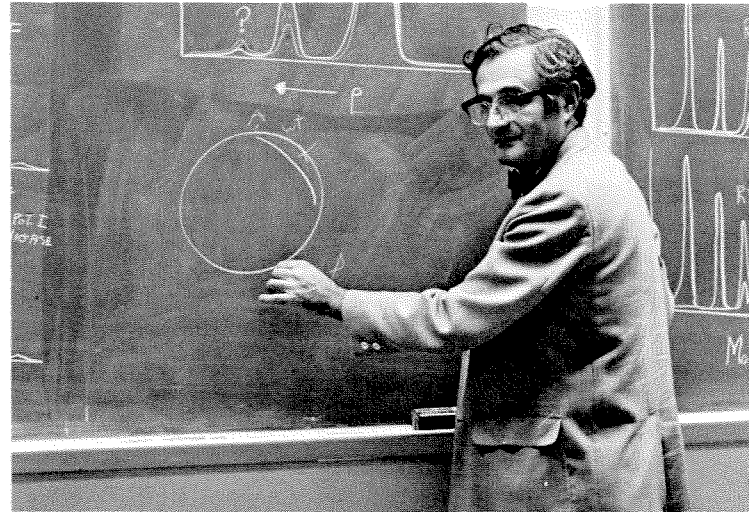


# CANCER RESEARCH: Down to the Basics

At Caltech it is an accepted fact that, in the long run, basic research is often the best kind of applied research. Although the results of a scientist's investigations may not be immediately useful, his discoveries often serve as the foundation upon which applied research may later be done.

This philosophy finds clear expression in the Institute's approach to the problem of cancer. While none of the Caltech biologists and chemists on these pages consider themselves cancer researchers, their investigations of fundamental biological problems may yield insights into the causes of this devastating disease.

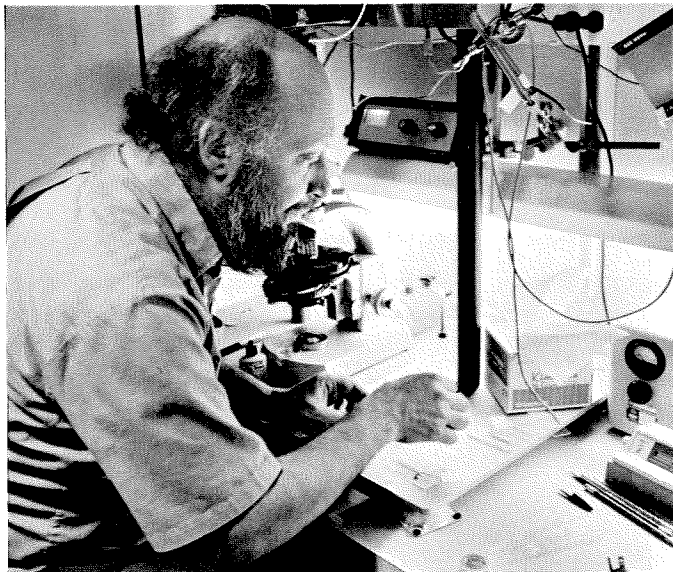


## Robert Sinsheimer

Research is more than just doing experiments; it is also reading, writing, discussing, evaluating, arguing, and planning. It takes place not only in the laboratory, but also in the office, the library, the hallway, the conference room, and at the blackboard. It is a team, rather than an individual, effort. In the division of biology, Robert Sinsheimer, chairman of the division and professor of biophysics, administers this diverse effort. In addition, he heads a group that is investigating a small DNA virus known as Phi X 174, which is made up of only nine genes. This relatively simple virus, like some cancer viruses, infects and destroys healthy cells in order to replicate itself. Studies of such simple organisms are vitally important to understanding the nature and behavior of the more complex cancer viruses.

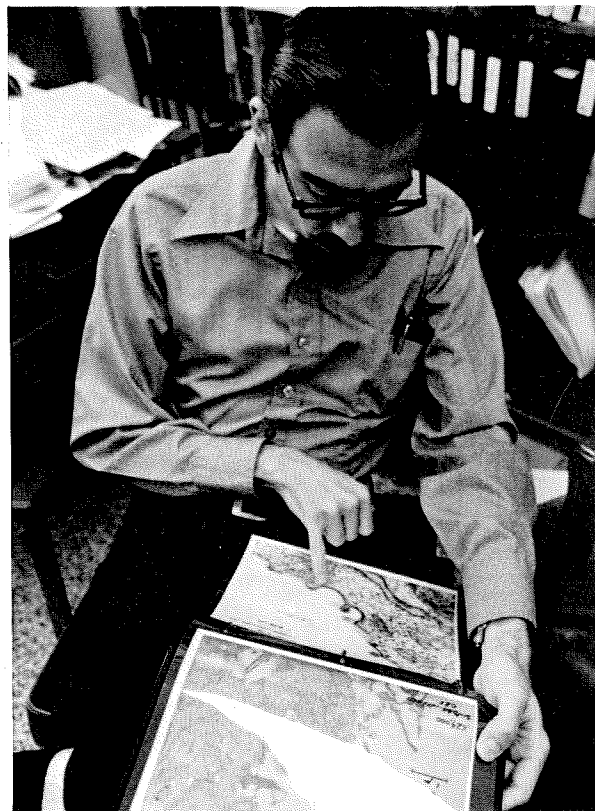
## William Wood

William Wood, professor of biology, and his research associates are studying a DNA virus, T4, which has only 150 genes. It looks like a microscopic hypodermic needle with legs, and the group is trying to learn how its various parts are produced and assembled inside the cells it infects and destroys in the act of reproducing itself. An understanding of how new virus particles are assembled—and the roles the infected bacterial cells play in the assembly—may help reveal how tumor viruses are involved in the production and growth of cancers.



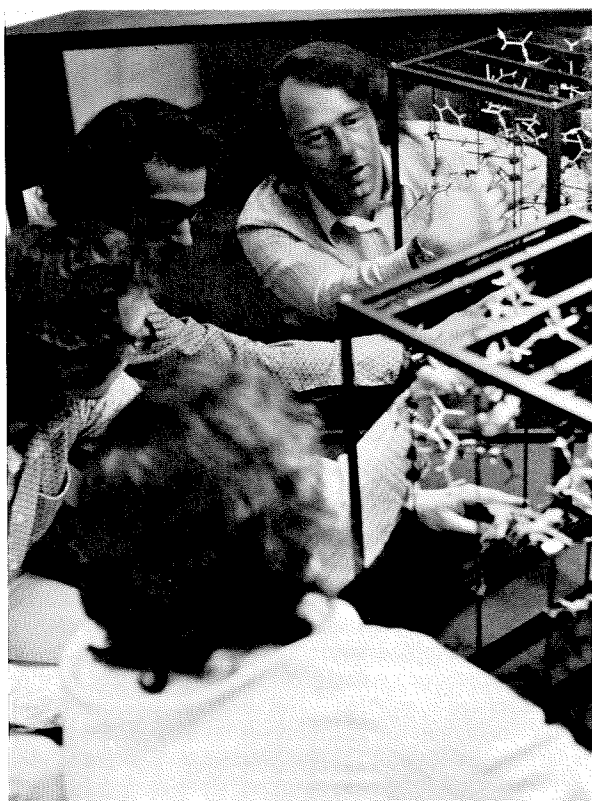
### Jean-Paul Revel

Jean-Paul Revel, professor of biology, examines photographic slides of a cell surface taken with an electron microscope. Studies of the nature of cell surfaces and how cells connect to one another can lead to an understanding of how the surfaces of cancer cells differ from those of normal cells.



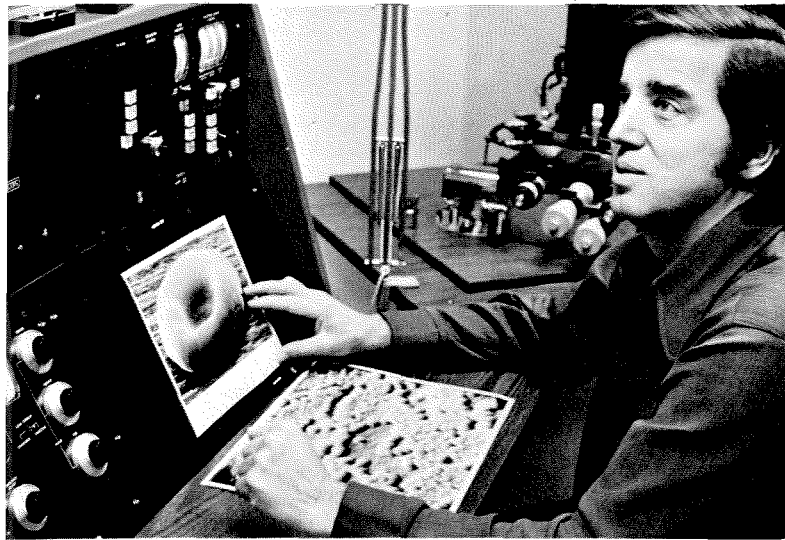
### James Strauss

Electron microscope photographs enable scientists to see the genes, viruses, bacteria, and cells they study through the use of sophisticated—but indirect—tests in the laboratory. Here, James Strauss, professor of biology, examines a photograph of a Sindbis virus that has been enlarged 250,000 times. Sindbis is an RNA virus made up of a single thread of genetic material covered by lipoproteins (combinations of proteins and fats). It infects animal cells, but does not produce cancer; yet, both in its makeup and behavior, it resembles some of the cancer-producing RNA viruses. Strauss is studying how the Sindbis virus reproduces within the cells it has infected, and how it manufactures the lipoproteins to wrap itself in.



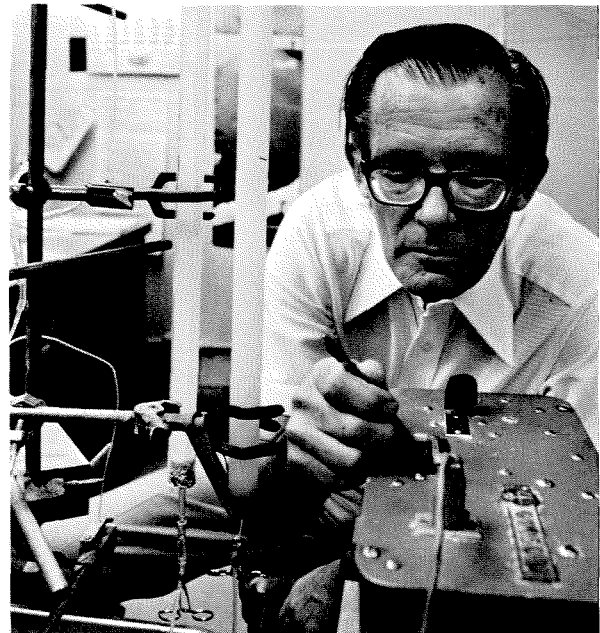
### Robert Stroud

Robert Stroud, Noyes Research Instructor in Chemistry, and members of his research group work with a model of the structure of a protein's nucleic acids. The group is studying the makeup of glycoproteins (proteins with sugar residues attached), which are involved in the specialized surfaces of different cell types. Changes in the condition of a cell's outer membrane seem to be associated with the regulation of normal cell growth and the unrestrained growth of cancer cells.



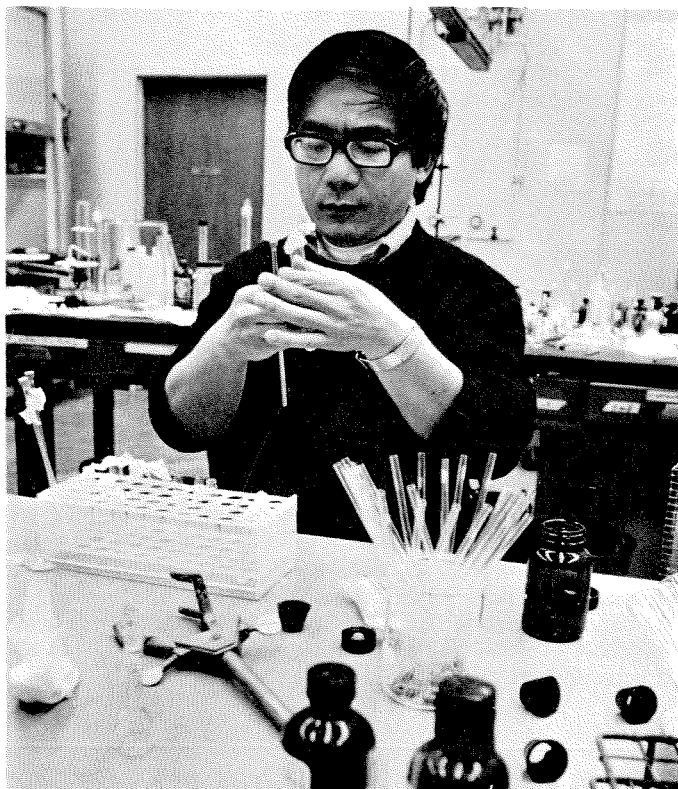
### William Dreyer

William J. Dreyer, professor of biology, analyzes two photographs taken with a scanning electron microscope—one of a normal human red blood cell, the other of specially designed polymeric spheres with antibody molecules on their surfaces that will react only with specific substances on the blood cell. Working with Alan Rembaum of Caltech's Jet Propulsion Laboratory, Dreyer is trying to develop molecular "smart bombs" that will attack only certain types of cancer cells. This work grows out of Dreyer's basic research on the system of surface recognition codes used by normal cells as they move and touch each other. These codes probably enable the cells to fit together correctly and to grow in a controlled fashion, in contrast to the defective surface recognition code system of cancer cells which permits abnormal growth.



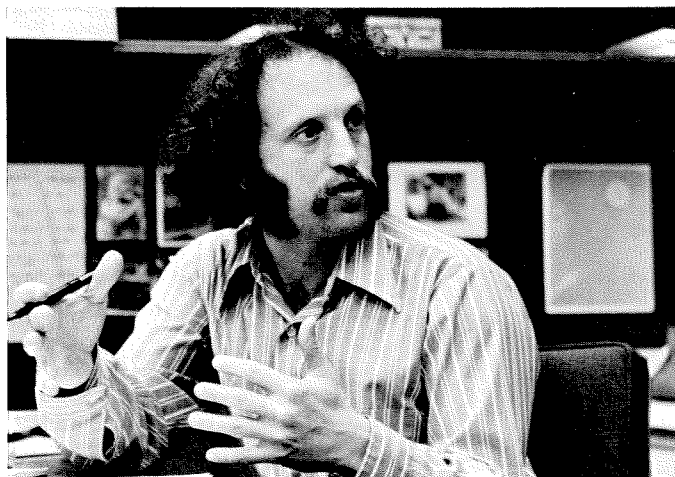
### James Bonner

James Bonner, professor of biology, and his research group are trying to learn more about normal, controlled growth, and what biochemical signals turn cells on and off—that is, what starts cells growing and what stops them. The group studies rat liver regeneration to find out what turns this organ's cells on when it has been seriously damaged, and what turns them off when it has returned to normal size. Knowing why and how this happens is important in understanding cancerous tissue, where cells do not respond to the signals that limit and control their growth.



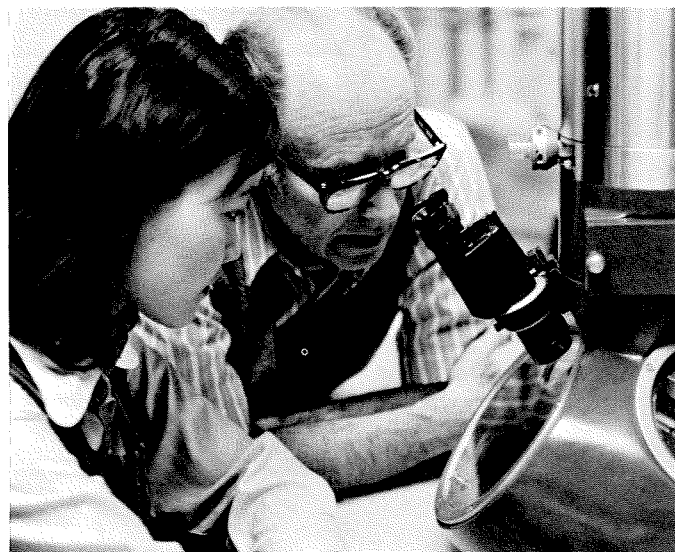
### Sunney Chan

Sunney Chan, professor of chemical physics, gauges the growth of a culture of artificial lipid bilayer membranes that he and his group use to simulate natural cell surfaces. They are investigating the way the outer membrane of a cell controls the flow of materials in and out of the cell. Utilizing weak radiofrequency signals, which are absorbed and emitted by the molecules in the membrane when the cell is placed in a high magnetic field, they are attempting to build a detailed picture of the atoms and molecules involved in this dynamic, changing system. An important goal of their work is to unravel those secrets and principles underlying the chemistry of the cell surface—particularly those relating to how glycoproteins modify the surface of the cell and control its properties and function. Some of the information gained from these studies will lead to an understanding of the phenomenon of "contact inhibition"—the way normal cells cooperate and stop growing when they touch each other—and why cancer cells exhibit no such organized control.



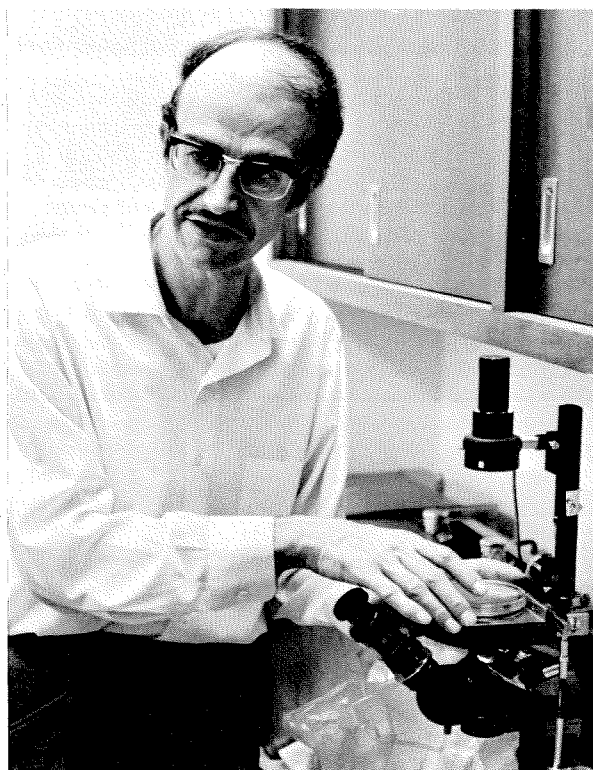
### Eric Davidson

Working with the cells of frogs, sea urchins, and snails, Eric Davidson, associate professor of biology, and his co-workers are investigating the regulation of genes—the mechanism that determines the growth and development of an organism. The sequence in which groups of genes in a cell have been turned on and off—and the timing of the appearance of new patterns of gene activity—determines the kind of tissue the cell will become. It is believed that cancer may be the result of an abnormal regulation of a cell's genes; some that normally should be turned off are somehow turned on, or else the timing mechanism has malfunctioned.



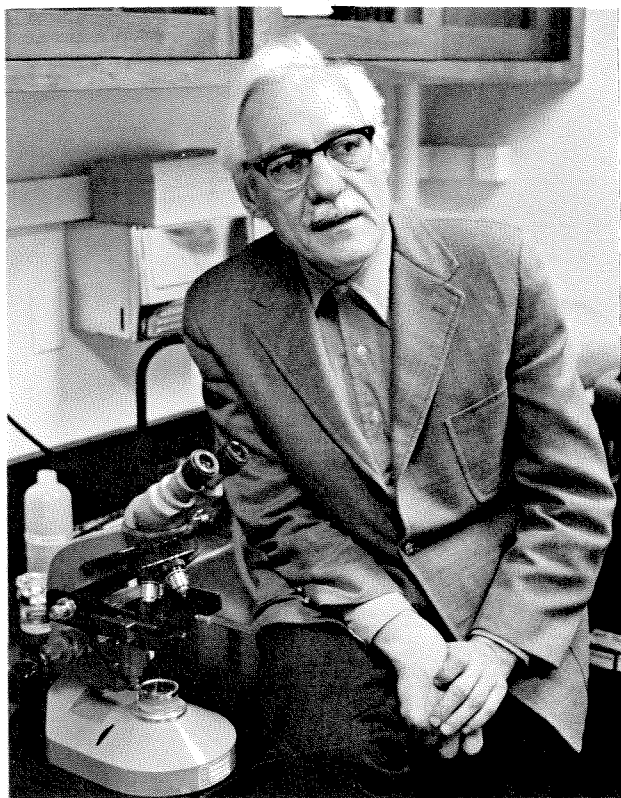
### Norman Davidson

With the aid of an electron microscope, Norman Davidson, professor of chemistry, and graduate student Sylvia Shaw-fen Hu study the sequence of genes on a strand of viral DNA. The development of the virus depends on the order in which its genes are turned on and off. In studies of viruses, bacteria, and cells, Davidson and his co-workers have found that this on-off mechanism is regulated in some unknown way by control sequences that are interspersed between the genes. In trying to determine the relative positions of the control sequences and the genes, the Davidson group has mapped sequences in DNA molecules of viruses and bacteria containing from 10 to 5,000 genes, and it is now trying to do the same with the higher animals, including man, whose DNA contains many thousands of genes. This information could tell us why most cells remain normal, but some become cancerous and grow out of control.



### Giuseppe Attardi

With a specially designed microscope, Giuseppe Attardi, professor of biology, is able to study living cancer cells growing in a petri dish. He and his group of researchers are trying to learn more about the nature and function of mitochondrial DNA genes of human cells—both normal and cancerous. Information on these genes is read and translated into unique proteins that only mitochondria—the power sources of the cell—can produce. Attardi's group is working at isolating and identifying the proteins synthesized by mitochondria which are essential for energy production and for keeping these cellular powerhouses "alive."

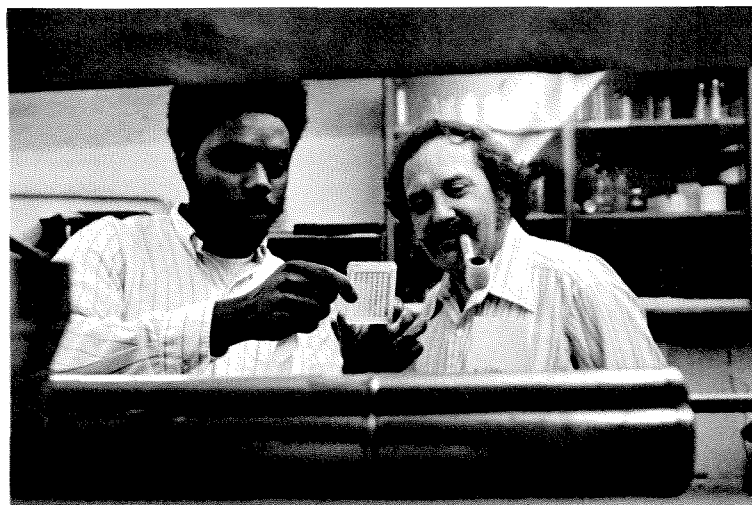


### Jerome Vinograd

Jerome Vinograd, professor of biology, and his research associates are studying the mitochondria, sausage-shaped structures within a cell that supply it with energy. Mitochondria also have their own chromosomes, independent of the cell. These are double strands of DNA genes that are twisted together and formed into rings. The researchers have found that the mitochondrial DNA rings in the cells of circulating human cancers (leukemias) are twice the size of those in normal adult cells. The same size differences are also found when normal cells are compared to the cells of many—but not all—solid human cancers. If scientists can find out why this occurs, it will help them understand the differences between cancerous and normal cells.

### John Richards

John Richards, professor of organic chemistry, right, and graduate student Dale Kooistra insert an antibody protein specimen in a nuclear magnetic resonance (NMR) spectrometer. NMR spectroscopy was developed originally for use in the physical sciences, but has turned out to be a powerful tool in biology as well. With this instrument, one can examine the fine details of the environments of particular nuclei in a molecule. Such information allows Richards and his research group to learn more about the structure and action of proteins. In this research, they are investigating various antibody molecules—proteins created by the body to combine with and neutralize disease-causing organisms which may invade the body, such as cancer viruses and bacteria.



### Ray Owen

Ray Owen, professor of biology, right, and Price Walker, a senior in biology, assess the effectiveness of an antibody against a series of cell specimens on a titer plate. This test is part of a study of the immune system in mice and humans. One reason cancer does not affect more people than it does may be because the body has a specific defense network that recognizes cancer cells as being "foreign" and sends antibody molecules out to destroy them. This important body mechanism is the basis for immunotherapy—a treatment for cancer involving artificial stimulation of the immune system.

