Two minds about odors

Leslie M. Kay*
Department of Psychology, Institute for Mind and Biology, University of Chicago, Chicago, IL 60637

It has long been suggested that synchronous fast oscillations in central sensory systems facilitate formation of neural assemblies that represent sensory objects. This hypothesis derives from the olfactory system, where odor-evoked fast oscillations of 40 Hz and above in the local field potential of the mammalian olfactory bulb (OB) were first reported by Adrian (1). Similar oscillations (~20 Hz) were observed half a century later in the insect mushroom body (MB) driven by antennal lobe (AL) synchrony (2). Two reports have shown empirical evidence that the relative power of fast oscillatory activity represents underlying neural synchrony and correlates in a general way with the ability of the animals (mice and honey bees) to discriminate chemically similar stimuli (3, 4). These studies together suggest that more oscillatory synchrony allows better discriminability and that less synchrony degrades discriminability of chemically similar odors. What these studies do not address is the advantage of not discriminating odors in some circumstances, of clustering odors by chemical or other features.

In this issue of PNAS, a computational model by Sivan and Kopell (5) addresses odor clustering in the insect olfactory system. The authors ask how the same system can be very efficient at both sensory object clustering and fine discrimination of similar objects. This is indeed an important question, particularly when we consider the functional structure of olfactory systems in diverse animals. Sivan and Kopell show that the modular structure of the insect system is capable of accomplishing both of these tasks in parallel pathways, so that discriminating individual odors is anatomically separate from, but simultaneous to, odor clustering.

Computational Nature of Odor Discrimination and Clustering

The striking similarity of separately evolved olfactory systems in insects and mammals drives speculation that convergent evolution has yielded a good solution to the odor coding and discrimination problem (6, 7), and, by focusing on their similarities, we may better understand the puzzling nature of odor quality. Despite the number of decades over which olfactory psychophysics and neurophysiology have been studied, we have surprisingly few insights into the definition of olfactory space. This may be because of the likelihood that olfactory space is partially represented by receptor families that could yield hundreds of dimensions (8, 9). Until recently, even the structure of sensory input to the AL and OB appeared indefinable; we now know that there is probably a receptor-defined input space in insects and mammals (10, 11). A spatial structure to neural responses appears at the first olfactory relay in insects and anesthetized or passive mammals and depends, at least partially, on molecular class; such structure has been shown to be perceptually relevant in some cases (12–15). Classes have been defined provisionally by similarities and differences in chemical structure, presumed to represent a lock-and-key mechanism in binding to olfactory receptors (ORs). However, we still have little insight into the nature of the structural features that define perceptual similarities, the odors that may group into perceptual classes, and the rules that govern such grouping. Recent analysis of connectivity in the very similar insect and mammalian olfactory systems may now allow systematic approaches to this previously intractable problem (16, 17). Computational models may be one of the major factors in the solution, allowing development of multiple testable hypotheses derived from existing anatomical and physiological data.

The olfactory system has been modeled in many forms, and the similarity of structure across phyla facilitates generalizations of functional architecture across models of invertebrate and vertebrate systems. Some models aim at biological detail at levels spanning from single cells to large populations, using only the simplifications necessary for the scale being addressed. Other models focus on functional realism without explicit cellular precision, attempting to capture the essence of system-level phenomena. The differences between these modeling strategies may not be as large as they appear at first glance. The goal of modeling is often to simplify a system to its functional essence appropriate to the question at hand, either to make predictions about unknown processes or to understand the computational nature of known processes. If these processes involve specific cell physiology, then biological details are essential. If these processes involve system-level behavior, then less biological realism may be essential in some cases to avoid ever-expanding parameter sets. One of the difficulties in developing a functional model lies in the choice of the amount and type of detail to retain.

Several models have addressed fine odor discrimination since publication of the phenomenon (4), and each has implemented synchrony and the failure of fine discrimination in a different way. One model proposes cell assemblies within the AL that develop during learning (18). Another invokes a metabotropic GABA receptor to account for slow temporal patterning, with complete discrimination of odorants requiring longer time frames in some cases (19). In this issue of PNAS, Sivan and Kopell (5) also provide a mechanism for fine discrimination, but this model is novel in that it proposes clustering mechanisms that do not rely on chemical similarity. They address this problem at a functional level but adhere to anatomical realism in both system connections and relative numbers of neurons. The neurons themselves are rather simple integrate and fire units, and there is no attempt to include the details of infrastructural connectivity. They directly address the role that synchrony and oscillations play in fine tuning odor discrimination. They also discuss the advantages of odor clustering without making specific assumptions about molecular features that may be used for this. The authors do this with relative simplicity, invoking structural information derived from two insect species, fruit flies and locusts, and by using combinatoric inferences to predict the average size of functional subsets (FSSs) composed of nonoverlapping sets of projection neurons (PNs), Kenyon cells (KCs), and lateral horn inhibitory neurons.

How can the same system be efficient at sensory object clustering and fine discrimination of similar objects?
neurons (LHIs). Odor class responses are produced by the broad responses in the lateral horn, whereas fine discrimination is accomplished by KC odor specificity, requiring precise timing of spikes from a number of PNs. The modular architecture is based on PN classes that purposely remain undefined. It is this last point that makes the model very evocative for thinking about odor representations.

Implications of Functional Subsets and Odor Clusters

It is important to remember that animals do generalize behaviorally to chemically similar odors in some circumstances, even though they are quite capable of discriminating any two odors with an intact olfactory system. Generalizations may go beyond the dimensions of chemical similarity, particularly when an animal encounters odor mixtures, which are closer to natural stimuli than monomolecular compounds. In many cases it may be desirable to “mistake” one odor for another, as viable food sources appear at different ambient temperatures or within a window of acceptable decomposition. The functional subset hypothesis therefore suggests some predictions regarding odor classes and perceptual similarity that may in fact be independent of chemical structure. Functional subsets appear to exist anatomically, at least in Drosophila (17). The structure suggests that there may be classes of ORs that evolved and develop together, and that may respond to a set of odors that belongs to a specific class by virtue of structural similarities or even a common food source. Structural similarities predict as-yet-unknown similarities among the ligands for these receptors. Clustering independent of ligand structure suggests even more interesting possibilities and gets at the confusing and conflicting nature of odor mixture quality. It may be possible to understand what defines an odor class in an ethological sense by working backwards from LHIs to identify classes of odor receptors and, in turn, using these receptor classes and their ligands to understand features that contribute to a perceptual class. Several recent studies of OR neurons have succeeded in uncovering ligand repertoires for individual ORs and families of ORs (20). A recent study has used 3D molecular reconstruction to suggest a fine structure to activation subregions in rat OB glomeruli (21). Comparative work has begun to address the structural determinants of perceptual similarity by using behavioral discrimination of similar aliphatic molecules and enantiomers (22–24) and mixture component recognition (25, 26). However, there remain many problems with understanding complexities of mixture perception that seem to defy the receptor ligand–molecular similarity argument. Working backwards from anatomical subsets may be one of the important missing pieces and may, in fact, decrease the dimensionality represented by the number of ORs.

The model presented by Sivan and Kopell (5) also suggests hypotheses regarding development and evolution of FSs. These subsets of PNs could be hard-wired and may develop from the same deutocerebral neuroblast progenitor cells (27), or predetermined subsets may organize during development to define the FSs (28). The structure suggests an evolutionary process in which more primitive organisms had smaller numbers of subsets that still contained enough variability of receptors within each FS to capture the repertoire of odors that the organism might encounter. This hypothesis is similar to that seen in iteration of insect body segments and genes in vertebrates and invertebrates (29, 30). There is some evidence that this evolutionary model exists in mammalian sensory cortex as well (31). These and other hypotheses await a convergence of recently developed tools in molecular biology, anatomical tracing, and sophisticated physiological and behavioral studies (4). Such technical advances together with the model proposed by Sivan and Kopell put us in a good position to begin to understand odor space.

Clustering independent of ligand structure gets at the confusing and conflicting nature of odor mixture quality.