



ELSEVIER

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

Computational
Biology and
Chemistry

Computational Biology and Chemistry 27 (2003) 121–133

www.elsevier.com/locate/cbac

Towards an odor communication system

D. Harel^{a,*}, L. Carmel^a, D. Lancet^b

^a Department of Computer Science and Applied Mathematics, The Weizmann Institute of Science, Rehovot 76100, Israel

^b Department of Molecular Genetics, The Weizmann Institute of Science, Rehovot 76100, Israel

Received 25 September 2002; received in revised form 27 September 2002; accepted 12 November 2002

Abstract

We propose a setup for an odor communication system. Its different parts are described, and ways to realize them are outlined. Our scheme enables an output device—the whiffer—to release an imitation of an odorant read in by an input device—the sniffer—upon command. The heart of the system is the novel algorithmic scheme that makes the scheme feasible. We are currently at work researching and developing some of the components that constitute the algorithm, and we hope that the description of the overall scheme in this paper will help to get other groups to join in this effort.

© 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Odor communication system; Palette odorants; Odor space; Odorant mixing; Sniffer; Whiffer

1. Introduction

It is generally accepted that the sensory world of most humans is built up mainly from visual and auditory impressions, and that other senses, such as smell, have smaller impact. Nevertheless, it seems that the sense of smell is often underestimated, and its impact actually may be overwhelming, directly influencing ancient, primitive, brain paths; see Schmidt (1978). Interestingly, humanity has already recognized this a long time ago, perhaps subconsciously, with scents already playing a significant role in ancient religious rituals. In our era, fragrances and flavors have an even greater influence, as exemplified by their intensive use in the blooming industries of food and beverage, perfumes and cosmetics, detergents, and many more. These many applications require some means of controlling the odor world. A repertoire of methods in fragrance production and synthesis has been developed, aiming at safe, cheap, and reproducible odor fabrication techniques. Still, hard labor is required for each individual odor fabrication

process, involving tedious, expensive, time consuming research.

In the last few decades, there have been efforts to integrate odors into the rapidly evolving world of modern communication. Adding smells to a personal computer, a video, a television set, or a mobile phone, would give rise to a vast number of possible applications, in the fields of commerce, marketing, computer games, and many others. However, available odor technologies seem to be incapable of supporting such applications, making it necessary to develop novel technologies. Today, only simple odor manipulations can be carried out. For example, scented cards are often inserted as sales promoters in magazines, dispensing a fragrance when scratched. Similar ‘scratch and sniff’ devices sometimes accompany movies or home television. Some recent model of mobile phones contains small capsules, emitting pre-determined scents when certain people call. There have even been attempts to introduce odors by means of air-conditioning systems in movie theaters and in the workplace. Still, none of the above comes close to the technological advances in vision and audition. One of the most salient expressions of this gap is in modern multimedia. Pictures and sound are routinely transmitted and exhibited on television, video or the personal computer. This has not happened yet with odors.

* Corresponding author. Tel.: +972-8-9344050; fax: +972-8-9344122.

E-mail addresses: dharel@weizmann.ac.il (D. Harel), liran.carmel@weizmann.ac.il (L. Carmel), doron.lancet@weizmann.ac.il (D. Lancet).

What is so difficult about odor communication? Probably, a combination of technological barriers and limited understanding of the relevant biology and psychophysics. Some of the major problems seem to be the following:

- The underlying physics is complex. Vision and audition also involve complex physical phenomena, but photons and sound waves are well-defined physical objects that follow well-known equations of a simple basic nature. Specifically, in both cases sensory quality is related to well-known physics. On the other hand, the smell of an odorant is determined by the complex, and only partially understood, interactions between the ligand molecule and the olfactory receptor (OR) molecule.
- The biological detection system is high-dimensional. The nose contains hundreds of different types of ORs, each of them interacting in different ways with different kinds of odorants. Thus, the dimensionality of the sense of smell is at least two orders of magnitude larger than that of vision, which can make do with only three types of color receptors.
- Odor delivery technology is immature. While artificial generation of desired visual and auditory stimuli is done in high speed and with high quality, smells cannot be easily reproduced. Nowadays, the best that can be done is to interactively release extracts that were prepared in advance.

Much effort has been invested in trying to better understand the sense of smell and its means of expression. Relating the smell of a molecule to its three-dimensional structure (see e.g. the review in Chastrette (1997)), as well as characterizing ligand–receptor interactions (see Araneda et al., 2000), are the subject of intensive research. However, while much progress is constantly reported, no theory adequately dealing with olfaction is currently at hand.

In this paper, we focus on the problem of odor communication, and tackle it from a novel perspective. We provide a precise definition of an odor communication system, which would make it possible to release in a distant location a faithful imitation of any desired odor recorded elsewhere (even if that odor is not present at the point of release). We describe both the technological and the mathematical aspects of such a system. The ‘brains’ of our system is in an algorithmic process that instructs an output device as to how best to imitate any specific odor by accurately mixing and releasing its available odors.

We believe that our system is the first to propose a scheme for actually carrying out odor communication, and it is likely to overcome the most disturbing aspects of the major difficulties mentioned above. Constructing the algorithm and filling its different blocks with content

requires intensive research, which our group is in the midst of pursuing. The work combines an experimental facet, which is needed to quantify odors, as well as a theoretical facet, which is needed in order to devise the algorithm.

The next section is devoted to presenting the overall structure of the odor communication system, and to describing its various components. Section 3 discusses the various mathematical spaces of odors relevant to the algorithm, and their underlying ideas. The algorithmic scheme itself, with its mixing algorithm, is discussed in more detail in Section 4. Some additional relevant issues are dealt with in Section 5, while a summary and discussion appear in Section 6.

2. An odor communication system

We would like to address the entire problem of ‘reading in’ an unknown odor, and ‘printing it out’ as faithfully as possible. We believe that the most general building blocks of such an odor communication system are as depicted in Fig. 1. At a remote location (Fig. 1a), we want to use an input device—the *sniffer*—to take in the odor and transform it into a digital fingerprint. At a different location (Fig. 1b), the fingerprint will be analyzed—by the *mix-to-mimic (MTM) algorithm*, which will instruct an output device—the *whiffer*—to emit a mixture of odorants that will mimic the input odor well enough to fool a human into thinking that he/she actually smells it. Prior to all of this, there is also a considerable amount of preprocessing and preparation. All of this will be discussed later on.

This setup is in direct analogy with other communication systems. For example, if we replace the sniffer by a camera, and the whiffer by a printer, we get a visual communication system, with the various color coding (RGB, CMYK, etc.) being analogous to our mixing technique.

2.1. The sniffer

In the most general sense, a sniffer is a physical device that can record, or digitize, odorants. In other words, it takes chemical data and turns it into numbers. Upon the introduction of an odorant in its inlet, the sniffer produces a numerical output, which becomes (usually after some further manipulation) a representation, or a *fingerprint*, of the odorant. To be useful in our odor communication system, we shall further require from a sniffer to be sufficiently discriminatory, in that it produces unique fingerprints for all odorants. Moreover, we would like its fingerprints to exhibit some correlations with the smell perception of their sources. This is for now a vague requirement, and we shall return

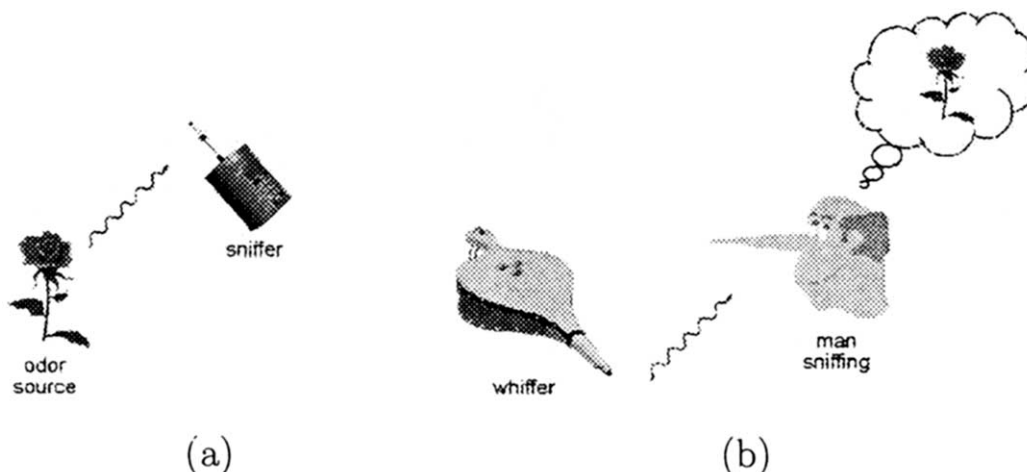


Fig. 1. The building blocks of an odor communication system.

to it in Section 4.3, when we talk about mappings between sniffer fingerprints and smell perception.

Ignoring this last requirement, many devices can pass as candidate sniffers. Any instrument that quantifies a certain property of chemicals in a unique and reproducible way suffices. In principle, an apparatus capable of measuring the boiling point of an odorant could become a sniffer. However, we can expect the correlation of boiling points with odor perception to be rather difficult. A more realistic example is the combination of a gas chromatograph (GC) and a mass spectrometer (MS). The GC/MS combination is very popular in analytical chemistry, and is used to precisely identify the compounds of a mixture. However, we doubt that it would make a good sniffer, since we have no reason to believe that the output it produces has anything to do with smell perception. From a commercial point of view, GC/MS suffers from additional disadvantages: it is expensive, it is large and bulky, and it is complicated to use, requiring carefully-trained operators. Moreover, analyzing its results is time consuming, and often sample preparation is tedious too.

In our opinion, the best candidates to serve as sniffers are the instruments collectively grouped under the term *electronic noses* (eNoses)—for details see Gardner and Bartlett (1999) or Nagel et al. (1998)—which are used for detecting vapor chemicals. These are analytic devices, whose main component is an array of non-specific chemical sensors, i.e. sensors that interact with a broad range of chemicals with varying strengths. Consequently, an incoming analyte stimulates many of the sensors in the array, and elicits a characteristic response pattern. These patterns are then further analyzed for the benefit of the specific application. The fact that the biological smelling system also relies on an array of non-specific receptors (see Section 3.1), gives hope that we may be able to find significant relationships between the

biological nose and its artificial counterpart. Indeed, we shall supply strong evidence for the existence of such relationships in Section 4.3, and they are expected to become even tighter as sensor technology improves. This is especially true in light of the promising work on bioelectronic noses (see Gopel et al., 1998; Ziegler et al., 1998), in which the usual chemical sensors are replaced by biosensors that are supposed to work in essentially the same way as the biological receptors in the nose. From a commercial point of view, eNoses enjoy several desired properties: they can be made small and cheap; they are easy to use, fast to operate, and for most applications they do not require any special sample preparation.

The first eNoses were developed during the early 1980s (Persaud and Dodd, 1982), and since then many different types have been designed, implementing a variety of sensor technologies. Some are even commercially available. Classification tasks, i.e. determining the identity of incoming samples, are by far the most popular applications of eNoses (for more on this, see Carmel et al. (2002b)). For example, eNoses are used for quality assessment of food products (Hahn et al., 2000; Di Natale et al., 2001), for medical diagnostics (Lin et al., 2001), for environmental control (Negri and Reich, 2001), and even in the automobile industry (Guadarrama et al., 2002).

In the electronic realm, as in the biological one, the desire for sensitivity does not always go well with the desire for non-specificity. Sensors (or receptors) that are designed to respond to an assortment of stimuli are normally characterized by low sensitivity. Indeed, eNoses are typified by relatively high detection thresholds, on the order of 1–10 ppm. Although seemingly problematic, this is not a true stumbling block for an odor communication system. First, many odor sources release higher concentrations than this in their immedi-

ate vicinity. Second, a preliminary step of concentration enrichment can be always carried out if necessary.

From now on, when we talk about sniffers, we assume that they are actually eNoses.

2.2. The whiffer

The whiffer is the part of the system that emits the smell imitation to the surroundings. It must include a palette of reservoirs containing the odorants it can mix (hereinafter—the *palette odorants*), a technology to accurately mix them, and means for releasing them to the outside world in accurate quantities and with precise timing. For use by mass consumers, the sniffer should also have small physical dimensions and be of low cost.

This definition of a whiffer strongly relies on the assumption that mixtures from within a set of odorants can mimic, to a reasonable level, any desired smell. This is reminiscent of the characteristics of RGB color mixing in vision. The question of whether this assumption is true for odors has a long history, and has never been unequivocally decided. It is a delicate issue indeed, and we will return to it in detail in Section 4.4. We should point out, however, that the issue of adequate palette odorants is not identical to the issue of true primary odors; we actually have reasons to believe that a palette of about 100 odorants would suffice for most applications.

The requirements from a whiffer seem simple, but it turns out that numerous technological barriers must be overcome in order to satisfy them. In fact, whiffers, as we have defined them, are not commercially available. The devices that are closest to being whiffers are the *olfactometers*, which have been in use for many years and are capable of accurately mixing gas samples and releasing the mixture to the surroundings. They are most often used together with human panelists for the purpose of assessing odor emission levels. However, an olfactometer is not a true whiffer, since it is designed mainly for diluting carefully prepared gaseous samples.

We think of a whiffer as being more akin to a printer (say, an ink-jet), with the palette of odorants being analogous to the color cartridge. Actually, our group was involved in a startup company, SenseIt Technologies, Ltd., which later became the R&D branch of DigiScents Inc., whose goal was to add smells as equal-rights members to the world of modern communication. In this company, we developed a whiffer—the iSmell® personal scent synthesizer—which contained a replaceable cartridge of 60 palette odorants. Unfortunately, the crash wave that befell so many high-tech companies in early 2001 did not spare DigiScents, which had to stop all its activities, sending the iSmell device into hibernation.

2.3. The mix-to-mimic algorithm

So far, we have discussed the two pieces of hardware. The heart of the system, however, is in its mathematical and algorithmic parts. The ultimate role of these is to instruct the whiffer, based on the input odor detected by the sniffer, as to how to mix the palette odorants so as to produce the desired odor perception.

The algorithmic scheme we propose here consists of several parts, and requires some carefully defined notation. We now discuss the mathematical spaces of odor relevant to the scheme, and in the subsequent section—the main section of the paper—we present the scheme itself, with its justification.

3. Odor spaces

For a proper formulation of the mixing algorithm and the algorithmic processes around it, we should introduce the notion of *odor space*, which will prove to be of a fundamental importance.

We have already mentioned that a sniffer yields a numerical representation of molecules. However, it is not the only entity that does so. Our brain carries out a similar operation when we sniff, producing a measurable electrical neuronal activity pattern. We use the term *odor space* for any end product of a process that represents numerically the olfactory information stored in odor ligands. Specifically, in this paper we are interested in three kinds of odor spaces—the *sniffer space*, the *sensory space*, and the *psychophysical space*.

To start with, we use $(o; c)$ to describe an odorant o in concentration c . An odor space represents $(o; c)$ by the set of numbers $d(o; c)$, which we call the *odorant vector*, the length of this vector is the *dimension* of the odor space.

3.1. The sensory space

The sense of smell is a primeval sense, originating in early single-cell organisms. In principle, it functions by taking a sample of the ambient environment and analyzing its chemical contents. In air-breathing organisms, volatile odorants enter the nasal cavity, where the primary organ of smell, the olfactory epithelium, resides. This pseudostratified neuroepithelium contains 10–100 million bipolar sensory neurons, each having a few dozen mucus-bathed hair-like cellular extensions known as olfactory cilia. The ciliary membranes harbor the OR proteins (Lancet and Ben-Arie, 1993), as well as components responsible for the chemoelectric transduction process. ORs have all been identified as belonging to the 7-transmembrane superfamily of G-protein coupled receptors (Buck and Axel, 1991). The stereospecific binding of odorant molecules to the ORs

initiates a cascade of biochemical events that result in action potentials that reach higher brain centers.

The number of distinct types of ORs, r , called the *olfactory repertoire size*, is believed to be around 1000 in all mammals (see Carmel et al., 2001). Only recently, the full sequence of more than 900 human OR genes has been reported, based on genomic databases (Glusman et al., 2001). Only about 300 of them are functional in humans, and the rest are pseudogenes. However, in other mammals the pseudogene fraction could be much smaller.

The recognition of odorant molecules occurs in the brain by a non-covalent binding process akin to that encountered in many other receptor types, including hormone and neurotransmitter receptors. However, while for ‘standard’ receptors there is usually only one, or very few, natural ligands, ORs are functionally promiscuous. Therefore, when an odorant ($o; c$) approaches the epithelium, it interacts with many receptor types, and can be characterized by the vector

$$d^B(o; c) = \begin{pmatrix} R_1(o; c) \\ R_2(o; c) \\ \vdots \\ R_r(o; c) \end{pmatrix}$$

with $R_i(o; c)$ being the response of the i th type of receptor molecule to the odorant ($o; c$). We deliberately do not specify the details of the response, which can be the fraction of bound receptors, the concentration of some second messenger, or some other relevant entity. It is often, in fact, a dynamic function of time. We shall see later that the exact definition of $R_i(o; c)$ is irrelevant to our algorithm. The r -dimensional odorant vector $d^B(o; c)$ describes the way by which the biological sensory machinery responds to the odorant, so that terming this odor space the *sensory space* is appropriate.

An important observation is that all the 10^5 – 10^6 OR molecules in the same sensory cell are of the same type, and thus r is also the number of distinct types of olfactory sensory neurons.

The olfactory neurons send their axons to the olfactory bulb (OB), passing in bundles through the cribriform plate. Here, the first, and rather significant stage of the higher processing takes place (see Mori et al., 1999). It is widely believed that important aspects of odor quality and strength (concentration) perception are carried out in the OB, and studies have in fact shown that the OB responds with odor-specific spatio-temporal patterns (see Joerges et al., 1997). Successive stimulations with the same odorant have been shown to lead to reproducible patterns of activity. Patterns evoked by low concentrations were topologically nearly identical to those evoked by high concentrations, but with reduced signal amplitude. Within the OB, the OR axons form contacts with secondary neurons inside ellipsoidal synaptic conglomerates, called glomeruli. A glomerulus

serves as a synaptic target for neurons expressing only a single OR type. Consequently, it is not surprising that the number of glomeruli, estimated to be between 1000 and 2000, is of the same order of magnitude as r . From our point of view, the important conclusion is that the OB is stimulated by approximately r distinct types of nerve cells, which tells us that the entire olfactory pathway is triggered by the vector $d^B(o; c)$.

3.2. The psychophysical space

Upon sniffing, three major tasks are performed by the brain: a qualitative classification of the incoming odorant, a quantitative estimation of its strength, and a hedonic decision about its acceptability. The first two are objective tasks (measuring molecule types and concentrations), while the last one is more subjective and will not be dealt with here.

Olfactory classification of a pure chemical or a mixture is a rather elaborate task. Unlike vision, audition and even gustation, olfaction is multidimensional, and is believed to involve dozens, if not hundreds of quality descriptors. Quantitative assessment of these qualities poses real challenges to research in olfactory psychophysics. Several experimental techniques have been proposed, but none with sweeping success (Wise et al., 2000). They all utilize panels of human assessors, either trained experts or laymen.

One technique, *odor profiling*, is a direct approach that uses human panels to break down an odor into its qualities. Many olfactory laboratories have each configured their own idiosyncratic odor vocabularies to achieve odor descriptions that are as objective as possible. Some vocabularies have been designed for specific fields like winery (see Chapter 4 of Margalit, 1997; Noble et al., 1984, 1987), or perfumery, while others have been designed for general purposes (see e.g. the 146-descriptor vocabulary proposed by Dravnieks (1985)). Methods have been developed to assign descriptors to an odor, and to give relative weights of dominance to the different descriptors. The entire procedure is normally carried out by a human panel of experts who are familiar with the technique, and who are capable of distinguishing the different descriptors with a high degree of accuracy. As appealing as this might sound, it is quite difficult to obtain coherent results with profiling, since exact verbal descriptions of odor perception are too demanding. Human subjects often find it difficult to describe odor quality verbally, an observation supported by the fact that most natural languages have a poor vocabulary for odors, and these are sometimes described using words borrowed from other sensory modalities (e.g. cool, green).

Alternatives to the profiling technique use panels to accomplish simpler, thus perhaps more reliable, tasks, such as various ways of sorting a group of odors,

comparing pairs or triples of odors, pointing out exceptions within groups of odors, etc. Some techniques collect enough statistics from the panels to be able to create a *distance matrix* that quantitatively expresses the level of dissimilarity between pairs of odors. Various kinds of multidimensional scaling (MDS) algorithms can then be applied to the data, resulting in a vector representation of the odors; see Schiffman et al. (1981).

Whatever quantitative quality assessment technique is used, an odorant ($o; c$) is eventually represented by the odorant vector $d^P(o; c)$. We use the symbol l to denote the dimensionality of the resulting odor space, which we call the *psychophysical space*. If one uses odor profiling, then l is normally in the range 20–200, and the i th element of $d^P(o; c)$ is the human panel's opinion regarding the weight of the i th descriptor. If one uses MDS, l is typically much lower (< 10), and the elements of $d^P(o; c)$ do not have precisely describable meaning. We should emphasize that $d^P(o; c)$ is concentration dependent, since the perception of an odorant might change with concentration.

We might say that while ($o; c$) represents the chemical o in concentration c , the odorant vector $d^P(o; c)$ represents the human perception of this odorant, or simply its odor. From this perspective, the psychophysical space is the one on which we should focus, since the odor communication system is designed to directly work within it.

There are profound inter-relations between the psychophysical space and the sensory space. The brain itself is the tool that maps the r -dimensional odorant vectors $d^B(o; c)$ into their corresponding l -dimensional odorant vectors $d^P(o; c)$. Ignoring dynamical phenomena, such as adaptation, this mapping is considered robust, in the sense that identical inputs $d^B(o; c)$, evoke approximately the same outputs $d^P(o; c)$. This suggests a way to 'fool' the human brain: if a certain odorant with a smell $d^B(o; c)$ elicits a neuronal response $d^B(o; c)$, then the same smell would be perceived if we succeed in developing a mixture of palette odorants that elicits the same neuronal response. The problem is that gathering data on the behavior of the olfactory neurons is hard, and not much information is currently available. Moreover, the effect of mixtures on neuronal response has not yet been completely unravelled, making the prediction of the effect of mixture perception impossible. For this reason, we would like to avoid the necessity of working with the odorant vectors $d^B(o; c)$, which leads to working with sniffers and human panels, as we shall see.

3.3. The sniffer space

The sensors inside an eNose are made using diverse technologies. Depending on the type of sensor, a certain physical property is changed as a result of exposure to a gaseous chemical. During the measurement process, a

signal is obtained by constantly recording the value of the physical property. Since a typical signal is comprised of a few hundred measured values, a process of feature extraction is frequently required, which is the process of finding a small set of parameters that somehow represent the entire signal. (For a recent way of dealing with this issue, see Carmel et al. (2002a).)

The set of features extracted from all the signals in a single measurement is called the *feature vector*, and if there are m features the vector can be viewed as an odorant vector in the m -dimensional *sniffer space*.

When exposed to mixtures of chemicals, eNoses produce a feature vector that reflects the combined effect of the mixture constituents. Yet, the feature vectors of a mixture do not noticeably differ in any aspect from those of pure chemicals, and in this sense eNoses do not distinguish pure chemicals from mixtures. Not only is this not a problem, but it is actually a highly desirable property of the sniffer space, since, as we shall see in Section 4.4, the same happens in the psychophysical space.

As the brain maps the sensory space into the psychophysical space, we can think of an analog algorithm that maps odorant vectors in the sniffer space to their corresponding odorant vectors in the psychophysical space. We shall call this the *mapping algorithm*, and denote it by the function f ; hence, $d^P(o; c) = f(d^S(o; c))$. Questions about whether such a mapping exists, and how to find it if it does, are postponed to Section 4.3. In the meantime, we simply state that the mapping algorithm is one of the major cornerstones of our overall algorithmic scheme.

4. The MTM algorithm

Now that we are equipped with notions of odor space, we can redefine the algorithmic scheme in more accurate terms. Let the whiffer contain n palette odorants, and let t_i stand for the i th of these. We use the generic term $p_i^E \cdot v_i$ to denote an odorant vector that constitutes a representation of palette odorant i in concentration v_i in some odor space E . For example, if E is the sniffer space S , then $p_i^S \cdot v_i$ would be the m -dimensional odorant vector $d^S(t_i; v_i)$. If E is the psychophysical space P , then $p_i^P \cdot v_i$ would be l -dimensional odorant vector $d^P(t_i; v_i)$. In this way, p_i^E can be viewed as an operator that is applied to the concentration v_i to yield some representation of the i th palette odorant in concentration v_i . Notice that we use the symbol v_i , rather than c , to denote the concentration of the i th palette odorant; this is to distinguish the palette odorants from other odorants, for which we use c . We define the *mixing vector* $v = (v_1, \dots, v_n)^T$ to be the list of palette odorant concentrations in a particular mixture. In accordance with our earlier notations, we represent a palette mixture

in the odor space E by $P^E \cdot v$, with v being the mixing vector and P^E being an as-of-yet unspecified operator.

Let $(o; c)$ be an arbitrary odorant. The role of the mixing algorithm is to find a mixing vector v , such that the perception of $P^E \cdot v$ is as similar as possible to that of $(o; c)$. More formally, we would like $d^P(o; c)$ to be as close as possible to $P^P \cdot v$; i.e. we are seeking

$$v = \arg \min_v \|d^P(o; c) - P^P \cdot v\| \quad (1)$$

with $\|\cdot\|$ some appropriately chosen norm. The general scheme of the mixing algorithm discussed above is described in Fig. 2. The sniffer provides the algorithm with a measured odorant vector $d^S(o; c)$. The mapping algorithm then transforms this vector into the odorant vector $d^P(o; c)$ in the psychophysical space. Following this, based on the specific palette that resides in the whiffer, the algorithm calculates from Eq. (1) the mixing vector v , and transmits it to the whiffer. The whiffer then prepares the corresponding mixture and releases it.

We are now in a position to describe our algorithm. In the interest of clarifying its dynamics, we have chosen to describe its development in three stages, each adding a further complication.

4.1. Fooling the sniffer

Let us consider first the problem of ‘fooling’ the sniffer. We want to find a way of presenting an eNose S with a palette mixture that mimics the original odor it

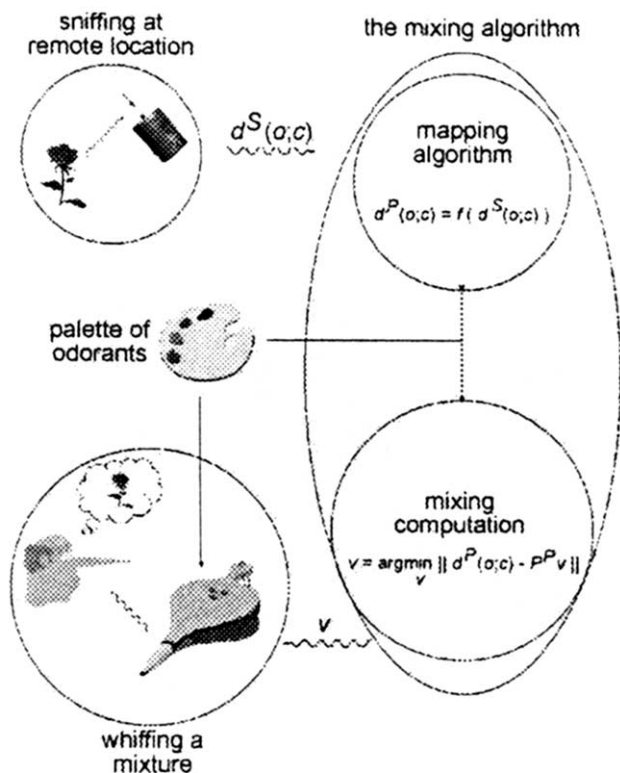


Fig. 2. The schematics of the mixing algorithm.

was given. Formally, let $(o; c)$ be an odorant, represented by the m -dimensional odorant vector $d^S(o; c)$. We want to find a mixing vector v such that when given $P^S \cdot v$ the sniffer S will produce a fingerprint as similar as possible to the one elicited by $(o; c)$ itself. This is a simplified version of the mixing problem. First, it does not require any space-to-space mapping, since we are working in a single space—the sniffer space. Second, fooling an eNose, whose fingerprints are relatively controllable and are easily measured and studied, seems on the face of it to be simpler than fooling the human perception. Dealing this problem first will provide us with insight regarding the solution of the more general problem.

In analogy with Eq. (1), our task is to find a vector v that satisfies

$$v = \arg \min \|d^S(o; c) - P^S \cdot v\|$$

Notice that unlike Eq. (1), here the odorant vectors are taken to be in the sniffer space too.

Let us now discuss such a P^S in a relatively simple special case. An m -dimensional sniffer space for a sniffer S is called *linear* if it has the following properties:

- 1) *Linearity of response*: For an odorant $(o; c)$, each of the elements $d_j^S(o; c)$, $1 \leq j \leq m$, is proportional to the odorant's concentration. That is, $d_j^S(o; c) = \alpha_j(o) \cdot c$, where $\alpha(o)$ is an odorant-dependent constant. Denoting $\alpha(o) = (\alpha_1(o), \alpha_2(o), \dots, \alpha_m(o))^T$, we can write this property in the compact form

$$d^S(o; c) = c \cdot \alpha(o) \quad (2)$$

- 2) *Additivity of mixtures*: The odorant vector describing the mixture $(o_1; c_1), (o_2; c_2), \dots, (o_k; c_k)$ is the vector sum of the odorant vectors of the individual elements,

$$d^S(o; c) = c_1 \cdot \alpha(o_1) + c_2 \cdot \alpha(o_2) + \dots + c_k \cdot \alpha(o_k) \quad (3)$$

For a linear sniffer, the operators p_i^S are simply multiplications by constant vectors, $p_i^S \cdot v_i = v_i \cdot \alpha(o_i)$. Similarly, the operator P^S is just a multiplication by a matrix, $P^S \cdot v = A \cdot v$, with $A_{ij} = \alpha_i(o_j)$. If we take $\|\cdot\|$ to be the standard Euclidean norm, then finding v is equivalent to solving the well-known *least-squares problem*,

$$v = \arg \min_v \|A \cdot v - d^S(o; c)\|$$

Actually, v is constrained to be a non-negative vector, so we have to solve a constrained version of the problem; the so-called *non-negative least-squares problem*, which is also well-studied; see Bjorck (1996).

Thus, had the sniffer space been linear, the mixing vector would have been easily calculated as the minimizer of a constrained least-squares problem. But how linear are real sniffer spaces? Well, within the kinds of concentration values we are interested in, and with the

sniffer we have been using, our experiments show that the space is adequately linear.

We have been using the MosesII eNose (Mitrovics et al., 1998), which is an accurate, laboratory-level, device. The one in our laboratory consists of 16 sensors made of two different technologies—eight metal oxide (MOX) sensors, and eight quartz crystal microbalance (QMB) sensors (see Gardner and Bartlett, 1999). The linearity of the sensors is nicely demonstrated in Fig. 3, where the responses of a typical MOX sensor (a) and a typical QMB sensor (b) are plotted as a function of odor concentration. We computed the response of the sensors from the time signal as the difference between the peak and the baseline (see Carmel et al., 2002a for details). Each dot represents a single measurement, and at least four repetitions were measured in each concentration. As can be seen, the concentration-dependency of the responses is linear to a high extent.

Sometimes, especially with some of the MOX sensors, we observed a certain deviation from linearity, mostly for high odor concentrations. However; such non-linearity does not bother us too much, for two reasons: first, more advanced concentration-dependency models can be used to linearize the response. Second, and maybe more importantly, we do not expect or desire to have to deal with high odor concentrations in real life applications. For example, we do not want end users in typical applications to have too much odor in their immediate vicinity, for various reasons, which include the need to be able to switch between odors very fast, the overwhelming nature of excessive quantities of odor to the user, as well as the inconvenience to the user's vicinity.

Hence, we have rather convincing evidence to the effect that the first property of linearity for sniffer spaces is adequately fulfilled for eNoses. We have recently

obtained initial encouraging indications that the second property is fulfilled too. To this end, we have carried out the following lab experiment: each of two chemicals is measured in several concentrations. We then prepare a 1:1 mixture of the two, and measure it in several concentrations, and we do the same for a 1:3 mixture. The data thus collected is multidimensional, and we project it onto two dimensions using principal component analysis (see Everitt and Dunn, 1991). As a characteristic example, Fig. 4 shows the results of this for ethyl acetoacetate and 4-methyl anisole. The things to notice are that both the pure chemicals and the mixtures come out plotted as linear-looking progressions in the principal components (PC) space, with

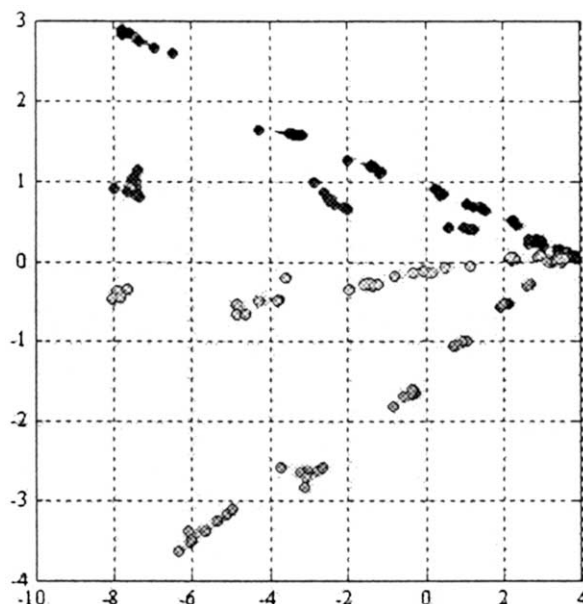


Fig. 4. Example of additivity of mixtures in an eNose space.

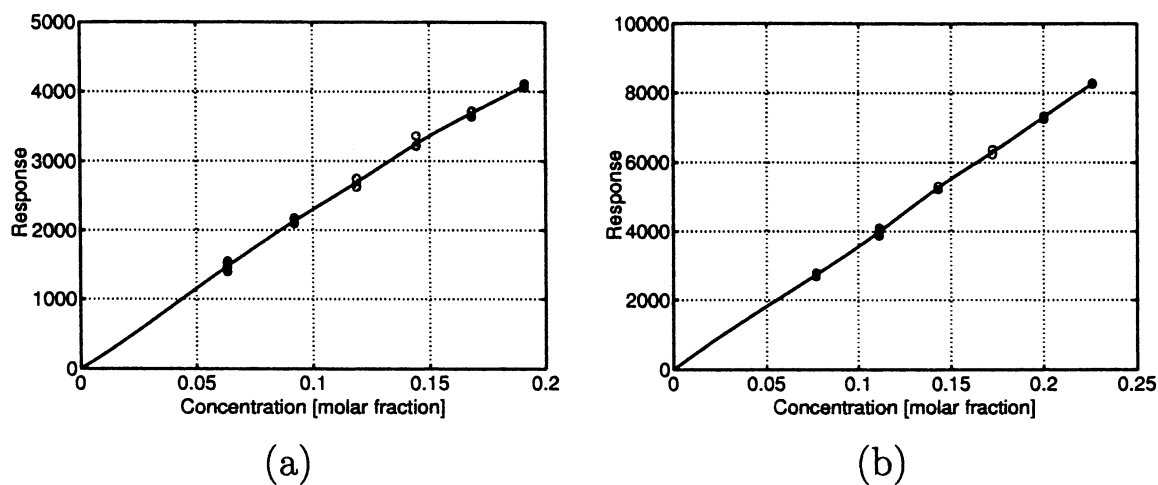


Fig. 3. Two examples of eNose sensor responses, illustrating their linearity: (a) a metal-oxide sensor response vs. amyl formate concentration; (b) a quartz-microbalance sensor response vs. toluene concentration. The dots are the measurements, and the solid line is an interpolation by piecewise cubic spline interpolation. Molar fractions are measured in poly ethylene glycol 400 solution.

larger concentrations located further from the origin, and that the 1:1 mixture vector is approximately the bisector of those of its constituents, and the 1:3 mixture vector is approximately the bisector of the 1:1 mixture vector and that of the 75% constituent. Thus we have both kinds of linearity showing up in the figure.

We are heavily involved these days in carrying out a detailed analysis of mixing experiments. We hope to be able to provide weighty evidence that the eNose space is adequately linear, so that finding the mixing vector can indeed be carried out by solving a constrained least-squares problem.

4.2. Fooling a different sniffer

Suppose now that we have two different sniffer spaces, S_1 and S_2 , with odorant vectors $d^{S_1}(o; c)$ and $d^{S_2}(o; c)$ of dimensions m_1 and m_2 , respectively. Can we digitize an odorant $(o; c)$ in the first sniffer and then produce a mixture of palette odorants such that the second sniffer will be fooled into thinking it to be $(o; c)$?

This problem adds an additional element to the one addressed above, because now we have to deal also with finding a mapping from one sniffer space to the other. To the best of our knowledge, no such mapping has ever been proposed. We are in the process of developing what we hope will be a satisfactory mapping between the MosesII eNose (Mitrovics et al., 1998), with its eight MOX sensors and eight QMB sensors, and the Cyranose320 eNose (<http://www.cyranosciences.com>), with 32 conducting polymer sensors. We hope to be able to exhibit a working mapping in the near future.

It is easy to think of specific simple examples where such a mapping does not exist. For example, the data provided by a single QMB sensor will probably not suffice to predict the response of some MOX sensor. Single sensor eNoes are, however, not realistic. We claim that for reasonable sniffers, with an adequate multitude of sensors, a good mapping can indeed be found. When a sniffer consists of an array of diverse sensors, it is likely to capture the physical information it needs for characterizing a certain odorant. At least in theory, this information is all that is needed in order to predict the response of another sniffer with similar information content. Put differently, finding the mapping $g: S_1 \rightarrow S_2$ is more likely to be possible when m_1 is large, and when the sensors are as diverse as possible. In our ongoing research, S_1 is the MosesII eNose, with its 16 different sensors made up of two completely different technologies. We feel that this should suffice to enable us to derive a good mapping function to the Cyranose320 eNose.

Once this mapping is found, we would read in the input odor in S_1 , yielding the m_1 -dimensional odorant vector $d^{S_1}(o; c)$, and then compute the mapping into the space S_2 , yielding the m_2 -dimensional odorant vector

$d^{S_2}(o; c)$. This vector would then be used, as in Section 4.1, to fool the second sniffer, S_2 .

4.3. Fooling the human brain

The human nose, with its hundreds of receptor types and complex biological machinery, can be viewed simply as a special case of a sniffer. Like any other sniffer, it takes an odorant $(o; c)$ and represents it by an odorant vector $d^P(o; c)$. However, mapping vectors from an artificial sniffer into the biological human 'sniffer' will probably be far more challenging than mapping one eNose into another.

The difficulty is in the fact that the two systems, the biological and the artificial, are very different in the detection mechanism. The ORs operate on very different principles than chemical sensors. As mentioned in Section 2.1, biosensors for eNoses are being developed by several research groups. Once they are eventually incorporated in eNoses, this difficulty can be expected to be removed. Our point here is that even for 'standard' eNoses that use conventional chemical sensors, there is evidence that the resulting fingerprints can be used to infer psychophysical data. For example, Frank et al. (2001) have shown that the MosesII eNose can be used to quantitatively predict the decision of a human panel regarding the amount of off-odor released from packaging material. Similar work by Gutierrez-Osuna et al. (2001), has demonstrated the possibility of using eNose to replace sensory analysis in assessing the effectiveness of biofilters.

An interesting question that arises in the spirit of Section 4.1 involves the degree of linearity of the psychophysical space. If we measure the psychophysical response as the intensity of perception I (which is not necessarily the optimal measure), then its concentration dependency is well studied. Above a certain odorant-dependent threshold, I grows with the odorant concentration until it reaches some odorant-dependent saturation value. Over a wide range of concentrations between the threshold and the saturation values, the intensity usually obeys a power law $I(o; c) = kc^n$, with k and n being odor-specific constants (see Schmidt, 1978). This is definitely not linear, but it has also been observed that n is usually close enough to 1 to allow for the linear approximation $I(o; c) \approx k'c$ to hold in a reasonable range of low concentrations. As explained earlier, real world applications require only low concentrations, thus this linear approximation might very well be adequate for the kind of odor communication system we propose.

So far we have discussed the linearity of response. But what about mixing additivity in the psychophysical realm? Well, here things are less clear. The way mixtures are perceived is still an open question, and no general rule has been suggested (see Frijters, 1987). It seems that a simple additive rule, like Eq. (3) will hold in many

cases. However, some strongly non-linear phenomena have also been found, see examples in Grosch (2001).

We would like to point out that the question of whether the psychophysical space is linear or not is academically interesting, but irrelevant to the scheme we propose. In our search for the mapping f , we do not assume linearity of the psychophysical space.

4.4. Palette odorants

Our odor communication system is based on the belief that there exists a set of palette odorants that can be mixed so as to mimic (up to a certain tolerance) any desired odor perception. Since to the best of our knowledge such an odorant palette has never been realized, the belief in its existence requires some justification. We start with a somewhat philosophical argument, and then provide some experimental observations to support it.

Relevant research indicates that we may assume that if two different stimuli elicit identical response of the ORs, the human perception thereof will be identical. Thus, it is the response of the receptors that has to be mimicked. An incoming stimulus elicits a spatio-temporal response of the olfactory nerve cells in the epithelium. This response is the combined result of many factors (such as the type of the odorant, its concentration, and its temporal behavior), and it reflects the entire available information regarding the specific stimulus. This information is encoded into the odorant vector d^B , which is considered to be the input for the cerebral analysis process. Since this process ends up with the ability to classify the odorant, to estimate its concentration, and to describe it, all this information must be somehow included in the response pattern, yielding the conclusion that identical response patterns will result in the same sensation regardless of the way they were formed. It is now reasonable to assume that any such set of responses can be viewed as a (possibly non-linear) superposition of patterns, which, when deciphered, can be reformulated as mixtures of suitably chosen palette odorants. Thus, if we can prepare a mixture of palette odorants, whose collective effect on the olfactory nerve cells is similar to the effect of the original odorant, the perception of the mixture will very closely resemble the perception of that odorant.

The fundamental experimental observation that should be considered here is the fact that a mixture is usually perceived by humans as a new odor. This is actually experienced by every individual on a daily basis, with the distinct aroma of food products, beverages, coffee, perfumes, etc. all being odorant mixtures comprising usually hundreds of different odorous volatile chemicals. However, it has also been shown experimentally on synthetic blends with only a few constituents (see Jinks and Laing (2001), and references therein).

Furthermore, the number of glomeruli activated when sniffing a mixture is similar to that activated when sniffing pure chemicals (Stewart et al., 1979). Similarly, the number of odor qualities perceived by a human panel responding to a mixture is similar to that perceived when responding to pure chemicals (Jinks and Laing, 2001).

Thus, mixtures can indeed carry out the mimicry we need. But how many compounds are needed for a typical mixture? And how many ingredients are shared by different mixtures? If, for example, a typical smell is adequately described by 100 unique compounds on the average, then it would drive the number of palette odorants to be impractically large. Fortunately, this is not the case. It is known that even the most complex odors can be mimicked by mixtures of a relatively small number of ingredients. This is nicely seen in the food industry, where people are interested in generating certain smell perceptions using simple artificial blends, known as *aroma models* (for a review see Grosch (2001)). Very complex aromas, such as those in wines, coffee brews, tomato paste, boiled beef and the like, are made of mixtures of many hundreds of chemicals. Yet, certain techniques have been designed to extract those compounds that have the strongest impact on the smell, and only those are used in the aroma models. Typically, the original smell is reproduced with 10–30 compounds at most. Moreover, as is exemplified in Grosch (2001), even aroma models of very different odors (such as wine and basil) may have common ingredients. At the risk of being overly speculative, we claim that a general-purpose palette of 100–300 odorants will be perfectly adequate for a broad range of applications.

We would like to end this discussion by emphasizing the differences between the concept of palette odorants, and the more familiar concept of primary odors. The latter term is used to describe odor qualities, i.e. the atomic descriptors of odors, whose discovery has turned out to be a very difficult problem, still unresolved today. The research on the subject seems to have been initiated by Amoore et al. (1964), who originally proposed seven primary odors. Since then, many followers have suggested alternative lists (Dravnieks, 1985); but none has been globally accepted. Even the attempts to isolate key molecular structures, and to identify them with specific perceptions have been only partially successful (see the review of Chastrette (1997)), and the general problem remains unsolved.

Thus, our palette odorants should not be erroneously identified with the notion of primary odors—i.e. a palette odorant does not (necessarily) represent an odor quality. In fact, the number and identity of the odor qualities is not needed for our purposes. We think of the palette odorants as a set of odorant vectors that adequately (and hopefully efficiently) span the psychophysical odor space. As such, the set of palette odorants

need not be unique, and there could be many satisfactory sets from among which one could choose, based on secondary factors, such as cost or palette size (more about this in Section 5).

4.5. Summary of the MTM algorithm

We may summarize the main operations that should be taken to devise, and then use, the mixing algorithm:

- Devising:
 - 1) Prepare a (preferably large) database of odorants, and pass them through an appropriate human panel, obtaining the odorant vectors $d^P(o; c)$ in the psychophysical space.
 - 2) Measure the same odorants by a sniffer S , obtaining the odorant vectors $d^S(o; c)$.
 - 3) Learn the mapping f between the sniffer and the psychophysical spaces.
 - 4) Choose a whiffer palette of size n .
 - 5) Compute the operator P^P for the palette odorants. (This is best done by measuring the palette odors directly by the human panel; alternatively, they can be measured by the sniffer S and then subjected to the mapping f .)
- Using:
 - 1) Sample an input odorant $(o; c)$ using the sniffer S , thus obtaining $d^S(o; c)$.
 - 2) Map the resulting fingerprint from the sniffer space to the psychophysical space, $d^P(o; c) = f(d^S(o; c))$.
 - 3) Find the non-negative mixing vector v as the minimizer of

$$v = \arg \min_v \|d^P(o; c) - P^P \cdot v\| \quad (4)$$
 - 4) Prepare and release a mixture of the palette odorants according to the vector v .

5. Additional topics

5.1. Choosing the hardware

The algorithmic scheme outlined above can work with any sniffer and any whiffer. Even an extremely poor sniffer, that yields very little information, and a primitive whiffer with a small number of palette odorants and a coarse mixing ability, can be used; the MTM algorithm will produce results and the whiffer will emit the computed mixture—the best possible under the circumstances. The point is that the results will be only as good as the hardware, and vice versa: better hardware will cause our scheme to produce better results.

The situation regarding sniffers is good. More and more eNose types are developed, using continuously improving sensor technologies. We hope that the ideas presented in this paper will have a productive effect on eNose manufacturers, since we envision a far broader spectrum of applications thereof.

Whiffers seem to evolve much more slowly. But, as we have shown in our design and construction of iSmell[®], the technology is available and the job can be done. We are confident that building and marketing high-quality commercial whiffing devices is possible. Indeed, it is inevitable.

5.2. Choosing the palette

One major aspect of the whiffer can benefit from the ideas presented here—the construction of the palette. The two key features of the palette are its size n and the particular palette odorants it contains. A palette designer should be concerned with determining both of these.

In a typical application of our scheme, we expect n to be given, being constrained by the limitations of the technology used, by the desired accuracy and by cost. Let us use the term *tolerance*, denoted δ , to represent a measure of the extent to which the perception of the computed mixture $P^P \cdot v$ deviates from that of the original odorant, $d^P(o; c)$. The exact formulation of the tolerance depends on the specific structure of the odor spaces involved.

In principle, a larger palette allows for a smaller tolerance. However, large palettes are more expensive and more difficult to build, hence a compromise between palette size and tolerance must be made. If there were no constraints on the palette, we could simply choose n to be large enough for the palette to contain all possible distinct aromas, which is at least in the order of 10^4 , and very far from the ability of current whiffer technology. To be realistic, we must assume that for the near future n will be under 300.

As to choosing the palette odorants themselves, we envision an algorithm which, given the desired size n and a large collection of candidate odorants, computes the ‘best’ n odorants for the palette. Such an algorithm can indeed be constructed, based on ideas similar to the ones reported upon here, and taking into account accumulated information about the psychophysical space (such as the density distribution of the various odorants). It is not out of the question that such an algorithm could also be used to tailor special palettes to specific application areas, to desired tolerance, to constraints on mixing ratios or quantities, etc.

Another interesting option in palette design is to adopt a multi-tier approach. There might be advantages in building the palette so that the palette odorants are arranged in tiers. In this way, mixtures can be prepared

by taking larger quantities from the higher levels (catering for coarser descriptions), adding lower level odorants to fine-tune the output—as a kind of ‘salt-and-pepper’ stage. Of course, the physical reservoirs for the palette odorants inside the whiffer can then be of different sizes, reflecting the differences in the typical use-rates of the various levels.

5.3. Choosing a tolerance

What is a reasonable value for δ ? We cannot give a number at this stage, but we can claim that for many applications, reasonably good performance is expected even with high tolerance (less accurate mixtures). As human beings, we are mainly driven by visual and verbal stimuli. Whenever these are in conflict with olfactory impressions, the brain tends to ‘twist’ these impressions so that they fit the visual or verbal input. This leads to the phenomena known as *olfactory illusions* (see Herz and von Clef, 2001), which can be as severe as causing subjects to think they are actually smelling an odorless liquid (Slosson, 1899). Consequently, for the average consumer, poor mimicking ability can be compensated by visual and verbal cues, at least to some extent. For example, sniffing a garlic-like substance while watching a TV pizza commercial, might suffice to convince many viewers that they are actually smelling pizza.¹

Of course, this entire discussion does not hold for specialized markets that require low tolerance. For example, a system designed for consumers to choose a perfume can obviously not allow itself to make any compromises regarding tolerance.

6. Summary and discussion

We have proposed a rather broad scheme for an odor communication system. We are hard at work expanding, refining and implementing its various parts. A notable part of our current work is in gathering and analyzing experimental data from eNoses and human panels. The results so far are very promising, and we shall report more fully on them in subsequent papers, beyond those developments appearing in Carmel et al. (2002a,b).

To some extent, our scheme decreases the importance of investigating structure–odor relationships (for the purpose of odor communication, that is). By investigating the psychophysical space via human panels, we use ‘records’ of the final mental/perception state following a sniffing, without having to understand the details of the machinery that led to this state.

The applications of odor communication are far-reaching, and diverse, and include scented movies, scented computer games, scented email attachments, scented commercials, and electronic purchase of odorous products (foods, perfumes, detergents, etc.). Some of the applications do not require the entire setup, and can do with only portions of the system. For example, sniffers can be left out of the day to day usage in cases where the output is known to be a member of a pre-determined set of odors; a preprocessing stage can be carried that will compute the required mixtures in advance.

Finally, we would like to stress that this paper exhibits ideas that still require much work in order to fully materialize. We hope to succeed in interesting other researchers in our vision, and would like to see broad efforts in these directions.

Acknowledgements

In 1998, Eli Fisch had the pioneering vision that an odor communication scheme might indeed exist, and he deserves a very special thanks for getting us to collaborate on this research at that time, and for following its materialization. We also thank him and Sagit Fink for their help in consolidating and improving the ideas expressed in the paper.

References

- Amoore, J.E., Johnston, J.W., Rubin, M., 1964. *Sci. Am.* 210, 42.
- Araneda, R.C., Kini, A.D., Firestein, S., 2000. *Nat. Neurosci.* 3, 1248.
- Bjorck, A., 1996. *Numerical Methods for Least Squares Problems*. SIAM, Philadelphia.
- Buck, L., Axel, R., 1991. *Cell* 65, 175.
- Carmel, L., Harel, D., Lancet, D., 2001. *Bull. Math. Biol.* 63, 1063.
- Carmel, L., Levy, S., Lancet, D., Harel, D., 2002. *Proc. 9th Int. Meeting on Chemical Sensors (ICS2002)*, Boston, USA.
- Carmel, L., Lancet, D., Harel, D., 2002. *Proc. 9th Int. Meeting on Chemical Sensors (ICS2002)*, Boston, USA.
- Chastrette, M., 1997. *SAR QSAR Environ. Res.* 6, 215.
- Di Natale, C., Macagnano, A., Martinelli, E., Paolesse, R., Proietti, E., D’Amico, A., 2001. *Sens. Actuators B* 78, 26.
- Dravnieks, A., 1985. *Atlas of Odor Character Profiles*. ASTM Data Series 61. Philadelphia.
- Everitt, B.S., Dunn, G., 1991. *Applied Multivariate Data Analysis*. Arnold, London.
- Frank, M., Ulmer, H., Ruiz, J., Visani, P., Weimar, U., 2001. *Anal. Chim. Acta* 431, 11.
- Frijters, J.E.R., 1987. *Ann. N. Y. Acad. Sci.* 510, 67.
- Gardner, J.W., Bartlett, P.N., 1999. *Electronic Noses, Principles and Applications*. Oxford University Press, Oxford.
- Glusman, G., Yanai, I., Rubin, I., Lancet, D., 2001. *Genome Res.* 11, 685.
- Gopel, W., Ziegler, C., Breer, H., Schild, D., Apfelbach, R., Joerges, J., Malaka, R., 1998. *Biosens. Bioelectron.* 13, 479.
- Grosch, W., 2001. *Chem. Senses* 26, 533.

¹ This example is a modern version of the one brought in Herz and von Clef (2001).

- Guadarrama, A., Rodriguez-Mendez, M.L., de Saja, J.A., 2002. *Anal. Chim. Acta* 435, 41.
- Gutierrez-Osuna, R., Schiffman, S.S., Nagle, H.T., 2001. Proc. 3rd European Congress on Odours. Metrology and Electronic Noses, Paris, France.
- Hahn, S., Frank, M., Weimar, U., 2000. Proceedings of the 7th international symposium on Olfaction and Electronic Nose (ISOEN 2000), pp. 49.
- Herz, R.S., von Clef, J., 2001. *Perception* 30, 381.
- Jinks, A., Laing, D.G., 2001. *Physiol. Behav.* 72, 51.
- Joerges, J., Kuttner, A., Galizia, G., Menzel, R., 1997. *Nature* 387, 285.
- Lancet, D., Ben-Arie, N., 1993. *Curr. Biol.* 3, 668.
- Lin, Y.-J., Guo, H.-R., Chang, Y.-H., Kao, M.-T., Wang, H.-H., Hong, R.-I., 2001. *Sens. Actuators B* 76, 177.
- Margalit, Y., 1997. Concepts in Wine Chemistry. Wine Appreciation Guild, San Francisco.
- Mitrovics, J., Ulmer, H., Weimar, U., Gopel, W., 1998. *Acc. Chem. Res.* 31, 307.
- Mori, K., Nagao, H., Yoshihara, Y., 1999. *Science* 286, 711.
- Nagel, H.T., Schiffman, S.S., Gutierrez-Osuna, R., 1998. *IEEE Spectrum* 35, 22.
- Negri, R.M., Reich, S., 2001. *Sens. Actuators B* 75, 172.
- Noble, A.C., Arnold, R.A., Masuda, S.D., Pecore, S.D., Schmidt, J.O., 1984. *Am. J. Enol. Vitic.* 35, 107.
- Noble, A.C., Arnold, R.A., Buechsenstein, J., Leach, E., Schmidt, J.O., Stern, P., 1987. *Am. J. Enol. Vitic.* 38, 143.
- Persaud, K., Dodd, G., 1982. *Nature* 299, 352.
- Schiffman, S.S., Reynolds, M.L., Young, F.W., 1981. Introduction to Multidimensional Scaling: Theory, Methods, and Applications. Academic Press, London.
- Schmidt, R.F., 1978. Fundamentals of Sensory Physiology, 3rd ed.. Springer-Verlag, New York.
- Slosson, E.E., 1899. *Psychol. Rev.* 6, 407.
- Stewart, W.B., Kauer, J.S., Shepherd, G.M., 1979. *J. Comp. Neurol.* 185, 715.
- Wise, P.M., Olsson, M.J., Cain, W.S., 2000. *Chem. Senses* 25, 429.
- Ziegler, C., Gopel, W., Hammerle, H., Hatt, J., Jung, G., Laxhuber, L., Schmidt, H.L., Schutz, S., Vogtle, F., Zell, A., 1998. *Biosens. Bioelectron.* 13, 539.