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The Measurement of Odours

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Abstract: The measurement of odours has been subject of many years of research in the flavour and fragrance industry. Still today it is a challenge to select the appropriate measurement technique to characterise odour performance which, beside the hedonistic qualities, is a key success criterion. Physicochemical parameters have been used for many years to obtain guidelines for improving fragrance performance but headspace measurements combined with olfactometry data are still among the most powerful methods which successfully help to extract additional information by linking detected signals obtained from an instrument with the sensory perception of a human nose.

Keywords: Fragrance performance · Headspace · Olfactometry · Partition coefficient · Substantivity

Introduction

The human sense of olfaction is known to be highly complex. For decades researchers have tried to understand odour perception and remarkable discoveries *e.g.* in molecular biology have been made through the last years [1]. Nevertheless no electronic nose-concept [2], nor understanding of underlying fundamental odorant-receptor mechanisms [3][4] or signal transduction pathways [5], or neurological discoveries made by brain-imaging experiments [6] have allowed until now a holistic understanding of how humans perceive and memorise smells generated by complex odour mixtures. A comprehensive theory of combinatorial receptor codes for odours is described in [7] but it is also known, as recent experiments on the perception of simple odour mixtures suggest, that so far unpredictable filtering mechanisms are present [8] which imply physiological limitations in the processing of components in odour mixtures. These findings seem to be neglected in press releases discussing a theory of digitising smell and taste or the 'RGB' [9] of odours: The theory is more wishful thinking than scientifically proven and validated. The concept of a very recently published patent in this area [10] is far from being proven.

The perfume and flavour industry provides products which are designed and developed to provide emotional benefits. Compared to the pharmaceutical or agrochemical industry, where scientific measurement methods are established and used to select the most successful molecules, there are no scientific parameters available which can guarantee the success of a flavour or fragrance product. Famous perfumers with outstanding skills of memorising and recreating scents as an art have accumulated over years an understanding of how to satisfy user preferences in hedonistic terms. They try with their experience to match the product quality with the requirements asked for by the customer and feedback obtained by market research tools. In parallel scientists have developed various systematic approaches in characterising odours through measurable parameters. It is not astonishing that many approaches are similar to the ones taken by *e.g.* medical drug design concepts. But it is not evident how to use the identified important parameters in the creative process: it is easier to find explanations of observed sensory phenomena by using measurable parameters than to predict them.

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Measurable Parameters *versus* Commonly Used Terms to Characterise Fragrance Performance

Perfumers and evaluators evaluate fragrance performance in rather empirical terms, which have evolved over many decades. This is shortly described in three particular examples:

- The property of a fine-fragrance to be perceivable on skin still after several hours of its application is expressed as 'long-lastingness'
- The ability to smell a fragrance on laundry even after the drying process is referred as 'substantivity'
- The capacity of being perceived at a farther distance from its source during a reasonably long time period is often described by 'diffusivity'.

A complementary description of such terminology can be found in [11] by Stora *et al.* Astonishingly such terms have survived over years without being directly measurable by quantitative analytical methods. They refer to a sensory experience, which is a result of very complex superposition of individual physical phenomena occurring simultaneously, which are even known to depend on each other and finally depend on the person's individual sensitivity and mental readiness to register a scent perception.

Measurement methods to quantitatively determine physicochemical effects, in contrary, have been well known for decades. This is done by characterising the isolated physical phenomenon, which unfortunately can only be partially used to obtain information about a complex fragrance application process. For each molecule it is possible to acquire data of vapour pressure, evaporation enthalpy, activity if used in diluted form, water-solubility, partition coefficients (solvent-air as well as solvent-solvent partitioning factors), adsorption and desorption behaviour. This list is not meant to be exhaustive.

Odour Value Concept

In most cases odour perception is induced through volatile chemical molecules which reach the olfactory epithelium. The very basic question of how many molecules are necessary to produce a perceivable signal has not yet been answered but there are standard methods available to measure sensory threshold concentrations [12]. Using such methods it is not, of course, possible to measure the number of molecules which will partition into the mucous membrane and finally will interact successfully with their corresponding receptor. Neuner and Etzweiler, however, have given a good description of how to work with a performance indicator called 'Odour Value (OV)' [13]. The OV of a pure ingredient is the ratio of the vapour pressure and its mean odour threshold concentration. This concept allows the determination of the ratio above threshold for any gaseous proportion of a selected ingredient even if it is used in a mixture of other ingredients. If an ingredient is used in diluted form, *e.g.* in solution or in a mixture, its vapour pressure is reduced and accordingly its OV is reduced as the threshold concentration is given for the ingredient. In a mixture the so-called partial vapour pressures can be determined according to Raoult's law or *via* quantitative headspace analysis. Practical approaches of how to use the OV in relation with fragrance performance on skin or on hair have been described in [14][15]. Neither the estimation according to the law of ideal gases nor the experimental quantification allows the psycho-physical measurements with humans to be neglected. This is required for the correlation of the perceived intensity *vs.* the presented concentration of the odorant used as stimulus. Such a graph is known as the dose/response curve and can be obtained by magnitude estimation or as known from more recent sensory research publications by labelled magnitude scaling [16]. Thus the OV concept can be correlated to the entire supra-threshold domain of odour concentrations as will be described later in this article. A novel olfactometer called the Cascade-Olfactometer was developed and patented [17] and good correlation of the labelled magnitude scale and the ASTM procedure for intensity measurements [18] could be obtained.

General Understanding of How to Improve Deposition Ratios in Perfumery and Other Fields

For years chemical engineers have tried to vary physicochemical properties of reactants or ingredients to achieve optimum conditions for physical and chemical interaction, reactions and processes. Remarkable results are known from the textile-dyeing industry, which increased dye-deposition ratios and minimised dye losses [19]. It was a successful approach to vary the pH of the dye solution to achieve the maximum amount of free anionic groups in structural cavities, which could host the cationic dye molecule. Concepts of enhancing the molecular weight by varying the anchor-part of the molecule while the chromophore was left untouched to maintain the dye's spectrum led successfully to higher dye-deposition ratios. Of course the dye-deposition yields of up to 99% or more which were achieved cannot directly be compared with the needs of the fragrance industry. Here it is necessary to find the optimum balance between deposition and the following sustained release (evaporation) of the molecules to make them perceivable by the human nose. Changing the molecular structure for optimum deposition results in changes of the odour quality as well as of the vapour pressure. More recent approaches in designing the size and weight of the molecule have been adopted from the medical drug development where small active ingredients were found to have no significant retention in the body. In such cases it is possible to design pro-drugs which can be activated through specific cleaving mechanisms (*e.g.* enzymes) which are initiated by the metabolism of the body, *e.g.* at the right organic location. Precursor technology and possible cleaving mechanisms are described [20] and can be regarded as the well-advanced scientific approach to increase deposition, followed by a sustained release of fragrance molecules.

The importance of using measurable parameters as a quantifiable approach to describe odour performance was recognised more than 30 years ago [21]. Van Abbé has discussed advantages and disadvantages of 'substantivity' achieved for cosmetic ingredients under a very interesting point of view [22]: He defined 'substantivity' as the prolonged association between a material and a substrate and points at the problematic observation that enhanced toxic effects are observed if cosmetic ingredients are deposited through physical means (*e.g.* special application media such as creams, emulsions) with more efficiency. Blakeway and Seu-Salerno [23] presented headspace-methods for analysing objectively the substantivity of fragrance molecules on hair. It is not unexpected that they identified the degree of substantivity as depending on the concentration of the applied fragrance, which they explain as a simple partitioning effect between water phase and the keratin fibres. A similar approach was used also by Etzweiler, Neuner-Jehle and Senn to get an insight about the various dependencies of stability and substantivity of fragrances in the washing cycle [24]. In 1984 Guy and Hadgraft gave a theoretical description of the effects of volatility and substantivity on percutaneous absorption [25]. The complex theoretical model included diffusion coefficients, local concentrations, exposed area as well as the ratio of concentrations of the applied product base over its concentration on skin. This model explicitly used the octanol-water partition coefficient (P_{OW}) as a key parameter. The latter became heavily used in drug-design, toxicology and agriculture to characterize structure-activity relationship as well as hydrophobicity and hydrophilicity respectively. Leo and Hansch [26], who published first articles already back in 1964, did very important work. The approach to use an indicator of hydrophobicity such as partitioning behaviour also in the fragrance industry was a logical consequence. A measurement method was published for analysing the water solubility of molecules with a very low solubility [27] but already earlier Müller *et al.* were basing their understanding of how to improve substantivity on water-solubility data [28]. Escher and Oliveros reported an equivalent method in describing substantivity dependent on P_{OW} [29]. Fig. 1a. visualises the trend of water-solubility and clog P_{OW} (= calculated log P_{OW}) *vs.* molecular weight. It is not astonishing that clog P_{OW} plotted against water solubility has a directly

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proportional dependence (see Fig. 1b). The influence of the presence of additives, namely surfactants, on the deposition behaviour has been reviewed in [30]. A more complex approach not to monitor substantivity as a phenomenon but to describe partitioning behaviour and guidelines how to use these parameters for reformulating perfumes and flavours was developed by PFW and Tastemaker [31].

Already many decades ago perfumers systematically based their creations on physico-chemical parameters as a result of practical experiments and experience. A key practical experiment is the evaluation of the dry-down notes on a smelling strip, a method which leads to large molecules with low vapour pressures and low detection thresholds. The combination of this knowledge with partitioning data was known already much more than ten years ago and used to estimate or improve substantivity or odour performance. It became the Holy Grail not only in the detergent business but also as a key to success in the segment of skin and hair care products. Summarising such perfumery experience, both Müller [28] and Escher [29] teach the principles for achieving substantivity. Namely that the higher the water insolubility/clog P_{OW} the greater the deposition efficiency and the higher the boiling point/lower the vapour pressure, the longer the material will endure on a treated substrate. The importance of being able to smell the small quantities remaining after a laundry cycle or after evaporation from skin is also taught by Müller using the principles of low threshold and high Odour Value.

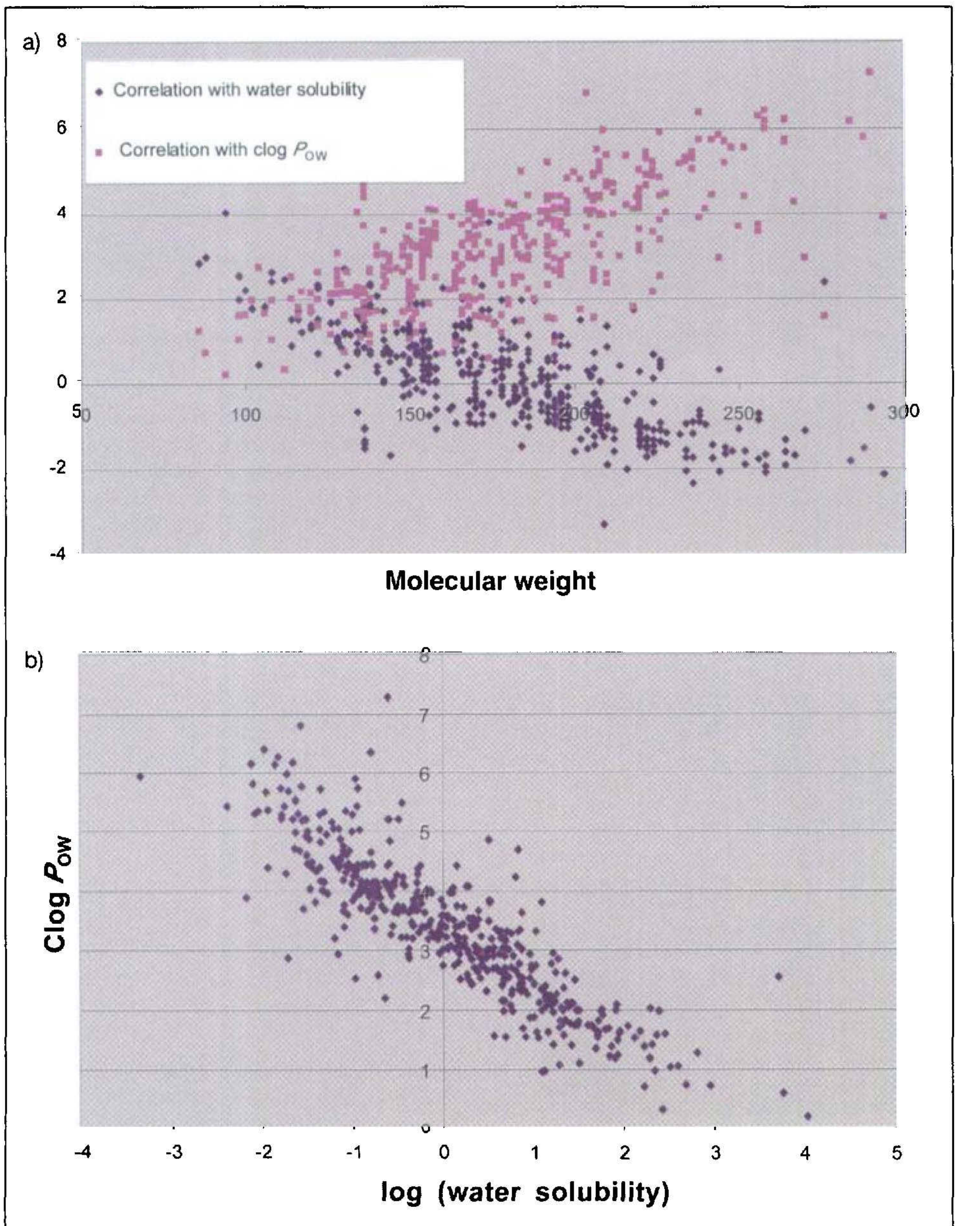

Fig. 1. a) Correlation of the *clog* P_{OW} and water solubility as two sets of data *vs.* the molecular weight. b) Correlation between the two parameters.

Hence, it was astonishing to see the series of patents [32] which claim an obvious extension of the prior art. The documents describe compositions consisting of ingredients with preferred physicochemical parameter-ranges or calculated parameters (*e.g.* clog P_{OW}) but they do not represent added scientific value to the broad perfumery experience.

State of the Art of Measuring Odours by Olfactometers

A very detailed review of how odour performance can be measured by olfactometric means was given in [13]. Over the following years the methods of measuring vapour pressure and determining sensory threshold concentrations for the raw materials was pursued in parallel with refinements of the technical measurement aspects. The successful development of the threshold olfactometer led to the Roche innovation award in 1993. The only restriction of the research tool was the limited dynamic range, which made it inappropriate for accurate and efficient dose/response measurements. The threshold-olfactometer was successfully used to give a measurable input in the odour evaluation process. A strong commitment in the development of molecules with a woody odour quality led over several years to the identification of first Sandela®, Sandalore®, Ebanol®, and finally Javanol® [20]. As a measure of the improvements it was found that the sensory threshold concentration was continuously lowered while maintaining a similar volatility of the molecules. The success story is visualised in Fig. 2. With the goal of opening an additional dimension of the OV concept in a long-term project, a new olfactometer was designed. It had to satisfy the need of a continuously tuneable dynamic range of seven orders of magnitude [17] to allow a fast and accurate presentation of any desired odour intensity stimulus between the saturated headspace of an ingredient and its threshold concentration. As an example the molecule Eucalyptol is cited of which the OV was determined to be 9 800 000. Eucalyptol is among the molecules with the highest OVs in our database. Fig. 3 shows that the instrument can access the entire dose-response curve of the molecule which has been measured with 16 test persons.

An other odour-related instrument with less quantitative character has been developed to enable the mixing of odours in the gas-phase. In various development steps it was possible to realise the Virtual Aroma Synthesizer™ (VAS) as a creative tool (Fig. 4). It is based on the principle described in a patent [33]. The VAS can be used to create perfume-skeletons or accords and allows the on-line study of the influence of a selected ingredient. Twenty identical channels can be controlled by a computer interface giving access to a tuneable range of 1:1000 for each ingredient. This tool allows *e.g.* the determination of the masking efficacy of an ingredient or a mixture if one of the channels contains a malodour. This gives perfumers and evaluators access to a measurable parameter.

Conclusion

The measurement of odours is not a simple determination of physicochemical parameters. The fragrance and flavour industry has developed a sound understanding of the deposition behaviour of fragrance molecules through parameters such as water solubility or partition coefficients. The findings, not unexpectedly, are in-line with perfumers' intuitive approaches to achieve higher substantivity or improve odour performance. The Odour Value concept is successfully used as a tool which can help to combine perfumery experience based on perception with objectively measurable parameters.

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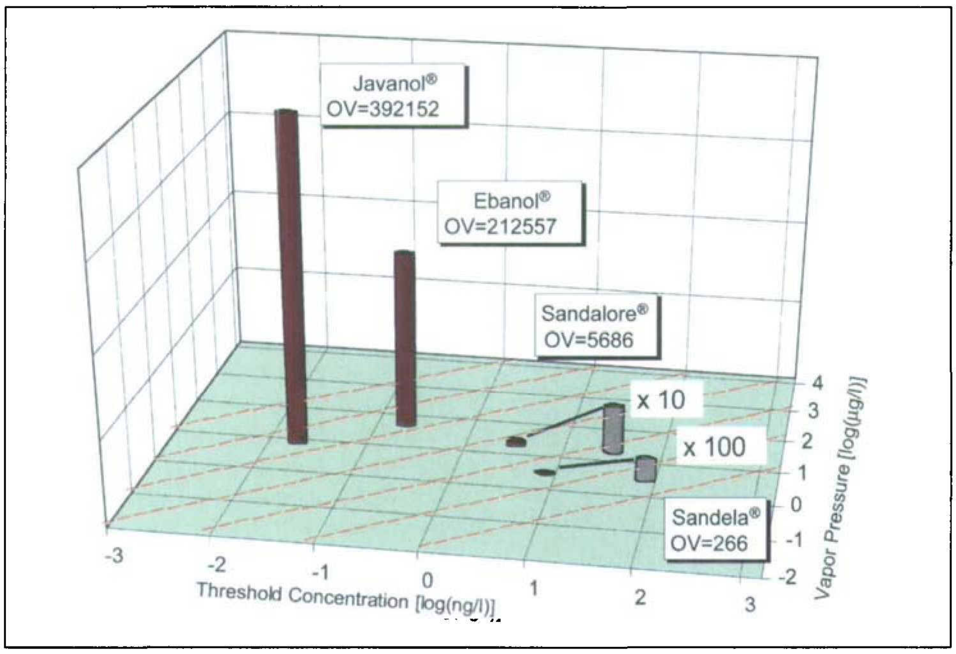

Fig. 2. Supporting the evaluation process of new 'woody' molecules led continuously to the identification of molecules with significantly lower sensory thresholds. While the vapour pressure of the identified molecules remained rather constant the lowering in threshold led to an important increase of the Odour Value (Sandela® OV=266, Javanol® OV= 392152)

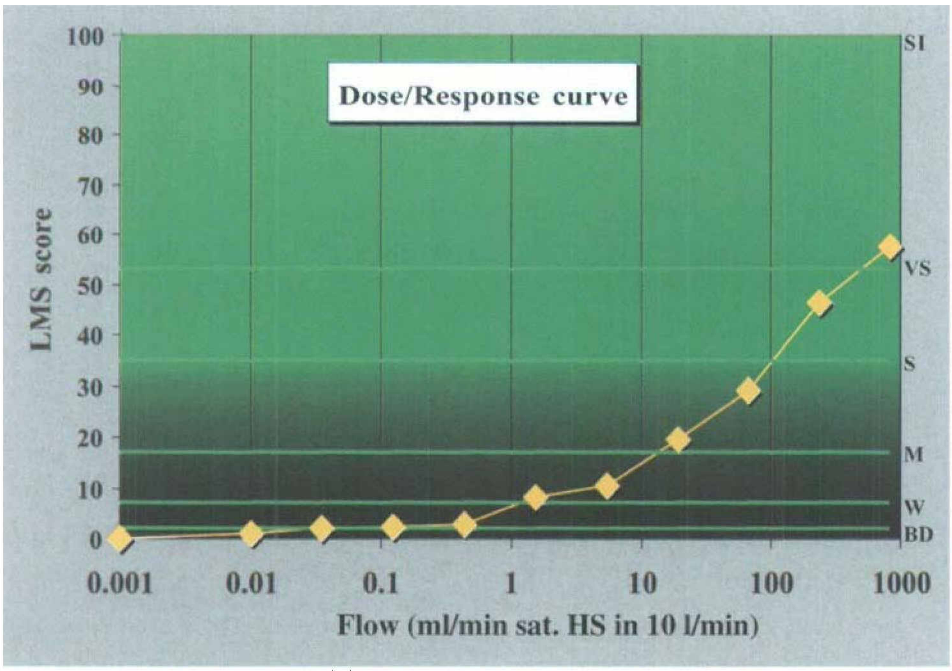

Fig. 3. The dose/response curve of Eucalyptol measured with the new Cascade olfactometer. The odour intensity was recorded on the labelled magnitude scale, the labels are named: strongest imaginable (SI), very strong (VS), strong (S), medium (M), weak (W) and barely detectable (BD)

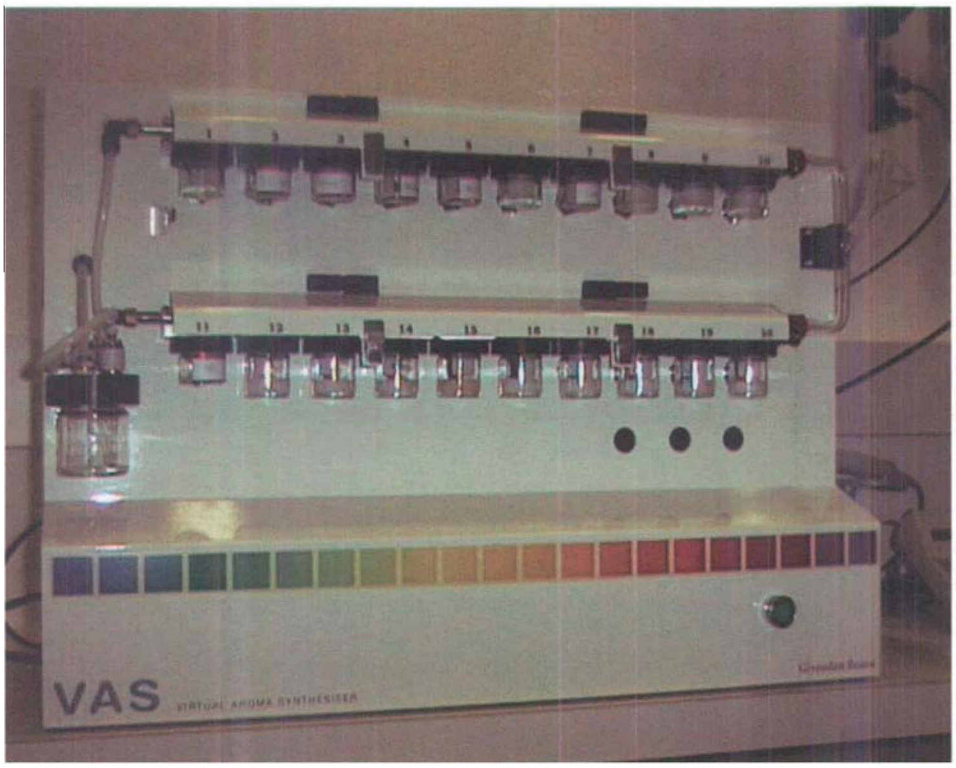

Fig. 4. The Virtual Aroma Synthesizer™, a creation tool, enabling online-mixing in the gasphase of 20 ingredients controlled by a computer interface. The instrument is especially useful to quantify malodour masking and to create simple fragrance accords.

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