## Watching the Brain at Work

Caltech's Derek Fender is trying to find out what goes on in the brain when it's thinking, and what patterns nerve impulses follow when they are activated by light. What goes on in the brain when it's thinking? What patterns, if any, do the nerve impulses follow when they are activated by a simple stimulus such as a flash of light?

In short, how does the brain work?

The problems in answering questions like these seem at first to be nearly insurmountable. For example, the inherent fragility and complexity of the brain itself, as well as the electronic speed of its activities, defy investigation. Even if direct observation were possible, the observer wouldn't be able to see anything, since the brain's activity occurs through countless electrochemical circuits at electrical potentials on the order of millionths of a volt.

Nevertheless, Derek Fender, professor of biology and applied science, and his graduate assistant Robert Kavanagh, have found some preliminary answers to the question of how the brain works. Through an apparatus they have designed and assembled in the Booth Computing Center, together with some computer software painstakingly developed over the past 24 months, they have reached the threshold of being able to visually follow the interactions among the parts of the brain as it performs some low-level perceptual and cognitive processes.

The technique with which Fender "sees" what happens in the brain involves using a helmet bristling with electrodes that are linked up to an IBM 360-75 computer. Looking like an exotic hair dryer, the helmet is custommade for each subject, air-conditioned, and vacuum-fitted to the head so that each electrode makes a good contact with the scalp. The brain waves are picked up, recorded on digital tape, and transmitted to the computer. The computer in turn is programmed to translate the digital signals into a visual pattern on a cathode ray tube somewhat like a television tube. The result is a picture of the brain waves—a contour map of the peaks and troughs of electrical activity as "seen" through the top of the subject's head.

Each picture on the tube is photographed and ends up as a frame in a movie, which is then studied to see how the brain waves emanate from the various regions of the brain. Fender and Kavanagh have made two such movies, each a little over a minute long, representing the brain wave activity in a quarter of a second—but slowed down 250 times.

Fender and Kavanagh have studied the brain wave patterns of 27 people. One of the things their investigation has already shown them is that perception of a simultaneous light flash and clicking noise will stimulate activity in three distinct locations of the brain. One area analyzes visual images. The second analyzes sound signals. Fender thinks the third area is the one that tries to decide whether the flash and the noise come from the same place.

People have been studying brain waves for 40 years, but there have been numerous obstacles to overcome. Investigators in the past have usually affixed only a few



These three frames from a computer-generated movie illustrate the brain wave pattern that follows a flash of light to each eye separately (left and right) or to both eyes simultaneously (center). The potential field on the surface of the head at 115 milliseconds after a light flash is displayed as contour lines. Dotted areas show negative potential, and the small ellipse on the midline denotes the vertex of the head.

electrodes to the skull, and then have tried to deduce what was going on in the brain from what those few electrodes told them. In fact, though, at least nine electrodes, strategically placed, are needed just to locate a single brain wave source—a point where a cluster of brain cells has fired in collaboration.

Pinpointing the locations of two sources, whose waves may be intermingled by the time they radiate outward to the surface of the scalp, requires a minimum of 30 electrodes in any practical scheme. At present, Fender's system employs a helmet with 49 electrodes.

So, one of the chief features about Fender's helmet is that it gathers a sufficient amount of data. But probably the crucial aspect of the system, and the characteristic which distinguishes it from all other techniques for evaluating electroencephalographic (EEG) data, is the logic reflected in the computer software itself.

When a brain wave signal reaches the surface, its strength as measured by any given electrode will vary depending on how close the source was to the electrode, and what direction the source fired in. Sometimes the strength of a signal makes it appear as though the source were located directly beneath an electrode, when in fact it could be the combined signal resulting from two sources firing from points farther away—but pointed at that electrode.

The only way to tell such cases apart is to do the careful electrical engineering calculations that, in effect, plot the signals picked up from several electrodes on a graph, and then use the resulting curve to deduce the location of the brain wave source. That's where the software comes in.

The software contains the logic—reflected in the form of algorithms—for thousands of such curves, each curve representing the pattern of electrical values that would be picked up by the electrodes if a specific brain wave source should happen to fire.

In a way, the software produces a kind of catalog of electrical curves, each one representing a series of differential equations—and all of them solved by Kavanagh. That's why it took him two years to write it.

In sharp contrast with this technique is what Fender calls the "classical" EEG method: First of all it is based on signals picked up from a limited number of electrodes. Then, looking at a strip-chart recording of the signals, the EEG specialist deduces the location of a given signal source. The potential for serious errors using this "eyeball" method is obvious. (It's no accident that a brain surgeon normally removes a segment of skull bone many times larger than the brain area he plans to work on. He needs a considerable margin of safety.)

And even if the EEG specialist could somehow plot the curves for each pattern of signals picked up by his electrodes, he still could not recognize the subtle—but crucial—differences among patterns with the accuracy or rapidity of a computer.

Fortunately for this experiment, most of man's thinking is done at very shallow depths of the brain—in the cortex at the surface of the hemispheres—rather than in the brain's deeper structures. This makes it easier to locate active neural populations from measurements taken on the scalp.

Another major obstacle has resulted from the low voltage of the brain waves themselves, which range in amplitude from 5 to 100 microvolts (millionths of a volt). Because of the brain's low voltage, the interference problem is severe—not only because of stray voltages constantly surrounding the subject (such as fluorescent lights, line voltages, and radio transmissions), but also because of frequencies produced by other organs and muscles of the body. The heart muscles, for example, produce a twentieth of a volt. Even the muscles of the arteries of the head produce signals. All of this adds up to an enormous data "cleaning" problem.

To deal with this problem, Fender and Kavanagh

conduct their tests in a specially built cubicle with copper mesh walls that take care of the stray signals coming from outside. To solve the problem of the interference from the muscles and organs in the subject's own body, special data recording and processing techniques are used, plus Kavanagh's software which instructs the computer to recognize—and ignore—those unwanted signals.

One of the biggest difficulties in brain research is the sheer volume of data that has to be handled, even in very basic functions like recognizing light flashes and buzzers. But Fender's technique, which makes it possible to record and analyze 1.25 million pieces of information in a quarter-second of brain activity caused by a light flash, appears to have overcome this hurdle.

Even so, the computer time required to translate this data into a series of pictures on the cathode ray tube amounts to 44 minutes—and that is a very long time to spend on any task with a third-generation machine like the IBM 360-75, which can do most tasks in a few seconds.

Fender's work, which is supported by the U.S. Public Health Service, will help bridge the enormous gap in understanding between the neurophysiological work which records and explains the activity of a single neuron or of small groups of neurons, and the work on the complex neural control of behavior in humans.

Individual neurons are very "nonlinear" devices. If even a small number, say 20 or so, are connected together in a network, then however much we might know about the individual cells, it is still very difficult to predict how the network will behave. And yet, the human brain operates on populations of cells that number in the millions. It is the statistical function of the population that carries on, so if some of the cells die, the statistics of the populations are not substantially altered. That's why we can be nearly as efficient at age 70 as we are when we are young.

If the function of the human brain is to be understood by building up from the work done on single cells, the investigations clearly have a long way to go. Present knowledge would not allow us to predict even what a 20-cell network would do.

Work on single cells is further complicated because it requires surgical procedures that would not be tolerated on humans and must be done on animals. This means that measurements made on the brains of cats and monkeys must be used to predict how the human brain works, and this represents an added complication.

Brain research needs people working at many levels, including those who work empirically from the single cell up, those who work on the human being and use theoretical and mathematical techniques to work down, and those who work on populations of cells in between.

Fender expects the work of all these groups to join up one day and form a coherent story of how the human brain really works.