Olfaction: A Window into the Brain

by Gilles Laurent

On the facing page, postdoc Glenn Turner (PhD '00) savors the aroma of a fresh cup of coffee. As the many different volatile chemicals in coffee waft into his nose, the olfactory receptors detect tens to hundreds of them, but his brain doesn't let him know it, because by a two-stage process of pattern recognition, his brain reconstructs this complex blend into one percept, "coffee." At the top of this page are some of the odors used in the Laurent lab.

Smell is an "old" sense. In primates, including humans, olfaction has been overtaken by vision, but it has kept its ancient connections to the emotional parts of the brain. In this article, I will try to summarize some of what we know about the inner workings of the olfactory brain, and the possible implications for our understanding of the nature of memories.

Natural odors often contain tens and sometimes hundreds of different types of molecules. The volatile oil secreted by scent glands inside a ranunculus flower, for example, contains 3,4,5-trimethoxytoluene, 2-phenylethylacetate, dimethyl salicylate, ten fatty-acid derivatives, six benzenoids, and much more besides. The smell of freshly ground coffee is a cocktail of 200 to 300 volatile components. And perfumes—man-made fragrances—are complex mixtures of both animal and plant oils or their synthetic analogs. Yet we perceive these odors as single entities—"ranunculus," "coffee," "Chanel No. 5." And having bound them into single entities, it's very hard for our brains to dissect out the chemical constituents again. This was demonstrated in 1998 by two Australian scientists, Andrew Livermore and David Laing, who prepared eight bottles of odors, the first of which contained one odor component, the second a mixture of two components, and so on, and asked people to smell each bottle and identify the components. Fifty percent got it right when there was just one component, but the success rate dropped to 15 percent with two components, and 4 percent with three, while with four components or more, no one could dissect out any of the odors. Even "Noses," people who design complex odors such as perfumes, fared no better.

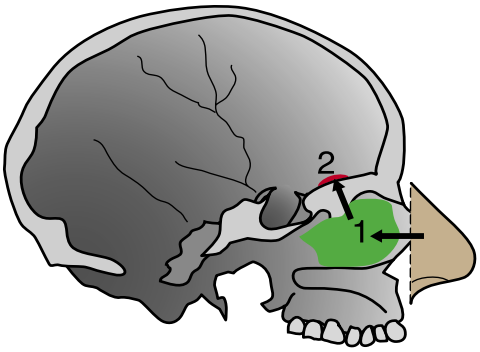
This illustrates a key aspect of olfaction. It's a "synthetic" sense that puts many disparate chemicals, each with its own associated percept, or sensory impression, together into a singular percept from which the components cannot be dissected out. Olfaction has another interesting property, common to the other senses also: the perception of an odor usually varies little over a wide range of intensities. If you smell jasmine at a variety of different strengths, you still identify it as being the same thing, jasmine.

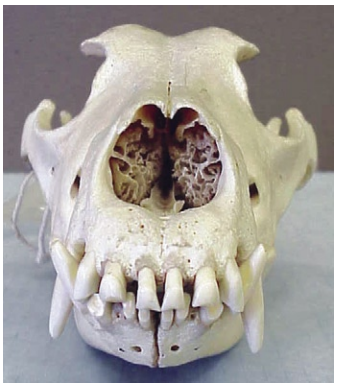
We call this property concentration invariance. The way the brain forms singular and invariant percepts from very complex stimuli, such as chemical mixtures, is a fundamental pattern-recognition problem. Brains solve pattern-recognition problems much better than any machine built today. Sensory neurobiology, which is what we do in my lab, helps us understand how brains solve these problems.

Complex chemical mixtures are not the only odors animals deal with. There are other kinds of smells used by animals as signals for very particular purposes, such as cues to locate food sources. The life cycle of the female malaria mosquito, *Anopheles gambiae*, for example, depends on one meal of human blood, and it locates its prey—us—by detecting a single chemical, 4-methylphenol, that is present in our sweat, but whose concentration varies between one person and another. This is the opposite of the way "general" odors are perceived: the mosquito seeks just one particular component within a complex smell.

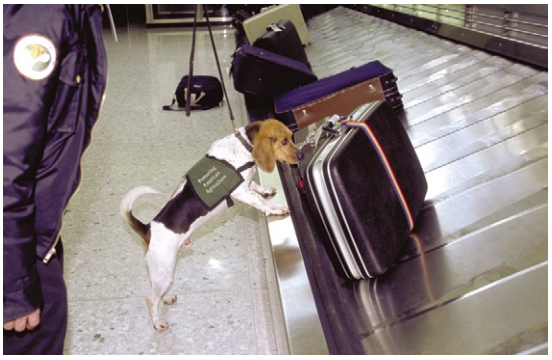
There are also smells, often referred to as pheromones, that convey information between members of the same species. Octyl acetate is one such example; released by honeybees from a gland in their abdomen, this odor orients other bees to the location of their hive, and bees drop some in the flowers they've visited so that other bees are guided to the food source. Sex pheromones are another example. In animals from worms to elephants, they're secreted by one sex to attract the other, and can be detected in minute amounts over very large distances.

So the olfactory sense is quite complex. At one extreme, mixtures of hundreds of components are perceived as single odors, while at the other extreme, specific signals that are very simple chemi-

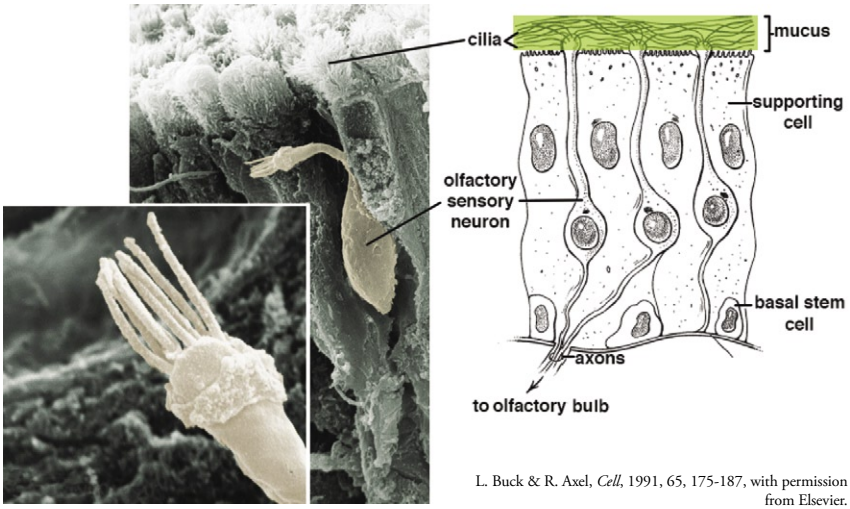




Above: In humans, odors are detected by neurons lining the nasal cavity (1), and processed in the olfactory bulb (2). Right: Dogs owe much of their olfactory superiority to the turbinate bones at the back of the nose. (Old English sheepdog skull courtesy of the Mammalogy Section, Natural History Museum of L. A. County.)



USDA beagles are trained to sniff out fruit from airline passengers' luggage to prevent the accidental introduction of harmful fruit flies into California. Neurobiologists like fruit flies, citrus growers don't. (Photo: Ken Hammond, USDA.)



L. Buck & R. Axel, *Cell*, 1991, 65, 175-187, with permission from Elsevier.

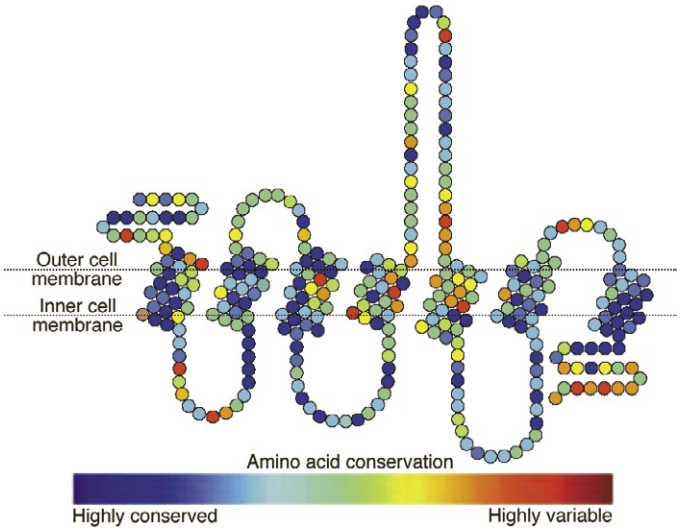
The proteins that catch odor molecules are in the membranes of cilia sprouting out of the top of receptor neurons. One neuron that has slipped down from its supporting cells is shown above, with the head magnified 17,500 times in the inset. Intact neurons still embedded in the epithelium have even more cilia. (SEMs courtesy of R. M. Costanzo, Virginia Commonwealth University.)

cally can be perceptually extracted from a complicated context. How do our brains make sense of this kind of chemical world?

The odor detection pathway begins in our nose, when we breathe in. Air goes into the nasal cavity, and affects a large population of receptor neurons—specialized nerve cells—embedded in a nasal epithelium, or mucosal layer, that carpets bony structures at the rear of the cavity. These bony projections are called turbinates, and they greatly increase the surface area of the nasal epithelium, and hence the number of receptor neurons. Turbinates are particularly well-developed in dogs, which explains in large part why dogs are so good at detecting odors. In a medium-sized dog, the turbinates have a total surface area the size of a large pizza. In humans, they're the size of a large cookie.

Growing out of the ends of the receptor neurons, and projecting into the nasal cavity, are many hairlike cilia. These lie in a layer of mucus—one with which we're all intimately acquainted—to stop them from drying out. The cell membranes of these cilia contain specialized receptor proteins. Odorant molecules in the air bind to these receptors and start a series of reactions that transform the chemical signal of the odor into a set of electrical signals that the brain can deal with.

In 1991, Linda Buck, working in Richard Axel's lab at Columbia University, identified the molecular structure of these receptor proteins, a discovery for which the two scientists were awarded the 2004 Nobel Prize in Physiology or Medicine. Many people had spent years trying to identify the olfactory receptors without success, but Buck decided to narrow her search of the genome to genes for G-protein-coupled receptors—a large receptor family characterized by a looped protein chain that crosses the cell membrane seven times—because they were already known to be receptors for some of the other senses, and for certain chemical neurotransmitters. She also hypothesized that these kinds of receptors would have a large number of variants,



P. Mombaerts, *Nature Reviews Neuroscience*, 2004, 5, 263-278, adapted from A. H. Liu *et al.*, *Genomics*, 2003, 81, 443-456, with permission from Nature Publishing Group & Elsevier.

The G-protein-coupled odorant receptor protein is a long chain of amino acids that loops seven times through the cell membrane. In this diagram, the amino acids have been colored according to their variability in the many types of this receptor protein. It's thought that odor molecules bind in one of the pockets formed where the chain crosses the membrane.

to detect many different odor molecules, and that they would be present at high density in the olfactory epithelium and nowhere else. Using this logic, and a lot of hard work, Buck finally identified the olfactory receptors.

We still don't know the three-dimensional structure of these receptors, but we can make educated guesses based on the known structure of related proteins. We think that some of the loops that cross the membrane may form little pockets in which the odorant molecules find binding sites. When they bind, the receptor protein probably changes shape, and this sets up a cascade of molecular events that ends with the generation of electrical impulses for signaling to the brain.

Although Buck and Axel had expected to find a lot of variation in the gene sequences of these receptors, they were still astonished at what they found. In parts of the looping receptor protein chain, the order in which the amino acids are strung together is so variable that some animals, such as the rat, have over 1,200 different receptor types. On average, mammals have about 1,000 types, fish and birds between 100 and 200, roundworms (*Caenorhabditis elegans*) 1,000, and fruit flies 60. Humans have only 600 different odorant receptor genes, but almost half of these are "pseudogenes" that no longer function, leaving us with only 350 receptor types in our nasal mucosa.

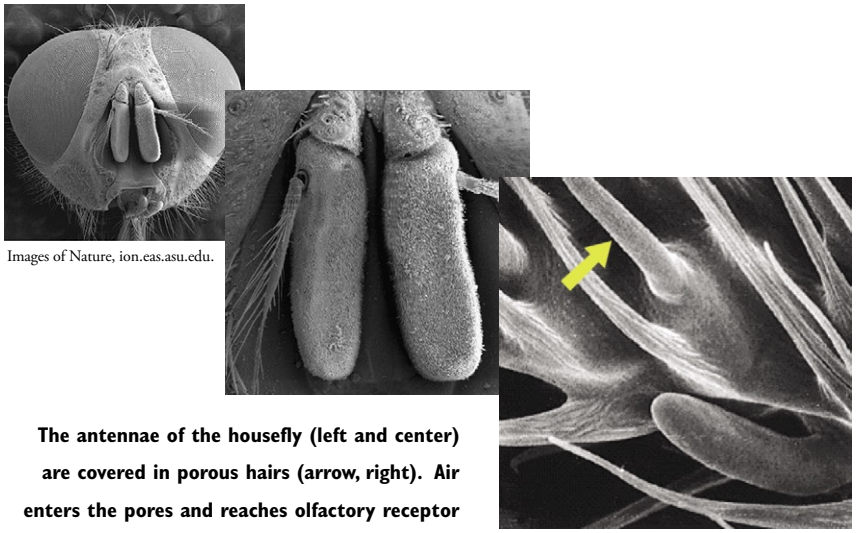
It's still much more than the receptor types found in other senses. Our sense of vision, for example, uses only four types of photoreceptor, and three of these have very slightly different sensitivities to wavelengths of light so that we can see color. (The largest number of photopigments known so far in a single eye is about 12, in the mantis shrimp.)

Interestingly, when the receptor genes of mammals, flies, and worms were compared, no sequence homology was found. In other words, the genes had probably not evolved from a common ancestor: different types of animals had come up with their own particular (but related) designs for olfactory receptors independently throughout evolutionary history. Such convergent evolution, as it's called, happens a lot in biological systems. The single-lens eye design, for example, has evolved independently at least eight times in the animal kingdom.

(As an aside, the system that generates responses to pheromones is in another region of the nose called the vomeronasal organ, and this organ sends its output to a different part of the olfactory bulb. The vomeronasal system also has a large number of G-protein-coupled receptor types, about 300 in mammals, that are separate from the ones that deal with other odors. But that's for another article.)

Individual receptor neurons in the cilia of the nasal epithelium express, or turn on, only one type of receptor gene. This implies that each receptor neuron, in principle, has a single sensitivity, given to it by the order of the amino acids in its receptor protein. Receptor neurons that express the same gene are sprinkled around the nasal epithelium in a fairly random fashion within large, overlapping "zones." All these neurons send their axons to the olfactory bulb, where they terminate in ball-shaped structures called glomeruli. But here's the surprise—all axons of the same receptor type converge on the same glomerulus. By implication, this means there are about as many glomeruli as there are receptor types. And with the exception of the roundworm, this extraordinary organization is

In an amazing feat of organization during development, each type of receptor neuron, near right, sends its axon to the same glomerulus, far right.



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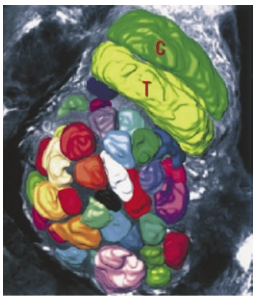
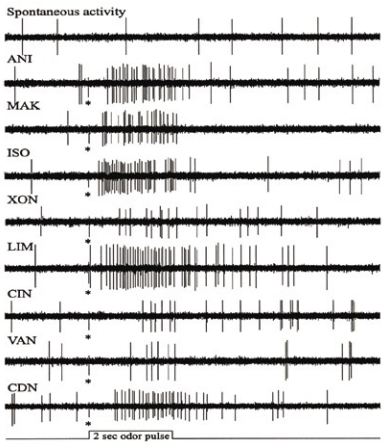
The antennae of the housefly (left and center) are covered in porous hairs (arrow, right). Air enters the pores and reaches olfactory receptor neurons at the base of each hair.

J. Riesgo-Escovar *et al.*, *J. Comp. Physiol. A.*, 1997, 180, 151-160 by permission of Springer Science & Business Media

R. Kanzaki *et al.*, *Chemical Senses*, 2003, 28, 113-130, Oxford University Press.



This male silkmoth's glomeruli, packed into the antennal lobe, have been individually colorized. The big ones labeled C and T are part of the pheromone system.



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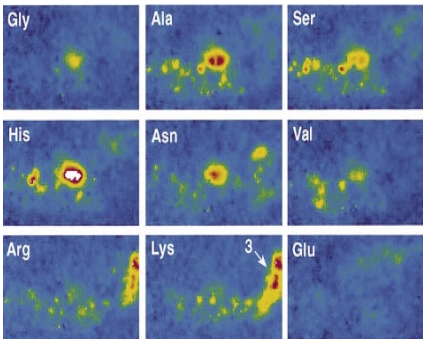
Left: The top row is an electrical recording from a resting rat olfactory receptor neuron, while each row below corresponds to a different odor given for two seconds to the same neuron. All the odors caused a change in the firing pattern, but in different ways.

Below: In the zebrafish olfactory bulb, different subsets of glomeruli fluoresced on receiving impulses from the receptor neurons in response to nine odors—in this case, amino acids.



R. W. Friedrich & S. I. Korsching, *Neuron*, 1997, 18, 737-752, with permssion from Elsevier.

found in almost all the animal species that have so far been looked at.

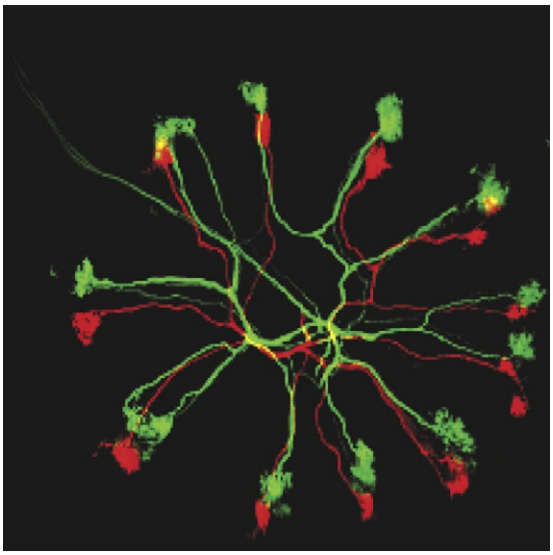
Much of the work in my lab is focused on insects, whose equivalent of a nose is a pair of antennae covered in porous hairs. These pores allow air to diffuse in and reach sets of receptor neurons at the base of each hair. The total number of receptor neurons depends on the species of insect, but some very olfactory insects such as moths can have several hundred thousand. The fruit fly *Drosophila melanogaster* has 1,300 in total, which express 60 different receptor types. The output of the receptor neurons goes to the antennal lobe, a structure analogous to our olfactory bulb, and terminates in about 45 glomeruli. This small number of glomeruli makes the fly, and other small animals, very useful for olfactory studies: the glomeruli can be characterized, named, and recognized from one animal to the next within the same species.

Does each olfactory receptor respond to a single odor molecule, or to a set of different molecules? Some receptors do seem to be specific to just one molecule. Recent results from Sperry Professor of Biology David Anderson's lab indicate that when a fruit fly is presented with carbon dioxide, a molecule that flies recognize as aversive, only a single glomerulus is activated. This suggests that the receptors connected to that glomerulus respond mainly (possibly solely, though this is hard to prove) to carbon dioxide, and (again possibly) no other glomeruli in the antennal lobe detect it.

If, however, one receptor always responded only to one single molecule, flies, which have only 60 receptor types, would be able to smell just 60 different chemicals. We know that is not the case. We also know, from physiological studies, that when individual receptor neurons are presented with different odors, they react to quite a number of them. We see this when we record their action potentials, as shown on the left. If a single receptor neuron, with only one type of odorant receptor, can respond to a variety of odors, it implies that an odor is detected by a population of different receptor neurons. In other words, each odor is defined by a certain combination of receptors; the code is combinatorial.

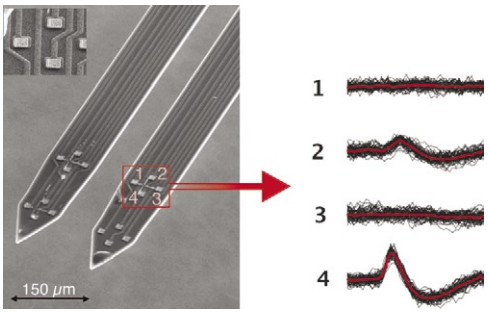
As different receptor neurons converge on different glomeruli, a single odor should also activate several glomeruli. Two German scientists, Rainer Friedrich and Sigrun Korsching, devised an experiment to test this. They added single odors—amino acids—to the water of zebrafish, and monitored the activity in the fishes' olfactory bulbs. Different amino acids did indeed activate different populations of glomeruli. The perception of an odor must therefore result from the brain's interpretation of combinatorial activity patterns. My group studies how the brains of insects (locusts, honeybees, and fruit flies), zebrafish, and rats do this.

In the glomeruli, the receptor neurons connect with other neurons called projection neurons.



In this locust antennal lobe imaged by Sarah Farivar (PhD '05), two projection neurons, one red and one green, connect with at least 12 different glomeruli.

Silicon probes with tetrads of electrodes fused to the surface, below, simultaneously record the electrical activity of up to 25 neurons in an insect's brain. Each probe records pulses from neurons in the vicinity, and software decodes the distribution of the signals. If the neuron is close to electrode 2, electrode 2 records a large signal, but if the neuron is even closer to electrode 4, this electrode records an even larger signal. Electrodes 1 and 3, farther away, detect very small signals.



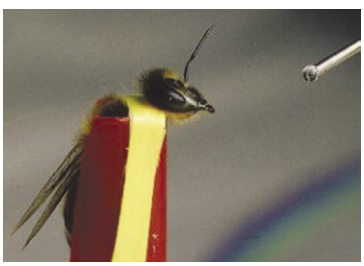
M. Roukes

These come in different shapes in different species: in fish, reptiles, and amphibians, a single projection neuron connects with several glomeruli, while in mammals and flies, one projection neuron connects with only one glomerulus. The locust has about 800 projection neurons, plus 300 neurons of another kind called local neurons, which have no axons, but have many branches that cover most of the glomeruli, and are critical for shaping and synchronizing the activity of the projecting neurons.

With 100,000 receptor neurons converging on just 800 projection neurons, what is being computed? To find out, we can insert tiny glass, metal, or silicon probes into the locust's olfactory circuits, give it an odor to smell, and observe the effect. Some of our probes carry groups of four electrodes, each of which detects electrical signals generated by neurons in the vicinity. The distribution of signals picked up by these electrodes can be decoded by triangulation in such a way that we can record and characterize the responses of up to 25 neurons simultaneously. By repeating these recordings many times, we can follow the activity of a large fraction of all the neurons present.

We also use another technique in which we penetrate the membranes of individual neurons with ultrafine glass microelectrodes, which allows us to record the electrical activity of single neurons while the animal is responding to odors.

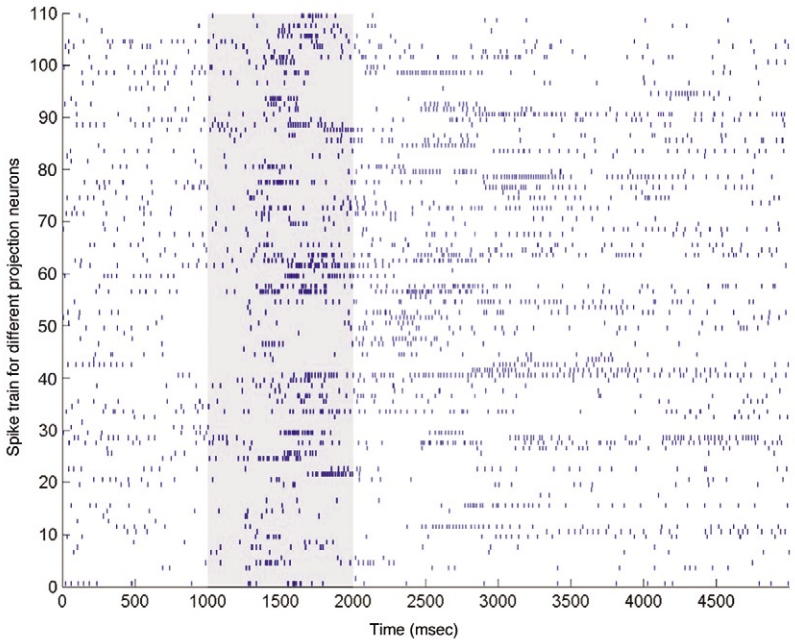
We can record all this electrical activity, but how can we gauge the insect's perception of odors and its discriminative power? To shed some light on this, we've also been doing behavioral studies on honeybees using the classical paired-stimulus conditioning experiments developed by a German scientist, Randolf Menzel, and colleagues. We put the bee in a harness that leaves the head free, and give it a puff of odorant. If the bee has never experienced the odor before, it orients its antennae, and that is pretty much it. Then we puff the odor again, and at the same time give the bee a drop of sugar solution at the same concentration as flower nectar. The bee learns to associate the odor with this sugar reward, and the next time it smells that odor, it sticks its tongue out in anticipation (even if it doesn't get a reward). This learned behavior is called a proboscis extension reflex; we can use this to probe the bee's ability to recognize an odor, and to distinguish it from other odors. By analyzing the time it takes for the bee to extend its proboscis, and the consistency or persistence of its responses, Mark Stopfer, a postdoctoral fellow in my lab at the time, was able to quantify the degree to which it can recognize odors, and get some idea of how it senses and perceives them.



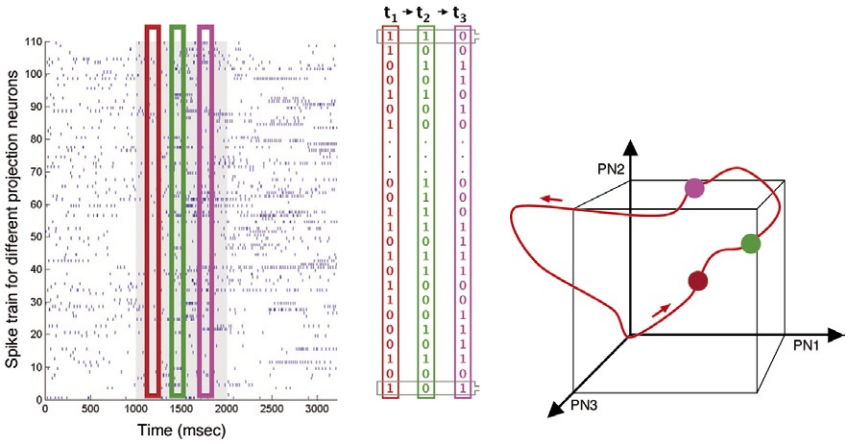
When a honeybee recognizes an odor, the antennae move forward and the bee sticks out its tongue, or proboscis, in anticipation of a reward. (Courtesy of Brian Smith, Ohio State University.)

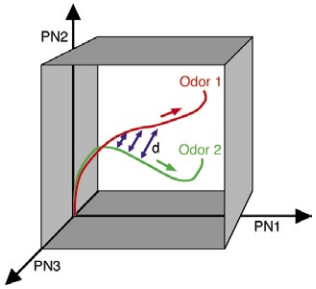
Going back to our electrophysiological recordings, the chart on the next page shows the kind of data we get when we use silicon probes to record

Mark Stopfer, NIH



Each row of the chart above is a recording of pulse patterns from a different locust projection neuron before, during (shaded box), and after a puff of odor. Each of the 110 projection neurons responds to the odor in a different way, characteristic of that neuron and that odor. Imagine the chart as sheet music—the neurons are drummers, and each one beats a different rhythm. To make sense of the cacophony, the score is broken down into very small time slots, below, each one drum-beat wide. During one interval, each drummer either hits the drum (1) or doesn't (0). When done for the entire score, a 110-dimensional graph of the activation trajectories over time can be drawn, like the one on the right (for three dimensions only).





Right: When the pulse patterns for two similar odors are superimposed, right, distance d between the trajectories increases over time—though it's a very short time. It takes less than 0.3 seconds for the brain to optimize the differences between the odors.

from populations of projection neurons before, during, and after the locust experiences an odor. Each line represents the activity of a different projection neuron. You can see that many of the neurons change their response patterns in a very characteristic way when the odor is presented: some respond early, some late, and yet others have complicated pulse patterns that are typical of that neuron and that odor. If the odor is changed, we see a different activation pattern across the neuronal population.

To make sense of charts like this, we break the activity pattern into very short windows of time, during which each neuron will have either fired or not fired. Then we transform the data into a column of ones (neuron fired) and zeros (neuron didn't fire), as in computer binary code. By moving the window forward incrementally, we can digitize the whole data set and draw a multidimensional graph (for the chart shown here, it would be a 110-dimensional graph) that plots the activity of each neuron. This gives us a trajectory for the activation pattern of the neurons over time in response to one odor. We can then repeat the experiment with other odors, and compare the trajectories defined by the same neurons.

This becomes interesting when we superimpose the graph of one odor onto that of a very similar odor. The two trajectories are more or less the same at first, but move further and further apart with time in a process we call decorrelation. As each odor activates the system, the system starts to interact with itself, and the representations of the odors become more and more characteristic—that is, they overlap less and less with the representations of other odors. This happens so quickly that the representations are optimally separated within 100 to 300 milliseconds.

Billiards provides a useful analogy of what's happening here. Imagine that the population of neurons that displays this complicated pattern is a set of red balls, and the odor is a white cue ball.

M. Heisenberg, *Nature Reviews Neuroscience*, 2003, 4, 266-274,
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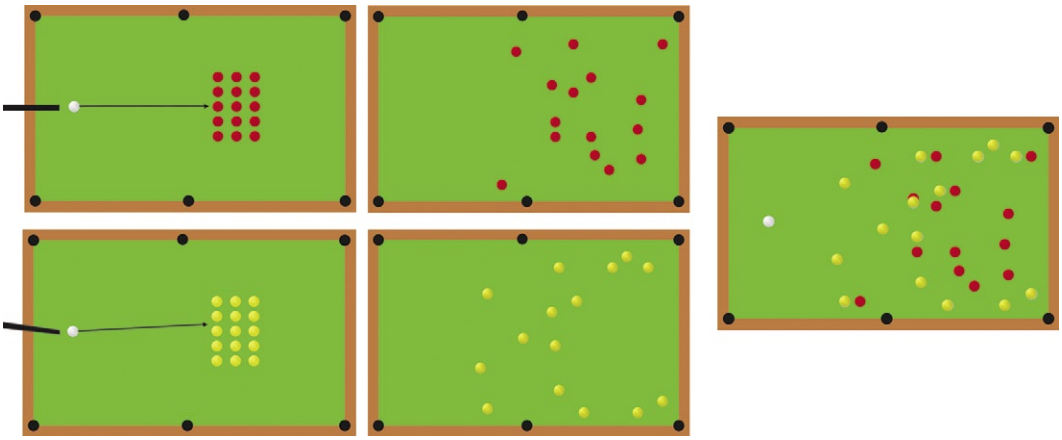
Behind a fruit fly's lovely big eyes is a very complex brain. Areas connected with olfaction include the antennae (red dot and arrow), the antennal lobes (red), and the two mushroom bodies (blue). Kenyon cell dendrites are in the swollen upper part of the mushroom body above the stalk, the calyx. The optic lobes (green), subesophageal ganglia (yellow), and central complex (orange) are also shown.

We hit the cue ball and, after some time, the red balls spread out into a particular pattern as a result of interacting with each other—like the projection neurons in the brain. We repeat this on an adjoining table with a set of yellow balls, but this time change the input just a bit by hitting the cue ball at a slightly different angle. The cue ball now hits the first ball at a different position, and the yellow balls spread in a different way than the red balls. When we compare the positions of the red and yellow balls, we can see quite a difference. Although the difference between the two input conditions was very small, the change in the output is very large. In other words, the difference has been amplified. That's basically what we think is taking place in this olfactory circuit. The remarkable thing is that this near-chaotic process is very sensitive to the input, but very reliable nevertheless. Finding the rules of such nonlinear dynamical problems is one of our goals.

It seems wasteful that hundreds of thousands of olfactory receptor neurons converge on their respective glomeruli in an amazingly precise way, but that this precision is then thrown away when seemingly disordered patterns of activation are generated in the projection neurons. But there's a good reason for it. A system that amplifies small differences in signals runs the risk of also amplifying noise, in this case noise coming from the receptors. Noise fluctuations would make the output of the projection neurons unreliable: the averaging that results from this kind of convergent design is precisely one way to reduce such fluctuations.

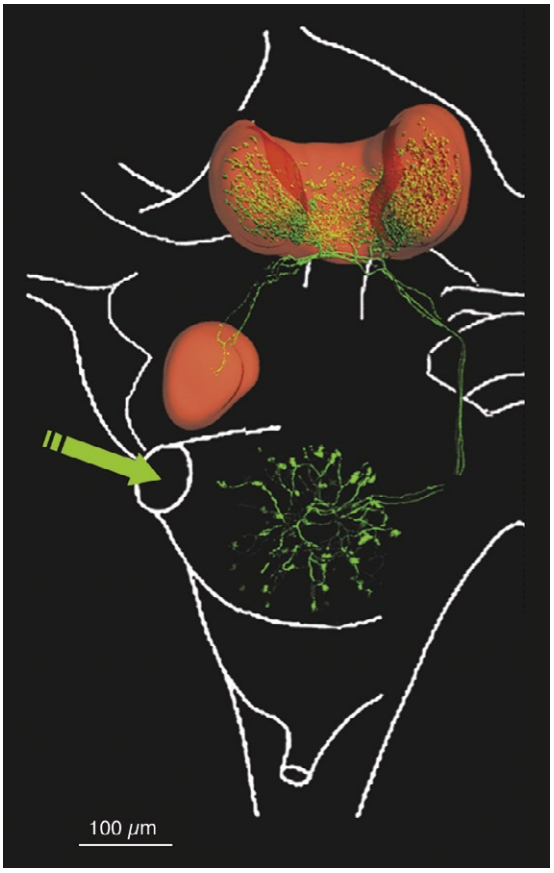
The projection neurons—which now contain all the information the animal has about the odor—go to a region of the insect brain called the mushroom body, a structure analogous to the vertebrate olfactory cortex. Here they connect with tens to hundreds of thousands of tightly packed neurons called Kenyon cells. From behavioral and molecular work in other insects, we know that the mushroom body plays a key role in the formation and recall of olfactory memories. Knowing how Kenyon cells represent odors thus promises to get us closer to understanding the nature of odor memories.

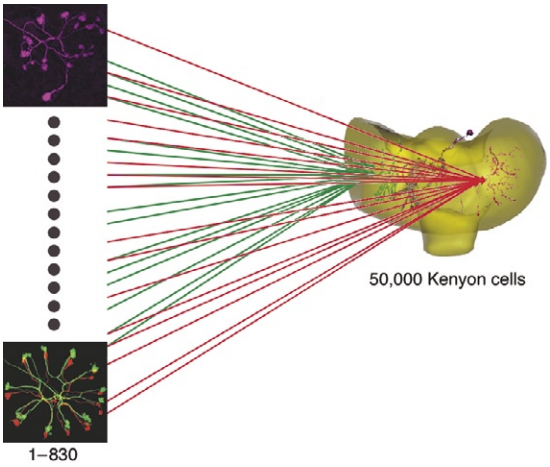
The locust has 800 projection neurons connecting to 50,000 Kenyon cells. With such a large mismatch in numbers, how are these nerve-cell populations interconnected? When Ron Jortner, a graduate student in my lab, recorded simultaneously from both projection neurons and individual Kenyon cells to assess the probability of connec-



In these two billiard games, one with red balls and the other one with yellow, a small change in the angle of the cue stick when it hits the white ball causes a large change in the way the balls eventually disperse.

In this composite of a locust's olfactory brain prepared by Sarah Farivar, the arrow shows where the antennal nerve brings input from one of the antennae. To the right of the arrow, green projection neurons connect with glomeruli in the antennal lobe. Their long axons run up to connect with Kenyon cells in the calyx of the red mushroom body at the top, and some also connect with the egg-shaped lateral protocerebrum, also colored red.





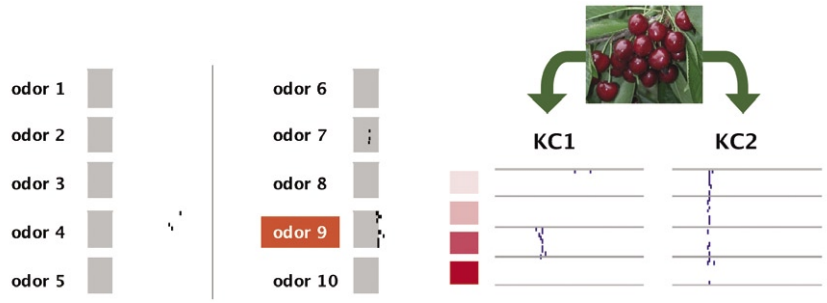
This is a simplified schematic of the linkages between projection neurons and two Kenyon cells. The real picture is far more complex, as each of the 50,000 Kenyon cells is estimated to connect with about 400 projection neurons out of 830.

tion between them he found, surprisingly, that the probability was about 0.5. In other words, each Kenyon cell seems to connect on average to half of the input population, that is, to 400 projection neurons. The number of ways in which 400 neurons can be selected out of 800—the number of possible connection patterns—is about 10^{240}. It's an *enormous* number. To put it in context, there are about 10^{10} seconds in a century, and there have been about 10^{19} seconds since the beginning of the universe. With 10^{240} possible combinations of projection neurons to choose from—assuming random connectivity—almost every Kenyon cell is likely to sample a combination of inputs that is very different from that sampled by the other Kenyon cells. Each cell will therefore gain a picture of the state of the projection neuron population very different from that gathered by any other Kenyon cell.

It follows that the responses of individual Kenyon cells will be very specific; a given cell should respond only to particular combinations of activated projection neurons, maximally different on average from those experienced by the other Kenyon cells. This is what two of my graduate students, Javier Perez-Orive (PhD '04) and Ofer Mazor, found when they sampled the responses of a selection of Kenyon cells to a wide variety of odors. Most of the Kenyon cells could not be activated by any of the odors they used in their experiments, but this was not unexpected, as with tens of thousands of simple odors and a near-infinite number of ways to combine them, it would have been practically impossible to test all possible odor stimuli. They did, however, find a "successful" stimulus for some, and of those successfully stimulated cells, most responded to only one odor among 20–30 odors tested.

With results such as these, we may begin to explain the synthetic nature of olfaction—the fact that when we smell cherry, we don't smell all the chemicals that make the odor of cherry. If our own brains contain bottlenecks equivalent to the Kenyon cells of insects, we can see how their synthetic property—their tuning to particular combinations of chemicals and only to those combinations—provides no information about the odor components. There's no receptor neuron in the antennae or nasal epithelium that recognizes cherry as such. There's no projection neuron in the antennal lobe or olfactory bulb that recognizes cherry as such. But in the mushroom body (and possibly in the olfactory cortex) lie cells that recognize cherry from the specific pattern of neural activation generated by the particular combination of chemicals contained within that odor.

Interestingly, monomolecular odors also often activate many different receptor types, and are therefore effectively identical to mixtures. Each odor, whether simple or complex, is represented by a specific pattern of coactivation in the antennal lobe (where the receptor neurons converge on the projection neurons) that is in turn recognized by



Kenyon cells are so specific that they only recognize one, or at most a few, odors. In the experiment on the left, in which 10 odors where tested on one Kenyon cell by Javier Perez-Orive, PhD '04, the cell responded reliably only to odor 9. The odor of cherries, right, produced the same pattern of electrical activation in Kenyon cell 2 over four different odor concentrations, while Kenyon cell 1 responded to this odor only at a certain concentration.

very few cells within a large population of pattern recognizers, each of which is tuned to different combinations. In other words, Kenyon cells have no way of knowing whether an odor is made of one or more molecular components. This may explain why we generally fail to perceive, when smelling an odor, whether it is mono- or multimolecular (as illustrated by Livermore and Laing's experiment that I described at the beginning of this article). Kenyon cell responses provide no information about this feature.

Neurons that respond highly selectively, as Kenyon cells do, have in a few instances also been found in other parts of the brain. Researchers of vision hypothesized their existence some forty years ago, and named them "grandmother" cells, following the proposition that a unique pair of cells might encode one's maternal and paternal grandmothers. No one really believes that representations in the brain are this specific. Such uniqueness is dangerous—a random activation of one cell could cause erroneous perception, or damage to one's grandmother cells would erase their memory for ever—but there is increasing evidence that the brain contains very sparse representations carried by extremely specific and invariant neurons. This makes such neurons very difficult for physiologists to find. If you put an electrode in a randomly selected neuron, you would have to try an enormous set of possible stimuli before you got a response (as my graduate students found). Our research into olfaction is, however, giving some valuable insights into how such kinds of high-level synthetic representations arise from the organization and dynamics of neural circuits.

The study of the sense of smell is a fascinating area of neuroscience. It already allows us to explain some perceptual qualities of olfaction, and may provide us with relatively simple solutions to complex and general pattern-recognition problems. Classifying and recognizing patterns is, after all, what our brains do best. □

PICTURE CREDITS:
42, 43 – Bob Paz; 42, 44 – Doug Cummings

Enjoying a day out of the Beckman Institute's basement are, left to right: front row, Bede Broome, Ofer Mazor, Vivek Jayaraman, Benjamin Rubin, Laurent Moreaux, Mala Murthy, and Sarah Farivar; back row, Gilles Laurent, Maria Papadopoulou, Jonathan Young, Roni Jortner, Glenn Turner, Kai Shen, Stijn Cassenaer, and Mattias Westman. Laurent lab members who missed out on the beach are Cindy Chiu, Suzi Yorozu, Mikko Vähäsöyrinki, and Sidra Golwala.

Gilles Laurent, the Lawrence A. Hanson Jr. Professor of Biology and Computation and Neural Systems, grew up in Morocco and France, and spent his student days in Toulouse, where, in 1985, he earned both a PhD from the University of Toulouse and a doctorate in veterinary medicine from the Ecole Nationale Vétérinaire. He then left both France and veterinary science to study neuroscience and electrophysiology at the University of Cambridge, before joining Caltech as an assistant professor in 1990. He became an associate professor in 1996, a full professor in 2000, and was named the Hanson Professor in 2002. His current interest is olfaction, but he also studies how single neurons perform nonlinear operations such as multiplication. He is married to another Caltech neuroscientist, Professor of Biology and Howard Hughes Medical Institute Associate Investigator Erin Schuman. This article is adapted from a Watson lecture given on February 23, 2005, which can be viewed on Caltech's Streaming Theater website, http://today.caltech.edu/theater/.