Computer Scents

A computer sniffs out how rats learn to distinguish odors

By STEFI WEISBURD

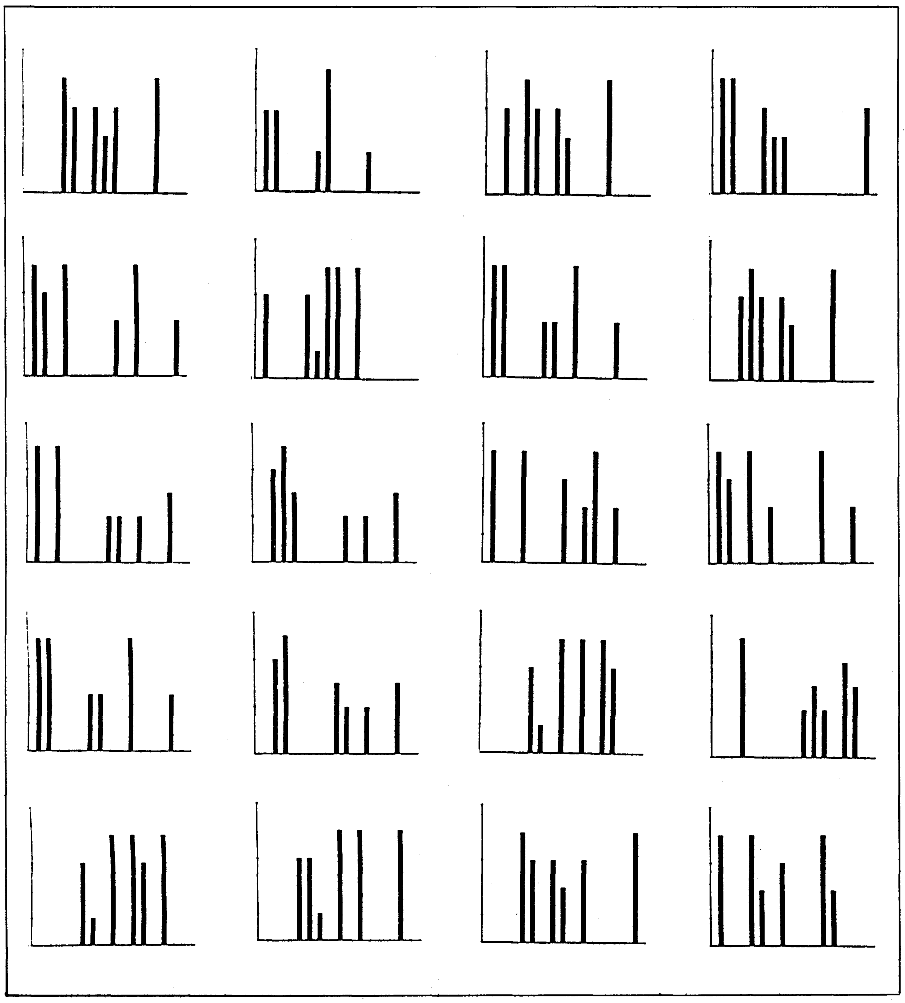
The brain is truly a case of the whole being greater than the sum of its parts. And untangling its complex circuitry in order to decipher how animals and humans store and recall information is a daunting biological task. In the last few decades, scientists have made enormous advances in understanding two ends of the learning and memory spectrum: By focusing on molecules and cells, they have uncovered chemical and physical changes in individual neurons thought to be involved in memory; and by observing psychology and behavior, they have classified forms of memory and linked them to different, general regions of the brain.

But how does one jump from the actions of a single neuron to the metropolis of hundreds of thousands of nerve cells interacting in myriad brain circuits and architectures? This is the question that in the last few years has spurred a remarkable meeting of minds among neurobiologists, psychologists, computer scientists, physicists and philosophers.

And it has sparked a revival of interest in computer simulations of the brain's neural networks (SN: 8/1/87, p.76) — work first brought into vogue in the early 1960s. If scientists cannot directly observe and dissect memory and learning processes in biological brains, perhaps silicon ones, able to handle highly interconnected webs of processing elements, may help fill in the gaps, they reason.

However, while they are inspired by the brain's learning abilities, most neural network modelers until now have only loosely been basing their computer designs on biological data. Though this "top down" approach may give rise to computer programs that can accurately recognize voices and faces, among other tasks, they are of limited use to *biologists*, who are attempting to use computers to answer real neurobiological questions, such as how the brain learns, remembers and recalls.

At the third conference on the Neurobiology of Learning and Memory, hosted by the University of California at Irvine (UCI) last fall, the problem of how to improve the translation between neurobiology and computer models took center stage. Participants repeatedly remarked that computer scientists and biologists were at last talking the same language. And it was evident from most of the lectures that modelers are increasingly incorporating the results of neurobiological experiments into their neural-net simulations.



Illustrations: Lynch, Granger/U.C. Irvine

When a rat sniffs an odor, the chemicals in that scent stimulate specific patches of the olfactory bulb. The activated bulb cells then send a unique pattern of electrical signals to the brain. In Lynch and Granger's computer simulation, each odor is represented as a bar graph, indicating the patches and number of cells within each patch that have been stimulated.

Perhaps the most biologically rooted neural-net model to date is the brainchild of neurobiologist Gary Lynch, computer scientist Richard Granger and their colleagues at UCI, who have built a simulation of one layer of neurons, called layer II, in the rat's pyriform, or olfactory, cortex – a brain area that has been linked to the sorting and storage of smells. The researchers decided to model the olfactory cortex because it is one of the anatomically simplest and best-understood regions of the brain and because it constitutes one of the shortest routes between memory and the outside world.

Their work, comments neurophysiologist Howard Eichenbaum at Wellesley (Mass.) College, "is one of the very few enterprises . . . which really takes advantage in an extended way of the known electrophysiology and anatomy [of the brain]."

In contrast to most other work, Lynch's group took a "bottom up" approach. The researchers threw together what they had learned in experiments about the physiological properties of pyriform neurons and how they interconnect, gave the computer a set of stimuli representing odors and, without asking it to solve any particular problem, simply watched what the simulation did. And much of what happened, say the researchers, came as a complete surprise. The computer organized information in unexpected ways and predicted a number of physiological phenomena, which the researchers have since confirmed with live rats and pyriform slices in the laboratory.

"I have no idea of what the computational significance of the [biological] rules [we used] is," says Lynch. "We just put them in because they're in the brain." The results, he says, are "mind-blowing. It's wild stuff."

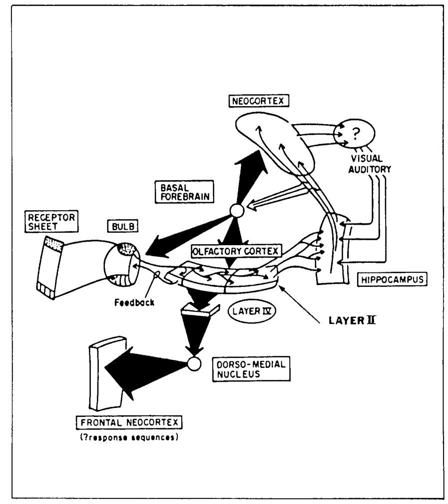
According to Lynch, most neurobiologists have been trying to explain a form of memory that associates different ideas or objects occurring together. Associative memory would link, for example, Rome with Italy or swallows with Capistrano. Lynch and Granger had anticipated that the pyriform-cortex simulation would exhibit associative memory as well.

But after being presented several times with a set of aromas – each represented as an electrical pattern resembling a supermarket bar code – the computer began organizing the odors by categorizing them. This means that instead of linking Rome with Italy, for example, the simulation would have grouped Rome with Los Angeles, Zurich and other cities, and it would have classified swallows with parrots, robins and other birds. This was surprising, says Lynch, because "categorization is a memory operation that is not immediately intuitive."

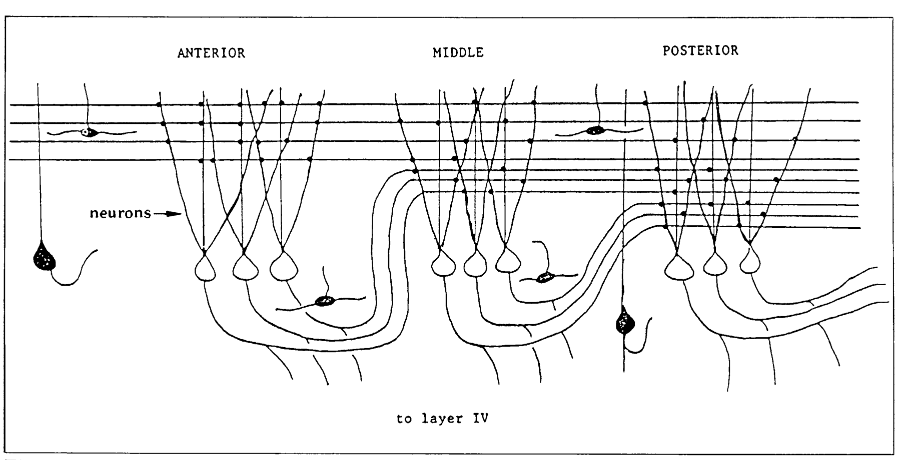
How does the computer show that it is categorizing? Lynch and Granger examined the patterns of neurons that fire in the simulation after the computer "sniffs" an odor, and they discovered that the patterns greatly emphasize the *similarities* among different odors, essentially bringing out the patterns' underlying and unifying theme.

In one experiment, for example, the researchers gave the computer a number of odors whose common properties would have stimulated the same 60 percent of cells in the rat's olfactory bulb, which is the first way station between the olfactory receptors in the nose, the pyriform cortex and the rest of the brain. But after the computer took these inputs and encoded them within the layer-II array as specific patterns of firing and nonfiring neurons, the fraction of shared neurons rose to 85 percent. After the first sniff, says Granger, the patterns can be thought of as members of a category of somewhat similar odors, like those arising from different kinds of cheese.

On subsequent sniffs, however, Lynch and Granger found that the simulation then began to tease out the *differences* between odors. By the third sniff, for example, only about 20 percent of the layer-II output cells were shared by encodings of different aromas. From the simulation, the researchers learned that the cells that are recruited for encoding differences between odors lie farther downstream from the cells activated during the first sniff. And they found that these downstream cells get their chance to fire because, once excited, the upstream cells are unable to refire for at least one second, and in that time the rat has restimulated its cortex neurons by taking a few additional sniffs. As the simulation shows, this arrangement enables the brain to identify smells first by looking at their similarities and then by highlighting their differences.



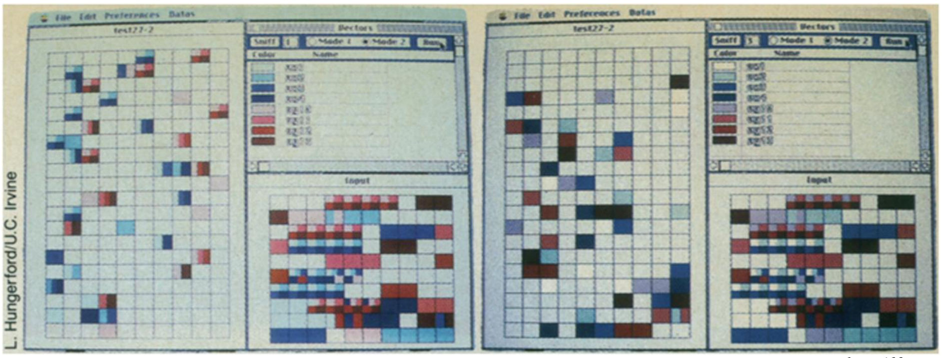
Odors are sensed by the receptor sheet in the nose and then are translated into electrical signals that travel down a number of pathways in the mammalian forebrain. Lynch and Granger are focusing on layer II of the olfactory cortex because it is extensively connected to the hippocampus and the dorsomedial nucleus of the thalamus, two structures thought to be especially important for memory processing.



The computer simulation is based on the anatomical arrangement of nerve cells in "layer II" of the pyriform cortex. A map of how these neurons connect to one another is shown above. The top four horizontal lines are the pathways along which the incoming "smells" travel.

Granger says the simulation also illustrates how the brain uses a specific rhythm of electrical activity to orchestrate and synchronize the many biological events that must come together in learning. In particular, it highlights a connection made in recent years between the sniff rate of rats and electrical rhythms in the brain. Rats naturally sniff every 200 milliseconds, and it appears that this 5-hertz sniff rate exploits a natural pattern of electrical signals in the brain, called the theta rhythm, which has the same 5-hertz frequency and which is known to be triggered during learning activities.

Moreover, in other work, Lynch's group has found that this same rhythm of electrical signals is the optimal rhythm for strengthening connections, or synapses, between nerve cells. And a tenet of neuroscience this century has been that memories are encoded as specific patterns of strengthened synapses within the web of neurons. It's as if the brain's neural network were a fisherman's net,



L. Hungerford/U.C. Irvine

These pictures show how the computer encodes odors as it takes a number of sniffs. The input pattern shown in each screen represents two general groups of eight smells; the various shades of red could be different cheese aromas, for example, and the blue scents could be different perfumes. As seen on the large panel of the left screen, most of the pyriform output neurons active after the computer's first sniff respond to either all the red odors or all blue scents, but are not stimulated by both groups; on the first sniff, the computer highlights general categories of smells. By the third sniff (right screen), however, each scent has been assigned a nearly unique output pattern, so the simulation can now tell the difference between Edam and cheddar.

with each cross-link representing a synapse that can be fortified by tying a knot around it; in this picture, every time a person stores a memory – whether it's a phone number or an odor – it is mapped onto the net as a particular pattern of knots.

In preliminary tests of their computer model, Lynch's group has found support for the idea that after learning, specific brain cells are activated by some odors but not others. In separate experiments, the researchers implanted electrodes into different layer-II cells of live rats that were learning to discriminate scents. The rats were given a series of odor pairs, each containing one scent that led to the reward of a drink of water and another scent that led only to a flashing light. The researchers found that during the first sniff of a new odor, one monitored cell fired extensively, but after several sniffs of a reward-linked odor, the cell became much quieter, firing in a complex burst only 200 milliseconds after the odor had been smelled. After several introductions to a nonreward odor, the same cell became inactive, while in other cells, the opposite was true: These responded to nonreward odors only. "This strengthens the argument that these cells are learning to become odor-specific," says Granger.

He adds that since the rats are presented with dozens of different odor pairs only a few times each – and yet, one month later, they still remember which odors correspond to a reward – their learning is very different from the standard classical conditioning (which involves hundreds of trials with one pair of stimuli) studied in most learning experiments. Moreover, the rats in Lynch's experiments are exhibiting a "kind of learning that presumably underlies normal human learning," he says. Next, the researchers plan to study how one cell responds to very similar odors. They also hope to be able to record activity from a number of cells at once.

Traditionally, says Granger, neurobiology has been a data-rich and theory-poor pursuit. But with the computer neural net, he says, the wealth of data begins to give rise to a coherent picture that wasn't seen before.

And that picture may extend beyond the pyriform cortex. In spite of its relative simplicity, the researchers believe that biologically based computer simulations of this region may lead to a deeper understanding of the much more complex neocortex. This area – which accounts for 80 percent of the human brain and is suspected of playing a role in everything from language processing to spatial tasks – is thought to have evolved from and retained many of the features of the more primitive olfactory region.

As a neurophysiologist who records electrical signals from single cells, Eichenbaum expects that Lynch and Granger's kind of computer model will be invaluable to the biosciences. Some scientists have suggested, he says, that the single-cell approach taken by neurophysiologists is akin to trying to understand how a television works simply by measuring the voltage of each transistor. "We can't take the brain apart," he says. "We can follow global connections, cables, but we can't follow the individual wires that are so important [in learning and memory]." With these computer simulations, however, "we really do for the first time have a hope of understanding the circuit diagram in the brain." □