Are We Finding a Way To Study the Action of the Mind?

"Memory, experience, learning are also facts, the laws of which can be investigated. . . ."

So said Hermann von Helmholtz, first to ally physics, biology, and mathematics in the experimental study of perception. Helmholtz would probably be pleased if he could drop in at certain sessions of the 132nd meeting of the American Association for the Advancement of Science this year in Berkeley. It seems likely that the researcher whom Kelvin called "unique in grandeur" would decide that progress is at last being made in study of the action of the mind.

Perhaps one of the best starts in the century since Helmholtz toward some understanding of how 10 billion neurons act in the cortex of the human brain is a study at Massachusetts Institute of Technology of what the frog's eye tells the frog's brain.

While his eyes do not move as ours do, a frog hunts on land and escapes his enemies mainly by seeing. Whether he leaps to capture a bug or dives into the darkest part of the pool to escape an enemy is a split-second matter determined by stimuli received by the one million rods and cones of his retina.

The meaning of signals carried from retinal photoreceptors to the frog's brain by the half-million ganglion cells of the optic nerve has been at least partly unraveled by an M.I.T. researcher, Jerome Lettvin, who will give a Moving Frontiers of Science lecture on Tuesday, 28 December.

Lifting a small flap of bone just behind the frog's eye, Lettvin was able to insert a platinum microelectrode in single fibers of the half-million axons of the optic nerve. As forms of different sizes and shapes were moved in the frog's visual field, he picked up signals that eventually made it possible for him to describe four different visual operations and to find, but not describe, a fifth.

Lettvin was able to report that each visual operation is conducted in the optic nerve by a different group of ganglion cells—each group is distinguishable by the size and shape of a characteristic dendritic tree, differing from others as clearly as the profiles of each species of tree in a forest. In this unparalleled undertaking, Lettvin and associates in the M.I.T. electronic research laboratories were guided by electron micrographs made by H. R. Maturana, who found ten times the number of ganglion cells in the frog's optic nerve than had been estimated by light microscopy.

Organization below the Brain

"The eye speaks to the brain in a language already organized and interpreted," Lettvin said. "There is also an odd discrimination in these cells, which, though one would not be surprised to find it in the whole animal, is somewhat startling in single units so early behind the retina."

The visual responses studied were limited to perception of form or silhouette—response to color was not part of the work so far published. Lettvin's method differed from almost all other experimental study of vision because he did not use flashing lights. Instead he used a wide range of visual stimuli: forms that looked like things the frog could eat or figures it would flee from. But they all moved. "The frog would starve to death surrounded by food if it is not moving," Lettvin says.

An M.D. who passed specialty boards in both neurology and psychiatry, Lettvin taught himself electronics in order to design the equipment needed to study the electrical pattern of perception. At M.I.T. he gives a course in circuit building as well as one in the physiology of perception. While Lettvin's meticulous study of vision in the frog has brought him an international reputation, this work has so far been published in just two tightly written papers. He may decide to discuss not-yet-published work on color perception at the AAAS lecture.

Lettvin's finding that a large amount of visual perception is organized below the brain supports other new approaches to study of learning and memory. Until recent decades these complex mental activities, whose development has made the human species dominant over other forms of life, were thought to be fairly well centralized in the cerebral cortex, absent or only partly developed in all other species. But now researchers have shown that rats, pigeons and even fish and flatworms can learn. Indeed, workers have even reported that learning can occur in a single nerve ganglion of a cockroach.

A psychologist, Edward M. Eisenstein of the State University of New York at Stony Brook, is one of the researchers inquiring whether a headless cockroach can learn leg position.

Discussing drug effects on learning, work done with Lewis Petrinovich, Eisenstein will be one of several dozen participants in an interdisciplinary symposium on behavior, brain and biochemistry arranged for the AAAS annual meeting by David Krech of the University of California.

Krech is a psychologist widely known for studies, with Mark Rosenzweig, of the correlation of various aspects of behavior with the amount of acetylcholine and cholinesterase in the central nervous system. Krech's work indicates that maze-bright rats have more of both the neural transmitter and the enzyme that destroys it than do maze-dull rats. The Krech group has bred strains of bright and dull rats, now widely used by other researchers in learning experiments.

For the 2-day (27 and 28 December) symposium, Krech has lined up a group of workers whose specialties ally neurophysiology, biochemistry, genetics and behavioral psychology in study of the nervous system. Thus participants will range from a neuroanatomist who will report that effect of rearing in the dark is visible in certain cells of a cat's cerebral cortex to psychologists whose experiments give particular promise that psychology may be succeeding in its struggle to become a science.

While others have reported that rearing experimental animals in the dark has blocked the development of retinal cells and of ganglion cells of the optic nerve, Paul Coleman, University of Maryland Medical School, is the first to observe this effect on dendrites of cells in the cerebral cortex. He did this by turning back to a 19th century technique: Golgi's silver stain as developed by the great Spanish neuroanatomist, Santiago Ramón y Cajal. It was this technique that made it possible for Cajal to reveal the neural structures in elegant drawings like his study of the frog retina shown below and, in 6 years of work, to transform understanding of the function of the nervous system.

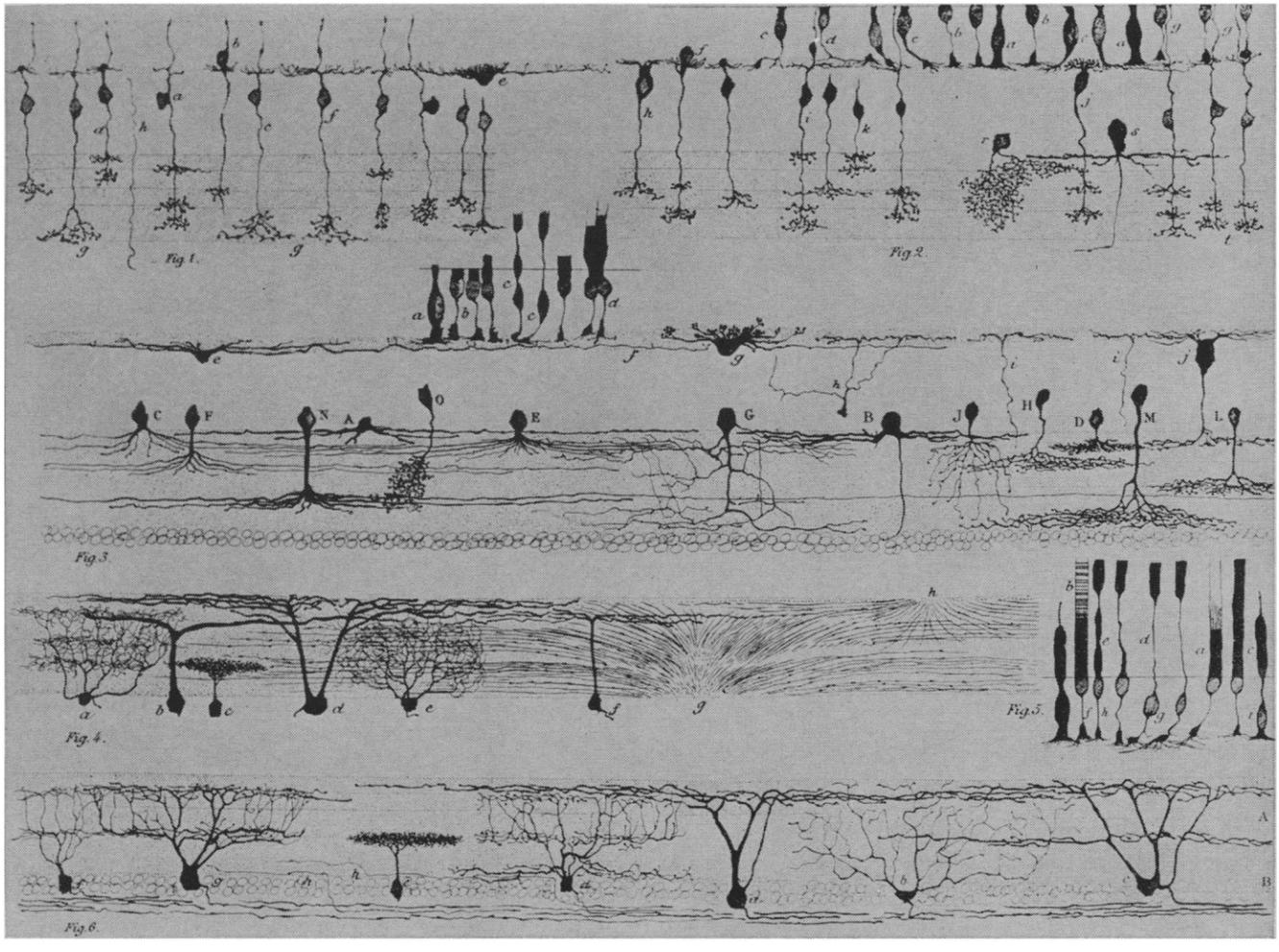
Cajal was not an experimentalist and it has remained for 20th-century workers to confirm many of the insights he derived from study of neural microanatomy. One of these was his suggestion that cortical dendrites grow in response to stimuli and are dwarfed if function is absent. In an experiment with cats raised in the dark, Coleman used Cajal's method to observe dendrite branching of stellate cells in visual centers of the cerebrum. He will tell what he found out, at the 28 December session of the behavior, brain, and biochemistry symposium.

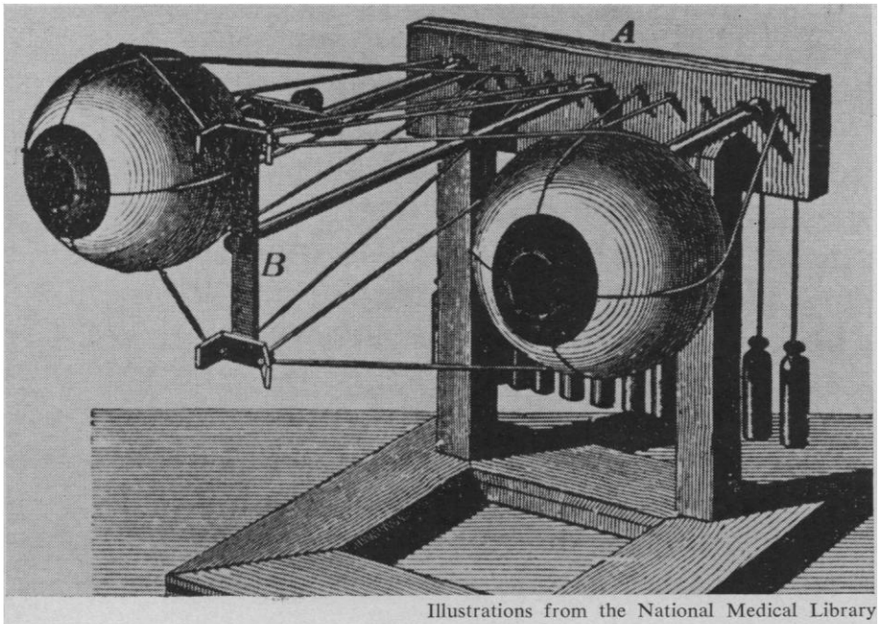
When Sweden's Holger Hydén reported that after a rat learns a balancing task nuclear RNA decreases in the large vestibular nerve cells and increases in the surrounding glial cells, researchers the world over were encouraged to look for the molecular basis of memory. Working under a stereomicroscope, Hydén uses a steel thread about 1/10 the diameter of a human hair to tease fresh nerve cells away from the glial cells into which they push their roots like plants in the soil. Since not many other workers have been able to make this delicate separation in quantities sufficient to permit analysis, Hydén's method has not spread beyond the University of Göteborg. But from that center provocative reports have continued to come.

Other workers have tried in other ways to examine RNA changes and protein synthesis in nerve cells, and several outstanding studies of this sort will be discussed at the AAAS symposium. One approach is to use agents such as puromycin, a nucleoside amino acid thought to interfere with protein synthesis by blocking transfer of amino acid from RNA to protein. Bernard Agranoff, University of Michigan, examined the effect of puromycin on memory in goldfish in a two-year study with Roger Davis and John Brink. Agranoff will tell how this work suggests that goldfish have both a short-term and long-term memory.

Using an autoradiographic technique, Joseph Altman of the Massachusetts Institute of Technology has been able to measure concentration of radio-

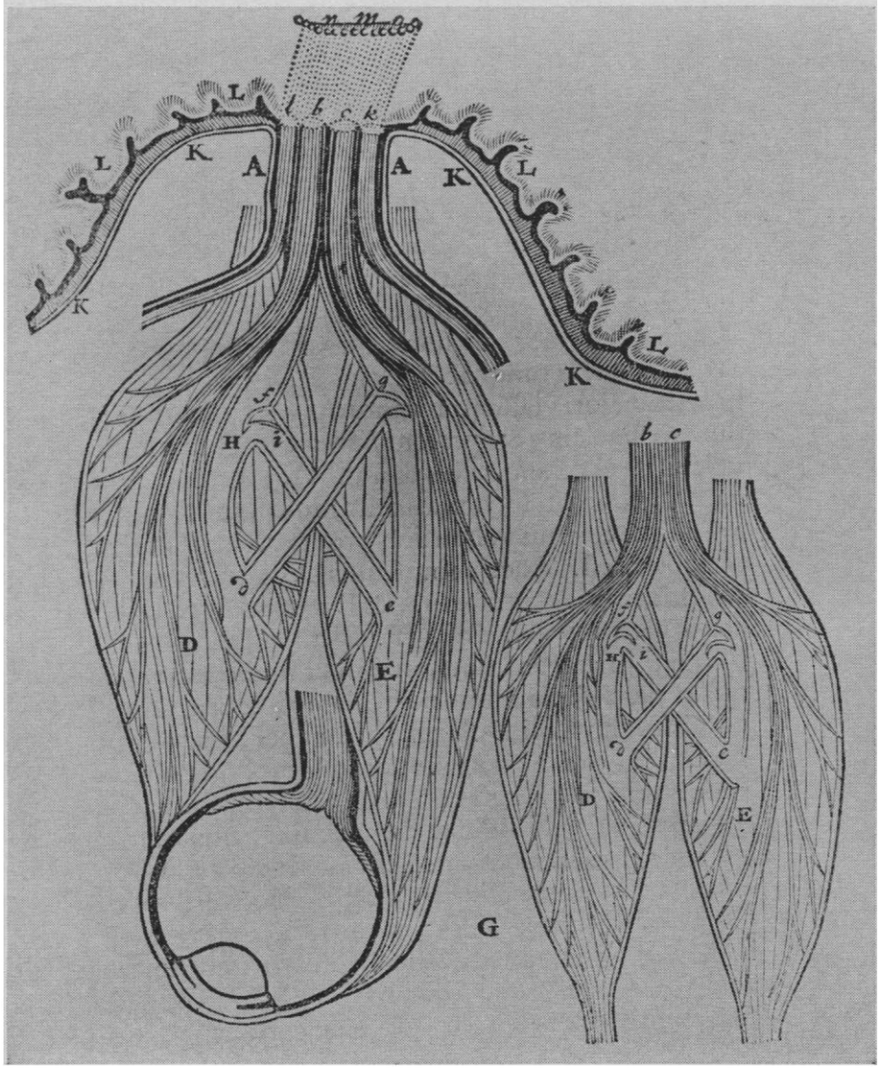
Cells transmitting visual stimuli from frog retina to brain were first clearly differentiated by Ramón y Cajal. In optic nerve, Cajal disclosed five types of ganglion cells, each showing a different shape of dendritic tree (figure 5). Jerome Lettvin has found five different visual operations in these ganglion cells.





Illustrations from the National Medical Library

Helmholtz used ophthalmotrope (above) in 19th-century study of vision. Descartes offered a 16th-century explanation of the eye (see below): Nerves have skins, which originate in the brain. These form little tubes, through which a subtle air flows from the cavities of the brain, activating muscles.



leucine in very small brain areas and even cells. With this amino acid as a gauge of protein formation in rats, Altman found that high rates of protein formation are associated with stress, but not, in animals adapted to stress, with motor activities or visual tasks. At the symposium he will tell why he thinks the powerful effects of emotional stress and arousal must be controlled in study of the relation between learning and protein formation.

Despite this and other indications of the complexities that surround the search for chemical correlates of learning, interest in RNA has been supported by such well-known experiments as the work with planaria by James McConnell and others at the University of Michigan. McConnell taught flatworms to associate light with shock and reported that he was able to transfer this learning to other flatworms by feeding them cut-up portions of trained worms. When D. Ewen Cameron of Montreal reported that RNA extracted from yeast seemed to improve memory in aged (but not senile) patients, it seemed likely that a pharmaceutical with this sort of action would soon follow.

Now N. Plotnikoff, pharmacologist, and A. J. Glasky, biochemist, may have arrived at such a drug, and Plotnikoff has succeeded in synthesizing it in Abbott Laboratories. With L. Simon, a biochemist at Illinois State Pediatric Institute, the Abbott researchers will report at the AAAS symposium that the drug enhances nucleic acid synthesis, learning, and memory in experimental animals. An application for approval from the Food and Drug Administration for use of the drug in humans has been made.

The above is only a sampling of the reports that will be made at the symposium on brain, biochemistry, and behavior, which will be held as a part of AAAS general sessions.

No one interested in the chemical basis of behavior will want to miss Bernard Brodie's lecture on biochemical aspects of mental disease on 30 December. Head of the National Heart Institute's Laboratory of Chemical Pharmacology, Brodie has published more than 265 papers covering many aspects of drug function. When he found that reserpine impairs the mechanism that stores serotonin and reduces this substance in the brain, many began work to try to show that serotonin is a neurohormone acting on the brain whose absence may cause mental disease.