Odors, Oscillations, and Waves: Does It All Compute?

D. W. Tank, A. Gelperin, D. Kleinfeld

Science, New Series, Volume 265, Issue 5180 (Sep. 23, 1994), 1819-1820.

Odors, Oscillations, and Waves: Does It All Compute?

D. W. Tank, A. Gelperin, D. Kleinfeld

Half a century ago Lord Adrian led wires from the olfactory bulb and cortex of a hedgehog to an amplifier and recorded an "induced wave" of coherent 50-Hz oscillations in response to stimulation of the olfactory mucosa (*1*). Similar oscillations of neural activity have now been recorded from olfactory systems in a variety of vertebrates [see references in (*2*)], including those in bony fish, frog, turtle, rodent, opossum, rabbit, cat, and humans. At least one vertebrate, the tiger salamander (*3*), shows odor-induced but nonrhythmic dynamics. The ubiquity of fast oscillations in the olfactory bulb suggests that they are fundamental to the computations performed to process odor stimuli. Two recent findings in invertebrates, one in a mollusk (*4*) and the other in the locust, as reported by Laurent and Davidowitz on page 1872 of this issue (*5*), add support to this notion.

The findings in a mollusk are oscillations and waves of electrical activity in the procerebral lobe of *Limax maximus*, a large terrestrial slug. *Limax* uses olfaction as its primary sensory modality and shows complex forms of associative conditioning to odor stimuli. The procerebral lobe is a prominent appendage to the cerebral ganglion that contains about 100,000 interneurons and receives projections from both superior and inferior tentacles the sites of olfactory sensory epithelia. Field potential recordings show that the lobe produces robust 0.7-Hz oscillations in vitro (*4*) as well as in vivo. The oscillations in *Limax* are continuously present, a finding consistent with the continuous monitoring of airborne odors by these animals and different from that in vertebrates, where oscillations occur only during the sniff cycle. Beyond the purely temporal nature of the oscillations in *Limax*, experiments that employ optical imaging techniques show that the oscillations are part of a repetitive traveling wave of electrical activity that sweeps along the length of the lobe (*6*). The application of natural odor stimuli to the olfactory receptors causes the activity along the lobe to transiently switch from the state with traveling waves to one with spatially uniform oscillations. Thus the appearance of odor, but apparently not its identity, is signaled by coincident activity of neurons throughout the lobe.

The most recent discovery in invertebrate olfaction involves oscillations in the olfactory system of the locust, as discussed by Laurent and Davidowitz (*5*). This study builds on Laurent's previous finding of odor-induced oscillations in the electrical activity of neurons in the mushroom body (*7*), an area of the locust cerebral ganglion that receives secondary input from the olfactory receptors and is known to be important in olfactory-based associative learning in *Drosophila* (*8*). The oscillation has a frequency near 20 Hz and appears as a rhythmic synaptic drive to Kenyon cells, the intrinsic interneurons of the mushroom bodies. In the present report, Laurent and Davidowitz demonstrate that the oscillation is, in fact, produced in the antennal lobe, a structure that provides input to the mushroom body. The antennal lobe has many anatomical features, such as dense spherical glomeruli which contain olfactory receptor axon terminals and the dendrites of interneurons, that suggest that the antennal lobe is a structural analog of the vertebrate olfactory bulb. The major excitatory neurons in the antennal lobe are the projection neurons (PNs), so named because they are the major output projection from the lobe. The PNs appear to be functionally analogous to mitral cells, the PNs in the vertebrate olfactory bulb. One of the remarkable discoveries presented in the new work with the locust is the similarity between the firing properties of PNs and those previously demonstrated for mitral cells in the bulb.

We focus on three similarities between PNs in the locust antennal lobe and mitral cells in the vertebrate olfactory bulb. First, those neurons that actively spike during an odor response tend to do so in phase with the field potential oscillation; the absolute phase is relatively constant across the antennal lobe or olfactory bulb (*9*). Intracellular recordings from PNs or mitral cells show subthreshold oscillations in membrane potential at the frequency of the field potential (*10*) [compare Fig. 1A with figure 2A in (*5*)]. Second, both cell types respond to more than one odor but not all odors in a test sequence. This implies that there is a subset of neurons in the lobe or bulb whose

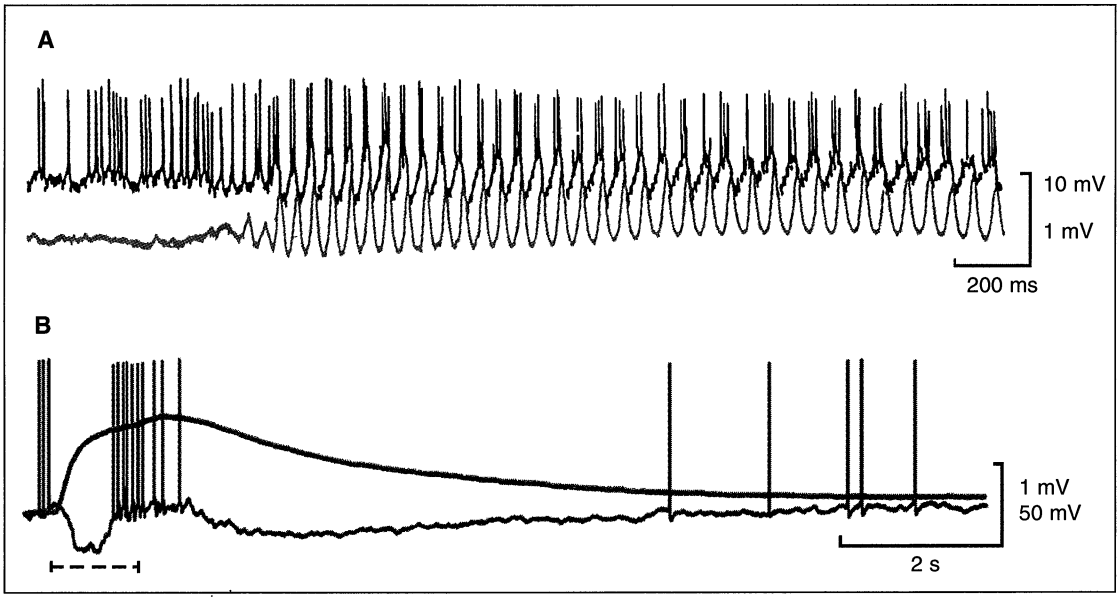

Fig. 1. (**A**) Intracellular recording of membrane potential from a mitral cell (upper trace) and simultaneously recorded odor-induced oscillations in extracellular field potential (lower trace) in the olfactory bulb of the carp. [Data of T. Hasegawa, M. Satou, and K. Ueda, adapted from (*10*)] (**B**) Intracellular recording from a tiger salamander mitral cell showing sequential phases of inhibition and excitation (lower trace) in response to a puff of odor (dashed line) and concomitant potential at the olfactory receptor epithelia (upper trace). [Adapted from Hamilton and Kauer (*11*)]

The authors are in the Biological Computation Research Department, AT&T Bell Laboratories, Murray Hill, NJ 07974, USA.

firing can uniquely identify each odor but that the subsets of neurons that respond to different odors overlap. Last, with respect to the odor-induced response that occurs on a time scale long compared to the fast oscillations, a given PN or mitral cell can have several transient phases of excitation and inhibition [compare figure 1B and figure 4 in (5)]. Kauer and others have studied this slow behavior extensively in the olfactory bulb of vertebrates and demonstrated that the time course of activity is associated with differences in odor concentration (*11*); this issue has yet to be explored in the locust. In toto, these features imply that the response to an olfactory stimulus is a temporal sequence of oscillating neuronal subpopulations. The specific subpopulations in the sequence are odor-dependent, which suggests that the spatiotemporal dynamics of neuronal firing may constitute a code, with different spatiotemporal patterns labeling different odors.

Freeman and colleagues have reached a different conclusion from other researchers, including Laurent and Davidowitz, with regard to when an odor-specific, spatiotemporal code is observed. Freeman performed an extensive series of experiments to record spatial patterns of oscillations from the awake rabbit with an array of electroencephalogram (EEG) electrodes implanted on the surface of the olfactory bulb (9). He and his colleagues find that spatial patterns of the oscillatory activity that are odor-specific are observed only when an animal performs an odor-discrimination task and even then, only in the first few odor presentations. Changes in the EEG pattern for different odors are subtle and require extensive processing of the data to resolve. In contrast, the intracellular measurements of Laurent and Davidowitz and others (*10,11*) suggest that spatiotemporal codes for a given odor are a robust phenomenon at the single-cell level and are stable over long periods of time. To reconcile Freeman's EEG results with the intracellular results, it may be that information about individual odors is coded on a spatial scale that is unresolved by the averaging inherent in measurements of surface potentials (*12*).

The observation of oscillations and odor-induced responses with similar features in olfactory interneurons from species as different as the locust and fish is truly remarkable. But what, if any, is the functional role of oscillations in the processing of odor stimuli? Unfortunately, the new results in invertebrates shed no additional light on this crucial question. There are, however, several current hypotheses to guide future experiments.

One idea for the functional role of oscillation revolves around the issue of readout and coordination of spatially distributed neuronal populations. In general, synchronized spiking that produces maximum summation of postsynaptic potentials should be more effective than random spike events at the same mean rate for the activation of specific postsynaptic neuronal populations. Why might the olfactory system require an internal mechanism for achieving synchrony? The timing of olfactory signals is likely to be relatively coarse for vertebrates, on the 0.1- to 1-s time scale of a sniff, and possibly as coarse for insects as they follow odor plumes. Thus, a fast clock may provide a mechanism to synchronize otherwise temporally uncorrelated spike events from receptor neurons on the tens of milliseconds time scale of dendritic integration. Electrophysiological properties at the cellular level that could provide the basis for this type of synchrony have been reported by Lampl and Yarom (*13*) for the response of neurons in the inferior olive.

A related role of oscillations may be to modulate the synchrony of populations of neurons that simultaneously process multiple odors. This idea has been suggested in the context of the stimulus-dependent 40-Hz oscillations observed in the cat visual cortex [reviewed in (*2*)]. In that system, the synchrony between oscillating activity in two regions of cortex depends on features of the stimuli; similarly moving bars can lead to strong synchrony between neurons in the two regions, whereas dissimilarly moving bars yield independent oscillations in each cortical region that are not phase locked to each other. It is intriguing to think whether a similar phenomenon might be produced in the olfactory bulb or locust antennal lobe by the simultaneous presentation of two well-known odors.

Last, a role for oscillations complementary to those above may be to activate synaptic plasticity. In the mammalian hippocampus, spike activity at the theta rhythm is highly effective in producing synaptic plasticity. Of particular relevance to the work reported here is the enchancement of synaptic potentiation in the mammalian piriform cortex, the target of mitral cell output, when stimuli arrive at the theta frequency (*14*). Although the frequency of the theta rhythm is slower than that for the fast oscillations seen in vertebrate olfactory bulbs and the locust antennal lobe, the synchronous oscillation of neurons in olfactory circuits may nevertheless be a "write" signal for changing the strengths of their mutual synaptic connections or of their connections with neurons downstream. In this view, oscillations will contribute to the formation of cell assemblies for different odors.

A most exciting aspect of the new work on the locust is that this preparation seems to offer significant technical advantages over vertebrates as a means to address the functional role of oscillations. In particular, a fundamental and unresolved question is whether nervous systems use synchrony on a cycle-by-cycle basis to shape behavior or rather make use of spiking activity averaged over many cycles. In locust olfaction, as has been done for fly vision, it may be possible to sense the intended motion produced by an immobilized insect in response to pulses of odor and thus measure behavioral responses concurrent with electrical activity on the time scale of the oscillation. Further, the olfactory system in the locust is homologous to that in *Drosophila*, opening the possibility of constructing olfactory mutants of *Drosophila* to test hypotheses derived from measurements on the locust. The data provided by such experiments will be needed before we can truly answer the question: "Does it all compute?"

References

1. E. D. Adrian, *J. Physiol. (London)* **100**, 459 (1942).
2. C. M. Gray, *J. Comput. Neurosci.* **1**, 11 (1994); K. L. Ketchum and L. B. Haberly, in *Olfaction: A Model System for Computational Neuroscience*, J. L. Davis and H. Eichenbaum, Eds. (MIT Press, Cambridge, 1991), p. 69.
3. J. A. Kauer, *Nature* **331**, 166 (1988).
4. A. Gelperin and D. W. Tank, *ibid.* **345**, 437 (1990).
5. G. Laurent and H. Davidowitz, *Science* **265**, 1872 (1994).
6. K. R. Delaney *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **91**, 669 (1994); D. Kleinfeld *et al.*, *J. Neurophysiol.* **72**, 1402 (1994).
7. G. Laurent and M. Naraghi, *J. Neurosci.* **14**, 2993 (1994).
8. R. H. Davis, *Neuron* **11**, 1 (1993); J. S. deBelle and M. Heisenberg, *Science* **263**, 692 (1994).
9. W. J. Freeman, *Electroencephalogr. Clin. Neurophysiol.* **44**, 586 (1978); F. H. Eeckman and W. J. Freeman, *Brain Res.* **528**, 238 (1990).
10. M. Satou, *Prog. Neurobiol.* **34**, 115 (1990).
11. J. A. Kauer, *J. Physiol. (London)* **243**, 695 (1974); T. A. Harrison and J. W. Scott, *J. Neurophysiol.* **56**, 1571 (1986); K. A. Hamilton and J. A. Kauer, *ibid.* **62**, 609 (1989).
12. W. J. Freeman and B. Baird, *Behav. Neurosci.* **101**, 393 (1987); G. Viana Di Prisco and W. J. Freeman, *ibid.* **99**, 964 (1985).
13. I. Lampl and Y. Yarom, *J. Neurophysiol.* **70**, 2181 (1993)
14. E. D. Kanter and L. B. Haberly, *Brain Res.* **525**, 175 (1990); M. W. Jung, J. Larson, G. Lynch, *Synapse* **6**, 279 (1990).