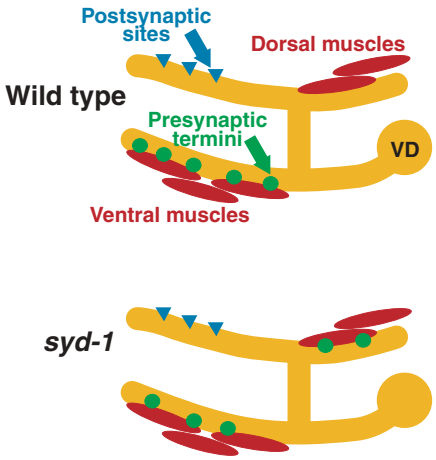

Fig. 1. Each VD neuron extends a single process that is spatially segregated into dendritic and axonal branches in wild-type worms. The dorsal branch functions as the dendrite and contains no presynaptic terminals; the ventral branch functions as the axon and forms synapses onto ventral muscles. In *syd-1* mutants, the formation of dorsal and ventral branches is unaltered, but the dorsal branch accumulates presynaptic components and forms synapses onto dorsal muscles.

The presence of a potential rhoGAP domain in SYD-1 suggested a possible connection between SYD-1 and the control of actin dynamics. As the Rho family of small GTPases is important in regulating actin dynamics, rhoGAPs can have powerful effects on neuronal morphogenesis[8]. This is especially intriguing given the contribution of F-actin dynamics to axon formation in culture (see above). However, the sequence of the rhoGAP-related region in SYD-1 contains unusual amino acids at positions important for the catalytic activity of other rhoGAPs. Hallam *et al.*[1] examined this issue further by creating a series of mutant forms of SYD-1 and reintroducing them into wild-type and *syd-1* mutant worms. Interestingly, none of the point mutations predicted to alter GAP function had dramatic effects on SYD-1 function in the animal. However, expression of a SYD-1 lacking the GAP domain caused strong dominant disruptions in neurite outgrowth. Thus, the GAP domain is important for appropriate SYD-1 function, but it may not function like a traditional GAP.

The next step will be to determine what the targets of SYD-1 are and how they act to control the localization of presynaptic components to the appropriate neurite. Mutations that disrupt the SAD-1 protein kinase, a relative of the PAR-1 kinase that regulates the polarity of asymmetric cell divisions, also cause presynaptic markers to be inappropriately sorted into presumptive dendrites[9], and it will be of interest to examine the relationship between SAD-1 and SYD-1. Determining the mechanism by which SYD-1 is specifically localized to axons will also shed light on upstream regulators of SYD-1. Detailed analysis of early stages of neuronal development and the use of conditional mutants may help determine the stage at which SYD-1 is required during outgrowth. Such work would be greatly facilitated by molecular markers permitting dendritic characteristics to be assessed with ease. Nonetheless, the identification of SYD-1 provides a springboard for uncovering the mechanisms that permit the processes from a single neuron to acquire such remarkably distinct identities.

1. Hallam, S. J., Goncharov, A., McEwen, J., Baran, R. & Jin, Y. *Nat. Neurosci.* **5**, 1137–1146 (2002).
2. Bradke, F. &. Dotti, C. G *Curr. Opin. Neurobiol.* **10**, 574–581 (2000).
3. Andersen, S. S. L. & Bi, G. *Bioessays* **22**, 172–179 (2000).
4. Bradke, F. & Dotti, C. G. *Science* **283**, 1931–1934 (1999).
5. Esch, T., Lemmon, V. & Banker, G. *J. Neurosci.* **19**, 6417–6426 (1999).
6. Nonet, M. J. *J. Neurosci. Methods* **89**, 33–40 (1999).
7. Hallam, S. J. & Jin, Y. *Nature* **395**, 78–82 (1998).
8. Luo, L. *Nat. Rev. Neurosci.* **1**, 173–180 (2000).
9. Crump, J. G. *et al. Neuron* **29**, 115–129 (2001).

AMPA autoreceptors fill the gap in olfactory temporal coding

W. Martin Usrey

A new study uncovers a possible mechanism, involving gap junctions and AMPA autoreceptors, to promote near-synchronous activity in mitral cells of the mammalian olfactory bulb.

Since the earliest recordings from sensory neurons by Adrian[1,2] and Hartline[3], it has been recognized that sensory information is encoded in the firing rate of individual neurons. Generally speaking, as the intensity of a sensory stimulus increases, so does the firing rate of specific neurons along that sensory pathway. Although such 'rate codes' are certainly prevalent in the nervous system, information may also be encoded in the precise timing of neural responses. Synchronized or correlated activity among ensembles of neurons has been proposed to carry sensory information (reviewed in ref. 4). It is hotly debated whether temporal coding occurs in the mammalian nervous system, but there is general agreement that spike timing is involved in information processing in the olfactory system of insects. For instance, odor discrimination in the honeybee is impaired if the activity of neurons in the antennal lobe and mushroom body becomes desynchronized[5]. In this issue, Schoppa and Westbrook describe a mechanism for the production of near-synchronous (< 10 ms) correlated spikes by pairs of mitral cells in the mammalian olfactory bulb[6].

The mammalian olfactory bulb, the earliest stage of odor processing, is an attractive model for information processing in the brain. The surface of the olfactory bulb is covered with numerous glomeruli that are approximately 30–50 m in diameter. Each glomerulus consists of a spherical region of neuropil containing axons of olfactory receptor neurons, processes of periglomerular cells and apical dendrites of mitral and tufted cells (**Fig. 1**). A major breakthrough in our understanding of olfactory processing occurred in the mid-1990s, when it was recognized that individual glomeruli receive input only from olfactory receptor neurons that express the same odorant receptor[7,8]. As a result, mitral cells that extend dendrites into common glomeruli receive input from the same class

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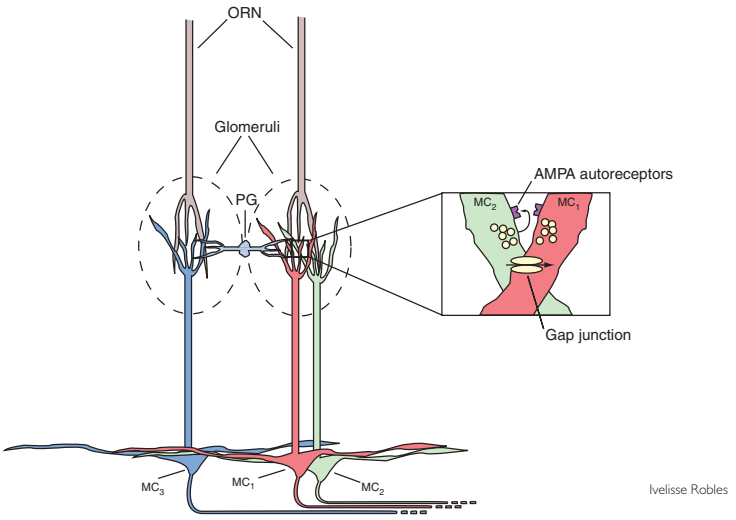

Fig. 1. Synaptic organization of olfactory bulb. Surrounding the olfactory bulb is an array of spherical glomeruli. Within each glomerulus, axons of olfactory receptor cells (ORN) form synapses with the apical dendrites of mitral cells($MC_{1,2\ and\ 3}$)—the only output cells of the olfactory bulb. Periglomerular (PG) cells also extend processes into each glomerulus. Although not shown here, in the mouse, each glomerulus contains the apical dendrites of ~25 mitral cells and the axon terminals of ~25,000 olfactory receptor cells. Schoppa and Westbrook[6] propose that mitral cells (e.g., $MC_{1\ and\ 2}$) that project to the same glomerulus can synchronize activity via AMPA autoreceptor activation and subsequent passage of current through gap junctions.

of olfactory receptors. Individual glomeruli, therefore, can be viewed as both anatomically and functionally defined modules for processing olfactory information.

Correlated oscillations (1–2 Hz) in neural activity have been reported for pairs of mitral cells that extend dendrites into the same glomerulus[9]. These slow oscillations depend on NMDA receptor activation and are presumed to result from spillover of neurotransmitter within the interior of individual glomeruli[9,10]. Because mitral cells are not directly connected to each other by chemical synapses[11–13], it was assumed that synchronous or fast correlations were not possible. Recent reports by Urban and Sakmann[14] as well as Schoppa and Westbrook[6] now demonstrate that nearly synchronous (< 10 ms) excitatory coupling and fast correlations also exist between pairs of mitral cells that extend apical dendrites into the same glomerulus. This finding opens the door for the possibility that fast correlations in mitral cell activity might be involved in odor processing in mammals, as previously suggested for insects.

Within the nervous system, fast correlations typically result from gap junction coupling, common excitatory inputs, or release from common inhibition (reviewed in ref. 4). Although gap junction coupling was not thought to occur between mitral cells, Schoppa and Westbrook now present evidence for gap junctions in this system[6]. The authors found gap-junctional coupling and near-synchronous activity between mitral cells that extend apical dendrites into the same glomerulus, but never between mitral cells that target different glomeruli with their apical dendrites.

In response to an initial depolarization, only a small amount of current passes through the gap junctions that couple one mitral cell with another[6]. This current is greatly amplified, however, by a new mechanism involving the activation of AMPA autoreceptors (**Fig. 1**). According to the authors' model[6], an action potential within a given mitral cell leads both to the passage of a small amount of current (insufficient to drive spikes) through gap junctions to adjacent mitral cells and to dendritic release of glutamate within the glomerulus. The released glutamate then binds to nearby AMPA autoreceptors located on the same mitral cell, and the cell responds with a much stronger depolarization. This AMPA-amplified signal is then passed via gap junctions to coupled mitral cells and, if above threshold, leads to near-synchronous discharge of action potentials in the two cells. Because correlated activity between pairs of mitral cells is extremely fast, the entire process of AMPA autoreceptor–amplified signaling must take just a few milliseconds to complete.

Whether or not correlated activity in the mammalian olfactory system is important for odor discrimination is an unresolved issue. Neurons in the antennal lobe of insects have been likened to those in the mammalian olfactory bulb, and disruption of correlated activity among antennal lobe neurons is known to degrade odor discrimination[5]. Although the experiment would be technically difficult, it would be extremely useful to know whether disruption of either the slow (1–2 Hz) oscillatory[9] or near-synchronous[6,14] activity of mitral cells has a similar influence on odor discrimination in mammals. Because individual glomeruli receive input only from olfactory receptor neurons that express the same odorant receptor[7,8], synchronously firing mitral cells with apical dendrites that target the same glomerulus can be viewed as members of a collective ensemble. In the visual system, synchronous activity among pairs of LGN cells increases the probability of driving postsynaptic spikes in the cortex[15]. If synchronous mitral cell spikes were to interact in a similar fashion, then these spikes would help ensure the processing of the olfactory signal originating from a given class of odorant receptors. There has been considerable debate over the years as to whether spike timing and correlated activity carry information in the visual, auditory and somatosensory pathways of mammals. With recent progress and promise in our understanding of information processing in the olfactory system, it seems likely that this system will be the first to provide a conclusive answer.

1. Adrian, E. D. *J. Physiol. (Lond.)* **61**, 49–72 (1926).
2. Adrian, E. D. & Mathews, R. *J. Physiol. (Lond.)* **63**, 378–414 (1927).
3. Hartline, H. K. & Graham, C. H. *J. Cell. Comp. Physiol.* **1**, 277–295 (1932).
4. Usrey, W. M. & Reid, R. C. *Annu. Rev. Physiol.* **61**, 435–456 (1999).
5. Stopfer, M., Bhagavan, S., Smith, B. H. & Laurent, G. *Nature* **390**, 70–74 (1997).
6. Schoppa, N. E. & Westbrook, G. L. *Nat. Neurosci.* **5**, 1194–1202 (2002).
7. Ressler, K. J., Sullivan, S. L. & Buck, L. B. *Cell* **79**, 1245–1255 (1994).
8. Mombaerts, P. *et al. Cell* **87**, 675–686 (1996).
9. Schoppa, N. E. & Westbrook, G. L. *Neuron* **31**, 639–651 (2001).
10. Isaacson, J. S. *Neuron* **23**, 377–384 (1999).
11. Price, J. L. & Powell, T. P. *J. Cell Sci.* **7**, 631–651 (1970).
12. Pinching, A. J. & Powell, T. P. *J. Cell Sci.* **9**, 347–377 (1971).
13. White, E. L. *Brain Res.* **37**, 69–80 (1972).
14. Urban, N. N. & Sakmann, B. *J. Physiol. (Lond.)* **542**, 355–367 (2002).
15. Alonso, J.-M., Usrey, W. M. & Reid, R. C. *Nature* **383**, 815–819 (1996).