Neural Code Breakers

What language do neurons use to communicate?

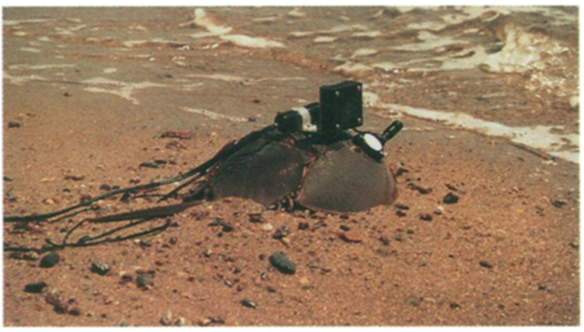
By RICHARD LIPKIN

A Paris bistro, along the sidewalks of Montmartre. A bespectacled man, a woman in a shawl. Before them, two crystal glasses, a basket of bread, a bottle of wine. He reaches for a piece of bread, refills her glass, replaces the bottle.

What could be simpler? Two people enjoying the evening and a fine Merlot.

Yet behind the scenes, within the communication channels of their bodies, a set of silent, surreptitious conversations makes this rendezvous possible. This is the chatter of their nervous systems, which are busy signaling, processing, and relaying information back and forth among a trillion neurons. Sensory systems capture and encode the raw pictures and sensations of their surroundings, then dispatch that information as electric pulses through neural pathways to the brain. There, after cerebral circuits collate and process those signals, a plan emerges. The brain issues commands for action. A sequence of electric signals pulses through the neurological network back down to the body's extremities.

Receiving their marching orders, fingers come together, an arm rises, a hand hovers. Two glasses clink, and a toast is made.


Linda M. Golder

Toting a video camera on its shell, a horseshoe crab heads for the surf. The "crab cam" records the animal's visual scene. The camera's output is fed into a computational model of the crab's eye.

To achieve such moments of poise, the nervous systems of these two diners must speak a language of attention, balance, and movement. Yet exactly how do each person's trillions of neurons constantly share and compute information? Intrigued by this mystery, interdisciplinary teams of neuroscientists and physicists are trying to decipher that language's subtle code.

Like cryptographers during a war, these researchers are intercepting and analyzing encoded transmissions. They eavesdrop among neurons that are communicating with one another as an organism monitors the world.

Each neuron behaves like a small signal processor. En masse, a community of neurons creates a buzz of information. To the eavesdroppers, the electric pulses of the cells appear as spikes on the recording equipment.

"An organism's response to external or internal stimuli must be made solely on the basis of information contained, or encoded, within relatively brief segments of such spike trains," says John W. Clark, a physicist at Washington University in St. Louis. "Within this generally held picture, some of the most basic questions are still unresolved or at best have only fragmentary answers: What variables are encoded in neural activity? What forms are taken by neural codes? How are these codes processed?"

When he regards the nervous system as a network of processors, further questions arise. Clark asks, "How reliable is spike timing? At what rate does information flow? Is most of the information carried in neuronal firing rates, or is the actual pattern of spikes over relevant encoding intervals of crucial importance?"

Collectively, these queries boil down to one fundamental question: Is it possible to decode the language of the nervous system?

"Wiggle your head," says Laurence Abbott, a biophysicist at Brandeis University in Waltham, Mass. "Do you perceive an earthquake? Does the world around you undulate wildly? No. It remains stable. Somehow, the brain corrects for your head's motion.

"On the other hand, if there's a real earthquake, you do perceive the world shaking," he says. "This distinction requires the brain to make an enormously complicated calculation, which it does automatically."

To execute even a relatively simple task, such as seeing an apple on a table and reaching for it, says Abbott, "information about the apple's location must get from the eye to the arm." Yet much more information about the relationship between the person's body and the object is needed.

"If I'm reaching for an apple and I turn my body, for example, the apple is still in the same location, but the motion I need to grab it is quite different," Abbott says. "Somehow, my brain is able to gather and process this information, then put it into a form that allows my body to make the necessary adjustments in its reaching motions."

Inevitably, the brain must represent information about an object's location in a way that both facilitates processing and moves it most efficiently through the nervous system, he says. It's unlikely that the nervous system would translate data important to its survival into many different forms.

What makes this problem difficult to solve, says Abbott, is that the kinds of information required by various parts of the nervous system appear quite different. "The eye deals with spatial information, while the motor system uses a different set of parameters, including body position and balance."

Abbott and Emilio Salinas, also at Brandeis, propose in the October 1995 JOURNAL OF NEUROSCIENCE a computational model that mimics the way the nervous system uses information gathered from sensory neurons to drive motor neurons. From the model, they predict, for example, that in one visual area of the brain the complex interconnections among a group of neurons can lead to the type of signal amplification necessary to trigger a motor response.

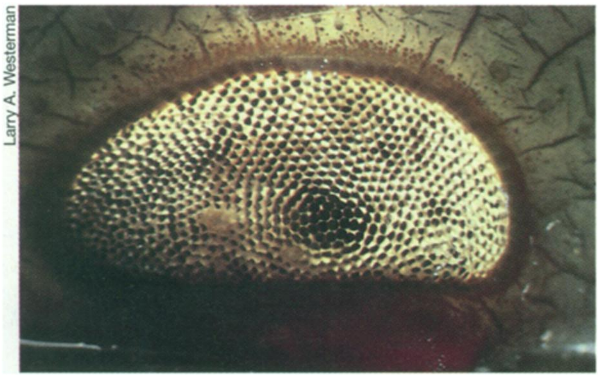
Just as DNA, the bearer of genetic information, eventually yielded its informational language to scientific code breakers, researchers believe that nervous system spike trains will soon reveal themselves as the neural equivalents of words and sentences.

"At the moment, we're not even sure if the symbols of the neural code are made up of one, two, three, or more spikes," says John P. Miller, a molecular biologist at the University of California, Berkeley. "In the genetic code, it took a long time to discover that each word, so to speak, in the code is three base-pairs long.

"Our approach to understanding the neural code is to derive and apply mathematical operations that allow us to decode the spike sequences from real neurons in a simple sensory system."

Miller and his colleagues have turned their attention to the cercal sensory system of the cricket. This system uses two antennalike cerci studded with a thousand tiny hairs to stabilize itself during flight and to detect subtle changes in air currents that enable the insect to sense encroaching predators or potential mates. When air currents tickle these hairs, neurons at the bases of the hair follicles send out signals that are funneled through a narrow band of neurons, or ganglion, on the cricket's abdomen to a cluster of primary sensory interneurons, which relay the signal to the insect's higher nervous system.

Miller and biophysicist Jacob E. Levin, also of Berkeley, and their colleagues have been decoding the signals generated by those cricket cercal neurons. They've built a miniature wind tunnel in which they can expose a cricket to a variety of air currents and record the electric pulses elicited by this stimulation. Using the mathematical tools of information theory to analyze the possible content of the signals obtained from the crickets, they have "characterized aspects of the information-carrying capability of the nerve cells in terms of bits and baud rates, the same measures used for performance specifications of electronic signal transmission devices," says Miller.



Larry A. Westerman

The pea-sized lateral eye of a male horseshoe crab contains 1,000 facets, each containing a lens and light-sensitive cells.

"We've determined that the transfer rates for information about air current velocity ranged from about 100 to 250 bits per second for the sensory receptors and between 10 and 60 bits per second for the primary sensory interneurons," Miller observes. On further analysis, they were surprised to find that each spike has the capacity to transfer as much as 3 bits of information. "These are remarkably high rates of information transfer, from an engineer's standpoint, indicating a high level of encoding efficiency," Miller says.

Moreover, Miller and Levin have found that the cricket neurons have adapted themselves to take advantage of background noise to enhance their sensory perceptions. They find that the noise actually increased the capacity of the cricket's cercal system to sense its surroundings, the scientists explain in the March 14 NATURE. They also report similar findings for wasps and cockroaches.

In many respects, the hairs of the cricket's cercal system resemble the hairs in the human ear, says Levin. "We believe that the neurons of different organisms have more similarities than differences. I look at the understanding of all nervous systems as one great project."

Using mathematical methods to seek a unified theory of neural coding, neuroscientists Charles H. Anderson and David C. Van Essen at the Washington University School of Medicine in St. Louis are grappling with an information-processing problem more subtle than sensory perception. They're trying to understand how organisms are able to pay close attention to some objects while screening out others.

The mere act of walking down a busy street or driving a car, for example, presents the viewer with an overload of visual stimulation. Somehow, individuals must filter that information, paying attention to key details and ignoring the rest.

"This requires an unbelievably complicated set of computations in the brain," says Anderson. Anderson and Van Essen are using ideas from information theory to clear up ambiguities that they say have arisen as a result of comparing the brain and nervous system to computers.

One critical difference between nervous systems and digital processors, says Anderson, is the way they deal with uncertainty. Whereas the processing and response signals of conventional electronic devices are highly regular, the nervous system has to deal with much more variability. As a result, he says, the nervous system can respond more effectively than the average computer to situations in which it is deluged with large amounts of conflicting and uncertain information—such as the flood of signals a driver receives in traffic.

The brain's ability to pick out the salient features to which it must pay attention, says Anderson, has arisen out of the unique way that ensembles of neurons encode and process information. "We need to develop general theories to explain how neuronal systems perform such a rich repertoire of information-processing functions," Anderson says.

What could be more important to an animal than finding a mate? To understand how the nervous system encodes and transmits visual information from the eye to the brain, Robert B. Barlow Jr., a neuroscientist at Syracuse (N.Y.) University, focuses on the male horseshoe crab, *Limulus polyphemus,* as it searches for a female. Mounting video cameras on the animal's shell, Barlow sends the primitive creature into its native waters and records the visual stimuli that it receives along the way.

Limulus vision is poor overall, note Barlow and fellow neuroscientists Christopher Passaglia and Frederick Dodge, both at Syracuse. Underwater, however, a male crab's eye enhances any image that looks like a female, the team explains in the January VISUAL NEUROSCIENCE.

"We think that image of the female crab pops out of the background when the male *Limulus* sees it," Barlow says.

He and his colleagues compared the impulses produced by the male crab's optic nerves to video images captured during a mating patrol. By feeding that information into a computer model of *Limulus*' lateral eye, they have simulated at least part of the horseshoe crab's neural code for vision.

Thinking along similar lines, Fred Rieke of Stanford University and William Bialek of the NEC Research Institute in Princeton, N.J., have been tracking the neural encoding that occurs when a bullfrog hears the nearby croaking of its fellow lily pad dwellers.

"We're interested in the coding of natural sounds, which is why we're working with frogs," says Rieke. "It's clear what their natural sounds are."

Rieke's team has been exposing frogs to two types of sounds—white noise, in the form of electric static, and bullfrog mating calls, recorded one night on a lake in New Jersey. In each case, the distinctive sound waves trigger a specific signature of electric activity within the roughly 10,000 neurons of a frog's auditory nerve.

Mating calls and white noise each tripped off a sequence of electric impulses with a "characteristic fingerprint," the researchers observed. In fact, the frog calls elicited electric impulse patterns that were more specific and carried up to six times as much information as the white noise did, Rieke's group reported in the Dec. 22, 1995 PROCEEDINGS OF THE ROYAL SOCIETY OF LONDON B.

This report supports other recent evidence indicating that much of the filtering takes place in the sensory neurons before information reaches the brain, Rieke says.

"My hope is that if we study the same kinds of sensory problems in several different animal systems, then perhaps we can see some overall rules used in all nervous systems, including our own." ☐