PRINCIPLES OF ODOR CODING AND A NEURAL NETWORK FOR ODOR DISCRIMINATION

DETLEV SCHILD
Physiologisches Institut der Universität Göttingen, Abteilung Neuro- und Sinnesphysiologie, D-3400 Göttingen, Federal Republic of Germany

ABSTRACT A concept of olfactory coding is proposed. It describes the stimulus responses of all receptor cells by the use of vector spaces. The morphological convergence pattern between receptor cells and glomeruli is given in the same vector space as the receptor cell activities. The overall input of a glomerulus follows as the scalar product of the receptor cell activity vector and the vector of the glomerulus' convergence pattern. The proposed coding concept shows how the network of the olfactory bulb succeeds in discriminating odors with high selectivity. It is concluded that sets of mitral cells coding similar odors work very much in the way of mutually inhibited matched filters. This solves one main problem both in olfaction as well as real-time odor detection by an artificial nose, i.e., how the fairly low degree of selectivity of receptor cells or sensors is overcome by the neural network following the receptor stage. The formal description of olfactory coding suggests that quality perception which is invariant under concentration shifts is accomplished by an associative memory in the olfactory bulb.

1. INTRODUCTION

In the past, there have been several theories of olfaction, most of which regarded the interactions between the molecular structure of odorants and the response of sensory cells in the mucosa. Amoore published a "site-fitting" theory that related odor quality to the chemical constitution of the odorants. Originally, he proposed seven primary odors; later, he suggested the existence of many more primaries (2, 3).

Davies (11) postulated that odorous molecules are adsorbed to the protein-lipid membrane of olfactory cilia; this adsorption would then dislocate membrane molecules, allowing an exchange of charges across the membrane and the depolarization of the cell. Wright (86, 87) correlated odor with vibrational modes of the odorous molecules transmitted and selectively received by receptor cells. Beets (5) proposed a "profile-functional group concept" according to which odor quality is determined by a specific functional group of a molecule as well as the shape and size of the whole molecule.

The difficulty that lies in all these older approaches is the lack of knowledge about the molecular receptors of odorous molecules. Possibly, the central points of all these theories will be unified in the near future by a theory based upon new results from biochemical and patch clamp approaches to the olfactory transduction problem (10, 53, 60, 66, 82). Solving this problem is, however, by no means equivalent to understanding information processing of olfactory stimuli in general. Beidler (6) wisely pointed out that olfactory discrimination may result not from a few highly specific cells (as was suggested by pheromone receptor cells in some insects, an exception), but from the more diffuse activity of a large number of cells. Moulton and Beidler (59) concluded from this "that more attention should be paid to neural coding in mammalian systems."

To my knowledge, there is only one paper (28) treating the complete information channel between receptor cells and mitral cells on the basis of information theory. Though this work has many simplifications and specific assumptions concerning only one species, it was the first time that concepts of information and coding theory were applied to the olfactory system. Since then (1954) no other attempts of this kind have appeared, probably because the gap between theory and experiments was too large and offered too much space for speculation. Freeman (16–19) has described the signal processing in the olfactory system in terms of interacting nerve cell assemblies. He was able to interpret odor detection in the olfactory bulb as a match between a template and an odor-elicited activity pattern. In this nonlinear approach different odors provoke different dynamical states in the state space of ensemble neuronal activities.

During the last 15 years a host of new and interesting results have been accumulated which are related to certain subchannels of the system. Some of these are particularly significant for the coding problem; they concern the topographic projection from receptor cells to the bulb (7, 15, 40, 47–50), the morphology of the olfactory bulb (45, 51, 63, 68, 77), single-unit temporal response patterns of receptor cells (13, 22, 25, 26, 32, 79) and of mitral cells (31, 39, 52, 54–56, 61, 69, 74, 75), as well as spatial 2-DOG patterns of the olfactory bulb (37, 38, 46, 76, 80, 81) and, more recently, the first spatio-temporal activation

patterns recorded with the voltage-sensitive dye method (41, 42, 65). An important point for the purpose of this paper is that PCA and factor analysis have clearly shown that more than three dimensions are needed for an adequate representation of odor responses at receptor level.

A coding concept that considers the action of all system elements and that takes into account the cited experimental evidence is presented in this paper. It might be useful also in real-time detection of chemical compounds in air or water. Though they are of increasing economic and technical importance, real-time odor measurements are hampered by the fact that artificial chemoreceptors are only weakly selective for most compounds (14, 20, 57, 67, 71, 85). However, the same applies also to most biological chemoreceptors. Because selectivity enhancement in biological systems is accomplished by the neural network following the receptor cells, studying this network from a formal point of view might thus shed some light not only on the principles of olfactory coding, it could also be valuable for the design of an "artificial nose" with high selectivity. The biological neural network for odor discrimination incorporates mainly local interactions, only a few cell types, and, at least in some species such as snails, only a reasonably low number of elements (e.g., 20 glomeruli per tentacle, [8]). In principle, construction of simplified models appears therefore both intriguing and feasible. This paper is also intended as a step in this direction.

In the following, I briefly outline the basic structure of the periphery of the olfactory system and the signals generated at its subsequent stages. Then I delineate a novel concept of olfactory coding that explains the mapping of olfactory stimuli onto the two-dimensional layers of the olfactory bulb. The underlying mathematics have been used in a similar form by Widrow (84), Rosenblatt (72), and Kohonen (43). The effect of the proposed mapping is that stimuli detected by many relatively unselective sensors are discriminated with high selectivity at the next stage of information processing. Therefore this coding concept suggests some ideas of how an "intelligent" artificial nose (i.e., a network that, as a whole, is more selective than its single sensors) could be built. It comprises parallel processors performing an (orthogonal) decomposition of the system's input signal. Then another array of parallel processors is needed to calculate and represent images of the stimuli whereby the connections between the processors guarantee a high selectivity of stimuli. It is particularly interesting that the biological system shows a certain degree of plasticity, i.e., the capability of self-programming. Parallels to self-organizing multiprocessor programming are thus obvious and could, in fact, find applications in a special purpose computer for odor detection.

2. DESIGN OF THE SYSTEM

The detailed organization of the periphery of the olfactory system differs from species to species. However, when only the principal steps of information processing are considered, all systems show common features. These features are of interest here and drawn in Fig. 1. The first stage is made up of receptor cells which may be inserted in a mucosa as it happens in vertebrates or which may be situated on quite different parts of the body such as antennae or legs. Olfactory receptor cells are numerous in all species (for a comparison, see reference 8); 10^7 cells can be taken as a mean value for vertebrates. A typical vertebrate receptor cell is not very selective; experimental evidence indicates that a cell can respond to a large number of stimuli, though with different activities (70). Fig. 2 exemplifies the responses of two different cells to 10 stimuli.

Despite the divergent receptor cell locations in different species their connections to the next stage of the system are rather similar. The receptor cell axons leaving the mucosa form the olfactory nerve which enters the olfactory bulb; there the axons end in so-called glomeruli which are spherically shaped conglomerates of synapses primarily between receptor axons and mitral/tufted cells, the output neurones of the olfactory bulb. Activation of glomeruli appears to be homogeneous when the system is stimulated as shown by 2-deoxyglucose studies (46). Mitral cells get their input signals from the glomeruli in their vicinity, either by a few dendrites that enter adjacent glomeruli (34, 35, 45, 64) or by one main dendrite that receives input from the gomerulus it enters and from neighboring glomeruli through excitatory interneurones (as in higher vertebrates [77]). Orthogonal to this direction of information flow from receptors to the central nervous system, there are local circuits incorporating periglomerular cells, short axon

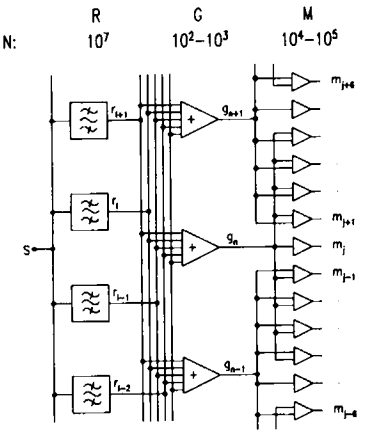

FIGURE 1 Block diagram of information flow from stimulus to mitral cells. A one-dimensional simplified model without interneurones is shown. S is the stimulus. Receptor cell classes are shown as filters. The connections between receptor cell classes and glomeruli (G) have a data bus structure. r_l is the activity of the lth receptor class. g_n is the overall input activity of the nth glomerulus. The connections between glomeruli and mitral cells (M) are local data buses so that a glomerulus gives input to mitral cells in its neighborhood only. m_j is the overall input the jth mitral cell receives from glomeruli. The orders of magnitude of the numbers of receptor cells (R), glomeruli (G), and mitral cells (M) are indicated above the diagram.

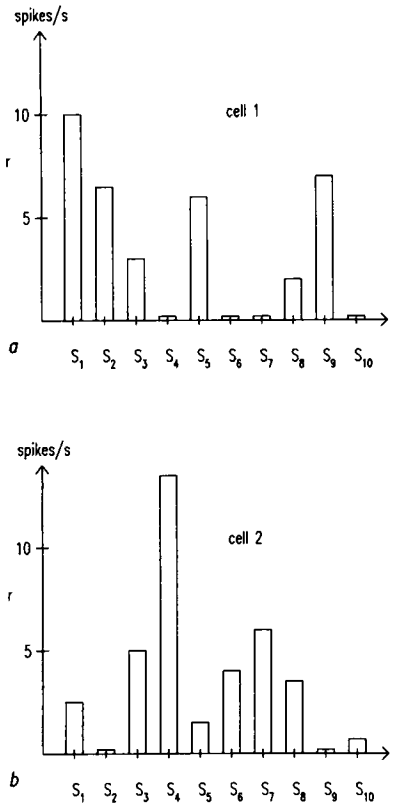

FIGURE 2 Response activity r of two different receptor cells to the same set of 10 odor stimuli S^1 through S^{10}. Because of the different response activity profiles $r(S^k)$ the cells must be assigned to two different receptor cell classes.

cells, and granule cells mediating inhibitory (23, 36) as well as excitatory (62) signals between mitral/tufted cells. The inhibitory interneurones are under efferent control. Granule cells stimulated by mitral/tufted cells inhibit the mitral/tufted cells in their neighborhood, i.e., they also inhibit the mitral/tufted cells by which they have been excited. Recent evidence (4, 78) indicates that self inhibition might be at least as important as lateral inhibition. The exact action of periglomerular and short axon cells is less clear. These cell types are therefore not included in the coding concept proposed in this paper, though some ideas of their possible role in the information processing are discussed (see section 5.4).

The signals at the receptor and mitral cell level of the system are as follows. Receptor cells fire action potentials of relatively low rate, about 0–15 spikes/s. The spontaneous rate is well below 1 spike/s (for a review of receptor cell function, see reference 23). The response to a step-shaped odor pulse is clearly dynamic-static, beginning with a dynamic overshoot followed by a fairly constant activity (25). The spike interval distribution is (except for short intervals) approximately exponential (83), i.e., spike occurrence is random and receptor cell spike trains are realizations of a Poisson process. Receptor axons converge onto mitral cells with ~1,000 axons per mitral cell, however, because there are about 25 times more mitral cells than glomeruli, the convergence factor of receptor to glomeruli is ~25,000. These numbers vary from species to species and are to be taken as rather coarse estimates; however, they show clearly an enormous convergence of receptor cells upon glomeruli and a following divergence from glomeruli to mitral cells. The precise numbers are not crucial in this context. Considering that ~1,000 spike trains with a mean rate of, say, 1 spike/s form the input of a mitral cell, the overall input to the mitral cell is ~1,000 spike/s corresponding to a mean spike interval of 1 ms. Given the fairly long excitatory time constant of mitral cells of >100 ms (30, 58), it is obvious that the overall input to a mitral cell is a smooth function that largely follows the dynamic-static time course of the receptor cell activity. This is in fact what has been measured in goldfish mitral cell discharges (74): a dynamic overshoot followed by a nonadapting static activity. The overshoot is often positive as in receptor cells, but equally often it is negative and followed by an activity depression (relative to prestimulus activity); this is exactly what one would expect from simple model considerations concerning the lateral inhibitory network (73).

There is another, maybe more significant aspect of the convergence from receptor cells to mitral cells. As mentioned, receptor cell spike trains are in good approximation Poisson processes; because the sum of Poisson processes is also a Poisson process, the total input to a mitral cell is a Poisson process. The activity of the summed spike train is approximately proportional to the number N of summed trains. Van Drongelen et al. (83) have pointed out that this leads to an increase in sensitivity of the system. The standard deviation of the summed process increases, however, only proportional to $\sqrt{N}$. In other words, the relative noise amplitude (r.m.s.) decreases as $N^{-1/2}$. Noisy activity fluctuations are the limiting factor of sensitivity, resolution, information content, and information channel capacity; it is therefore clear that this decrease of noise increases the information capacity of the channel "receptors → mitral cells" markedly.

The above sketch of the system, though incomplete, elucidates features common to the periphery of all olfactory systems. Only these general features are needed for the formulation of the following olfactory coding concept.

3. A VECTOR SPACE CODING CONCEPT

3.1 Receptor Cell Activities

The mapping of odors S^k, $k = 1, 2, \ldots, K$, onto the activity of all receptors can be described by vectors $\mathbf{r}(S^k)$,

$$f_1 : S^k \rightarrow \mathbf{r}(S^k) \epsilon R = R^L,$$

where R has an orthonormal basis $\mathbf{r}_1, \mathbf{r}_2, \ldots, \mathbf{r}_L$.

Here, indices indicating stimuli are written as superscripts and those indicating vector components as subscripts. The lth component r_l of $\mathbf{r}(S^k)$ is the ensemble mean

response to odorant S_k of the lth receptor cell class. A receptor cell class is viewed as an ensemble of receptor cells that all respond in the same way to any set of successively applied stimuli.

In the trivial case that no two receptor cells respond in the same way to all stimuli, the number L of receptor cell classes equals the number of receptor cells. The number L is currently unknown, however there is some recent evidence for the existence of biochemically different receptor cell classes (1, 21). The impact of the number of receptor classes on the information processing is discussed in section 3.2.

In the following, the vector components are treated just as variables; one has however to keep in mind that they are actually time functions, namely the ensemble mean activity responses of receptor classes.

The physiological dissimilarity D of two odors S^k and S^i can be described in R as the length $D(k, i)$ of the difference vector between $\mathbf{r}^k$ and $\mathbf{r}^i$:

$$D = |\mathbf{r}^k - \mathbf{r}^i|.$$

An alternative definition of stimulus similarity at the receptor level is the correlation coefficient $C_r(k,i)$ between the vector components r_l^k, $l = 1, 2, \ldots, L$ and r_l^i, $l = 1, 2, \ldots, L$ of two stimuli k and i.

$$C_r(k,i) = \sum_{l=1}^{L}(r_l^k\, r_l^i)/L = (\mathbf{r}^k \cdot \mathbf{r}^i)/L.$$

It is an interesting question how stimuli of different concentrations but of the same molecular structure and composition are represented at the receptor level. Existing evidence indicates that there is a recruitment of receptor cells with increasing concentration; an example is shown in Fig. 3 where, for simplicity, monotonic dose-response curves as well as identical maximum response activities are assumed. As a consequence, an increase in concentration will usually result in both an increase in length and a change of direction of $\mathbf{r}$. Concentration is thus not only coded by an increase of single cell firing rate but also by the across fiber pattern of active receptor classes. The various views of how concentration influences receptor cell activities are summarized in Fig. 3. The vector $\mathbf{r}$ viewed as a function of concentration gives a curve $\mathbf{r}(c)$ in the receptor activity space R (for the two-dimensional case, see Fig. 3 c). Two odors S^k and S^i are physiologically distinguishable at the receptor level if the curves $\mathbf{r}^k(c)$ and $\mathbf{r}^i(c)$ don't intersect; if the curves $\mathbf{r}(c)$ of two odors coincide at a certain concentration, these odors are identically coded at this concentration. Amazingly, however, this ambiguity at receptor level can be removed in a later stage of the system (see next paragraph and section 5.4).

As a last point in this paragraph, let us just touch the invariance problem in olfaction. In other sensory systems, invariant perceptions are well known: seventh chords, e.g., are perceived per se, invariant under transposition though different chords have different representations at the receptor level. In olfaction, there is a fairly analogous phenomenon: imagine an experimenter who measures the responses to two successively applied stimuli, say A and B, recording simultaneously from four receptor cells. Assume that he knows neither qualities nor concentrations of the stimuli, nor from which receptor classes he is recording. If the two stimuli result in the measurement of two across fiber patterns such as those of c_1 and c_5 in Fig. 3 b, then

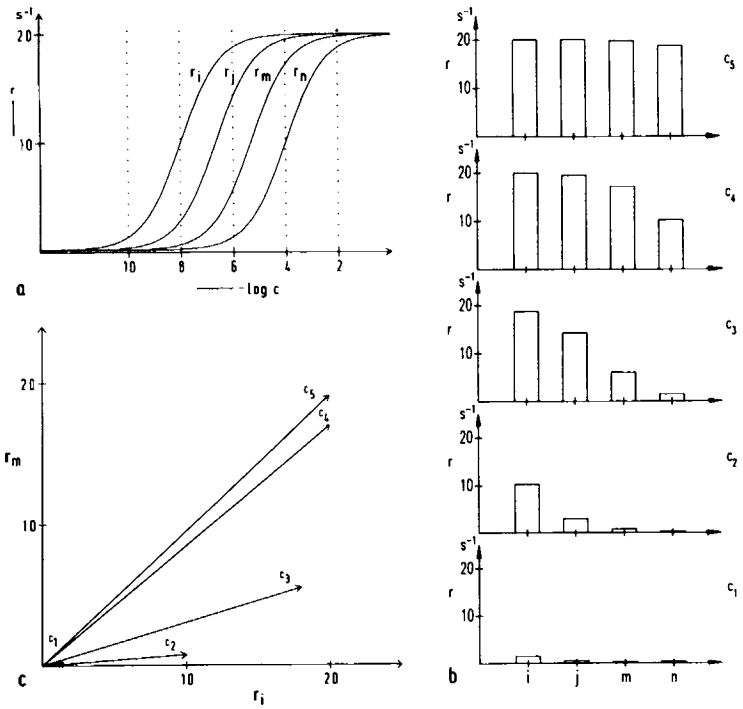

FIGURE 3 Receptor class activities as a function of concentration c. (a) Response activities r of four different receptor cell classes i, j, m, and n as a function of the negative logarithm of the concentration c; the activity of class i is r_i, etc. Five specific concentrations c_1 through c_5 (10^{-10}, 10^{-8}, 10^{-6}, 10^{-4}, and 10^{-2} M/liter) are indicated by dotted lines. (b) The response activities r_i, r_j, r_m, and r_n are shown as histograms, one histogram for each of the concentrations c_1 through c_5. (c) The response activities r_i and r_m are shown for the five indicated concentrations as receptor cell activity vectors. The quality of a stimulus, i.e., the stimulus independent of its concentration, corresponds to the curve connecting these vectors. In this representation concentration is a parameter, whereas it is a variable in Fig. 3 a.

there is no way for him to decide whether or not the stimuli have the same quality. In other words, concentration and quality coding are not well separated at receptor level; stimuli of the same quality but of different concentrations are not mapped to the same sets of receptor classes. The invariance of quality perception (which holds for most stimuli) means that a curve $\mathbf{r}^k(c)$ is seen as a whole at another stage of information processing. Therefore, punctual overlapping of $\mathbf{r}^k(c)$ with another curve is only of minor importance. The only physical variables which could be used by the system to establish such an invariant perception are the joint probabilities of the activated receptor classes involved in the coding of specific odor qualities. This point is discussed later in section 5.4.

3.2 Receptor-Glomerular Convergence

Receptor cell fiber convergence onto glomeruli can adequately be described by coefficients c_{ln}, where c_{ln} means the number of receptor fibers of class l that enter the nth glomerulus. Then the mapping f_2 of receptor class activities on the total input activities of the glomeruli,

$$f_2: R \rightarrow G = R^N,$$

is given by

$$g_n = \sum_{l=1}^{L} c_{ln} r_l. \qquad (1)$$

The input of all glomeruli is then

$$\mathbf{g} = (g_1, g_2, g_3, \ldots, g_N).$$

At the level of glomeruli, the stimuli S^k, $k = 1, 2, \ldots, K$, are thus represented in an N-dimensional space. The number N of glomeruli can be as low as 20 in the tentacle of a snail (8, 9); in higher vertebrates, a reasonable estimate is 3,000 (Meisami, personal communication).

When the coefficients c_{ln} are written in matrix form $C = (c_{ln})$, then the linear relation between $\mathbf{r}$ and $\mathbf{g}$ is

$$\mathbf{g} = C\,\mathbf{r},$$

or when the stimulus is indicated,

$$\mathbf{g}^k = C\,\mathbf{r}^k.$$

The coefficients c_{ln} are unknown; this does, however, not preclude some comments of their meaning: (*a*) All coefficients c_{ln} are positive or zero. The transform is therefore not a rotation of the coordinate system, because for this purpose negative coefficients would also be needed.

(*b*) The coefficients c_{ln} of the nth glomerulus give the vector

$$\mathbf{c}_n = (c_{ln}, c_{2n}, \ldots, c_{Ln}),$$

and the overall input g_n to the nth glomerulus (Eq. 1) can be written as the scalar product

$$g_n = \mathbf{c}_n \cdot \mathbf{r}.$$

Overall glomerular input is maximal if $\mathbf{c}_n$ and $\mathbf{r}$ are parallel. The receptor-glomerular convergence can thus be well visualized as follows: imagine for every glomerulus a morphologically predetermined vector $\mathbf{c}_n$ so that the convergence pattern can be viewed as a number of vectors $\mathbf{c}_n$ in the space of receptor classes. When a stimulus represented by $\mathbf{r}^k$ is applied, the projections of $\mathbf{r}^k$ upon all vectors $\mathbf{c}_n$ multiplied by $|\mathbf{c}_n|$ are the glomerular input pattern.

Another view of this fact is that the sum in Eq. 1 is nothing but the nonnormalized cross-correlation coefficient between the components of the vectors $\mathbf{c}_n$ and $\mathbf{r}$. With $\mathbf{r}$ parallel to $\mathbf{c}_n$, the correlation is maximal and the nth glomerulus receives maximal input; the stimulus is "optimally mapped" onto this glomerulus. Other glomeruli, whose convergence vectors are not orthogonal to $\mathbf{c}_n$, also receive input from this stimulus. Given the enormous number of potential stimuli and the limited number of glomeruli in some species (e.g., molluscs and several fishes), it is clear that most stimuli cannot be mapped optimally on single glomeruli. "Optimal mapping" at glomerular level does therefore not appear to be an optimal coding principle. Another serious objection against the hypothesis of exclusive optimal mapping at the glomerular level is that signal transmission seems to work well even if a considerable part of the bulb is removed (33).

Up to this point, the convergence vectors have been regarded as fixed, whereas the stimuli were variable. The opposite might also be important in view of the plasticity of the system. If there were a predominant stimulus ($\mathbf{r}^k$) and a receptor-glomerular convergence which could vary over time, then the input to a certain glomerulus would become maximal if the c_{ln} changed such that $\mathbf{c}_n$ ended up parallel to $\mathbf{r}^k$. In this case, the receptor activity vector would be optimally mapped on one glomerulus and the "correlator glomerulus" would be a matched filter and a self-organized feature detector as outlined by Kohonen (43). An analogous self-organizing convergence can be imagined for more than one glomerulus (see section 5.3).

(*c*) The numbers L and N, and particularly their ratio L/N influence the kind of information processing considerably. N can, at least in principle, be measured. L remains presently unknown, so that three cases need to be discussed: $L < N$, $L = N$, and $L > N$. In the first case, the matrix C has more rows than columns, and N different odors could be optimally mapped on glomeruli in the sense of the preceding paragraph *b*. For all other stimuli, the vectors $\mathbf{r}^k$ do not coincide with any of the convergence vectors $\mathbf{g}_n$, and the glomerular input pattern of these stimuli is a linear combination of the optimally mapped stimuli. The glomerular representation of a stimulus $\mathbf{r}^k$ is then more redundant the larger the ratio N/L is. This redundancy, which is also suggested by experiments showing that only a small part of the system is sufficient for transmitting almost all of the necessary information (33), guarantees a very safe information transmission. If, on the other hand, the spaces R and G have the same number of

dimensions ($L = N$), the vectors $\mathbf{r}^k$ are merely transformed into another coordinate system; the mapping may be as described above ("optimal map"), but there are also other reasonable possibilities (see Discussion). If the connections between glomeruli and the following layers of the system work in the way of an associative memory, which seems most plausible, the entire odor information could be retrieved from only a part of the system even in the case $L = N$. The experiments cited above give therefore no hint about the magnitude of L.

If $L > N$, it is important to know the number L_0 of linearly independent vectors $\mathbf{r}^k$. It is well possible that there are less, say $L_0 < L$, independent receptor activity vectors than there are receptor classes (a simple example of such a case would be a number of vectors on a plane of arbitrary orientation in a three-dimensional coordinate system). If $L_0 > N$, then, of course, information is lost. In this case, different odors might have identical representations. In the opposite case ($L_0 < N$), the transform C could reduce the dimensionality of the space in which odors are represented.

(*d*) A slight variation of a stimulus ($\mathbf{r} \rightarrow \mathbf{r} + \mathbf{dr}$) results in a proportionally slight variation of the vector $\mathbf{g}$ at the glomerular level. In other words, whatever the coefficients of the matrix C, similar stimuli are mapped onto similar glomerular input activity patterns. This crucial property is discussed in section 5.2.

3.3 Glomerular-Mitral Cell Projection

The mapping from glomeruli to the input of mitral cells is given by

$$f_3: G \rightarrow M = R^J$$

with $m_j^k = \Sigma_{n=1}^{N} p_{nj}\, g_n^k$ or, with the matrix written as $p = (p_{nj})$,

$$\mathbf{m}^k = P\,\mathbf{g}^k.$$

As there are about 25 times more mitral cells than glomeruli, $J \approx 25\,N$. The matrix P has special properties: it is a projection matrix with nonvanishing, positive elements on and in the neighborhood of the diagonal. This property corresponds to the locally restricted divergence from glomeruli to mitral cells. The information of S^k, $\mathbf{r}^k$, and $\mathbf{g}^k$ is decomposed and projected on different subspaces of M corresponding to different areas of the olfactory bulb's mitral cell layer.

As odors are represented in (at most) N dimensions (the maximal dimension of the space G), there cannot be more than N linearly independent mitral cell input activity vectors. Assuming 25 times more mitral cells than glomeruli, this means that 24 N mitral cells, i.e., most of them, have input vectors that are linearly dependent and principally unnecessary for the information conveyence of one specific odor. However, the combination of the cells involved in information transmission changes from stimulus to stimulus.

A particular mitral cell, say the jth, gets its inputs according to the vector

$$\mathbf{p}_j = (p_{1j}, p_{2j}, \ldots, p_{Nj}),$$

where the p_{nj} vanish outside a certain neighborhood of the jth mitral cell, e.g.,

$$\mathbf{p}_j = (0, \ldots, 0, p_{n-1,j}, p_{nj}, p_{n+1,j}, 0, \ldots, 0).$$

An adjacent mitral cell gets its input from (almost) the same glomeruli, though with different weighting factors

$$\mathbf{p}_{j+1} = (0, \ldots, 0, p_{n-1,j+1}, p_{nj+1}, p_{n+1,j+1}, 0, \ldots, 0).$$

The input activities of these cells are $m_j = \mathbf{p}_j \cdot \mathbf{g}$ and $m_{j+1} = \mathbf{p}_{j+1} \cdot \mathbf{g}$. The cell with the projection vector $\mathbf{p}$ which fits better with $\mathbf{q}$ gets the larger input. Extending this to all mitral cells, we see that there are sets of optimally activated mitral cells, one set for every glomerular activation pattern.

3.4 Lateral Inhibition

In the olfactory bulb, lateral inhibition is found mainly between adjacent glomeruli on the one hand, and between mitral cells on the other. The exact connection patterns as well as the synaptical strengths are, however, not known in much detail. It is therefore presently impossible to assess precisely the effects of these lateral inhibitory circuits. Here, it is only assumed that lateral inhibition acts as a spatial high-pass filter enhancing the contrast of a spatial activity pattern. Possible other effects such as activity-dependent gain, etc., are not considered here. Let mitral cell input be transformed into mitral cell output by

$$f_4: M \rightarrow M, \text{ with}$$

$$b_i^k = \sum_{j=1}^{J} s_{ji}\, m_j^k, \text{ or}$$

$$\mathbf{b}^k = S\,\mathbf{m}^k, \tag{2}$$

whereby the (suppression) matrix S has negative values near the diagonal and vanishing values otherwise. Negative activities b_i^k are discarded as insignificant for spike generation

$$a_i^k = \max\,(0, b_i^k). \tag{3}$$

The vector $\mathbf{a}^k$ gives a coarse approximation of the mitral cell activities due to stimulus S^k. A strong lateral suppression may inhibit all activities but one within a certain subspace; in this way, a vector which before the action of lateral inhibition had several positive components in a subspace, is transformed into a vector which has only one positive component. This orthogonalizing effect is brought about by Eq. 2 and the nonlinear transformation (Eq. 3) rather than by an orthogonal transformation. Further it is a transformation which acts separately on many small areas of the olfactory bulb rather than on all mitral cells together.

4. AN ALTERNATIVE DESCRIPTION: ACTIVITY IMAGES

In the foregoing, the geometrical arrangement of glomeruli and mitral cells is obscured by the specific construction of the spaces G and M. In the following, I briefly sketch an alternative and equivalent description that explicitly takes into account the geometrical position of glomeruli and mitral cells on the respective layers. A specific position on a layer is conveniently given in spherical coordinates (written as α, β or ϕ, δ) with origin in the middle of the bulb.

4.1 Glomerular Activity Image

Imagine a discrete vector field such that to every glomerulus a vector ("convergence" vector) $\mathbf{c}(\alpha, \beta)$ is assigned the lth component $c_l(\alpha, \beta)$ of which is the number of fibers of the lth receptor class that enter the glomerulus at α, β. Then, assuming stimulus S^k, let $\mathbf{r}^k$ be projected onto glomeruli according to

$$g(\alpha, \beta) = \mathbf{c}(\alpha, \beta) \cdot \mathbf{r}^k$$

for every pair α, β. The main difference from the previous description is that $g(\alpha, \beta)$ depends on two geometric coordinates instead of being a vector component. The components of $\mathbf{c}(\alpha, \beta)$ and $\mathbf{c}_n$ are identical for the same glomerulus.

$\mathbf{r}^k$ is mapped into a two-dimensional array $g(\alpha, \beta)$, which can be interpreted as a spatial image of the odor with analogue values at discrete points (the glomeruli) on a surface. The further processing of this image can thus be understood in terms of digital image processing and digital filtering.

4.2 Mitral Cell Input

The locally restricted glomerular mitral cell projection is given by

$$m(\phi, \delta) = \sum_{\alpha,\beta} p_{\alpha,\beta}(\phi, \delta)\, g(\alpha, \beta)$$

with $p_{\alpha,\beta}(\phi, \delta) = 0$ for $|\alpha - \phi| \geq \Delta\phi$ and $|\beta - \delta| \geq \Delta\delta$, and $p_{\alpha,\beta}(\phi, \delta) \geq 0$ otherwise.

The values $\Delta\phi$ and $\Delta\delta$ are determined by the spatial input range of a mitral cell (including excitatory interneurones). The filter coefficients $p_{\alpha,\beta}(\phi, \delta)$ determine the filter type: for every ϕ, δ, they equal zero except in a small region of the α, β-plane, the filters are thus spatial low-pass filters. If the filter coefficients were stationary in the spatial sense, i.e., $p_{\alpha,\beta}(\phi, \delta) = p(\alpha - \phi, \beta - \delta)$, Eq. 3 would become

$$m(\phi, \delta) = \sum_{\alpha,\beta} p(\alpha - \phi, \beta - \delta)\, g(\alpha, \beta),$$

where the sum is taken only for some small values $\alpha - \phi$ and $\beta - \delta$. This has the form of a convolution, and the low-pass character is more obvious. It might, however, well be (and seems, in fact, more plausible) that for every mitral cell the filter coefficients are different, i.e., the coefficients are not stationary. In any case, every mitral cell acts as a low-pass on the glomerular image, sampling and processing only a small part of it. The glomerular image is low-pass-filtered by 25 times more mitral cells than there are glomeruli. Adjacent mitral cells, which get input from (almost) the same set of glomeruli, therefore get similar inputs that differ in being different linear combinations of the filter input.

4.3 Mitral Cell Output Image

The mitral cell input function m^k is transformed into a mitral cell output function b^k by

$$b^k(\phi, \delta) = \sum_{\alpha,\beta} s_{\alpha,\beta}(\phi, \delta)\, m^k(\alpha, \beta).$$

Again, negative values are discarded: $a^k(\phi, \delta) = \max [0, b^k(\phi, \delta)]$. a^k is a function which assigns to the mitral cell at (ϕ, δ) the activity $a^k(\phi, \delta)$. a^k is thus the spatial activity pattern of mitral cells on the two-dimensional mitral cell layer.

5. DISCUSSION

5.1 Topographical Projection vs. Specificity Projection

The view of olfactory coding in this paper is different from previous approaches with respect to three points: (*a*) A topological description of the system has not been made previously. (*b*) The multidimensionality of the problem and the mapping of the multidimensional receptor activity space on certain subspaces has not been taken into account in a formal way. (*c*) The receptor-bulbar projection is usually considered as a geometrical projection, i.e., the mapping of a specific point or area of the mucosa onto the olfactory bulb (47–50). The experiments concerning this question have revealed, however, that specificities seem to be distributed over the mucosa in a mosaic-like way (40). On the other hand, it has been known from electrophysiological experiments (32,79) that a proper description of odorous stimuli demands more than two dimensions. A two-dimensional order of the receptor sheet could thus not be expected. But if there is little or no order with respect to specificity in the mucosa, then there is the question of how the system succeeds in mapping multidimensional events (odor stimuli) onto the two-dimensional layers of the bulb so that no information is lost. The concept proposed here maintains that receptor cells and fibers are mapped on certain glomeruli according to their receptor specificity rather than to the receptor cell coordinates in the mucosa. In other words, specificities are the starting points of projection, fairly independently of receptor position and, of course, from how specificity was established. This does not exclude that there might exist some sort of order in the mucosa due to development and regeneration. If one assumes, for instance, the existence of only three specifici-

ties (three receptor classes) the coding mechanism described above is easy to imagine (the multidimensional case is merely an extension). If each of three receptor cells shows a certain activity in response to a stimulus, these three activities correspond to a point in a three-dimensional vector space, imaginable, e.g., as a room. The points corresponding to many different odors can obviously not be mapped uniquely onto two dimensions. One could, however, take the projection of every point on two walls (subspaces) of the room. The two projected points corresponding to a stimulus are equivalent to the position of one point in three dimensions. In more dimensions, the same principle is realized by projecting a multidimensional point in the space R on many subspaces in the space M, i.e., on many small areas of the mitral cell layer. The special point here is that points in a region of a higher dimensional space, the receptor class activities, can be represented by points in several lower dimensional spaces, the mitral cell activities, in an equivalent way without any loss of information. The precise structure of the mitral cell activity pattern depends obviously on the coefficients that define the connectivities which in turn may depend on the species studied. The relative structure of two patterns corresponding to two similar stimuli follows from the fact that a small difference between receptor activity vectors is proportional to small variations of all values $m^k(\phi, \delta)$, i.e., when switching from a stimulus S^k to a similar stimulus S^i, the spatial input pattern of mitral cells is only slightly altered. Similarity of odors (in the multidimensional space R) is transformed into geometrical vicinity of activated cells on a two-dimensional surface. These predictions, which result from the proposed coding concept, will probably soon be checked by spatial activity measurements with voltage-sensitive dyes.

5.2 Two Kinds of Discrimination

From the paragraphs 3.2*d* and 3.3 it is clear that odors which are similar in the receptor cell activity space are mapped on similar and spatially adjacent glomerular and mitral cell activity patterns. Thereby a (necessary) spatial order relation among odors is introduced.

To elucidate the essence of this mapping, imagine a response vector **r** as a histogram or component profile, each bar of which gives the activity of a receptor cell class. Assuming five receptor cell classes we could have a histogram as in Fig. 4 *a*. This histogram is basically different from those in Fig. 2 in that it is the system's point of view observing one stimulus, whereas the histograms in Fig. 2 are rather the electrophysiologist's point of view observing the responses of one cell to several stimuli. Now it is important to note that the coding problem of the olfactory system is not to filter histograms like this (Fig. 4 *a*) to get some components more pronounced and others suppressed. The problem is rather to distinguish one histogram of this type as a whole from others which may be very similar (Fig. 4 *b*). This aim could, of course, not be accomplished

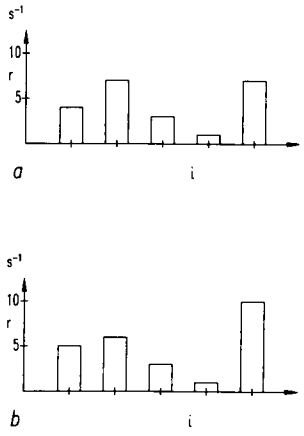

FIGURE 4 Activity spectra for two stimuli. The response activities r of five receptor cell classes $i = 1, 2, 3, 4$, and 5 are shown. The stimuli in parts *a* and *b* of the figure differ only slightly.

by a network of mutually inhibited neurones the first of which receives input only from receptor class 1, the second only from class 2, etc. Such a network would act as a high-pass on every single (input) histogram, sharpening the contrast of the bars within the histogram. In fact, the olfactory system works in a different way in that one component profile stimulates a certain set of mitral cells and that a similar component spectrum, i.e., a similar stimulus, stimulates a spatially slightly different pattern. Mutual lateral inhibition of these patterns means that the one pattern suppresses the other one or vice versa depending on which stimulus is stronger. Lateral inhibition at the mitral cell level has thus the effect that the contrast between the images of component profiles is enhanced. Similar odors can thus be well discriminated at mitral cell level.

5.3 Connection Pattern and Self-Organization

The construction of an intelligent artificial nose corresponding to a biological system poses one major practical problem: how should the connections between the three main element types (receptor cells, glomeruli, and mitral cells) be arranged? At present these connections are not known; it is therefore impossible to copy them. However, during the last years some interesting ideas about the formation of glomeruli have emerged: based on substantial experimental evidence, Graziadei has put forward the idea that "the glomerulus is determined by the reciprocal recognition of subsets of complementary axons originating from different areas of the sensory sheet and converging in the fiber plexus" (27). In this view, recognition can be of molecular nature and does not necessarily need targets other than receptor cells. The problem with Graziadei's hypothesis is that we can presently not define what is meant exactly by "complementary." One possibility would be that receptor cells which are complementary in Graziadei's sense show a high probability for being simultaneously active when stimulated. The joint probability for receptor cells to be active at the same time is highest for fibers of the same receptor class. Accordingly, every

glomerulus would receive input from one receptor class only, and there would be only one nonzero component in every convergence vector **c**. At the first glance, such a convergence pattern is appealing in that every two convergence vectors are orthogonal,

$$\mathbf{c}_n \cdot \mathbf{c}_l = 0 \quad \text{for } n \neq 1,$$

i.e., every vector **r** is decomposed into its receptor cell class components. A mitral/tufted cell receiving input from glomeruli $n-2$, $n-1$, n, $n+1$, and $n+2$ is therefore tuned (due to its morphological input pattern) to some linear combination of the receptor class activities $n-2$, $n-1$, n, $n+1$, and $n+2$.

A modified kind of the same type of self organization follows. It might occur that two (or more) receptor classes respond almost always in a proportional way to stimuli. These cells could be defined complementary. In this case the joint probability for being simultaneously active is almost as high as for cells of the same receptor class, and axons of both classes would enter the same glomerulus. As the activity of either class is redundant with respect to the other, this convergence does not mean a loss of information. It merely corresponds to a reduction of dimensionality as mentioned above.

One might also imagine a third kind of self organization of this type. As a natural stimulus hardly ever occurs at one precise concentration, the receptor fibers of all those classes that are involved in the coding of the mean concentration range of this stimulus would enter one glomerulus. This mechanism would lead to a competition of receptor classes for glomeruli because the total number of fibers per glomerulus is finite and fibers of many receptor classes would tend to enter the same glomeruli. The convergence pattern that would evolve would then depend on the specific (currently unknown) self-organization rule.

Considering these various possibilities of self-organization is certainly useful in that it suggests new behavioral, electrophysiological, and morphometrical experiments. It might, however, be even more useful to have somewhat more precise hypotheses for the design of new experiments. These can be obtained by applying Monte Carlo simulations on the system. Such simulations can show the effects of certain stimulus variations upon the spatial mitral cell activity pattern. In particular, it is possible to allow the coefficients $c_1(\alpha, \beta)$, $p_{\alpha,\beta}\, c(\phi, \delta)$, and $s_{\alpha,\beta}\, c(\phi, \delta)$, to vary with time; in this way, hypotheses on glomerulogenesis can be tested and processes of adaptation, habituation, and regeneration after injury (88) can be investigated.

5.4 Quality Detection and Associative Memory

An artificial nose built according to the principles above (receptors, orthogonal decomposition of receptor cell class activities, and linear combination of these) would work quite well if the patterns of interest were filed up in a library and if odor-induced spatial patterns were compared with the library patterns. Of course, it would be much simpler if all spatially different patterns belonging to the same stimulus quality would be seen as a whole. There is, however, no experimental evidence how the olfactory system might associate the same quality with the different sets of mitral cells activated by different concentrations. Among the various possibilities, two are particularly easy. Either all patterns of a quality converge to the same set of cells in the next stage of information processing, or the quality association is made by excitatory connections within the olfactory bulb. In vertebrates, there appear to be several cell types in the olfactory bulb that mediate excitation (for the variety of occurring transmitters, see references 12 and 29). If such connections formed between simultaneously active mitral cells, the spatial pattern of the positions of active mitral cells would be identical for all concentrations of an odor though the single cell activities within the pattern would vary with concentration. In other words, the invariant perception of odor quality would be accomplished by an associative memory mechanism within the olfactory bulb (for a thorough treatment of associative and content-addressable memories, see reference 44). As in all cases of associative memory, partial input information (only one specific concentration of a stimulus) provokes complete output information (the quality pattern associated with all concentration values). The fact that the output of the olfactory bulb does not enter a closed nucleus such as the bulb itself, and that mitral/tufted cell fibers make contact with a large variety of nuclei, might suggest that the quality invariance is, in fact, established before information spreads to many parts of the brain, i.e., within the olfactory bulb. However, more detailed morphological evidence concerning mutually excitatory cell connections as well as multi-unit electrophysiological recordings are needed to confirm or reject this mechanism experimentally.

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