Herschel Kenworthy Mitchell
1913 — 2000

Herschel Mitchell in 1988, photographed by his wife, Annamarie.

by Norman Horowitz, Professor of Biology, Emeritus

Emeritus Professor of Biology Herschel K. Mitchell died on April 1, following a stroke, his second in a period of 10 years. The first stroke confined him to a wheelchair, but he retained the ability to speak and was frequently seen on campus with his attendant, Douglas Ross.

Mitch, as he was known to his friends, played an important role in the advances that revolutionized the science of biology in the 20th century. Born on November 27, 1913, in Los Nietos, California, near Los Angeles, he attended Pomona College and graduated in 1936 with honors in chemistry. This was followed in 1938 by a master's degree in chemistry from Oregon State College and, in 1941, a PhD in chemistry from the University of Texas.

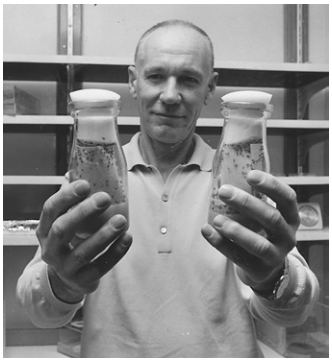
At Oregon State, Mitchell worked with biochemists R. J. Williams and E. E. Snell, and he accompanied them when they moved to the University of Texas in 1940. His most significant research in those years dealt with the B vitamins folic and pantothenic acid. He was the discoverer of folic acid and was primarily responsible for its initial isolation from four tons of spinach.

From Texas, Mitchell moved, in 1943, to Stanford University as a research associate in the laboratory of George Beadle. The Beadle lab was investigating the role of genes in metabolism—work that had been made possible by Beadle and Tatum's discovery of mutations in the mold Neurospora that blocked the synthesis of specific vitamins, amino acids, and nucleic acid bases. At the time, Neurospora was the only genetically well-understood microorganism. Its genetic organization and metabolic properties made it ideal for the revolutionary program initiated by Beadle and Tatum that succeeded in uniting genetics and biochemistry. Mitchell occupied a unique position in the Beadle group. He was a genuine glassblowing chemist with little knowledge of genetics, whereas the others were geneticists, largely self-trained in chemical procedures. Mitch, for his part, had to learn basic genetics, which he soon did.

When Beadle left Stanford in 1946 to become chairman of the Division of Biology at Caltech, he took Mitch with him, along with other senior members of his research group. In 1949, Mitchell became associate professor of biology at Caltech, and in 1953 full professor. He retired in 1984 as professor emeritus.

Over the years, Mitch and the excellent students and postdocs he attracted to his laboratory made important contributions to the developing field of biochemical genetics. Among the most consequential of these was the first demonstration of an enzyme missing from a Neurospora mutant. Such a demonstration was one of the early goals of the Beadle lab. Up to that point, the evidence had established that specific gene mutations cause blockage of specific biosynthetic reactions, and it was assumed that loss of the enzyme catalyzing the reaction was responsible. The demonstration by Mitchell and Lein that the enzyme

In 1995 Mitchell attended Ed Lewis's Nobel Prize celebration. From left: biologists Norman Horowitz, Lewis, Seymour Benzer, Mitchell, Norman Davidson, and Ray Owen, all professors emeriti.



Mitchell appeared in the January 1972 *E&S* with some of his Drosophila—in this case miniflies he had produced by injecting two-day-old larvae with a polypeptide derived from bee venom.

(tryptophan synthetase in this case) was absent from the mutant but present in the wild type from which the mutant arose was an essential step in the argument that eventually established that genes control metabolism by producing (in a manner not then understood) the enzymes required for specific chemical reactions, the rule being that one gene governed the synthesis of one particular enzyme. Beadle called this the "one-gene-one-enzyme" hypothesis. It later was refined to become "one-gene-one-protein" and, finally, since some proteins are composed of more than a single polypeptide, each with its own gene, "one-gene-one-polypeptide." Other refinements are now recognized, but all are reducible to the idea of a simple relation between genes and proteins.

Mitch's interests were wide ranging. His published works include papers dealing with the biosynthesis in neurospora of adenine, pyrimidine nucleosides, nicotinic acid, lysine, histidine, and tryptophan; and they include studies on topics as diverse as maternal inheritance and temperature-sensitive mutants in this organism.

In the early '50s, Mitchell became interested in the problem of development in higher organisms and turned his attention to the genetically important insect Drosophila. Development can be described, at one level, as the programmed synthesis of specific proteins through time. Since the structure of every protein of an organism is encoded in the organism's genes, development involves the activation of specific genes at the time and place the proteins they encode become needed for production of the organism.

The problem that came to occupy Mitch's attention starting in the 1970s and to which he made important contributions was the phenomenon of heat-shock. Heat-shock refers to the effect of brief exposure to heat on the biochemistry of cells and tissues. It had been known since the early '60s that heat-shock causes "puffing" of specific regions of the giant salivary chromosomes of Drosophila, and it had been suggested that puffing was an indicator of gene activity. In 1973 Mitchell, together with Swiss biochemist Alfred Tissières, began to work on heat-shock. They made the basic discovery that heat-shock induces the production of a small number of proteins and inhibits the production of most others. This was the first chemical work ever done on heat-shock, and it gave rise to a large amount of research on its mechanism and biological role. It has recently been found that the proteins induced by heat-shock are principally "chaperones" that function in the refolding of proteins damaged by heat stress. The phenomenon is not restricted to Drosophila, but has been found in all species examined, from bacteria to man—indicating that it is very ancient and also very important. Since 1973, the study of heat-shock has become a new area of biological research, one for which Mitchell was a founding father. □

Meyerowitz New Chair

Elliot Meyerowitz, a specialist in the genetics of flowering plants, has been named chair of the Division of Biology at the California Institute of Technology. Meyerowitz replaces Mel Simon, who is returning to full-time faculty and research duties after serving five years in the office.

A member of the Caltech faculty since he arrived as an assistant professor in 1980, Meyerowiz has been professor of biology since 1989 and was executive officer from 1995 to 2000. His primary research interest is the genes that control the formation of flowers, and how altering these genes will affect flower development. He has identified mutations that cause petal cells to develop into stamens instead, and another mutation that causes these same embryonic petals to become sepals (see *E&S*, 1997, No. 4).

Meyerowitz earned his bachelor's degree in biology, summa cum laude, at Columbia University in 1973, and his doctorate at Yale University in 1977. He received the John S. Nicholas Award for Outstanding Biology Dissertation from Yale for his doctoral reserach. He came to Caltech following a postdoctoral appointment at Stanford.