THE BUZZ

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OLFACTORY CODING IN THE INSECT ANTENNAL LOBE

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For most insects, olfaction is the most important sense. Odors are used for mate finding, social communication, finding appropriate egg-laying substrates, or food sources. Some of these behaviors rely on highly stereotypical odors. For example, sexual pheromones emitted by female moths attract only males from their own species, amidst a variety of other odors – and even pheromones from other species – in the air. Similarly, ants follow a specific trail odor over long distances on their foraging trips. Other odors are more varied. For example, honeybees learn the odor of a flower that is rich in nectar, and communicate that odor, by means of the traces trapped in their hair, to their sister bees.

The questions that we ask in our lab are: how are odors processed in the insect's brain? And what is the molecular organization of the olfactory system?

Interestingly, the basic physiology of olfactory coding is remarkably similar across species, be it insects or vertebrates, including humans. Odors consist of volatile substances that float in the air, and hit olfactory receptors. In insects, these are on the antennae, and in some species also on other appendages, such as the maxillary palps. Each species has a characteristic complement of a limited number of receptor cell types, defined by the olfactory receptor type that is expressed. In an adult *Drosophila*, this number is about 43, in honeybees much more. Each receptor cell responds to some, but not all, odors. Indeed, some receptor cells are exquisitely selective, and in the natural environment of a species may only respond to a single molecule, e.g., a component of a conspecific pheromone. Other receptor cells are more broadly tuned. A responding cell will send that information as a barrage of action potentials via its axons into the brain. Within the brain, a specialized area (i.e., the olfactory lobe, or antennal lobe) collects all that incoming information. Within this antennal lobe, incoming axons are sorted according to their response spectrum, or the expressed olfactory receptor. All axons of the same type coalesce into a single locus, forming a spheroid structure, called the olfactory glomerulus. *Drosophila* has 43 such glomeruli, moths number about 60-70, and honeybees 160. Consequently, when an odor hits the antenna, the activity that it elicits across the olfactory receptors is transformed into a characteristic activity pattern of olfactory glomeruli.

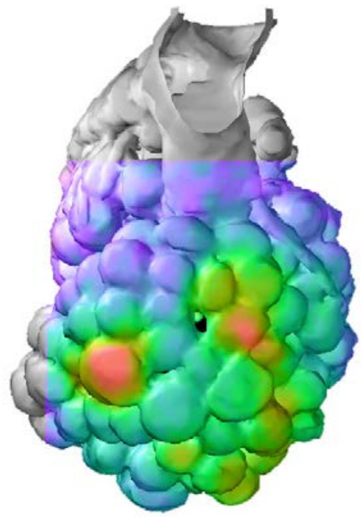
Cartoon view of a honeybee flying through a cloud of odors deriving from three flowers. Note the patchy and irregular distribution of odor plumes, leading to occurrences of low-concentration areas close to the source, as well as high-concentration areas far away. Also note that plumes can intermingle, creating imperfect odor mixtures, i.e. mixtures where the relative concentration of the components varies in time and space. An animal able to navigate in an olfactory environment needs to process a rapidly changing and highly complex landscape of odor plumes.

The logic of the olfactory code resides in these patterns of active glomeruli. Because all receptors are exposed to each odor stimulus, and because each receptor type will respond to some but not all odors, and because most odor stimuli will elicit responses in more than one receptor type, the resulting code is a combinatorial one. In other words: knowing that a particular receptor type is active will not give much information about an odor, but knowing the activity pattern across all receptors of a species allows one to identify the stimulus with confidence. The combinatorial logic greatly expands the coding capacity of the system: if each glomerulus (or receptor type) were used exclusively for a single odor, *Drosophila*, with its 43 glomeruli, would cover an olfactory space of a mere 43 odors. By exploiting its combinatorial power, it can code a much greater variety.

It is necessary to do behavioral experiments in order to know how good an animal is at discriminating odors. In the particular case of *Drosophila*, we have no precise indication of how many odors can be encoded, but the olfactory system of the honeybee, with its 160 glomeruli, appears to be almost unlimited.

Giving importance to temporal aspects, such as spike timing, may further refine the power of these systems and several research groups, including ours, are active in this area. The role of the antennal lobe is not limited to collecting information from like receptor neurons. Rather, a dense network of local neurons interconnects those glomeruli, and further refines olfactory information. The precise role that these networks play is as yet unknown. However, their understanding is crucial for understanding how odors are encoded.

We have developed techniques to measure odor-evoked activity patterns in the antennal lobes of a variety of insects. Among these techniques, calcium imaging is the most prominent. Intracellular calcium concentration is an ideal monitor for neural activity, and there are a variety of substances that, when introduced into the cells of interest, change their optical properties as a function of intracellular calcium concentration. Some of these indicators are of synthetic origin. We have used such dyes to characterize odor-responses in moths, ants and honeybees. We found that the activity patterns are characteristic within a species. In other words, it is possible to create a physiological atlas of odor representation by naming the active glomeruli. Indeed, we could show that it is possible to 'hindcast' an odor on the basis of the elicited calcium activity pattern. Other indicators are genetically engineered. In combination with the molecular biology tools available in *Drosophila*, these can be used to dissect olfactory processing along its cellular steps. We are now characterizing the olfactory response profiles of a series of olfactory receptors in great detail. Ultimately, this endeavor will lead to knowing the complete 'olfactome' of the species, i.e., to know what the primary information is that reaches the brain. The strength of using *Drosophila* lies in the fact that the calcium indicator can be expressed specifically in all cells that express a specific receptor, and only in these cells. Consequently, the response profile of that cell can be measured *in vivo*, with all auxiliary mechanisms in place. In a similar fashion, it is possible to selectively measure odor responses in the local neurons, or in the output cells of the antennal lobe, in order to understand the computations performed in the brain along the olfactory processing steps.



False-color coded image of an odor response in the antennal lobe of a honeybee (odor: clove oil extract). Active areas are shown in red and yellow, non-active areas in purple and blue. The image is superimposed onto an image of the three-dimensional arrangement of the antennal lobe. Note the glomerular arrangement, reminiscent of a cluster of grapes

Using similar techniques, we have done such an analysis in honeybees. In collaboration with Christian Linster at Cornell, Ithaca, we have created a computer model of the antennal lobe, and tested what kind of connections are needed within the antennal lobe in order to explain the observed patterns. Ultimately, we assume that these patterns will create an efficient means of olfactory coding. Knowing that most connections within the antennal lobe are inhibitory, we have tested three alternatives: connections are random, connections are spatially dictated by the neighborhood relationship of glomeruli, or connections are functionally dictated by the response profiles of the connected glomeruli. We found that the functional arrangement best explains the observed data.

The group is currently split with a lab in Europe (Berlin) and one in Riverside. In Berlin, research is done by 4 Ph.D. students, 2 research assistants, and 2 student assistants. In Riverside, **Rick Vetter** (SRA) is studying olfactory processing in honeybee projection neurons, and **Amy Sage** (student assistant) develops techniques to study olfactory processing in moths, in collaboration with **Kris Justus** and **Ring Cardé** (Entomology, UCR). Computational models are developed in collaboration with **Stefano Lonardi** (Computer Science, UCR). The lab in Berlin will be transferred to Riverside as the students complete their studies, with the last student due to finish in October 2005.

Insects rely heavily on their olfactory sense. Understanding how odors are encoded in their brain will allow us to develop better and environmentally safer approaches to controlling pests, as well as promoting beneficial insects. Furthermore, due to the fundamental similarity of olfactory systems across phyla, these studies help understanding our own sense of smell.

Giovanni Galizia joined the department in January 2003 as an Associate Professor. His Ph.D. is from Cambridge University (UK) and his undergraduate, postdoctoral and Assistant Professor work was - among other places - at the Free University of Berlin.

Honors and Awards

The Academic Senate has selected **Brian Federici** as a 2004 Faculty Research Lecturer and **Tim Paine** has received the Distinguished Teaching award for 2004. The Distinguished Teaching Award and the Faculty Research Award are the top honors awarded annually by the Academic Senate. **Jeremy Allison** has been awarded a $300 Graduate Dean's dissertation Research Grant and **Apostolos Kapranas** has been awarded a $500 Graduate Dean's dissertation Research Grant. **Keith Willingham**, Director of the Technical and Training division at Western Exterminator Company, presented the Karl Strom scholarships to graduate students **Dong-Hwan Choe, James Keenan, Raj Saran**, and **Andrew Soeprono**. The Carl Strom/Western Exterminator Scholarship is an ongoing fund to support both graduate and undergraduate studies relative to urban pest management.