Journal of Biology

BioMed Central

Minireview

Lateral inhibition and concentration-invariant odor perception

Susy M Kim and Jing W Wang

Address: Section for Neurobiology, Division of Biological Sciences, University of California-San Diego, 9500 Gilman Drive, MC 0368, La Jolla, CA 92093-0368, USA.

Correspondence: Jing W Wang. Email: jw800@ucsd.edu

Published: 26 January 2009

Journal of Biology 2009, **8**:4 (doi:10.1186/jbiol106)

The electronic version of this article is the complete one and can be found online at http://jbiol.com/content/8/1/4

Abstract

Sensory identity usually remains constant across a large intensity range. Vertebrates use lateral inhibition to match the sensitivity of retinal ganglion cells to the intensity of light. A new study published in *Journal of Biology* suggests that lateral inhibition in the *Drosophila* antennal lobe is similarly required for concentration-invariant perception of odors.

Adaptation is a fundamental neural mechanism for stable sensory perception in a changing environment. For example, our perception of the contrast between the black text and the white background of a page remains constant under a variety of illumination conditions ranging from indoor lighting to bright sunlight. In a manner similar to this, the olfactory system must be able to perceive the same odor identity across a wide range of concentrations. Why might this be important?

To navigate towards an odor source, a *Drosophila* larva must be able to recognize odor intensity as well as concentration-invariant odor identity. From physiological studies, however, we know that the odor response of odorant receptor neurons (ORNs) normally saturates within one or two orders of magnitude [1]. In addition, the number of ORNs activated by an odor increases with odor concentration - thus creating a shifting odor representation in the antennal lobe. Despite this, *Drosophila* larvae can navigate towards an attractive odor source across a much broader range of odor concentrations [2]. How does the olfactory system accomplish this? In this issue of *Journal of Biology*, Asahina *et al.* [3] use a highly effective synthesis of genetics, behavioral analyses and calcium imaging to uncover a neural circuit at early stages of the olfactory system for concentration-invariant odor perception. The data [3] suggest that properties of lateral inhibitory neurons are the key to understanding how perceptual constancy is achieved in olfactory circuits.

How might lateral inhibitory connections support adaptive functions in a sensory system? The well-studied vertebrate retinal circuitry is one of the best examples for sensory adaptation. Horizontal cells, a type of lateral inhibitory interneuron in the retina, integrate inputs from many cone photoreceptors and make inhibitory synapses back onto the presynaptic terminals of each cone photoreceptor. Neural activity in horizontal cells thus represents ambient light intensity and presynaptic inhibition of the corresponding cone photoreceptor scales with the ambient light intensity (Figure 1a). This effectively results in the transmission of information about the difference between local and ambient light intensity to the corresponding bipolar and retinal ganglion cells [4].

Analogous to the horizontal cells in the vertebrate retina, lateral inhibitory interneurons in the *Drosophila* adult olfactory system receive inputs from many ORNs of different glomeruli [5] and feed back onto presynaptic ORN terminals

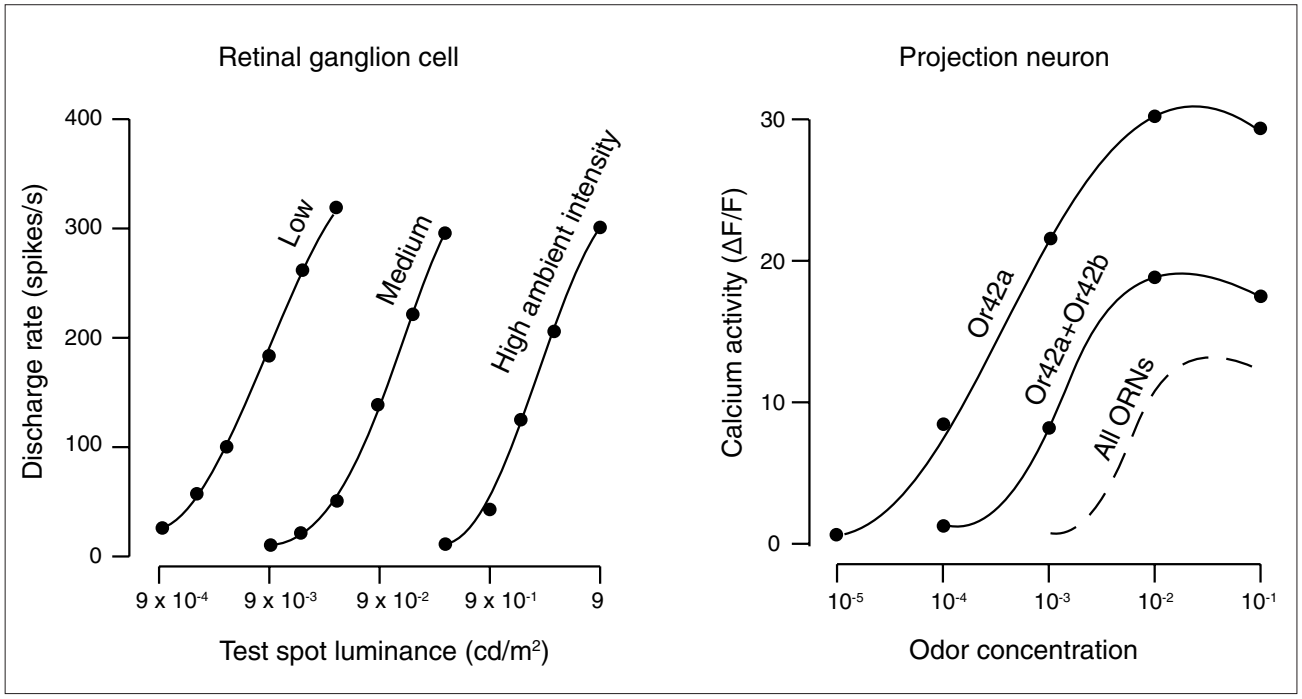

Figure 1
Similarities between lateral inhibition in the vertebrate retinal system and the insect olfactory system. **(a)** Ambient light intensity modulates light sensitivity in retinal ganglion cells. Modified from [4]. **(b)** Similarly, high odor concentrations recruit more odorant receptor neurons, down shifting the sensitivity of the corresponding projection neuron in *Drosophila* antennal lobe. Modified from Figure 7 of Asahina *et al.* [3], with the dashed line indicating potential projection neuron response in normal larvae.

through inhibitory connections. Two recent studies show that these local interneurons (LNs) provide a gain control mechanism to modulate olfactory sensitivity [6,7]. *Drosophila* larvae have a relatively simple olfactory system, with only 21 ORNs in the dorsal organ, each of which expresses a unique odorant receptor gene [8]. ORNs make synapses with specific projection neurons (PNs) in the antennal lobe, which carry olfactory information to higher brain centers for further processing. Despite its simpler anatomical organization, the larval antennal lobe also contains GABAergic LNs that innervate different glomeruli.

Using a novel larval preparation that is amenable to calcium imaging, Asahina *et al.* [3] confirm the observations in adult flies - that a given odorant excites multiple ORNs and a given ORN responds to multiple odorants [1,9]. In principle, a combinatorial code using the glomerular pattern can encode more odors than the number of receptor types available. However, higher concentrations of a given odorant may also activate more ORNs. Therefore, odor identity is potentially confounded by a change of concentration [10], which is a problem that has attracted much speculation from researchers in the field of olfaction. Indeed, in this study [3], Asahina *et al.* report that high concentrations of the attractive odorant ethyl butyrate excite three ORNs - those expressing the olfactory receptor gene *Or35a*, *Or42a* or *Or42b*. Yet the response thresholds of these three ORNs are orders of magnitude apart, with the *Or42b* and *Or35a* ORNs showing the highest and lowest sensitivities to ethyl butyrate, respectively. Thus, depending on the ethyl butyrate concentration, the number of recruited glomeruli can switch from one to three.

In order to study the physiological and behavioral response properties of isolated ORN channels, Asahina *et al.* [3] created larvae with only one functional ORN using an elegant genetic trick. The *Or83b* gene is normally expressed and required for odor detection in all larval ORNs. Targeted expression of the wild-type *Or83b* in the *Or83b* mutant background generates larvae with just one functional ORN type, which they term *OrX*-functional. These Or83b rescue experiments allowed them to show that one functional ORN is sufficient for odor navigation towards an attractive odorant. In addition, the behavioral threshold for each isolated ORN channel is similar to its physiological threshold as measured by calcium imaging in this study and electrophysiology in a previous work [11].

This study [3] and a recent publication [11] provide unprecedented resolution on olfactory behaviors of *Drosophila* larvae with the *Or42a* and *Or42b* ORNs. Both studies show that control larvae can navigate toward attractive odorants over a large range of concentrations. Both studies also report that loss of function in certain ORNs causes a reduction in attraction or even avoidance to high concentrations of odorants. Kreher *et al.* [11] showed that *Or42b* mutant larvae exhibit reduced attraction to low concentrations of ethyl acetate, whereas *Or42a* mutant larvae avoid high concentrations of ethyl acetate. One interpretation of the avoidance behavior offered by the authors [11] is that hyperactivation of the *Or42b* ORN or downstream neurons, which is normally balanced by the activation of the *Or42a* ORN, causes a switch from attraction to aversion.

However, Asahina *et al.* [3] show that simultaneous functional restoration of Or42a and Or42b is not sufficient to recapitulate the wild-type attraction behavior. This result led them to investigate other cell types in the antennal lobe. They discovered that LNs fail to respond to odor stimulation when only one ORN channel is present, but that LNs respond to the summed stimulation of *Or42a* and *Or42b* ORNs. In parallel, they showed that PN output is suppressed by the simultaneous activation of these two ORNs (Figure 1b).

Together, these results paint a picture in which the firing rate of the GABAergic LNs scales with the number of receptor inputs and serves as a mechanism to dampen PN response. It is interesting to note that the LN response in the *Or42a+Or42b*-functional larvae is still less than that of wild-type larvae. Based on the data in these two papers [3,11], one might imagine a model whereby Or42a ORNs offer the greatest contribution towards balancing out Or42b hyperactivation through inhibitory LNs. Contributions from the total ORN ensemble may be necessary for sufficient LN recruitment to suppress hyperactivation. Future experiments to investigate the role of inhibitory LNs in the behavioral switch from attraction to aversion will be necessary for a conclusive answer.

The traditional view of GABAergic LNs in the olfactory system is that they serve to increase contrast between odors of similar glomerular patterns by lateral inhibition [12]. The findings of Asahina *et al.* [3], together with two other recent studies [6,7], offer compelling evidence that inhibitory LNs may instead mediate automatic gain control to expand the dynamic range of odor responses. Although horizontal cells in the retina and inhibitory LNs in the olfactory system seem to share functional similarities, their exact synaptic wiring diagrams may have differences. Besides targeting the axonal terminal of ORNs [6,7], LNs also synapse with PNs. LNs, in principle, can thus mediate both feedback and feedforward inhibition. $GABA_B$ receptor-mediated feedback inhibition is important for efficient odor-tracking behaviors [7]. Feedforward inhibition may be mediated by postsynaptic GABA receptors that reduce dendritic excitability. Future efforts to assess the relative contributions from feedback and feedforward mechanisms in perceptual constancy and adaptation will be crucial for understanding how early olfactory processing shapes incoming olfactory information and how this information is used to generate behavior.

References

1. de Bruyne M, Foster K, Carlson JR: **Odor coding in the *Drosophila* antenna.** *Neuron* 2001, **30:**537-552.
2. Louis M, Huber T, Benton R, Sakmar TP, Vosshall LB: **Bilateral olfactory sensory input enhances chemotaxis behavior.** *Nat Neurosci* 2008, **11:**187-199.
3. Asahina K, Louis M, Piccinotti S, Vosshall LB: **Intensity coding with an ensemble of odorant receptors.** *J Biol* 2009, **8:**9.
4. Sakmann B, Creutzfeldt OD: **Scotopic and mesopic light adaptation in the cat's retina.** *Pflugers Arch* 1969, **313:**168-185.
5. Ng M, Roorda RD, Lima SQ, Zemelman BV, Morcillo P, Miesenbock G: **Transmission of olfactory information between three populations of neurons in the antennal lobe of the fly.** *Neuron* 2002, **36:**463-474.
6. Olsen SR, Wilson RI: **Lateral presynaptic inhibition mediates gain control in an olfactory circuit.** *Nature* 2008, **452:**956-960.
7. Root CM, Masuyama K, Green DS, Enell LE, Nassel DR, Lee CH, Wang JW: **A presynaptic gain control mechanism fine-tunes olfactory behavior.** *Neuron* 2008, **59:**311-321.
8. Vosshall LB, Stocker RF: **Molecular architecture of smell and taste in *Drosophila*.** *Annu Rev Neurosci* 2007, **30:**505-533.
9. Wang JW, Wong AM, Flores J, Vosshall LB, Axel R: **Two-photon calcium imaging reveals an odor-evoked map of activity in the fly brain.** *Cell* 2003, **112:**271-282.
10. Stopfer M, Jayaraman V, Laurent G: **Intensity versus identity coding in an olfactory system.** *Neuron* 2003, **39:**991-1004.
11. Kreher SA, Mathew D, Kim J, Carlson JR: **Translation of sensory input into behavioral output via an olfactory system.** *Neuron* 2008, **59:**110-124.
12. Mori K, Nagao H, Yoshihara Y: **The olfactory bulb: coding and processing of odor molecule information.** *Science* 1999, **286:**711-715.