Universidade do Porto
Faculdade de Engenharia
FEUP

Perfume Performance and Classification: Perfumery Quaternary-Quinary Diagram (PQ2D®) and Perfumery Radar

A dissertation presented to the
FACULDADE DE ENGENHARIA DA UNIVERSIDADE DO PORTO
For the Degree of Doctor in Chemical and Biochemical Engineering

by

Miguel André Abreu Teixeira

Supervision: Professor Alírio E. Rodrigues
Co-supervision: Dr. Oscar Rodríguez
Dr. Vera Mata

LSRE
LABORATORY OF SEPARATION AND REACTION ENGINEERING

Laboratory of Separation and Reaction Engineering
Department of Chemical Engineering - University of Porto

Porto, Portugal, 2011

Miguel André Abreu Teixeira, 2007-2011
Laboratory of Separation and Reaction Engineering (LSRE)
Department of Chemical Engineering - University of Porto
Printed by Cromotema – Artes Gráficas, Vilar do Paraíso, Gaia, 2011

Acknowledgements

First of all, I would like to express my deepest gratitude to my supervisor, Professor Alírio Rodrigues, one of those responsible for having followed the path of research. I'm thankful for accepting me as his PhD student and for the excellent guidance, valuable advices, encouragement and patience throughout the course of my research. I will remember his many great stories and to finalize what I once said on the occasion of his 65th birthday, "*it was a pleasure to learn even more "aromatically" with you*".

I am also grateful to Dr. Oscar Rodríguez, someone with whom I worked on a daily basis, for his guidance and advising in many situations, the helpful discussions we had in various issues and for sharing with me moments of discouragement and victory. A word of appreciation also to Dr. Vera Mata for her contribution in the initial research plan of my thesis.

A strong word of thanks to Nuno Lourenço and José Luís Moreira, two tireless men who helped me in countless situations and also for the great conversations we had.

I would like to express my gratitude to the Associate Laboratory - Laboratório de Engenharia de Reacção e Separação (LSRE) for all the support and facilities given, as well as to Faculdade de Engenharia da Universidade do Porto (FEUP) and to Departamento de Engenharia Química (DEQ).

I am also very grateful for the financial support I received for the PhD grant from the FCT - Fundação para a Ciência e a Tecnologia without which it would not have been possible to develop this work.

Finally, I would like to thank **all** those who, directly or indirectly, helped me to complete this thesis.

Para a minha família

Pelo seu amor e compreensão que me ajudou a completar este capítulo da minha vida.
Estou ansioso pelo próximo.

"After a certain high level of technical skill is achieved, science and art tend to coalesce in aesthetics, plasticity, and form. The greatest scientists are always artists as well."

Albert Einstein (1879-1955)

Resumo

O trabalho desenvolvido ao longo deste doutoramento e apresentado nesta tese resultou no desenvolvimento de novos dados experimentais e modelos teóricos, metodologias e ferramentas inovadoras para a quantificação e previsão da nossa percepção dos cheiros. Para tal, esteve na base deste trabalho, a partir de uma perspectiva macroscópica do problema, considerar-se um perfume como uma mistura líquida de *N* fragrâncias químicas e solventes que se vai evaporando para o ar. A partir daí as fragrâncias vão difundir no ar até serem percepcionadas pelo nosso nariz, onde podemos identificar e reconhecer os cheiros. A nível da mistura líquida é sabido que ocorrem interacções a nível molecular, uma vez que as fragrâncias apresentam diferentes propriedades físico-químicas, o que influencia a velocidade de evaporação de cada componente. Com o aumento da concentração de odorantes na fase gasosa, a intensidade da percepção sensorial aumenta (através de uma dada lei ou relação psicofísica), pelo que, numa mistura de *N* componentes, haverá alguns que serão mais fortemente sentidos pelo olfacto do que outros, definindo-se, deste modo, o carácter ou a qualidade do odor.

Neste sentido desenvolveu-se uma nova metodologia, intitulada "Perfumery Quaternary-Quinary Diagram® (PQ2D)", no seguimento do seu antecessor, o "Perfumery Ternary Diagram (PTD®)". Esta metodologia é capaz de prever e mapear num diagrama quaternário a intensidade e o carácter do cheiro de uma mistura de fragrâncias. Esta ferramenta foi aplicada a diferentes misturas, permitindo avaliar o efeito do tipo e concentração da nota de base e o efeito da água na evaporação das fragrâncias. Obtiveram-se resultados que mostraram a importância de métodos de previsão na pré-formulação de perfumes e que foram, aliás, validados por evidências experimentais da indústria de perfumaria.

O fenómeno de evaporação de diferentes misturas de fragrâncias foi, também, alvo de medições experimentais e previsões utilizando quatro métodos termodinâmicos de contribuição de grupos (UNIFAC, ASOG, UNIFAC-Dortmund e A-UNIFAC), tendo-se verificado uma boa concordância entre os resultados obtidos. Além disso, efectuaram-se avaliações olfactivas sensoriais com painéis de avaliadores, obtendo bons resultados para a determinação do carácter de misturas.

A nível da difusão de fragrâncias no ar, foi projectado e construído um tubo com diferentes portas de amostragem para se efectuar a medição experimental de perfis de concentração e difusividades de fragrâncias no ar. Aplicou-se, também, um modelo

simples baseado na 2ª Lei de Fick para modelar o processo de difusão e avaliar a performance de fragrâncias no tempo e no espaço. Obtiveram-se resultados experimentais para os perfis das fragrâncias e misturas destas no tempo e no espaço semelhantes aos previstos pelos modelos.

Por outro lado, no que diz respeito à percepção de odorantes, desenvolveu-se um modelo para a previsão de limiares de detecção de componentes químicos, tendo sido proposta uma nova equação baseada em apenas três parâmetros para a previsão desta importante propriedade. Efectuou-se, igualmente, um estudo comparativo de três modelos de previsão da intensidade de cheiros e avaliações olfactivas sensoriais para uma série de misturas. Os resultados obtidos foram concordantes e a partir dos modelos de previsão para o odorante mais fortemente percepcionado verificou-se que o modelo de Stevens (Power Law) foi aquele que obteve um melhor resultado global.

Por fim, desenvolveu-se o "Perfumery Radar", uma metodologia baseada em pressupostos científicos e com potencialidades de previsão para a classificação sistemática de perfumes comerciais em famílias olfactivas. Esta metodologia inovadora foi validada experimentalmente com classificações de perfumistas e, ainda, por análise de concentrações de *headspace*.

Em suma, um dos principais objectivos desta tese residiu no desenvolvimento de técnicas e metodologias de estandardização de processos que a nível industrial são ainda governados pelos perfumistas, a arte e o conhecimento empírico. Dela resultaram dados experimentais e novas ferramentas que têm relevância para a formulação, classificação e avaliação da performance de fragrâncias.

Abstract

This thesis presents a series of experimental results, new methodologies, theoretical models and innovative tools that seek to describe, assess, quantify and predict the way we perceive odors and fragrance materials. At the basis it was considered that a perfume can be approximated to a liquid mixture of *N* fragrance ingredients and solvents that is evaporating into the air above it. For that, it is known that fragrance molecules have different physicochemical properties and that interactions will be occurring at the molecular level, influencing the release rate of each component. Then, odorant molecules will diffuse in the air until they reach the human nose where they can be identified and recognized. As the concentration rises, it is expected that the perceived sensation magnitude will also increase following some relationship and within a mixture of odorant molecules some will be more strongly perceived than others, thus defining the character or quality of the mixture.

In this way, a novel tool called the Perfumery Quaternary-Quinary Diagram® (PQ2D) was developed as an extension of its predecessor, the Perfumery Ternary Diagram® (PTD), towards the prediction and mapping of the odor intensity and character of mixtures of fragrance ingredients. The PQ2D® methodology was used to predict the effect of different base notes as well as water in perfume formulation, obtaining results that are evidences in the perfumery business.

Moreover, the evaporation process of fragrance ingredients within a mixture was experimentally measured for several mixtures. These results have shown a good agreement when compared with those predicted using four different G^E methods based on the group-contribution concept. Furthermore, their comparison with an olfactory evaluation performed by panelists has shown a relatively good agreement.

Then, for the diffusion of fragrances in air a diffusion tube was built for the measurement of experimental data and a simple model based on Fick's 2nd law was used to characterize the diffusion and performance of each odorant. Experimental data was obtained for the diffusion profiles of fragrance components and mixtures showing good agreement with simulations.

For the perception of odors, a new equation based on a proposed model for odor detection thresholds was derived for the prediction of this property using only three readily available parameters. Moreover, different odor intensity models were compared for the perception of fragrance mixtures, highlighting their differences and applicability.

Finally, a novel tool called the Perfumery Radar methodology was developed for the classification of perfumes with predictive power and showing good agreement with both the classifications from perfumers and experimentally measured concentrations.

Concisely, the search for the standardization of methodologies that at the industry are still ruled by empirical knowledge, art and experts was an objective of this thesis. That led to the development of new tools that can play their role in formulation, classification and performance evaluation of fragrances at the industrial level.

Résumé

Le travail élaboré au long de ce doctorat et présenté dans cette thèse a été fait à partir de nouveaux donnés expérimentaux et de modèles théoriques, en utilisant des méthodologies tout à fait innovatrices pour quantifier et prévoir la perception des odeurs. Dans une perspective macroscopique du problème on a considéré un parfum comme un mélange liquide d'un certain nombre de fragrances chimiques et de solvants qui s'évaporent et diffusent dans l'air. Et, donc, à partir de ce moment le nez humain les sent, les identifie et les reconnaît. On sait, évidemment, que, dans ce mélange, il y a des interactions au niveau moléculaire, car ces fragrances ont des propriétés physiques et chimiques différentes et leur procès d'évaporation se produira à des vitesses différentes. Avec une concentration croissante des odorants dans la phase gazeuse, on constate, selon une loi ou relation psychologique, qu'il y a une meilleure et plus grande perception sensorielle. Ainsi dans un mélange de plusieurs composants il y aura quelques-uns qui seront plus facilement aperçus que d'autres. Cela permettra connaître la famille olfactive ou la qualité de l'odeur. De cette manière on a développé une nouvelle méthode, appelée "Perfumery Quaternary-Quinary Diagram® (PQ2D)", capable de prévoir et présenter dans un diagramme quaternaire l'intensité et le type de l'odeur n'importe quel mélange de fragrances. Avec ce donné on a pu évaluer l'effet de concentration des notes de fond et l'effet de l'eau dans l'évaporation des fragrances. Effectivement, on a même obtenu des résultats consistants et certifiés par l'industrie de parfumerie. Le phénomène d'évaporation a été mesuré par les prévisions en utilisant quatre méthodes thermodynamiques de contribution de groupes (UNIFAC ASOG, UNIFAC–Dortmund et A-UNIFAC) et on a vérifié que les résultats étaient en accord. En outre, des évaluations sensorielles olfactives ont été réalisées avec l'aide de quelques évaluateurs et on a eu de bons résultats pour déterminer le caractère des mélanges.

À propos de la diffusion des fragrances dans l'air on a planifié et construit un tube avec plusieurs portes d'évaluation afin de mesurer les profils de diffusion des fragrances. Le modèle utilisé est simple et basé dans la deuxième Loi de Fick pour analyser le procès de diffusion et évaluer la performance des fragrances dans le temps et aussi dans l'espace.

D'autre part, en ce qui concerne à la perception des odorants, on a développé un nouveau modèle pour prévoir les seuils de détection des composants chimiques et une

nouvelle équation basée en trois paramètres a été proposée de façon à permettre prévoir cette propriété.

On a aussi élaboré une étude comparative de trois modèles de prévision de l'intensité des odeurs et les évaluations sensorielles olfactives pour une série de mélanges. On a constaté que les résultats étaient en accord et du point de vue de la prévision de l'odorant plus fortement reconnu on a confirmé que le modèle de Stevens (Power Law) a été celui qui a réussi un meilleur résultat global.

Finalement, on a développé une nouvelle méthodologie, le Perfumery Radar, conçue et basée sur des hypothèses scientifiques et qui permettra classer, d'une forme systémique, les parfums commerciaux en familles olfactives. Cette méthodologie totalement innovatrice a été ratifiée par des expériences, par les classifications des parfumeurs et aussi par l'analyse des concentrations de headspace.

En conclusion, l'un des objectifs de cette thèse est celui de développer des techniques et des méthodologies standard pour des procès qui, au niveau des entreprises, sont faits par les parfumeurs et régis par la connaissance empirique et aussi par l'expérience. De cette façon, ces donnés tout à fait originaux et aussi les nouveaux outils auront un rôle bien important dans la formulation, la classification et l'évaluation de la performance des fragrances.

Table of Contents

List of Figures

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

Chapter 7

Chapter 8

List of Tables

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

Chapter 7

Chapter 8

Chapter 1

Introduction

"How many smells are there? The answer leads to psychology ("How do you count smells?"), technology ("How do you take apart a complex odor?"), and secrets of the trade ("How do you become a perfumer?")"
(Avery Gilbert, 2008)

1.1. Relevance and Motivation

Fragrances are widely used by people in modern societies, as they are present in a number of different daily products like cosmetics, toiletries, household cleaners, or perfumes. They are incorporated in different products with the purpose of influencing the consumer to buy them, either by enhancing its benefits, or simply by signaling it to be easily recognizable. Consumers, on their part, are extremely attracted to perfumed products because they influence their image, mood, or personality among other effects. This bilateral relationship of interests is explained by the power of the sense of olfaction that surpasses frontiers which other senses can not reach.

The Flavor & Fragrance (F&F) business is a multi-billion dollar market spread all over the world (Leffingwell and Leffingwell, 2011). It comprises two different fields of operation: *i)* production of raw materials either obtained from natural sources or chemically synthesized; *ii)* blending of flavors and fragrances into high added value

products. In terms of product development, and considering the exclusive fine fragrance market, the industry released over 1500 fine fragrances only in 2009 (compared with less than 50 in twenty years ago) (Brechbill, 2010). Perfumes are added-value products, luxurious and expensive. Surprisingly or not, nowadays, in modern societies, there will hardly be any people who do not use a perfume or any type of functional perfumed product (*e.g.* fragranced shampoos, detergents, or candles). Consequently, the pressure of the market is massive and its increasing competition will lead to fierce the creation of new scents and sensations, a process which has to be faster and faster. However, the formulation of a perfume is a lengthy and costly process. Moreover, the knowledge in this field is limited due to the secrecy imposed by major companies in such a profitable business, but also because it still remains as an art developed by experienced professionals (the perfumers). Nevertheless, the latter problem is perhaps a consequence of the lack of knowledge in understanding the sense of olfaction. Moreover, the chemical complexity arising from perfumes is mainly due to the desire of their creators to deliver perceptual complexity and intensity to consumers. However, it adds significantly to the perfume costs. Recent works suggest that it is possible to reduce the number and quantity of chemicals used in perfume formulation through the use of scientific principles, without any measurable reduction in perceptual complexity (Cussler, *et al.*, 2010; Bagajewicz, *et al.*, 2011). Although this is a complex process to be achieved, an opportunity shows up at the development of more sophisticated and sensitive tools aimed at the perception of fragrance mixtures: novel powerful fragrant molecules, improved technical analysis, or application of predictive models and computer simulators.

All the aforementioned reasons are enough to draw the conclusion that the perception of perfumed products is indeed complex, especially when the number of available chemicals involved is in the order of thousands. It may be argued that the perception and characterization of single fragrances may be easier than it is for multi-component mixtures. And although in both cases, odors are represented in the brain as complex patterns, it may be simpler to start by understanding the way single fragrance molecules are detected and perceived at diluted concentrations in air – the odor detection and recognition thresholds (Chastrette, 1998). These parameters are of great importance in different fields of our society, constituting regulatory limit values for atmospheric environment control, soil and drinking water contamination levels, food chemistry,

cosmetics and fragrance products. Although there is a large number of odor threshold data available in the literature, their experimental measurement is difficult, time consuming, labor intensive, and presents a large variability, mainly because this parameter has physiological variability. The search for a theoretical model that could be capable of predicting these values with more or less accuracy for a first estimate has been sought by many, but we are still far from the solution (Chastrette, 1997, 1998; Hau and Connell, 1998; Abraham, *et al.*, 2002).

Recalling perfume mixtures, these are generally liquid solutions of odorant chemicals and solvents (plus stabilizers) that evaporate into the air and diffuse through it over time and distance until the airborne molecules reach our nose. The study of this chain of processes includes in its fundamentals multidisciplinary sciences, starting from thermodynamics to transport phenomena, and from biochemistry and cellular biology to psychophysics. The combination of these sciences (or at least some) for their application to perfume design, might be performed by Product Engineering, an emerging paradigm of the last decade (Ulrich and Eppinger, 2000; Cussler and Moggridge, 2001; Bagajewicz, 2007; Wesselingh, *et al.*, 2007; Rodrigues, 2008). In terms of scientific studies and experimental data on the evaporation and diffusion of fragrances there is, once more, a lack of available literature. This way, not only the development and implementation of theoretical models but also the experimental validation of those will contribute to the evolution of the knowledge and understanding of the behavior of perfume mixtures. Moreover, it will enhance the evaluation of the performance of perfumed products released from any supporting material (base or substract) into the air.

It is a fact that much of what concerns the formulation of perfumed products involves experimental evaluation and classification. The characterization of a scent is not like defining a color that we visualize or a texture that we feel: we need a lot more words to describe an odor than it does for other senses because olfaction is influenced not only by our physical aptitudes but also by our psychological behavior and past experiences. Translating words like “clean” or “fresh” into product specifications is a big challenge to perfumers. This way, the number of classifications of fragrances and perfumes is large and diversified (Poucher, 1955; Thiboud, 1991; Chastrette, 1998; Société-Française-des-Parfumeurs, 2006). As if not enough, once again, adversities arise in

disclosing perfume mixtures: perfumes commonly list “fragrance” as an ingredient, rather than naming the specific chemicals involved, thus withholding information. Nevertheless, it is important to aim at looking for a uniform classification of perfumes by introducing some scientific basis behind it, as a target of Product Engineering.

In sum, the combination of knowledge from the field of olfaction with that coming from Chemical Engineering opens a window for Product Engineering applied to fragrances and perfumed products.

It should be mentioned that research on Perfume Engineering started at the LSRE more than 10 years ago with the post-doc of Vera Mata and continued with the PhD thesis and post-doc of Paula Gomes (Gomes, 2005; Mata, *et al.,* 2005). A spin-off company has also been created (i-sensis, 2010). Thus, it was supported on some previously developed bases but with an eye towards new applications and discoveries that this thesis has grown.

1.2. Objectives and Outline

After presenting the relevance and motivation for this work, it becomes clear that its main objectives are focused on: the development of tools for the formulation, quantification and classification of perfumed products in a scientific way; and the evaluation and prediction of the performance of perfumed products, thus contributing to lower production costs and manufacturing time at the industrial level.
Having this in mind, this thesis was oriented to start from the present level of knowledge of the literature and, then, extend that to other levels. A brief description of the Chapters is presented ahead.

An introduction to important fields within the Flavor & Fragrance world is presented in Chapter 2, reviewing the current state-of-the-art for product development of perfumes. Their evaluation and characterization is addressed considering different perspectives of some relevant processes like the evaporation, diffusion and olfactive perception of fragrances and odorants. From that point, it is important to quantify and characterize a key parameter for Product Engineering: the performance of perfumed products. To accomplish that, a new methodology called the Perfumery Quaternary-Quinary Diagram

(PQ2D®) is presented in Chapter 3 in order to predict and graphically represent the perceived odor of multi-component fragrance mixtures. However, to quantify odors there is an important parameter that must be taken into account: the odor detection threshold (ODT). In this way, this parameter must be calculated from experimental data or predicted using suitable models. This issue is reviewed in Chapter 4, together with the development of a new simple predictive model using physical properties only. Then, the evaporation process and organoleptic evaluation of fragrance ingredients being released from different mixtures is experimentally performed in Chapter 5 and compared with the results predicted from different thermodynamic models. In Chapter 6, the diffusion of fragrance raw materials is measured using a diffusion tube and compared with the models to assess perfume performance. After that, the perception of odors is revisited in Chapter 7 from the perspective of Psychophysics, using different odor intensity models to establish a term of comparison. On Chapter 8, a novel methodology is presented for the classification of perfume mixtures called the Perfumery Radar. Finally, the major conclusions drawn from this work and some hot topics in F&F are highlighted and suggested for future work in Chapter 9.

1.3. References

Abraham, M. H., Gola, J. M. R., Cometto-Muniz, J. E., Cain, W. S., A model for odour thresholds, *Chemical Senses*, 27, (2): 95-104, 2002

Bagajewicz, M., On the Role of Microeconomics, Multi-scale Planning and Finances in Product Design, *AIChE Journal*, 53, (12): 3155- 3170, 2007

Bagajewicz, M., Hill, S., Robben, A., Lopez, H., Sanders, M., Sposato, E., Baade, C., Manora, S., Coradin, J. H., Product Design in Price-Competitive Markets: A Case Study of a Skin Moisturizing Lotion, *AICHE Journal*, 57, (1): 160-177, 2011

Brechbill, G. O., Fragrance's & Their Stories, New Jersey (USA), Fragrance Books Inc., 2010

Chastrette, M., Trends in structure-odor relationships, *SAR and QSAR in Environmental Research*, 6, 215-254, 1997

Chastrette, M., Data management in olfaction studies, *SAR and QSAR in Environmental Research*, 8, (3-4): 157-181, 1998

Cussler, E. C., Moggridge, G. D., Chemical Product Design, Cambridge, Cambridge University Press, 2001

Cussler, E. L., Wagner, A., Marchal-Heussler, L., Designing Chemical Products Requires More Knowledge of Perception, *AIChE Journal*, 56, (2): 283-288, 2010

Gomes, P. B., Engineering Perfumes. Department of Chemical Engineering. Porto, University of Porto Faculty of Engineering. PhD Thesis, 2005

Hau, K. M., Connell, D. W., Quantitative structure-activity relationships (QSARs) for odor thresholds of volatile organic compounds (VOCs), *Indoor Air-International Journal of Indoor Air Quality and Climate*, 8, (1): 23-33, 1998

i-sensis, S. João da Madeira, Portugal, from www.i-sensis.com, Last Accessed on 2011

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AIChE Journal*, 51, (10): 2834-2852, 2005

Poucher, W. A., A classification of odors and its uses, *Journal Soc. Cosmet. Chem.*, 81-95, 1955

Rodrigues, A. E., da Silva, F. A., Granato, M., Lamia, N., Grande, C., Gomes, P. S., Propane/Propylene separations: from molecular simulation to process development, XXXIII Reunión Ibérica de Adsorción, Madrid (Spain), 2008

Société-Française-des-Parfumeurs, Société Française des Parfumeurs, Classification des Parfums, from http://www.parfumeur-createur.com/article.php3?id_article=68, Last Accessed on May 2010

Thiboud, M., Empirical Classification of Odors, Art, Science & Technology, Muller and Lamparsky, Oxford (UK), Kluwer Academic Publishers, 253-286, 1991

Ulrich, K. T., Eppinger, S. D., Product Design and Development, New York, McGraw-Hill, 2000

Wesselingh, J. A., Kiil, S., Vigild, M. E., Design & development of biological, chemical, food and pharmaceutical products, Chichester, U.K., Wiley, 2007

Chapter 2

Insight into Flavors & Fragrances: Art, Experiments and Science

"An effective chemical engineer is someone who relates his or her special expertise to other areas of concern, someone who may focus on one part of a practical problem but also retains an overall view of where the special area intersects with others."
(J. M. Prausnitz, 1996)

Throughout this chapter a detailed overview of the state of the art in some fields of Flavors & Fragrances (F&F) will be presented. The main context of this Chapter will follow three major topics: *i)* fragrance ingredients and their use in the formulation of perfumes; *ii)* detection and interpretation of odorants as odors by the human nose through the olfactory mechanism and, *iii)* the emerging paradigm of Product Engineering applied to the performance of perfumed products with high added-value for their design and classification.

First, a synopsis about the F&F industry in the world will be presented, followed by a more particular perspective of the Portuguese market. A brief description of the regulatory context to which this industry is subjected will also be addressed.

Then, the processes underlying the formulation of perfumes and the blending of fragrance ingredients will be reviewed, with particular emphasis on the structure and

mixture properties, manufacture, and classification. Accordingly, the types and classifications of raw materials used to formulate perfumes as well as a picture of the different processes used to obtain and purify them will be addressed, highlighting also some innovative techniques. Nevertheless, perfumes are designed to be perceived by people and so they are composed by volatile components that evaporate and diffuse in air. For that, the evaporation and diffusion of fragrance chemicals will be analyzed, focusing on both experimental techniques and predictive models. The evaluation of the performance of fragranced products as a function of the evaporation and diffusion processes will also be addressed. To quantify a fragrance product's performance it is also important to understand the way the human being perceives airborne odorant molecules. This phenomenon will be explored, first from the perspective of the biological mechanism of olfaction, and later from the application of psychophysics. The relevance of odor concentration thresholds for the perception of odors will be investigated as well as the use of scientific equipments, devices, or novel techniques for odor measurement. Moreover, the classification of fragrance raw materials and perfumes in terms of quality or character will be approached. Issues on the interpretation and classification of odors will be presented and qualitative classifications will be compared.

Finally, the emergence of Perfume Engineering as an application of Product Engineering is tackled. The importance of introducing some science into an empirical and artistic field like the perfumery business is scrutinized and its main issues that are yet to unravel are identified and classified as major objectives of this thesis.

2.1. Flavor & Fragrance industry

The Flavor and Fragrance (F&F) business is a multi billion dollar market with economic impact and relevance all over the world (Leffingwell and Leffingwell, 2010). Within this business there is a large number of companies working at different levels: starting from those responsible for the extraction, processing, synthesis, and separation/purification of raw materials, up to those companies that generate more value in their products, namely by the blending of fragrances and/or aromas. Furthermore, there are industries from very diverse fields that are also closely linked to the F&F business like packaging, marketing, or retail chain companies.

In this way, the global market of F&F is large and has been continuously growing at high rates over the last decade. Even throughout the 2009-2010 world economic and financial crisis its sales have only leveled off but the upturn of the market has already been seen over the last year (Leffingwell and Leffingwell, 2010). From the analysis of companies and market reports, attention should be paid to the effect of sales on local currencies and the equivalent to the US dollar (Leffingwell and Leffingwell, 2010). Hence, Figure 2.1 presents a retrospective view of the evolution of both the global F&F market (in billion US$) and the growth rates in local currencies for the ten-year period of 1999-2009.

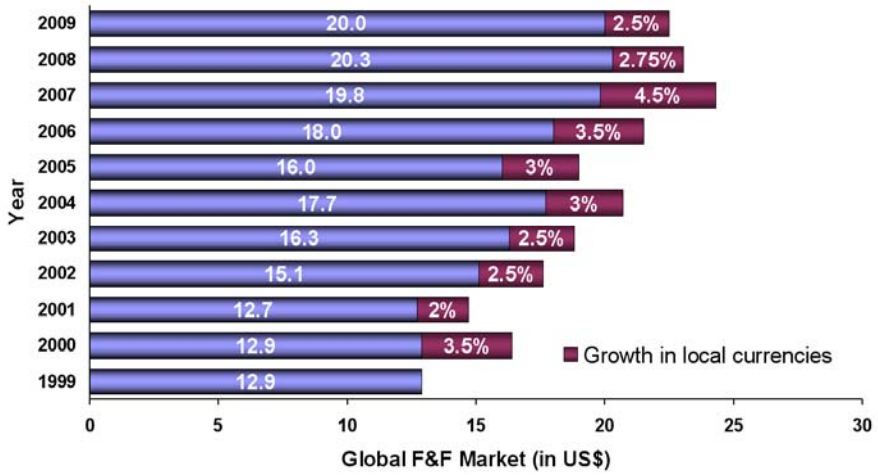


Figure 2.1 – Evolution of the global F&F market in billion US$ for period 1999-2009.

In its early days, the F&F industry was initially positioned in Europe and only later evolved to the United States of America (USA) where up to the Second World War was already dominating the world scene. However, after that episode, the Central-Western European companies have re-conquered the leadership of the global market (Ziegler, 2007). Nowadays, although it may be said that it is a worldwide market, it is also true that it is mainly controlled by a group of 10 companies or so, who are based in the central Europe, North America, Japan, and the Middle East, as shown in Figure 2.2 and Figure 2.3. In fact, this is the general trend of many industrial sectors, where some companies through mergers or acquisitions tend to get a multinational dimension and dominance. It is important to highlight the relative impact of Japan as a worldwide player, on one hand because their civilization is much more oriented to functional perfumed products than for fine fragrances (which represent an important class), and on the other hand because it has a much smaller territorial area than Europe or the USA. Altogether, these 10 companies gather a total of 72.5% of the market share and the top 5

companies account for more than 60% alone (Leffingwell and Leffingwell, 2010). It may be convenient to make a note here, to remember that these numbers were taken from evaluations of companies' sales throughout the last decade and considering nearly 400 F&F companies with relevance for the total market size (million dollar companies). In this way, it can be said that the F&F business still remains a closed and strong market that is controlled by a small group of companies. These are perhaps some of the reasons behind the existing secrecy. Beyond the biggest players shown in Figure 2.3 and Table 2.1, there are some other international and national companies that closely follow them and should also be referred although their operational results are not often published due to private ownership, like Danisco, Shiono, McCormick, Treatt, or Mastertaste (Ziegler, 2007). Additionally, it should be said that the results extracted from market reports are always subjected to errors, like controversial issues in double estimating sales when intermediaries are involved in the process. An example of that are the sales of perfumery goods in shopping websites and online auctions in the internet which are difficult to account, although these are subjected to regulatory conditions and market supervision.

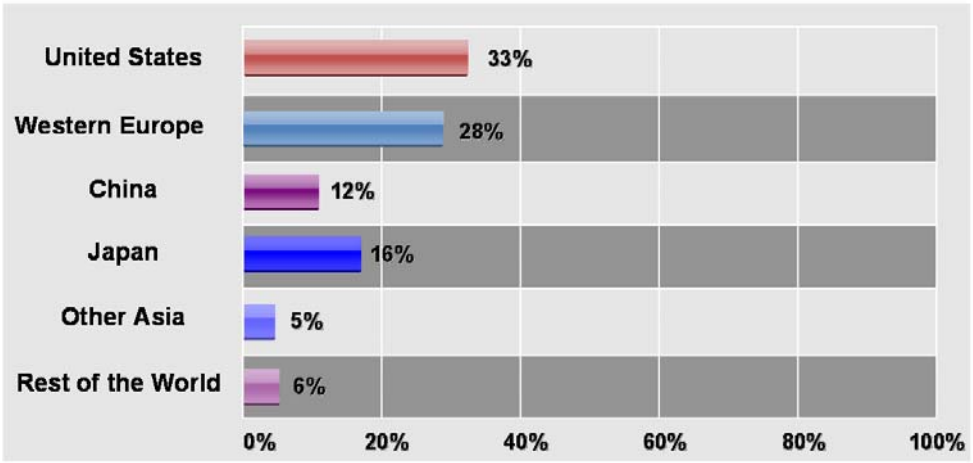


Figure 2.2 – World consumption of F&F products in 2010.

Before proceeding let us make a stop here to reflect on the names of the leading F&F companies appearing in Figure 2.3. To a layman or a regular consumer of perfumes, these names will be mostly unfamiliar since they do not appear on the shelves of perfume shops or on the packaging of perfumes. Probably, companies' names such as Christian Dior, Dolce & Gabbana, Estée Lauder or Hugo Boss will sound more familiar. However, the fact is that a vast majority of these companies (which work as brand managers) do not produce the perfumes themselves nor have perfumers in their staff. In

fact, what happens is that when these brand companies spot a gap in their portfolio, then, they brief the fragrance houses who develop the perfume. Thus, companies like Givaudan, Firmenich or International Flavors & Fragrances (IFF) are global suppliers of fragrances and flavorings (including raw materials and active ingredients for perfumes, cosmetics and foods) but also manufacturers of perfumes and perfumed products.

Figure 2.3 – Geographical distribution of the top 10 F&F companies in the world in 2009: *1. Givaudan; 2. Firmenich; 3. IFF; 4. Symrise; 5. Takasago; 6. Sensient Flavors; 7. Mane SA; 8. T. Hasegawa; 9. Robertet SA; 10. Frutarom.*

Table 2.1 – Market share of the top 10 F&F companies in 2009 (values in million US$) (Tisi, 2009; Leffingwell and Leffingwell, 2010).

Rank	Company	US$	Market Share
1	Givaudan	3824	19.1%
2	Firmenich	2729	13.6%
3	IFF	2326	11.6%
4	Symrise	1952	9.8%
5	Takasago	1257	6.3%
6	Sensient Flavors	549	2.7%
7	Mane SA	539	2.7%
8	T. Hasegawa	465	2.3%
9	Robertet SA	437	2.2%
10	Frutarom	425	2.1%
Top 10	-	14503	72.5%
All others	-	5495	27.5%
Total Market	-	$19998	100.0%

To put the question of market share in numbers, it should be said that the worldwide market has more than doubled in the past 15 years, from US$9.6 billion in 1995 to US$20 billion in 2009, as partially shown in Figure 2.1 (Leffingwell and Leffingwell, 2010). However, the analysis of these numbers must also be accompanied by the inflation rise indexed to the corresponding years, and for that it was registered a parallel increase in almost 41% (Gardner, 2011).

While watching the present, reputable companies keep carrying out forecast analysis for the F&F worldwide market. According to these, it is expected that the trend for flavors and fragrances demand will continue to rise in the upcoming years. Through 2012, the cosmetic and toiletry market is foreseen to record great advances, with skin care products taking the lead over traditional soaps and body washes. Nevertheless, fragrances will also continue to experience healthy gains through 2012, spurred by food applications, essential oils and natural extracts, fine perfumery products, and growth in aromatherapy and functional perfumes (Freedonia, 2010). Finally, a brief comment on the position of essential oils: it is possible to say that although the development of synthetic alternatives will play an important role due to lower costs, the essential oils market will continue to rise since the "natural" label is seen as a positive feature and is usually preferred by consumers (Freedonia, 2010).

2.1.1. Materials and applications at the F&F industry

Both fragrance and flavor ingredients are odorous organic chemical compounds that can be used in perfumes or scented products, as well as for the flavoring of foods and beverages. Hence, their classification as fragrance or flavor depends whether they are mainly perceived by the sense of olfaction or gustation, that is if they are applied in fragrance or food products, respectively (Surburg and Panten, 2006).

Thus, the core business of the F&F industry can be divided in two main groups, namely the fragrances and the flavors. They nearly share the same percentage of sales although the flavor market has been gaining little ground during the last decade as shown in Figure 2.4. This increasing need for flavors is explained by the dramatic shift in human life style and philosophy. At the turn of the XXI century, the trend in the food industry started to be oriented for healthy, fitness and diet products (moved by the slogan *"you are what you eat"*).

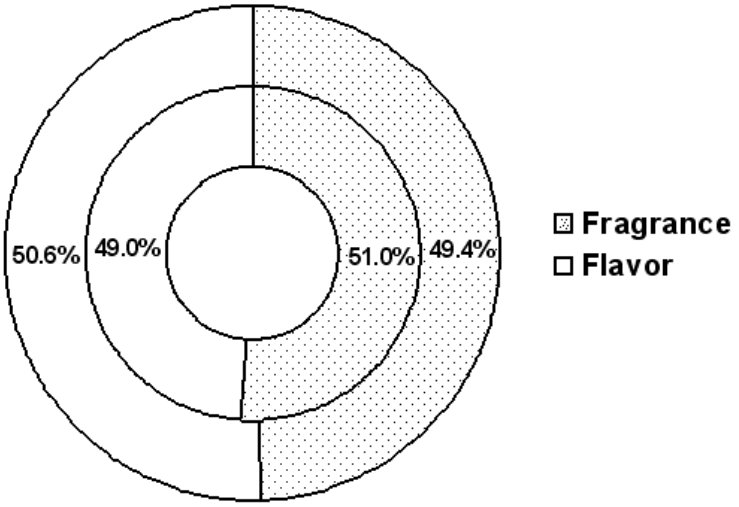


Figure 2.4 – Global market for flavors and for fragrances (values estimated according to Consultants, 2007; Leffingwell and Leffingwell, 2010).

In each one of these two core fields, it is possible to consider the following sub processes:

i) Fragrances: essential oils or natural extracts, and fragrance blends;

ii) Flavors: aroma chemicals and flavor blends.

These have different preponderance in the F&F industry with more weight for the blends than for extracts and chemicals only, as depicted in Figure 2.5 (Somogyi, 2007).

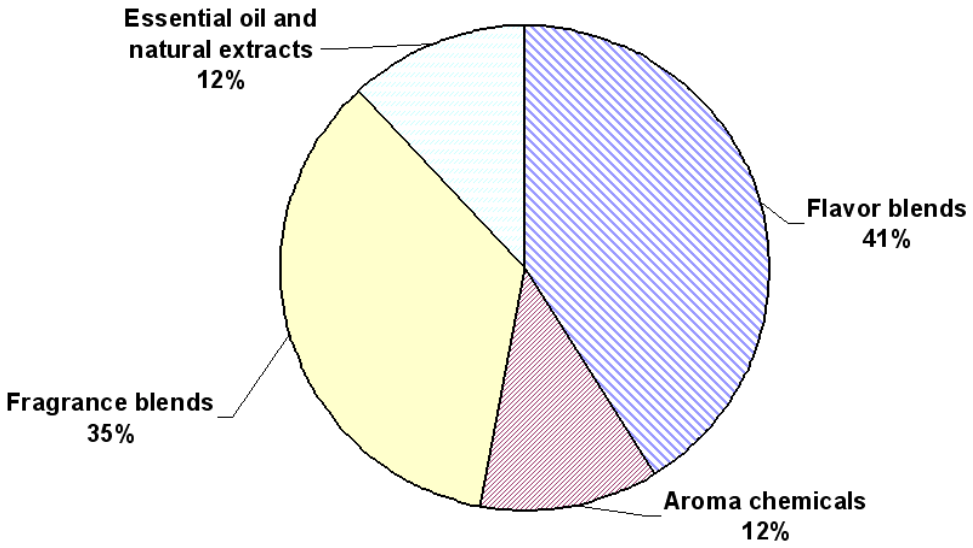


Figure 2.5 – Market share for each sub-sector in the fields of flavors and fragrances in 2002 (estimated by the Freedonia Group - Freedonia, 2010).

There are multiple applications for the final products in each of these sub-sectors inside the F&F industry as shown in Figure 2.6. Mainly, they are aimed at enhancing human quality of life by striving for increased pleasure and enjoyment. In the field of flavors, aromas are essentially designed for beverages, bakery, savory, and meat products. In the case of the fragrance field the largest application goes to functional perfumes which are products with fragrances in their formulation but designed for everyday use. Examples of these products are soaps, detergents, toiletries and household cleaners. However, the development of fine fragrances, which are more expensive and have higher added value, is also significant reaching 21% of the fragrance market.

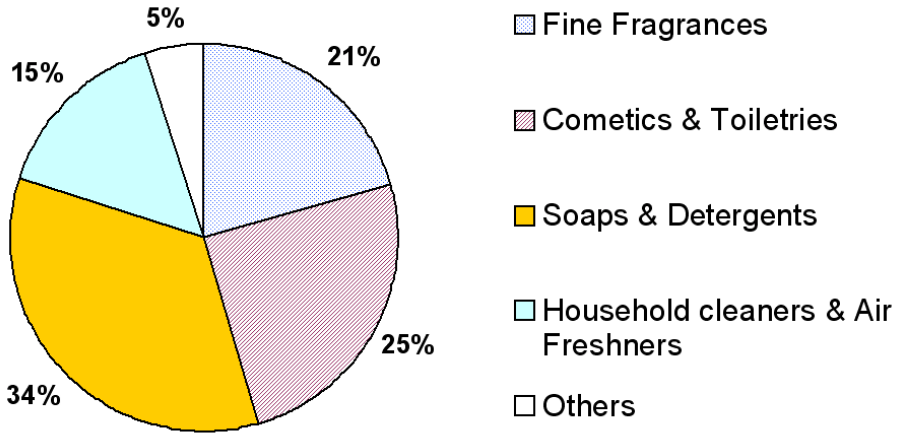


Figure 2.6 – Global Market for fragrances by application in 2006 (estimated values according to Consultants, 2007; Leffingwell and Leffingwell, 2010).

In terms of fine fragrances only, the market share per company, shows the same trend as for the global F&F market previously observed in Table 2.1. In this way, Givaudan is the world leader company followed by Firmenich and IFF as depicted in Figure 2.7.

In a more confined perspective, the branch of fine fragrances and cosmetics falls in what is commonly called the global luxury retail market. It includes a wide variety of luxury products, although the terminology is very subjective: what is luxury for someone might be granted for others. Nevertheless, it is important to highlight here the significance of fine fragrances and cosmetics in this market of high added value products, as shown in Figure 2.8.

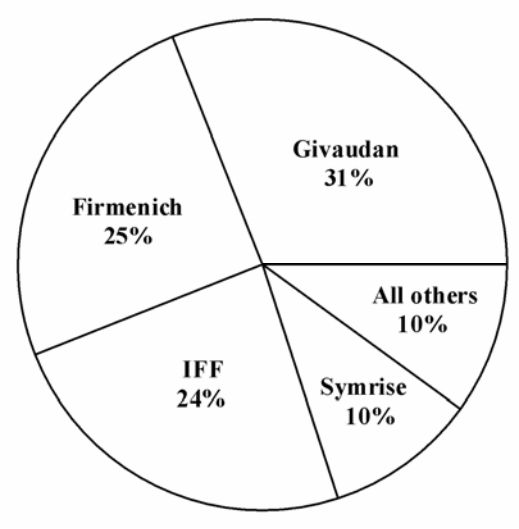


Figure 2.7 – Fine fragrance market in terms of F&F companies (From Leffingwell and Leffingwell, 2010).

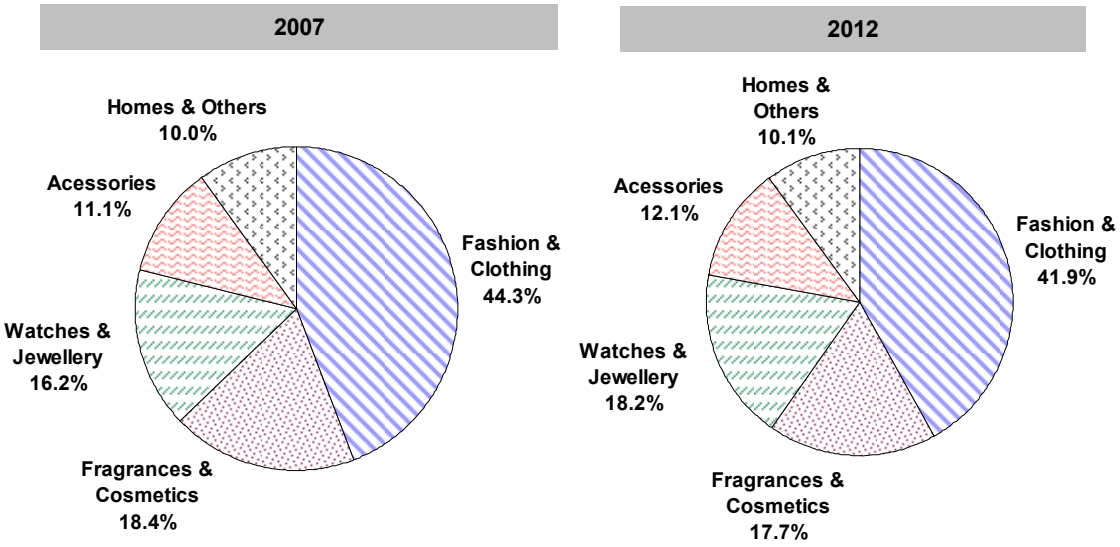


Figure 2.8 – Luxury market in 2007 and predictions for 2012 (Verdict, 2007; FOCUS, 2008).

While in 2007 fragrances & cosmetics were ranked in second place on the luxury goods market, it is expected a slight shift towards an increase of watches & jewellery until 2012. Nevertheless, it is undisputable that the fragrance market is, once more, large and prominent within this market. According to the corporate consultants Bain & Company, the sales for the luxury worldwide market stood at €146 billion in 2006, increasing up to €159 billion in 2007 (FOCUS, 2008). Within this business, the largest market share is dominated by Europe with 38%. It is here, mainly in Italy and France, that the most important luxury businesses have been built.

2.1.2. F&F market: the Portuguese case

Portugal is the most western country of mainland Europe, located on the Iberian Peninsula with the Atlantic archipelagos of the Azores and Madeira. It is a small country with little tradition on production or extraction of perfumery raw materials and formulation of perfumes. The vast majority of the F&F trade in Portugal is developed by resellers of perfumery, cosmetic or flavor products. In Portugal, about 15 to 25% of the perfumed products are sold through non-specialized outlets, and most is sold through specialist perfumery shops. These are often located in shopping centers or large commercial areas, widely accessible to the public.

In terms of the extraction of essential oils in Portugal, the most relevant ones are obtained from plants like the turpentine (from the Pine or "Pinheiro") and acacia (from "Mimosa") essential oils. The absolute obtained from the flowers of the acacia tree yields an extremely warm, spicy and at the same time herbaceous and floral odor according to Arctander. Figure 2.9 shows some pictures of these plants whose essential oils have added-value for perfumery and are much appreciated by consumers.

Figure 2.9 – *Pinus pinaster* trees and *acacia melanoxylon* leaves from Nazaré, Portugal.

In what concerns to the international trade of essential oils, cosmetics and perfumery raw materials, it was reported that the exports have been growing in recent years, despite representing only 11.1%, 17.4% and 20.8% of the corresponding imports for the triennial of 2001-2003 (INE, 2003). The main destination of these Portuguese goods is the United Kingdom with 30% of the market, followed by Spain and Germany with 21% and 13%, respectively. In the case of imports of essential oils, Spain was the main contributor in the beginning of the decade but later on was surpassed by the United Kingdom. The perfumery imports and exports represent only an average of merely

0.85% and 0.25% of the totals for the country, respectively. These data were collected from the 2003 International Trade Statistics Report published from the Instituto Nacional de Estatística de Portugal (INE) and are presented in Figure 2.10 (INE, 2003).

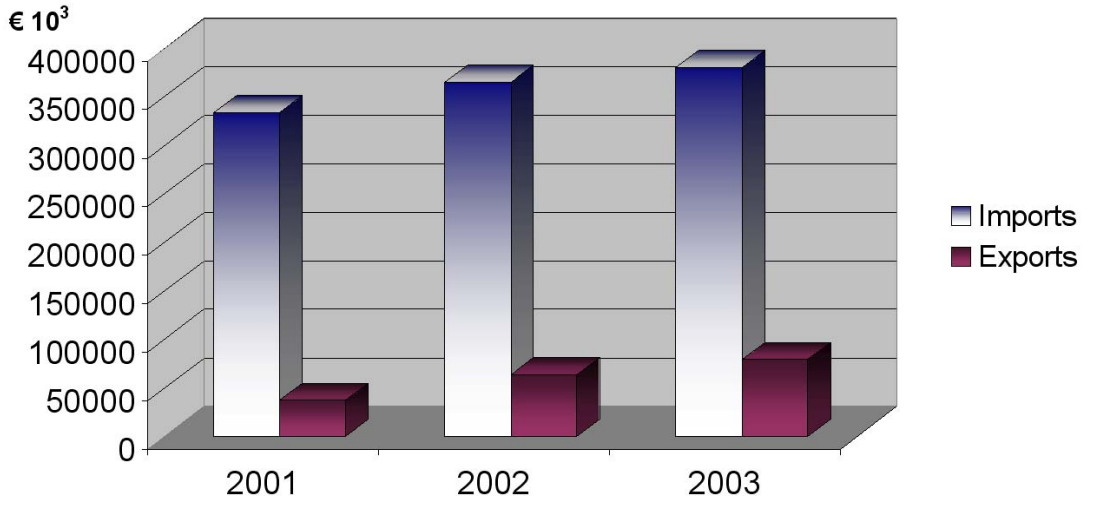


Figure 2.10 – Importations and exportations of *merchandises* from and to Portugal (values in € 10^3) (INE, 2003).

The number of born and raised Portuguese companies operating in F&F is small and distributed over different application fields from the trade of essential oils to the olfactive marketing, from functional perfumes to the development of fine fragrances. The first ever Portuguese factory of soaps and perfumes was founded in Porto in 1887 by Ferdinand Claus and Georges Schweder, two Germans that were living in Portugal. The company was called *"Fábrica de Produtos Chimicos CLAUS & SCHWEDER, SUCRS"*. Due to a number of unexpected problems the company was closed and reopened under the name of *"Ach. Brito & Cª Lda"* which endures to this day. It keeps the brand name of Claus Porto for their products, and today is a well established and recognized company worldwide. Among their private clients it should be mentioned the famous American television host, producer, and philanthropist, Oprah Winfrey (2010).

A similar example of this last company is the "Confiança – Saboaria e Perfumaria" which was founded in 1894 in the north of Portugal (Braga). This centenary company is also devoted to the development of different types of soaps and perfumed cleaning products (Confiança, 2011).

Another example is the Helmut Kreutz Portugal (HKP), a company created in 1994, oriented to the marketing and distribution of raw materials for different industries. Its core business is not directly the development of F&F products, although they present a

palette of a few hundreds of essential oils from different olfactive families like floral, citrus, spices, herbaceous, or woody (Helmut-Kreutz, 2010).

On the other hand, in the field of perfume formulation and olfactory marketing, a spin-off company called i-sensis should me mentioned. It was created in 2004 from two Portuguese researchers that had previously developed their research in perfumes at the LSRE (FEUP). Their company hosted in São João da Madeira (Portugal) is focused on two targets: the development of custom-made private label perfumes and also the new trend, called olfactive marketing. While in the former they develop fine fragrances for private customers, in the later they provide perfumed environments for commercial facilities like shops, hotels, or ceremonies (i-sensis, 2010).

Finally, in 2009 a new Portuguese company was created focusing on the development of fine fragrances and cosmetics. The company called Laboratórios Vidaurre is located in Cantanhede and has developed its first commercial perfume in 2010.

Although so far we have talked about F&F, considering both the fragrance business (oriented to perfumes and functional perfumery) and the flavor business (oriented for foods and beverages) we will now primarily focus on fragrance ingredients and their blending, the so-called perfumes. Their development is a complex and long process which is subjected to restrict regulatory standards as we will discuss ahead.

2.1.3. The regulatory standards

Fragrances are considered a type of added-value product but despite their price they are used by millions of consumers around the world. Their derivative products, whether or not containing added value, from the field of cosmetics or household products (what we may refer as functional perfumery), also present a massive consumption worldwide. Since such products are designed for personal use and so to have contact with the human body (skin, nose, eyes) and because they are universally spread, there must be a strict regulation on their composition to control their possible effects on human health.

For these reasons, the F&F industry is facing new challenges from regulators, particularly from Europe and the United States, which have been limiting the use of possible allergenic or toxic chemical compounds into their products. There are some organizations with impact all over the world that are aware of possible health problems arising from fragrance use. In other words, they want to give higher protection to human health and the environment. For that purpose they keep track of the identification of

intrinsic properties of chemical substances. These main organizations are the Research Institute for Fragrance Materials (RIFM), the International Fragrance Association (IFRA), and the REACH (Registration, Evaluation, Authorization and Restriction of Chemical substances). The major suppliers and fragrance houses generally have a close relationship with these regulators, contributing with a large amount of information on a wide range of fragrance chemicals.

The regulators also perform evaluations on chemical properties and their use, and collect data from the published scientific literature or suppliers' reports. The results of all these studies have been published over the years in extensive series of authoritative monographs covering various issues for each of the chemicals analyzed (Abbe, 2000). Alongside these efforts, IFRA regularly publishes a "Code of Practice", accompanied by detailed recommendations when appropriate, which can be used as voluntary guidelines by the industry to restrict the use of chemicals that are believed to be potentially harmful for the human being. Additionally, some fragrance companies also apply an in-house "black list", thus imposing an even more stringent restriction on the raw materials that their perfumers can use (Abbe, 2000).

However, there has been some noise in the industry, especially against the high levels of restrictions proposed by the regulators, since they will cost hundreds of thousands of dollars to the industry in reformulation, ingredient stock adjustments, costs of buying in substitution stock, and re-labeling. The current legislation for fine fragrance producers defines that they have to declare on packaging if a perfume contains any chemical compound of a list of considered allergens. Consequently, this is undesirable because consumers may tend to reject buying these products for health reasons. Moreover, these restrictions limit the range of possible combinations on perfume formulation, hampering the perfumer's job.

For example, very common essential oils like orange oil or lemon oil must be used in limited concentrations in perfume applications due to sensitizing and phototoxicity effects according to IFRA (Davies, 2009). Other raw materials have already been banned from use, like some chemicals from the musk class. According to Leffingwell *"if you took all these things away from the perfumers, they'd have real difficulty making nice fragrances"*. But the F&F industry is responding positively to these changes, either by reducing the concentration of such ingredients or by replacing them by equivalents. However, the reformulations of classic perfumes, due to introduction of these modern regulatory requirements, have led (in some cases) to some disappointment amongst their

long-term devotees. Jean-Paul Gautier said that *"it is a bit more difficult when clients want you to take these molecules out of existing perfumes without having any change. We do have replacers but they are not exactly equivalent. To have the same organoleptic, physical and economic properties is a challenge"* (Davies, 2009).

In order to overcome such difficulties, the industry has long been looking for synthetic molecules capable of reproducing the pleasant smell of naturals but with less to none toxic or allergenic effects. For this reason, synthetics are, nowadays, widely used in the formulation of perfumes, though they may, of course, introduce other impurity problems. The most important examples of pioneers for synthetic chemicals (natural identical) were methyl salicylate, cinnamon aldehyde, benzyl aldehyde, and vanillin (Ziegler, 2007). For example, vanillin is considered to be responsible, in some part, to the foundation of perfumes belonging to the oriental olfactory family. In 2009, IFRA's 44th Amendment first included vanillin as a restricted compound based on studies showing sensitization effects, but this restriction is currently suspended (IFRA, 2011).

One point to keep in mind about allergic responses is also the recognized "positive effect" observed in mixtures of fragrance ingredients. In other words, one reason for the relative harmlessness associated to perfumes containing ingredients that have sensitizing potential is, apparently, that some other constituents are able to exert a 'quenching' effect. In this way, the sensitizing potential on skin of cinnamic aldehyde, for example, is reduced by D-limonene which acts as a quenching agent (Butler, 2000).

It is a fact that several possible perfume ingredients are allergenic to some degree or, in other words, they have potential for inducing skin sensitization but the same happens with many physical environments around us. The green leaves of trees and plants continuously emit α- and β-pinenes, limonene and other terpene chemicals that are considered as potential sensitizers but, clearly, these are often tolerated reasonably well by most people. Moreover, some authors even say that one European forest would be responsible for releasing more chemicals into the environment that the whole European chemical industry (Burfield, 2010).

In brief, it should be highlighted that perfumery products available on the market are subjected to strict regulations and control, so that these products may be considered as safe and, thus, finding health problems in humans by their use is unlikely to happen.

2.2. Processes underlying the formulation of perfumes

Perhaps perfumes were not originally liquids, but a form of incense. The word perfume is derived from the Latin *'per fumum'*, which means 'by smoke' or 'through smoke', as incense was used by our ancestors to convey their prayers to the heavens for the contemplation of the Gods (Gautschi*, et al.*, 2001). Since then, a restricted audience of priests, kings, pharaohs and emperors used perfumes for both personal and spiritual purposes. It was not until the twentieth century, as a result of the development of our knowledge in chemistry and other scientific fields, together with the Industrial Revolution, that fragrances became available to the rest of mankind as beauty, religious, and spiritual products.

2.2.1. Role of a fragrance

We experience fragrances almost everyday and everywhere, from the fresh scented shower gel we use in the morning to the odor of a classic perfume we put at the evening dinner. Today, fragrances are an everyday item and are part of the culture of many civilizations. More and more, women and men have several perfumes, which they wear depending on their mood. The main function of a fragrance is probably the need to instill a pleasant and harmonious odor to the product in which it has been incorporated. Even so, fragrance ingredients may also be used or designed to perform other roles in the product, which may be more important than the smell itself (*e.g.* antioxidant properties). When incorporated in a shampoo, a fragrance will give the idea that one is washing the hair more cleanly; or when in a perfumed deodorant will appear to impart more freshness. There are also many cosmetic products on the market that have a mild odor, which is the result of some raw materials used in their formulation (Williams and Schmitt, 1992). Mostly, the odor of these "bases" is harmless but sometimes they can be awkward or unpleasant so that they should be masked by using a fragrance. However, there are some very pungent bases that are almost impossible to mask like permanent-wave lotions (Williams and Schmitt, 1992). There are countless products on the market that may contain fragrance ingredients from household cleaning products, through fine fragrances till the toothpaste. Thus, in short, fragrances have the role of enhancing products' performance and attractiveness from consumers. If a fine fragrance, commonly called as perfume, is specially designed to impart a pleasant odor when people are using it, a functional perfumed product often has the objective of masking

malodors (*e.g.* fragranced deodorant). Fine fragrances as those presented in Figure 2.11 are very expensive and often commercialized in small volumes, in the order of tens of milliliters. Additionally, the higher the concentration of fragrance raw materials in the perfume (compared to the amount of solvent) the more expensive the product will tend to be.

Figure 2.11 – Examples of masculine (left) and feminine (right) commercial perfumes.

In sum, fragrances can be used in different perfumery products in order to enrich their organoleptic properties, thus increasing their appreciation from consumers, and therefore their value.

2.2.2. Perfumery raw materials (PRM)

Until the XIX century the vast majority of chemical compounds used in perfumery were mainly obtained from natural sources, since the demand of fragranced products was not compared with today's demand and was mostly intended for the "wealthiest society". As we have seen, the current conjecture is quite different from the ancient times and fragrances are now part of our lives, habits and cultures.

Perfumery raw materials and essential oils vary considerably in cost and volume produced each year. The exact balance between these two variables depends on different factors such as the ease of cultivation, extraction yields, manpower (involved for all the process) or valuable organoleptic properties. For example, while lavender is produced at 250–300 tonnes/year and is a relatively inexpensive oil (€17–35/kg), rose and jasmine are produced at 15–20 tonnes/year and 12 tonnes/year respectively, but in return are much more expensive with prices of €1150-3500/kg, depending on quality (Sell, 2006). Eucalyptus oil, for instance, has one of the biggest production volumes in the world, reaching nearly 2000 tonnes/year and, consequently, is also one of the

cheapest oils on the market (€6/kg) (Sell, 2006). Some perfumery raw materials can be produced in much higher quantities like linalool (8000-10000 tonnes/year), benzyl acetate (7000-9000 tonnes/year), Galaxolide® (7000-8000 tonnes/year), Hedione® (4000-5000 tonnes/year) or Iso E Super® (2500-3000 tonnes/year), depending whether they are natural or synthetic. A simple perspective of the map of natural essential oils in the European continent is shown in Figure 2.12. Of course product cost has an influence on its production volume, but the organoleptic properties obtained from the natural material most influences their demand. On a general trend, perfumery raw materials that are detected by the human nose at very low concentrations are also produced in less quantity (*e.g.* kilograms per year) (Gautschi*, et al.*, 2001). However, the limitations on the available land for cultivation and product stability under storage together with the industrial age and the development of organic chemistry, led to the discovery of synthetic chemicals in the middle of the XIX century. Consequently, this has boosted the fragrance industry as well.

Figure 2.12 – European map of essential oils according to the Treatt Company [Reproduced from The Treatt Company Essential Oils of the world, in http://www.treatt.com/EssentialOil WorldMap.aspx].

In fact, modern perfumery would not sustain itself with natural ingredients only, and so the use of synthetics began to grow. Nowadays, the industry uses several thousands of synthetics. Many natural identical are also used, some of which – like vanillin or the damascones - were first obtained from natural sources and, later, synthesized (Calkin and Jellinek, 1994). Synthetic fragrances can have different origins, beginning with those who mimic the smell of natural fragrances (called natural-identical) to those that have born from the imagination and expertise of a chemist and so have a distinct smell from any odorant molecule previously discovered (Calkin and Jellinek, 1994). And as

with many things in life, several novel odorants were discovered by serendipity. Synthetic fragrances are generally cheaper, easier to obtain throughout the whole year (once they are industrially produced in high volumes). They may also present toxicity levels much lower than the corresponding natural fragrance ingredients which use has been limited by the regulators. In what concerns the price, a simple example that clearly illustrates this idea can be seen for the case of vanillin, one of the most widely used fragrance ingredients in perfumery: considering the same purity (≥97%, FCC, Kosher, FG) the retail price obtained from Sigma-Aldrich is €65.10/Kg and €472.50/Kg for synthetic and natural vanillin, respectively (Sigma-Aldrich, 2010). However, not all currently known pathways for the synthesis of fragrant molecules are viable from a chemical or economical point of view. Moreover, it should be mentioned that the use of natural fragrances still is (and I believe it will continue to be) very important and appreciated by consumers. This is due to their valued organoleptic properties and the significance of the "natural product" tag, that costumers usually prefer.

As the origin of the perfumery ingredients have become more diverse, the processes to extract and purify the natural ones have also evolved through the ages accompanying the technological expansion. Currently, the extraction of perfumery ingredients from natural raw materials can be carried out by processes like distillation (dry, hydro or steam distillation), expression, or solvent extraction (including alcoholic and supercritical CO_2 extraction), just to mention the most important processes (Sell, 2006). In this way, for the process of distillation, it can be performed by three different ways (Sell, 2006):

i) Dry distillation is a common and simple process. It uses high temperatures to heat the plant material which in most cases is performed by direct flame to the vessel. This technique is more appropriated for high boiling point oils (*e.g.* typically woods), since high temperatures are necessary to vaporize their chemical components.

ii) Hydrodistillation is the traditional method of extraction where the raw material is submerged in boiling water. The potential risk of this technique is that the still can run dry, or be overheated, thus changing the properties of the fragrances and so producing an essential oil with low organoleptic value. In order to avoid these problems, hydrodistillation is sometimes carried out under reduced pressure, allowing it to perform at low temperatures.

iii) Steam distillation uses an outside source of steam that usually flows under pressure through the fragrance material. The immiscible oil is generally separated from water by means of a Florentine flask, since they have different densities.

On the other hand, the process that involves the least scientific knowledge of all and which was probably used before distillation is called expression. In this process, mechanical pressure or compression is used to force the essential oils to come out of the vegetal material (*e.g.* leaves, fruit, flower). It generally uses no heat sources and can be performed by different methods, one of which is by cold pressing. Many citrus and fruity oils are obtained at the industry through this process as is the case of the lemon, orange, grapefruit, or bergamot essential oils.

Finally, extraction of essential oils using volatile solvents is widely applied in industry for obtaining perfumery ingredients. Through this process it is possible to obtain different types of natural extracts, depending on the selected technique: extraction with ethanol (*e.g.* vanillin and ambergris), *enfleurage* (where the raw material is brought into contact with purified fat and is nowadays of little commercial impact), or the simple solvent extraction using other solvents. In the latter technique, benzene was traditionally the solvent of choice but due to health concerns (benzene has recognized toxicity, mutagenic and carcinogenic effects) it has now been superseded by other solvents like petroleum ether, acetone, hexane, or ethyl acetate, together with various combinations of these (Sell, 2006). Solvent extraction is one of the methods of choice in the industry having the advantages of using lower temperature than distillation processes, and a resulting extract that is often more rich in natural odor. Its main disadvantage is that non-volatile compounds like waxes are co-extracted during the process, implying further processing by distillation or chromatography. Moreover, there has been recently an increasing interest in supercritical fluid extraction (SFE) which is a branch inside solvent extraction processes. This is considered a “clean” technology in the perspective that the obtained extracts are solvent residue-free and present increased odor naturalness. It is known that supercritical CO_2 provides major organoleptic advantages in essential oil fractionation and that it has the Food and Drug Administration (FDA) GRAS status (Generally Recognized As Safe). Although this process may imply higher costs than the others mentioned before, it is already used at industrial scale by some major F&F companies (*e.g.* Danisco, Denmark) to obtain floral extracts of jasmine, tuberose, and rose. Finally, other processes or solvents with different properties that have been

proposed for obtaining essential oils like microwave radiation, or the use of phytosol solvents (*e.g.* tetrafluoroethane) (Lis-Balchin, 2006) can be referred though we will not go into their details here.

2.2.3. The structure of a perfume

A fragrance ingredient is, typically, defined as an organic compound with a volatile disposition, an appreciated odor quality, and a varying degree of detectability by the human nose. It certainly has valuable properties for its use in perfumery products of different types (*e.g.* fine fragrance or perfume). For its part, the simplest definition of a perfume consists of a mixture of fragrance ingredients, essential oils and fixatives which possess valuable organoleptic properties, together with stabilizers and solvents (water, ethanol, among others). Within the perfumery industry the terms fragrance, perfume, or juice are often used to represent a fragranced mixture (Williams and Schmitt, 1992; Burr, 2008), while in the literature it is common to find definitions of fragrance as the raw material only. Apart from this, a perfume is not just the artistic result of a set of fragrance ingredients randomly mixed to produce a pleasant smell (Calkin and Jellinek, 1994). Instead, it has a well-defined structure in its essence, where at the molecular level, a multiplicity of chemical interactions are simultaneously occurring, thus influencing the volatiles present in air. According to the definition of two recognized perfumers, R. Calkin and J. Jellinek, *"a perfume is a blend of odiforous materials, which is perceived as having its own unique and aesthetically appropriate identity… It must be sufficiently strong, it must be diffusive (which is not quite the same thing), it must be persistent, and it must retain its essential character throughout its period of evaporation"* (Calkin and Jellinek, 1994). This way, a perfume mixture is an ordered arrangement of fragrance ingredients and notes with different physicochemical (and also sensorial) properties that, as a whole, produce a pleasant perceived smell from the beginning of its evaporation. A note, for itself, defines the olfactory impression of a single smell, or more specifically it is the perceived scent of a single or mixture of fragrance ingredients and/or essential oils (Calkin and Jellinek, 1994). Psychophysically it is the perceived odor sensation induced by a stimulus magnitude (Stevens, 1957).

A renowned perfumer of the last century, Jean Carles, in his studies on perfume formulation considered a tripartite structure for a perfume, considering three types of

fragrant notes: top, middle and base notes (Carles, 1962). The three groups of olfactory notes described above may have different psycho-physico-chemical properties but within each group or type of note they share a similar volatility. The fragrant notes constitute the pieces that are needed to formulate a perfume, just as we need bricks to build a house. According to Carles, the structure of a well-bodied perfume is like a pyramid with a large, heavier bottom and a small, lighter top as presented in Figure 2.13.

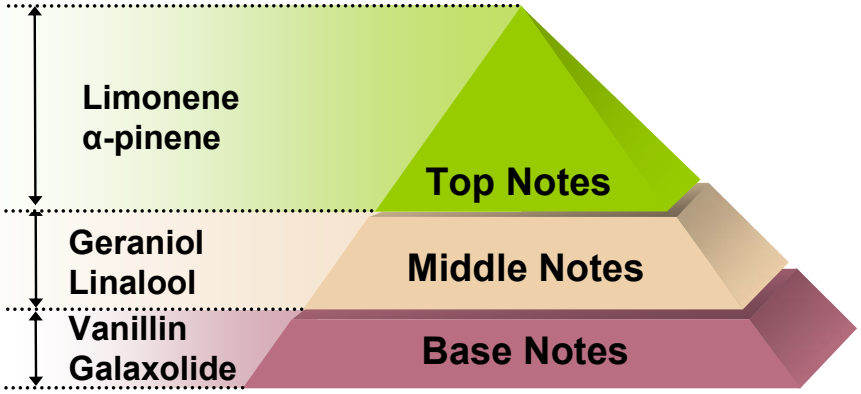


Figure 2.13 – Perfume pyramid considering the top, middle, and base notes in the concentrate of a perfume with some examples of raw materials.

He considered that at the top of the pyramid were the lightest and fastest evaporating scents - the top notes. These are the most volatile fragrances and so, hypothetically, they would be smelled in first place, like during the first seconds through the initial minutes after application of the perfume. As the top notes start to fade (once they evaporate faster and are also absorbed into the skin for example), the perceived odor would evolve into the middle notes as their perception gets more noticeable (Kasting and Saiyasombati, 2003). These are also called as heart or bridge notes since some experts consider that they make a smoother transition between the different scent notes. In some cases, middle notes are used to mask the initial unpleasant odor of some base notes and so they can last from minutes to several hours (Calkin and Jellinek, 1994). Finally, at the bottom of the pyramid were placed the base notes which would be the last to be perceived since they would have the lowest volatility and so would remain longer in the liquid phase. Some of the base notes are often used as fixatives because they can change the tendency of evaporation of both the top and middle notes, thus allowing the perfume to last longer. The base notes are also called end or dry out notes. They can be smelled more strongly some hours after application, persisting for days or even months (*e.g.* for someone who uses perfume on a regular basis, a typical example is when one smells a sweater which was used a week ago). One common family of these base notes are the

(macrocyclic) musks. This group of ingredients is extremely important for the industry because they have valuable organoleptic properties and some are also used as fixatives, producing an effect on other ingredients in the perfume mixture. Originally, they had their natural source in the musk pods of the musk deer. Nowadays, these odorants are mostly obtained by chemical synthesis (synthetic), although they are getting increasingly subjected to restrictions by the regulators, see section 2.1.3. and (Davies, 2009).

The proposed pyramid structure of Carles suggested the following composition relationship between the different olfactive notes: top notes are present in lower percentage, 15–25%; followed by middle notes, 30–40%; and, finally, the core of the perfume concentrate would be the base notes, 45–55% (Poucher, 1955; Butler, 2000; Rowe, 2005). This traditional view holds that perfumes can be seen as blends, composed of three notes together with solvents (mainly water and alcohol among others). However, in terms of perception of the different olfactory notes this is an oversimplification: all fragrant species are evaporating from the moment the perfume is applied though at different rates (which depend on volatility, composition, molecular structure, and molecular interactions), as will be discussed later. Moreover, throughout the evaporation of the perfume it is expected that its main character or accords are kept similar over time, so that the perfume will keep its identity. However, in perfumery there are many puzzling observations which are difficult to explain. Either in the formulation of the perfume or during its evaporation, synergies or molecular interactions between the fragrant materials may occur, resulting in distinct odors from the ingredients separately.

The perfumer, for his part, has a deeper and more detailed perspective of the structure of a perfume, dividing it into three important aspects: *i)* the perfumery accord (aesthetical pleasantness of a mixture of fragrances), *ii)* the relationship between top, middle, and base notes (composition), *iii)* and the balance between simplicity and complexity (number of ingredients) (Calkin and Jellinek, 1994). The perfumer also needs to make a balance between the nature and quality of the raw materials he selects for the juice, together with their corresponding price which will influence the cost of the final product. Figure 2.14 shows a simplified perspective of the properties and price of the fragrant notes that can be used in a perfume. Perfumers may prefer to work with reliable pure materials (from natural or synthetic origin) or choose a commercial grade instead. However, there are some natural fragrance ingredients with an organoleptic

performance that is very hard to emulate with a synthetic one. One of the greatest and most famous perfumes of the last century, Chanel 19 (1971), has a typical floral-green character with a noticeable presence of orris which is a major component. This is a fragrance ingredient widely used in perfumery due to its appreciated sensorial properties and although synthetic irone exists (its major ingredient) the performance of the natural material is often preferred (Calkin and Jellinek, 1994).

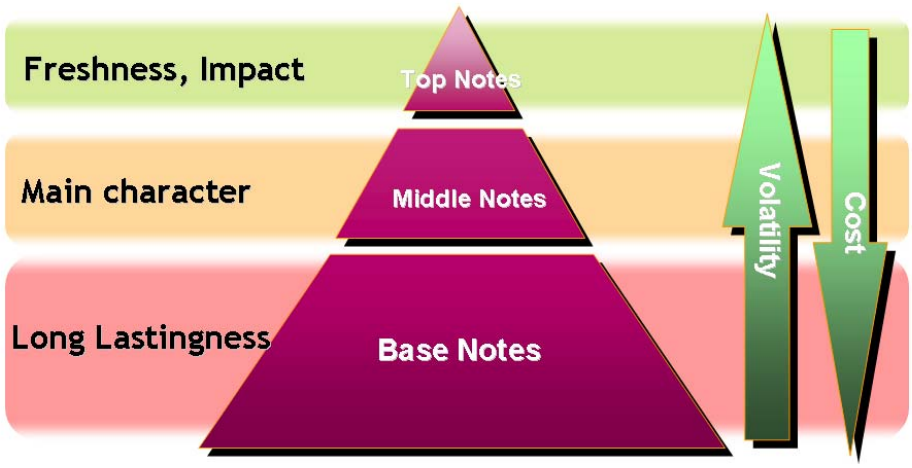


Figure 2.14 - Basic perspective of the perfume structure along with the properties and price of the fragrant notes (Carles, 1962; Kerschner, 2006).

Recently, a new style of perfumery has emerged in the past years with the creation of perfumes with a linear or monolithic structure. This technique initially had its origin in the USA, where consumers preferred strong, sweet, floral, and immediate smelling perfumes. They are characterized for having a simple structure consisting of 5-10 main fragrance ingredients (typically synthetic), all of which tend to be long lasting. These are used at very high concentrations, up to 25% or more, constituting 80% of the total composition. This line of perfumes tends to keep the same perceived scent during evaporation (Calkin and Jellinek, 1994). As an example, Trésor (Lancôme, 1990) – considered a best seller perfume - represents this type of formulation, having four major ingredients in its composition: approximately equal amounts of hedione, iso-E-super, galaxolide, and methyl ionone, which make up about 80% of the formula (Calkin and Jellinek, 1994).

Finally, and following this line of thought, there are some countries and cultures which appreciate highly concentrated perfume oils, like India. These perfumes are highly concentrated in fragrance ingredients, non-alcoholic and long lasting. Their structure may (probably!) not follow any of the conventions addressed in this Chapter, and although they are quite cheap the quality controls they are subjected to are often dubious.

Nevertheless, they are generally applied in very small quantities and sold in small volume bottles (*e.g.* 10 mL).

2.2.4. The development of a perfume

Gone are the days when product manufacturers contacted two or three favorite perfume house suppliers to develop a new fragrance (to be released on the market). Today, the main objective of the fragrance houses' development units is to deliver the best product for their clients instead of proposing a bunch of applications from which the best is selected. For that part, the perfume's brief plays an important role on the development of such products. The brief is a meeting that happens when the different people involved in the development of a perfume meet together and carry out a brainstorming of what it will be like. In the brief many characteristics concerning the perfume are defined: who the perfume should appeal to and why, what the scent should say to the contractor (if one exists) or to the consumers, what forms the fragrance will take (*e.g.* spray, *parfum*, after-shave, soap), where and for how long the product will be sold (*e.g.* Europe or America, 1 or 2 years), among many other questions. The answers collected from the brief will influence the selection of fragrance ingredients for the target product. In short, the brief is a creative and detailed definition of what the new fragrance is supposed to be. As in an analogy it may be compared with the Product Engineering framework based on the needs-ideas-selection-manufacture arrangement which will be discussed in detail later. However, nowadays, it is observed an exponential increase in the release of new perfumes due to a higher competitive market and demand for even greater profits within the industry. This situation sometimes may change the orientation of the brief, which would be to create a new and unique piece of art but to ask the perfumer to develop a fragrance that will sell millions of dollars and that is appealing to all types of people (Burr, 2008). In either case, the brief is the beginning of the development of the perfume, which is first created in the imaginary of an expert in the art of perfumery (called in French *"le nez"* - the nose or perfumer). Today, the "secret formula" of a perfume is idealized by them, experts with a high level of experience in the perception of scents (detection and recognition) as well as in the art of creating accords and perfumes. They select the ingredients to be used and define their proportions based on their expertise. Their selection depends on the theme of the fragrance house they work for or the consumer desire, and may include fragrance ingredients from different sources (natural, synthetic or natural-identical fragrance ingredients or essential oils). The perfumer must

be aware of the differences between these perfumery raw materials and understand how their different qualities perform in a mixture. They have a palette of pure fragrance ingredients, so they can develop their test formulations, as shown in Figure 2.15. For example, young perfumers usually begin by knowing natural products and highly pure synthetics (and mixtures with them) before going on to work with the so-called commercial qualities and more complex essential oils (Calkin and Jellinek, 1994). Then, the recipe is delivered to laboratory technicians who formulate the fragrance and later deliver it back to the perfumer, who will perform an olfactory evaluation and propose further changes, until the desired scent is obtained (Burr, 2008).

Figure 2.15 – Disposition of a palette of fragrance ingredients used in perfumery in the so called "perfume organ". [Reproduced from http://en.wikipedia.org/wiki/Perfume]

Once the perfume's formula is defined, probably after several trials, it may be ready for the production at industrial scale. Throughout this process, the essential oils and fragrance ingredients composing the concentrate (in general terms) are blended with solvents (alcohol, water, etc), antioxidants (tocopherol, butylated hydroxytoluene), stabilizers (paraben, phenoxyethanol, benzyl alcohol), UV filters (benzophenone, octyl salicylate) and coloring agents, among others (Cheong*, et al.*, 2010; Lopez-Nogueroles*, et al.*, 2010). After that, it must be left for ageing in tanks for several weeks. During this period, organoleptic and chemical changes may occur due to the precipitation or possible chemical reactions of some of the fragrance ingredients (Lopez-Nogueroles*, et al.*, 2010). This stage is called the maceration of the perfume and frequently exceeds the minimum time needed to obtain the organoleptic characteristics of the desired perfume. Later, sediments and other small solids are removed through filtration, and the blended mixture is allowed to stabilize for a period around two weeks ("maturation process"), prior to the expedition to sellers in the perfume bottles. This maturation process for perfumes is essential to ensure the stability of the product, so that its performance, odor character, intensity, or color is guaranteed to remain unvaried. The stability of

perfumery raw materials are mainly influenced by chemical interactions occurring at the molecular level, external agents, or evaporation processes. This way, prior to the release of the product on the market it is important to evaluate: *i)* its chemical stability (*e.g.* pH variations, oxidation); *ii)* the color stability (*e.g.* light exposure may lead to discoloration, reactions between aldehydes and amines may change the color as well as formation of complexes of iron); *iii)* other physical factors may be responsible for perfume degradation like hydrolytic breakdown, bacterial decomposition, or inactivation of the preservative by the plastic container (Calkin and Jellinek, 1994).

Whenever the perfume meets these standards and other regulatory standards previously referred in Section 2.1.3 for human health safety, it can be launched in the market. But the success of a perfume is not only due to the compliance with regulatory norms and to its pleasant odor character. It is also known that the consumer expects to find a product that is indistinguishable from the one he bought the last time, and if bought for the first time, he expects it to perform equally throughout the product's lifetime (Calkin and Jellinek, 1994). For the case of a fine fragrance, it is expected that it will remain stable and invariant to the sight of the ordinary consumer, for a period not shorter than 18 to 24 months. In this way, we conclude that a fragranced product is not just the scent that emerges from the liquid solution (in the case of a fine fragrance) or a stick bar (in the case of a dishwashing detergent). In order to succeed in the market, it must have a combination of scents and colors (fragrance), shapes (bottle and package), along with powerful marketing techniques to increase consumers likeability. That means to see a product in a holistic way. From that, consumers will buy it, test it and enjoy the perceived odor as the perfume evaporates and diffuses through air.

2.3. Evaporation and diffusion of fragrances

The process of dissipation of a fragrance from a specific substrate presents itself as an important step for the design and evaluation of novel fragrance materials or products containing fragrance ingredients. But it is also used as an instrument to aid in the risk assessment of fragranced products, namely for skin sensitization (Kasting and Saiyasombati, 2003). The importance of this Section 2.3 is almost certainly because it is known that a wide range of factors influence the way we perceive a perfumed product that is evaporating and diffusing in air. The product in this case may be some substrate/base containing fragrance ingredients which, ultimately, is intended to be

applied on the skin and then perceived by the human nose. However, the evaporation of fragrance materials from the skin varies from person to person. Additionally, it should be underscored that the evaporation arising from a paper blotter may also be different from that of skin or a piece of cloth. This way, the evaporation of a fragrance mixture from a substrate or a base depends on its physicochemical properties, molecular interactions with fragrance molecules, temperature, or pH, just to mention a few. In fact, one problem commonly found by perfumers in the pre-formulation stage of a fine fragrance is the fact that often their perfume formulations do not present the same behavior when applied on a paper blotter and on the skin (Burr, 2008). In this way, the study of all the phenomena involved in the formulation, behavior, release, diffusion and perception of fragrances is of great importance: *i)* it encircles the evaluation of both vapor-liquid and liquid-liquid (or even vapor-liquid-liquid) equilibrium of mixtures composed by fragrance ingredients at different temperatures which may provide important information for fragrance development (Arce*, et al.*, 2002; de Doz*, et al.*, 2008); *ii)* measurement of phase interactions for multi-component mixtures composed by surfactant(s), water, and fragrance ingredient(s) is also valuable for the industry (Tokuoka*, et al.*, 1994; Friberg*, et al.*, 2009); *iii)* other studies concerned with the solubility of fragrance materials in water and alcohols are of great importance to evaluate skin disorders, since they are used in a number of cosmetic products (Domanska*, et al.*, 2008; Domanska*, et al.*, 2010); *iv)* additionally, studies involving humans for the experimentation step are also of relevance like estimating the evaporation and absorption of fragrances from the skin, evaluate the kinetics for fragrance ingredients applied to human skin *in vitro*, and perform some modeling to predict these phenomena (Kasting and Saiyasombati, 2003). Several studies can be found in the literature concerning different topics within the evaporation and diffusion of fragrances in air and released from different substrates or bases. A non-extensive selection of reference works on these fields is presented in Table 2.2.

2.3.1. Evaporation from different media

As aforementioned, the role and behavior of fragrance chemicals have been widely studied in different media from macro-dispersions, emulsions or colloid solutions, to molecular solutions. In respect to this, a particular case on fragrance evaporation is that of emulsions which are of great importance in many fields, such as functional perfumery, food, or pharmaceuticals (Friberg, 2007, 2008, 2009; Friberg*, et al.*, 2009).

Table 2.2 - Summary of some relevant previous studies on evaporation and diffusion of fragrances.

Approach	References
From the skin	
Measurement of the evaporation rates of fragrance ingredients alone and in multicomponent mixtures with and without fixatives using dynamic headspace.	Vuilleumier *et al.* , *Int. J. Cosmetic. Sci.* , 17, 61-76, **1995**
Release of perfume from the skin and evaluation of the physical and chemical interactions between them using headspace analysis with trap adsorbents.	Behan *et al.* , *Int. J. Cosmetic. Sci.,* 18, 237-246, **1996**
Evaporation of fragrances using a skin substitute (*in vitro*) and *in vivo* measurements with headspace techniques.	Schwarzenbach *et al.* , *Int. J. Cosmetic. Sci.,* 23, 85-98, **2001**
Evaporation of fragrances from the human forearm under *in vivo* conditions considering evaporation and absorption rate constants and estimation of the release using physico-chemical properties following nearly first-order kinetics. Measurement and modelling of the evaporation rates of fragrance ingredients in multicomponent mixtures with and without fixatives using dynamic headspace.	Kasting *et al.* , *Int. J. Cosmetic. Sci.* , 23, 49-58, **2001**; Kasting *et al.* , *Int. J. Cosmetic. Sci.* ,25, 235-43, **2003;** Saiyasombati *et al.* , *J. of Pharma. Sci.* , 93, 2, **2004**
Measurement of fragrance intensity and base odor above skin using panellists and a labeled magnitude scale (LMS) .	Cortez-Pereira *et al.* , *J. Sens. Stud.* , 24, 6, 871-901, **2009**
Evaluation of the effect of skin properties on the release of fragrances from the skin using dynamic headspace traps and the odor value concept.	Baydar *et al.* , *Perfum Flavor.,* 20,45-53, **1995**
Study of fragrance performance with measurement of vapor concentrations overtime after application and evaluation of the pleasantness of the aroma in the vicinity of the fragranced skin.	Baydar *et al.* , *Cosmetics & Toilletries* , 111,49-57, **1996**
Comparison of the vapor phase around a plant material and that of the oil applied on the skin using SPME technology and study of the effect of skin properties on the release of fragrances using different perfume formulations.	Mookherjee *et al.* , *Perfum Flavor.* , 23, **1998**; Mookherjee *et al.* , Perfum Flavor., 23, **1998**
From liquid mixtures	
Evaporation from ethanol-water solutions was measured in a wind tunnel using a circular cell and modelled with Gibbs adsorption equation.	O'Hare, *Langmuir* , 9, 1408-1413, **1993**
Development of a methodology for the prediction of the perceived odor of ternary to quaternary mixtures using the Perfumery Ternary Diagram (PTD) and the diffusion of fragrance mixtures in the air using the Fick's law.	Mata *et al.* , *AIChE J.* , 5, 2834-2852, **2005**
Prediction of the evaporation and diffusion of fragrance mixtures in the air using vapor-liquid equilibrium methods and a model based on the Fick's law.	This Thesis
Measurement of vapor compositions in equilibrium with the liquid phase of fragrance mixtures and comparison with different VLE predictive methods and human olfactory evaluations	This Thesis
From emulsions	
Calculation and measurement of evaporation paths of several fragrance in oil emulsions using phase diagrams and modeling by algebraic methods using physico-chemical properties. Different emulsion systems were evaluated mostly of the type surfactant-fragrance-water. Different properties of these systems with influence on the evaporation rate were evaluated.	Friberg, *Int. J. of Cosm. Sci.* , 22, 181-199. **2000**; Friberg, *J. of Disp. Sci. and Tech.* , 28:2, 207 - 212. **2007**; Friberg, *J. of Disp. Sci. and Tech.* , 28:1, 11 - 20. **2007**; Friberg *et al.* , *Colloids and Surfaces A: Physicochem. Eng. Asp.* , 338, 102-106, **2009**; Friberg, *J. Phys. Chem. B* , 113, 3894-3900, **2009**; Friberg *et al.* , *Flavour Fragr. J.* , **2009**; Friberg *et al.* , Colloids and Surfaces A: Physicochem. Eng. Asp., **2010**; see Review of Friberg, *Adv. in Coll. and Int. Sci.* , 75, 181-214. **1998**
Evaluation of the hypothesis that odor intensity is controlled by the concentration of the aqueous phase of na oil-in-water emulsion using the headspace technique.	Brossar *et al.* , *J. of Sensory Studies* , 17, 511-525, **2002**
Measurement of the release of fragrances (and study of the presence of ethanol) from amphiphilic multiarm star-block copolymers using thermogravimetry and dynamic headspace analysis.	Ternat *et al.* , *Macromolecules* , 41, 19, 7079-89, **2008**
Others	
Evaluation of the substantivity of fragrances applied in laundered and dry-out fabrics. Correlation of the affinities of fragrances in standard fabric softener and detergent solutions using the octanol-water partition coefficient.	Escher *et al.* , *J. of the Am. Oil Chem. Soc.* , 71, 1, 31-40, **1994**
Evaluation of the deposition of fragrances on textiles and their evaporation using perfumed fabric softeners was measured in an headspace cell.	Stora *et al.* , *Chimia* , 55, 406-412, **2001**
Olfactory evaluation of the odor intensity of different types of fabrics finished with cyclodextrins and impregnated with fragrances was performed for over an year using odor values.	Martel *et al.* , *J. of Inc. Phen. and Macroc. Chem.* , 44, 439-442, **2002**
Microencapsulation of fagrances for industrial application on fabrics and evaluation of the release upon abrasion and washing cycles.	Rodrigues *et al.* , *Chem. Eng. J.* , 149, 463-472, **2009**
Impregnation of different types of microcapsules containing fragrances in fabrics and evaluation of the released fragrance before and after washing using an electronic nose.	Specos *et al.* , *J. of Ind. Text.* , 40, 1, **2010**
Online measurement of fragrance release from cotton towels impregnated with microcapsules containing fragrances by low thermal mass gas chromatography using a cryogenic system for headspace analysis.	Haefliger *et al.* , *Anal. Chem.* , 82, 729-737, **2010**
Measurement and prediction of the evaporation of fragrances from microencapsulated textiles and their diffusion plus odor perception in the surrounding air.	This Thesis

Friberg and co-workers have been developing an extraordinary work in the field of fragrance chemicals release from emulsion systems combining phase diagrams with algebraic calculations to withdraw information from these ternary diagrams as illustrated in Figure 2.16. In this example, the evaporation paths in linalool emulsions were experimentally determined and compared to those calculated from vapor pressures for a series of emulsions with different oil/water (O/W) ratios. In the ternary diagrams of Figure 2.16 the three-phase regions consist of triangular areas delimited by three tie lines which are defined by the points of composition of the aqueous liquid (Aq), of the liquid crystal (LC) and of the oil phase (Oil). This is of relevance since most studies on this subject do not address the variation of the conditions (*e.g.* composition or the number and structures of the emulsion phases) during a prolonged evaporation which is experienced in most emulsion applications.

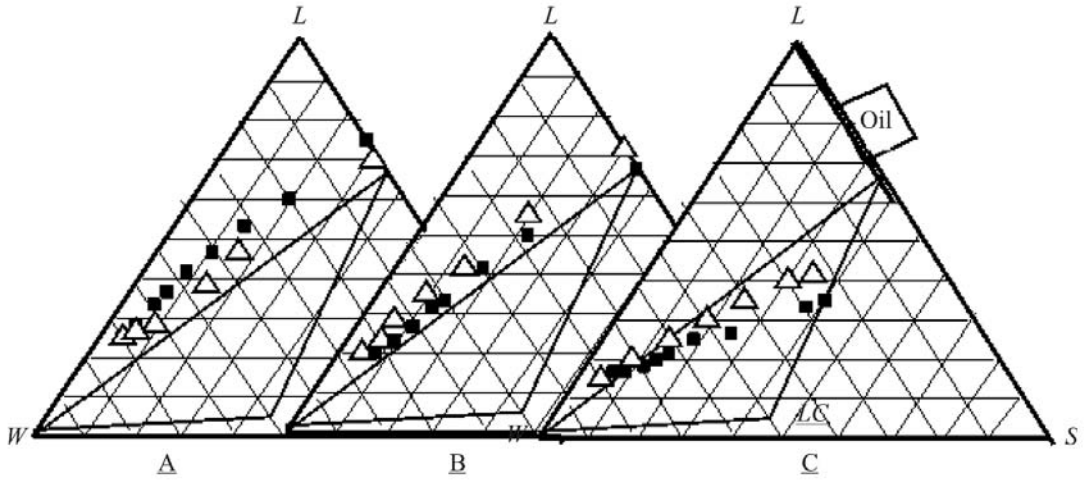


Figure 2.16 - Evaporation paths for three series of emulsions with different initial compositions (A, B, C) for the ternary system of water (*W*), linalool (*L*) and surfactant laureth-4 (*S*). Open symbols represent experimental values (triangles) and closed symbols are calculated compositions (squares). [Reproduced from Al-Bawab A *et al.* Flavour and Fragrance Journal. 2009; 24(4):155-159].

Through their methodology it becomes possible to predict the evaporation path or the change in the vapor pressure during the evaporation process of fragrance chemicals from an oil/water emulsion. Other effects were also evaluated to account for deviations from equilibrium conditions in the evaporation of emulsions like the weight of relative humidity on the evaporation rate or the growth and reduction of phase volumes at non-equilibrium conditions (Bozeya*, et al.*, 2009).

On the other hand, important studies on the evaporation of fragrance materials are also concerned to those that involve clinical trials such as the release from the skin (*e.g.*

forearm). The available research experiments of *in vivo* release of fragrant chemicals are scarce in the literature. Experiments performed at one of the major F&F companies relied on dynamic headspace measurements using adsorbent materials (*e.g.* Tenax, Porapak Q or activated charcoal). In this way, the volatiles released from the skin could be identified and quantified, and then the odor intensity could be calculated over time, using for example the odor value (OV) which is defined by the ratio of the concentration in the gas phase and the odor detection threshold (Baydar*, et al.*, 1995; Baydar*, et al.*, 1996). From the literature it is also possible to obtain valuable information about parameters influencing the evaporation process: the effect of physical properties of the skin, the absorption mechanism into the skin, and the kinetics of the release, among others. It is known that the skin is not an inert surface, as discussed before. It interacts with fragrance chemicals and appears to substantially slow down its evaporation (for some components and especially with oily skin see Baydar*, et al.*, 1995) when compared with free evaporation from a glazed surface (Behan*, et al.*, 1996). This has to do with complex fragrance-skin interactions. The same effect is seen when a fragrance evaporates from a paper blotter since it has a different affinity for fragrance molecules than the skin. The skin effect on each component of a fragrance mixture varies depending on its nature (*e.g.* polarity, molecular size). Within this issue, it would be reasonable to expect that moderately hydrophobic ingredients would present higher affinity for the oil phase on the skin, and thus be held more strongly than others. Conversely the presence of perspiration may drive off very hydrophobic materials such as terpenes (Behan*, et al.*, 1996). Another consideration is that the skin, like a biological tissue, may act as a reservoir for fragrance chemicals which can be absorbed and provoke skin sensitization. To evaluate the balance between percutaneous penetration and evaporative losses of fragrance from the skin, the ratio of the chemical-physical properties of vapor pressure to the product of its octanol-water partition coefficient and its aqueous solubility can be calculated to give some reasonable approximation of the phenomena (Guy, 2010).

Finally, it is also important to address the application of fragrance materials on fabrics and evaluate its release and diffusion through air. There are several studies on the development of polymeric microcapsules containing fragrances inside for impregnation into fabrics and posterior evaluation of the released fragrance after dry washing or abrasion cycles using headspace gas chromatography, cryogenic systems coupled with chromatography, electronic noses, or olfactory evaluations, as shown in Table 2.2.

In this way, when a perfume is incorporated into a product (*e.g.* liquid soap, detergent, or bath oil) it is not surprising to observe a variation in the vapor composition which will change fragrance intensity and/or character as perceived by the nose. The primary explanation would arise from the dilution process itself which has to do with the psychophysical properties of the fragrance and the solvent (*e.g.* saturated vapor pressure, molecular weight). Yet, for different product bases which themselves have very weak odors, it is seen that using the same perfume dilution results in a significantly different odor perception. For that, molecular interactions within a product play an important role in the evaporation of the fragrance ingredients.

High impact odorants vs fixatives

The search for new fragrance ingredients which are responsible for the main characteristic odor of a perfume (or an essential oil) is usually driven by different factors or a combination of them: the high price or the scarcity of other powerful ingredients which leads to the need to replace them; or simply the enthusiasm for the discovery of novel ingredients that induce a pleasant or a blooming odor. The characteristic odor elicited from a perfume or an essential oil may be due to a single ingredient with a major composition or to a trace component that evaporates rapidly and has a low odor detection threshold. Anyway, in most cases the characteristic odor evaporating from a mixture is the result of a multi-component combination of different odors. And it is within this vapor blend that some ingredients show up, usually having low impact on the odor but with great influence in the release of the other fragrances (*e.g.* retaining them in solution). These are called fixatives and their role within a mixture was already discussed in this Chapter (see section 2.2.3: The structure of a perfume). From the perspective above it is not correct to define a fragrance ingredient as highly-blooming only based on its odor threshold, despite the fact that a fragrance material with an ODT lower than 10^{-4} mg/m^3 will generally be considered as a powerful odorant (Clery, 2010). For example, p-menthane-8-thiol-3-one has one of the lowest ODTs in air reported by Givaudan as 0.17 ng/L while geosmin, a popular example of a high-impact odorant, has an ODT in the order of 10^{-3} ng/L (Clery, 2010). Nevertheless, it should be pointed out that these ODTs come from the company's database which are probably obtained using their perfumers and so are lower than those that can be obtained from the compilation of van Gemert (van Gemert, 2003), for example. Even so,

there are other fragrance materials like 1,8-cineole, thymol, linalool, or geraniol with low ODTs and thus, depending on their composition in the mixture, may also have a high-impact.

From the physicochemical point of view, there are some variables that may have a role on the release of fragrance chemicals from a mixture or the skin, like the saturated vapor pressure, the octanol-water partition coefficient, the boiling point, the solubility in water, or even the molecular weight. The study of high blooming odorants is also very important for fragrance products like detergents or shampoos which are generally applied in high water dilution conditions. For these cases, it is considered that the physical properties of the fragrant molecules may play a role on the perfume burst so that odorants with a partition-coefficient of at least 3.0 and a boiling point of less than 260° C would be considered as having superior release properties (Fadel*, et al.*, 2008). Nonetheless, it is obvious that this is a simplified perspective of the problem because even in an emulsion system (as these cases apply), molecular interactions are occurring which may change the release. Moreover, one should not forget the importance of the odor detection/recognition threshold which can also influence the human perception of a fragrance material.

2.3.2. Diffusion in air and fragrance performance

As aforementioned, the perfume is evolving during its evaporation and diffusion in the surrounding air. Throughout that time some fragrance ingredients are more rapidly volatilized than others or diffuse quicker trough air, thus changing the equilibrium state at the gas-liquid interface and the perceived sensation. At a glance, not only the properties of the fragrant notes come into account for this effect but also their molecular diffusivities. The diffusion of a molecule in air is a physical process and the rate of diffusion of a fragrance, in a simplified manner, can be said to be proportional to the square root of its molecular weight. Thus, considering the narrowed range of molecular weights among the fragrance raw materials (~100 to 300 g/mol), it is fair to say that their molecular diffusivities will only be marginally different (the lightest molecules will travel 1.5 times faster than the heavier ones) (Cortez-Pereira*, et al.*, 2009). Through this point of view, it appears that the differences in the volatility of the fragrance raw materials (considering their saturated vapor pressures), will be the significant driving force for their release. However, when blended with others or with a solvent or applied

in a substrate, the persistence of each ingredient will also depend on the concentration (higher dosages will tend to increase persistence), and the strength of the attraction forces between perfumery ingredients and the base or substrate to which it is applied. (A parenthesis is made here, to underline that we should not confuse the term persistence used in this context with the perceived olfactory intensity over time since this will also be a function of the odor threshold. It, thus, refers to the remaining liquid that lasts longer prior to volatilize.) Even so, the combination of both processes of evaporation and diffusion will contribute to the evolution of the perceived scent from the initial sensation (the impact or the kick) through its core scent (the development), until at last, it completely fades away. Between these three "olfactory stages" the different fragrance notes (top, middle, and base) naturally overlap in terms of perceived odor, thus contributing to a balanced perfume structure as shown in Figure 2.17.

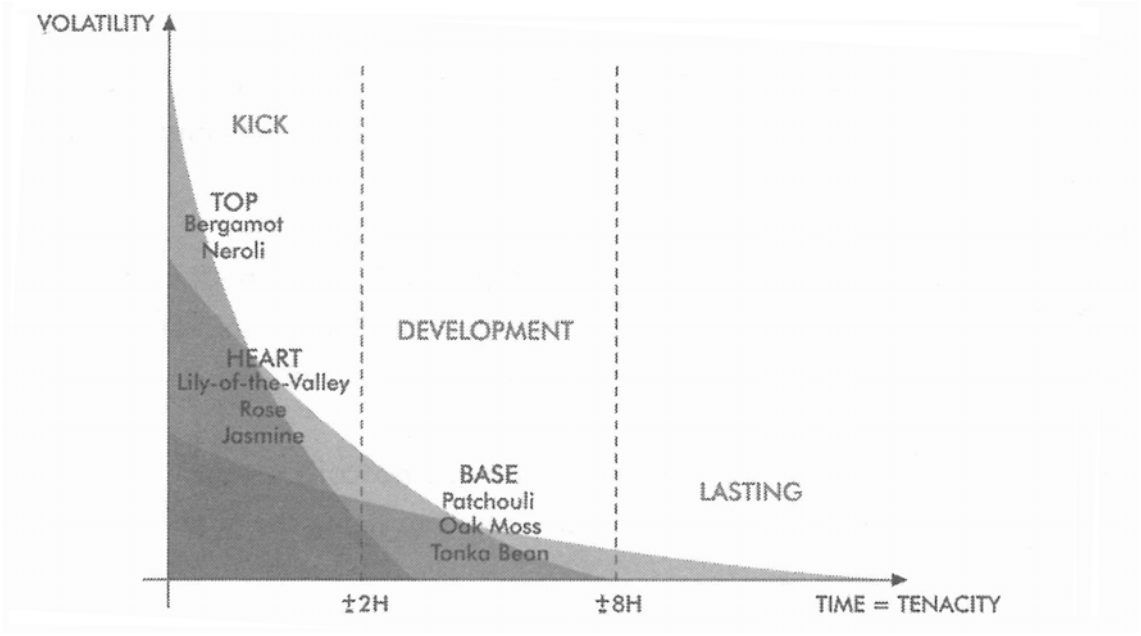


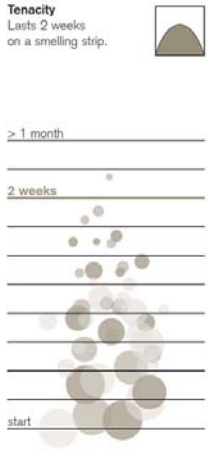
Figure 2.17 – Simple perspective of the evaporation and perception of the different fragrant notes near the source of the perfume. [Reproduced from Paris Parfum, The fragrance guide to Paris, 2011]

It is then understood that the perceived odor of a mixture of fragrance ingredients is evolving over time (and also distance) both in terms of intensity and quality/character. To account for this change, the performance of a perfumed product must be evaluated. An overview of some relevant works on the evaluation of the performance of perfumes is presented in Table 2.3. The term performance is commonly used in perfumery as a measure of the long lastingness or strength of a perfume/fragrance as shown in Figure

2.18. These terms are generally related to the persistence of a fragrance on a paper blotter over time, although such an evaluation may be too simplistic. In fact, within the perfumery industry, the sensory evaluation of a perfume, a fragrance ingredient or a scented product is primarily based on the quantification of human responses to physicochemical stimuli (olfactory evaluation often carried out by perfumers). Of course, this process involves using the human noses as measuring tools, mainly for a qualitative and descriptive analysis (Cortez-Pereira*, et al.*, 2009). According to Calkin and Jellinek, the performance of a perfume is represented by its ability to become noticeable. Thus, the performance of a perfumed product starts in the optimization of its composition, in order to obtain the maximum desired odor effect at the lowest possible concentration. Yet, several questions still remain to be unfolded: does the performance of a perfume depends on the intrinsic performance of its constituents? Does the art of perfumery involved in the formulation of the product also play a role in the performance of the product? How should the performance of a perfumed product be measured and better yet, predicted?

Table 2.3 - Summary of some relevant literature on performance of fragrances.

Approach	References
Measurement of fragrance intensity and base odor above skin using panelists and a labeled magnitude scale (LMS) for performance evaluation	Cortez-Pereira *et al.*, *J. Sens. Stud.*, 24, 6, 871-901, **2009**
Evaluation of perfume performance based on chemical structure related properties and physicochemical properties of the chemicals together with calculation of the perceived odor intensity	Stora *et al.*, *Chimia*, 55, 406-412, **2001**
Combination of headspace measurements with olfactometry data and correlation of physicochemical properties for evaluation of fragrance performance	Gygax *et al.*, *Chimia*, 55, 401-405, **2001**
Definition of performance parameters like impact, tenacity, diffusion, volume and substantivity as well as important properties for the evaluation of performance like the odor value, odor threshold or log P	Calkin and Jellinek, Perfumery: Practice and Principles, New York, John Wiley, **1994**
Prediction of the perceived odor of mixtures using the PTD® methodology and also of their performance in terms of time and distance using a model based on Fick's laws and performance parameters commonly used by the industry	Mata *et al.*, *AIChE J.*, 5, 2834-2852, **2005;** Gomes, P. B., Engineering Perfumes PhD Thesis, FEUP, **2005**
Proposal of perfume compositions comprising non-substantive fragrance materials in order to enhance product shelf life, delivery effectiveness and substantivity on different substrates	Duprey et al., Quest, US Patent 7,713,922 B2, **2010**
Methods of formulating fragrance products to mask the malodor of ammonia	Faddel et al., Givaudan, US Patent 7,585,833 B2, **2009**
Perfume compositions designed for use in wash-off systems to provide a high initial bloom with minimal residual perfume on the targeted system and a long sustained release of fragrance	Faddel et al., Givaudan, US Patent 7,446,079 B2, **2008**
Methods and compositions of perfume mixtures to improve the release of fragrance materials from an entrapment structure on a surface over time	Heltovics et al. The Procter & Gamble Company, US 2004/0097398 A1, **2004**



STABILITY & PERFORMANCE

RECOMMENDED APPLICATIONS	STABILITY	TYPICAL % USE	SUBSTANTIVITY & REMARKS			
fine fragrances	■■■■	1 - 10%	Heart and base note			
shampoo	■■■■	1 - 5%	wet:	■■■■	dry:	■■■■
shower gel	■■■	1 - 5%	bloom:	■■■		
soap	■■■	0.5 - 5%	foam:	■■■■	dry hand:	■■■■
detergent	■■■	0.5 - 5%	wet:	■■■	dry:	■■■
softener	■■■■	0.5 - 5%	wet:	■■■■	dry:	■■■■
APC	■■■	0.5 - 5%	–			
candle	■■■	0.5 - 5%	cold wax:	■■■	burning:	■■■

Figure 2.18 – Typical evaluation compendium for fragrance ingredients (*e.g.* Habanolide®) from Firmenich. [From Firmenich Catalogue, http://www.firmenich.com/e-catalog/index.lbl]

In order to obtain a more precise and scientific perspective of how a perfumed product will be perceived, one should account not only for the time variable, but also for space (or distance from the source of application of the perfume). This way, the perfume is evaporating and diffusing through the surrounding air over time and distance, and will be perceived differently depending on where we stand on these two variables. For that, there are some important performance parameters that must be evaluated in order to define the lowest possible perfume dosage that allows the desired maximum odor effect (Cortez-Pereira*, et al.*, 2009). These odor performance parameters are time and distance dependent as schematically shown in Figure 2.19, and can be categorized as follows:

i) Impact: is an immediate olfactory sensation because it is a measure of the intensity of a perfume in the first moments after an application. An example is when sniffing a perfume from a blotter or right after its application onto the skin;

ii) Tenacity: is the ability of a fragranced mixture to retain its characteristic odor during the called dry down stage. It is a performance index that measures the persistence of a fragrance for long times after its application but near the evaporating source, like how long lasts the perfume in the skin after applying it;

iii) Diffusion: refers to the efficacy of a perfume at some distance from the source, representing how fast a fragrance radiates in space and permeates into the surrounding environment;

iv) Volume: is the effectiveness of a perfume over distance, some time after application.

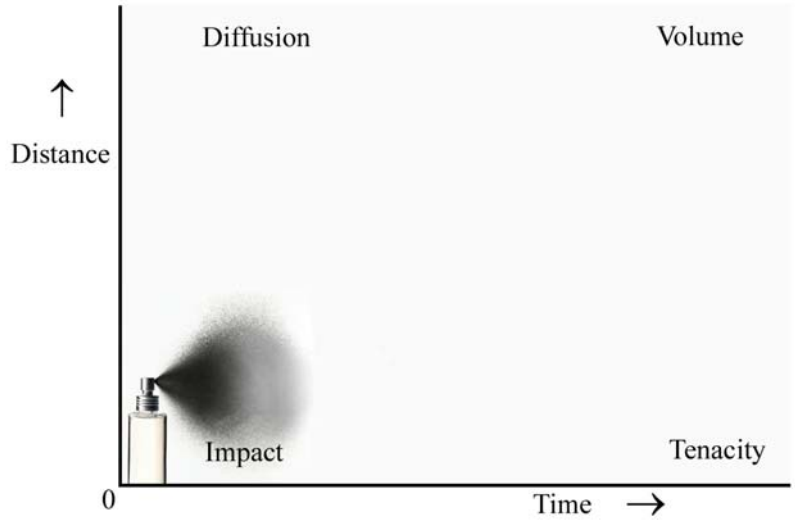


Figure 2.19 – Parameters used by perfumers to evaluate the performance of a perfume as a function of the intensity and character of the perceived odor with time and distance.

There are other performance parameters like the odor life of a fragrance that is also another quantitative measure of how long a fragrance note persists in the gas phase above a liquid mixture (headspace) with intensity higher enough to be smelled (*e.g.* with a concentration above the odor threshold value). Another parameter that must be referred here is the term fragrance substantivity: it deals with the tendency of an essential oil or fragrance ingredient when applied in a diluted solution of water, to bind itself to a solid surface like the skin. This property measures the adhesion of a fragrance to the substrate where it is applied, like its affinity to stay on a surface when this is moistened (Calkin and Jellinek, 1994; Cortez-Pereira*, et al.*, 2009). Some of the aforementioned odor performance parameters can be evaluated quantitatively or qualitatively using different experimental techniques or models that will be discussed later in this Chapter - Section 2.5.

2.4. The perception of odors and fragranced products

The detection, recognition and quantification of odors are truly multidisciplinary fields inside what is often called the perception of odors. Olfactory studies have been a subject of interest for long in different scientific fields, including environmental science,

chemistry, chemical engineering, biotechnology, medicine, flavor & fragrance, psychology (and psychophysics) or social sciences (like demography, ethnography, anthropology, geography or sociology), just to mention some (Rouby*, et al.*, 2002). This is so because though they may be imperceptible for us most of the times, odors play an important role in our daily lives. Odors are relevant for health and safety concerns, not only at regulatory levels but also for in-situ monitoring that can be performed by operators (for example in the detection of diseases to anticipate their medical treatment). Odors are also crucial in social sciences to understand the evolution of population and its relationship with the city and environment. In other words, it is important to quantify and evaluate the effects of the relationships between odorant concentrations and their psychophysical interpretations which encircle the knowledge of the olfactory mechanism.

2.4.1. The olfaction mechanism

It is known that an odor is the result of an interaction between chemical molecules and the olfactory system, eliciting a bio-psychological response or sensation. They are originated by volatile species accompanying gaseous emissions or evaporating from solids or liquids. It is thought that only volatile molecules can act as odorants, because the odorant molecules have to be in the gas phase to be perceived by the olfaction mechanism. Moreover, their concentration in air must be above a certain limit in order to be detected and recognized: the odor detection (ODT) and recognition thresholds (ORT), respectively. In olfaction, faint odors are perceived just above the detection threshold and often have no semantic quality while at higher concentrations odorants can be pleasant or even pungent (*e.g.* have irritating effects). A simple perspective of the process of olfaction is schematically presented in Figure 2.20 and can be depicted as follows: odorant molecules which are present in the air get into the nose nostrils when breathing or sniffing and reach the upper section of the nose. Once there, part of these odorant molecules will dissolve in the mucus layer and then bind to specific olfactory receptor (OR) proteins located on the cilia of olfactory sensory neurons (OSN) on the nasal epithelium.

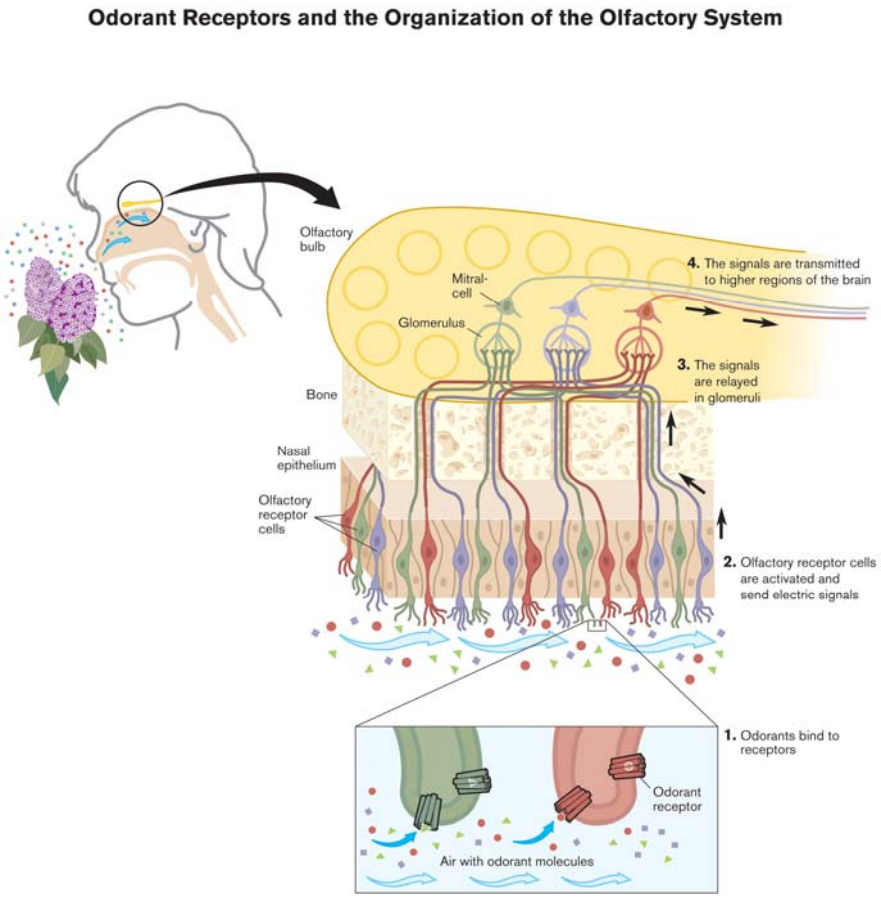


Figure 2.20 - Schematic view of the organization of the olfactory system. Highlighted is the section where the odorant receptors are located, showing their interaction with the airborne odorant molecules. [Reproduced from http://nobelprize.org/nobel_prizes/medicine/laureates/2004/press.html]

Figure 2.20 shows a simple and schematic view of this process for a type of olfactory receptors. OSNs are bipolar neurons with a dendrite formed by tens of cilia that elongate into the olfactory mucus. This way, chemical odorant molecules bind to the olfactory receptor protein (a 7-TM or trans-membrane protein) at the surface of the cilia membrane (Haddad*, et al.*, 2008; Kato and Touhara, 2009; Spehr and Munger, 2009). After being received by the sensory neurons, the olfactory signals are projected to the olfactory bulb (Mandairon and Linster, 2009; Matsumoto*, et al.*, 2009). This mechanism activates a response of the G protein and triggers a nerve process (chemical stimulus) transmitted through the olfactory neuron to the glomeruli within the olfactory bulb (Saito*, et al.*, 2004; Khafizov*, et al.*, 2007; Periole*, et al.*, 2007; Spehr and Munger, 2009). With about 391 olfactory receptors, humans also have the same number of glomeruli in the olfactory bulb where the pattern of activation is decoded by the brain as a perceived odor. These are complex processes responsible for our perception of thousands of different odors. For example, if we assume that a glomerulus could only be

on or off (though in reality many intermediate activation states occur), this would result in $2^{391} \approx 5 \times 10^{117}$ potential odor impressions (Kraft and Mannschreck, 2010). Moreover, the combinatorial binding process between odorant molecules and ORs make it even more complex to envision this process as we will discuss ahead. It is a fact that ORs are being thoroughly investigated (those from humans, other mammals or insects), resulting in an accelerated growth of knowledge at this level though it still remains short. The discovery of a number of different types of receptors involved in the detection of olfactory signals has revealed a structural and functional diversity that was not expected until few years ago (Saito*, et al.*, 2004; Tian*, et al.*, 2005). Scanning electron micrographs (SEM) of the human mucosal surface showing the structure of ORs is presented in Figure 2.21.

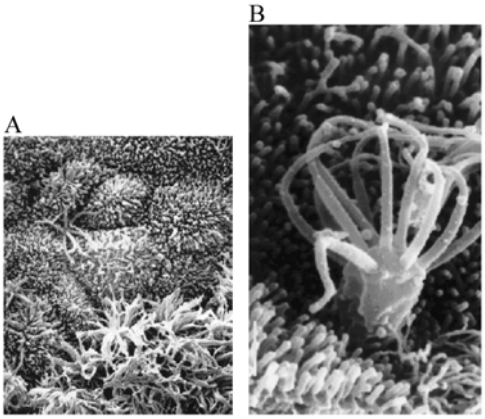


Figure 2.21 – SEM images of the human olfactory mucosal surface (A) and olfactory receptor cells and cilia (B). [Reproduced from Jackson, R. S., Wine Science: Principles, Practice, Perception, USA, Elsevier Science & Technology Books, 2000]

It is believed that a better understanding of their function and interaction with odorants may significantly enhance the knowledge of the mechanism lying behind odor perception. Despite all the advances, several questions remain unanswered and many puzzling observations on odor perception are still unsolved.

It is known that there are about a few hundred different ORs, and thousands of odorants. Additionally, different odorants may bind to the same type of ORs, as well as a given type of odorants can also bind to different types of ORs. This way, our knowledge about the ORs and odorant(s) interaction(s) is still limited. But do these different bindings of the couple odorant-ORs result in similar threshold concentrations or provoke the same sensation? Will the perceived intensity scales be the same? Why do we perceive vanilla as a sweet warm scent and not anything else? The answer to these questions is not more than a mere attempt, and so the process of odor perception remains unsolved. Indeed,

the prediction of olfactory perception is still considered from some, as almost impossible to be successfully achieved in the near future (Sell, 2006).

Still, this lack of knowledge is disturbing and at the same time stimulating for scientists. Odors are pervasive in our daily life, influencing, for instance, our mood or likeability of a product but that is not all. With every breath we take we are sampling the environment for dangers, food, or even sexual attraction to other individuals (*e.g.* pheromones). Just like the other human senses as hearing, sight, touch or taste, the sense of smell allows us to gather messages about the environment around us. However, there is a big difference between the senses of taste and smell from all others: they are "chemical senses". In other words, the information that is sent to the brain deals with cognitive areas that are more complex of being understood. The sense of olfaction is peculiar not only because it is always active and with a close connection with the brain but it has also crucial importance in the lives of many organisms. For example, animals have to recognize a massive amount of odorant chemicals related to food, predators or mating partners in order to fight for their survival and reproduce their species, respectively (Fleischer*, et al.*, 2009). The fruit fly, for example, can rapidly detect the presence of an odor when first sniffing a plume, and rapidly redirect its flight trajectory within 250 ms. On the other hand, the human olfaction mechanism can detect an odor in a single sniff and modify the airflow through the nose within 160 ms (Johnson*, et al.*, 2003).

Finally, in what concerns the human being there are also significant differences in the perception of odors among people. These can be attributed to age, gender, smoking habits, or nasal allergies, among others. As an example, non smokers show greater olfactory acuity than smokers and females have a keener perception than males, in general (Powers, 2004). Having said that, there is no doubt that the olfaction mechanism is complex and omnipresent, constituting a powerful system for our survival.

2.4.2. Odor detection and recognition

There is the common idea that the human olfactory system is rather limited when compared to that of other species like dogs or mice. Even so, the fact is that humans can detect a large number of different odors, in the range of thousands (Jacobson*, et al.*, 2001; Gilbert, 2008), even at extremely low concentrations as parts per billion (ppb) or parts per trillion (ppt) (*e.g.* methanethiol) (van Gemert, 2003; Powers, 2004; Goldstein,

2005). However, from the human health point of view, the type and duration of exposure is also an essential parameter to take into account when analyzing (health) harmful effects and this encompasses: odor concentration (intensity), duration of exposure, frequency, offensiveness of the odor as well as tolerance and expectation of the receptor (Wang*, et al.*, 2004; Pritchard, 2009). Table 2.4 presents an example of the relationship between toxicity effects with exposure time and concentrations for ammonia, which is one of the bulk chemicals with largest production in the world. In addition to the risks that chemicals alone may bring to the human health, it can not be disregarded the possible effects coming from their blending. Mixing of chemicals may produce a combination of toxic odorants in the gas phase which are not all perceived by the nose due to masking effects of odors (and so may be responsible for severe health injuries). As a result, regulatory actions often include odor thresholds, concentration, frequency, and duration as controlling parameters within the compliance protocol.

Table 2.4 - Toxicological effects following acute exposure to ammonia by inhalation (Singh*, et al.*, 1999; Amshel*, et al.*, 2000).

Exposure Concentrations (ppm)	Duration	Effects
20		Decreased disease resistance
20-50	2 hours	Mild discomfort and pungency depending on individual odor detection threshold
50		Smell
50	< 1 day	Eye and throat irritation, cough
100	2 hours	Nuisance eye and throat irritation though it may be tolerated by some people
100	6 weeks	Impaired pulmonary function
<150	< 1 day	Scarring of upper and lower airway, need to leave exposure area
500-1000	30 min	Tearing of the eyes, sore nose and throat coughing
1000-4000		Pulmonary edema, irritation of upper respiratory tract, severe coughing
4000-5000	30 min	Severe damage of the upper and lower respiratory tract, irreparable respiratory injuries
5000-10000	few min	Rapidly fatal due to airway obstruction
>10000		Promptly lethal

Nevertheless, the measurement of odors must be performed both quantitatively and qualitatively according to EN 13725, 2003: *i)* detectability (detection or recognition thresholds); *ii)* intensity scale (the perceived sensation with concentration increase); *iii)* perceived character or quality (classification into olfactive families like floral or citrus); *iv)* hedonic tone (the degree of pleasantness or annoyance of an odor).

2.4.3. Odor thresholds

The definition of perception thresholds in the literature can be misleading, as different descriptions are currently used to express them, albeit not always are well applied (Lawless and Heymann, 1998; Meilgaard*, et al.*, 2007). The nomenclature referring to the types of odor thresholds involves several terms like perception, sensory, olfactory, or sensitive thresholds. The differences among their peers are few to none and from here onwards we will not make any distinction between them. Instead four major parameters should be considered for the perception of odors: detectability, recognition, intensity, and character, as aforementioned. While the last is concerned with the hedonic tone (qualitative) of odors, the first deals with the bottom of the scale (the minimum perceptible). The mid parameters are concerned with the identification or classification of odors and with the perceived intensity (quantitative), respectively. It is then understood that the use of odor thresholds involves a careful evaluation of such parameters, as could only be for a unit that is so important in different areas of human life. Surprisingly, in the past there were even those who questioned the existence of an odor threshold (Swets, 1961). In other words, it was questioned the existence of a threshold concentration value that could be independent of the probability of a false-positive report (Swets, 1961). However, nowadays not only their existence but also their importance is widely recognized as they are applied in a multitude of fields (AIHA, 1989; Cain and Schmidt, 2009). Even so, experimental threshold data are not universal, but rather open to criticism. Due to the aforementioned variability it is sometimes reported that threshold data should be a last resort tool for analysts, unless no other method could be applied (Swets, 1961; Chambers and Wolf, 1996). Nevertheless, whether it is due to insufficient scientific knowledge on olfaction or to the lack of alternative methodologies, odor threshold data are often used. And, to our point of view, their application has proved so far to provide fair to good results in a variety of issues like atmospheric environment control, commodities purity, soil and drinking water contamination, food chemistry, cosmetics and fragrance products among many others (AIHA, 1989; Young*, et al.*, 1996; Ferreira*, et al.*, 2000; Gostelow*, et al.*, 2001; Nicell, 2003; Rosenkranz and Cunningham, 2003; Rodrigues*, et al.*, 2009; Teixeira*, et al.*, 2009a; van Wezel*, et al.*, 2009).

Four types of odor thresholds can be found in the literature: the detection threshold (also called as absolute odor threshold, Thr^d or *ODT*), the recognition threshold (Thr^r or *ORT*),

the terminal threshold (also defined sometimes as pungency threshold, Thr^{ter}), and the difference threshold (Thr^{dif}) (Meilgaard, *et al.*, 2007). The latter represents a relative or comparative odor evaluation: it is a measure of the degree of change in the stimulus (*e.g.* gas concentration) necessary to produce a noticeable difference in the perceived response. Its experimental determination is often made by comparison between a standard and a variable stimulus, using a metric scale. The metric scale was first proposed by Fechner, who postulated that each increment of sensation was defined by a unitary *"just noticeable difference"* (Stevens, 1957; Shigemoto, 2002, 2004). The relationship between the odorant concentration in air and the perceived sensation is shown in Figure 2.22, together with the positioning of these odor thresholds in the scale.

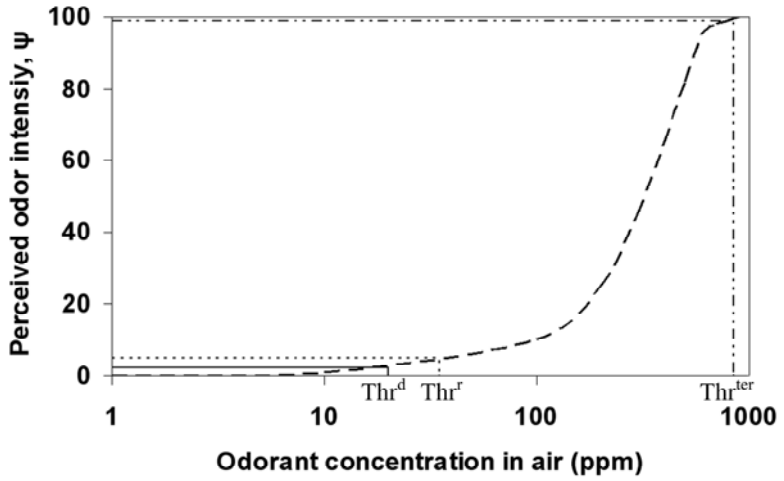


Figure 2.22 – Typical representation of the perceived odor intensity as a function of odorant concentration in air with the representation of the different odor concentration thresholds. [Reproduced from Teixeira, MA *et al.*, Advances in Environmental Research, Chapter 1: Odor Detection & Perception: An Engineering Perspective, NovaPublishers, Volume 14, 2011]

For its part, the terminal threshold (Thr_{ter}) is concerned with the maximum of that metric scale as shown in Figure 2.22: It is the concentration limit value above which humans cannot discriminate any increase in the perceived intensity produced by a corresponding increase in the stimulus. It is often observed pain above this threshold value (Meilgaard, *et al.*, 2007), and so it is sometimes used for hedonic (qualitative) purposes as a boundary between pleasantness and unpleasantness scents. These two types of person-specific thresholds are less common in practice for odor evaluation. The most widely used (and economically important) odor thresholds are the detection (ODT) and the recognition (ORT) thresholds. The first is defined as the minimum

concentration of an odorant that can be detected by humans, while the latter represents the lowest odorant concentration at which its recognition becomes possible (see for example Appell, 1969; Calkin and Jellinek, 1994; van Gemert, 2003; Teixeira*, et al.*, 2011). Below the ODT an odorant is not perceived mostly because the number of activated olfactory receptors (ORs) is not sufficient or there are insufficient odorant molecules to elicit a response. Above this value, higher concentrations produce higher perceived intensities, at least up to the limit of perception, the odor terminal threshold (Thr^{ter}) as presented in Figure 2.22. The terms absolute and detection thresholds are the same in theory, though they sometimes are misunderstood and considered apart. It is sometimes called as absolute once the scale measurement of detection thresholds is an absolute scale. For example, in the Russian literature the detection threshold is defined as the absolute threshold, that is the minimum concentration to cause a physiological change (*e.g.* as an electroencephalogram (EEG) signal) in the most sensitive humans (AIHA, 1989). However, a systematic definition of the odor threshold comes from the ASTM (Method E 679-91) which defines it as *"the concentration of an odorous compound at which the physiological effect elicits a response 50% of the time"* (Mayer*, et al.*, 2005). For experimental purposes the ODT represents the lowest odorant concentration that induces a sensory individual stimulation in the olfactory receptors (so that it can be perceived) for a definite percentage of the tested panel. This is often defined as 50% (the mean of the panel), thought it can be sometimes defined as 100% (including the most insensitive) or 10% (only the most sensitive) (AIHA, 1989). It is noteworthy to mention that the ODT does not necessarily represent a recognized odor (quality) sensation. Instead it defines only a responsiveness of the presence of some chemical odorant, making the response all-or-nothing. One common error found in the literature when defining detection thresholds is that they are considered as the concentration detected at a definite percentage of significance, instead of being the concentration detected by 50% of the panel (Laing, 1987). Odor threshold concentrations of chemical substances that evoke a smell are often particularly low (in the ppb or ppt range). The odor recognition threshold (ORT), on the other hand, is the lowest odorant concentration at which an odorant is recognized as having a characteristic odor quality by a definite percentage of the sensory panel tested (often 50% of the population). The recognition threshold differs from the detection threshold in the subject's sense and characterization of the odorant, instead of the traditional yes/no detection. In this way, the panel members have not only to identify the presence

of an odorous chemical but also to associate it to a cognitive interpretation (hedonics). At first glance it may be thought that the concentration recognition threshold should always be higher than the detection threshold, once to characterize an odorant one will first need to detect it (if it is not there, it is not quantifiable). However, it is common to find in the literature odor recognition thresholds equal or even lower than the corresponding odor detection thresholds, when reported from different authors (van Gemert, 2003). This is due to differences in the measurement technique, protocol, equipment used or, most important of all, to interpersonal variability (mainly psycho-physiological variability). Nevertheless, for the same individual, in theory, the recognition threshold of an odorant should always be equal or higher than its corresponding detection threshold. For this case recognition thresholds are typically higher than detection ones by a factor of 1.5 to 10 (Dravnieks and Jarke, 1980). The recognition threshold is perhaps more significant that the detection one, although it may not always be easy to accurately determine it. The task of recognizing and classifying through words what is being smelled, is mostly individual dependent and complex, even when its identity is known (Appell, 1969; Marshall*, et al.*, 2006), as will be discussed in Section 2.6 of this Chapter. It crosses a multipart system of neuronal impulses and signal transduction, eliciting memories and past experiences. Since this matter is not fully understood, it could be said that considering the same adequate experimental procedures, detection thresholds would be more reliable than recognition ones (Doty*, et al.*, 1995). Nevertheless, attention should be taken when measuring either type of olfactory thresholds or using olfactory threshold data from the literature, since experimental conditions, type of equipment used and applied methodologies are possible sources that influence the obtained results.

Odor threshold measurement

Olfactometry is aimed at characterizing odors. It is a sensory technique or experimental procedure for the measurement of human odor sensitivity, including odor thresholds, odor intensity, or odor character (*e.g.* annoyance or nuisance assessments) among others. These procedures are time consuming and labor intensive: the correct determination of odor thresholds, for example, should involve hundreds of experiments as well as a large group of panelists (trained and non-trained, covering different ages and from both sexes). The calculation of odor thresholds can be performed using different techniques and equipments. In Figure 2.23 is shown a dynamic olfactometer which implies one of

the most suitable and acceptable techniques for odor threshold measurement (other methods comprise plastic squeeze or glass bottles, triangular odor bag method, etc). Thus, by mapping the distribution of relative sensitivity of a large population to a chemical odorant, an average odor threshold value can be obtained. Indeed, at the end, the final result will be a single threshold value (or an estimated range of values with the corresponding confidence limits) although there were a large number of experimental tests behind that single value (Chambers and Wolf, 1996). Nevertheless, variability and response bias will always be present. Olfactory perception, even when performed for the same panel, may vary among individuals and experiments: ~ 2 up to 4-fold within the same experiment (Chambers and Wolf, 1996). Inter-personal variability is even higher, sometimes reaching differences as high as three orders of magnitude, as we have discussed before in Section 2.4.3: Odor Thresholds (van Gemert, 2003; Cain and Schmidt, 2009). Even more surprisingly, a difference of six orders of magnitude can be found for very particular cases like partial or total anosmia for a single odorant. In this way, it is important to have a series of replicates of experimental judgments, obtained from a statistically significant population and using a standardized procedure in order to acquire reliable odor threshold data.

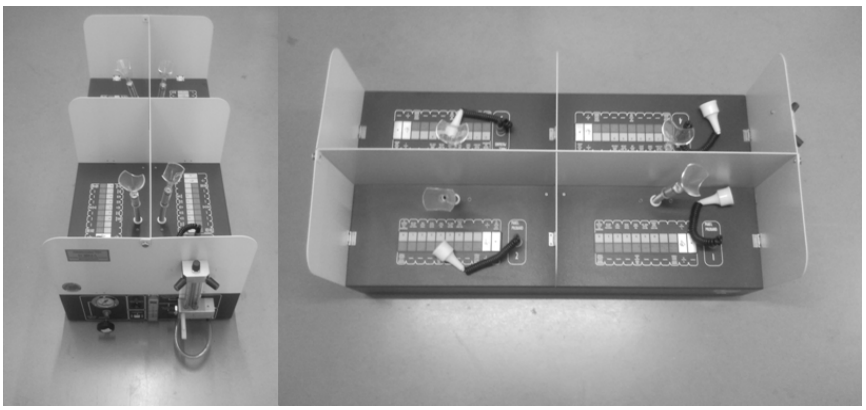


Figure 2.23 – Olfactometer TO7 from Ecoma (Germany) available at the LSRE lab.

Typically, when measuring data for odor thresholds, a Gaussian dose–response curve is obtained. The threshold value calculated at the 50%-point can be accurately determined after transformation of the positive experimental judgments from panelists. In Figure 2.24, a conventional notion of the detection odor threshold (solid line) and the typical averaged experimental data (open triangles) with smooth fitting (dashed line) for determination of personal threshold data is presented. Additionally, a typical histogram with the number of experimenters having positive judgments (closed dots) for each

odorant concentration in air is also included. It is from the panelists' evaluation that the intensity curve can be calculated as well as the odor threshold. We will not discuss here, in detail, the experimental protocol and statistical treatment for the calculation of odor thresholds, but we direct the reader towards the following references (AIHA, 1989; Gomes*, et al.*, 2008; Teixeira*, et al.*, 2011).

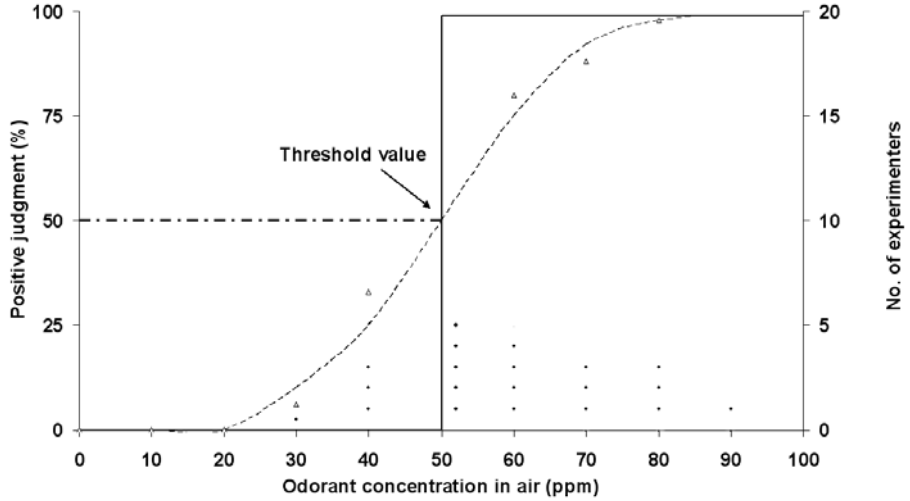


Figure 2.24 – The conventional notion of the odor detection threshold (solid line) and the typical experimental data (open triangles) with smooth fitting (dashed line). The typical histogram with the number of positive judgments from experiments (closed dots) for each odorant concentration should be read on the right ordinates' axis. [Reproduced from Teixeira, MA *et al.*, Advances in Environmental Research, Chapter 1: Odor Detection & Perception: An Engineering Perspective, NovaPublishers, Volume 14, 2011]

2.5. Psychophysics of olfaction

How do we perceive and process a stimulus coming from the environment around us? What stimuli are we capable of interpreting? Which is the relationship between the stimulus magnitude and the corresponding perceived sensation? The pursuit for the answer of some of these questions started to be drawn only by the end of the 19th century. Since then and until now, the search for the primary question is still going on: How precisely does a perceived sensation (output) vary with a stimulus (input)?

2.5.1. Odor perception: intensity and character

Perception can be defined as the means by which we receive, collect and interpret information from the outside world. It is the sensory experience by which we gain information about the properties of the surrounding environment, allowing us to interact with it. In what concerns to odor perception, we have already seen that the olfactory

system is capable of detecting and identifying thousands of odorants (Buck and Axel, 1991). It is even able to collect scents at lower concentrations than analytical instruments such as gas chromatographs (GC). Additionally, the odor sensations can be perceived from single odorants and also from mixtures of them, which may have hundreds of compounds. In the latter case a complex summation or suppression of odor intensities occurs, turning difficult to characterize it in a neurophysiologic way and often resulting in a unitary perception of a smell. This phenomenon is quite common and is defined as a synthetic process (Gottfried*, et al.*, 2006): the smell of coffee has around 800 different compounds but a non-trained nose perceives it as plain coffee only. Even for an expert with a well trained nose, it may be possible to identify just a few species from the whole mixture. In nature there are plenty of examples like this, where a mixture of dozens, if not hundreds, of volatile organic compounds (VOC), are seamlessly perceived by the olfactory system as a single odor. In this way, the perception of a mixture of odorants may not have anything similar to that of each of its chemicals independently.

Even more puzzling observations can be seen for the perceived quality of single odorants. For example, the odor character of ethyl acetate (widely found in wines) at concentrations below 50 mg/L is pleasant, adding a subtle complexity to the wine fragrance, although above 150 mg/L it resembles an unpleasant sour vinegar odor (Jackson, 2000). As discussed earlier in Section 2.4.1: The olfaction mechanism, this phenomenon is though to be due to the combinatorial code occurring at the odorant-OR level. For these reasons (and some that will be addressed later) it is important to measure and predict the perceived intensity of single odors and mixtures of them.

2.5.2. Models for odor intensity of single odorants

The first attempts to explain the way human beings perceived exterior stimuli came from Psychophysics. This branch of Psychology deals with the understanding between physical stimuli and their psychological interpretation by giving some mathematical relationships for that. Psychophysics approached all types of sensorial perception, involving the five senses (sight, hearing, touch, smell and taste). Within that, different models were developed to describe the odor intensity of single odorants and of multi-component mixtures (unfortunately, mainly binary and ternary mixtures only). These are empirical models that invariably derive from fittings of experimental data to

establish such relationships. In fact, the first derived laws from Psychophysics of sensory perception still remain in use till our days. Here, a brief description of the most significant odor intensity models will be presented. Their pros and cons are discussed in more detail in Annex A, together with the presentation of some examples of application. First, we will explore the models for odor intensity of single odorants and later those relating to mixtures shall be addressed.

Although, nowadays, biochemistry is known to play an important role on the perception of odors (specially at the microscopic level), the science of Psychophysics evaluated it for long by performing external experiments of sensory perception as a function of stimulus intensity (macroscopic level). The most important models for odor perception of single odorants started to be sketched in the XIX century with the Weber-Fechner law (Shigemoto, 2002). It stated that the perceived intensity increased arithmetically with the geometrical increase of the stimulus magnitude so that:

$$\psi = k \cdot log\left(\frac{S}{S_0}\right) \tag{2.1}$$

where ψ is the sensation magnitude, k is a positive constant factor, S is the stimulus magnitude and S_0 is the threshold of the magnitude of the physical stimulus. In the mid of the XX century Stevens (Stevens, 1957) proposed the psychophysical law (also known as Power Law), considering that sensation magnitude was proportional to the magnitude of a physical stimulus raised to an exponent n, as expressed in equation 2.2.

$$\psi = k.S^n \tag{2.2}$$

Stevens's experiments were based on direct measurements and judgments performed with different senses. This was considered an advance compared to the Weber-Fechner indirect methods. Even more important, the power law has been observed for perceptual judgments of physical stimuli like brightness, loudness, taste, smell or size, and so it was generalized as the psychophysical law. Equally interesting was also the discovery by Stevens that the value of the exponent n was different for each perceptual continuum (Stevens, 1957). Table 2.5 presents a selection of different perceptual continua and their corresponding exponents.

Table 2.5 – Exponents for different perceptual continua.

Perceptual Continua	n
brightness (point source)	0.5
loudness (sound pressure)	0.6
smell (for heptane)	0.6
taste (for sucrose)	1.3
(for salt)	1.4
electric shock (current trough the fingers)	3.5

It is feasible to admit that odor perception follows such a law, where at some point the increase in the odorant concentration will not produce an increase in the odor perception due to the saturation of the odor receptor cells. For olfaction the exponents are generally equal or lower than unity having a recommended average value of 0.35 (Devos*, et al.*, 2002). The effect of this parameter on the odor perception intensity is presented graphically in Figure 2.25.

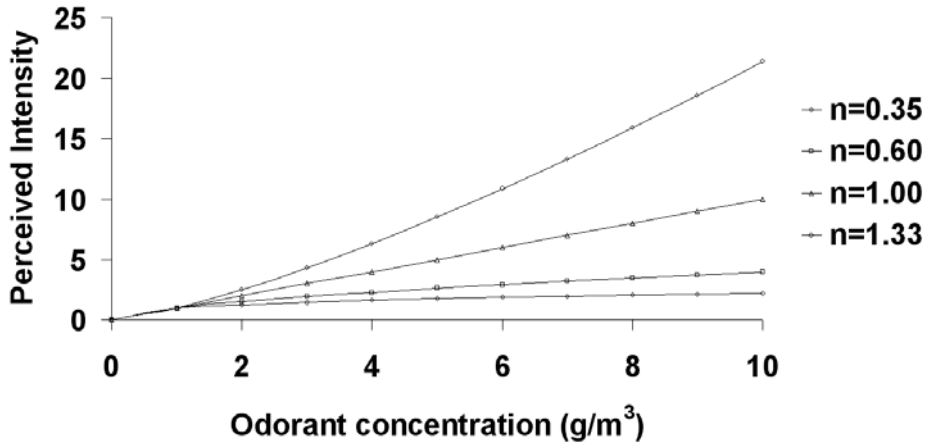


Figure 2.25 – Perceived intensity as a function of the odorant concentration for different exponents using the Stevens' power law. [Reproduced from Teixeira, MA *et al.*, Advances in Environmental Research, Chapter 1: Odor Detection & Perception: An Engineering Perspective, NovaPublishers, Volume 14, 2011]

Another model for odor perception which is widely used in the fragrance industry is the Odor Value (OV) (Appell, 1969; Calkin and Jellinek, 1994). It defines a linear relationship between the magnitude of a physical stimulus and its perceived sensation magnitude which when applied to olfaction takes the form of equation 2.3.

$$OV = \frac{C^g}{ODT} \tag{2.3}$$

where C^g is the concentration of an odorant in the gas phase ($g.m^{-3}$), *ODT* is the odor detection threshold in air ($g.m^{-3}$). It is easily perceptible that the difference between the Power Law and the odor value models, rests on the exponent ($n \neq 1$ for the Power Law and $n = 1$ for the OV).

A few studies have been devoted to compare the differences among the Stevens Power Law and the OV model (see for example Teixeira*, et al.*, 2010). Despite the fact that at low odorant concentrations (near-threshold values) the differences can be neglected, the power law should be preferred especially in cases when high odorant concentrations are considered, though the lack of available data (for exponent values) would be an issue.

Nonetheless, some authors point out that this linear law does not hold for all the range of stimuli magnitude, and particularly at high values of the stimulus where it deviates from experimental data (Zwislocki, 2009). So far, experimental studies performed on sensory perception have shown that at sufficiently high concentrations, the experimental data based on human sensory panels followed approximately power functions with exponents smaller than unity. However, at lower concentrations, and especially near-threshold concentrations, the slope of the curves was close to unity (Zwislocki, 2009).

2.5.3. Models for odor intensity of mixtures

The recognition and, more important, the intensity of a mixture of odors is far more complex than it is for single odors (Gilbert, 2008). There is no doubt that the generation of complex patterns at the brain centers for processing of olfactory signals occurs both when smelling pure chemicals or mixtures of odors. But the discrimination and identification of their constituents is much more complex for mixtures, as mentioned before (Jinks and Laing, 1999). Nevertheless, on a daily basis we often contact with mixtures of odors instead of single odorants. However, since the knowledge about how single odorants in complex mixtures have an effect on the perception of each other is scarce, it becomes difficult to develop correlations for the prediction of the character and intensity of such mixtures. For example, effects of hyperadditivity or hypoadditivity of odors are not uncommon, albeit the perceived intensity of a mixture will generally lie somewhere between those extremes. Even more problematic is the prediction of odorant

emissions from a source at different distances from that, which would include diffusion and convection models (Laing*, et al.*, 1994; Teixeira*, et al.*, 2009a).

Even so, different models attempting to calculate the perceived odor intensity of mixtures have been presented over the years. Here, we will briefly report those which are more significant while a more detailed view of their advantages and drawbacks is presented in Annex A.

First, it is to highlight that the majority of these models were derived from experiments with binary or (at most) ternary odorant mixtures. In this way, they present an initial limitation if they are intended to be applied to multi-component perfumes. Nevertheless, some of the models may provide a first approximation of the odor intensity of such mixtures. The most valuable models relating the stimuli magnitudes with the intensity of the perceived sensation came from Psychology like the vectorial, U, and Stronger Component (SC) models, or from Psychophysics as is the case of the UPL2, Additivity, Euclidean additivity (EA) and the Equiratio (ERM) models (see the reviews of Laffort and Dravnieks, 1982; Cain*, et al.*, 1995). In a general trend, the Psychological models gave better correlation coefficients, but lack explanatory power. Moreover, among all the aforementioned models the Stronger Component (SC) model is probably the most suitable one, easier to implement for predictive purposes and is often one of the best when used in experiments and compared with other models. The SC model also allows performing an approximation to other important parameter within the perception of odors: the perceived quality or character.

In this way, there are several models that attempt to describe the odor intensity of mixtures which have been proposed over the years. However, among a number of drawbacks, all the models presented in this Chapter 2 (and detailed in Annex A) have shown deviations between predictions and experimental data, especially for multi-component mixtures of odorants. The number of studies addressing the question of odor-intensity interaction for complex mixtures (three or more components) is also very scarce, independently of the selected approach (Laffort and Dravnieks, 1982; Laing*, et al.*, 1994). To overcome the limitation of binary mixtures and achieve better reliability for multi-component mixtures is the key for a successful model. They generally fail to explain all of the variance, and are not supported by analytical principles. This is so because none considers in deep the odorant-olfactory receptor (odorant-OR) binding mechanisms, nor considers neuronal decoding processes that underlie the perception of odors (Doty and Laing, 2003). It is axiomatic that future studies have to be performed

incorporating physicochemical parameters as well as considering information about the neuronal processes controlling odor interaction (Cain*, et al.*, 1995).

For that purpose, molecular simulation techniques are a promising tool suitable for determination of odor-related properties such as molecular shape, molecular electrostatic potential (MEP), polarizability or free energies of solvation (Gilson and Zhou, 2007; Garrido*, et al.*, 2009). Molecular modeling studies are known to be widely used in pharmaceutical applications, though they have already been used in the field of olfaction, mainly focusing ligand-receptor interactions at the molecular level. Recent research on this topic considers not only configurations of stereoisomers but also their most favored conformations and interactions with olfactory receptors (Singer and Shepherd, 1994; Chastrette, 1997, 1998; Hajjar*, et al.*, 2006). However, these are complex methodologies that need deep knowledge of the principles involved and are still in development for this kind of biological mechanisms.

However, the perception of odors includes the binomial intensity-quality. So far, we have addressed the main topics on measuring odor intensity only, from its lower limit, the threshold concentration, up to the measurement and prediction of the intensity scale. But the perceived odor character or quality is also an important parameter when measuring odors. Yet it has probably received less attention in research fields than the corresponding intensity and so the rules underlying the classification of the character of odors and mixtures are still lacking (Lapid*, et al.*, 2008).

2.6. The classification of fragrance ingredients and perfumes

The expression of the sensory stimuli that we constantly perceive has to be quantified through a physical intensity magnitude but should be also complemented by dimensions of quality, duration, feel, or pleasantness. However, as we have seen so far the characterization of perceived odors by the human nose together with brain encoding is a combination of very complex phenomena, either for single or for mixtures of odors. Materializing the perceived scents by words or qualities is difficult, even for experts in the art of smell. Likewise we are also far from being able to predict the odor quality of scents. The reason for this is that we are still taking small steps in understanding the way we perceive the quality of odors. Whatever is the physiology behind that, the sense of smell is keener than that of any other sense. A practical example to illustrate this fact

can be seen in a comparison when people describe the colors they see or the smell they perceive. Usually, a general description of a color is done through the use of 1-2 words (at most) which often explicitly translates the color that any other individual with good visual acuity would also describe. On the opposite, the same is not often true with the description of odors or smells. When one tries to describe the smell elicited by a rose, for example, it will require multiple words, representing feelings, emotions, or memories of the individual. Moreover, different people will use different adjectives or classes to characterize the scent of a rose. One of the reasons for that is because we are not taught for different odors as we are for colors, shapes or sounds. Other reasons are related to the inter-personal variability and the complexity of the human olfactory system (together with neuronal encoding). That is, once again we are back to the question of how the human being interprets odorant molecules and characterizes them in terms of odors. For the human vision, we know that there are three broadly-tuned receptors that perceive the entire visible range of wavelengths. However, in olfaction we have about 391 olfactive receptors which allow us to perceive thousands of different odorants and multiple combinations between them (Saito*, et al.*, 2009).

Several examples can be found in nature where enigmatic effects on odor perception are observed. In some cases, mixtures of odors can produce unpredictable odor perceptions. Even among single odorants there are some which are perceived differently as its concentration increases. This means that an odorant is not perceived with the same quality by the human nose at low and high concentrations. The general trend is that unpleasant odors are perceived at high concentrations. For example, some thiols evidence a harmonious fruity odor at very low concentrations (near its odor detection threshold) but unpleasant (and sometimes nauseous) sulfurous odors at higher concentrations. One other puzzling odorant molecule is trans-non-2-enal, because its perceived character is highly appreciated for fragrance purposes at low concentrations but is unpleasant for high ones, as shown in Figure 2.26 (Fisher and Scott, 1997). Since its odor quality changes with the concentration, it has different recognition thresholds, and that is why it appears to be classified has a green, cucumber, aldehydic, and fatty odorant with a citrus nuance. Other examples were observed for macrocyclic ketones which have a faint cedarwood odor when concentrated and a musky odor when diluted (Chastrette, 1998).

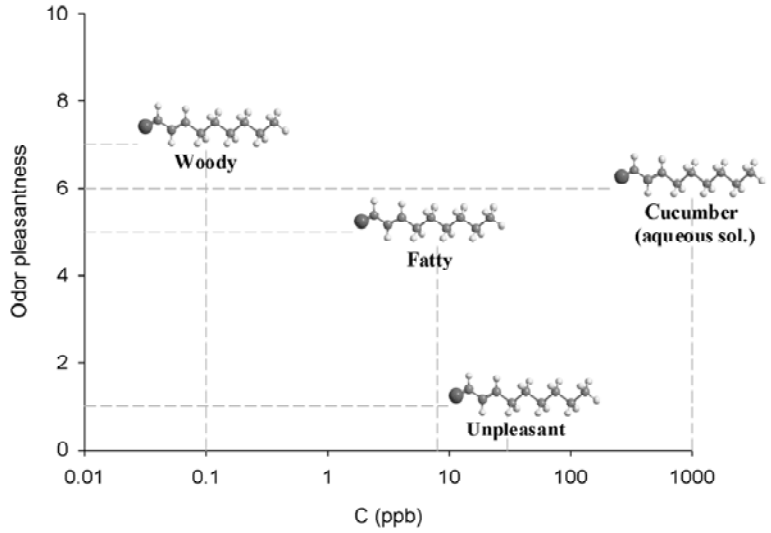


Figure 2.26 – Effect of concentration on the perceived odor character of trans-non-2-enal. [Reproduced from Teixeira, MA *et al.*, Advances in Environmental Research, Chapter 1: Odor Detection & Perception: An Engineering Perspective, NovaPublishers, Volume 14, 2011; and Teixeira, MA *et al.*, Jornadas de Bioengenharia, FEUP, 2010]

However, within the F&F industry the task of sensory perception, evaluation, and classification of odors or mixtures are part of the job of perfumers. These specialists are highly trained for many years to detect, recognize, and classify raw materials and complex perfumes. The nose of a perfumer is capable of recognizing a few hundreds of different odorant chemicals, keeping them as a memory database. Their classification generally consists of assigning odors to olfactory families or classes, which often include *"nuances"*. A *nuance* is a subtle or secondary odor in the main olfactory sensation of a pure chemical or a perfume. Typical olfactory families are citrus, floral, green, fruity, herbaceous, musk, oriental, spicy, tobacco, woody, chypre, aromatic, or fougère among many others, although they often change within fragrance houses or perfumers. These terms can be seen as descriptors of the type of odor, and are commonly sided by quality terms like heavy or light, sharp or round, just to mention a few. It is important to highlight though that this nomenclature is difficult to be interpreted by the typical consumer who is not familiarized with the terminology. Non-experts usually classify odors using more traditional terms and expressions that resemble some of their memories or past experiences. However, even among perfumers there is not a complete agreement of which olfactory families should be used or in which to include the perceived scents. Additionally, care should be taken when performing comparisons of classifications because the odor of a rose, for example, may vary from species to species and so one may have a floral note, or an aromatic note or a

green note, while for other variety of roses the combinations may be completely different and with singular *nuances*.

In terms of classification of odors or mixtures of them there are several examples that have been defined over the times. One of those is presented in Figure 2.27, along with a proposed gradient for coding scents in the same way as color codes.

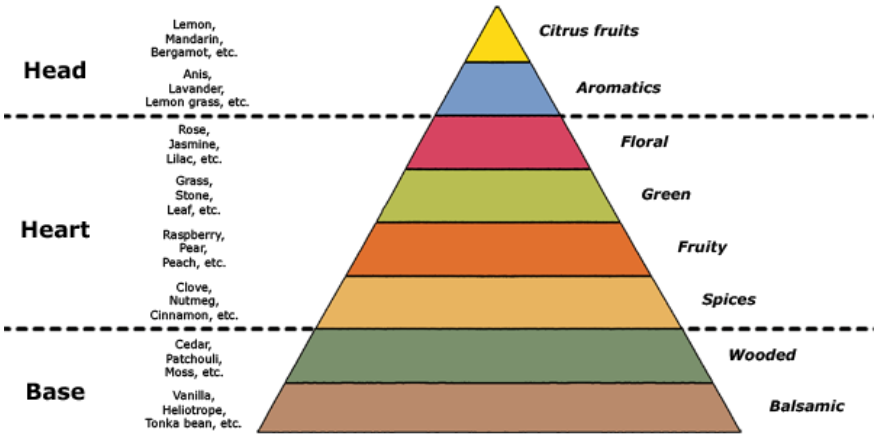


Figure 2.27 – Olfactory families of some fragrance ingredients along with their type of olfactive notes (top or head, middle or heart, and base notes).
[From www.roseraieduvaldemarne.com/roseraie_internet/rose_roseraie_article.php3?id_article=525]

The classification of scents into olfactive families presents some general trends with the perfume pyramid structure proposed by Carles and previously discussed in this Chapter in Section 2.2.3: The structure of a perfume. For example, citrus scents are usually related to some top notes while the woody family is related to base notes. Moreover, in the classification of perfumes there are some olfactive families that result from the combination of different notes and scents like the Fougère or the Chypre family. In 1882, perfumer Paul Parquet created the perfume *"Fougère Royale"* using an accord composed of coumarin, oakmoss, geranium and bergamot, which resulted in a novel family (Firmenich, 2009). On the other hand, the Chypre family gave its name to its homonymous perfume developed by François Coty in 1917, although those types of fragrances became fashionable only much later (Firmenich, 2009).

Just as there are classifications of fragrances into olfactory families, other organoleptic classifications were also developed over time for different types of products that are strongly dependent on sensorial perception. Some examples are the olfactory classification of wines and beer as shown in Figure 2.28 and Figure 2.29, respectively.

Figure 2.28 – The classification of olfactory families for wines.

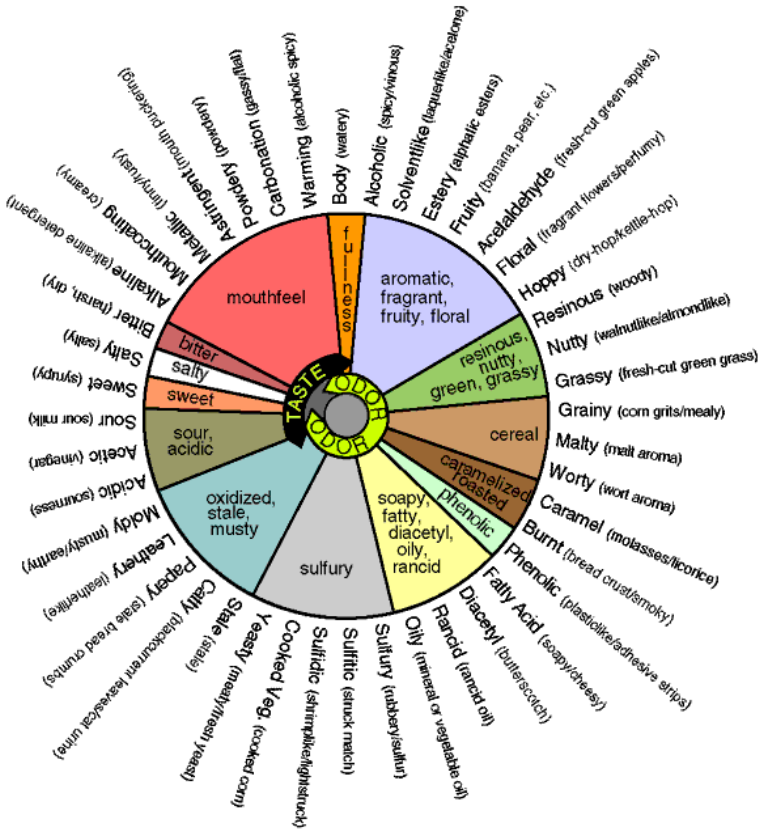


Figure 2.29 – The Beer Flavor Wheel.

The Beer Wheel presented in Figure 2.29 dates back to the 1970s and considers both the classifications of flavors (gustatory sense) and odors (olfactory sense) of beers. It was developed by Morten Meilgaard and was later adopted as the flavor analysis standard by the European Brewery Convention, the American Society of Brewing Chemists, and the Master Brewers Association of the Americas (Bamforth*, et al.*, 2008).

Thus, after this synopsis about the classification of odors in terms of their quality or using olfactory families we have seen a great diversity of classifications that are due to the biophysical properties of the olfactory system and brain decoding of the human being. For that and for many other issues previously highlighted in this Chapter on fragrance formulation and odor perception, one concludes that a more theoretical approach for the evaluation and classification of odors and fragrances is needed.

2.7. Scientific knowledge from Product Engineering: application to perfumed products

The development of novel and innovative products to meet consumer needs comprises two interrelated fields of scientific knowledge in Chemical Engineering: what we want to produce, that is Product Engineering, and how we should produce it, which is the scope of Process Engineering (Cussler and Moggridge, 2001; Wei, 2002; Ulrich and Eppinger, 2003; Costa*, et al.*, 2006; Wesselingh*, et al.*, 2007). Figure 2.30 illustrates this relationship within Chemical Engineering. In the classical view of this discipline, the general path followed by chemical engineers was oriented, in the past, to bulk chemical products where the manufacture of commodity chemicals was made in large scale. By the middle of the XX century, the chemical industry was at its peak, boosted by a previous exponential growth. Industrial processes were diversified and optimized, seeking for high yields and, consequently, better profit margins. But since then, the chemical industry has been shifting due to constant changes in consumer and market needs. And today, that classical view of Process Engineering alone might not be sufficient on its own to give an affirmative answer to consumer needs, or in other words, for product-design.

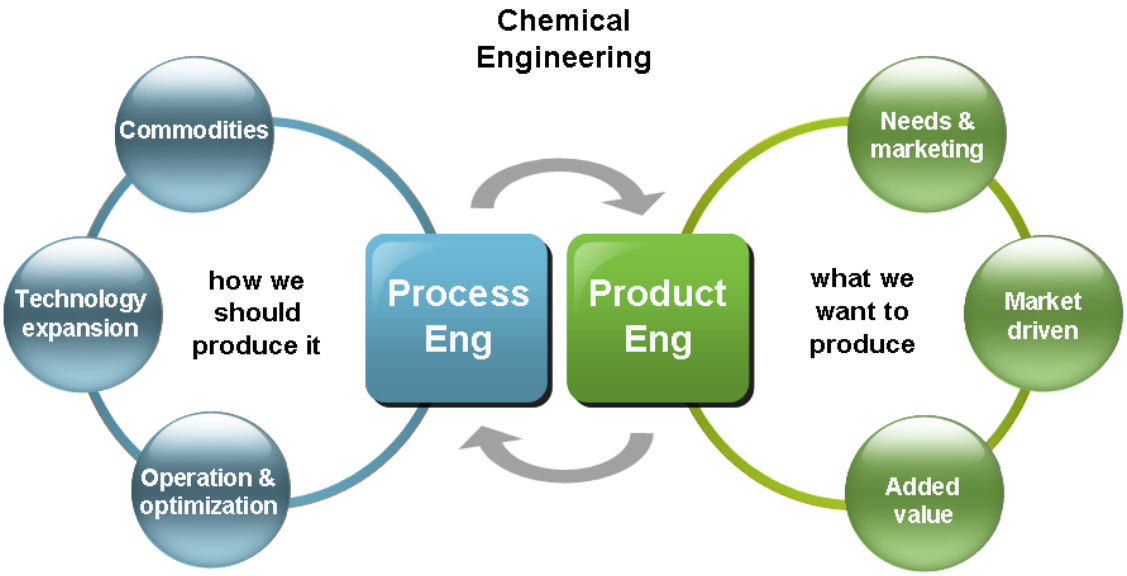


Figure 2.30 – Relationship of Product and Process Engineering as two branches within Chemical Engineering.

Within the last couple decades, the chemical industry has switched from the capital intensive bulk chemicals towards the manufacture of high added-value products. Hitherto, development was mainly driven by technological expansion, but now it is more market-driven. New trends in market innovations for the development of new products and the information technology and computational chemistry have been growing. It is a fact, that the development of new, high added-value products and the processes to produce them demand both Process and Product Engineering knowledge. First and foremost, such products have to go through several stages till reaching the market: design, development, optimization, production, and testing (Charpentier, 1997; Cussler and Moggridge, 2001; Wei, 2002; Ulrich and Eppinger, 2003; Wesselingh, *et al.*, 2007). This is the reason why product engineers need to have knowledge and expertise in multiple scientific fields and technical aspects, but also about customer needs and marketing (Wesselingh, 2001; Wesselingh, *et al.*, 2007). Extending the current limits of product's performance has now become a key factor for Product Engineers who must hand out innovative and valued products, technologies and services to the market. For Product Engineers the various disciplines they learn can be schematically represented by the triangular diagram in Figure 2.31. That should not be interpreted as a strict rule, but *"instead a catalyst for thought"* (Cussler and Moggridge, 2001). Either way, what is important to emphasize here is that they should learn from physical sciences, chemical sciences and Chemical Engineering. Their role within

Chemical Product Design/Engineering will follow the general stages of needs-ideas-selection-manufacture to obtain novel and profitable products to put on the market (Cussler and Moggridge, 2001; Cussler, 2003; Ulrich and Eppinger, 2003).

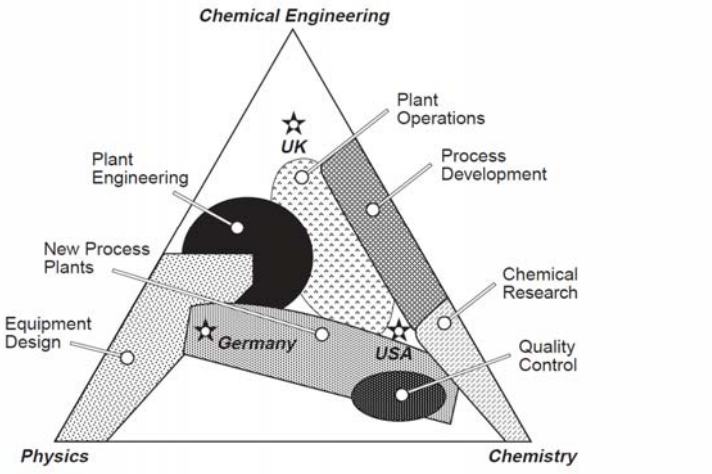


Figure 2.31 - Perspective of the traditional skills learned by Chemical Engineers as suggested by Cussler and Moggridge. [Reproduced from Cussler, E., Moggridge, G., Chemical Product Design, Cambridge University Press, 2001]

In sum, although Process Engineering has attained a high degree of scientific maturity over the last half century, Product Engineering is still growing and maturing its basis in Chemical Engineering fields.

Product Engineering allows the extension of the Chemical Engineering methodology to product-oriented engineering, following the triplet of ‘‘molecular processes-product-process” (Charpentier, 2002), or more recently the equation ChemEng = M^2P^2Eng (M for Molecular and Materials, P for Process and Product) as shown in Figure 2.32 (Rodrigues, 2008; Teixeira*, et al.*, 2009b). The objective is to develop new products that are more effective to satisfy customers’ needs and/or less threatening to the environment.

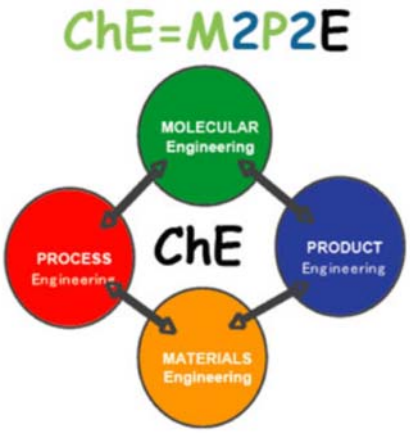


Figure 2.32 – The today’s vision of Chemical Engineering from A. E. Rodrigues.

The development of Perfume Engineering itself represents a particular case in the field of Product Engineering, inside the Flavor & Fragrance industry. For its part, F&F represents a commercially relevant and profitable area where scientific knowledge must be combined with creativity (Wesselingh, 2001; Costa*, et al.*, 2006). In our modern society, fragrances and flavors, whether they are used as perfumes or flavorants, play a central role in people's daily life – from showering to scenting a home or from sweetening a cake to flavoring a meal. Thus, mainly for these reasons, it is seen that fragrance companies continue to seek over the years for new, pleasant and lastingness fragrances not only extracted from natural products but especially those obtained from synthetic paths due to its simplicity and lower production cost (Curtis, 1994).

As aforementioned in this Chapter, there have been great advances on the understanding of the olfaction process in humans in recent years, but we are still far from decoding the olfactory sense. For that reason, and many others, the process of developing fragrances remains mostly empirical, based on the experience and know-how of perfumers. For example, the perfume "Bois de Paradis" launched in 2005 and developed by Michel Roudnitska took more than two years and nearly 300 formulation trials until he got the desired fragrance. Another example, is the fragrance "Tommygirl" that took eleven hundred iterations to arrive at the market (Wolfson, 2005). In this way, the aim of this work on Perfume Engineering is, in a straightforward perspective, to introduce more science in this process using basic concepts from Chemical Engineering and other scientific fields (*e.g.* Psychophysics, Biology).

2.7.1. Equipments and techniques for perfume design

In order to introduce science within this field, one needs experimental measurements. It is known that the detection and measurement of the perceived intensity scale of odors has been studied for long by scientists from different scientific fields but also from the F&F industry as well. As we have seen throughout this Chapter, literature data on the detection and recognition of odorant chemicals as well as their odor intensity scales covers more than a century. However, all the way through this period, the development of new equipments and innovative methods for odor evaluation has guided and revitalized both the academic and industrial sectors. They no longer rely solely on the subjectivity of the human nose, even though the use of panelists is still widely used today due to the complexity lying behind odor evaluation.

The F&F industry itself, where perfumers play a decisive role in the formulation and characterization of fragrances, already uses a panoply of technological devices that help and support their various processes concerning the development of fragrances. Equipments like gas chromatographs coupled with mass spectroscopy (GC-MS) or with olfactometry (GC-O, also called GC-Sniff) are used by the industry. But they have also infrared spectrometry (IR) equipments, electronic noses (e-noses), and comprehensive two-dimensional GC hyphenated to a time-of-flight MS (GC-TOF-MS) for the detection and characterization of odorant fingerprints (Rochat*, et al.*, 2009). The use of a wide number of technological equipments comes from the fact that the disadvantages of one may be complemented by the advantages of others, as presented in Table 2.6.

Table 2.6 – Properties, advantages and disadvantages of some common equipments used by the perfumery industry.

Technology	Avg. Analysis Time / sample (min/sample)	Advantages	Disadvantages
IR Spectrometry	0.5 (Fast)	Structural information Easy online implementation	Aqueous sample require special cells Non linear response to many analytes Difficult to determine trace analytes
Gas Chromatography	>15 (Slow)	Linear response Excellent selectivity Analyze low volatile species	Column bleed and fouling Higher resolution, increases analysis time Short and long term drift
E-nose (solid state sensors)	5-15 (Moderate)	Responds to various analytes Minimal sample preparation Can be miniaturized Easy online implementation	Sensor poisoning No structural information Time consuming calibration Short and long term drift Alcohol and water interfere Small range of linearity response (< 2 orders of magnitude)
Headspace Mass Spectrometry	3-5 (Low-Moderate)	Responds to all volatiles Structural information Minimal sample preparation Fast method development	Can not distinguish optical isomers Vacuum pump required Subject to tuning inconsistencies

One technological breakthrough came in 1987 with the first appearance of the electronic nose technology although their first equipments only came to market in 1993 (Bonnefille, 2007). The e-nose was probably the first attempt to mimic the human sense of smell by using a series of sensors, predominantly of conducting-polymer, metal-oxide, or infrared sensors. Although these equipments have shown greater accuracy for detection of some chemicals than GC-MS techniques or panelist evaluations, it should be mentioned that hedonic evaluation remains a specificity of the human nose, given that it is related to preference (Bonnefille, 2007). E-noses have been improving over the

last ten years, being considered valuable equipments for complementary evaluation in many research fields like air quality and control, flavors and fragrances, cosmetics, and pharmaceuticals, among others.

2.7.2. Reverse engineering

It is a common practice within the F&F industry to use reverse engineering tools for the evaluation of the fragrance ingredients contained within a competitor's best-selling perfume. This is generally run through GC-MS techniques for the quantification and identification of chemicals. GC-MS equipments are robust, easy to use technologies which offer great precision and reproducibility for analytical measurements. These coupled techniques are also of use for the detection of adulterated or fake perfumes and to evaluate degradation processes undergoing in old perfumes as it is known that some of their components are somehow reactive over time.

2.7.3. Headspace (HS) Analysis

The analysis of the gas phase above a mixture of fragrance raw materials (headspace) is another method to isolate flavor and fragrance compounds. It is widely used although it presents a large number of issues for quantification purposes, especially when dealing with liquid perfume mixtures. There are two types of headspace analysis, static and dynamic. The former involves the sampling of the air equilibrated above a mixture sample (*e.g.* using gas tight or SPME syringes) and its injection into a gas chromatograph-mass spectrometer (GC-MS) for further identification and quantification. The main drawback of this method is concerned with the low concentration level at which the volatile compounds are often present. GC-MS equipment usually has an analysis detection limit of around 10^{-5} - 10^{-6} g/L. Consequently, volatiles must be present at levels equal to or greater than that. As an example, the concentration of fragrant volatiles above perfume mixtures may be in the range of 10^{-11} to 10^{-1} g/L. Therefore it is common that only the most abundant volatiles will be detected. On the other hand, dynamic headspace involves a carrier gas and usually a purge and trap system. This allows concentrating the volatiles which are subsequently desorbed in a GC-MS equipment. Here, the objective is the isolation of single volatile components instead of a fraction or collection of chemicals (Friedrich and Acree, 1998). Both techniques are valuable for the evaluation of volatiles released into air, depending on the purpose of the work.

2.7.4. Scientific tools for perfume design

Over the past years, there have been great advances, both through the application of new experimental techniques or new technologies, which contributed for the creation of knowledge in the field of flavors and fragrances. Remarkably, it is also undisputable that a significant part of that knowledge remains under wraps, mainly due to the million dollar market of F&F, which consequently leads to secrecy. Nevertheless, the importance of enhancing scientific knowledge in an area like F&F with direct application in the development of products for the consumer is especially relevant for two reasons: *i)* the number of fragrance ingredients is in the order of thousands (and increasing) which makes an almost infinite number of possible formulations for different applications and, thus, a corresponding number of trial-and-error evaluations; *ii)* it is still dependent on the high skills and expertise of the perfumers.

Thus, as we have already seen throughout this Chapter, although the industry uses a vast array of technological tools (mainly for analytical evaluations), it still remains dependent from the human physiology for the perception of odors. Consequently, either on this matter, either on others like the creation of new flavor and fragrance chemicals, it is important to introduce scientific knowledge to enhance productivity or performance and to reduce costs and time for product development.

At the experimental level, developments in the extraction processes for fragrance raw materials have been seen, either by improving the efficiency of the already known processes either by the application of new techniques such as the supercritical CO_2 extraction at industrial-scale or the extraction of headspace aromas and odorants from living flowers (The Living Flower® from IFF) (IFF, 2005). Another technique developed by IFF that must be highlighted is the Aura of Aroma® (used to enhance fragrance substantivity) (Mookhejee*, et al.*, 1998). Furthermore, the discovery of economic valuable pathways for the synthesis of natural-identical or new fragrant molecules has been a hot topic within the industry mainly for economic reasons (see detailed reviews of Rossiter, 1996; Fritter*, et al.*, 1998). Besides in terms of consumer evaluation, a new method called Mood Mapping™ was recently developed: it is designed to measure mood associations with aromas coming from pure fragrance ingredients or finished fragrances presented in consumer products (Warrenburg, 2005). Even more astonishing discoveries were made like when IFF sent a miniature of a rose

plant aboard NASA's STS-95 Discovery space shuttle and found out that its odor radically changed at zero gravity (IFF, 2005)!

On the other hand, there has been valuable research in the development of tools for the quantification and characterization of odors (some of those were already mentioned throughout this Chapter). Among these, it is important to highlight the application of quantitative structure-activity relationships (QSAR) techniques for the screening of new potential fragrance chemicals using computer aroma design (Kovatcheva*, et al.*, 2004; Korichi, 2008). Important reviews on this topic are available in the literature (Chastrette, 1997, 1998). Following this line of thought, it is also worth mentioning the studies on molecular modeling (*e.g.* finding potential molecules through energetically favored conformations) and the application of statistical methods to correlate properties or qualities of fragrances (see reviews of Rossiter, 1996; Chastrette, 1997).

Independently of the pathway followed, the development of a fragrance product includes several issues that need to be addressed. So, from the point of view of the perception of fragrances incorporated into consumer products the topics that must be taken into account are listed below: some are known and controlled (unmarked), other need to be better understood and controlled (marked with *), and, finally, there are others more problematic topics that are still in need of new technical routes and innovative approaches for their accurate and reproducible measurement (marked with #) (Kerschner, 2006).

i) odor threshold of each perfume ingredient
ii) amount of product used by the consumer
iii) mixing of fragrance ingredients
iv) fragrance evaporation from mixtures*
v) minimum concentration used in the product*
vi) odor quality of the base*
vii) degree of interaction with the base*
viii) effect of processing the product*
ix) fragrance perception by consumers#
x) stability of the perfume during storage#
xi) interaction with the packaging#
xii) amount of perfume deposited and retained after the wash#
xiii) rate of release of the perfume over time and perfume performance#

Of course, the product design of a fragrance mixture is different depending on the final application of the product: for example, a fine fragrance is intended to leave a pleasant long lasting odor on the skin or on the clothes while a fragrance for a dishwashing detergent is engineered not to leave residual odors on the surface of plates but, at the same time, to release a pleasant odor during the wash experience.

Some of the topics listed above have already been studied at the LSRE laboratory in the recent past, and others will be focused in some Chapters of this Thesis. In fact, different themes involving fragrances have also been studied over the last years at the LSRE, aiming at the extraction of essential oils and fragrance raw materials with different techniques, or the prediction of the odor intensity and character of mixtures. A product of that work resulted in the development of a new methodology called the Perfumery Ternary Diagram (PTD®) for the prediction and representation of the odor character of ternary mixtures of odorant chemicals (Gomes, 2005; Mata, *et al.*, 2005a; Mata, *et al.*, 2005b; Mata, *et al.*, 2005c; Mata and Rodrigues, 2006; Gomes, *et al.*, 2008). The methodology makes use of engineering tools, like the ternary diagrams that are commonly used in different fields, to show the effect of the predicted odor in the headspace as a function of the composition of the chemical ingredients (*e.g.* mole fraction). In this way, is possible to include in the perfume formulation a top, middle, and a base note as is expected for the perfume concentrate. These diagrams allow a simple but fast theoretical and visual evaluation of the odor character for any possible mixture of three fragrance ingredients as presented in Figure 2.33.

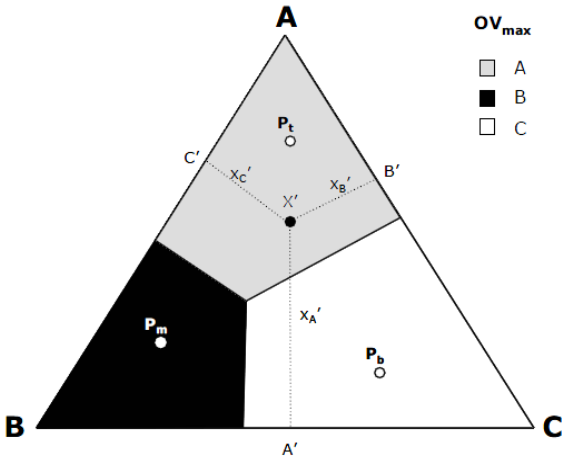


Figure 2.33 – Scheme of the Perfumery Ternary Diagram (PTD®), showing the different odor zones where fragrance ingredients A (grey), B (black), and C (white) have a dominant odor. [Reproduced from Gomes, P. B., Engineering Perfumes, Department of Chemical Engineering, University of Porto Faculty of Engineering. PhD Thesis, 2005].

Once perfumes have one or more solvents in their formulation, the PTD® methodology also allows showing the qualitative character of quaternary mixtures. If a solvent is introduced, a four component mixture is obtained and the predicted odor is represented in the PTD® by recalculating the mole fractions of each component (*e.g.* solvent free basis). This methodology used the concept of the Odor Value (OV) which is defined as the ratio between the concentration of an odorant chemical in the gas phase and its corresponding odor threshold value, as previously defined.

A detailed study to evaluate the effect of non-idealities in the liquid mixture was also performed using this methodology. It was shown that in multi-component mixtures the effect of intermolecular interactions was significantly important and should be considered, especially when concentrated fragrance ingredients are present. For that, the UNIFAC method was included in the methodology for the prediction of activity coefficients in the liquid phase (γ_i), and so the vapor-liquid equilibrium (VLE) of such mixtures. Finally, the PTD® methodology was used as a predictive tool for different ternary systems with or without a solvent, showing that changing the fragrance ingredients, resulted in different PTDs. As a result, it was shown that the perception of fragrances is not a straightforward job of looking solely at the physicochemical properties of a single component isolated from the mixture. Rather it must include the properties of all fragrance ingredients mixed in the perfume. Finally, the methodology was experimentally validated using a ternary mixture of limonene, geraniol and vanillin with or without ethanol as a solvent. It was shown good agreement between the predicted OVs and those experimentally measured for the case of limonene and geraniol, though for vanillin were poorly estimated (Gomes, 2008). In this way, further improvements are necessary either from thermodynamic models, either from a better understanding of odor perception.

In sum, the mechanisms underlying detection, quantification and characterization of odors have been widely investigated although we are still far from understanding it as a whole. There are numerous puzzling observations in odor perception but this fact will only stimulate and increase the interest of the scientific community for discovering the processes that regulate the sensory perception of odors. Furthermore, the commercial applications on the olfactory field have been tremendously growing over the past years, influencing consumers' likeability and, thus, looking for higher profits. The opportunities in the fields of fragrances and odor perception are just around the corner:

either at unraveling the sense of smell, either at applying olfactory techniques to product development (Baydar*, et al.*, 1995).

2.8. References

Ach Brito & Ca., S.A., from www.clausporto.com / www.achbrito.com, Last Accessed on 2011

Abbe, N. J. V., Perfumes: their manufacture in products and psychology in use, Poacher's Perfumes, Cosmetics and Soaps, Butler, Dordrecht, The Netherlands, Kluwer Academic Publishers, 2000

AIHA, Odor Thresholds for Chemicals With Established Occupational Health Standards, Fairfax, VA (USA), American Industrial Hygiene Association, TRC - Environmental Consultants, 1989

Amshel, C. E., Fealk, M. H., Phillips, B. J., Caruso, D. M., Anhydrous ammonia burns case report and review of the literature, *Burns*, 26, 493-7, 2000

Appell, L., Physical foundations in perfumery - VIII. The minimum perceptible, *American Perfumer and Cosmetics*, 84, 45-50, 1969

Arce, A., Marchiaro, A., Rodriguez, O., Soto, A., Liquid-liquid equilibria of limonene plus linalool plus diethylene glycol system at different temperatures, *Chemical Engineering Journal*, 89, (1-3): 223-227, 2002

Bamforth, C. W., Russell, I., Stewart, G., Handbook of Alcoholic Beverages Series - Beer: A quality perspective, Academic Press, 2008

Baydar, A., Carles, A., Decazes, J. M., McGee, T., Purzycki, K., Behavior of fragrances on skin, *Cosmetics & Toilletries*, 111, 49-57, 1996

Baydar, A., McGee, T., Purzycki, K. L., Skin Odor Value Technology for Fragrance Performance Optimization, *Perfumer & Flavorist*, 20, 45-53, 1995

Behan, J. M., Macmaster, A. P., Perring, K. D., Tuck, K. M., Insight into how skin changes perfume, *International Journal of Cosmetic Science*, 18, (5): 237-246, 1996

Bonnefille, M., Electronic noses: sniffing fast, safe and objective. NutraCos - Cosmetics: 9-12, 2007

Bozeya, A., Al-Bawab, A., Friberg, S. E., Guo, R., Equilibration in a geranyl acetate emulsion, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 373, (1-3): 110-115, 2009

Buck, L., Axel, R., A Novel Multigene Family May Encode Odorant Receptors: A Molecular Basis for Odor Recognition, *Cell*, 65, 175-187, 1991

Burfield, T., Is excessive regulation destroying the perfumery art?, British Society of Perfumers - Safety and Regulatory symposium, Cropwatch, 2010

Burr, C., The Perfect Scent: A Year Inside the Perfume Industry in Paris and New York, Henry Holt and Co., 2008

Butler, H., Poucher's Perfumes, Cosmetics and Soaps, Kluwer Academic Publishers - Boston / London, 2000

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Cain, W. S., Schmidt, R., Can we trust odor databases? Example of t- and n-butyl acetate, *Atmospheric Environment*, 43, (16): 2591-2601, 2009

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994
Carles, J., A method of creation in perfumery, *Soap Perfumery Cosmet.*, 35, 328-335, 1962
Chambers, E., Wolf, M. B., Sensory Testing Methods, Philadelphia, PA (USA), ASTM International, 1996
Charpentier, J. C., Process Engineering and Product Engineering, *Chemical Engineering Science*, 52, (18): 3-4, 1997
Charpentier, J. C., The triplet "molecular processes-product-process" engineering: the future of chemical engineering?, *Chemical Engineering Science*, 57, 4667-4690, 2002
Chastrette, M., Trends in structure-odor relationships, *SAR and QSAR in Environmental Research*, 6, 215-254, 1997
Chastrette, M., Data management in olfaction studies, *SAR and QSAR in Environmental Research*, 8, (3-4): 157-181, 1998
Cheong, S. H., Choi, Y. W., Myung, K. B., Choi, H. Y., Comparison of Marketed Cosmetic Products Constituents with the Antigens Included in Cosmetic-related Patch Test, *Annals of Dermatology*, 22, (3): 262-268, 2010
Clery, R., High-impact odorants in essential oils, *Flavour and Fragrance Journal*, 25, (3): 117-120, 2010
Confiança, Saboaria e Perfumaria, from http://www.confiancasoaps.com/, Last Accessed on 2011
Consultants, I., An overview of the global flavours and fragrances market, UK, 2007
Cortez-Pereira, C. S., Baby, A. R., Kaneko, T. M., Velasco, M. V. R., Sensory approach to measure fragrance intensity on the skin, *Journal of Sensory Studies*, 24, (6): 871-901, 2009
Costa, R., Moggridge, G. D., Saraiva, P. M., Chemical product engineering: an emerging paradigm within chemical engineering, *AIChE Journal*, 52, (6): 1976-1986, 2006
Curtis, T., Williams, D. G., Introduction to Perfumery, New York, Ellis Horwood, 1994
Cussler, E. C., Moggridge, G. D., Chemical Product Design, Cambridge, Cambridge University Press, 2001
Cussler, E. L., Wei, J., Chemical Product Engineering, *AIChE*, 49, (5): 1072-1075, 2003
Davies, E., The sweet scent of success, *Chemistry World*, 40-44, 2009
de Doz, M. B. G., Cases, A. M., Solimo, H. N., (Liquid plus liquid) equilibria of (water plus linalool plus limonene) ternary system at T = (298.15, 308.15, and 318.15) K, *Journal of Chemical Thermodynamics*, 40, (11): 1575-1579, 2008
Devos, M., Rouault, J., Laffort, P., Standardized olfactory power law exponents, Dijon - France, Editions Universitaires-Sciences 2002
Domanska, U., Morawski, P., Piekarska, M., Solubility of perfumery and fragrance raw materials based on cyclohexane in 1-octanol under ambient and high pressures up to 900 MPa, *Journal of Chemical Thermodynamics*, 40, (4): 710-717, 2008
Domanska, U., Paduszynski, K., Niszczota, Z. K., Solubility of fragrance raw materials in water Experimental study, correlations, and Mod UNIFAC (Do) predictions, *Journal of Chemical Thermodynamics*, 43, (1): 28-33, 2010
Doty, R. L., Laing, D. G., Psychophysical Measurement of Human Olfactory Function, Including Odorant Mixture Assessment, Handbook of Olfaction and Gustation - Revised and Expanded, Laing, New York (USA), Marcel Dekker Inc., 2003
Doty, R. L., McKeown, D. A., Lee, W. W., Shaman, P., A study of the test-retest reliability of ten olfactory tests, *Chemical Senses*, 20, (6): 645-656, 1995

Dravnieks, A., Jarke, F., Odor threshold measurement by dynamic olfactometry: significant operational variables, *Journal of the Air Pollution Control Association*, 30, (12): 1284-1289, 1980

Fadel, A., Turk, R., Mudge, G., Mattila, J., Esteves, J., Ranciato, J., Perfumes for rinse-off systems. Corporation. United States Patent. US 7,446,079 B22008

Ferreira, V., Lopez, R., Cacho, J. F., Quantitative determination of the odorants of young red wines from different grape varieties, *Journal of the Science of Food and Agriculture*, 80, (11): 1659-1667, 2000

Firmenich, Osmoz Encyclopedia, from http://www.osmoz.com/, Last Accessed on May 2011

Fisher, C., Scott, T. R., Food Flavours: Biology and Chemistry, Cambridge (UK), The Royal Society of Chemistry, 1997

Fleischer, J., Breer, H., Strotmann, J., Mammalian olfactory receptors, *Frontiers Cellular Neuroscience*, 3, 9, 2009

FOCUS, The luxury market, FOCUS Magazin, Verlag GmbH, Munich, 2008

Freedonia, Industry Study, US Flavors & Fragrances Market, 2010

Friberg, S. E., Evaporation from a Limonene Emulsion, *Journal of Dispersion Science and Technology*, 28, 11-20, 2007

Friberg, S. E., Constant vapor pressure evaporation from emulsions, *Colloid Polym. Sci.*, 286, 47-50, 2008

Friberg, S. E., Phase Diagram Approach to Evaporation from Emulsions with n Oil Compounds, *Journal of Physical Chemistry B*, 113, (12): 3894-3900, 2009

Friberg, S. E., Al-Bawab, A., Odehb, F., Bozeya, A., Aikens, P. A., Emulsion evaporation path. A first comparison of experimental and calculated values, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 338, (1-3): 102-106, 2009

Friedrich, J. E., Acree, T. E., Gas chromatography olfactometry (GC/O) of dairy products, *International Dairy Journal*, 8, (3): 235-241, 1998

Fritter, G., Bajgrowicz, J. A., Kraft, P., Fragrance Chemistry, *Tetrahedron*, 54, (report number 456): 7633-7703, 1998

Gardner, B., The US Inflation Calculator, from http://www.usinflationcalculator.com/, Last Accessed on June, 2011

Garrido, N. M., Queimada, A. J., Jorge, M., Macedo, E. A., Economou, I. G., 1-Octanol/Water Partition Coefficients of n-Alkanes from Molecular Simulations of Absolute Solvation Free Energies, *Journal of Chemical Theory and Computation*, 5, (9): 2436-2446, 2009

Gautschi, M., Bajgrowicz, J. A., Kraft, P., Fragrance chemistry - Milestones and perspectives, *Chimia*, 55, (5): 379-387, 2001

Gilbert, A., What the Nose Knows - The Science of Scent in Everyday Life, New York, Crown Publishers, 2008

Gilson, M. K., Zhou, H.-X., Calculation of Protein-Ligand Binding Affinities, *Annual Review of Biophysics and Biomolecular Structure*, 36, 21–42, 2007

Goldstein, B., Handbook of Sensation and Perception, USA, Blackwell Publishing Ltd, 2005

Gomes, P. B., Engineering Perfumes. Department of Chemical Engineering. Porto, University of Porto Faculty of Engineering. PhD Thesis, 2005

Gomes, P. B., Mata, V. G., Rodrigues, A. E., Experimental Validation of Perfumery Ternary Diagram Methodology, *AIChE*, 54, (1): 310-320, 2008

Gomes, P. B., Mata, V. G., Rodrigues, A. E., Experimental Validation of Perfumery Ternary Diagram Methodology, *AIChE*, 54, (1): 310-320, 2008

Gostelow, P., Parsons, S. A., Stuetz, R. M., Odour measurements for sewage treatment works, *Water Research*, 35, (3): 579-597, 2001

Gottfried, J. A., Winston, J. S., Dolan, R. J., Dissociable codes of odor quality and odorant structure in human piriform cortex, *Neuron*, 49, (3): 467-479, 2006

Guy, R. H., Predicting the Rate and Extent of Fragrance Chemical Absorption into and through the Skin, *Chemical Research in Toxicology*, 23, (5): 864-870, 2010

Haddad, R., Lapid, H., Harel, D., Sobel, N., Measuring smells, *Current Opinion in Neurobiology*, 18, (4): 438-444, 2008

Hajjar, E., Perahia, D., Debat, H., Nespoulous, C., Robert, C. H., Odorant binding and conformational dynamics in the odorant-binding protein, *Journal of Biological Chemistry*, 281, (40): 29929-29937, 2006

Helmut-Kreutz, from http://www.helmutkreutzportugal.pt/, Last Accessed on 2011

i-sensis, S. João da Madeira, Portugal, from www.i-sensis.com, Last Accessed on 2011

IFF, International Falvors & Fragrances Inc. Press Kit, 2005

IFRA, International Fragrance Association, from http://www.ifraorg.org/, Last Accessed on 2011

INE, International Trade Statistics Report published from the Instituto Nacional de Estatística de Portugal (INE), 2003

Jackson, R. S., Wine Science: Principles, Practice, Perception, USA, Elsevier Science & Technology Books, 2000

Jacobson, L., Lorimor, J., Bicudo, J., Schmidt, D., Emission from Animal Production Systems - Lesson 40: Measuring Outdoor Air Quality (OAQ) Components, MidWest Plan Service (MWPS)2001

Jinks, A., Laing, D. G., A limit in the processing of components in odour mixtures, *Perception*, 28, (3): 395-404, 1999

Johnson, B. N., Mainland, J. D., Sobel, N., Rapid olfactory processing implicates subcortical control of an olfactomotor system, *Journal of Neurophysiology*, 90, (2): 1084-1094, 2003

Kasting , G. B., Saiyasombati, P., Two stage kinetics analysis of fragrance evaporation and absorption from skin, *International Journal of Cosmetic Science*, 25, 235-243, 2003

Kato, A., Touhara, K., Mammalian olfactory receptors: pharmacology, G protein coupling and desensitization, *Cellular and Molecular Life Sciences*, 66, (23): 3743-3753, 2009

Kerschner, J., Fragrances in Consumer Products. International Flavor and Fragrances - Bergen Academy 2006

Khafizov, K., Anselmi, C., Menini, A., Carloni, P., Ligand specificity of odorant receptors, *Journal of Molecular Modeling*, 13, (3): 401-409, 2007

Korichi, M., et al., Computer Aided Aroma Design. I – Molecular Knowledge Framework, *Chemical Engineering and Processing*, 10, 2008

Kovatcheva, A., Golbraikh, A., Oloff, S., Xiao, Y. D., Zheng, W. F., Wolschann, P., Buchbauer, G., Tropsha, A., Combinatorial QSAR of ambergris fragrance compounds, *Journal of Chemical Information and Computer Sciences*, 44, (2): 582-595, 2004

Kraft, P., Mannschreck, A., The Enantioselectivity of Odor Sensation: Some Examples for Undergraduate Chemistry Courses, *Journal of Chemical Education*, 87, (6): 598-603, 2010

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Laing, D. G., Eddy, A., Best, D. J., Perceptual characteristics of binary, trinary, and quaternary odor mixtures consisting of unpleasant constituents, *Physiology & Behavior*, 56, (1): 81-93, 1994

Laing, G. G., Optimum Perception of Odours by Humans, Report, CSIRO Division of Food Research, North Ryde, N.S.W., Australia, 1987

Lapid, H., Harel, D., Sobel, N., Prediction models for the pleasantness of binary mixtures in olfaction, *Chemical Senses*, 33, (7): 599-609, 2008

Lawless, H. T., Heymann, H., Sensory Evaluation in Food: Principles and Practices, New York (USA), Chapman & Hall, 1998

Leffingwell, J. C., Leffingwell, D., 2005 - 2009 Flavor & Fragrance Industry Leaders, 2010

Lis-Balchin, M., Aromatherapy science: a guide for healthcare professionals, Great Britain, Pharmaceutical Press, 2006

Lopez-Nogueroles, M., Chisvert, A., Salvador, A., A chromatochemometric approach for evaluating and selecting the perfume maceration time, *Journal of Chromatography A*, 1217, (18): 3150-3160, 2010

Mandairon, N., Linster, C., Odor Perception and Olfactory Bulb Plasticity in Adult Mammals, *Journal of Neurophysiology*, 101, (5): 2204-2209, 2009

Marshall, K., Laing, D. G., Jinks, A. L., Hutchinson, I., The capacity of humans to identify components in complex odor-taste mixtures, *Chemical Senses*, 31, (6): 539-545, 2006

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Effect of nonidealities in perfume mixtures using the perfumery ternary diagrams (PTD) concept, *Industrial & Engineering Chemistry Research*, 44, (12): 4435-4441, 2005a

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AIChE Journal*, 51, (10): 2834-2852, 2005b

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Perfumery ternary diagrams (PTD): a new concept applied to the optimization of perfume compositions, *Flavour and Fragrance Journal*, 20, (5): 465-471, 2005c

Mata, V. G., Rodrigues, A. E., A new methodology for the definition of odor zones in perfumery ternary diagrams, *AIChE*, 52, (8): 2938-2948, 2006

Matsumoto, H., Kashiwadani, H., Nagao, H., Aiba, A., Mori, K., Odor-Induced Persistent Discharge of Mitral Cells in the Mouse Olfactory Bulb, *Journal of Neurophysiology*, 101, (4): 1890-1900, 2009

Mayer, V. A., Fazio-Fluehr, P. C., Arendt, S. A., ASTM Dictionary of Engineering Science & Technology, Mayfield, PA (USA), ASTM International, 2005

Meilgaard, M., Civille, G. V., Carr, B. T., Sensory evaluation techniques, Boca Raton (USA), CRC Press, Taylor & Francis Group, 2007

Mookhejee, B., Patel, S., Trenkle, R., Wilson, R., A Novel Technology to Study the Emission of Fragrance from the Skin, *Perfumer&Flavorist*, 1, (23): 1998

Nicell, J. A., Expressions to relate population responses to odor concentration, *Atmospheric Environment*, 37, (35): 4955-4964, 2003

Periole, X., Huber, T., Marrink, S. J., Sakmar, T. P., G protein-coupled receptors self-assemble in dynamics simulations of model bilayers, *Journal of the American Chemical Society*, 129, (33): 10126-10132, 2007

Poucher, W. A., A classification of odors and its uses, *Journal Soc. Cosmet. Chem.*, 81-95, 1955

Powers, W., The science of smell part 1: Odor perception and physiological response, 2004

Pritchard, J. D., Ammonia - Health Effects of Acute / Single Exposure (Human), Health Protection Agency (HPA)2009

Rochat, S., Egger, J., Chaintreau, A., Strategy for the identification of key odorants: Application to shrimp aroma, *Journal of Chromatography A*, 1216, (36): 6424-6432, 2009

Rodrigues, A. E., da Silva, F. A., Granato, M., Lamia, N., Grande, C., Gomes, P. S., Propane/Propylene separations: from molecular simulation to process development, XXXIII Reunión Ibérica de Adsorción, Madrid (Spain), 2008

Rodrigues, S. N., Martins, I. M., Fernandes, I. P., Gomes, P. B., Mata, V. G., Barreiro, M. F., Rodrigues, A. E., Scentfashion®: Microencapsulated perfumes for textile application, *Chemical Engineering Journal*, 149, 463–472, 2009

Rosenkranz, H. S., Cunningham, A. R., A substructure-based SAR model for odor perception in humans relevant to health risk assessments, *Sar and Qsar in Environmental Research*, 14, (3): 215-222, 2003

Rossiter, K. J., Structure-odor relationships, *Chemical Reviews*, 96, (8): 3201-3240, 1996

Rouby, C., Schaal, B., Dubois, D., Gervais, R., Holley, A., Olfaction, Taste, and Cognition UK, Cambridge University Press, 2002

Rowe, D., Chemistry and Technology of Flavours and Fragrances, United States, Blackwell Publishing Ltd - CRC Press, 2005

Saito, H., Chi, Q. Y., Zhuang, H. Y., Matsunami, H., Mainland, J., Odor coding by a mammalian receptor repertoire, *Neuroscience Research*, 65, S76-S76, 2009

Saito, H., Kubota, M., Roberts, R. W., Chi, Q. Y., Matsunami, H., RTP family members induce functional expression of mammalian odorant receptors, *Cell*, 119, (5): 679-691, 2004

Sell, C., The Chemistry of Fragrances - From Perfumer to Consumer, Cambridge (UK), RSC Publishing, 2006

Shigemoto, K., Weber-Fechner's Law and Demand Function, *Tezukayama Academic Review*, 9, (41-46): 2002

Shigemoto, K., Weber-Fechner's Law and Demand Function, *Microeconomics 0412001, EconWPA*, 2004

Sigma-Aldrich, from http://www.sigmaaldrich.com/, Last Accessed on 2011

Singer, M. S., Shepherd, G. M., Molecular modeling of ligand-receptor interactions in the OR5 olfactory receptor, *Neuroreport*, 5, (10): 1297-1300, 1994

Singh, S., Malhotra, P., Jain, S., Varma, S., Gastro-esophageal burns following domestic liquid ammonia ingestion: report of two cases, *J. Assoc. Physicians India*, 47, 647, 1999

Somogyi, L., Kishi, A., Mueller, S., Yang, W., Flavors and Fragrances, from www.sriconsulting.com/SCUP/Public/Reports/FLAVO000/, Last Accessed on November, 2010

Spehr, M., Munger, S. D., Olfactory receptors: G protein-coupled receptors and beyond, *Journal of Neurochemistry*, 109, (6): 1570-1583, 2009

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Surburg, H., Panten, J., Common Fragrance and Flavor Materials - Preparation, Properties and Uses, Weinheim, WILEY-VCH Verlag GmbH & Co., 2006

Swets, J. A., Detection theory and psychophysics - A review, *Psychometrika*, 26, (1): 49-63, 1961

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009a

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009b

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE Journal*, 56, (4): 1090-1106, 2010

Teixeira, M. A., Rodrìguez, O., Rodrigues, A. E., Chapter 1: Odor Detection & Perception: An Engineering Perspective, Advances in Environmental Research, USA, NovaPublishers, Volume 14: 2011

Tian, C. L., Breyer, R. M., Kim, H. J., Karra, M. D., Friedman, D. B., Karpay, A., Sanders, C. R., Solution NMR spectroscopy of the human vasopressin V2 receptor, a G protein-coupled receptor, *Journal of the American Chemical Society*, 127, (22): 8010-8011, 2005

Tisi, D. A., The Taste of Success, *Pharmaceutical Formulation and Quality*, (11.2): 14-18, 2009

Tokuoka, Y., Uchiyama, H., Abe, M., Phase-diagrams of surfactant water synthetic perfume ternary-systems, *Colloid and Polymer Science*, 272, (3): 317-323, 1994

Ulrich, K., Eppinger, S., Product design and development, New York, McGraw Hill, 2003

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

van Wezel, A., Puijker, L., Vink, C., Versteegh, A., de Voogt, P., Odour and flavour thresholds of gasoline additives (MTBE, ETBE and TAME) and their occurrence in Dutch drinking water collection areas, *Chemosphere*, 76, (5): 672-676, 2009

Verdict, Global Luxury Retailing Report, 2007

Wang, L. K., Pereira, N. C., Hung, Y.-T., Air Pollution Control Engineering, Totowa, New Jersey (USA), Humana Press Inc., 2004

Warrenburg, S., Effects of fragrance on emotions: Moods and physiology, *Chemical Senses*, 30, I248-i249, 2005

Wei, J., Molecular Structure and Property: Product Engineering, *Ind. Eng. Chem. Res.*, 41, 1917-1919, 2002

Wesselingh, J. A., Structuring of products and education of product engineers, *Powder Technology*, 119, 2-8, 2001

Wesselingh, J. A., Kiil, S., Vigild, M. E., Design & development of biological, chemical, food and pharmaceutical products, Chichester, U.K., Wiley, 2007

Williams, D. F., Schmitt, W. H., Chemistry and Technology of the Cosmetics and Toiletries Industry, Glasgow, Blackie Academic & Professional, Chapman & Hall, 1992

Wolfson, W., In the fragrance molecule smells business, the right like money, *Chemistry & Biology*, 12, (8): 857-858, 2005

Young, W. F., Horth, H., Crane, R., Ogden, T., Arnott, M., Taste and odour threshold concentrations of potential potable water contaminants, *Water Research*, 30, (2): 331-340, 1996

Ziegler, H., Flavourings: Production, composition, applications, regulations, Weinheim, Germany, WILEY-VCH Verlag GmbH & Co., 2007

Zwislocki, J. J., Sensory Neuroscience: Four Laws of Psychophysics, New York, Springer Science+Business Media, 2009

Chapter 3

Scientific Methodologies for Engineering Perfumes*

"The utilization of a balance between art, science, logic and imagination, known as the 'Da Vinci Principle' can be utilized in every step of product development to reach higher efficiency through this 'whole-brain' development approach"

Herta Ziegler (2007)

In this Chapter the Perfumery Ternary Diagram (PTD®) methodology is revisited and extended to the Perfumery Quaternary Diagram (later registered as Perfumery Quaternary-Quinary Diagram, PQ2D®) methodology. This tool can be applied to quaternary and quinary perfumery systems through the use of tetrahedric diagrams for the prediction of their headspace odor character and odor intensity. To present this new methodology, the effect of different base notes was studied in quaternary systems of the type (limonene + geraniol + base note + ethanol). Moreover, the effect of solvent concentration was evaluated together with their corresponding ternary subsystems. In this study the selected base notes were: vanillin, tonalide, ambrox, and galaxolide. The PQ2Ds of these perfumery systems evidenced different headspace odor qualities, with ambrox and galaxolide dominating most of the composition spectrum (OV_{max}). The methodology was also applied to a quinary mixture (limonene + geraniol + vanillin +

* This Chapter is partly based on the paper from Teixeira, MA, Rodríguez, O, Mata, VG, Rodrigues, AE, Perfumery Quaternary Diagrams for Engineering Perfumes, AIChE J., 55, (8): 2171-2185, 2009

tonalide + ethanol) to evaluate the effect of different concentrations of the fixative (tonalide). Other quinary mixtures were also presented to compare the perceived odor in the headspace with that of the corresponding quaternary mixtures. Finally, a last effort was put on the graphical representation capabilities of the PQ2D® methodology which was extended to incorporate octonary mixtures within a three-dimensional diagram.

3.1. Application of Product Engineering to F&F

Last Chapter ended with a discussion on the relevance of Product Engineering and the contribution of scientific knowledge to the field of Flavors & Fragrances (F&F). In this way, the application of Product Engineering to (F&F) has exactly the crucial objective of implementing technical and scientific knowledge into a so far empiric and experimental area. As we have seen in Chapter 2, the creation of perfumes is still today an art, developed by well trained perfumers, within a variety of raw materials. It is highly specialized and individualistic. A wide palette of ingredients, in the order of thousands and differing greatly in chemical structure and physicochemical properties, are available to perfumers. They are, in some way, like an experienced pastry chef who imagine in their mind a combination of chemicals, extracts, essential oils and distillates selectively chosen and know exactly what decimal quantity of essence to put in the formula (Guentert, 2007). There is no doubt that the key for perfume formulation is the blending of different fragrant species with the main objective of producing an aesthetically pleasant scent for consumers. The experience and olfactory perception combined with creativity and inspiration are the key qualities of an experienced perfumer.

However, even for those, a large number of trial and error experiments have to be performed prior to obtain the desired fragrance combination (Curtis, 1994). It is, thus, in this context that raises an imperative objective of developing techniques, tools or models that may characterize (and ultimately predict) the olfactory perception of a mixture of any number of fragrances and solvents.

Recently, a scientific methodology for the prediction of the odor character and intensity in the headspace above a liquid perfume mixture of three fragrant species and a solvent matrix was developed (Mata*, et al.*, 2005; Mata and Rodrigues, 2006). The concept, called the Perfumery Ternary Diagram (PTD®), as briefly presented in Chapter 2, results from the combination of the classic perfume pyramid structure and the ternary

phase diagrams, especially used in the fields of engineering and physical-chemistry. In this Chapter 3, an extension of that concept, called the Perfumery Quaternary-Quinary Diagram (PQ2D®) methodology is presented, using tetrahedric 3-dimensional diagrams to map the perceived odor of multi-component perfume mixtures.

3.2. Methodology

The odor strength or odor intensity can be described by a quantitative parameter known as the odor value (OV) (Calkin and Jellinek, 1994). As aforementioned, the OV is defined as the ratio between the concentration of an odorant species *i* in the headspace, C_i^g, and its odor detection threshold in air, ODT_i (both in g/m^3):

$$OV_i = \frac{C_i^g}{ODT_i} \tag{3.1}$$

Only the volatiles with an OV higher than unity may be detected by the human nose and thus contribute to the overall scent. In what concerns to the odor threshold, it is important to consider both the detection (ODT_i) and the recognition (ORT_i) thresholds of a fragrant component *i*. As discussed before, odor detection thresholds are more reliable than recognition ones and thus, the formers were selected to be used in this study. Extensive compilations of odor threshold values can be found in the literature for odorant substances in air and water (Calkin and Jellinek, 1994; van Gemert, 2003; Leffingwell and Leffingwell, 2011).

For a liquid mixture of *N* fragrant components it is possible to evaluate its behavior using some basic thermodynamics: the composition of the different fragrant components in the gas phase above the liquid can be calculated from a modified Raoult's law for vapor-liquid equilibria (VLE) as presented in Equation 3.2.

$$y_i \phi_i P = x_i \gamma_i P_i^{sat} \tag{3.2}$$

where y_i and x_i stand for the vapor and liquid mole fractions of component *i*, while ϕ_i and γ_i are the vapor and liquid activity coefficients of component *i*, respectively. *P* is the total pressure and P_i^{sat} is the saturation pressure of pure component *i*. At atmospheric

pressure, ideal gas behavior can be assumed and thus, $\phi_i = 1$. Consequently, the concentration of odorant species in the headspace C_i^g can be calculated as:

$$C_i^g = \frac{y_i M_i P}{RT} = x_i \gamma_i \frac{M_i P_i^{sat}}{RT} \tag{3.3}$$

where M_i is the molecular mass of component *i*, *R* is the universal gas constant and *T* is the absolute temperature.

The activity coefficient (γ_i) accounts for deviations of the liquid phase from ideal behavior, reflecting the affinity and interactions of each molecule with its surrounding medium. For an ideal solution $\gamma_i = 1$, while for a non-ideal solution $\gamma_i \neq 1$, evidencing deviations from the Raoult's Law. In a perfume mixture, γ_i can be understood as a measure of the tendency of a molecule *i* to stay in the liquid medium or to be "pushed out" into the headspace. If $\gamma_i > 1$, the concentration of the fragrant component *i* in the headspace will be higher than for an ideal solution, that is, the molecules will be "pushed out" from the solution into the gas phase. When $\gamma_i < 1$, lower concentrations of the odorant species *i* will be found in the headspace and so there will be a higher retention of these odorous molecules into the liquid phase due to a higher affinity to the surrounding medium (Mata*, et al.*, 2005).

Combining Equations 3.1 and 3.3, the OV of each fragrant component can be calculated as:

$$OV_i = \gamma_i x_i \left(\frac{P_i^{sat} M_i}{ODT_i} \right) \left(\frac{1}{RT} \right) \tag{3.4}$$

Thus, the odor intensity of each species can be obtained from pure component data (composition in the liquid phase, molecular weight, saturated vapor pressure and odor threshold) together with the activity coefficient (γ_i). This activity coefficient can be calculated from experimental vapor-liquid equilibrium (VLE) data or with suitable predictive methods. In this work we have used the UNIFAC method (Fredenslund*, et al.*, 1975; Poling*, et al.*, 2004) for prediction of the vapor-liquid equilibrium and the activity coefficients of the fragrance components.

Furthermore, when considering a perfume mixture with *N* fragrant components, it is expected that *N* different odor values can be calculated in the headspace, each one corresponding to a single fragrant species *i*. In order to account for the odor character of such mixtures, the Stronger Component (SC) model has been considered. It states that among all the odorant components present in the gas phase, the one that is more strongly perceived and recognized by the human nose is the one having the highest odor value, although there is a mixture of perceived scents in the air (Laffort and Dravnieks, 1982; Cain*, et al.*, 1995):

$$OV_{mix} = max\{OV_i\}, \qquad i = 1,...,N \tag{3.5}$$

Like this, if we consider a quaternary perfume mixture, Equation 3.5 reduces to:

$$OV_{mix} = max\{OV_A, OV_B, OV_C, OV_S\} \tag{3.6}$$

where subscripts are as: A – top note, B – middle note, C – base note and S – solvent.
It is important to highlight that this PQ2D® methodology presented here is not limited to the selected models or the small number of fragrance ingredients considered in this study. That is, different models may be used to calculate the activity coefficient - *e.g.* correlations such as NRTL (Renon and Prausnitz, 1968) or UNIQUAC (Abrams and Prausnitz, 1975), or predictive methods like ASOG (Tochigi*, et al.*, 1990) or COSMO-RS (Klamt, 2005), or other models can be used to evaluate the odor intensity and perception. The models used here were selected attending to their simplicity and, most especially, the widespread availability of data needed for their application. Moreover, the developed methodology works for any number of fragrant compounds considered in a mixture, although to visualize the results in a graphical representation, a small number of components has been selected.

3.3. Perfumery Ternary Diagram (PTD®)

The concept of PTD® (Mata*, et al.*, 2005; Mata and Rodrigues, 2006) relies on the engineering ternary diagrams, where it is possible to express singular compositions by a set of ternary fractions (molar, volume, weight). In the PTD®, the three components,

$i = A, B \text{ and } C$, represent the three types of fragrant notes used in a typical perfume formulation: *A* represents the top note, *B* the middle note and *C* the base note. In this study, though, some of the test mixtures considered the presence of ethanol (solvent, *S*) in order to differentiate from the concentrated perfume mixtures and also to simulate a more realistic perfume formulation. For these four component systems it is possible to define pseudo-ternary compositions using solvent-free basis compositions, by recalculating the ternary molar fractions of the three other components as follows:

$$x_A' = \frac{x_A}{x_A + x_B + x_C}, \quad x_B' = \frac{x_B}{x_A + x_B + x_C}, \quad x_C' = \frac{x_C}{x_A + x_B + x_C} \tag{3.7}$$

where x'_i indicates a pseudo-ternary composition for each of the three fragrant components (*A, B, C*) in the quaternary system (*A, B, C, S*). The selected odorant components, their chemical structures and their physical and sensorial properties are presented in Table 3.1 and Figure 3.1.

Table 3.1 – Properties of the odorant components.

	Name	Molecular Formula	M. W.$_i$ (g/mol)	P_i^{sat} (Pa)	ODT_i (g/m^3)	$\frac{P_i^{sat} \cdot M_{wi}}{ODT_i \cdot R \cdot T}$	$D_{i,air}$ (m^2/h)
A	Limonene[a]	$C_{10}H_{16}$	136.2	20.5×10^{1}	2.45×10^{-3}	4.60×10^{3}	2.214×10^{-2}
	α-pinene[a]	$C_{10}H_{16}$	136.2	5.13×10^{2}	5.44×10^{-4}	5.18×10^{4}	2.000×10^{-2}
B	Geraniol[a]	$C_{10}H_{18}O$	154.3	26.7×10^{-1}	2.48×10^{-5}	6.70×10^{3}	2.138×10^{-2}
	Linalool[a]	$C_{10}H_{18}O$	154.3	2.21×10^{1}	1.26×10^{-5}	1.09×10^{5}	2.124×10^{-2}
	Vanillin[a]	$C_8H_8O_3$	152.2	16.0×10^{-3}	1.87×10^{-7}	5.25×10^{3}	4.111×10^{-2}
C	Tonalide[a]	$C_{18}H_{26}O$	258.4	67.0×10^{-6}	1.82×10^{-5}	3.84×10^{-1}	1.941×10^{-2}
	Ambrox	$C_{16}H_{28}O$	236.4	12.5×10^{-1}[b]	2.90×10^{-6}[c]	4.11×10^{4}	1.670×10^{-2}
	Galaxolide	$C_{18}H_{26}O$	258.4	72.7×10^{-3}[d]	6.30×10^{-7}[e]	1.20×10^{4}	1.924×10^{-2}
S	Ethanol[a]	C_2H_6O	46.0	72.7×10^{2}	5.53×10^{-2}	2.44×10^{3}	4.469×10^{-2}

[a]From (Calkin and Jellinek, 1994); [b]from (Chemspider, 2010); [c]from (Leffingwell and Leffingwell, 2011); [d]from (Balk and Ford, 1999); [e]from (Fráter, *et al.*, 1999).

The PTD® shows the most strongly perceived component, the one having the maximum OV (OV_{max}), for a ternary perfume mixture (or even a quaternary mixture if one of the compositions is fixed according to Equation 3.7). The calculation of the OV using Equation 3.4 allows mapping the whole PTD® with different odor zones where the

relation $OV_{max} = OV_i$ for $i = A, B$ *and* C is valid. These odor zones represent the range of compositions where each fragrant ingredient dominates the perceived scent among all others. These zones are limited by the Perfumery Binary Lines (PBL), which correspond to compositions where two different notes have the same and maximum OV. The Perfumery Ternary Points (PTP) are found at the intersection of the PBLs, where $OV_A = OV_B = OV_C = OV_{max}$. The procedure to calculate the Perfumery Binary Lines and Perfumery Ternary Points has been explained before (Mata and Rodrigues, 2006).

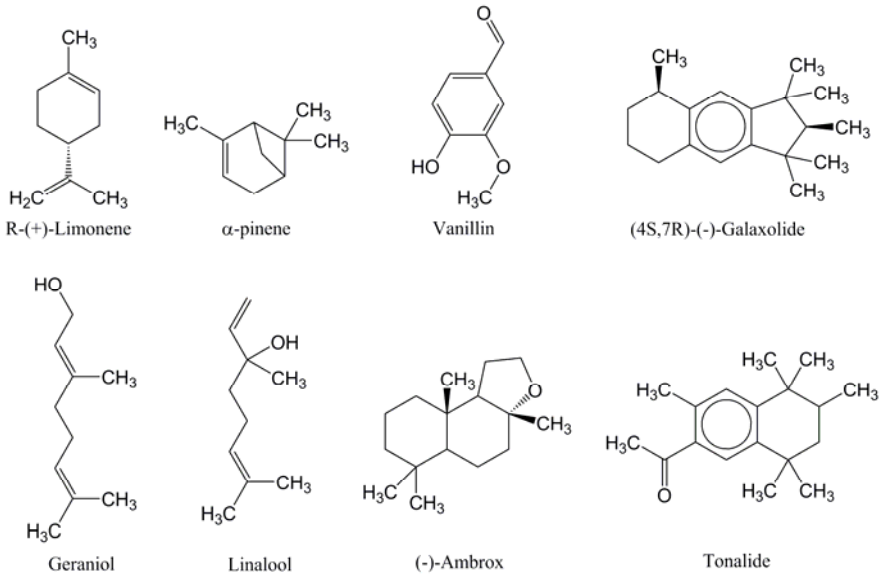


Figure 3.1 – Chemical structures of the fragrant components.

3.4. Extension of the Perfumery Ternary Diagram (PTD®) to the Perfumery Quaternary-Quinary Diagram (PQ2D®)

As it was previously said, perfumes are commonly formulated as the combination of three different types of notes (top, middle and base) together with a solvent matrix (and other ingredients – additives - which we will not focus here, as for example, for chemical stability). The PTD® is used to represent the odor character of a ternary fragrant mixture, and it can also be used for quaternary mixtures if the fourth component has a fixed composition (and so, the remaining components are represented as in a solvent-free basis). But in that way, the complete behavior of the quaternary mixture is not shown. Thus, an extension of the PTD® methodology for quaternary mixtures is needed, so that the odor character of all possible mixtures with three fragrance notes and a solvent can be seen.

For that purpose, the regular tetrahedron has been commonly used in phase equilibria thermodynamics to represent the behavior of quaternary systems. This is so because of an important property of the regular tetrahedron (similar to the equilateral triangle): the sum of the distances from a given point inside the tetrahedron to its four faces (*e.g.* the sum of the heights of that point in respect to each face) is a constant value, *k*, which equals the total height of the tetrahedron (Wei, 1983):

$$\sum_i h_i = k \tag{3.8}$$

where h_i is the height of some point inside the tetrahedron with respect to its face *i*. In this way, if we build a tetrahedron of unit length edges (so the edges can be used as axis to denote fraction compositions), we can use it to represent the composition (in mole, mass or volume fraction) of any quaternary system, given that:

$$\sum_i x_i = 1 \propto \sum_i h_i \tag{3.9}$$

where x_i stands for the composition of component *i* (in mole, mass or volume fraction). Following this line of thought, the vertex opposite to face *i* represents the pure component *i* in the quaternary mixture. Each edge of the tetrahedron represents a binary subsystem (composed of the two pure components at both ends of the edge), each face represents a ternary subsystem (without the component placed in the opposite vertex) and, finally, the points inside the tetrahedron represent any possible mixture of the quaternary system. All points in a plane parallel to a given face *i* are at the same distance of that face and, thus, have the same composition for component *i*.

For the construction of such a diagram, it is necessary a coordinate transformation from a system of tetrahedric coordinates (quaternary compositions, in mole, mass or volume fraction) to the 3-dimensional, cartesian space. Considering a regular tetrahedron (ABCS) with unitary edges as presented in Figure 3.2, it is possible to locate any quaternary composition point $P = \phi(x_A, x_B, x_C, x_S)$ in the three dimensional space $\phi(X, Y, Z)$ by summing the relative projections of each of the quaternary compositions in each of the orthogonal axis (*X, Y, Z*). In all the diagrams made throughout this work it was assumed the vertex C, as the origin of the orthogonal three dimensional space, that

is $(X,Y,Z)\big|_C = (0,0,0)$. The edge $\overline{CA}$ is placed over the *X* axis, and the edge $\overline{CB}$ is in the *XY* plane. Following Wallas (Walas, 1985), a schematic representation of the transformation of coordinates together with a PQ2D is illustrated in Figure 3.2.

The transformation matrix of the tetrahedric-quaternary variable system to the cartesian one, then results in the summation of the projection of the four variable system, (x_A, x_B, x_C, x_S), into an orthogonal axis *(X, Y, Z)* that can be mathematically described by:

$$\begin{bmatrix} x \\ y \\ z \end{bmatrix} = \begin{bmatrix} 1 & \cos\left(\pi/3\right) & \cos\left(\arctan\left(\sqrt{2}\right)\right)\cos\left(\pi/6\right) \\ 0 & \sin\left(\pi/3\right) & \cos\left(\arctan\left(\sqrt{2}\right)\right)\sin\left(\pi/6\right) \\ 0 & 0 & \sin\left(\arctan\left(\sqrt{2}\right)\right) \end{bmatrix} \begin{bmatrix} x_A \\ x_B \\ x_S \end{bmatrix} \tag{3.10}$$

From this point, the procedure to use the tetrahedric diagrams is similar to that of the PTD® (*e.g.* it shows for each composition of a quaternary mixture which component has the OV_{max}). However, once the tetrahedric diagram is three-dimensional, it is divided into odor volumes (instead of odor zones only), where any inside composition has the same dominant note (OV_{max}) for the corresponding fragrance ingredient.

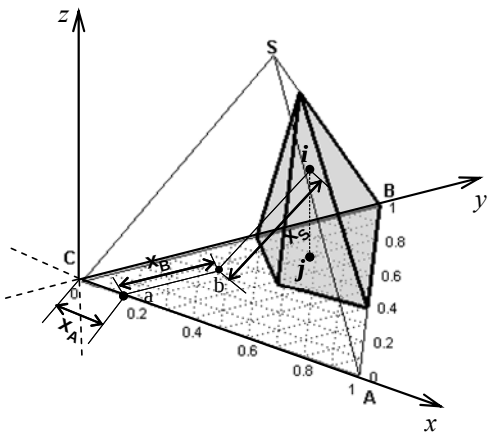


Figure 3.2 - Relationship between the Perfumery quaternary-quinary diagram (PQ2D) and the engineering quaternary diagrams.

The Perfumery Quaternary-Quinary Diagram (PQ2D®) covers the whole range of possible compositions between different combinations of four fragrant components presented in a liquid perfume mixture. The calculation of the odor value (OV) using Equation 3.4 allows mapping the whole PQ2D, by defining the regions (odor volumes) where one component dominates the overall odor. In the PQ2D shown in Figure 3.2 it is possible to see an illustrative odor volume for component B (light shaded volume)

which comprises all the quaternary compositions where the odorant species B has the maximum headspace odor value ($OV_{max} = OV_B$). The definition of the odor volumes is described by the relationship where $OV_{max} = OV_i$ for $i = A, B\ C\ or\ S$. That is, the odor volumes are limited by surfaces where the OV_{max} is shared by two components and delimited by lines where the OV_{max} is shared by three components. A new concept of Perfumery Binary Surfaces (PBS) and Perfumery Ternary Lines (PTL) is introduced here. The distribution of the odor value (OV) for a quaternary perfume mixture represented in a perfumery quaternary diagram as in Figure 3.2 shows that it is possible to have for each perfume system different odor volumes. These are delimited by interior Perfumery Binary Surfaces (PBS) and externally, by the odor zones of the corresponding ternary subsystems that constitute the faces of the tetrahedric diagram. The PBS defines the interior region of the quaternary compositions where:

$$OV_{max} = OV_j = OV_k \tag{3.11}$$

with j, k as fragrant components and $j \neq k$. The Perfumery Ternary Lines (PTL) represent the set of quaternary compositions where remains valid the following relationship:

$$OV_{max} = OV_j = OV_k = OV_l \tag{3.12}$$

with j, k, l as fragrant components and $j \neq k \neq l$. The PTL results from the intersection of three different PBS. This means that a PTL crosses the quaternary diagram in the thin region where three fragrant components have the same maximum odor value (OV_{max}). Table 3.2 shows the conditions established for the PBS and PTL, considering a quaternary perfume system. Moreover, in a quaternary mixture it is considered that a Perfumery Quaternary Point (PQP) exists between four different fragrant components j, k, l and m when the following relationship is valid:

$$OV_{max} = OV_j = OV_k = OV_l = OV_m \tag{3.13}$$

where $j, k, l\ and\ m$ are fragrant components and $j \neq k \neq l \neq m$. Analogously, the composition of the PQP is also set by the intersection point of three different PTL.

Moreover, for a perfumery quaternary system there is only one type of PQP which is fully determined by the conditions stated on Table 3.2.

Table 3.2 – Conditions of the non-linear system for the PBS, PTL and PQP.

PBS: j + k	*PTL: j + k + l*	*PQP: j + k + l + m*
$OV_j = OV_k = OV_{max}$	$OV_j = OV_k = OV_l = OV_{max}$	$OV_j = OV_k = OV_l = OV_m = OV_{max}$
$\gamma_j x_j K_j = \gamma_k x_k K_k$	$\gamma_j x_j K_j = \gamma_k x_k K_k$	$\gamma_j x_j K_j = \gamma_k x_k K_k$
	$\gamma_k x_k K_k = \gamma_l x_l K_l$	$\gamma_k x_k K_k = \gamma_l x_l K_l$
		$\gamma_l x_l K_l = \gamma_m x_m K_m$
$\sum_{i=1}^{N} x_i = 1$	$\sum_{i=1}^{N} x_i = 1$	$\sum_{i=1}^{N} x_i = 1$
$0 \le x_i \le 1$	$0 \le x_i \le 1$	$0 \le x_i \le 1$

A computer program was developed to calculate the Perfumery Quaternary-Quinary Diagram (PQ2D®) and the Perfumery Ternary Diagram (PTD) methodologies which were run using the MATLAB software. Routines and functions for the determination of the PBLs, PTPs, PBSs and PTLs were developed in MATLAB as well as the prediction of the activity coefficients (γ_i) using the UNIFAC method (for further details on the UNIFAC method see Annex B).

The iterative methods for solving the non-linear systems of equations were numerically computed using the optimization toolbox package from MATLAB, adapted to the nature of the problem studied (Chapman, 2000). The *fsolve* routine was used to compute the perfumery binary and ternary lines, perfumery ternary points and perfumery binary surfaces. The numerical method of Levenberg-Marquardt (LM) with line search was used to solve the nonlinear system of algebraic equations. The choice of the LM method relied on its robustness and precision, although it may have occasionally poorer efficiency than other methods (*e.g.* higher number of function evaluations than the Gauss-Newton method, when the residual is zero at the solution). The line search algorithm uses a combined quadratic and cubic polynomial interpolation and extrapolation methods. The tolerance was set equal to 10^{-6} for both the dependent variable and the calculated function value, and a maximum of 300 function evaluations was defined. Although it is considered that the Levenberg-Marquardt method is more robust than the Gauss-Newton method and iteratively more efficient than an unconstrained method, the main routine was programmed to choose and shift among the

different available methods for solving non-linear systems of equations, when a solution was not found using the LM method (Nocedal and Wright, 1999; MathWorks, 2002). This way, the most efficient iterative method was dynamically selected to reach stable solutions for the system of equations.

The algorithm for the iterative methods used for the determination of the Perfumery Binary Surfaces (PBS) is presented in Figure 3.3 for the case of the PBS between components A+B. Moreover, it is important to remark that the algorithm for the Perfumery Ternary Lines (PTL) is analogous to the one used for the PBS, though the non-linear system of equations must be updated for the one presented in Table 3.2.

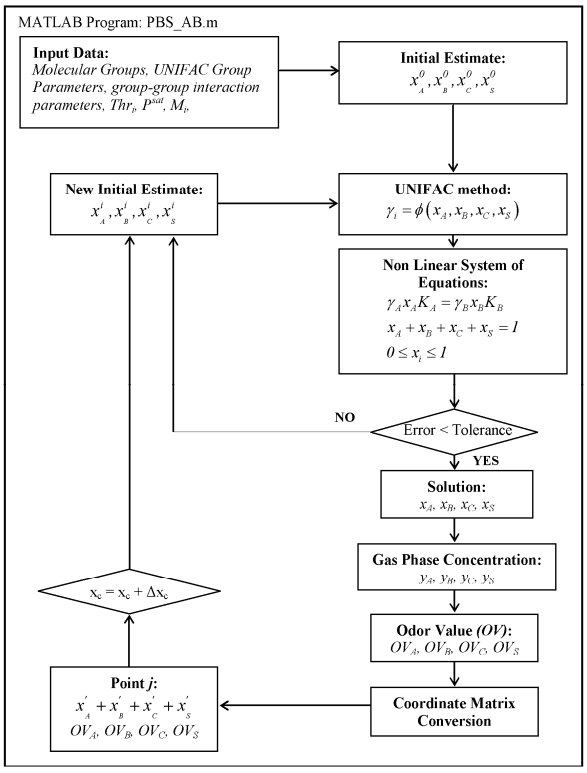


Figure 3.3 - Iterative method for the resolution of the nonlinear system of Equations for the case of a PBS between a top note (A) and a middle note (B).

3.5. Effect of the base note on the perceived odor

In order to illustrate the application of the Perfumery Quaternary-Quinary Diagram (PQ2D®), the effect of different base notes on the perceived headspace odor of different perfume mixtures has been studied using the proposed methodology. The top note (A - limonene), middle note (B - geraniol) and solvent (S - ethanol) were the same in the four quaternary systems studied. Four different base notes (C) were selected to be

incorporated in the different quaternary systems: vanillin, tonalide, galaxolide and ambrox. The applicability of the PQ2D to quinary mixtures with two base notes is also shown for the perfumery systems: limonene + geraniol + vanillin + tonalide + ethanol. Moreover, the presence of water on perfume formulation is evaluated for the systems: limonene + geraniol + vanillin + ethanol + water and limonene + geraniol + galaxolide + ethanol + water. The chemical structures and some relevant physical properties of these chemicals were shown in Figure 3.1 and Table 3.1, respectively.

3.5.1. Application of the PTD®

The prediction of the odor character above a perfume liquid mixture is first analyzed to the light of the PTD® methodology. The PTDs for the different quaternary perfume systems studied in this work are presented in Figure 3.4 to Figure 3.7 for the concentrated perfume mixtures (ethanol free) and for some selected mole fractions of ethanol in solution. These PTD® represent the cross plans of the tetrahedric diagrams at the specific height proportional to the ethanol mole fraction, thus showing the evolution of the perfume mixture as the solvent concentration rises. The Perfumery Binary Lines (PBL) are also represented (solid lines), dividing the PTD® into its different odor zones.

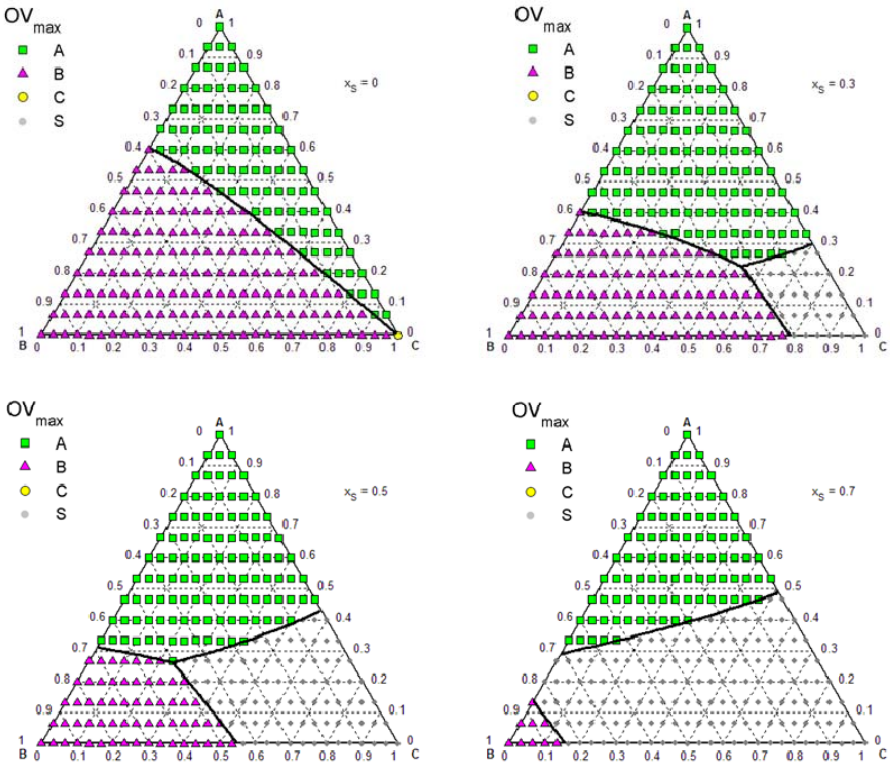


Figure 3.4 – PTD® for different initial mole fractions of solvent in the quaternary system of limonene (A) + geraniol (B) + tonalide (C) + ethanol (S).

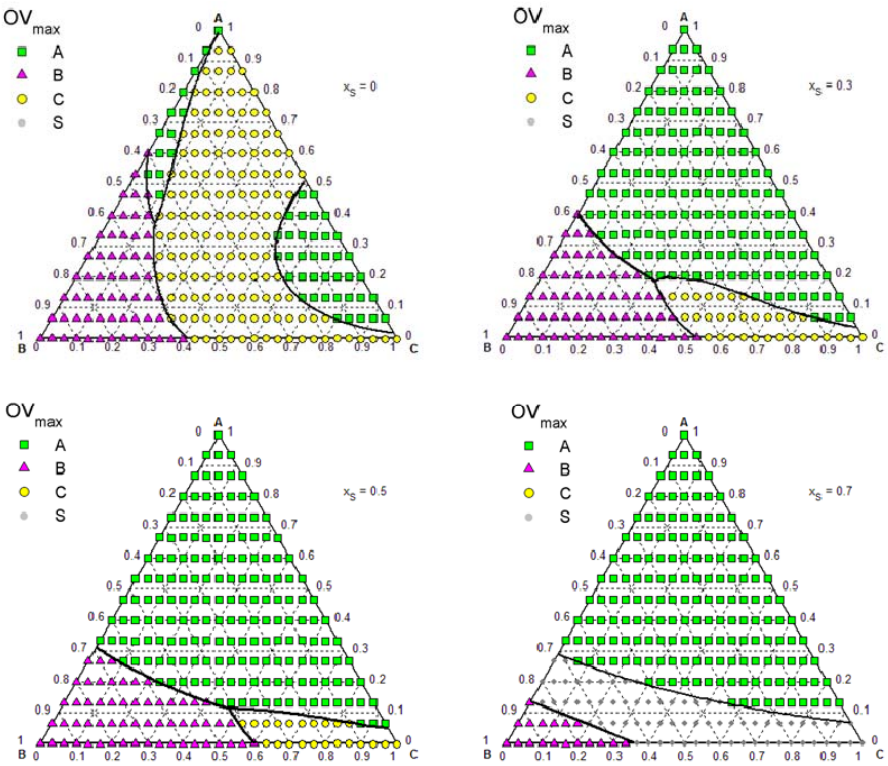


Figure 3.5 - PTD® for different initial mole fractions of solvent in the quaternary system of limonene (A) + geraniol (B) + vanillin (C) + ethanol (S).

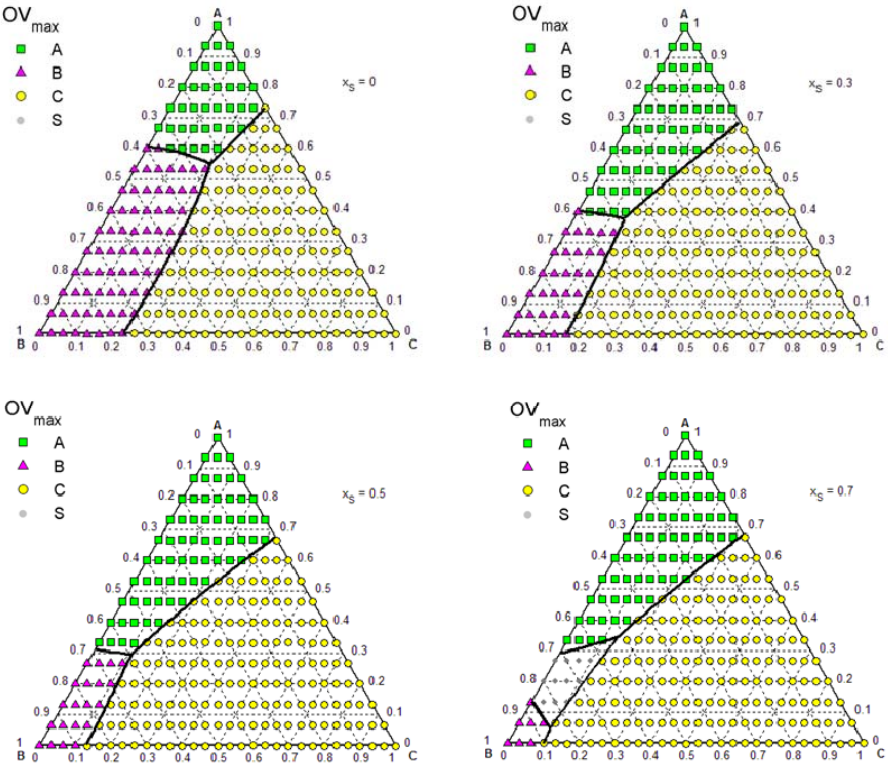


Figure 3.6 - PTD® for different initial mole fractions of solvent in the quaternary system of limonene (A) + geraniol (B) + galaxolide (C) + ethanol (S).

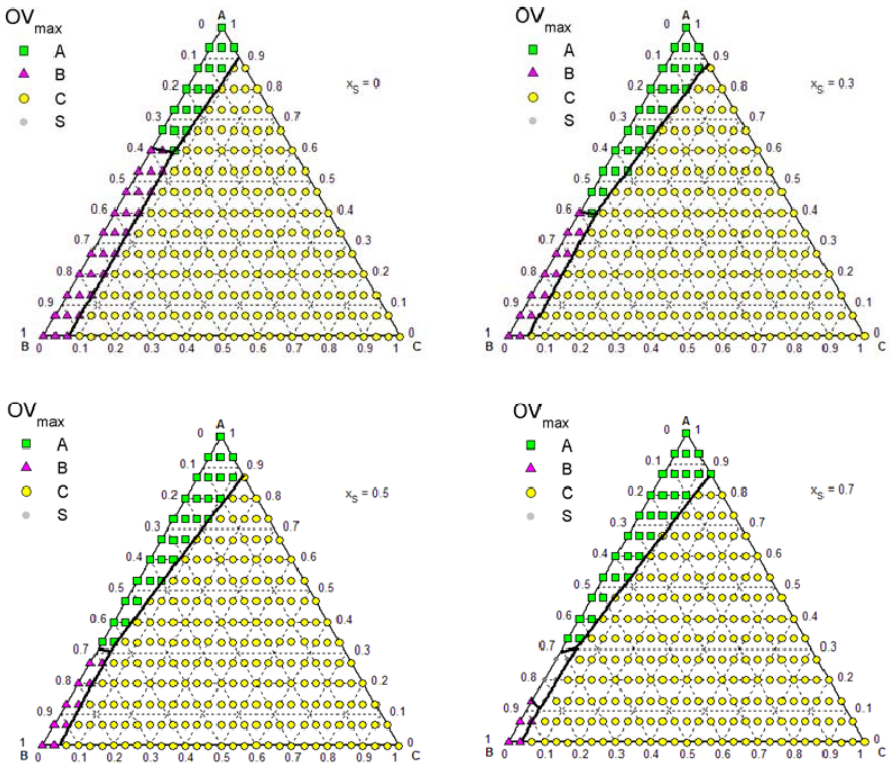


Figure 3.7 - PTD® for different initial mole fractions of solvent in the quaternary system of limonene (A) + geraniol (B) + ambrox (C) + ethanol (S).

Another feature of the PTD is that it is also able show the odor intensity of a fragrance ingredient by combining the intensity of the odorants in the ternary diagram. Like this, it is possible to map the contours of odor intensity for each component (*e.g.* isolines of odor value) as presented for the system limonene + geraniol + vanillin in Figure 3.8. It is important to make some considerations about the obtained results for the odor intensity: while for geraniol (middle note) the maximum odor intensity is reached when it is presented at high concentrations in the mixture, the same is not seen for limonene (top note) and vanillin (middle note). In fact, the behavior of these two fragrance ingredients is quite curious because it is seen that the predicted odor intensity for limonene reaches its maximum for ternary mixtures with high concentrations of vanillin. This effect, if not expected, is explained by the relative low polarity of limonene which is highly "pushed out" of the solution when present in low concentrations, thus increasing its perceived odor intensity in the air. A similar phenomenon is predicted for the odor intensity of vanillin, thus showing a good agreement with experimental observations. However, if one includes ethanol in a mole fraction equal to $x_i = 0.50$ in order to obtain the quaternary mixture of limonene (top note) + geraniol (middle note) + vanillin (base note) + ethanol (solvent) the PTD changes significantly as was previously seen in Figure 3.5 as well as the odor intensity maps represented in Figure 3.9.

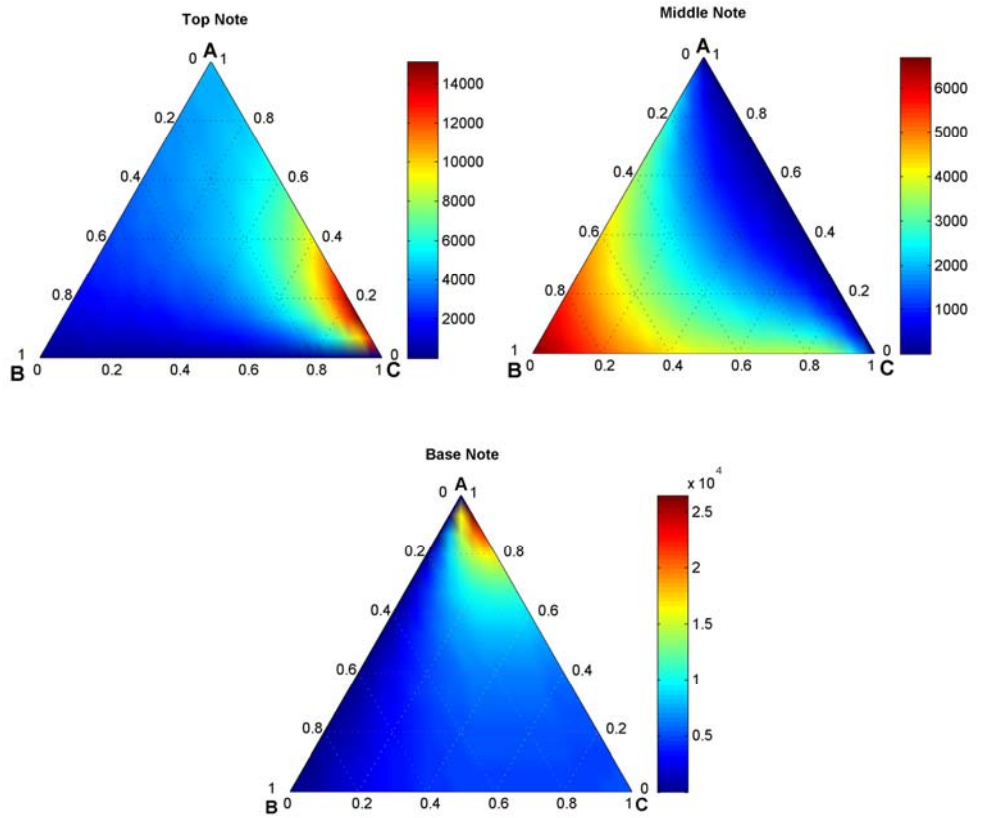


Figure 3.8 – PTDs showing the odor intensity map for each fragrance ingredient in the ternary mixture of limonene (top note) + geraniol (middle note) + vanillin (base note).

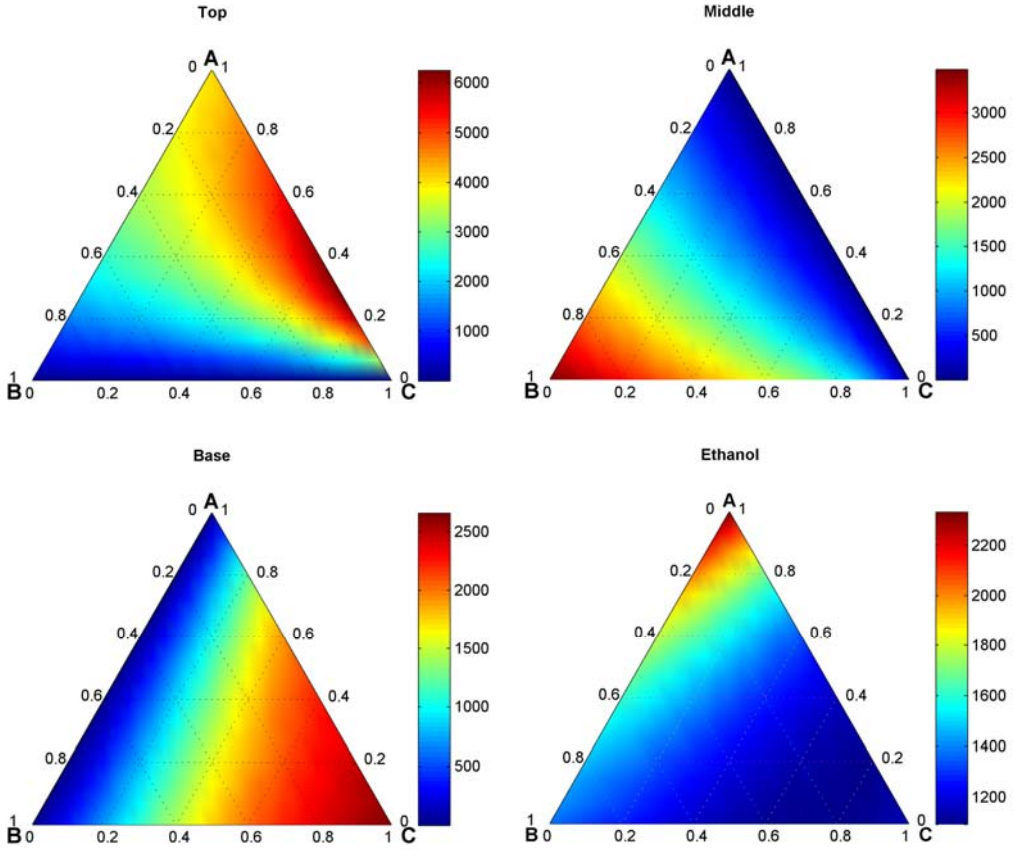


Figure 3.9 - Odor intensity map of each fragrance ingredient in the ternary mixture of limonene (top note) + geraniol (middle note) + vanillin (base note) + ethanol ($x_i = 0.50$, solvent).

Despite this type of projections may serve to provide some insights of the quaternary behavior, it is clear that only with the Perfumery Quaternary-Quinary Diagram (PQ2D®) the whole composition range can be shown.

Nevertheless, the PTD® can be used to show the behavior of the quaternary system (A + B + C + S), when applied to its four ternary subsystems: (A + B + C), (A + B + S), (A + C + S), and (B + C + S). As aforementioned, the four faces of the tetrahedric diagram match with the four ternary subsystems that compose the perfume quaternary mixture. Thus, in order to facilitate the comprehension of the following tetrahedric diagrams, the PTD® of the four ternary subsystems for each quaternary mixture were calculated. The different PTDs of the four quaternary systems (limonene + geraniol + base note + solvent) are represented together in Figure 3.10 as the projection of the faces of the tetrahedron. The tetrahedron can be constructed from each diagram just "pushing up" the three outer vertices (S), so they join together in the space above the central triangle (base of the tetrahedron). It is important to mention that Figure 3.10 only shows the limits (faces) of the tetrahedron, thus no information about the quaternary system behavior is given.

The effect of the base note on perfume formulation can be clearly seen in the PTDs showed before and especially in Figure 3.10, since the perceived odor character presented in the PTDs is significantly different for the perfume mixtures. On one side, it should be highlighted that tonalide will only be noticed for very high concentrations, that is nearly pure, since it has a very low vapor pressure (see Table 3.1). This odorant was widely used in perfume formulations (although its use is currently more restricted), acting as a fixative in the perfume mixture, thus influencing the molecular interactions between the different fragrant species and their evaporation. On the other side, both galaxolide and ambrox present a dominant character over all other components for a wide range of compositions in the PTD®. In this way, it is seen that the effect of the base note on the perceived odor character of these quaternary systems increases in the order of dominance as: tonalide << vanillin < galaxolide < ambrox (Figure 3.10 – (1), (2), (3) and (4), respectively).

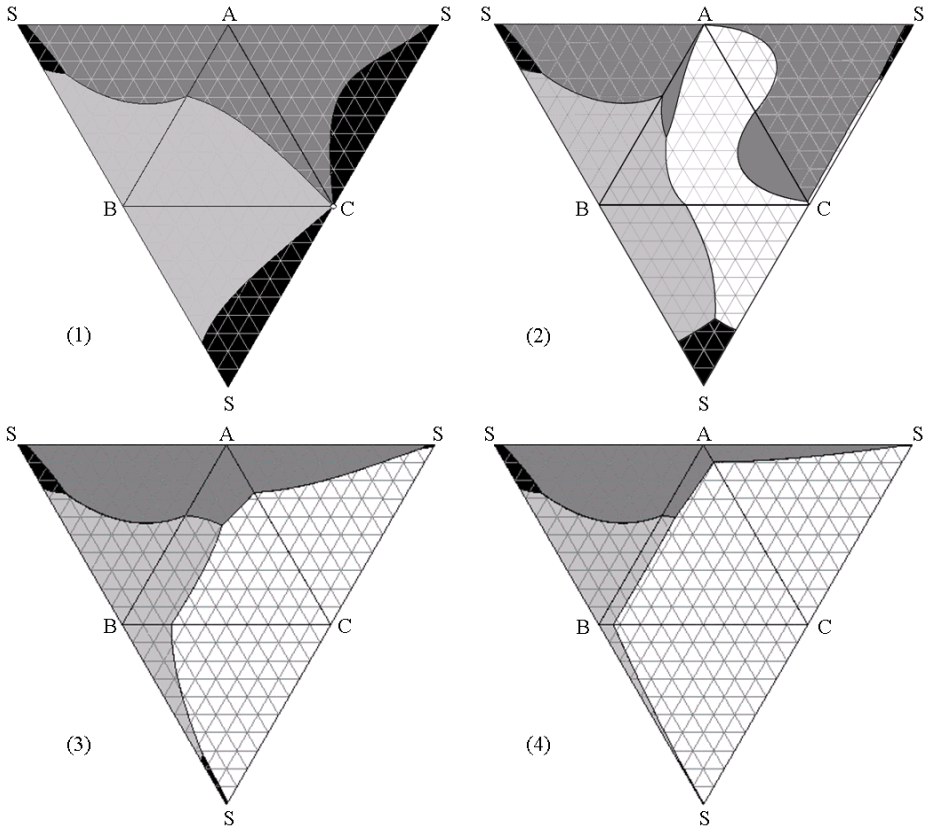


Figure 3.10 – PTD® of the ternary subsystems for the four quaternary perfume mixtures. The figures are the projection of the tetrahedron faces. (A) Top note (Dark gray, Limonene); (B) Middle note (Light grey, Geraniol); (C) Base note (White, 1: Tonalide, 2: Vanillin, 3: Galaxolide, 4: Ambrox); (S) Solvent (Black, Ethanol).

Each PTD® on the top left side of the projection of the tetrahedron faces in Figure 3.10 corresponds to the ternary subsystem (A + B + S) and is equal for all four quaternary systems. As it was stated before, the diagrams in Figure 3.10, represent only the outside of the tetrahedron (the ternary subsystems), and no information of the inside (the quaternary system itself) is given. Thus, it shows the limiting behavior of the PTD® methodology when applied to quaternary systems. Nevertheless, it is easier to visually and understand the whole tetrahedron once its outer surface is known. The Perfumery Quaternary-Quinary Diagrams (PQ2D®) for the four perfume quaternary systems studied are shown and discussed ahead.

3.5.2. Application of the PQ2D®

In order to show the whole behavior of the perfume system, each fragrance odor volume is presented separately in Figure 3.11 to Figure 3.14. The PQ2Ds confirm what was expected from inspection of the PTD® diagrams of the ternary subsystems and quaternary mixtures: the size of the odor volume for the different base notes increases in

the order of tonalide <<< vanillin < galaxolide < ambrox. Accordingly, the sizes of the odor volumes for the other three components in the mixture (limonene, geraniol and ethanol) decrease as the size of the base note odor volume increases. The perception of tonalide is restricted to nearly the pure component, and it will not be perceived in almost any mixture (at least strongly). Galaxolide and ambrox present the largest odor volumes, which dominate most of the tetrahedric diagram (and thus, most of the composition spectrum). The size of the vanillin odor volume is somewhere in the middle.[1]

The high saturated vapor pressure of ambrox which is of the same order of magnitude as the middle note (geraniol) is responsible for this unexpected behavior. The fact is that the ratio of $K_{odor} = (P^{sat}{}_C M_{wi})/(ODT_C RT)$ presented in Table 3.1 which is used for the calculation of the OV (using Equation 3.4), is significantly high for both ambrox and galaxolide, resulting in very volatile base notes. This is why perfumers usually use them in low molar fractions or highly diluted, when they introduce these fragrances in a perfume formulation.

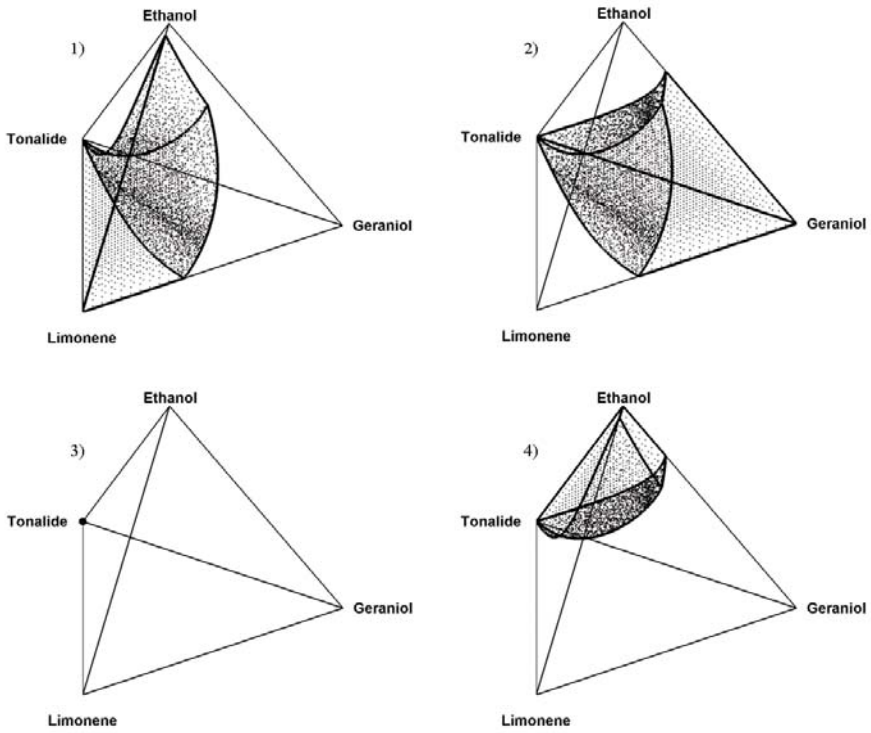


Figure 3.11 - Perfumery fragrance volumes: 1) limonene, 2) geraniol, 3) tonalide, 4) ethanol.

[1] All PQ2Ds can be seen elsewhere as a video file to show how the different odor volumes match together in the tetrahedron.

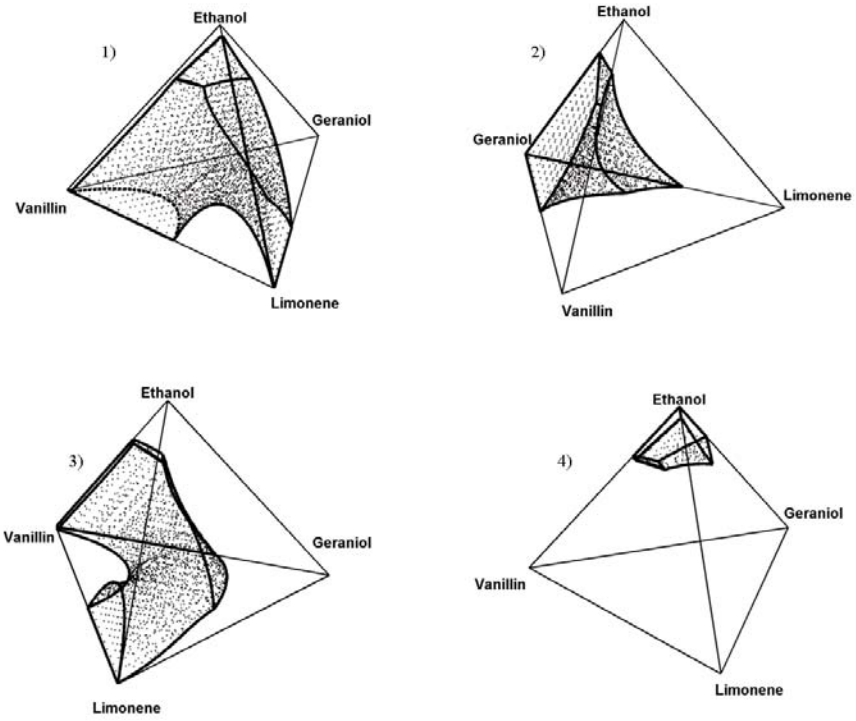


Figure 3.12 - Perfumery fragrance volumes: 1) limonene, 2). geraniol, 3) vanillin, 4) ethanol.

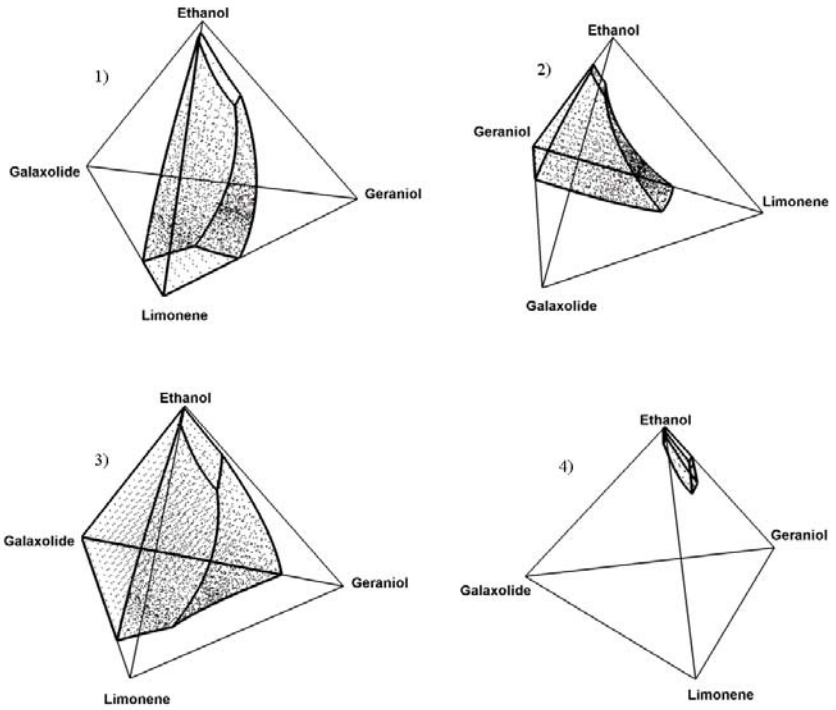


Figure 3.13 - Perfumery fragrance volumes: 1) limonene, 2) geraniol, 3) galaxolide, 4) ethanol.

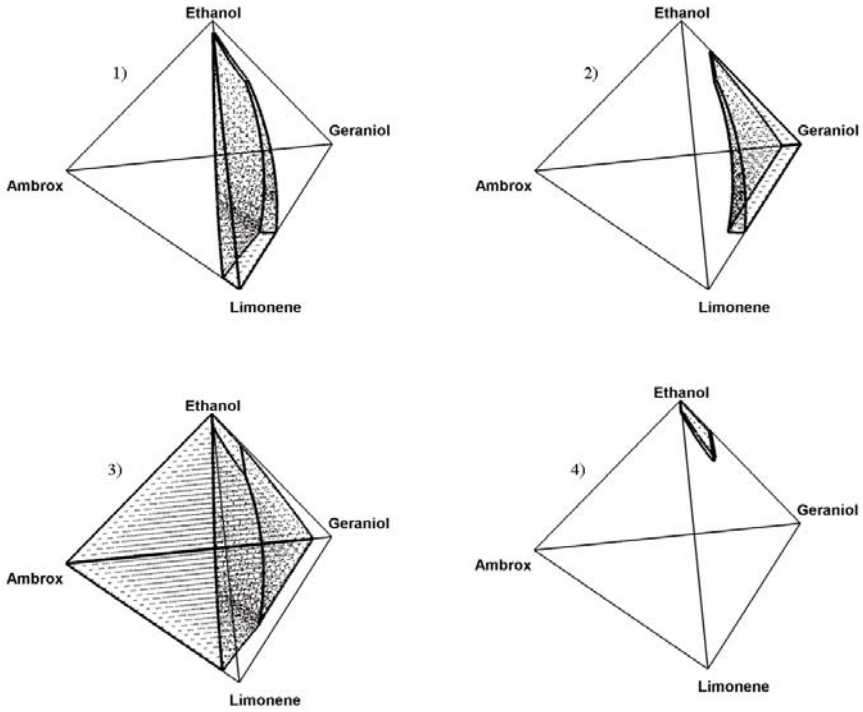


Figure 3.14 - Perfumery fragrance volumes: 1) limonene, 2) geraniol, 3) ambrox, 4) ethanol.

The factors governing the behavior of the odor value in the perfume mixtures have been detailed above. To provide some more insights, we can rewrite Equation 3.4 as:

$$OV_i = \gamma_i \cdot x_i \cdot \left(\frac{P_i^{sat} \cdot M_i}{ODT_i \cdot R \cdot T} \right) \tag{3.14}$$

Among the three factors in Equation 3.14 the composition, x_i, varies from 0 to 1, while the activity coefficient (γ_i) can vary about one or two orders of magnitude. The third factor (K_{odor}) is a constant value which depends on the experimental temperature (T), and the pure component properties (saturated vapor pressure, molecular weight and odor threshold). Table 3.1 presents the values for this constant *(K_{odor})* calculated for each component used in the fragrance mixtures while in Figure 3.15 it is shown a comparison for the base notes only.

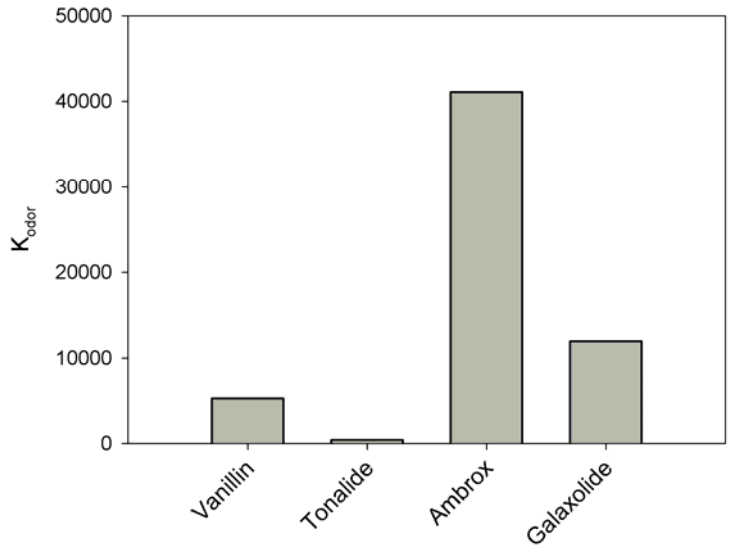


Figure 3.15 - Variation of the K_{odor} value for the different base notes.

It is clearly seen that the value of the constant K_{odor} increases in the same way as the size of odor volumes for the base notes: tonalide <<< vanillin < galaxolide < ambrox. The increase is especially significant from tonalide to vanillin, which may explain why the first can not be perceived when mixed with other fragrant components. It is to highlight also that tonalide has the lowest saturated vapor pressure and the highest odor threshold, resulting in a K_{odor} value that is several orders of magnitude lower than the others. Both ambrox and galaxolide have a high ratio (see Table 3.1) which explains why they are strongly perceived by the human nose for a wide range of perfume compositions.

3.5.3. Application of the PQ2D® to perfumery quinary systems

The PQ2D methodology can also be extended to perfumery quinary mixtures in the same way that quaternary mixtures could be applied to the PTD® methodology, although with some (graphical) limitations. When the PQ2D methodology is to be used with a quinary mixture, it is necessary to define pseudo-quaternary compositions. These are obtained by recalculating the quaternary molar fractions of some four fragrant components in a free basis of the fifth component, as follows:

$$x_A^{'} = \frac{x_A}{x_A + x_B + x_C + x_S},\ x_B^{'} = \frac{x_B}{x_A + x_B + x_C + x_S},$$

$$x_C^{'} = \frac{x_C}{x_A + x_B + x_C + x_S},\ x_S^{'} = \frac{x_S}{x_A + x_B + x_C + x_S} \tag{3.15}$$

where x'_i indicates a pseudo-quaternary composition for each of the four fragrant components (*A, B, C, S*) in the quinary system (*A, B, C, D, S*).

The first predicted quinary system consists of a top note (limonene), a middle note (geraniol), two different base notes (vanillin and tonalide) and a solvent (ethanol). First, the component used at fixed compositions has to be chosen. As tonalide is only perceived when nearly pure (Figure 3.10 and Figure 3.11) it was selected as fixed component. The PTDs for the different quinary systems simulated are presented in Figure 3.16, considering constant mole fractions of tonalide: $x_{tonalide} = 0.10$, $x_{tonalide} = 0.15$ and $x_{tonalide} = 0.20$, respectively. The distribution of the odor character in terms of the odor volumes for this system is presented in Figure 3.17 to Figure 3.19 using the PQ2D® methodology. Once more each fragrance odor volume is presented separately in order to have a better perception of the distribution of the perceived odor.

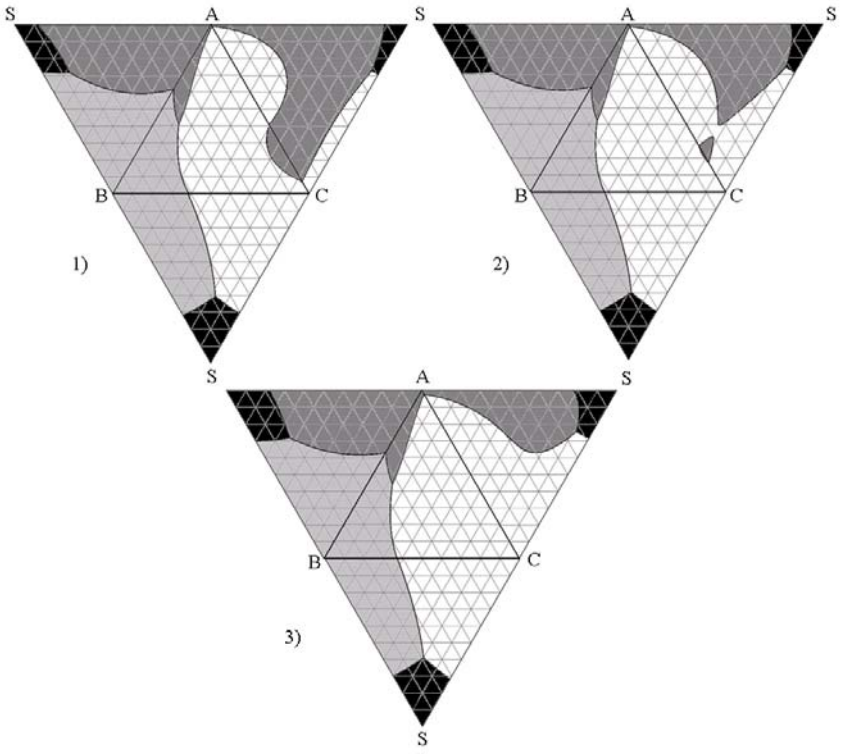


Figure 3.16 - PTD® of the ternary subsystems for the three quinary perfume mixtures: 1) $x_{tonalide} = 0.10$, 2) $x_{tonalide} = 0.15$, 3) $x_{tonalide} = 0.20$. (A) Top note (Dark gray, Limonene); (B) Middle note (Light gray, Geraniol); (C) Base note (White, Vanillin); (S) Solvent (Black, Ethanol).

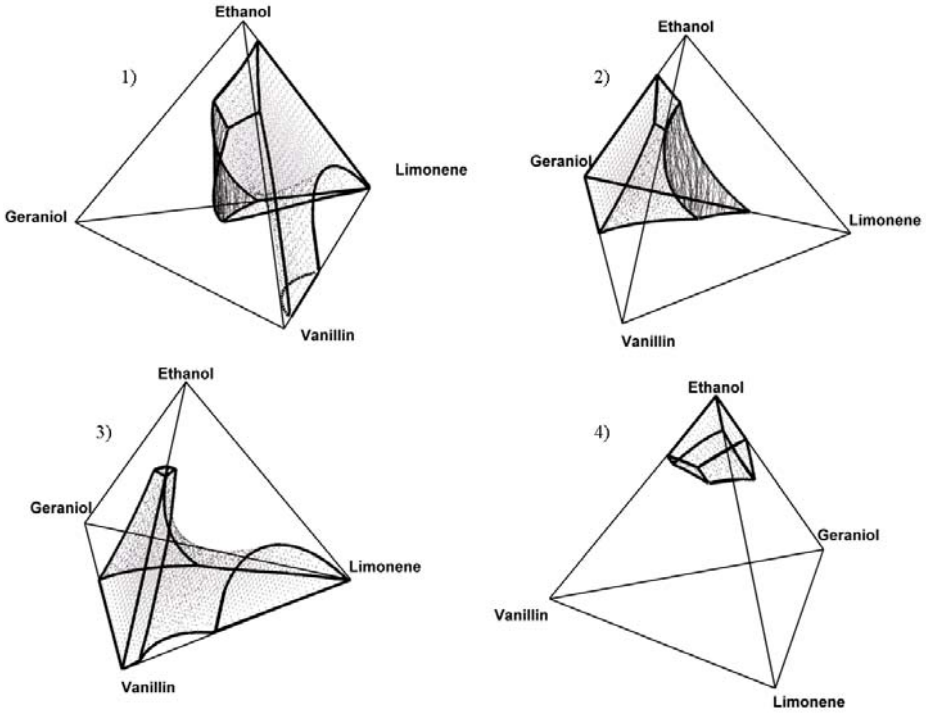


Figure 3.17 - Odor volumes for each fragrance of the quinary mixture with $x_{tonalide}$= *0.10*: 1) limonene, 2) geraniol, 3) vanillin, 4) ethanol.

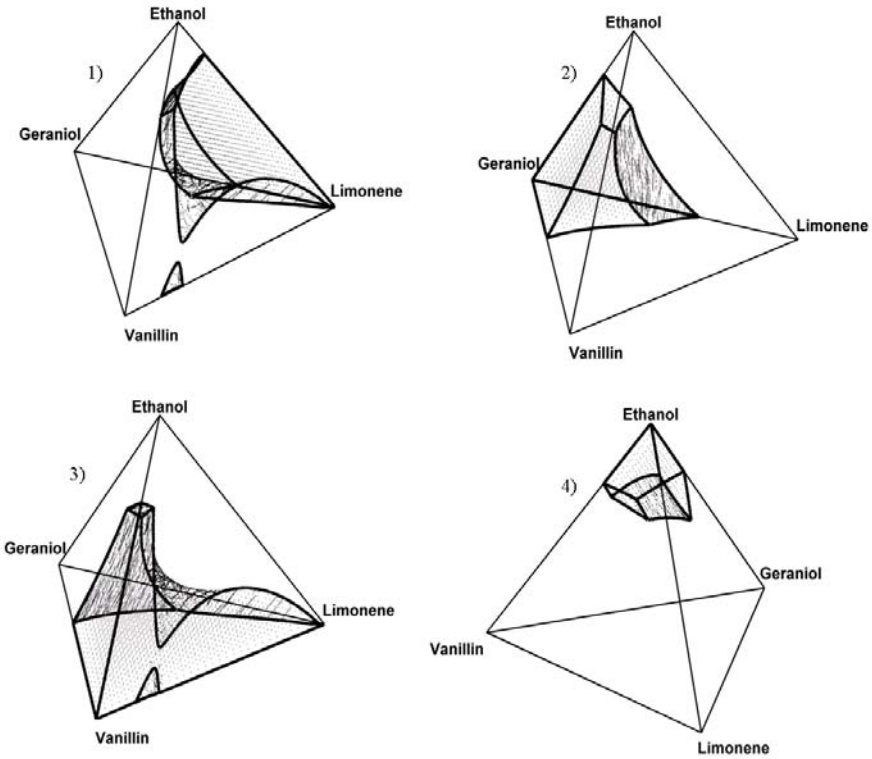


Figure 3.18 - Odor volumes for each fragrance of the quinary mixture with $x_{tonalide}$= *0.15*: 1) limonene, 2) geraniol, 3) vanillin, 4) ethanol.

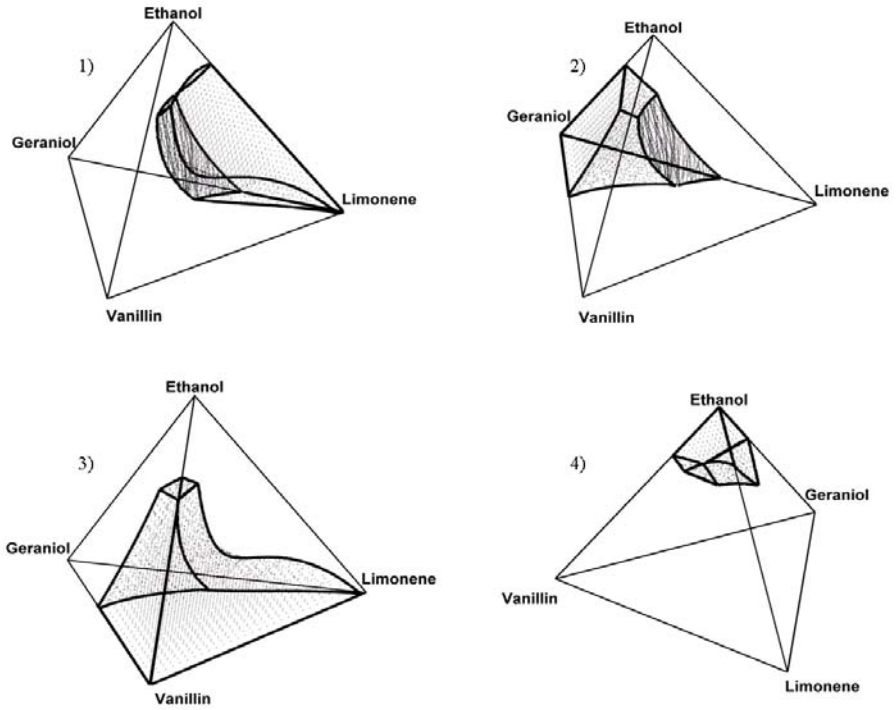


Figure 3.19 - Odor volumes for each fragrance of the quinary mixture with $x_{tonalide}= 0.20$: 1) limonene, 2) geraniol, 3) vanillin, 4) ethanol.

For the perfume quinary system it is possible to see that incorporating a second base note (tonalide) in the perfume formulation, results in different predictions of the odor character (Figure 3.12 and Figure 3.16 to Figure 3.19). In this way, when the mole fraction of tonalide is increased in the perfume mixture, the odor volume for limonene tends to diminish and for $x_{tonalide} = 0.20$ it is restricted to a volume near the corner of the pure component. On the opposite direction, the odor volume for vanillin increases with the concentration of tonalide in the mixture, showing that it tends to be more easily "pushed out" of the solution and, thus, more intensely perceived by the human nose. Middle note (geraniol) and ethanol odor volumes remain similar to those of the quaternary mixture – without tonalide (see Figure 3.12). This indicates that the fixative properties of tonalide have a retention effect on limonene, allowing it to evaporate slower and so changing the vapor-liquid equilibrium of the perfume mixture. On the opposite direction, it pushes out vanillin to the headspace so that it gets more strongly perceived.

Within the formulation of perfumes not only ethanol but also water is an essential component (especially in more diluted fragrances) in order to obtain the so desired aroma of fragrances. In this way, water was included in two of the previous perfumery

systems to show its influence in the resulting quinary systems (x_{water} = *0.45*). The behavior of the quinary systems of limonene + geraniol + vanillin or galaxolide + ethanol + water is presented in Figure 3.20 to Figure 3.22.

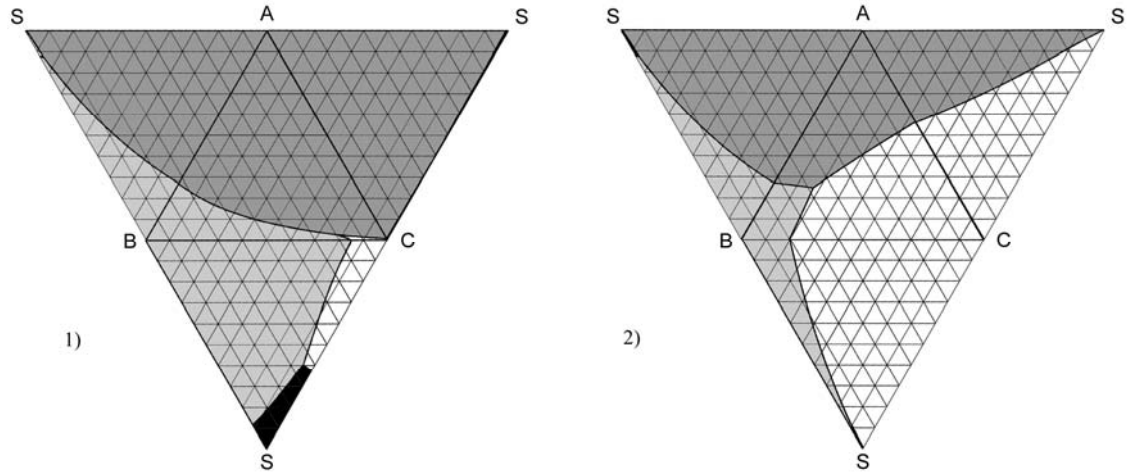


Figure 3.20 - PTD® of the ternary subsystems for the quinary perfume mixtures: 1) limonene + geraniol + vanillin + ethanol + water and 2) limonene + geraniol + galaxolide + ethanol + water. (A) Top note (Dark gray, Limonene); (B) Middle note (Light gray, Geraniol); (C) Base note (White, Vanillin or Galaxolide); (S) Solvent (Black, Ethanol).

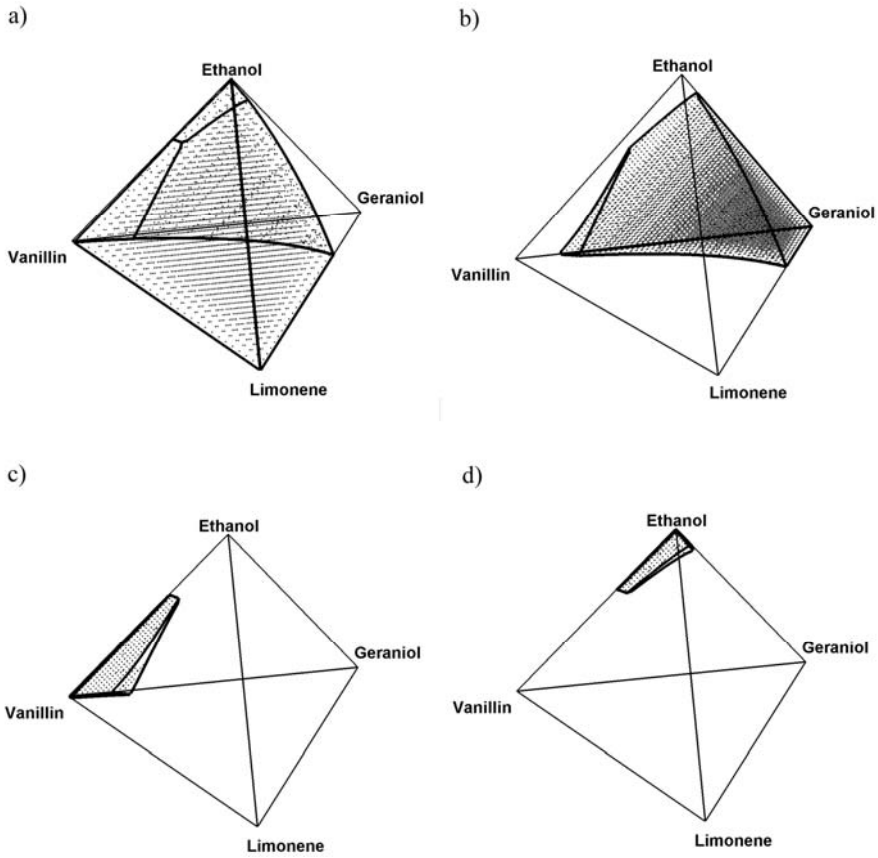


Figure 3.21 - Perfumery fragrance volumes for the quinary system 1) limonene + geraniol + vanillin + ethanol + water: a) limonene, b) geraniol, c) vanillin, d) ethanol. Water composition was set equal to 45% (mol/mol).

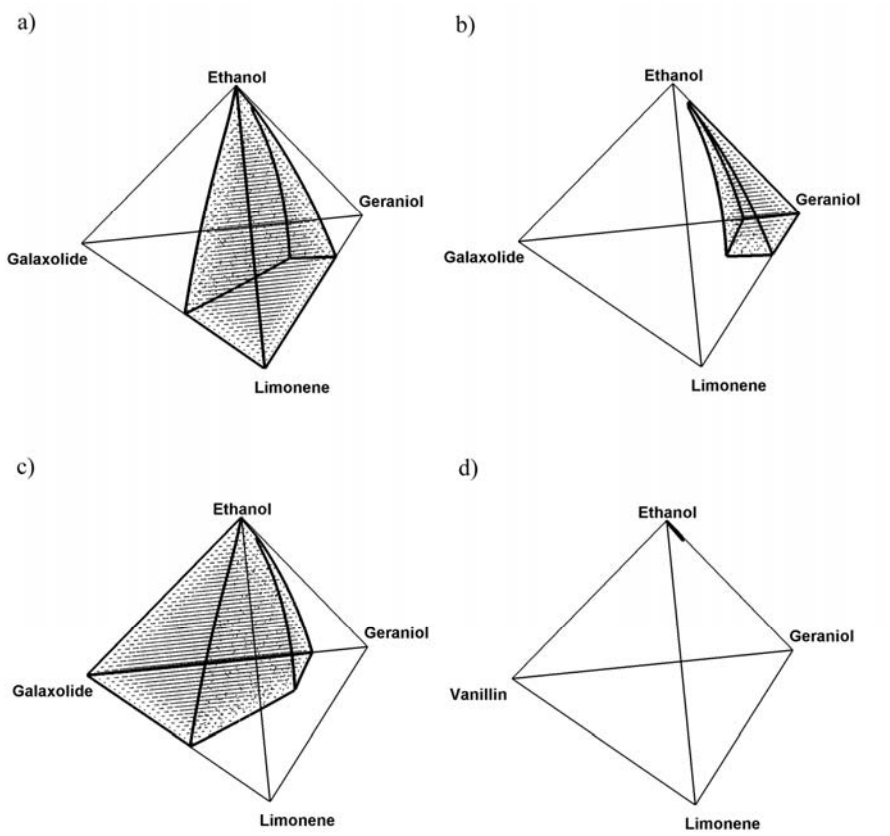


Figure 3.22 - Perfumery fragrance volumes for the quinary system 2) limonene + geraniol + galaxolide + ethanol + water: a) limonene, b) geraniol, c) galaxolide, d) ethanol. Water composition was set equal to 45% (mol/mol).

It is seen that introducing water the perfume formulation completely changes the shapes of the odor volumes for the different components. Even more striking is the fact that two interesting phenomena are seen for both systems: the non-polar limonene seems to be pushed out of the solution more strongly in the presence of water and so its odor volume is larger; and the polar component ethanol is more retained in the solution when water is included, thus slowing down its evaporation rate and limiting its initial perception. Remarkably, these phenomena are supported by experimental evidences from perfumery: Later on Chapter 7, we will address this question of the effect of water with a deeper analysis.

3.6. Perfumery octonary system

As previously seen, the developed PQ2D® methodology uses a graphic representation of a three dimensional view using a tetrahedron to map the perceived odor of quaternary and quinary fragrance mixtures. However, if we want to introduce more fragrance

ingredients it becomes difficult (or even impossible) to visualize it in its entirety since plotting and understanding of more than three dimensions on a plane paper is quite complex. Thus, although the methodology works for *N* component mixtures of fragrance ingredients (as well as the developed software), it is restricted by our own limitation of the visual perception. It is not possible to represent in a visual way (*e.g.* using a polyhedron) higher dimensional systems in their entirety, once equation 3.8 has to be satisfied. One way to tackle this problem would be by performing projections and cuts to reduce dimensionality. This visualization approach was already used in high-dimensional liquid-liquid equilibrium (LLE) phase diagrams, using the Jänecke or normalization projection, the parallel or lumping projection, the Cruickshank projection or different isobaric and isothermal cuts (Harjo*, et al.*, 2004). Despite being valuable for reducing dimensionality, some of these projections continue to be difficult to visualize.

In this work, an octonary perfume system was considered and its odor character was predicted using the PQ2D® methodology. This perfume mixture included six fragrance ingredients (Limonene + α-pinene + Geraniol + Linalool + Vanillin + Galaxolide) and two solvents (Ethanol + Water). Then, this fragrance system consists of two top notes, two middle notes and two base notes in a binary solvent matrix. In order to be possible to represent the headspace behavior of this octonary mixture in a three dimensional view using the PQ2D®, a constraint was introduced in the chemical compositions of the components. For that reason, in each vertex of the tetrahedron two components of the mixture were placed like two top notes, two middle notes, and two base notes. Moreover, wherever in the PQ2D, a specific ratio of those two components must be verified so that the composition relationship of each couple is kept constant. In this case, two different component ratios were considered: one for the fragrance ingredients and another for the solvents as shown in Equations 3.16 and 3.17.

$$x_j = \frac{0.55}{0.45} x_i \tag{3.16}$$

$$x_{S_2} = \frac{0.60}{0.40} x_{S_1} \tag{3.17}$$

where *i* and *j* correspond to each fragrance couple placed in a vertex of the tetrahedron, while s_1 and s_2 correspond to ethanol and water, respectively. Following this reasoning, in each vertex of the tetrahedron there will be a binary mixture with a specific ratio of

composition and across each edge there will be a quaternary mixture where every two components have a composition that is determined by its couple.

The odor character of the subsystems composing the octonary perfume mixture is shown in Figure 3.23 for the different PTDs of the tetrahedron diagram.

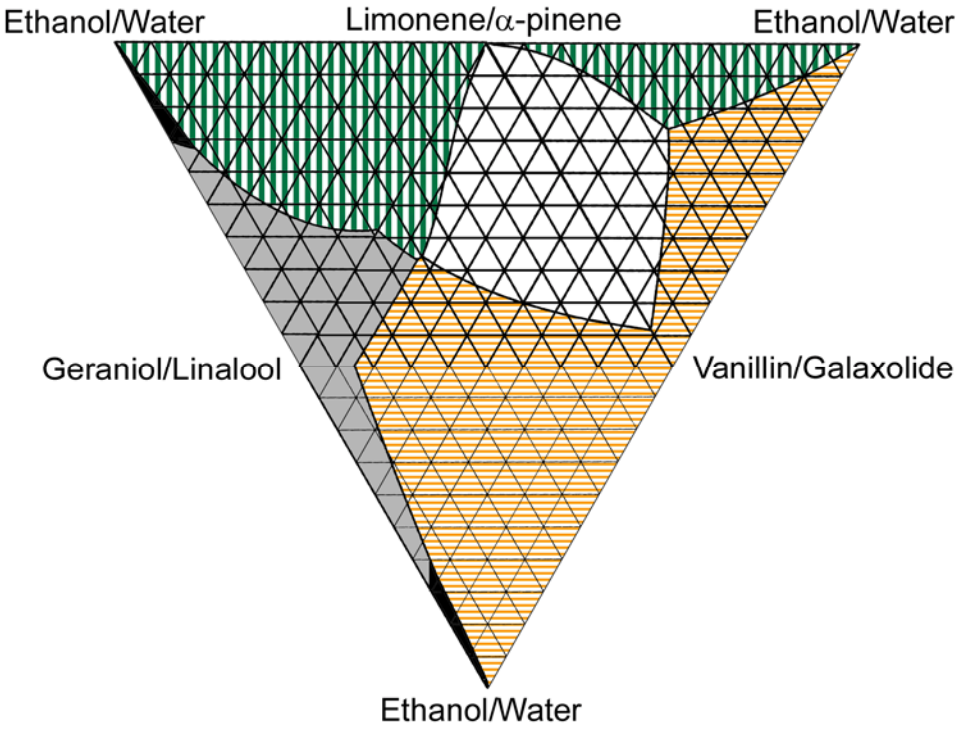


Figure 3.23 – PTD® of the subsystems composing the octonary perfume mixture. The figures are the projection of the tetrahedron faces. Limonene: no odor; α-pinene: bold vertical stripes; Geraniol: light grey; Linalool: no odor; Vanillin: white; Galaxolide: light horizontal stripes; Ethanol: black; water: no odor.

The whole behavior of the octonary perfume system can be seen by using the PQ2D® diagrams, showing the odor volumes of each component within the mixture as presented in Figure 3.24. Some of the fragrance ingredients and solvents have no representative odor volume for this mixture once they are not more intensely perceived than the other fragrances. Nevertheless, they may contribute to the odor as a *nuance* or a secondary odor. Moreover, there will not be an odor volume for water since we know it is odorless. From the predicted results obtained for this octonary mixture of fragrance ingredients it is possible to draw some conclusions: *i)* in a multi-component mixture not all fragrance components are strongly perceptible by the human nose; *ii)* the combination of top notes may lead to a stronger initial perception of only one of those (depending on the composition) which explains the fact that limonene has no odor volume; *iii)* base notes play an important role in perfumery not only for the fixative and long lastingness effects

but also because their smell may be perceived from the beginning as background odors (odor volumes of vanillin and galaxolide); *iv)* a stronger perception of the fragrance ingredients reduces the range of compositions (odor volume) where ethanol is strongly perceived which is undesired to be smelled for the perfume product.

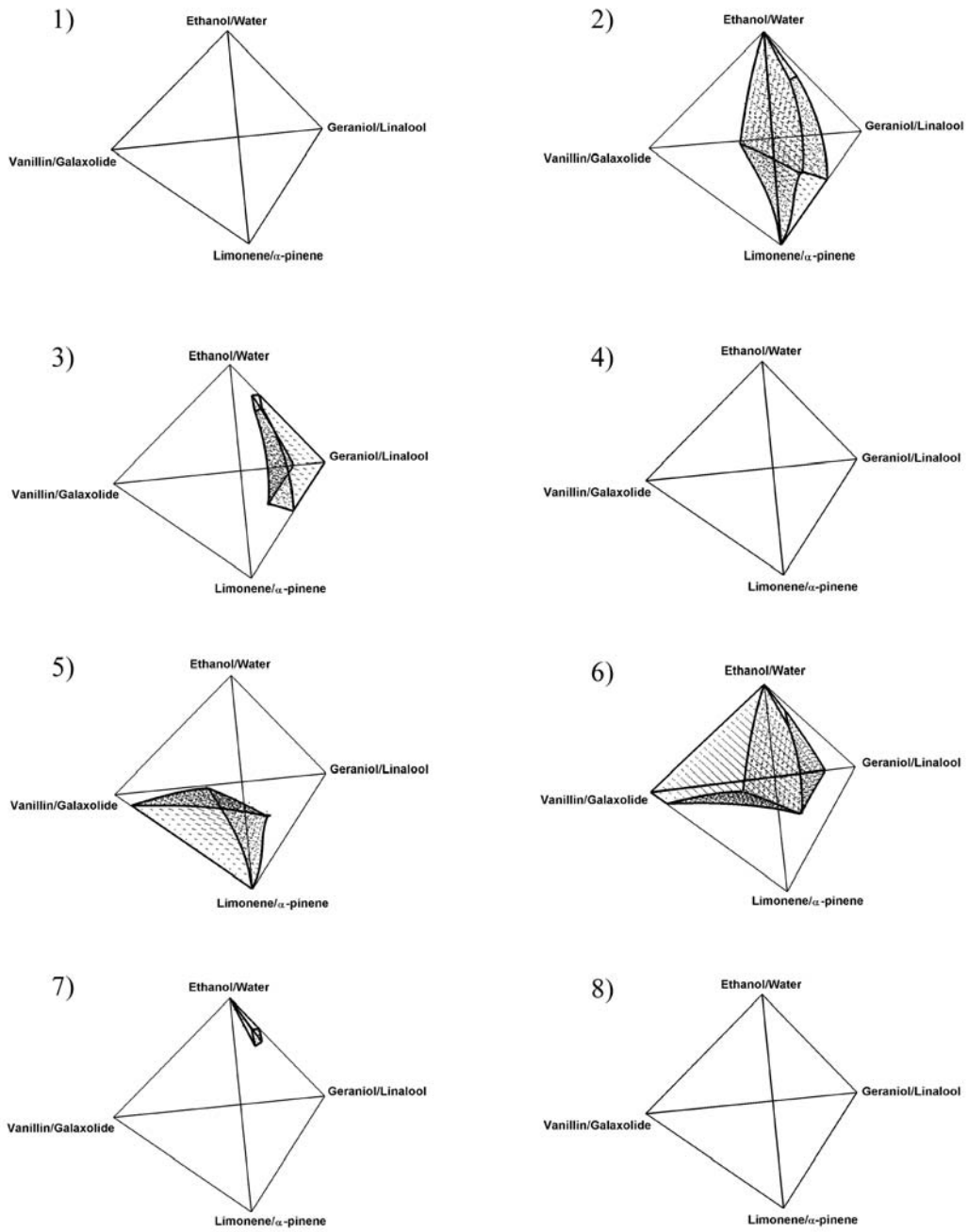


Figure 3.24 - Perfumery fragrance volumes for the octonary perfume system: 1) limonene, 2) α-pinene, 3) geraniol, 4) linalool, 5) vanillin, 6) galaxolide, 7) ethanol, and 8) water.

3.7. Conclusions

A methodology to describe the odor perception of quaternary perfume mixtures in the headspace has been presented. The methodology uses the concept of Perfumery Quaternary-Quinary Diagrams (PQ2D®) which employs tetrahedric diagrams to represent the composition of quaternary and quinary systems. For this representation it is necessary a coordinate transformation from tetrahedric to Cartesian coordinates, which has been given.

As an example of this methodology, the effect of four different base notes (Tonalide, Vanillin, Galaxolide and Ambrox) in the perception of quaternary perfume mixtures of the type (Limonene + Geraniol + base note + Ethanol) has been studied. The odor perception through the whole composition spectrum has been calculated and was presented here. The influence of the physicochemical properties of the pure components in the odor perception has also been highlighted.

The application of the methodology to quinary systems, keeping one component at a fixed composition, has also been shown for different perfumery systems. Finally, the PQ2D® was also applied to octonary mixtures by reducing dimensionality and allowing mapping the perceived scent of more complex mixtures with two types of top, middle and base notes plus two solvents.

The methodology presented here also confirms some experimental evidences from perfume formulation: tonalide is known in perfumery as a fixative, because it retains more volatile compounds in the perfume; the simulations presented confirm a retention effect on limonene; galaxolide and ambrox are powerful base notes used and that is why they are commonly used in high dilution for perfume formulations.

This methodology is fast and convenient for the prediction of the odor perception of the headspace of perfume mixtures. In this way, repetitive trial-and-error experimental assays can be avoided in perfume formulation.

3.8. References

Abrams, D., Prausnitz, J. M., Statistical thermodynamics of liquid mixtures: A new expression for the excess Gibbs energy of partly or completely miscible systems, *AIChE Journal* 21, 116–128, 1975

Balk, F., Ford, R., Environmental risk assessment for the polycyclic musks AHTN and HHCB in the EU - I. Fate and exposure assessment, *Toxicology Letters*, 111, 57–79, 1999

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Chapman, J., MATLAB programming for engineers, California, Brooks Cole Publishing Company, 2000

Chemspider, Database of Chemical Structures and Property Predictions - Royal Society of Chemistry, from http://www.chemspider.com/Default.aspx, Last Accessed on February, 2011

Curtis, T., Williams, D. G., Introduction to Perfumery, New York, Ellis Horwood, 1994

Fráter, G., Müller, U., Kraft, P., Preparation and Olfactory Characterization of the Enantiomerically Pure Isomers of the Perfumery Synthetic Galaxolide, *Helvetica Chimica Acta*, 82, 1656-1665, 1999

Fredenslund, A., Jones, R., Prausnitz, J. M., Group-contribution estimation of activity coefficients in nonideal liquid mixtures, *AIChE Journal*, 21, (6): 1086-1099, 1975

Guentert, M., The Flavour and Fragrance Industry - Past, Present, and Future, Flavours and Fragrances - Chemistry, Bioprocessing and Sustainability, Berger, Berlin, Springer - Verlag, 2007

Harjo, B., Ng, K. M., Wibowo, C., Visualization of High-Dimensional Liquid-Liquid Equilibrium Phase Diagrams, *Industrial & Engineering Chemistry Research*, 43, (3566-3576): 2004

Klamt, A., COSMO-RS: from quantum chemistry to fluid phase thermodynamics and drug design, Amsterdam, Elsevier, 2005

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AIChE Journal*, 51, (10): 2834-2852, 2005

Mata, V. G., Rodrigues, A. E., A new methodology for the definition of odor zones in perfumery ternary diagrams, *AIChE*, 52, (8): 2938-2948, 2006

MathWorks, Partial Differential Equation Toolbox - ComsoLab MATLAB's Users Guide, 2002

Nocedal, J., Wright, S., Numerical Optimization, New York, Springer, 1999

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Renon, H., Prausnitz, J., Local compositions in thermodynamic excess functions for liquid mixtures, *AIChE*, 14, 135–144, 1968

Tochigi, K., Tiegs, D., Gmehling, J., Kojima, K., Determination of new ASOG parameters, *Journal of Chemical Engineering Japan*, 23, (4): 453-463, 1990

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

Walas, S., Phase equilibria in chemical engineering, Boston, Butterworth, 1985

Wei, N., The 3-dimensional phase diagram in quaternary systems of polymers and solvents, *J. Appl. Polym. Sci.*, 28, 2755-2766, 1983

Chapter 4

Modeling of Odor Detection Thresholds using Basic Physical Properties*

"Prediction is very difficult, especially about the future!"

Nils Bohr (1885 - 1962)

For the perception of odors, the human being needs, at first, that his olfactory mechanism detects the presence of odorant molecules and, finally, the neuronal processes to transmit some coded information. In this Chapter 4, the olfactory mechanism and the processes behind the detection of odors are introduced. Odor detection thresholds (ODT) are at the bottom of the perceived intensity scale of odors and so they play an important role for both their detection and quantification. The experimental determination of ODTs is laborious and because it involves experiments with humans, it is dependent of physiological variability. In this way, the prediction of ODTs would be of great interest. However, such predictions proved to be too difficult to obtain. Nevertheless, several models for odor detection thresholds have been proposed and are reviewed in this Chapter, highlighting their pros and cons. Moreover, a simple physicochemical model based on physical properties (vapor pressure, solubility in water and octanol/water partition coefficient) has been derived. The principles underlying this model are the transport processes of the odorants from air to the olfactory neurons in the nasal epithelium. A linear regression was applied to ODTs measured from different

* This Chapter is partly based on the paper from Rodríguez, O, Teixeira, MA, Rodrigues, AE, Prediction of odor detection thresholds using partition coefficients, Flavour and Fragrance Journal, in press.

authors separately, showing similar regression parameters. Finally, a general linear regression was obtained for odor detection threshold data from several authors for a total of 121 odorant chemicals. This regression allows a preliminary estimation of ODTs with fair accuracy using available literature data only.

4.1. Introduction

Sensory perception refers to the human five senses (olfaction, gustation, vision, audition and touch) and how environmental stimuli are detected and subsequently interpreted by the brain. Although the three latter senses are reasonably understood, the mechanisms underlying the former two perceptual continua are still not clear. Nevertheless, they are relevant for a number of everyday situations and for different research fields (biophysics, physiology, neuroscience, food & fragrance chemistry). Recently, the interest has also been driven by economic factors, since sensory perception influences life quality and provides valuable information for product design & marketing (Cussler*, et al.*, 2010). For this, understanding and modeling customer perception of a product is critical for the development of added-value and performance products (Costa, 2006; Bagajewicz, 2007; Herrmann, 2007; Cussler*, et al.*, 2010). For these reasons, over the last two decades, the understanding of the biophysical mechanisms involved in the olfactive process has been thoroughly improved (Fleischer*, et al.*, 2009). Despite this recent upsurge of interest in the field of olfaction and the importance of the landmark work from Buck and Axel (Buck and Axel, 1991; Axel, 2005; Buck, 2005), there are several issues that still remain not completely understood.

4.1.1. Odor perception mechanism

Nowadays, the olfaction process at the biological level can be considered as the following sequence of events (Hau and Connell, 1998; Hau*, et al.*, 1999; Abraham*, et al.*, 2002; Meierhenrich*, et al.*, 2004): the odorant molecules present in air enter the nose when breathing or sniffing. There, part of them will dissolve in the mucus layer and then, bind to olfactory receptor (OR) proteins (G coupled proteins with seven transmembrane domains) located on the cilia of olfactory sensory neurons (OSN) in the nasal epithelium (Buck and Axel, 1991; Meierhenrich*, et al.*, 2004). OSNs are bipolar neurons with a dendrite formed by tens of cilia that elongate into the olfactory mucus.

This process triggers signal transduction cascades within OSNs, constituting a key step in the primary olfactory perception. OSNs are linked to the olfactory bulb and each one synapses in only one glomerulus, transmitting signals to the olfactory cortex. Nevertheless, prior to reach the ORs, odorants have to cross the aqueous mucus phase. This process can be done with the help of odorant binding proteins (OBP) which may be possible carrier candidates for odorant molecules. OBPs are small soluble proteins found in the mucus layer of the olfactory epithelium of many vertebrate species. These proteins reversibly bind to odorants having dissociation or binding constants in the micromolar range and different mechanisms of their role have been proposed (Getz and Lansky, 2001; Taylor*, et al.*, 2008). These mechanisms are supported by experiments (mainly) performed under equilibrium conditions, although little is known about the dynamics of the transport process. Even so, it is seen a fast mass transfer of odorant molecules from air to OBPs, although its interaction with ORs is still not clear (Taylor*, et al.*, 2008; Yabuki*, et al.*, 2010). In turn, the binding of odorant molecules with ORs shows a multiplicity of combinatorial coding which hampers the understanding and modeling of olfactory perception: an OR may recognize different odorants and simultaneously, each odorant may bind to different ORs (Firestein, 2001). Additionally, different odorants can be recognized by different combinations of ORs. Moreover, for a single odorant, the variation of its concentration can change its receptor code, since it is observed that at higher concentrations more ORs are involved in the odor perception (Buck, 2005). Anyway, the odorant-OR biochemical binding process may be evaluated by a dissociation constant which would represent a measure (of the strength) of the affinity between receptors and their ligands (odorants). In general, if we assume the concentration of odorants as [O], the concentration of unbound ORs as [OR] and, finally, the concentration of bound ORs as [O-OR], then the odorant-olfactory receptor binding process can be represented by:

$$[O]+[OR] \rightleftharpoons [O-OR] \tag{4.1}$$

where the equilibrium constant of this reaction is given by:

$$K = \frac{[O][OR]}{[O-OR]} = \frac{1}{K_D} \tag{4.2}$$

where K_D is the dissociation constant previously referred (Taylor*, et al.*, 2008).

In this way, the discovery of a number of different types of receptors involved in the detection of olfactory signals has revealed a structural and functional diversity that was not expected until few years ago (Spehr and Munger, 2009). In Figure 4.1 a simple and schematic view of this process is presented for a type of olfactory receptors.

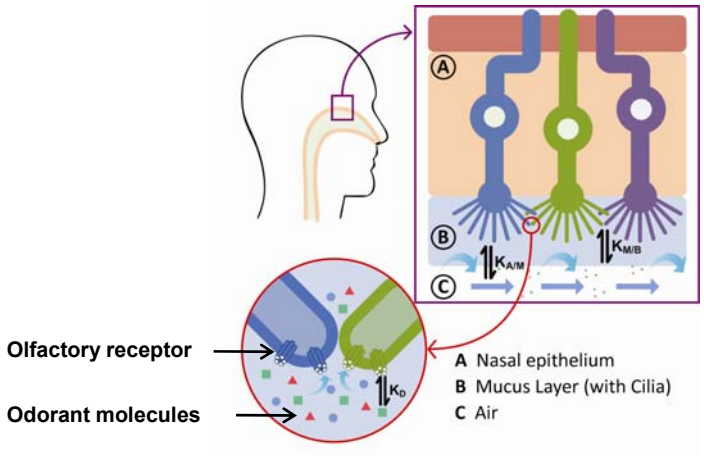


Figure 4.1 - Schematic view of the odorant perception mechanism.

It is known that there are about a few hundred different ORs (approximately 391 functional ORs) (Niimura and Nei, 2005), and a few thousand odorants (Chastrette, 1997; Fisher and Scott, 1997). Thus, taking into account this fact and considering the combinatorial coding scheme between odorants and ORs, it is understood that the human olfactory mechanism is capable of discriminating a vast number of odorants, turning it difficult to model. Like so, our knowledge about the odorant-OR interaction and how the brain translates this odorant combinatorial receptor code is quite limited, except for a few cases (Saito*, et al.*, 2009).

However, and despite all the advances in the knowledge of the olfactory function, several questions remain unanswered: How are these odorant-OR interactions related to the odor detection thresholds? When different odorants bind to the same olfactory receptor or the same odorant binds with different ORs, do we perceive similar sensations? And probably more complex will be to understand how the perceived sensation changes with stimulus concentration over the intensity scale: when the concentration of odorants increases other effects may arise throughout the perceived intensity scale (*e.g.* competition between odorants) since it is not only dependent on odorant-OR relationships but also brain integration. The processes underlying OR signaling through the olfactory bulb to the primary olfactory cortex and from there to

higher order cortical regions and to the limbic system also make the perception of odorant chemicals complex to model. As aforementioned, the perceived odor character for some chemicals may change with its concentration in air: an example previously presented in Chapter 2 is that for trans-non-2-enal which has more than one odor recognition threshold, because it presents a woody character at 0.1 ppb, but a fatty odor at 8 ppb and becomes unpleasant above 30 ppb (Fisher and Scott, 1997). Another example was observed for macrocyclic ketones which have a faint cedarwood quality when concentrated and a musky odor when diluted (Chastrette, 1997). In fact, for the reasons highlighted so far, there are those who foresee that the prediction of olfactory perception is still almost impossible to be successfully achieved (*e.g.* how a new potential ligand would bind to an OR) (Sell, 2006).

Nevertheless, it is the human nature to discover the unknown. Thus, the first fundamental theories concerning olfactory perception were the classical stereochemical theory (shape, or *"lock and key"* theory), originally proposed by Pauling, and the vibration theory of Wright and Dyson, later rejuvenated by Turin (Meierhenrich*, et al.*, 2004; Rowe, 2005). Several objections were raised to these theories once there are experimental evidences not clearly explained by them. Among the main controversies of the stereochemical theory were the multiple examples of odorant molecules with very similar shapes but different odor character and intensity. Examples for these are isomers (in particular, enantiomers) or molecules with certain different functional groups (*e.g.* exchanging hydroxyl and thiol groups) (Rossiter, 1996; Rowe, 2005). One other phenomenon commonly found is that odorant molecules with different structures may have similar odor intensities and character while others with similar structures exhibit different odor properties or even none (odorless) (Sell, 2006). In the vibration theory, objections arise when cases of optical isomerism and isotopic substitution are present in odorant molecules (Rossiter, 1996; Chastrette, 1997; Rowe, 2005). In conclusion, both theories have pros and cons, but none is able to explain the whole olfactory mechanism.

However, recently, the study from a biochemical perspective has shown a rather different picture of the olfactory perception. It has been focused on the olfactory receptors and binding interactions between them and the odorant molecules (Spehr and Munger, 2009; Yabuki*, et al.*, 2010). It was shown that these interactions are the starting biochemical processes for odorant perception and that the large and complex sets of ORs are responsible for the chemosensory capacity of the olfactory system as aforementioned.

4.2. Odor thresholds

The topic of odor detection thresholds (ODT) is intimately related with odor perception: it is the minimum concentration of an odorant (in the air) at which it can be detected by the human nose. Below the ODT an odorant is not perceived, while above this value higher concentrations will produce higher perceived intensities. The relationship between the odorant concentration in air and its perceived odor intensity has not yet been clarified, with different models still under discussion although the Stevens' Power Law is probably more recognized (Stevens, 1957; Cain*, et al.*, 1995; Zwislocki, 2009; Teixeira*, et al.*, 2010).

Odor detection thresholds though are important in different scientific fields and also for the understanding of the olfaction mechanism. Odor thresholds are psychophysical values that have to be calculated with great care and with adequate equipment. As discussed in Chapter 2, the experimental determination of odor detection thresholds is best performed using dynamic olfactometers (Schmidt and Cain, 2010), where panels of experts and/or untrained people are exposed to increasing concentrations of the odorant until they identify the detection concentration limit. The stimulus generation methodology, environmental and equipment operating conditions have evolved for the last century and can be found elsewhere (see for example Schmidt and Cain, 2010). Nevertheless, it is important to note here the relevance of the panelist selection (trained/untrained, age, sex, and health condition), the stimulus generation, room and equipment operating conditions (calibration, dilution ratio, contamination), the odorant supplying media (air, water or other media), and its flow rate. The determination of psychophysical properties such as odor thresholds, if not performed under standardized conditions, may lead to significant differences: it is complex, time consuming, and labor intensive. It is important to highlight that olfactory data depend on the individual physiology, and thus physiological differences may raise the inter-individual variability. Therefore it becomes extremely important to control all of the aforementioned variables in order to obtain standardized ODTs which could be more reproducible. As previously referred, a large variability is found in literature data for ODTs, and even for the same chemical if it is obtained from different sources it often differs in one to four orders of magnitude (considering, for example, the chemicals used in this Chapter). Moreover, there are examples where the observed variability can be as high as five or six orders of

magnitude (for 1-butanol or vanillin, respectively), (see van Gemert, 2003; Leffingwell and Leffingwell, 2011).

It may be argued that odor thresholds are influenced by physiological variables (since it shows inter-individual differences), and that averaged odor thresholds represent the response of the hypothetical "average person". Still, the use of average values obtained from a large population is the best solution: the only alternative would be the use of tailored methods (adapted to each individual like in-house measurements), which seems unpractical and with limited applications.

Nevertheless, whether it is due to insufficient scientific knowledge on olfaction or to the lack of alternative methodologies, odor threshold data are often used (*e.g.* for determination of odor values or health exposure risks). And there is no doubt that their application has proved so far to provide fair to good results in a variety of fields like atmospheric environmental control, purity of commodities, soil and drinking water contamination, food chemistry, cosmetics and fragrance products, among many others (see for example AIHA, 1989; Ferreira*, et al.*, 2000; Gostelow*, et al.*, 2001).

4.2.1. Modeling of odor detection thresholds and odor quality

In the modeling of odor detection thresholds and odor character/quality, most efforts have been directed towards Quantitative Structure-Activity Relationships (QSAR), with acceptable success for certain chemical families (namely esters, alcohols, amines or ketones – see for example Hau and Connell, 1998; Hau*, et al.*, 1999; Abraham*, et al.*, 2002; Kovatcheva*, et al.*, 2004). Another approach for the modeling of odors is based on olfactophore models which have been applied to different olfactory notes for the representation of molecular features that are responsible for a given odor (Bajgrowicz*, et al.*, 2003). Further details can be obtained from review works in the field (Rossiter, 1996; Chastrette, 1997; Kraft*, et al.*, 2000; Sell, 2006). Many of these studies (also called Structure-Odor Relationships or SOR) are concerned with the odor character of odorant molecules rather than with its perceived intensity (detection or recognition thresholds, suprathreshold intensity). However, odor detection thresholds are considered far more economically relevant. The reason for the lack of work on this matter relies on the fact that it is much more difficult and expensive to measure and quantify odors experimentally than to assess their quality (Sell, 2006).

Odorant molecules typically present one or more functional groups in their molecular arrangement. These groups are sometimes considered as responsible for the odor of the molecule but the fact is that there are several cases that disrupt this theory (Sell, 2006). Molecule structural substitution has shown that small changes in the structure of an odorant molecule can induce significant changes in its odor properties while in other cases they have little or no effect at all (for further details see Sell, 2006).

4.2.2. Theoretical Model

Recalling the olfactory mechanism depicted in Section 4.1.1: Odor perception mechanism (Figure 4.1), it all starts with the dissolution of odorant molecules from air into the mucus layer and then into the nasal epithelium (hereafter called biophase). As the interest here is the minimum concentration that provides a response of the olfactory system, it may be reasonable to assume that odorant-OR interactions will not be the limiting step, since most of the ORs would be available. Thus, the controlling step would be the transport processes from air through the mucus to the epithelium. Furthermore, if we assume that the transport phenomena is fast, then equilibrium between the air/mucus and mucus/OR phases is reached and the question reduces to the partitioning of the odorants between the different phases. This idea was tackled before by Doleman and co-workers (Doleman*, et al.*, 1998) who compared the performance of electronic noses with human olfaction for the measurement of odor detection thresholds. Their results showed similar responses for odor detection thresholds, concluding that the odorant perception was dependent on its equilibrium concentration on the polymeric detector material (or the physical sorption in the biophase for the human nose). Deviations were considered to be due to interactions of the odorants with the olfactory receptors (the biochemical process of odorant-OR binding) (Doleman*, et al.*, 1998). This same approach was also used by Hau & Connell (Hau and Connell, 1998; Hau*, et al.*, 1999) in the correlation of odor detection and pungency thresholds. In fact, a similar idea was successfully applied by Abraham and co-workers (Abraham*, et al.*, 1994) for the correlation of gaseous toxicity and narcosis. Moreover, Abraham and co-workers concluded that the biological processes analyzed (nonreactive toxicity and narcosis) were controlled by the gas phase/receptor reaction equilibrium or by the gas phase/receptor phase equilibrium. Following that line of reasoning, there should be a

relationship between odor detection thresholds and the partition coefficients of the odorants which can be expressed by equation 4.3:

$$C_i^{air} \xleftrightarrow{K_{air/mucus}=\frac{C_i^{mucus}}{C_i^{air}}} C_i^{mucus} \xleftrightarrow{K_{mucus/biophase}=\frac{C_i^{biophase}}{C_i^{mucus}}} C_i^{biophase} \quad (4.3)$$

where C_i is the concentration of an odorant *i* in the phase indicated as superscript, and K is the partition coefficient between the phases indicated as subscript. The partition coefficient between air and the biophase, $K_{air/biophase}$, can be obtained as the product of the air/mucus and the mucus/biophase partition coefficients (*e.g.* $K_{air/biophase} = K_{air/mucus} \cdot K_{mucus/biophase}$). A model based on these partition coefficients would be impractical due to the lack of available data. In order to facilitate their calculation (or prediction) some assumptions may be taken. First, the mucus (aqueous) phase can be assumed as water, so that $K_{air/mucus} = K_{air/water} = K_{AW}$ (Fisher and Scott, 1997; Hau and Connell, 1998; Hau*, et al.*, 1999). Then, the 1-Octanol/water partition coefficient, K_{OW}, can be used as a good representation of the biophase/aqueous partitioning (Leo*, et al.*, 1971; Sangster, 1997). As the mass transport goes on the opposite direction (*e.g.* from the aqueous phase to the biophase), it can be written that $K_{mucus/biophase} = 1/K_{OW}$. 1-Octanol/water partition coefficients are widely available for many different substances due to their environmental and toxicological relevance (Sangster, 1997). Alternatively, there are also predictive tools based on chemical structure, with an acceptable precision for an estimative (Chemspider, 2010). However, we make a parenthesis here to highlight that great care should be taken into account when dealing with octanol/water partition coefficients from different sources. This is so because it is dependent on the properties of the medium in which it is calculated, especially the pH of the solution. Moreover, K_{AW} can be obtained from Henry's Law constants in water (accepting that the ideal gas law prevails, which is reasonable at ambient conditions), that is, the ratio of saturation vapor pressure to water solubility, for a given odorant *i* (Reinhard and Drefahl, 1999):

$$K_{AW} = \frac{P_i^s}{C_{i,W} RT} \quad (4.4)$$

where P_i^s is the saturation vapor pressure and $C_{i,W}$ the water solubility for chemical *i*, R

is the universal gas constant, and T is the absolute temperature. Thus, the partition coefficient between air and the biophase, $K_{air/biophase}$, can be approximated by the partition coefficient between air and octanol, $K_{air/octanol}$ (Sepassi and Yalkowsky, 2007), subsequently calculated as the ratio of air/water and 1-octanol/water partition coefficients. Alternative methods for the estimation of $K_{air/octanol}$ have also been derived (Sepassi and Yalkowsky, 2007).

Considering the assumptions above and the definition of the odor detection threshold, it is postulated here that the latter will be directly proportional to the ratio of partition coefficients:

$$ODT_i \propto \frac{K_{AW}}{K_{OW}} = \frac{P_i^s}{K_{OW} C_{i,W} RT} \tag{4.5}$$

Equation 4.5 shows that a simple relationship may be found between the odor detection thresholds of odorants with three readily accessible physical properties. However, it should be noted that this relationship presents some obvious limitations such as: *i)* it is only applied to odorants with partial miscibility with water; *ii)* values for the physical properties must be obtained at the same temperature or range of temperatures (in this work, temperature was set to 298 K); *iii)* inability to distinguish among enantiomers, since the physical properties are the same (but ODTs are not); *iv*) it neglects existing biochemical effects, especially the interactions occurring at the odorant-OR level. Among these limitations, the latter is the most relevant, since olfaction is, in fact, the result of the biochemical interaction of odorants with our sensory system. But the ODT is the lowest concentration that can be detected by the human nose, and so it may be assumed that at this low concentration the transport process to the OR, rather than the biochemical process at the OR, is the limiting step in the whole olfaction process. Of course, the same cannot be assumed for suprathreshold perception.

4.3. Results & Discussion

As aforementioned in Chapter 2, a large variability is found in the literature for data on odor detection thresholds. Most of it is systematic due to variation in the method of stimulus delivery and careful control of this factor can reduce the variation in ODT

significantly (Schmidt and Cain, 2010). Taking into account the importance of such variables, the relationship presented in equation 4.5 was applied to different and independent sources of odor detection thresholds (since each author may use its own methodology, procedure, and protocol). Some authors (see Table 4.1) with vast experience in the field were selected. All the three physical properties on the right side of equation 4.5 can be easily measured experimentally, obtained from literature to thousands of components or even predicted with acceptable accuracy (Leo*, et al.*, 1971; Derawi*, et al.*, 2001; Poling*, et al.*, 2004). In this work, saturation vapor pressures and 1-octanol/water partition coefficients were obtained from the Royal Society of Chemistry's Chemspider Database (Chemspider, 2010), and water solubilities were obtained from the compilation of Yalkowsky and He (Yalkowsky and He, 2003).

First, equation 4.5 was applied to data from Patte, Etcheto and Laffort (PEL) (Patte*, et al.*, 1975). That is a collection of data from different authors, with a semi-empirical weight coefficient attributed to each author, instead of performing a simple compilation of original values for human olfactory thresholds. The procedure looks for multilateral coherence and lack of coherence between odor threshold data from different authors. This resulted in a single average value for the odor detection threshold of each chemical substance. The linear regression of 29 ODTs with the physical properties as in equation 4.5 provided the following results:

$$log\left(ODT_i\right) = (0.9 \pm 0.1) \cdot log\left\{\left[P_i^s \Big/ \left(K_{OW} C_{i,W} RT\right)\right]\right\} + (4.4 \pm 0.5) \tag{4.6}$$

with $r^2 = 0.637$ and $F = 47$ for $n = 29$ chemical compounds plus 1 outlier.

Another source for odor detection thresholds is the dataset of Nagata (NAG) and co-workers (from the Japan Environmental Sanitation Center) who measured odor detection thresholds for a large amount of chemical substances in experiments carried out from 1976 to 1988 (Nagata, 2003). The measurement was performed using the triangular odor bag method, which is the standardized method for odor measurement in Japan (Nagata, 2003). The application of equation 4.5 to these data resulted in:

$$log\left(ODT_i\right) = (0.84 \pm 0.06) \cdot log\left\{\left[P_i^s \Big/ \left(K_{OW} C_{i,W} RT\right)\right]\right\} + (2.5 \pm 0.2) \tag{4.7}$$

with $r^2 = 0.649$ and $F = 172$ for $n = 95$ chemical compounds with 6 outliers.

Odor detection thresholds were also compiled from Cometto-Muniz and co-workers (van Gemert, 2003; Cometto-Muniz and Abraham, 2009a, 2009b, 2010). These ODTs were divided in two separate sets, once the methodologies used for stimulus delivery are different for each case: plastic 'squeeze bottles' were used up to 2003 (CM1), but later changed to dynamic olfactometry (CM2). This way, the first regression obtained from Cometto-Muniz and collaborators (CM1) resulted in:

$$log\left(ODT_i\right) = (0.9 \pm 0.1) \cdot log\left\{\left[P_i^s / \left(K_{OW} C_{i,W} RT\right)\right]\right\} + (4.9 \pm 0.6) \quad (4.8)$$

with $r^2 = 0.637$ and F = 42 for n = 26 chemical compounds. The most recent data of this research group (CM2) provided the following result:

$$log\left(ODT_i\right) = (0.9 \pm 0.2) \cdot log\left\{\left[P_i^s / \left(K_{OW} C_{i,W} RT\right)\right]\right\} + (2.6 \pm 0.6) \quad (4.9)$$

with $r^2 = 0.769$ and F = 23 for n = 10 chemical compounds.

As can be seen from equations 4.6 to 4.9, the regression parameters obtained are somehow similar. It is important to note that odor detection thresholds were measured by different authors, who used different methodologies, panelists, and/or protocols. Even so, all slopes in equations 4.6 to 4.9 are in the range of 0.8 – 0.9, while the intercepts are concentrated around two range values: 2.5-2.6 and 4.4-4.9. The results are summarized in Table 4.1 where similarities are clearly seen between the regression parameters obtained from different authors' data. This finding suggests that different methodologies for measuring odor detection thresholds may result in comparable data. A similar conclusion was already obtained by Cometto-Muniz and co-workers (Cometto-Muniz and Abraham, 2009a, 2010). Thus, it will be also plausible to apply equation 4.5 to a broader set of data including odor detection thresholds obtained by different authors over the years in order to make its application more generalized. This way, odor detection thresholds would not be limited to in-house determinations, but some comparison could be made between available data and predicted values.

Table 4.1 – Regression results for different sources of odor detection thresholds: slope, intercept, coefficient of determination (r^2), Fisher coefficient, number of data points (n), and number outliers.

Eq #	ODT source	Slope	Intercept	r^2	F	n	*Outliers*
(4.6)	PEL	0.9±0.1	4.4±0.5	0.637	47	29	1
(4.7)	NAG	0.84±0.06	2.5±0.2	0.649	172	95	6
(4.8)	CM1	0.9±0.1	4.9±0.6	0.637	42	26	-
(4.9)	CM2	0.9±0.2	2.6±0.6	0.769	23	10	-
(4.10)	Various	0.97±0.05	4.2±0.2	0.770	399	121	2

In order to find a more general relationship, all the previous odor detection thresholds in air, and others from different authors for a total of 121 chemical components were collected (Patte*, et al.*, 1975; van Gemert, 2003; Cometto-Muniz and Abraham, 2009a, 2009b). Special emphasis was given to fragrance ingredients, representing different functional groups. Table 4.2 presents the percentage of the functional groups found in the odorant molecules considered in this work. It is important to highlight not only the variety of functional groups in the dataset but also the fact that odorant molecules with several functional groups are present in great number (thus summation in Table 4.2 exceeds 100%). All these data with the respective references are compiled in Table S1 (see end of Chapter).

Table 4.2 – Percentage of the different functional groups in the odorants dataset used.

Functional Group	**%**
Acid	1.7
Alcohol	23.1
Aldehyde	8.3
Amine	1.7
Aromatic	43.0
Epoxide	0.8
Ester	14.9
Ether	7.4
Haloalkane	9.9
Hydrocarbon	12.4
Ketone	8.3
Nitrile	1.7
Nitro	2.5
Terpenoid	6.6

In order to reduce variability from literature data (sample size, methodology bias) the geometric mean was considered for any of the parameters in equation 4.5 whenever

different data were available. Figure 4.2 shows the logarithms of ODTs as a function of the logarithm of the ratio on the right side of equation 4.5, for the 121 components. It is important to highlight that both sides in equation 4.5 range over ten orders of magnitude, with $\left(x \in \left[10^{-9}, 10^{1}\right], y \in \left[10^{-5}, 10^{5}\right]\right)$. This way, a logarithmic transformation of the original data was necessary. An attempt to plot the data using a linear scale would result in failure to represent the smaller values and a regression performed in this way would have no statistical meaning (Rousseeuw and Leroy, 1987).

Applying logarithms to equation 4.5, resulted in a good regression of all but 2 data points (see Table S1):

$$log\left(ODT_i\right) = (0.97 \pm 0.05) \cdot log\left\{\left[P_i^s \Big/ \left(K_{OW} C_{i,W} RT\right)\right]\right\} + (4.2 \pm 0.2) \qquad (4.10)$$

with a correlation coefficient r = 0.877, an adjusted correlation coefficient r^2_{adj} = 0.769, and a Fischer statistics parameter F = 399 for n = 121 data points. The r^2_{adj} value indicates that the independent variable accounts for 77% of the variance in the threshold data (Wilcox, 2009).

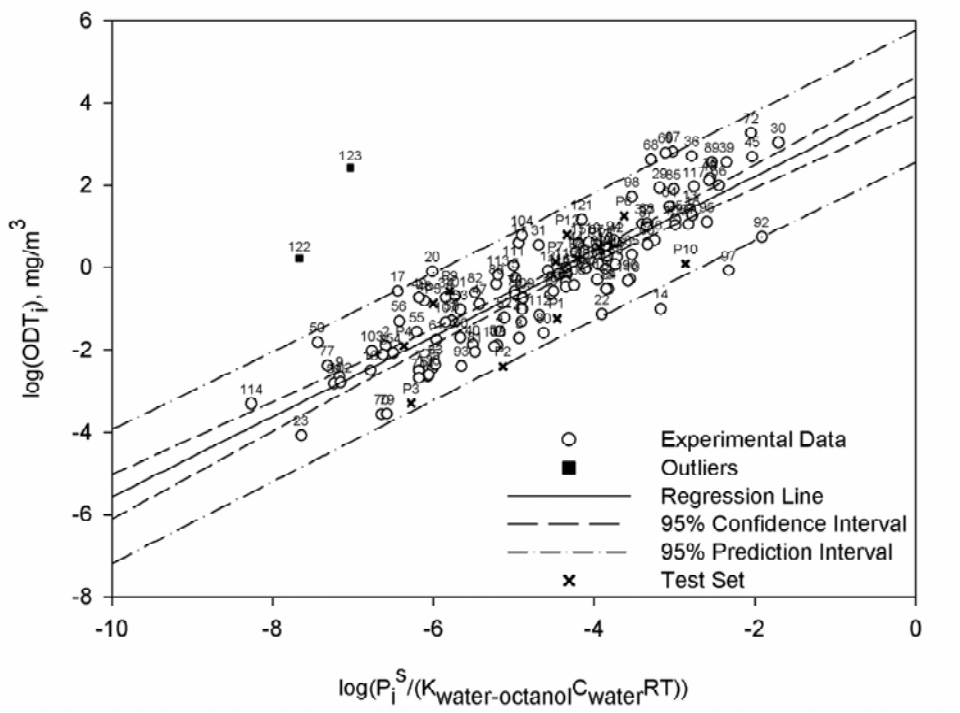


Figure 4.2 - Regression for the *log(ODT$_i$)* versus the logarithm of the physical properties (see equation 4.10). Labels for each data point can be found in Table S1. Chemicals 122 and 123 are considered as outliers and, thus, were not used in the regression.

This represents a fairly good result for the prediction of odor detection thresholds taking into account their large experimental variability. In order to validate the predictive capacity of equation 4.10, a new data set of odorants (test set with 12 different chemicals – see Table S1) was used. These points were included in Figure 4.2, and it was seen that all values lied within the 95% prediction interval previously obtained. Moreover, the average absolute deviation for this prediction was 0.77 (log units). In this way, once the average absolute deviation obtained in the regression (equation 4.10) was 0.60 (log units), the predictive capacity of the model can be considered as good. Moreover, considering that only three physical properties for each pure component are needed, the model presents a simple and easy-to-apply method that provides a good first estimate of the odor detection threshold for any chemical. This type of estimate is important for engineering purposes, before going to experimental measurements that are expensive and laborious. Once more, it is possible to see that the parameters for the general regression are comparable to those obtained in the author-specific regressions, thus showing its applicability.

The results obtained herein with the proposed model compare favorably with other models from the literature. First, the work of Hau and Connell should be mentioned (Hau and Connell, 1998), who have also used a partitioning model to predict odor detection thresholds for different chemical families of odorants. In their work, 4 groups of odorants (acetates, alcohols, ketones and amines) were analyzed separately for a small number of odorant molecules (6 to 9), resulting in coefficients of determination (r^2) ranging from 0.70 – 0.90. Abraham *et al.* developed a general equation for the prediction of odor detection thresholds using QSAR methodologies with five descriptors and a set of 40 odorants with r^2 = 0.77 (Abraham*, et al.*, 2002). Increasing the number of descriptors to 7 led to an increase in r^2 up to 0.85. The QSAR methodology was also applied by Anker *et al*. to 53 alcohols with a series of 4 descriptors, resulting in r^2 = 0.86 (Anker*, et al.*, 1990). Later, Chastrette *et al.* applied neural networks with a nonlinear relationship between the logarithm of the odor detection threshold and its descriptors to a set of 45 camphoraceous alcohols (Chastrette, 1997). The result was that 78% of the predicted odor thresholds lied within the range of the logarithm of the minimum and the maximum experimental odor threshold plus a constant, which is quite vague. More recently, Kraft and Eichenberger developed the olfactophore model for the correlation of structure-odor properties for a small class of 20 marine odorants, obtaining "*a correlation of 0.59*" (Kraft and Eichenberger, 2003).

A summary of these results for the authors who followed a similar approach is shown in Table 4.3, comparing the number of descriptors, parameters and chemicals (*n*) used, and also the reported value for the coefficient of correlation (r^2). In sum, in terms of predictive power our results compare favorably with previous models. As the correlation coefficient value is similar in all cases, the predictive capacity of the different models can be considered as similar. However, the proposed model brings three advantages: *i*) it is applied to a larger set of odorants and, more important, independent of chemical families; *ii*) it uses a limited set of adjustable parameters (only two); *iii*) the model and parameters have a physical meaning with a direct interpretation (which can be viewed as a plus when comparing with QSPR methods).

Table 4.3 – Comparison of models for the prediction of odor thresholds.

	Hau and Connell (Hau and Connell, 1998)	Abraham *et al.* (Abraham, *et al.*, 2002)	Anker *et al.* (Anker, *et al.*, 1990)	This work
properties or descriptors	2	5-7	4	3
parameters	2	6-9	5	2
n	6-9	50-60	49	121
r^2	0.7-0.9	0.77-0.85	0.86	0.77

The dispersion of the data points in Figure 4.2 can be attributed to different sources of error: *i*) the approximation of odor detection to partitioning processes, neglecting the biochemical odorant-OR binding process; *ii*) the assumptions that $K_{air/mucus} \approx K_{AW}$ and $K_{mucus/biophase} \approx 1/K_{OW}$; *iii*) the assumption of a constant minimum odorant concentration in the biophase; *iv*) the variability on the experimental odor detection thresholds.

Additionally, from the obtained results it was possible to see that the average absolute deviation between experimental and predicted odor detection threshold for the dataset used in the regression was 0.60 log units. This value is similar to the average geometric deviation observed within the experimental odor detection thresholds selected for this work (0.54, see Table S1). This effect is best perceived in Figure 4.3, where a comparison between the experimental and predicted odor detection thresholds is presented. The logarithms of the geometric mean deviation for the experimental odor detection thresholds of each chemical compound found in the literature are shown in Figure 4.3 as error bars.

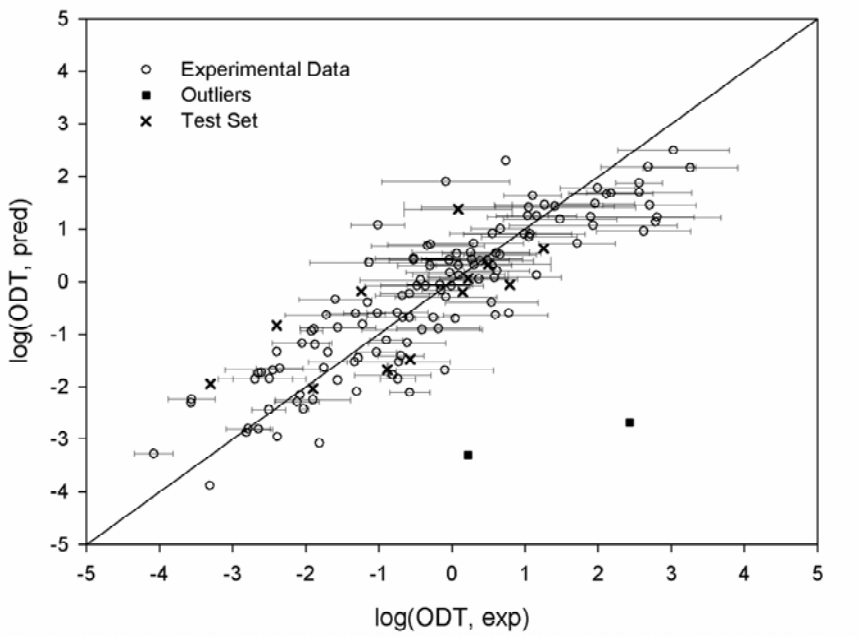


Figure 4.3 - Comparison of experimental and predicted odor detection thresholds. Error bars indicate the geometric mean deviation of experimental odor threshold data found in the literature.

Considering both the experimental and predicted odor detection thresholds described by equation 4.10, it is reasonable to say that the predicted values are fairly well correlated. Additionally, disregarding the thresholds for which there is only a single experimental value available, it is seen that 81% of the predicted thresholds lie within the minimum and maximum odor thresholds reported in the literature.

It is important to highlight that the proposed model does not account for optical isomerism (enantiomers), since it is based on physicochemical properties that do not distinguish enantiomers. It is known that chirality plays an important role in odor perception both at the detection and recognition threshold levels, as mentioned before. Perhaps one of the largest differences is that of the enantiomers (4R,4aS,6R)-(+) and (4S,4aR,6S)-(-) of nootkatone: while the first has an ODT of 30 ppm (and a typical odor of grapefruit), the latter has an ODT of nearly 66000 ppm (and a woody - spicy character) (Bentley, 2006). The differences among enantiomers arise from the biochemical process, the odorant binding to the ORs in the neurons' cilia, which is not considered in the model. However, it should be mentioned that recent research has shown that not all ORs are able to distinguish between structurally-similar compounds like enantiomers (Saito*, et al.*, 2009). Even so, the proposed model differentiates structural isomers (since they have different physical properties) and these were considered in the odorants' dataset used.

That being said, the results obtained from the regression in equation 4.10 suggest that the assumptions taken are, to a certain extent, correct. It is then worth exploring their implications. The general picture presented above is that the odor thresholds are controlled by the partitioning of the odorants from air to the biophase in the nasal epithelium. From equation 4.3 we can define the odor detection threshold as a function of the partition coefficients $K_{air/mucus}$ and $K_{mucus/biophase}$:

$$ODT_i = C_{i,min}^{air} = K_{air/mucus} \cdot K_{mucus/biophase} \cdot C_{i,min}^{biophase} = K_{air/biophase} \cdot C_{i,min}^{biophase} \quad (4.11)$$

where the definition of the variables are as above, and subscript *min* stands for the minimum in the concentrations that allow for odor detection. Applying logarithms to this equation results:

$$log\left(ODT_i\right) = log\left(K_{air/biophase}\right) + log\left(C_{i,min}^{biophase}\right) \quad (4.12)$$

Comparison between equations 4.10 and 4.12 is straightforward: the slope obtained in equation 4.10 is 0.97, thus, close to unity as predicted by equation 4.12. The intercept in equation 4.10 should correspond to the logarithm of the minimum odorant concentration in the biophase in equation 4.12. Nevertheless, it should be noted that this concentration does not have to be the same (a constant) for all odorants. It is a result of an assumption taken for the application of the model, since there are neither such data available in the literature nor perhaps an experimental method to quantify it. This minimum odorant concentration in the biophase points out that a certain concentration is needed at the biophase so that the OR produces a response that triggers the brain to detect the odorant. Decreasing the odor concentration inherently reduces its binding to the ORs and, at sufficiently low values (near threshold concentrations), it results in a single active glomerulus, making the response all-or-nothing (Pifferi*, et al.*, 2010).

It is clear that the elucidation of the mechanism for olfaction will have a large contribution from the biochemical relationships between the coupling odorant-OR. The simplified mechanism presented here constitutes a good predictive estimate for odor detection thresholds whenever experimental values are not available. Nevertheless, further development of this model (or any other for olfaction) should account not only for the transport of odorants to the OR but the biochemical binding process odorant-OR.

Such can be done for example through the use of dissociation constants (K_D) of the odorant-OR pairs as depicted in equation 4.2. Once values for these equilibrium constants are known, they can be used in equation 4.12 to allow the substitution of its intercept, that is, the minimum odorant concentration in the biophase:

$$\log\left(C_{i,\min}^{biophase}\right) = \log\left(\frac{[O-OR]}{K_D[OR]}\right) \tag{4.13}$$

Such approach would allow relating the ODT to the biochemical reaction between the odorant and the receptors. Still, we are far from knowing all the ORs which are responsible for the perception of each odorant.

4.4. Conclusions

A new model is proposed for the prediction of odor detection thresholds in air from elemental physical properties of odorants: saturation pressure, water solubility and 1-octanol-water partition coefficient. The model is based on a linear regression and was applied to a large number of chemical odorants with different functional groups. This model was also obtained from different sets of data showing marginal differences when applied to different authors. Our results have shown a fairly good estimate of odor detection thresholds for odorants, independently of their chemical family and the odor detection threshold source. The regression demonstrated that these physical properties can account for 77% of the odor threshold variance. This result indicates that equation 4.10 can be used as a predictive tool for engineering purposes.

Table S1. Name, CAS number, chemical formula, molecular weight and relevant physicochemical properties for the chemical odorant compounds used throughout this work.

	Component	CAS Number	Chemical Formula	M_i (g/mol)	Log Threshold (mg/m^3)[(a)]	Log δ_{geo}	Vapor Pressure (Pa)[(b)]	Log (K_{OW})[(b)]	S_w (mol/L)[(c)]	Log $(P^S/(K_{OW}*S_w*R*T))$
1	Limonene	7721-11-1	$C_{10}H_{16}$	136.23	-0.165	0.447	2.05E+02	4.45	6.39E-05	-4.337
2	Linalool	78-70-6	$C_{10}H_{18}O$	154.25	-1.901	0.515	1.21E+01	3.28	1.00E-02	-6.593
3	Nonanal	124-19-6	$C_9H_{18}O$	142.24	-1.716	0.567	7.09E+01	3.56	6.75E-04	-4.933
4	Eucalyptol	470-82-6	$C_{10}H_{18}O$	154.25	-1.559	0.519	2.20E+02	2.82	2.01E-02	-5.175
5	p-Cymene	99-87-6	$C_{10}H_{14}$	134.22	-0.255	0.281	1.95E+02	4.02	7.20E-04	-4.982
6	Benzyl Acetate	140-11-4	$C_9H_{10}O_2$	150.17	-0.575	0.076	2.19E+01	1.93	9.97E-03	-4.983
7	p-Cresol	106-44-5	C_7H_8O	108.14	-2.496	0.499	2.81E+01	1.94	1.95E-01	-6.176
8	Eugenol	97-53-0	$C_{10}H_{12}O_2$	164.20	-2.119	0.304	1.39E+00	2.20	1.50E-02	-6.628
9	Methyldihydro jasmonate	24851-98-7	$C_{13}H_{22}O_3$	226.31	-2.643	0.191	9.47E-02	2.50	1.77E-03	-7.165
10	Coumarin	91-64-5	$C_9H_6O_2$	146.14	-2.504	0.234	1.73E-01	1.39	1.71E-02	-6.777
11	Aniline	62-53-3	C_6H_7N	92.13	0.594	0.716	9.77E+01	0.94	3.91E-01	-4.936
12	Benzaldehyde	100-52-7	C_7H_6O	106.13	-0.081	0.692	1.30E+02	1.64	4.52E-02	-4.576
13	Benzene	71-43-2	C_6H_6	78.11	1.406	0.815	1.35E+04	2.20	2.18E-02	-2.804
14	Butanal	123-72-8	C_4H_8O	72.11	-1.014	0.364	1.28E+04	0.91	9.44E-01	-3.172
15	1-Butanol	71-36-3	$C_4H_{10}O$	74.12	0.580	0.915	1.14E+03	0.88	9.49E-01	-4.196
16	o-Xylene	95-47-6	C_8H_{10}	106.17	0.382	0.735	7.99E+02	3.14	1.71E-03	-3.866
17	Linalyl Acetate	115-95-7	$C_{12}H_{20}O_2$	196.29	-0.577	0.277	1.55E+01	3.83	2.55E-03	-6.441
18	Ethyl Acetate	141-78-6	$C_4H_8O_2$	88.11	1.263	0.685	1.49E+04	0.71	7.05E-01	-2.779
19	Furfural	98-01-1	$C_5H_4O_2$	96.09	-0.677	0.369	2.97E+02	0.73	7.84E-01	-4.545
20	1-Heptanol	111-70-6	$C_7H_{16}O$	116.20	-0.099	0.667	4.33E+01	2.47	6.09E-02	-6.012
21	2-Heptanone	110-43-0	$C_7H_{14}O$	114.19	-0.363	0.608	6.31E+02	1.97	6.08E-02	-4.348
22	Hexanal	66-25-1	$C_6H_{12}O$	100.16	-1.135	0.806	1.45E+03	1.97	4.99E-02	-3.900
23	Vanillin	121-33-5	$C_8H_8O_3$	152.15	-4.078	0.261	5.12E-02	1.10	7.24E-02	-7.645
24	Isoamyl Acetate	123-92-2	$C_7H_{14}O_2$	130.19	-0.522	0.527	7.57E+02	2.12	1.53E-02	-3.821
25	Isopropyl Acetate	108-21-4	$C_5H_{10}O_2$	102.13	1.156	0.550	8.09E+03	1.06	2.76E-01	-2.987

26	Isoamyl Alcohol	123-51-3	$C_5H_{12}O$	88.15	-0.477	0.713	5.55E+02	1.22	3.02E-01	-4.351
27	Methacrylonitrile	126-98-7	C_4H_5N	67.09	1.048	1.465	7.53E+03	0.74	3.69E-01	-2.825
28	3-Nitrobenzaldehyde	99-61-6	$C_7H_5NO_3$	151.12	0.477	-	1.29E+00	1.75	6.62E-05	-3.855
29	Nonane	111-84-2	C_9H_{20}	128.26	1.933	1.149	6.17E+02	5.54	1.10E-06	-3.186
30	Pentane	109-66-0	C_5H_{12}	72.15	3.028	0.763	7.03E+04	3.41	5.57E-04	-1.703
31	1-Pentanol	71-41-0	$C_5H_{12}O$	88.15	0.543	0.633	3.75E+02	1.41	2.85E-01	-4.685
32	2-Pentanone	107-87-9	$C_5H_{10}O$	86.13	1.056	0.656	5.15E+03	0.91	6.43E-01	-3.401
33	3-Pentanone	96-22-0	$C_5H_{10}O$	86.13	1.066	0.567	4.77E+03	0.91	5.19E-01	-3.341
34	Phenol	108-95-2	C_6H_6O	94.11	-0.731	0.706	8.19E+01	1.48	7.61E-01	-5.842
35	Propyl Acetate	109-60-4	$C_5H_{10}O_2$	102.13	0.661	0.400	4.69E+03	1.24	1.92E-01	-3.246
36	Tetrachloromethane	56-23-5	CCl_4	153.82	2.702	0.637	1.51E+04	2.86	5.10E-03	-2.783
37	Toluene	108-88-3	C_7H_8	92.14	0.990	0.832	3.69E+03	2.68	6.87E-03	-3.344
38	Trichloromethane	67-66-3	$CHCl_3$	119.38	2.173	0.578	2.67E+04	1.76	6.72E-02	-2.556
39	1,1,1-Trichloroethane	71-55-6	$C_2H_3Cl_3$	133.41	2.560	0.316	1.63E+04	2.11	1.14E-02	-2.349
40	2-Chlorophenol	95-57-8	C_6H_5ClO	128.56	-1.874	0.194	1.17E+02	2.04	1.39E-01	-5.510
41	Acetophenone	98-86-2	C_8H_8O	120.15	-1.315	0.405	3.99E+01	1.67	2.77E-02	-4.906
42	Chlorobenzene	108-90-7	C_6H_5Cl	112.56	0.605	0.615	1.49E+03	2.81	4.93E-03	-3.723
43	Cyclohexane	110-82-7	C_6H_{12}	84.16	2.111	0.481	1.25E+04	3.39	7.60E-04	-2.569
44	Cyclohexanone	108-94-1	$C_6H_{10}O$	98.15	0.368	0.531	3.99E+02	0.76	4.72E-01	-4.228
45	Dichloromethane	75-09-2	CH_2Cl_2	84.93	2.687	0.650	5.97E+04	1.19	1.68E-01	-2.033
46	p-Xylene	106-42-3	C_8H_{10}	106.17	0.258	0.804	1.06E+03	3.14	1.59E-03	-3.711
47	Ethyl Benzoate	93-89-0	$C_9H_{10}O_2$	150.18	-0.897	0.224	2.40E+01	2.73	4.79E-03	-5.425
48	1-Octanol	111-87-5	$C_8H_{18}O$	130.23	-0.810	0.520	1.52E+01	3.00	7.85E-03	-6.107
49	Nonanol	143-08-8	$C_9H_{20}O$	144.26	-0.740	0.240	5.43E+00	3.53	9.70E-04	-6.177
50	Dodecanol	112-53-8	$C_{12}H_{26}O$	186.34	-1.813	-	2.79E-01	5.13	2.30E-05	-7.441
51	p-Anisaldehyde	123-11-5	$C_8H_8O_2$	136.15	-2.646	0.079	3.32E+00	1.70	3.15E-02	-6.071
52	Camphor	76-22-2	$C_{10}H_{16}O$	152.24	-1.219	-	3.00E+01	2.13	1.17E-02	-5.117
53	Carvone	6485-40-1	$C_{10}H_{14}O$	150.22	-1.030	0.275	8.75E+00	2.27	8.65E-03	-5.660
54	Citronellol	106-22-9	$C_{10}H_{20}O$	156.27	-2.075	-	2.44E+00	3.38	1.28E-03	-6.494

	Component	CAS Number	Chemical Formula	M_i (g/mol)	Log Threshold (mg/m^3)[a]	Log δ_{geo}	Vapor Pressure (Pa)[b]	Log (K_{OW})[b]	S_w (mol/L)[c]	Log ($P^S/(K_{OW}*S_w*R*T)$)
55	Diphenylmethane	101-81-5	$C_{13}H_{12}$	168.24	-1.565	-	2.13E+00	4.21	8.49E-05	-6.204
56	Menthol	89-78-1	$C_{10}H_{20}O$	156.27	-1.303	-	4.31E+00	3.20	2.92E-03	-6.426
57	Methyl Benzoate	93-58-3	$C_8H_8O_2$	136.15	-1.885	-	4.53E+01	2.20	1.85E-02	-5.205
58	Methyl Salicylate	119-36-8	$C_8H_8O_3$	152.15	-1.283	-	9.33E+00	2.23	1.31E-02	-5.772
59	Phenylacetic Acid	103-82-2	$C_8H_8O_2$	136.15	-2.813	-	6.08E-01	1.51	1.29E-01	-7.232
60	Phenylethylalcohol	60-12-8	$C_8H_{10}O$	122.17	-1.696	-	1.85E+01	1.38	1.43E-01	-5.662
61	Thymol	89-83-8	$C_{10}H_{14}O$	150.22	-1.751	-	2.59E-01	1.19	6.12E-03	-5.958
62	n-Butyl Acetate	123-86-4	$C_6H_{12}O_2$	116.16	0.302	0.516	1.53E+03	1.77	9.31E-02[d]	-3.948
63	Isobutyl Acetate	110-19-0	$C_6H_{12}O_2$	116.16	0.558	0.589	2.40E+03	1.59	5.39E-02	-3.336
64	Methyl Ethyl Ketone	78-93-3	C_4H_8O	72.11	1.476	0.777	1.53E+04	0.37	3.03E+00	-3.060
65	Methyl Isobutyl Ketone	108-10-1	$C_6H_{12}O$	100.16	0.298	0.681	2.43E+03	1.25	1.85E-01	-3.526
66	Propylene Oxide	75-56-9	C_3H_6O	58.08	1.993	0.514	7.63E+04	0.13	6.39E+00	-2.447
67	Heptane	142-82-5	C_7H_{16}	100.21	2.809	0.867	6.03E+03	4.48	8.43E-05	-3.020
68	n-Octane	111-65-9	C_8H_{18}	114.23	2.621	0.641	1.89E+03	5.01	1.46E-05	-3.291
69	1-Octyne	629-05-0	C_8H_{14}	110.20	2.785	-	1.92E+03	3.66	2.18E-04	-3.109
70	2,4-Dichlorophenol	120-83-2	$C_6H_4Cl_2O$	163.00	-3.569	-	1.81E+01	3.00	3.22E-02	-6.644
71	N,N-Dimethylaniline	121-69-7	$C_8H_{11}N$	121.18	-1.018	0.467	6.16E+01	2.33	9.12E-03	-4.895
72	2,4-Dimethylpentane	108-08-7	C_7H_{16}	100.21	3.260	0.645	1.26E+04	4.11	4.36E-05	-2.043
73	Cumene	98-82-8	C_9H_{12}	120.20	-0.527	0.643	5.97E+02	3.56	4.66E-04	-3.846
74	m-Cresol	108-39-4	C_7H_8O	108.14	-2.690	0.510	2.76E+01	1.94	1.94E-01	-6.181
75	o-Cresol	95-48-7	C_7H_8O	108.14	-2.451	0.650	5.05E+01	1.94	2.37E-01	-6.006
76	2-Hexanone	591-78-6	$C_6H_{12}O$	100.16	0.085	0.382	1.77E+03	1.44	2.31E-01	-3.950
77	1-Naphthol	90-15-3	$C_{10}H_8O$	144.17	-2.387	-	1.85E-01	2.71	3.03E-03	-7.318
78	Nitrobenzene	98-95-3	$C_6H_5NO_2$	123.11	-0.675	0.498	3.65E+01	1.95	1.59E-02	-4.982
79	Indole	120-72-9	C_8H_7N	117.15	-3.563	0.320	3.97E+00	2.14	4.40E-02	-6.578
80	Octanal	124-13-0	$C_8H_{16}O$	128.22	-1.596	0.500	2.76E+02	3.03	4.37E-03	-4.624
81	Guaiacol	90-05-1	$C_7H_8O_2$	124.14	-2.053	0.406	2.39E+01	1.19	1.88E-01	-5.481

82	Anethole	104-46-1	$C_{10}H_{12}O$	148.21	-0.615	0.526	9.16E+00	3.17	7.49E-04	-5.477
83	Cinnamaldehyde	104-55-2	C_9H_8O	132.16	-2.355	0.318	3.53E+00	2.12	1.02E-02	-5.975
84	Acetic Acid	64-19-7	$C_2H_4O_2$	60.05	0.271	0.691	1.85E+03	-0.29	1.00E+01	-3.838
85	Butyl Formate	592-84-7	$C_5H_{10}O_2$	102.13	1.900	1.414	3.55E+03	1.36	6.40E-02	-3.011
86	Cyclohexanol	108-93-0	$C_6H_{12}O$	100.16	-0.407	0.822	1.17E+02	1.34	3.51E-01	-5.213
87	Cyclooctane	292-64-8	C_8H_{16}	112.22	0.556	-	6.08E+02	4.51	7.04E-05	-3.968
88	Ethylbenzene	100-41-4	C_8H_{10}	106.17	0.069	0.200	1.23E+03	3.21	1.65E-03	-3.731
89	Hexane	110-54-3	C_6H_{14}	86.18	2.560	0.718	2.01E+04	3.94	3.20E-04	-2.535
90	Hexyl Acetate	142-92-7	$C_8H_{16}O_2$	144.22	-0.581	0.398	1.85E+02	2.83	3.54E-03	-4.505
91	Anisole	100-66-3	C_7H_8O	108.14	-0.038	0.820	5.65E+02	2.13	1.20E-02	-3.852
92	Isoprene	78-79-5	C_5H_8	68.12	0.740	-	7.32E+04	2.41	9.43E-03	-1.914
93	2-Methylnaphthalene	91-57-6	$C_{11}H_{10}$	142.20	-2.398	-	8.07E+00	3.91	1.78E-04	-5.648
94	Isobutyl Alcohol	78-83-1	$C_4H_{10}O$	74.12	0.657	0.500	2.19E+03	0.69	1.01E+00	-3.750
95	Acrylonitrile	107-13-1	C_3H_3N	53.06	1.102	0.394	1.29E+04	0.19	1.33E+00	-2.595
96	Styrene	100-42-5	C_8H_8	104.15	-0.292	0.584	8.28E+02	2.70	2.36E-03	-3.550
97	Vinyl Acetate	108-05-4	$C_4H_6O_2$	86.09	-0.084	0.877	1.57E+04	0.73	2.49E-01	-2.324
98	Undecane	1120-21-4	$C_{11}H_{24}$	156.31	1.713	0.522	7.52E+01	6.60	2.58E-08	-3.530
99	Mesitylene	108-67-8	C_9H_{12}	120.20	0.092	0.629	3.09E+02	3.60	4.38E-04	-4.145
100	1,2,4-Trimethylbenzene	95-63-6	C_9H_{12}	120.20	-0.431	0.827	2.56E+02	3.60	4.62E-04	-4.251
101	Iodoform	75-47-8	CHI_3	393.73	-0.701	0.314	4.52E+00	3.51	3.00E-04	-5.726
102	2,4,6-Trichlorophenol	88-06-2	$C_6H_3Cl_3O$	197.45	-2.787	0.300	2.36E+00	3.58	3.58E-03	-7.155
103	Diphenyl Ether	101-84-8	$C_{12}H_{10}O$	170.21	-2.026	0.069	2.97E+00	4.21	4.28E-04	-6.763
104	Pentylbenzene	538-68-1	$C_{11}H_{16}$	148.25	0.778	-	4.81E+01	4.80	2.43E-05	-4.897
105	Pentyl Acetate	628-63-7	$C_7H_{14}O_2$	130.19	-0.026	0.604	5.24E+02	2.30	1.33E-02	-4.098
106	1-Octene	111-66-0	C_8H_{16}	112.22	1.036	0.281	2.39E+03	4.50	2.96E-05	-2.988
107	2-Octanol	123-96-6	$C_8H_{18}O$	130.23	-1.331	0.634	4.08E+01	2.82	1.73E-02	-5.843
108	2-Nitrophenol	88-75-5	$C_6H_5NO_3$	139.11	-1.921	0.151	1.32E+01	1.71	1.80E-02	-5.239
109	Naphthalene	91-20-3	$C_{10}H_8$	128.18	-0.748	0.417	2.12E+01	3.45	2.31E-04	-4.882
110	Methyl Methacrylate	80-62-6	$C_5H_8O_2$	100.12	-0.331	0.773	4.92E+03	1.35	3.36E-01[(d)]	-3.579

	Component	CAS Number	Chemical Formula	M_i (g/mol)	Log Threshold (mg/m^3)[a]	Log δ_{geo}	Vapor Pressure (Pa)[b]	Log (K_{OW})[b]	S_w (mol/L)[c]	Log ($P^S/(K_{OW}*S_w*R*T)$)
111	(-)-Menthone	14073-97-3	$C_{10}H_{18}O$	154.25	0.046	-	3.41E+01	2.63	3.22E-03	-4.999
112	1-Hexen-3-ol	4798-44-1	$C_6H_{12}O$	100.16	-1.155	-	4.80E+02	1.58	2.45E-01	-4.683
113	1-Hexanol	111-27-3	$C_6H_{14}O$	102.18	-0.187	0.572	1.26E+02	1.94	9.13E-02	-5.193
114	Galaxolide	1222-05-5	$C_{18}H_{26}O$	258.41	-3.311	-	7.27E-02	5.90	6.77E-06	-8.263
115	2-Ethyl-1-Butanol	97-95-0	$C_6H_{14}O$	102.18	-0.009	0.440	2.41E+02	1.75	3.90E-02	-4.353
116	1,2-Dichlorobenzene	95-50-1	$C_6H_4Cl_2$	147.00	-0.149	0.263	1.61E+02	3.28	9.35E-04	-4.437
117	1-Chlorobutane	109-69-3	C_4H_9Cl	92.57	1.960	0.543	1.37E+04	2.56	8.69E-03	-2.755
118	Butyl Ether	142-96-1	$C_8H_{18}O$	130.23	-0.300	0.446	9.47E+02	3.11	2.70E-03	-3.959
119	Bromobenzene	108-86-1	C_6H_5Br	157.02	0.614	0.446	5.49E+02	2.99	2.62E-03	-4.062
120	Borneol	507-70-0	$C_{10}H_{18}O$	154.25	-2.604	-	5.31E+00	2.71	4.78E-03	-6.059
121	Propylbenzene	103-65-1	C_9H_{12}	120.1916	1.158	-	4.12E+02	3.74	4.29E-04	-4.152
	Outlier Data									
122	Dodecanoic acid	143-07-7	$C_{12}H_{24}O_2$	200.32	0.222	-	8.81E-02	5.03	1.55E-05	-7.669
123	Acetanilide	103-84-4	$C_6H_5NH(COCH_3)$	154.25	2.431	-	1.16E-01	1.08	4.21E-02	-7.034
	max	-	-	393.73	3.26	1.47	7.63E+04	6.60	1.00E+01	-1.70
	min	-	-	53.06	-4.08	0.07	5.12E-02	-0.29	2.58E-08	-8.26
	average	-	-	123.98	-0.30	0.54	4.70E+03	2.46	2.79E-01	-4.59

Test Set

Component	CAS Number	Chemical Formula	M_i (g/mol)	Log Threshold (mg/m^3)[(a)]	Log δ_{geo}	Vapor Pressure (Pa)[(b)]	Log (K_{OW})[(b)]	S_w (mol/L)[(c)]	Log ($P^S/(K_{OW}*S_w*R*T)$)
Butylbenzene	68411-44-9	$C_{10}H_{14}$	134.22	-1.237	-	1.40E+02	4.27	8.79E-05 [(d)]	-4.462
2,6-Dichloroanisole	1984-65-2	$C_7H_6Cl_2O$	177.03	-2.398	-	2.51E+01	3.24	7.91E-04	-5.133
2,3-Dimethylphenol	526-75-0	$C_8H_{10}O$	122.17	-3.301	-	1.24E+01	2.40	3.74E-02	-6.274
2,4-Dimethylphenol	105-67-9	$C_8H_{10}O$	122.17	-1.900	0.010	1.72E+01	2.40	6.44E-02	-6.368
2,5-Dimethylphenol	95-87-4	$C_8H_{10}O$	122.17	-0.879	0.005	1.71E+01	2.40	2.75E-02	-6.001
Isobutyl Isobutyrate	97-85-8	$C_8H_{16}O_2$	144.22	1.255	-	6.80E+02	2.47	3.95E-03	-3.629
4-Methyl-2-pentanol	108-11-2	$C_6H_{14}O$	102.18	0.146	-	4.91E+02	1.57	1.60E-01	-4.478
1-Penten-3-ol	616-25-1	$C_5H_{10}O$	86.13	0.227	0.541	1.49E+03	1.05	8.80E-01	-4.215
Methyl Cinnamate	103-26-4	$C_{10}H_{10}O_2$	162.19	-0.569	-	1.49E+00	2.18	2.50E-03	-5.798
Thiophene	110-02-1	C_4H_4S	84.14	0.085	0.740	1.09E+04	1.95	3.58E-02	-2.861
Tribromomethane	75-25-2	$CHBr_3$	252.75	0.500	0.852	6.89E+02	2.29	1.23E-02	-3.935
1,3,5-Trichlorobenzene	108-70-3	$C_6H_3Cl_3$	181.45	0.792	-	3.56E+01	4.04	2.83E-05	-4.334
max	-	-	252.75	1.26	0.852	1.09E+04	4.27	8.80E-01	-2.86
min	-	-	84.14	-3.30	0.005	1.49E+00	1.05	2.83E-05	-6.37
average	-	-	140.90	-0.61	0.429	1.21E+03	2.52	1.11E-01	-4.79

(a) L. J. van Gemert, Compilations of odour threshold values in air, water and other media, Oliemans Punter & Partners BV, The Netherlands, 2003.
(b) Royal Society of Chemistry, Chemspider - Database of Chemical Structures and Property Predictions, http://www.chemspider.com/Default.aspx.
(c) S. H. Yalkowsky, Y. He, Handbook of Aqueous Solubility Data, CRC Press LLC, Boca Raton, Florida (USA), 2003.
(d) D. Mackay, W. Y. Shiu, K.-C. Ma, S. C. Lee, Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Vol. I-IV, CRC Press, Taylor & Francis Group, Boca Raton, Florida (USA), 2006.

4.5. References

Abraham, M. H., Gola, J. M. R., Cometto-Muniz, J. E., Cain, W. S., A model for odour thresholds, *Chemical Senses*, 27, (2): 95-104, 2002

Abraham, M. H., Nielsen, G. D., Alarie, Y., The Ferguson principle and an analysis of biological-activity of gases and vapors, *Journal of Pharmaceutical Sciences*, 83, (5): 680-688, 1994

AIHA, Odor Thresholds for Chemicals With Established Occupational Health Standards, Fairfax, VA (USA), American Industrial Hygiene Association, TRC - Environmental Consultants, 1989

Anker, L. S., Jurs, P. C., Edwards, P. A., Quantitative structure retention relationship studies of odor-active aliphatic-compounds with oxygen-containing functional-groups, *Analytical Chemistry*, 62, (24): 2676-2684, 1990

Axel, R., Scents and sensibility: A molecular logic of olfactory perception (Nobel lecture), *Angewandte Chemie-International Edition*, 44, (38): 6110-6127, 2005

Bagajewicz, M., On the Role of Microeconomics, Multi-scale Planning and Finances in Product Design, *AIChE Journal*, 53, (12): 3155- 3170, 2007

Bajgrowicz, J. A., Berg-Schultz, K., Brunner, G., Substituted hepta-1,6-dien-3-ones with green/fruity odours green/galbanum olfactophore model, *Bioorganic & Medicinal Chemistry*, 11, (13): 2931-2946, 2003

Bentley, R., The nose as a stereochemist. Enantiomers and odor, *Chemical Reviews*, 106, (9): 4099-4112, 2006

Buck, L., Axel, R., A Novel Multigene Family May Encode Odorant Receptors: A Molecular Basis for Odor Recognition, *Cell*, 65, 175-187, 1991

Buck, L. B., Unraveling the sense of smell (Nobel lecture), *Angewandte Chemie-International Edition*, 44, (38): 6128-6140, 2005

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Chastrette, M., Trends in structure-odor relationships, *SAR and QSAR in Environmental Research*, 6, 215-254, 1997

Chemspider, Database of Chemical Structures and Property Predictions - Royal Society of Chemistry, from http://www.chemspider.com/Default.aspx, Last Accessed on February, 2011

Cometto-Muniz, J. E., Abraham, M. H., Olfactory detectability of homologous n-alkylbenzenes as reflected by concentration-detection functions in humans, *Neuroscience*, 161, (1): 236-248, 2009a

Cometto-Muniz, J. E., Abraham, M. H., Olfactory psychometric functions for homologous 2-ketones, *Behavioural Brain Research*, 201, (1): 207-215, 2009b

Cometto-Muniz, J. E., Abraham, M. H., Odor Detection by Humans of Lineal Aliphatic Aldehydes and Helional as Gauged by Dose-Response Functions, *Chemical Senses*, 35, (4): 289-299, 2010

Costa, R., Moggridge, G. D., Saraiva, P. M., Chemical product engineering: an emerging paradigm within chemical engineering, *AIChE*, 52, (6): 1976-1986, 2006

Cussler, E. L., Wagner, A., Marchal-Heussler, L., Designing Chemical Products Requires More Knowledge of Perception, *AIChE Journal*, 56, (2): 283-288, 2010

Derawi, S. O., Kontogeorgis, G. M., Stenby, E. H., Application of group contribution models to the calculation of the octanol-water partition coefficient, *Industrial & Engineering Chemistry Research*, 40, (1): 434-443, 2001

Doleman, B. J., Severin, E. J., Lewis, N. S., Trends in odor intensity for human and electronic noses: Relative roles of odorant vapor pressure vs molecularly specific odorant binding, *Proceedings of the National Academy of Sciences of the United States of America*, 95, (10): 5442-5447, 1998

Ferreira, V., Lopez, R., Cacho, J. F., Quantitative determination of the odorants of young red wines from different grape varieties, *Journal of the Science of Food and Agriculture*, 80, (11): 1659-1667, 2000

Firestein, S., How the olfactory system makes sense of scents, *Nature*, 413, (6852): 211-218, 2001

Fisher, C., Scott, T. R., Food Flavours: Biology and Chemistry, Cambridge (UK), The Royal Society of Chemistry, 1997

Fleischer, J., Breer, H., Strotmann, J., Mammalian olfactory receptors, *Frontiers in cellular neuroscience*, 3, 9, 2009

Getz, W. M., Lansky, P., Receptor dissociation constants and the information entropy of membranes coding ligand concentration, *Chemical Senses*, 26, (2): 95-104, 2001

Gostelow, P., Parsons, S. A., Stuetz, R. M., Odour measurements for sewage treatment works, *Water Research*, 35, (3): 579-597, 2001

Hau, K. M., Connell, D. W., Quantitative structure-activity relationships (QSARs) for odor thresholds of volatile organic compounds (VOCs), *Indoor Air-International Journal of Indoor Air Quality and Climate*, 8, (1): 23-33, 1998

Hau, K. M., Connell, D. W., Richardson, B. J., Quantitative structure-activity relationships for nasal pungency thresholds of volatile organic compounds, *Toxicological Sciences*, 47, (1): 93-98, 1999

Herrmann, A., Controlled release of volatiles under mild reaction conditions: From nature to everyday products, *Angewandte Chemie-International Edition*, 46, (31): 5836-5863, 2007

Kovatcheva, A., Golbraikh, A., Oloff, S., Xiao, Y. D., Zheng, W. F., Wolschann, P., Buchbauer, G., Tropsha, A., Combinatorial QSAR of ambergris fragrance compounds, *Journal of Chemical Information and Computer Sciences*, 44, (2): 582-595, 2004

Kraft, P., Bajgrowicz, J. A., Denis, C., Frater, G., Odds and trends: Recent developments in the chemistry of odorants, *Angewandte Chemie-International Edition*, 39, (17): 2981-3010, 2000

Kraft, P., Eichenberger, W., Conception, characterization and correlation of new marine odorants, *European Journal of Organic Chemistry*, (19): 3735-3743, 2003

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Leo, A., Hansch, C., Elkins, D., Partition coefficients and their uses, *Chemical Reviews*, 71, (6): 525-616, 1971

Meierhenrich, U. J., Golebiowski, J., Fernandez, X., Cabrol-Bass, D., The molecular basis of olfactory chemoreception, *Angewandte Chemie-International Edition*, 43, (47): 6410-6412, 2004

Nagata, Y., Measurement of odor threshold by triangle odor bag method. Odor measurement review. Office of Odor: 118–127, 2003

Niimura, Y., Nei, M., Evolutionary changes of the number of olfactory receptor genes in the human and mouse lineages, *Gene*, 346, 23-28, 2005

Patte, F., Etcheto, M., Laffort, P., Selected and standardized values of suprathreshold odor intensities for 100 substances, *Chemical Senses & Flavour*, 1, (3): 283-305, 1975

Pifferi, S., Menini, A., Kurahashi, T., The Neurology of Olfaction, Boca Raton, Florida (USA), CRC Press, Taylor & Francis Group, 2010

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Reinhard, M., Drefahl, A., Handbook for Estimating Physicochemical Properties of Organic Compounds, USA, John Wiley & Sons, 1999

Rossiter, K. J., Structure-odor relationships, *Chemical Reviews*, 96, (8): 3201-3240, 1996

Rousseeuw, P. J., Leroy, A. M., Robust Regression and Outlier Detection, Canada, John Wiley & Sons, 1987

Rowe, D., Chemistry and Technology of Flavours and Fragrances, United States, Blackwell Publishing Ltd - CRC Press, 2005

Saito, H., Chi, Q. Y., Zhuang, H. Y., Matsunami, H., Mainland, J. D., Odor Coding by a Mammalian Receptor Repertoire, *Science Signaling*, 2, (60): 2009

Sangster, J., Octanol Water Partition Coefficients: Fundamentals and Physical Chemistry, Chichester (England), John Wiley & Sons Ltd, 1997

Schmidt, R., Cain, W. S., Making Scents: Dynamic Olfactometry for Threshold Measurement, *Chemical Senses*, 35, (2): 109-120, 2010

Sell, C. S., On the unpredictability of odor, *Angewandte Chemie-International Edition*, 45, (38): 6254-6261, 2006

Sepassi, K., Yalkowsky, S. H., Simplified estimation of the octanol-air partition coefficient, *Industrial & Engineering Chemistry Research*, 46, (7): 2220-2223, 2007

Spehr, M., Munger, S. D., Olfactory receptors: G protein-coupled receptors and beyond, *Journal of Neurochemistry*, 109, (6): 1570-1583, 2009

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Taylor, A. J., Cook, D. J., Scott, D. J., Role of Odorant Binding Proteins: Comparing Hypothetical Mechanisms with Experimental Data, *Chemosensory Perception*, 1, (2): 153-162, 2008

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE Journal*, 56, (4): 1090-1106, 2010

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

Wilcox, R. R., Basic Statistics: Understanding Conventional Methods and Modern Insights, Oxford (UK), Oxford University Press, Inc., 2009

Yabuki, M., Portman, K. L., Scott, D. J., Briand, L., Taylor, A. J., DyBOBS: A Dynamic Biomimetic Assay for Odorant-Binding to Odor-Binding Protein, *Chemosensory Perception*, 3, (2): 108-117, 2010

Yalkowsky, S. H., He, Y., Handbook of Aqueous Solubility Data, Boca Raton, Florida (USA), CRC Press LLC, 2003

Zwislocki, J. J., Sensory Neuroscience: Four Laws of Psychophysics, New York, Springer Science+Business Media, 2009

Chapter 5

The Evaporation of Fragrance Mixtures: a thermodynamic and organoleptic analysis*

"The present state of research in olfaction is characterized by a plethora of tantalizing clues and a paucity of definitive results."

(T. E. Graedel, 1984)

After predicting the intensity of odorants evaporating from fragrance mixtures with new methodologies and evaluating the role of odor detection thresholds to account for that perceived intensity, it appears to be important to experimentally validate the evaporation of such fragrances. In this Chapter, several predictive G^E methods based on the group-contribution concept have been evaluated for the prediction of multi-component vapor liquid equilibria (VLE) of fragrance mixtures. The evaluation covered 24 binary, 20 ternary and 21 quaternary mixtures combining six different fragrances typically used in perfume formulation and ethanol as the solvent. The selected predictive methods are the original UNIFAC (updated to the last revision), the UNIFAC-Dortmund, the ASOG, and the A-UNIFAC. The equilibrium compositions were experimentally measured at 23 ºC by headspace gas chromatography (HS-GC). For each liquid composition, the corresponding experimental and predicted vapor compositions were compared. Moreover, from the vapor compositions the odor intensity and character of the fragrance

* This Chapter is partly based on the paper from Teixeira MA, Rodríguez, O, Mota, FL, Macedo, EA, Rodrigues, AE, Evaluation of group-contribution methods to predict VLE and odor intensity of fragrances, *Industrial & Engineering Chemistry Research*, accepted.

mixtures were calculated using a previous developed model (see Chapter 3) which considers the Stevens' Power Law for the intensity scale and the Stronger Component model for quality of perception. The odor intensity and character of fragrance mixtures was also predicted and compared to experimental and sensorial evaluations performed by panelists.

5.1. Introduction

Fragrances are important sensory components that companies of consumer goods have been using, more and more often, to differentiate their products from others (Calkin and Jellinek, 1994; Butler, 2000; Cussler*, et al.*, 2010; Teixeira*, et al.*, 2010b). Consequently, they are willing to increase the appreciation that customers have for their products and thus increase their market share, distancing themselves from their nearest competitors. Manufacturers either develop different variations of their products or adapt the existing ones to the market needs, offering consumers an increasingly broad choice of products which hopefully have added value. Accordingly, fragrances are known to be appellative and appreciated by consumers, so that their incorporation in a wide variety of products brings with it an increase in products' value.

However, considering the number of available fragrances (in the order of several thousands), the possible combinations of fragrance ingredients for a perfumer are endless. Thus, as stated before, the formulation of fragranced products (either fine fragrances or functional perfumes like soaps, household cleaners, detergents amongst others) is a complex and lengthy process often developed by experts in the art of odor perception, called perfumers (Calkin and Jellinek, 1994). It involves a long and costly trial-and-error process for testing the perceived odor of hundreds of different samples. Moreover, when a perfume is incorporated into a product (*e.g.* liquid soap, detergent, or bath oil) it is usual to observe a variation in the headspace composition due to the change of the perfume base or matrix and the interactions between them. The result can be a different perception of fragrances' intensity and/or character. For that, molecular interactions within a matrix play an important role in the evaporation of fragrance ingredients, especially in liquid solutions (Behan and Perring, 1987). For this reason, companies are increasing their investment in the design steps of their fragranced products using tools, for example, for the prediction of vapor liquid equilibria of

fragrance ingredients. With an eye towards this goal comes the so-called Product Engineering, which congregates different scientific fields together with materials and processes for a common end: product development (Ulrich and Eppinger, 2000; Costa, *et al.*, 2006; Wei, 2007; Hill, 2009).

As for perfumes and fragranced products, the evaporation of the ingredients used in their formulation is a critical issue for product design. Recently, Friberg and co-workers have been developing a significant work on the release of fragrance chemicals from emulsion systems, combining phase diagrams with algebraic calculations to withdraw information from ternary diagrams. Their methodology allows to predict the evaporation path of fragrances in water/oil and three-phase emulsions, and the effect of different parameters on their evaporation rate (*e.g.* relative humidity, surfactant concentration, growth and reduction of phase volumes at non-equilibrium conditions) (Friberg, 2007, 2008, 2009; Friberg, *et al.*, 2009).

Here several thermodynamic models for the prediction of the VLE compositions of fragrance mixtures will be evaluated. It is intended to validate the use of group-contribution methods to model the VLE, both in terms of the composition in the gas phase and the perceived odor intensity. Towards this purpose, several fragrance mixtures were formulated, their headspace was evaluated by gas chromatography and by olfactory analysis and, finally, the experimental results were compared with those predicted from the VLE models.

5.1.1. Methodology for odor perception

The processes for the perception of scents released from a perfume mixture can be divided into four steps as shown in Figure 5.1: *i)* it starts with a liquid mixture of fragrance ingredients and solvents with known molar compositions (x_i) that customers spray on the skin or clothes (as first approached in Chapter 3); *ii)* then, this liquid mixture begins to evaporate into the air at ambient conditions, accompanied by a change in the compositions of the gas (y_i) and liquid (x_i) phase (as will be discussed in this Chapter); *iii)* subsequently the vapors of the fragrant components diffuse through the surrounding air (as will be explored in Chapter 6); *iv)* finally, some of the fragrance molecules will eventually reach the nose of the customer or other people around, who will perceive the odors with a certain intensity and character (which will be the topic on Chapters 7 and 8, respectively). As aforementioned, this process encompasses different

scientific fields including Thermodynamics, Transport Phenomena and Psychophysics, being schematically depicted in Figure 5.1.

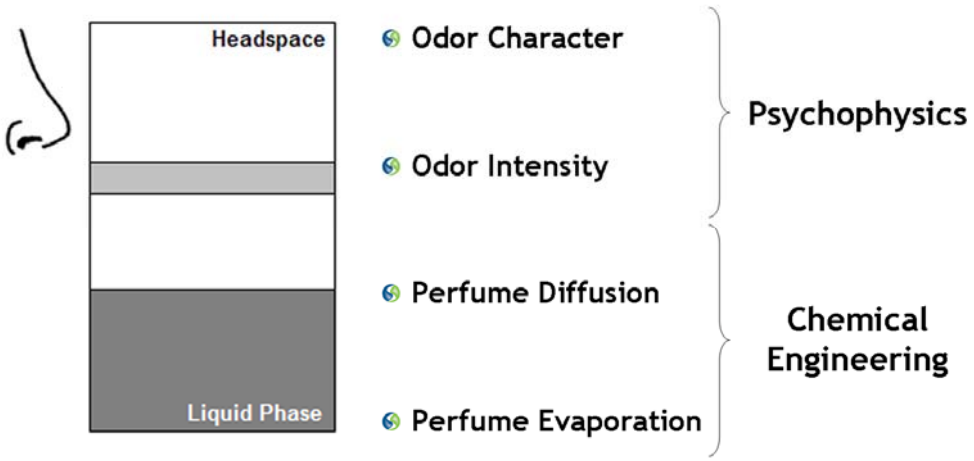


Figure 5.1 – Schematic representation of the steps involved in the odor perception model for fragrance mixtures.

From a Product Engineering point of view, it is of prime interest to obtain a reliable model for this process, so that the olfactory effect of a given formulation can be identified. Moreover, if the mathematical model is predictive, these effects can be known in advance and it can be used to obtain suitable preliminary formulations for the perfume. Consequently, this is expected to reduce the number of trial-and-error experiments and decrease the consumption of raw materials (some of which are quite expensive), and thus improve the development process for the final product.

Nevertheless, from the stepwise process shown in Figure 5.1, a mathematical model is needed to establish the relationship between the odorant concentration and its odor perception. For that purpose we recall Psychophysics, a branch of Psychology dealing with mathematical relationships between sensorial perception and external physical stimuli. In what concerns to olfaction, there are several models used to relate odor intensity as a function of the odorant concentration in air, as previously reviewed in Chapter 2 and Annex A. The Stevens Psychological Law (also known as the Power Law) set forth that the sensation (Ψ) is proportional to the stimulus (S) raised to an exponent (n). This Power Law has been observed for perceptual judgments of different physical stimuli like brightness, loudness, taste, or smell, and even for nonphysical stimuli like the utility of money (Stevens, 1957, 1958, 1964; Graedel, 1984; Teixeira, *et al.*, 2010a). For the measurement of the odor intensity, the power law can be expressed as:

$$\Psi_i = \left(\frac{C_i}{ODT_i} \right)^{n_i} \tag{5.1}$$

where the subscript *i* refers to a given odorant, and Ψ_i, C_i, ODT_i, and n_i are its odor intensity, concentration in air, odor detection threshold, and olfactory power law exponent, respectively. Both C_i and ODT_i should have the same units (*e.g.* mg/m^3). Odor detection threshold concentrations and exponents for the power law can be obtained in the open literature from compilations of hundreds of odorant species (see Chapter 4 and Devos*, et al.*, 1990; Calkin and Jellinek, 1994; Devos*, et al.*, 2002; van Gemert, 2003; Leffingwell and Leffingwell, 2011). As previously reported, the odor recognition thresholds may be more meaningful for perfume formulation and evaluation because they represent an odor quality, but experimental values are scarce and more difficult to obtain with confidence. Thus, odor detection thresholds (ODT) were used for all components involved in this study.

Equation 5.1 relates the odor intensity of a given component to its concentration in air which can be measured by analytical methods. However, when several components are present in the air, what will be perceived is a blend of those odorants. The way we perceive and classify a mixture of odorants is a complex process, far from being completely understood (Graedel, 1984; Sell, 2006; Gilbert, 2008). Hitherto, several models have been proposed to explain the quality perception of odorants in mixtures (for further details see Annex A), among which can be highlighted the Stronger Component, Vectorial, U, and Γ models (together with some modifications or extensions of them). Different comparisons of these models can be found in the literature, resulting in different conclusions, since none has yet imposed universally over the others (Laffort and Dravnieks, 1982; Olsson and Berglund, 1993; Cain*, et al.*, 1995; Olsson, 1998; Laffort*, et al.*, 2002). From all the referred models, the Stronger Component is the simplest, but it has also proved to consistently be one of the best models when all these are compared (Laffort and Dravnieks, 1982; Cain*, et al.*, 1995). Moreover, a series of experiments on the odor perception of binary mixtures has shown that the perceived odor intensity tends to present a certain trend: the overall odor intensity is somewhat in the middle of the intensity of their binary components, but tends to fall closer to the stronger of the unmixed compounds: $\Psi_i < \Psi_{ij} < \Psi_j$ (Laffort

and Dravnieks, 1982; Berglund and Olsson, 1993; Olsson, 1998). The Stronger Component model states that in a mixture of *N* odorants, the one with the highest odor intensity is the most strongly perceived, as mathematically expressed by equation 5.2:

$$\Psi_{mix} = max(\Psi_i), \ \forall \ i = 1,\ldots,N \tag{5.2}$$

This model has been used by several authors in the past showing good results (Cain, *et al.*, 1995; Mata, *et al.*, 2005b; Teixeira, *et al.*, 2009b) and so it will be used in this work to account for the odor character of mixtures.

Combining equations 5.1 and 5.2, the dominant odor in a mixture can be found from their compositions in air. But perfumes are liquid mixtures, and so before these equations may be of any help in the perfume formulation process, the odorant concentration in air (C_i) must be calculated from that in the liquid phase (the composition of the perfume mixture). In order to do so, the vapor-liquid equilibrium (VLE) compositions can be calculated using a modified Raoult's law (Poling, *et al.*, 2004):

$$y_i \cdot P = x_i \cdot \gamma_i \cdot P_i^{sat} \tag{5.3}$$

where y_i and x_i are the mole fractions of component *i* in the gas and liquid phases, respectively. *P* is the total pressure, P_i^{sat} is the vapor pressure of component *i* and γ_i is its activity coefficient in the liquid phase. Non-idealities in the gas phase can be neglected, since we are dealing with atmospheric pressure, temperature conditions and odorants will be highly diluted in air. In this way, combining equations 5.1 and 5.3, the odor intensity of an odorant *i* can be calculated as follows:

$$\Psi_i = \left(\frac{x_i \cdot \gamma_i \cdot P_i^{sat} \cdot M_i}{R \cdot T \cdot ODT_i} \right)^{n_i} \tag{5.4}$$

where M_i is the molecular weight of component *i*, *R* is the universal gas constant, *T* is the absolute temperature and all other variables have been previously defined.

It is important to highlight that variables in equation 5.4 involve the experimental conditions (temperature, *T*), physicochemical properties of the components used in the

perfume formulation (vapor pressure, P_i^{sat}, molecular weight, M_i, odor detection threshold, ODT_i, and olfactory power law exponent, n_i), the molar compositions used for that formulation (x_i) and, finally, the activity coefficient of each component in the liquid phase (γ_i). All these variables are known in advance except for the activity coefficients. These must be calculated from experimental data, or predicted using suitable models. It is evident that for preliminary results, predictions of activity coefficients may provide sufficient information. The predictions can be used *a priori* to give estimates of perfume formulations (namely in the pre-formulation step), thus reducing the trial-and-error experiments commonly used in the development of fragranced products.

5.1.2. Prediction of activity coefficients

The activity coefficients of chemicals in liquid mixtures can be calculated using a range of thermodynamic models. Among them, excess Gibbs energy (G^E) models based on the group-contribution approach (Gmehling, *et al.*, 1993; Poling, *et al.*, 2004) present relevant advantages. Other approaches would rely on the use of equations of state (which often need critical properties) or molecular modeling tools, both of which are difficult to apply to this particular problem. On the other hand, the group-contribution concept considers the system as a mixture of functional groups, rather than molecules. The interaction parameters are obtained from experimental data involving molecules containing those functional groups (but not necessarily the same molecules). As these parameters are available in the literature, the model can be used to predict activity coefficients of any molecule involving the same functional groups. It is important to note here that the only information needed to calculate the activity coefficients of each component in a liquid mixture is just its composition. Then, the molecules of each component have to be divided into the appropriate functional groups to obtain their number and type. All structural and interaction parameters for the groups needed in the calculations should be found in the literature. In this work, four (group-contribution) thermodynamic models have been selected to predict and compare the VLE compositions with experimental data: UNIFAC (Skjold-Jorgensen, *et al.*, 1979; Wittig, *et al.*, 2003), UNIFAC-Dortmund (Weidlich and Gmehling, 1987; Jakob, *et al.*, 2006), A-UNIFAC (Fu, *et al.*, 1995; Mengarelli, *et al.*, 1999; Ferreira, *et al.*, 2005) and ASOG (Tochigi, *et al.*, 1990). In general, these methods consider the activity coefficient as the

sum of two contributions, one accounting for conformational effects (C, also referred as combinatorial or entropic contribution) and other for group interactions (R, referred as residual or enthalpic contribution). The A-UNIFAC introduces a third term for associative interactions (A). In the liquid phase, the non-ideal behavior can be described using any of these methods as the summation (of logarithms) of these two or three contributions:

$$ln\,\gamma_i = ln\,\gamma_i^C + ln\,\gamma_i^R + \left(ln\,\gamma_i^A\right) \tag{5.5}$$

The ASOG (Analytical Solution Of Groups) method was the first to be developed, combining the Flory-Huggins theory and the Wilson equation for the entropic and enthalpic contributions of the activity coefficient, respectively (Tochigi, *et al.*, 1990; Gmehling, *et al.*, 1993). The selected parameters for the ASOG method were obtained from the literature (Tochigi, *et al.*, 1990). In this way, the activity coefficient is calculated according to:

$$\ln\gamma_i^C = 1 + \ln\left(\frac{\nu_i^C}{\sum_j \nu_j^C x_j}\right) - \frac{\nu_i^C}{\sum_j \nu_j^C x_j} \tag{5.6}$$

$$\ln\gamma_i^R = \sum_k \nu_{ki}\left(\ln\Gamma_k - \ln\Gamma_k^*\right) \tag{5.7}$$

$$\ln\Gamma_k = 1 - \ln\sum_l X_l a_{kl} - \sum_l \frac{X_l a_{kl}}{\sum_m X_l a_{lm}} \tag{5.8}$$

$$X_k = \frac{\sum_{i=1}^{n} x_i \nu_{ki}}{\sum_l \sum_{j=1}^{n} x_j \nu_{lj}} \tag{5.9}$$

$$a_{kl} = \exp\left(m_{kl} + \frac{n_{kl}}{T}\right);\ \left(a_{kl} \neq a_{lk}\right) \tag{5.10}$$

where m_{kl} and n_{kl} are group interaction parameters, independent of the temperature, ν_i^C is the number of atoms (not hydrogen) in molecule i, ν_{ki} is the total number of atoms (not hydrogen) in group k of molecule i, and x_i is the mole fraction of molecule i. Γ_k

represents the activity coefficient for group *k*, and superscript * refers to the reference state (a solution of molecules of type *i*).

In a similar way, the UNIFAC (UNIversal Functional Activity Coefficient) method uses the UNIQUAC equation (which contains *per se* the summation of the entropic and enthalpic contributions) for the activity coefficient of the functional groups (Fredenslund, *et al.*, 1975; Anderson and Prausnitz, 1978; Skjold-Jorgensen, *et al.*, 1979; Wittig, *et al.*, 2003). Further details on the UNIFAC method can be found in Annex B. Starting from equation 5.5, the expressions for the calculation of the activity coefficient become:

$$\ln \gamma_i^C = \ln \frac{\Phi_i}{x_i} + \frac{z}{2} q_i \ln \frac{\theta_i}{\Phi_i} + l_i - \frac{\Phi_i}{x_i} \sum_j x_j l_j \tag{5.11}$$

$$\theta_i = \frac{q_i x_i}{\sum_j q_j x_j}; \quad \Phi_i = \frac{r_i x_i}{\sum_j r_j x_j}; \quad l_i = \frac{z}{2}(r_i - q_i) - (r_i - 1) \tag{5.12}$$

$$r_i = \sum_k \nu_k^{(i)} R_k; \quad q_i = \sum_k \nu_k^{(i)} Q_k \tag{5.13}$$

$$\ln \gamma_i^R = \sum_k \nu_k^{(i)} \left(\ln \Gamma_k - \ln \Gamma_k^{(i)} \right) \tag{5.14}$$

$$\ln \Gamma_k = Q_k \left(1 - \ln \sum_m \Theta_m \Psi_{mk} - \sum_m \frac{\Theta_m \Psi_{km}}{\sum_n \Theta_n \Psi_{nm}} \right) \tag{5.15}$$

$$\Theta_m = \frac{Q_m X_m}{\sum_n Q_n X_n}; \quad X_m = \frac{\sum_i x_i \nu_m^{(i)}}{\sum_j \sum_n x_j \nu_n^{(j)}} \tag{5.16}$$

$$\Psi_{mn} = \exp\left(-\frac{U_{mn} - U_{nn}}{RT} \right) = \exp\left(-\frac{a_{mn}}{T} \right) \tag{5.17}$$

where $a_{mn} = (U_{mn} - U_{nn})/R$ are the group interaction parameters (in Kelvin, with $a_{mn} \neq a_{nm}$), R_k and Q_k are the group volume and surface parameters, r_i and q_i are the molecule volume and surface parameters, Γ_k represents the group k residual activity coefficient and $\Gamma_k^{(i)}$ the group k residual activity coefficient in a reference solution containing only i molecules. Θ and θ are group and molecule surface fraction, respectively, while Φ is the molecule volume fraction. The coordination number, z, has been set equal to 10 as suggested by Wong and Eckert, 1971).

Over the years, the original UNIFAC method has gone through expansions in the number of parameters (and their values) for the functional groups defined, thus improving the performance of the model. Its predictive capability has been enhanced by including more experimental data in the parameter regression, filling the gaps (not available parameters) in the group parameter matrix and also including new groups on it. The parameters used in this work were taken from the most recent available versions (Skjold-Jorgensen, *et al.*, 1979; Wittig, *et al.*, 2003; Poling, *et al.*, 2004). Besides, several modifications of the UNIFAC method have been proposed and can be found in the literature (Prausnitz, *et al.*, 1999; Poling, *et al.*, 2004). Two of these modifications were also selected for this work. The UNIFAC-Dortmund (UNIFAC-D) introduces changes in the volume parameter, r_i, and extends the interaction parameters as quadratic functions of temperature (Weidlich and Gmehling, 1987; Jakob, *et al.*, 2006). It should be noted that the UNIFAC-Dortmund method presents a more detailed group division, and so has more interaction parameters than the other models. The parameters for the UNIFAC-D method have also suffered several revisions and the latest was used in this work (Jakob, *et al.*, 2006). The group volume fraction defined in equation 5.12 is now calculated as:

$$\Phi'_i = \frac{r_i^{0.75} x_i}{\sum_j r_j^{0.75} x_j} \tag{5.18}$$

Furthermore, the group interaction parameter in equation 5.17 was also re-defined to:

$$\Psi_{mn} = exp\left(-\frac{a_{mn} + b_{mn}T + c_{mn}T^2}{T}\right) \tag{5.19}$$

The A-UNIFAC method, instead, introduces a new term in the activity coefficient calculation (see equation 5.5) to account for associative interactions. This introduction requires the estimation of new association parameters (energy and volume), and also a re-parameterization of the group interaction parameters since association is now explicitly taken into account. This correction is pertinent when dealing with mixtures that have functional groups (*e.g.* hydroxyl, acid, ether, ester) which participate in such interactions. Remarkably, these groups are frequently found in fragrant molecules. The combinatorial and residual contributions are kept as in the original UNIFAC method (see equations 5.11-5.17). A new association contribution, based on Wertheim's theory for fluids with highly directed attractive forces, is introduced as follows (Mengarelli*, et al.*, 1999; Ferreira*, et al.*, 2005):

$$\ln \gamma_i^A = \sum_{k=1}^{NGA} \left\{ \nu_k^j \sum_{A_k} \left[\ln\left(\frac{X^{A_k}}{X_i^{A_k}} \right) + \frac{X^{A_k} - 1}{2} \right] + r_i \rho_k \sum_{A_k} \frac{1 - X^{A_k}}{2} \right\} \tag{5.20}$$

$$X^{A_k} = \frac{1}{1 + \sum_{j=1}^{NGA} \sum_{B_j} \rho_j \Delta^{A_k B_j} X^{B_j}} \tag{5.21}$$

$$X_i^{A_k} = \frac{1}{1 + \sum_{j=1}^{NGA} \sum_{B_j} (\rho_j)_i \Delta^{A_k B_j} X_i^{B_j}} \tag{5.22}$$

$$\rho_j = \frac{\sum_{i=1}^{NC} \nu_j^i x_i}{\sum_{i=1}^{NC} r_i x_i}; \quad (\rho_j)_i = \frac{\nu_j^i}{r_i} \tag{5.23}$$

$$\Delta^{A_k B_j} = \kappa^{A_k B_j} \left[\exp\left(\frac{\varepsilon^{A_k B_j}}{kT} \right) - 1 \right] \tag{5.24}$$

where *NGA* stands for the number of associating groups and *NC* for the number of components, subscripts *k* and *i* refer to associating groups and components, respectively. X^{Ak} represents the fraction of non-bonded sites, ρ_j the associating group density and Δ^{AkBj} the associating strength between site *A* of group *k* and site *B* of group *j*. Similarly, X_i^{Ak} and $(\rho_j)_i$ is the fraction of non-bonded sites and the associating group density in pure component *i*, respectively. r_i is the (UNIQUAC) molecular volume of species *i*, and it is calculated from the UNIFAC group volume parameters R_k (equation 5.13).

Finally, κ^{AkBj} and ε^{AkBj}, in equation 5.24, are the volume and energy of association, respectively.

The group interaction parameters for the A-UNIFAC method were obtained from the literature and are presented in Annex C as well as for the remaining methods (Mengarelli, *et al.*, 1999; Ferreira, *et al.*, 2005; Andreatta, *et al.*, 2008; Mota, 2010). The procedure for parameterization involves the correlation of equilibrium data (vapor-liquid and liquid-liquid equilibrium and infinite dilution data) of representative associative molecules. As the dataset for parameterization in the A-UNIFAC is much smaller than in other methods (namely UNIFAC), the number of interaction parameters is also more limited, but affects groups that do not participate in the association term. In particular, there are no parameters for the following groups: double bonded hydrocarbons (group 2, C=C), aldehyde (group 10, CHO) or ether (group 13, CH_2O). Whenever there is interaction between two non-associating groups whose group-interaction parameters are not in the A-UNIFAC table, the UNIFAC parameters were used. These parameters, as well as the association energy and volume parameters, have been tabulated for some functional groups showing self- and/or cross-association (like carboxyl, hydroxyl, ester, aromatic rings and water) and we have used the latest available data in the literature (Ferreira, *et al.*, 2005; Andreatta, *et al.*, 2008; Mota, 2010).

As already indicated above, the only requirements to calculate activity coefficients using the referred methods are the compositions of all components involved in the liquid phase, and the availability of the interaction parameters involved. That may be a problem when dealing with fragrances, as these molecules may have several functional groups (hydroxyl, carbonyl, ether, ester, aromatic rings, and double bonds) in the same molecule. Thus, it is necessary that interaction parameters among all these functional groups exist in the database. All the methods presented above, at least to some extent, obey this premise. That is especially true for the UNIFAC and UNIFAC-Dortmund models for which the parameter table is very extensive.

The compositions of the odorant mixture in the gas phase were experimentally measured in this work by headspace gas chromatography (HS-GC) in closed cap vials, as will be presented in detail ahead. A flash calculation was performed to compute the vapor compositions in equilibrium with the liquid perfume. The iterative procedure for the resolution of the equilibrium equations using the group contribution methods is schematically presented in Figure 5.2. The UNIFAC, ASOG, and UNIFAC-Dortmund

methods were implemented in the MATLAB software (Chapman, 2000; Teixeira, *et al.*, 2009b; Teixeira, *et al.*, 2010a) while the A-UNIFAC method was developed in FORTRAN language (Ferreira, *et al.*, 2005).

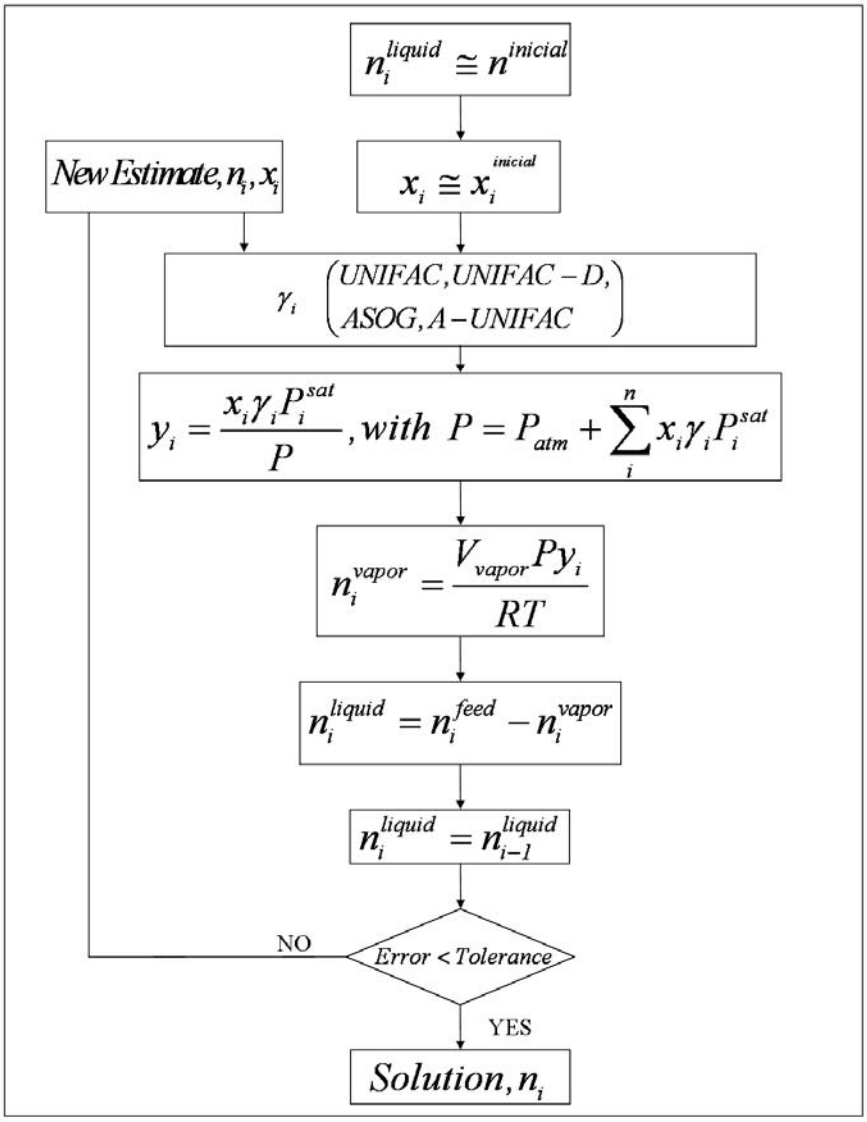


Figure 5.2 – Iterative procedure for the calculation of the vapor-liquid compositions.

In terms of experimental evaluations, different fragrance systems (24 binary, 20 ternary and 21 quaternary systems) were analyzed through headspace gas chromatography (HS-GC), comprising a total of six fragrant compounds: (R-(+)-limonene (LIM), (-)-α-pinene (PIN), geraniol (Ger), (±)-linalool (LOH), linalyl acetate (Lin. ac.), and vanillin (Van), plus ethanol (EtOH) as the solvent. A comparison was performed between the gas phase compositions experimentally measured and those predicted by the group contribution models. Moreover, olfactory evaluations of selected mixtures were also

performed. Finally, a previously developed model (see Chapter 3 equations 3.4 and 3.5 and Teixeira, *et al.*, 2009b; Teixeira, *et al.*, 2010a) was used to predict the odor character or the dominant smell of these perfume mixtures, and results were compared with those measured by gas chromatography and by the olfactory panel.

5.2. Experimental methodology

5.2.1. Materials

R-(+)-Limonene (CAS # 5989-27-5, >97%, >98%, ee) and Geraniol (CAS # 106-24-1, >98%) were obtained from Sigma-Aldrich. (±)-Linalool (CAS # 78-70-6, >97%, GC) and (-)-α-Pinene (CAS # 7785-26-4, >98%, purum) were obtained from Fluka. Linalyl acetate (CAS # 115-95-7, >97%, FCC) and Vanillin (CAS # 121-33-5, >97%, FCC) were supplied by Aldrich. Ethanol (Absolute GR for analysis, >99.9%) was supplied by Merck. All reagents were used as received without further purification. All chemicals together with the values for the properties used throughout this work are presented in Table 5.1.

Table 5.1 – Properties of the components obtained from the literature, molecular formula, molecular weight (M.W.), vapor pressure at 296 K (P^{sat}), boiling point (T_b), odor detection threshold (ODT), an olfactory power law exponent (n).

Fragrance Chemicals	Mol. Form.	M.W. / (g.mol^{-1})	P^{sat} / (Pa)[§]	T_b / (ºC)	ODT / (g.m^{-3})[‡]	n[¶]
Limonene (Lim)	$C_{10}H_{16}$	136.2	1.96×10^{2} [#]	178.0	6.84×10^{-4}	0.37
α-pinene (Pin)	$C_{10}H_{16}$	136.2	5.13×10^{2} [#]	155.5	5.44×10^{-4}	0.49
Linalool (LOH)	$C_{10}H_{18}O$	154.3	2.21×10^{1} [#]	198.5	1.26×10^{-5}	0.35
Geraniol (Ger)	$C_{10}H_{18}O$	154.3	4.00×10^{0} [*]	225.0	1.63×10^{-5}	0.36
Ethanol (EtOH)	C_2H_6O	46.0	7.05×10^{3} [#]	78.2	1.21×10^{-1}	0.58
Linalyl Acetate (Lin. ac.)	$C_{12}H_{20}O_2$	196.3	1.48×10^{1} [*]	220.0	2.65×10^{-4}	0.35
Vanillin (Van)	$C_8H_8O_3$	152.2	2.44×10^{-2} [†]	282.6	8.35×10^{-8}	0.31

[§] vapor pressures for pure components were obtained at 296K.
[#] From DIPPR 801 Database.
[*] From Chemspider Database of Chemical Structures and Property Predictions - Royal Society of Chemistry (Chemspider, 2011).
[†] From Mackay, D.; Shiu, W. Y.; Ma, K.-C.; Lee, S. C, Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals. CRC Press (Mackay, *et al.*, 2006).
[‡] From van Gemert, L. J., Compilations of odour threshold values in air, water and other media. Oliemans Punter & Partners BV: The Netherlands, 2003.
[¶] *n* is the olfactory power law exponent as expressed in Equation 5.1 and literature data was obtained from Devos, M.; Rouault, J.; Laffort, P., Standardized olfactory power law exponents. Editions Universitaires-Sciences Dijon - France, 2002.

5.2.2. Sample preparation and analysis of the vapor phase

First, liquid mixtures of fragrances, with or without ethanol, were prepared gravimetrically using an Adam Equipment balance model AAA250L, with a precision of ±0.2 mg. Four replicates of each mixture (1 mL) were placed on 20 mL closed-cap headspace vials as shown in Figure 5.3 and allowed to equilibrate for at least 24 h. This required time for equilibration proved to be enough in preliminary experiments considering the volume of liquid and vials used in the experiments.

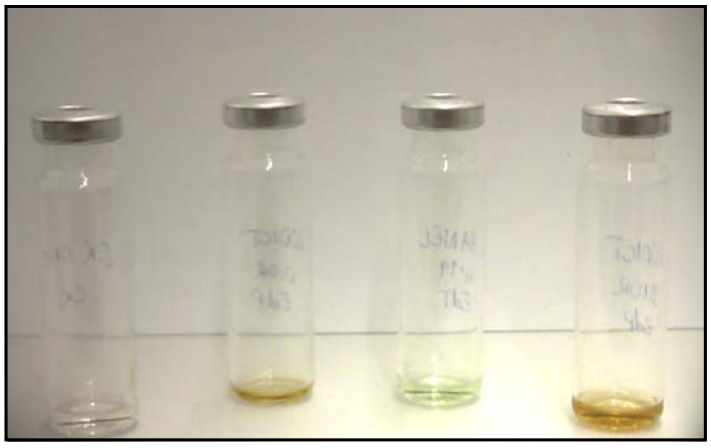


Figure 5.3 – Picture of the closed-cap headspace vials used to evaluate gas phase compositions.

In order to significantly reduce evaporation losses of the volatile fragrant ingredients during weighing, syringes were used to collect pure fragrance components and place them into headspace vials that were previously cap sealed. From the resulting mixture, four aliquots of 1 mL were pipetted and each one was placed in cap sealed 20 mL vials, constituting the four replicates. The temperature at which the experiments were performed (including equilibration and analysis) was controlled in the lab through an air-conditioning system to 23 ± 1 ºC.

Moreover, a washing procedure for the vials was followed which consisted of one washing with tap water and three washings with deionized water (demineralized water or DI water) in an ultrasonic cleaning bath.

The composition in the gas phase was assessed by headspace gas chromatography (HS-GC) using a Varian CP-3800 (presented in Figure 5.4) equipped with a split/splitless injector, FID detector and a capillary column Chrompack CP-Wax 52 CB, 50 m length, 0.25 mm i.d., 0.2 μm film thickness.

Figure 5.4 – Picture of the gas chromatograph with mass spectrometer (GC-MS) used at the LSRE.

The oven temperature was programmed isothermal at 60 ºC for 7 min, heated up to 100 ºC at a heating rate of 20 ºC/min, held isothermal for 3 min, then heated up to 220 ºC at a heating rate of 20 ºC/min, and finally held isothermal for 5 min. The injector and detector ports were set at 240 and 250 ºC, respectively. Injection volume for the gas phase was 0.5 ml with a split ratio of 1:25. Injection was performed using a gas-tight syringe from SGE and a headspace auto sampler HT250D by HTA S.r.L. The carrier gas was helium (He N60) with a constant flow rate of 1 ml/min. Calibration lines were obtained for the pure fragrant components of each system using liquid samples and analyzed in triplicate. These calibration curves are presented in Figure 5.5. The GC was operated with the same temperature program for the analysis of liquid samples as for the headspace samples, although the injection volume used for the liquid was 0.1 μl and the split ratio was set at 1:150.

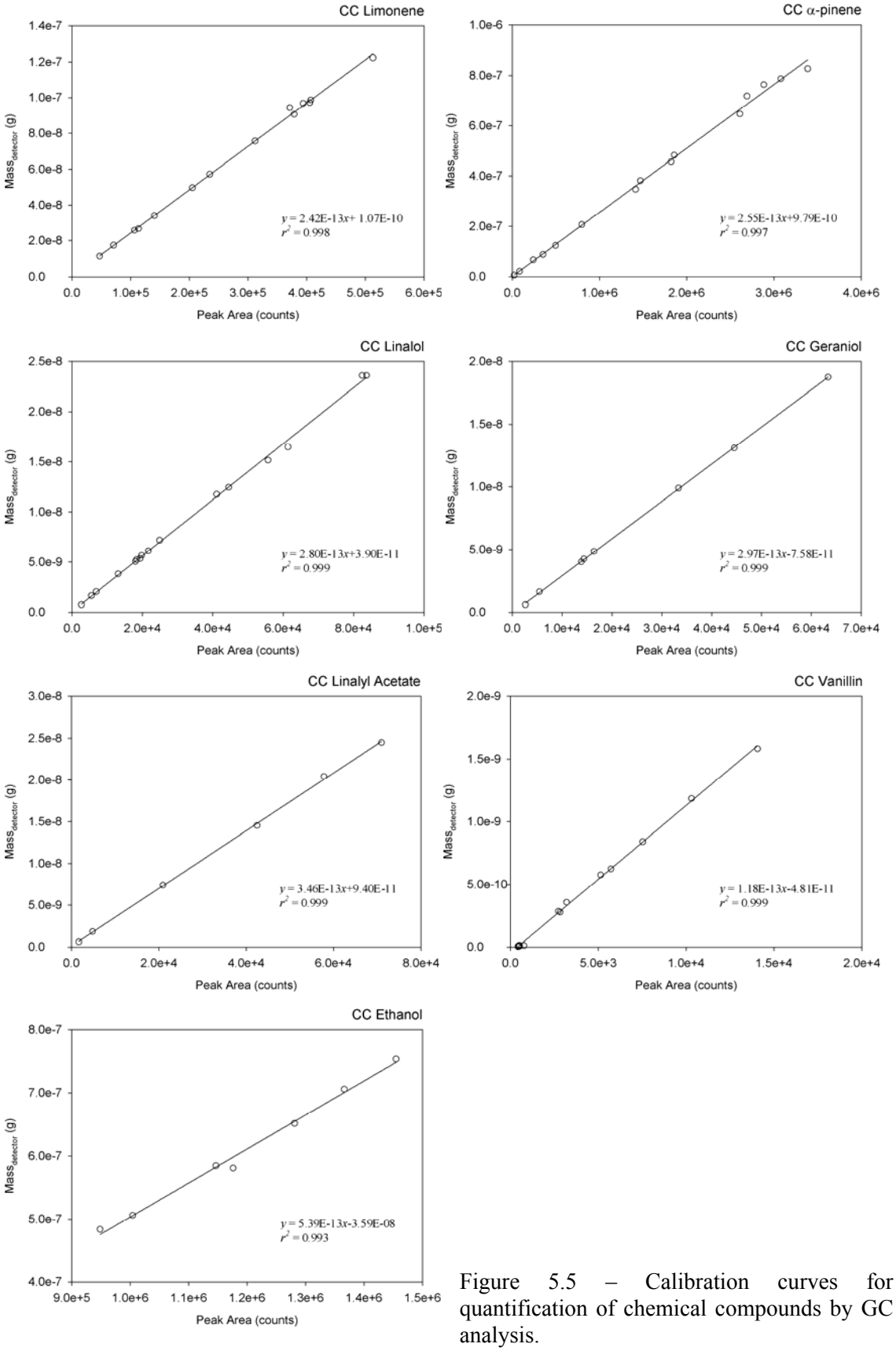


Figure 5.5 – Calibration curves for quantification of chemical compounds by GC analysis.

5.2.3. Olfactory analysis

Some selected perfumery systems studied in this work were subjected to an experimental olfactory analysis. Two non-trained male panelists (26 and 35 years old), non-smokers with normal olfactory function were chosen. The olfactory evaluations were performed during three days in a temperature-controlled environment (23 ± 1ºC), were not intensive and were carried out at the same time of the day per mixture stimulus and subject. The testing protocol allowed the panelists to be aware of what fragrances composed the system under evaluation (*e.g.* for a binary mixture the two components were known) and to smell each pure fragrance compound, prior to the evaluation of the samples. Throughout that test, subjects were given time to make meaningful associations that would help them remembering the odor of the pure fragrances. In between evaluations the panelists smelled coffee beans to remove the previous odors. Each system was evaluated separately from the others, and the samples were presented randomly, so panelists did not know the composition of each one. Overall, 31 different samples (with four replicates each) were evaluated by each panelist, including binary, ternary, and quaternary mixtures. For each sample/replicate the panelists had to choose the strongest perceived odor and whenever two (or more) fragrance ingredients were perceived with the same intensity they were both assigned to that mixture.

5.3. Results & Discussion

First, it should be said that the selection of the fragrant species obeys to the typical formulation and composition of perfumery products. These are normally constituted by three types of notes (top, middle and base notes, according to their volatility and sensorial properties) and one or more solvents (ethanol and water, though they may also include other chemicals such as stabilizers). Top notes (*e.g.* limonene or α-pinene) comprise those chemicals that are most volatile, and so tend to have an impact in the first seconds or minutes after applying the mixture; then, as their smell starts to fade, the scent of the middle or heart notes (*e.g.* geraniol or linalool) becomes more noticeable and can be perceived for hours; finally, the odor would evolve to the scent given by the base notes (*e.g.* vanillin) which often have the lowest volatility and so remain longer, persisting for several hours or even days. The selected solvent (ethanol) is the lightest of

all the compounds. Water was not included since we use a GC with a flame ionization detector (FID) which is not suitable for water measurement. Moreover, no stabilizers or UV filters were considered as well. Nevertheless there is a large range of volatilities among the fragrant components used throughout this work (see Table 5.1). At a glance, this traditional perfume composition holds that perfumes can be viewed as blends, composed of top, middle, and base notes together with solvents as previously discussed in Chapters 2 and 3. However, in terms of its olfactory perception, it is known that all fragrant species will be evaporating simultaneously, though at different rates (depending on volatility, composition, molecular structure, and molecular interactions) from the time the perfume is applied (Teixeira*, et al.*, 2009a). The group assignment for the UNIFAC and ASOG methods is presented in Table 5.2 for all the components studied in this work while the systems are shown in Table 5.3.

Table 5.2 - UNIFAC and ASOG group assignment for the selected fragrant components. The UNIFAC-D and A-UNIFAC methods use the same group assignment as the original UNIFAC.

Compound	UNIFAC groups assignment	ASOG groups assignment
Limonene	2 x CH_3, 3 x CH_2, CH, CH_2=C, CH=C	ν_{ki} = 2 x CH_2, 4 x C=C, 3.8 x CyCH; ν_i^{FH} = 10
α-pinene	3 x CH_3, 2 x CH_2, 2 x CH, C, CH=C	ν_{ki} = 3 x CH_2, 2 x C=C, 4.1 x CyCH; ν_i^{FH} = 10
Linalool	3 x CH_3, 2 x CH_2, C, CH_2=C, CH=C, OH	ν_{ki} = 5.5 x CH_2, 4 x C=C, OH; ν_i^{FH} = 11
Geraniol	3 x CH_3, 3 x CH_2, CH=C, OH	ν_{ki} = 6 x CH_2, 4 x C=C, OH; ν_i^{FH} = 11
Ethanol	CH_3,CH_2, OH	ν_{ki} = 2 x CH_2, OH; ν_i^{FH} = 3
Linalyl Acetate	3 x CH_3, 2 x CH_2, C, CH=CH_2, CH=C, CH_3COO	ν_{ki} = 6.5 x CH_2, 4 x C=C, 3 x COO; ν_i^{FH} = 14
Vanillin	3 x ACH, 2 x AC, ACOH, CHO, CH_3O	ν_{ki} = CH_2, 6 x ArCH, OH, O, CHO; ν_i^{FH} = 11

Table 5.3 – Fragrance systems studied in this work comprising binary, ternary and quaternary mixtures.

	Components			
FS1	α–pinene + Linalool			
FS2	Limonene + Linalool			
FS3	α–pinene + Limonene			
FS4	α–pinene + Limonene	+ Linalool		
FS5	α–pinene + Geraniol			
FS6	α–pinene + Limonene	+ Geraniol		
FS7	α–pinene + Linalool	+ Geraniol		
FS8	Linalool + Geraniol			
FS9	Limonene + Geraniol			
FS10	Limonene + Linalool	+ Geraniol		
FS11	α–pinene + Limonene	+ Linalool	+ Geraniol	
FS12	α–pinene + Linalyl acetate			
FS13	Limonene + Linalyl acetate			
FS14	α–pinene + Limonene	+ Linalyl acetate		
FS15	Limonene + Linalool	+ Geraniol	+ Ethanol	
FS16	Limonene + Geraniol	+ Vanillin	+ Ethanol	

It should be highlighted that the UNIFAC-D and A-UNIFAC methods use the same group assignment as the original UNIFAC. In Table 5.3 are presented all the binary, ternary and quaternary systems studied, while in Table 5.4 the experimental results obtained for the molar compositions in the liquid and vapor phases of all these systems at 296 K are shown.

Table 5.4 – Experimental compositions of the liquid (x_i) and vapor (y_i) phases for the different binary, ternary and quaternary systems studied in this work.

N	x_{Lim}	x_{LOH}	x_{Pin}	x_{Ger}	x_{EtOH}	$x_{Lin.\ ac.}$	x_{Van}	y_{Lim}	y_{LOH}	y_{Pin}	y_{Ger}	y_{EtOH}	$y_{Lin.\ ac.}$	y_{Van}
1	-	2.04E-01	7.96E-01	-	-	-	-	-	2.01E-02	9.80E-01	-	-	-	-
2	-	5.84E-01	4.16E-01	-	-	-	-	-	5.29E-02	9.47E-01	-	-	-	-
3	-	7.64E-01	2.36E-01	-	-	-	-	-	1.03E-01	8.97E-01	-	-	-	-
4	8.02E-01	1.98E-01	-	-	-	-	-	9.43E-01	5.67E-02	-	-	-	-	-
5	4.21E-01	5.79E-01	-	-	-	-	-	8.49E-01	1.51E-01	-	-	-	-	-
6	2.45E-01	7.55E-01	-	-	-	-	-	7.46E-01	2.54E-01	-	-	-	-	-
7	2.12E-01	-	7.88E-01	-	-	-	-	9.66E-02	-	9.03E-01	-	-	-	-
8	5.33E-01	-	4.67E-01	-	-	-	-	2.93E-01	-	7.07E-01	-	-	-	-
9	7.64E-01	-	2.36E-01	-	-	-	-	5.26E-01	-	4.74E-01	-	-	-	-
10	1.83E-01	6.34E-01	1.82E-01	-	-	-	-	2.20E-01	8.40E-02	6.96E-01	-	-	-	-
11	4.38E-01	2.14E-01	3.48E-01	-	-	-	-	2.95E-01	3.21E-02	6.73E-01	-	-	-	-
12	1.28E-01	6.25E-02	8.09E-01	-	-	-	-	5.59E-02	1.14E-02	9.33E-01	-	-	-	-
13	8.53E-01	6.38E-02	8.32E-02	-	-	-	-	7.50E-01	2.08E-02	2.29E-01	-	-	-	-
14	-	-	8.08E-01	1.92E-01	-	-	-	-	-	9.98E-01	2.44E-03	-	-	-
15	-	-	4.22E-01	5.78E-01	-	-	-	-	-	9.95E-01	5.31E-03	-	-	-
16	-	-	1.94E-01	8.06E-01	-	-	-	-	-	9.89E-01	1.14E-02	-	-	-
17	1.44E-01	-	1.68E-01	6.88E-01	-	-	-	2.11E-01	-	7.79E-01	1.47E-02	-	-	-
18	4.67E-01	-	2.96E-01	2.37E-01	-	-	-	3.55E-01	-	6.40E-01	4.59E-03	-	-	-
19	1.35E-01	-	7.83E-01	8.22E-02	-	-	-	6.30E-02	-	9.35E-01	2.18E-03	-	-	-
20	8.78E-01	-	5.47E-02	6.70E-02	-	-	-	8.33E-01	-	1.62E-01	5.90E-03	-	-	-
21	-	1.66E-01	1.85E-01	6.49E-01	-	-	-	-	1.69E-02	9.68E-01	1.47E-02	-	-	-
22	-	4.37E-01	3.57E-01	2.06E-01	-	-	-	-	3.53E-02	9.60E-01	4.59E-03	-	-	-
23	-	1.41E-01	7.84E-01	7.51E-02	-	-	-	-	1.32E-02	9.85E-01	2.18E-03	-	-	-
24	-	8.45E-01	7.95E-02	7.53E-02	-	-	-	-	1.64E-01	8.30E-01	5.90E-03	-	-	-
25	-	7.79E-01	-	2.21E-01	-	-	-	-	9.40E-01	-	5.99E-02	-	-	-
26	-	3.65E-01	-	6.35E-01	-	-	-	-	7.61E-01	-	2.39E-01	-	-	-
27	-	1.97E-01	-	8.03E-01	-	-	-	-	5.73E-01	-	4.27E-01	-	-	-
28	8.13E-01	-	-	1.87E-01	-	-	-	9.72E-01	-	-	2.79E-02	-	-	-
29	4.23E-01	-	-	5.77E-01	-	-	-	9.70E-01	-	-	3.05E-02	-	-	-
30	1.78E-01	-	-	8.22E-01	-	-	-	9.43E-01	-	-	5.70E-02	-	-	-
31	1.65E-01	1.46E-01	-	6.88E-01	-	-	-	8.96E-01	5.78E-02	-	4.61E-02	-	-	-
32	3.75E-01	3.86E-01	-	2.39E-01	-	-	-	8.85E-01	1.06E-01	-	9.73E-03	-	-	-
33	8.27E-01	1.14E-01	-	5.88E-02	-	-	-	9.66E-01	3.00E-02	-	3.80E-03	-	-	-
34	8.73E-02	8.47E-01	-	6.54E-02	-	-	-	4.73E-01	5.13E-01	-	1.35E-02	-	-	-
35	9.95E-02	5.28E-01	6.72E-02	3.06E-01	-	-	-	2.50E-01	1.33E-01	6.01E-01	1.50E-02	-	-	-
36	1.87E-01	2.13E-01	1.03E-01	4.97E-01	-	-	-	3.36E-01	4.23E-02	6.09E-01	1.29E-02	-	-	-
37	1.56E-01	7.51E-02	5.30E-02	7.16E-01	-	-	-	4.40E-01	1.56E-02	5.21E-01	2.39E-02	-	-	-
38	5.84E-01	4.93E-02	7.53E-02	2.92E-01	-	-	-	7.04E-01	7.86E-03	2.79E-01	8.89E-03	-	-	-
39	2.31E-01	1.26E-01	5.13E-01	1.30E-01	-	-	-	1.39E-01	1.41E-02	8.44E-01	3.04E-03	-	-	-
40	2.94E-01	5.05E-02	1.43E-01	5.13E-01	-	-	-	3.92E-01	6.13E-03	5.93E-01	9.13E-03	-	-	-
41	-	-	8.54E-01	-	-	1.46E-01	-	-	-	9.90E-01	-	-	1.03E-02	-
42	-	-	5.02E-01	-	-	4.98E-01	-	-	-	9.49E-01	-	-	5.11E-02	-
43	-	-	2.78E-01	-	-	7.22E-01	-	-	-	8.95E-01	-	-	1.05E-01	-
44	8.29E-01	-	-	-	-	1.71E-01	-	9.53E-01	-	-	-	-	4.65E-02	-
45	4.75E-01	-	-	-	-	5.25E-01	-	8.30E-01	-	-	-	-	1.70E-01	-
46	2.75E-01	-	-	-	-	7.25E-01	-	6.96E-01	-	-	-	-	3.04E-01	-
47	1.89E-01	-	2.07E-01	-	-	6.04E-01	-	1.95E-01	-	7.16E-01	-	-	8.88E-02	-
48	4.67E-01	-	3.58E-01	-	-	1.75E-01	-	3.10E-01	-	6.73E-01	-	-	1.68E-02	-
49	1.19E-01	-	8.39E-01	-	-	4.22E-02	-	5.28E-02	-	9.45E-01	-	-	2.70E-03	-
50	8.64E-01	-	9.16E-02	-	-	4.44E-02	-	7.54E-01	-	2.39E-01	-	-	6.25E-03	-
51	1.41E-01	2.24E-01	-	2.77E-01	3.58E-01	-	-	4.77E-02	4.45E-03	-	1.09E-03	9.47E-01	-	-
52	1.38E-01	1.04E-01	-	4.20E-01	3.37E-01	-	-	5.07E-02	2.01E-03	-	1.73E-03	9.46E-01	-	-
53	1.82E-01	1.08E-01	-	4.70E-01	2.40E-01	-	-	7.65E-02	2.68E-03	-	2.59E-03	9.18E-01	-	-
54	1.53E-01	1.00E-01	-	3.61E-01	3.86E-01	-	-	4.98E-02	1.89E-03	-	1.31E-03	9.47E-01	-	-
55	2.06E-01	2.36E-01	-	1.19E-01	4.39E-01	-	-	6.44E-02	6.05E-03	-	3.82E-04	9.29E-01	-	-
56	5.99E-02	1.28E-01	-	2.42E-01	5.70E-01	-	-	2.68E-02	2.67E-03	-	8.81E-04	9.70E-01	-	-
57	1.91E-01	1.35E-01	-	2.62E-01	4.12E-01	-	-	6.71E-02	3.24E-03	-	1.07E-03	9.29E-01	-	-
58	3.61E-01	1.27E-01	-	1.42E-01	3.70E-01	-	-	9.11E-02	3.38E-03	-	5.09E-04	9.05E-01	-	-
59	2.03E-02	-	-	2.27E-01	6.63E-01	-	9.03E-02	1.21E-02	-	-	3.90E-04	9.88E-01	-	6.53E-07
60	2.67E-02	-	-	2.47E-01	6.39E-01	-	8.71E-02	1.49E-02	-	-	3.84E-04	9.85E-01	-	2.67E-07
61	1.33E-02	-	-	4.93E-01	4.35E-01	-	5.92E-02	6.63E-03	-	-	7.43E-04	9.93E-01	-	4.90E-07
62	3.27E-01	-	-	1.56E-01	4.56E-01	-	6.21E-02	7.84E-02	-	-	1.38E-03	9.20E-01	-	7.28E-07
63	2.06E-01	-	-	1.84E-01	5.37E-01	-	7.31E-02	6.52E-02	-	-	1.61E-03	9.33E-01	-	9.17E-07
64	5.27E-01	-	-	1.90E-01	2.48E-01	-	3.38E-02	8.83E-02	-	-	1.93E-03	9.10E-01	-	1.28E-06
65	1.66E-01	-	-	6.53E-01	1.60E-01	-	2.17E-02	8.20E-02	-	-	1.81E-02	9.00E-01	-	3.94E-06

5.3.1. Evaluation of vapor compositions

The comparison of group-contribution methods and experimental data is presented graphically through Figure 5.6 to Figure 5.9. The quaternary system FS11, composed of two top notes (limonene and α-pinene), a middle note (linalool) and a middle-to-base note (geraniol) is presented first. The molar compositions for the liquid and vapor phases (experimental and predicted with different models) of the corresponding binary and ternary subsystems (FS1 to FS10) are shown graphically in Figure 5.6, while the behavior of the quaternary mixture (FS11) is shown in a tetrahedric diagram in Figure 5.7. Figure 5.8 shows the ternary diagram with the liquid and predicted vapor compositions for the ternary system FS14, composed by two top notes (limonene and α-pinene) and a middle note (linalyl acetate). In order to bring us closer to a real perfume formulation, two quaternary systems, consisting of top, middle, and base notes plus a solvent (ethanol) were evaluated. The tetrahedric representations for quaternary systems of Limonene + Geraniol + Linalool + Ethanol (FS15) and Limonene + Geraniol + Vanillin + Ethanol (FS16) are presented in Figure 5.9. Both systems can be viewed as more representative of the initial perfume formulation, having three different notes within a solvent matrix.

Visual inspection of Figure 5.6 to Figure 5.9 shows small differences among all predictive methods and the experimental data: vapor compositions are grouped around the experimental value in most cases, with some exceptions in Figure 5.6 and Figure 5.8. Towards a quantitative comparison, the average relative deviations (ARD, %) between experimental and predicted values were calculated as:

$$ARD(\%) = \frac{100}{NP}\sum_{1}^{NP}\frac{\left|y_i^{\exp.} - y_i^{calc.}\right|}{y_i^{\exp.}} \tag{5.25}$$

where NP stands for the number of experimental data points, y_i for the vapor molar fraction of component i and superscripts *exp.* and *calc.* for experimental or calculated compositions, respectively. The relative deviations for each single composition ($\delta y = 100|y_i^{exp.} - y_i^{calc.}|/y_i^{exp.}$) between the experimental data and those predicted with the four methods are presented in Table 5.5. Results can be as good as 0.001% or as bad as 530% (observed for only one system, the quaternary mixture FS16, with the A-

UNIFAC) depending on the method, fragrance components and compositions considered.

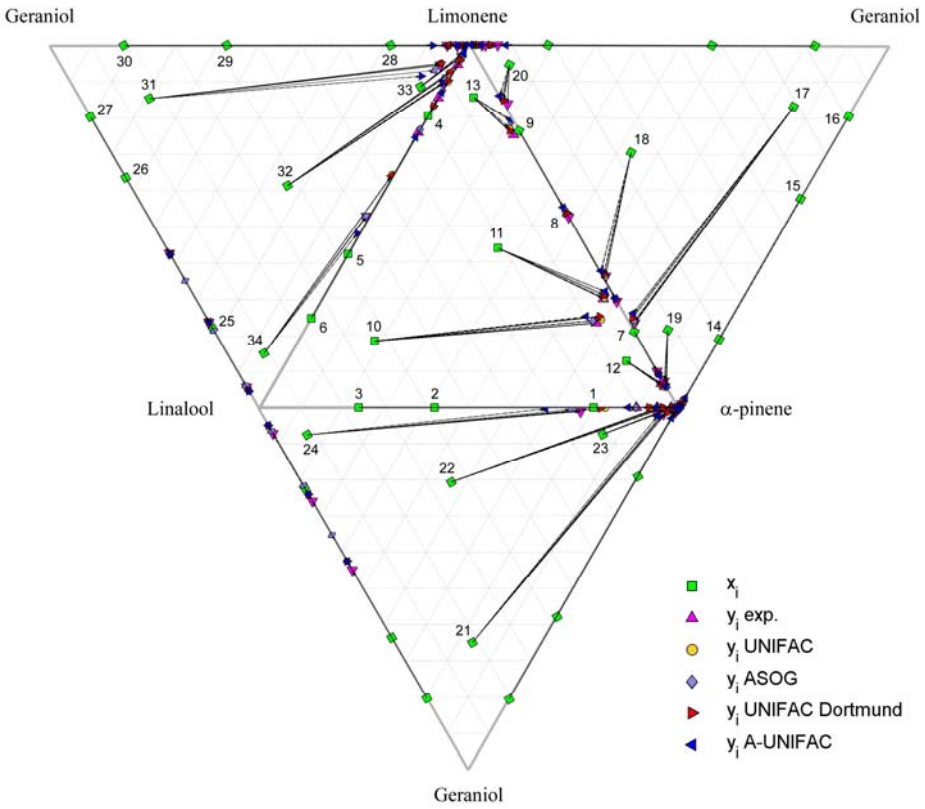


Figure 5.6 – Representation of the liquid composition and comparison between the experimental and predicted vapor compositions for the binary and ternary subsystems in the quaternary system [Limonene + α-pinene + Linalool + Geraniol].

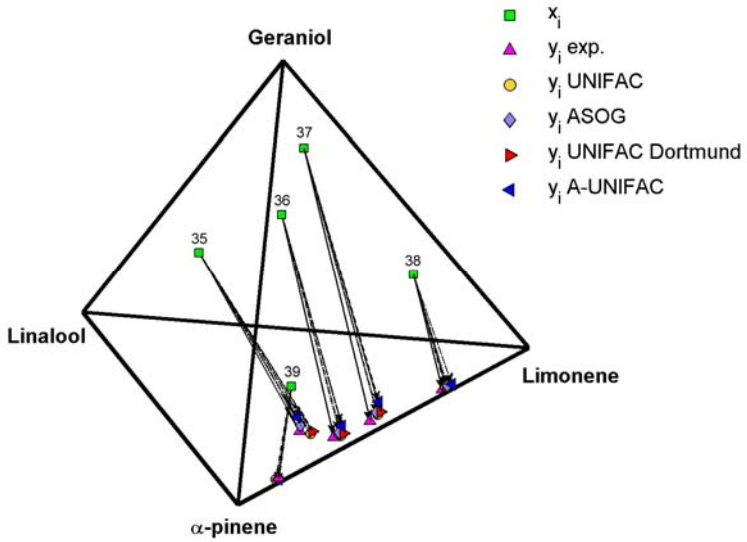


Figure 5.7 - Representation of the liquid composition and comparison between the experimental and predicted vapor compositions for the quaternary system [Limonene + α-pinene + Linalool + Geraniol].

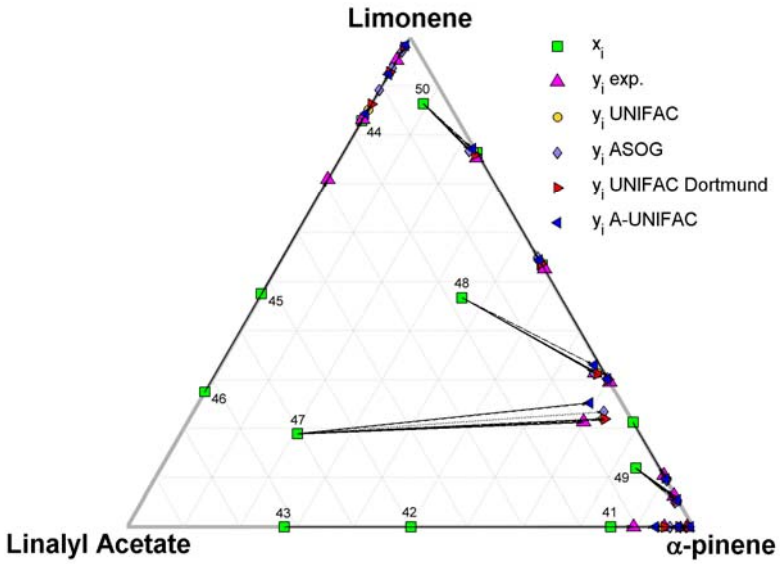


Figure 5.8 - Representation of the liquid composition and comparison between the experimental and predicted vapor compositions for ternary system [Limonene + Linalyl acetate + α-pinene].

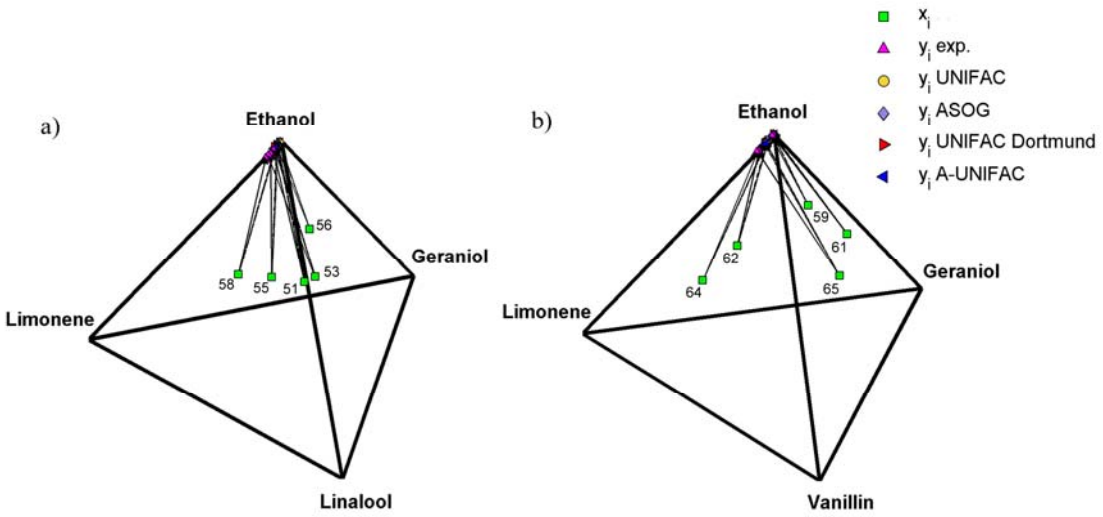


Figure 5.9 - Representation of the liquid composition and comparison between the experimental and predicted vapor compositions for the quaternary systems of: a) [Limonene + Geraniol + Linalool + Ethanol]; b) [Limonene + Geraniol + Vanillin + Ethanol].

Table 5.6 summarizes the results for each system and component. At the bottom of Table 5.6 are shown the global average deviations for each component. Here, it is clear that results are really good for the most volatile components (ethanol and α-pinene, with ARD's of 3.7 and 2.0%, respectively) and not so much for the less volatile fragrances.

Table 5.5 – Average relative deviations (ARD) between experimental and predicted vapor compositions for all fragrance ingredients in each sample for all fragrance systems.

	UNIFAC							ASOG							UNIFAC Dortmund							A-UNIFAC						
N	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin. ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin. ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin. ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin. ac.}$	δy_{Van}
1	-	1	0.02	-	-	-	-	-	33	1	-	-	-	-	-	10	0.2	-	-	-	-	-	17	0.3	-	-	-	-
2	-	24	1	-	-	-	-	-	1	0.1	-	-	-	-	-	24	1	-	-	-	-	-	21	1	-	-	-	-
3	-	32	4	-	-	-	-	-	0.4	0.05	-	-	-	-	-	29	3	-	-	-	-	-	24	3	-	-	-	-
4	1	18	-	-	-	-	-	3	45	-	-	-	-	-	1	22	-	-	-	-	-	1	20	-	-	-	-	-
5	5	31	-	-	-	-	-	3	16	-	-	-	-	-	6	33	-	-	-	-	-	6	34	-	-	-	-	-
6	11	32	-	-	-	-	-	2	7	-	-	-	-	-	11	33	-	-	-	-	-	12	35	-	-	-	-	-
7	1	-	0.1	-	-	-	-	3	-	0.3	-	-	-	-	2	-	0.3	-	-	-	-	0.01	-	0.001	-	-	-	-
8	3	-	1	-	-	-	-	3	-	1	-	-	-	-	3	-	1	-	-	-	-	3	-	1	-	-	-	-
9	3	-	4	-	-	-	-	4	-	5	-	-	-	-	2	-	2	-	-	-	-	3	-	4	-	-	-	-
10	9	22	0.3	-	-	-	-	8	4	3	-	-	-	-	14	22	2	-	-	-	-	24	19	5	-	-	-	-
11	2	11	0.3	-	-	-	-	5	37	1	-	-	-	-	4	19	1	-	-	-	-	9	18	3	-	-	-	-
12	2	7	0.2	-	-	-	-	2	61	1	-	-	-	-	7	9	1	-	-	-	-	6	2	0.4	-	-	-	-
13	2	2	8	-	-	-	-	5	59	10	-	-	-	-	1	14	6	-	-	-	-	3	21	10	-	-	-	-
14	-	-	0.1	49	-	-	-	-	-	0.1	41	-	-	-	-	-	0.1	31	-	-	-	-	-	0.1	22	-	-	-
15	-	-	0.2	40	-	-	-	-	-	0.2	42	-	-	-	-	-	0.2	41	-	-	-	-	-	0.2	44	-	-	-
16	-	-	0.5	42	-	-	-	-	-	1	48	-	-	-	-	-	1	53	-	-	-	-	-	1	62	-	-	-
17	7	-	2	4	-	-	-	8	-	3	1	-	-	-	12	-	4	2	-	-	-	23	-	7	2	-	-	-
18	0.3	-	0.5	30	-	-	-	1	-	1	28	-	-	-	2	-	1	16	-	-	-	7	-	4	20	-	-	-
19	2	-	0.1	21	-	-	-	4	-	0.2	17	-	-	-	3	-	0.3	15	-	-	-	3	-	0.3	6	-	-	-
20	2	-	8	30	-	-	-	2	-	11	29	-	-	-	1	-	5	20	-	-	-	2	-	11	13	-	-	-
21	-	11	0.1	9	-	-	-	-	58	1	9	-	-	-	-	19	0.3	3	-	-	-	-	27	1	3	-	-	-
22	-	9	1	39	-	-	-	-	14	1	11	-	-	-	-	7	0.4	39	-	-	-	-	3	0.3	36	-	-	-
23	-	2	0.1	40	-	-	-	-	37	1	8	-	-	-	-	8	0.2	47	-	-	-	-	14	0.3	50	-	-	-
24	-	5	1	53	-	-	-	-	54	11	10	-	-	-	-	11	2	50	-	-	-	-	20	4	46	-	-	-
25	-	1	-	18	-	-	-	-	0.4	-	7	-	-	-	-	1	-	18	-	-	-	-	1	-	18	-	-	-
26	-	0.1	-	0.4	-	-	-	-	3	-	10	-	-	-	-	0.1	-	0.5	-	-	-	-	0.1	-	0.3	-	-	-
27	-	1	-	1	-	-	-	-	13	-	18	-	-	-	-	1	-	1	-	-	-	-	1	-	1	-	-	-
28	2	-	-	69	-	-	-	2	-	-	70	-	-	-	2	-	-	71	-	-	-	2	-	-	70	-	-	-
29	1	-	-	32	-	-	-	1	-	-	32	-	-	-	1	-	-	35	-	-	-	1	-	-	37	-	-	-
30	1	-	-	13	-	-	-	1	-	-	11	-	-	-	1	-	-	12	-	-	-	1	-	-	17	-	-	-
31	1	15	-	9	-	-	-	1	19	-	4	-	-	-	1	13	-	7	-	-	-	2	18	-	13	-	-	-
32	4	29	-	13	-	-	-	1	16	-	44	-	-	-	4	31	-	16	-	-	-	4	33	-	17	-	-	-
33	0.2	4	-	28	-	-	-	1	45	-	1	-	-	-	0.4	7	-	31	-	-	-	0.3	5	-	28	-	-	-
34	35	31	-	63	-	-	-	9	8	-	21	-	-	-	34	30	-	62	-	-	-	37	32	-	64	-	-	-
35	20	26	2	31	-	-	-	14	2	7	19	-	-	-	24	23	4	28	-	-	-	37	21	10	26	-	-	-
36	10	30	3	2	-	-	-	9	11	5	25	-	-	-	13	29	5	1	-	-	-	23	27	11	2	-	-	-
37	10	5	9	8	-	-	-	10	33	10	18	-	-	-	12	2	11	11	-	-	-	21	1	18	12	-	-	-

N	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}
38	2	3	4	2	-	-	-	3	21	6	6	-	-	-	2	6	5	11	-	-	-	5	5	12	8	-	-	-
39	1	7	0.3	20	-	-	-	0.2	37	1	11	-	-	-	4	16	0.3	28	-	-	-	9	17	1	28	-	-	-
40	4	1	3	24	-	-	-	5	9	4	33	-	-	-	7	3	5	20	-	-	-	14	0.2	10	23	-	-	-
41	-	-	0.3	-	-	27	-	-	-	0.1	-	-	14	-	-	-	1	-	-	90	-	-	-	1	-	-	49	-
42	-	-	3	-	-	49	-	-	-	3	-	-	56	-	-	-	3	-	-	51	-	-	-	2	-	-	46	-
43	-	-	6	-	-	48	-	-	-	7	-	-	61	-	-	-	7	-	-	57	-	-	-	4	-	-	36	-
44	3	-	-	-	-	60	-	2	-	-	-	-	36	-	3	-	-	-	-	54	-	3	-	-	-	-	64	-
45	12	-	-	-	-	56	-	13	-	-	-	-	63	-	12	-	-	-	-	58	-	11	-	-	-	-	55	-
46	22	-	-	-	-	51	-	28	-	-	-	-	64	-	24	-	-	-	-	55	-	21	-	-	-	-	48	-
47	12	-	2	-	-	44	-	20	-	1	-	-	54	-	1	-	6	-	-	51	-	29	-	3	-	-	36	-
48	1	-	0.1	-	-	31	-	2	-	1	-	-	8	-	2	-	2	-	-	18	-	7	-	2	-	-	42	-
49	1	-	0.1	-	-	9	-	4	-	0.2	-	-	152	-	2	-	0.2	-	-	39	-	2	-	0.02	-	-	45	-
50	2	-	5	-	-	33	-	2	-	8	-	-	84	-	0.5	-	1	-	-	16	-	2	-	6	-	-	45	-
51	56	81	-	71	3	-	-	67	58	-	71	4	-	-	57	66	-	69	3	-	-	52	65	-	69	3	-	-
52	57	80	-	70	3	-	-	62	43	-	69	4	-	-	59	63	-	69	3	-	-	53	62	-	68	3	-	-
53	58	79	-	71	5	-	-	61	46	-	69	5	-	-	58	62	-	69	5	-	-	52	60	-	68	5	-	-
54	56	82	-	71	3	-	-	62	49	-	70	3	-	-	58	67	-	69	3	-	-	53	66	-	69	3	-	-
55	63	89	-	73	5	-	-	74	77	-	74	6	-	-	64	79	-	70	5	-	-	60	80	-	71	5	-	-
56	64	87	-	76	2	-	-	73	60	-	78	2	-	-	70	76	-	75	2	-	-	65	76	-	76	2	-	-
57	64	87	-	77	5	-	-	71	67	-	77	5	-	-	65	76	-	75	5	-	-	62	76	-	75	5	-	-
58	66	90	-	76	7	-	-	71	78	-	75	7	-	-	63	80	-	73	7	-	-	61	80	-	74	6	-	-
59	55	-	-	41	1	-	22	58	-	-	37	1	-	22	65	-	-	40	1	-	25	51	-	-	34	1	-	133
60	55	-	-	36	1	-	94	57	-	-	31	1	-	101	65	-	-	34	1	-	88	51	-	-	28	1	-	513
61	55	-	-	17	0.4	-	23	56	-	-	10	0.4	-	68	62	-	-	17	0.4	-	22	50	-	-	8	0.3	-	510
62	56	-	-	91	5	-	5	55	-	-	90	5	-	17	55	-	-	90	5	-	4	49	-	-	90	4	-	370
63	54	-	-	91	4	-	36	55	-	-	90	4	-	25	58	-	-	90	4	-	32	48	-	-	90	4	-	163
64	51	-	-	89	5	-	16	45	-	-	87	5	-	7	43	-	-	88	4	-	16	40	-	-	87	4	-	531
65	46	-	-	91	6	-	82	41	-	-	90	6	-	68	47	-	-	91	6	-	82	37	-	-	90	5	-	66
ARD (%)	21	30	2	41	4	41	40	22	32	3	38	4	59	44	23	28	2	40	4	49	38	23	29	4	40	3	47	327

Table 5.6 – Average relative deviations (ARD) between experimental and predicted vapor compositions for all fragrance ingredients in each fragrance system. Average deviations are presented at the bottom for each ingredient in different systems containing or not ethanol.

	UNIFAC							ASOG							UNIFAC Dortmund							A-UNIFAC						
System	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}	δy_{Lim}	δy_{LOH}	δy_{Pin}	δy_{Ger}	δy_{EtOH}	$\delta y_{Lin.\ ac.}$	δy_{Van}
FS1	-	19	2	-	-	-	-	-	12	0.3	-	-	-	-	-	21	2	-	-	-	-	-	21	1	-	-	-	-
FS2	6	27	-	-	-	-	-	3	23		-	-	-	-	6	29		-	-	-	-	6	30	-	-	-	-	-
FS3	2	-	2	-	-	-	-	3	-	2	-	-	-	-	2	-	1	-	-	-	-	2	-	2	-	-	-	-
FS4	4	11	2	-	-	-	-	5	40	4	-	-	-	-	7	16	2	-	-	-	-	10	15	5	-	-	-	-
FS5	-	-	0.3	44	-	-	-	-	-	0.3	43	-	-	-	-	-	0.3	42	-	-	-	-	-	0.3	43	-	-	-
FS6	3	-	3	21	-	-	-	4	-	4	19	-	-	-	5	-	3	13	-	-	-	9	-	5	10	-	-	-
FS7	-	7	0.3	35	-	-	-	-	41	3	10	-	-	-	-	11	1	35	-	-	-	-	16	1	34	-	-	-
FS8	-	1	-	6	-	-	-	-	6	-	11	-	-	-	-	1	-	6	-	-	-	-	1	-	6	-	-	-
FS9	1	-	-	38	-	-	-	1	-	-	38	-	-	-	1	-	-	39	-	-	-	1	-	-	41	-	-	-
FS10	10	20	-	28	-	-	-	3	22	-	18	-	-	-	10	20	-	29	-	-	-	11	22	-	30	-	-	-
FS11	8	12	4	14	-	-	-	7	19	5	19	-	-	-	10	13	5	17	-	-	-	18	12	10	16	-	-	-
FS12	-	-	3	-	-	41	-	-	-	3	-	-	44	-	-	-	3	-	-	66	-	-	-	2	-	-	44	-
FS13	12	-		-	-	56	-	14	-		-	-	54	-	13	-	-	-	-	56	-	12	-		-	-	56	-
FS14	4	-	2	-	-	29	-	7	-	3	-	-	74	-	1	-	2	-	-	31	-	10	-	3	-	-	42	-
FS15	60	84		73	4	-	-	68	60	-	73	5	-	-	62	71	-	71	4	-	-	57	71	-	71	4	-	-
FS16	53	-	-	65	3	-	40	52	-	-	62	3	-	44	56	-	-	64	3	-	38	46	-	-	61	3	-	327
All systems																												
ARD (%)	21	30	2	41	4	41	40	22	32	3	38	4	59	44	23	28	2	40	4	49	38	23	29	4	40	3	47	327
All systems without ethanol																												
ARD (%)	6	13	2	26	-	41	-	5	24	3	21	-	59	-	7	16	2	25	-	49	-	10	16	4	25	-	47	-

Table 5.7 – Predicted activity coefficients for all fragrance ingredients in each perfumery system with different models.

	UNIFAC							ASOG							UNIFAC Dortmund							A-UNIFAC						
N	γ_{Lim}	γ_{LOH}	γ_{Pin}	γ_{Ger}	γ_{EtOH}	$\gamma_{Lin. ac.}$	γ_{Van}	γ_{Lim}	γ_{LOH}	γ_{Pin}	γ_{Ger}	γ_{EtOH}	$\gamma_{Lin. ac.}$	γ_{Van}	γ_{Lim}	γ_{LOH}	γ_{Pin}	γ_{Ger}	γ_{EtOH}	$\gamma_{Lin. ac.}$	γ_{Van}	γ_{Lim}	γ_{LOH}	γ_{Pin}	γ_{Ger}	γ_{EtOH}	$\gamma_{Lin. ac.}$	γ_{Van}
1	-	2.08	1.13	-	-	-	-	-	1.26	1.02	-	-	-	-	-	1.91	1.15	-	-	-	-	-	1.76	1.15	-	-	-	-
2	-	1.12	1.61	-	-	-	-	-	1.05	1.15	-	-	-	-	-	1.10	1.57	-	-	-	-	-	1.08	1.50	-	-	-	-
3	-	1.03	1.91	-	-	-	-	-	1.01	1.23	-	-	-	-	-	1.03	1.81	-	-	-	-	-	1.02	1.69	-	-	-	-
4	1.09	1.90	-	-	-	-	-	1.01	1.16	-	-	-	-	-	1.13	1.88	-	-	-	-	-	1.14	1.94	-	-	-	-	-
5	1.48	1.11	-	-	-	-	-	1.09	1.03	-	-	-	-	-	1.52	1.10	-	-	-	-	-	1.56	1.11	-	-	-	-	-
6	1.72	1.03	-	-	-	-	-	1.13	1.01	-	-	-	-	-	1.73	1.03	-	-	-	-	-	1.80	1.03	-	-	-	-	-
7	1.04	-	1.00	-	-	-	-	1.01	-	1.00	-	-	-	-	1.08	-	1.01	-	-	-	-	1.04	-	1.00	-	-	-	-
8	1.01	-	1.02	-	-	-	-	1.00	-	1.01	-	-	-	-	1.03	-	1.04	-	-	-	-	1.01	-	1.02	-	-	-	-
9	1.00	-	1.04	-	-	-	-	1.00	-	1.01	-	-	-	-	1.01	-	1.07	-	-	-	-	1.00	-	1.04	-	-	-	-
10	1.55	1.08	1.71	-	-	-	-	1.09	1.03	1.18	-	-	-	-	1.60	1.07	1.67	-	-	-	-	1.67	1.06	1.55	-	-	-	-
11	1.10	1.89	1.17	-	-	-	-	1.01	1.19	1.05	-	-	-	-	1.16	1.78	1.21	-	-	-	-	1.18	1.77	1.16	-	-	-	-
12	1.04	4.05	1.02	-	-	-	-	1.01	1.42	1.00	-	-	-	-	1.11	4.17	1.03	-	-	-	-	1.09	3.74	1.03	-	-	-	-
13	1.01	3.18	1.08	-	-	-	-	1.00	1.28	1.03	-	-	-	-	1.03	3.79	1.14	-	-	-	-	1.04	4.02	1.08	-	-	-	-
14	-	-	1.12	2.20	-	-	-	-	-	1.12	2.09	-	-	-	-	-	1.14	1.98	-	-	-	-	-	1.13	1.84	-	-	-
15	-	-	1.61	1.13	-	-	-	-	-	1.58	1.12	-	-	-	-	-	1.56	1.10	-	-	-	-	-	1.50	1.09	-	-	-
16	-	-	2.00	1.02	-	-	-	-	-	1.93	1.02	-	-	-	-	-	1.86	1.02	-	-	-	-	-	1.75	1.01	-	-	-
17	1.65	-	1.80	1.06	-	-	-	1.62	-	1.75	1.05	-	-	-	1.67	-	1.73	1.04	-	-	-	1.78	-	1.61	1.05	-	-	-
18	1.11	-	1.20	1.80	-	-	-	1.12	-	1.18	1.75	-	-	-	1.18	-	1.24	1.67	-	-	-	1.21	-	1.18	1.69	-	-	-
19	1.04	-	1.03	3.56	-	-	-	1.02	-	1.04	3.46	-	-	-	1.12	-	1.05	3.44	-	-	-	1.11	-	1.05	3.18	-	-	-
20	1.01	-	1.09	3.15	-	-	-	1.01	-	1.06	3.19	-	-	-	1.03	-	1.15	3.68	-	-	-	1.04	-	1.09	4.02	-	-	-
21	-	1.02	2.01	1.02	-	-	-	-	1.26	1.73	1.06	-	-	-	-	1.02	1.87	1.01	-	-	-	-	1.01	1.75	1.01	-	-	-
22	-	1.08	1.71	1.09	-	-	-	-	1.03	1.28	1.52	-	-	-	-	1.07	1.65	1.07	-	-	-	-	1.05	1.57	1.06	-	-	-
23	-	2.01	1.14	2.02	-	-	-	-	1.16	1.06	2.86	-	-	-	-	1.85	1.16	1.83	-	-	-	-	1.70	1.16	1.72	-	-	-
24	-	1.00	2.20	1.01	-	-	-	-	1.00	1.34	1.59	-	-	-	-	1.00	2.04	1.01	-	-	-	-	1.00	1.86	1.01	-	-	-
25	-	1.00	-	1.00	-	-	-	-	1.03	-	1.36	-	-	-	-	1.00	-	1.00	-	-	-	-	1.00	-	1.00	-	-	-
26	-	1.00	-	1.00	-	-	-	-	1.23	-	1.07	-	-	-	-	1.00	-	1.00	-	-	-	-	1.00	-	1.00	-	-	-
27	-	1.00	-	1.00	-	-	-	-	1.39	-	1.02	-	-	-	-	1.00	-	1.00	-	-	-	-	1.00	-	1.00	-	-	-
28	1.08	-	-	2.00	-	-	-	1.08	-	-	1.95	-	-	-	1.12	-	-	1.95	-	-	-	1.14	-	-	2.06	-	-	-
29	1.48	-	-	1.12	-	-	-	1.48	-	-	1.11	-	-	-	1.51	-	-	1.10	-	-	-	1.58	-	-	1.11	-	-	-
30	1.86	-	-	1.02	-	-	-	1.81	-	-	1.02	-	-	-	1.81	-	-	1.01	-	-	-	1.94	-	-	1.02	-	-	-
31	1.87	1.01	-	1.02	-	-	-	1.64	1.29	-	1.05	-	-	-	1.83	1.01	-	1.01	-	-	-	1.95	1.01	-	1.01	-	-	-
32	1.54	1.08	-	1.10	-	-	-	1.21	1.03	-	1.45	-	-	-	1.57	1.07	-	1.07	-	-	-	1.63	1.08	-	1.09	-	-	-
33	1.07	2.06	-	2.09	-	-	-	1.03	1.12	-	2.76	-	-	-	1.11	2.05	-	2.05	-	-	-	1.12	2.12	-	2.18	-	-	-
34	1.97	1.00	-	1.01	-	-	-	1.20	1.00	-	1.61	-	-	-	1.93	1.00	-	1.01	-	-	-	2.05	1.00	-	1.01	-	-	-
35	1.85	1.01	2.05	1.02	-	-	-	1.31	1.04	1.45	1.31	-	-	-	1.83	1.01	1.93	1.01	-	-	-	1.95	1.01	1.76	1.02	-	-	-
36	1.67	1.04	1.84	1.05	-	-	-	1.42	1.14	1.55	1.15	-	-	-	1.68	1.04	1.77	1.04	-	-	-	1.78	1.04	1.63	1.04	-	-	-
37	1.80	1.02	1.99	1.02	-	-	-	1.66	1.32	1.82	1.04	-	-	-	1.78	1.02	1.87	1.02	-	-	-	1.90	1.02	1.72	1.02	-	-	-
38	1.21	1.43	1.34	1.45	-	-	-	1.18	1.06	1.26	1.51	-	-	-	1.26	1.37	1.38	1.37	-	-	-	1.30	1.39	1.28	1.41	-	-	-
39	1.13	1.74	1.20	1.76	-	-	-	1.06	1.09	1.11	2.23	-	-	-	1.23	1.62	1.22	1.61	-	-	-	1.25	1.56	1.19	1.58	-	-	-

40	1.47	1.12	1.62	1.13	-	-	-	1.40	1.17	1.52	1.16	-	-	-	1.51	1.10	1.59	1.10	-	-	-	1.58	1.10	1.48	1.11	-	-	-
41	-	-	1.02	-	-	1.56	-	-	-	1.08	-	-	2.61	-	-	-	1.16	-	-	0.24	-	-	-	1.00	-	-	1.06	-
42	-	-	1.18	-	-	1.11	-	-	-	1.49	-	-	1.21	-	-	-	1.35	-	-	1.22	-	-	-	1.02	-	-	1.02	-
43	-	-	1.34	-	-	1.03	-	-	-	1.84	-	-	1.05	-	-	-	1.69	-	-	1.05	-	-	-	1.04	-	-	1.00	-
44	1.01	-	-	-	-	1.24	-	1.08	-	-	-	-	2.13	-	1.02	-	-	-	-	1.43	-	1.01	-	-	-	-	1.11	-
45	1.10	-	-	-	-	1.05	-	1.43	-	-	-	-	1.17	-	1.17	-	-	-	-	1.09	-	1.04	-	-	-	-	1.03	-
46	1.17	-	-	-	-	1.02	-	1.72	-	-	-	-	1.04	-	1.04	-	-	-	-	1.10	-	1.08	-	-	-	-	1.01	-
47	1.11	-	1.28	-	-	1.05	-	1.54	-	1.66	-	-	1.11	-	1.18	-	1.58	-	-	1.09	-	1.08	-	1.03	-	-	1.01	-
48	1.01	-	1.07	-	-	1.32	-	1.07	-	1.13	-	-	2.18	-	1.01	-	1.14	-	-	1.62	-	1.02	-	1.02	-	-	1.07	-
49	1.04	-	1.01	-	-	1.80	-	1.01	-	1.01	-	-	5.04	-	1.07	-	1.01	-	-	2.76	-	1.06	-	1.00	-	-	1.08	-
50	1.00	-	1.06	-	-	1.40	-	1.01	-	1.04	-	-	3.88	-	1.00	-	1.12	-	-	1.78	-	1.00	-	1.05	-	-	1.14	-
51	2.23	0.84	-	0.83	1.13	-	-	1.69	1.14	-	0.85	1.17	-	-	2.02	0.85	-	0.84	1.07	-	-	2.57	0.97	-	0.96	1.20	-	-
52	2.21	0.85	-	0.84	1.13	-	-	1.86	1.30	-	0.83	1.07	-	-	2.00	0.85	-	0.84	1.08	-	-	2.55	0.98	-	0.97	1.20	-	-
53	1.82	0.80	-	0.80	1.15	-	-	1.57	1.14	-	0.81	1.07	-	-	1.70	0.81	-	0.81	1.07	-	-	2.25	0.98	-	0.98	1.26	-	-
54	2.24	0.82	-	0.81	1.11	-	-	1.87	1.28	-	0.81	1.06	-	-	2.02	0.83	-	0.83	1.05	-	-	2.61	0.97	-	0.96	1.20	-	-
55	2.05	0.75	-	0.74	1.08	-	-	1.51	0.98	-	0.76	1.16	-	-	1.87	0.77	-	0.76	1.01	-	-	2.54	0.94	-	0.93	1.25	-	-
56	3.66	0.98	-	0.95	1.09	-	-	2.72	1.68	-	0.89	1.08	-	-	2.98	0.97	-	0.96	1.06	-	-	3.60	1.00	-	0.98	1.10	-	-
57	2.09	0.77	-	0.77	1.09	-	-	1.69	1.13	-	0.77	1.07	-	-	1.89	0.79	-	0.78	1.03	-	-	2.54	0.95	-	0.94	1.24	-	-
58	1.26	0.60	-	0.60	1.06	-	-	1.06	0.74	-	0.62	1.04	-	-	1.22	0.62	-	0.61	0.94	-	-	2.00	0.94	-	0.94	1.47	-	-
59	6.58	-	-	1.21	1.02	-	1.11	5.92	-	-	1.23	0.97	-	1.05	5.02	-	-	1.22	1.01	-	1.05	6.81	-	-	1.30	0.98	-	3.17
60	6.07	-	-	1.18	1.03	-	1.15	5.44	-	-	1.19	0.98	-	1.13	4.69	-	-	1.19	1.02	-	1.10	6.27	-	-	1.25	0.98	-	3.44
61	3.89	-	-	1.05	1.10	-	1.41	3.51	-	-	1.05	1.01	-	1.77	3.23	-	-	1.05	1.09	-	1.38	3.98	-	-	1.08	1.01	-	6.44
62	2.53	-	-	0.89	1.39	-	2.13	2.33	-	-	0.91	1.27	-	2.38	2.35	-	-	0.92	1.28	-	2.13	2.65	-	-	0.93	1.25	-	9.47
63	3.49	-	-	0.94	1.20	-	1.55	3.15	-	-	0.95	1.12	-	1.69	3.03	-	-	0.97	1.14	-	1.56	3.63	-	-	0.99	1.11	-	5.86
64	1.58	-	-	1.03	2.04	-	4.88	1.52	-	-	1.05	1.76	-	5.36	1.59	-	-	1.02	1.77	-	4.26	1.66	-	-	1.04	1.76	-	31.81
65	2.19	-	-	0.99	1.36	-	2.19	2.09	-	-	0.99	1.19	-	3.31	2.06	-	-	0.99	1.30	-	2.06	2.27	-	-	0.99	1.21	-	17.69

However, it should be underlined that the use of relative errors leads to situations like this, although absolute deviations may not be as significant given the magnitude of the compositions studied. Careful inspection of values either on Table 5.5 or Table 5.6 raises the cause for such disparity: the large differences in the volatilities of the different components studied. The perfume formulation combining top, middle and base notes produces mixtures with volatilities covering a range of several orders of magnitude. For the case studied here, this range is of 5 orders of magnitude (see Table 5.1). Thus, it leads to compositions in the vapor phase (*e.g.* mole fractions) also differing in several orders of magnitude, from 0.90 or higher for ethanol and 0.5-0.9 for α-pinene, down to 10^{-2} - 10^{-3} for linalool and geraniol or even to 10^{-6} - 10^{-7} for vanillin (see Table 5.4).
As mole fractions should sum for unity, errors in the most volatile component below 5%, which are good for a prediction, lead to large relative errors in other components with much lower volatility and vapor compositions. This fact is clearer when errors in limonene compositions are inspected in Table 5.6: independently of the predictive method chosen, errors for limonene are acceptable (1 to 14 %) except for systems with ethanol (quaternary systems FS15 and FS16). This is, when a component significantly more volatile is introduced in the mixture. For this reason, ARD values were also calculated for all components excluding these quaternary systems FS15 and FS16 and are presented at the bottom of Table 5.6. These values are acceptable for all components except perhaps geraniol and linalyl acetate where higher deviations were found. But again, these are middle (or middle-to-base) notes, with a large difference in volatility when compared to top notes such as limonene or α-pinene. Even so, it should be emphasized that in most cases the order of magnitude of the composition is well predicted for all components: even for vanillin in system FS16 (which involves ethanol, and a difference in their vapor composition of seven orders of magnitude), errors using the UNIFAC the UNIFAC-D or the ASOG methods are around 40%.

5.3.2. Evaluation of predicted activity coefficients

As the key function of group contribution methods is the prediction of activity coefficients, it is pertinent here to analyze the differences among them. The activity coefficients obtained from different methods are presented in Table 5.7. It is important to highlight that the predicted activity coefficients do not deviate much from ideality for binary mixtures, while greater deviations are observed in some ternary and quaternary

mixtures. In this regard, mixtures with structurally similar components present activity coefficients close to unity (*e.g.* binary geraniol-linalool). However, it is also seen that in some cases where activity coefficients significantly deviate from ideality, the liquid composition (x_i) for the corresponding component is also low, and consequently it will not produce significant differences in the perceived odor as will be discussed later.

The relevance of activity coefficients can be understood better when comparing the effect of ethanol in fragrance evaporation. As mentioned earlier, ethanol is commonly used as solvent in perfumery. Careful inspection of systems FS10 and FS15 (for samples N = 31 and 32 with 52 and 55, from Table 5.4 & Table 5.7) is pertinent and allows such a comparison as presented in Table 5.8. It is possible to see that for the pairs N = 31 & 52 and N = 32 & 55 the liquid compositions of the ternary mixtures (x_i) are very similar to the quaternary ones calculated in a solvent free basis (x'_i). However, the vapor compositions (y_i and for a solvent free basis, y'_i) obtained and presented in Table 5.8 are significantly different, especially for linalool (LOH) and geraniol (Ger).

Table 5.8 – Evaluation of the effect of ethanol on the activity coefficients and vapor compositions of similar mixtures. Compositions are presented for the ternary (x_i *and* y_i) and for the quaternary mixtures with ethanol in a solvent free basis (x'_i *and* y'_i).

N	x_{Lim}	x_{LOH}	x_{Ger}	γ_{Lim}	γ_{LOH}	γ_{Ger}		y_{Lim}	y_{LOH}	y_{Ger}
31	0.165	0.146	0.688	1.87	1.01	1.02	-	8.96E-01	5.78E-02	4.61E-02
32	0.375	0.386	0.239	1.54	1.08	1.10	-	8.85E-01	1.06E-01	9.73E-03
N	x'_{Lim}	x'_{LOH}	x'_{Ger}	γ_{Lim}	γ_{LOH}	γ_{Ger}	γ_{EtOH}	y'_{Lim}	y'_{LOH}	y'_{Ger}
52	0.208	0.157	0.634	2.21	0.85	0.84	1.13	9.31E-01	3.70E-02	3.17E-02
55	0.367	0.421	0.211	2.05	0.75	0.74	1.08	9.09E-01	8.54E-02	5.39E-03

In this way, if we analyze the vapor compositions once more in a solvent free basis, it is possible to see that the presence of ethanol has a retention effect on the release of geraniol and linalool while the relatively non-polar component, limonene, is slightly pushed out of the solution. This behavior is reflected by changes in the components' activity coefficients: it increases for limonene and has a marginal decrease for linalool and geraniol. This happens in a similar extent for all group-contribution methods, being less pronounced with ASOG.

5.3.3. Issues and selection of VLE predictive method

In order to select a predictive method, the ARD for each system and for all systems are presented in Table 5.9. The UNIFAC method resulted in the lowest errors, whether the quaternary systems with ethanol are considered or not. Nevertheless differences among all the used methods are not large. In general, A-UNIFAC performed worse than other methods, despite this is the most complete equation and includes associative interactions. The group assignments used in A-UNIFAC were the same as in the UNIFAC method (as showed in Table 5.2). Linalool, geraniol and ethanol have the hydroxyl associative group, and vanillin has the hydroxyl and aromatic carbon groups. The two-site hydroxyl group is able to self- and cross-associate and the one-site aromatic ring can only cross-associate in presence of an electropositive site. Linalyl acetate has the ester group, but it can only cross-associate in the presence of an electropositive site, such as hydroxyl or carboxyl group which do not appear in that system. Most of the molecules under study have the double bond group which is not included in the A-UNIFAC interaction group parameters' table. However, this is a non-associative group, and so UNIFAC parameters were used. The same was done for vanillin, except for the group –ACOH, whose parameters were recently obtained in-house (Mota, 2010). The use of UNIFAC parameters (which do not separate associative interactions) in the A-UNIFAC method (which separate these interactions) may be behind the worse results obtained with this method, especially for the system containing vanillin. The issue of available parameters is related to the size of the experimental database used in the parameterization itself (which in our opinion may be the limitation of A-UNIFAC). This database (see references of Ferreira*, et al.*, 2005; Andreatta*, et al.*, 2008; Mota, 2010) cannot be compared in number of experimental points and/or types of components with the Dortmund Databank used in the UNIFAC and UNIFAC-D revisions (a larger database with more experimental data to obtain the interaction parameters somehow corrects the lack of the associative term). These assumptions may be behind the slightly worse results obtained with A-UNIFAC, although its theoretical foundations are more suitable for this kind of molecules. Even so, considering systems without ethanol, the A-UNIFAC predicted comparable results with other models, as shown in Table 5.9. It is also important to note that for some systems involving predominantly alcohols (like geraniol and linalool) ASOG performed slightly better overall. This finding was already shown by Gupte and Daubert (Gupte and Daubert, 1986) who compared a large

experimental VLE database with predictions from ASOG and UNIFAC. They have shown that for ternary systems (at low pressures) containing alcohols and water, the ASOG method gave marginally better predictions. From their work it was also possible to see that systems with chemically similar components tended to be better predicted by the ASOG method.

Table 5.9 - ARD obtained for each system in terms of vapor compositions with different models.

	UNIFAC	ASOG	UNIFAC Dortmund	A-UNIFAC
FS1	10	6	11	11
FS2	16	13	18	18
FS3	2	3	2	2
FS4	6	16	8	10
FS5	22	22	21	22
FS6	9	9	7	8
FS7	14	18	16	17
FS8	4	8	4	4
FS9	20	20	20	21
FS10	19	14	20	21
FS11	9	12	11	14
FS12	22	24	35	23
FS13	34	34	34	34
FS14	12	28	12	18
FS15	56	51	52	51
FS16	40	40	41	109
	All systems			
ARD (%)	24	25	29	35
	All systems without ethanol			
ARD (%)	13	16	14	15

Moreover, other studies found in the literature have pointed out slightly better predictions obtained from the ASOG method when compared with the UNIFAC method (for example in mixtures with ketones) (Pereiro, *et al.*, 2005). However, the ASOG method gives much higher deviations for system FS14 (α-pinene + limonene + Linalyl acetate) probably due to the presence of esters in solution (Camacho, *et al.*, 2007). Besides, the ASOG method has not been updated for many years. On the opposite, UNIFAC has been continuously (and recently) updated and extended (Wittig, *et al.*, 2003), covering a larger number of functional groups and their interactions, thus making this method strongly recommended.

An example of this limitation of the ASOG method is seen for vanillin which was used in this work. Vanillin (4-hydroxy-3-methoxybenzaldehyde) is constituted by a benzene ring with aldehyde, methoxy and hydroxyl groups linked in the aromatic carbons 1, 3 and 4, respectively. As the hydroxyl group is linked to an aromatic carbon, it should be considered "aromatic" (group 7 in the ASOG parameters' matrix, instead of group 6) (Tochigi, *et al.*, 1990). The problem here is that there are not available interaction parameters for this group 7 with groups 4, 10 and 11. This is a major problem for group-contribution methods. For the particular systems studied in this work, the limitation was overcome simply by considering the normal hydroxyl group (group 6). Nevertheless, such solution would not be possible for other molecules and/or functional groups. Considering the number of different functional groups present in fragrance molecules and the large number of components used in perfume formulation, the problem is likely to happen with ASOG, rather than with the more developed methods (*e.g.* UNIFAC and UNIFAC-Dortmund), similarly to what happens for A-UNIFAC with other functional groups.

5.3.4. Prediction of perceived odor and olfactory evaluations

The relevance of the data presented so far concerning the compositions in the liquid and gas phases is increased when applied to the prediction of the dominant fragrance odors as they are perceived by the human nose. Following Stevens' Power Law for olfaction, as presented in equation 5.1, the odor intensity of each fragrance ingredient in each mixture was calculated from the vapor phase concentration measured by HS-GC. These odor intensities can then be compared with those predicted using equation 5.4, which uses the thermodynamic models presented before for the estimation of activity coefficients. The results were also compared with an olfactory analysis performed by two panelists (for details see section 5.2. Experimental Methodology – 5.2.3: Olfactory analysis). In this way, two types of comparisons are made here: *i)* between odor intensities experimentally obtained and predicted using models; *ii)* between the dominant odors classified by sensory evaluations using panelists and predicted using an odor character model.

A compilation of these results is presented in Table 5.10. A very good agreement has been found between the experimental and predicted perceived dominant odorant. Considering all the fragrance mixtures studied in this work (binary, ternary, and

quaternary for a total of $N = 65$ samples) similar deviations for the different predictive models were observed between the predicted dominant odor and experimental values. Using the UNIFAC and UNIFAC-D methods for the prediction of the activity coefficients, the dominant odor is correctly predicted in 95.4% of the cases, while the ASOG and the A-UNIFAC performed marginally poorer with 93.8% and 90.8%, respectively.

However, it should be highlighted that deviations were only observed for quaternary mixtures having ethanol in its composition, except for the ASOG that failed to predict the dominant odor of one ternary mixture (see Table 5.10, for N = 33). Binary and ternary systems have shown a full agreement between dominant odors obtained by predicted and experimental gas compositions. Additionally, it should be noted that when deviations were found for the quaternary mixtures, it was observed that the predicted strongest odorant corresponded to the second more intense obtained from the experimental measurements. This fact shows once more the good predictability of the model for odor perception, regardless of the thermodynamic model used for the vapor-liquid equilibrium.

Despite these results, the use of a group-contribution model could be questioned: could the fragrance mixture be considered ideal ($\gamma = 1$) and then reduce the computing effort? In fact, the calculation time for this type of problems is not even significant and so one can neglect that factor *a priori*. On the other hand, it can also be said that if a group contribution method is taken into account there will be the need and expertise to program the corresponding equations to compute the activity coefficients. Nevertheless, this question was previously studied in our group, showing significant differences in the perceived odor when non-idealities are not considered (Mata*, et al.*, 2005a; Mata*, et al.*, 2005b). Moreover, in this case here, considering an ideal solution for the liquid phase for all the fragrance systems, it is observed that the dominant odor is only correctly predicted in 73.4% of the times, comparing with experimental headspace measurements. Thus, if non-idealities are not considered in the context of the problem, significant errors will be introduced in the calculation of the vapor compositions and a lower agreement will be obtained for the prediction of the dominant perceived odorant.

As explained above, the olfactory evaluation of some fragrance mixtures was also performed in order to evaluate and validate the odor intensity model and involved two panelists. For the olfactory analyses, four replicates were used and classified in terms of the strongest fragrance odor by the panelists. In some of the selected mixtures a

similarity for the odor character classification was observed between two fragrance ingredients, so that two olfactory descriptors were assigned, as presented in Table 5.10. The olfactory evaluations when compared with the dominant note experimentally obtained (using chromatographic analysis) have shown an agreement of 65% and 68% for panelist 1 and panelist 2, respectively. The vast majority of the differences were seen for ternary and quaternary mixtures which are more difficult to assess by the nose at the sensory point of view.

In fact, if the average sniffing duration is about 1.6 s (Laing, 1983), and if only one sniff is enough to correctly identify distinct pure odorants (Laing, 1986), it is also true that the identification of odors within mixtures is far more difficult. According to the literature, humans have difficulty in the identification of single odorants in mixtures containing three or more compounds (Chastrette, 1998; Marshall*, et al.*, 2006; Goyert*, et al.*, 2007), although this process may be significantly improved after presenting the pure components of the mixture to the panelists (as was done in this work) (Goyert*, et al.*, 2007).

Finally, it was seen an average agreement of 54% (panelist 1) and 59% (panelist 2) between the olfactory evaluation and the dominant odor obtained with the predictive method using the different thermodynamic models. The majority of the mismatches were observed for the quaternary mixtures with ethanol in the composition. It was seen that for those, the prediction of the dominant odor intensity often indicated a stronger ethanol perception, although from the perfumery point of view, ethanol will be a solvent that evaporates quickly and thus is not expected to be perceived (at least perfumers formulate perfumes with that in mind). This fact has mainly to do with the psychophysical model used for the odor intensity scale and the high exponent value *(n)* for ethanol (see Table 5.1). It is also to note that these predictions are performed at time zero, that is, at equilibrium conditions without considering diffusion or convection effects. It was previously observed by the authors that predicted odor intensities using this model for systems containing ethanol, resulted in stronger perceptions of this component than in other perception models like the OV model (Teixeira*, et al.*, 2010a). In short, the odor character evaluation performed by sensorial analysis has shown a good correlation with the odor character obtained from the headspace concentrations measured by gas chromatography and also with those from the predictive methods.

Table 5.10 – Odor intensities and character of perfumery mixtures measured by headspace gas chromatography and by olfactory evaluation (panelists), compared with the predicted values obtained using thermodynamic models and equation 5.4.

	Experimental Data								Panel		UNIFAC							
N	**ψ_{Lim}**	**ψ_{LOH}**	**ψ_{Pin}**	**ψ_{Ger}**	**ψ_{EtOH}**	**$\psi_{Lin.\ ac.}$**	**ψ_{Van}**	**max ψ**	**Pan 1**	**Pan 2**	**ψ_{Lim}**	**ψ_{LOH}**	**ψ_{Pin}**	**ψ_{Ger}**	**ψ_{EtOH}**	**$\psi_{Lin.\ ac.}$**	**ψ_{Van}**	**max ψ**
1	-	37	168	-	-	-	-	Pin	-	-	-	43	195	-	-	-	-	Pin
2	-	47	140	-	-	-	-	Pin	-	-	-	50	169	-	-	-	-	Pin
3	-	51	111	-	-	-	-	Pin	-	-	-	53	139	-	-	-	-	Pin
4	29	36	-	-	-	-	-	LOH	-	-	34	41	-	-	-	-	-	LOH
5	25	46	-	-	-	-	-	LOH	-	-	30	50	-	-	-	-	-	LOH
6	21	49	-	-	-	-	-	LOH	-	-	26	53	-	-	-	-	-	LOH
7	18	-	152	-	-	-	-	Pin	-	-	20	-	183	-	-	-	-	Pin
8	24	-	119	-	-	-	-	Pin	-	-	29	-	142	-	-	-	-	Pin
9	28	-	87	-	-	-	-	Pin	-	-	32	-	103	-	-	-	-	Pin
10	18	46	93	-	-	-	-	Pin	Lim	Pin/Lim	22	51	116	-	-	-	-	Pin
11	23	37	108	-	-	-	-	Pin	Lim	Lim	27	42	132	-	-	-	-	Pin
12	15	29	154	-	-	-	-	Pin	Pin	Pin	17	36	187	-	-	-	-	Pin
13	29	28	53	-	-	-	-	Pin	Lim/LOH	Lim	34	33	63	-	-	-	-	Pin
14	-	-	160	17	-	-	-	Pin	Pin	Pin	-	-	195	24	-	-	-	Pin
15	-	-	142	20	-	-	-	Pin	Pin	Pin	-	-	170	28	-	-	-	Pin
16	-	-	111	22	-	-	-	Pin	Ger/Pin	Pin	-	-	129	30	-	-	-	Pin
17	18	-	98	21	-	-	-	Pin	-	-	21	-	114	29	-	-	-	Pin
18	25	-	105	18	-	-	-	Pin	-	-	28	-	123	24	-	-	-	Pin
19	15	-	149	15	-	-	-	Pin	-	-	17	-	185	21	-	-	-	Pin
20	28	-	41	16	-	-	-	Pin	-	-	34	-	52	18	-	-	-	Pin
21	-	25	105	24	-	-	-	Pin	Pin	Pin	-	30	126	28	-	-	-	Pin
22	-	38	128	18	-	-	-	Pin	Pin	Pin	-	43	161	19	-	-	-	Pin
23	-	31	158	16	-	-	-	Pin	Pin	Pin	-	36	194	16	-	-	-	Pin
24	-	46	74	14	-	-	-	Pin	LOH	LOH	-	53	87	13	-	-	-	Pin
25	-	42	-	16	-	-	-	LOH	-	-	-	53	-	19	-	-	-	LOH
26	-	30	-	20	-	-	-	LOH	-	-	-	41	-	27	-	-	-	LOH
27	-	23	-	21	-	-	-	LOH	-	-	-	33	-	30	-	-	-	LOH
28	26	-	-	25	-	-	-	Lim	Lim	Lim	34	-	-	23	-	-	-	Lim
29	23	-	-	23	-	-	-	Lim/Ger	Lim	Lim	30	-	-	28	-	-	-	Lim
30	19	-	-	25	-	-	-	Ger	Ger	Ger	24	-	-	30	-	-	-	Ger
31	19	25	-	23	-	-	-	LOH	Lim	Lim	23	30	-	28	-	-	-	LOH
32	24	39	-	17	-	-	-	LOH	Lim	Lim	29	43	-	20	-	-	-	LOH
33	29	29	-	14	-	-	-	LOH/Lim	LOH	Lim	34	35	-	15	-	-	-	LOH
34	14	52	-	14	-	-	-	LOH	LOH/Lim	LOH	19	55	-	12	-	-	-	LOH
35	15	43	63	20	-	-	-	Pin	Pin	Pin/LOH	19	47	78	21	-	-	-	Pin
36	19	32	75	21	-	-	-	Pin	Lim/Pin	Pin/Lim	23	34	91	25	-	-	-	Pin
37	18	20	57	23	-	-	-	Pin	LIM	LIM	22	24	68	29	-	-	-	Pin

38	27	19	55	19	-	-	-	Pin	LIM	LIM	31	23	67	24	-	-	-	Pin
39	19	29	131	17	-	-	-	Pin	Pin	Pin	22	34	162	19	-	-	-	Pin
40	22	18	82	20	-	-	-	Pin	Pin/Lim	Pin	26	21	100	26	-	-	-	Pin
41	-	-	159	-	-	10	-	Pin	-	-	-	-	192	-	-	11	-	Pin
42	-	-	128	-	-	15	-	Pin	-	-	-	-	159	-	-	15	-	Pin
43	-	-	101	-	-	16	-	Pin	-	-	-	-	126	-	-	17	-	Pin
44	28	-	-	-	-	12	-	Lim	-	-	34	-	-	-	-	11	-	Lim
45	23	-	-	-	-	16	-	Lim	-	-	28	-	-	-	-	15	-	Lim
46	19	-	-	-	-	17	-	Lim	-	-	24	-	-	-	-	17	-	Lim
47	17	-	87	-	-	15	-	Pin	-	-	20	-	107	-	-	16	-	Pin
48	23	-	106	-	-	10	-	Pin	-	-	27	-	128	-	-	11	-	Pin
49	14	-	155	-	-	6	-	Pin	-	-	16	-	189	-	-	8	-	Pin
50	29	-	55	-	-	6	-	Pin	-	-	34	-	66	-	-	7	-	Pin
51	19	30	-	18	30	-	-	EtOH	-	-	25	34	-	20	37	-	-	EtOH
52	19	22	-	21	29	-	-	EtOH	-	-	24	26	-	23	36	-	-	EtOH
53	20	22	-	22	24	-	-	EtOH	-	-	26	26	-	24	31	-	-	EtOH
54	20	23	-	20	31	-	-	EtOH	-	-	26	26	-	22	39	-	-	EtOH
55	24	36	-	14	35	-	-	LOH	-	-	28	34	-	15	43	-	-	EtOH
56	17	28	-	19	38	-	-	EtOH	-	-	21	29	-	19	45	-	-	EtOH
57	23	28	-	19	33	-	-	EtOH	-	-	28	28	-	19	41	-	-	EtOH
58	27	30	-	15	35	-	-	EtOH	-	-	32	28	-	16	43	-	-	EtOH
59	8	-	-	9	17	-	5	EtOH	EtOH/Lim	EtOH	17	-	-	20	46	-	10	EtOH
60	9	-	-	9	17	-	3	EtOH	EtOH	EtOH/Lim	18	-	-	21	45	-	10	EtOH
61	7	-	-	10	16	-	4	EtOH	Lim/Ger	Lim	12	-	-	25	38	-	10	EtOH
62	17	-	-	14	17	-	5	Lim	Lim	Lim	33	-	-	16	44	-	11	EtOH
63	16	-	-	15	17	-	5	EtOH	Lim	Lim	32	-	-	17	45	-	11	EtOH
64	17	-	-	15	16	-	5	Lim	Lim/Ger	Lim	33	-	-	18	39	-	12	EtOH
65	13	-	-	27	11	-	6	Ger	Lim	Lim	25	-	-	27	24	-	8	Ger
							Deviations (%)		35.5	32.3								4.6

Table 5.11 – (continued)

N	ASOG								UNIFAC Dortmund								A-UNIFAC							
	ψ_{Lim}	ψ_{LOH}	ψ_{Pin}	ψ_{Ger}	ψ_{EtOH}	$\psi_{Lin. ac.}$	ψ_{Van}	max ψ	ψ_{Lim}	ψ_{LOH}	ψ_{Pin}	ψ_{Ger}	ψ_{EtOH}	$\psi_{Lin. ac.}$	ψ_{Van}	max ψ	ψ_{Lim}	ψ_{LOH}	ψ_{Pin}	ψ_{Ger}	ψ_{EtOH}	$\psi_{Lin. ac.}$	ψ_{Van}	max ψ
1	-	36	185	-	-	-	-	Pin	-	42	197	-	-	-	-	Pin	-	41	196	-	-	-	-	Pin
2	-	49	143	-	-	-	-	Pin	-	50	167	-	-	-	-	Pin	-	50	163	-	-	-	-	Pin
3	-	53	112	-	-	-	-	Pin	-	53	135	-	-	-	-	Pin	-	53	131	-	-	-	-	Pin
4	33	35	-	-	-	-	-	LOH	35	41	-	-	-	-	-	LOH	33	57	-	-	-	-	-	LOH
5	27	48	-	-	-	-	-	LOH	30	50	-	-	-	-	-	LOH	32	49	-	-	-	-	-	LOH
6	22	53	-	-	-	-	-	LOH	26	53	-	-	-	-	-	LOH	27	53	-	-	-	-	-	LOH
7	20	-	183	-	-	-	-	Pin	21	-	183	-	-	-	-	Pin	21	-	183	-	-	-	-	Pin
8	28	-	142	-	-	-	-	Pin	29	-	144	-	-	-	-	Pin	29	-	143	-	-	-	-	Pin
9	32	-	102	-	-	-	-	Pin	32	-	105	-	-	-	-	Pin	32	-	103	-	-	-	-	Pin
10	20	50	97	-	-	-	-	Pin	23	51	115	-	-	-	-	Pin	24	50	114	-	-	-	-	Pin
11	26	36	125	-	-	-	-	Pin	28	42	134	-	-	-	-	Pin	27	51	126	-	-	-	-	Pin
12	17	25	185	-	-	-	-	Pin	17	36	188	-	-	-	-	Pin	17	52	185	-	-	-	-	Pin
13	34	24	61	-	-	-	-	Pin	34	35	65	-	-	-	-	Pin	34	54	62	-	-	-	-	Pin
14	-	-	195	23	-	-	-	Pin	-	-	197	23	-	-	-	Pin	-	-	197	22	-	-	-	Pin
15	-	-	168	27	-	-	-	Pin	-	-	167	27	-	-	-	Pin	-	-	164	27	-	-	-	Pin
16	-	-	127	30	-	-	-	Pin	-	-	124	30	-	-	-	Pin	-	-	121	30	-	-	-	Pin
17	21	-	113	29	-	-	-	Pin	21	-	112	29	-	-	-	Pin	22	-	112	28	-	-	-	Pin
18	28	-	123	23	-	-	-	Pin	29	-	125	23	-	-	-	Pin	28	-	118	28	-	-	-	Pin
19	17	-	185	20	-	-	-	Pin	18	-	186	20	-	-	-	Pin	17	-	183	30	-	-	-	Pin
20	34	-	51	18	-	-	-	Pin	34	-	53	19	-	-	-	Pin	34	-	51	31	-	-	-	Pin
21	-	32	118	28	-	-	-	Pin	-	30	122	28	-	-	-	Pin	-	31	121	28	-	-	-	Pin
22	-	42	140	21	-	-	-	Pin	-	43	158	19	-	-	-	Pin	-	44	159	18	-	-	-	Pin
23	-	30	187	18	-	-	-	Pin	-	35	196	16	-	-	-	Pin	-	43	187	19	-	-	-	Pin
24	-	53	68	15	-	-	-	Pin	-	53	84	13	-	-	-	Pin	-	55	81	13	-	-	-	Pin
25	-	54	-	21	-	-	-	LOH	-	53	-	19	-	-	-	LOH	-	53	-	19	-	-	-	LOH
26	-	44	-	28	-	-	-	LOH	-	41	-	27	-	-	-	LOH	-	41	-	27	-	-	-	LOH
27	-	37	-	30	-	-	-	LOH	-	33	-	30	-	-	-	LOH	-	33	-	30	-	-	-	LOH
28	34	-	-	22	-	-	-	Lim	35	-	-	22	-	-	-	Lim	33	-	-	33	-	-	-	Lim
29	30	-	-	27	-	-	-	Lim	30	-	-	27	-	-	-	Lim	32	-	-	27	-	-	-	Lim
30	24	-	-	30	-	-	-	Ger	24	-	-	30	-	-	-	Ger	25	-	-	30	-	-	-	Ger
31	22	32	-	29	-	-	-	LOH	23	30	-	28	-	-	-	LOH	24	30	-	28	-	-	-	LOH
32	27	42	-	22	-	-	-	LOH	29	43	-	20	-	-	-	LOH	31	42	-	19	-	-	-	LOH
33	34	28	-	17	-	-	-	Lim	35	35	-	15	-	-	-	LOH	34	51	-	22	-	-	-	LOH
34	16	55	-	14	-	-	-	LOH	19	55	-	12	-	-	-	LOH	19	55	-	12	-	-	-	LOH
35	17	47	65	23	-	-	-	Pin	19	47	75	21	-	-	-	Pin	20	47	74	21	-	-	-	Pin
36	22	35	84	26	-	-	-	Pin	23	34	89	25	-	-	-	Pin	25	34	89	25	-	-	-	Pin
37	22	26	65	29	-	-	-	Pin	22	24	66	29	-	-	-	Pin	24	24	65	29	-	-	-	Pin

38	31	21	65	24	-	-	-	Pin	32	23	68	23	-	-	-	Pin	32	23	64	24	-	-	-	Pin
39	21	29	156	21	-	-	-	Pin	22	33	163	18	-	-	-	Pin	22	37	155	20	-	-	-	Pin
40	26	22	97	27	-	-	-	Pin	27	21	99	26	-	-	-	Pin	28	21	99	26	-	-	-	Pin
41	-	-	197	-	-	14	-	Pin	-	-	204	-	-	6	-	Pin	-	-	190	-	-	10	-	Pin
42	-	-	178	-	-	16	-	Pin	-	-	169	-	-	16	-	Pin	-	-	148	-	-	15	-	Pin
43	-	-	148	-	-	17	-	Pin	-	-	141	-	-	17	-	Pin	-	-	112	-	-	17	-	Pin
44	34	-	-	-	-	13	-	Lim	34	-	-	-	-	12	-	Lim	33	-	-	-	-	11	-	Lim
45	31	-	-	-	-	16	-	Lim	29	-	-	-	-	16	-	Lim	28	-	-	-	-	15	-	Lim
46	27	-	-	-	-	17	-	Lim	22	-	-	-	-	17	-	Lim	23	-	-	-	-	17	-	Lim
47	23	-	121	-	-	16	-	Pin	3	-	119	-	-	16	-	Pin	21	-	96	-	-	16	-	Pin
48	28	-	131	-	-	14	-	Pin	27	-	132	-	-	12	-	Pin	29	-	125	-	-	11	-	Pin
49	16	-	189	-	-	11	-	Pin	17	-	189	-	-	9	-	Pin	32	-	189	-	-	6	-	Pin
50	34	-	65	-	-	10	-	Pin	34	-	67	-	-	8	-	Pin	20	-	65	-	-	7	-	Pin
51	22	38	-	20	38	-	-	LOH	24	34	-	20	36	-	-	EtOH	27	35	-	20	35	-	-	LOH
52	23	30	-	23	35	-	-	EtOH	24	26	-	23	35	-	-	EtOH	17	27	-	24	33	-	-	EtOH
53	24	30	-	24	30	-	-	LOH	25	27	-	24	29	-	-	EtOH	34	27	-	25	28	-	-	Lim
54	24	30	-	22	38	-	-	EtOH	25	26	-	22	38	-	-	EtOH	27	26	-	22	36	-	-	EtOH
55	25	38	-	15	45	-	-	EtOH	27	35	-	15	41	-	-	EtOH	31	35	-	15	39	-	-	EtOH
56	19	35	-	19	45	-	-	EtOH	19	29	-	19	45	-	-	EtOH	21	29	-	20	44	-	-	EtOH
57	25	32	-	19	41	-	-	EtOH	27	29	-	20	40	-	-	EtOH	30	29	-	20	38	-	-	EtOH
58	30	30	-	16	43	-	-	EtOH	31	28	-	16	41	-	-	EtOH	35	28	-	16	37	-	-	EtOH
59	16	-	-	20	45	-	10	EtOH	15	-	-	20	46	-	10	EtOH	18	-	-	20	47	-	15	EtOH
60	18	-	-	21	44	-	10	EtOH	17	-	-	21	45	-	10	EtOH	19	-	-	21	46	-	16	EtOH
61	12	-	-	25	36	-	10	EtOH	11	-	-	25	37	-	10	EtOH	12	-	-	25	38	-	18	EtOH
62	32	-	-	16	42	-	12	EtOH	32	-	-	16	42	-	11	EtOH	40	-	-	16	40	-	16	Lim
63	31	-	-	17	43	-	11	EtOH	30	-	-	17	43	-	11	EtOH	38	-	-	18	42	-	16	EtOH
64	33	-	-	18	36	-	12	EtOH	34	-	-	18	36	-	11	EtOH	34	-	-	18	40	-	25	EtOH
65	24	-	-	27	22	-	9	Ger	24	-	-	27	23	-	8	Ger	26	-	-	28	22	-	16	Ger
						Deviations (%)		9.2								4.6								6.2

5.4. Conclusions

The vapor-liquid compositions of several fragrance systems were evaluated by HS-GC and compared with those predicted by four group-contribution methods. The results have shown that the UNIFAC method is a suitable model for predicting the headspace composition, performing marginally better than the remaining methods, while the A-UNIFAC performed poorer. Moreover, a methodology to describe the odor character of multi-component mixtures was applied using the predicted vapor compositions from perfumery mixtures, showing very good agreement with the experimental measurements. Besides, their comparison with an olfactory evaluation has shown a relatively good agreement. From this point of view, it can be said that this methodology is suitable for the prediction of the odor character of fragrance mixtures. In this way, the repetitive and costly trial-and-error experimental assays in perfume formulation may be reduced. This type of predictions will speed up the pre-formulation process and reduce final product costs, enhancing the development of perfumed products.

5.5. References

Anderson, T. F., Prausnitz, J. M., Application of UNIQUAC equation to calculation of multicomponent phase-equilibria - 1. Vapor-liquid-equilibria, *Industrial & Engineering Chemistry Process Design and Development*, 17, (4): 552-561, 1978

Andreatta, A. E., Casas, L. M., Hegel, P., Bottini, S. B., Brignole, E. A., Phase equilibria in ternary mixtures of methyl oleate, glycerol, and methanol, *Industrial & Engineering Chemistry Research*, 47, (15): 5157-5164, 2008

Behan, J. M., Perring, K. D., Perfume interactions with sodium dodecyl-sulfate solutions, *International Journal of Cosmetic Science*, 9, (6): 261-268, 1987

Berglund, B., Olsson, M. J., Odor-intensity interaction in binary and ternary mixtures, *Perception & Psychophysics*, 53, (5): 475-482, 1993

Butler, H., Poucher's Perfumes, Cosmetics and Soaps, Kluwer Academic Publishers - Boston / London, 2000

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Camacho, A. G., Moll, J. M., Canzonieri, S., Postigo, M. A., Vapor-liquid equilibrium data for the binary methyl esters (butyrate, pentanoate, and hexanoate) (1) plus propanenitrile (2) systems at 93.32 kPa, *Journal of Chemical and Engineering Data*, 52, (3): 871-875, 2007

Chapman, J., MATLAB programming for engineers, California, Brooks Cole Publishing Company, 2000

Chastrette, M., Data management in olfaction studies, *Sar and Qsar in Environmental Research*, 8, (3-4): 157-181, 1998

Chemspider, Database of Chemical Structures and Property Predictions - Royal Society of Chemistry, from http://www.chemspider.com/Default.aspx, Last Accessed on February, 2011

Costa, R., Moggridge, G. D., Saraiva, P. M., Chemical product engineering: an emerging paradigm within chemical engineering, *AIChE Journal*, 52, (6): 1976-1986, 2006

Cussler, E. L., Wagner, A., Marchal-Heussler, L., Designing Chemical Products Requires More Knowledge of Perception, *AIChE Journal*, 56, (2): 283-288, 2010

Devos, M., Patte, F., Rouault, J., Laffort, P., Gemert, L. J. v., Standardized Human Olfactory Thresholds, Oxford, IRL press at Oxford University Press, 1990

Devos, M., Rouault, J., Laffort, P., Standardized olfactory power law exponents, Dijon - France, Editions Universitaires-Sciences 2002

Ferreira, O., Macedo, E. A., Bottini, S. B., Extension of the A-UNIFAC model to mixtures of cross- and self-associating compounds, *Fluid Phase Equilibria*, 227, (2): 165-176, 2005

Fredenslund, A., Jones, R., Prausnitz, J. M., Group-contribution estimation of activity coefficients in nonideal liquid mixtures, *AIChE Journal*, 21, (6): 1086-1099, 1975

Friberg, S. E., Evaporation from a Limonene Emulsion, *Journal of Dispersion Science and Technology*, 28, 11-20, 2007

Friberg, S. E., Constant vapor pressure evaporation from emulsions, *Colloid and Polymer Science*, 286, 47-50, 2008

Friberg, S. E., Phase Diagram Approach to Evaporation from Emulsions with n Oil Compounds, *Journal of Physical Chemistry B*, 113, (12): 3894-3900, 2009

Friberg, S. E., Al-Bawab, A., Odehb, F., Bozeya, A., Aikens, P. A., Emulsion evaporation path. A first comparison of experimental and calculated values, *Colloids and Surfaces a-Physicochemical and Engineering Aspects*, 338, (1-3): 102-106, 2009

Fu, Y. H., Sandler, S. I., Orbey, H., A modified uniquac model that includes hydrogen-bonding, *Industrial & Engineering Chemistry Research*, 34, (12): 4351-4363, 1995

Gilbert, A., What the Nose Knows - The Science of Scent in Everyday Life, New York, Crown Publishers, 2008

Gmehling, J., Fischer, K., Li, J., Schiller, M., Status and results of group contribution methods, *Pure and Applied Chemistry*, 65, (5): 919-926, 1993

Goyert, H. F., Frank, M. E., Gent, J. F., Hettinger, T. P., Characteristic component odors emerge from mixtures after selective adaptation, *Brain Research Bulletin*, 72, (1): 1-9, 2007

Graedel, T. E., The Perceived Intensity of Natural Odors, *Journal of Chemical Education*, 61, (8): 681-686, 1984

Gupte, P. A., Daubert, T. E., Prediction of low-pressure vapor-liquid-equilibria of non-hydrocarbon-containing systems Asog or Unifac, *Industrial & Engineering Chemistry Process Design and Development*, 25, (2): 481-486, 1986

Hill, M., Chemical Product Engineering-The third paradigm, *Computers & Chemical Engineering*, 33, (5): 947-953, 2009

Jakob, A., Grensemann, H., Lohmann, J., Gmehling, J., Further development of modified UNIFAC (Dortmund): Revision and extension 5, *Industrial & Engineering Chemistry Research*, 45, (23): 7924-7933, 2006

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Laffort, P., Walsh, R. M., Spillane, W. J., Application of the U and Gamma ' models in binary sweet taste mixtures, *Chemical Senses*, 27, (6): 511-520, 2002

Laing, D. G., Natural sniffing gives optimum odour perception for humans, *Perception*, 12, (2): 99-117, 1983

Laing, D. G., Identification of single dissimilar odors is achieved by humans with a single sniff, *Physiology & Behavior*, 37, (1): 163-170, 1986

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Mackay, D., Shiu, W. Y., Ma, K.-C., Lee, S. C., Handbook of Physical-Chemical Properties and Environmental Fate for Organic Chemicals, Boca Raton, Florida (USA), CRC Press, Taylor & Francis Group, 2006

Marshall, K., Laing, D. G., Jinks, A. L., Hutchinson, I., The capacity of humans to identify components in complex odor-taste mixtures, *Chemical Senses*, 31, (6): 539-545, 2006

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Effect of nonidealities in perfume mixtures using the perfumery ternary diagrams (PTD) concept, *Industrial & Engineering Chemistry Research*, 44, (12): 4435-4441, 2005a

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005b

Mengarelli, A. C., Brignole, E. A., Bottini, S. B., Activity coefficients of associating mixtures by group contribution, *Fluid Phase Equilibria*, 163, (2): 195-207, 1999

Mota, F. L., Solubility Studies with Pharmaceutical Applications. Department of Chemical Engineering. Porto, University of Porto. PhD 2010

Olsson, M. J., An integrated model of intensity and quality of odor mixtures, *Olfaction and Taste Xii*, 855, 837-840, 1998

Olsson, M. J., Berglund, B., Odor-intensity interaction in binary and ternary mixtures, *Perception & Psychophysics*, 53, (5): 475-482, 1993

Pereiro, A. B., Rodriguez, A., Canosa, J., Tojo, J., Vapor-liquid equilibria for systems of diethyl carbonate and ketones and determination of group interaction parameters for the UNIFAC and ASOG methods, *Fluid Phase Equilibria*, 235, (1): 83-91, 2005

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Prausnitz, J. M., Lichtenthaler, R. N., Azevedo, E. G. d., Molecular Thermodynamics of Fluid - Phase Equilibria, New Jersey, Prentice Hall, 1999

Sell, C. S., On the unpredictability of odor, *Angewandte Chemie-International Edition*, 45, (38): 6254-6261, 2006

Skjold-Jorgensen, S., Kolbe, B., Gmehling, J., Rasmussen, P., Vapor-liquid-equilibria by unifac group contribution. Revision and Extension, *Industrial & Engineering Chemistry Process Design and Development*, 18, (4): 714-722, 1979

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Stevens, S. S., The surprising simplicity of sensory metrics, *Psychological Bulletin*, 55, (4): 29-39, 1958

Stevens, S. S., Concerning the psychophysical power law, *Quarterly Journal of Experimental Psychology*, 16, (4): 383-385, 1964

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009a

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009b

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE Journal*, 56, (4): 1090-1106, 2010a

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., Perfumery Radar: A Predictive Tool for Perfume Family Classification, *Industrial & Engineering Chemistry Research*, 49, 11764–11777, 2010b

Tochigi, K., Tiegs, D., Gmehling, J., Kojima, K., Determination of new ASOG parameters, *Journal of Chemical Engineering Japan*, 23, (4): 453-463, 1990

Ulrich, K. T., Eppinger, S. D., Product Design and Development, New York, McGraw-Hill, 2000

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

Wei, J., Product engineering. Molecular structure and properties, New York, Oxford University Press, 2007

Weidlich, U., Gmehling, J., A modified unifac model .1. Prediction of VLE, h^E, and γ^∞, *Industrial & Engineering Chemistry Research*, 26, (7): 1372-1381, 1987

Wittig, R., Lohmann, J., Gmehling, J., Vapor-liquid equilibria by UNIFAC group contribution. 6. Revision and extension, *Industrial & Engineering Chemistry Research*, 42, (1): 183-188, 2003

Wong, K. F., Eckert, C. A., Dilute Solution Behavior of Two Cyclic Anhydrides, *Industrial Engineering Chemistry Fundamentals*, 10, (1): 20-23, 1971

Chapter 6

Diffusion & Performance of Fragrance Ingredients and Mixtures*

"Fruitful as the miscibility of the gases has been in interesting speculations, the experimental information we posses…is that gases of different nature, when brought into contact, do not arrange themselves according to their density, the heaviest undermost, and the lighter uppermost, but they spontaneously diffuse, mutually and equally, and so remain in the intimate state of mixture for any length of time."
(Thomas Graham, 1833)

In this Chapter, two interrelated topics for the evaluation of fragrances and scented products will be addressed: the diffusion of odorant mixtures in air and the assessment of their performance in terms of olfactory perception. In the first section (Part I) of this Chapter, a predictive model to account for the diffusion of fragrances in air was applied to several mixtures of fragrance ingredients and their performance using perfumery concepts is studied. In this way, a simple diffusion model based on Fick's Law for diffusion was developed to simulate the evaporation/diffusion rate of small volumes of perfume liquid mixtures over time and distance. The UNIFAC group-contribution method was used to account for the vapor-liquid equilibrium (VLE), since fragrance

* This Chapter is partly based on the paper from Teixeira, MA, Rodríguez, O, Mata, VG, Rodrigues, AE, The Diffusion of Perfume Mixtures and Odor Performance, Chemical Engineering Science, 64, 2570-2589, 2009.

solutions were considered as non-ideal liquid mixtures. The diffusion model was applied to concentrated ternary mixtures but also to quaternary mixtures, which included ethanol as solvent. The PTD® and PQ2D® methodologies were recalled for the representation of the perfume evaporation paths using Evaporation Lines (EL) plotted in the diagram. The performance of these perfume mixtures was also analyzed considering the odor intensity and lastingness of the odorants at different distances from the point of application of the perfume and over time. Perfumery performance parameters, namely impact, tenacity, diffusion and volume, were studied to the light of the diffusion model. The use of different base notes in the formulation of perfumes and their role on the performance was studied as well as the impact of ethanol in fragranced mixtures.

In the second section (Part II) experimental data was measured for the diffusion profiles in air of pure components (ethanol, α-pinene) and a binary mixture of them. A quaternary mixture composed by α-pinene, linalool, tonalide and ethanol was also experimentally evaluated. For that purposed a diffusion tube with different sampling ports was designed and built. The measured profiles were then compared with a diffusion model, showing its application to the physical system studied.

Part I – Concept: modeling diffusion and performance

6.1. Introduction

The description of the diffusion process involves the use of a mathematical model based on some fundamental law or hypothesis. For such a law, there are essentially two common choices: the most fundamental, the Fick's law of diffusion, which defines a diffusion coefficient parameter and is commonly used to describe diffusion processes; and another one, that involves the use of a mass transfer coefficient (which is a measure of a reversible rate constant) (Bird, 2002; Cussler, 2007). The preference of one approach from the other is, according to Cussler, the result of a *"compromise between ambition and experimental resources"*. If on one hand, it is desirable to follow a more fundamental perspective, diffusion coefficients should be preferred but if a more approximate and phenomenological experiment is desired, then, such approximation would lead to mass transfer coefficients (Cussler, 2007).

But diffusion is a classical phenomenon, which has been studied for long. For that purpose, two men have contributed much (at the beginning) to what we know today

about this process: Thomas Graham and Adolf Fick. The former, constructed a diffusion tube apparatus to study the diffusion of gases under constant pressure but also addressed tests for diffusivity of liquids, showing that diffusion in liquids was at least several thousand times slower than in gases (Philibert, 2006; Cussler, 2007). Later, Fick has also carried out important studies in this field (and curiously in another completely different one, namely physiology, for which he became also remembered). Fick has postulated that a diffusion law, as in symmetry with the Fourier's law for heat conduction or the Ohm's law for electrical conduction, could be described using a similar mathematical basis. From then, until now, the fundamental law of diffusion (commonly called Fick's 2nd law) can be expressed by the partial differential equation (PDE) for a constant section as presented in equation 6.1:

$$\frac{\partial}{\partial t}c(x,t) = D\nabla^2 c(x,t) \tag{6.1}$$

where c can be a concentration and D is the diffusion coefficient. Moreover, by definition $c(x, t)$ is described as a function that gives the distribution probability of finding a perfectly average particle in the small vicinity of the point x at the specific time t (Crank, 1975; Cussler, 2007). In simple terms, this equation states that the diffusion process is characterized by the random molecular motion of molecules at the microscopic level that leads to complete mixing. Additionally, it should be noted that pure diffusion motion should occur in environments where viscous forces dominate (*e.g.* at low Reynolds numbers). According to Ursell (Ursell, 2007), *"given a group of non-interacting particles immersed in a fluctuating (Brownian) environment, the movement of each individual particle is not governed by the diffusion equation. However, many identical particles each obeying the same boundary and initial conditions share statistical properties of their spatial and temporal evolution."* In this way, if it would be possible to visualize the movement of individual molecules, it would be seen that in a dilute solution they would not have a preferred direction of motion. Thus, they would sometimes travel towards higher concentrations, sometimes towards lower concentration regions. Nevertheless, the average of the group of molecules will follow Fick's law as showed in his experiments with salt and water, resulting in a defined net transfer of molecules (for further details see Philibert, 2006; Cussler, 2007). Also postulated by Graham, was that the rate at which diffusion occurs is a function of the

surrounding medium: while in gases, diffusion may progress at a rate of ~ 5 cm/min, it drops to ~ 0.05 cm/min in liquids, and even more in solids, where it is only ~ 0.00001 cm/min (Cussler, 2007). Another important point to underline is that equation 6.1 does not account for convection effects (in the same direction of diffusion) which are common in several problems and so it often points to diluted solutions (Cussler, 2007).

In what concerns to odors and their perception, diffusion plays a very important role, as for example in the dispersion of odorants in the air which can have several consequences (*e.g.* malodor spread from an industry or the pleasant fragrance dispersion in a commercial store). Because diffusion is a slow process, it often occurs simultaneously or sequentially with other phenomena making it so important in many physicochemical processes. For that, diffusion is also interrelated with the evaporation mechanism which for chemical fragrances will play an important role on odor performance. This is so, because performance is usually evaluated in terms of perceived odor intensity and character at different distances from the source. However, the performance of fragrance products has been studied mainly by R&D departments at the major fragrance houses, thus remaining a trade secret, as discussed earlier in Chapter 2 (see Table 2.3). Although many of these companies use modeling tools to predict odor dispersion and measure odor intensity (profiles) they also generally report only experimental measurements due to the difficulty of working with extensive properties.

Nevertheless, the aim of the study here on the diffusion and performance of fragrance materials is to introduce some scientific knowledge in these processes using concepts from Chemical Engineering combined with Psychophysics for human sensory perception. For that purpose, the proposed odor model presented in Chapter 5 (see Figure 5.1) will continue to be explored. After studying the evaporation process in the previous Chapter, here the diffusion step will be addressed in more detail. Within that point of view, it can be summarized at this time that perfumes are liquid solutions of fragrant components diluted in a suitable solvent. For their typical use, they are sprayed (*e.g.* on the skin or clothes) and allowed to vaporize. The vapors diffuse through the surrounding space and are then perceived by the people around. Chemical Engineering provides suitable models for vapor-liquid phase equilibria and gas diffusion, which can be used to describe these steps for the releasing of a fragrance into air (see Chapter 5). Models for odor intensity and odor perception can be taken from Psychophysics (as presented in Chapter 3 and as will be addressed in more detail in Chapter 7). Altogether, this provides a suitable tool for understanding and evaluating perfume behavior.

6.1.1. Perfume structure, evaporation and diffusion

As previously discussed in Chapter 2, the pyramidal structure for a perfume is based on physical, chemical and sensorial properties of the fragrant notes that compose its formula, especially in terms of volatility, molecular structure, polarity, and odor threshold (Carles, 1962; Calkin and Jellinek, 1994). Following this line of thought, it is expected that, theoretically, the perceived scent of a perfume evaporating and diffusing into the air should be evolving with time and changing through the surrounding space. In this way, top notes, which comprise the most volatile species, would be smelled in first place, like when the perfume bottle is opened or during the first minutes after application on a paper blotter or on our body. The top notes form a person's initial impression about the perfume and so are remarkably important. Then, as these start to progressively fade away, the tonality (the dominant note in the vapor phase) would shift to the middle or heart notes as the evaporation process takes place. These notes are the main body of the perfume, often masking the initial unpleasant impact of the base notes (which tend to become more pleasant with time) and can last for hours in the air. Finally, the perceived odor slowly changes with time to the base notes which have the lowest volatility, thus lasting in air from hours to days. Some base notes are often used as fixatives, influencing the molecular interactions in the liquid solution and so changing the evaporation rate of the top and middle notes (Calkin and Jellinek, 1994; Vuilleumier, 1995; Teixeira*, et al.*, 2009b). From this point of view, Carles considered that perfumes were blends of fragrances that would evaporate following these rules, independently of the combination of odorants. The fact is that, as we will see, this traditional view of the naturally occurring process of evaporation is too simplistic. It is purely a qualitative organoleptic analysis. Thus, depending on physical properties like the volatility of the fragrant molecules or the molecular interactions existing in the liquid, all fragrant species start to evaporate at a faster or slower rate, right after application of the perfume. Then, as the evaporation and diffusion processes take place, a blending of vapor fragrances is evolving in the air above the liquid and the human nose simultaneously perceives these single odorants, though with different intensities.

6.2. Methodology

One important parameter that must be recapped for the discussion here is the odor intensity of a fragrant species which has to be considered in the function for quantifying odor performance. The character/quality perceived from an odorant is an important attribute for measuring its performance but it is also strongly dependent on people preferences and cultures. In this way, establishing a relationship between performance of a perfume mixture and its (liquid) composition is of prime interest. For that, the methodology for odor perception presented in Chapters 3 and 5 presents itself as a powerful tool.

In psychophysics, several models are often referred to relate odor intensity with concentration: the Weber-Fechner logarithmic law (Shigemoto, 2002), the Stevens Power Law (Stevens, 1957), and the Odor Value (OV) model (Calkin, 1994; van Gemert, 1999). Here, the Odor Value (OV) concept which defines the odor intensity of a fragrant species in the gas phase as the ratio between its concentration and its detection limit (Calkin, 1994; van Gemert, 1999) will be addressed as follows:

$$OV_i = \frac{C_i^g}{ODT_i} \tag{6.2}$$

where C^g_i is the concentration of the odorant species i in the vapor phase (g/m^3) and ODT_i is the concentration threshold value in air (g/m^3). As reported by several authors in the literature (Calkin, 1994; Baydar, 1995, 1996; Grosch, 2001; Rappert, 2005; Boatright, 2000), this is a suitable model to account for odor intensity because of its simplicity and data availability, whenever there is no information on the intensity curve (like the power law exponent).

The concentration threshold can be obtained from the literature in data series for numerous fragrant species studied over the years by different authors (Calkin and Jellinek, 1994; van Gemert, 2003; Leffingwell and Leffingwell, 2011). On the other hand, the headspace concentration (above the liquid mixture) can be calculated by the ideal gas law, once it was considered for this study an ideal gas phase. This assumption relies on the fact that fragrant components are highly diluted in air. Moreover, for low pressure values and a non-ideal liquid phase, it is possible to describe the vapor-liquid

equilibrium (VLE) by a modified Raoult's Law (Smith, 1996) and so equation 6.2 can be reformulated as:

$$OV_i = \gamma_i x_i \left(\frac{P_i^{sat} M_i}{ODT_i} \right) \left(\frac{1}{RT} \right) \tag{6.3}$$

where y_i represents the headspace mole fraction of component i in a mixture with N components, M_i is the molecular mass of component i (g/mol), P_i^{sat} is the saturated vapor pressure of i (Pa), P is the total pressure in the gas phase (Pa), R is the ideal gas constant and T is the temperature (K). Further details on the derivation of equation 6.3 from equation 6.2 were previously detailed in Chapter 3.

In what refers to a qualitative odor analysis, it is important to highlight that the odor character of a perfume mixture results from the combination of different smells that not only evaporate at different rates but are also perceived differently by the olfactory receptor cells located in the human nose. The perceived scent is then a mixture of different fragrances, where one or more might prevail due to their odor intensity. Thus, the already mentioned Stronger Component model (SC) was used throughout this Chapter as the odor character model.

6.2.1. Odor performance

The performance of any kind of consumer product relies as the ultimate proof that a product accomplishes the function for which it was made (*e.g.* that a deodorant masks the malodor of the human body). In this Chapter, it was intended to predict and evaluate how a perfume mixture would perform, quantitatively and qualitatively, over time and distance. Quantitatively, refers to the odorant intensity or strength in the headspace (gas phase) which our nose can smell. Qualitatively relates to the odor quality, tonality or character of a perfume, that is, the dominant note in the gas phase which is more strongly perceived.

The study of the odor value distribution over time at different distances from the releasing source enables the evaluation of the diffusion fragrance properties. Different perfumery performance parameters, namely: impact, tenacity, diffusion and volume are important factors to which perfumers look to optimize as presented in Figure 6.1 (Calkin, 1994; Mata*, et al.*, 2005). Impact represents an immediate olfactory sensation

because it is a measure of the intensity of a perfume in the first moments after an application ($z \in [0, 0.3] m$ and $t \in [0, 5] min$). An example is when sniffing a perfume from a paper blotter or right after its application onto the skin. Diffusion refers to the efficacy of a perfume at some distance from the source ($z \in [1, 2] m$ and $t \in [0, 5] min$), representing how fast a fragrance radiates in space and permeates into the surrounding environment.

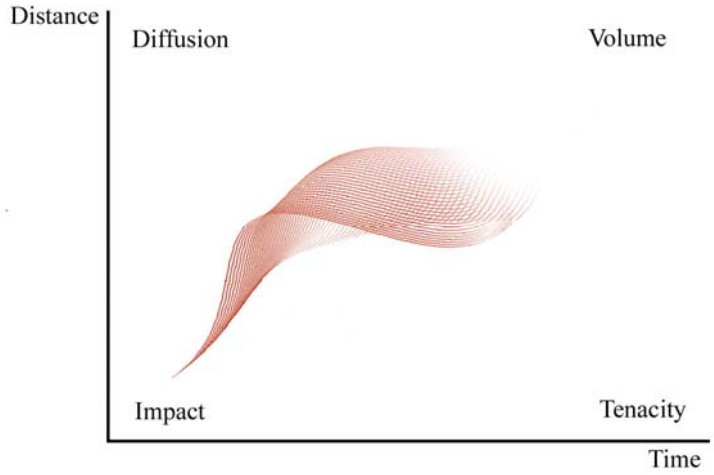


Figure 6.1 - Evaluation parameters for perfume performance: impact, tenacity, diffusion, and volume.

Tenacity is the ability of a fragranced mixture to retain its characteristic odor during the called dry down stage. It is a performance index that measures the persistence of a fragrance for long times after its application but near the evaporating source, like how long lasts the perfume in the skin after applying it ($z \in [0, 0.3] m$ and $t \in [10, 20] h$). Finally, volume is the effectiveness of a perfume over distance, some time after application ($z \in [1, 2] m$ and $t \in [10, 20] h$) (Calkin and Jellinek, 1994; Stora*, et al.*, 2001; Mata*, et al.*, 2005; Teixeira*, et al.*, 2009a). Moreover, odor life is also another quantitative parameter related to how long a fragrance note persists in the headspace with intensity higher enough to be smelled (Stora*, et al.*, 2001).

6.2.2. Perfume diffusion model

In this study a diffusion model to simulate the evaporation rate of a liquid perfume mixture over time *(t)* and distance *(z)* was developed. The physical system considered here is presented in Figure 6.2 and consists of a very small volume of liquid perfume that is evaporating in the air over time and diffusing upward through the gas phase

above it (headspace). It was considered a non-ideal liquid mixture with a small volume like that of a spray application of perfume. Because of the low volume of perfume considered (1 mmol, ≈ 50 to 100 µL), it is expected that the mass transfer resistance in the liquid phase can be neglected. This assumption is based on the following: the methodology is being applied to perfume utilization, that is, when a perfume is sprayed on the skin or clothes. The area of the liquid-gas interface was set to 0.071 m^2 (0.3 m diameter), which gives a liquid thickness of approximately 10^{-6} m. Under these conditions, we are well below the film thickness usually considered for mass transfer resistance in the film theory (10^{-4}-10^{-5} m for liquids, see *e.g.* Taylor and Krishna, 1993). Because of that, mass transfer resistance in the liquid phase was neglected and the liquid was assumed as perfectly mixed.

Moreover, the volume and composition of the liquid changes with time as the perfume evaporates. The liquid composition is represented by the number of moles of each component *(n_i)* while the composition of the gas phase is determined by the molar concentration *(c_i)* of each species. Moreover, it is assumed constant pressure *(P)* and temperature *(T)* while evaporation takes place.

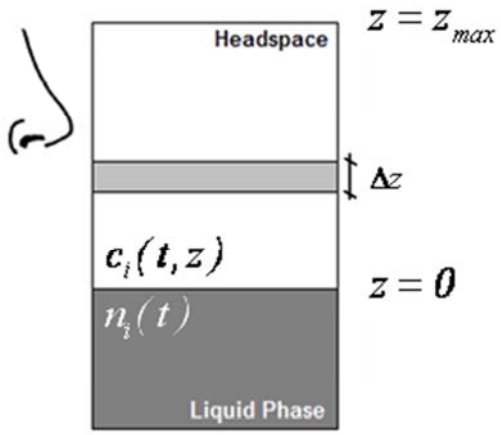


Figure 6.2 - Scheme of the simulated liquid and gas phases of the perfume system.

Gas Phase

It is considered that the diffusion of the fragrant molecules in the gas phase occurs in the axial direction only (z, 1-dimensional). It is assumed that the surrounding air is not soluble in the liquid mixture, that there are no simultaneous convection processes and that there are no significant interactions between the fragrant gas molecules and the surrounding air molecules (ideal gas phase).

The species mass balance in the gas phase is calculated over the gas control volume, $\Delta V = A\Delta z$, where V is the total gas volume, A is the cross section area and z the axial coordinate, as shown in Figure 6.2. This perfume diffusion model is based on Fick's 2nd Law for diffusion and the vapor-liquid equilibrium (VLE) relationship links the compositions of the liquid and gas phases at the interface. The use of Fick' law neglects interactions between gas molecules, which is suitable for a diluted gas. On the other hand, for a concentrated gas phase, the Maxwell-Stefan theory for diffusion could be used to take into to account binary interactions (Crank, 1975; Taylor and Krishna, 1993; Bird, 2002). Considering the above conditions the unsteady-state mass balance is described by the partial differential equation *(PDE)*:

$$\frac{\partial y_i}{\partial t} = D_{i,air} \frac{\partial^2 y_i}{\partial z^2} \tag{6.4}$$

where y_i is the mole fraction of species i in the gas phase and related to the concentration by $y_i = c_i/c_T$, being $c_T = P/RT$ a constant once the gas is considered ideal; t is the time variable and $D_{i,air}$ is the diffusivity of component i in the gas phase. The diffusion coefficients were calculated by the method of Fuller *et al.* (for further details see Annex D) as it is stated that this procedure for the calculation of $D_{i,air}$, yielded the smallest average error among many other analyzed methods (Poling*, et al.*, 2004). The diffusion coefficients calculated for the fragrant species considered in this study are presented in Table 6.1.

Table 6.1 – Diffusion coefficients calculated and physical properties ratio *(K_{odor})*.

	$D_{i,air}$	$\frac{P_i^{sat} \cdot M_{wi}}{ODT_i \cdot R \cdot T}$
Species	(m^2/h)	
Limonene	2.214×10^{-2}	4.60×10^{3}
Geraniol	2.138×10^{-2}	6.70×10^{3}
Vanillin	4.111×10^{-2}	5.25×10^{3}
Tonalide	1.941×10^{-2}	3.84×10^{-1}
Ambrox	1.670×10^{-2}	4.11×10^{4}
Galaxolide	1.924×10^{-2}	1.20×10^{4}
Ethanol	4.469×10^{-2}	2.44×10^{3}

Liquid Phase

In the liquid phase it was considered a non-ideal mixture of fragrances with or without ethanol as solvent. The VLE was predicted using the UNIFAC method for the activity coefficients (γ_i), as described in Chapter 5 and in the literature (Gmehling, 2003; Poling, 2004). When ethanol is considered for the quaternary systems, the representation of molar fractions in the PTD® is changed for a solvent-free basis. The concentration and volume of the liquid phase change with time *t* through the evaporation process and it is assumed a homogeneous concentration in the liquid mixture.

The mass balance in the liquid phase is obtained by considering the mass transfer of component *i* through the interfacial layer, as presented by the following ordinary differential equation *(ODE)*:

$$\frac{dn_i}{dt} = D_{i,air} A_{lg} c_T \left. \frac{\partial y_i}{\partial z} \right|_{z=0} \tag{6.5}$$

where n_i is the number of moles of component *i* in the liquid phase and A_{lg} is the area of the liquid-gas interface.

Initial Conditions (IC)

The applicable initial conditions to the stated system of equations are defined as follows:

Gas Phase

$$t = 0: \quad y_i = y_{i_0} = 0 \tag{6.6}$$

Liquid Phase

$$t = 0: \; n_i = n_{i_0} \text{ or } x_i = x_{i_0} \tag{6.7}$$

where x_i is the mole fraction of component *i* in the solution and x_{i_0} is the initial mole fraction of component *i* in the perfume liquid mixture.

Boundary Conditions (BC)

The formulation of the designed model requires the definition of two boundary conditions (one at the left and another at the right side of the domain) for the resolution of the partial differential equation (PDE), as follows:

$t > 0$:

$$z = 0 : y_i = \frac{\gamma_i P_i^{sat}}{P} x_i = \frac{\gamma_i P_i^{sat}}{P} \frac{n_i}{\sum_i n_i} \tag{6.8}$$

$$z = z_{max} : y_i = 0 \tag{6.9}$$

where y_i is the mole fraction of the ith component of a mixture of N components and at $z = 0$ it represents the composition in equilibrium with the corresponding component mole fraction in the liquid phase, x_i.

As aforementioned, the diffusion model based on Fick's equations for diffusion considers no interactions between the fragrant gas molecules while diffusing in air. The gas phase was considered ideal but molecular interactions were considered in the liquid mixture, thus making the evaporation rate dependent on the group-group interactions. Though the model might be simple, the assumption of ideal gas is plausible once the volume of the initial perfume mixture is small and so the evaporated molecules will be highly diluted in the gas phase.

6.3. Numerical Solution

Considering ternary or quaternary perfume liquid mixtures, the model has six or eight paired differential equations, respectively. The system of equations was computed in MATLAB using the *pdepe* package for numerical computation of partial differential equations *(PDE)*. This routine solves initial-boundary value problems for systems with parabolic and elliptic PDEs in one space variable *(z)* and time *(t)* (MathWorks, 2002). The calculations over the space variable include second order approximations to the solution on the specified space mesh. The ordinary differential equations *(ODE)* resulting from the discretization in space were integrated using the *ODE15s* solver package to obtain the approximate solutions over time *(t)*. The ODE solver is applicable to initial value problems with stiff ordinary differential equations, different orders and differential algebraic equations. This solver is based on the numerical differentiation formulae (NDFs) which are implemented with backward differences. These are generally more efficient than the backward differentiation formulas (BDF), although for higher orders they are less stable (Shampine and Reichelt, 1996). Moreover, the solver

uses the method of finite differences for the discretization of the space variable (Nocedal, 1999; Chapman, 2000; Chapra, 2002).

The system of equations was solved in the domain of $z \in [0, z_{max}]$, where $z = 0$ corresponds to the liquid-gas interface. This means that the domain of integration considered for computing the model equations was restricted only to the gas phase *(headspace)*. Thus, the calculated values for the moles of each component *i* at the interfacial layer, $z = 0$, represent the liquid composition for the component *i*, assuming an homogeneous solution, while the mole values for the case of $z > 0$, become meaningless, representing dummy variables. The time integration was calculated over the domain of $t \in [0, t_{max}]$, where the limit on the right side could vary from hours to days, depending on the scope of the study. The iterative algorithm used to solve the non-linear system of equations for the diffusion model is presented in Figure 6.3.

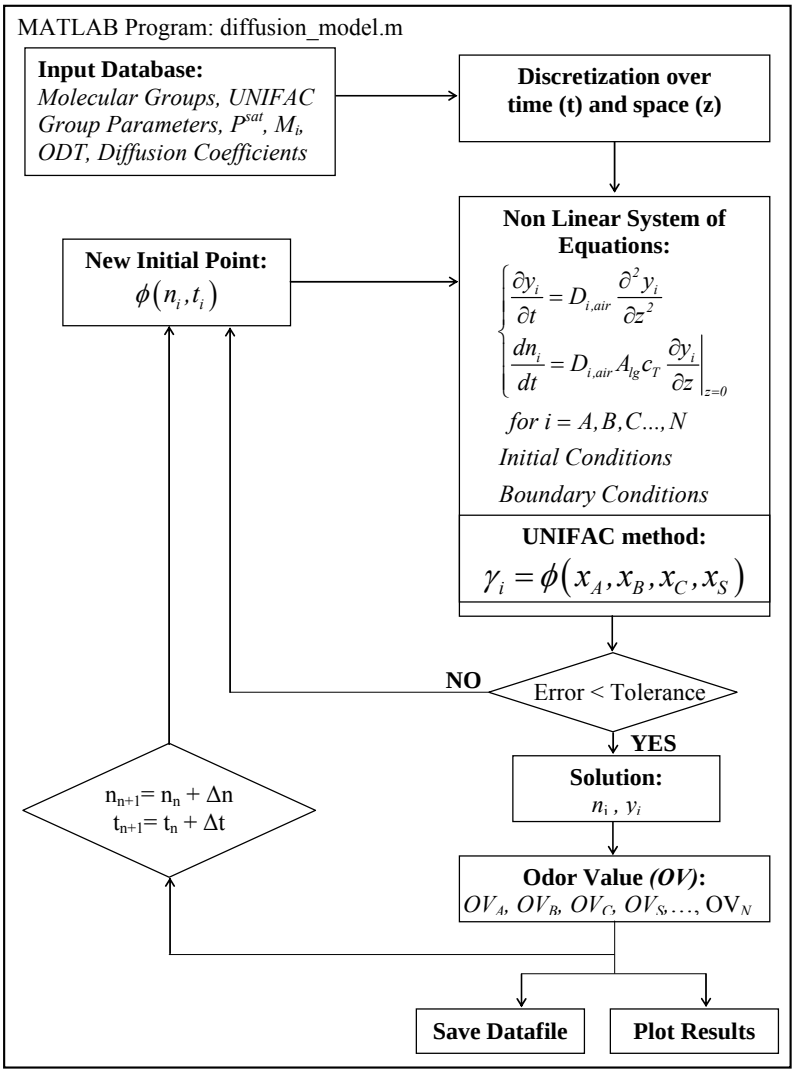


Figure 6.3 - Iterative method for resolution of the diffusion model equations.

6.4. Results & Discussion

6.4.1. Evaluation of ternary and quaternary systems

The perfume diffusion model was applied to simulate the evaporation behavior of multi-component perfume liquid mixtures. In the case of ternary mixtures, three components, like typical top, middle and base notes were used as a concentrated perfume while for the quaternary mixtures, ethanol was added as a solvent, representing a general perfume composition. The fragrance systems presented in Table 6.2 were studied in this Chapter considering the same top and middle notes but changing the base note. In these ternary systems it was introduced ethanol to evaluate the effect of a solvent matrix on the release rate and performance of the fragrance ingredients.

Table 6.2 - Fragrance systems simulated for the diffusion and performance analysis.

Fragrance system	Top note	Middle note	Base note
1	limonene	geraniol	vanillin
2	limonene	geraniol	tonalide
3	limonene	geraniol	ambrox
4	limonene	geraniol	galaxolide

For the perfume liquid mixtures simulated in the test cases, it was considered the following physical conditions: pressure, P = 1 bar, temperature, T = 298.15 K, total number of moles, $n_T = \sum_i n_i = 1$ mmol and area of liquid-gas interface, $A_{lg} = 0.071$ m^2.

The physical, chemical and sensorial properties for the fragrant species studied are presented in Table 6.3.

The performed simulations considered the study of:

i) the effect of the solvent, ethanol (S), in the odor value measured in the headspace above the fragrant mixture;

ii) the variation of the mole fraction of a fragrant species in the liquid compared to the predicted mole fraction in the gas phase (in terms of the OV);

iii) the Evaporation Lines (EL) for ternary mixtures with and without ethanol and its application into the PTD methodology;

iv) the study of the odor performance parameters for each fragrance (impact, tenacity, diffusion and volume);

v) the effect of the base note on perfume evaporation and diffusion.

Table 6.3 – Properties of the odorant components.

	Name	Molecular Formula	M_i ($g.mol^{-1}$)	P_i^{sat} (Pa)	ODT_i ($g.m^{-3}$)
A	Limonene[a]	$C_{10}H_{16}$	136.2	20.5×10^{1}	2.45×10^{-3}
B	Geraniol[a]	$C_{10}H_{18}O$	154.3	26.7×10^{-1}	2.48×10^{-5}
C	Vanillin[a]	$C_8H_8O_3$	152.2	16.0×10^{-3}	1.87×10^{-7}
	Tonalide[a]	$C_{18}H_{26}O$	258.4	67.0×10^{-6}	1.82×10^{-5}
	Ambrox	$C_{16}H_{28}O$	236.4	12.5×10^{-1} [b]	2.90×10^{-6} [c]
	Galaxolide	$C_{18}H_{26}O$	258.4	72.7×10^{-3} [d]	6.30×10^{-7} [e]
S	Ethanol[a]	C_2H_6O	46.0	72.7×10^{2}	5.53×10^{-2}

[a] From (Calkin and Jellinek, 1994), [b] from (Chemspider, 2011), [c] from (Leffingwell and Leffingwell, 2011), [d] from (Balk and Ford, 1999); [e] from (Fráter, *et al.*, 1999).

6.4.1.1. System 1: Limonene, Geraniol and Vanillin

Evaporation Profiles

A ternary system composed by a top note, limonene (A), a middle note, geraniol (B), and a base note, vanillin (C) was first studied. The effect of a solvent matrix in this perfume system was also analyzed for comparison between the concentrated mixture (free of ethanol) and diluted mixtures with different mole fractions of the solvent. The results showing the diffusion of the fragrant components are presented over time and distance for different initial compositions of the liquid mixture. First, the evaporation profiles are presented for the selected initial compositions specified in Table 6.4.

The initial composition points P1 and P2 represent typical concentrated perfume mixtures while the others are the corresponding diluted ones, considering the same relative composition for the fragrant notes. A comparison between the odorant profiles for the ternary mixtures with and without ethanol is shown in Figure 6.4.

Table 6.4 – Initial compositions (x_{i0}), activity coefficients (γ_i) and odor values for system 1.

Point	x_{A0}	x_{B0}	x_{C0}	x_{S0}	γ_A	γ_B	γ_C	γ_S	OV_A	OV_B	OV_C	OV_S
P1	0.780	0.200	0.020	-	1.12	1.69	23.82	-	4028	2271	2503	-
P2	0.400	0.400	0.200	-	1.98	0.90	4.55	-	3633	2418	4781	-
P3	0.390	0.100	0.010	0.500	2.13	0.86	2.00	1.56	3823	577	105	1904
P4	0.200	0.200	0.100	0.500	3.54	0.95	1.68	1.14	3257	1273	880	1397
P5	0.234	0.060	0.006	0.700	3.59	0.86	1.05	1.21	3864	347	33	2060
P6	0.120	0.120	0.060	0.700	5.34	1.05	1.09	1.06	2947	840	343	1815

It is possible to see that for mixture P6, ethanol is the most volatile component, so that in the first minute after application of the perfume, more than 87% of the solvent evaporates. Moreover, the presence of ethanol in the solution triggers a fast theoretical

evaporation of the top note (limonene). This phenomenon is due to the fact that increasing the ethanol mole fraction in the liquid (P1, P3 and P5 or P2, P4 and P6), increases its average polarity. Thus, the relatively non-polar top note, limonene, tends to be "pushed out" of the solution more rapidly, while base and middle notes (less volatile and more polar) will have a tendency to remain in the liquid.

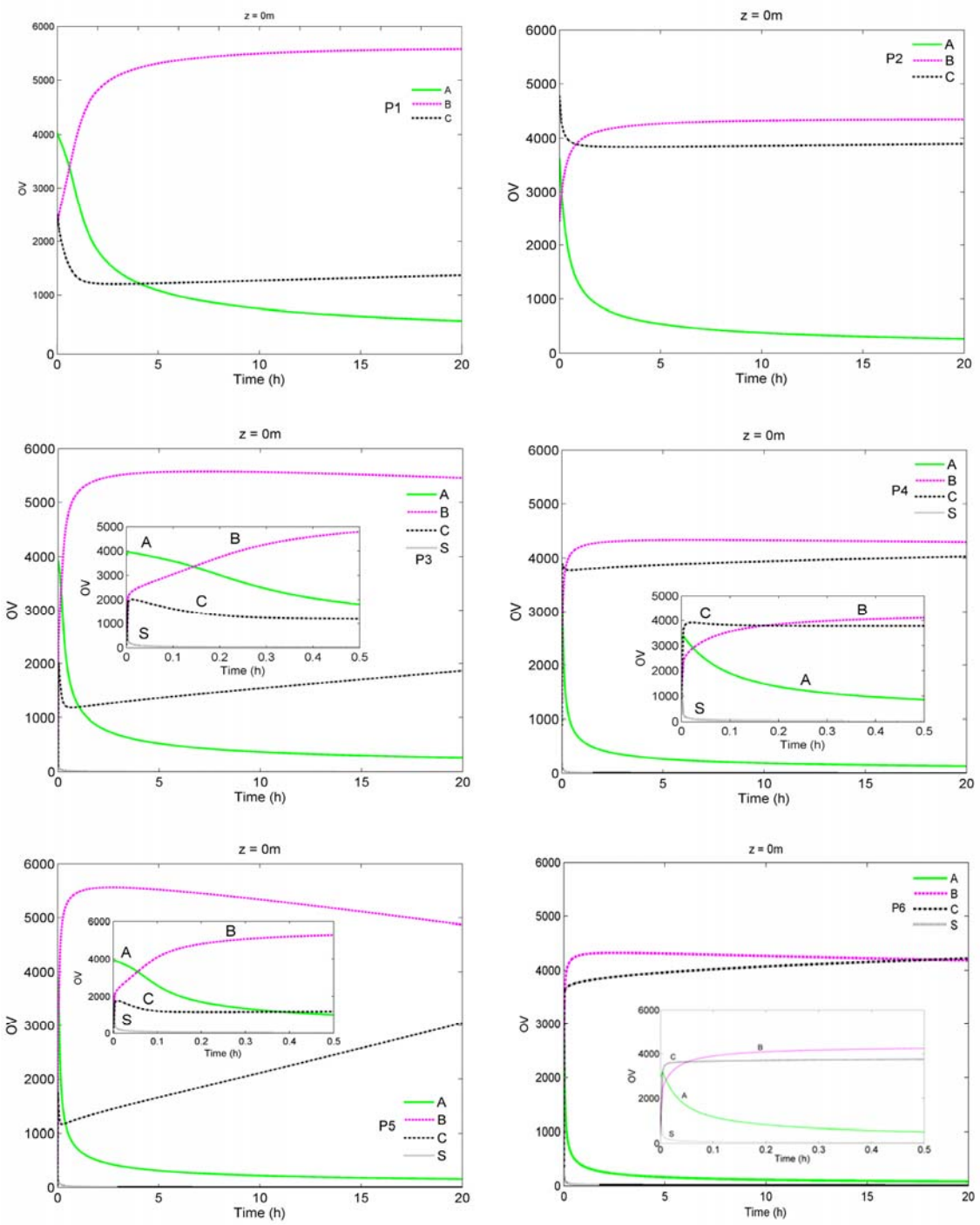


Figure 6.4 - Odor profiles of the odorants over time for different perfume mixtures of system 1.

As evaporation takes place, the liquid composition changes and the thermodynamic behavior between the liquid and gas phases can be seen in Figure 6.5 where the mole fraction of each component in the liquid phase *(x_i)* and the corresponding headspace OV (measured at $z = 0$) are analyzed over time for a typical mixture like that of point P6 (see Table 6.4).

The relationship between the liquid and gas phases is not linear, since it greatly depends on the activity coefficients due to the molecular interactions, volatility and polarity of the fragrant species. However, it is easily perceptible by analyzing the profiles in Figure 6.5 that the most volatile components are ethanol and limonene (as expected), whose mole fractions fall more sharply in the first minutes after application of the perfume. In opposite direction, the mole fractions of both the middle and base notes increase significantly in the liquid phase, since they are less volatile. In this way, one hour after the evaporation has started, the liquid mixture remains essentially as a binary solution of these two last fragrant species that will slowly evaporate and diffuse into the air.

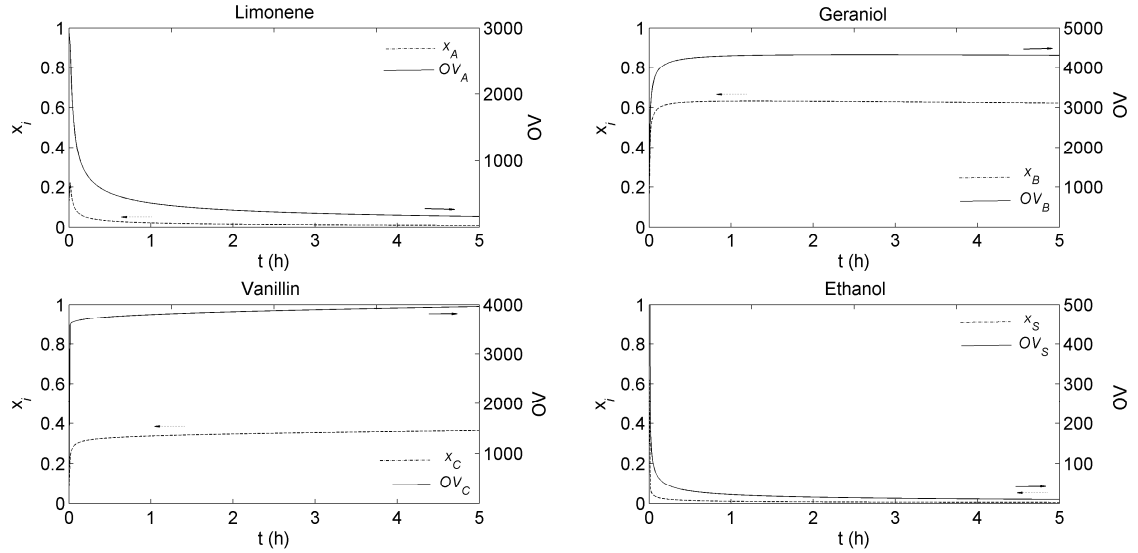


Figure 6.5 - Variation of the odor value (OV) and liquid composition (x_i) over time for each fragrance in mixture P6 (system 1).

Perfume Performance

Considering the initial composition of mixture P6 (presented in Table 6.4) it is possible to analyze the odor profiles for each species at different values of the axial coordinate *(z)*. It is like if the human nose was at some distance from the liquid mixture that was evaporating into the headspace and so the customer would smell the fragrances from

that static point as they diffuse through the surrounding air. Figure 6.6 shows a quantitative comparison of the 3-D odor profiles over the time and distance domains. However, a qualitative analysis of the odor value distribution can be made by plotting its maximum (OV_{max}) for the mapped scale of time and distance. This is shown with performance plots in Figure 6.7 for the same mixture P6. In what concerns to perfume performance parameters it is possible to see that limonene shows to have the highest impact, while vanillin evidences greater diffusion and volume properties. This is in agreement to what should be expected for a top note since it has the highest volatility and so it will be perceived more intensely over the first minutes after application of the perfume.

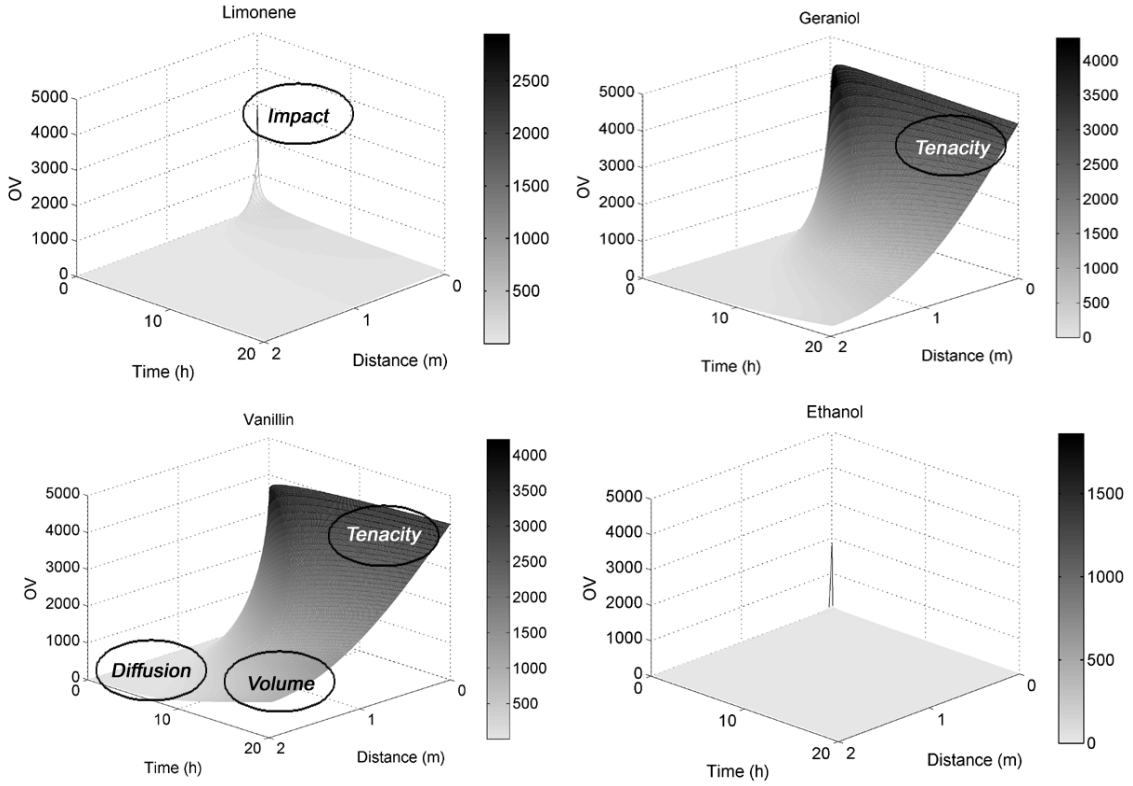


Figure 6.6 - Evaporation profiles over time and distance for each fragrance in mixture P6 (system 1).

On the other hand, the base note is considered to last long in the liquid phase (it has the lowest volatility), thus being more strongly noticed by the human nose only after a few hours. Additionally, it is noteworthy to mention that vanillin has the highest diffusion coefficient among all the fragrant species (see Table 6.1), thus allowing it to have a higher diffusion performance parameter. Simultaneously, geraniol and vanillin show to have higher tenacity properties, though increasing the ethanol mole fraction results in

the increasing of the tenacity of vanillin only (Figure 6.4, mixtures P1, P3 and P5). Finally, except for the solvent, the odor life of limonene is the shortest of all the fragrances, as it would be expected, once it is a very volatile top note. The reduction of the limonene mole fraction in the liquid phase over the first half hour of evaporation is about 74.5%, while its decrease in OV reaches as much as 83%. Performance plots can be used to map the distribution of the OV_{max} over time and distance as in Figure 6.7 allowing a qualitatively analysis of the tonality or dominant note in the surrounding air. Moreover, odor isolines (equal odor intensity) are plotted in order to express the perceived odor intensity over the domain of prediction.

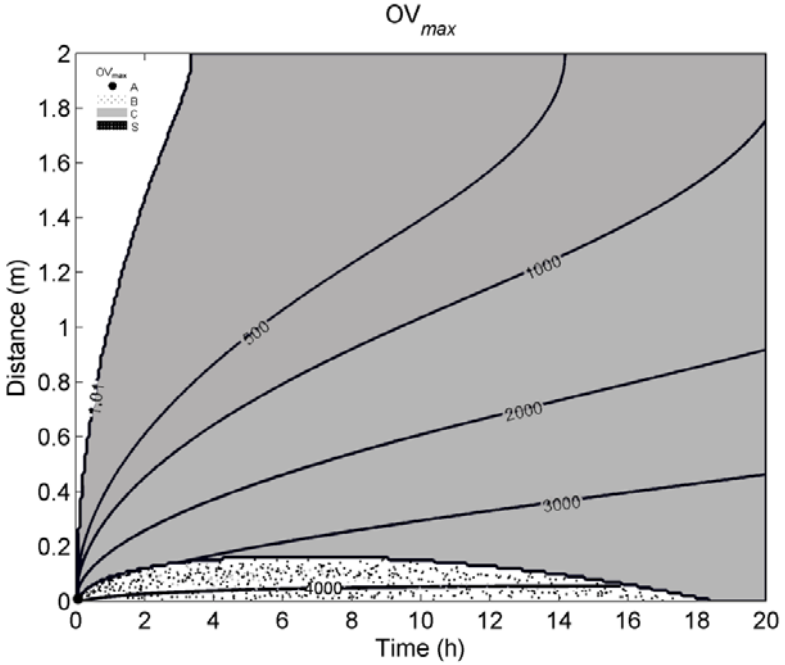


Figure 6.7 - Distribution of the OV_{max} over time and distance for system 1 and mixture P6. A – limonene, B – geraniol, C – vanillin, S - ethanol.

Perfume Evolution

The evolution of the perceived smell along with the evaporation process can be followed by Evaporation Lines (EL) plotted in the Perfumery Ternary Diagram (PTD®) for the fragrant mixtures with the initial compositions defined in Table 6.4. For that purpose, Figure 6.8 shows the evaporation paths for the concentrated perfume mixtures (P1 and P2) in the PTD. In quaternary systems containing a matrix of ethanol, it is still possible to represent the evaporation lines in the PTD, as shown in Figure 6.9 for the initial perfume mixture P6. For this case it is important to take into account the following: in the PTD it is possible to represent ternary compositions only or like for

this case, compositions in a solvent-free basis, considering a constant mole fraction of a fourth component (*e.g.* ethanol, $x_s = 0.7$). Nevertheless, along the evaporation line the mixture composition in the liquid phase is changing at a rate equal to the rate of evaporation of the fragrant components. This means that the solvent composition is changing through time along with the evaporation process.

Due to this dynamic shift, it is shown in Figure 6.10, some of the mapped PTDs at specific times for the mixture P6, thus showing the evaporation line along with the evolution of the headspace odor distribution with time. The quantitative mixture compositions for the selected times are shown in Table 6.5 with the corresponding OVs.

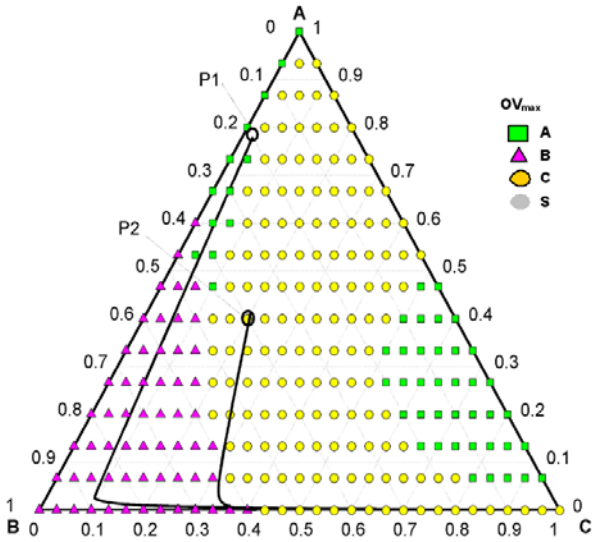


Figure 6.8 - Evaporation lines (EL) for the initial mixture compositions (system 1).

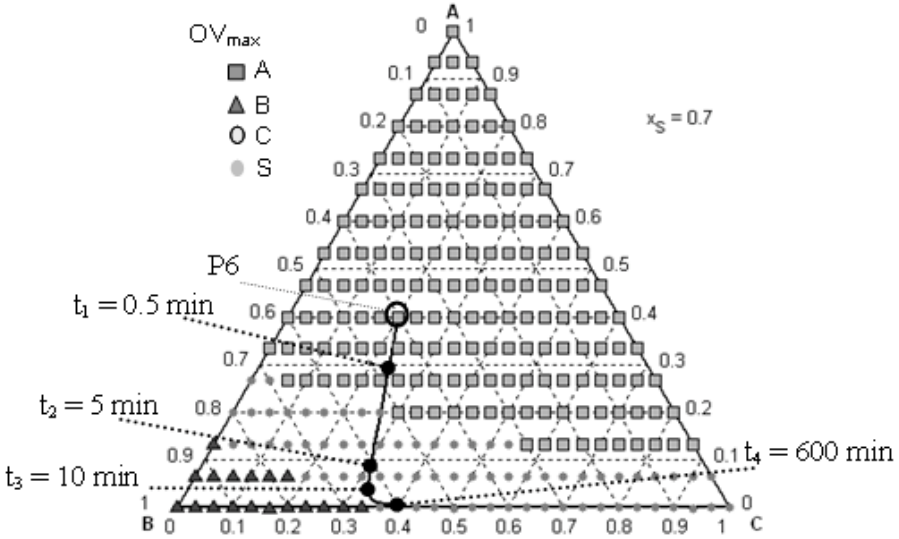


Figure 6.9 - Evaporation line and mapped PTD for point P6 (system 1).

During the simultaneous processes of evaporation and diffusion the headspace odor values are changing, which means that through the time the liquid composition changes and so the activity coefficients and the perceived odor. For the presented case of P6 it is perceptible that in the very first moments after application of the perfume, the most strongly perceived note is the fresh smell of limonene (Figure 6.4-P6, and Figure 6.9). As the vapors start to diffuse into the air above it, the sweet scent of vanillin becomes more intensely perceptible, after half a minute (see Figure 6.10a), though geraniol will have the highest OV when the evaporation time reaches approximately 5 minutes and will remain the strongest scent for some hours (Figure 6.4-P6, and Figure 6.10b). After a time around 10 hours, the base note will theoretically tend to overcome the middle note: it gets the highest OV and thus it is perceived more intensely. This analysis of the different PTDs over time along with the evaporation lines allows us to see the evolution of this unexpected change of odors and scents that a perfume can produce.

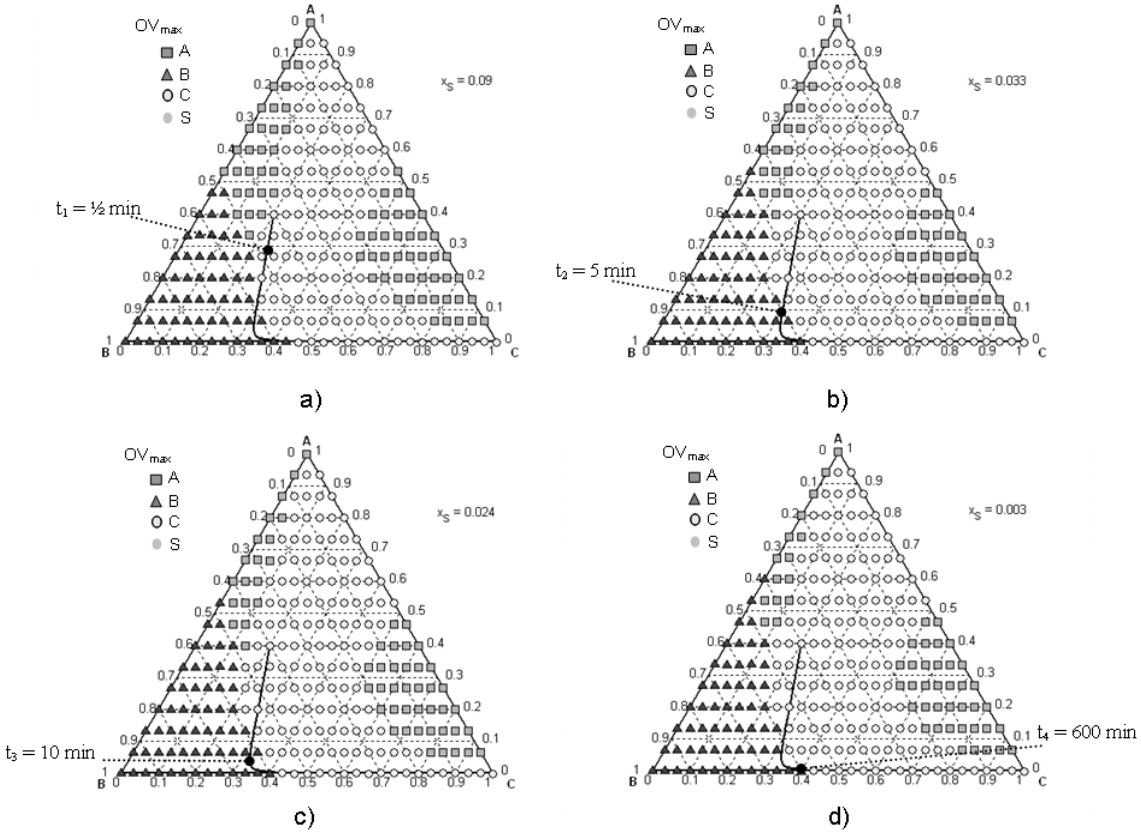


Figure 6.10 - PTDs at different times of evaporation and correspondent evaporation line for mixture P6 (system 1): (a) ½ min; (b) 5 min; (c) 10 min; and (d) 600 min.

Table 6.5 – Liquid composition at different times and corresponding headspace OVs for mixture P6.

Time (min)	x_A	x_B	x_C	x_S	OV_A	OV_B	OV_C	OV_S
0.0	0.120	0.120	0.060	0.700	2947	840	343	1815
0.5	0.259	0.433	0.217	0.090	3026	2641	3491	251
5	0.085	0.585	0.297	0.033	1296	3825	3661	76
10	0.056	0.609	0.311	0.024	900	4042	3693	53
600	0.006	0.607	0.383	0.003	113	4270	4075	7

Additionally, it is also possible to show the evaporation lines through time and composition using a triangular prism. If one considers the superposition of $i = 1,2,3,...,n$ plans of the PTDs with increasing mole fractions of solvent ($x^i_S < x^{i+1}_S < ... < x^{n-1}_S < x^n_S$) with $x^i_S = 0$ for the base plan and $x^n_S = 1$ for the top one, it is possible to represent in a 3D diagram a triangular prism that shows the different sets of compositions for a quaternary mixture. For perfume system 1 (see Table 6.2) it is shown in Figure 6.11 the triangular prism with the PTDs for $x^i_S = 0, 0.3$ and 0.7 and the evaporation line for the initial mixture composition of P6 as presented in Table 6.4. Only three PTDs are shown so that the reader can easily see the odor zones and the interceptions of the evaporation line with them. Nevertheless, the best way to visualize the evolution of the composition and perceived odor over time can be done by representing evaporation lines in the PQ2D®. This is shown in Figure 6.12 for the fragrance mixture P6, where it is possible to see (using a color scheme) that the dominant odor through the evaporation line is changing over time, from the top note to the base note.

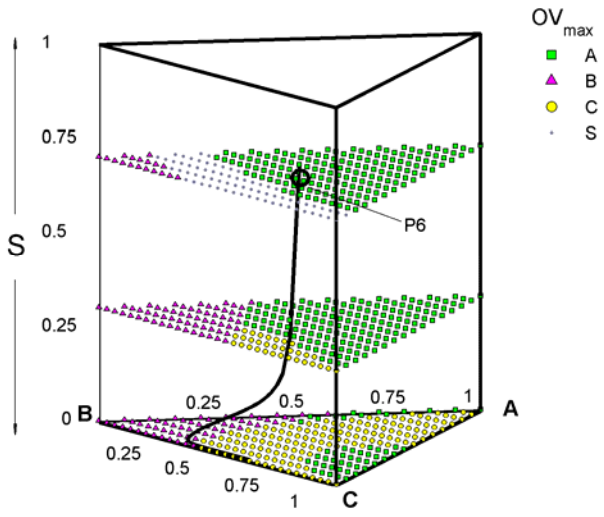


Figure 6.11 - Triangular prism with evaporation line for point P6 (system 1).

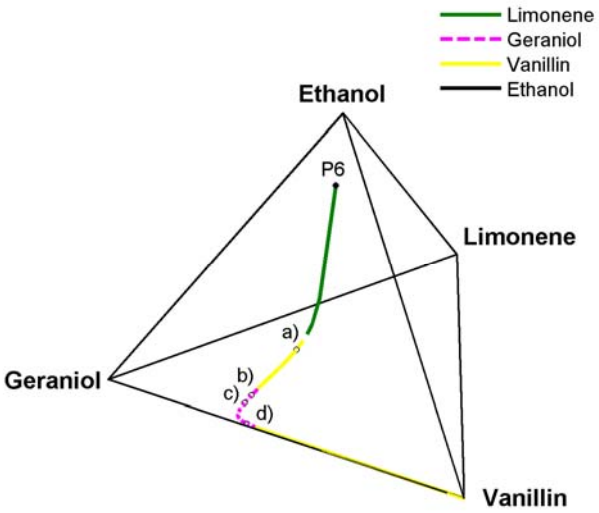


Figure 6.12 - PQ2D® with the evaporation line of mixture P6: a) t = 0.5 min, b) t = 5 min, c) t = 10 min, d) t = 600 min.

6.4.1.2. System 2: Limonene, Geraniol and Tonalide

Evaporation Profiles

The odor profiles for ternary system 2 comprising limonene (A) geraniol (B) and tonalide (C) with and without ethanol (S) are shown in Figure 6.13a for some different initial compositions presented in Table 6.6.

Table 6.6 – Initial compositions (x_{i0}), activity coefficients (γ_i) and odor values for system 2.

Point	x_{A0}	x_{B0}	x_{C0}	x_{S0}	γ_A	γ_B	γ_C	γ_S	OV_A	OV_B	OV_C	OV_S
P1	0.780	0.200	0.020	-	1.09	1.91	1.76	-	3904	2558	0.013	-
P2	0.400	0.400	0.200	-	1.31	1.34	1.47	-	2400	3596	0.113	-
P3	0.390	0.100	0.010	0.500	2.06	0.87	1.95	1.60	3695	582	0.007	1953
P4	0.200	0.200	0.100	0.500	2.45	0.95	2.10	1.39	2250	1270	0.081	1697
P5	0.234	0.060	0.006	0.700	3.5	0.86	2.85	1.22	3755	345	0.007	2081
P6	0.120	0.120	0.060	0.700	3.94	0.96	3.11	1.16	2174	773	0.069	2030

At first sight, the main considerations that can be done for this system are that, independently of the initial mixture concentration, the base note (tonalide) has always an OV lower than the human limit of detection and recognition (and so $OV_C < 1$). This behavior is due to the very low saturated vapor pressure of tonalide and also a relatively high odor threshold value when compared to the other base notes studied here (see Table 6.1 and Table 6.3). Tonalide is a polycyclic musk that is used in a wide variety of consumer products, usually as a fixative, having the ability to "fix in" the liquid some of the other notes and so producing a long lasting fragrance with an increased performance.

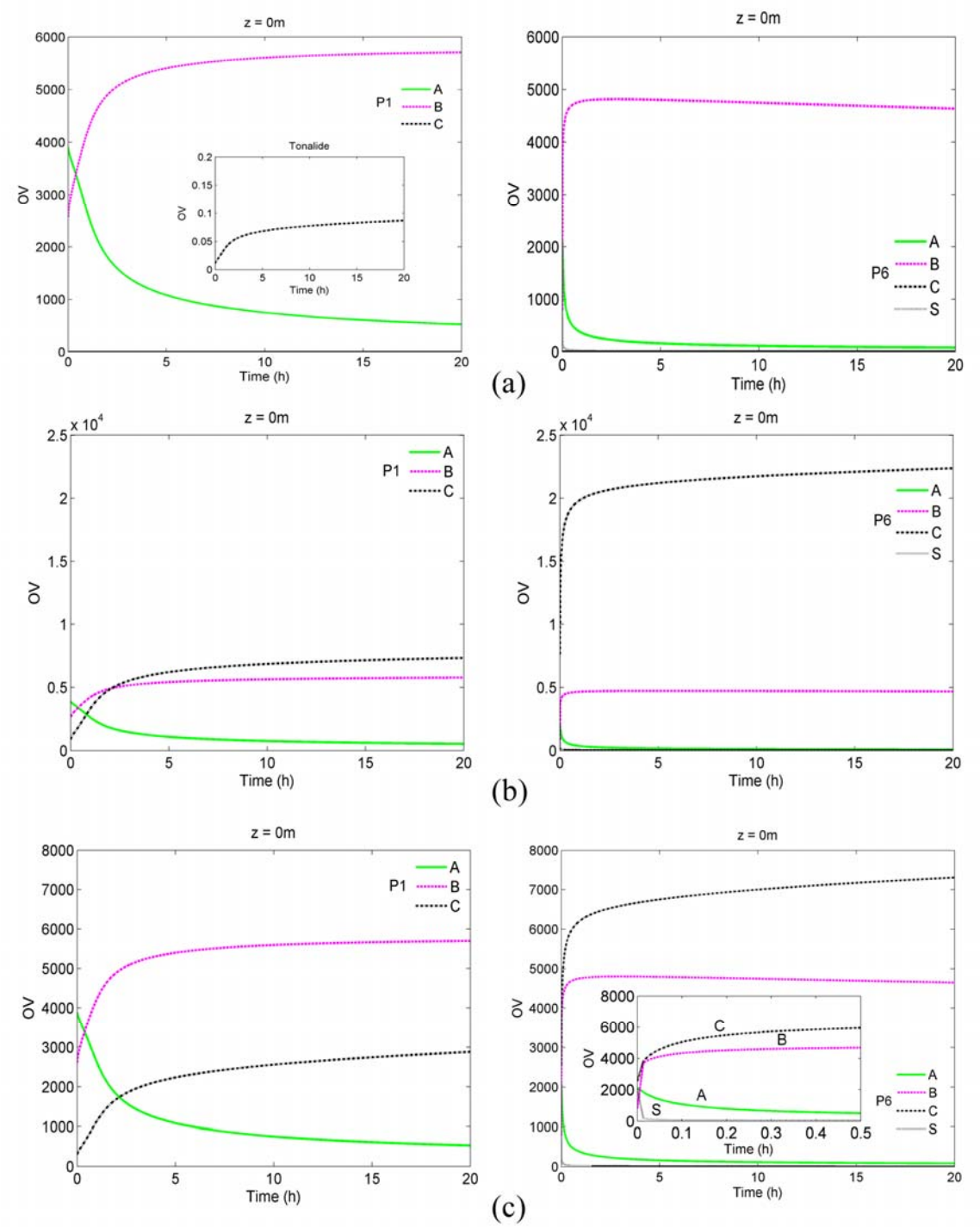


Figure 6.13 - Odor profiles of the odorants over time for different perfume mixtures: (a) system 2; (b) system 3; and (c) system 4 as defined in Table 6.2.

The presence of ethanol in this system leads (once more) to a faster evaporation of limonene due to the increase of polarity in the liquid, pushing the relatively non-polar top note out of the solution (Figure 6.13a). The relationship between the liquid and the gas phase over time for this system 2 (mixture P6) is shown in Figure 6.14. The volatile species, limonene and ethanol, evaporate faster than the middle and base notes: after 1

hour of the application of the perfume mixture, there is a decrease in 58.5% for the top note and 99% for the solvent in the liquid phase mole fraction.

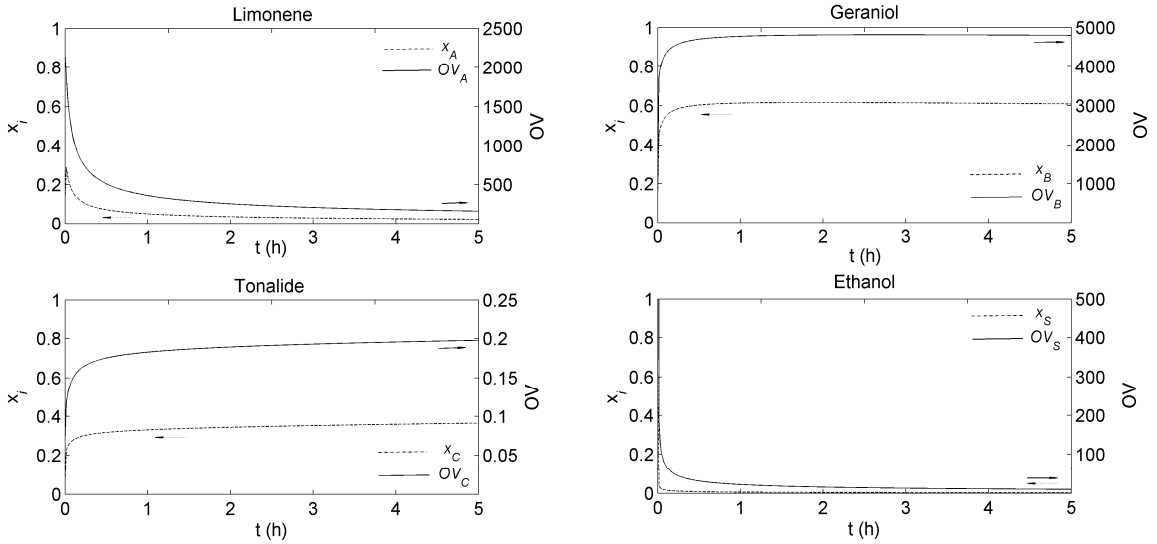


Figure 6.14 - Variation of the odor value (OV) and liquid composition (x_i) over time for each fragrance in mixture P6 (system 2).

Perfume Performance

The dispersion in the gas phase of the perfume mixture P6 over time and distance for system 2 is presented in Figure 6.15 for each species. It is seen that limonene (top note), when compared to system 1, has a lower impact over the first minutes after application of the perfume, due to the fixation induced by the base note. However, it is still the first fragrance note to be strongly perceived, though for only a few seconds. The middle note has higher tenacity and volume properties (dominant note at short and long distances from the perfume after a long time) than the other odorants in this perfume mixture, thus having a strong lastingness in the surrounding headspace. Limonene has a higher diffusion parameter, as expected from its higher diffusion coefficient when compared to geraniol (see Table 6.1).

The performance plot represented in Figure 6.16 allows mapping the OV_{max} over time and distance and, thus, having a general perspective of the behavior of the mixture. It is seen that the tonality in the gas phase is essentially that of geraniol, with exceptions for the initial point (smells strongly to limonene) and some place at short distance from the source of the perfume at initial times (smells strongly to ethanol).

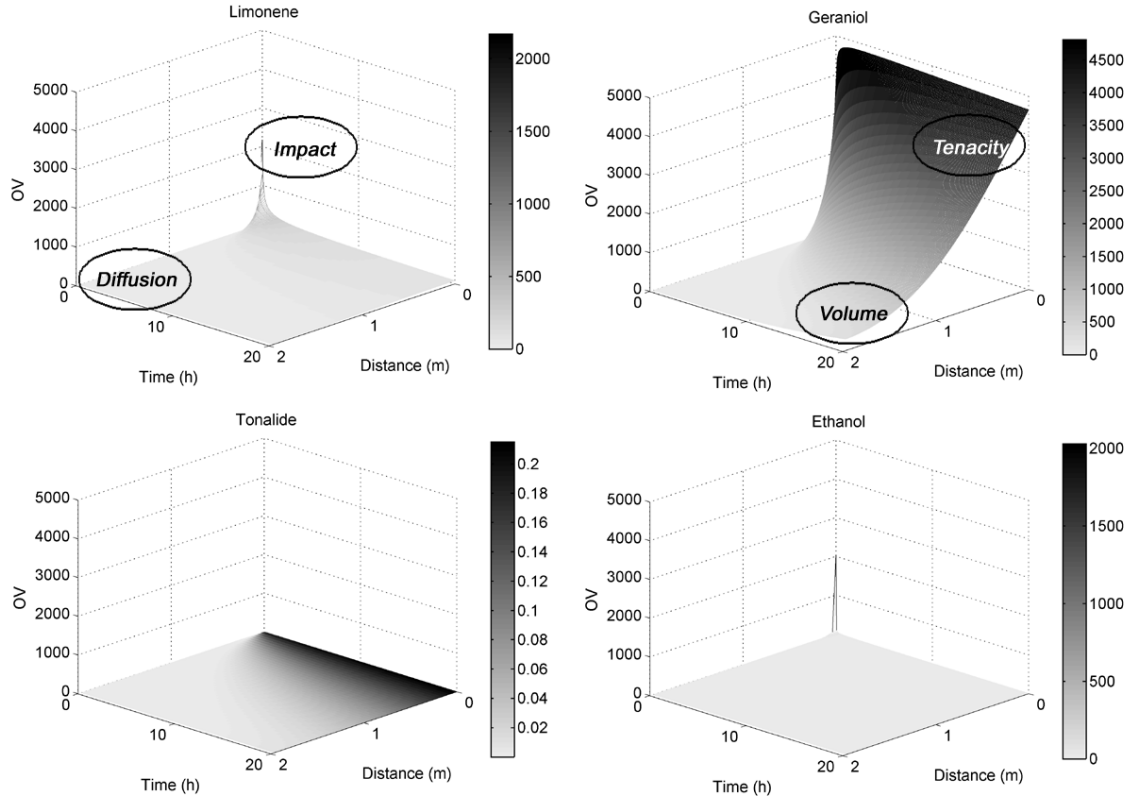


Figure 6.15 - Evaporation profiles over time and distance for each fragrance in mixture P6 (system 2).

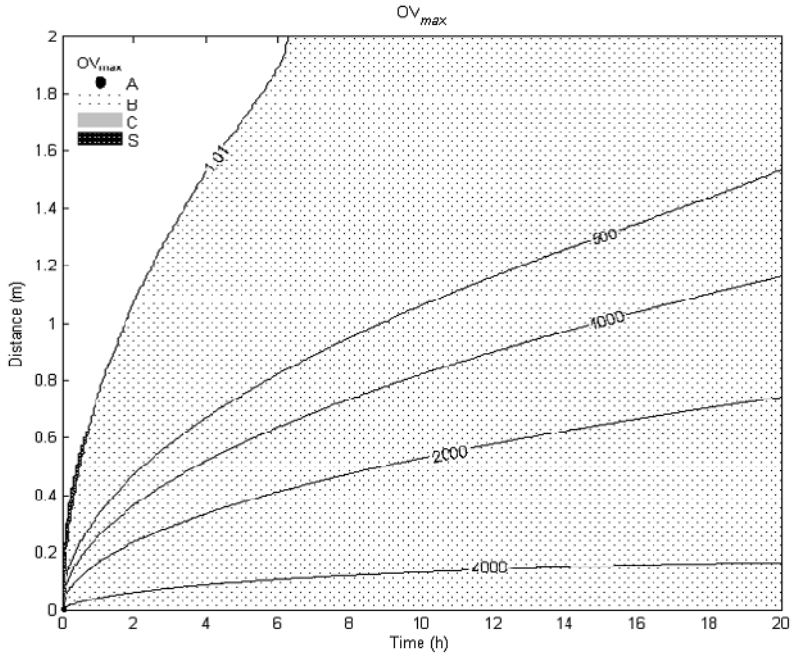


Figure 6.16 - Distribution of the OV_{max} over time and distance for system 2 and mixture P6. A – limonene, B – geraniol, C – tonalide, S - ethanol.

Perfume Evolution

A comparison between the evaporation lines for ternary (ethanol free) and quaternary mixtures is presented in Figure 6.17 and Figure 6.18 for some of the initial mixtures selected from Table 6.6. The evaporation lines for mixtures P2 and P6 seem quite similar in shape when plotted in the PTD, though they cross different odor zones (areas in the PTD where the OV of one species prevails over the others). This results in a significantly different odor perception over time. On one hand, for the ternary mixture P2 the initial impact is that of geraniol which will remain for several hours until it has vanished (near corner C in Figure 6.17a).

It is important to highlight though, that tonalide will probably never be strongly perceived, except when it is the pure component in the liquid, since its OV is smaller than unity and so below its detection limit. However, it should be noted also that this happens here for this specific perfume system which has a significantly low content in tonalide and relatively low volume of liquid. On the other hand, for the mixture P6 the first odor impact is that of limonene, which evolves to a geraniol scent in less than a minute after application. The liquid compositions and corresponding headspace OV for different times are presented in Table 6.7 for the points specified in Figure 6.17b and Figure 6.18.

Table 6.7 – Liquid composition at different times and corresponding headspace OVs for mixture P6.

Time (min)	x_A	x_B	x_C	x_S	OV_A	OV_B	OV_C	OV_S
0.0	0.120	0.120	0.060	0.700	2174	773	0.069	2030
0.5	0.312	0.426	0.214	0.049	2032	3519	0.110	250
5	0.170	0.539	0.274	0.017	1169	4287	0.147	76
10	0.123	0.571	0.293	0.013	867	4488	0.160	53
600	0.016	0.594	0.388	0.002	113	4747	0.205	7

The fixative properties of the base note used in this perfume system are well understood by analyzing the evaporation lines and the evolution of the ternary or quaternary mole fractions over time (Table 6.7). It is possible to see that for the top note (most volatile species) these are invariably higher than in perfume system 1, considering the same time after application of the perfume. This means that the presence of tonalide “fixes” the limonene in the liquid phase, thus remaining longer as a perceived scent than what was observed in system 1.

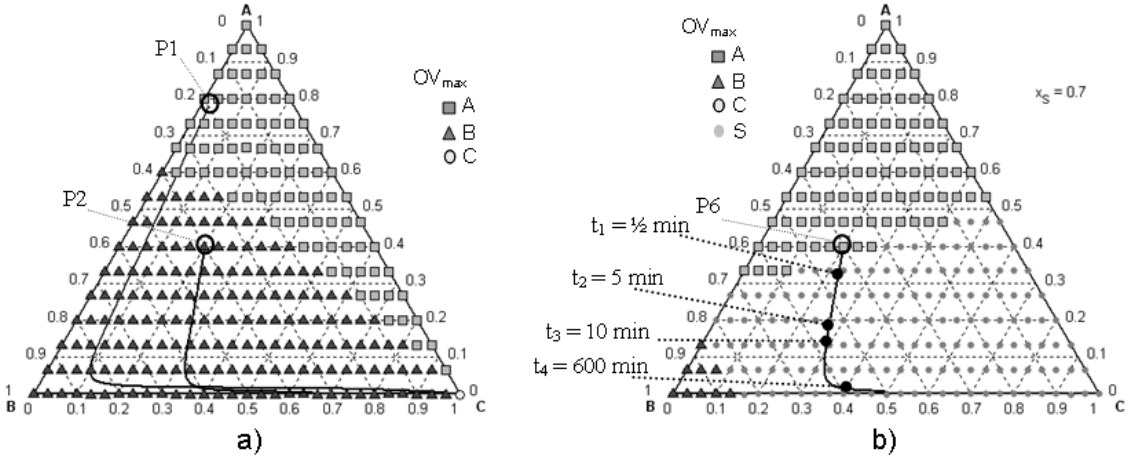


Figure 6.17 - Evaporation lines (EL) for initial mixtures compositions (system 2): (a) ternary mixture and (b) quaternary mixture.

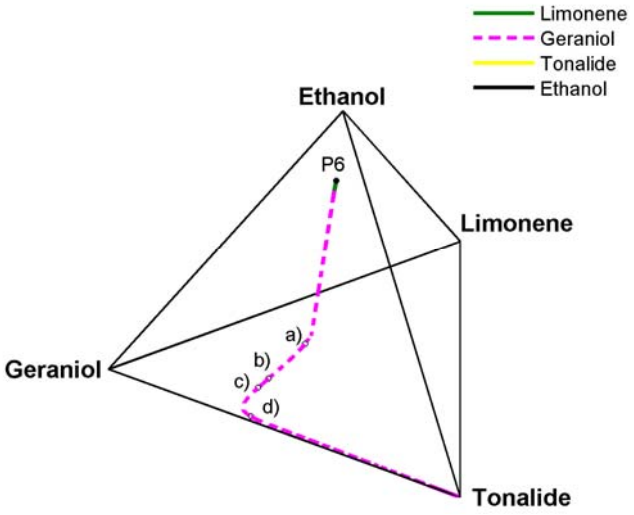


Figure 6.18 - PQ2D® with the evaporation line of mixture P6: a) t = 0.5 min, b) t = 5 min, c) t = 10 min, d) t = 600 min.

6.4.1.3. System 3: Limonene, Geraniol and Ambrox

Evaporation Profiles

The odor profiles showing the diffusion of odorants for perfume system 3 composed by limonene (A) geraniol (B) and ambrox (C) with and without ethanol (S) matrix for some different initial compositions (Table 6.8) of the liquid mixture are shown in Figure 6.13b. The odor profiles for this system 3 shows that ambrox is a powerful base note, evidencing a strong perceived odor in the headspace above the liquid perfume.

Table 6.8 – Initial compositions (x_{i0}), activity coefficients (γ_i) and odor values for system 3.

Point	x_{A0}	x_{B0}	x_{C0}	x_{S0}	γ_A	γ_B	γ_C	γ_S	OV_A	OV_B	OV_C	OV_S
P1	0.780	0.200	0.020	-	1.09	1.92	1.08	-	3894	2578	890	-
P2	0.400	0.400	0.200	-	1.26	1.34	1.23	-	2319	3597	10130	-
P3	0.390	0.100	0.010	0.500	2.06	0.87	1.63	1.65	3689	581	668	2006
P4	0.200	0.200	0.100	0.500	2.41	0.93	2.01	1.44	2214	1240	8257	1751
P5	0.234	0.060	0.006	0.700	3.49	0.86	2.60	1.25	3753	344	641	2135
P6	0.120	0.120	0.060	0.700	3.92	0.95	3.09	1.19	2165	760	7630	2030

Although it is a base note it produces a significantly high OV (P1 and P6), due to its physical and sensorial properties considered in this study. This can be seen by the highest dimensionless ratio for ambrox as presented in Table 6.1. Only for mixtures with very low content in ambrox (like P1) it is possible to have a "competition effect" for the strongest perceived odor in the first minutes after the perfume has started to evaporate. Otherwise, it is seen in Figure 6.13b that this soft, persistent and amber-like odorant with a velvety effect is always quantitatively predominant, having the highest OV. This trend can also be verified by comparison of the liquid and headspace compositions presented in Figure 6.19 for mixture P6. Additionally, the effect of ethanol on limonene is once more visible: increasing its mole fraction in solution, increases the tendency to "push out" of the mixture the top note, limonene. It is seen that OV_A strongly decreases over the first hour of evaporation, though it is seen a greater reduction when the ethanol fraction increases in the mixture, like a 52% and 83% decreasing in OV_A for mixtures P2 and P6, respectively.

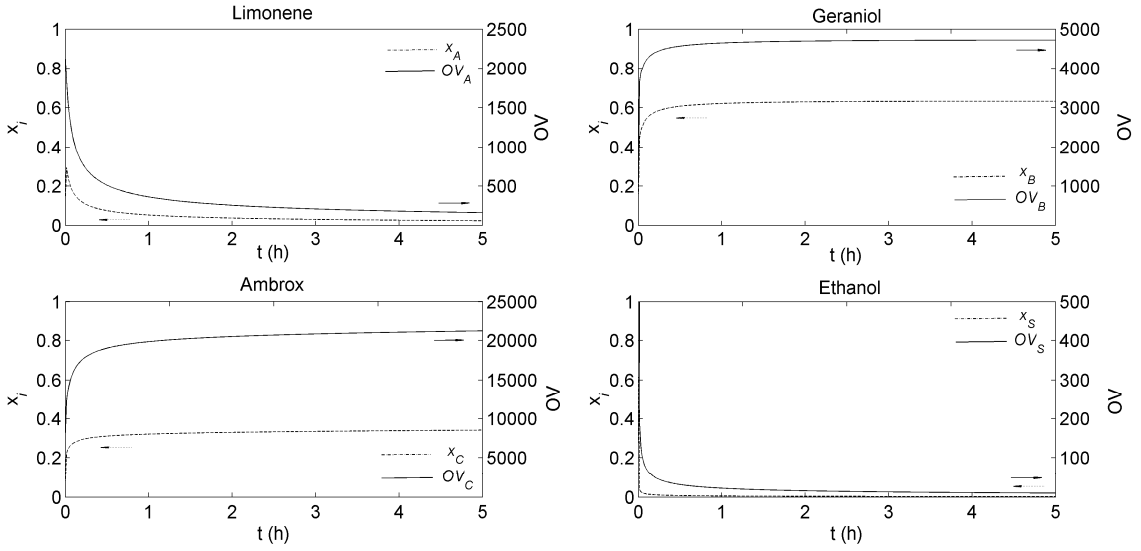


Figure 6.19 - Variation of the odor value (OV) and liquid composition (x_i) over time for each fragrance in mixture P6 (system 3).

Although the liquid composition remains mainly as a binary mixture of geraniol and ambrox from the first hour onwards, it is possible to see that OV_C is an order of magnitude higher than OV_B (Figure 6.19). This effect is due to a similar saturated vapor pressure of ambrox and geraniol (in the same order of magnitude, although it is a base note) and has a lower odor threshold. Figure 6.19 shows also that ethanol and limonene have fast predicted evaporation rates.

Perfume Performance

The diffusive effects over time and distance can be seen in Figure 6.20, where it is possible to quantitatively interpret the perfumery performance parameters. Although being a base note, ambrox shows to have not only higher tenacity and volume properties but also a higher impact in what concerns to the performance of this mixture. The middle note geraniol evidences a slightly higher diffusion performance parameter than ambrox, thus being more strongly perceived at a long distance from the perfume source in the first minutes after application. This is in agreement with the fact that geraniol has a diffusion coefficient higher than ambrox (see Table 6.1). The later has a low saturated vapor pressure, which leads to this equilibrium or little predominance of the base note.

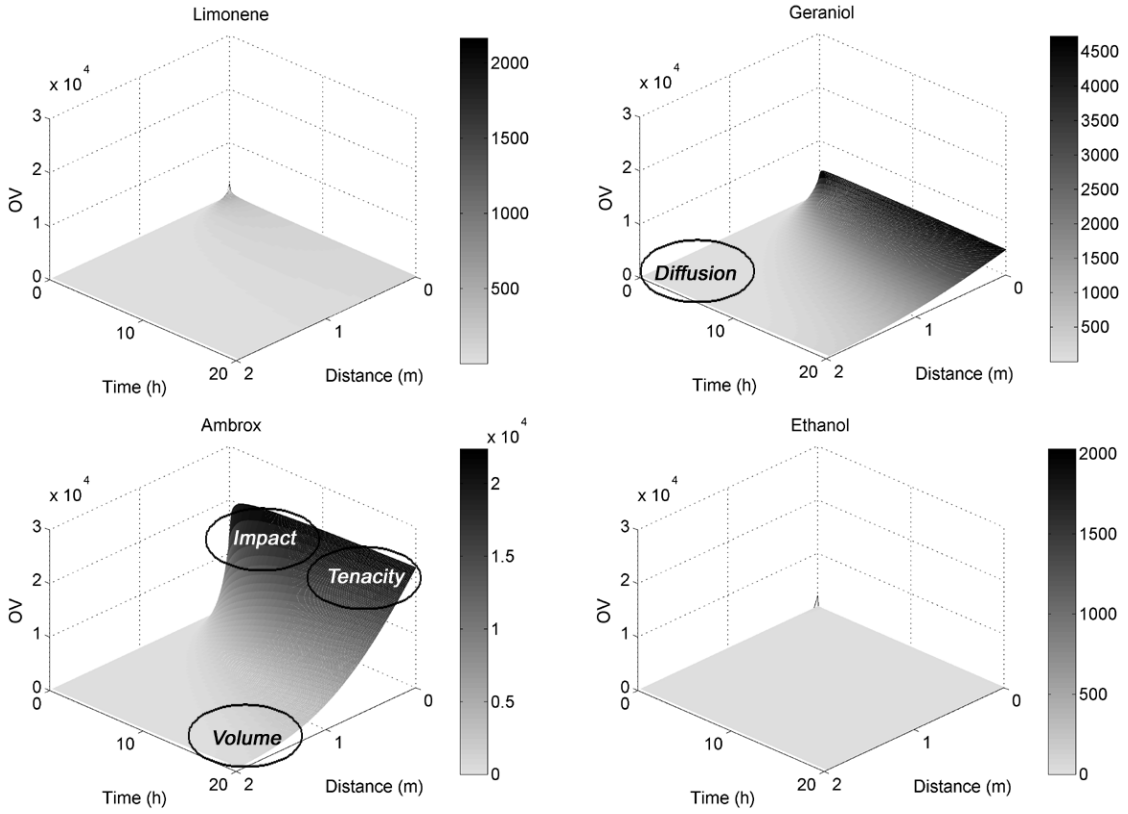


Figure 6.20 - Evaporation Profiles over time and distance for each fragrance in mixture P6 (system 3).

An analysis of the OV_{max} distribution over time and distance in the performance plot of Figure 6.21 shows a qualitative view for the tonality of the perfume over time and distance. It is seen that ambrox has the maximum odor value for a large range of time over the surrounding space (dark grey), except at initial times after starting to diffuse at some distance from the perfume source and some minor area where ethanol prevails (black with open dots). Once more, it should be noted that this predicted blooming effect from ambrox is due to its physicochemical properties obtained from the literature. However it is known from perfumery that despite the fact that ambrox has a pleasant sweet-amber odor it may not be always so intensely perceived.

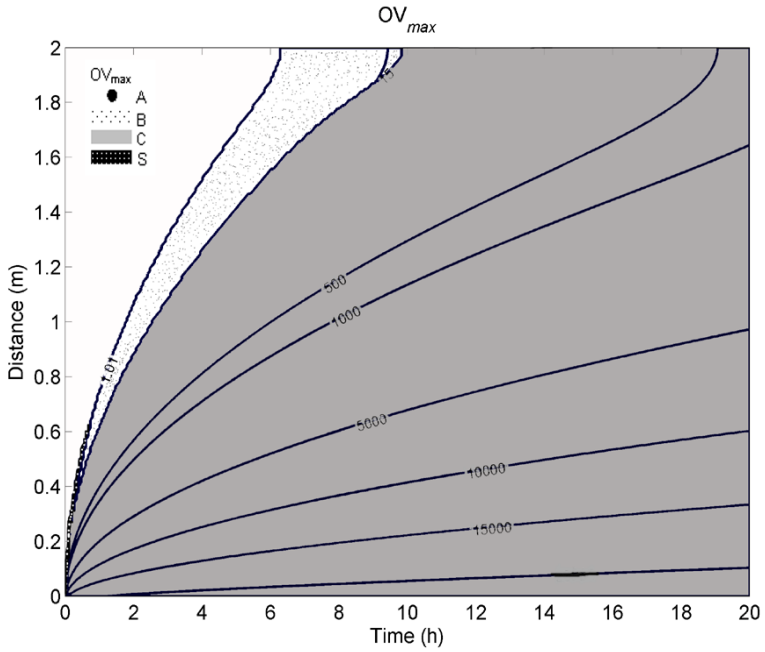


Figure 6.21 - Distribution of the OV_{max} over time and distance for system 3 and mixture P6. A – limonene, B – geraniol, C – ambrox, S - ethanol.

Perfume Evolution

The evaporation lines for system 3 are shown in Figure 6.22 and Figure 6.23 for some concentrated and diluted mixtures specified before in Table 6.8. The evaporation lines showing the scent evolution over time strongly depend upon the selection of the initial mixture composition as it can be seen for P1 and P2, the concentrated perfume mixtures, in Figure 6.22. Mixture P2 has always an amber scent, while mixture P1 starts to have an impact of limonene and finishes with an amber odor after passing through a rose geraniol scent. For its part, mixture P6 has a prevailing amber scent through all time

since it starts to evaporate and diffuse as can be seen in Table 6.9. Although the PTD for the quaternary mixture changes over time (Figure 6.22b), once the ethanol composition is changing along with the evaporation process, the fact is that ambrox, actually, prevails with the maximum OV over the entire range of simulated time.

Table 6.9 – Liquid composition at different times and corresponding headspace OVs for mixture P6.

Time (min)	x_A	x_B	x_C	x_S	OV_A	OV_B	OV_C	OV_S
0.0	0.120	0.120	0.060	0.700	2165	760	7630	2030
0.5	0.309	0.429	0.215	0.047	1941	3505	11687	249
5	0.173	0.539	0.272	0.016	1142	4189	15802	76
10	0.127	0.571	0.289	0.012	856	4369	17243	53
600	0.016	0.630	0.352	0.002	113	4714	21747	7

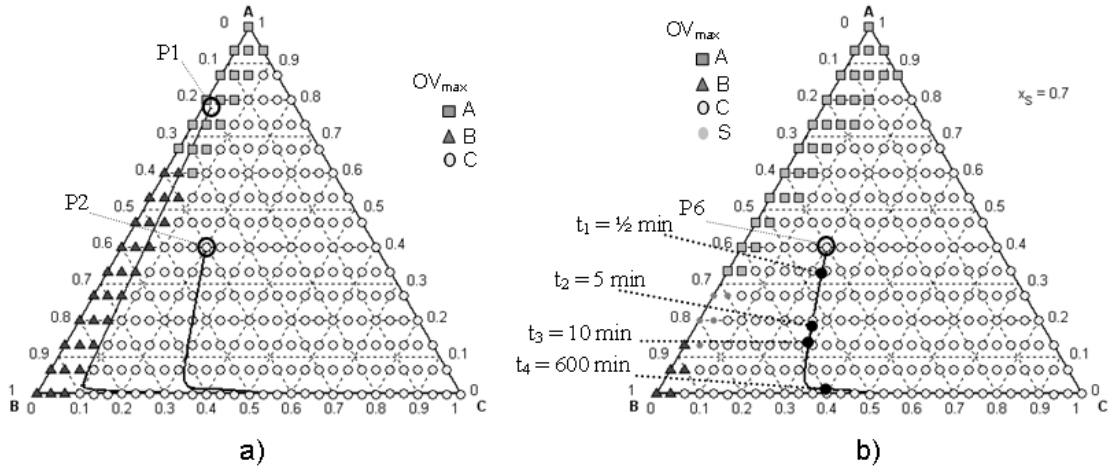


Figure 6.22 - Evaporation lines (EL) for initial mixtures compositions (system 3): (a) ternary mixture and (b) quaternary mixture.

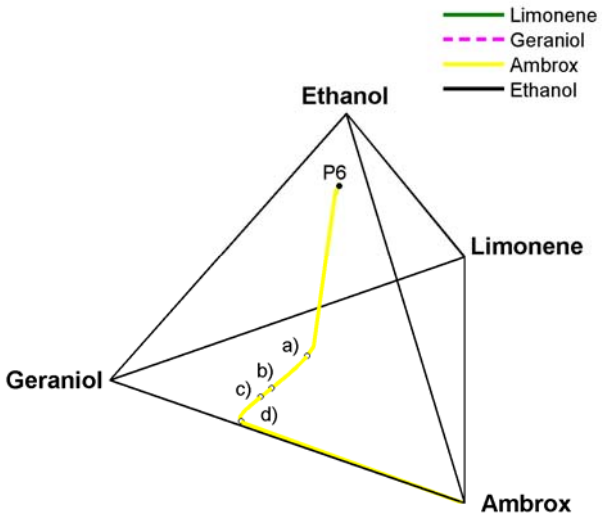


Figure 6.23 - PQ2D® with the evaporation line of mixture P6: a) t = 0.5 min, b) t = 5 min, c) t = 10 min, d) t = 600 min.

6.4.1.4. System 4: Limonene, Geraniol and Galaxolide

Evaporation Profiles

The odor profiles for the perfumery ternary and quaternary systems of limonene (A) geraniol (B) and galaxolide (C) with and without an ethanol (S) matrix are shown in Figure 6.13c, considering the initial mixtures presented in Table 6.10.

Table 6.10 – Initial compositions (x_{i0}), activity coefficients (γ_i) and odor values for system 4.

Point	x_{A0}	x_{B0}	x_{C0}	x_{S0}	γ_A	γ_B	γ_C	γ_S	OV_A	OV_B	OV_C	OV_S
P1	0.780	0.200	0.020	-	1.086	1.92	1.245	-	3894	2579	300	-
P2	0.400	0.400	0.200	-	1.262	1.37	1.332	-	2321	3662	3204	-
P3	0.390	0.100	0.010	0.500	2.06	0.87	1.874	1.646	3686	582	225	2007
P4	0.200	0.200	0.100	0.500	2.39	0.94	2.224	1.443	2198	1256	2675	1760
P5	0.234	0.060	0.006	0.700	3.49	0.86	3.082	1.251	3749	344	222	2136
P6	0.120	0.120	0.060	0.700	3.88	0.95	3.545	1.193	2141	764	2558	2038

The incorporation of a higher mole fraction of ethanol in the perfume mixture leads to a typical effect of faster evaporation of the more volatile fragrance note (limonene), as it can be seen by the steepest negative slope for the OV profile curves at initial times (Figure 6.13c). The evolution of the liquid phase composition with the OV for mixture P6 (see Table 6.10) can be seen in Figure 6.24 for all different odorants of system 4. The evaporation rate of ethanol is the fastest among all the species, considering the stated evaporation conditions, though it is present in a much higher percentage in the solution. The top note, limonene, also shows a fast evaporation during the first hour after the application of the perfume while geraniol and galaxolide remain longer in solution and so will be perceived more intensely in the remaining hours.

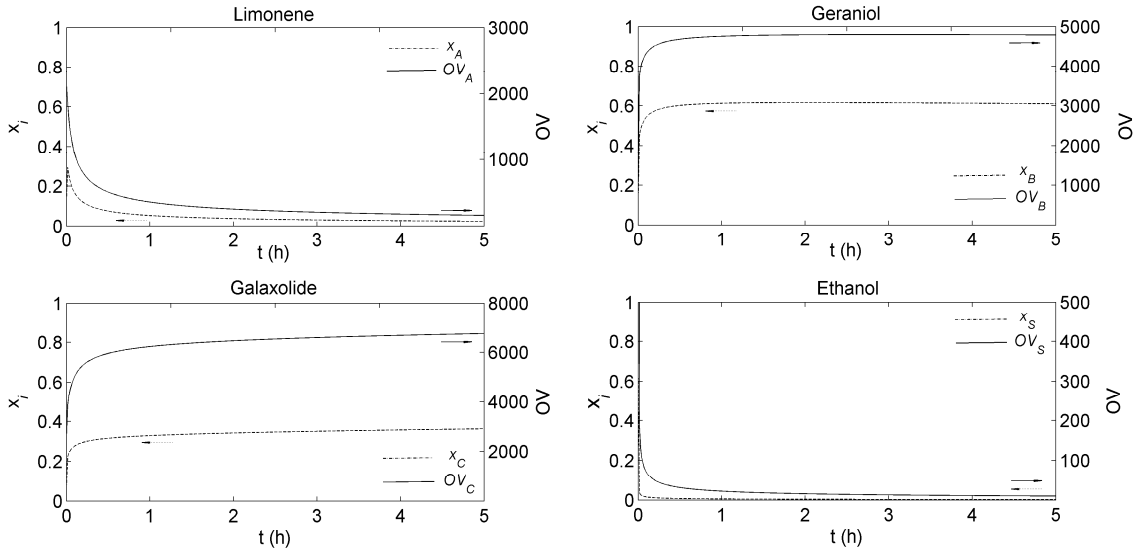


Figure 6.24 - Variation of the odor value (OV) and liquid composition (x_i) over time for each fragrance in mixture P6 (system 4).

Perfume Performance

The analysis of the performance for this system 4 can be carried out with the OV distribution over time and distance for each of the odorants as presented in Figure 6.25 for an initial mixture composition like P6 (see Table 6.10). Galaxolide evidences higher impact than the other odorants (Figure 6.25 and Table 6.10) which means that it will be strongly perceived in the first couple minutes after the perfume has started to diffuse. Although geraniol has a low OV for the initial mixture at the liquid-gas interface, it does increase rapidly over the first minutes but it is always quantitatively lower than the OV of galaxolide. This unexpected behavior is due to the fact that the base note has the lowest odor threshold value of all the base notes studied here (Table 6.3). Thus, the tonality in the air over time and distance *(OV_{max})* shown in the performance plot of Figure 6.26 is mainly that of galaxolide. There is a small area where the strongly perceive odor is ethanol (black pattern with white dots) which is undesirable from the perfumery point of view; and also a small odor intensity zone where geraniol prevails due to its diffusion properties (light grey). Thus, diffusion property is controlled by geraniol. This is similar to system 3, but here the area for geraniol is larger so impact for galaxolide is smaller than for ambrox.

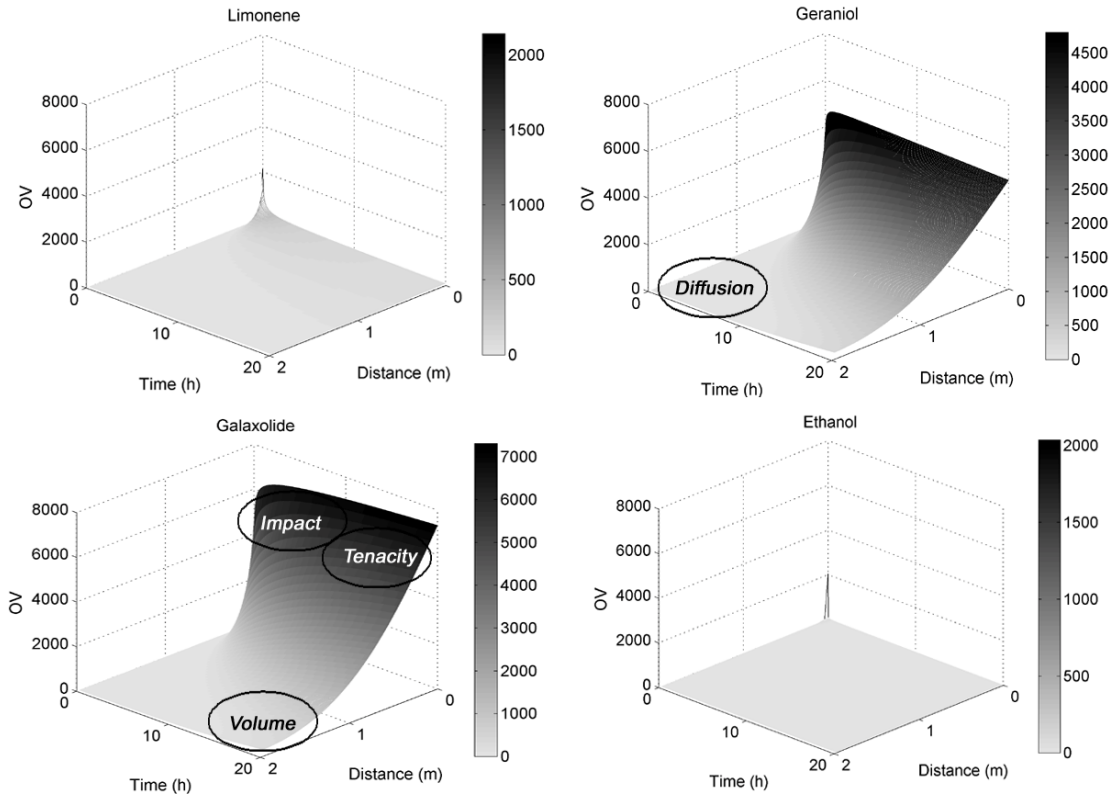


Figure 6.25 - Evaporation profiles over time and distance for each fragrance in mixture P6 (system 4).

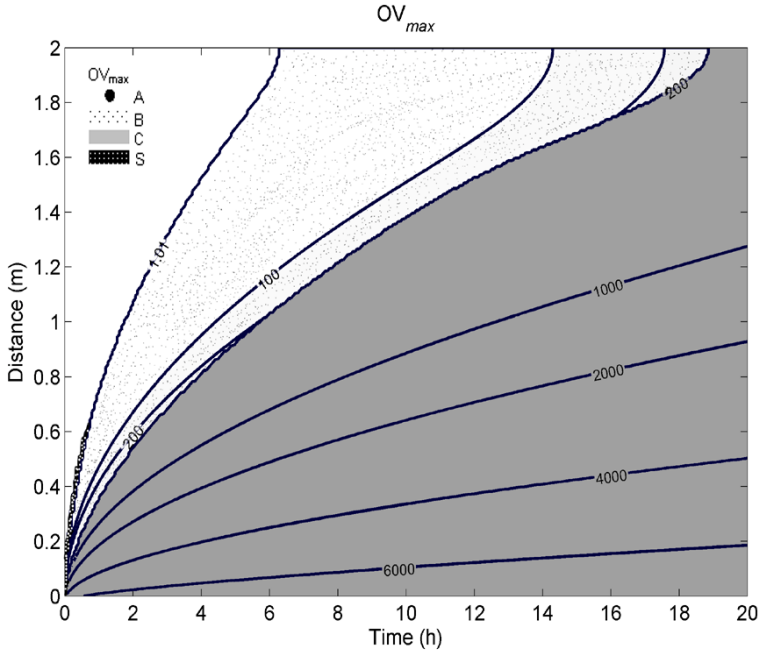


Figure 6.26 - Distribution of the OV_{max} over time and distance for system 4 and mixture P6. A – limonene, B – geraniol, C – galaxolide, S - ethanol.

Perfume Evolution

The evaporation lines showing the theoretical perceived scent over time for a point near the perfume source are presented in Figure 6.27 and Figure 6.28 for the mixtures listed in Table 6.10. The evaporation lines of the concentrated mixtures shown in Figure 6.27 highlight the importance of the selection of the initial perfume concentration. As it is seen, for an initial mixture like P1 the first odor impact is that of limonene, which then progresses to geraniol through time and, finally, ends up with a galaxolide scent. However, if one selects a mixture like the one of P2, initially a geraniol scent is strongly perceived which then shifts into a galaxolide odor for the remaining hours or days, having no prevalence of the limonene fresh odor ever during the evaporation process.

However, if an ethanol matrix is incorporated in the perfume formulation, the resulting PTD changes significantly as the liquid concentration is dynamically evolving during the evaporation process. The representation of the evaporation line for mixture P6 of system 4 is shown in Figure 6.27b for the initial PTD (with $x_S = 0.7$) and in the PQ2D in Figure 6.28 where it is seen that as evaporation proceeds, the liquid composition moves towards the galaxolide corner.

Table 6.11 – Liquid composition at different times and correspondent headspace OVs for mixture P6.

Time (min)	x_A	x_B	x_C	x_S	OV_A	OV_B	OV_C	OV_S
0.0	0.120	0.120	0.060	0.700	2142	764	2559	2038
0.5	0.309	0.429	0.215	0.047	1940	3580	3684	249
5	0.173	0.537	0.273	0.016	1139	4294	4950	76
10	0.128	0.569	0.292	0.012	854	4480	5396	53
600	0.017	0.596	0.386	0.002	113	4745	7003	7

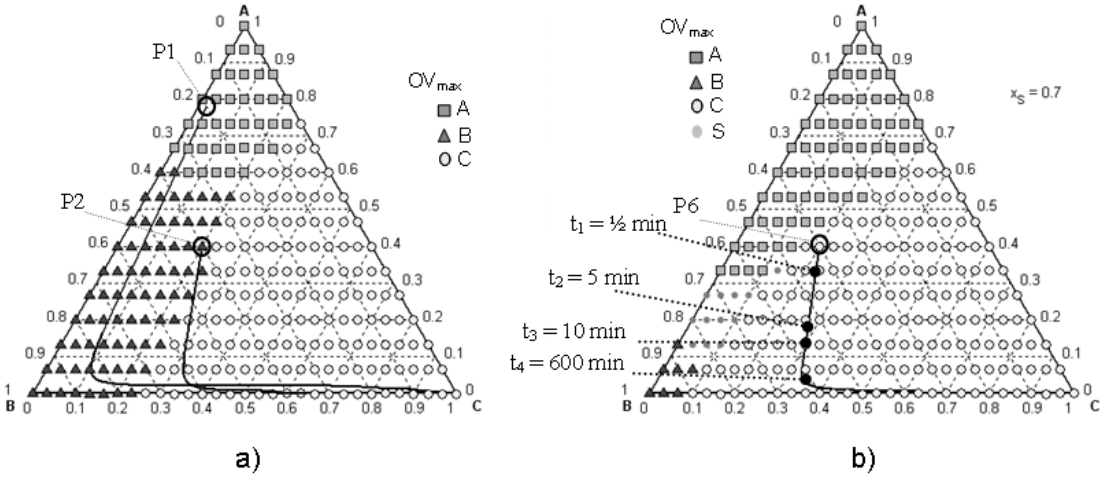


Figure 6.27 - Evaporation lines (EL) for initial mixtures compositions (system 4): (a) ternary mixture and (b) quaternary mixture.

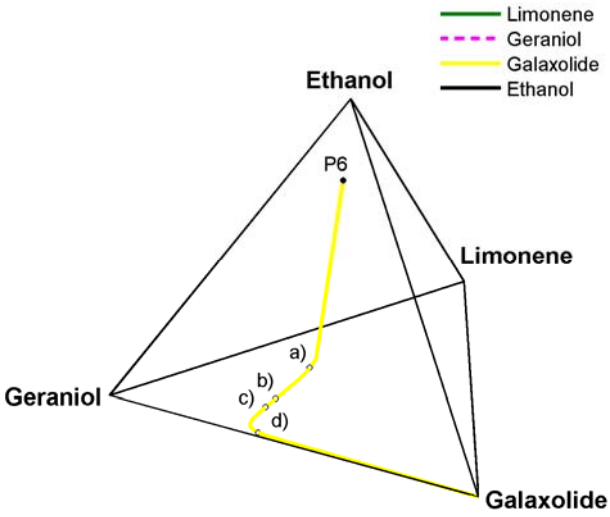


Figure 6.28 - PQ2D® with the evaporation line of mixture P6: a) t = 0.5 min, b) t = 5 min, c) t = 10 min, d) t = 600 min.

6.4.2. Evaluation of commercial perfumes

So far, we have been studying ternary to quaternary mixtures of a defined and known composition. However, it is unquestionable that for the fragrance business it is common practice to use larger number of fragrance ingredients in a formulation. Perfume mixtures can differ in complexity and be applied in different products with different bases/matrices. Here, the evaporation and diffusion of two commercial perfumes will be addressed without delving into much detail due to the complexity of its nature and the difficulty of its validation. The odor profiles for Gloria (Cacharel) and L'air du Temps (Nina Ricci) are presented in Figure 6.29 and Figure 6.30, respectively.

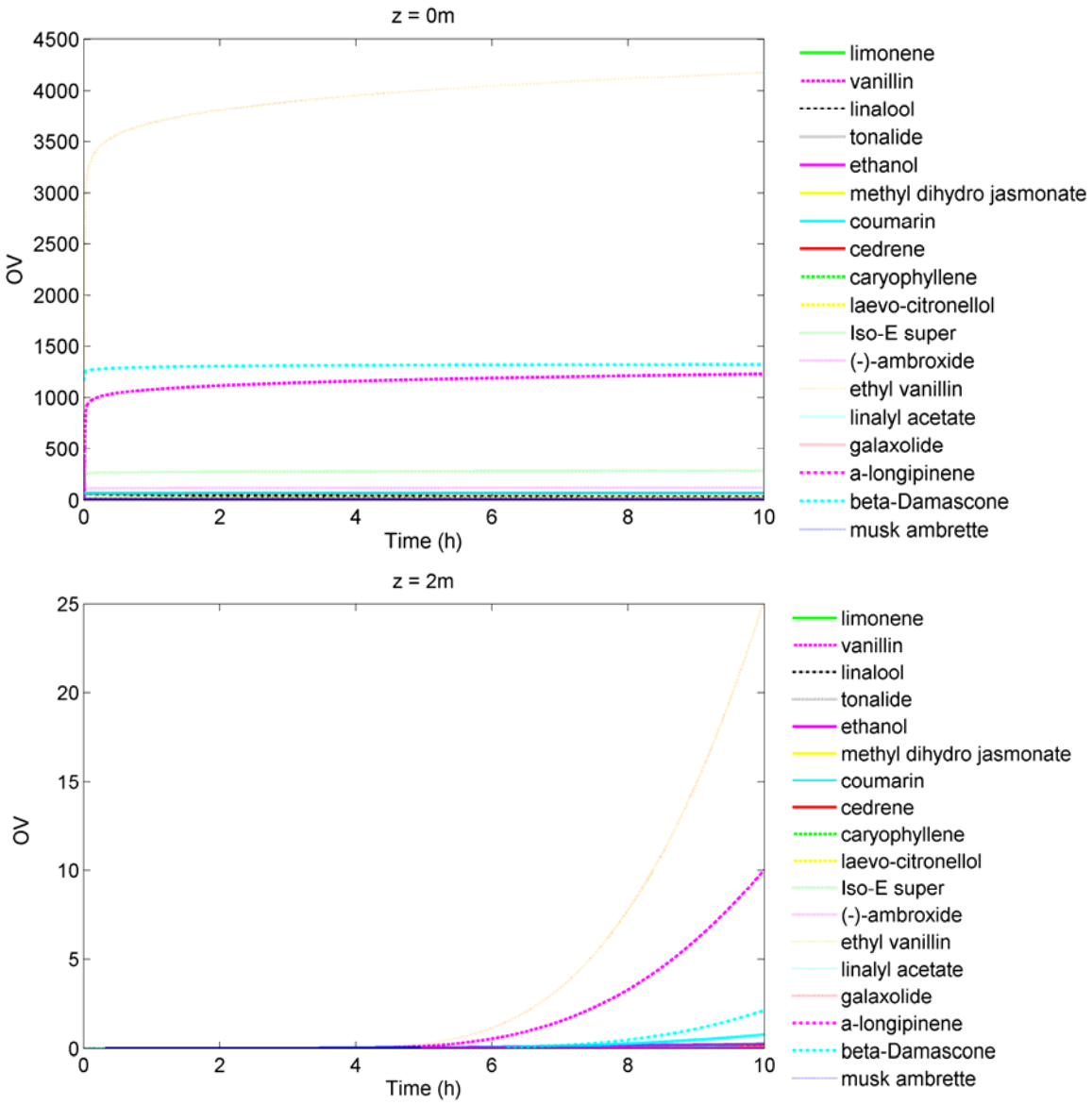


Figure 6.29 - Diffusion profiles for the commercial perfume Gloria (Cacharel) at z = 0 m and z = 2 m from the releasing source.

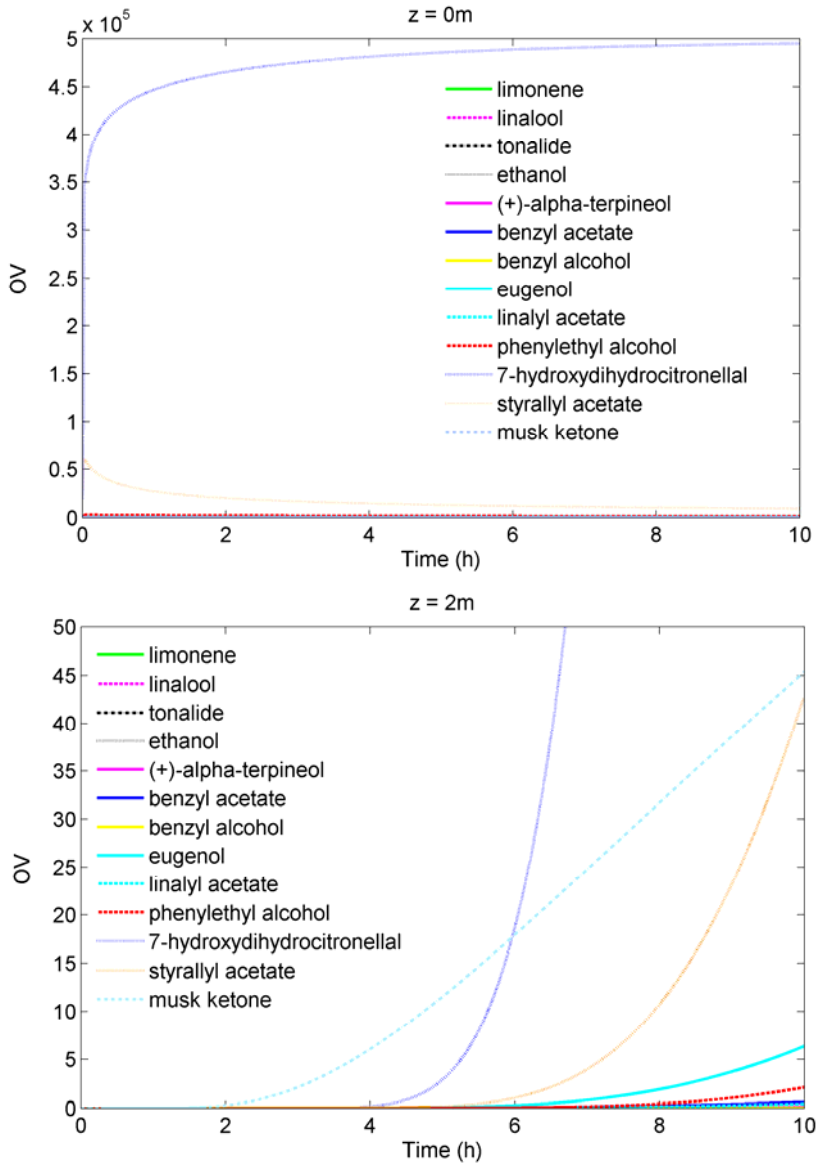


Figure 6.30 - Diffusion profiles for the commercial perfume L'air du Temps (Nina Ricci) at z = 0 m and z = 2 m from the releasing source.

These commercial perfumes were analyzed by gas chromatography coupled with mass spectrometry (GC-FID-MS) for the quantification and identification of the major fragrance ingredients. Further details on this procedure will be discussed ahead on Chapter 8. Nevertheless, the purpose here is to show a qualitative perspective obtained for more complex mixtures. From that point, the odor model presented in this Chapter was applied for the diffusion of the different components. It is possible to observe that there is a large number of fragrance ingredients in these perfumes with different roles in it. Some are more strongly perceived than others (higher OV) depending on the time and distance from the source, thus contributing for the perceived overall odor. This is one of the reasons behind the complexity and success of perfumes.

Part II – Proof of concept: experimental validation

6.5. Introduction

Recalling equation 6.1 for diffusion as proposed by Fick, it can be noted that, more than a century ago, he faced difficulties to prove its validity throughout his experiments with salt solutions (Philibert, 2006). Nevertheless, he did succeed in performing experiments at the steady state regime. For that reason also, in this study it was first performed the measurement of diffusion profiles for pure components until they reach the steady state. The modeling of the diffusion process was performed considering the fundamental approach based on the Fick's law of diffusion.

However, there could be a preference for mass transfer coefficients, especially in the case where the resistance to mass transfer in the liquid phase exceeds that in the gas phase. Here, a parenthesis is made to analyze this question. The type of geometry and liquid volume plays an important role in this phenomenon. Considering the particular "geometry" obtained from perfume spray which is the case considered here it is possible to do some rough calculations to evaluate the resistance to mass transfer both in the liquid and gas phases, as follows: The mass transfer coefficient is defined as $k = D/\delta$ where D is the diffusion coefficient (m^2/s) and δ is the film thickness (m) (Taylor and Krishna, 1993; Wesselingh and Krishna, 2000; Bird, 2002; Cussler, 2007). Typical values for these parameters are presented in Table 6.12.

Table 6.12 – Typical values of D and $\boldsymbol{\delta}$ for gases and liquids.

	Gas	Liquid
D (m^2/s)*	(10^{-4} to 10^{-6}) ~ 10^{-5}	(10^{-8} to 10^{-10}) ~ 10^{-9}
δ (m)†	10^{-3} - 10^{-4}	10^{-4} - 10^{-5}‡

* Perry and Green, *in* Perry's Chemical Engineer's Handbook; Bird, Stewart and Lightfoot, *in* Transport Phenomena.

† Taylor and Krishna, *in* Multicomponent Mass Transfer.

‡ Cussler, *in* Diffusion: Mass transfer in fluid systems, recommends a value of $\delta = 10^{-4}$ for liquids.

The mass transfer coefficients in the gas and liquid phases are then calculated as $k_g = 10^{-1} - 10^{-2}\, m/s$ and $k_l = 10^{-4} - 10^{-5}\, m/s$, respectively, which are in good agreement with the mass transfer coefficients published by Wesselingh and Krishna (Wesselingh and Krishna, 2000): $k_g = 10^{-1}\, m/s$ and $k_l = 10^{-4}\, m/s$.

Now, the overall mass transfer coefficient, assuming a linear model for the description of the vapor-liquid equilibrium (VLE) can be given by $\frac{1}{k_{Tot}} = \frac{1}{k_g} + \frac{1}{k_l}\frac{c_g^T}{c_l^T}K_i$ with k_{Tot} as the overall mass transfer coefficient, $c^T{}_g$ and $c^T{}_l$ the total concentrations in gas and liquid phases, respectively, and K_i as the equilibrium ratio ($y_i = K_i\, x_i$).

The ratio of gas to liquid concentrations can be calculated for some of the perfume mixtures presented in this Chapter – Part I (*e.g.* system 1: Limonene, Geraniol, Vanillin and Ethanol) near the interface at initial times after evaporation has started. For this case it was obtained a ratio of $\frac{c_g^T}{c_l^T} = \frac{2.32 mol/m^3}{11.15\times10^3 mol/m^3} = 2.08\times10^{-4}$. Moreover, the equilibrium ratios, K_i, can be determined using the UNIFAC method. Considering the case of limonene near the interface at relatively short times after the evaporation process takes place, it was obtained that:

$$\begin{cases} K_i = \frac{y_i}{x_i} = \frac{1.3\times10^{-3}}{1.2\times10^{-1}} \approx 10^{-2} & at\ t = t_0 = 0 seg \\ K_i = \frac{y_i}{x_i} = \frac{1.4\times10^{-3}}{2.8\times10^{-1}} \approx 0.5\times10^{-2} & at\ t = 16 seg \end{cases}$$

Additionaly, it is presented in Table 6.13 some of the initial values of the equilibrium ratios for the different fragrant species in system 1.

Table 6.13 – K_i values for the different species.

$K_{i\ (Limonene)}$	$K_{i\ (Geraniol)}$	$K_{i\ (Vanillin)}$	$K_{i\ (Ethanol)}$
1.10×10^{-2}	2.79×10^{-5}	1.74×10^{-7}	7.93×10^{-2}
5.05×10^{-3}	2.44×10^{-5}	5.03×10^{-7}	8.64×10^{-2}

Using the values presented above it is possible to estimate the resistance to mass transfer in the gas and liquid phases, respectively, considering the case of limonene: $\frac{1}{k_g} \cong 10$; $\frac{1}{k_l} \cong 10^4$; and $\frac{1}{k_l}\frac{c_g^T}{c_l^T}K_i \cong K_i \cong 10^{-2}$. In this way, with a simple calculation, it can be said that the resistance to mass transfer in the gas phase would exceed that in the liquid phase, and not the opposite. However, in a different system, with a different

geometry, like in a bottle of perfume (with a larger volume of liquid), opened and evaporating into the atmosphere, it may be reasonable to consider the approach using mass transfer coefficients.

The physical system for the diffusion of fragrances studied in this Part II of Chapter 6 is very similar in phenomenological terms to the Stefan Tube problem (Lee and Wilke, 1954; Heinzelmann*, et al.*, 1965). This is expressed by a liquid A that evaporates into a stagnant gas film B with a gas stream of air at the top as depicted in Figure 6.31. This gas stream is passed at a rate sufficient to assume the concentration of the diffusing gas as zero but low enough to prevent turbulence inside the tube.

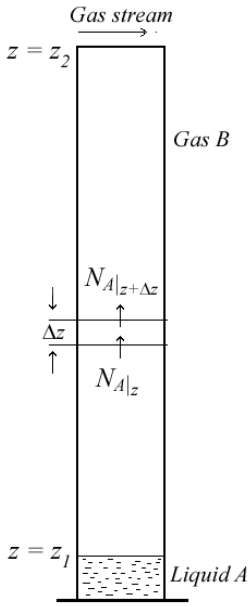


Figure 6.31 - Schematic representation of the diffusion of A through stagnant B.

The solution of Fick's first law as a function of the molar flux relative to stationary coordinates for a single component can be derived as follows (Bird*, et al.*, 1960):

$$N_{A_z} = -c_T D_{AB} \frac{\partial x_A}{\partial z} + x_A \left(N_{A_z} + N_{B_z} \right) \tag{6.10}$$

where N_{AZ} is the number of moles of A that go through the unit area per unit of time (molar flux) with the unit area fixed in space. c_T is the total concentration, D_{AB} is the diffusion coefficient of species A in species B, x_A is the mole fraction of A and N_{BZ} is the corresponding flux for species B. If a steady state condition is assumed and species B (in this case, air) is considered as a stagnant fluid ($N_{BZ} = 0$), then equation 6.10 can be rewritten as:

$$N_{A_z} = \frac{-c_T D_{AB}}{1-x_A}\frac{dx_A}{dz} \tag{6.11}$$

Moreover, performing a mass balance to the volume element depicted in Figure 6.31 in steady state, $dN_A/dz = 0$, then equation 6.11 is expressed as:

$$\frac{dN_{A_z}}{dz} = \frac{d}{dz}\left(\frac{c_T D_{AB}}{1-x_A}\frac{dx_A}{dz}\right) = 0 \tag{6.12}$$

Considering ideal solution in the gas phase, T and P constant, and D_{AB} approximately independent of the concentration, and c_T a constant, it is possible to integrate equation 6.12 which returns (Bird*, et al.*, 1960):

$$\frac{1}{1-x_A}\frac{dx_A}{dz} = C_1 \tag{6.13}$$

$$-\ln\left(1-x_A\right) = C_1 z + C_2 \tag{6.14}$$

and with respect to the Boundary Conditions (BC):

$$z = z_1 \qquad\qquad x_A = x_{A_1} \tag{6.15}$$

$$z = z_2 \qquad\qquad x_A = x_{A_2} \tag{6.16}$$

In this way, solving equation 6.14 for $z = z_1$ gives that $C_2 = -ln(1-x_{A1})-C_1 \cdot z_1$ and substituting into equation 6.14 solved for z = z_2 gives that:

$$C_1 = \frac{\ln\left(\frac{1-x_{A_1}}{1-x_{A_2}}\right)}{z_2 - z_1} \tag{6.17}$$

and, then, the integration constant C_2 can be calculated as:

$$C_2 = \frac{z_1 \ln\left(1-x_{A_2}\right) - z_2 \ln\left(1-x_{A_1}\right)}{z_2 - z_1} \tag{6.18}$$

Therefore, having determined the constants and substituting into equation 6.14, it is possible to represent the concentration profile of A as defined by Bird *et al.* (Bird*, et al.*, 1960):

$$\left(\frac{1-x_A}{1-x_{A_1}}\right)=\left(\frac{1-x_{A_2}}{1-x_{A_1}}\right)^{\frac{z-z_1}{z_2-z_1}} \tag{6.19}$$

Thus, from the previous equation 6.19 it is possible to calculate the steady state concentration inside the tube for a fragrant species that is diffusing upwards.

On the other hand, if we recall Equation 6.11 and seek for an unsteady state solution (transient state), then the mass balance to the volume element is given by $\partial N_A/\partial z = \partial C_A/\partial t$, and it can be written that:

$$\frac{\partial N_{A_z}}{\partial z}=\frac{\partial}{\partial z}\left(\frac{c_T D_{AB}}{1-x_A}\frac{\partial x_A}{\partial z}\right)=c_T\frac{\partial x_A}{\partial t} \tag{6.20}$$

which by derivation gives:

$$\frac{\partial x_A}{\partial t}=\frac{D_{AB}\left[\left(\frac{\partial x_A}{\partial z}\right)\left(\frac{\partial x_A}{\partial z}\right)+\left(1-x_A\right)\frac{\partial^2 x_A}{\partial z^2}\right]}{\left(1-x_A\right)^2} \tag{6.21}$$

Moreover, it can be considered the mass balance to the liquid phase described by:

$$\frac{dn_A}{dt}=D_{AB}A_{gl}c_T\left.\frac{\partial x_A}{\partial z}\right|_{z=0} \tag{6.22}$$

with the following initial (IC) and boundary conditions (BC):

I.C.	$t = 0$,	(z = 0)	$n_A = n_{A0}$	(6.23)
B.C.	$t > 0$,	z = 0	$x_A = x_{A0} = x_{Aeq}$	(6.24)
		z > 0	$x_A = 0$	(6.25)

The solution of the coupled equations 6.21 and 6.22 gives the concentration profiles over time for each species in the unsteady regime. Both the approaches, steady state and unsteady state, were considered for the modeling of the diffusion systems considered here, with pure components and mixtures of them. The resolution of the coupled system of equations (ODE + PDE) was performed in Matlab and the numerical methods used were the same as previously reported in Section 6.3: Numerical Solution.

The diffusion profiles of fragrance raw materials in air were also experimentally evaluated at constant temperature on a diffusion tube designed for the purpose using gas chromatographic techniques for dynamic headspace analysis. Measurements were performed for ethanol (solvent), α-pinene (top note), a binary mixture of them and a quaternary mixture. At the top of the diffusion tube a sweep fan was placed which was operated in some of the experiments to make the concentration null at that point. The modeling of the process was performed with the diffusion models presented above.

6.6. Experimental methodology

6.6.1. Materials

(-)-α-Pinene (CAS # 7785-26-4, >98%, purum) and (±)-Linalool (CAS # 78-70-6, >97%, GC) were obtained from Fluka. Ethanol (Absolute GR for analysis, >99.9%) was supplied by Merck and Tonalide (CAS # 21145-77-7) was purchased from Aroma & Fine Chemicals. All reagents were used as received without further purification. The physicochemical properties of these components are presented in Table 6.14. Molecular diffusivities were calculated from the method of Fuller *et al.* (Fuller*, et al.*, 1966; Poling*, et al.*, 2004) as described in Annex D.

Table 6.14 – Properties of the components obtained from the literature, molecular formula, molecular weight (M.W.), vapor pressure at 296 K (P^{sat}), boiling point (T_b), odor detection threshold (ODT), an olfactory power law exponent (n).

Chemicals	Mol. Form.	M.W. / (g.mol^{-1})	P^{sat} / (Pa)[§]	T_b / (ºC)	ODT / (g.m^{-3})[‡]	$D_{i,air}$ (m^2/h)[¶]
α-pinene (Pin)	$C_{10}H_{16}$	136.2	5.13×10^{2} [#]	155.5	5.44×10^{-4}	2.200×10^{-2}
Linalool	$C_{10}H_{18}O$	154.3	2.21×10^{1} [#]	198.5	1.26×10^{-5}	2.124×10^{-2}
Tonalide	$C_{18}H_{26}O$	258.4	67.0×10^{-6} [*]	356.8	1.82×10^{-5}	1.941×10^{-2}
Ethanol (EtOH)	C_2H_6O	46.0	7.05×10^{3} [#]	78.2	1.21×10^{-1}	4.469×10^{-2}

[§]vapor pressures for pure components were obtained at 296K; [#]From DIPPR 801 Database; [*]From Chemspider Database of Chemical Structures and Property Predictions - Royal Society of Chemistry (Chemspider, 2011); [‡]From van Gemert, L. J., Compilations of odour threshold values in air, water and other media. Oliemans Punter & Partners BV: The Netherlands, 2003; [¶]Estimated by Fuller *et al.* (see Annex D).

6.6.2. Equipments & Methods

A diffusion tube with 2 m long and five sampling ports (SP) positioned at different heights from the gas-liquid interface which is located at the bottom of the tube was designed as presented in Figure 6.32a. The diffusion tube was constructed with a constant nominal pipe size (NPS) of 1 (corresponding to an internal diameter of 2.41 cm from the top to the bottom including the conical section to screw in the glass vessel) and is presented in Figure 6.32 b,c. The tube was made of stainless steel and jacketed in case non-ambient temperature is required. The sampling ports positioned at distances of 0.13, 0.38, 0.63, 1.13 and 1.63 m from the gas-liquid interface, were also made of stainless steel and consisted of perforated pieces for screwing in the tube. These were designed to tighten a PTFE silicone septum that is flanked by two perforated rings of PTFE with a central diameter hole of 2 mm. These rings were used in both sides of the septum in order to increase their contact area and eliminate leaks. In all sampling ports high vacuum grease from Dow Corning was used prior to screwing them, first by hand and then tight ¼ with a wrench. Moreover, during the experiments they were plugged with a rubber cap and covered with tape to further reduce gas leaks. Moreover, at the top of the diffusion tube a sweep fan was placed to make the concentration null at that point.

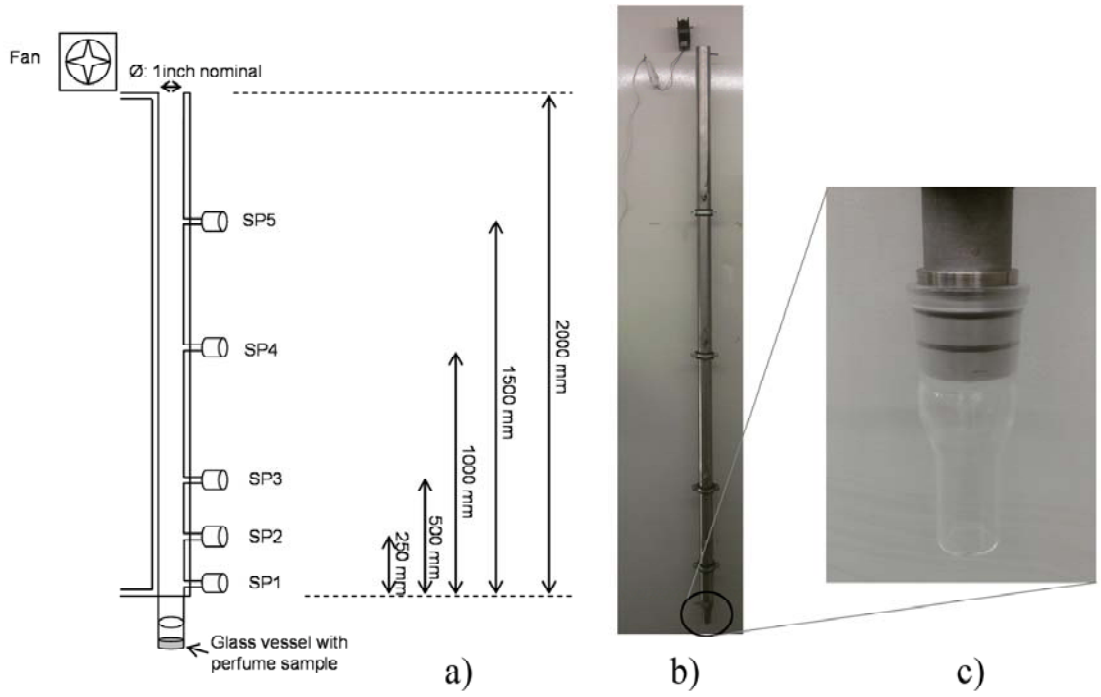


Figure 6.32 - Schematic representation of the projected diffusion tube (a), photograph of the system in the lab (b) and of the glass vessel to place the sample (c).

For the measurement of odor diffusion profiles of raw materials, a volume of 1 mL of the pure component or mixture of fragrance ingredients was pipetted and placed in the glass vessel presented in Figure 6.32c. For the case of mixtures of fragrances, these were prepared gravimetrically using an Adam Equipment balance model AAA250L, with a precision of ±0.2 mg. The liquid mixture was allowed to evaporate and diffuse upwards (1-dimensional diffusion) and headspace samples were being collected over time from the different sampling ports using gas-tight syringes. Samples were injected in a gas chromatograph (GC) with FID detector for quantification. All experiments were run at room temperature (23 ± 1 ºC), controlled through an air-conditioning system. The vapor compositions were determined by headspace gas chromatography (HS-GC) using a Varian CP-3800 (see Chapter 5 – Figure 5.4) equipped with a split/splitless injector and a capillary column Chrompack CP-Wax 52 CB, 50 m length, 0.25 mm i.d., 0.2 μm film thickness. For the case of ethanol and α-pinene the oven temperature was programmed isothermal at 60 ºC for 7 min only, while for mixtures it was then heated up to 100 ºC at a heating rate of 20 ºC/min, held isothermal for 3 min, then heated up to 220 ºC at a heating rate of 20 ºC/min, and finally held isothermal for 5 min. The injector and detector ports were set at 240 and 250 ºC, respectively. Injection volume for the gas phase was 0.1 ml with a split ratio of 1:2. Injection was performed using gas-tight syringes from SGE of 0.1 mL or 1mL. The carrier gas was helium (He N60) with a constant flow rate of 1 ml/min.

Calibration lines were obtained from the headspace composition of pure components. For that, 1 mL of the liquid raw material was placed in a 20 mL cap-sealed vial and allowed to equilibrate for at least 24 hrs at a controlled temperature of 23 ± 1 ºC. Then, 0.5 mL of the gas phase were sampled using a headspace auto sampler HT250D from HTA S.r.L. equipped with a gas-tight syringe from SGE. Several points were obtained for calibration curves and each was analyzed in triplicate until achieving a low standard deviation. In these experiments, the split ratio was changed from 15 to 225 and in some cases the sample volume was reduced to 0.25 mL in order to extend the range of the calibration line. In this way, the mass of each sample at the detector was calculated using equation 6.26 and correlated with the integrated average peak area.

$$m_{\text{det}} = \frac{P^{sat} \cdot V_{inj} \cdot M_{wi}}{R \cdot T \cdot split} \tag{6.26}$$

where m_{det} is the calculated mass at the detector of the GC (g), P^{sat} is the saturation vapor pressure (Pa), V_{inj} is the sample volume injected (mL), M_{wi} is the molecular mass (g/mol), R is the universal gas constant ($Pa \cdot m^3 \cdot mol^{-1} \cdot K^{-1}$), T is the absolute temperature (K) and *split* is the split ratio used in the GC injector. The obtained calibration curves for ethanol and α-pinene are presented in Figure 6.33.

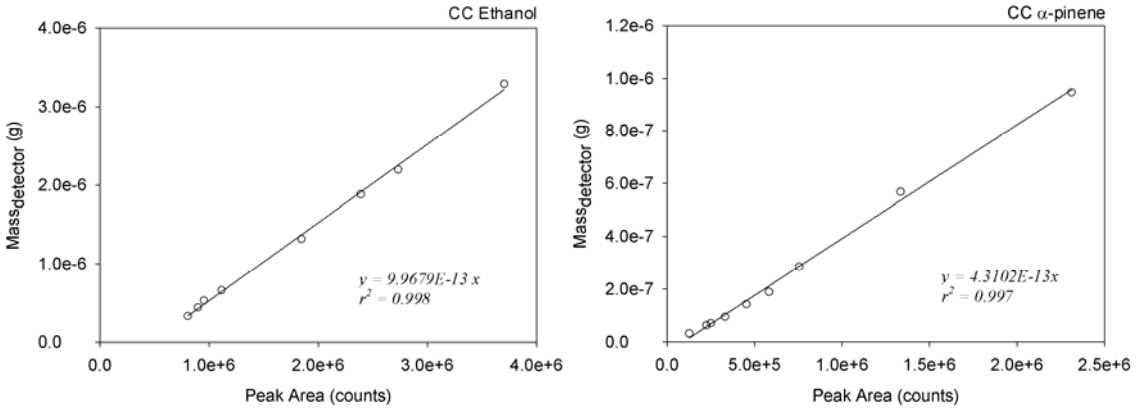


Figure 6.33 - Headspace calibration curves for quantification of chemical compounds by GC analysis.

6.7. Results & Discussion

Diffusion profiles were obtained for ethanol using the conditions described before. The experimental data were compared with those obtained from the model using the steady state condition as defined by equation 6.19. The concentration profiles are presented separately in Figure 6.34 for different sampling ports due to the differences in magnitude of concentrations.

It is to be noted that the model fits well the experimental data for short times (≤ 10 hrs), thus meaning that the diffusion coefficient estimated for ethanol in this study can be acceptable. For that, the diffusion coefficients in air were estimated by the method of Fuller *et al.* (Fuller*, et al.*, 1966) at 296K (23 ºC) and for ethanol it was equal to $D_{ethanol,air}$ = 4.469 x 10^{-2} m^2/h. This value compares favorably with those experimentally measured at 298K from Wilke and Lee (Lee and Wilke, 1954) and Lugg (Lugg, 1968) which were 4.860 x 10^{-2} and 4.252 x 10^{-2} m^2/h, respectively. The correlation of Fuller *et al.* is considered as one of the methods with lower associated errors (Perry, 1997) and the estimated diffusion coefficient is expected to be within an error of 5.4% as reported in the literature (Fuller*, et al.*, 1966; Perry, 1997; Poling*, et al.*, 2004). Moreover, the steady state concentrations were fairly well predicted by the model when compared to

experimental data, although they tend to be slightly over predicted. The concentrations of ethanol determined on the long run (steady state concentrations measured in the different *plateaus* observed in Figure 6.34) can be used to trace the concentration profile of ethanol as a function of the distance from the source of release, as presented in Figure 6.35. Experimental values were measured after more than 30 hrs from the beginning of the run and a comparison with those is also performed using the results predicted from equation 6.19 for steady state and those computed in Matlab. The experimental measurements presented in Figure 6.35, are the result of averaged values from several determinations and so the standard deviation is also presented as error bars.

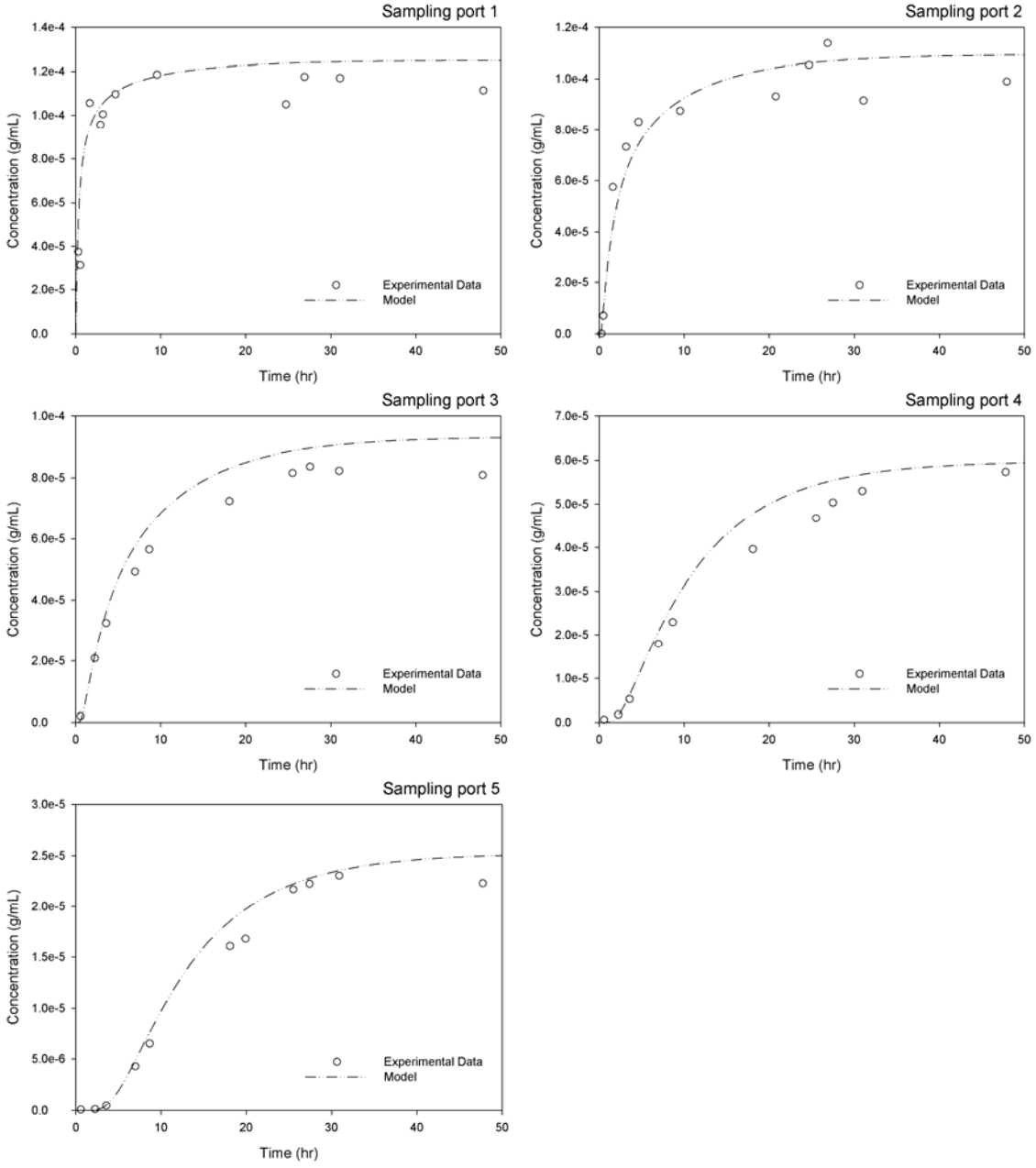


Figure 6.34 – Experimental data (open symbols) for diffusion of ethanol in air measured at different heights from the source (different sampling ports) and modeling using equation 6.19.

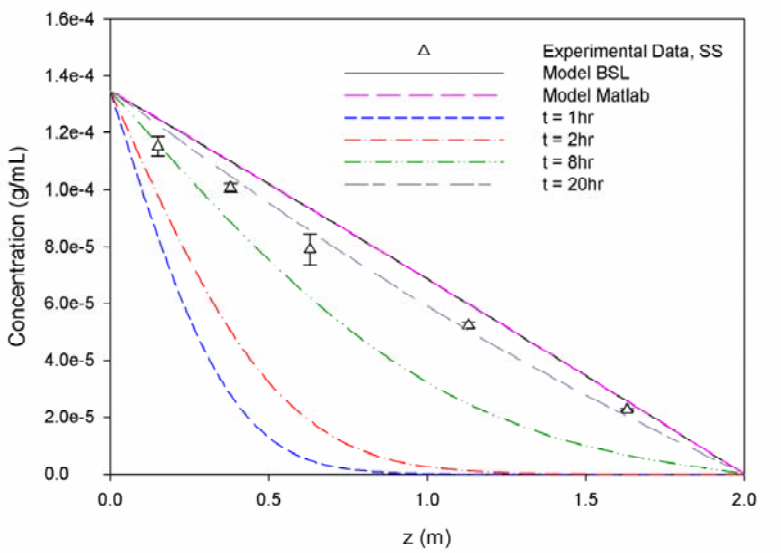


Figure 6.35 – Experimental data for the steady state concentrations measured at different heights for ethanol (open triangles), and simulations using equation 6.19 (BSL) and the coupled equations 6.21 and 6.22 (Matlab).

It is possible to see from Figure 6.35, that the solution obtained from the algebraic equation 6.19 and the coupled equations 6.21 and 6.22 give the same result as the lines are superposed. Moreover, some deviations are observed between the model curves for ethanol concentrations in steady state and the experimental data measured in the diffusion tube. For that experimental errors should be taken into consideration, especially because when measuring extensive properties like the concentration of an odorant in the gas phase, great care should be taken in the sampling procedure. In this way, an imperfect sampling or a slight variation of the collected volume in the gas-tight syringe from the user might lead to differences in the concentration measured by gas chromatography.

Moreover, it is seen that for sampling port 5 the measured vapor concentration is close to that predicted although for the remaining ports these were below the predicted values. However, in relative terms, relative error deviations between the measured and predicted steady state concentrations were of 7.8%, 8.4%, 15.3%, 12.6% and 11.8%, for sampling ports 1, 2, 3, 4, and 5, respectively.

Diffusion experiments were also performed for α-pinene using the same conditions, technique and protocol as for the experiments with ethanol. The experimental data for the diffusion profiles of α-pinene in the diffusion tube are presented in Figure 6.36 for each sampling port together with the predicted model.

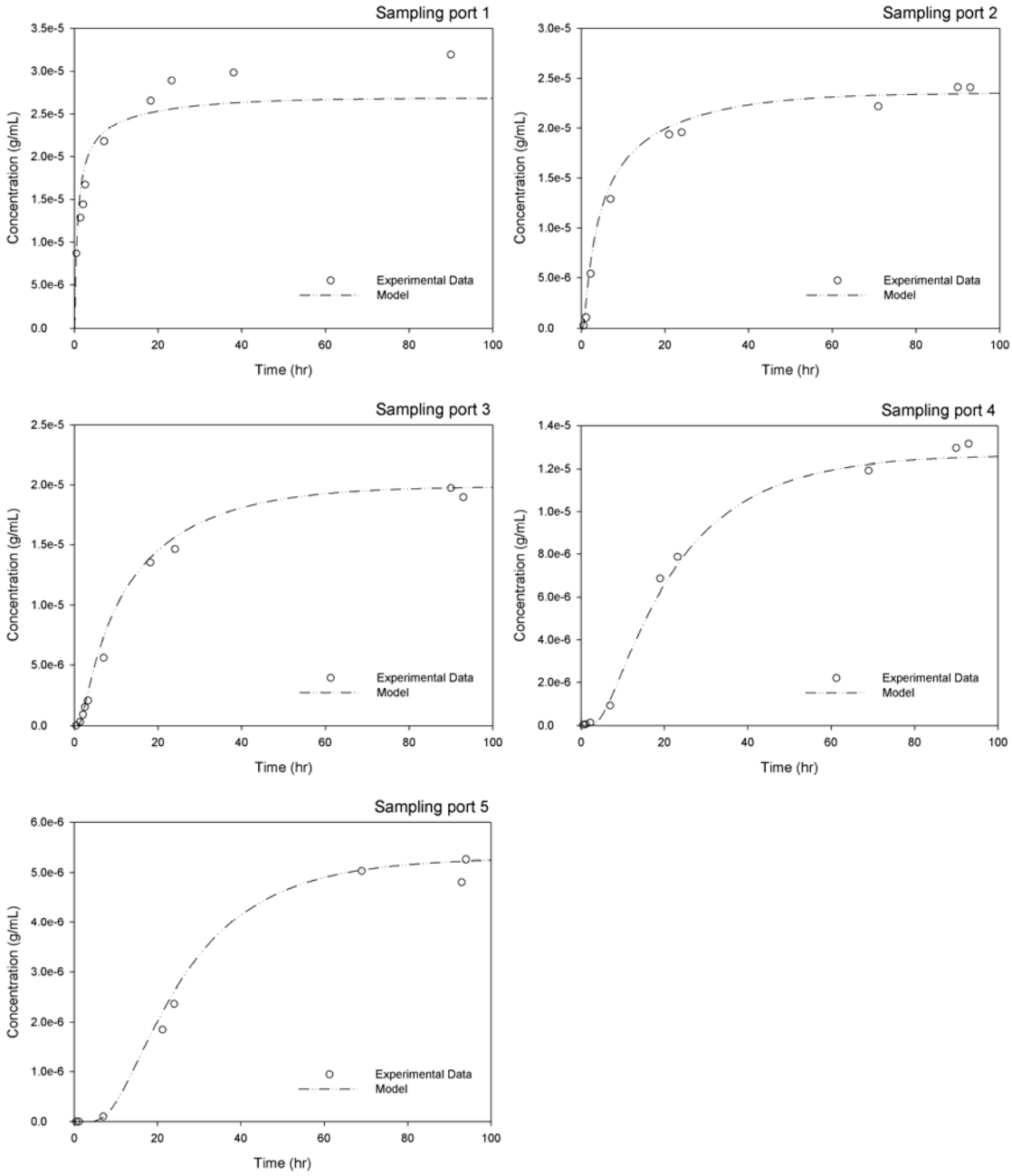


Figure 6.36 – Experimental data (open symbols) for diffusion of α-pinene in air measured at different heights from the source (different sampling ports) and modeling using equation 6.19.

It is observed a good agreement between the measured experimental data and the model for the concentration profiles of α-pinene, except for sampling port 1 where the model under predicts the steady state concentration. These experiments were performed for longer times (~ 100 hrs) than ethanol because α-pinene is also less volatile. It should be said also that after 1 hr and 50 hrs the vaporization rates reached nearly 50% and 99% of that measured at the stationary *plateau*. Moreover, it is seen that the predicted

diffusion profiles on the different sampling ports fit well the experimental data for short times, thus showing that the diffusion coefficient estimated for α-pinene in this study is satisfactory. The concentrations for α-pinene measured on the long run (≥ 90 hrs) and averaged from several measurements can be used to plot its corresponding concentration profile as a function of the distance from the source of release, as shown in Figure 6.37.

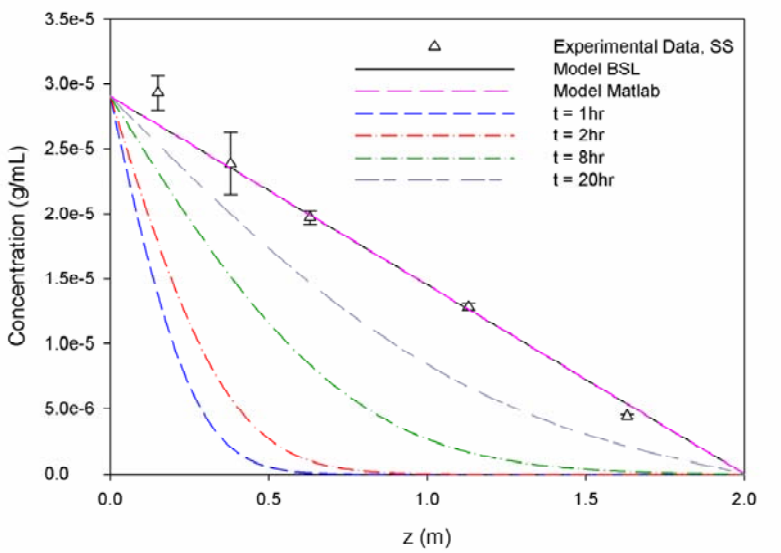


Figure 6.37 - Experimental data for the steady state concentrations measured at different heights for α-pinene (open triangles), and simulations using equation 6.19 (BSL) and the coupled equations 6.21 and 6.22 (Matlab).

It is possible to see from Figure 6.37 that with the exception of sampling port 1, there is a very good agreement between the experimental steady state concentrations and those predicted by the model. In this case, relative deviations for the different sampling ports 1, 2, 3, 4, and 5 were found to be of 9.1%, 1.4%, 1.0%, 1.7%, and 13.3%, respectively.

On the other hand, diffusion of the binary system of ethanol and α-pinene was also studied using a mixture with a molar composition of $x_{Ethanol} = 0.891$ and $x_{\alpha\text{-}pinene} = 0.109$. The experimental data together with the modelling for the concentration profiles of both components using equations 6.21 and 6.22 for the transient diffusion is presented in Figure 6.38. Firstly, it can be observed from Figure 6.38, that ethanol presents significantly higher concentrations in air than α-pinene at both time and distance to the source. This behavior was expected due to its higher concentration in the mixture but also a much higher vapor pressure and diffusivity than α-pinene (see Table 6.14). Moreover, it can be said that this experimental methodology allows the measurement of

the concentration profiles over time and distance with fair accuracy, although deviations may be found for some experimental points.

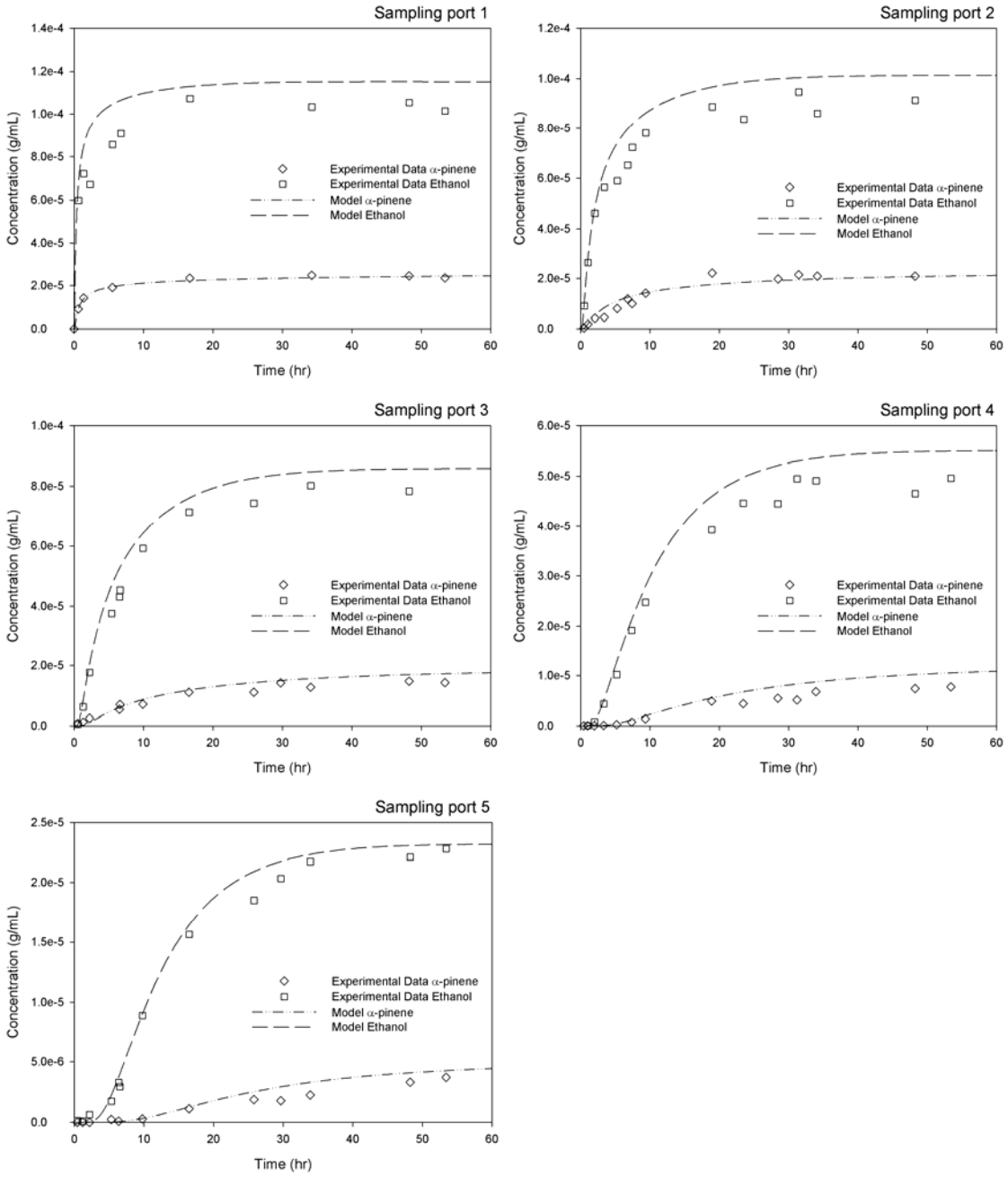


Figure 6.38 – Experimental data (open symbols) for diffusion of ethanol in air measured at different heights from the source (different sampling ports) and modeling using equations 6.21 and 6.22.

Additionally, performing a similar analysis as before for the pure components, it is possible to represent the concentrations of each species at the steady state as a function of the distance from the source. This experimental data along with the predicted curves are shown in Figure 6.39.

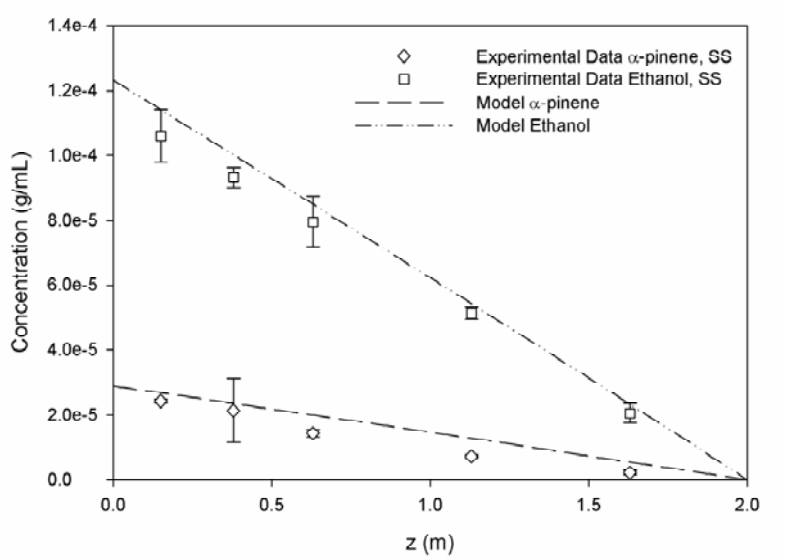


Figure 6.39 - Experimental data for the steady state concentrations measured at different heights for ethanol (open squares) and α-pinene (open diamonds) with simulations using coupled equations 6.21 and 6.22 (Matlab).

Finally, the diffusion of a quaternary fragrance system composed by α-pinene (top note), linalool (middle note), tonalide (base note) and ethanol was studied. For that, it was intended to evaluate the effect of the base note (which in this case is a fixative) on the release of the most volatile components. Tonalide was chosen as the base note for this system due to its fixative effect (as aforementioned in section 6.4.1.2: System 2), easiness in experimental handling and also for the availability of parameters for prediction of the vapor-liquid equilibrium. In this way, the diffusion of two quaternary mixtures (Q1 and Q2) with a similar composition except for tonalide was evaluated. These mixtures present an analogous composition in a tonalide free-basis as presented in Table 6.15. The diffusion profiles for these quaternary systems are shown in Figure 6.40 for ethanol and α-pinene only because the concentrations of linalool and tonalide in the gas phase were very low and difficult to measure for the concentrations used.

Table 6.15 – Mass, molar and mole fraction composition of the Q1 and Q2 quaternary fragrance mixtures.

	Q1			Q2		
Component	mass (g)	mol	x_i	mass (g)	mol	x_i
α-pinene	1.04280	7.668E-03	0.37	0.91317	6.714E-03	0.32
Linalool	1.48824	9.664E-03	0.46	1.42235	9.236E-03	0.44
Tonalide	0.11263	4.434E-04	0.02	1.48217	5.835E-03	0.28
Ethanol	0.14634	3.181E-03	0.15	0.12369	2.689E-03	0.13

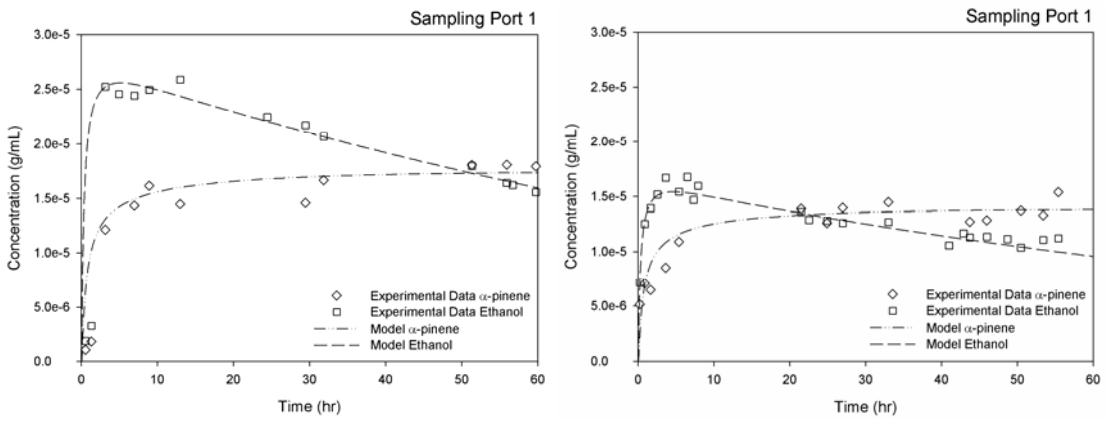


Figure 6.40 - Diffusion profiles for ethanol and α-pinene in the quaternary mixtures Q1 (left) and Q2 (right) for sampling port 1 over time.

The predicted diffusion profiles for the most volatile components in both quaternary mixtures fit well the experimental data. It is observed an initial increase and dominance in the concentration of ethanol but as it vanishes in the liquid, its concentration in the gas phase decreases with time. Nevertheless, it is important to highlight here the verification of the fixative effect of tonalide on the most volatile species. It is seen that for mixture Q2 (reach in tonalide) the maximum measured concentrations for ethanol and α-pinene are lower than for mixture Q1. Moreover, the concentration of α-pinene exceeds that of ethanol in a shorter period of time than for Q1, showing that tonalide has a higher retention effect on ethanol.

6.8. Conclusions

The odor profile of a multi-component mixture of fragrances is the odor fingerprint of a fragrance solution. In the first part of this Chapter, these predicted profiles in terms of the OV showed that at $z = 0\ m$ (liquid-gas interface), the tonality and odor intensity change with time, depending whether fixatives or solvents are used or not. Increasing the ethanol mole fraction in the perfume composition will tend to "push out" of the solution the non-polar notes (limonene). In fact the F&F industry usually considers the incorporation of a solvent matrix in a well bodied perfume, which in this case leads to a faster release into the headspace of a fresh-citrus scent of limonene. Nevertheless, the odor intensity of ethanol in the perfume mixtures simulated here is often lower than that of the remaining odorants. Thus it is not perceived by the human nose which is a rule widely used in perfumery.

A comparison between different base notes studied in this Chapter, allows to conclude that the evaporation rate of each fragrance is a function of the initial composition (x_i) and the molecular interactions (activity coefficient, γ_i) but is especially dependent on the physicochemical and psychological properties (diffusivity, saturated vapor pressure, molecular weight, threshold concentration). In this way, it was seen that the tonality or dominant smell in the headspace follows fairly well the ratio of physical properties - the constant $K_{odor} = (P_i^{sat} \cdot M_{wi})/(ODT_i \cdot R \cdot T)$ - presented in Table 6.1: $K_{odor}^{Tonalide} < K_{odor}^{Vanillin} < K_{odor}^{Galaxolide} < K_{odor}^{Ambrox}$. In fact, tonalide is hardly smelled while vanillin dominates sometimes depending on the initial composition. Galaxolide is quite similar to ambrox, though this last base note provides quantitative higher odor values.

The relationship between the composition in the liquid and gas phases is difficult to predict at first sight, since the system of equations solved numerically is highly non-linear. However, it is possible to say that limonene and ethanol were the components that evaporated faster, showing a significant decrease during the first hour after application of the perfume.

The evaporation lines strongly depend on the initial mixture composition, thus influencing not only its initial tonality (dominant note) but also the evolution scents that will be smelled as the evaporation and diffusion processes take place. The combination of the PTDs with the evaporation lines allows seeing whether the predicted odor will cross or not different odor zones, thus changing its odor character through time.

In this way, the performance of a perfume mixture is a function of different properties like the initial mixture composition or the palette of odorants chosen (molecular interactions, chemical structure, molecular weight, vapor pressure, diffusion coefficients, etc). For composition mixtures with $x_S = 0.7$ (mixtures P6) it was shown using performance plots where the OV_{max} is represented over time and distance, that limonene has higher impact for perfume systems 1 and 2 while for systems 3 and 4 the base notes ambrox and galaxolide, respectively, were dominant from the start of the evaporation process. The only base note to have a higher diffusion parameter than the remaining odorants was vanillin (system 1), since it has the smallest molecular weight among the base notes and has the highest diffusion coefficient $(D_{i,air})$ of all the fragrances.

On the Part II of this Chapter, experimental data for fragrance profiles over time and distance were measured. These results compared favorably with the modeling based on Fick's equation for diffusion when applied to ethanol, α-pinene and a binary mixture of them. For that it is important two highlight two points: *i)* the steady state concentrations

were well predicted from the model, although the experimental error should not be forgotten; *ii)* the predicted concentration profiles fitted well the experimental data for initial times, showing that the diffusion coefficient used in this study was adequate. Finally, the diffusion of typical quaternary fragrance mixtures comprising three different notes and a solvent was evaluated. For that, the effect of the base note (fixative) previously highlighted in Part I of this Chapter was evaluated. It was observed a good fitting of the model with the experimental data and that tonalide had a retention effect on the most volatile components.

6.9. References

Balk, F., Ford, R. A. (1999). Environmental risk assessment for the polycyclic musks AHTN and HHCB in the EU - I. Fate and exposure assessment, Toxicology Letters, 111, 57-79.

Balk, F., Ford, R., Environmental risk assessment for the polycyclic musks AHTN and HHCB in the EU - I. Fate and exposure assessment, *Toxicology Letters*, 111, 57–79, 1999

Baydar, A., Charles, A., Decazes, J. M., McGee, T., Purzycki, K., Behavior of Fragrances on Skin, *Cosmetics and Toiletries magazine*, 111, 49-57, 1996

Baydar, A., McGee, T., Purzycki, K., Skin Odor Value Technology for Fragrance Performance Optimization, *Perfumer & Flavourist*, 20, 45-53, 1995

Bird, R., Stewart, W., Lightfoot, E., Transport Phenomena, Singapore, John Wiley & Sons, 1960

Bird, R., Stewart, W., Lightfoot, E., Transport Phenomena, New York, John Wiley & Sons, 2002

Boatright, W. L., Lei, Q., Headspace Evaluation of Methanethiol and Dimethyl Trisulfide in Aqueous Solutions of Soy-protein Isolates, *Journal of Food Science*, 65, (5): 2000

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Carles, J., A method of creation in perfumery, *Soap Perfumery Cosmet.*, 35, 328-335, 1962

Chapman, J., MATLAB programming for engineers, California, Brooks Cole Publishing Company, 2000

Chapra, S., Canale, R., Numerical methods for engineers: with software and programming applications, Boston, McGraw Hill, 2002

Chemspider, Database of Chemical Structures and Property Predictions - Royal Society of Chemistry, from http://www.chemspider.com/Default.aspx, Last Accessed on February, 2011

Crank, J., The Mathematics of Diffusion, Oxford, Oxford Science Publications, 1975

Cussler, E. L., Diffusion: Mass Transfer in Fluids, Cambridge, UK, Cambridge University Press, 2007

Fráter, G., Müller, U., Kraft, P., Preparation and Olfactory Characterization of the Enantiomerically Pure Isomers of the Perfumery Synthetic Galaxolide, *Helvetica Chimica Acta*, 82, 1656-1665, 1999

Fuller, E. N., Schettler, P. D., Giddings, J. C., A new method for prediction of binary gas-phase diffusion coefficients, *Industrial and Engineering Chemistry*, 58, (5): 19-27, 1966

Gmehling, J., Potential of group contribution methods for the prediction of phase equilibria and excess properties of complex mixtures, *Pure Appl. Chem.*, 75, (7): 875–888, 2003

Grosch, W., Evaluation of the key odorants of foods by dilution experiments, aroma models and omission, *Chemical Senses Review*, 26, 533-545, 2001

Heinzelmann, F. J., Wasan, D. T., Wilke, C. R., Concentration profiles in a Stefan diffusion tube, *Industrial & Engineering Chemistry Fundamentals*, 4, (1): 55-61, 1965

Lee, C. Y., Wilke, C. R., Measurements of vapor diffusion coefficient, *Industrial and Engineering Chemistry*, 46, (11): 2381-2387, 1954

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Lugg, G. A., Diffusion Coefficients of Some Organic and Other Vapors in Air, *Analytical Chemistry*, 40, (7): 1072-1077, 1968

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005

MathWorks, Partial Differential Equation Toolbox - ComsoLab MATLAB's Users Guide, 2002

Nocedal, J., Wright, S., Numerical Optimization, New York, Springer, 1999

Perry, R. H., Perry's chemical engineers' handbook, United States of America, McGraw-Hill, 1997

Philibert, J., One and a Half Century of Diffusion: Fick, Einstein, Before and Beyond, *Journal for the Basic Principles of Diffusion Theory, Experiment and Application*, (Diffusion Fundamentals), 4, (6.1 - 6.19): 2006

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Poling, B., Prausnitz, J., O'Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Rappert, S., Müller, R., Odor compounds in waste gas emissions from agricultural operations and food industries, *Waste Management*, 25, 887–907, 2005

Shampine, L. F., Reichelt, M. W., The MATLAB ODE suite, The MathWorks, Inc.1996

Shigemoto, K., Weber-Fechner's Law and Demand Function, *Tezukayama Academic Review*, 9, (41-46): 2002

Smith, J. M., Van Ness, H.C., Abbot, M.M., Introduction to chemical engineering thermodynamics, New York, McGraw Hill, 1996

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Stora, T., Eschera, S., Morris, A., The Physicochemical Basis of Perfume Performance in Consumer Products, *Chimia*, 55, 406-412, 2001

Taylor, R., Krishna, R., Multicomponent Mass Transfer, Ney York, John Wiley & Sons, 1993

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009a

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009b

Ursell, T. S., The Diffusion Equation A Multi-dimensional Tutorial, Pasadena, California USA, Department of Applied Physics, California Institute of Technology, 2007

van Gemert, L. J., Compilation of Odor Threshold Values in Air and Water, The Netherlands, TNO Nutrition and Food Research Institute (BACIS), 1999

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

Vuilleumier, C., Flament, I., Sauvegrain, P., Headspace analysis study of evaporation rate of perfume ingredients applied onto skin, *International Journal of Cosmetic Science*, 17, 61-76, 1995

Wesselingh, J. A., Krishna, R., Mass transfer in multicomponent mixtures, Delft, Netherland, Delft University Press, 2000

Chapter 7

The Perception of Fragrance Mixtures: comparison of odor intensity models*

"If you are ambitious to find a new science, measure a smell."

(Alexander Graham Bell, 1914)

So far we have seen how to evaluate the evaporation and diffusion of fragrances in the air, as well as how to calculate thresholds for odor detection which are important parameters for quantifying odors. Throughout this Chapter 7, we will evaluate a variable that is quite difficult to measure quantitatively: odor intensity. A comparison of psychophysical odor intensity models and their effect on the prediction of the odor character of perfume mixtures will be shown. The Odor Value (OV) and Power Law models have been applied (together with the previously developed Perfumery Ternary Diagram - PTD® - and Perfumery Quaternary-Quinary Diagram - PQ2D® - methodologies) to map the perceived smell of quaternary and quinary fragrance mixtures. A simple diffusion model, previously reported in Chapter 6, was used to simulate the evolution of the concentrations in the liquid and gas phases. The composition paths were predicted through evaporation lines plotted in the PQ2D®. The two odor intensity models present some differences in the initial perfume impact, but after some time tend to similar profiles. It was also seen that the Power Law predicted

* This Chapter is partly based on the paper from Teixeira, MA, Rodríguez, O, Rodrigues, AE, The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE J.*, 56(4), 1090-1106, 2010.

higher ethanol intensities than the OV model, due to the parameter *n* that corresponds to its exponent in the model. Moreover, the effect of water in the formulation was evaluated, showing that it fixes the ethanol in the solution, thus reducing the initial alcohol perception. Finally, some of the fragrance mixtures presented in Chapter 5 for evaluations of the vapor-liquid equilibria (VLE) are presented here, and the experimental results are compared to those predicted with the OV, the Power Law and the Weber-Fechner Law.

7.1. Introduction

The formulation of perfumes involves the combination of a wide variety of fragrances (from natural, natural-identical and synthetic origin) in the order of thousands. It is the role of the perfumer, to combine different fragrant notes in a trial and error procedure, until the desired scent or odor character is found. The perfumer has to smooth the odor profile of a formulation so that there will be no discontinuities in the perceived odor as the different fragrant notes evaporate. The amount of concentrated fragrances (or essential oils) in a perfume formulation can vary from trace levels (ppm) for some compounds up to 10–20% for others. In the formulation process, the concentrate is usually incorporated within solvents (*e.g.* ethanol). Additionally, water is also used in higher quantities for the more diluted formulations (Schreiber, 2005). The classification of perfumes can be done with respect to the concentration of the perfume concentrate (Pybus and Sell, 1999) or its olfactory family (Teixeira*, et al.*, 2010). In what concerns here, the first is highlighted for the purpose of the study of the odor intensity as described in Table 7.1. According to its composition a perfume may be classified into different types, as defined by the ratio of concentrate and solvent (ethanol/water).

Table 7.1 – Perfume classification in terms of the composition of perfume concentrate, ethanol and water (in volume) (Poucher, 1955).

Type	Concentrate (% v/v)	Ethanol (% v/v)	Water (% v/v)
Extrait or Parfum	15-30	74-77	1-3
Eau de parfum	8-15	75-80	9-13
Eau de toilette	4-15	72-81	10-18
Eau de cologne	3-5	58-77	20-40
After shave	2-8	47-67	30-50
Splash cologne	2-3	49-68	30-50

The amount of water that is introduced into the perfume mixture depends on the nature of the perfume composition and the percentage of oil. Water is desirable because it reduces the sharp odor of alcohol and the price of the final product (Rowe, 2005). The selection of the fragrances and their exact combination to design a perfumed product relies on a variety of parameters like: odor contribution to the overall scent, product stability, the performance of the product to be perfumed (impact, tenacity, diffusion and volume) (Calkin and Jellinek, 1994; Mata*, et al.*, 2005b; Teixeira*, et al.*, 2009a), product safety/toxicity or product's final cost. During the development of a fragrance, perfumers experimentally evaluate the odor character as it evaporates off a paper blotter and diffuses in the air above it. While both processes occur, the character or tonality of the perceived odor (the dominant smell) necessarily changes, once fragrant species do not evaporate at the same rate, although it is desirable that the perfume fingerprint does not change much (Herman, 2002; Ternat*, et al.*, 2008).

We know that perfume mixtures are complex systems due to the multiplicity of interactions and the number of components present in solution which renders it difficult to predict *a priori* the perceived odor (Perring, 2006). Additionally, fragrant molecules have to be captioned by the human olfactory receptor cells and its interpretation in the brain has to be considered. Here, two aspects are relevant: on one hand, the quantification of the odor intensity of a fragrance; and on the other hand, the discrimination and identification of the overall odor character and the fragrance ingredients present in a multi-component mixture. For its part, the odor intensity will be discussed in this Chapter along with the prediction of the odor character in the surrounding air.

The scientific study of the phenomena of perception has inspired perfumers and psychophysicists for long time with several questions still remaining unanswered: How do we perceive and interpret a stimulus coming from the outside world? What stimuli are we capable of process? Which is the relationship between a stimulus magnitude and the sensation perceived?

Nowadays, the search for these answers within the perception of odors is mainly performed at the molecular level: the olfactory system is remarkably capable of detecting and identifying thousands of odorants through olfactory receptor (OR) cells (Buck and Axel, 1991), followed by complex brain integration patterns as highlighted in Chapter 4. However, this scientific pathway is still far from being completely understood and thus reaching its end.

In this way, as reviewed in Chapter 2 – 2.5.2: Models for odor intensity of single odorants, the answer for some of the aforementioned questions may come from Psychophysics, a science that deals with human perception. For that purpose, perception can be defined as the means by which we receive, collect and interpret information from the outside world. It is the sensory experience by which we gain information about the properties of the environment around us, allowing us to act within it.

7.2. Odor intensity models and methodology

The search for the measurement of odors has been done for long, following the words of Galileo (1564-1642) *"Count what is countable, measure what is measurable. What is not measurable, make measurable"*. The applications of Psychophysics cover different perceptual continua (including the five senses we have), attempting to establish relationships between physical stimuli and its psychological interpretation using some mathematical relationships for that. There are different models within this area which are based on experimental studies to establish these relationships. A brief description of the most significant models with application on olfaction is given ahead (further details can be seen in Chapter 2 and Annex A).

In this way, the Odor Value (OV) model (Appell, 1969; Calkin and Jellinek, 1994; Baydar*, et al.*, 1995; Teixeira*, et al.*, 2009b) and the Stevens' Power Law (Stevens, 1957, 1958, 1964) will be compared throughout this study using some Chemical Engineering methodologies, like the PTD® and the PQ2D® for the representation of the odor intensity and character (see Chapter 3). Briefly, the OV is calculated as the headspace concentration of an odorant species *i*, C_i^g, divided by its corresponding odor detection threshold in air, ODT_i (both in g/m^3):

$$OV_i = \frac{C_i^g}{ODT_i} \tag{7.1}$$

On the other hand, the Stevens' Power Law considers that the perceived sensation magnitude, ψ, is given by the ratio between the headspace concentration and the odor detection threshold, raised to an exponent *n*, so that:

$$\psi = \left(\frac{C^g}{ODT} \right)^n \tag{7.2}$$

Finally, the Weber-Fechner Law (Shigemoto, 2002; Zwislocki, 2009; Teixeira, *et al.*, 2011) which was in fact the first to be postulated, will be compared with the Stevens' Power Law and the OV model for a series of fragrance mixtures which were also tested with an olfactory evaluation from panelists. The Weber-Fechner considered that the perceived sensation magnitude, ψ, was given by:

$$\psi = k_w \cdot log\left(\frac{S}{S_0} \right) \tag{7.3}$$

where ψ is the sensation magnitude, k_w is the Weber-Fechner constant (often a positive factor), S is the stimulus magnitude and S_0 is the threshold of the magnitude of the physical stimulus (Zwislocki, 2009).

It is known that these Psychophysical models are generally based on human experiments (using direct or indirect methods) and as a result are vulnerable to interpersonal variability among other variables previously reviewed (see Annex A) (Green, 1974; Graedel, 1984; Luce, 1990, 2002).

As previously reported the effect of water on perfume formulation will be addressed, once it is a component widely used in perfumery, and playing an important role in the release of the fragrances and the odor character. A simple diffusion model previously developed will be applied to the release and diffusion of fragrance mixtures.

The studied odorant components and their physical and sensorial properties are presented in Table 7.2.

Table 7.2 - Properties for the odorant components considered in this study.

	Name	Molecular Formula	M_i (g/mol)	P_i^{sat} (Pa)	ODT_i (g/m^3)	$\frac{P_i^{sat} \cdot M_{wi}}{ODT_i \cdot R \cdot T}$	$D_{i,air}$ (m^2/h)	n^d
A	Limonene[a]	$C_{10}H_{16}$	136.2	20.5×10^{1}	2.45×10^{-3}	4.60×10^{3}	2.214×10^{-2}	0.37
B	Geraniol[a]	$C_{10}H_{18}O$	154.3	26.7×10^{-1}	2.48×10^{-5}	6.70×10^{3}	2.138×10^{-2}	0.36
C	Vanillin[a]	$C_8H_8O_3$	152.2	16.0×10^{-3}	1.87×10^{-7}	5.25×10^{3}	4.111×10^{-2}	0.31
	Galaxolide	$C_{18}H_{26}O$	258.4	72.7×10^{-3} [b]	6.30×10^{-7} [c]	1.20×10^{4}	1.924×10^{-2}	0.36
S	Ethanol[a]	C_2H_6O	46.0	72.7×10^{2}	5.53×10^{-2}	2.44×10^{3}	4.469×10^{-2}	0.58
	Water	H_2O	18.01	3.17×10^{3}	-	-	9.132×10^{-2}	-

[a]From (Calkin and Jellinek, 1994); [b](Balk and Ford, 1999); [c](Fráter, 1999); [d](Devos, *et al.*, 2002).

The simulations for the Perfumery Ternary Diagram (PTD®) and the Perfumery Quaternary-Quinary Diagram (PQ2D®) methodologies were run using the MATLAB software. Routines and functions were developed in MATLAB as well as the prediction of the activity coefficients (γ_i) using the UNIFAC method. The calculations over the space variable were set to second order approximations to the solution on the specified mesh values. The computation of the non-linear systems of equations were solved numerically using the optimization toolbox from MATLAB, adapted to the nature of the problem studied (Nocedal and Wright, 1999; Chapman, 2000; MathWorks, 2002). The *fsolve* routine was used to compute the perfumery binary and ternary lines, perfumery ternary points and perfumery binary surfaces. The numerical method of Levenberg-Marquardt (LM) with line search was used to solve the nonlinear system of algebraic equations. The tolerance was set equal to 10^{-6} for both the dependent variable and the function value calculation and a maximum of 300 function evaluations was defined. The diffusion equations were solved using the *pdepe* routine which is designed to solve initial-boundary value problems for parabolic-elliptic PDEs in 1-D. The ordinary differential equations (ODEs) resulting from discretization in space were integrated to obtain approximate solutions at specified times with the *ODE 15s* using relative and absolute tolerances of 10^{-8}. This solver is based on the numerical differentiation formulae (NDFs) and uses the method of finite differences for the discretization of the space variable (Nocedal, 1999; Chapman, 2000; Chapra, 2002). Further details on these methods were previously explained in Chapter 6.

7.3. Results & Discussion

The two odor intensity models considered in the first part of this study (Power Law and OV) were applied for the simulation of different quaternary and quinary fragrance systems. The top note (A – Limonene) and the middle note (B – Geraniol) were the same for all systems, while the selected base notes (C) were vanillin and galaxolide for system 1 and 2, respectively. Moreover, the selected solvent (S) was ethanol for the quaternary systems, while a mixture of ethanol/water was used for quinary systems as presented in Table 7.3.

Table 7.3 – Fragrance systems used for the comparison of odor intensity models.

Fragrance system	Top note	Middle note	Base note	Solvents	
1	limonene	geraniol	vanillin	Ethanol	-
2	limonene	geraniol	galaxolide	Ethanol	-
3	limonene	geraniol	vanillin	Ethanol	Water
4	limonene	geraniol	galaxolide	Ethanol	Water

The effect of the selected odor perception model is first analyzed using the PTD® methodology as presented in Figure 7.1 instead of the PQ2D®, since it is easier to get a better perception of the variations in the odor zones by plotting the ternary subsystems that constitute the quaternary system. These ternary subsystems represent the faces of the PQ2D® tetrahedric diagram, where there are $n-1$ components present in the mixture. Figure 7.1 shows the corresponding four ternary subsystems (A+B+C), (A+B+S), (A+C+S) and (B+C+S) for the quaternary perfume systems studied in this work, considering both the OV (top) and the Power Law (bottom) models.

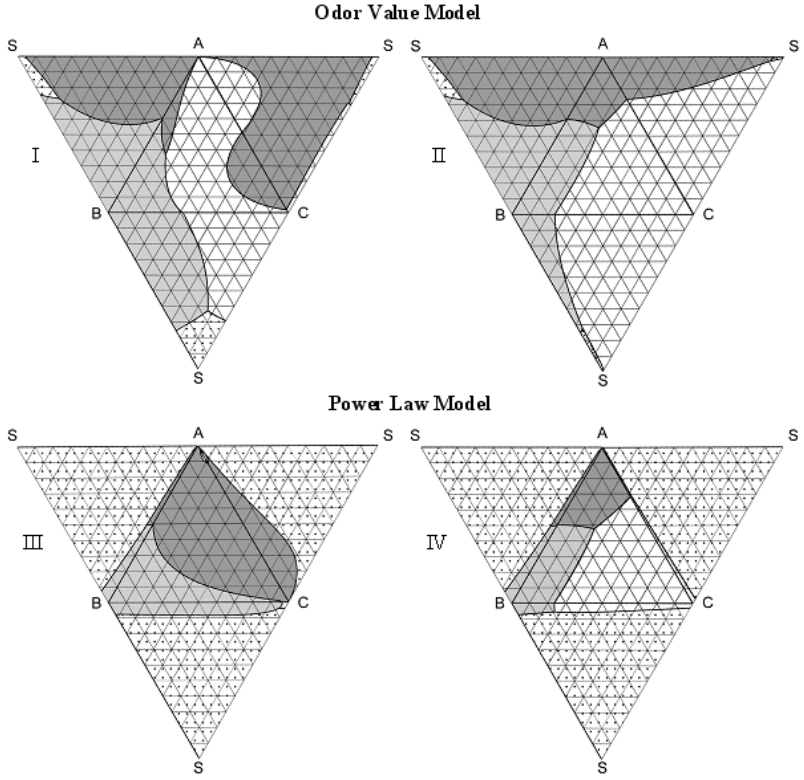


Figure 7.1 – PTD® of the different ternary subsystems of the two quaternary mixtures. A: Top Note (Dark grey, Limonene), B: Middle note (Light grey, Geraniol), C: Base note (White, I-III: Vanillin, II-IV: Galaxolide), S: Solvent (Dotted, Ethanol). Top diagrams simulated using the OV model (I-II), bottom diagrams with Power Law model (III-IV).

Through Figure 7.1 it can be easily seen that there are significant differences in the shapes of the odor zones and in the distribution of the odor character when the two odor intensity models are applied. Comparing the top diagrams (OV model) with the bottom ones (Power Law model) the predominance of the odor of the solvent increases significantly. This is due to the fact that ethanol has an exponent for the power law much higher than all other components, resulting in higher initial odor intensities (see Table 7.2). It is seen that for the ternary mixture of Limonene + Geraniol + Vanillin of perfume system 1, the application of the Power Law changes significantly the odor character, since vanillin is only perceived near the corner C. On the other hand, for system 2, the simulation with the Power Law does not change much the inner PTD.

However, viewing these ternary subsystems does not give us any specific insight into the quaternary perfume mixture, that is, the composition points located inside the tetrahedron. In order to see the whole behavior of the quaternary perfume system, it is presented in Figure 7.2 to Figure 7.5 the PQ2Ds, for the two fragrance systems using both odor intensity models, with the different fragrance volumes highlighted for each component.

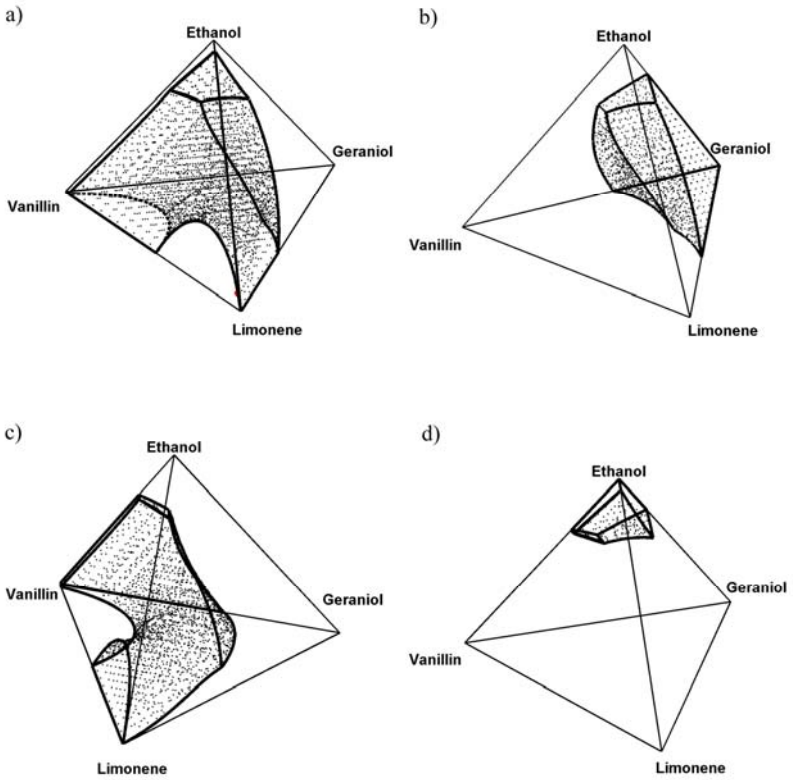


Figure 7.2 – Perfumery fragrance volumes considering the OV model for the odor perception in system 1: a) Limonene, b) Geraniol, c) Vanillin, and d) Ethanol.

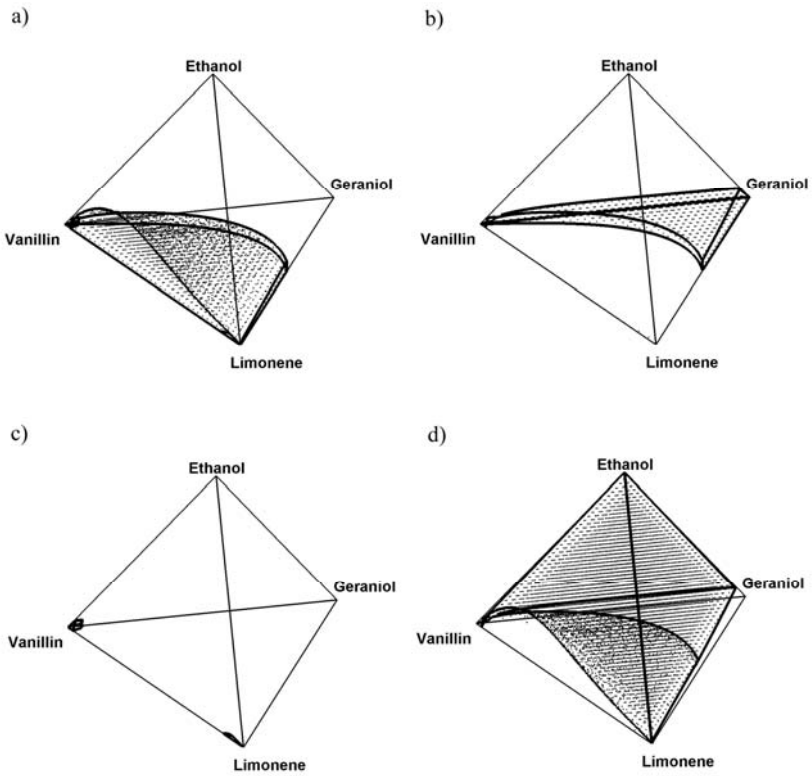


Figure 7.3 – Perfumery fragrance volumes considering the Power Law model for the odor perception in system 1: a) Limonene, b) Geraniol, c) Vanillin, and d) Ethanol.

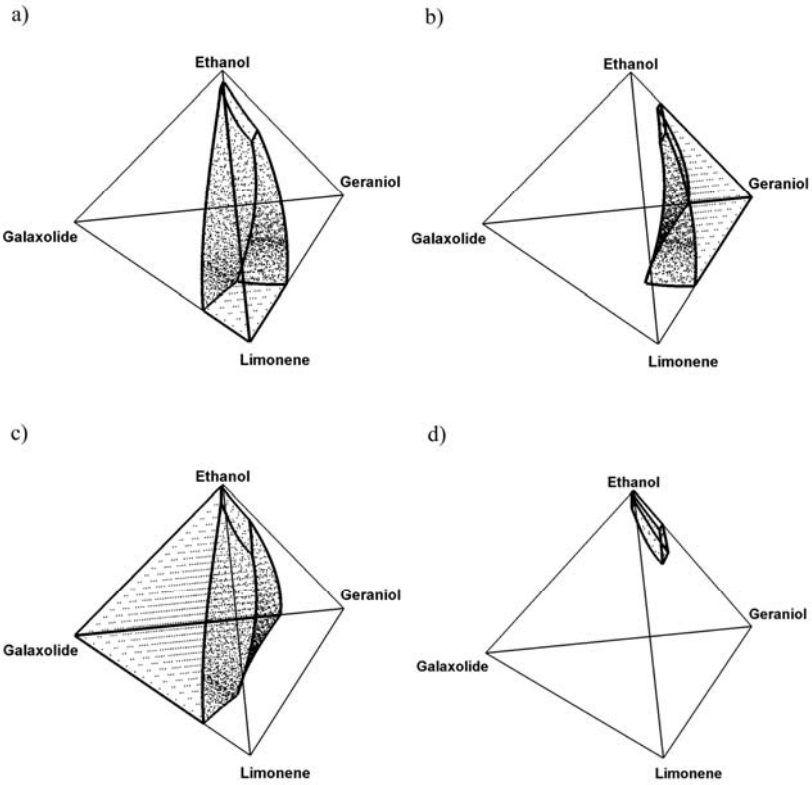


Figure 7.4 – Perfumery fragrance volumes considering the OV model for the odor perception in system 2: a) Limonene, b) Geraniol, c) Galaxolide, and d) Ethanol.

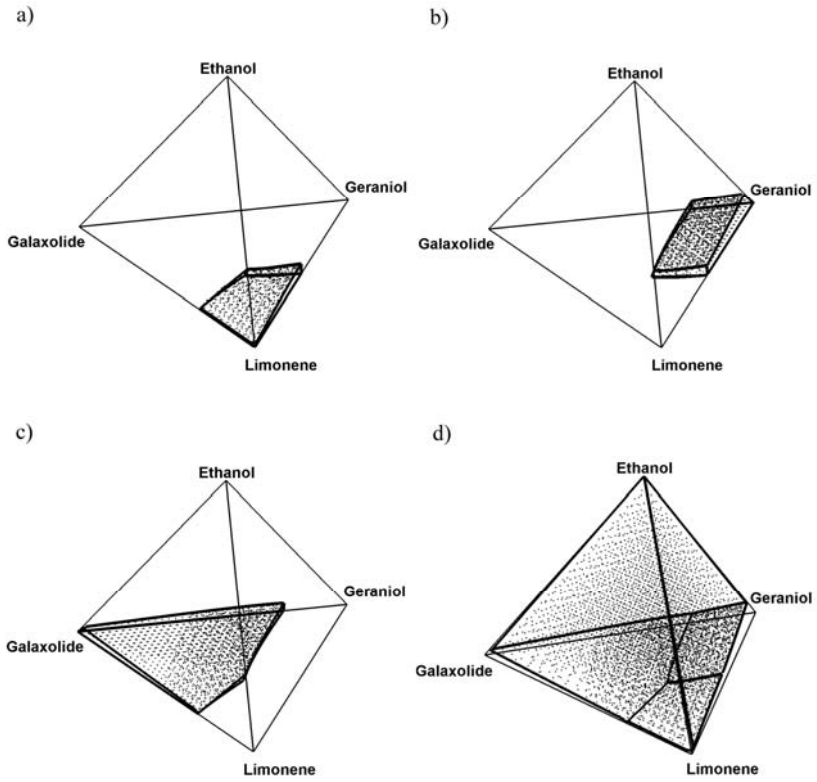


Figure 7.5 – Perfumery fragrance volumes considering the Power Law model for the odor perception in system 2: a) Limonene, b) Geraniol, c) Galaxolide, and d) Ethanol.

The PQ2Ds for both perfume systems studied here show that when the Power Law model is applied to account for the odor intensity, the fragrance volumes of the odorant compounds are significantly reduced while the fragrance volume of ethanol increases. It is observed when comparing Figure 7.2 and Figure 7.3 that the odor volume for vanillin is significantly smaller when the Power Law model is considered, being reduced to two small volumes near the corners of Limonene and Vanillin. This means that when considering a non-linear odor intensity model, the Stevens' Law as opposed to the linear OV model, the result is that the range of simulated compositions where ethanol has higher intensity is greater. It is important to highlight that the PQ2D methodology maps the odor character near the source of the perfume mixture (at the gas-liquid interface). This effect in the prediction of the odor intensity near the source is mainly dependent on the exponent *(n)* for the single fragrances. A comparison between the two different odor intensity models can be seen in Figure 7.6, where the Power Law model is plotted against the linear OV concept, considering the exponents *(n)* in Table 7.2 for each fragrance. The use of a Power Law to relate odor stimuli and the perceived olfactive sensation, results in a significant difference in odor intensity relatively to the linear law, especially at higher odor intensities.

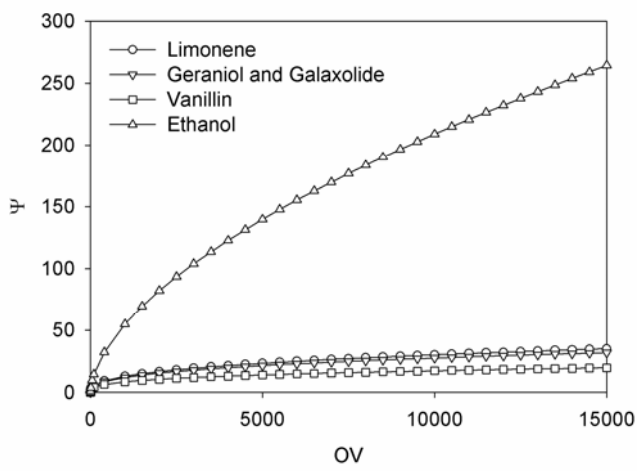


Figure 7.6 – Effect of the exponent (n) on the odor intensity of the fragrant molecules.

It is seen also from Figure 7.6, that the predicted odor intensity of ethanol reaches values much higher than for other fragrant components, due to the fact that its exponent is significantly higher than all others. Additionally, the slope of the ethanol curve when the Power Law is applied is higher than for the other components, thus sharply increasing its odor intensity. The curves for geraniol and galaxolide in Figure 7.6 are overlapped since they have the same exponent while vanillin, the less volatile component, has the lowest curve (Devos*, et al.*, 2002).

The truth is that perfumers generally follow a rule that says that a perfume should never smell to the alcohol solution, once it is not aesthetically pleasant for consumers. However, when smelling a perfume in a paper blotter or on our body we generally give it some time prior to smell it (thus introducing diffusion or convection effects which speed up the release of the lightest components). Moreover, a perfume mixture is formulated with a wide number of odorant components (in the order of dozens) having some fixatives in their composition which influence the release of other fragrance ingredients. It is designed to be smelled and perceived differently with time and at different distances from the point of application, although keeping its fingerprint all the way at the same time. The effect of the diffusion of the perfume mixtures studied here and their odor intensity over time and away from the source will be seen ahead. Additionally, one of the major components widely used in commercial perfumes as a solvent is water, usually in a mixed solution of water/alcohol (Pybus and Sell, 1999; Rowe, 2005). For that purpose, it is important to understand the effect of the highly polar water molecules in a perfume mixture and how they will affect the odor intensity and character of the headspace above the fragrance solution.

7.3.1. The effect of water on fragrance mixtures

The effect of water in perfume mixtures was studied considering the same quaternary systems previously analyzed in this Chapter and adding water as the fifth component in a fixed mole fraction (see Table 7.3). It is important to highlight that although water can not be smelled or perceived by the human nose, it modifies the molecular interactions in the perfume mixture, thus changing the evaporation profile and odor perception. Two different quinary fragrance systems were studied (see Table 7.3) and are recalled here:

- System 3: Limonene (A), Geraniol (B), Vanillin (C), Ethanol (S) and Water (S')
- System 4: Limonene (A), Geraniol (B), Galaxolide (C), Ethanol (S) and Water (S')

The mole fraction of water *(x_S)* was fixed to 45% (mol/mol) of the solution. In the formulation of fine fragrances this corresponds to the case of *Eau de parfum* or *Eau de toilette*, as shown before in Table 7.1 (Pybus and Sell, 1999). The results showing the odor distribution for these quinary systems are presented in Figure 7.7 for the pseudo-quaternary subsystems that constitute the quinary one. The whole distribution of the odor character for these two quinary mixtures can be shown using the PQ2Ds for the different odor intensity models as presented in Figure 7.8 to Figure 7.11.

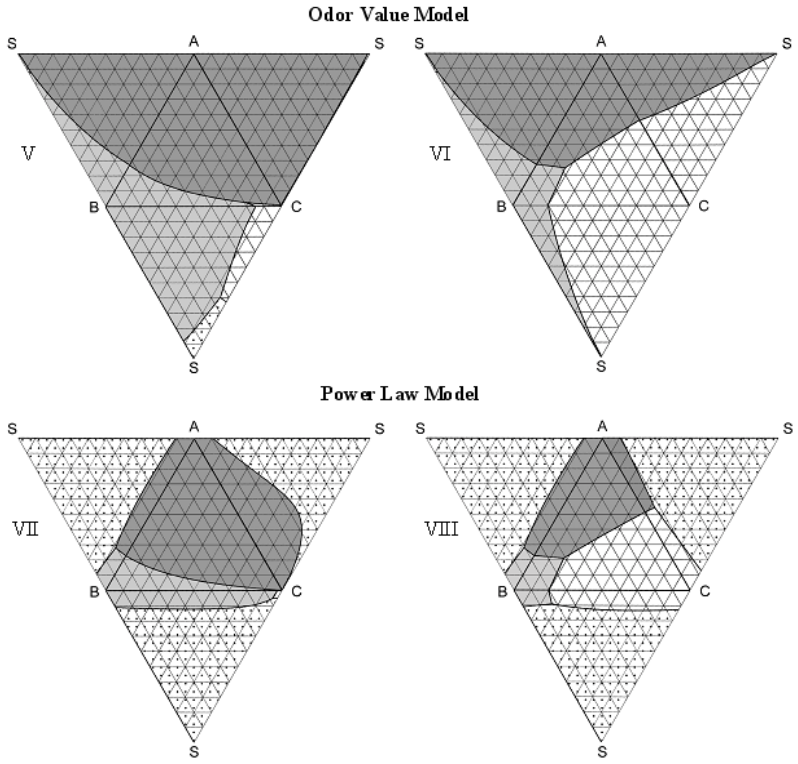


Figure 7.7 – PTD® of the different pseudo-quaternary subsystems of the two quinary mixtures. A: Top Note (Dark grey, Limonene), B: Middle note (Light grey, Geraniol), C: Base note (White, V-VII: Vanillin, VI-VIII: Galaxolide), S: Solvent (Dotted, Ethanol). Top diagrams simulated using the OV model (V-VI), bottom diagrams with Power Law model (VII-VIII). All systems include 45% water.

When considering the OV model alone to account for the odor intensity it is possible to compare from Figure 7.1 (I-II) and Figure 7.7 (V-VI) that in both perfume systems the presence of water molecules induces a larger odor zone for the top note (limonene). This can be explained by the fact that when including water in the system the average polarity of the mixture increases, and so tends to push out of the solution the less polar component, limonene (Pybus and Sell, 1999; Mata*, et al.*, 2005a). This effect was previously seen in an experimental study where the activity coefficients (γ_i) of three fragrant components were measured in three different media (aqueous surfactant, diethyl phthalate and water). The authors showed that for the case of limonene, activity coefficients in water were two or three orders of magnitude higher than in other solvents (Pybus and Sell, 1999). In the same way, the ethanol odor zones seem to be significantly reduced probably due to the strong water-ethanol interactions (through hydrogen bonding) which retain ethanol in the liquid phase. The same effect is seen when the Power Law model is considered, since these effects are independent of the sensory model selected.

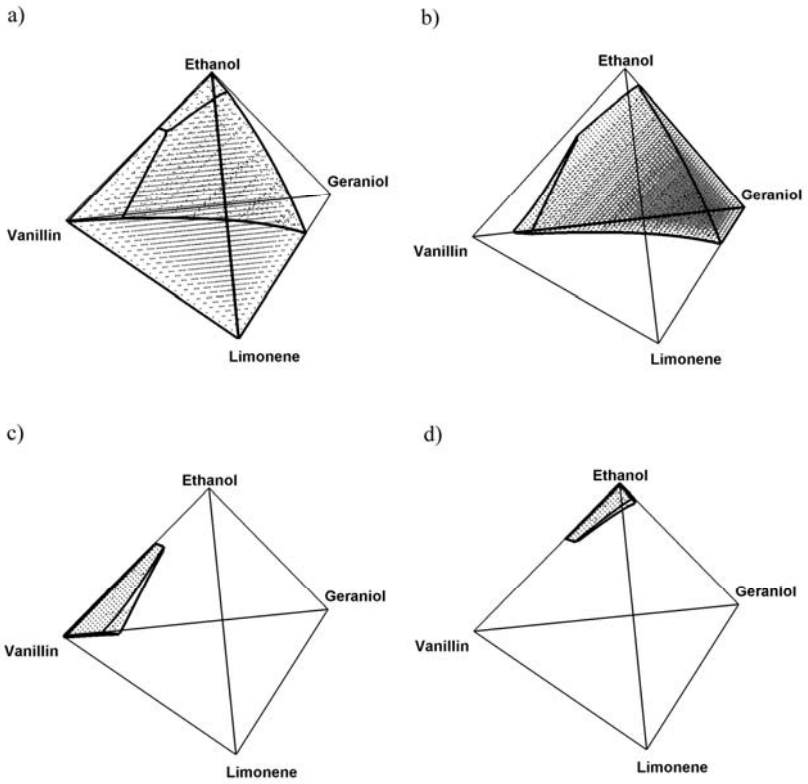


Figure 7.8 – Perfumery fragrance volumes considering the OV model for the odor perception in system 3: a) Limonene, b) Geraniol, c) Vanillin, and d) Ethanol. Water composition was set equal to 45% (mol/mol).

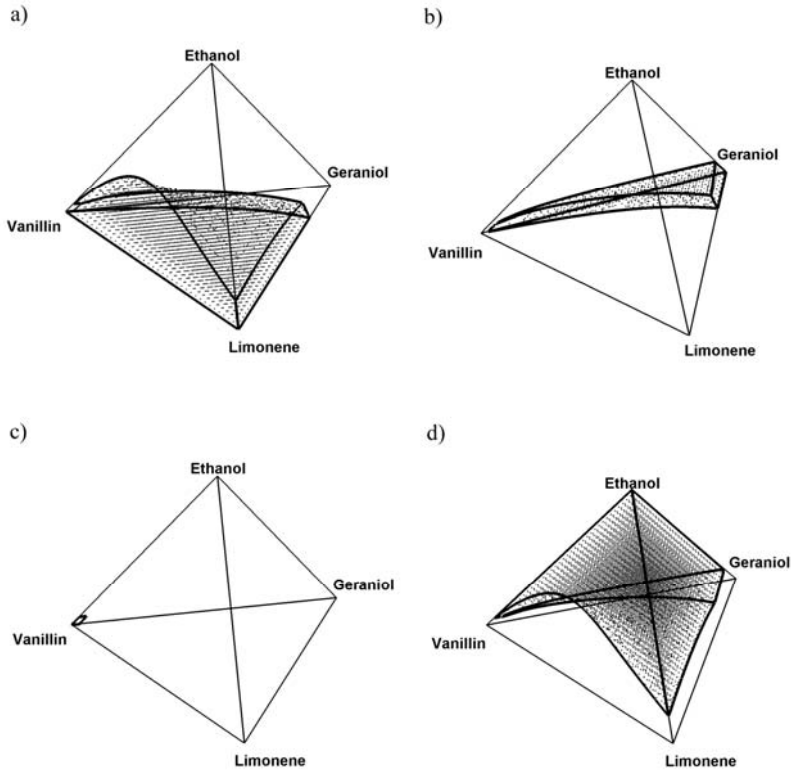


Figure 7.9 – Perfumery fragrance volumes considering the Power Law model for the odor perception in system 3: a) Limonene, b) Geraniol, c) Vanillin, and d) Ethanol. Water composition was set equal to 45% (mol/mol).

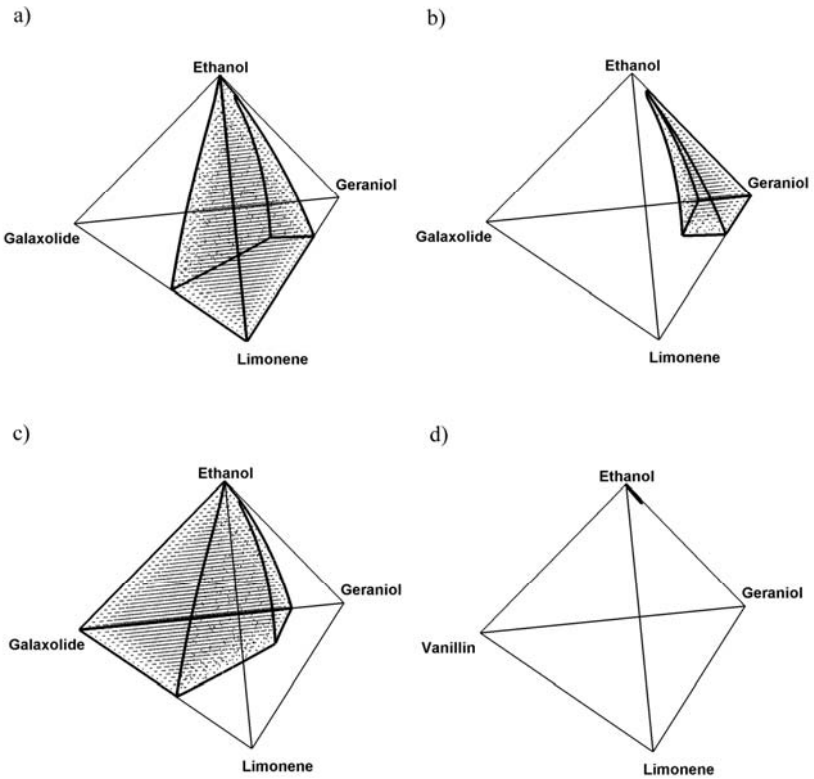


Figure 7.10 – Perfumery fragrance volumes considering the OV model for the odor perception in system 4: a) Limonene, b) Geraniol, c) Galaxolide, and d) Ethanol. Water composition was set equal to 45% (mol/mol).

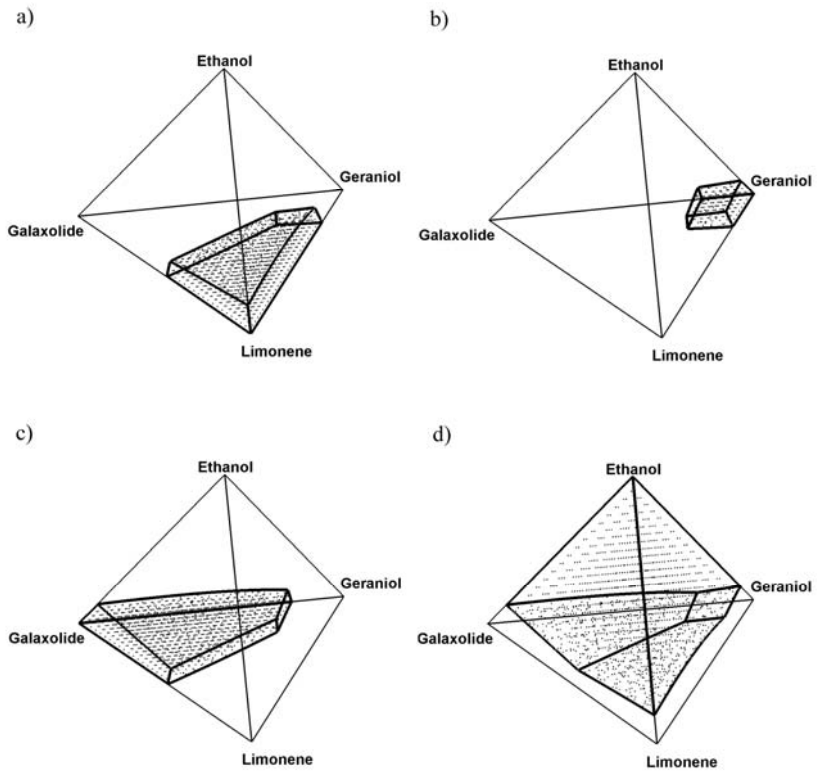


Figure 7.11 – Perfumery fragrance volumes considering the Power Law model for the odor perception in system 4: a) Limonene, b) Geraniol, c) Galaxolide, and d) Ethanol. Water composition was set equal to 45% (mol/mol).

Comparing Figure 7.1 (III-IV) and Figure 7.7 (VII-VIII) it is slightly perceptible that the ethanol odor zone is reduced, though this effect is far less evident than in the OV model. The effect of water molecules in these quinary perfume mixtures can also be seen through the odor volumes represented in the PQ2Ds for the different fragrant species (Figure 7.8 to Figure 7.11). In fact, various molecules may dissolve in each other when they have similar polarities. In the case of water and ethanol, this is the situation: the -OH group of ethanol is polar and may hydrogen bond to an oxygen of a water molecule. Thus, hydrogen bonding among ethanol and water molecules is a strong interaction that may be behind this fixative effect on ethanol so that it is not strongly perceived (as it is desirable from the perfumery viewpoint). This water-ethanol effect has already been reported to the light of perfumery, mainly as an empiric verification but nothing has been proved at the molecular level (Pybus and Sell, 1999). Although water has shown to have a retention effect on ethanol for the quinary mixtures studied here, it is important to note that in the formulation of a real perfume a large number of fragrant species is involved, and some (*e.g.* base notes) can have also a strong fixative effect (Mata*, et al.*, 2005b; Teixeira*, et al.*, 2009a).

7.3.2. Diffusion of quaternary fragrance mixtures

As seen before, the use of different odor intensity models have an effect on the prediction of the odor character of fragrance mixtures in the first moments after the application of a perfume. However, it is important to see how these models will influence or not the performance of the perfume mixtures over time and distance. Perfumes and fragranced products are designed to be used over time and it is desirable that their smell diffuses over the surrounding space with time. Therefore, the question here is whether the use of one model or another will significantly change the odor perception and performance of fragrance mixtures over time and distance.

A simple diffusion model based on Fick's 2nd Law (see Chapter 6) was applied to the perfume mixtures studied in this Chapter (previously presented in Table 7.3) to simulate the evaporation and diffusion processes of quaternary mixtures. This model simulates a physical system with a small volume of a liquid mixture evaporating over time *(t)* and diffusing upward *(z)* through the gas phase above it (headspace). The odor profiles obtained for the diffusion simulations for perfume system 1, using both odor intensity models, for the initial mixture composition of P1 (Table 7.4) are shown in Figure 7.12.

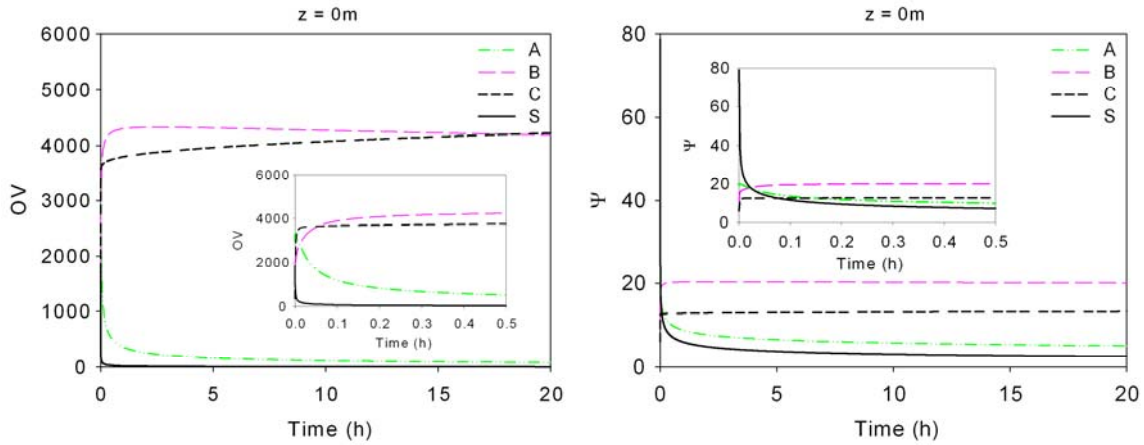


Figure 7.12 – Comparison of the odor profiles for perfume mixture P1 of the quaternary system 1, using the OV (left) and the Power Law (right) as odor intensity models.

The odor profiles presented in Figure 7.12 show that despite the first odor impression is different using the OV or the Power Law model (as seen before in the PQ2Ds), after some time of evaporation the dominant smell is that of component B (geraniol) for both cases. The fact is that as seen in Table 7.4 for this initial composition of the perfume mixture, it takes nearly 80 seconds until the odor intensity of component B becomes higher than the solvent when the Power Law model is used and ~200 seconds when the

OV model is considered. Thus, at this point will it make sense to say that the odor prediction done by the Power Law invalidates the previous one using the OV model?

In fact, both odor intensity models give similar odor profiles with time, except for short times after the evaporation process has started. An example of this case might be seen when one sprays a perfume in a paper blotter, fans it and then, after a few seconds, smells it. The typical initial impression would be that of the top notes, and it is undesirable that the alcohol solution might be perceived at this point. Nevertheless, in this particular experimental case, we would be introducing convection flows by first agitating the paper blotter in the air, and so speeding up the evaporating process. In our diffusion model, no convection is considered, and only the simple diffusion process is present which turns the evaporation slower than the depicted real case. Additionally, it is important to note that the high impact of ethanol predicted with the power law model can be decreased by introducing water in the solution (as will be shown ahead) or using a polar fixative odorant that has the capacity to retain in the liquid the more polar components (as it is often done in perfume formulation).

Table 7.4 – Comparison of the OV and Power Law models at different times during evaporation, for perfumery systems 1 and 2. Marked values represent maximum odor intensity.

		Mole Fractions				OV				Power Law			
	time (s)	x_A	x_B	x_C	x_S	OV_A	OV_B	OV_C	OV_S	ψ_A	ψ_B	ψ_C	ψ_S
System 1 - Mixture P1													
$P1_{initial}$	0.0	0.120	0.120	0.060	0.700	**2947**	840	343	1862	19	11	6	**79**
$P1_A$	14.4	0.288	0.391	0.196	0.125	**3246**	2396	3237	365	20	16	12	**31**
$P1_B$	72.1	0.192	0.497	0.250	0.061	2476	3108	**3614**	156	18	18	13	**19**
$P1_C$	198.4	0.110	0.565	0.286	0.039	1612	**3653**	3646	94	15	**19**	13	14
System 2 - Mixture P1													
$P1_{initial}$	0.0	0.120	0.120	0.060	0.700	2142	764	**2559**	2038	17	11	17	**83**
$P1_A$	14.4	0.332	0.401	0.201	0.067	2089	3337	**3421**	361	17	19	19	**30**
$P1_B$	72.1	0.274	0.463	0.233	0.030	1730	3837	**4032**	156	16	19	**20**	19
$P1_C$	198.4	0.207	0.514	0.260	0.019	1340	4155	**4640**	94	14	20	**21**	14

The results obtained by simulation using both odor intensity models can be seen to the light of the PTD®, if they are plotted as a function of time. These are shown in Figure 7.13 for some selected times of Table 7.4.

The PTDs simulated at different times (14.4 s, 72.1 s and 198.4 s) during the evaporation and diffusion process show significant differences in the odor zones over time and, additionally, present differences depending on the odor intensity model used. These PTDs represent only the initial times after the application of the perfume mixture, when the evaporation of ethanol is more significant and thus more evident on the PTDs of the right side of Figure 7.13 (due to the exponent for this component). However, after

approximately 3 minutes and for a long period of time both odor intensity models predict that component B (geraniol) will be the most strongly perceived. There is therefore a slight difference between the models for the prediction of the odor intensity for short times after the evaporation has started but then they tend to be similar in odor character (although there will always be some differences).

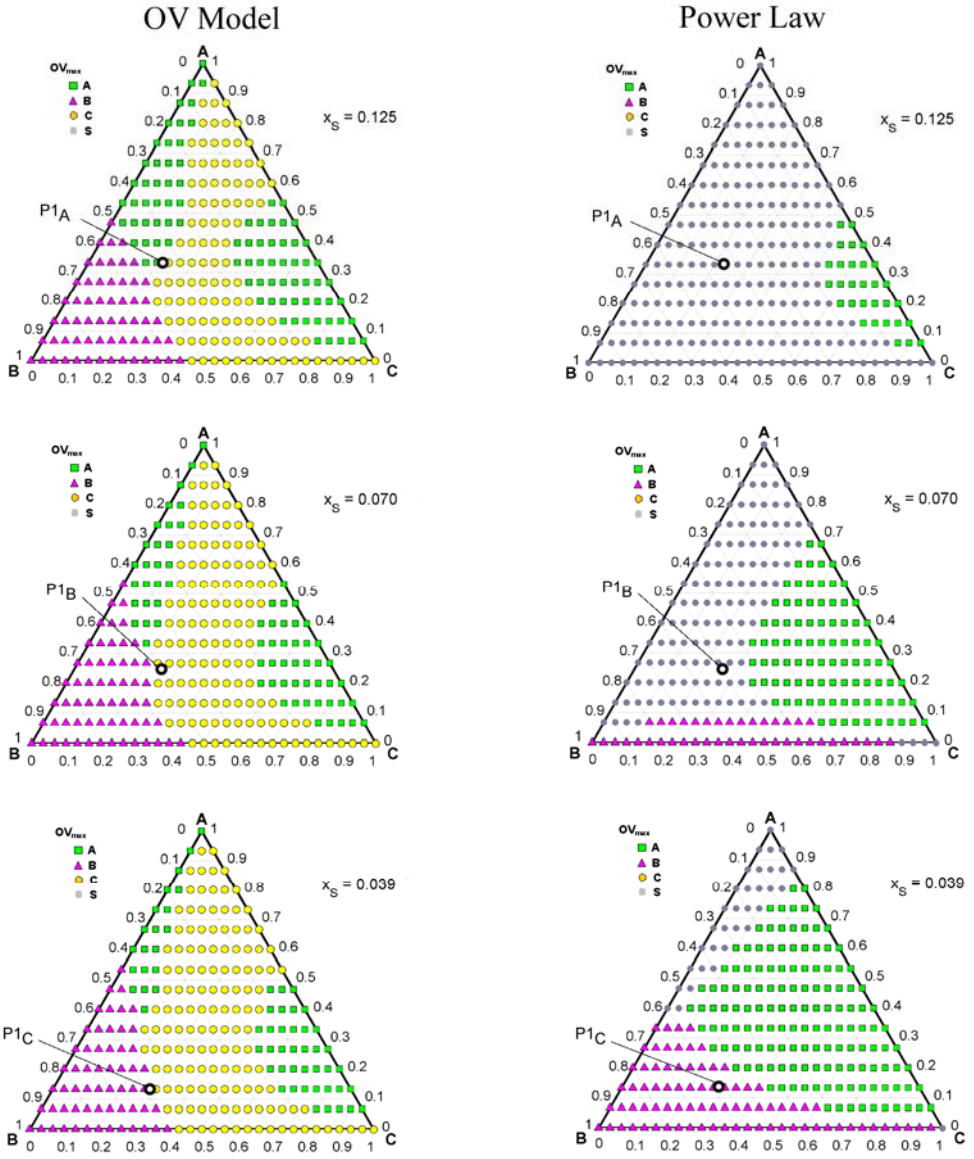


Figure 7.13 – PTD® of perfume system 1, using the OV model (left) and the Power Law (right) at different times after application (14.4s, 72.1s and 198.4s).

For the case of perfume system 2, where a different base note is used (galaxolide), it is possible to compare in Figure 7.14 the odor profiles using the OV and the Power Law models, for some initial mixture composition (Table 7.4). The similarities in the odor profiles of this perfume quaternary system are visible for times over 3 minutes, as seen

in Table 7.4, where after this time the base note galaxolide dominates the odor character, followed by the middle note (geraniol) and top note (limonene). At initial times after the perfume has started to evaporate there are some differences in the prediction of the odor character between the two models. As in the case of system 1, the ethanol is strongly perceived and dominates the first impact when the Power Law is used, while galaxolide is more strongly perceived when the OV model is applied.

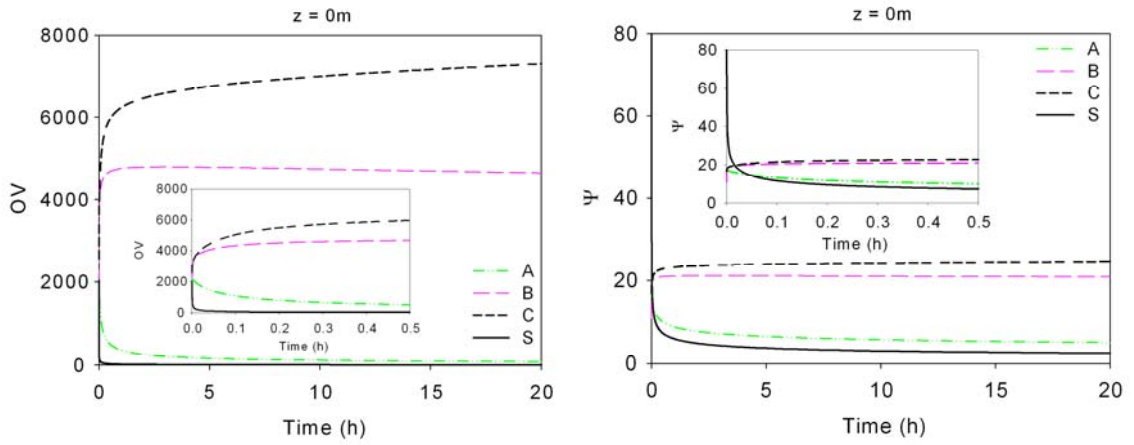


Figure 7.14 – Comparison of the odor profiles for perfume mixture P1 of the quaternary system 2, using the OV (left) and the Power Law (right) as odor intensity models.

As long as the evaporation takes place, the odorant molecules will diffuse into the surrounding air above the liquid. Additionally, since the liquid composition is changing and the fragrant molecules have different rates of evaporation and diffusion, the odor character evolves with time and distance. Taking into account this effect between the composition in the liquid perfume mixture and the odor character perceived by the human nose, it is possible to represent evaporation lines in the PQ2D®. In Figure 7.15 the evaporation paths of some perfume mixtures are shown considering the Power Law model only for some initial mixture compositions: P1 ($x_A = 0.120$, $x_B = 0.120$, $x_C = 0.060$, $x_S = 0.700$); P2 ($x_A = 0.234$, $x_B = 0.060$, $x_C = 0.006$, $x_S = 0.700$); and P3 ($x_A = 0.200$, $x_B = 0.100$, $x_C = 0.200$, $x_S = 0.500$). The evaporation lines represent the evolution of the perfume composition in the liquid and at the same time the odor character in the gas phase. Over the time of the dual process of evaporation and diffusion, evaporation lines cross different odor volumes in the PQ2D® (Figure 7.15). This means that the dominant smell is changing as the liquid composition changes too. It is possible to see that these evaporation paths are dependent on the initial mixture concentration, though all follow the same trend: initially, a steep curve due to the fast

evaporation of ethanol; then the evaporation lines approximate the geraniol-vanillin binary edge, once the top note (limonene) is very volatile; and, finally, at the end they tend to the vertex of the base note (vanillin or galaxolide) since it is the fragrant species that lasts longer.

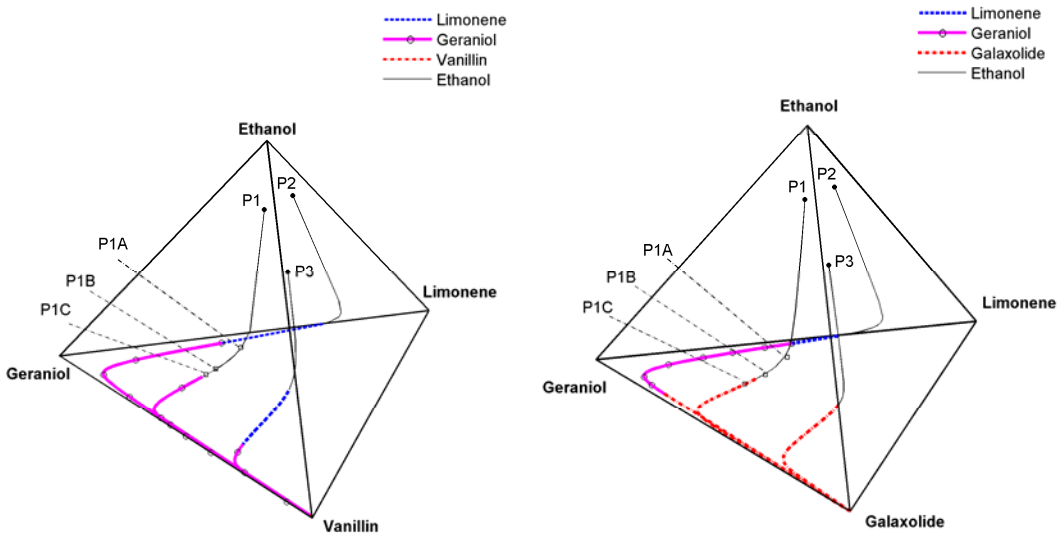


Figure 7.15 – Perfumery evaporation lines plotted in the PQ2D® for the quaternary system 1 (left) and system 2 (right) with different initial mixture compositions.

7.3.3. Diffusion of quinary fragrance mixtures

In order to come closer of a real perfume formulation it would be necessary to include several components (fragrances and others) in the formulation process. One of the most important constituents of perfume mixtures is water, which we have included here in this study. The effect of water in the initial odor impact has already been presented. The next question to be addressed is if water has different or similar effects when the evaporation and diffusion processes are taken together into account.

For the purpose of this study, the effect of water in fragrance diffusion was analyzed for the quinary systems 3 and 4. The number of moles in the initial quinary mixture was kept the same as in the quaternary ones, for all the fragrances and the ethanol. In this way, the quantity of matter in the quinary systems is higher than 1 mmol, since water was included in a mole fraction of 45%. For comparison purposes, the mole fractions in a water free basis remain the same in the quinary and in the quaternary systems. The initial mixture composition is given by: $x_A = 0.066$, $x_B = 0.066$, $x_C = 0.033$, $x_{EtOH} = 0.385$, $x_{H2O} = 0.450$. In Figure 7.16 the evaporation profiles of two quinary perfume mixtures are presented considering the Power Law as the odor intensity model. Table

7.5 shows some compositions of the mixture and its predicted odor intensity at different times during the evaporation process.

When a comparison is made between the quaternary (Table 7.4) and the quinary mixtures (Table 7.5) for the Power Law model, it is possible to see that in the latter, ethanol is less dominant when water is included in the formulation of the perfume. In fact, the simulations for the odor intensity have shown that both quaternary systems 1 and 2, exhibit higher initial odor intensity for ethanol than in the quinary systems (3 and 4, where water is included). Thus, it can be seen that water has a retention effect on ethanol, preventing its faster evaporation from the liquid mixture and reducing its high initial odor intensity. The presence of water in the perfume formulation showed another effect on the release of the fragrances by increasing the odor intensity of limonene. This is due to the fact that incorporating water in the solution increases its polarity, thus pushing out of the solution the non polar top note, limonene.

Table 7.5 – Odor intensity values using the Power Law model at different times during evaporation for the quinary mixtures 3 and 4. Marked values represent maximum odor intensity.

		Mole Fractions					Power Law				
	time (s)	x_A	x_B	x_C	x_S	x_{H2O}	Ψ_A	Ψ_B	Ψ_C	Ψ_S	Ψ_{H2O}
						System 3 - Mixture P1					
$P1_{initial}$	0.0	0.066	0.066	0.033	0.385	0.450	24	11	3	**53**	-
$P1_A$	14.4	0.233	0.331	0.166	0.145	0.125	20	16	10	**32**	-
$P1_B$	72.1	0.173	0.466	0.234	0.063	0.064	18	18	12	**19**	-
$P1_C$	198.4	0.103	0.541	0.273	0.040	0.044	15	**19**	12	14	-
						System 4 - Mixture P1					
$P1_{initial}$	0.0	0.066	0.066	0.033	0.385	0.450	21	10	16	**54**	-
$P1_A$	14.4	0.301	0.368	0.184	0.078	0.069	17	18	18	**32**	-
$P1_B$	72.1	0.262	0.448	0.225	0.032	0.033	16	19	**20**	19	-
$P1_C$	198.4	0.201	0.503	0.254	0.020	0.023	14	20	**21**	14	-

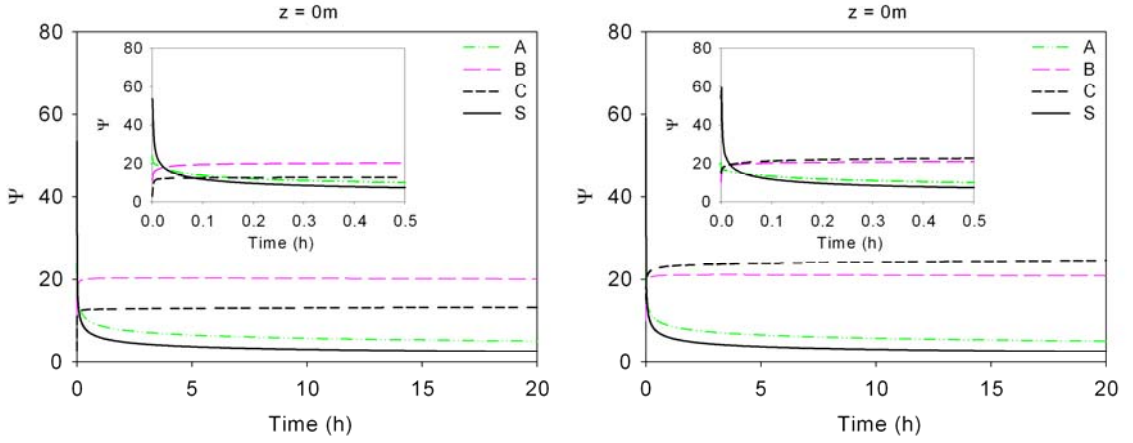


Figure 7.16 – Evaporation profiles of the quinary mixtures of system 1 (left) and system 2 (right) using the Power Law model.

Once more, it is important to highlight that although ethanol shows a high odor impact (in the first moments), which is not expected from the point of view of a perfumer, we are considering here only diffusion effects (free of convection). Moreover, the fragrance systems considered were for quaternary and quinary mixtures only, while commercial perfumes have a larger number of constituents (some of which may have larger or lesser effect on the retention or release of others).

7.4. Olfactory evaluations and comparison with odor intensity models

So far, we have analyzed the predicted odor intensity of different fragrance raw materials present in several mixtures using both the PTD® and the PQ2D® methodologies. Within these methodologies two odor intensity models were used: the OV model and the Steven's Power Law. The predicted odor intensities and dominant olfactive notes have shown some differences but also some similarities between the two models.

Thus, at this point, it is important to evaluate experimentally the perceived character (the dominant odor) of some fragrance mixtures and establish a comparison with predictive models. For that purpose, the predictive capacity of the Steven's Power Law was already presented in Chapter 5 with different fragrance mixtures. Here, those samples (comprising several binary, ternary and quaternary mixtures) will be evaluated with three different models: the OV, the Steven's Power Law and also the Weber-Fechner model.

For the latter, the positive constant factor (k_w) which appears in the Weber-Fechner Law (see equation 7.3 or for further details Annex A) was assumed as 2.33 for all calculations since this is considered as a median value for a number of odorants in olfactive perception (Ruijten*, et al.*, 2009). The methodology, sample preparation, olfactory analysis and further details can be seen on Chapter 5. The experimental results for all the 65 samples together with the predicted odor intensities using the UNIFAC method and the three different odor intensity models are presented in Table 7.6.

First, it is possible to see that different models, result as expected in different odor intensity scales. Furthermore, they also predict different fragrance components with the maximum odor intensity (OV_{max}) for some mixture. In terms of predictive capability of

the models for the component with the maximum odor intensity it was obtained a good agreement between the olfactory evaluations performed by the panelists and all the models. There were slight differences between the panelists' evaluations but overall the odor intensity models resulted in similar prediction for the maximum odor scent. Moreover, for the 31 samples evaluated by the panelists, an agreement of 64.5% was obtained between the predicted odor character for all models and the olfactory evaluation. However, the majority of the deviations occurred for quaternary mixtures which are more complex to evaluate, as aforementioned in section 7.1: Introduction. Additionally, for mixtures with a high content of ethanol (N = 59 to N = 63) the Power Law tends to predict higher odor intensities for that component due to its high exponent (see Table 7.2) which were not accompanied by the panelists' evaluations. Disregarding these mixtures containing ethanol in its composition, the Power Law performed better than the remaining models with an agreement of 75% in the predicted odor character.

7.5. Conclusions

The comparison of different psychophysical intensity models to account for the odor perception of fragrance mixtures has shown differences in the prediction of the odor character for initial times after application of the perfume. The Power Law model predicted that ethanol was more strongly perceived than when using the OV model, for the beginning of the evaporation of the perfume, mainly for mixtures with high concentration of it and due to its large exponent. However, for the end-use of fragranced products it is desirable that they have high performance over time (long lastingness). It was shown that when evaporation and diffusion effects were considered, these two odor intensity models tend to get the same odor character after some time of the processes.

The incorporation of water in the perfume formulation has shown two interesting phenomena that are supported by experimental evidences from perfumery: *i)* non-polar fragrances (as limonene) tend to be pushed out of the solution and thus are more strongly perceived by the human nose; *ii)* water has a retention effect on more polar components like ethanol, preventing them to evaporate fast and limiting its initial perception. The predictions of the odor intensity and character with water in solution have shown that its use in perfumes is not only ruled by the cost factor, but also by the odor performance and impact of the perfume.

The evaporation paths for different perfume mixtures presented with the PQ2D® methodology showed that the odor character (the dominant note) is evolving over time as the evaporation of the perfume goes on. These paths evidenced that in the evaporation and diffusion of a perfume mixture there can be seen two stages: first the rapid evaporation of ethanol and water as seen by the steepest descent curvatures, and then a more pronounced evaporation of the fragrance components.

The comparison of the OV model, the Steven's Power Law and the Weber-Fechner Law with an olfactory evaluation test performed by two panelists have shown a good agreement between them for the predicted odor character. All models performed well but for mixtures without ethanol the Power Law was the best with an agreement of 75% for the dominant note out of 24 samples (including binary, ternary and quaternary mixtures).

In brief, the comparison of psychophysical models for odor intensity showed slight differences (especially for short times but similar predictions after that). Thus, it can be concluded that the universality of a psychophysical law definitely established for perceptual continua and sensory perception must continue to be tested, in quest of possible exceptions.

Table 7.6 - Odor intensities and character of fragrance mixtures evaluated by olfactory measurements (panelists) compared with the predicted odor character calculated using the different odor intensity models (Power Law, OV and Weber-Fechner).

	Experimental Data		Power Law								OV								Weber-Fechner							
N	**Pan 1**	**Pan 2**	**Lim**	**LOH**	**Pin**	**Ger**	**EtOH**	**Lin.Ac.**	**Van**	**max**	**Lim**	**LOH**	**Pin**	**Ger**	**EtOH**	**Lin.Ac.**	**Van**	**max**	**Lim**	**LOH**	**Pin**	**Ger**	**EtOH**	**Lin.Ac.**	**Van**	**max**
1	-	-	-	43.10	194.53	-	-	-	-	Pin	-	46755	46923	-	-	-	-	Pin	-	10.88	10.91	-	-	-	-	Pin
2	-	-	-	50.06	168.61	-	-	-	-	Pin	-	71713	35046	-	-	-	-	LOH	-	11.31	10.57	-	-	-	-	LOH
3	-	-	-	53.43	138.57	-	-	-	-	Pin	-	86381	23485	-	-	-	-	LOH	-	11.50	10.13	-	-	-	-	LOH
4	-	-	34.01	41.31	-	-	-	-	-	LOH	13788	41440	-	-	-	-	-	LOH	9.65	10.76	-	-	-	-	-	LOH
5	-	-	30.02	49.82	-	-	-	-	-	LOH	9837	70736	-	-	-	-	-	LOH	9.30	11.30	-	-	-	-	-	LOH
6	-	-	26.00	53.20	-	-	-	-	-	LOH	6669	85364	-	-	-	-	-	LOH	8.91	11.49	-	-	-	-	-	LOH
7	-	-	20.46	-	182.72	-	-	-	-	Pin	3492	-	41295	-	-	-	-	Pin	8.26	-	10.76	-	-	-	-	Pin
8	-	-	28.51	-	142.41	-	-	-	-	Pin	8556	-	24831	-	-	-	-	Pin	9.16	-	10.26	-	-	-	-	Pin
9	-	-	32.44	-	102.90	-	-	-	-	Pin	12133	-	12793	-	-	-	-	Pin	9.52	-	9.60	-	-	-	-	Pin
10	Lim	Pin/Lim	22.48	50.95	115.90	-	-	-	-	Pin	4504	75421	16308	-	-	-	-	LOH	8.51	11.36	9.79	-	-	-	-	LOH
11	Lim	Lim	27.28	42.39	132.25	-	-	-	-	Pin	7597	44598	21349	-	-	-	-	LOH	9.04	10.83	10.12	-	-	-	-	LOH
12	Pin	Pin	16.96	35.93	186.92	-	-	-	-	Pin	2102	27802	43255	-	-	-	-	Pin	7.74	10.35	10.81	-	-	-	-	Pin
13	Lim/LOH	Lim	33.88	33.27	63.10	-	-	-	-	Pin	13650	22317	4715	-	-	-	-	LOH	9.63	10.13	8.61	-	-	-	-	LOH
14	Pin	Pin	-	-	194.87	23.57	-	-	-	Pin	-	-	47092	6490	-	-	-	Pin	-	-	10.89	8.88	-	-	-	Pin
15	Pin	Pin	-	-	169.55	27.58	-	-	-	Pin	-	-	35446	10035	-	-	-	Pin	-	-	10.60	9.32	-	-	-	Pin
16	Ger/Pin	Pin	-	-	129.08	29.97	-	-	-	Pin	-	-	20318	12645	-	-	-	Pin	-	-	10.04	9.56	-	-	-	Pin
17	-	-	21.02	-	114.36	28.68	-	-	-	Pin	3756	-	15871	11195	-	-	-	Pin	8.33	-	9.79	9.43	-	-	-	Pin
18	-	-	28.11	-	123.35	23.68	-	-	-	Pin	8236	-	18520	6570	-	-	-	Pin	9.12	-	9.94	8.89	-	-	-	Pin
19	-	-	17.29	-	184.93	20.66	-	-	-	Pin	2214	-	42318	4500	-	-	-	Pin	7.79	-	10.78	8.51	-	-	-	Pin
20	-	-	34.26	-	51.50	18.37	-	-	-	Pin	14067	-	3115	3247	-	-	-	Lim	9.67	-	8.14	8.18	-	-	-	Lim
21	Pin	Pin	-	29.87	126.47	27.71	-	-	-	Pin	-	16404	19489	10174	-	-	-	Pin	-	9.82	10.00	9.34	-	-	-	Pin
22	Pin	Pin	-	42.80	160.74	18.79	-	-	-	Pin	-	45854	31791	3456	-	-	-	LOH	-	10.86	10.49	8.24	-	-	-	LOH
23	Pin	Pin	-	35.82	194.02	16.32	-	-	-	Pin	-	27554	46674	2337	-	-	-	Pin	-	10.35	10.88	7.85	-	-	-	Pin
24	LOH	LOH	-	52.52	87.23	12.72	-	-	-	Pin	-	82276	9132	1169	-	-	-	LOH	-	11.45	9.23	7.15	-	-	-	LOH
25	-	-	-	53.28	-	18.70	-	-	-	LOH	-	85704	-	3410	-	-	-	LOH	-	11.49	-	8.23	-	-	-	LOH
26	-	-	-	40.88	-	27.32	-	-	-	LOH	-	40215	-	9780	-	-	-	LOH	-	10.73	-	9.30	-	-	-	LOH
27	-	-	-	32.99	-	29.72	-	-	-	LOH	-	21783	-	12350	-	-	-	LOH	-	10.11	-	9.53	-	-	-	LOH
28	Lim	Lim	34.08	-	-	22.59	-	-	-	Lim	13863	-	-	5764	-	-	-	Lim	9.65	-	-	8.76	-	-	-	Lim
29	Lim	Lim	30.12	-	-	27.51	-	-	-	Lim	9933	-	-	9971	-	-	-	Ger	9.31	-	-	9.32	-	-	-	Ger
30	Ger	Ger	23.74	-	-	30.15	-	-	-	Ger	5220	-	-	12859	-	-	-	Ger	8.66	-	-	9.57	-	-	-	Ger
31	Lim	Lim	23.19	29.82	-	28.27	-	-	-	LOH	4895	16328	-	10746	-	-	-	LOH	8.60	9.82	-	9.39	-	-	-	LOH
32	Lim	Lim	29.20	42.86	-	19.87	-	-	-	LOH	9135	46040	-	4035	-	-	-	LOH	9.23	10.87	-	8.40	-	-	-	LOH
33	LOH	Lim	34.19	34.96	-	15.11	-	-	-	LOH	13987	25719	-	1887	-	-	-	LOH	9.66	10.28	-	7.63	-	-	-	LOH

N	Pan 1	Pan 2	Lim	LOH	Pin	Ger	EtOH	Lin.Ac.	Van	max	Lim	LOH	Pin	Ger	EtOH	Lin.Ac.	Van	max	Lim	LOH	Pin	Ger	EtOH	Lin.Ac.	Van	max
34	LOH/Lim	LOH	18.66	54.92	-	12.10	-	-	-	LOH	2723	93466	-	1018	-	-	-	LOH	8.00	11.58	-	7.01	-	-	-	LOH
35	Pin	Pin/LOH	19.15	46.69	77.60	21.13	-	-	-	Pin	2920	58787	7193	4790	-	-	-	LOH	8.07	11.11	8.99	8.58	-	-	-	LOH
36	Lim/Pin	Pin/Lim	23.27	34.38	90.98	25.45	-	-	-	Pin	4941	24522	9950	8030	-	-	-	LOH	8.61	10.23	9.31	9.10	-	-	-	LOH
37	LIM	LIM	22.40	23.68	68.07	28.75	-	-	-	Pin	4462	8448	5504	11270	-	-	-	Ger	8.50	9.15	8.72	9.44	-	-	-	Ger
38	LIM	LIM	31.45	22.97	66.51	23.57	-	-	-	Pin	11160	7740	5251	6486	-	-	-	Lim	9.43	9.06	8.67	8.88	-	-	-	Lim
39	Pin	Pin	21.81	34.21	161.52	18.87	-	-	-	Pin	4148	24167	32107	3500	-	-	-	Pin	8.43	10.21	10.50	8.26	-	-	-	Pin
40	Pin/Lim	Pin	26.24	21.31	99.84	26.46	-	-	-	Pin	6837	6254	12029	8944	-	-	-	Pin	8.94	8.85	9.51	9.21	-	-	-	Pin
41	-	-	-	-	191.55	-	-	11.27	-	Pin	-	-	45470	-	-	1013	-	Pin	-	-	10.85	-	-	7.00	-	Pin
42	-	-	-	-	158.88	-	-	15.37	-	Pin	-	-	31043	-	-	2459	-	Pin	-	-	10.47	-	-	7.90	-	Pin
43	-	-	-	-	126.19	-	-	17.03	-	Pin	-	-	19400	-	-	3296	-	Pin	-	-	9.99	-	-	8.20	-	Pin
44	-	-	33.56	-	-	-	-	10.99	-	Lim	13302	-	-	-	-	942	-	Lim	9.61	-	-	-	-	6.93	-	Lim
45	-	-	28.15	-	-	-	-	15.38	-	Lim	8267	-	-	-	-	2463	-	Lim	9.13	-	-	-	-	7.90	-	Lim
46	-	-	23.52	-	-	-	-	17.00	-	Lim	5089	-	-	-	-	3277	-	Lim	8.64	-	-	-	-	8.19	-	Lim
47	-	-	20.10	-	107.19	-	-	16.11	-	Pin	3326	-	13904	-	-	2813	-	Pin	8.21	-	9.65	-	-	8.04	-	Pin
48	-	-	27.09	-	128.33	-	-	11.33	-	Pin	7452	-	20078	-	-	1027	-	Pin	9.02	-	10.03	-	-	7.02	-	Pin
49	-	-	16.47	-	188.66	-	-	7.67	-	Pin	1943	-	44082	-	-	338	-	Pin	7.66	-	10.82	-	-	5.89	-	Pin
50	-	-	33.92	-	65.52	-	-	7.16	-	Pin	13685	-	5092	-	-	277	-	Lim	9.64	-	8.64	-	-	5.69	-	Lim
51	-	-	24.68	34.20	-	20.02	37.22	-	-	EtOH	5793	24154	-	4123	511	-	-	LOH	8.77	10.21	-	8.42	6.31	-	-	LOH
52	-	-	24.39	26.20	-	23.31	35.90	-	-	EtOH	5615	11275	-	6288	480	-	-	LOH	8.74	9.44	-	8.85	6.25	-	-	LOH
53	-	-	25.60	26.48	-	24.31	30.71	-	-	EtOH	6398	11633	-	7072	367	-	-	LOH	8.87	9.47	-	8.97	5.97	-	-	LOH
54	-	-	25.66	25.73	-	21.94	38.96	-	-	EtOH	6438	10707	-	5318	553	-	-	LOH	8.87	9.39	-	8.68	6.39	-	-	LOH
55	-	-	28.36	34.41	-	14.58	42.91	-	-	EtOH	8439	24568	-	1707	653	-	-	LOH	9.15	10.23	-	7.53	6.56	-	-	LOH
56	-	-	20.89	28.68	-	19.37	45.31	-	-	EtOH	3691	14600	-	3763	717	-	-	LOH	8.31	9.70	-	8.33	6.65	-	-	LOH
57	-	-	27.58	28.41	-	19.46	41.09	-	-	EtOH	7827	14222	-	3809	606	-	-	LOH	9.07	9.68	-	8.34	6.48	-	-	LOH
58	-	-	31.56	27.65	-	15.57	43.45	-	-	EtOH	11265	13152	-	2050	667	-	-	LOH	9.44	9.60	-	7.72	6.58	-	-	LOH
59	EtOH/Lim	EtOH	16.98	-	-	20.20	46.10	-	10.24	EtOH	2109	-	-	4228	739	-	1815	Ger	7.75	-	-	8.45	6.68	-	7.59	Ger
60	EtOH	EtOH/Lim	18.24	-	-	20.60	45.41	-	10.22	EtOH	2560	-	-	4466	720	-	1805	Ger	7.94	-	-	8.50	6.66	-	7.59	Ger
61	Lim/Ger	Lim	11.95	-	-	25.41	37.53	-	9.66	EtOH	817	-	-	7996	518	-	1502	Ger	6.79	-	-	9.09	6.32	-	7.40	Ger
62	Lim	Lim	33.35	-	-	15.78	44.38	-	11.14	EtOH	13077	-	-	2129	692	-	2380	Lim	9.59	-	-	7.75	6.62	-	7.87	Lim
63	Lim	Lim	31.70	-	-	17.08	44.78	-	10.63	EtOH	11402	-	-	2650	703	-	2048	Lim	9.45	-	-	7.98	6.63	-	7.72	Lim
64	Lim/Ger	Lim	33.43	-	-	17.88	38.97	-	11.94	EtOH	13157	-	-	3010	553	-	2981	Lim	9.60	-	-	8.11	6.39	-	8.10	Lim
65	Lim	Lim	24.62	-	-	27.47	23.75	-	8.12	Ger	5761	-	-	9931	235	-	858	Ger	8.76	-	-	9.31	5.53	-	6.83	Ger
							% Match panelists 64.5								% Match panelists 64.5								% Match panelists 64.5			

7.6. References

Appell, L., Physical foundations in perfumery - VIII. The minimum perceptible, *American Perfumer and Cosmetics*, 84, 45-50, 1969

Balk, F., Ford, R., Environmental risk assessment for the polycyclic musks AHTN and HHCB in the EU - I. Fate and exposure assessment, *Toxicology Letters*, 111, 57–79, 1999

Baydar, A., McGee, T., Purzycki, K., Skin Odor Value Technology for Fragrance Performance Optimization, *Perfumer & Flavorist*, 20, 45-53, 1995

Buck, L., Axel, R., A Novel Multigene Family May Encode Odorant Receptors: A Molecular Basis for Odor Recognition, *Cell*, 65, 175-187, 1991

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Chapman, J., MATLAB programming for engineers, California, Brooks Cole Publishing Company, 2000

Chapra, S., Canale, R., Numerical methods for engineers: with software and programming applications, Boston, McGraw Hill, 2002

Devos, M., Rouault, J., Laffort, P., Standardized olfactory power law exponents, Dijon - France, Editions Universitaires-Sciences 2002

Fráter, G., Müller, U., Kraft, P., Preparation and Olfactory Characterization of the Enantiomerically Pure Isomers of the Perfumery Synthetic Galaxolide, *Helvetica Chimica Acta*, 82, 1656-1665, 1999

Graedel, T. E., The Perceived Intensity of Natural Odors, *Journal of Chemical Education*, 61, (8): 681-686, 1984

Green, D., Luce, D., Variability of magnitude estimates: A timing theory analysis, *Perception & Psychophysics*, 15, (2): 291-300, 1974

Herman, S. J., Chemistry and Technology of Flavors and Fragrances, Blackwell, 2002

Luce, R. D., "On the possible psychophysical laws" revisited: Remarks on cross-modal matching, *Psychological Review*, 97, (1): 66-77, 1990

Luce, R. D., A psychophysical theory of intensity proportions, joint presentations, and matches, *Psychological Review*, 109, (3): 520-532, 2002

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Effect of nonidealities in perfume mixtures using the perfumery ternary diagrams (PTD) concept, *Industrial & Engineering Chemistry Research*, 44, (12): 4435-4441, 2005a

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005b

MathWorks, Partial Differential Equation Toolbox - ComsoLab MATLAB's Users Guide, 2002

Nocedal, J., Wright, S., Numerical Optimization, New York, Springer, 1999

Nocedal, J., Wright, S., Numerical Optimization, New York, Springer, 1999

Perring, K. D., The Chemistry of Fragrances - From Perfumer to Consumer, Cambridge, RSC Publishing, 2006

Poucher, W. A., A classification of odors and its uses, *Journal Soc. Cosmet. Chem.*, 81-95, 1955

Pybus, D. H., Sell, C. S., Chemistry of Fragrances, RSC Paperbacks, 1999

Rowe, D., Chemistry and Technology of Flavours and Fragrances, United States, Blackwell Publishing Ltd - CRC Press, 2005

Ruijten, M. W. M. M., Doorn, R. v., Harreveld, A. P. v., Assessment of odour annoyance in chemical emergency management. 609200001/2009, National Institute for Public Health and the Environment, BA Bilthoven, the Netherlands, RIVM2009

Schreiber, W. L., Perfumes, *Kirk-Othmer Encyclopedia of Chemical Technology*, 18, 1-40, 2005

Shigemoto, K., Weber-Fechner's Law and Demand Function, *Tezukayama Academic Review*, 9, (41-46): 2002

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Stevens, S. S., The surprising simplicity of sensory metrics, *Psychological Bulletin*, 55, (4): 29-39, 1958

Stevens, S. S., Concerning the psychophysical power law, *Quarterly Journal of Experimental Psychology*, 16, (4): 383-385, 1964

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009a

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009b

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., Perfumery Radar: A Predictive Tool for Perfume Family Classification, *Industrial & Engineering Chemistry Research*, 49, 11764–11777, 2010

Teixeira, M. A., Rodrìguez, O., Rodrigues, A. E., Chapter 1: Odor Detection & Perception: An Engineering Perspective, Advances in Environmental Research, USA, NovaPublishers, Volume 14: 2011

Ternat, C., Ouali, L., Sommer, H., Fieber, W., Velazco, M. I., Plummer, C. J. G., Kreutzer, G., Klok, H. A., Manson, J. A. E., Herrmann, A., Investigation of the Release of Bioactive Volatiles from Amphiphilic Multiarm Star-Block Copolymers by Thermogravimetry and Dynamic Headspace Analysis, *Macromolecules*, 41, (19): 7079-7089, 2008

Zwislocki, J. J., Sensory Neuroscience: Four Laws of Psychophysics, New York, Springer Science+Business Media, 2009

Chapter 8

Perfumery Radar (PR): A Predictive Tool for Perfume Family Classification*

"Science makes important first step towards the smelloscope
Smells make a vivid impression, but are nearly impossible to describe."
(Esther Inglis-Arkell in io9.com about the PR methodology, 2010)

The classification of perfumes can be done in two ways, either in terms of chemical composition (quantitative) or in terms of olfactory families (qualitative). If until now we have focused the discussion on the quantification of the odor intensity of fragrances, in this Chapter we will address the qualitative classification of perfumes into olfactory families. A methodology called Perfumery Radar (PR) that predicts the classification of perfumes within different olfactive families that perfumers often use is presented. The classification of perfumes into families or classes has been done for years by Flavor & Fragrance companies on the basis of sensorial analysis or odor descriptors. These are mainly performed by their experts (perfumers), but significant differences are observed when comparing these classifications and so none has attained universal acceptance. The PR introduces some scientific basis, reducing the arbitrariness of perfume classification to the empirical classification of pure odorants as will be shown later. The odor intensity of pure fragrances in a liquid mixture is predicted using the Odor Value (OV) concept, considering molecular interactions between components. Radar plots are

* Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., Perfumery Radar: A Predictive Tool for Perfume Family Classification, *Industrial & Engineering Chemistry Research*, 49, 11764–11777, 2010

used to represent olfactory families and transform quantitative information into qualitative. In the first part of this Chapter, several perfumery radars were obtained for essential oils and commercial feminine perfumes and were compared with existing experimental classifications. Another validation was also performed using headspace gas chromatographic analysis of feminine perfumes and applying that data in the PR methodology to obtain experimental perfumery radars.

In the second part of this Chapter, the PR methodology was also applied for two different studies: *i)* quantitative analysis of olfactory families using similar perfumes but with different compositions, mainly in the concentration of water/ethanol (*e.g.* same brand and model of the types *Eau de toillete* versus *Eau Fraîche*); *ii)* evaluation of the role of unisex fragrances and their typical descriptors and classifications. In this first topic, radar plots were obtained for two different fragrance mixtures, combining the qualitative approach of this methodology with a quantitative evaluation of the odor intensity of each olfactive family. Finally, in the last topic the PR methodology was applied to commercial unisex perfumes which are new trend in the market which is still not completely understood.

8.1. Introduction

In what concerns to the industry and research of Flavors & Fragrances, it should be emphasized that although they go hand in hand in some issues such as chemical synthesis (*e.g.* new fragrant molecules), they are still far in others such as predicting odor quality. The reason for this is that we are still taking small steps in understanding the perception of odors. Whatever the physiology of odor perception may be, the sense of smell is keener than any other sense. The human nose, together with the olfactory receptor cells and their transduction with the brain, results in a complex but somewhat limited system for perceiving odors. In fact, as previously reviewed in Chapter 2, among hundreds of different odors present in a mixture, the human nose can only simultaneously distinguish few (*e.g.* one common example is that of coffee, see Parliment, 2002). Much has been done in recent decades to understand the mechanism of olfaction. In the recent past, the 2004 Nobel Prize in Physiology or Medicine was attributed to researchers working on olfactory perception. Throughout their work, they discovered the large family of olfactory receptors (OR), a good example of the

relevance and progress in this scientific field (Buck and Axel, 1991; Axel, 2005; Buck, 2005). Additionally, in food chemistry and flavor science much has been done aiming to characterize the odor of food and drinks (Fisher and Scott, 1997). For example, different studies were performed to evaluate the aroma profile of wines, spirits and soft-drinks, often using radar plots to relate the composition with their odor character based on perceptual judgments of enologists or flavorists (Ferreira, *et al.*, 2000; Buettner and Schieberle, 2001; Caldeira, *et al.*, 2002; Moyano, *et al.*, 2002).

Analogously, at the fragrance industry, major companies have within their technical staff not only chemists, biologists, or engineers but also perfumers, who are specialists in the art of smell by producing and formulating their fragrance mixtures. These experts are able to identify, characterize and classify different odors based on their appraisal and sensorial perception. The classification of odors has long been studied though it was not found yet the master key that opens the "Pandora box" for a universal classification of odors (Chastrette, 1997, 1998; Distel, *et al.*, 1999; Lawless, 1999; Pintore, *et al.*, 2006; Gilbert, 2008; Haddad, *et al.*, 2008). The number of classifications available (either from top F&F companies or experts) is large but the agreement between them is limited. Yet, there are several reasons that contribute to this uncertainty in olfaction (Milotic, 2003):

i) Perception of fragrances varies within people because the human olfactory system presents sensory-chemical differences (*e.g.* physiological).

ii) It is very difficult to characterize fragrances and scents by words, since people are not taught for different odors as they have with colors, shapes or sounds.

iii) People tend to associate smells to past experiences, objects, feelings and emotions which leads to a variety of classifications. Perfumers can be considered an exception as they tend to use the same language or olfactory descriptors which are more accurate (Jaubert, *et al.*, 1995).

iv) Fragrance companies do not share publicly a great amount of information about their fragrances or discoveries due to the high competition and money involved in this market.

v) Science behind perfume formulation is proprietary, so that the success of commercial perfumes is always unpredictable and mainly consumer-driven.

The way the human mind interprets the smell of the fragrances that reach our olfactory receptors is complex to be described. In a simple perspective it can be characterized by the pyramid of scents shown in Figure 8.1 that mimics a hierarchical process for the perception of scents (Teixeira, *et al.*, 2010). First, it is strongly influenced by our emotions, expressed by past experiences and memories, being the basis of all the following interpretations (Distel, *et al.*, 1999; Wilson, 2009). It is based on this primary knowledge that a person will then characterize a fragrance. Second, the reception of other sensory stimuli (sight, touch, taste, and hearing) will influence our decision-making (Morrot, *et al.*, 2001). It is only after these two steps that the classification of a fragrance really begins, first with a subjective analysis, and subsequently with an objective classification. In the former a large number of different sensations expressed by words like cool or warm, dry, fatty or powerful, and so on is commonly used to describe fragrances, especially by consumers (Milotic, 2003). This classification is usually wide and ambiguous, individual dependent and difficult to materialize. Finally, at the top of the pyramid of scents relies the most objective classification which is often given by perfumers (Milotic, 2003). It is more concise, formal and technical although the classification terms may also be ambiguous and different for the same fragrance ingredient or perfume mixture.

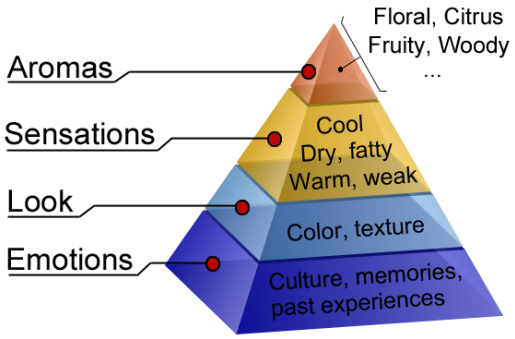


Figure 8.1 – The pyramid of scents perception.

Following this pyramidal structure it is possible to understand that the way we detect, recognize and classify the odors that we perceive is complex and involves neuronal processes. Thus, being a good perfumer entails using all four cognitive layers, cross-referenced. A deeper discussion on the use of “objective” and “subjective” descriptors for odors can be found elsewhere (Thiboud, 1991).

The interpretation and discrimination of odors seems to be easier for pure chemicals than for complex mixtures (Gilbert, 2008). Even though the attribution of a class or family to certain mixtures of scents might become simpler than for single chemicals (*e.g.*

for coffee blends or essential oils), the fact is that in the former what is being identified by the nose is only a limited number of components while the background ones are being neglected. This idea was first tackled by Laing (Laing, 1983, 1986; Gilbert, 2008), intrigued by the number of smells that the nose alone could pick out from a complex mixture. In his work, Laing proved that neither amateurs nor professionals could identify more than three to four odors (or volatile components) from mixtures. Moreover, as further odors are added to the mixture, the difficulty to identify even one of them increased. Recalling that the human nose can detect single smells at extraordinarily low concentrations, he concluded that *"we do a better job of collecting smells than we do of tracking them in a complex mixture"* (*in* Gilbert, 2008). In brief, the classification of single chemicals might be more concise, complete and truthful of its whole character than it is for mixtures (Jinks and Laing, 2001; Gilbert, 2008).

In the case of perfumes they can be classified according to the concentration of the perfume concentrate (*e.g. Eau de Parfum, Eau de Toillete, Eau Frâiche*) or to its olfactory family (*e.g.* Floral, Citrus, Woody) (Pybus and Sell, 1999; Zarzo, 2008). The amount of concentrate or essential oil in a perfume formulation can vary widely, depending on the purpose of the perfumed product. The composition of fragrance components ranges from 10–30% for some compounds, down to trace levels (ppm) for others. Solvents are also used in the formulation process, being ethanol and water the most common, as well as diethyl phthalate (DEP) or dipropylene glycol (DPG) (Schreiber, 2005; Sell, 2006; Surburg and Panten, 2006).

8.2. Classification of odors

The classification of odors has long been discussed and different classifications have been proposed, based on arbitrary distinctions among empirical, semi-empirical and statistical as will be presented briefly in this section. It should be noted though that a comparison between these classifications must be cautious since not all were developed with similar aims or supported by the same theoretical foundations.

The classification of single (pure) fragrances into families has been performed using different methodologies and techniques, as for perfume mixtures. The oldest classifications used to have a small number of olfactive families while recent ones tend to increase this number. Sometimes odorants are classified into one family only, while

others are assigned subfamilies or *nuances*. A *nuance* is a subtle change in the main olfactory sensation of a pure chemical or a mixture of fragrances.

The majority of these classifications were based on the human sensorial perception of experts, while others sought to describe the human olfactory space using statistical descriptors based on odor profiles, semantic descriptions and similarity data (Callegari, *et al.*, 1997; Chastrette, 1997; Wise, *et al.*, 2000; Mamlouk, *et al.*, 2003; Mamlouk and Martinetz, 2004). However, few comprehensive semantic odor-profile databases have been published until now (Arctander, 1969; Sigma–Aldrich, 2003 and for further details see Zarzo and Stanton, 2009). At this point, it is important to highlight that common terms are found in many of these perfume classification systems (as well as some differences) suggesting that an universal system for fragrance classification may be reasonable (Milotic, 2003).

Some of the first attempts to classify odors in family classes relied on empirical classifications and date back to the end of the XIX century when Zwaardemaker, the first major olfactory psychologist, proposed a classification based on degrees with 9 families (Zwaardemaker, 1927; Wise, *et al.*, 2000). At the beginning of the XX century Henning (see Wise, *et al.*, 2000) proposed a semi-empirical classification of primary odors attempting to clarify the idea of "complex odors" using an odor prism. Henning's prism comprised six corners labeled as putrid, fragrant, spicy, resinous, burned and ethereal. However, experimental tests produced great variations in where the different odors should be placed on the prism, and so Henning's theory fell out of favor (Wise, *et al.*, 2000). Later, Crocker and Henderson (Crocker and Henderson, 1927) proposed another semi-empirical classification system based on four families (fragrant, acid, burnt, caprylic) which was presented with a sample kit of 32 odorants (Ross and Harriman, 1949). On the other hand, there are several empirical classifications of fragrances based on the human olfactory interpretation, mainly developed by experienced perfumers of the most popular fragrance companies. Here can be referred the Odor Descriptor Wheel by St. Croix Sensory Company (McGinley, *et al.*, 2000) having eight families and dozens of subfamilies or the Rosace of Firmenich from 1972 (Chastrette, *et al.*, 1991) with thirteen families.

Furthermore, it is important to mention the work of Amoore (Amoore, *et al.*, 1975; Amoore and Forrester, 1976; Amoore and Hautala, 1983) which represents a more theoretical view of olfaction. His stereochemical theory was based on assertion of the relationship between odor and molecular chemical structures. This theory led him to

search for a limited number of discrete primary odor sensations based on specific anosmia studies that could express the sense of smell. It started to comprise 7 primary odors (ethereal, camphoraceous, musky, floral, minty, pungent, and putrid) which were later extended to 25 though there may exist hundreds of them (Amoore, *et al.*, 1975; Amoore and Forrester, 1976; Chastrette, 1998; Weiner, 2006; Haddad, *et al.*, 2008). From the most recent studies, it should be mentioned the works of Dravnieks with the Atlas of odor character in 1985 (Wise, *et al.*, 2000), the Field of Odors in 1987 from J.N. Jaubert *et al.* (Jaubert, *et al.*, 1995), the olfactory space in 1997 from P. Laffort *et al.* (Callegari, *et al.*, 1997), and, more recently, the perceptual space in 2008 from M. Zarzo (Zarzo, 2008) which tried to classify fragrances by structure odor relationships (SOR) or similarity tests using extensive databases of descriptors (for further details see Chastrette, 1997, 1998; Pintore, *et al.*, 2006; Haddad, *et al.*, 2008). However, on simple perceptual grounds the lack of clarity for the interpretation of these multidimensional scaling analyses with n-dimensional spaces is a difficulty for their application by non-experts.

In conclusion, in the past years we have enlarged the available database of odors and chemical structures and learned in a more detailed level the mechanism between odorants and olfactory receptors. However, we are still far away from understanding their exact structure, and the way signal transduction and interpretation are processed (especially for character recognition), which limits any deeper interpretation of the olfactory mechanism (Rowe, 2005).

In this work four databases were selected for the assignment of olfactory families to single fragrances (pure compounds). The literature databases of Brechbill (Brechbill, 2006), Sturburg and Panten (Surburg and Panten, 2006), The Good Scent Company (2009) and an in-house developed compilation of olfactive families from several perfume companies were considered, including more than 2000 fragrant species. However, it should be mentioned that the Brechbill database was the first reference of choice while the remainder were used when the former had no classification assigned. Whenever more than one family was attributed, the most representative family was considered as primary family and the following classes were considered as subfamilies or *nuances*. Additionally, when there were discrepancies between the primary families assigned in different databases the criterion was to consider the families of the Brechbill's database and then include as subfamilies the classifications of the remaining databases. The relative distribution of each family or descriptor according to the

Brechbill's dataset is represented in Figure 8.2. It is readily apparent that the Floral family is the one that holds the largest share of the distribution among the fragrance raw materials (21%), not overlooking that the families named "Rose" (11%) and "Jasmine" (3%) also represent scents of flowers and are not negligible. This fact mirrors what is observed in commercial perfumes, where the number of floral fragrances is very significant, especially in women's perfumes.

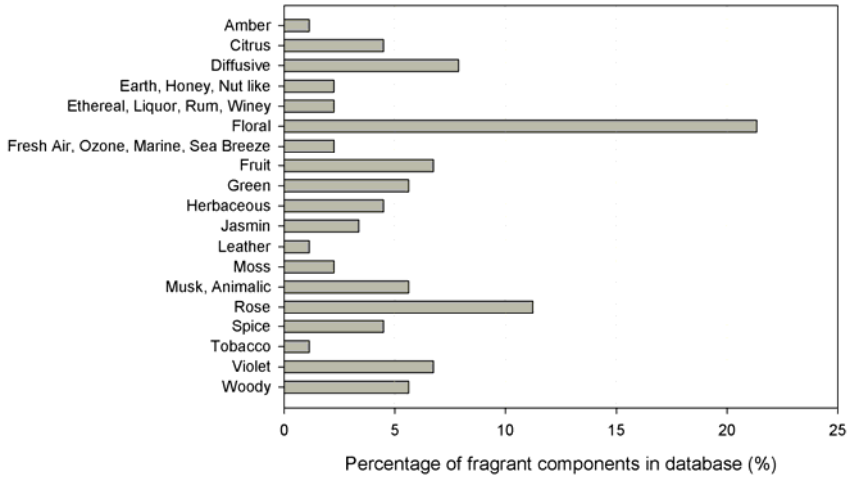


Figure 8.2 – Relative distribution of each olfactory family or descriptor in the database used for this work.

8.3. Classification of perfumes

In what concerns to perfumes, several attempts have been made in the past trying to associate such complex mixtures to olfactory families. This type of classification is often called fragrance genealogy. Perfumes generally have around 50-100 fragrant components in their formulation, with several functional groups within this high number of molecules (hydroxyl, carbonyl, ether and many others). Due to this complexity, they are often qualitatively classified into olfactory families attending to the dominant fragrant notes. Although the Flavor & Fragrance industry employs sophisticated analytical tools in perfumery (*e.g.* GC/MS, olfactometers, electronic-noses), so far there is not yet a standard classification of perfumes in view of their olfactory nature (perfume families). Nowadays, each perfume is empirically attributed to a class or family (floral, citrus, chypre, oriental, etc), with or without subfamilies or *nuances* in it. This classification process is often done by experienced perfumers based on their large experience categorizing commercial fragrances into families. Thus, it is mainly experimental, person-sensitive and, perhaps more important of all, it is only applied in the post-formulation step. The fact is that even among these experts in the art of

perfumery there are biological differences in their olfactory response to fragrance stimuli, resulting in different classifications (Jinks and Laing, 2001; Gilbert, 2008). However, it is important to point out that the classification of perfumes could also be performed by consumers that have little to no experience in the art of perception of odors. In 1992, Jellinek tried to follow this hypothesis and presented a consumer-based classification for perfumes in its "Map of the world of fragrances" and "Odour effect diagram" (Milotic, 2003). In what concerns to the empirically-based classifications there are some available in the literature, most of which were developed by Flavor & Fragrance companies. Jean Carles (Carles, 1962), a famous perfumer of the last century, classified fragrances in a series of perfumery notes when proceeding with his methodology for perfume design. Additionally, an extensive study from the survey of all perfumed products developed since 1782, lead to the "*Classification des Parfums et Terminologie*" by the French Society of Perfumers (1984) (Société-Française-des-Parfumeurs, 2006). It was divided into five main olfactory families, plus several secondary families or *nuances*. Later on, a second study outlined in 1989 included the contribution of two new families, citrus and woody, and the addition of secondary families (Société-Française-des-Parfumeurs, 2006). Besides, some fragrance companies like Avon (USA) (Avon, 2009) classifies perfumes into six different families, each one comprising two subfamilies or *nuances*, while the Fragrance Wheel developed by perfumer Michael Edwards (1983) considers four standard family notes having each one three subfamilies as presented in Figure 8.3 (Edwards, 2009).

Figure 8.3 – The fragrance wheel from Michael Edwards (Edwards, 2009).

This acclaimed perfumer has developed an extensive database for perfume classification, the well known Fragrances of the World encyclopedia, that comprises fourteen primary

families and has been recently incorporated into The Fragrance Foundation library (Edwards, 2009). Edwards has already classified more than 5700 commercial perfumes using these fourteen categories displayed around a central hub, except for aromatic/fougère, which in some cases is placed at the center of the wheel as it will be discussed later (Zarzo and Stanton, 2009).

Another very good classification map for fragrances or perfumes is the "Drom Fragrance Circle" (DROM, 2011) shown in Figure 8.4. It considers sixteen olfactive families classified by perfumers (outside band) and consumers (inner band) related terms. In the middle band some examples of essential oils are given for each family. Moreover, in the center of Figure 8.4 is shown an example for a classification of an essential oil where the intensity of the olfactory families is represented through five (in this case) colored intensity slices, thus generating a stellar map.

Figure 8.4 - Drom Fragrance Circle: different layers are used to relate the classifications of essential oils using perfumers related terms and those from consumers.

The experimental classifications of Osmoz by Firmenich (Firmenich, 2009) has a six group family criteria for both women and men with various *nuances* in each one. Scent Direct (ScentDirect, 2009) and H&R Genealogy by former company Haarman & Reimer (H&R, 2002) divide their classification in six and four families with different subfamilies, respectively. Octagon, by former company Dragoco, now merged with Haarman & Reimer into Symrise, has nine perfume families. It is curious that there is a more detailed description of the floral family in this classification differentiating between simple and complex floral accords. Finally, a compilation study on thousands of commercial perfumes made by Luca Turin and Tania Sanchez (LT & TS), a recognized scientist and a perfumer, classifies fragrances into a large number of olfactive families, always giving a touch of their personal assessments about them

(Turin and Sanchez, 2008). However, it should be mentioned that in some cases the definition of the correspondent family was somewhat ambiguous. Finally, it is to be said that other fragrance classifications have been proposed but in most cases, their details still remain confidential (Zarzo and Stanton, 2009).

In this work a new approach for perfume classification has been developed. The aim of the Perfumery Radar (PR) methodology is to predict the classification of perfumes into olfactive families as performed by perfumers using physicochemical models and qualitative descriptors. The methodology combines the use of radar graphs (to present qualitative information) with some Product Engineering tools and concepts previously developed (Mata, et al., 2004). The Osmoz, Scent Direct, H&R Genealogy, Octagon, The Fragrance Foundation, and Luca Turin & Tania Sanchez perfume classifications were used for comparison with the proposed methodology for the classification of perfumes. All these classifications of perfumes defined along with the one from this work are presented in Table 8.1.

Table 8.1 - Perfume families used from different fragrance companies and in this work.

	FSP [a)]	FSP [b)]	AVON [c)]	TFW [d)]	Osmoz [e)]	SD [f)]	H&R [g)]	Octagon [h)]	This work
Citrus		x	x	x	x				x
Floral	x	x	x	x	x	x	x		x
Green				x					x
Fruity				x					x
Herbaceous									x
Musk									x
Oriental			x	x	x	x	x	x	x
Woody		x	x	x	x			x	x
Chypre	x	x	x		x	x	x	x	
Fougère	x	x	x			x	x	x	
Leather	x	x							
Amber	x	x							
Fresh				x					
Dry Woods				x					
Floral-Oriental				x		x			
Mossy Woods				x					
Soft-Floral				x					
Soft-Oriental				x					
Water				x					
Woody-Oriental				x					
Aromatic					x				
Aromatic-Fougère				x					
Cedar						x			
Aromas								x	
Eau de cologne								x	
Floral Simple								x	
Floral Transparent								x	
Floral Bouquet								x	

[a)] French Society of Perfumers (FSP, 1984); [b)] French Society of Perfumers (FSP, 1989); [c)] AVON; [d)] The Fragrance Wheel (TFW) by Michael Edwards in The Fragrance Foundation (1983); [e)] Osmoz by Firmenich; [f)] Scent Direct (SD); [g)] Haarmann & Reimer (H&R); [h)] Octagon by Dragoco.

8.4. Perfumery Radar (PR) methodology

The proposed Perfumery Radar (PR) methodology intends to improve perfume classifications based not only on a classification of pure fragrances, but also their evaporation process and their odor intensity. This will allow reducing the arbitrariness to the empirical classification of pure fragrance chemicals for the prediction of the odor character of perfumes and assign them to olfactive families. The PR methodology considers that among all the fragrant species present in a perfume mixture there will be some that produce a stronger sensation, thus contributing more significantly to its overall scent. The proposed PR methodology can be structured into the following steps:

1. Classification of pure fragrances in olfactory families;
2. Prediction of the odor intensity for each fragrance using the Odor Value (OV) concept (Teixeira, *et al.*, 2009b);
3. Determination of the OV for each olfactory family and representation in the Perfumery Radar;

Once then, a comparison between the predicted Perfumery Radar and the classifications from the perfumers is established for commercial perfumes. A schematic representation of the PR methodology along with the main steps and procedures followed for its validation are presented in Figure 8.5.

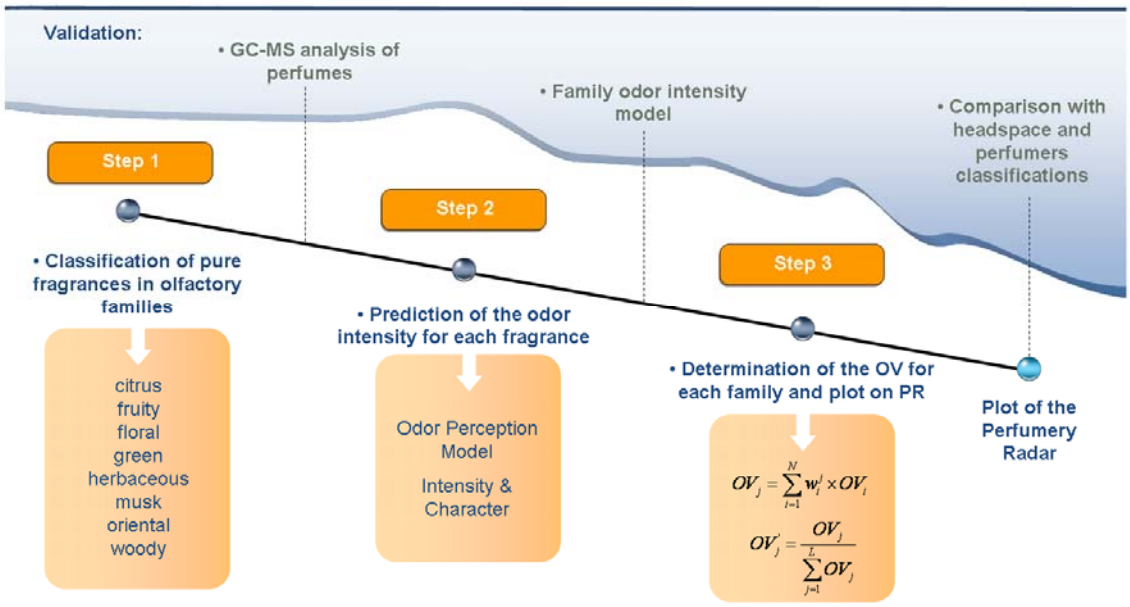


Figure 8.5 – Schematic view of the PR methodology.

In this way, the first step consisted in the compilation of an extensive database for the classification of pure fragrances and selection of the olfactive families, as previously mentioned. In the PR methodology eight olfactory families (citrus, floral, green, fruity, herbaceous, musk, oriental, and woody) were considered for perfume classification based on the criteria of the most commonly used terms for the classification of pure fragrances. The positioning of the families around the radar axis took into account the traditional subfamilies or *nuances* existing in each family, so that closer axis usually traduce families that blend well in perfumery products. Since the number of classifications available in the literature is vast and here only eight families were selected, a brief description of each family will be presented ahead (Poucher, 1955; Calkin and Jellinek, 1994; Butler, 2000; Brechbill, 2006; Edwards, 2009; Firmenich, 2009; Leffingwell and Leffingwell, 2011):

i) *Citrus:* freshness and lightness from citrus fruits like lemon or orange. The first *"Eau de Cologne"* ever made belonged to this family.
ii) *Fruity:* from natural fruits like apple, banana, or raspberry.
iii) *Floral:* made up of flowers (*e.g.* geranium, jasmine or rose) is one of the most widely used families for feminine fragrances.
iv) *Green:* typical botanical notes with scents of fresh leaves or stalks and mown grass or with reminiscent freshness. Examples are vertocitral, or hexenyl benzoate.
v) *Herbaceous:* more complex scents than green, often found in low-growing plants. Typical examples are sage and mint.
vi) *Musk:* characteristic from the musk deer and musk oxen. The odorants of this family when used in perfumes often act as fixatives (components that fix other fragrances in the solution).
vii) *Oriental:* associated to amber species, often including warm scents. The classifications found in the literature for scents like spicy, earth, balsamic, tobacco, leather, waxy, and mossy were included in this family.
viii) *Woody:* generally as woods like cedar, sandalwood, or patchouli. A classification of fragrances as camphoraceous was included in this family.

Then, in step 2, several commercial feminine perfumes were analyzed through gas chromatographic techniques (GC/FID/MS) to identify and quantify single fragrant

components. The composition of each perfume (x_i, mole fraction of each fragrant compound) was normalized according to the parameters defined in Table 7.1 – Chapter 7 and Annex E, and a definite amount of water (solvent) was considered for each perfume type (*Eau de Parfum, Eau de Toilette, Eau Frâiche*). For the prediction of the Odor Value (OV), several physicochemical and psychophysical properties (molecular weight, vapor pressure, UNIFAC interaction parameters, odor detection threshold) were needed. These were compiled for all the fragrant compounds. Here, it should be mentioned that for the odor intensity the OV concept was preferred in detriment to the well known Stevens' Power Law (Stevens, 1957) due to the lack of available data (the number of published exponents is less than 10% of the number of existent fragrant compounds). Furthermore, the vapor-liquid equilibrium (VLE) was predicted using the UNIFAC method for the calculation of activity coefficients (γ_i) in the liquid phase. For this, molecules were fractioned in functional groups and the group-group interaction parameters were selected from the literature (Poling, *et al.*, 2004). This step ended with the calculation of the OV for each fragrant compound (see Chapter 3, equation 3.4). In step 3, the overall OV (summation of the OVs of all the fragrant components) of each olfactory family was calculated considering the pure fragrance classification. However, it should be mentioned that the summation of the OVs for the quantification of the olfactive family intensity is an approximation considered in our model. Effects like hypoadditivity of odors (the perceived odor intensity of a mixture to be lower than the sum of the perceived odor intensities of the single components) are not considered here. There are several models in the literature attempting to express the odor intensity and character of mixtures of odors (Vector, U and Γ models, among others) but they are valid for binary to quaternary mixtures only (which is insufficient for perfume mixtures). Moreover, none of them has imposed over the others, as has been shown in different comparisons in the literature (Laffort and Dravnieks, 1982; Olsson and Berglund, 1993; Cain, *et al.*, 1995). Thus, possible effects of mixtures of odors have been neglected in this methodology for perfume perception (Cain, *et al.*, 1995; Cometto-Muniz, *et al.*, 2005). Other particular olfactory effects are also out of the scope of the model since its purpose is to obtain a qualitative analysis in terms of olfactory families. Here, since literature classifications differ or attribute one or more families/subfamilies to the fragrances, a weighing criterion was considered in order to take into account the presence of *nuances*, as presented in Table 8.2. This way, a family odor intensity model was developed, accounting for weights in each olfactive family, as will be seen ahead.

Moreover, the quantification of odor intensity was done by means of the odor value (OV) concept as aforementioned (Mata, *et al.*, 2005; Teixeira, *et al.*, 2009b).

Table 8.2 - Distribution of weights (w_i) for each olfactive family.

Number of Families	Family		
	Primary	Secondary	Tertiary
1	100%	-	-
2	70%	30%	-
3	60%	30%	10%

Finally, the PR methodology ends with the representation of the predicted odor intensity for each olfactory family using radar plots and their comparison with the classifications from perfumers. Thus, this methodology will allow the prediction of the OV to determine the olfactory family of perfumes using radar plots.

The experimental validation of the PR methodology was done, first using simple essential oils, and later with commercial feminine and unisex perfumes already classified into olfactory families by experienced perfumers. The former are simple mixtures with 30 or less fragrant compounds in their composition while the later (the perfumes) are more complex having 50-100 or more components. A validation of the predictive power of the PR methodology was also performed by analyzing the gas phase above the perfume (headspace) in equilibrium conditions using GC-FID/MS and then calculating the PR from real (not predicted) gas compositions.

8.4.1. The Odor Value (OV) Concept

The Odor Value (OV) has been thoroughly used and discussed in previous Chapters. It is a dimensionless quantitative parameter that measures the odor intensity of fragrant molecules. It is calculated as the concentration of an odorant species *i* in the gas phase above a liquid mixture, C_i^g , divided by its concentration odor threshold, ODT_i, as expressed by equation 8.1.

$$OV_i = \frac{C_i^g}{ODT_i} \tag{8.1}$$

The odor detection threshold is a psychophysical parameter which is remarkably important for the prediction of the OV, and so, an analysis of its data availability,

application, and validity will be discussed later in this Chapter. Furthermore, the concentration in the gas phase (headspace) of a single fragrant, C^g_i, can be predicted using the modified Raoult Law for vapor-liquid equilibrium (VLE), so that the OV can be expressed as:

$$OV_i = \gamma_i x_i \left(\frac{P_i^{sat} M_i}{ODT_i} \right) \left(\frac{1}{RT} \right) \tag{8.2}$$

where M_i is the molecular mass of component i, R is the universal gas constant, and T is the absolute temperature. This way, the OV accounts for non-idealities in the liquid phase by means of the activity coefficient, reflecting the interactions of the molecules with their surrounding medium. All activity coefficients were predicted using the UNIFAC group contribution method (Poling, *et al.*, 2004). The application of predictive methods like UNIFAC for multi-component VLE is complex and deviations are expected to occur. The details on the application and validation of the UNIFAC method were already discussed in Chapter 5. However, it is a thoroughly developed tool, suitable for the purpose of this work, allowing it to give a qualitative view of the olfactory character instead of a quantitative one. It should be noted that alternative odor intensity models may be used in the PR methodology, such as the Stevens' Power Law (Stevens, 1957). Nevertheless, this model uses one further parameter, the Power Law exponent, which is obtained experimentally. Literature data for these exponents are scarce, which limits the application of the model. Thus, for engineering and predictive purposes, the OV has been preferred.

8.4.2. Odor thresholds databases

The measurement of odor thresholds has been studied by researchers from different scientific fields for more than a century. The reported values and measurement techniques have increased since then. Data on odorant thresholds cut across a large number of fields in the scientific literature (AIHA, 1989; Cain and Schmidt, 2009). There are some compilations of odor thresholds available in the literature (van Gemert and Nettenbreijer, 1977; Fazzalari, 1978; Amoore and Hautala, 1983; AIHA, 1989; Devos, *et al.*, 1990; Calkin and Jellinek, 1994; van Gemert, 1999; van Gemert, 2003). In this work the most recent compilation of van Gemert (2003) was used for collecting the

odor detection thresholds of the fragrances (van Gemert, 2003). Although odor recognition thresholds are of great value for the evaluation of odor quality, detection thresholds were selected due to a larger number of available data in comparison with that for recognition thresholds. Considering the number of different odorant compounds involved in these perfumes, many fragrances would have to be neglected due to the lack of available odor recognition thresholds. While being very useful, these databases on odor thresholds present also some flaws. The fact is that these compilations report either average values or ranges of thresholds without criticizing the experimental methodologies used in the original references (Cain and Schmidt, 2009). Additionally, they cover a period of more than a century, during which analytical methods and scientific equipments have evolved. Olfactory data is dependent on the individual physiological differences, measurement techniques and psychological factors (Chastrette, 1998). Among the variables that influence threshold measurement it is important to highlight the olfactometric equipment used, the nature of the panelist (age, sex, expertise), the stimuli type (water, gas vapor or other media) and flow rate, and the type of threshold measured (detection, recognition or difference threshold) (Consultants, 1989; Chastrette, 1998). Hence, it is often recognized that heterogeneous databases have a wide variability of data, meaning that its handling has to be careful. These issues on odor threshold data were also presented earlier in Chapter 4. An example of the variability of odor thresholds found in literature databases is the well known and widely used n-pentyl acetate (banana odorant). Comparing its odor threshold data from Devos et al. (1990) and from van Gemert (1999) it is seen a variation of three orders of magnitude. However, if we consider the geometric means, it obtained values of 139 ppb and 212 ppb, respectively. This evidences the need of using some criteria when analyzing and using odor threshold data (Cain and Schmidt, 2009). Additionally, for n-butyl acetate (also banana scent) the range of values varies four orders of magnitude. In sum, since odor thresholds are obtained from individuals, the use of any single investigation could suffer limitations of small sample sizes and bias of methodology (Consultants, 1989; Grosch, 2001; Cain and Schmidt, 2009). It is desirable to use averaged or recommended best estimate values compiled from a large set of data. The geometric mean value was used in this work since it is a recommended procedure, commonly used in sensory analyses (Cain and Schmidt, 2009). The use of averaged values minimizes differences between data and allows predictions of the model based

on population averages. Moreover, when threshold data were presented as a range of values, the average of the two extremes was considered.

8.4.3. Perfume diffusion model

A previously developed diffusion model was applied to account for the evaporation and diffusion of commercial perfumes in air over time *(t)* and distance *(z)* (Teixeira, *et al.*, 2009a). This model is based on Fick's law for diffusion and allows the prediction of the perceived odor over time and distance for the commercial perfumes. The model considers a small volume of liquid perfume like when it is sprayed on a paper blotter or in the surface of the body. Then, this liquid is allowed to evaporate over time and diffuse upward through the gas phase above it (headspace). This way it is possible to mimic the spraying of a perfume on a surface and its evaporation into the air by simulating its diffusion. The volume and composition of the liquid perfume will be changing with time as the evaporation process takes place. This model has been presented in detail in Chapter 6 and in (Teixeira, *et al.*, 2009a). The application of the diffusion model in this study with feminine perfumes will allow predicting the evolution of the odor character shown in the perfumery radar with time.

8.4.4. Olfactory family odor intensity model

It is known that perfumes are complex mixtures with tens of components and thus a complex pattern is developed in the brain for their interpretation. This pattern generation at the brain centers used in processing of olfactory signals is also created when smelling pure chemicals. However, their discrimination at identifying its constituents is more complex for mixtures, as mentioned before. Perfumes (and even pure fragrances) are often classified in subfamilies or *nuances* to further describe their perceived odors.

The first simulations performed with the PR methodology considered the summation of all the OVs of the fragrances attributed to each olfactive family according to equation 8.3:

$$OV_j = \sum_{i=1}^{N} OV_i \tag{8.3}$$

where *j* represents a family type, *i* the single fragrant species in perfume which belongs to family *j*, and *N* the total number of fragrant species identified in the perfume belonging to family *j*.

However, this procedure showed some flaws since in most cases just one family dominated the overall scent, so that the effect of *nuances* in the smell of perfume mixtures was lost. In order to overcome this, and following what experience dictates in the evaluation of complex, multi-component odors, the model was improved considering primary, secondary and tertiary families. The pure fragrance classification of Brechbill (Brechbill, 2006) was used, which has a primary odor family and provides some comments or a description of the fragrance quality. Thus, the primary odor family is the first family indicated by Brechbill and whenever other families were referred, these were used as secondary (and tertiary) families according to the order of appearance or relevance given. Moreover, weight factors were assigned to each family. The distribution considered that the primary olfactive family is more strongly perceived than the secondary, followed by other families with smaller weights. A tripartite structure was defined as presented in Table 8.2. There were considered only three families or subfamilies since for pure substances an average value of 3 descriptors per odor is considered sufficient (Chastrette obtained an average of 2.8 for thousands of odorants - Chastrette, 1998). Thus, equation 8.3 becomes:

$$OV_j = \sum_{i=1}^{N} w_i^j \times OV_i \tag{8.4}$$

where w_i^j is the weight factor of component *i* for family *j* according to Table 8.2. The selection of the weight factors was arbitrary, considering the more intense perception of the primary over the secondary family, and that over the tertiary. It should be highlighted that these weights may vary from odorant to odorant but the fragrance classifications do not present any quantitative information concerning that point, and the same weight factors were used for all fragrances. In order to make the Perfumery Radars independent of the total odor intensity, these family odor values (OV_j) were normalized according to:

$$OV_j^{'} = \frac{OV_j}{\sum_{j=1}^{L} OV_j} \tag{8.5}$$

where $OV_j^{'}$ is the normalized odor value for family j and L is the number of olfactory families defined (in this work L = 8). This allows comparing all the Perfumery Radars in a scale independent of the odor intensity.

8.5. Materials & Methods

Commercial perfumes studied in this work correspond to real perfumes of recognized brands and in excellent state of preservation. The essential oils were obtained from Mondeconatur (Spain). The liquid composition of these essential oils and the selected commercial perfumes was analyzed through gas chromatography coupled with FID and MS detectors to quantify and identify fragrant species, respectively. The simultaneous analyses were carried out in a Varian CP-3800 instrument equipped with two parallel split-splitless injectors and two CP-Wax 52 CB bonded fused silica polar columns, 50m length, 0.25mm i.d., 0.2μm film thickness. The detection system was composed of a Varian FID detector and a Varian Saturn 2000 MS ion-trap mass spectrometer, both controlled by the Saturn 2000WS acquiring software. The oven was initially set at 50 ºC for 5 min, then raised up to 200 ºC at a rate of 2º C/min, and finally hold isothermal for 40 min. The temperature of both injectors was 240 ºC, with a split ratio of 1:50 for FID and 1:200 for MS. The FID detector was set at 250 ºC, and helium N60 was used as carrier gas with a flow rate of 1 ml/min. Sample volume injected in the GC equipment was 1μL of essential oil or commercial perfume mixture. For the FID data, a lower-limit value of peak area (<10000 counts) was considered in the integration process to exclude components or residues present in the analysis of the perfumes. It is known that at very low peak areas the noise-to-signal ratio in FID detectors is high, thus introducing errors in the composition. Moreover, the peak identification performed by MS turns also more difficult whenever the chromatographic peaks are too small. Additionally, accounting for peaks much below this limit (*e.g.* 1000 counts) would significantly increase the number of components and so make its identification too laborious and almost impractical. However, care should be taken with this rejection, once powerful odorants

may be present in trace amounts (have small chromatographic peak areas). Nevertheless, a lower limit is necessary to avoid misidentification of peaks in the analysis of the perfume. The analysis of the MS data for pure component identification was performed using the NIST98 spectral library, an in-house library (with pure reference species) and literature data. The headspace FID-MS analyses for the selected perfumes were performed with SGE gas-tight syringes using 1mL of gas sample. The chromatographic experimental conditions were the same as for the liquid analyses, except that the split ratio was set to 1:2 for FID.

All calculations done throughout this work for the UNIFAC method and the radar plots were run using the MATLAB® software. For the diffusion model, the non-linear system of 2*N* equations (with *N* equal to the number of identified components in a perfume with an integrated peak area above 10000 counts) was solved in MATLAB. The program used the *pdepe* package for numerical computation of partial differential equations (PDE). The program developed solves initial-boundary value problems for systems with parabolic and elliptic PDEs in one space variable *(z)* and time *(t)* (MathWorks, 2002). From the discretization in space the ordinary differential equations (ODE) obtained were integrated using the *ODE15s* solver package to approximate solutions over time *(t)*. The ODE solver is applicable to initial value problems and is based on the numerical differentiation formulae (NDFs), using the finite differences method for the discretization of the space variable (Nocedal and Wright, 1999; Chapman, 2000; Chapra, 2002).

8.6. Results: applications of the PR methodology

In the first part, the Perfumery Radar (PR) methodology was first applied to simple essential oils of orange and lemon (citrus), jasmine (floral), and thyme (herbaceous). Then, 14 feminine commercial perfumes belonging to various perfume families were selected to validate the PR methodology comparing simulations with experts' results. In this study, the radar plots were first performed at time t = 0 min, which means sniffing immediately after opening the bottle of perfume. Diffusion or convection processes were not considered for the purpose, only evaporation was taken into account. Additionally, a diffusion model was applied to two commercial perfumes in order to mimic the usual procedure for perfume testing and to show the evolution of the

perfumery radars with time. In the second part, the PR methodology was applied to unisex fragrances.

8.6.1. Essential oils

The classification of the essential oils in olfactive families is presented in Table 8.3 and the perfumery radars are shown in Figure 8.6. The essential oils of orange and lemon are both classified as citrus in the literature, and the two radars are similar, as expected. It should be emphasized that these essential oils although they are both obtained from citrus fruits, it is axiomatic that they will smell different. In fact, their composition is similar but there are some odorants in one essential oil and not in the other, making their perceived scents different. Although their perfumery radars evidence subfamilies or *nuances*, there is a predominance of the citrus axis with 44% and 49% for orange and lemon oils, respectively. As expected from everyday experience, lemon has a stronger "citrus" character than orange. Attending to their subfamilies, the orange essential oil shows predicted woody-fruity-floral *nuances* while lemon essential oil has a fruity-floral-woody character. It is to highlight that the difference in their order comes from the difference in their intensity, which will be traduced in differences in their perception. However, the major difference between both essential oils is the green character perceived in the orange but not in the lemon essential oil. The essential oil of jasmine is a classic floral mixture commonly used in perfumery. Its perfumery radar reveals a dominant floral scent (71%) with a fruity *nuance* (27%). Finally, the thyme essential oil is usually obtained from extraction of a perennial shrub (*Thymus vulgaris L.*) and is used in medicinal, food and fragrance products. It has a characteristic herbal scent which is also seen from the predicted perfumery radar where the herbaceous family dominates (48%), together with certain citrus and fruity *nuances*.

Table 8.3 - Olfactive families of the essential oils based on the database of Brechbill (Brechbill, 2006).

Essential Oils	Family
Orange	Citrus
Lemon	Citrus
Jasmine	Floral
Thyme	Herbaceous

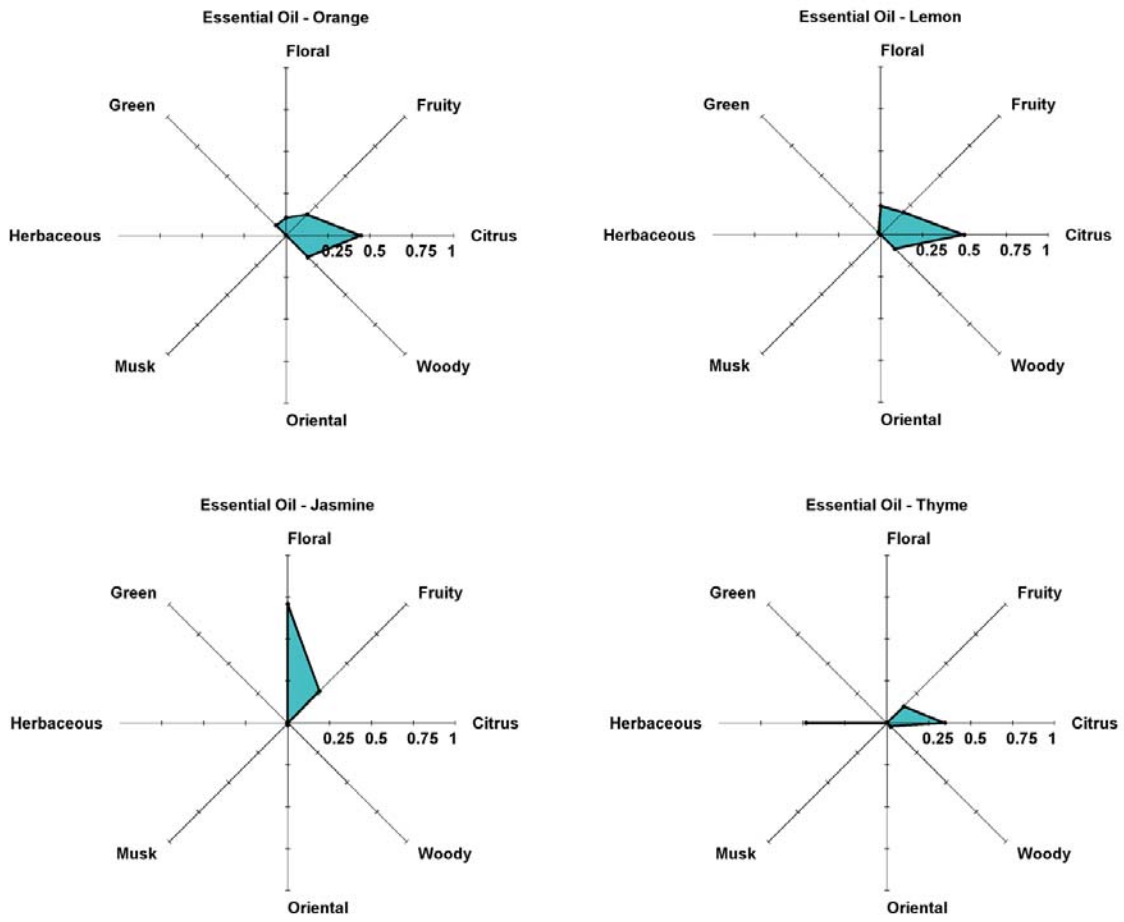


Figure 8.6 – Perfumery Radars of the essential oils.

Thus, the perfumery radars of the analyzed essential oils show some subfamilies or *nuances* in their perceived odor, however it is seen that the predicted primary olfactive family always hits the classification from the perfumers.

8.6.2. Feminine commercial perfumes

Relatively to the analyses and simulations of feminine commercial perfumes, Table 8.4 presents their commercial name, brand, and the olfactive family according to six different classifications together with the PR classification. As previously stated, it is important to remember that these classifications are based on empirical evaluations made by perfumers of the respective company. Among the perfumes listed in Table 8.4, it is clearly seen that some of them are classified equally in the primary olfactive family by the majority of the companies while others (P12-P14) have different classifications. However, significant differences are seen among them for the classification of the secondary and tertiary olfactive families.

Table 8.4 - Commercial name, brand, and family classification of the selected perfumes.

#	Perfume	Brand	Osmoz (Firmenich)	Scent Direct	H & R	Dragoco	The Fragrance Foundation	LT & TS	This work
P1	L'air du temps	Nina Ricci	Floral-Spicy	Floral	Floral	Floral Bouquet	Floral	Floral-Green	Floral-Green
P2	Paris	YSL	Floral-Rose Violet	Floral	Floral	Floral Simple-Rose	Floral	Rose	Floral
P3	Chanel 19	Chanel	Floral-Green	Floral-Green	Floral-Green-Fruity	Floral Simple-Green	Soft Floral	Green-Floral	Floral
P4	Eau de Givenchy	Givenchy	Floral-Fruity	Floral-Fruity	Floral-Fruity	Floral Transparent	Floral	Green-Floral	Floral
P5	Addict	Dior	Oriental-Vanilla	Oriental-Floral	-	-	-	-	Oriental-Woody
P6	Addict EdF	Dior	Oriental-Floral	-	-	-	-	-	Oriental-Fruity-Green
P7	Gloria	Cacherel	Oriental-Woody	Oriental-Fresh	-	-	-	Amber-Rose	Fruity-Oriental
P8	Eau de Rochas	Rochas	Citrus-Aromatic	Chypre-Fresh	Chypre-Fresh	-	-	Citrus-Woody	Chypre
P9	Ô de Lâncome	Lâncome	Citrus-Aromatic	Chypre-Fresh	Chypre-Fresh	-	-	Fresh-Citrus	Chypre
P10	Miss Dior	Dior	Chypre-Floral	Chypre-Floral-Animalic	Chypre-Fruity	Chypre-Green	-	Dry Chypre	Chypre-Green
P11	Ma Griffe	Carven	Chypre-Floral	Chypre-Floral	Chypre-Animalic	Chypre-Fruity	Mossy Woods	Green-Chypre	Floral-Green
P12	Jungle Tigre	Kenzo	Oriental-Spicy	-	Chypre-Fruity	Floral-Fruity	-	-	Floral-Green
P13	CK One	Calvin Klein	Citrus-Aromatic	Chypre-Fresh	Chypre-Fresh	Floral Transparent	-	Citrus	Woody-Fruity
P14	Le Feu d'Issey Light	Issey Miyake	Floral-Woody-Musk	-	Oriental-Spicy	Woody-Spicy	Soft Floral	Milky Rose	Green-Floral-Musk

The chemical analyses by GC/FID/MS provided the composition of the fragrances and ethanol, but not water. Thus, water concentration was fixed according to the type of perfume (*"Eau de parfum"*, *"Eau de toilette"*, *"Eau de cologne"*) and literature data shown in Table 7.1 – Chapter 7. The composition of all other components was calculated directly from gas chromatographic peak areas without any correction factor (see Appendix E). The Perfumery Radars simulated at initial times (t = 0 s) for the commercial perfumes with primary olfactive families, Floral, Oriental and Chypre are presented in Figure 8.7 to Figure 8.9, respectively. Perfumes with a heterogeneous classification are presented in Figure 8.10.

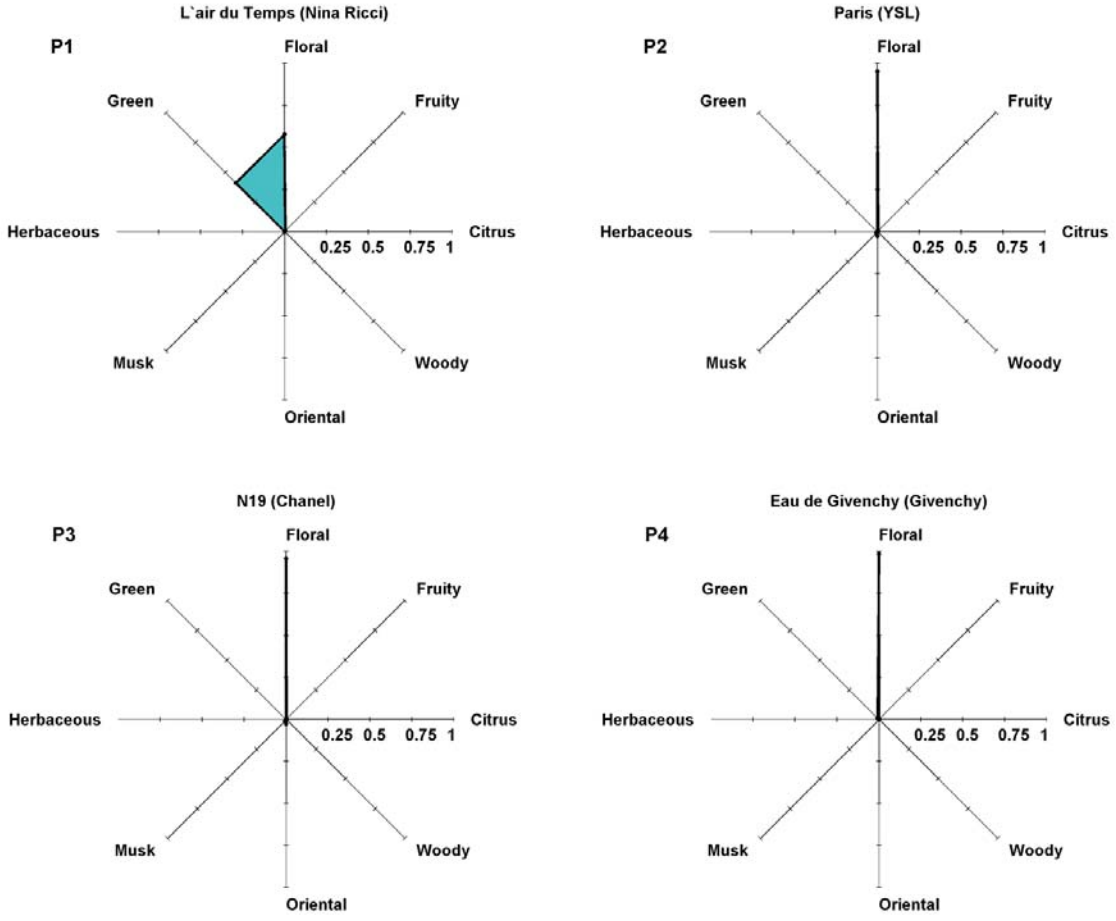


Figure 8.7 – Perfumery radars for perfumes P1-P4 (Floral primary olfactive family).

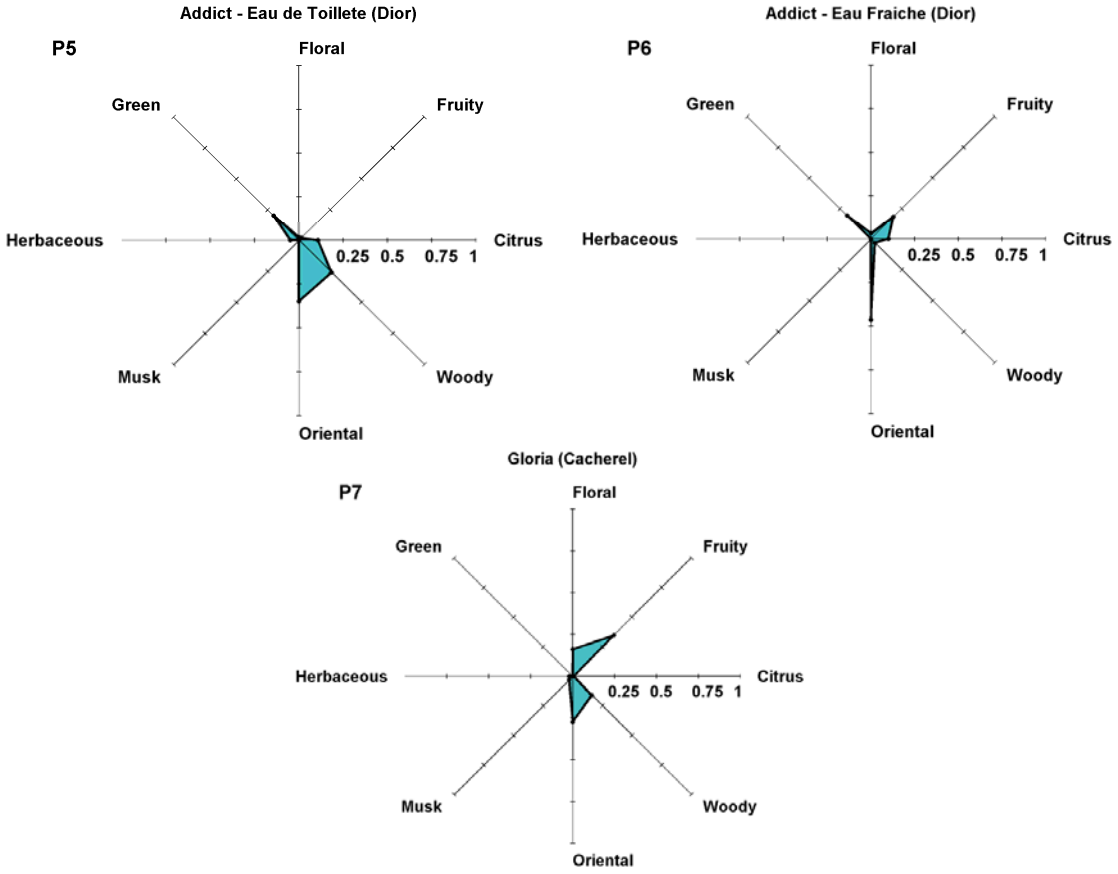


Figure 8.8 – Perfumery radars for perfumes P5-P7 (Oriental primary olfactive family).

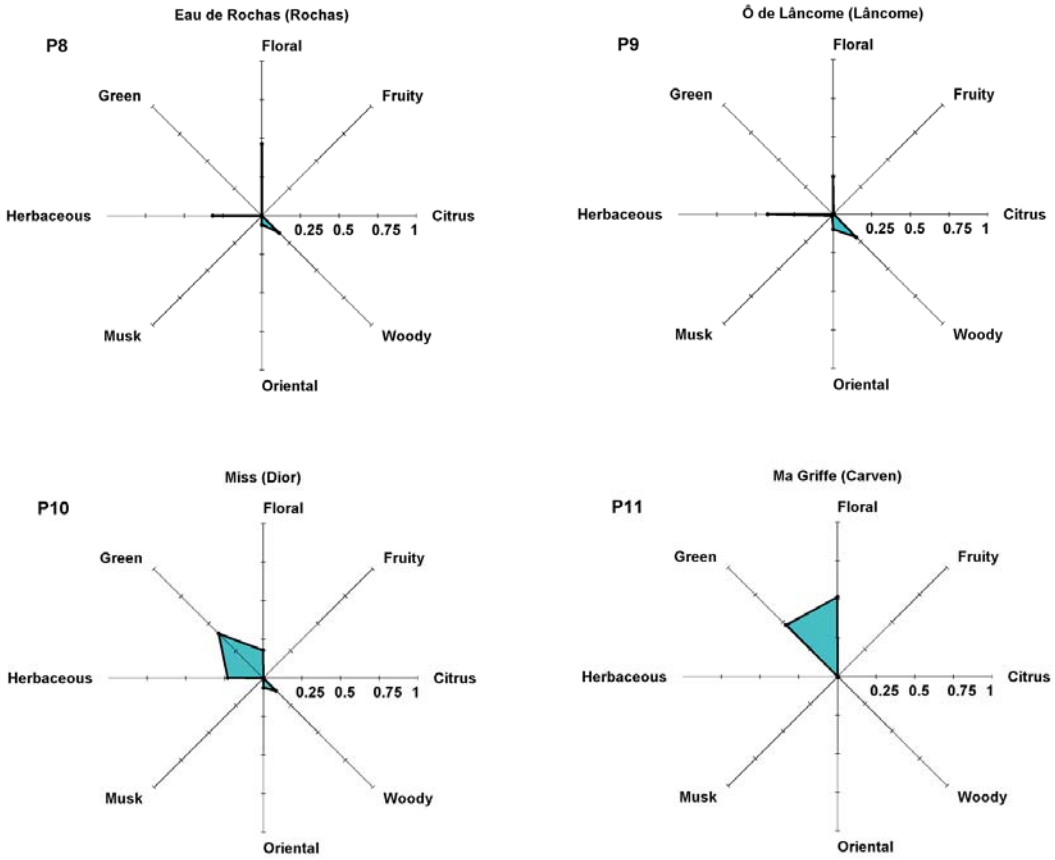


Figure 8.9 – Perfumery radars for perfumes P8-P11 (Chypre primary olfactive family).

Considering the perfumery radars obtained for the floral perfumes (Figure 8.7) it is possible to see that in all cases there is a predominant floral scent (always higher than 50%). In perfume P1 there is also a significant contribution of the green subfamily, which can be found only in the classification by LT & TS (see Table 8.4). As aforesaid, the green scent is closely linked with the floral one, so that its perception in floral perfumes is understandable. It is also classified as "Floral Bouquet" by Dragoco (Table 8.4) which resembles different types of botanical flowers (Sturm and Peters, 2005). In the case of perfumes P2 to P4 the floral scent was nearly alone (> 95%), so no significant *nuances* were found. All the empirical classifications agreed with that for perfume P2, while Fragrance Foundation agreed for P3 and P4, and Dragoco for P4. Other classifications assigned *nuances* for P3 and P4.

Oriental perfumes as P5-P7 traditionally resemble warm and spicy compositions. The radars in Figure 8.8 show the expected oriental character, in agreement with Osmoz and Scent Direct classifications. In fact, for perfume P5 the oriental family (42%) dominates the overall scent, followed by secondary woody (17%), green (16%), and citrus notes (8%). In what concerns P6, it is the *Eau Fraîche* version of perfume P5 and it is also dominated by oriental family (65%), with a fruity *nuance* (27%). Empirical classifications from Osmoz and Scent Direct refer different secondary families for them. For perfume P7, a fruity-oriental character is predicted, with floral and woody *nuances*. It is classified by LT & TS as amber-rose (Turin and Sanchez, 2008) (which corresponds to our oriental-floral) and as oriental-woody and oriental-fresh by Osmoz and Scent Direct (fresh has been defined elsewhere as citrus-green - Surburg and Panten, 2006 and citrus-green-fruity-water - Edwards, 2009). According to our PR methodology, it shows a fruity-oriental character with floral and woody subfamilies, which in general terms could be considered in agreement with the former literature classifications.

Perfumes P8 to P11 are classified as Chypre by the majority of the perfumists although some differences are seen (Table 8.4). Their perfumery radars are shown in Figure 8.9 and care should be paid when analyzing this family since these commercial perfumes are more difficult to assign into olfactive families due to their complexity in the combination of odorants. This classic perfume family (Chypre) does not have an axis in the PR methodology, as mentioned before. In the literature, the Chypre family is described as containing the scents of bergamot (Fruity), rose (Floral), patchouli (Herbaceous-Woody), and oak moss (earthy, mossy, woody) (Calkin and Jellinek, 1994;

Firmenich, 2009). Thus, a certain variation in the radars of Chypre perfumes can be expected: since this family is a combination of other families or radar axes (fruity, floral, herbaceous and woody), different perfumes (with different compositions) will present differences in the strength of each axis.

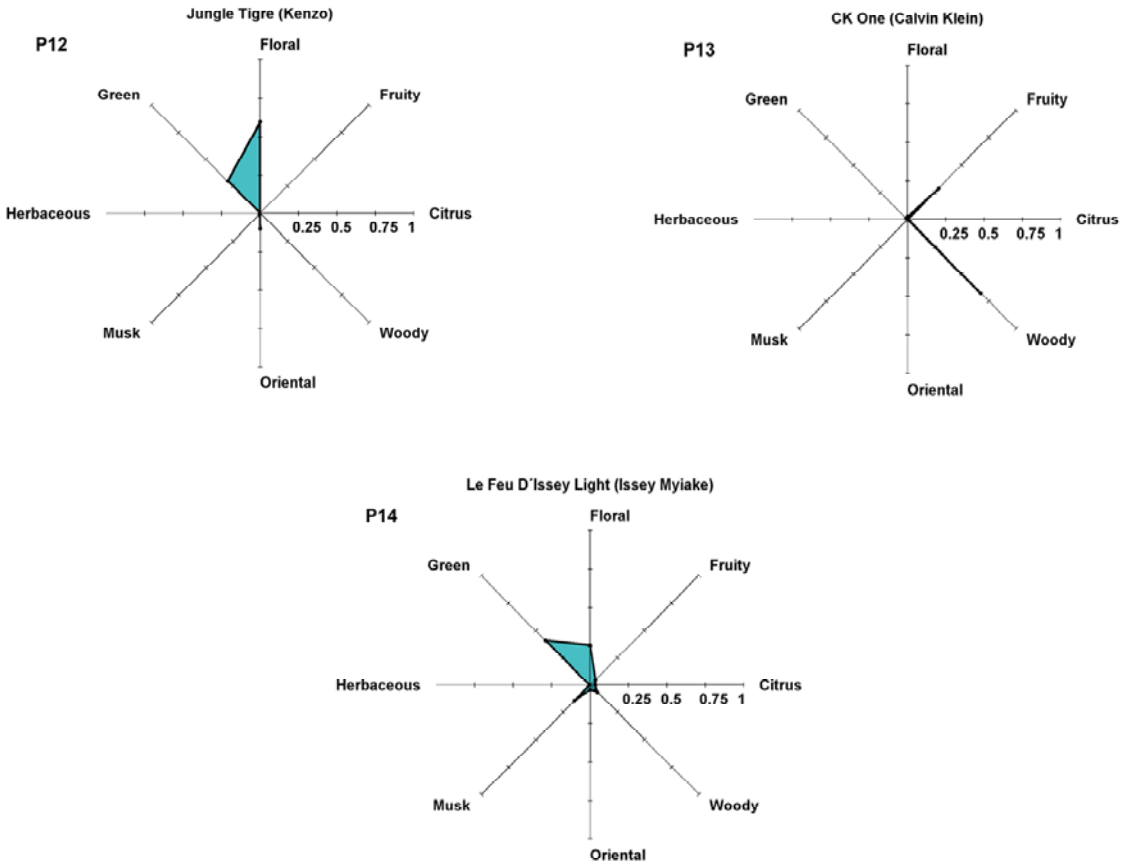


Figure 8.10 – Perfumery radars for perfumes P12-P14 (Heterogeneous classifications).

For the Chypre perfumes studied here (Figure 8.9) a radar pattern could be identified. Perfumery radars for P8, P9 and P10 have similar shapes with floral-herbaceous families being dominant and combined with woody-oriental (as a *nuance*) clearly appearing in the lower section of the radar. This pattern is clear for P8 and P9, while in P10 there is also an important contribution from the green axis. It is important to highlight here that although the formulation of these perfumes is quite different (both in species and composition) the predicted perfumery radars show a similar shape. This shape can be assigned as the radar pattern for the Chypre family. For the case of perfume P11, a different perfumery radar is seen where the woody-oriental *nuance* does not appear and the floral-green axes are predominant. This green character could only be compared with P10, though the herbaceous family is not present for P11. In fact,

perfume P11 follows the description of LT & TS (see Table 8.4) who classified this perfume as "*a classic green-chypre, less herbaceous…more floral than most*" (Turin and Sanchez, 2008). This green scent is significantly influenced by the presence in their composition of a main component: styrallyl acetate. The ratio between its vapor pressure and odor threshold is very high, which contributes to a high OV for the component (see equation 3) and thus the families assigned to it: green and floral.

Finally, the perfumery radars for some selected perfumes with heterogeneous classifications are presented in Figure 8.10 for perfumes P12 to P14. In the case of perfume P12 its predicted perfumery radar shows a strong floral character (59%), having green and oriental subfamilies. This matches the classification given by Dragoco for the primary olfactive family, but all empirical classifications are in disagreement. For perfume P13, it is clearly seen a woody and fruity character, which are families belonging to the chypre-fresh perfumes as mentioned before. This way, this perfumery radar shows only some of the families that constitute those attributed by the experts, since they attribute different classifications to this perfume. Finally, P14 shows a green-floral character due to the presence of mefloral (green-floral), with a musk *nuance* mainly due to a high composition in galaxolide (a sweet musk fragrance - Brechbill, 2006; Surburg and Panten, 2006). Both floral and musk families are present in the classifications of the perfumers (Osmoz, Fragrance Foundation and LT & TS).

In brief, the predicted perfumery radars match most of the primary olfactive families assigned in the empirical classifications from the perfumers, and the secondary olfactive families are well predicted in several cases (see Table 8.4).

Experimental validation of the PR methodology

The PR methodology was also experimentally validated, in order to assess for its predictive character. These experiments were carried out by measuring the headspace composition of four commercial perfumes belonging to different olfactive families, and then calculating the corresponding PR from the real concentrations in the gas phase. Figure 8.11 shows a comparison between perfumery radars predicted from the liquid composition and those obtained from headspace GC measurements.

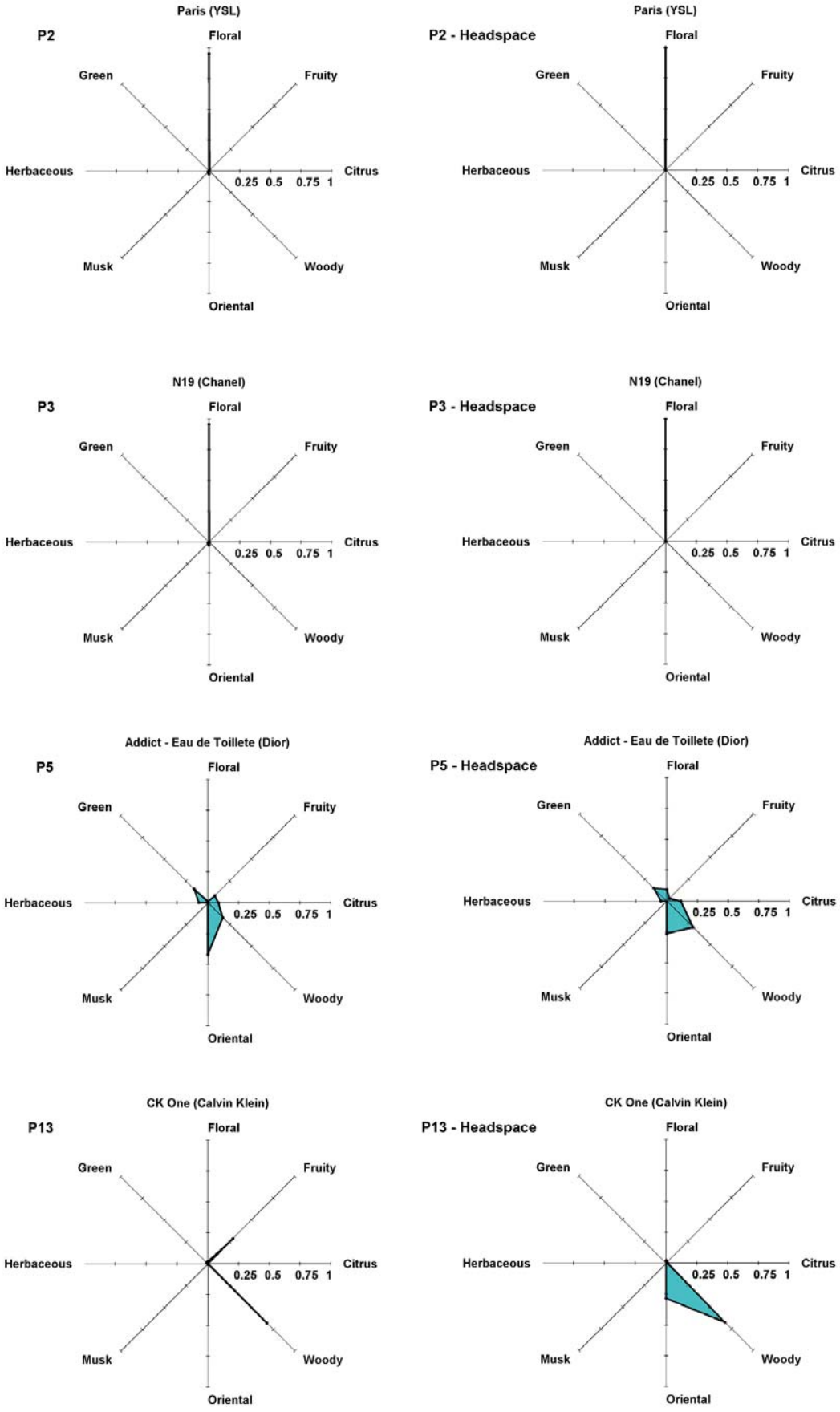


Figure 8.11 – Comparison between perfumery radars predicted from the liquid composition and those obtained from headspace GC-FID-MS measurements.

It is possible to see that the experimental perfumery radars are very similar to the predicted ones for perfumes P2, P3 and P5. Perfume P13 is more complex and heterogeneous, being the one where none of the classifications agree (those from the perfumers and the PR). Nevertheless, the primary olfactive family that was predicted with the PR methodology matches the one from the experimental perfumery radar, although the fruity nuance does not. That being said, the experimental headspace classification shows that the predicted PR methodology is very close to the experimental odor character of the tested perfumes. Moreover, through the headspace analyses of the perfumes it was possible to see that the most powerful fragrances that were detected by GC-FID-MS were also predicted by the PR methodology. Finally, it should be said that the analysis of the headspace gas phase is much more limited than it is for the liquid perfume. The problem here resides in the fact that gas concentrations are highly diluted in air which makes it difficult to analyze and detect even in a GC-FID-MS equipment. These experimental analyses of the headspace of perfume mixtures have also another implication: they have shown that the UNIFAC method is suitable for the prediction of the VLE of multi-component mixtures where a qualitative evaluation is performed although some deviations may appear. Here, a parenthesis is made to highlight the importance of using activity coefficients in multi-component mixtures. In these cases large deviations to ideality are expected for the prediction of the vapor-liquid equilibrium, although it will depend on the composition. Even so, in the case studied here using the PR methodology we were more interested in the qualitative classification of perfumes and so, it could be argued to make a simplification and consider an ideal liquid solution. However, when comparing the results obtained for both cases, despite the fact that in some of them that qualitative evaluation may smooth the differences, in the majority of the perfumes large differences in their classification are found. In this way, considering idealities for the liquid perfume mixture can lead to erroneous classifications.

Evolution of the PR with evaporation and diffusion

The diffusion model was applied on two selected commercial perfumes classified in different olfactory families to simulate the evaporation of a sprayed perfume on a paper blotter and to characterize its behavior over time. The perfumery radars after 30 and 60 seconds of evaporation and diffusion are presented in Figure 8.12 for perfumes P1 and

P7. The evaluation of a perfume is usually done after spraying and fanning it on a paper blotter, thus allowing the ethanol to evaporate and dilute the perceived smell. The evolution of the perfume can be described by the diffusion model presented before.

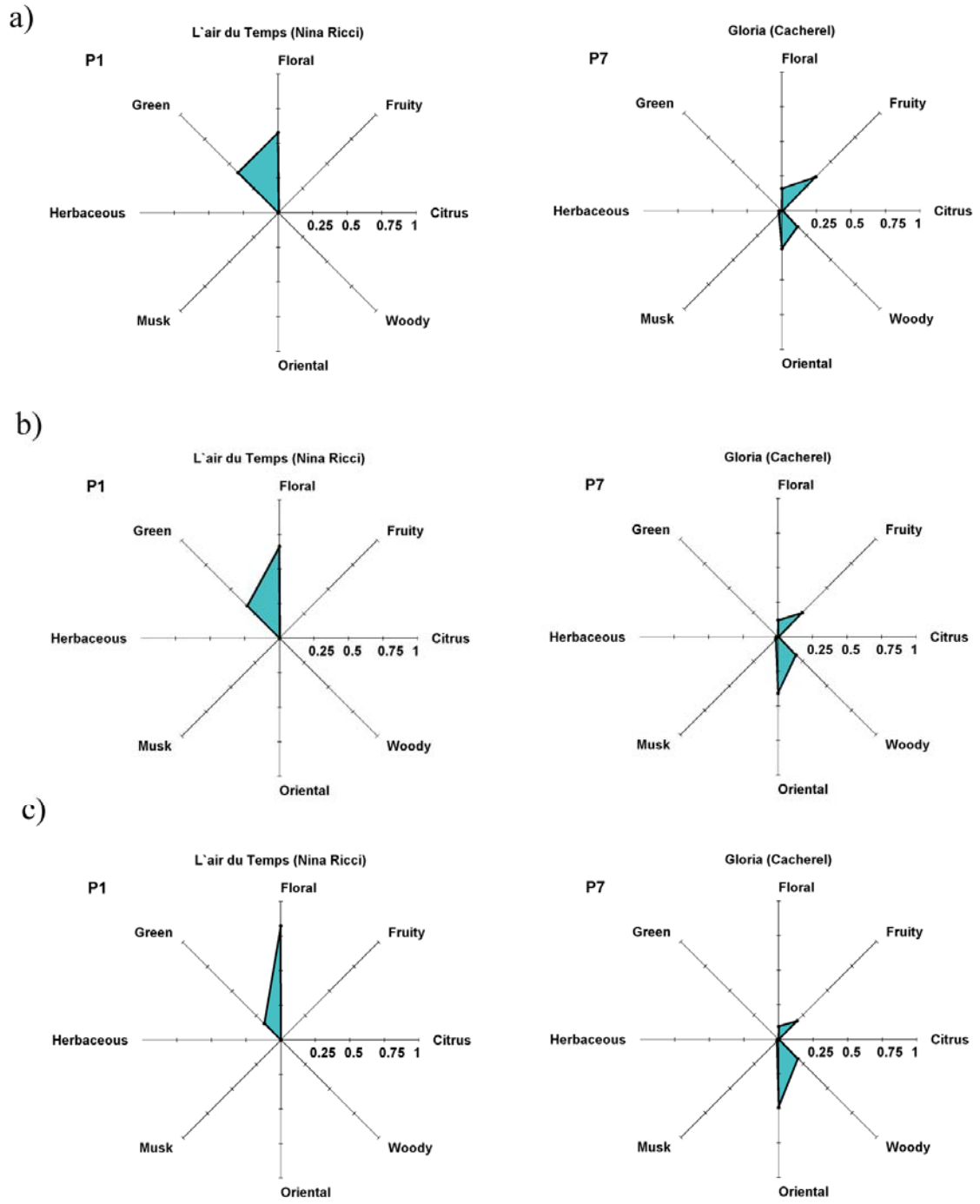


Figure 8.12 – Evolution of the perceived character of the perfumes P1 and P7 using the PR methodology with evaporation and diffusion over time: a) t = 0 s; b) t = 30 s; c) t = 60 s.

When diffusion is considered, the concentration of the perfume evolves with time as perfume evaporates. Thus, its perfumery radar changes with time. For perfume P1 the

initial floral-green scent changes to a more intense floral character over time, although the green *nuance* is still perceived. For perfume P7, the Fruity-Oriental scent evolves to a stronger oriental-woody character with time diffusing. This way, it is seen that when considering the diffusion of the perfumes, their predicted olfactory families slightly change over time. The incorporation of the diffusion model in the PR methodology tends to mimic the experimental procedure used for perfume classification and so predicts the olfactive families for the commercial perfumes. The application of the PR methodology to classify commercial perfumes in olfactive families has proven to give accurate predictions, although the following remarks should be taken into account. It is important to highlight that differences between the simulations obtained for the olfactive families and the classifications based on the olfactory perception of experienced perfumers may have to do with some factors discussed ahead. First, the fact that gas chromatographic analysis were performed in a GC-FID-MS excludes the detection of water, since FID detector is not suitable for detection of water molecules and MS operates in non-moisture mode. This way, the normalized compositions of the commercial perfumes used here have approximated values for the water content (solvent) adapted to the type of perfume (*Eau de toilette* or *Eau fraîche*) as presented in Annex E. Moreover, the application of the Perfumery Radar (PR) methodology, accounts for a large number of fragrant species and, thus, the evaluation of the OV for each is dependent on the availability of physicochemical (P_i^{sat}, M_i, UNIFAC interaction parameters) and psychophysical (ODT_i) data. For this reason, throughout this work some other perfumes could not be considered due to the limitation of threshold data or the impossibility of attributing group parameters (UNIFAC) for fragrant molecules present in the perfume. Nonetheless, the PR methodology has shown to be a valuable tool for the prediction and classification of perfumes in olfactory families. The PR methodology presents a modular construction since it is possible to change or update the experimental database for the classification of pure fragrances, the liquid-vapor equilibrium model, the odor intensity model for any other that might suit or the graphic representation for the olfactive families (radar, prism, or bar plot). It is expected though that perfumers will continue to stick to their personal framework and use their nose and experience to evaluate perfumes. However, the PR methodology can be adapted to follow the preferences of a certain perfumer or company. This is especially true for the pure fragrance classification and the type and number of olfactive families used, as aforementioned. The use of the PR methodology, even adapted as said, presents two

major advantages: it is a predictive tool that can be applied in the pre-formulation stage of the perfume, so there is no need for experimental evaluation, and would provide a standard basis for comparison of different perfumes or compositions. Thus, it would contribute to the *a priori* product design, reducing cost and time of production.

8.6.3. Evaluation of odor intensities of similar perfumes

As stated in the beginning of this Chapter 8, perfumes can be classified in terms of their chemical composition (depending on the desired type of application) or their olfactory families (for character or quality analysis). Here, we will compare both the perceived odor intensity and character of similar perfumes (same brand and model) that were designed to be fine fragrances (*e.g. Eau de Toilette*) or used as lighter fragrances (*e.g. Eau Fraîche or After Shave*). For that, two fragrances were selected: one feminine which was previously evaluated in terms of odor character only – Addict (Dior) – with its two versions *Eau de toilette* and *Eau Fraîche*; and one masculine fragrance - Euphoria Intense (Calvin Klein) – with the *Eau de toilette* and *After Shave* versions. A comparison between these perfumery radars is shown in Figure 8.13.

The PR methodology was applied to these different fragrance versions which, as we know, will differ in their composition, especially in terms of alcohol and water content. First of all, a comparison between the compositions of these fragrances has shown that although they have almost the same fragrant components within the mixture, some of those are present in significantly different concentrations, despite the obvious differences in ethanol and water content. For example, in Addict, limonene and linalyl acetate are, respectively, 3 and 5 times more concentrated in the *Eau de toilette* than in the *Eau Fraîche* while they have 8 and 4 times more concentration in the Euphoria Intense *Eau de toilette* than in the *After Shave*.

From the analysis of Figure 8.13, it is clear that there are differences in both intensity and character between the two versions of Addict tested here (left) while for Euphoria Intense (right) the perceived character is similar though with little differences in the intensities of the olfactive families. Moreover, in terms of odor intensity, it is seen that the OVs for the dominant notes of each perfume are much higher in the woody note for Euphoria Intense ($max\ OV_j$ = 18000) than in the oriental note for Addict ($max\ OV_j$ = 5800).

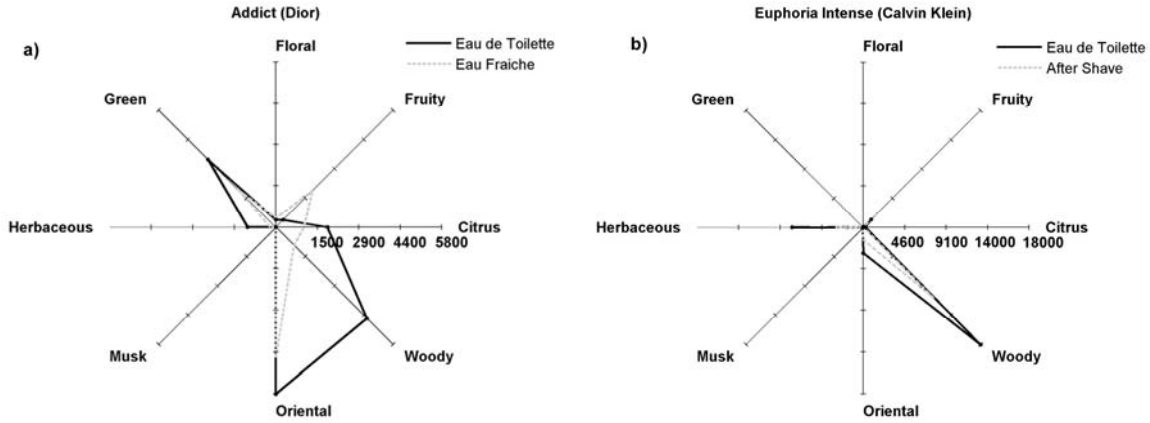


Figure 8.13 - Comparison between the odor intensities of the olfactive families of two different fragrances: a) *Eau de toilette* vs *Eau Fraîche* versions of the commercial perfume Addict (Dior) and b) *Eau de toilette* and *After Shave* versions of Euphoria Intense (Calvin Klein).

In terms of character, Euphoria Intense is classified by experts as woody-aromatic by Osmoz (Firmenich, 2009) and ISIPCA (ISIPCA, 2010) and as woody-oriental by The Fragrance Foundation (Edwards, 2009) and the Perfume Intelligence (Perfume-Intelligence, 2011). In this work, it is predicted as woody with powerful herbaceous and oriental *nuances*, thus showing good agreement.

8.6.4. Unisex commercial fragrances

A curious point in the fragrance industry that has not yet been discussed here, concerns to one other type of fragrance classification: the classification in gender. In analogy with the sense of smell, for example, one has the visual sense: studies using semantic differential scales have shown that pink, yellow and purple colors are considered more feminine, while blue, brown and gray are most commonly classified as masculine (Zellner, *et al.*, 2008). We all know that some fragrances are typically more feminine whilst others tend to show a more typical masculine scent. However, this distinction has mostly to do with the perceived smell and trends, personal and cultural preferences. Women's fragrances tend to be lighter and floral while masculine ones often have a stronger character of a citrus-woody type. And apart from these two genera, there still exists (especially more recently) a line of unisex fragrances, which aims at pleasing both the feminine as the masculine side. These differences depend on the composition of the perfume and are clearly evident in the main olfactory families in which they fall under. A comparison of perfume classifications in terms of olfactive families distributed by gender and type of notes is presented in Table 8.5 considering a compilation of 5730 fragrances (3463 women, 1717 men, and 550 unisex) contained in the 2008 edition

Michael Edwards' guide (Donna, 2009; Zarzo and Stanton, 2009). It should also be highlighted that the number of feminine fragrances considered is much larger than that for men (as in the line with market), mainly because the latter is a seasonal market (with its busiest period in the Christmas season), while the women's sector covers equally the entire year.

Table 8.5 – Percentage of fragrances by category/descriptors commonly used in perfumery and gender according to Edward's guide and frequency of these descriptors in the H&R Fragrance Guide [Reproduced from (Donna, 2009) and (Zarzo and Stanton, 2009)].

	Number of Fragrances			% of Fragrances by gender[a]			Frequency of occurrence, by gender, of descriptors used by H&R Fragrance Guide[b]					
							Top notes		Middle notes		Base notes	
Category	Women	Men	Unisex	Women	Men	Unisex	%women	%men	%women	%men	%women	%men
Floral	1446	17	44	41.8	1.0	8.0	18.5	0.5	96.0	67.0	10.4	0.0
Soft Floral	354	10	23	10.2	0.6	4.2						
Floral Oriental	533	1	6	15.4	0.1	1.1						
Soft Oriental	97	18	19	2.8	1.0	3.5						
Oriental	145	15	31	4.2	0.9	5.6	0.0	0.0	0.0	0.0	0.7	0.0
Woody Oriental	352	361	65	10.2	21.0	11.8						
Woods	71	263	63	2.1	15.3	11.5	0.0	0.8	5.5	38.4	34.2	40.9
Mossy woods	175	70	15	5.1	4.1	2.7						
Dry woods	47	156	43	1.4	9.1	7.8						
Fougère	8	572	21	0.2	33.3	3.8						
Citrus	146	138	167	4.2	8.0	30.4	3.5	11.2	0.0	0.0	0.0	0.0
Water/marine	35	81	21	1.0	4.7	3.8	0.0	0.0	0.2	0.0	0.0	0.0
Green	33	15	29	1.0	0.9	5.3	34.2	23.2	5.3	3.0	0.2	0.0
Fruity	21	0	3	0.6	0.0	0.5	32.5	1.1	4.6	0.8	0.7	0.0
Total	**3463**	**1717**	**550**	**100.0**	**100.0**	**100.0**						
Fresh[c]	235	234	220	6.8	13.6	40	52.1	92.6	2.9	13.6	0.2	1.9

[a] Based on 5730 fragrances (3463 women's, 1717 men's and 550 unisex) contained in the 2008 ed. of Edward's guide.
[b] Percentage of times categories on this Table are used as descriptors of top, middle and base notes of the 820 commercial fragrances (453 women's and 367 men's) contained in the H&R Fragrance Guide, by fragrance gender.
[c] Fresh = citrus + water + green + fruity, according to Edward's guide.

According to Zarzo and Stanton, the analysis on the trend of each family can be performed in a simple way by considering that families whose percentage is higher for women, tend to be feminine or gynogenic (perceived with female characteristics), whereas if it is greater for men than it is regarded as masculine or androgenic (Zarzo and Stanton, 2009). Following the same analysis, it is possible to say that families with similar number of perfumes (equally distributed) may be associated with unisex fragrances as is the case for woody-oriental or citrus, although there are exceptions. Unisex fragrances are not perceived strictly as masculine or feminine. In this way, it

seems that olfactive families like citrus, woody-oriental or woody are in the boundary between femininity and masculinity. For example, floral-oriental or fruity are feminine descriptors and contain (almost) only women's and unisex fragrances.

Another important family to evaluate is the mossy woods which corresponds to the chypre family (Zarzo and Stanton, 2009). Here, there is a slight discrepancy: from Table 8.5 it is seen that in the mossy woods family there are more feminine than masculine fragrances, so that it would be gynogenic, but according to the H&R guide, there are 23.8% of feminine fragrances and 35.7% of masculine fragrances classified as chypre, showing that it is more androgenic. This reflects once more the difficulty in the classification of "more complex" scents (like the chypre family) by the human nose, even when experts' opinions are used.

However, it is clear that all these analyses and discussions are not sufficient to define what the ideal perfume is for a woman or a man. A recent study performed by the Fragrance Foundation showed that age is also an important factor to take into account in this matter. Through a survey, they concluded that women under 18 have a higher propensity for citrus fragrances, whilst in the 18-25 range they prefer fruity-floral notes and above 35 years of age women mostly choose musky notes (TFF, 2011).

Thus, one concludes that there is still a long way to go in the classification of odors and their tendency towards women or men is difficult to predict *a priori*. For this, the Perfumery Radar methodology was applied to 11 unisex commercial fragrances from several brands. The selected perfumes and their classifications into olfactive families according to different fragrance houses and experts are presented in Table 8.6. These classifications were compiled from the literature and correspond to Osmoz (Firmenich), Scent Direct, Luca Turin & Tania Sanchez (LT & TS), The Fragrance Foundation, Haarman & Reimer (H&R), the Perfume Intelligence, and Institut Supérieur International du Parfum de la Cosmétique et de l'Aromatique Alimentaire (ISIPCA).

These commercial unisex fragrances correspond to real perfumes of recognized brands and were used in excellent state of preservation. Their liquid compositions were analyzed through gas chromatography coupled with FID and mass spectrometry following the same sample preparation, procedure and analysis conditions as before. In terms of identification of chemical components, the only difference here was that a new lower-limit value for peak area was considered for the FID data equal to 2000 counts. In this way, only components with an area below that value were excluded.

Table 8.6 - Commercial name, brand, and family classification of the selected unisex perfumes. Their gender from each fragrance house or experts is also presented: feminine (F), masculine (M) or unisex (U) fragrances.

#	Perfume	Brand	Year	Osmoz (Firmenich)	Scent Direct	LT & TS	The Fragrance Foundation	H&R	Perfume Intelligence	ISIPCA	This work
U1	Aqua Allegoria Herba Fresca	Guerlain	1999	-	-	Weird mint	-	-	Summer garden (U)	Aromatic-Citrus (U)	Green-Citrus
U2	Aqua Allegoria Pamplelune	Guerlain	1999	Citrus-Aromatic (F)	-	Floral-Glowing grapefruit	-	-	Citrus Rich (U)	Citrus (U)	Floral-Fruity-Citrus
U3	Bulgari Extrême	Bulgari	1996	Woody-Aromatic (M)	-	Woody-Spicy (M)	-	Fresh-Green (F); Fresh-Citrus (M)	-	Floral-Woody-Citrus (U)	Floral-Green
U4	Eau Parfumée	Bulgari	1992	Citrus-Aromatic (U)	Chypre-Fresh (F)	-	-	Chypre-Fresh (F)	Fresh-Citrus (U)	Floral-Woody-Citrus (F)	Musk-Woody-Floral
U5	CK Be	Calvin Klein	1998	Floral-Woody-Musk (U)	-	Fougère	Aromatic-Fougère-Fresh (U)	Fougère-Fresh-Woody (M)	Fresh-Woody-Oriental (U)	Floral-Musky (U)	Floral-Musk-Fruity
U6	Cologne	Thierry Mugler	2001	Citrus-Aromatic (U)	-	Steam clean-Floral (M)	-	-	Citrus-Fruity-Musk (U)	Musky-Citrus (U)	Musk-Citrus
U7	Gaultier 2	J. Paul Gaultier	2005	Oriental-Vanilla (F)	-	Musk-Floral-Green	Woody-Oriental-Classical (U)	-	-	Floriental (F)	Green-Floral
U8	Eau de Cartier	Cartier	2001	Citrus-Aromatic (U)	Floral-Fresh (F)	violet leaf-woods-citrus	Citrus-Rich (U)	Chypre-Fresh (F)	-	Floral-Woody-Citrus (U)	Oriental-Citrus-Fruity
U9	Voyage d'Hermès	Hermès	2010	Woody-Floral-Musk (U)	-	-	Woody-Fresh-Citrus-Fruity (U)	-	Fresh-Musk-Woody (U)	-	Woody-Fruity
U10	Eau de Gentiane Blanch	Hermès	2009	Woody-Floral-Musk (M)	-	-	Woody-Crisp-Green (U)	-	(U)	-	Woody-Musk
U11	Eau de Campagne	Sisley	1976	Floral-Green (F)	-	-	Green-Classical (U)	-	(U)	-	Floral-Citrus-Green

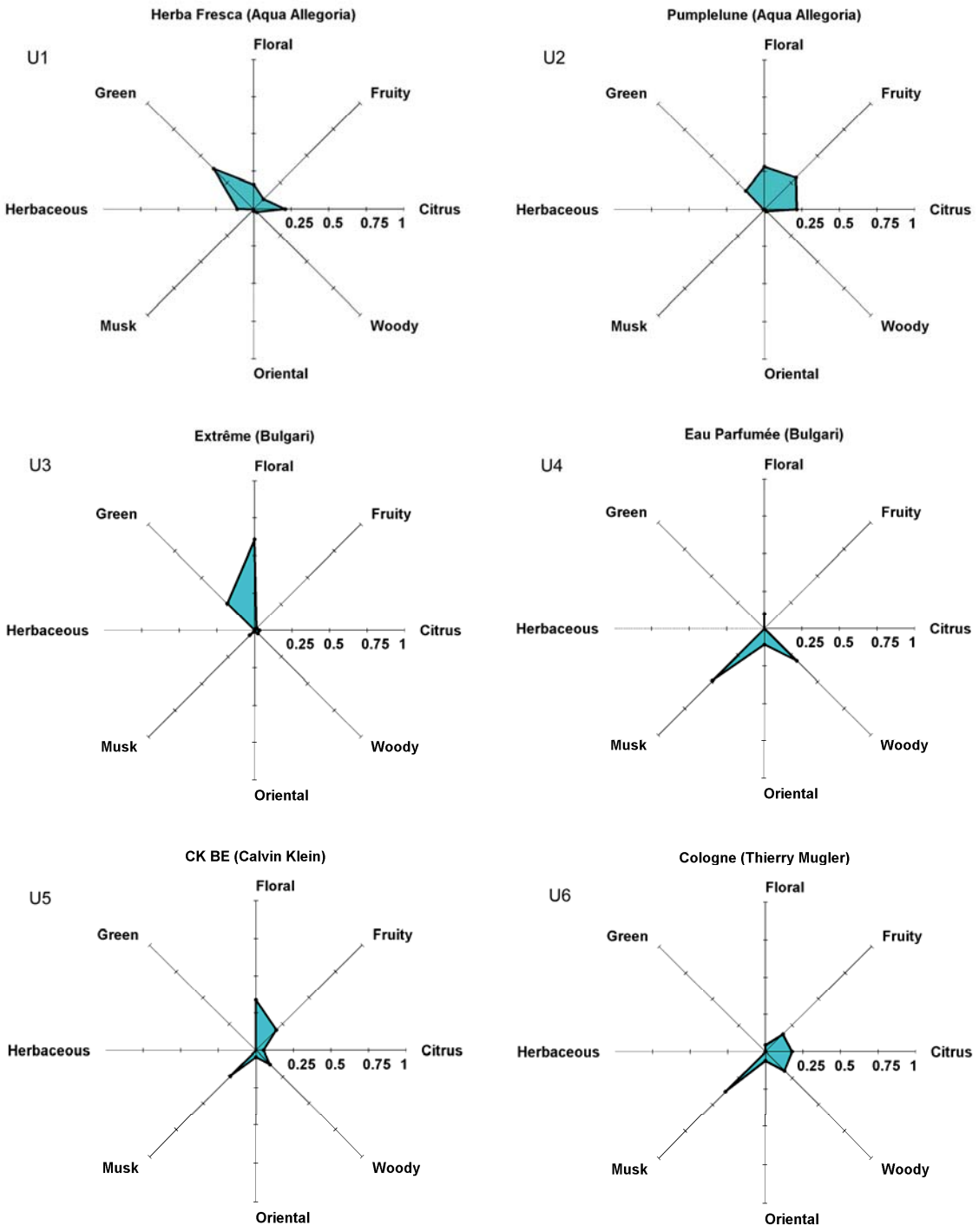


Figure 8.14 - Perfumery radars for Unisex perfumes U1-U6.

First of all, it can be observed that, as for the feminine perfumes studied before in this Chapter, there are several discrepancies in the classifications obtained for the same fragrance. It is also seen that there are typical olfactive families in the unisex fragrances analyzed here: citrus, woody and fresh. This is in agreement with the evaluation of Zarzo and Stanton shown in Table 8.5.

Moreover, it should be noted that for some of these commercial perfumes there is not unanimity on the classifications as to their unisex (U) character, as shown in Table 8.6. With the exception of Voyage d'Hermès (Hermès), all the other perfumes present at least one classification as feminine (F) or masculine (M) fragrance. This evidences what was aforementioned, so that not only in the character classification but also in the gender assignment there are some differences.

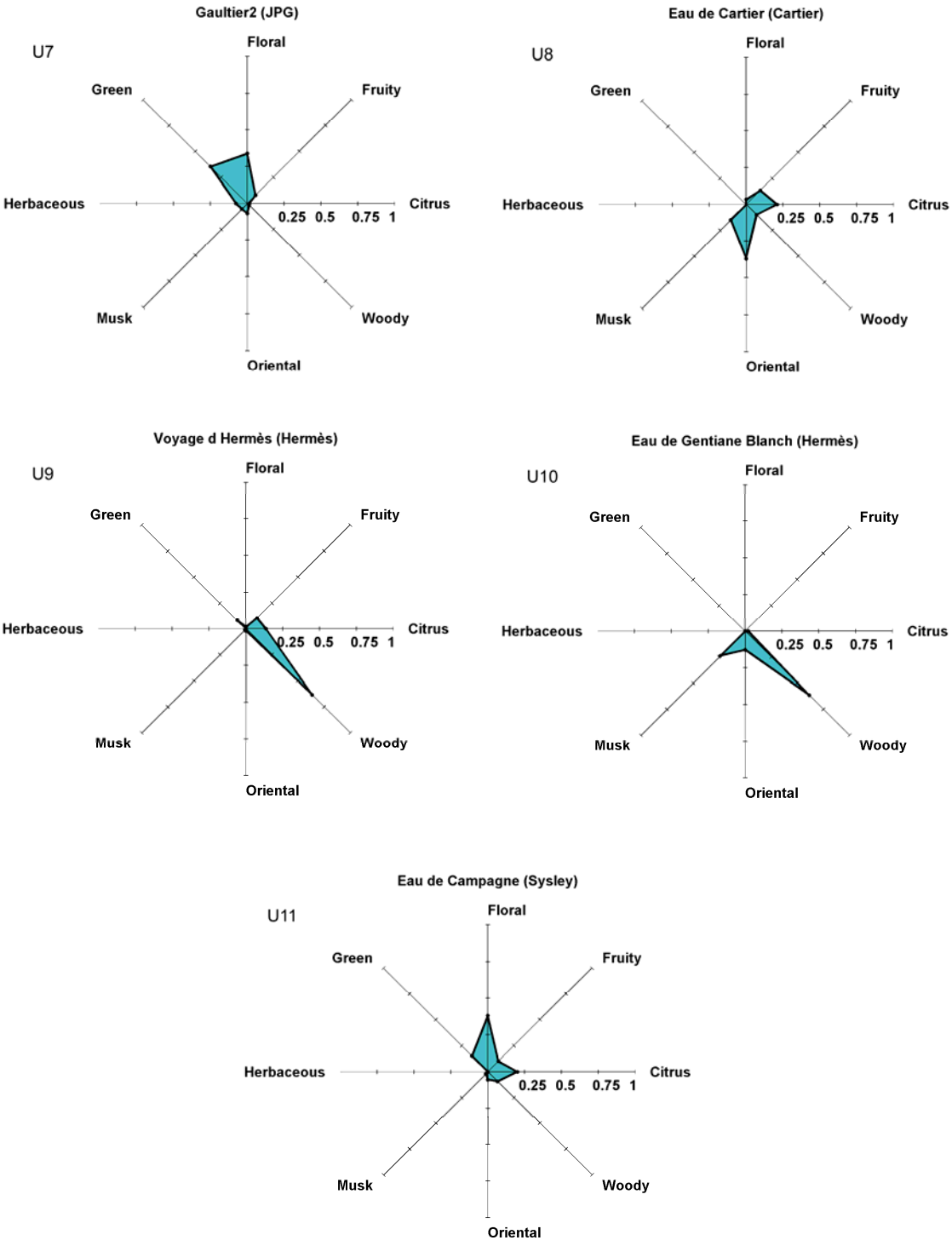


Figure 8.15 - Perfumery radars for Unisex perfumes U7-U11.

From the comparison of the perfumery radars predicted in this work and the classifications shown on Table 8.6 it is possible to see a very good agreement. For the great majority of the commercial perfumes, the PR methodology predicts the primary olfactive family, with few exceptions for Eau Parfumée (U4) and Eau de Cartier (U8) for which only secondary families were well predicted. Nevertheless, for perfumes like U9, U10 or U11 were obtained predictions that match perfectly well all the classifications from the experts.

As a curiosity, it should be noted for these unisex perfumes the presence of the musk family, which gives sweetness to the perceived scent and which was not that common on the feminine perfumes studied before.

8.7. Conclusions

The PR methodology has shown to correctly predict the primary olfactive family of four essential oils and several commercial perfumes of different types or gender. The PR methodology uses scientific models for the prediction of the vapor-liquid equilibrium and diffusion of fragrances for a qualitative classification of perfumes, instead of relying on the sensorial perception of perfumers only. This way, the arbitrariness of the classification of perfumes is confined to the experimental descriptors of the pure fragrance chemicals. Further advantages are its flexibility, since it is possible to easily change or add perfume families to the radar plots, include or exclude fragrant components, add new data or even change the models used to account for the evaporation, diffusion or odor intensity. It is a valuable technique for the prediction of perfumes' olfactive families, giving important guidelines when designing perfumed products.

8.8. References

The Good Scents Company, from http://www.thegoodscentscompany.com/, Last Accessed on May 2010

AIHA, Odor Thresholds for Chemicals With Established Occupational Health Standards, Fairfax, VA (USA), American Industrial Hygiene Association, TRC - Environmental Consultants, 1989

Amoore, J. E., Forrester, L. J., Specific anosmia to trimethylamine: the fishy primary odor, *J. Chem. Ecol.*, 2, (1): 49-56, 1976

Amoore, J. E., Forrester, L. J., Buttery, R. G., Specific anosmia to 1-pyrroline: the spermous primary odor, *J. Chem. Ecol.*, I, (3): 299-310, 1975

Amoore, J. E., Hautala, E., Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution, *Journal of Applied Toxicology*, 3, (6): 272-290, 1983

Arctander, S., Perfume and flavor chemicals (aroma chemicals), Montclair, NJ, 1969

Avon, AVON Company from http://knowledgeonline.youravon.com/content/beautyboost/2008B24/0808_quick_guide.pdf, Last Accessed on May 2010

Axel, R., Scents and sensibility: A molecular logic of olfactory perception (Nobel lecture), *Angewandte Chemie-International Edition*, 44, (38): 6110-6127, 2005

Brechbill, G. O., A Reference Book on Fragrance Ingredients, New Jersey - USA, Creative Endeavor Books, 2006

Buck, L., Axel, R., A Novel Multigene Family May Encode Odorant Receptors: A Molecular Basis for Odor Recognition, *Cell*, 65, 175-187, 1991

Buck, L. B., Unraveling the sense of smell (Nobel lecture), *Angewandte Chemie-International Edition*, 44, (38): 6128-6140, 2005

Buettner, A., Schieberle, P., Evaluation of aroma differences between hand-squeezed juices from valencia late and navel oranges by quantitation of key odorants and flavor reconstitution experiments, *Journal of Agricultural and Food Chemistry*, 49, (5): 2387-2394, 2001

Butler, H., Poucher's Perfumes, Cosmetics and Soaps, Kluwer Academic Publishers - Boston / London, 2000

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Cain, W. S., Schmidt, R., Can we trust odor databases? Example of t- and n-butyl acetate, *Atmospheric Environment*, 43, (16): 2591-2601, 2009

Caldeira, I., Belchior, A. P., Climaco, M. C., de Sousa, R. B., Aroma profile of Portuguese brandies aged in chestnut and oak woods, *Analytica Chimica Acta*, 458, (1): 55-62, 2002

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Callegari, P., Rouault, J., Laffort, P., Olfactory quality: From descriptor profiles to similarities, *Chemical Senses*, 22, (1): 1-8, 1997

Carles, J., A method of creation in perfumery, *Soap Perfumery Cosmet.*, 35, 328-335, 1962

Chapman, J., MATLAB programming for engineers, California, Brooks Cole Publishing Company, 2000

Chapra, S., Canale, R., Numerical methods for engineers: with software and programming applications, Boston, McGraw Hill, 2002

Chastrette, M., Trends in structure-odor relationships, *SAR and QSAR in Environmental Research*, 6, 215-254, 1997

Chastrette, M., Data management in olfaction studies, *Sar and Qsar in Environmental Research*, 8, (3-4): 157-181, 1998

Chastrette, M., Desaintlaumer, J. Y., Sauvegrain, P., Analysis of a system of description of odors by means of 4 different multivariate statistical-methods, *Chemical Senses*, 16, (1): 81-93, 1991

Cometto-Muniz, J. E., Cain, W. S., Abraham, M. H., Odor detection of single chemicals and binary mixtures, *Behavioural Brain Research*, 156, (1): 115-123, 2005

Consultants, T. E., Odor Thresholds for Chemicals with Established Occupational Health Standards, Fairfax, VA, AIHA, 1989

Crocker, E. C., Henderson, L. F., Analysis and classification of odors: an effort to develop a workable method, *Am Perf Essent Oil Rev*, (22): 325–56, 1927

Devos, M., Patte, F., Rouault, J., Laffort, P., Gemert, L. J. v., Standardized Human Olfactory Thresholds, Oxford, IRL press at Oxford University Press, 1990

Distel, H., Ayabe-Kanamura, S., Martinez-Gomez, M., Schicker, I., Kobayakawa, T., Saito, S., Hudson, R., Perception of everyday odors - Correlation between intensity, familiarity and strength of hedonic judgement, *Chemical Senses*, 24, (2): 191-199, 1999

Donna, L., Fragrance Perception: Is everything relative?, *Perfumer & Flavorist*, 34, (12): 26-35, 2009

DROM, DROM Fragrance Circle, from http://www.drom.com/, Last Accessed on 2011

Edwards, M., The Fragrance Wheel, from http://www.fragrancedirectory.info/usadirectory/, Last Accessed on May 2011

Fazzalari, F. A., Compilation of Odor and Taste Threshold Values Data, Philadelphia, American Society For Test Mate, 1978

Ferreira, V., Lopez, R., Cacho, J. F., Quantitative determination of the odorants of young red wines from different grape varieties, *Journal of the Science of Food and Agriculture*, 80, (11): 1659-1667, 2000

Firmenich, Osmoz Encyclopedia, from http://www.osmoz.com/, Last Accessed on May 2010

Fisher, C., Scott, T. R., Food Flavours - Biology and Chemistry, Cambridge (UK), RSC Paperbacks, 1997

Gilbert, A., What the Nose Knows - The Science of Scent in Everyday Life, New York, Crown Publishers, 2008

Grosch, W., Evaluation of the key odorants of foods by dilution experiments, aroma models and omission, *Chemical Senses*, 26, (5): 533-545, 2001

H&R, Haarmann & Reimer Fragrance Guide: Feminine Notes, Masculine Notes, Holzminden, Germany, 2002

Haddad, R., Lapid, H., Harel, D., Sobel, N., Measuring smells, *Current Opinion in Neurobiology*, 18, (4): 438-444, 2008

ISIPCA, Classification officielle des parfums et terminologie, Grasse (France), 2010

Jaubert, J. N., Tapiero, C., Dore, J.-C., The Field od Odors: Toward a Universal Language for Odor Relationships, *Perfumer & Flavorist*, 20, (May/June): 1-15, 1995

Jinks, A., Laing, D. G., The analysis of odor mixtures by humans: evidence for a configurational process, *Physiology & Behavior*, 72, (1-2): 51-63, 2001

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Laing, D. G., Natural sniffing gives optimum odour perception for humans, *Perception*, 12, (2): 99-117, 1983

Laing, D. G., Identification of single dissimilar odors is achieved by humans with a single sniff, *Physiology & Behavior*, 37, (1): 163-170, 1986

Lawless, H. T., Descriptive analysis of complex odors: reality, model or illusion?, *Food Quality and Preference*, 10, (4-5): 325-332, 1999

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Mamlouk, A. M., Chee-Ruiter, C., Hofmann, U. G., Bower, J. M., Quantifying olfactory perception: mapping olfactory perception space by using multidimensional scaling and self-organizing maps, *Neurocomputing*, 52-4, 591-597, 2003

Mamlouk, A. M., Martinetz, T., On the dimensions of the olfactory perception space, *Neurocomputing*, 58, 1019-1025, 2004

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Science Behind Perfume Design, Second European Symposium on Product Technology (Product Design and Technology), Groningen, The Netherlands, 2004

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005

MathWorks, Partial Differential Equation Toolbox - ComsoLab MATLAB's Users Guide, 2002

McGinley, M. A., McGinley, C. M., Mann, J., Olfactomatics: Applied Mathematics For Odor Testing, WEF Odor / VOC 2000 Specialty Conference

Cincinnati, OH., St. Croix Sensory Inc. / McGinley Associates, P.A., 2000

Milotic, D., The impact of fragrance on consumer choice, *Journal of Consumer Behaviour*, 3, (2): 179-191, 2003

Morrot, G., Brochet, F., Dubourdieu, D., The color of odors, *Brain and Language*, 79, (2): 309-320, 2001

Moyano, L., Zea, L., Moreno, J., Medina, M., Analytical study of aromatic series in sherry wines subjected to biological aging, *Journal of Agricultural and Food Chemistry*, 50, (25): 7356-7361, 2002

Nocedal, J., Wright, S., Numerical Optimization, New York, Springer, 1999

Olsson, M. J., Berglund, B., Odor-intensity interaction in binary and ternary mixtures, *Perception & Psychophysics*, 53, (5): 475-482, 1993

Parliment, T., Solvent Extraction and Distillation Techniques, Flavor, Fragrance and Odor Analysis, Marsili, New York, USA, Marcel Dekker, Inc., 2002

Perfume-Intelligence, Perfume Intelligence Encyclopaedia, from http://www.perfumeintelligence.co.uk/, Last Accessed on 2011

Pintore, M., Wechman, C., Sicard, G., Chastrette, M., Amaury, N., Chretien, J. R., Comparing the information content of two large olfactory databases, *Journal of Chemical Information and Modeling*, 46, (1): 32-38, 2006

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Poucher, W. A., A classification of odors and its uses, *Journal Soc. Cosmet. Chem.*, 81-95, 1955

Pybus, D. H., Sell, C. S., Chemistry of Fragrances, RSC Paperbacks, 1999

Ross, S., Harriman, A. E., A Preliminary Study of the Crocker-Henderson Odor-Classification System, *The American Journal of Psychology*, 62, (3): 399-404, 1949

Rowe, D., Chemistry and Technology of Flavours and Fragrances, United States, Blackwell Publishing Ltd - CRC Press, 2005

ScentDirect, Fragrance Genealogy, from http://www.scentdirect.com/, Last Accessed on May 2010

Schreiber, W. L., Perfumes, Kirk-Othmer Encyclopedia of Chemical Technology, New York, John Wiley & Sons, Inc., 18: 1-40, 2005

Sell, C., The Chemistry of Fragrances - From Perfumer to Consumer, Cambridge (UK), RSC Publishing, 2006

Sigma–Aldrich, Fine Chemicals Company. Flavors and fragrances 2003-2004 catalog, Milwaukee, WI, 2003

Société-Française-des-Parfumeurs, Société Française des Parfumeurs, Classification des Parfums, from http://www.parfumeur-createur.com/article.php3?id_article=68, Last Accessed on May 2010

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Sturm, W., Peters, K., Perfumes, Ullmann's Encyclopedia of Industrial Chemistry, Weinheim, Wiley-VCH Verlag GmbH & Co, DOI: 10.1002/14356007.a19 171: 2005

Surburg, H., Panten, J., Common Fragrance and Flavor Materials - Preparation, Properties and Uses, Weinheim, WILEY-VCH Verlag GmbH & Co., 2006

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009a

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009b

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., Perfumery Radar: A Predictive Tool for Perfume Family Classification, *Industrial & Engineering Chemistry Research*, 49, 11764–11777, 2010

TFF, The Fragrance Foundation. Key Fragrance Findings from The Premium Market Report 2010/11, from http://www.fragrancefoundation.org.uk/market-research.htm#top10, Last Accessed on

Thiboud, M., Empirical Classification of Odors, Art, Science & Technology, Muller and Lamparsky, Oxford (UK), Kluwer Academic Publishers, 253-286, 1991

Turin, L., Sanchez, T., Perfumes - The Guide, London, Viking Penguin 2008

van Gemert, L. J., Compilation of Odor Threshold Values in Air and Water, The Netherlands, TNO Nutrition and Food Research Institute (BACIS), 1999

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

van Gemert, L. J., Nettenbreijer, A. H., Compilation of Odour Threshold Values in Air and Water, Voorburg, Netherlands, National Institute for Water supply, 1977

Weiner, I. B., Handbook of Psychology, New Jersey (USA), John Wiley & Sons, Inc., 2006

Wilson, D. A., Pattern Separation and Completion in Olfaction, *International Symposium on Olfaction and Taste*, 1170, 306-312, 2009

Wise, P. M., Olsson, M. J., Cain, W. S., Quantification of odor quality, *Chemical Senses*, 25, (4): 429-443, 2000

Zarzo, M., Relevant psychological dimensions in the perceptual space of perfumery odors, *Food Quality and Preference*, 19, (3): 315-322, 2008

Zarzo, M., Stanton, D. T., Understanding the underlying dimensions in perfumers' odor perception space as a basis for developing meaningful odor maps, *Attention Perception & Psychophysics*, 71, (2): 225-247, 2009

Zellner, D. A., McGarry, A., Mattern-McClory, R., Abreu, D., Masculinity/femininity of fine fragrances affects color-odor correspondences: A case for cognitions influencing cross-modal correspondences, *Chemical Senses*, 33, (2): 211-222, 2008

Zwaardemaker, H., The sense of smell, *Acta Oto-Laryngologica*, 11, (1): 3 - 15, 1927

Chapter 9

Conclusions, Perspectives and Further Studies

"Problems cause still more problems. Although research and development have a beginning, there really is no end. The more we know, the more we discover how much we don't know."
(Takasago Private Report)

In the opening remarks presented in Chapter 2 of this thesis, several topics within olfactory perception, odor modeling or engineering perfume design were highlighted. However, it was known that not all these issues could be addressed here, nor answers would be found for all the questions raised. The vastness and complexity of the main areas involved in this thesis together with their interdisciplinary nature make any attempt to exhaust all matters remarkably difficult.

Even so, throughout this thesis, several topics concerning the formulation of fragrances, prediction of odor intensity and character classification, olfactory analysis or detection, and evaluation of the performance of perfumed products were addressed. It is now time to summarize the major conclusions withdrawn from this work, covering some issues and misfortunes experienced, but also emphasizing the pleasure of some achievements. After that, a brief journey through some current *"hot topics"* within the research fields of this thesis will be highlighted along with a perspective of the application of R&D to the industry.

Finally, over the course of this work different paths of research were being shaped as it progressed and so new windows of opportunities have also been created: as said before some were explored in this thesis, other remained on the shelf to mature their ideas. Therefore, some topics that have been flourishing throughout these years will be presented as an opportunity for future studies.

9.1. Conclusions

The first part of the work presented in this thesis was oriented to the extension of the previously developed Perfumery Ternary Diagram (PTD®) methodology which represented the perceived odor character of ternary mixtures (or quaternary ones if considering, for example, a solvent-free basis). For that, in Chapter 3 the Perfumery Quaternary-Quinary Diagram (PQ2D®) was developed as an extension of this methodology based on a graphical tool using tetrahedric diagrams to map the perceived odor of quaternary or quinary mixtures. With the PQ2D® it is possible to study the whole behavior of a simple structured perfume with a top, middle and a base note plus a solvent by representing and visualizing its odor character simultaneously in a 3-D plot. The PQ2D® methodology was used to evaluate the effect of different base notes in perfume formulation. It was shown that some had a fixative effect on the remaining components confirming experimental evidences from the perfumery business. The effect of water on perfume formulation and consequently on the perceived odor was also addressed in quinary systems of the type: limonene + geraniol + (vanillin or galaxolide) + ethanol + water. It was shown that water tends to fixate polar compounds like ethanol, thus preventing it from being strongly perceived at initial times which would be undesirable from the consumer point of view. Finally, this tool was, once more, extended to octonary fragrance mixtures, thus incorporating two different fragrances for each note and two solvents. Although this representation presents restrictions for the perfume formulation, it allows mapping the perceived odor of mixtures with a higher number of fragrance ingredients. Moreover, it can be thought that the application of this PQ2D® methodology to the fragrance industry would allow reducing the number of trial-and-error formulations, but also decrease time and cost for fragrance product design.

For the quantification of the odor intensity and consequently the perceived character of a mixture of odorants there is one important parameter to take into consideration: the odor detection threshold (ODT). Its calculation from experimental data is laborious and requires both panelists and adequate equipment. Moreover, literature data for the same odorant may present large deviations as 2 or 3 orders of magnitude. For these reasons, modeling ODTs would be of great value, since it would allow having an estimate of such parameter without having the skills, reagents or equipments needed. For that, a model for olfactory detection and a new regression was proposed for prediction of ODTs in air using only three widely available physical properties: vapor pressure, water solubility and 1-octanol/water partition coefficient. The theory behind this model was based on the physicochemical phenomena occurring from the moment that odorant molecules are present in air to their binding with the olfactory receptors (OR). In this way, biochemical processes at the molecular level which are still far from being understood were neglected. The proposed correlation was developed with 121 chemical odorants with different functional groups and validated with a test set showing good results for estimating ODTs in air. It was obtained a correlation coefficient of 0.77 which compares favorably with others in the literature and shows a fairly good reliability of the model for such a complex physical phenomena.

Following the outlined methodology for odor perception developed at the beginning of this thesis, it was also important to evaluate the vapor-liquid equilibria (VLE) of fragrance mixtures. For that several fragrance systems were evaluated by headspace-gas chromatography (HS-GC). Different techniques were tested due to the difficulty of the experimental procedure (in part because of the high volatility of components, complexity of handling solid base notes, types of vials and syringes) until the protocol was optimized with low standard deviations between replicates. The obtained results were compared with those predicted by four group-contribution methods (UNIFAC, ASOG, UNIFAC-Dortmund and A-UNIFAC). This comparison with experimental data considered both the relationship between liquid and vapor compositions and the olfactory analysis for the perceived dominant odor. It was shown that all group-contribution methods performed well, and that the original UNIFAC (with its updates) was the best model. Most important of all, in terms of product design, the dominant odor within the different multi-component fragrance mixtures calculated from the predicted vapor compositions showed a very good agreement of 95.4% (UNIFAC) with

the experimental measurements. Moreover, their comparison with a panelist olfactory evaluation resulted in a relatively good agreement of 54% and 59% for panelist 1 and 2, respectively. From this study, it could be said that the VLE of fragrance mixtures is well predicted from group-contribution methods. Consequently, the application of the odor perception model (where VLE takes its part) showed that the prediction of the odor character of fragrance mixtures was in good agreement with experimental measurements.

After the evaporation process, fragrances will diffuse in the air, so that a perfume will be perceived differently over time and distance. In this process, one important variable for product design and formulation should be highlighted: product performance. In the fragrance industry this is evaluated in terms of the perceived intensity and character of a perfume with time and distance from the releasing source. The concept is a simple perfume diffusion model based on Fick 2nd law which was developed and implemented in MATLAB which was applied to different fragrance systems to predict their performance. In a first stage, several experimental evidences were extracted from the predicted results, thus showing the applicability of the model. Moreover, as a proof of concept, a vertical stainless steel diffusion tube was specifically designed for the purpose of evaluating the diffusion of fragrance chemicals. The experimental protocol proved to be difficult to implement for gaseous measurements (for example, gas leaks from septa in the sampling ports or sampling losses from gas tight syringes). After several trials, leaks were minimized and the experimental protocol was optimized to give good and reproducible results. Experimental measurements were performed in this equipment obtaining diffusion profiles for odorants in time and distance. The performance of different fragrance mixtures was also evaluated showing the effect of ethanol and fixatives in the perfume formulation.

From the evaporation and diffusion of fragrances in air it is time to address the way the human olfactory system perceives odors and mixtures of them at suprathreshold concentrations. The last step of the methodology behind the PQ2D® is probably one of the most complex and difficult to unravel within the sense of smell. That deals with Psychophysics for the evaluation of the odor intensity and character. The latter is definitely much more difficult to understand: it deals with character classification of single molecules and so it remains tied to the experimental olfactory classification from

experts. However, in terms of the prediction of odor intensity there are several models derived over the years like the Weber-Fechner Law, the Steven's Power Law or the Odor Value (OV) model which were all tested in this study for several fragrance mixtures. These psychophysical intensity models use different metric scales, so their comparison must be done in terms of the prediction of perceived dominant odor. Some differences were observed for the prediction of the odor character at initial times after application of the perfume: the Power Law model predicted that ethanol was more strongly perceived than the OV model, but for longer times there were no significant differences. Finally, the comparison of these models for the predicted odor character with human olfactory evaluations has shown a good agreement among them. All the models performed well but for mixtures without ethanol the Power Law was better with an agreement of 75% for the dominant note.

The classification of the olfactive character of fragrances is performed by experts (perfumers) at the industry but large discrepancies are observed in perfume classifications between fragrance houses. This fact is mainly attributed to the interpersonal physiological variability of the human being. In order to overcome this issue, a new methodology called Perfumery Radar (PR) was developed in this work aiming for a scientific and standardized classification of perfumes. It uses models for the prediction of the VLE, diffusion of fragrances and Psychophysics for a qualitative classification of perfumes, instead of relying on the sensorial perception of perfumers only. It was shown that the PR methodology correctly predicted the primary olfactive family of four essential oils and several commercial perfumes. In this way, this is a new and valuable technique for the prediction of perfumes' olfactive families.Its application in the industry could give important guidelines for the design of perfumed products. From this work, several essential oils and commercial perfumes of different types were analyzed by GC-FID-MS. From that, it was developed a compilation of ~250 chemical odorants with their corresponding properties: physicochemical (name, C.A.S., molecular weight and formula, vapor pressure, odor thresholds), olfactory properties (primary, secondary and tertiary families) and structural group assignments (UNIFAC). This in-house database was implemented in the software developed for the PR methodology so that it can work with any possible mixture of fragrance chemicals.

9.2. Perspectives & Further Studies

9.2.1. The Holy Grail in Olfaction

As aforementioned, throughout this thesis, there is a wide range of opportunities for research & development within fragrance design, formulation and perception. These should also be of great interest for the fragrance industry. A great part of that stems from the complexity of the olfactory system and the lack of knowledge we have from it. The olfactory system is an incredible receiving and integrating mechanism that is continually collecting multiple (supra-threshold) odor sensations. It is also a powerful chemical sense that is closely linked to the brain's emotional center. Thus, it is not surprising that it can play a strong role on our attitudes, moods or decisions. It can influence people's cardiac rhythm, make us salivate or stir our memories of pleasant times in our lives. For all this, smell can also make us buy products, which adds an economically relevant perspective. In this way, it is undisputable the relevance of the olfactory system in our lives.

However, several system-level organizations of olfaction still remain unexplored and so the mechanisms behind olfactory detection and recognition are still far from being completely understood. For it, I believe that the Holy Grail within this field, which consequently will have an effect on others, will be the discovery and understanding of the biochemical and neurological mechanisms behind odor detection, recognition and intensity (Gazzaniga, 2004; Reed, 2004). From that point, it will be possible to understand how we detect, recognize and associate words to odors at the molecular and neuronal levels. Only with that level of knowledge one may establish more complex and reliable models for olfaction, unless it is by serendipity (Sell, 2006). Thus, it is difficult to point a way to find those answers, but it is likely that it will encompass molecular genetics and neuroscience studies. In the former, there is a large number of research groups around the world who have been focusing on the study of the interactions between odorant binding proteins (OBP), and its peers odorants and olfactory receptors (OR) (Taylor, *et al.*, 2008; Yabuki, *et al.*, 2010). In the latter, it is also believed that neuroscience may help understanding the role of ORs in human olfaction and, thus, contribute to unravel the sense of smell (Fleischer, *et al.*, 2009; Saito, *et al.*, 2009). Despite all this, it is my opinion that the discovery of the functioning of these phenomena at molecular level will take long. Until then, small steps will be taken in little discoveries, some of which are postulated ahead.

9.2.2. Extension of the PQ2D® methodology

On the other hand, it may be argued that Perfume Engineering can also help (in part) for this knowledge but definitely it can play an important role in the evaluation of molecular interactions in liquid solutions, gas diffusion in air and in predicting the intensity of the smell of mixed fragrances. It is known that the fragrance and related industries that deal with other products containing fragrances (*e.g.* household cleaners) currently use some tools similar to those developed in this work for the development of their own products. For that reason and considering that fragrance products often contain a large number of ingredients, it would be of great interest to continue extending the PQ2D® methodology developed in this thesis for *N* component mixtures. The software developed in this work is perfectly suitable for the calculation of the odor intensity and character of *N* fragrant components. The purpose in this topic would be to find a graphical representation that would make possible to easily visualize the distribution of the (initial) odor intensity and character of such a multi-component mixture (instead of having a large amount of numbers dispersed in tables or projection cuts of *N* dimensional planes that are hard to see).

9.2.3. Fragrance stability

Closely related to this last topic, is the fact that the fragrance industry is "speeding up", or in other words, is producing different fragrance products in larger numbers and in shorter times. Twenty-five years ago, less than a hundred perfumes were introduced each year but only in 2008 there were around a thousand launched on the market (although many of these will ultimately not succeed and be discontinued). A reason for this exponential growth is because unlike 30 years ago, the life of a perfume today, is relatively short. According to J. Lefingwell, *"in many cases now a fragrance will be very popular for a year or two, then the consumers move on" in* (Davies, 2009). This interpersonal "volatility" of tastes crosses continents and cultures, because it is a consequence of the evolution of our society, and so pushes the industry to produce new formulations faster. If the PQ2D® methodology may speed up the design process of new fragrances, there may be other limiting steps for the formulation of the final product like the evaluation of product stability or maceration time. For the former, stability issues are most commonly related to the addition of fragrances to functional products,

although some considerations are also taken into account in fine fragrances. From a consumer point of view, fragrance products must be unvarying in terms of quality. For that, the main issues include: *i)* chemical interactions between fragrance ingredients or components of the product base (where pH plays an important role also); *ii)* compatibility with the container or package material (*e.g.* should avoid evaporation losses); *iii)* the possibility of product discoloration (*e.g.* due to complex formation with iron or other metal ions or UV irradiation effects); *iv)* compound oxidation (*e.g.* unsaturated terpenes are likely to undergo air oxidation); *v)* and loss of perfume strength by evaporation that leads to a change in odor character (Poucher, 1955; Calkin and Jellinek, 1994). The problem is that although the majority of the reactions leading to perfume instability are known and understood (and so its behavior could be predicted *a priori*), in practice the combination of such factors may turn it difficult to foresee. On the other hand, the maceration time for a perfume is usually long (several weeks or even months), in order to guarantee that (eventual) reactive processes are controlled and that the product is kept stable ("steady-state"). The problem here is that the maceration period often exceeds the time that would be really necessary to obtain the desired organoleptic properties for the perfume (Lopez-Nogueroles, *et al.*, 2010). In this way, a further study that would encompass the prediction of the stability of fragrance products and minimum maceration time needed, would then contribute to decrease product formulation time and economic costs.

9.2.4. Fragrance performance: different routes

Another important topic inside the fragrance industry is related with the performance of their products. Fragrances are volatile compounds that do not often last long in air (especially if convection phenomena is involved), so that the performance of fragranced products is often measured by its pleasantness together with the lastingness and the diffusivity of the fragrance ingredients (Gygax and Koch, 2001). However, lastingness can be improved by means of controlled release mechanism or devices. There are a number of typical routes to develop long lasting fragrances that can be related to the chemical synthesis of new odorant molecules, use of pro-fragrances, microencapsulation techniques, among others. The increase of fragrance concentrations in air or any other media presents several advantages: it is not only socially enjoyable but it is also useful for applications like masking malodors. Whenever a persistent odor

remains in the clothes, on our body or in the air, the use of techniques for slow fragrance release and long lasting scents is valuable.

In this way, one of the approaches relies on chemical synthesis of new odorant molecules (or simply by changing small parts of it, the so-called group substitution). For example, it is possible to reduce the odorant volatility without changing its odor characteristics. These methods are already used at the industry with the Doremox® molecule, which is a derivative of the rose oxide, chemically modified by increasing its molecular weight and resulting in a 10-fold less volatile molecule than its precursor (Watkins, *et al.*, 1993).

Another technique is the use of dynamic mixtures where fragrances are mixed together with fragrance precursors, called pro-fragrances, and reversible covalent reactions occur (Levrand, *et al.*, 2006; Herrmann, 2007). In this process, the fragrance is chemically produced after a trigger is activated, and then it is released. Different triggers may be used: enzymes, light, temperature or pH change, hydrolysis, or dynamic equilibrium (Levrand, *et al.*, 2006). This process is expected to produce a slow release of fragrance materials in the air, thus producing a long-lasting perceived odor sensation (Herrmann, 2007). This concept (which is widely used by the pharmaceutical industry) was introduced to functional perfumery by Firmenich in the mid 90's (Gautschi, *et al.*, 2001). Back then, for textile applications they used lipases in their detergent formulations to hydrolyze esters of fragrant alcohols, which in turn had better affinities towards fabrics than other fragrance ingredients.

Nevertheless, the most common process for the controlled release of highly volatile odorants has its origin in drug release techniques: the encapsulation of odorants into matrices or specifically designed capsules. This technology often makes use of polymeric microcapsules which act as small containers of a liquid solution to be released from the inner core under controlled conditions to address a specific purpose. In this way, it slows down their release and improves the lastingness of the fragranced product (Rodrigues, *et al.*, 2009).

The performance of fragrances was one of the topics addressed in this thesis for several fragrance mixtures. A diffusion tube with several sampling ports was used to evaluate that for pure fragrances and liquid solutions, along with a simple diffusion model for the prediction of the odor concentration profiles in air. In terms of performance, models were also applied for a fragrance application to textiles. However, the evaluation of the performance of fragrance products is not exhausted here, and many other applications of

interest as those aforementioned should be explored. Thus, it would be of interest to perform further studies on the evaluation of the performance of fragrance ingredients mixed with different bases (*e.g.* ethanol, dipropylene glycol, diethyl phthalate, polyethylene glycol, waxes, gels, emulsions), applied in different substracts (*e.g.* different textiles, skin, paper blotter) or combined with some other techniques like microencapsulation. There are a large number of fragranced products available in the market with different properties and functions like detergents, shampoos, creams and so on. For that, it would be important to: *i)* determine the lowest possible perfume dosage to achieve the (maximum) desired odor effect; *ii)* study the effect of fixatives (materials of low volatility) in the evaporation of more volatile perfume components and on the perfume odor profile with time and distance; *iii)* determine the olfactive changes during the evaporation of test perfumes and of some commercial ones from wet to dry substrates using panelists for olfactory evaluations; *iv)* Development of different diffusion models in MATLAB or gProms software for the modeling of the above physical processes considering: 1) only a liquid perfume mixture; 2) the adsorption mechanism fragrance-subtract when a perfume is deposited on a wet substrate; *v)* evaluate the changes in the perfume odor profile as a function of time and distance, using the previously developed PR methodology.

9.2.5. Olfactive marketing

Another application of fragrance performance deals with a recent trend in the industry called brand scenting or olfactive marketing. It is a growing fashion in merchandising places although the power of scent and its influence on people is still not fully understood, as we have seen before. Companies typically had their brand marketing driven only by visual images or fashionable music (Moeran, 2007). However, there has been a shift in recent years towards aesthetic or sensory branding. The idea remains the same: attract consumers by appealing to their senses (sight, hearing or olfaction) and induce them to stop, smell and buy their products. Having said that, why marketing of brands should not be oriented to olfactory sensations or emotions instead?

In fact, companies have already started to associate pleasant scents to their brands, trying to make the scent recalling the brand to the consumer. To render this idea of sensorial marketing, there are plenty of examples with scenting applications: shops, malls, supermarkets, casinos, hotels, office buildings, cinemas or department stores just

to mention a few (Whiff Solutions, 2008; I-sensis, 2010; Scent Marketing Institute, 2011). As a result, in 2007 the scent marketing industry was billed at $100 million and future predictions pointed to reach up to $1 billion by 2015 (Bradford and Desrochers, 2009). Additionally, it was considered as one of the top ten trends to be watched in the upcoming years (Thomaselli, 2006). Nonetheless this effect of smell on consumer decision-making behavior, it is rather surprising that olfactory marketing still remains comparatively undeveloped as a discipline (Moeran, 2007). The method of application is typically by using air conditioning systems together with fragrance diffusing apparels, which are used for the diffusion of the fragrances in the surrounding environment. One important task would be to model this release and dispersion phenomena in closed environments, for which Chemical Engineering has plenty of tools. The principle for the modeling of odor perception should use the concepts of odor threshold concentration and perception of odor quality as its basis. Then the determination of the exact concentration of fragrance needed so that it is perceived by the customers as a pleasant odor around the room is a function of the diffusivities and those two previous parameters. For that, the modeling of such environments together with the dispersion of the odor using mathematical diffusion models or computational fluid dynamics (CFD) techniques would be of great value for this industry.

9.2.6. New applications and extension of the Perfumery Radar

One of the major topics addressed in this thesis was the Perfumery Radar as a theoretical tool for the classification of multi-component complex mixtures in olfactive families or classes. The PR methodology was applied to essential oils, feminine and unisex commercial perfumes being validated with the classifications from perfumers and by performing experimental perfumery radars using chromatographic techniques. However, it should also be important to extend this methodology to masculine perfumes and evaluate several aspects like: *i)* number and type of olfactive families; *ii)* layout of the olfactive families in the radar; *iii)* location of the fougère family (typically masculine) which is a combination of different scents/families; *iv)* development of a theoretically-based weighing criteria for subfamilies. Another application of the PR methodology that could be explored would be for wine science and classification. As suggested in *The Economist* magazine when reporting on the Perfumery Radar*"It might also find a use in other trades that require a good nose. A wine radar would settle any*

argument between oenophiles as to whether a slight whiff of soggy cardboard indicates that a $1000 bottle of claret has become corked" (Kaplan, 2010). Although there are differences in the composition of perfumes and wines, the PR methodology could be applied to this field with some changes and adaptations.

9.2.7. Integrative approach for product development: the role of microeconomics and planning strategies

It was already highlighted in this thesis the skills a product engineer must have and, consequently, the approach that must be followed when developing a new product for the market. In this thesis the classical perspective of Product Engineering which encloses the Needs-Ideas-Selection-Manufacture was generally followed: it starts with the identification of consumer needs, which leads to the development of ideas and, then, their selection is made up to the manufacture of the product (Ulrich and Eppinger, 2000; Cussler and Moggridge, 2001; Wesselingh, *et al.*, 2007). There are several approaches that have been proposed for chemical product development over the last decade which are very similar in their definition of stages. However, it is also equally true that recently some valuable contributions have been inputted to those approaches, especially dealing with microeconomics for a sustainable product development. For that, it was already mentioned the industry framework of the Stage-Gate™ Product Development Process (STPDP) which uses product design strategies based on decision analysis (Cooper, 2001; Seider, *et al.*, 2010) and the approach of Bagajewicz (Bagajewicz, 2007), who applies microeconomics evaluations from the beginning of product design.

In this way, it would be of great value to perform an economic evaluation/prediction of the product cost, potential and (eventual) success in the market for a new fragranced product or a new commercial perfume to be developed. It is known though, that it is extremely difficult to evaluate consumer preferences for a perfume, and thus to predict its success. So far, the triumph of a perfume in the market has been put on the hands of the perfumers (who develop the fragrance), the brand or celebrity that signs the product and the money that is spent on marketing and publicity. Nevertheless, the development of a model or approach that would consider a pre-evaluation of consumer demand by introducing pricing and microeconomics models in order to define the best properties for the desired product would be an excellent task for further studies and also, without a doubt, for the industry as well.

In sum, there are plenty of opportunities and new applications for fragrance research in the future ahead. For that, the understanding of how do humans perceive odors and mixtures of them will be crucial for the success in many different fields. Nevertheless, odors will always make part of our lives, ruling somehow our behavior.

9.3. References

Bagajewicz, M., On the Role of Microeconomics, Multi-scale Planning and Finances in Product Design, *AIChE Journal*, 53, (12): 3155- 3170, 2007

Bradford, K. D., Desrochers, D. M., The Use of Scents to Influence Consumers: The Sense of Using Scents to Make Cents, *Journal of Business Ethics*, 90, 141-153, 2009

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Cooper, R. G., Winning at new products: accelerating the process from idea to launch, New York, Perseus Publishing, 2001

Cussler, E. C., Moggridge, G. D., Chemical Product Design, Cambridge, Cambridge University Press, 2001

Davies, E., The sweet scent of success, *Chemistry World*, 40-44, 2009

Fleischer, J., Breer, H., Strotmann, J., Mammalian olfactory receptors, *Front Cell Neurosci*, 3, 9, 2009

Gautschi, M., Bajgrowicz, J. A., Kraft, P., Fragrance chemistry - Milestones and perspectives, *Chimia*, 55, (5): 379-387, 2001

Gazzaniga, M. S., The cognitive neurosciences, Cambridge, USA, The MIT Press, 2004

Gygax, H., Koch, H., The measurement of odours, *Chimia*, 55, (5): 401-405, 2001

Herrmann, A., Controlled release of volatiles under mild reaction conditions: From nature to everyday products, *Angewandte Chemie-International Edition*, 46, (31): 5836-5863, 2007

I-sensis, S. João da Madeira, Portugal. November, 2010, from www.i-sensis.com, Last Accessed on

Kaplan, M., Making sense of scents - A new way to describe a fragrance. The Economist. Science & technology. 2010

Levrand, B., Ruff, Y., Lehn, J. M., Herrmann, A., Controlled release of volatile aldehydes and ketones by reversible hydrazone formation - "classical" profragrances are getting dynamic, *Chemical Communications*, (28): 2965-2967, 2006

Lopez-Nogueroles, M., Chisvert, A., Salvador, A., A chromatochemometric approach for evaluating and selecting the perfume maceration time, *Journal of Chromatography A*, 1217, (18): 3150-3160, 2010

Moeran, B., Marketing scents and the anthropology of smell, *Social Anthropology*, 15, (2): 153–168, 2007

Poucher, W. A., A classification of odors and its uses, *Journal Soc. Cosmet. Chem.*, 81-95, 1955

Reed, R. R., After the holy grail: Establishing a molecular basis for mammalian olfaction, *Cell*, 116, (2): 329-336, 2004

Rodrigues, S. N., Martins, I. M., Fernandes, I. P., Gomes, P. B., Mata, V. G., Barreiro, M. F., Rodrigues, A. E., Scentfashion®: Microencapsulated perfumes for textile application, *Chemical Engineering Journal*, 149, 463–472, 2009

Saito, H., Chi, Q. Y., Zhuang, H. Y., Matsunami, H., Mainland, J., Odor coding by a mammalian receptor repertoire, *Neuroscience Research*, 65, S76-S76, 2009

Scent Marketing Institute, from http://www.scentmarketing.org/, Last Accessed on 2011

Seider, W. D., Seader, J. D., Lewin, D. R., Widagdo, S., Product and Process Design Principles: Synthesis, Analysis and Evaluation, Asia, John Wiley & Sons, Inc., 2010

Sell, C. S., On the unpredictability of odor, *Angewandte Chemie-International Edition*, 45, (38): 6254-6261, 2006

Taylor, A. J., Cook, D. J., Scott, D. J., Role of Odorant Binding Proteins: Comparing Hypothetical Mechanisms with Experimental Data, *Chemosensory Perception*, 1, (2): 153-162, 2008

Thomaselli, R., Trends to Watch in 2007, *Advertising Age*, 77, (51): 10, 2006

Ulrich, K. T., Eppinger, S. D., Product Design and Development, New York, McGraw-Hill, 2000

Watkins, H., Liu, O. C., Krivda, J. A., Use of tetra:hydro-4-methyl -2-phenyl-2H-pyran as a perfume ingredient - capable of imparting a very fresh and green odour note with a rosy character. Firmenich SA1993

Wesselingh, J. A., Kiil, S., Vigild, M. E., Design & development of biological, chemical, food and pharmaceutical products, Chichester, U.K., Wiley, 2007

Whiff Solutions, L., from www.whiffsolutions.com, Last Accessed on

Yabuki, M., Portman, K. L., Scott, D. J., Briand, L., Taylor, A. J., DyBOBS: A Dynamic Biomimetic Assay for Odorant-Binding to Odor-Binding Protein, *Chemosensory Perception*, 3, (2): 108-117, 2010

Annex A

A. Models for odor intensity

Here, a detailed overview of the most significant odor intensity models for single odorants and for mixtures of them will be performed. The analysis of the experimental methodologies and the pros and cons of the models will be discussed.

A.1. Models for odor intensity of single fragrance ingredients

The Weber-Fechner Law

The first relationship between a stimulus and its perceived sensation to be postulated in the history of Psychophysics was based on Weber's theory, first published in 1851 (Weber, 1905). His theory gained attention a few decades later, in the 1870s, when Weber's empirical hypothesis were mathematically expressed by Fechner (Stevens, 1957; Shigemoto, 2004; Zwislocki, 2009). From that the Weber-Fechner law stated that as stimulus strength grew geometrically (by constant ratios) the sensation magnitude increased arithmetically, or in other words, the magnitude of the psychological sense would be proportional to the logarithm of the ratio of physical stimulus by the threshold magnitude:

$$\psi = k_w \cdot log\left(\frac{S}{S_0}\right) \qquad \text{(A1)}$$

where ψ is the sensation magnitude, k_w is the Weber-Fechner constant (often a positive factor), S is the stimulus magnitude and S_0 is the threshold of the magnitude of the physical stimulus (Zwislocki, 2009).

Physicists and psychologists have agreed that this logarithmic law could not be applicable to all perceptual continua. Nonetheless, the model persisted for more than a century mainly due to the fact that there were only contrary arguments, but not a widely-accepted model. In this way, two important issues have been raised against the Weber-Fechner Law:

(i) Metrics of the measurement of sensation: Fechner considered each unitary increment in sensation (defined as a *"just noticeable difference"* or *j.n.d.*) as a constant increment. This would result in a proportional interval scale for measuring the intensity of a sensation provoked by an input stimulus which is not observed for several examples (*e.g.* the perception of sound is not linearly proportional as the stimulus magnitude is increased since at a pain level, for example, we do not equally define an increase in sound intensity, so that the *j.n.d.* would not be a constant increment) (Stevens, 1957).

(ii) It is based on indirect experiments and indirect measurements of magnitude sensation; modern psychophysicists support their ideas on direct measurements, which reduces errors that are difficult to eliminate in such a sensorial science (Stevens, 1957; Teixeira*, et al.*, 2010).

Even so, despite being criticized by many, the Weber-Fechner law is still used today for several applications like olfactory analyses of odors eluting from drinking water, release of odorants from municipal solid waste landfills or for the evaluation of indoor air quality (see for example (Jokl, 2000; Sarkar and Hobbs, 2002; Omur-Ozbek and Dietrich, 2008)). There also some recent reports that consider the Weber-Fechner law as a suitable model for the description of odorants intensity in air (Sarkar and Hobbs, 2002; Heidelberger, 2004). Nevertheless, prior to draw any inference about the application of this model it is necessary to consider its range of applicability, array of odorant concentrations and their perceived intensity. However, at the beginning of the XX century many psychophysicists criticized the theories proposed by Weber-Fechner but they still failed to propose an alternative. It was not until the 30s that the first direct methods were applied in the area of Psychophysics.

The Power Law

A general mathematical equation relating sensation magnitude with physical stimulus for all perceptual continua was proposed by the American psychologist Stanley Smith Stevens (1906-1973). The Stevens Psychophysical Law, or the power law, set forth that the sensation magnitude, ψ, is proportional to the stimulus S raised to an exponent n, so that:

$$\psi = k.S^n \qquad \text{(A2)}$$

The derivation of this relationship was based on the fitting of experimental data for different perceptual continua. One of the landmarks of Stevens' work is the development of sensorial experiences based on direct measurements and judgments for many different types of sensorial perceptions. This was a fundamental change in respect to Weber-Fechner indirect experiences (Stevens, 1957, 1961, 1964; Dalton, 2002). The use of direct methods showed that, at least to a first order approximation, the ratio scale of magnitude perception followed a power function. Adapting Equation A2 for the measurement of odor intensity, it is obtained:

$$\psi = \left(\frac{C^g}{ODT} \right)^n \tag{A3}$$

where C^g is the concentration of an odorant in the gas phase ($g.m^{-3}$), *ODT* is the odor detection threshold in air ($g.m^{-3}$) while *n* represents the odor power exponent. This equation can be plotted in a log-log scale to obtain a linear relationship between the stimulus and its perceived sensation where the slope equals the exponent *n* and the intercept is a function of the odor threshold. Compilations of odor concentration threshold and exponents for the power law are available in the open literature for several hundreds/thousands of odorant chemicals (see for example (Calkin and Jellinek, 1994; van Gemert, 2003; Leffingwell and Leffingwell)).

The principle of the power law lays on the assumption that equal stimulus ratios tend to produce equal sensation ratios (Stevens, 1957). In fact, Stevens' experiments consisted of asking observers that were presented with different intensity stimuli to make a numerical or category judgment of their subjective experience. The use of direct methods in opposition to the indirect methods revealed that a power law was behind the explanation for perceived intensity in different perceptual continua.

It is a straightforward reasoning that the psychophysical power law is a nonlinear relationship between the strength of some stimulus and its sensory magnitude. However, if one plots it in a log-log scale a linear relationship will be obtained, being the power exponent defined by the slope, as presented in Figure A1.

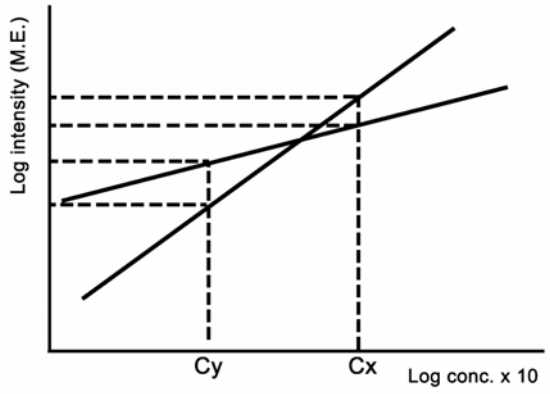


Figure A1 – Logarithm of the perceived intensiy as a function of the logarithm of the fragrance concentration for two distinct odorants. [Reproduced from Cortez-Pereira *et al.*, Journal of Sensory Studies. 2009; 24(6):871-901]

If the exponent is lower than unity ($n < 1$), it is called compressive and the odor intensity increases slowly with the concentration; for exponents equal to unity ($n = 1$) there is a linear relationship between concentration and perceived sensation which would then be linearly proportional; and finally, if the exponent is higher than unity ($n > 1$), it is said to be expansive and the odor intensity increases more rapidly with the concentration (Teixeira*, et al.*, 2010). Whereas sugars tend to produce power function exponents for sweetness slightly greater than 1 with a mean of 1.33, acids have a propensity to give exponents smaller than 1 for sourness (Kamadia*, et al.*, 2006). In olfaction, the majority of the odorants seem to generate power functions with exponents equal or smaller than unity, and it is suggested an average value of 0.35 whenever the exponent is not known (Devos*, et al.*, 2002).

However, it is worth to mention that although the power law has had great impact and applicability since it was postulated, it also has some controversies. In this way, its major drawbacks were first seen from Stevens' experiments and are reported below.

i) Throughout its experiments it was not performed a straight test of the power law, but a fitting to experimental data that showed to be correlated by a power function (Luce, 2002).

ii) Stevens' tests also missed out any personal differences between the subjects. In fact, the power function did not always hold when data were considered separately from individual respondents (Green and Luce, 1974).

iii) When backgrounds are introduced in continua measurements (*e.g.* background noise in loudness or background scents in olfaction) the shape of the magnitude estimation function sharply deviates from the power function (Luce, 1990).

There are some other variables that affect perception magnitude like adaptation or human sensory modification, among others (Stevens, 1964).

Following this line of thought, there were some authors that have a more critical perspective of the power law as well as the previous Weber-Fechner law, even disproving their applicability to different perceptual continua (Weiss, 1981; Krueger, 1989; Augustin, 2008). Nevertheless, as for olfaction, it can be said that the Stevens power law is a suitable model and perhaps the most accepted one for odor intensity scales (Dalton, 2002; Sarkar and Hobbs, 2002; Kamadia*, et al.*, 2006; Ryan*, et al.*, 2008).

The Odor Value

The Odor Value (OV) concept expresses the relationship between stimuli and perception by a linear function. This way there will be a linear relationship between odorant concentration and its perceived intensity. This linear law is shown in Equation A4, where the OV stands as a measure of the odor intensity (see for example(Calkin and Jellinek, 1994; Baydar*, et al.*, 1995; van Gemert, 2003; Mata*, et al.*, 2005)).

$$OV = \frac{C^g}{Thr} \qquad \text{(A4)}$$

This linear law can be considered as a special case of the aforementioned power law for n = 1. For this linear response the perceived odor intensity is directly proportional to the odorant concentration across all the range. It is a fact that the OV model is easier to be applied once values for odor concentration threshold (detection or recognition) can be obtained from the literature in data series for numerous fragrant species, as previously reported, while power law exponents data are limited (Devos*, et al.*, 1990; Devos*, et al.*, 2002).

Other models of relevance

On the other hand, despite the recognized value of the aforementioned models, it should be highlighted that others were developed for the perception of single odorants. Following this trend, Beidler (Beidler, 1966) derived a mathematical equation for the relationship between the stimulus concentration and its perceived steady-state magnitude of response. The proposed model was oriented for both taste and olfaction. It

was based on the biological mechanisms of excitation of taste and olfactory receptors which according to Beidler depended upon adsorption of the flavor or odorant molecules to the receptor surfaces. In this model the relationship between the response magnitudes with the concentration for the case of olfaction is presented in Equation A5:

$$\Psi = \frac{R_s K C^g}{K C^g + 1} \tag{A5}$$

where ψ is the neural response or sensation magnitude, R_s is the maximum neural response from a particular type of olfactory receptor at the saturation level, C^g is the odorant concentration in air and K is the equilibrium constant of the reaction between the stimulus and the receptor. Beidler's equation presents certain similarities both with the Langmuir adsorption isotherm, and the equations used to describe enzyme-substrate reactions (Beidler, 1966; Sarkar and Hobbs, 2002).

Later, Laffort (Sarkar and Hobbs, 2002) proposed a modification for the fundamental taste equation to describe psychophysical functions of odor intensity. This model is based on the Stevens' power function and is mathematically represented by Equation A6:

$$\Psi = \left(\frac{C^g}{1 + C^g \Psi_{max}^{-1/n}} \right)^n \tag{A6}$$

where ψ is the neural response or sensation magnitude, ψ_{max} is the maximum neural response from a particular type of olfactory receptor at the saturation level, C^g is the odorant concentration in air and n is the power exponent which is different for each odorant chemical. Both Beidler's and Laffort's equations imply that at high perceived sensations, equal ratio increments in stimulus would cause smaller increments in sensation, as expected from any power law (Sarkar and Hobbs, 2002).

Very recently, another scientific approach resulted in a linear law as a function of sensation magnitude, called the law of asymptotic linearity (Zwislocki, 2009). This law states that all subjective magnitudes grow linearly with the stimuli intensity at near threshold values.

In brief, multisensory experiments together with its biophysical and biological fundamentals have been thoroughly discussed in the scientific community. Recent results found in the literature for the application of these models have shown good agreement for sensory perception in different perceptual continua. Nevertheless, care should be taken when choosing the model depending on the physical situation to be tested, experimental variables and availability of data for prediction purposes.

A.2. Models for odor intensity of mixtures

The result of the combination of two odorants can produce a mystifying perceived odor, either in terms of intensity or character. Moreover, the most common experimental techniques for the measurement of the odor intensity also present some drawbacks. Generally the experimental methodologies are based on ranking methods and referencing methods. In the former, odors are evaluated by panelists who rank the odor potency or the odor offensiveness of different samples using an arbitrary scale, usually limited from 0 to 10 (with 0 being the lowest intensity detected and 10 the highest). In the referencing methods, the intensity of odor samples is evaluated in comparison to a standard (usually 1-butanol). This type of measurements though, presents the disadvantage of using panelists which have inter-personal differences in the evaluation of odors (each person has a unique odor acuity.) Moreover variability in the sensitivity of a person from one day to the next can be as much as three times, due to mood, fatigue, or many other reasons.

Nevertheless, different series of experiments on odor perception for binary mixtures have shown some general rules that often apply for addition of two odorants (Laffort and Dravnieks, 1982; Berglund and Olsson, 1993; Olsson, 1998):

i) The mixture intensity tends always to be weaker than the arithmetic sum (*e.g.*, $\Psi_{ij} < \Psi_i + \Psi_j$) and stronger than the arithmetic mean (*e.g.*, $\Psi_{ij} > (\Psi_i + \Psi_j)/2$) of the odor intensity of each component present alone. This is called hypoaddition.

ii) The odor intensity of the resulting mixture is always higher than the weakest component, *e.g.*, $\Psi_{ij} > \min(\Psi_i, \Psi_j)$.

iii) The odor intensity of mixtures tend to show a certain compromise, which means that the overall intensity is within the intensity of their binary components, but tend to fall closer to the stronger of the unmixed compounds: $\Psi_i < \Psi_{ij} < \Psi_j$.

iv) Other findings less agreed upon include asymmetries in mixture summation, like the fact that the mixture intensity when compared to the additivity indicated by the specific power function for each component, tends to be of the same size as the self-additivity of the one with the smallest exponent ($\Psi_{ij} \approx 2 \cdot \Psi|_{min(i,j)}$).

There are two general approaches for measuring the overall odor perception of binary mixtures: one is the classical method which relates the olfactive perception to the concentrations of the single components (C_i and C_j), known as the psychophysical approach; the other method considers the perceived intensity of the two single odorants when they are presented alone (Ψ_i and Ψ_j), known as the perceptual approach (Berglund and Olsson, 1993). The former was mainly employed in early studies for mixture perception, while the later prevails in recent research. Following this trend, different mathematical models have been proposed, attempting to express the odor intensity of mixtures of odorants as a function of the odor intensities of the single constituents.

The Vectorial model

One of the first models to be proposed for the perception of odorant mixtures came to light in 1974 which was called the vectorial model (Laffort and Dravnieks, 1982). This model for the olfactory interaction of odorants in mixtures considers the vector addition of the perceived intensity of single odorants (within a mixture) to account for the overall intensity of the odorant mixture. It was first derived for binary mixtures and later extended for multi-component mixtures resulting in the generalized vectorial model which can be mathematically represented by Equation A7.

$$\psi_{mix} = \sqrt{\sum_{i=1}^{N} \psi_i^2 + \sum_{i=1}^{N-1} \sum_{i=1+1}^{N} 2\psi_i \psi_j \cos \alpha_{ij}} \qquad \text{(A7)}$$

where ψ represents the perceived odor intensity, i and j are odorant components, and $\cos \alpha_{ij}$ is an interaction constant. This interaction constant is a limitation of this model since it is empirically calculated for components of equal perceived intensities from a subset of the data or from previous results obtained for that particular mixture and later extrapolated for any mixture (Olsson, 1998). Generally, it is considered almost

independent of the concentrations of the odorants in the mixture (Laffort, *et al.*, 2002). So far it is not know any relationship of this parameter with the properties of the unmixed components, but it typically presents values in the range of 90-130° (Cain, *et al.*, 1995).

In the generalized model which was intended for more complex mixtures of odors, it was assumed that single or double "area" of interaction would be activated, depending whether binary or ternary mixtures were considered. However, experimental data collected for quaternary and quinary mixtures (but not three odor mixtures) evidenced only one common interaction "area" for all components in the mixture. Thus, this implied that the degree of odorant interaction was less than expected for the ternary mixtures (Berglund and Olsson, 1993; Cometto-Muniz, *et al.*, 2005). However, the main counterpart in the application of the vector model to experimental data relies in the difficulty and low reproducibility of measuring the olfactory interaction coefficient, $cos\ \alpha$ (Laffort and Dravnieks, 1982). Moreover, it does not account for hyperadditivity effects, where the perceived intensity of a mixture exceeds the sum of the perceived intensities of the unmixed components (Cain, *et al.*, 1995).

The U model

Patte and Laffort (1979) proposed the U Model attempting to overcome the limitations of its precedent vectorial model. The U model was first developed for binary mixtures by fitting experimental data which was previously obtained by Cain and Drexler (1974) (Laffort and Dravnieks, 1982; Cain, *et al.*, 1995). Later this model was extended to multi-component mixtures as presented in Equation A8.

$$\Psi_{mix} = \frac{1}{p}\left(\sum_{1}^{N}\Psi_{(N-1)} + \sum_{1}^{N}\Psi_{1}\right) + \frac{2\cos\alpha_{(N)}}{N}\sum_{1}^{N}\sqrt{\Psi_{(N-1)}\cdot\Psi_{1}} \qquad \text{(A8)}$$

where $cos\,\alpha_{(N)}$ is an interaction parameter that mirrors not only a sensory odor interaction but is also a consequence of the psychophysical power law. It should be highlighted though that this parameter of interaction is not related with a real angle α as happened with the vectorial model (Laffort, *et al.*, 2002). Instead this parameter is defined as:

$$\cos\alpha_{(N)} = \frac{\sum_{BIN=1}^{p(p-1)/2} \cos\alpha_{(BIN)} \cdot \Psi_{(BIN)}}{\sum_{BIN=1}^{p(p-1)/2} \Psi_{(BIN)}} \quad \text{(A9)}$$

where $\cos\alpha_{(BIN)}$ is experimentally determined using Equation A10.

$$\cos\alpha_{(BIN)} = \cos\alpha_{ij} = \frac{\Psi_{ij} - \Psi_i - \Psi_j}{2\sqrt{\Psi_i \Psi_j}} \quad \text{(A10)}$$

The U model overcomes (at some point) the difficulty of the vector model in measuring the $\cos\alpha$ parameter with reliability and reproducibility. Additionally, for literature data based on the magnitude estimation method, it was shown to predict better odor intensities than the vectorial model (Laffort and Dravnieks, 1982). However, both these two models consider that the intensity of the mixture is an additive function of the single intensities of their components apart. As it was aforementioned, the addition of an odorant to itself may not always follow arithmetic additivity for the whole range of concentrations (*e.g.* Weber-Fechner law, Power law and others).As a consequence of that assumption these models fail to take into consideration the mechanisms underlying odor perception (*e.g.* odorant-olfactory receptor binding, neural decoding).

The UPL2 model

Looking to overcome some of the flaws of the U model, Laffort and Dravnieks (1982) proposed a psychophysical model called the UPL model (as the U model but with PL as Power Law) for mixtures of odorants. This model was later improved for the UPL2 model where the exponents previously defined for the unmixed odorants were included, considering that a non-linear relationship would rule the odor interaction (Cain*, et al.*, 1995). The UPL2 model is mathematically expressed by Equation A8 (the same as the

U model), although in this case the term $cos\,\alpha_{(N)}$ is replaced by the term $cos\,\alpha_{(UPL2)}$ which considers the power law equation $\left(\psi = k.S^n\right)$ and is defined by Equation A11:

$$cos\,\alpha_{(UPL2)} = \frac{\Psi_i\, cos\,\alpha_i + \Psi_j\, cos\,\alpha_j}{\Psi_i \Psi_j} \tag{A11}$$

where each parameter is defined as:

$$cos\,\alpha_i = \frac{1 - P^{n_i} - \left(1-P\right)^{n_i}}{2P^{n_i/2}\left(1-P\right)^{n_i/2}}$$
$$cos\,\alpha_j = \frac{1 - P^{n_j} - \left(1-P\right)^{n_j}}{2P^{n_j/2}\left(1-P\right)^{n_j/2}} \tag{A12}$$

$$P = \frac{\psi_j^{1/n_j}}{\psi_i^{1/n_i} + \psi_j^{1/n_j}} \tag{A13}$$

It should be highlighted that in the case of binary mixtures $cos\,\alpha$ is supposed to remain constant at all reciprocal concentrations for both the vectorial and the U models, whereas in the UPL model it should vary with the reciprocal concentration (Laffort and Dravnieks, 1982). Since the UPL model is based on the power law it becomes necessary to know or obtain the olfactory exponents for the power function, which are only available in the literature for a limited number of odorant compounds (Devos*, et al.*, 2002). Additionally, they can be experimentally determined for single odorants which is not always easy to calculate. Nevertheless, the UPL model did not show significant improvements for the prediction of other intensity in mixtures compared to the previous U and vectorial models (Laffort and Dravnieks, 1982).

The Stronger component (SC) model

As aforementioned in the general rules observed for binary mixtures, their perceived intensity (especially for binary mixtures) tends to show some compromise, and it often falls close to the intensity of the stronger of the unmixed components. The Stronger Component (SC) model (sometimes misnamed as the Strongest Component Model) for a two-component mixture states that among all the odorant species present in the gas

phase, the one that is more strongly perceived and recognized by the human nose is the one having the highest odor intensity, although there is a mixture of perceived scents in the air. This way, the odor intensity of the mixture would be approximately equal to the intensity of the strongest component within it (Laffort and Dravnieks, 1982; Cain*, et al.*, 1995). This model presents also some suitability to represent the odor perception of multi-component mixtures, being mathematically defined by Equation A14.

$$\psi_{mix} = max\left(\psi_i\right) \qquad i = 1,...,N \tag{A14}$$

From experimental data it was verified that this model inhibits any odorant intensity additivity (as expected due to its definition – Equation A14), avoiding over-predicted intensities and resulting in a quite robust model (Laffort and Dravnieks, 1982). The SC model is a rough and simple model since it does not reflect the whole olfactory mechanism (*e.g.* weaker odors can increase or decrease the intensity of a strong odor). It is an easy method for the prediction of odor intensities of mixtures, which makes that the intensity of a mixture will not be grossly larger than the odor intensity of the strongest odorant. Nevertheless, when experimental data is fitted to the SC model, reasonable results are obtained and when compared to other models it appears to give reasonably good predictions (Laffort and Dravnieks, 1982).

The Additivity model

The additivity model (ADD), for its part, considers that the odor intensity of the mixture is equal to the sum of the intensities of its components:

$$\psi_{mix} = \sum_{1}^{N} \psi_i \qquad i = 1,...,N \tag{A15}$$

The Euclidean additivity (EA) model

The Euclidean additivity model (EA) is a simple model and a particular case of the vectorial model where $cos\,\alpha_{(N)} = 0$ which can be mathematically represented by Equation A16.

$$\psi_{mix} = \sqrt{\sum_{1}^{N} \psi_i^{\,2}} \qquad i = 1,\ldots,N \tag{A16}$$

Experimental data compared to prediction values obtained from the additivity and the Euclidean additivity models have shown that they tend to over-predict the odor intensity of mixtures regardless of the odor measurement method used. They generally give poor correlation coefficients between the experimental and the model-predicted intensities (Laffort and Dravnieks, 1982).

The Equiratio Model (ERM)

Finally, it is to mention only the Equiratio Model (ERM) which was originally proposed for the gustatory sense and later applied for olfaction (Schiet and Frijters, 1988; Cain*, et al.*, 1995). This model assumes a constant ratio of concentrations of the components *i* and *j* in a binary mixture and defines it perceived sensation as:

$$\psi_{mix} = k_{ij} C_{ij}^{n_i + n_j} \tag{A17}$$

where n_i, n_j are the power exponents of each odorant, and the constant k_{ij} is estimated using the constants k_i and k_j obtained from $\psi_i = k_i C_i^{n_i}$ and $\psi_j = k_j C_j^{n_j}$ together with the proportions of each odorant in the mixture as:

$$k_{ij} = \frac{p k_i / C_i + q k_j / C_j}{p / C_i + q / C_j} \tag{A18}$$

where *p* and *q* are the proportions of odorant *i* and *j*, respectively. Although this model has shown good matching results for gustatory perception, it resulted in poor results when applied to olfaction.

A.3. References

Augustin, T., Stevens' power law and the problem of meaningfulness, *Acta Psychologica*, 128, (1): 176-185, 2008

Baydar, A., McGee, T., Purzycki, K. L., Skin Odor Value Technology for Fragrance Performance Optimization, *Perfumer & Flavorlst*, 20, 45-53, 1995

Beidler, L. M., Chemical excitation of taste and odor receptors, *Advances in Chemistry Series*, (56): 1-&, 1966

Berglund, B., Olsson, M. J., Odor-intensity interaction in binary and ternary mixtures, *Perception & Psychophysics*, 53, (5): 475-482, 1993

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Calkin, R., Jellinek, S., Perfumery: Practice and Principles, New York, John Wiley, 1994

Cometto-Muniz, J. E., Cain, W. S., Abraham, M. H., Odor detection of single chemicals and binary mixtures, *Behavioural Brain Research*, 156, (1): 115-123, 2005

Dalton, P., Chapter 17: Olfaction, Stevens' handbook of experimental psychology, Pashler, New York (USA), John Wiley & Sons, Inc., Volume 1: Sensation and Perception: 2002

Devos, M., Patte, F., Rouault, J., Laffort, P., Gemert, L. J. v., Standardized Human Olfactory Thresholds, Oxford, IRL press at Oxford University Press, 1990

Devos, M., Rouault, J., Laffort, P., Standardized olfactory power law exponents, Dijon - France, Editions Universitaires-Sciences 2002

Green, D. M., Luce, R. D., Variability of Magnitude Estimates - Timing Theory Analysis, *Perception & Psychophysics*, 15, (2): 291-300, 1974

Heidelberger, M., Fechner's (wider) conception of psychophysics – then and now, Contribution to "Fechner Day 2004" XXth Meeting of the International Society for Psychophysics, Coimbra (Portugal), 2004

Jokl, M. V., Evaluation of indoor air quality using the decibel concept based on carbon dioxide and TVOC, *Building and Environment*, 35, (8): 677-697, 2000

Kamadia, V. V., Yoon, Y., Schilling, M. W., Marshall, D. L., Relationships between odorant concentration and aroma intensity, *Journal of Food Science*, 71, (3): S193-S197, 2006

Krueger, L. E., Reconciling Fechner and Stevens - toward a unified psychophysical law, *Behavioral and Brain Sciences*, 12, (2): 251-267, 1989

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Laffort, P., Walsh, R. M., Spillane, W. J., Application of the U and Gamma ' models in binary sweet taste mixtures, *Chemical Senses*, 27, (6): 511-520, 2002

Leffingwell, J. C., Leffingwell, D., from http://www.leffingwell.com/odorthre.htm, Last Accessed on May 2011

Luce, R. D., "On the possible psychophysical laws" revisited: Remarks on cross-modal matching, *Psychological Review*, 97, (1): 66-77, 1990

Luce, R. D., A psychophysical theory of intensity proportions, joint presentations, and matches, *Psychological Review*, 109, (3): 520-532, 2002

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AIChE*, 51, (10): 2834-2852, 2005

Olsson, M. J., An integrated model of intensity and quality of odor mixtures, *Olfaction and Taste Xii*, 855, 837-840, 1998

Omur-Ozbek, P., Dietrich, A. M., Developing hexanal as an odor reference standard for sensory analysis of drinking water, *Water Research*, 42, (10-11): 2598-2604, 2008

Ryan, D., Prenzler, P. D., Saliba, A. J., Scollary, G. R., The significance of low impact odorants in global odour perception, *Trends in Food Science & Technology*, 19, (7): 383-389, 2008

Sarkar, U., Hobbs, S. E., Odour from municipal solid waste (MSW) landfills: A study on the analysis of perception, *Environment International*, 27, (8): 655-662, 2002

Schiet, F. T., Frijters, J. E. R., An investigation of the equiratio-mixture model in olfactory psychophysics: A case study, *Perception & Psychophysics*, 44, (4): 304-308, 1988

Shigemoto, K., Weber-Fechner's Law and Demand Function, *Microeconomics 0412001, EconWPA*, 2004

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Stevens, S. S., To honor Fechner and repeal his law - a power function, not a log function, describes operating characteristic of a sensory system, *Science*, 133, (344): 80-86, 1961

Stevens, S. S., Concerning the psychophysical power law, *Quarterly Journal of Experimental Psychology*, 16, (4): 383-385, 1964

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE Journal*, 56, (4): 1090-1106, 2010

van Gemert, L. J., Compilations of odour threshold values in air, water and other media, The Netherlands, Oliemans Punter & Partners BV, 2003

Weber, E. H., Tastsinn und Gemeingefühl, W. Engelmann, 1905

Weiss, D. J., The impossible dream of Fechner and Stevens, *Perception*, 10, (4): 431-434, 1981

Zwislocki, J. J., Sensory Neuroscience: Four Laws of Psychophysics, New York, Springer Science+Business Media, 2009

Annex B

B.1. Original UNIFAC Method

The UNIFAC (UNIversal Functional Activity Coefficient) is a group contribution method that uses the UNIQUAC equation (which contains *per se* the summation of the entropic and enthalpic contributions) for the calculation of the activity coefficient (γ_i) (Fredenslund*, et al.*, 1975; Fredenslund*, et al.*, 1977). In this way, the UNIFAC method uses the concept of functional groups considers the activity coefficient as the sum of two contributions: one accounting for conformational effects (C, also referred as combinatorial or entropic contribution) and other for group interactions (R, referred as residual or enthalpic contribution) (Fredenslund*, et al.*, 1975; Anderson and Prausnitz, 1978; Skjold-Jorgensen*, et al.*, 1979; Wittig*, et al.*, 2003):

$$ln\,\gamma_i = ln\,\gamma_i^C + ln\,\gamma_i^R \tag{B.1}$$

The combinatorial term (C) takes into account the non-idealities in the liquid phase due to the effect of molecular size and molecular shape. It considers the molecule volume fraction (Φ) and the molecule surface fraction (θ). Only pure component properties enter into this part and it is calculated using Equations B.2 to B.4.

$$ln\,\gamma_i^C = ln\frac{\Phi_i}{x_i} + \frac{z}{2}q_i\,ln\frac{\theta_i}{\Phi_i} + l_i - \frac{\Phi_i}{x_i}\sum_j x_j l_j \tag{B.2}$$

$$\theta_i = \frac{q_i x_i}{\sum_j q_j x_j};\quad \Phi_i = \frac{r_i x_i}{\sum_j r_j x_j};\quad l_i = \frac{z}{2}\left(r_i - q_i\right) - \left(r_i - 1\right) \tag{B.3}$$

$$r_i = \sum_k \nu_k^{(i)} R_k;\quad q_i = \sum_k \nu_k^{(i)} Q_k \tag{B.4}$$

where θ is the molecule surface fraction while Φ is the molecule volume fraction. The coordination number, z, has been set equal to 10 (as is common practice). R_k and Q_k are the group volume and surface area parameters (given by Bondi, 1968), r_i and q_i are measures of molecular van der Waals volumes and molecular surface areas, respectively.

The residual part is calculated by the solution-of-groups concept (Poling*, et al.*, 2004). The residual term quantifies the group energetic interactions and is calculated from Equations B.5 to B.8:

$$ln\,\gamma_i^R = \sum_k \nu_k^{(i)}\left(ln\,\Gamma_k - ln\,\Gamma_k^{(i)}\right) \tag{B.5}$$

$$ln\,\Gamma_k = Q_k\left(1 - ln\sum_m \Theta_m \Psi_{mk} - \sum_m \frac{\Theta_m \Psi_{km}}{\sum_n \Theta_n \Psi_{nm}}\right) \tag{B.6}$$

$$\Theta_m = \frac{Q_m X_m}{\sum_n Q_n X_n};\quad X_m = \frac{\sum_i x_i \nu_m^{(i)}}{\sum_j \sum_n x_j \nu_n^{(j)}} \tag{B.7}$$

where Γ_k represents the group k residual activity coefficient, $\Gamma_k^{(i)}$ is the group k residual activity coefficient in a reference solution containing only i molecules, and Θ is the group surface area fraction. The Boltzmann factor (ψ_{mn}) can be calculated from the interaction parameters a_{mn} between the corresponding groups n and m:

$$\Psi_{mn} = exp\left(-\frac{U_{mn} - U_{nn}}{RT}\right) = exp\left(-\frac{a_{mn}}{T}\right) \tag{B.8}$$

where U_{mn} is a measure of the energy of interaction between groups m and n while $a_{mn} = (U_{mn} - U_{nn})/R$ are the group interaction parameters (in Kelvin, with $a_{mn} \neq a_{nm}$).

Finally, it should be remarked that the original UNIFAC model is designed for vapor-liquid equilibria (VLE) but is not able to adequately represent liquid-liquid equilibria (LLE), excess enthalpy data (h^E) or infinite dilution activity coefficients (γ^∞) data using the same set of parameters. Several modifications have been proposed since then to improve the method for other applications.

B.2. References

Anderson, T. F., Prausnitz, J. M., Application of UNIQUAC equation to calculation of multicomponent phase-equilibria .1. Vapor-liquid-equilibria, *Industrial & Engineering Chemistry Process Design and Development*, 17, (4): 552-561, 1978

Fredenslund, A., Gmehling, A., Rasmussen, P., Vapor-Liquid Equilibria using UNIFAC, Amesterdam, Elsevier, 1977

Fredenslund, A., Jones, R., Prausnitz, J. M., Group-contribution estimation of activity coefficients in nonideal liquid mixtures, *AIChE Journal*, 21, (6): 1086-1099, 1975

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Skjold-Jorgensen, S.*, et al.*, Vapor-liquid-equilibria by unifac group contribution. Revision and Extension, *Industrial & Engineering Chemistry Process Design and Development*, 18, (4): 714-722, 1979

Wittig, R., Lohmann, J., Gmehling, J., Vapor-liquid equilibria by UNIFAC group contribution. 6. Revision and extension, *Industrial & Engineering Chemistry Research*, 42, (1): 183-188, 2003

Annex C

C.1. Parameters used for the different group-contribution methods

UNIFAC

Table C1.1 - Group-interaction parameters for the (original) UNIFAC (Fredenslund, *et al.*, 1975; Wittig, *et al.*, 2003).

a_{mn}	1. CH_2	2. C=C	3. ACH	5. OH	8. ACOH	10. CHO	11. CCOO	13. CH_2O
1. CH_2	0.0	86.0	61.1	986.5	1333.0	677.0	232.1	251.5
2. C=C	-35.4	0.0	38.8	524.1	526.1	448.8	37.9	214.5
3. ACH	-11.1	3.4	0.0	636.1	1329.0	347.3	6.0	32.1
5. OH	156.4	457.0	89.6	0.0	-259.7	-203.6	101.1	28.1
8. ACOH	275.8	217.5	25.3	-451.6	0.0	-271.1	-449.4	-162.9
10. CHO	505.7	56.3	23.4	529.0	-155.6	0.0	-110.3	304.1
11. CCOO	114.8	132.1	85.8	245.4	-36.7	185.1	0.0	-235.7
13. CH_2O	83.4	26.5	52.1	237.7	-178.5	-7.8	461.3	0.0

ASOG

Table C1.2 - Group-interaction parameters for the ASOG (Tochigi, 1990).

m_{kl}	1. CH_2	2. C=C	3. ArCH	4. CyCH	6. OH	10. O	11. CHO	12. COO
1. CH_2	0.0	0.7767	-0.7457	0.1530	-41.2503	-1.3836	0.1147	-15.2623
2. C=C	-0.4816	0.0	-0.0622	-1.0732	-4.1886	-0.0489	3.3580	-2.4963
3. ArCH	0.7297	0.0744	0.0	-0.3288	2.2682	-0.4061	0.1448	-0.5812
4. CyCH	-0.1842	1.2487	0.5301	0.0	-11.9939	-0.4055	0.1354	-2.0465
6. OH	4.7125	-0.4867	-0.5859	5.6308	0.0	0.4251	-1.7642	0.0583
10. O	0.7666	-0.8602	-2.4476	0.1546	-1.2619	0.0	-0.4918	-7.8816
11. CHO	-1.1266	-4.9564	-0.5546	-1.2628	0.9824	0.4562	0.0	-1.1887
12. COO	-0.3699	-0.1323	-0.1541	-0.0991	-0.0296	1.0050	0.5393	0.0

n_{kl}	1. CH_2	2. C=C	3. ArCH	4. CyCH	6. OH	10. O	11. CHO	12. COO
1. CH_2	0.0	-94.4	146.0	2.1	7686.4	606.4	0.1	515.0
2. C=C	-58.9	0.0	-140.0	263.4	566.7	-407.5	-1057.2	-31.6
3. ArCH	-176.8	88.8	0.0	156.3	-1111.5	370.9	0.1	-249.3
4. CyCH	0.3	-347.0	-251.0	0.0	-2231.6	0.1	0.1	10.5
6. OH	-3060.0	-751.8	-939.1	-3221.4	0.0	-474.9	0.1	-455.3
10. O	-444.0	476.9	562.6	0.2	380.7	0.0	0.0	-0.3
11. CHO	0.2	1355.3	-0.1	0.1	-0.1	0.1	0.0	0.0
12. COO	162.6	114.2	97.5	2.4	2.6	0.7	0.1	0.0

UNIFAC-Dortmund

Table C1.3 - Group-interaction parameters for the UNIFAC-Dortmund (Jakob, *et al.*, 2006).

a_{mn}	1. CH_2	2. C=C	3. ACH	5. OH	8. ACOH	10. CHO	11. CCOO	13. CH_2O
1. CH_2	0.0	190	114.2	2777.0	1381.0	875.85	98.66	233.1
2. C=C	-95.4	0.0	174.1	2649.0	1207.0	476.25	980.74	733.3
3. ACH	16.1	-157.2	0.0	3972.0	1356.0	-365.5	-274.54	-87.08
5. OH	1606.0	1566.0	3049.0	0.0	83.91	-281.4	973.8	816.7
8. ACOH	1987.0	191.6	2340.0	465.4	0.00	5.6	-212.9	-329.3
10. CHO	256.21	202.49	1011.0	1590.0	-410.21	0.00	-208.4	209.0
11. CCOO	632.22	-582.82	622.73	310.4	-224.4	389.7	0.00	195.3
13. CH_2O	-9.65	-844.3	179.0	650.9	-80.58	235.7	824.2	0.00

b_{mn}	1. CH_2	2. C=C	3. ACH	5. OH	8. ACOH	10. CHO	11. CCOO	13. CH_2O
1. CH_2	0.0	-0.2723	0.0933	-4.6740	-0.9977	0.0	1.9294	-0.3155
2. C=C	0.0617	0.0	-0.5886	-6.5080	-1.9550	0.0	-2.4224	-2.5090
3. ACH	-0.2998	0.6166	0.0	-13.160	-2.1180	1.8740	0.9149	-0.1859
5. OH	-4.7460	-5.8090	-12.770	0.0	-1.2620	2.3790	-5.6330	-5.0920
8. ACOH	-4.6150	0.4936	-5.0430	-1.8410	0.0	0.0	0.0	0.0
10. CHO	0.0	0.0	-2.1670	-24.570	0.0	0.0	0.0	-0.6241
11. CCOO	-3.3912	1.6732	-1.7605	1.5380	0.0	0.0	0.0	-9.7500
13. CH_2O	-0.0324	2.9450	0.0562	-0.7132	0.0	0.1314	-6.0090	0.0

c_{mn}	1. CH_2	2. C=C	3. ACH	5. OH	8. ACOH	10. CHO	11. CCOO	13. CH_2O
1. CH_2	0.0	0.0	0.0	0.0016	0.0	0.0	-0.0031	0.0
2. C=C	0.0	0.0	0.0	0.0048	0.0	0.0	0.0	0.0
3. ACH	0.0	0.0	0.0	0.012	0.0	0.0	0.0	0.0
5. OH	0.0009	0.0052	0.014	0.0	0.0	-0.0067	0.0077	0.0061
8. ACOH	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
10. CHO	0.0	0.0	0.0	0.062	0.0	0.0	0.0	0.0
11. CCOO	0.0039	0.0	0.0	-0.0049	0.0	0.0	0.0	0.0405
13. CH_2O	0.0	0.0	0.0	0.0008	0.0	0.0	-0.0083	0.0

A-UNIFAC

Table C1.4 - Group-interaction parameters for the A-UNIFAC (Ferreira, *et al.*, 2005; Andreatta, *et al.*, 2008; Mota, 2010).

a_{mn}	1. CH_2	2. C=C	3. ACH	5. OH	8. ACOH	10. CHO	11. CCOO	13. CH_2O
1. CH_2	0.0	86.02 [a]	61.13 [a]	50.4	-55.4	677.0 [a]	232.1 [a]	251.5 [a]
2. C=C	-35.36 [a]	0.0	38.81 [a]	524.1 [a]	526.1 [a]	448.8 [a]	37.85 [a]	214.5 [a]
3. ACH	-11.12[a]	3.446 [a]	0.0	20.9	-42.9	347.3 [a]	-	32.14 [a]
5. OH	387.4	457.0 [a]	359.6	0.0	-410.1	-203.6	325.5	28.06 [a]
8. ACOH	343.4	217.5 [a]	74.0	-722.6	0.0	-271.1 [a]	-	-162.9 [a]
10. CHO	505.7 [a]	56.30 [a]	23.39 [a]	529.0 [a]	-155.6 [a]	0.0	-	304.1 [a]
11. CCOO	114.8 [a]	132.1 [a]	-	-8.433	-	-	0.0	-
13. CH_2O	83.36 [a]	26.51 [a]	52.13 [a]	237.7 [a]	-178.5 [a]	-7.838 [a]	-	0.0

[a] parameters from UNIFAC method.

Table C1.5 – Self- and cross- association parameters for the A-UNIFAC (Ferreira, *et al.*, 2005; Andreatta, *et al.*, 2008).

		ε/k (K)	κ
Self-association			
COOH		4100.0	0.0020
OH		3125.0	0.0062
H2O		3125.0	0.0062
i	*j*	*εij/k(K)*	*κij*
Cross-association			
COOH	OH	3612.5	0.0035
	H_2O[a]	3612.5	0.0035
	COOR	2912.0	0.0038
	Aring	1810.0	0.0030
OH	COOR	1975.0	0.0710
	Aring	1690.0	0.0635
	H2O	3125.0	0.0062

[a] With $k_{COOH,H2O}$ = 0.63.

C.2. References

Andreatta, A. E., Casas, L. M., Hegel, P., Bottini, S. B., Brignole, E. A., Phase equilibria in ternary mixtures of methyl oleate, glycerol, and methanol, *Industrial & Engineering Chemistry Research*, 47, (15): 5157-5164, 2008

Ferreira, O., Macedo, E. A., Bottini, S. B., Extension of the A-UNIFAC model to mixtures of cross- and self-associating compounds, *Fluid Phase Equilibria*, 227, (2): 165-176, 2005

Fredenslund, A., Jones, R., Prausnitz, J. M., Group-contribution estimation of activity coefficients in nonideal liquid mixtures, *AIChE Journal*, 21, (6): 1086-1099, 1975

Jakob, A., Grensemann, H., Lohmann, J., Gmehling, J., Further development of modified UNIFAC (Dortmund): Revision and extension 5, *Industrial & Engineering Chemistry Research*, 45, (23): 7924-7933, 2006

Mota, F. L., Solubility Studies with Pharmaceutical Applications. Department of Chemical Engineering. Porto, University of Porto. PhD2010

Tochigi, K., Tiegs, D., Gmehling, J., Kojima, K., Determination of new ASOG parameters, *Journal of Chemical Engineering Japan*, 23, (4): 453-463, 1990

Wittig, R., Lohmann, J., Gmehling, J., Vapor-liquid equilibria by UNIFAC group contribution. 6. Revision and extension, *Industrial & Engineering Chemistry Research*, 42, (1): 183-188, 2003

Annex D

D.1. Diffusion Coefficients Calculation using the Method of Fuller *et al.*

When the diffusion process takes place in a dilute and isotropic medium, it is reasonable to consider the diffusion coefficient as constant for each component *i* in air, *j*. This was the case assumed in Chapter 6 and, thus, the diffusion coefficients of fragrance ingredients and solvents in air were using the correlation proposed by Fuller *et al.* (Fuller, *et al.*, 1966; Poling, 2004) for a definite pressure and temperature, as follows:

$$D_{ij} = \frac{1.43\times10^{-7}\cdot T^{3/2}}{P\cdot M_{ij}\left[\left(\sum_v\right)_i^{1/3}+\left(\sum_v\right)_j^{1/3}\right]^2} \qquad \text{(D.1)}$$

where $D_{ij} =$ binary diffusion coefficient, in m^2/s

$T =$ temperature, in K

$M_i, M_j =$ molecular weights of *i* and *j*, in g/mol

$M_{ij} = 2\left[\left(1/M_i\right)+\left(1/M_j\right)\right]^{-1}$

$P =$ pressure, in Pa

$\sum_v$ = sum of the atomic diffusion volumes

The atomic and molecular volume increments for each group are presented in Table D1.

Table D1 – Atomic, Structural and Molecular Diffusion Volume Increments

Atomic and Structural Diffusion Volume Increments	
C	15.90
H	2.31
O	6.11
Aromatic Ring	-18.30
Heterocyclic Ring	-18.30
Diffusion Volumes of Simple Molecules	
Air	19.70

D.2. References

Fuller, E. N., Schettler, P. D., Giddings, J. C., A new method for prediction of binary gas-phase diffusion coefficients, *Industrial and Engineering Chemistry*, 58, (5): 19-27, 1966

Poling, B., Prausnitz, J., O'Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Annex E

E.1. Example of application for the PR methodology

The application of the Perfumery Radar (PR) methodology to a commercial perfume is described in detail here, step by step, considering the case of the perfume P1 - "L'air du Temps (Nina Ricci)" which is evaluated in Chapter 8.

The starting point for this process is the gas chromatographic analysis together with the mass spectrometry technique (GC/FID/MS). The FID chromatogram of the perfume P1 is presented in Figure E1.1. From this, it is possible to determine the composition of the liquid sample (FID) and to identify each fragrant component (MS) of the perfume by comparison with spectral libraries. For the FID analysis a peak rejection criterion was used, so that only peaks with an area higher than 10000 counts were considered for the feminine perfumes used in the PR methodology. Later on, for unisex perfumes this criterion was broadened and only peak areas below 2000 counts were rejected. For all these peaks, the MS data was analyzed, peak by peak, in order to identify each component within the mixture. These species were tentatively identified using two mass spectral databases, one from the National Institute of Standards and Technology (NIST) and another one which has been built in-house for more than a decade.

From that point, the composition of the commercial perfumes was calculated directly from gas chromatographic peak areas without any correction factor and considering a linear response factor for all species. Then, fragrant compounds were assigned their olfactive families according to the previously developed database and considering the distribution weights (w_i) for each olfactive family (primary, secondary and tertiary). After this, physicochemical properties (molecular formula, molecular mass, vapor pressure) and psychophysical data (threshold concentration) were assigned to each component. Moreover, the identified species were fractioned into functional groups so that it could be possible to predict the activity coefficients (γ_i) using the UNIFAC group contribution method. The composition extracted directly from the peak areas for all the fragrant components identified in the perfume sample P1 is presented in Table E1.1.

Table E1.1 – Psycho-physicochemical properties, olfactive families and molar composition of each component.

Peak No.	Retention Time (min)	Area (counts)	Molar Fraction (FID peak area)	Molar fraction (recalc.) x_i'	Name	C.A.S.	Molecular Formula	Molecular Mass (g/mol)	Primary Family	Secondary Family	Terceary Family	Threshold (mg/m^3) arithmetic	Threshold (mg/m^3) geometric	Standard deviation δ	Pressure Vapor (Pa)
1	6.186	9141700	84.70%	55.61%	Ethanol	64-17-5	C_2H_6O	46.070	Alcohol	-	-	1.23E+01	1.36E+00	1.25E+01	7.27E+03
2	15.492	10000	0.09%	0.06%	(S)-Limonene	7721-54-8	$C_{10}H_{16}$	136.234	Citrus	Fruity	-	1.23E+01	1.36E+00	1.25E+01	2.05E+02
3	36.202	86339	0.80%	0.53%	Linalool	78-70-6	$C_{10}H_{18}O$	154.249	Floral	-	-	3.72E-07	3.72E-07	0.00E+00	1.21E+01
4	36.697	107248	0.99%	0.65%	Linalyl acetate	115-95-7	$C_{10}H_{20}O_2$	196.286	Fruity	Citrus	Floral	2.53E+00	5.47E-01	2.96E+00	1.55E+01
5	44.336	23161	0.21%	0.14%	α-terpineol	98-55-5	$C_{10}H_{18}O$	154.249	Floral	-	-	2.28E-01	1.01E-01	2.67E-01	3.77E+00
6	44.539	10005	0.09%	0.06%	γ-terpineol	586-81-2	$C_{10}H_{18}O$	154.249	Floral	-	-	2.28E-01	1.01E-01	2.67E-01	3.60E+00
7	44.655	10062	0.09%	0.06%	1-phenylethyl acetate	93-92-5	$C_{10}H_{12}O_2$	164.201	Green	Floral	-	2.00E-04	2.00E-04	0.00E+00	2.71E+01
8	46.083	36800	0.34%	0.22%	Benzyl acetate	140-11-4	$C_9H_{10}O_2$	150.175	Floral	Fruity	-	1.72E-01	1.72E-01	0.00E+00	1.89E+02
9	52.229	139025	1.29%	0.85%	isomethyl ionone	127-51-5	$C_{14}H_{22}O$	206.324	Oriental	-	-	-	-	-	3.76E-01
10	53.82	10002	0.09%	0.06%	Benzyl alcohol	100-51-6	C_7H_8O	108.138	Oriental	-	-	1.18E+01	1.18E+01	0.00E+00	1.47E+01
11	55.492	204957	1.90%	1.25%	Phenylethyl alcohol	60-12-8	C8H10O	122.164	Floral	-	-	4.91E-02	2.03E-02	5.34E-02	9.88E+00
12	57.259	119170	1.10%	0.72%	Hydroxycitronellal	107-75-5	$C_{10}H_{20}O_2$	172.265	Floral	-	-	6.90E-06	6.90E-06	0.00E+00	4.24E-01
13	60.179	46980	0.44%	0.29%	Vetiveryl acetate	62563-80-8	$C_{17}H_{26}O_2$	262.387	Woody	-	-	-	-	-	1.60E-02
14	66.686	10955	0.10%	0.07%	Valencene	4630-07-3	$C_{15}H_{24}$	204.351	Citrus	-	-	-	-	-	1.51E+00
15	67.66	64820	0.60%	0.39%	Eugenol	97-53-0	$C_{10}H_{12}O_2$	164.201	Oriental	-	-	3.37E-01	4.50E-03	1.04E+00	1.39E+00
16	71.439	43057	0.40%	0.26%	α-Amylcinnamaldehyde	122-40-7	$C_{14}H_{18}O$	202.292	Floral	Herbaceous	-	-	-	-	3.11E-01
17	73.849	12525	0.12%	0.08%	Tonalide	1506-02-1	$C_{18}H_{26}O$	258.400	Musk	-	-	1.82E-02	1.82E-02	0.00E+00	6.70E-05
18	75.475	71014	0.66%	0.43%	α-Santalol	19903-72-1	$C_{15}H_{24}O$	220.351	Woody	-	-	-	-	-	1.57E-02
19	76.269	41788	0.39%	0.25%	Diethyl phthalate	84-66-2	$C_4H_{10}O_3$	106.120	odorless	-	-	odorless	odorless	odorless	6.25E-01
20	80.43	33554	0.31%	0.20%	Acetyl triethyl citrate	77-89-4	$C_{14}H_{22}O8$	318.320	odorless	-	-	odorless	odorless	odorless	2.73E-02
21	87.733	37702	0.35%	0.23%	Benzyl benzoate	120-51-4	$C_{14}H_{12}O_2$	212.244	Oriental	-	-	-	-	-	3.05E-02
22	93.947	75637	0.70%	0.46%	Benzyl dodecanoate	140-25-0	$C_{19}H_{30}O_2$	290.440	Unknown	-	-	-	-	-	1.03E-03
23	98.227	286450	2.65%	1.74%	Benzyl 2-hydroxybenzoate	118-58-1	$C_{14}H_{22}O_3$	228.243	Floral	-	-	-	-	-	2.33E-02
24	106.663	170590	1.58%	1.04%	Musk ketone	81-14-1	$C_{14}H_{18}N_2O_5$	294.303	Musk	-	-	6.50E-04	3.46E-04	7.78E-04	1.63E-03
-	-	-	-	34.34%	Water	7732-18-5	H_2O	18.015	odorless	-	-	odorless	odorless	odorless	3.17E+03
Totals:	-	10793541	100.00%	100.00%											

A normalization step was then applied to the composition in the liquid phase for each commercial perfume and will be detailed hereafter. The selected perfume is an *"Eau de Toilette"* type and its typical composition (in terms of solvents and perfume concentrate) with their calculated mean values according to the literature is presented in Table E1.2.

Table E1.2 – Typical composition (%, vol) in perfume concentrate, ethanol and water for an "Eau de Toilette".

	Concentrate	Water	Ethanol
φ_i	4-15	10-18	72-81
$\varphi_{i\ (average)}$	9.5	14	76.5

The typical composition is usually presented in volume fraction (φ_i, vol/vol) as is the case here so that it was necessary to recalculate it in a molar fraction basis (x_i, mol/mol). This way, an average molecular mass (M_i, g/mol) and density (ρ_i, g/m^3) for the concentrate were considered, taking into account typical values for this type of fragrance mixtures. It was assumed that $M_{concentrate}$ = 150 g/mol and $\rho_{concentrate}$ = 900 kg/m^3. The number of moles for the perfume concentrate, water and ethanol were calculated using equation E1, considering an injection volume of 1µl and the mean values of the volume fractions.

$$n_i = \frac{\varphi_i \times \rho_i}{M_i} \times V_{inj} \tag{E1}$$

where i represents concentrate, water or ethanol, φ_i is the volume fraction of i, M_i is the molecular mass of i, and ρ_i is the density of i. This way, the absolute molar compositions in the liquid phase (x_i) were calculated dividing each n_i by the total number of moles in solution (except those of water) as is shown in equation E2.

$$x_i = \frac{n_i}{\sum_{i=1}^{N} n_i} \tag{E2}$$

where N represents the perfume concentrate, water or ethanol. The number of moles and the molar compositions in the liquid phase are presented in Table E1.3.

Table E1.3 – Number of moles and molar compositions in the liquid phase for perfume concentrate, water and ethanol.

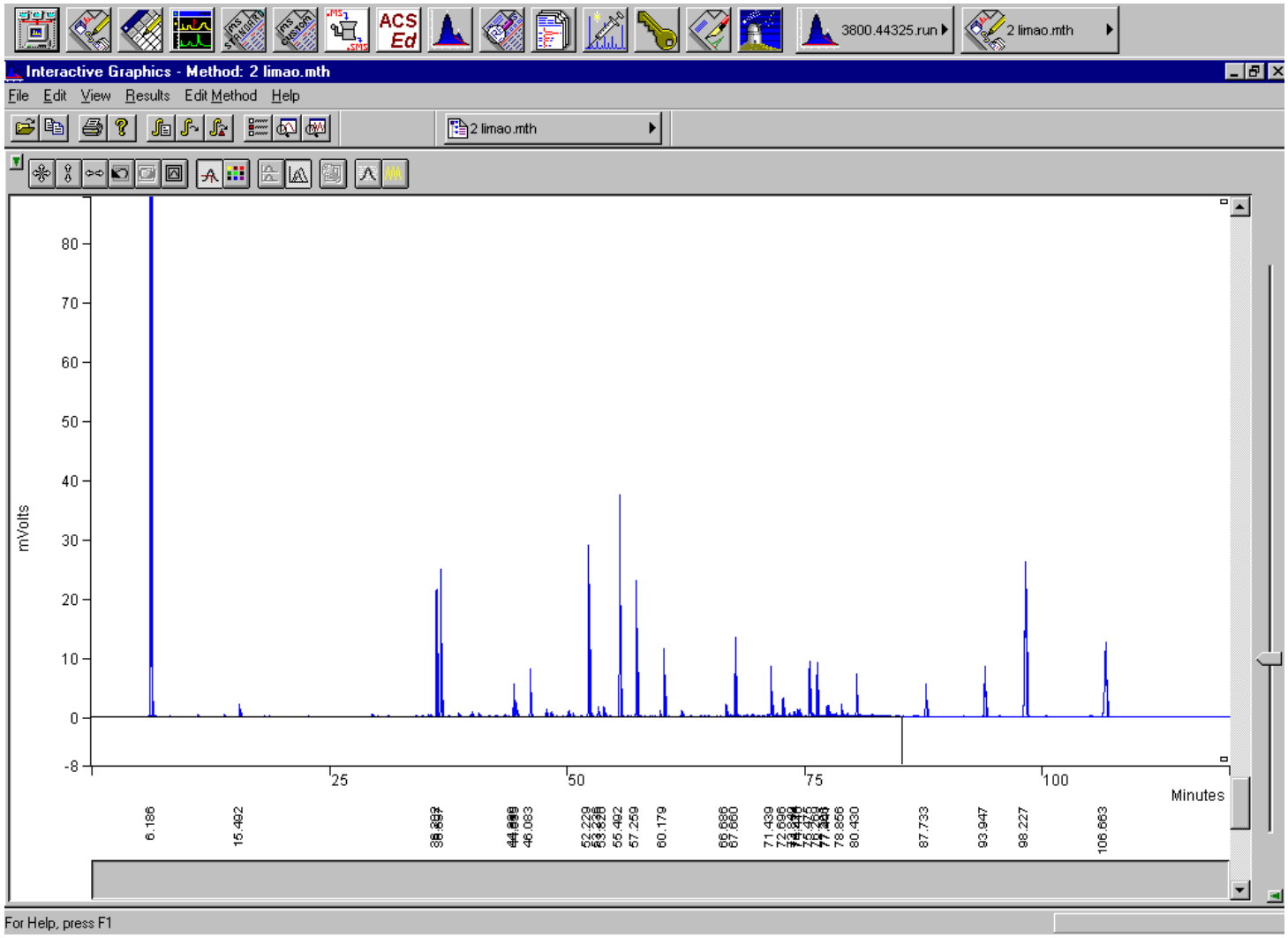
	Concentrate	Water	Ethanol
n_i	0.057	0.778	1.430
x_i	0.025	0.343	0.631

Considering this approach the mole fractions for water were set for all simulated commercial perfumes at 0.343, respectively; while the mole fractions of each fragrance ($x_i^{'}$) was recalculated using equation E3:

$$x_i^{'} = \frac{x_i}{1 + \frac{n_{H_2O}}{\sum_{i=1}^{N-1} n_i}} \qquad \text{(E3)}$$

where x_i is the initial absolute mole fraction of fragrance *i* as obtained from the peak areas (see Table E1.1), and n_{H_2O} is the number of moles of water molecules in solution. The normalized compositions are presented in Table E1.1 (as molar fractions recalc.). Then, the developed software for the PR methodology was ready to run, calculating the activity coefficients in the liquid phase (γ_i), the odor intensity for each fragrance chemical, the corresponding weighed odor intensity for each olfactive family and plotting the results in the radar graph.

Figure E1.1 – Software and chromatogram of the perfume P1 - “L’air du Temps (Nina Ricci)” analyzed by gas chromatography with FID.



Annex F

F. Applications to Product Engineering

Here, two examples of application of some of the methodologies developed throughout this thesis are applied to specific experiments within Product Engineering. First, the evaluation of the odor released from a mixture of perfumery raw materials applied over textiles is assessed and compared with the results obtained from a prediction model. Later, the performance of fragrance microencapsulated textiles is predicted using evaporation and diffusion models.

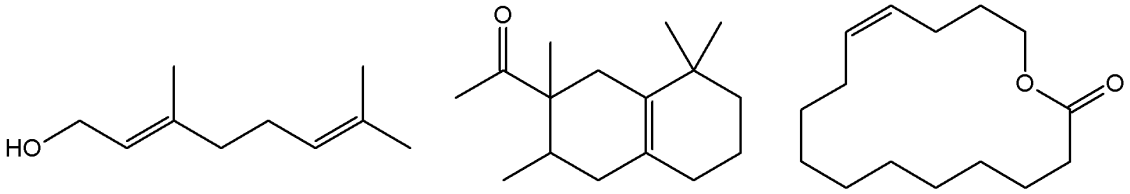
F1. Experimental measurement and prediction of the odor intensity of fragrance mixtures

This work resulted from a partnership between the LSRE and the Procter & Gamble Company (P&G). In this work, it was intended to assess the predictive power of a theoretical model for the determination of the odor intensity of different fragrance mixtures containing three perfumery raw materials (PRM) which were applied on textiles and are being released into the surrounding air. The aim was also to establish a correlation between the odor intensities predicted from the model and those measured by olfactory evaluations performed either by trained (experts) and non-trained (typical consumer) panelists. For that, P&G performed the experimental part of the work while the modeling was developed at LSRE.

F1.1. Methodology

Several fragrance mixtures containing three perfumery raw materials (PRM) which have different volatilities were tested. These PRMs can be classified as top, middle or base notes according to the definition of Carles (Carles, 1962): geraniol is a middle note, habanolide is a typical base note and also a fixative, and iso-E-super represents a low middle to base note. These fragrance ingredients were dissolved in a solvent matrix with low volatility and no odor character (odorless). In this way, a mineral oil of the type C_nH_{2n+2} was used to dissolve the PRMs which were mixed in different compositions for a total of 17 quaternary perfume mixtures. These were then applied on the surface of textiles (dry fabric) according to the procedure from P&G. The molecular structures of

the fragrant components studied in this work are presented in Figure F1.1 and their corresponding psycho-physicochemical properties are shown in Table F1.1.



Geraniol Iso-E-Super Habanolide

Figure F1.1 - Molecular structures of the perfumery raw materials (PRMs) used in the formulation of the studied mixtures.

Table F1.1- Properties of the chemical components used in this work.

Compound Name	CAS	Mol. Form.	Mol. Weight (g/mol)	ODT P&G* (mg/m^3)	Vapor Pressure (Pa) [a)]	log P [a)]	n	Odor Family
Mineral Oil	8042-47-5			odorless				odorless
considered as Hexadecane for calculations	544-76-3	$C_{16}H_{34}$	226.4	odorless	6.66×10^{-1}	8.86	-	odorless
Geraniol	106-24-1	$C_{10}H_{18}O$	154.2	0.077*	2.67×10^{-0}	4.95	0.36[b), *]	Floral
Habanolide	111879-80-2	$C_{15}H_{26}O_2$	238.4	13.717*	7.05×10^{-3}	4.95	0.80*	Amber-Musk
Iso-E-super	54464-57-2	$C_{16}H_{26}O$	234.4	0.107*	7.17×10^{-2}	5.29	0.68[b)]	Fresh-Woody

[a)]From Chemspider - RSC Database (Chemspider, 2011); [b)]From Devos *et al.*, 2002 (Devos*, et al.*, 2002); *Calculated from P&G data.

Perfume mixture formulation and application on textile

In this work, the formulation of the fragrance mixtures was performed by P&G perfumers, who defined the required concentrations of each perfumery raw material for each mixture in order to obtain a desired target olfactive scale as presented in Table F1.2. These target olfactive values were defined by the perfumers as objective values to obtain pleasant fragrance mixtures as perceived by our nose. For that, different fragrance mixtures were formulated comprising 7 quaternary, 6 ternary and 3 binary mixtures plus a blank and 2 validation samples. This set of samples was used to test a proposed predictive model for odor intensity. In all mixture formulations the PRMs (see Table F1.2) were made into respective one, two or three stock solutions (the perfume oils added gravimetrically into 10 ml of mineral oil) of varying ratios with aliquots of 100 µl taken and added to the fabric as per the design of experiments (DoE). After, fragrance solution was applied over a 10 x 10 cm square of cotton textile (dry textile). These samples were enclosed in tin foil and left to equilibrate for 2 hours prior to the

olfactory analysis of the headspace. It is to be noted, that other matrices were tested (*e.g.* pentane, ethyl ether, and an alcohol of low olfactive intensity) for the dissolution of the fragrance mixtures but these performed poorer than the mineral oil because they either left residues, significantly influenced the perceived odor or overwhelmed the column on the analytical technique chosen.

Olfactory evaluations

The headspace of the fragrance mixtures applied on the textiles was evaluated for several quaternary, ternary and binary mixtures. It should be highlighted that the solvent matrix is odorless and so should not be perceived in the olfactory evaluations. For the case of the binary mixtures, they consist of a single PRM dissolved in the odorless mineral oil matrix, thus what is expected to be perceived is the PRM only. Samples were evaluated through olfactory analysis made by perfumers and non-trained panelists from P&G. This panel was composed by 30 non-trained people, 13 men and 17 women aged between 17 and 57 years. The panelists presented averages of 31.6 and 35.9 years for male and female panelists, respectively. More information of the panel of consumers used is presented in Table F1.3. For the olfactory evaluations, samples were analyzed independently in blind tests (without knowing the concentrations). Each non-trained panelist evaluated five samples randomly (which could be repeated, although every sample was new and not reused) and rated those on a 10 cm line scale as described in the literature (Meilgaard*, et al.*, 1999). Moreover, fresh coffee beans were used to clear the nose receptors in between every evaluation.

Four perfumers also rated samples randomly using an olfactive scale. This intensity scale ranges from 0 to 200 units where values near 20-30 represent recognition thresholds, values above 120 may provoke nuisance and at the top end of the scale they are considered as painful as presented in Figure 1.2.

Figure F1.2 – Olfactive intensity scale for used from perfumers at Procter & Gamble.

Table F1.2 – PRM mixtures, compositions, predicted odor intensities (OV^n), concentration targets, and perfumer and panelist evaluations.

	Concentration (mg/fabric)			Mole Fraction				OV^n			Concentration (Target Olfactive Scale)			Intensity Grade	
N	Geraniol	Habanolide	Iso-E-super	Mineral Oil	Geraniol	Habanolide	Iso-E-super	Geraniol	Habanolide	Iso-E-super	Geraniol	Habanolide	Iso-E-super	Perfumer average	Panelist average
1	0.8	1	4	0.928	0.014	0.011	0.046	6.99	4.3E-03	3.47	105	90	80	108.8	6.2
2	0.8	1	0	0.973	0.015	0.012	0	7.49	4.7E-03	-	105	90	0	105.0	6.1
3	0.8	0	4	0.939	0.014	0	0.047	7.09	-	3.53	105	0	80	107.5	6.0
4	0.8	0	0	0.985	0.015	0	0.000	7.64	-	-	105	0	0	107.5	4.8
5	0	1	4	0.942	0	0.012	0.047	-	4.5E-03	3.61	0	90	80	65.0	5.0
6	0	1	0	0.988	0	0.012	0	-	5.0E-03	-	0	90	0	32.5	1.9
7	0	0	4	0.953	0	0	0.047	-	-	3.68	0	0	80	81.3	1.9
8	0	0	0	1.000	0	0	0	-	-	-	0	0	0	26.3	0.5
9	0.1	0.2	0.1	0.994	0.002	0.002	0.001	3.78	1.4E-03	0.32	50	20	40	63.8	3.6
10	0.1	0.2	0	0.996	0.002	0.002	0	3.78	1.4E-03	-	50	20	0	47.5	2.4
11	0.1	0.2	4	0.949	0.002	0.002	0.047	3.48	1.3E-03	3.65	50	20	80	71.3	5.4
12	0.1	0	0.1	0.997	0.002	0	0.001	3.79	-	0.32	50	0	40	43.8	4.3
13	0.1	1	0.1	0.985	0.002	0.012	0.001	3.73	5.0E-03	0.32	50	90	40	82.5	2.6
14	0	0.2	0.1	0.996	0	0.002	0.001	-	1.4E-03	0.32	0	20	40	45.0	1.5
15	0.8	0.2	0.1	0.982	0.015	0.002	0.001	7.60	1.3E-03	0.31	105	20	40	126.3	5.0
16	0.7	0.2	0.1	0.983	0.013	0.002	0.001	7.28	1.3E-03	0.31	100	20	40	97.5	6.6
17	0.3	0.4	0.3	0.986	0.006	0.005	0.004	5.47	2.4E-03	0.68	75	30	45	86.3	5.3

Table F1.3 – Reference number, age and gender of the non-trained panel.

Ref	Age	Gender
1	17	Male
2	43	Female
3	31	Female
4	19	Male
5	38	Female
6	29	Female
7	34	Female
8	53	Female
9	29	Female
10	25	Female
11	25	Male
12	48	Male
13	32	Female
14	38	Male
15	43	Male
16	32	Female
17	57	Female
18	35	Female
19	31	Female
20	19	Male
21	23	Male
22	26	Female
23	41	Male
24	51	Female
25	48	Male
26	29	Female
27	35	Female
28	35	Male
29	36	Male
30	19	Male
Averages	34.0	
	31.6	Male
	35.9	Female

For the perception of odors it is important to account for both quantitative and qualitative parameters. Although the latter is without a doubt very important from the consumer point of view, the former is easier to be evaluated. Nevertheless when measuring odors there are some parameters to be considered: *i)* detectability (detection or recognition thresholds); *ii)* intensity scale (the perceived sensation with concentration increase); *iii)* perceived character or quality (classification into olfactive families like floral or citrus); *iv)* hedonic tone (the degree of pleasantness or annoyance of an odor). For that, all these parameters were considered in this work: odor detection thresholds (ODT) and power law exponents (*n*) were calculated by P&G, the character classification of each PRM and an intensity scale were defined by their perfumers (see Table F1.1 and Figure F1.2). The data on ODTs were evaluated by perfumers and represent an averaged value obtained from a large number of evaluations. The power law exponents were also measured by P&G perfumers based on category scales, as

presented for geraniol and habanolide in Figure F1.3. It is important to note that the power law exponent calculated for geraniol is the same as that recommended by Devos *et al* (Devos*, et al.*, 2002). The power law exponent for habanolide was not available in the literature.

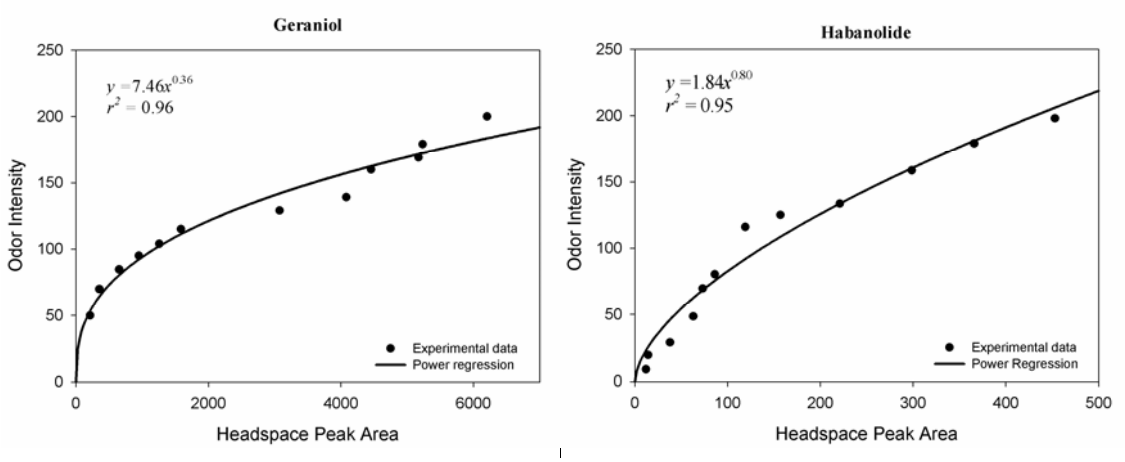


Figure F1.3 – Curves of odor intensity versus headspace peak area for geraniol and habanolide.

From the category scale experiments performed for geraniol and habanolide (Figure F1.3) it is possible to see that there is nonlinearity in the intensity scale, which means that for this perceptual continua (olfaction) and for these PRMs the perceived odor intensity increases slowly with the concentration ($n < 1$, compressive exponent). In other words, near the lower end of the scale (where discrimination is good) the slope of the function is steep while at the upper end (where a given change in the stimulus magnitude is more difficult to be detected) the slope declines (Stevens, 1957). This experiment shows the need to consider a power law to describe the magnitude of olfactory perception if the whole range of concentrations is considered. Even so, for low concentration mixtures it is also seen that a linearly dependent relationship between the perceived odor intensity and the headspace peak area could be approximated (*e.g.* odor value) (Mata*, et al.*, 2005; Teixeira*, et al.*, 2010).

Modeling of perceived odor

In order to establish a simple model that could replicate the physical experiments performed in this work, the theory behind the PTD® and PQ2D® methodologies was first considered. For that, it was assumed a dry fabric substrate where the fragrance ingredients were placed on it and started evaporating into the air. Since the perfumery mixtures contained only three odorant species, the PTD® methodology is perfectly

suitable to predict and represent graphically the perceived odor intensity and character of any ternary fragrant mixture (Mata*, et al.*, 2005; Teixeira*, et al.*, 2009). For that purpose, the odor intensity above a liquid mixture of any volatile PRM can be calculated using the Stevens' Power Law for olfaction as presented in equation F1.1 (for further details see, for example, Chapter 1).

$$OV^n = \psi = \left(\frac{C_i^g}{ODT_i} \right)^n \tag{F1.1}$$

where C_i^g is the concentration of an odorant i in the gas phase (g/m^3), ODT_i is its corresponding odor detection threshold (g/m^3), and n is the power law exponent for intensity perception. As previously mentioned the ODT and n parameters were calculated by P&G and a summary of those results is presented in Table F1.1 and Figure F1.3. Once we did not know the concentrations in the gas phase for each fragrance compound, we have used our predictive methodology which is based on the (liquid) mass composition of each fragrance ingredient (plus the solvent) applied in the fabric as experimentally developed by P&G. From that, mole fractions for those mixtures were calculated and then the perceived odor intensity (OV^n) of each PRM was predicted using our methodology (Mata*, et al.*, 2005; Teixeira*, et al.*, 2009). For that, in a mixture of N fragrant components it is necessary to account for the molecular interactions in the liquid phase and so the composition of the different fragrant components in the gas phase above the liquid can be calculated from the modified Raoult's law for vapor-liquid equilibria (VLE) as previously reported (see Chapter 3). That includes the determination of activity coefficients in the liquid phase (γ_i) due to non-idealities, reflecting the affinity and interactions of each molecule with the matrix. In this way, equation F1.1 can be re-written as:

$$OV_i^n = \psi_i = \left[\gamma_i x_i \left(\frac{P_i^{sat} M_i}{ODT_i} \right) \left(\frac{1}{RT} \right) \right]^n \tag{F1.2}$$

Thus, the odor intensity of each perfumery raw material can be predicted from pure component data (composition in the liquid phase, molecular weight, saturated vapor pressure and odor detection threshold) together with the activity coefficient (γ_i). This parameter is a function of the composition and can be experimentally calculated from

vapor-liquid equilibrium (VLE) data or predicted using suitable methods. In this work the UNIFAC group contribution method (Fredenslund*, et al.*, 1975; Poling*, et al.*, 2004) was used for the prediction of the VLE and the activity coefficients of the chemical components.

For the intensity of a mixture of PRMs with *N* fragrant components, there will be *N* different odor intensities, one for each component to be calculated in the headspace. In order to account for the odor intensity of such mixtures, the Stronger Component (SC) model was used. It states that the odorant with the highest odor intensity will be more strongly perceived and recognized by the human nose, although there is a mixture of perceived scents in the air (Laffort and Dravnieks, 1982; Cain*, et al.*, 1995). This model is expressed by equation F1.3:

$$OV_{max} = max\{OV_i\}, \qquad i = 1,...,N \tag{F1.3}$$

Finally, it is to note that in this odor perception model no interactions between the textiles and the PRMs were considered (*e.g.* adsorption of PRMs to the fibers and their partitioning between air and fibers). In this way, it was assumed that a thin film of a liquid mixture of PRMs was placed over a textile (dry fabric) and from that point the evaporation of PRMs at occurred different rates.

In this work, several fragrance quaternary samples were subjected to olfactory evaluations performed by perfumers and non-trained panelists who rated the intensity of the odor perceived above the wet fabrics. For each of these mixtures, the aforementioned odor perception model was applied for the quantification of the odor intensities of each PRM. It should be highlighted that, in general, PRMs are volatile chemicals that evaporate into the air and, thus, they contribute to the overall intensity of the perceived scent. In this case, the same happens and so there may be effects of hypoadditivity or hyperadditivity of odors which were neglected in the modeling so that the odor intensity was approximated by the strongest component model.

F1.2. Materials & Methods

The fragrance materials used in this work were supplied by IFF: Geraniol (3,7-dimethyl-2,6-octadien-1-ol, CAS # 106-24-1) and Iso-E-super (1-(1,2,3,4,5,6,7,8-

octahydro-2,3,8,8-tetramethyl-2-naphthalenyl)-ethan-1-one, CAS # 54464-57-2) while Habanolide (12E-Oxacyclohexadec-12-en-2-one, CAS # 423773-57-3) was obtained from Firmenich. The mineral (paraffinic) oil supplied by Sigma-Aldrich (CAS # 8042-47-5) was considered for all calculations as hexadecane (CAS # 544-76-3). The physicochemical properties of the fragrance ingredients compiled in Table F1.1 were used in all calculations which were computed in MATLAB software. Their group assignments for the UNIFAC method are shown in Table F1.4. For each fragrant molecule, it is presented the division into groups and subgroups; the number of groups of type *j* in molecule *i,* $v_j^{(i)}$; the parameters of molecular van der Waals volumes, $R_j^{(i)}$, and surface area, $Q_j^{(i)}$. Further details on the UNIFAC method can be obtained from Annex B or from the literature (Poling*, et al.*, 2004). The fabrics used were of cotton type and with dimensions of 10 x 10 cm.

Table F1.2 – UNIFAC for the perfumery raw materials with the corresponding volume and surface parameters.

Molecule (*i*)	Subgroup (*j*)	Group Number	Subgroup Number	$v_j^{(i)}$	$R_j^{(i)}$	$Q_j^{(i)}$
Geraniol	***CH_3***	1	1	3	0.9011	0.848
	CH_2	1	2	3	0.6744	0.540
	CH=C	2	8	2	0.8886	0.676
	OH	5	15	1	1.0000	1.200
Habanolide	***CH_2***	1	2	11	0.6744	0.540
	CH=CH	2	6	1	1.1167	0.867
	CH_2COO	9	19	1	1.6764	1.420
Iso-E-super	***CH_3***	1	1	4	0.9011	0.848
	CH_2	1	2	5	0.6744	0.540
	CH	1	3	2	0.4469	0.228
	C	1	4	1	0.2195	0.000
	C=C	2	70	1	0.6605	0.485
	CH_3CO	9	18	1	1.6724	1.488
Mineral Oil	***CH_3***	1	1	2	0.9011	0.848
	CH_2	1	2	14	0.6744	0.540

F1.3. Results & Discussion

Application of the PTD® methodology

The PTD® methodology together with the psychological Power Law for the perception of odor intensity and the stronger component model for mixture intensity and character were used to predict the perceived odor of any mixture with the selected three perfumery raw materials and a constant amount of solvent. The obtained PTDs are presented in Figure F1.4 showing the map of the perceived dominant odors for any possible mixture of three fragrant components (the perfume concentrate, left) and for

the quaternary mixtures (right) with an average molar composition of mineral oil (x_S=0.975) selected for the experiments. It is seen that the middle note (geraniol) and the middle-to-base note (iso-E-super) divide the left diagram into two parts, while the fixative (habanolide) is only strongly perceived when pure. This phenomenon was expected from the perfumery point of view since habanolide is a fixative. The odor zone for geraniol is also larger than for iso-E-super as expected for a middle and a middle-to-base note, respectively. On the other hand, it is also observed, a significant difference in the odor zones of the PTDs when the mineral oil is introduced. It appears that when the PRMs are dissolved in mineral oil, iso-E-super tends to be more retained in the solution and so, it is only strongly perceived when present at higher relative concentrations in respect to the remaining PRMs.

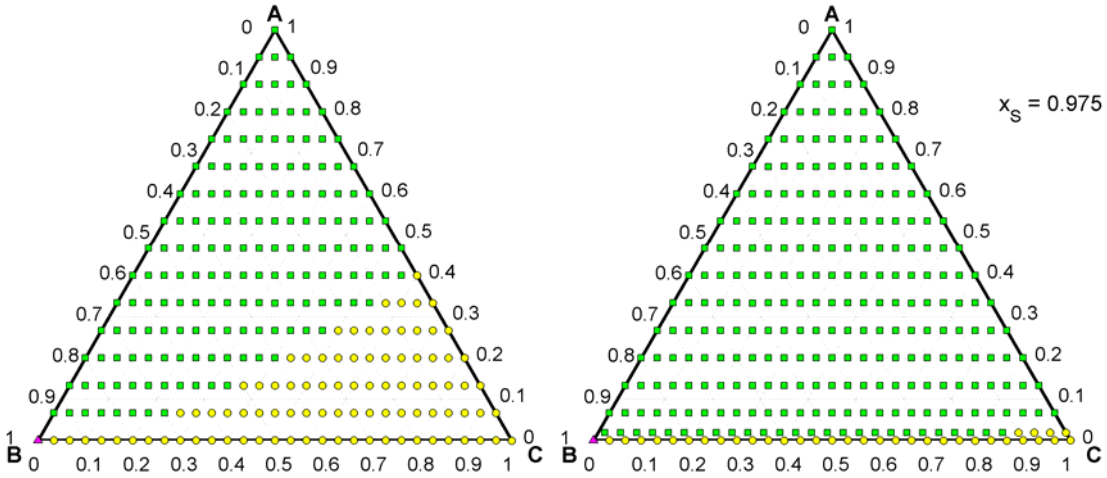


Figure F1.4 – PTDs for the ternary mixture (left) of geraniol (A, green squares) + habanolide (B, pink triangle) + iso-E-super (C, yellow circles) and quaternary mixture (right) including a fixed composition of mineral oil (x_S).

The PTD® can be used as tool to map the perceived odor character as shown in Figure F1.4 and it can also represent the perceived odor intensity of each PRM as a function of its concentration in a ternary mixture. In this way, the odor intensities for each perfumery raw material are shown separately in Figure F1.5 for the perfume concentrate. It is seen that the odor intensity scales plotted on the right of the PTDs have different ranges (so that the gradient colors for odor intensity can be discriminated), especially for habanolide whose odor intensity range is very low as expected for a fixative note. It is known from perfumery that this component is not strongly perceived but has an important role when in a mixture by retaining longer in the solution the other PRMs. Finally, it is also observed that geraniol has higher odor intensities than iso-E-super for

low concentrations of it (lower part of the diagram) because it is typically more volatile than the latter.

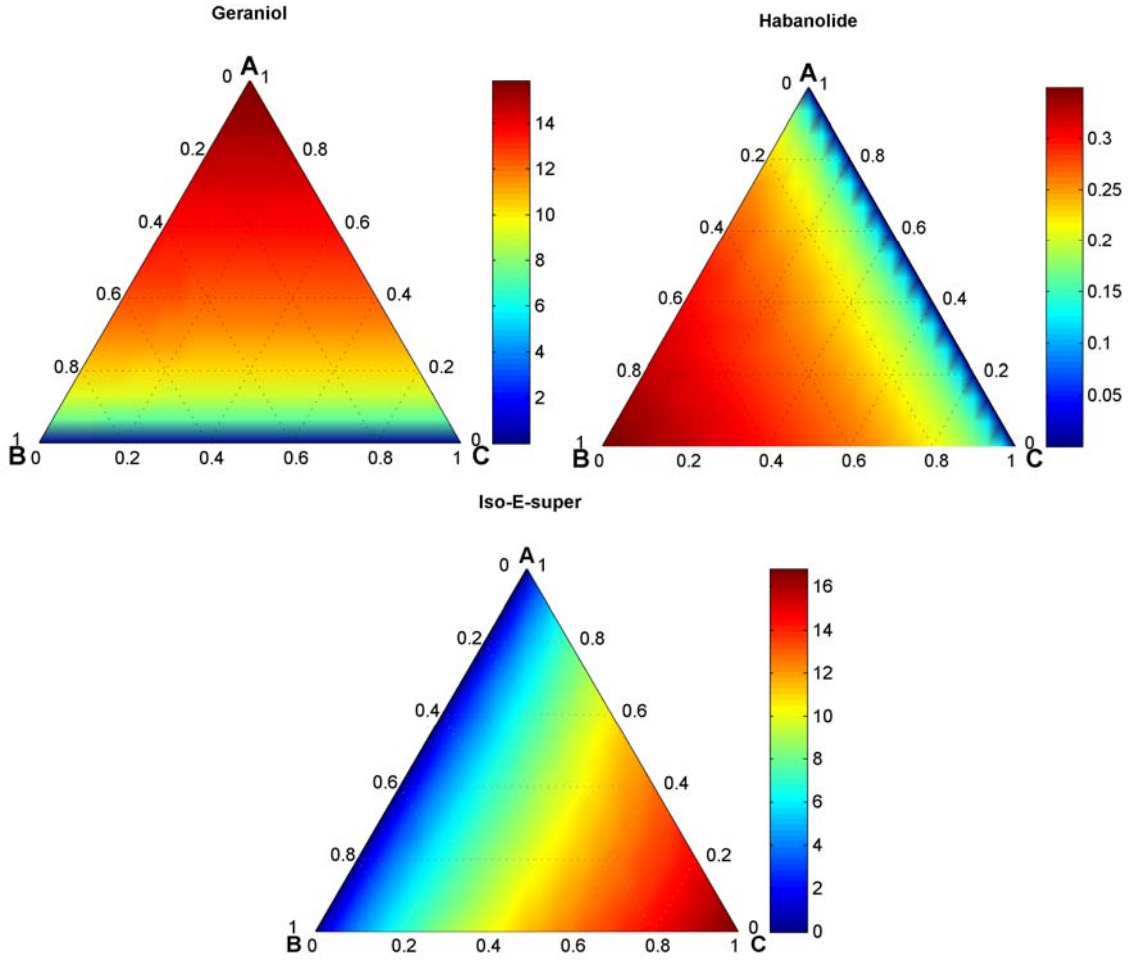


Figure F1.5 – Predicted odor intensities for each fragrance ingredient as a function of its composition in the ternary mixture (A: geraniol, B: habanolide, C: iso-E-super).

Comparison between olfactive evaluations and the model

One target of this work was also to evaluate the relationship between the olfactive evaluations carried by perfumers and the predicted odor intensity for each mixture (OV^n) using the proposed model. For that, the evaluations from the perfumers were arithmetically averaged (from four perfumers) as presented in Table F1.2 and Table F1.5. In this way, the average of the perfumers evaluations presented in these tables represents an experimental measure of the "Target olfactive scale" of the mixture. It is seen that in most of the cases, the reported perfumer average is very close to the maximum "Target olfactive scale" of the three fragrance ingredients. Thus, the use of the stronger component model on our approach may be suitable. In this way, a

correlation between the perfumer average evaluations and the predicted maximum odor intensity values was obtained. This correlation is presented in Figure F1.6 and it is seen that the coefficient of correlation between the two variables (r^2 = 0.85) is very good, thus showing a strong relationship between perfumers' evaluations and the maximum odor intensity predicted from the odor perception model. Moreover, if a comparison is made between the maximum predicted odor intensity and the maximum "Target olfactive scale" for each mixture, an agreement of 84.6% (11 out of 13 samples) for the desired strongest fragrance is observed. The two mismatch cases (N = 5 & 13), occur for mixtures where the maximum "Target olfactive scale" is that of habanolide, which from the model predictions is not strongly perceived (see Table F1.2). However, it is observed that for this PRM the perfumer average is often lower than its "Target olfactive scale", thus getting closer to the predicted values. It is also seen that the two validation samples are reasonably well predicted by the correlation represented on Figure F1.6 (squares). Once again, these results are very significant, once they consider human olfactory experiments which are difficult to model and predict.

Table F1.5 – PRM mixtures, compositions, and perfumer evaluations.

Sample	**Concentration (mg/fabric)**			**Perfumers Intensity Grade**				
N	Geraniol	Habanolide	Iso-E-super	1	2	3	4	average
1	0.8	1	4	125	100	140	70	108.8
2	0.8	1	0	120	120	90	90	105.0
3	0.8	0	4	130	100	130	70	107.5
4	0.8	0	0	100	115	115	100	107.5
5	0	1	4	90	50	50	70	65.0
6	0	1	0	20	20	80	10	32.5
7	0	0	4	80	100	140	5	81.3
8	0	0	0	5	40	40	20	26.3
9	0.1	0.2	0.1	95	75	60	25	63.8
10	0.1	0.2	0	40	90	30	30	47.5
11	0.1	0.2	4	95	80	60	50	71.3
12	0.1	0	0.1	50	65	10	50	43.8
13	0.1	1	0.1	90	80	110	50	82.5
14	0	0.2	0.1	20	70	70	20	45.0
15	0.8	0.2	0.1	135	150	120	100	126.3
16	0.7	0.2	0.1	120	100	110	60	97.5
17	0.3	0.4	0.3	95	80	100	70	86.3

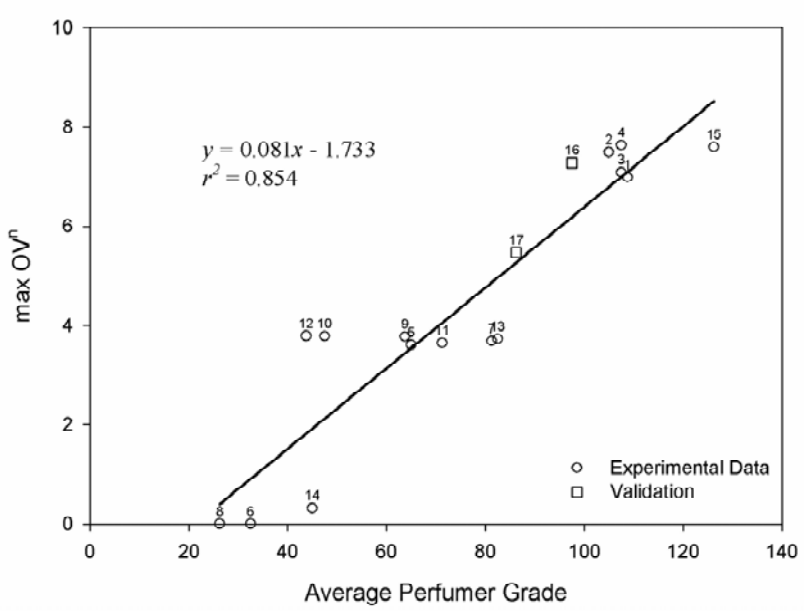


Figure F1.6 – Correlation between the predicted maximum odor intensity and the perfumer average grade.

On the other hand, although perfumers are recognized for playing a key role in the formulation and evaluation of fragrances, one should not forget that the final product will ultimately be evaluated by consumers. These are people non-trained to perceive and interpret smells, and their choice of a fragranced product over another is based mainly on their likeability of the odor they perceive. Therefore, it is also important to assess the perception of odors by an untrained panel. In this regard, it is possible to perform a quantitative (odor intensity) or qualitative (olfactory family) analysis. Though the latter is probably a decisive factor when buying a product, this is also the most difficult to evaluate by consumers because of their lack of sensorial language for classifying smells and their difficulty to express sensorial perceptions with similar words to those of perfumers. In this work, an olfactory analysis test of the perfumery samples was also performed by non-trained panelists at P&G. In this way, it was intended to correlate the maximum predicted odor intensity with the olfactory evaluations made from panelists. For that, each sample was rated from each non-trained panelist for at least 8 times (see Table F1.6). From these evaluations the arithmetic average, geometric average and the median were calculated and then correlated with the obtained results from the odor perception model. The best correlation was found using the arithmetic average of the panelists' evaluations (r^2 = 0.72) and those results are shown in Figure F1.7.

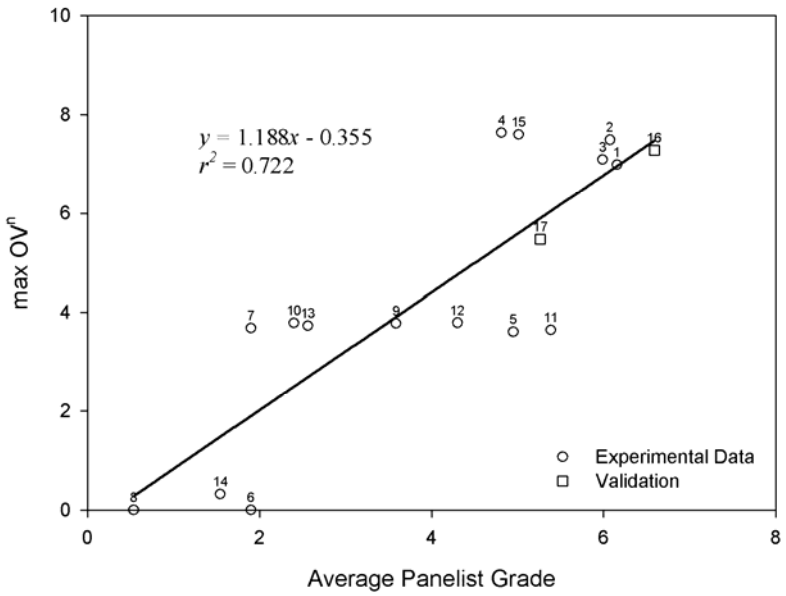


Figure F1.7 – Correlation between the predicted maximum odor intensity and the arithmetic average evaluations from panelists.

It is seen that the correlation performed with non-trained panelists is not as good as that obtained with perfumers. However, it should be emphasized that the use of a non-trained panel is likely to introduce more variability in the reported evaluations than with perfumery experts. Nevertheless, a good correlation was obtained between the predicted odor intensities and the evaluations from non-trained panelists (r^2 = 0.72). Thus, it seems reasonable to assume that to the light of the model applied here for odor intensity, the evaluations performed by panelists are not so different from those of the perfumers. This shows that, although in terms of qualitative classification, panelists have much more difficulty to assign fragrances to words than perfumers, in terms of quantifying odors, the olfactory mechanism presents smaller discrepancies (especially for higher concentrations).

Finally, it should be said that the exponent value (n) for iso-E-super was obtained from the literature. Since it is often used as a mixture of isomers (which exhibit very different olfactive properties) it would be of interest to obtain the experimental odor intensity versus headspace concentration curves in order to calculate that value more accurately. Finally, it would also be of value to measure the concentrations above the textiles (headspace) to obtain experimental data and establish a comparison with the predictions or the olfactive evaluations.

Table F1.6 –Reference number (Ref) and Intensity Grade (I.G.) evaluations of the PRM mixtures carried out by the panel of consumers.

Sample	Panelist										Average
1	Ref	4	12	20	24	25	25	26	26	30	
	I.G.	7.5	4.9	5.6	4.2	7.6	3.9	7.5	9.1	5.1	6.2
2	Ref	2	9	13	13	16	23	26	28		
	I.G.	8.7	9.6	7	3.9	4	6.2	5.4	3.8		6.1
3	Ref	1	9	9	10	11	12	21	23		
	I.G.	2.1	4.3	9	6.4	8.9	6.2	5.4	5.6		6.0
4	Ref	8	16	20	20	21	22	25	27		
	I.G.	8.9	3.3	2.2	3.1	4.9	8.5	3	4.6		4.8
5	Ref	3	3	7	11	17	18	23	27		
	I.G.	4.3	5.8	6.9	3.3	1.6	5	6.5	6.2		5.0
6	Ref	1	3	6	9	11	16	18	21		
	I.G.	0.6	0.4	3.7	1.9	5.1	0.3	2.8	0.4		1.9
7	Ref	2	5	6	9	13	15	18	22	29	
	I.G.	4.9	0.2	5.4	0.4	0	0.8	5.5	4.4	0.3	2.4
8	Ref	2	5	14	19	23	26	27	29		
	I.G.	0.3	0.1	0.7	0	2.1	0.2	0.8	0.1		0.5
9	Ref	1	2	4	7	10	14	17	23	28	
	I.G.	0.5	2.5	0.4	1.6	4.8	8.2	3.6	8.4	1.8	
	Ref	1	4	5	8	10	15	17	28		
	I.G.	0.9	2	1.4	5.9	1.8	10	2.9	4.3		3.6
10	Ref	2	12	13	14	14	18	19	21	24	
	I.G.	1.2	2.5	0	5.8	5	1.7	1	1.3	3.1	2.4
11	Ref	4	6	6	8	8	12	24	24		
	I.G.	5.3	6.4	5.1	6.1	8.2	6.8	1.4	3.8		5.4
12	Ref	6	7	10	15	15	17	20	22	27	
	I.G.	3.3	4.4	5.3	4.1	5.1	3.8	1.1	6.7	4.9	4.3
13	Ref	4	5	7	13	16	16	19	21		
	I.G.	6.7	1.5	4.5	2.7	1.2	1.5	2.1	0.3		2.6
14	Ref	1	7	8	11	11	12	19	25	30	
	I.G.	0.3	1.1	2.6	3.2	1.8	0.3	0.3	4	0.3	1.5
15	Ref	3	5	18	19	20	22	25	29		
	I.G.	8.1	3.6	5.5	2.6	3.6	9.8	2.5	4.4		5.0
16	Ref	10	22	24	27	28	28	30	30		
	I.G.	6.9	9.4	2.4	8.2	5.9	7.9	5.7	6.3		6.6
17	Ref	3	14	15	17	26	29	29	30		
	I.G.	7.3	4.9	6.1	5.2	7.1	3.3	3.6	4.6		5.3

F1.4. Conclusions

Two correlations were obtained between both the perfumer average and panelist average olfactory evaluations with an olfactory model for the prediction of the odor intensity of fragrance mixtures. The results have shown a good agreement between our model and the experimental evaluations involving human experiments which are very difficult to model at this level so far. In this way, it is possible to use the proposed odor perception model, which has its own metric scale for odor intensity, for comparison with the intensity rating scales obtained from perfumers or panelists. The achievements found in this work are of great relevance once a developed odor perception model can be applied for the prediction of the odor intensity of fragrance mixtures and, thus, be useful in the pre-formulation stages of a fragranced product.

F1.5. References

Cain, W. S., Schiet, F. T., Olsson, M. J., de Wijk, R. A., Comparison of Models of Odor Interaction, *Chemical Senses*, 20, 625-637, 1995

Carles, J., A method of creation in perfumery, *Soap Perfumery Cosmet.*, 35, 328-335, 1962

Chemspider, Database of Chemical Structures and Property Predictions - Royal Society of Chemistry, from http://www.chemspider.com/Default.aspx, Last Accessed on February, 2011

Devos, M., Rouault, J., Laffort, P., Standardized olfactory power law exponents, Dijon - France, Editions Universitaires-Sciences 2002

Fredenslund, A., Jones, R., Prausnitz, J. M., Group-contribution estimation of activity coefficients in nonideal liquid mixtures, *AIChE Journal*, 21, (6): 1086-1099, 1975

Laffort, P., Dravnieks, A., Several models of suprathreshold quantitative olfactory interaction in humans applied to binary, ternary and quaternary mixtures, *Chemical Senses*, 7, (2): 153-174, 1982

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005

Meilgaard, M., Civille, G. V., Carr, B. T., Sensory Evaluation Techniques, New York, CRC Press, 1999

Poling, B., Prausnitz, J. M., O´Connell, J., The Properties of Gases and Liquids, McGraw-Hill, 2004

Stevens, S. S., On the Psychological Law, *The Psychological Review*, 64, (3): 153-181, 1957

Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., Perfumery Quaternary Diagrams for Engineering Perfumes, *AIChE Journal*, 55, (8): 2171-2185, 2009

Teixeira, M. A., Rodríguez, O., Rodrigues, A. E., The Perception of Fragrance Mixtures: a comparison of odor intensity models, *AIChE Journal*, 56, (4): 1090-1106, 2010

F2. Performance of microencapsulated perfumes applied on textiles*

This work resulted from a joint cooperation between two research teams within LSRE, with the aim of evaluating the performance of an added-value product: microencapsulated perfumes applied on textiles. The design of the perfume, the microencapsulation and thermo fixation processes and the experimental measurement of the fragrance release upon dry washing and abrasion cycles was performed by other authors within LSRE (further details can be found in (Rodrigues*, et al.*, 2009)).

In this work, the idea was to combine different techniques (experimental and modeling) to assess the performance of perfumed suits for man. To accomplish that, several concepts of Product Engineering (previously reviewed in Chapter 2) were combined as presented in Table F2.1. These approaches consider the definition of several stages from the identification of consumer **needs** for the development of **ideas** and their **selection** up to the **manufacture** of the product (needs-ideas-selection-manufacture) (Ulrich and Eppinger, 2000; Cussler and Moggridge, 2001; Wesselingh*, et al.*, 2007).

Table F2.1 – Description of the four-step procedure considered in this work.

Needs	Fragrant suits for men
Ideas	Perfume + Microcapsule + Textile: define several perfume families and compositions, formaldehyde-free microcapsules and polymerization techniques, types of textile and binders
Selection	Composition of a masculine perfume + polyurethane-urea microcapsules by interfacial polymerization + impregnation in the foulard step + polyurethane binder + wool/polyester textile
Manufacture	Production of microcapsules with perfume + impregnation onto textiles + assessment of finished textile quality + evaluation of olfactive performance after dry washing and abrasion cycles

In order to assess the performance of this product, the perceived odor intensity and character of the perfume was predicted using the PQ2D® methodology and evaluated by headspace gas chromatography after equilibration. These results were then compared with those obtained by Rodrigues *et al.* (Rodrigues*, et al.*, 2009) for the dry cleaning and abrasion tests performed on the textiles. Moreover, it was predicted here the evaporation and diffusion profiles of the encapsulated fragrances, so that it could be

* This section is partly based on the paper from Teixeira, MA, Rodríguez, O, Rodrigues, S, Martins, I, Rodrigues, AE, A case study of Product Engineering: Performance of microencapsulated perfumes on textile applications, submitted.

possible to perform a first estimate of the performance in terms of perceived odor with the time and distance from the source. For a product like a perfumed suit, it has to fulfill some specific requirements as a function of dry washing and abrasion cycles: it has to satisfy the odor intensity (in order to be perceived that has to be higher than the odor detection threshold, *ODT*) and also the odor quality after these mechanical tests. For that reason the performance was evaluated by the persistence of the fragrance material in the textiles in terms of their odor intensity and character (*e.g.* .olfactive families).

F2.1. Materials and methods

The perfume formulation was obtained using four commercially available fragrances, namely (4R)-1-methyl-4-(1-methylethenyl)-cyclohexene (limonene), methyl-(2-amyl-3-oxocyclopentyl)acetate (methyl dihydrojasmonate, MDJ), methyl cedryl ketone (vetiver) and 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethylcyclopenta[g]-2-enzopyran (galaxolide) in a 50% diethyl phthalate (DEP) mixture. All fragrances were supplied by Sigma Aldrich and used without further purification. This mixture composition is based on the pyramidal structure proposed by Jean Carles (Carles, 1962) for a perfume which is based on the combination of a top (limonene), middle (MDJ), and base (vetiver and galaxolide) notes plus a solvent (DEP).

The part of the work with respect to the production of microcapsules of polyurethane-urea (PUU), their incorporation on textiles and evaluation of headspace concentrations after dry cleaning and abrasion cycles was performed by Rodrigues et al., so that further details on those processes can be seen at (Rodrigues*, et al.*, 2009).

F2.2. Results & Discussion

Perfume characterization

The fragrant components used in the formulation of the perfume together with their compositions and some physicochemical properties are presented in Table F2.2. For the evaluation of the performance of this perfume concentrate, a characterization of its olfactive intensity and character was performed using some perfumery tools previously developed. First, the odor character of the mixture was studied using the PTD® and

PQ2D® methodologies (see Chapter 3). These are graphical tools showing the dominant odor as a function of composition in triangular or tetrahedric diagrams, respectively. The dominant odor was calculated using the Stevens' Power Law for odor intensity together with the Stronger Component (SC) model as an odor perception model (see Chapters 2, 3, 7 and Annex A).

Table F2.2 - Perfume concentrate composition and their physicochemical properties.

Component	Molecular Formula	Molar composition, x_i	Molecular Weight, M_i (g/mol)	Odor Threshold, C^i_{Thr} (g/m^3)	Vapor Pressure, P_i^a (Pa)	n[e]
Limonene	$C_{10}H_{16}$	0.296	136.20	6.84×10^{-4} [b]	20.5×10^{1}	0.37
Methyl dihydrojasmonate	$C_{13}H_{22}O_3$	0.326	226.31	9.12×10^{-4} [c]	9.47×10^{-2}	0.35*
Methyl cedryl ketone	$C_{17}H_{26}O$	0.299	246.39	3.80×10^{-5} [d]	1.13×10^{-2}	0.35*
Galaxolide (in 50% DEP)	$C_{18}H_{26}O$	0.037	258.40	1.38×10^{-5} [c]	5.52×10^{-2}	0.36
Diethyl Phthalate (DEP)	$C_{12}H_{14}O_4$	0.043	222.23	odorless	2.22×10^{-1}	-

[a] Chemspider. Database of Chemical Structures and Property Predictions - Royal Society of Chemistry.[Database] November, 2010; Available from: http://www.chemspider.com/Default.aspx.
[b] van Gemert LJ, Compilations of odour threshold values in air, water and other media. The Netherlands: Oliemans Punter & Partners BV 2003.
[c] Leffingwell JC, Leffingwell D. May 2010; Available from: http://www.leffingwell.com/odorthre.htm.
[d] Measurement in our laboratory using an olfactometer.
[e] Devos M, Rouault J, Laffort P, Standardized olfactory power law exponents. Dijon - France: Editions Universitaires-Sciences 2002.
*Recommended average value.

Once the perfume concentrate is composed by four fragrances and an odorless solvent, the PQ2D® is perfectly suited to show in a single three dimensional graph the effect of the composition in the initial odor character near the source of release of the fragrance ingredients. The odor character of the ternary subsystems that compose the perfume mixture are presented in Figure F2.1. The presented PTD® diagrams match the faces of the PQ2D® which is presented in Figure F2.2 to show the whole behavior of the quaternary mixture. Each fragrant note will dominate above all others within a certain composition range, which in the PTD® is represented by an odor zone while in the PQ2D® is shown by an odor volume.

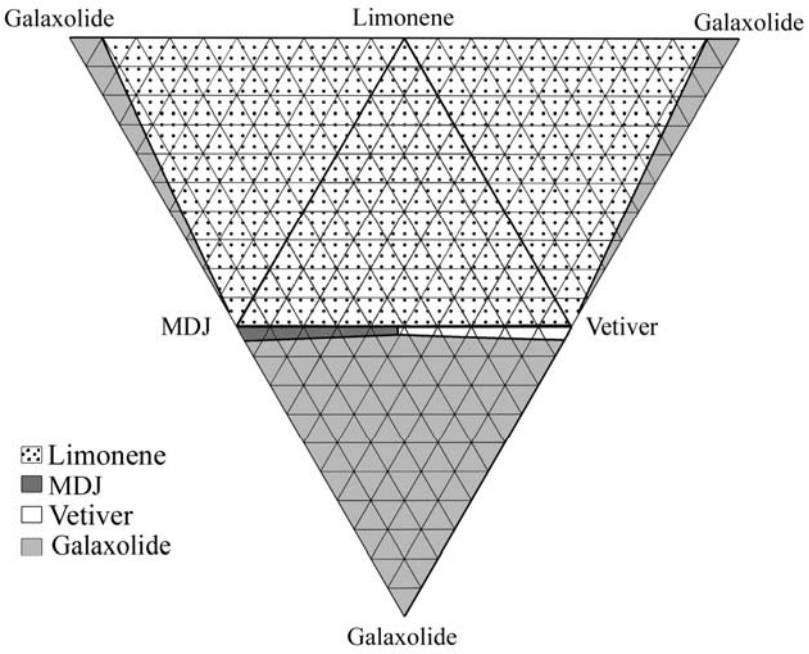


Figure F2.1 – PTD® for the ternary subsystems with the odor zones for each individual fragrance in the mixture.

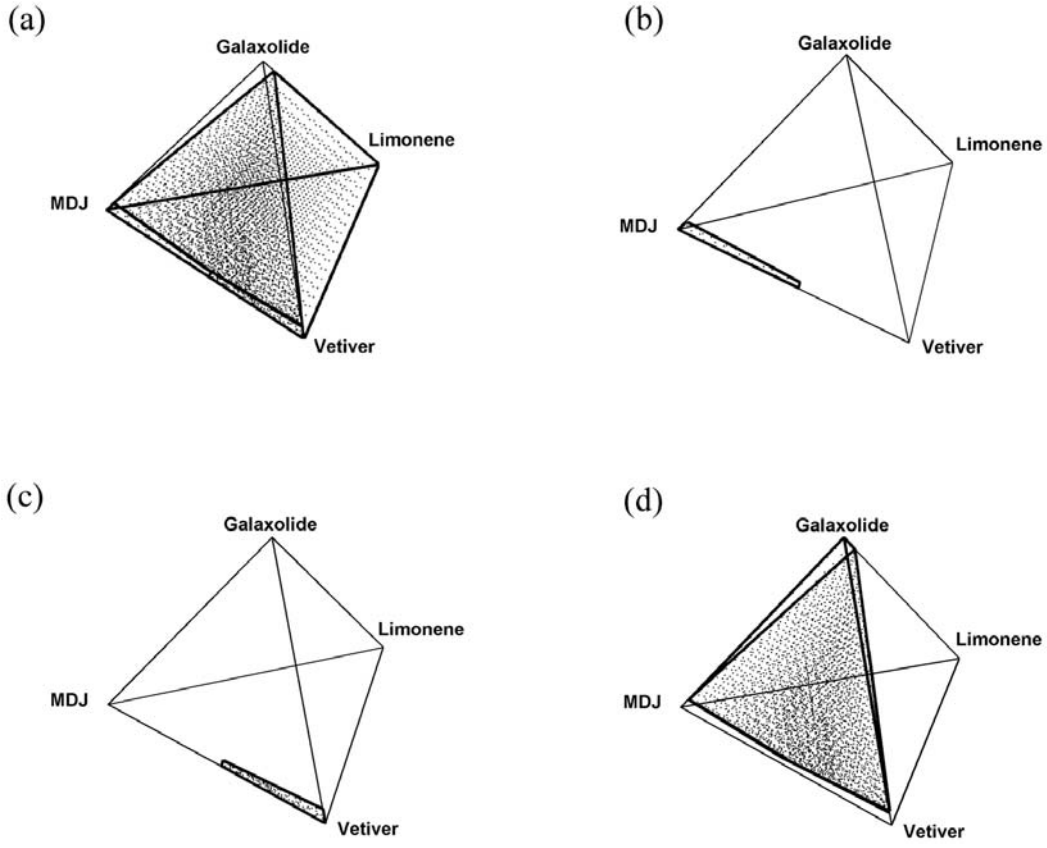


Figure F2.2 – PQ2D® with the odor volumes for each individual fragrance in the mixture: (a) limonene, (b) MDJ, (c) vetiver, (d) galaxolide.

In Figure F2.2 it is possible to visualize the shapes of the different odor volumes as a function of the liquid composition in the PQ2D® for the quaternary mixture (limonene + MDJ + vetiver + galaxolide). It is clear that limonene, the top note (and the most volatile component) has the dominant odor of the mixture for the majority of the composition range, and so its odor volume occupies nearly the whole tetrahedron. The odor volume for galaxolide dominates the odor space only for low limonene concentrations, appearing as a slice opposite to the limonene vertex. Both MDJ and vetiver (the floral and woody notes) make themselves more strongly perceptible only for very low concentrations of limonene and galaxolide. Thus, their odor volumes are like fine sticks near the axis linking their vertices. Considering the initial perfume composition and the PQ2D® on Figure F2.2, it is possible to see that this perfume mixture would initially present a dominant limonene scent. In order to assess the odor character or quality of this perfume formulation, the PR methodology was also applied, considering its molar composition (Table F2.2) and the classification of the pure fragrances into olfactive families as presented in Table F2.3.

Table F2.3 – Fragrance classification in terms of volatility and olfactive character.

Component	Fragrance note	Odor character[a]
Limonene	Top	Citrus, Fruity, Floral
Methyl dihydrojasmonate	Middle	Floral
Methyl cedryl ketone	Base	Woody, Oriental
Galaxolide (in 50% DEP)	Base	Musk, Floral, Woody
Diethyl Phthalate (DEP)	Solvent	odorless

[a]Brechbill GO, A Reference Book on Fragrance Ingredients. New Jersey - USA: Creative Endeavor Books 2006.

The obtained perfumery radars for the predicted and experimental (measured by headspace) compositions of the perfume mixture are shown in Figure F2.3. Both perfumery radars present stronger citrus family for the primary olfactive family, as a result of the blooming odor of limonene. In this way, in terms of olfactive families both the predicted and the experimental perfumery radars evidence an initial citrus-floral odor perception, although the fruity, woody and musk *nuances* have also their impact. These last two families will be more strongly perceived after the evaporation of the top note (limonene). Thus, considering the proposed olfactive families of the PR methodology, it can be possible to classify this perfume as citrus-floral with woody and

musk *nuances*. The experimental classification of this simple perfume mixture obtained from the nose evaluation of experts agreed with the Perfumery Radar, considering the powerful limonene odor (mainly citrus and fruity) to give lift and freshness, together with a background of sweet (musk) and woody *nuances* (see (Rodrigues*, et al.*, 2009)).

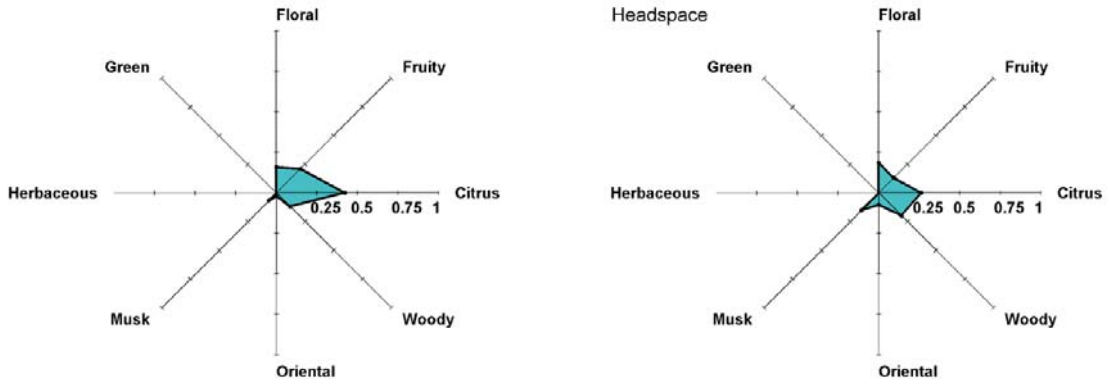


Figure F2.3 – Predicted (left) and experimental (right) perfumery radars for the selected perfume mixture that was encapsulated and impregnated in the fabrics.

However, as it is known, the perceived smell of a perfume does not remain the same over time although it may be expected its character does not change dramatically (in terms of dominant olfactive families). As mentioned before, perfumes are formulated as a combination of different types of fragrances and once it is applied in the body or clothes the different components will start to evaporate and diffuse at different rates. The same applies for a perfume released from microcapsules as is the case here. Thus, it is expected that the perceived odor of the perfume will evolve with time, and this effect must be taken into account for the evaluation of its performance. In order to evaluate that, a diffusion model previously developed (see Chapter 6) was used to predict the evolution of the odor intensity and character of the selected formulation (Mata*, et al.*, 2005; Teixeira*, et al.*, 2009). This diffusion model accounts for the change of the fragrances concentration, both in the liquid and gas phases. The combination of the diffusion model with the odor intensity and the perception models provides the tool to predict the odor intensity profiles for a given perfume composition. These intensity profiles are presented in Figure F2.4 for the selected perfume composition (Table F2.2) at two different distances from the source: 0 and 2 m. Despite the simplicity of the odor models, they provide basic information about the dominant note (character) of the perfume. This way, the diffusion profiles show that limonene is the odor note more intensely perceived for all the time considered. Even at longer distances from the release

point, limonene is more strongly perceived although the middle and the base notes present some background odor effects: vetiver gives an oriental-sweet *nuance* while the musk galaxolide acts as a fixative by retaining the other fragrances in the liquid and, thus, slowing down their evaporation.

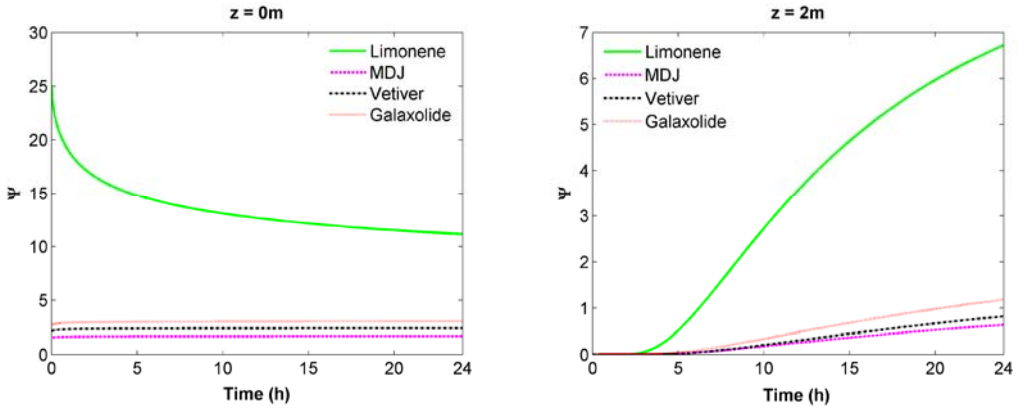


Figure F2.4 - Odor profiles for the perfume concentrate near the point of release (left) and at a distance of 2m from the source point (right).

Performance of fabrics with microencapsulated perfume

Generally, there are two ways of releasing the fragrance to the outside of an encapsulating agent: by molecular diffusion through the wall of the capsule and/or using a physical trigger to release the fragrance like scratch-and-sniff or by destruction of the capsule wall through mechanical action as is the case here (Nelson, 2002; Rodrigues*, et al.*, 2008; Rodrigues*, et al.*, 2009).

The encapsulated perfume is a homogeneous solution with constant composition in each microcapsule, which will be released to air from breakage of their polymeric walls. In order to evaluate the performance of the microencapsulated perfume when applied to the fabrics, the released odor intensity was compared to that of the pure perfume. Odor intensities for the fragrant components were calculated from the concentrations measured experimentally in the headspace of the perfume at equilibrium conditions, which were compared to those in the headspace of the microencapsulated textiles (prior to any washing cycles or abrasion tests as reported in (Rodrigues*, et al.*, 2009)) and they were also predicted from the perfume composition, considering the encapsulation

efficiencies reported by (Rodrigues*, et al.*, 2009). A comparison between the odor intensity of each fragrant component in these three situations is presented in Figure F2.5.

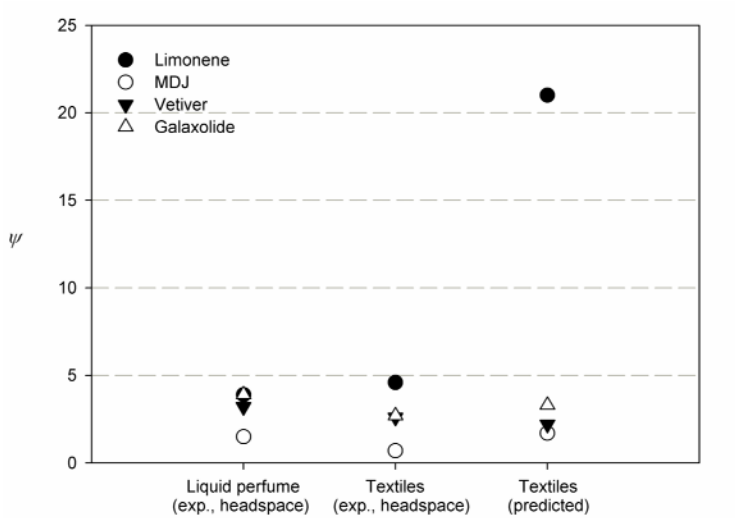


Figure F2.5 – Comparison between the odor intensities of the fragrant species in the headspace of the perfume (left) and the impregnated textiles (middle), together with those predicted by our models (right).

From Figure F2.5, it can be observed that limonene is the dominant fragrant note in all cases, followed by galaxolide, vetiver, and finally MDJ. Comparing the odor intensities obtained in the headspace of the liquid perfume mixture (left column) and in the headspace of the impregnated textiles (middle column) measured by Rodrigues *et al.*, it is possible to see that the top note (limonene) is the only species that has higher odor intensity when applied in the textiles. This may be attributed to the fact that limonene was the fragrance ingredient with the lowest reported encapsulation efficiency (of all the fragrance ingredients), and so much of it remained outside the microcapsules, being directly adhered to the fibers. In order to simulate the odor intensity of the fragrant compounds, they were also predicted using the composition of the liquid perfume, the encapsulation efficiencies obtained, and the UNIFAC method as described elsewhere. The predicted odor intensities for each fragrance compound are presented on the right column of Figure F2.5. The results show an over prediction for the odor intensity of limonene, while for the other fragrances it presents the same tendency as observed for the perfume and textiles headspace. The general trend of the perceived odor intensities is that Limonene > Galaxolide > Vetiver > MDJ for all the three cases.

As mentioned before, the impregnated textiles were subjected to dry cleaning and abrasion (mechanical) tests performed by Rodrigues *et al.* for the evaluation of their

performance in a daily use. Further details on the analysis and experimental results can be obtained from (Rodrigues*, et al.*, 2009). Here we will just present the simulations for the odor diffusion and summarize some of the experimental results which are important for comparison purposes.

On both tests of washing and abrasion cycles it was possible to see that limonene and vetiver were the most retained fragrances in the fabrics and with suprathreshold odor intensities. It is seen through this analysis that after a number of dry washing cycles or abrasion tests some of the notes (MDJ, galaxolide) have odor intensities below unity (sub-threshold). However, it should be emphasized that this does not mean that the fragrant species is not still impregnated in the fabrics, but that its concentration is below the detection limit. Thus, if the fragrant component remains in the perfume mixture, it continues to play a role in the evaporation rate of the other fragrances, influencing the overall perceived odor.

In order to assess the performance of these fragranced textiles it is important to evaluate the perceived odor intensity and character of the microencapsulated perfume either over time of usage of the suit, either at different distances from it. This is important to evaluate the perceived sensation of the fragranced suit on the user and surrounding people. The analysis of such parameters is quite difficult to predict (due to the randomness of microcapsule breakage and evolution of the perfume composition over time) or to evaluate experimentally (due to the complexity in sample collection and analysis at low or trace levels). However, for a simple evaluation, a diffusion model was used to estimate the performance of the perfumed suits in terms of the odor intensity and character over time and distance of application: The composition of the liquid perfume remaining on the textiles was estimated from the experimentally measured concentrations in the headspace of the impregnated textiles. A flash vapor-liquid equilibrium (VLE) calculation was performed using the UNIFAC method for estimating the activity coefficients (γ_i) in the liquid phase. From that point the diffusion model was applied using an estimated total number of moles of 1.0 mmol and an area of liquid-gas interface of 0.071 m^2. This analysis was performed for each dry washing cycle in order to evaluate the odor intensity and character of the perceived scents at different distances from the man suit and over time. The odor profiles obtained after the first and third dry washing cycle are shown in Figure F2.6.

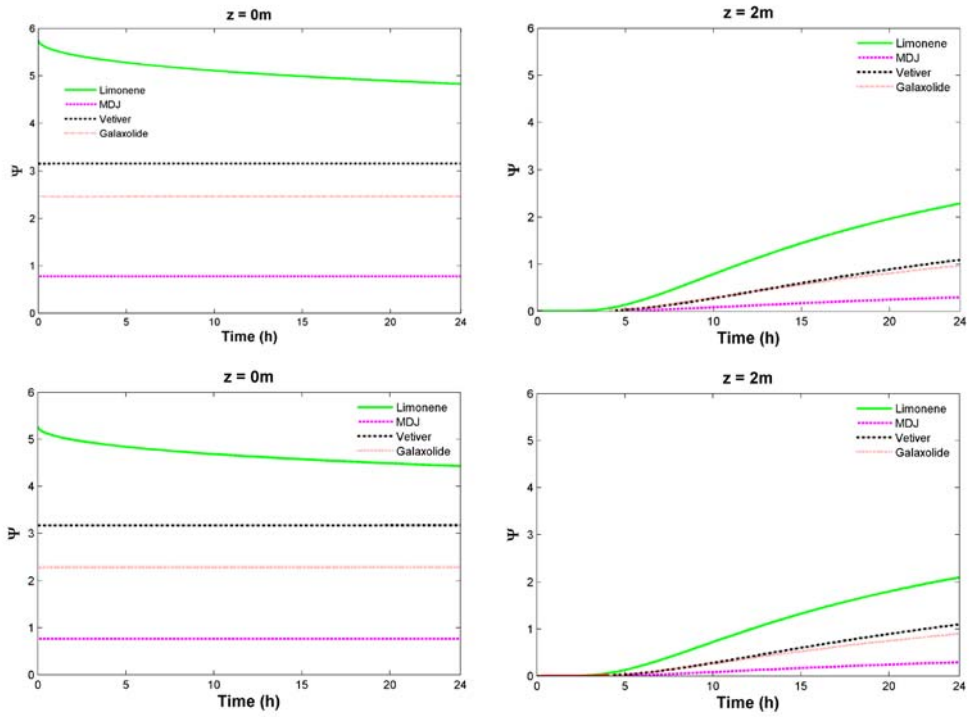


Figure F2.6 – Odor profiles for the perfume concentrate after the first (top) and third (bottom) dry washing cycles: near the point of release (left) and at a distance of 2 m from the source (right).

The predicted odor intensity profiles show that, from a very simplistic approach, the top note limonene would be more strongly perceived than the other fragrances after each dry cleaning cycle. Thus, limonene would have higher impact, tenacity, diffusion and volume parameters in terms of odor performance, though the character of the perceived scent might change as the concentration of the middle and base notes evolve through time and distance. Another important result is that although the perceived scent decreases in intensity after dry cleaning cycles (as expected), its character remains similar. This can be seen in Figure F2.6: comparison of top and bottom graphics shows that the relative proportion of the ingredients is kept. This is desirable from the consumer point of view, because it is expected that the perfume will maintain a similar scent and olfactive family after washing. Moreover, it should be noted that although convection effects were neglected in the model and the total mass of perfume impregnated in the textile was assumed as being small, the predicted odor intensity after 24 h is still higher than unity for some fragrances. This way, the perfume is expected to be perceived around the people wearing the suit for a considerable time. Nevertheless, it is important to highlight that this evaluation of performance considers only the

evaporation and diffusion of the fragrant components from the microcapsules into air, neglecting possible interactions of the fragrances with the textile and between themselves. In this case the releasing process starts by breakage of the microcapsule and then evaporation of the liquid perfume mixture into air. However, the binding of fragrant molecules to textile fibers would reduce the evaporation rate, thus enhancing the performance of the perfumed suit.

F2.3. Conclusions

In this work different predictive models (for odor intensity, odor character, diffusion) were combined with experimental methodologies for the assessment of the performance of an added-value product. The performance analyses of perfumed textiles have shown a reduction of the odor intensity of the perfume with the number of dry cleaning and abrasion cycles. However, even after being subjected to these tests, it is possible to detect fragrances released from the suits at suprathreshold concentrations. The prediction of the odor intensity for the headspace of both the perfume and the textiles has shown that limonene was the most strongly perceived fragrance which was confirmed experimentally. The relative odor intensity of the perfume ingredients predicted with the model was in agreement with the experimental headspace evaluations showing a general trend: Limonene > Galaxolide > Vetiver > MDJ. Moreover, it was observed that although galaxolide was strongly perceived after impregnation, it was less perceived than vetiver after the first dry cleaning or abrasion tests. In sum, this work has presented a performance analysis of fabrics with a microencapsulated perfume. For this type of application, and considering the perfume mixture selected, limonene showed a better performance in the perfume mixture, being the dominant note over time and distance.

F2.4. References

Carles, J., A method of creation in perfumery, *Soap Perfumery Cosmet.*, 35, 328-335, 1962

Cussler, E. C., Moggridge, G. D., Chemical Product Design, Cambridge, Cambridge University Press, 2001

Mata, V. G., Gomes, P. B., Rodrigues, A. E., Engineering Perfumes, *AICHE Journal*, 51, (10): 2834-2852, 2005
Nelson, G., Application of microencapsulation in textiles, *International Journal of Pharmaceutics*, 242, (1-2): 55-62, 2002
Rodrigues, S. N., Fernandes, I., Martins, I. M., Mata, V. G., Barreiro, F., Rodrigues, A. I., Microencapsulation of limonene for textile application, *Industrial & Engineering Chemistry Research*, 47, (12): 4142-4147, 2008
Rodrigues, S. N., Martins, I. M., Fernandes, I. P., Gomes, P. B., Mata, V. G., Barreiro, M. F., Rodrigues, A. E., Scentfashion®: Microencapsulated perfumes for textile application, *Chemical Engineering Journal*, 149, 463–472, 2009
Teixeira, M. A., Rodríguez, O., Mata, V. G., Rodrigues, A. E., The Diffusion of Perfume Mixtures and Odor Performance, *Chemical Engineering Science*, 64, 2570-2589, 2009
Ulrich, K. T., Eppinger, S. D., Product Design and Development, New York, McGraw-Hill, 2000
Wesselingh, J. A., Kiil, S., Vigild, M. E., Design & development of biological, chemical, food and pharmaceutical products, Chichester, U.K., Wiley, 2007

Annex G

G.1. Full papers in peer-reviewed international journals

(1) Miguel A. Teixeira, Oscar Rodríguez, Vera G. Mata, Alírio E. Rodrigues, The Diffusion of Perfume Mixtures and Odor Performance, Chemical Engineering Science, 64, 2570-2589, 2009.

(2) Miguel A. Teixeira, Oscar Rodríguez, Vera G. Mata, Alírio E. Rodrigues, Perfumery Quaternary Diagrams for Engineering Perfumes, AIChE Journal, accepted, 55(8), 2171-2185, 2009.

(3) Miguel A. Teixeira, Oscar Rodríguez, Alírio E. Rodrigues, The Perception of Fragrance Mixtures: a comparison of odor intensity models, AIChE Journal, 56(4), 1090-1106, 2010.

(4) Laura E. LeMire, Miguel A. Teixeira, Brian E. Reed, Removal of Arsenic (V) Using an Iron-Impregnated Ion Exchange Bead, Separation Science and Technology, 45(14), 2051-2063, 2010.

(5) Miguel A. Teixeira, Oscar Rodríguez, Alírio E. Rodrigues, Perfumery Radar: A Predictive Tool for Perfume Family Classification, Ind. Eng. Chem. Res., 49, 11764–11777, 2010.

(6) Oscar Rodríguez, Miguel A. Teixeira, Alírio E. Rodrigues, Prediction of odor detection thresholds using partition coefficients, Flavour & Fragrance Journal, In press.

(7) Miguel A. Teixeira, Oscar Rodríguez, Fátima L. Mota, Eugénia A. Macedo, Alírio E. Rodrigues, Evaluation of group-contribution methods to predict VLE and odor intensity of fragrances, Industrial & Engineering Chemistry Research, 50, 9390–9402, 2011.

(8) Miguel A. Teixeira, Oscar Rodríguez, Sofia Rodrigues, Isabel Martins, Alírio E. Rodrigues, A case study of Product Engineering: Performance of microencapsulated perfumes on textile applications, AIChE Journal, DOI 10.1002/aic.12715, 2011.

G.2. Chapters in Books

(1) Miguel A. Teixeira, Oscar Rodríguez, Alírio E. Rodrigues, Chapter 1 - Odor Detection and Perception: An Engineering Perspective, In: Advances in Environmental Research. Vol. 14, Edited by Justin A. Daniels, Nova Science Publishers, Inc., 2011, ISBN 978-1-61209-584-4.

G.3. Conference Proceedings

2007 – Poster presentation at the Regional Conference of the American Waterworks Association (AWWA) with the work "Removal of Arsenic(V) Using an Iron-Impregnated Ion Exchange Bead", with co-authors, Laura LeMire and Brian Reed, Maryland (EUA).

2009 - Poster presentation at the European Symposium on Applied Thermodynamics (ESAT2009) with the work "Product Engineering for Perfumes", with co-authors, Oscar Rodríguez and Alírio E. Rodrigues, Santiago de Compostela (Spain).

2009 – Oral presentation at the 8th World Congress of Chemical Engineering (WCCE8) with the work "Perfume Engineering: Odor Character, Diffusion and Performance", with co-authors, Oscar Rodríguez, Vera G. Mata, Alírio E. Rodrigues, Montreal (Canada).

2010 - Poster presentation at the Cosmetic Innovation Days (Cosm'Innov 2010) with the work "A model to predict the odor character of perfume mixtures", with co-authors, Oscar Rodríguez and Alírio E. Rodrigues, Orléans (France).

2010 - Poster presentation at the Cosmetic Innovation Days (Cosm'Innov 2010) with the work "A predictive methodology to assess perfume performance", with co-authors, Oscar Rodríguez and Alírio E. Rodrigues, Orléans (France).

2010 – Invited lecture presented at the II Conference of Bioengineering with the title "Engineering Perfumes", with co-authors Oscar Rodríguez and Alírio E. Rodrigues, FEUP, Porto (Portugal).

INTERNATIONAL PRESS RELEASES

FOR IMMEDIATE RELEASE

ACS News Service Weekly PressPac: December 1, 2010

“Perfumery radar” brings order to odors

“**Perfumery Radar: A Predictive Tool for Perfume Family Classification**”
Industrial & Engineering Chemistry Research

New perfumes may be developed faster using a new tool, called a “perfumery radar,” that brings scientific order to often arbitrary process of classifying odors that make-up the products.
Credit: iStock

Scientists are announcing development and successful testing of the first “perfumery radar (PR).” It’s not a new electronic gadget for homing in on the source of that Eau de Givenchy or Jungle Tiger in a crowded room. Rather, PR is a long-awaited new tool for bringing scientific order to the often arbitrary process of classifying the hundreds of odors that make-up perfumes. A report on the advance appears in ACS’ journal *Industrial & Engineering Chemistry Research*.

Alírio Rodrigues and colleagues note that the typical perfume has 50-100 fragrant ingredients. Experts who make perfumes have long described those ingredients with highly subjective terms like “floral,” “citrus,” “woody,” and “oriental.” Many different classification systems have been proposed, but they still leave perfumers describing the same smell with different words that often are arbitrary.

In an effort to bring order to odor classification, the scientists developed “perfumery radar” system, which relies on plots (see graphic), similar to the displays used to track aircraft. They used the PR to classify the primary odor families of 14 commercial perfumes and found th the results closely matched those of experienced perfume makers. With the PR, manufacturers could speed up the development of new perfumes — namely the called preformulation stage in which they experimentally evaluate the product — thus saving time and money, the report states.

Contact

Science Inquiries: **Michael Woods**, Editor, 202-872-6293
General Inquiries: **Michael Bernstein**, 202-872-6042

Perfume

Making sense of scents

A new way to describe a fragrance

Dec 9th 2010 | from PRINT EDITION

Comment (1) Recommend (3)
E-mail Share
Print Reprints & permissions

PERFUMES have colourful descriptions, such as floral or musky, to give buyers an inkling of their aromas. But perfumers often disagree about how to describe a particular fragrance, so the classification of scents is inconsistent. Now researchers have revealed a new system to bring some order to this odoriferous business.

A nose for the business

One reason why people describe smells differently is a weakness of the nose. Although the human sense of smell is keen, it is hampered by a lack of precision. When presented with hundreds of odours, the nose can simultaneously distinguish only a few. Keenly aware of these problems, Alírio Rodrigues at the University of Porto in Portugal and his colleagues compiled an extensive list of scent descriptions from the existing databases used by the perfume industry. They found that eight general terms for scents (citrus, floral, green, fruity, herbaceous, musk, oriental and woody) could work as families to which more than 2,000 specific scents could be assigned. The team then plotted these eight families onto a map that resembled the plots on a radar screen.

Dr Rodrigues then tested what the group calls its "perfumery radar" by presenting it with four essential scent oils: orange, lemon, jasmine and thyme. To do this, the oils were broken into their component parts and analysed using gas chromatography and mass spectrometry. This allows molecules of oil to be compared against a spectral library which could identify them chemically and assign each oil to one of the eight families.

The team already knew that lemon and orange should naturally fall into the citrus family, jasmine should be floral and thyme herbaceous. But would the perfumery radar make the same choices? Dr Rodrigues was pleased to discover it did. He then put it to work classifying 14 perfumes, including Chanel No 19, Dior's Addict and Kenzo's Jungle Tigre. The team compared their system's classification with those of industry experts, with noses that can discern fine details, working for three firms in the scent business, Osmoz, Scent Direct and Haarmann & Reimer (H&R).

Some perfumes, like Chanel No 19, described by all three firms as floral-green, offered little challenge to the radar. However, for perfumes like Jungle Tigre, described by Osmoz as "oriental-spicy" and by H&R as "chypre-fruity", the radar came up with a sensible midway description, declaring it to be strongly floral in character with green and oriental subfamilies.

Overall, as the researchers report in *Industrial & Engineering Chemistry Research*, their system agreed with assessments made by experts who had come to similar conclusions, and it provided logical descriptions for perfumes that are frequently disputed. The researchers plan to make their radar available as a product which they believe perfumers can use to save time and money developing new scents.

It might also find a use in other trades that require a good nose. A wine radar would settle any argument between oenophiles as to whether a slight whiff of soggy cardboard indicates that a $1,000 bottle of claret has become corked.

from PRINT EDITION | Science and Technology

Most commented | Most recommended

1. Global power: The dangers of a rising China
2. Germany and the euro: We don't want no transfer union
3. The future of the euro: Don't do it
4. Banyan: Lips, teeth and spitting the dummy
5. Breaking up the euro area: How to resign from the club
6. Lexington: The qualities of Sarah Palin
7. WikiLeaks: Unpluggable
8. WikiLeaks: Read cables and red faces
9. Chinese missile ranges: China's missiles
10. America's jobless recovery: Where are the jobs?

Over the past five days

Latest blog posts - All times are GMT

The Difference Engine: Birth of an icon
From **Babbage** - 2 hours 30 mins ago

Explain in vain
From **Asia view** - 3 hours 32 mins ago

Reading material
From **Prospero** - December 10th, 07:37

Principal departs, maybe principles too
From **Asia view** - December 10th, 07:15

American exceptionalism, American hypocrisy
From **Democracy in America** - December 10th, 04:47

Link exchange
From **Free exchange** - December 10th, 00:15

Better Obama odds in 2012?
From **Free exchange** - December 10th, 00:10

More from our blogs »

CORRIERE DELLA SERA.it

ESPERIMENTO ALL' UNIVERSITÀ DI PORTO

Un «grafico radar» scompone i profumi

Un naso capace di distinguere e separare tutti gli odori e le puzze del mondo, come quello di Jean-Baptiste Grenouille protagonista del romanzo «Il profumo» di Süskind, non esiste. Ma dove non arriva la natura, risolve la tecnologia. Con un nuovo metodo, chiamato «il radar di profumeria», i ricercatori dell' Università di Porto (Portogallo) sono in grado di scomporre ogni eau de toilette nelle sue essenze di base, senza affidarsi al giudizio olfattivo (soggettivo) degli esperti profumieri. La tecnica serve a catalogare i profumi commerciali in maniera oggettiva, universale e standard per tutti. Che cosa c' entra il radar? «Il profumo è rappresentato da un grafico radar con otto rette radiali che formano una specie di asterisco - dice Ines Mancini dell' Università di Trento -. Ogni retta rappresenta una delle otto famiglie olfattive principali in cui si dividono i profumi: floreale, fruttato, agrumi, legnoso, orientale, muschio, erbaceo e verde. L' area all' interno del grafico identifica esattamente la composizione del profumo». In pratica, l' area nel grafico fornisce le caratteristiche del profumo, come l' area di un radar per aerei indica la presenza di un veicolo in volo. Per realizzare la classificazione dei vari profumi Alirio Rodrigues e i suoi colleghi hanno usato strumenti tipici delle analisi chimiche. Con un gascromatografo associato a uno spettrometro di massa hanno ricavato i pesi molecolari delle sostanze e sono risaliti alla composizione dei bouquet, identificando dalle 50 alle 100 fragranze presenti in ogni miscela. Alla fine, per calcolare persistenza e diffusione dell' odore hanno usato equazioni classiche della termodinamica. I test eseguiti su 14 «eau» in commercio, da Chanel 19 a CK One, sono positivi. «Il metodo è scientifico - sottolinea Mancini -. Tutela la composizione della formula e può andare bene per programmare nuovi profumi a tavolino. Anche se ha un limite: rileva l' alcol etilico e non l' acqua, per cui funziona per i profumi in quanto questi contengono l' 80% circa di alcol, invece non funziona per i vini che hanno percentuali di alcol intorno al 13-14%». A intercettare aromi poco alcolici ci pensano i «nasi elettronici», attivi su inquinanti, esplosivi e gas di diverso genere. «I nasi elettronici possono misurare variazioni chimiche, elettriche o di tipo ottico - spiega Gian Giuseppe Bentini, ricercatore del Cnr di Bologna -. I sensori indicano al massimo i tre o quattro vapori più concentrati, quindi non tutti. I gas in tracce non vengono rilevati e spariscono nel rumore di fondo. Un naso elettronico per tutti i vapori non è stato ancora inventato». Paola Caruso

Caruso Paola

Pagina 34
(14 dicembre 2010) - Corriere della Sera

'Perfumery Radar' Brings Order to Odors

ScienceDaily (Dec. 2, 2010) — Scientists are announcing development and successful testing of the first "perfumery radar (PR)." It's not a new electronic gadget for homing in on the source of that Eau de Givenchy or Jungle Tiger in a crowded room. Rather, PR is a long-awaited new tool for bringing scientific order to the often arbitrary process of classifying the hundreds of odors that make-up perfumes.

See Also:

Matter & Energy
- Detectors
- Electronics
- Technology
- Engineering
- Energy Technology

Reference
- Engineering geology
- Altimeter
- Alcohol
- Doppler effect

A report on the advance appears in ACS' journal *Industrial & Engineering Chemistry Research*.

Alírio Rodrigues and colleagues note that the typical perfume has 50-100 fragrant ingredients. Experts who make perfumes have long described those ingredients with highly subjective terms like "floral," "citrus," "woody," and "oriental." Many different classification systems have been proposed, but they still leave perfumers describing the same smell with different words that often are arbitrary.

In an effort to bring order to odor classification, the scientists developed "perfumery radar" system, which relies on plots (see graphic), similar to the displays used to track aircraft. They used the PR to classify the primary odor families of 14 commercial perfumes and found that the results closely matched those of experienced perfume makers. With the PR, manufacturers could speed up the development of new perfumes -- namely the so-called preformulation stage in which they experimentally evaluate the product -- thus saving time and money, the report states.

***Disclaimer**: Views expressed in this article do not necessarily reflect those of ScienceDaily or its staff.*

Email or share this story: | More

Related Stories

Bacteria Manage Perfume Oi Production From Grass (Nov 2008) — Scientists in Italy hav bacteria in the root of a tropica whose oils have been used in the cosmetic perfumery ... > *read more*

Small Particles Show Big Promise in Bea Unpleasant Odors (Oct. 27, 2010) — Sci are reporting development of a new approa dealing with offensive household and other one that doesn't simply mask odors like toc room fresheners, but eliminates them at ... *more*

Sniffing Out Uses For The Electronic No (Mar. 12, 2008) — Despite 25 years of res development of an "electronic nose" even approaching the capabilities of the human s remains a dream, chemists in Germany cor an overview on the topic. ... > *read more*

Perfume classification system could help pre-formulation of fragrances

By Katie Bird , 16-Dec-2010

Related topics: Formulation & Science

A new way of classifying scents has been developed by researchers in Portugal which they claim could help take the arbitrariness out of fragrance categorisation.

The Perfumery Radar, developed by researchers at the University of Porto, is a tool that can classify perfumes into various olfactive or scent families regarding their composition.

Traditionally it is individual perfumers or perfume houses that categorise scents, which means the systems are not always easily comparable, explained the researchers in the study led by Professor Alírio Rodrigues.

In addition, the sense of smell itself is very personal and people tend to associate scents with past experiences and emotions, further complicating an attempt to find a universal classification system.

Scientific classification

However, according to Rodrigues, the Perfumery Radar, as a more scientific classification, provides a system that is less arbitrary.

"The Perfumery Radar is a methodology for the classification of perfumes into olfactive families like "citrus", "floral", "oriental", or "woody" among others. It assigns a fragrance to an olfactive family considering the composition in the liquid phase and the olfactive character of each single fragrance ingredient," he told CosmeticsDesign-Europe.com.

In order to test the Perfumery Radar, Rodrigues and the team classified a number of essential oils as well as commercially available female fragrances to see whether the classification agreed with perfumers' views.

According to the study, the Perfumery Radar correctly predicted the primary olfactive family of four essential oils (orange, lemon, jasmine and thyme) and a number of commercial perfumes.

Predictive power

For Rodrigues, this predictive quality is one the most useful characteristics of the Perfumery Radar for the industry.

"Its [uses for the industry are] *mainly focused on perfume classification and since it has predictable capabilities it can be used in the pre-formulation step of perfumes or other fragrant mixtures (e.g. functional perfumes),"* he said.

Although he believed experts would continue to stick with their own personal frameworks of classification, Rodrigues did say that a standardised framework is the only practical ways to perform comparisons and the Perfumery Radar would help towards that objective.

Source: *Industrial Engineering and Chemistry Research*

2010, Issue 49, pages 11764 – 11777
Perfumery Radar: A Predictive Tool for Perfume Family Classification
Miguel A. Teixeira, Oscar Rodríguez, and Alírio E. Rodrigues

MOST POPULAR NEWS

1. Industry urged to take precautions with triclosan
2. L'Oreal looks to emerging markets to capture a billion new consumers
3. Firmenich reveals how REACH compliance is impacting its business
4. Ads branded 'misleading' as L'Oreal's lumbered with conditional fine
5. Branding is more important than labelling a product as natural – expert

Science makes important first step towards the smelloscope

Smells make a vivid impression, but are nearly impossible to describe. Scientists have just created 'perfumery radar' - a classification system of smells that may pin down the elusive phenomenon.

The human sense of smell is much derided. Our noses are weak. We lean on our eyesight and our hearing to guide us through the world. One of the things holding back our ability to smell is the fact that smell is often so personal. There are some scents that the majority of people can recognize - roasting meat, smoke, maple syrup - but most scents remain undefinable. Unless people know the provenance of the smell, like food odors, there are relatively few words that describe what the smell is.

The words that humans do use to describe scents are heavily influenced by a person's experience and preferences. Expose an outdoorsey person to the smell of wet wood chips and they might describe the smell as 'organic' or 'green'. A city person, on the other hand, might associate those smells with the scents of vegetables left too long in the fridge and describe them as 'rotten' or 'stale'.

Even among people who smell things for a living, there is a wide variety of classifications for different smells. Over the years, odors have been classified into 'families,' smells that had common elements. Families were given all kinds of labels; putrid, resinous, oriental, floral, minty, camphoraceous. Little agreement could be reached between people that 'this' odor, even simple odors, belonged in 'that' family. When perfumes started layering scents, the classification became that much more difficult.

A new method, developed by researchers at the University of Porto, combines 'physicochemical models and qualitative descriptors,' to classify perfumes into families that can be universally recognized. It also incorporates their odor intensity and the evaporation process of the various different scens that make up complex fragrances.

The methodology is long, and complicated. It first separates the pure scents combined in a perfume into various basic scents like 'fruity' or 'citrus.' The perfumes are then subjected to gas chromatographic techniques to single out fragrance components. The researchers take those fragrance compounds and applied the Odor Value Concept, a dimensionless calculation that measures the intensity of the fragrance.

The results of the new methodology lined up very well with the classification of scents done by professional perfumers, and may form the basis of a classification of smells. Every *Futurama* viewer knows how many lives that could save in the future.

Via Industrial and Engineering Chemistry Research.

Send an email to Esther, the author of this post, at einglisarkell@gmail.com.

SCIENCE AND EDUCATION

'Perfumery radar' objectively quantifies scents

By Ben Coxworth
15:58 December 3, 2010

1 Comment
2 Pictures

The Perfumery Radar system uses gas chromatography to objectively analyze the different scents that make up a perfume (Photo: CC)

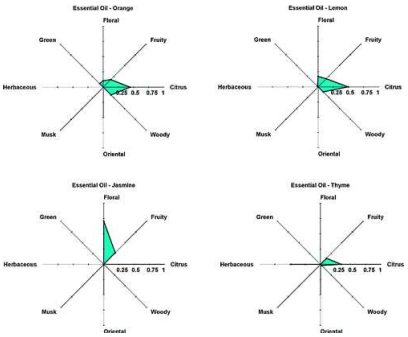
Image Gallery (2 images)

Making perfume is an art, and you can't objectively break art down into its individual components... right? In the case of perfume, it appears that perhaps you can. Dr. Alirío Rodrigues, a chemical engineer at Portugal's University of Porto, has devised a system called Perfumery Radar (PR). It is able to analyze the odor of perfumes, and map out what scents are present, and in what proportions.

Usually, the different component scents that make up perfumes are detected by human perfume experts, who use words like "floral" and "woody" to describe them. The ability to detect smells varies from person to person, however, as does their perception of those smells – one person might associate the smell of the sea with vacations, for instance, while another might associate it with almost drowning.

There's also the whole philosophical question to be asked, that applies to any sensual perception: how do I know that what you describe using given word (i.e: woody) is the same as what I think of when I hear that word? With a reported 50 to 100 fragrant ingredients going into a typical perfume, the margin for individual interpretation could be pretty big.

In the PR system, gas chromatography devices analyze the vapors from perfumes. Based on the vapor's molecular structure, its smell is then broken down into eight commonly-referenced families, namely citrus, fruity, floral, green, herbaceous, musk, oriental and woody... although there are many other families that this early version of the system does not yet recognize. The results are plotted out on a radar graph, indicating the relative strength of each of the families.

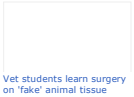


When 14 popular women's fragrances were tested on the system, the results were similar to those arrived at by human perfume experts.

A University of Porto paper on the technology stated, "PR introduces some scientific basis, reducing the arbitrariness of perfume classification to the empirical classification of pure odorants." Rodrigues hopes that the system could be used to speed up and economize the commercial development of perfumes in the future.

The research was recently published in the journal *Industrial & Engineering Chemistry Research*.

Recent popular articles in Science and Education


Vet students learn surgery on 'fake' animal tissue

NASA announces discovery of radical new life form - on Earth

Rubber device mimics bird song

Sweet way to make graphene - just add table sugar

First "potentially habitable" exoplanet discovered

Einstein's prediction finally witnessed one century later

NASA finds lost Soviet lunar rover after 40 years

Wonder why we don't crash like computers? Yale explains

Google Earth moves to become Google Universe

The Kno: A giant double-screen tablet to replace giant textbooks

Sections

Aero Gizmo
Around The Home
Automotive
Baby Gizmo
Childsplay
Digital Cameras
ecoGizmo
Electronics
Games
Good Thinking
Health and Wellbeing
Holiday Destinations
Home Entertainment
Inventors and Remarkable People
Laptops
Military
Mobile Technology
Motorcycles
Music
On the Water
Outdoors
Personal Computing
Pet Gizmos
Podcasts
Research Watch
Robotics
Science and Education
Sports
Spy Gear
Telecommunications
Urban Transport
Wearable Electronics

PORTUGUESE PRESS RELEASES

Portugueses criam radar dos perfumes

Alírio Rodrigues e Miguel Teixeira (Universidade do Porto): radar põe fim às disputas na indústria dos perfumes FOTO RUI

Pôr em ordem o **negócio dos aromas**

A classificação empírica dos aromas puros é arbitrária, dando origem a disputas na indústria de perfumes quanto à descrição de uma fragrância, o que tem um impacto negativo no tempo e dinheiro necessários para desenvolver novos perfumes.

Mas uma equipa de investigadores do Laboratório de Processos de Separação e Reação (LRSE) da Faculdade de Engenharia da Universidade do Porto, liderada por Alírio Rodrigues, criou uma metodologia científica para resolver o problema. Chama-se Radar de Perfumes, deu origem a um artigo no prestigiado jornal científico "Industrial & Engineering Chemistry Research" e mereceu destaque na revista britânica "The Economist" e no diário italiano "Corriere della Sera".

Os investigadores compilaram uma extensa lista de descrição de aromas a partir das bases de dados usadas na indústria de perfumes. E descobriram que oito designações gerais (ver caixa) funcionavam como famílias onde mais de dois mil aromas específicos podiam ser classificados.

Depois, distribuíram as oito famílias num gráfico-radar, um tipo de gráfico semelhante ao dos monitores de radar, que mostra informação quantitativa de forma mais visual, e testaram quatro óleos aromáticos — laranja, limão, jasmim e tomilho. Os óleos foram então decompostos nos seus componentes moleculares e analisados através da cromatografia de gases — para quantificar cada componente químico — e espectrometria de massa — para identificar o mesmo componente —, associando cada óleo a uma das oito famílias de aromas.

Metodologia preditiva

A intensidade aromática das fragrâncias puras numa mistura líquida foi prevista através do conceito de valor aromático, que considera as interações moleculares entre os seus componentes. Os investigadores conseguiram assim descrições lógicas de perfumes que antes eram frequentemente disputados na indústria. "Conseguimos fazer a validação experimental da nossa metodologia, o que significa que a partir de agora ela é preditiva, isto é, não precisa de mais experiências para ser usada", esclarece Alírio Rodrigues. E pode ser aplicada nos vinhos, onde os aromas são fundamentais, "mas com as devidas modificações, porque os vinhos pertencem a diferentes famílias olfativas e composições", ressalva Miguel Teixeira, investigador do LRSE.

"A classificação de perfumes em famílias olfativas foi feita durante anos apenas com base na análise sensorial, mas nenhum destes métodos alcançou uma aceitação universal", conta Alírio Rodrigues. Tudo porque o nariz humano, juntamente com as células recetoras olfativas e a sua relação com o cérebro, "resulta num sistema complexo mas limitado para distinguir os aromas". Entre centenas de aromas presentes numa mistura, o nariz humano só pode distinguir em simultâneo muito poucos. Um exemplo: o café tem 800 componentes químicos, mas só conseguimos concluir que a mistura cheira a café...

VIRGÍLIO AZEVEDO
vazevedo@expresso.impresa.pt

AS 8 FAMÍLIAS DE AROMAS

Cítrico De citrinos como o limão e a laranja
Frutado De frutos como maçã, banana ou framboesa
Floral Das flores
Verde De talos e gramíneas
Herbáceo De plantas de baixo crescimento (salva, hortelã)
Almíscar Característico do cervo e do boi almiscarado
Oriental Aromas quentes
Madeiras De madeiras como cedro, sândalo ou patchouli

TV news broadcast on Portuguese public television (RTP1)

*"To obtain **Knowledge**, add things everyday;*
*to get **Wisdom**, delete things everyday"*
Lao Tsu, Chinese philosopher