

Olfactory processing in a tiny microcircuit

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Each first-order olfactory receptor neuron (ORN) expresses just a single odorant receptor gene, which confers upon it a particular odor response profile. All the ORNs that express the same odorant receptor gene project their axons to the same compartment of neuropil (“glomerulus”) in the brain. Each second-order neuron receives direct ORN input from a single glomerulus. An odorant typically activates multiple types of ORNs, and thus olfactory information is represented as a distributed population code. Glomeruli are linked by local interneurons, but the function of inter-glomerular connections is unclear. Because the vertebrate olfactory system contains ~1000 glomeruli, each with a unique response profile, and with no simple spatial relationship between glomeruli, the logic of this system has been difficult to unravel.

My lab has been investigating olfactory processing in a more tractable system, the *Drosophila* antennal lobe. The basic organization of the fly antennal lobe is similar to that of the vertebrate olfactory lobe, but numerically this system is much simpler, with only ~50 glomeruli. Moreover, genetic tools allow us to label first- and second-order neurons corresponding to identified glomeruli. Extracellular and intracellular recordings from these neurons allow us to monitor their odor responses *in vivo*. We also use genetic tools and pharmacology to probe functional interactions between neurons in this circuit.

What transformations are occurring as olfactory information passes from ORNs to second-order neurons (called “projection neurons” or PNs)? We find that the odor responses of a PN show higher spike-count reliability than the responses of a cognate presynaptic ORN, likely reflecting the fact that PNs pool signals from many homotypic ORNs. We also find that weak ORN odor responses are amplified in postsynaptic PNs, but strong ORN responses are not amplified to the same degree. This mainly reflects synaptic and cellular nonlinearities intrinsic to each glomerulus. This transformation produces a type of reformatting that Simon Laughlin has called “histogram equalization”, with the result that distances between odor representations become more uniform. As a consequence, a linear discriminator classifies odors more accurately using PN spike trains as compared to an equivalent number of ORN spike trains.

What is the function of inter-glomerular connections? We were surprised to find that inter-glomerular input to PN dendrites is predominantly excitatory. The function of these excitatory connections is still something of a mystery. We were then again surprised to find that the net effect of inter-glomerular input to a glomerulus can actually be inhibitory. This is because there are inter-glomerular circuits that suppress neurotransmitter release from ORN axon terminals. So while the net effect of inter-glomerular input to a PN is generally excitatory, presynaptic inhibition generally dominates over postsynaptic excitation. The odor tuning of this inter-glomerular presynaptic inhibition is roughly similar across glomeruli, and is strongly correlated with the total ORN activity evoked by each odor. Thus, we propose that inter-glomerular presynaptic inhibition acts as a spatially diffuse gain control signal.