

that there are substantial energetic costs associated with maintaining eyes — even in the dark when they are not signalling — due to the movements of Na⁺ and K⁺ ions [11,12]. As is the case on islands, the high energetic cost of maintaining neural structures coupled with the limited access to energy would strongly favour a reduction in the size of redundant structures [13,14]. Moreover, the cave alleles at the 12 eye and lens loci identified in the Pachón population of *Astyanax* all cause a reduction in eye size, which is consistent with selection but not drift [5].

Maintenance of brain regions involved in the processing of visual information will also incur substantial energetic costs. It is unclear whether, in the absence of inputs from the eyes, these regions are co-opted for the processing of other sensory modalities in *Astyanax*. There is considerable potential for plasticity during development [15], especially in the nervous system. For example, in eyeless mouse mutants, circuits within the lateral geniculate nucleus that normally receive optic inputs are co-opted to process other extrinsic inputs [16]. This inherent plasticity within the nervous system may facilitate the processing of sensory information from other modalities in cave fish, which have often increased reliance on

non-visual senses, particularly mechanosensation. It is also likely that following isolation in caves the visual processing centres in the brain would be reduced in size whilst those processing mechanosensory information would expand.

Some key questions remain about the roles specific eye and lens loci play in eye loss in different *A. mexicanus* populations. It seems crucial to determine their identity and their relationship to genes known to promote eye size reduction such as those in the Hedgehog pathway. Intriguingly, some of these genes may also regulate development of other neural structures such as mechanoreceptors or brain regions.

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Department of Zoology, Downing Street, University of Cambridge, Cambridge, CB2 3EJ, UK; Smithsonian Tropical Research Institute, Apartado 0843-03092, Balboa, Ancón, Panamá, República de Panamá. E-mail: jen22@hermes.cam.ac.uk

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Olfactory Coding: Non-Linear Amplification Separates Smells

How does the nervous system encode complex sensory stimuli? A recent study reveals the fly olfactory system compensates for variability in sensory input as odor representations are restructured for enhanced discriminability and coding efficiency.

Baranidharan Raman and Mark Stopfer

Olfactory stimuli are often spatially and temporally irregular [1]. In addition to the chaotic structures of odor plumes, complex biophysical [2,3] and neural

mechanisms [4–6] conspire to make olfactory transduction a sometimes inconsistent and seemingly unreliable process. Yet, remarkably, behavioral and physiological studies show the olfactory system can reliably detect and recognize odorants.

In a recent study, Bhandawat *et al.* [7] used the relatively simple olfactory system of the fruitfly *Drosophila* to show how noisy, variable peripheral signals are transformed by early neural circuits into consistent, efficient and distinguishable odor representations.

In *Drosophila*, odorants are detected by a population of ~1200 olfactory receptor neurons (ORNs) in the antenna (~120 in the maxillary palp), each expressing one of ~60 types of odor receptor [8]. Although the ORNs are randomly distributed along the antennae, their axons

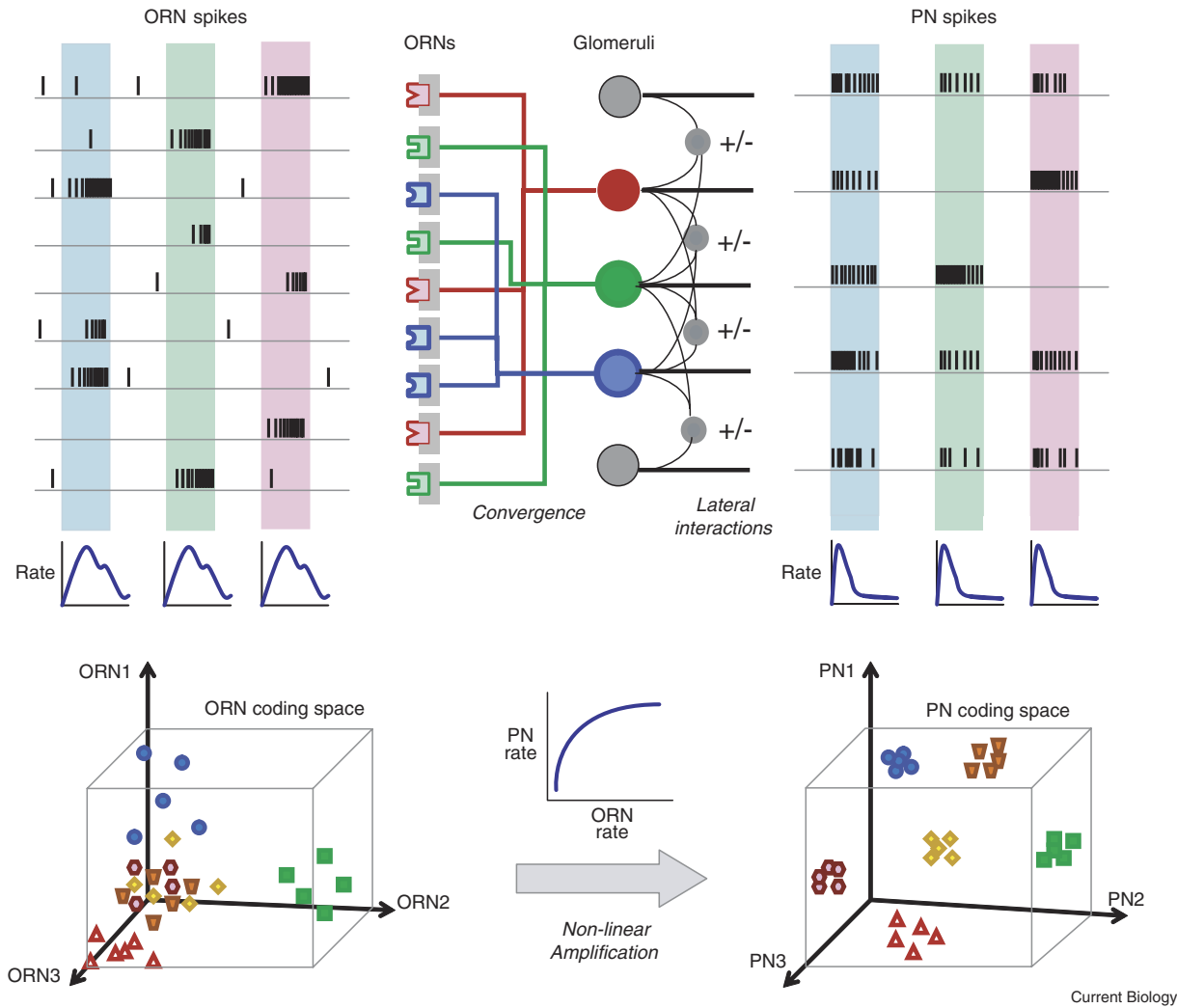


Figure 1. Olfactory computation by peripheral circuits.

Olfactory receptor neurons (ORNs) produce odor-elicited spike train responses that are noisy, highly variable, and grow relatively slowly in intensity. Second-order, projection neurons (PNs) in the antennal lobe receive convergent input within glomeruli from multiple, distributed copies of the same ORN type. When driven by odor, projection neurons show responses that are more reliable and that build more rapidly than responses in the ORNs. Lateral interactions within the antennal lobe circuitry result in a non-linear amplification of ORN inputs, restructuring odor-elicited patterns across projection neurons to become more uniformly distributed and distinct from one another, and thus enable more efficient coding.

are astonishingly well sorted such that receptor neurons expressing the same receptor converge within the antennal lobe onto single spherical structures of neuropil called glomeruli [9,10]. There, the ORN afferents synapse onto second-order projection neurons (which are like the mitral cells of vertebrates); most projection neurons receive input from 10–40 ORNs of the same type. This peripheral reorganization scheme is remarkably similar across species and phyla [1], suggesting a design optimized over evolutionary time to solve

a common information processing problem.

What computational role is provided by this convergence of redundant and spatially distributed sensory information? With a relatively small number of uniquely identifiable glomeruli (~50) and well-characterized ORN types that project onto them, the fly olfactory system provides an ideal preparation to study the functional role of this ubiquitous olfactory design. Recording extracellularly from the presynaptic ORNs and intracellularly from their postsynaptic projection neurons, Bhandawat *et al.* [7] compared

the trial-to-trial reliability of the inputs and outputs in seven different identified glomeruli. They found that the odor-evoked responses were less variable in the projection neurons than in the individual sensory neurons providing their direct inputs. By integrating inputs from multiple copies of the same ORN type, the projection neurons were able to average away uncorrelated variability in their inputs (Figure 1).

Integrating over multiple redundant inputs also allowed the olfactory system to recover extremely weak responses buried

in the relatively noisy responses of single ORNs. This form of sensitivity enhancement, where the detection limit for an integrated group of like elements is lower than that of any of its individual elements, is generally called 'hyperacuity'. Bhandawat *et al.* [7] found that the second-order neurons did indeed show measurable responses to odors that evoked no noticeable activity in their direct pre-synaptic ORNs. These results suggest a role for convergent wiring in heightening the sensitivity of the olfactory system. Excitatory local neurons recently reported in *Drosophila* [11,12] could potentially contribute to some of these observed differences as well.

Bhandawat *et al.* [7] found that the amplification provided by converging ORN inputs also allows for speedy responses from their follower projection neurons. Although the responses of ORNs to an odor puff generally build up slowly over time, projection neurons can respond swiftly and powerfully, even as converging presynaptic inputs from ORNs are still intensifying. This 'high-pass' filtering function may allow flies to alter behaviors rapidly when stimulated by odors [13].

Previous work suggested that lateral interactions in the antennal lobe dramatically restructure olfactory information, broadening the tuning curves of projection neurons relative to their presynaptic ORNs [14]. Here, with a larger dataset of seven test glomeruli, Bhandawat *et al.* [7] directly compared the tuning profiles of presynaptic ORNs with their corresponding postsynaptic projection neurons. Consistent with the earlier results, the authors found that projection neurons were less selective than ORNs, and that the broadening of the tuning profiles of projection neuron occurred independently of odorant concentration. Hence, these new results provide strong evidence for the dramatic transformation of olfactory codes within the antennal lobe.

And, interestingly, the transformation is non-linear: Bhandawat *et al.* [7] found that weaker inputs from ORNs to

projection neurons were amplified greatly, but stronger inputs were amplified less. One benefit of processing olfactory information in this non-linear fashion is that, compared to responses in ORNs, resulting responses in projection neurons were more evenly spaced within their available dynamic range, providing more efficient use of their coding capacity.

Within the antennal lobe, olfactory information is generally distributed across ensembles of projection neurons [15]. Are the various reformatting benefits detected in the responses of individual projection neurons also observed in the ensemble code? Bhandawat *et al.* [7] compared the arrangement of eighteen different odors in the multi-dimensional spaces defined by ORN and projection neuron responses. Again, they found that odor responses filled the projection neuron coding space more uniformly. Even those odorants that appeared clustered together in the ORN space became well separated, and thus more discriminable, in the projection neuron space (Figure 1). And, indeed, a classification analysis showed that odors that elicit non-linearly separable activity across ORNs are transformed into linearly separable response patterns in the projection neuron ensemble.

Processing of odor information in the antennal lobe, however, did not result in orthogonal coding channels. Rather, Bhandawat *et al.* [7] found that the responses of projection neurons were highly correlated with each other, as were responses within groups of ORNs. The existence of inhibitory and excitatory local neurons in the antennal lobe suggests that both competitive and associative interactions are possible. Purely inhibitory interactions between projection neurons would tend to decorrelate their responses; in an extreme case — a fully connected network — such interactions would lead to a 'winner-take-all' competition, resulting in a coding capacity greatly reduced to the number of available output channels. Purely excitatory interactions, on the other hand,

would decrease the independence of channels to lower than what is available in their inputs. Thus, the results of Bhandawat *et al.* [7] suggest that the network connectivity of the antennal lobe is delicately balanced to optimize its coding capacity.

Given these new results, it is interesting to speculate about how different aspects of information processing within the antennal lobe might be achieved by specific inhibitory and excitatory interactions. Excitation among projection neurons would tend to correlate instantaneous firing; such highly correlated activity would resemble the behavior of association networks for sensory memories that can recover partial and degraded inputs. Inhibition would tend to decorrelate firing, although over time [16]. Shifting the balance from inhibition to excitation, the antennal lobe circuits in *Drosophila*, depending on the network connectivity and plasticity, could potentially decorrelate representations for one set of odorants and cluster representations for another set.

The work by Bhandawat *et al.* [7] provides insights into the logic behind olfactory circuit design. It will be interesting to analyze how these results generalize to a larger set of odorants, and to other species. It will also be interesting to see whether these peripheral circuits play a role in insulating the neural signal-processing engine from the constant changes in the population of ORNs that occur throughout the lifetime of the animal. These fundamental olfactory processing principles are not only important for understanding how the brain interprets odor signals, but are also necessary for engineering solutions inspired by biological computations for addressing high dimensional and non-linear problems.

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National Institutes of Health, National Institute of Child Health and Human Development, 35 Lincoln Drive, Bethesda, Maryland 20892, USA.
E-mail: stopferm@mail.nih.gov

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Action Observation: Inferring Intentions without Mirror Neurons

A recent study has shown, using fMRI, that the mirror neuron system does not mediate action understanding when the observed action is novel or when it is hard to understand.

James M. Kilner¹
and Chris D. Frith^{1,2}

Social interaction depends upon the ability to infer beliefs and intentions in the minds of others [1]. It has been suggested that humans can infer the intentions of others through observation of their actions [2]. This notion that actions are intrinsically linked to perception was proposed by William James, who suggested that “every mental representation of a movement awakens to some degree the actual movement which is its object” [3]. The implication is that observing, imagining, preparing or in any way representing an action excites the motor program used to execute that same action [4,5]. Interest in this idea has grown recently following the neurophysiological discovery of mirror neurons and, in turn, the mirror neuron system. Mirror neurons, first discovered in monkey premotor area F5 and subsequently in inferior parietal lobule, discharge not only during action execution but also during

action observation [6]. This has led many to suggest that these neurons could be the neural substrate for automatic action understanding; however, the precise role of mirror neurons in action understanding is a matter of much debate [7–9].

Now Brass *et al.* [10] have reported in *Current Biology* that, in humans, action understanding in novel situations is not mediated by the mirror neuron network but rather by an inferential interpretive system. The authors used functional magnetic resonance imaging (fMRI) to measure brain activity from healthy human subjects whilst they watched a series of videos in which an actor made a very unusual action: switching on a light with their knee. The videos differed in the ease to which this unusual action could be understood. In the easy to understand videos, the actor was clearly unable to operate the switch with her hands as these were fully occupied holding some folders, whereas in the difficult to understand action, the actors

hands were free and consequently the actor's decision to operate the switch with their knee and not their hand is hard to understand. The authors argue that this latter condition should activate any system involved in action understanding more than the easy to understand action.

Brass *et al.* [10] found that activity in brain areas that are considered part of the mirror neuron system is not modulated by the ease of action understanding. Instead, such modulations are seen in brain areas that have previously been associated with social perception and mentalizing, namely the superior temporal sulcus (STS), the posterior STS and the anterior fronto-medial cortex (aFMC). This result demonstrates that the mirror neuron system is not sufficient for action understanding when the intention of the observed action is hard to understand. This would suggest that the mirror neuron system does not infer the high level intention of an observed action, in this example, why did the actor operate the switch with their knee?

Actions have to be understood at many different levels [11]: an intention level; a goal level that describes short-term goals necessary to realize the intention;