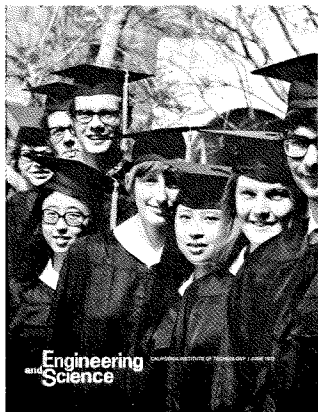# Engineering and Science

and

CALIFORNIA INSTITUTE OF TECHNOLOGY / JUNE 1973

In this issue

Trailblazers

On the cover—*E&S* salutes four historic women, Caltech's first female bachelors of science, the accomplished and attractive vanguard of a new subset of Caltech alumni. "Pioneer Women" (page 20) gives a glimpse of the interests, research, and plans of Stephanie Charles, Deborah Chung, Sharon Long, and Flora Wu.

In "Being a woman at Caltech has its own special set of challenges." (page 22), one of these women—Sharon Long—tells something of what it was like to be an undergraduate at Caltech. Sharon shares many of the experiences of the other women—including having graduated with honor. In addition, she received Caltech's coveted Hinrichs Award for contributions to the welfare of the student body and for outstanding qualities of character, leadership and responsibility.

Cancer Research and Caltech

Cancer is a disease we do not yet understand, but at Caltech there are at least 15 scientists whose investigations into fundamental biological problems may eventually lead to understanding. They are not cancer specialists in any narrow sense; rather, they are molecular biologists and protein chemists who work in fields that are basic to the cancer problem.

One of these men is Leroy Hood, associate professor of biology and author of "The ABC's of Cancer" (page 2), which is based on his May 14 Watson Lecture at Beckman Auditorium. Hood is well qualified to discuss both the basic science and the clinical aspects of cancer. He took his BS degree in biology at Caltech in 1960, and then went to the Johns Hopkins School of Medicine, obtaining an MD four years later. However, he decided he preferred medical research to medical practice, and came back to Caltech for a PhD in biochemistry, which he received in 1967. He then went to the National Cancer Institute for three years as a senior investigator studying the chemical structure of antibody molecules. He joined the Caltech faculty in 1970.
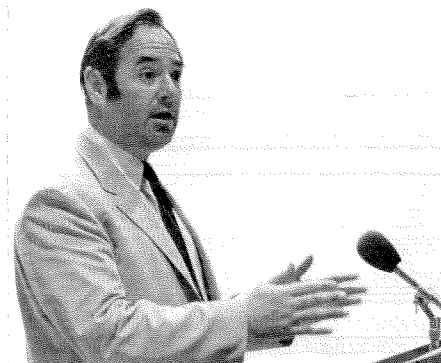
Work like Hood's—and that of 14 fellow Caltech researchers, which is described in "Cancer Research: Down to the Basics" (page 11)—offers one of the best hopes for progress toward the prevention and cure of cancer.

Atomic Electronics

Two members of the Caltech faculty are now doing the groundwork for what may someday result in atom-by-atom, custom-engineered semiconductor devices. In "Crystal Growth through Solid Metal" (page 16), James O. McCaldin, associate professor of applied science, and James W. Mayer, professor of electrical engineering, describe the work that may contribute to such a breakthrough.

Pilgrim's Progress

In "The Making of a Mahatma—Gandhi's South African Years" (page 24), Robert A. Huttenback, professor of history, chairman of the division of the humanities and social sciences, and a distinguished scholar in the field of British imperial history, tells something of what went into the evolution of the philosophy and political techniques of India's revered Mahatma Gandhi.

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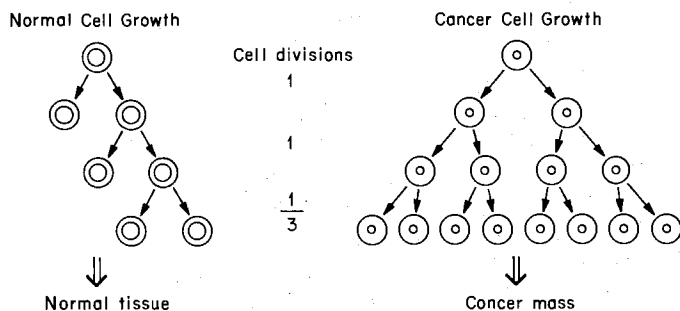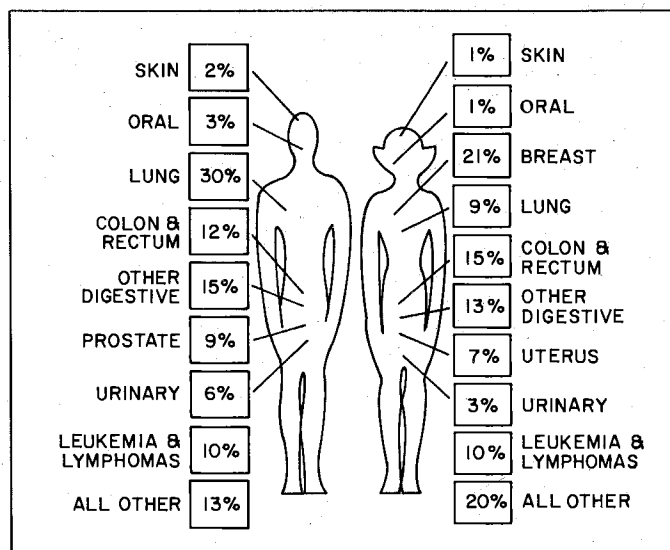
The ABC's of Cancer

C ancer has had a profound impact on human experience and, accordingly, various segments of society see this disease in different ways. To the physician, cancer is a vexing, frustrating, sometimes tractable, but more often incurable disease. To the research scientist, it is a fascinating enigma which may provide a model for understanding some of the most difficult puzzles of cellular biology. To the layman, it is an unknown, shaped by vague rumors, superstitions, haunting deaths, and most of all by fear.

What Is Cancer?

Cancer is a disease in which cells divide when they should not. Most cancers start as a single abnormal cell which at each step of cell division produces daughter cells that in turn divide to produce additional cancer cells. In contrast, normal cells divide asymmetrically so that only one of the two daughter cells generally has the ability to divide and produce additional daughter cells (below). Thus a single cancer cell divides again and again in an uncontrolled fashion to produce a tumor mass with three general properties that are of clinical importance. First, the tumor mass generally increases rapidly in size. Second, it invades and destroys surrounding normal tissues. Third, clumps of cancer cells can break away from the parent tumor mass, migrate through the blood and lymphatic vessels of the body, and eventually come to rest in distant tissues such as the lungs or the liver to

CANCER DEATHS BY SITE AND SEX—*It should be noted that the incidence of cancer in a particular tissue can be quite different from the incidence of cancer deaths at that same site. For example, 23 percent of the cancers arising in males occur in the skin, but only 2 percent of cancer deaths are attributable to skin cancer.*

A MODEL FOR NORMAL AND CANCER CELL GROWTH—*In general, each cancer cell can divide to produce two new daughter cells, but normal cells generally undergo an asymmetric cell division that leaves only one daughter cell with the capacity to undergo further cell division. In addition, the growth of normal cells is regulated by a variety of poorly understood mechanisms, while cancer cells divide in an unregulated fashion to produce a tumor mass.*

establish secondary tumor foci or metastases. The often explosive seeding and growth of these metastases present the physician with an extremely difficult clinical problem.

The prognosis for survival of a particular cancer patient correlates very well with the extent to which the cancer has spread. Patients whose tumor is discretely localized to a single site often have a favorable prognosis. Once the tumor has begun to invade the surrounding tissues the prognosis becomes only fair. Finally, when the tumor begins to metastasize to local and finally to distant sites, the prognosis becomes grave to terminal. Consequently, early cancer detection is an extremely important aspect of the clinical treatment of cancer.

Cancer can arise in any cell type, although it occurs much more frequently in certain tissues (above). In males, lung and colon cancer are major killers; in females, breast and colon cancer predominate. Cancer occurs most commonly in those tissues which cover various organs and are exposed to the external environment (i.e., air and food). Certain environmental agents or carcinogens may cause specific types of cancer.

Cancers of the same tissue may vary markedly in growth rate. For example, two women may each have a small and cancerous breast nodule about a half inch in

by Leroy E. Hood

diameter. After appropriate surgery, one woman will be alive and well 20 years later; in the second, the tumor will already have metastasized and spread throughout her lungs and bones, generally leading to death within a year. Thus the malignancy or the ability of a particular type of cancer to destroy the host varies enormously from one tumor to the next.

Cancer is also a disease that is related to the aging process. More than 50 percent of those cancers that eventually kill the host appear in individuals who are over 65.

Cancer is the second leading killer in the United States, falling only behind heart disease. Approximately one person in four will contract cancer at some point in his life, and two families in three will be affected by it. In 1973 more than 350,000 Americans will die of cancer.

A Clinical View of Cancer

From the clinical viewpoint of the physician there are three aspects to cancer as a disease entity—prevention, diagnosis, and therapy.

Prevention

Environmental agents, or carcinogens, can cause cancer. For example, in 1775 an English surgeon named Percival Pott noted there was an extremely high incidence of cancer of the scrotum in chimney sweeps. His investigations led him to conclude that soot was the causative agent. With the advent of modern heating, the profession of chimney sweep disappeared in England and with it disappeared this particular form of cancer.
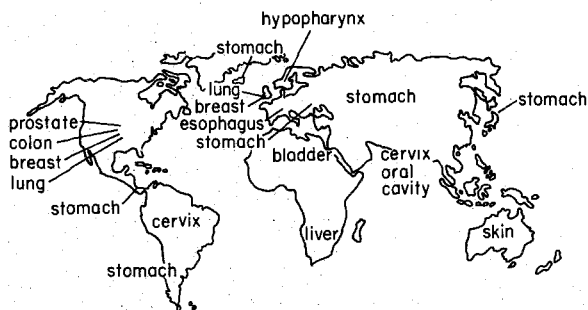
Leroy E. Hood

THE GEOGRAPHY OF CANCER—*Those forms of cancer with the highest incidence rates are shown for selected regions throughout the world.*
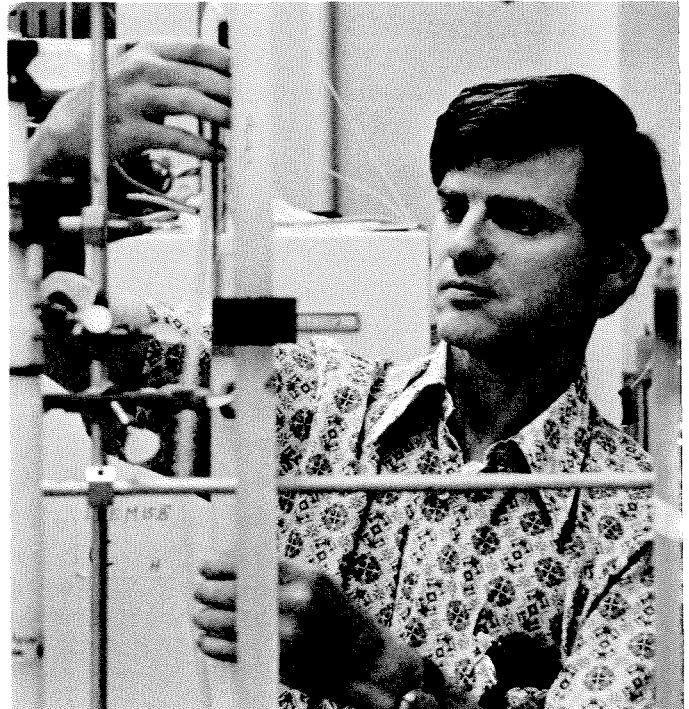
It was not until 150 years later that a second English physician discovered the carcinogen in soot that was responsible for scrotum cancer. Thus, cancer caused by an environmental agent such as soot can be prevented by avoiding the responsible agent, even though the molecular details of how the carcinogen causes cancer are unknown. This observation also suggests that geographically distinct populations which are presumably exposed to differing carcinogens should vary in their incidence of particular types of cancer. Indeed, the incidence of differing types of cancer in various parts of the world differs markedly from one locale to the next (left). For example, predominant types of cancer in the United States arise in the lung, breast, colon, and prostate; in Japan, in the stomach; in Australia, in the skin; and in Southern Africa, in the liver. One of the most interesting examples of the "geography of cancer" is the incidence of esophageal cancer seen in a narrow belt around the tip of the Caspian Sea in Iran. Within this belt the incidence of esophageal cancer, which is extremely rare throughout the rest of the world, varies more than a hundredfold in regions geographically a short distance apart.

Some cancer experts believe that between 80 and 95 percent of cancer is environmentally caused

This unusual distribution of esophageal cancer might have one of two explanations. First, the people living in the region of high incidence may have a genetic constitution which makes them highly susceptible to this particular kind of cancer. This explanation seems unlikely because migrant populations can move from a region of low cancer incidence to one of high cancer incidence and in time assume the cancer rate of the native population. So, it appears likely that the esophageal cancer seen in Iran is caused by some unknown environmental factor(s).

Cancer Death Rates in Groups of Males Throughout the World*

	High	Low
Mouth	61.3	1.3
Nasopharynx	35.9	0.0
Esophagus	110.5	2.1
Stomach	172.2	6.6
Colon	30.6	0.0
Rectum	23.3	0.0
Pancreas	18.3	0.4
Larynx	15.6	0.7
Lung	154.3	1.9
Prostate	40.8	0.7
Bladder	34.6	1.9
Thyroid	17.0	0.0
Leukemia	15.6	1.3
Total	730.0	17.0

*Average annual death rate per 100,000 for 35-64 age group.

By combining the statistics from Indian oral cancer, Mozambique liver cancer, Chinese nasopharyngeal cancer, Central Asia's esophageal cancer, and so forth, a hypothetical population with an extremely high incidence of cancer can be constructed (above). This hypothetical population would have a cancer incidence rate more than 40 times that of a population constructed from groups with low cancer rates. Is it possible that the incidence of cancer could be markedly reduced by the identification and avoidance of carcinogenic agents in our environment?

Certain cancer experts concluded that between 80 and 95 percent of cancer is environmentally caused and could be prevented by avoiding the responsible carcinogenic agents, which may include viruses, various forms of polycyclic compounds, pesticides, and a variety of other agents present in the environment of contemporary man. Epidemiology, which is the study of the distribution of— and factors that cause—cancer, will certainly be an important aspect of the future control of the disease.

The time factor is extremely important in the understanding of human cancer induction by carcinogenic agents. Cancers develop in man and animals long after the causative agent has been in contact with the target tissue. The time interval, or latent period, can be as long as 20 years or more. For example, in the table below the statistics are given for bladder tumors among 78 men engaged under conditions of heavy exposure in the distillation of 2-naphthylamine and benzidine, two highly carcinogenic dyestuff intermediates. The group of workers who were exposed for only four years did not show a response for the first ten years of observation, but after 20 years their bladder tumor incidence was up to 30 percent, and by 30 years it was as high as 80 percent. For the workers exposed for five years or more the incidence observed in 30 years went up to 94 percent.

Progressive increase of bladder tumors among 78 aromatic amine distillers with increasing length of exposure

Length of latent period in years	Length of exposure in years					
	Up to 1	1	2	3	4	5 & over
	Percentage of workers with tumors					
Up to 5	0	0	0	0	0	0
10	0	0	0	0	0	11
15	0	17	22	0	10	45
20	4	17	22	40	30	69
25	9	17	22	70	70	88
30	9	17	48	70	80	94

Exposures to chemical carcinogens which produce lower levels of tumor incidences would be more difficult to detect, particularly if they were spread throughout the general population. The fact that it may take 20 years to detect the cancers in man due to the exposure to a new chemical carcinogen means that the chemical can be given to people for 20 years under the false appearance of harmlessness. If the effect is then detected and properly attributed to the specific chemical, and this is then removed from the environment, the cancers it induced will continue to appear for the next 20 to 30 years. More effective screening techniques for rapidly detecting possible carcinogens are desperately needed. This, perhaps, should be one of the most important areas of fundamental research in modern cancer biology.

Diagnosis

The prognosis for a particular case of cancer depends primarily on the extent to which it has invaded surrounding tissues and metastasized to distant sites (right). The five-year survival rates can be three times as large in groups of patients with an early as opposed to a late cancer diagnosis. Thus, it is imperative that the earliest possible diagnosis be made. Two individuals play an important role in this early diagnosis—the patient and the doctor.

The patient can approach the problem of early diagnosis through an awareness of the early signs and symptoms of the most common forms of cancer (right). So the patient himself is the most important factor in the early diagnosis of cancer. For example, approximately 95 percent of the cases of breast cancer are detected by patients themselves. Unfortunately, cancer breast nodules can first be detected when they are about one-half inch in diameter, but it is just at this point that many breast cancers begin to metastasize—a fact that underscores the urgency of early diagnosis.

A thorough physical examination should include an inspection of the larynx, inspection of the colon and rectum, and for women a pelvic examination. The chest x-ray is almost the only diagnostic tool that is effective for lung cancer. Various blood and urine tests are also helpful. Most other tests for cancer are expensive, complicated, often ineffective, and to some degree risky for the patient. Indeed, these tests are not carried out unless there are specific indications for their use.

The ideal diagnostic test for cancer should be effective, simple, inexpensive, and relatively safe for the patient. There is at least one test that meets these criteria— the Papanicolau test, or pap smear, which detects cervical cancer by an examination of cells that can easily be scraped from this organ. This simple test has decreased by a factor of three the incidence of cervical cancer, which in the early 1930's was the leading killer of American women. Even today only about 50 percent of American women routinely have pap smears, yet it is obvious that cervical cancer deaths could virtually be eliminated from the American population if the pap smear was a routine,
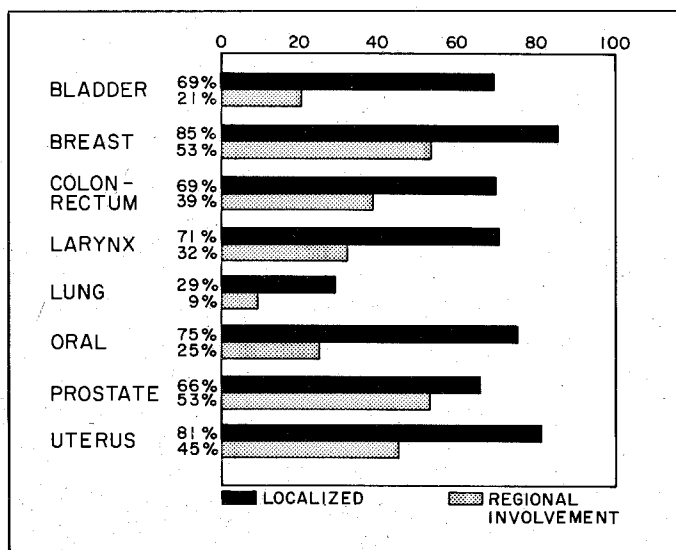
FIVE-YEAR SURVIVAL RATES FOR SELECTED CANCER SITES—*"Localized" indicates that the tumor has not yet started to metastasize. "Regional involvement" means that metastases have occurred in the nearby lymphatic system.*

Cancer's Seven Warning Signals

1. **Change in bowel or bladder habits**
2. **A sore that does not heal**
3. **Unusual bleeding or discharge**
4. **Thickening or lump in breast or elsewhere**
5. **Indigestion or difficulty in swallowing**
6. **Obvious changes in wart or mole**
7. **Nagging cough or hoarseness**

annual procedure for all women. A major effort in contemporary cancer research is directed at developing more of these simple, inexpensive, and routine screening procedures.

Therapy

Cancer patients fall into two classes—those who can be cured and those for whom treatment can merely extend life or alleviate suffering. The physicians' armamentarium contains three general therapeutic tools—surgery, radiation, and chemotherapy.

The oldest therapeutic approach is surgery. The rationale is that the tumor can be completely excised, and this approach is generally successful for well-localized tumors. For example, many skin cancers spread slowly and very high cure rates can be achieved with surgery. However, if the tumor is widely invasive or if it has metastasized, surgery is generally ineffective.

Radiation therapy can be effective for tumors that have started to spread. X-rays and radioisotopes kill rapidly dividing cells more readily than cells that are dividing at a slower rate. In general, cancer cells are rapidly dividing in comparison to most normal tissues and, accordingly, can be more readily killed by radiation. However, radiation therapy must be used carefully with organs which have rapidly dividing normal cells, such as the gastrointestinal tract.

Radiation therapy is useful because local tumor invasion and regional metastases can be destroyed by selecting an appropriately large field for radiation therapy. This type of therapy is probably used on more than 50 percent of the cancer patients treated today. For some types of cancer such as cancer of the cervix and the early stages of Hodgkins disease, the five-year cure rate with radiation is greater than 90 percent. Radiation therapy can, however, fail for a number of reasons. Some tumors are radiation resistant; often the tumor will have spread beyond the field of exposure; and, of course, the patient with widespread metastases is difficult to treat effectively with radiation therapy.

The final tool in the physicians' armamentarium is chemotherapy. The rationale for its use is that of the

Perhaps a "magic bullet" can be designed to kill cancer cells specifically without harming normal cells

"magic bullet." The hope is that a "magic bullet," a chemotherapeutic agent, can be designed to kill cancer cells specifically and not harm normal cells. This idea is based on the enormous success that antibiotics have had in killing the agents responsible for bacterial infections while not harming normal human cells. Unfortunately, cancer cells are derived from normal cells and so they are very similar to normal cells. Once again, chemotherapy depends on the fact that certain chemical agents can kill rapidly dividing cells more effectively than cells which divide at a slower rate. Most chemotherapeutic agents operate by blocking the synthesis of new DNA which, accordingly, blocks the production of new cells. For example, one class of chemotherapeutic agents, the anti-metabolites, are compounds which very closely resemble compounds that are used by the body in the normal synthesis of DNA. In some cases the only difference between the two is the positioning of one chemical group about a carbon atom. Yet this subtle difference between antimetabolite and metabolite can render the machinery for DNA synthesis ineffective.

Chemotherapy is generally the only approach effective against disseminated types of cancer, whether due to metastases from solid tumors or to cancer of various types of cells in the blood, such as leukemia, because these agents are injected directly into the bloodstream and, accordingly, distributed throughout the body. Chemo-therapy has a high five-year survival rate for a limited number of tumors (below), the most impressive of which is choriocarcinoma—cancer of the placenta, or the organ

Successful Results with Cancer Chemotherapy

Disease entity	5-year survival rate
Choriocarcinoma	95%
Burkitt lymphoma	75%
Wilm's tumor (kidney)	75%
Acute leukemia of childhood	50%

which attaches the fetus to the mother. This cancer is highly invasive, metastasizes early, and prior to chemotherapy was inevitably fatal; currently the five-year survival rate is greater than 95 percent.

In the past five to ten years more effective chemo-therapeutic approaches have been developed for dealing with one of the most tragic types of cancer, acute leukemia of childhood. The most effective therapies can now achieve a five-year survival rate of approximately 50 percent.

Surgery, radiation, and chemotherapy are now used effectively in various combinations. For example, large tumor masses are often excised, and regional or systemic metastases are countered with radiation or chemotherapy. It is very difficult to determine the optimal treatment for many types of cancer, particularly at the more advanced stages, as this determination requires the statistical analysis of large numbers of patients with appropriate controls. Such studies are rare in clinical cancer research; as a result, there is widespread controversy, even among cancer experts, as to the best therapeutic approach to many types of cancer.

The statistics on cancer survival are dismal. With current diagnostic and therapeutic techniques, for every six individuals who contract cancer, two are saved, one could be saved, and three will die. So new diagnostic or thera-peutic techniques are required if the present death rate in cancer patients is to be changed.

The Immune System

Modern research into the immune system and the role it plays in protecting man against cancer seems to offer enormous promise both with regard to the diagnostic possibilities for early cancer detection and the therapeutic possibilities of more effective cancer treatment.

The immune system is a complex entity comprised of a number of organ systems (such as lymph nodes, spleen, and thymus) and cell types (lymphocytes—or antibody-producing cells—and macrophages). One major function of this system is to defend man against invasive foreign organisms such as bacteria and viruses. This defensive system functions in part through the elaboration of serum proteins called antibody molecules (below). The foreign
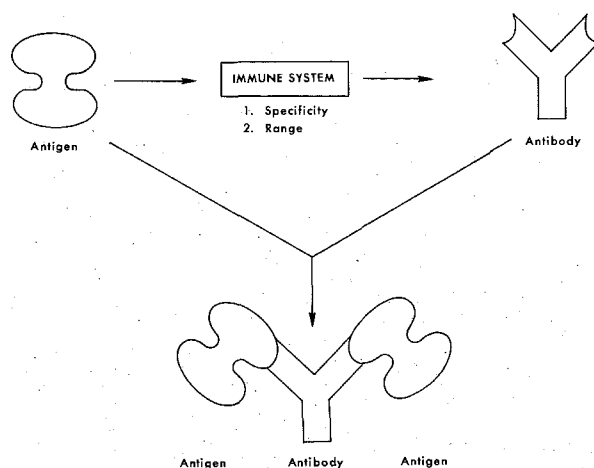
A SIMPLE MODEL OF THE IMMUNE RESPONSE—*When a foreign organism or antigen is exposed to man's immune system, the production of specific antibodies is initiated. The immune response has two remarkable features—specificity and range. Each immune response produces antibody molecules specific for the particular antigen that triggered their production. The immune system is capable of an enormous range of responses in that it has the potential of elaborating specific antibody molecules to more than a million different antigens.*

Precursor Antibody Producing Cell

Humoral Immunity
1. Acute Bacterial Infections
2. Acute Viral Infections

Cellular Immunity
1. Cancer Surveillance
2. Transplant Rejection
3. Certain Intracellular Infections
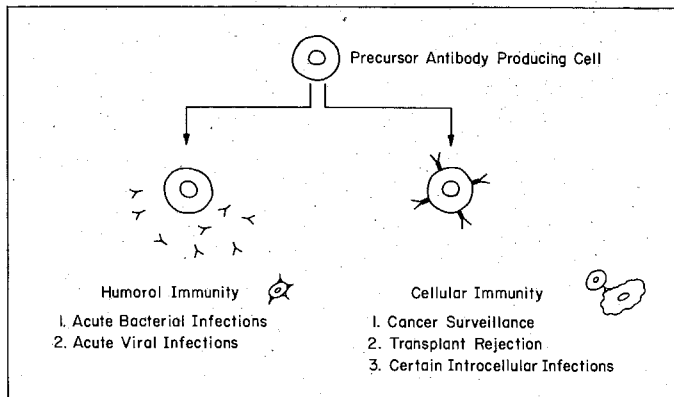
THE TWO IMMUNE SYSTEMS—*The humoral immune system is concerned primarily with acute bacterial and viral infections; and the cellular immune system with the destruction of newly arising cancer cells (cancer surveillance), the control of certain intracellular and parasitic infections, and—more recently—with the rejection of foreign organ transplants. Here, humoral antibodies are shown killing a bacterium, and a cellular lymphocyte is destroying a cancer cell.*

organism, designated an antigen, gains entry into man's body and evokes the production of specific antibody molecules from the immune system. The antibody molecules are specific because they can combine at the molecular level with the particular antigen in a complementary fashion much as a lock and key fit together. This interaction leads to the destruction of the foreign bacteria or virus by a variety of mechanisms. The cells that produce antibodies are called lymphocytes, or antibody-producing cells.

The immune system is actually composed of two components with distinct functions, the humoral immune system and the cellular immune system. The antibody-producing cells of the humoral immune system synthesize specific antibody molecules and secrete them into the blood where they can interact with antigens throughout the entire vascular system and at a distance from the cells which produced them (above). In contrast, the antibody-producing cells of the cellular immune system synthesize specific antibody molecules and place them on their own cell membranes. These membrane-bound antibody molecules interact with antigens, and this juxtaposition of lymphocytes and the foreign entity leads to the destruction of that entity.

The cellular immune system plays an important role in the protection of vertebrate organisms against cancer. Man is a complex creature constructed of perhaps 10^{14} cells. He is continually exposed to a variety of environmental carcinogens which can transform one or more of those 10^{14} normal cells into cancer cells. One function of the cellular immune system, cancer surveillance, is to recognize cancerous cells and destroy them as they appear.
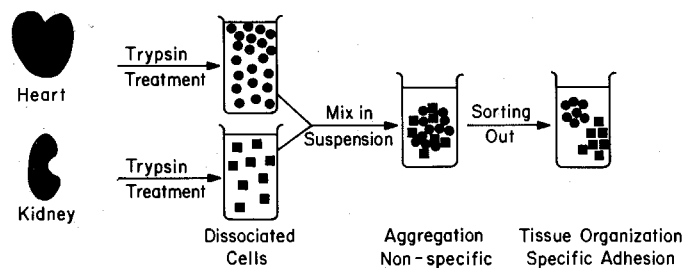
An impressive array of experimental evidence has been mustered to support the contention that the cellular immune system is involved in cancer surveillance. First, in patients who are to receive an organ transplant, immuno-suppressive agents are often used to destroy the cellular

immune system so that the foreign graft will not be rejected (left). In these "immunosuppressed" patients the incidence of cancer is approximately 100 times that of normal individuals. In fact, these patients exhibit extremely malignant forms of cancer which spread very rapidly. However, once the immunosuppressive agents are stopped, the patient's cellular immune system is regenerated, and these malignant cancers are rapidly destroyed. Second, the ability of patients to survive cancer depends on the effectiveness of their cellular immune system, and a simple skin test can determine that. Ninety-five percent of those patients surviving cancer surgery beyond two years do have a good cellular immune response, whereas 95 percent of those failing to survive cancer surgery have a poor cellular immune system. Third, the incidence of cancer increases with aging. In normal individuals, beginning at about 30 or 35 years of age the efficiency of the cellular immune system drops off in approximately a linear fashion; at this same time the incidence of cancer starts to increase. In each case the incidence increases when the efficiency of the cellular immune system is compromised.

Biochemical Properties of the Cancer Cell

How does the cellular immune system recognize cancer cells as being different from normal cells so that it can initiate the appropriate immune response and tumor cell destruction?

Cancer cells appear to have three biochemical properties—each related to the cell membrane—which can explain at least in part the general clinical properties of a growing tumor. First, cancer cells can no longer receive signals from nearby neighbor cells which regulate the rate of cell division. Consequently, cancer cells grow in an unchecked fashion, and there is no regulation on the size of the tumor mass that is produced. Second, normal cells derived from the kidney, for example, will clump together in a tissue-specific fashion (below). In

Heart — Trypsin Treatment → Dissociated Cells · Mix in Suspension · Sorting Out · Kidney — Trypsin Treatment →

Dissociated Cells · Aggregation Non-specific · Tissue Organization Specific Adhesion

SPECIFIC ADHESION OF CELLS FROM THE SAME TISSUE—*Normal organs such as the heart or kidney can be dissociated into single cells by appropriate chemical and enzymatic treatments. When dissociated cells from two normal organs are mixed together, at first they form nonspecific aggregates and later sort out into tissue-specific clumps. Tumor cells lose their ability to adhere in a tissue-specific fashion and form nonspecific aggregates when mixed with normal cells. Perhaps the loss of tissue-specific adhesion in cancer cells is due to the appearance of new molecules on their cell surfaces.*

"Cancer molecules" provide an opportunity for developing simple, safe, and early diagnostic tests for cancer
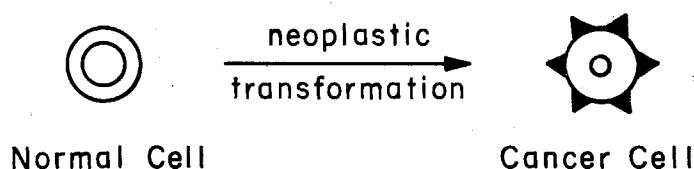
A SCHEMATIC OF THE "CANCER MOLECULES" ON A TUMOR CELL—
When a normal cell is transformed into a cancer cell, new molecules appear on the membrane surface which are here designated "cancer molecules."

contrast, cancer cells can readily break apart from their nearby neighbors, and it is perhaps this property which often leads tumors to metastasize to distant regions of the body. Finally, cancer cells appear to have molecules on their surface that are not present on normal cell surfaces (above). These "cancer molecules" are foreign, and the cellular immune system mounts a response against them which leads to the eventual destruction of the cancer cell.

Immunodiagnosis

"Cancer molecules" provide an opportunity for the development of simple, safe, and early diagnostic tests for cancer. An example of this was demonstrated in 1965 by a young physician in Montreal named Philip Gold, who decided to undertake the study of cancer as part of a PhD thesis project. He chose human colon cancer as a model system because of its prevalence in man. Dr. Gold examined the differences between normal and cancer cells by injecting the tumor tissue into rabbits to raise antibodies against the colon "cancer molecules." Then he removed that fraction of the antibodies reacting with normal cellular components by absorption with normal tissue. Thus he was able to produce antibodies that could react with cancer cells and not with normal cells, and these antibodies appeared to be specific for the "cancer molecules" on the surface of the colon cancer cells (right). Gold then demonstrated that the colon cancer sheds its "cancer molecules" to the blood. He examined the blood from 35 patients with colon cancer using the antibodies specific to the colon cancer cells. In 97 percent of the patients the blood gave a positive reaction with the specific cancer antibodies, indicating that antibodies raised

against "cancer molecules" may serve as a specific immunodiagnostic reagent for cancer detection.

The importance of such an early diagnostic test, once again, must be stressed, for in 1972 approximately 79,000 Americans contracted colon cancer. Of these, 47,000 died, and it is estimated that with early diagnostic techniques more than three-quarters of them could have been saved. In other words, if the simple and inexpensive immunodiagnostic test described above were specific and could be made a part of the general physical examination for all adults, approximately 35,000 deaths from colon cancer could be avoided every year. The future diagnostic potential for these immunodiagnostic techniques is even more exciting when we consider that six of the most common types of cancer cause approximately 60 percent of the cancer deaths seen in the United States. If simple immunodiagnostic tests could be devised for each of these six types of cancer, a tremendous saving of life would be possible (below).

Unfortunately, subsequent research has indicated that this kind of simple immunodiagnostic test has some difficulties. For example, the sera from patients with certain other types of cancer—and indeed that from certain patients with other types of disease—also react with the antibody molecules raised against the colon "cancer molecules." I think that eventually antibodies specific for a particular kind of cancer can be produced in one of two ways: through the use of sophisticated purification techniques to obtain homogeneous preparations of specific
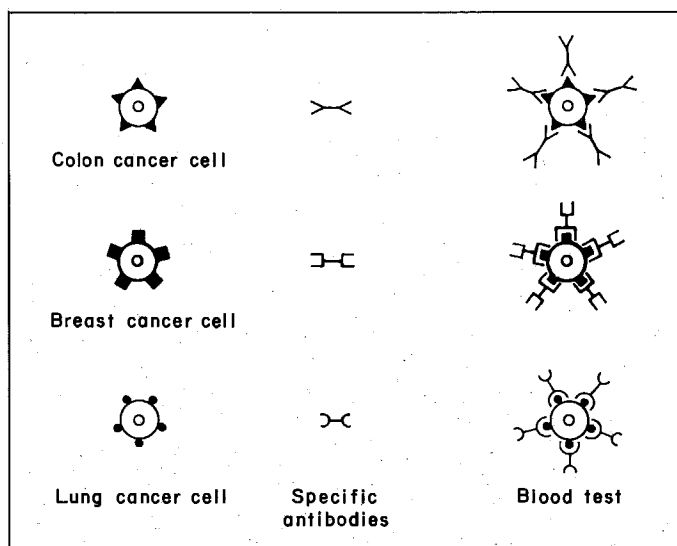
A SCHEMATIC OF THREE TYPES OF CANCER CELLS WITH THEIR SPECIFIC "CANCER MOLECULES"—*It appears likely that most types of cancer have "cancer molecules" that are different from those of other cancers. Thus if specific antibodies can be produced against each type of "cancer molecule," they could be used as diagnostic reagents for the detection of cancer cells (or "cancer molecules") in the patient's blood. Since these antibody reactions are specific and very sensitive, very small quantities of "cancer molecules" can be specifically detected. When perfected, these immunodiagnostic tests will be ideal for the early diagnosis of cancer.*

"cancer molecules," or through the use of complicated immunologic procedures to absorb out undesired reactivities. Each of these approaches will require a great deal of additional fundamental research, and the problem does not appear to be at a stage now where expensive mission-oriented research efforts will yield fruitful results.

The immunodiagnostic technique developed by Dr. Gold for colon cancer is extremely useful in one regard at present. It can be used to follow cancer patients postoperatively after surgery. The level of "cancer molecules" in the blood following cancer surgery drops and remains at a low level unless there is a recurrence of cancer. Thus, this specific immunodiagnostic technique can be used to detect early recurrences, and appropriate action can be initiated immediately.

Immunodiagnosis promises to yield a real breakthrough into the early diagnosis of cancer in the future. But it is clear that a great deal of fundamental research remains to be done before this tool can be employed effectively.

Immunotherapy

The rationale for immunotherapy is similar to that for generating immunity against specific bacterial or viral pathogens. For example, cancer cells of a particular type might be killed and then used to immunize an appropriate host. In this fashion cellular immunity could be generated against the specific "cancer molecules," and this immunity could protect the host from that type of cancer. In practice, this type of approach can fail for a number of different reasons. One in particular is interesting because it demonstrates that under certain circumstances the two immune systems can oppose one another.

A husband and wife cancer research team in Seattle, the Hellstroms, made a series of interesting observations on a type of brain cancer found in small children, the neuroblastoma. Tumor cells were taken from a child in whom the tumor was actively growing, and they were cultured in a small petri dish. Since this tumor was growing in the child, the Hellstroms predicted that lymphocytes, or antibody-producing cells, taken from that same child and placed in the petri dish with the tumor cells would fail to kill the cancer cells. To their surprise, however, the lymphocytes from the tumor patient were very effective in killing the tumor cells—as long as these antibody-producing cells were removed from the patient's own blood. Why could the lymphocytes kill the patient's tumor cells in the petri dish, but not in his body? Because cancer cells shed their cancer molecules into the blood and stimulate the production of a specific type of humoral antibody which combines with the specific cancer molecule to form what is termed "blocking factor." Blocking factor, as its name indicates, apparently blocks the cellular immune system from effectively destroying cancer cells.

One possible mechanistic explanation for the behavior
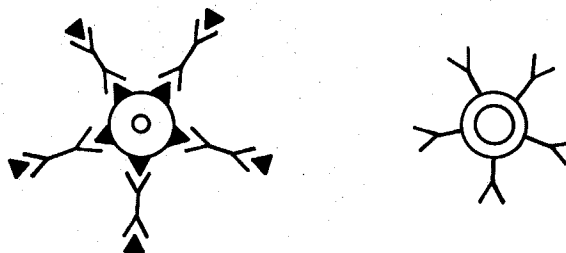
ONE POSSIBLE MECHANISM BY WHICH BLOCKING FACTOR PROTECTS CANCER CELLS FROM IMMUNOSURVEILLANCE—*Blocking factor, a combination of a humoral antibody molecule and a specific "cancer molecule," may enhance tumor growth by shielding it from the cellular immune system.*

of blocking factor is that it can cover the "cancer molecules" and prevent lymphocytes from the cellular immune system from interacting with cancer cells (above). The blocking factor seems to form a protective coat around cancer cells, which then grow even in the presence of lymphocytes that are capable of destroying them once the blocking antibodies are removed. Thus, the effects of the two immune systems can oppose one another.

The neuroblastoma of childhood is also interesting because it undergoes spontaneous remissions at the rate of 1 to 2 percent; that is, tumors occasionally disappear in relatively short periods of time. These spontaneous remissions appear to be an immunologic phenomenon in which a second type of humoral antibody appears that has the ability to remove the blocking factor. Appropriately enough, this second type of antibody is called "unblocking factor," and in its presence the cancer cells can once again be killed by lymphocytes, even in the presence of blocking factor.

The existence of unblocking factor raises some interesting possibilities with regard to cancer therapy. They are illustrated by the clinical history of a young doctor from New York State. He came from a family with a history of hypernephroma, a kidney tumor. Hypernephromas are, like neuroblastomas, tumors that occasionally undergo spontaneous regression. This young physician contracted a hypernephroma which was presumed to be successfully removed by surgery. But six months later it was learned that the hypernephroma had metastasized to his lungs. A second surgical procedure removed most but not all of the tumor from the lungs. The prognosis was grave.

The young physician, however, was aware of an uncle who had some years earlier contracted a hypernephroma which later underwent a spontaneous regression. Knowing of the Hellstroms' work, he reasoned that unblocking factors must be present in the serum of his uncle, so he underwent a bimonthly series of serum transfusions from his uncle for a period of more than two years. Now, some four years later, the young physician is completely free of

cancer. The Hellstroms checked the serum from this young physician and were able to demonstrate blocking factors and unblocking factors at appropriate times throughout the clinical course of his disease. Of course, the young physician's tumor may have actually undergone a spontaneous remission just as did the tumor of his uncle in the past. We will never know whether the uncle's unblocking factor really contributed to the young physician's recovery, but this clinical course points out one exciting possibility for immunotherapy.

The general problem with regard to immunotherapy is to learn how to manipulate the two immune systems independently of one another. How can we immunize individuals so that blocking factor is not produced? How can the cellular immune system be specifically stimulated to provide immunity against various types of cancer? These are difficult questions which will require concerted efforts in fundamental research before immunotherapy will be an effective and safe tool for the physician. Immunotherapy offers enormous possibilities for a cancer cure, but that cure will not come in the near future.

Some Social and Ethical Aspects of the Cancer Problem

There is an undeniable statistical correlation which links cigarette smoking and lung cancer (right). In the past, smoking has been a matter of personal choice and, indeed, it has been viewed as a fundamental right by many. These attitudes may have to change in the future because it is clear that cigarette smoke is just as harmful to people who do not smoke as to those who do. Since this is so, those who have sat on a plane for four or five hours inhaling someone else's cigarette smoke may feel that their basic rights are being infringed.

This question of the infringement of rights has much broader sociologic implications. For example, suppose that smog is carcinogenic. Can a certain subset of the population, perhaps a majority, choose to risk an increased incidence of cancer in order to have unlimited use of cars and other concomitants of smog? Can this majority force a minority to accept environmental conditions that are unhealthy? This question can also be posed for those environmental carcinogens, such as DDT, which are economically beneficial but dangerous. Society is going to have to identify these environmental carcinogens and balance the economics and convenience of their use against their potential risk as carcinogenic agents.

Euthanasia or mercy-killing is an ethical consideration which relates to the problem of cancer in at least two regards. First, most of us have seen at least one example of the agony and suffering of terminal cancer patients where in certain cases even the most powerful drugs fail
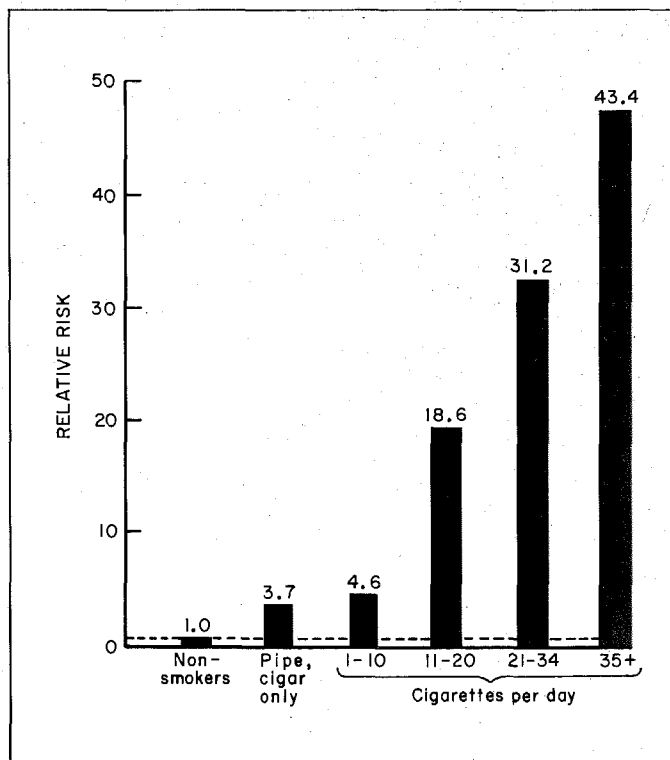
THE RELATIVE RISK OF INCURRING LUNG CANCER AMONG NONSMOKERS AND VARIOUS GROUPS OF SMOKERS—*Those who smoke more than 35 cigarettes per day, for example, are more than 43 times as likely to develop cancer as those who do not smoke.*

to alleviate suffering. The response to this suffering can be extreme. For example, in August of 1967 a young man was arrested because he had killed his mother. She was dying of leukemia and had for three weeks begged him to end her life because of the agony and hopelessness of the terminal stages of this disease. How should society view this crime? Should an individual be able to choose to terminate his life under such circumstances? Second, the extremely sophisticated life-support systems that physicians now have make it possible to keep terminal cancer patients alive for protracted periods of time. In the future these life-support systems will become more sophisticated, and patients could be kept alive for even longer periods of time —prolonging the suffering and agony that families must go through, as well as incurring enormous expenses. Clearly the question of euthanasia is an issue that society—laymen and physicians alike—must deal with in the near future.

Cancer is a disease entity which poses complex social and ethical questions as well as challenging clinical problems and exciting opportunities for probing the innermost workings of the human cell. The future for the eventual control of cancer is very promising, but a great deal of fundamental research is still required. Do not expect too much too soon. □

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.
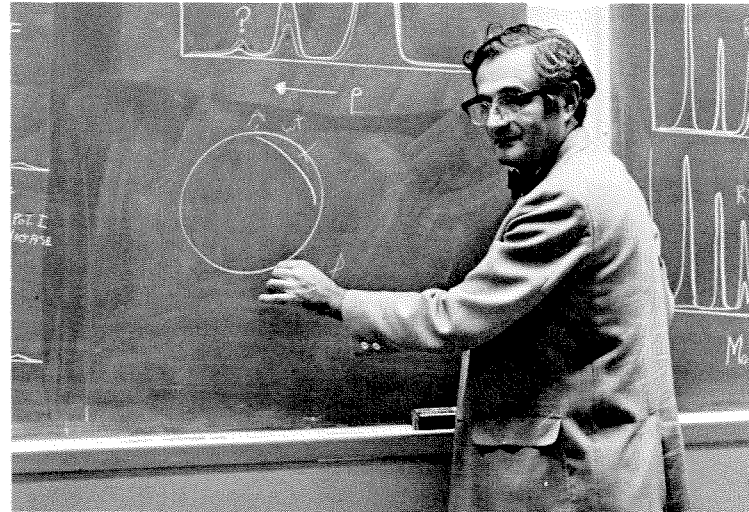

Robert Sinsheimer

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.
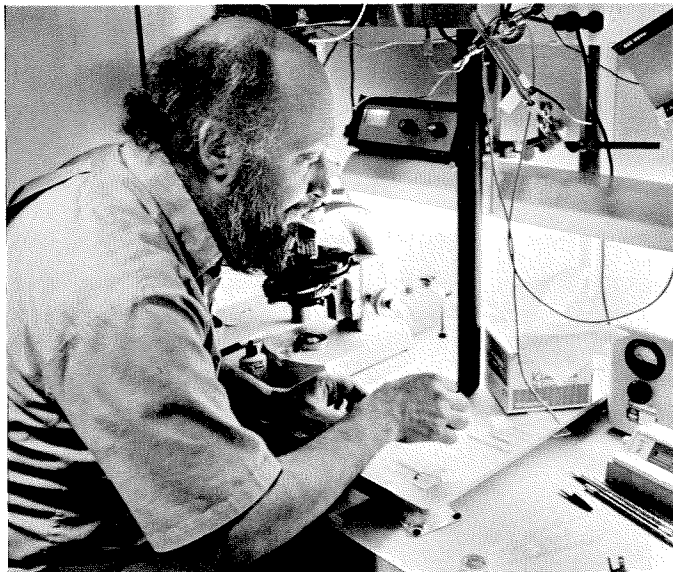
Jean-Paul Revel

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.
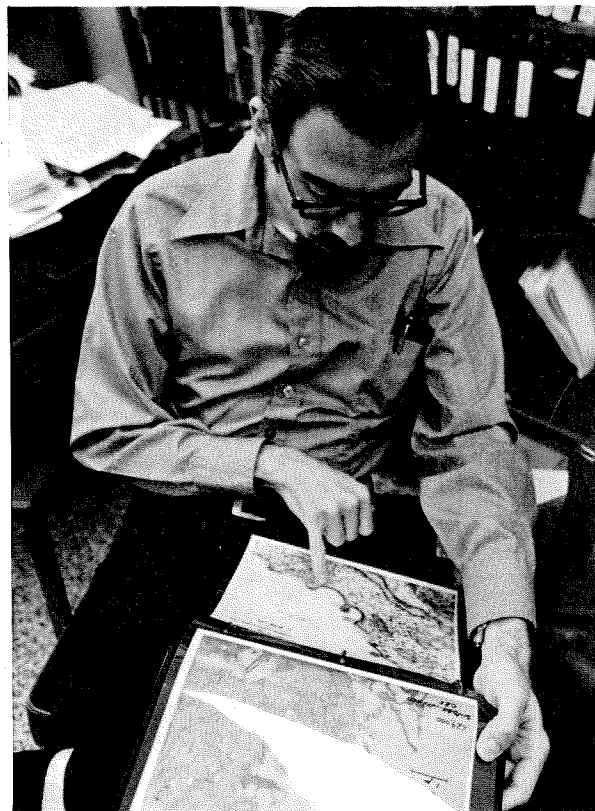
James Strauss

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.
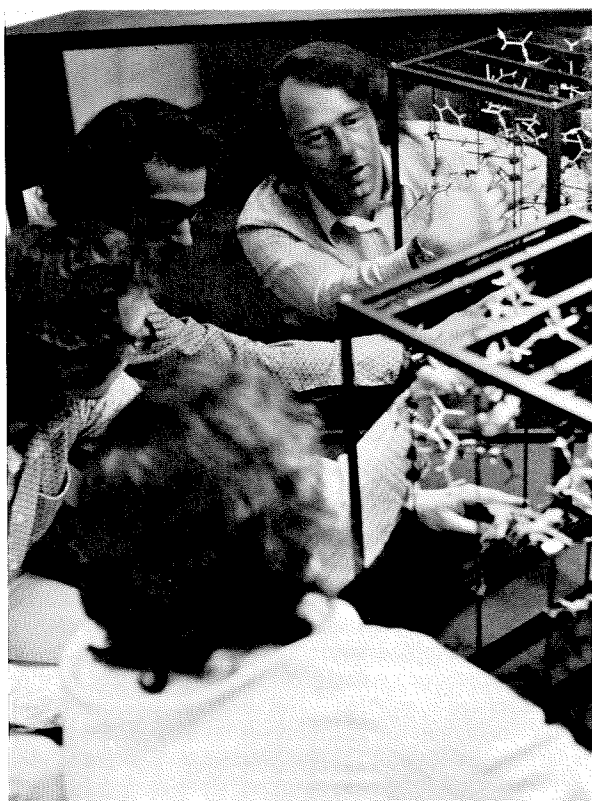
Robert Stroud

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.
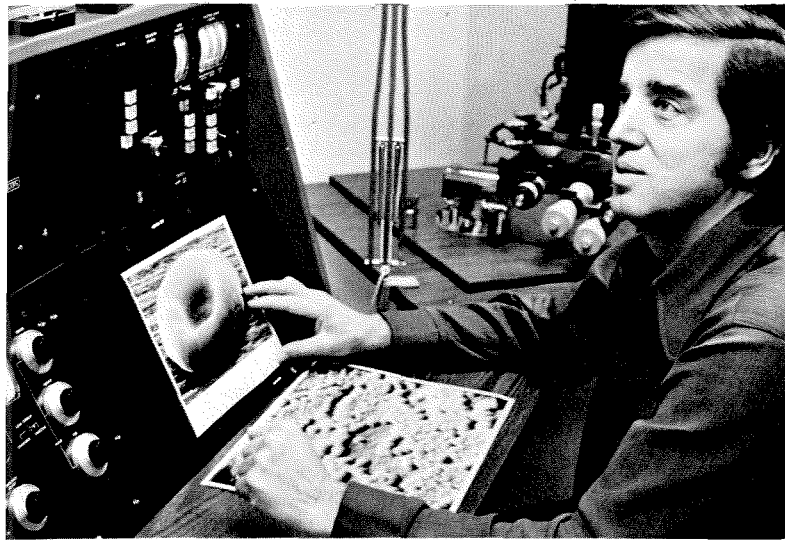
William Dreyer

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.
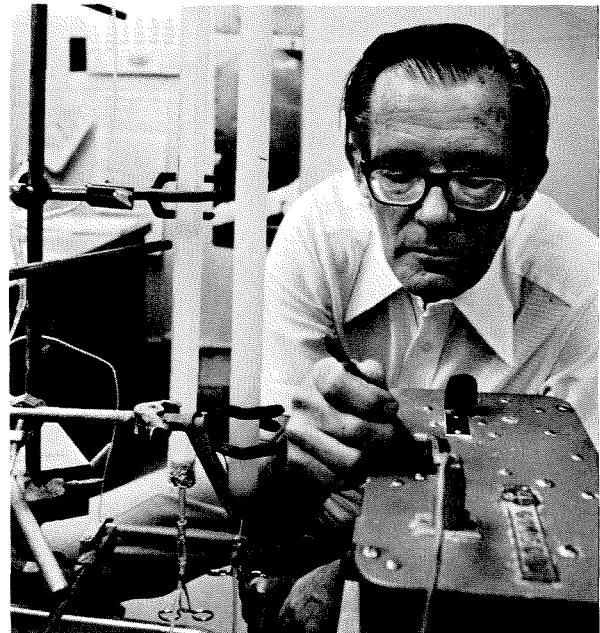
James Bonner

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.
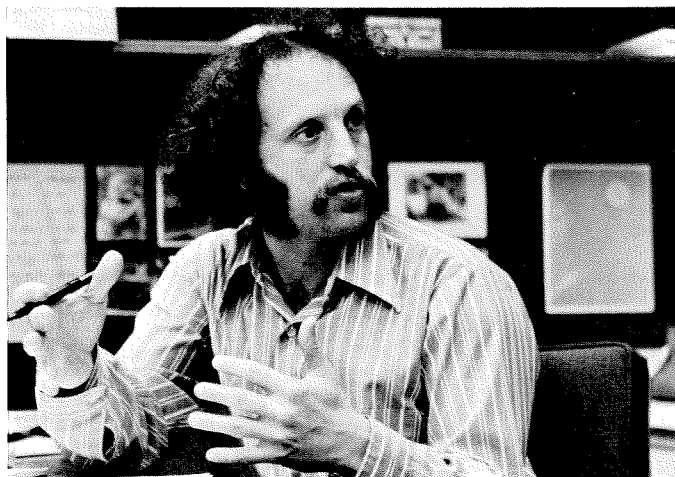
Eric Davidson

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.
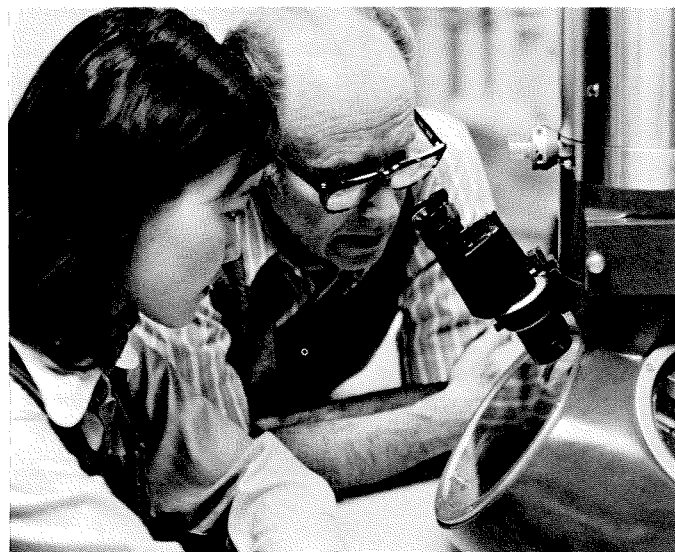
Norman Davidson

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.
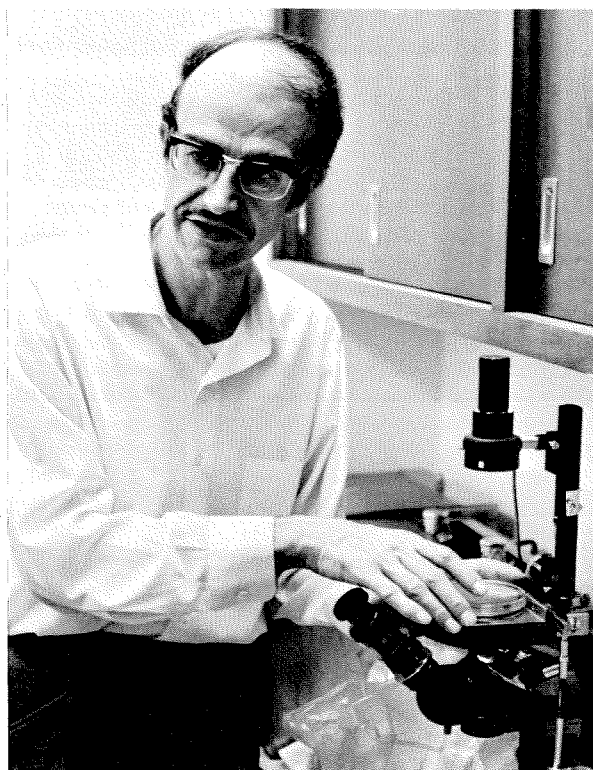
Giuseppe Attardi

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."
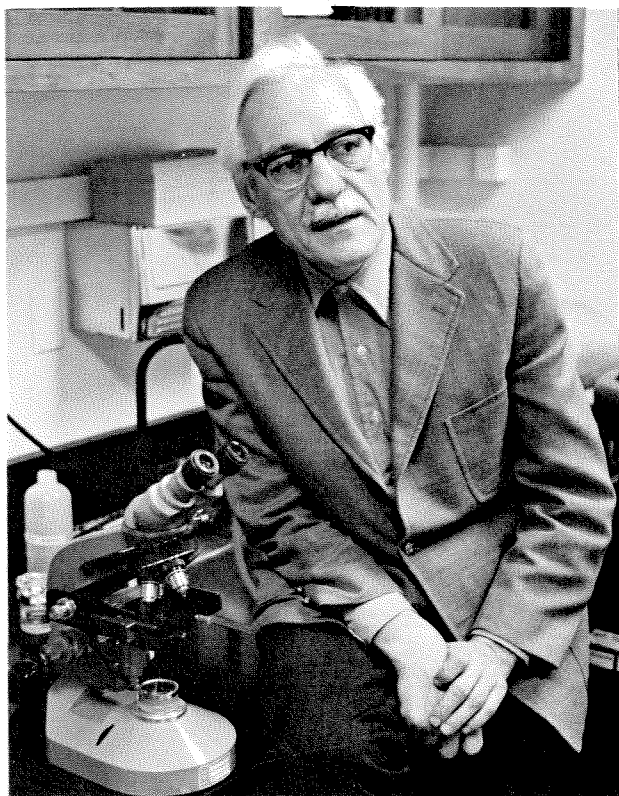
Jerome Vinograd

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.
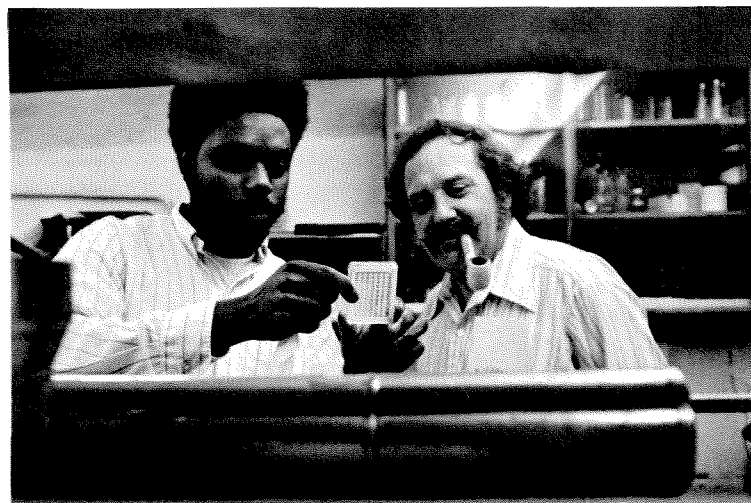
Ray Owen

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.

Crystal Growth through Solid Metal

An attempt to understand a relatively minor aspect of semiconductor processing has led to a new understanding of transistors

Transistors and integrated circuits have had a profound effect on our lives. They have made possible a vast array of miniaturized devices—from truly portable radios and television sets to hearing aids and heart pacemakers. Because of them we have worldwide communication through satellites in space, where reduced size, weight, and electrical power consumption are vital. They have also greatly increased the power and versatility of computers. Even so, we are only at the beginning of developing applications for their use. Our colleague Carver Mead, professor of electrical engineering, notes that the trend toward miniaturizing electronic components is increasing so rapidly that within a decade almost every facet of our society will be automated to some degree (*E&S*, February 1972).

In spite of their revolutionary impact, transistors and integrated circuits are basically very simple mechanisms. Both are made from semiconductors—materials that are neither metals nor non-metals, but somewhere in between, capable of carrying an electric current under certain conditions. Transistors are usually made from single crystals of semiconductor material in which chemical impurities are distributed in three layers like a sandwich. Depending on how the layers are placed, and how the impurities are manipulated, the transistor can function as either an amplifier, a detector, or a switch. In the same manner, a complete electronic network can be formed on a semiconductor crystal to produce an integrated circuit.

Transistors are components in integrated circuits, with one circuit containing many thousands of transistors inside a square only one-tenth of an inch on a side.

Among the things that make transistors and integrated circuits work are the contacts between the semiconductors and the metals used in them. Such contacts are necessary to connect transistors to each other and to the outside world, but the nature of these contacts is not well understood. As a result, the crucial connections between the various layers in the transistor are made by processes developed by trial and error. A number of special formulations or recipes have been developed to produce the necessary contacts—but there has been little understanding of why they work.

To discover more about it, our research group recently undertook a study of what happens at the contact between metals and semiconductors during the actual fabrication of transistors and other integrated circuit components. But what began as an attempt to understand a relatively minor aspect of semiconductor processing—contact forming—has led instead to an entirely new way of looking at the reactions between metals and semiconductors in electronic devices.

Over the short term, what we have learned may allow manufacturers to ease the constraints under which integrated circuits are fabricated. Eventually, it may lead to techniques for producing these devices at lower temperatures—and more simply and cheaply than is now possible. And over a still longer term, it points the way to molecule-by-molecule and atom-by-atom engineering of semiconductor devices in much smaller sizes than are now available.

The techniques for "forming" metal-semiconductor contacts have not changed much over the 25 years since the introduction of transistors. The contact fabrication then involved a procedure called "electrical forming," in which direct current was applied for seconds, or less, to the metal-semiconductor interfaces. For some reason this input of energy greatly enhanced the transistor action. Semiconductor devices generally still undergo a forming

by James O. McCaldin and James W. Mayer
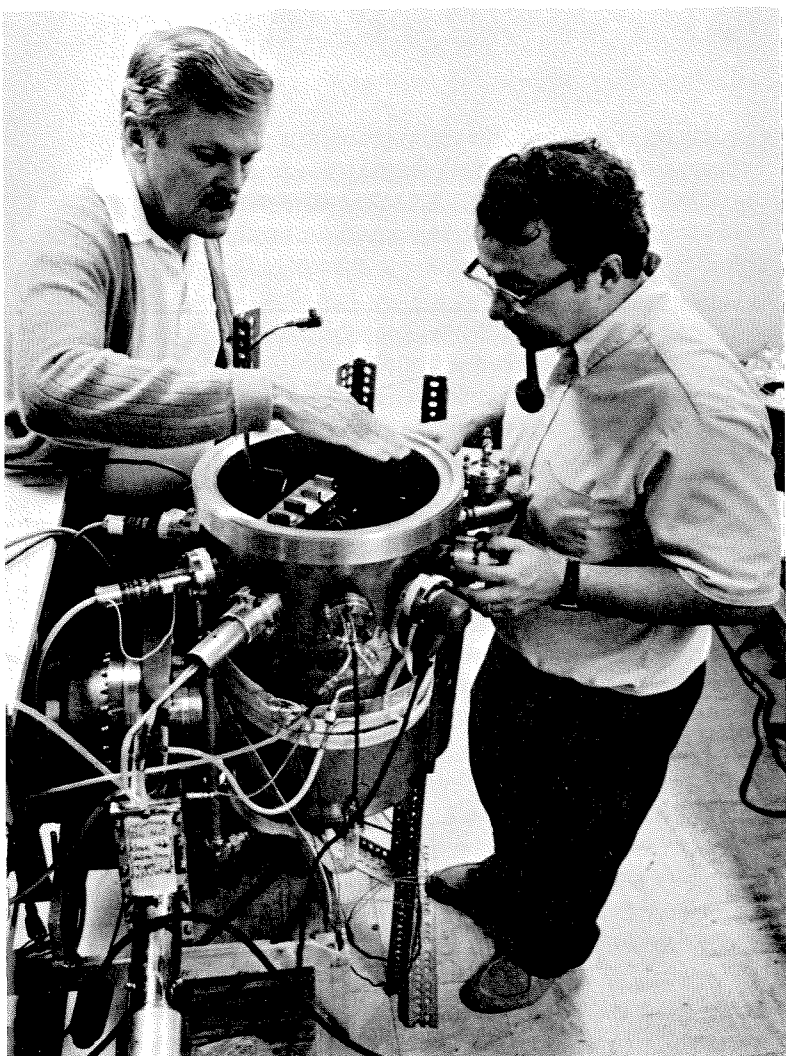
Thin layers of metal are evaporated onto semiconductor crystals in this metal evaporation chamber—the first step in a new and simpler way of producing transistors. The process was developed by McCaldin (left) and Mayer, working with research fellows Gianpiero Ottaviani and Dag Sigurd and graduate students Vince Marrello and Haluk Sankur.

process, but today it involves heat treatment to temperatures near 500 degrees Centigrade.

In a macroscopic sense, a formed contact provides the necessary electrical capabilities for semiconductor devices like transistors. (Note for the specialist: The formed contact can be either a good ohmic contact, a blocking contact, or a contact capable of injecting minority carriers.) However, the physical processes that lead to the behavior observed at the contacts are determined over extremely small dimensions—so small, in fact, that it takes instruments with considerably higher resolving power than optical microscopes to observe what is happening.

Fortunately, there are at least three kinds of instruments with the necessary resolving power available at Caltech and the Jet Propulsion Laboratory. First, there are the scanning electron microscopes, which are used routinely to distinguish structures of sub-optical size—usually at resolutions 10 to 30 times finer than that of the best optical microscopes. To supplement the information provided by the electron microscopes, there is the electron microprobe, which can identify local atomic composition and detailed movements of atoms at the metal-semiconductor interface. Finally, there is the million-electron-volt accelerator at the Kellogg Radiation Laboratory, which is capable of resolving atom depth distributions to within a few hundred Angstroms (an Angstrom being four-billionths of an inch long). In the latter case, the accelerator is used for depth microscopy rather than for the lateral resolution provided by the electron microprobe.

Using these instruments, our group found—to our surprise—that atoms move across the metal-semiconductor interface at temperatures as low as that of boiling water. For example, silicon moves through a thin film of gold about 1,000 Angstroms thick in a few minutes at 100 degrees Centigrade. Only in rare instances do atoms move through a solid medium at such a low temperature.

We have found it possible to grow semiconductor crystal layers by utilizing the fact that semiconductor atoms move through solid metal films. To illustrate what

## A simple way to build a transistor is to evaporate aluminum on both sides of a thin wafer of n-type germanium and heat it to 150 degrees on a hot plate

SOURCE

DISSOLUTION

↓

DIFFUSION

↓

GROWTH

5"
4"
3"
2"
1"
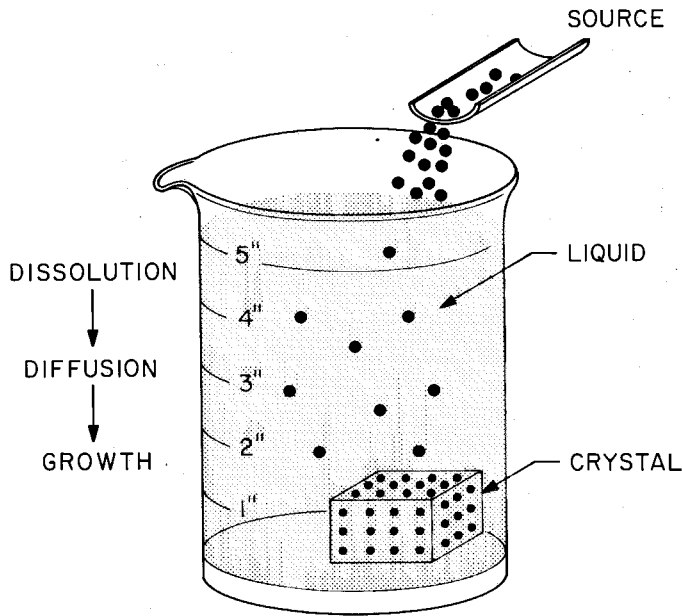
LIQUID

CRYSTAL

In transistors, the necessary contacts between metals and semi-conductors can be grown by a process very similar to growing crystals in a liquid—though on a much smaller scale. If, for example, solid material is dissolved in a beaker filled with a liquid, it is transported to the seed crystal at the bottom of the beaker, where the crystal grows in an orderly, regular fashion.

The solid phase growth of metal-semiconductor contacts occurs in the same way (below). The layer of loosely arranged semiconductor on top provides a source of material that dissolves in the solid metal and is transported to the seed crystal below. There it rearranges itself into a form necessary for transistor action. All of this happens in a space with a thickness of less than one micron—four hundred-thousandths of an inch.

DISSOLUTION ↓

DIFFUSION ↓

GROWTH ↓

SOURCE

METAL

CRYSTAL

1 MICRON
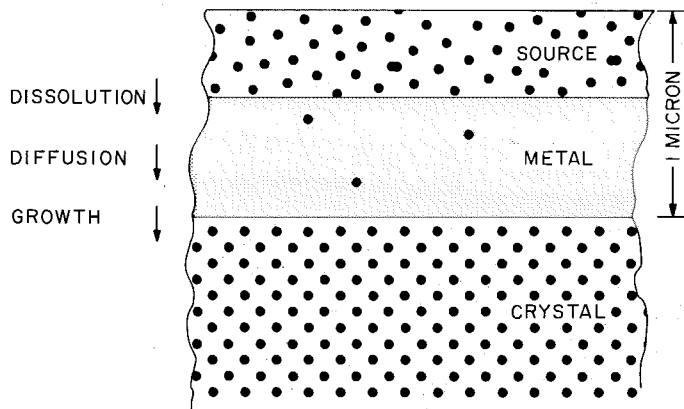
is going on in this case, we can go back to a well-known experiment from high school chemistry—growing solid crystals in a liquid solution. A beaker filled with a liquid is fed from the outside with loose grains of sodium chloride—ordinary table salt—for example. The grains dissolve in the liquid, which allows the salt atoms to diffuse to the bottom of the beaker where a "seed" crystal has been placed. The seed is usually a solid crystal of the same material as that dissolved in the liquid—in this case, salt. But it may be of any composition as long as it has an orderly, crystalline shape for the dissolved salt to stick to and re-arrange itself. The seed will grow, fed by the dissolved salt.

In a similar manner, semiconductor crystals capable of exhibiting transistor action grow through a solid metal film which takes the place of the liquid in the beaker. The film provides a medium through which the nutrient material is dissolved. The nutrient—a layer of loosely arranged semiconductor material on the metal surface—is unable under normal conditions to rearrange its atoms into the regular crystalline form necessary for transistor action to take place.

We have assumed for many years that it was necessary to supply quite a bit of extra energy—either through application of direct current or by heating to hundreds of degrees—to make this rearrangement occur. But we have made this assumption without understanding the key role of the metal film. The solid metal enables the disorderly semiconductor material to dissolve and diffuse, atom by atom, to a crystalline substance on the bottom of the metal-semiconductor sandwich. The function of this crystal is the same as that of the seed in the liquid: to provide a template for further crystal growth. We refer to the technique as solid phase epitaxy.

We have demonstrated this process in the laboratory with germanium-aluminum mixtures where the diffusion temperature of these atoms is strikingly low. We have obtained transistor action at the contacts in a single treatment at temperatures just slightly above that of boiling water. One of the simplest ways to build a transistor is as

follows: Take a thin wafer of n-type germanium, evaporate aluminum on both sides, and heat it to 150 degrees on a hot plate. When removed from the hot plate, the structure clearly exhibits transistor action.

By comparison, the technology currently in use requires much higher temperatures, excruciatingly clean environments, and special mixtures of gases to protect the semiconductors during the fabrication process. The solid phase epitaxy technique is much simpler.

We believe that our newly developed technique will speed up the trend to smaller and smaller transistors and semiconductor devices. A typical integrated circuit chip is about a tenth of an inch long and a tenth of an inch wide. The size of this chip will not change. What will change is the number and size of the transistors that can be put on the chip. Where we can now fit as many as 10,000 components on a standard chip, we will soon be able to put 100,000—or a million. Most of the progress in this direction has been made by reducing the length and width (the lateral dimensions) of the transistors.

As the ability to reduce the lateral dimensions of transistors develops, we need to develop a comparable ability to reduce their depth dimensions. They should be no larger than required by the electronic functions performed—in contrast to the present thicknesses, which are artificially large because of the limitations of current technology.

Our studies indicate that the behavior we have observed in the metal-semiconductor contacts arises from structures that are much smaller than anyone has supposed. The thicknesses produced by the techniques we have developed are typically from a maximum of 3,000 Angstroms down to as thin as we can measure with present instrumentation —a few hundred Angstroms.

This means that our solid-state metal-semiconductor sandwiches have dimensions much closer to what nature requires to obtain the necessary electronic functions. With improvements in instrumentation and fabrication skills, it may soon be possible to reduce this thickness to, perhaps, atomic dimensions. □
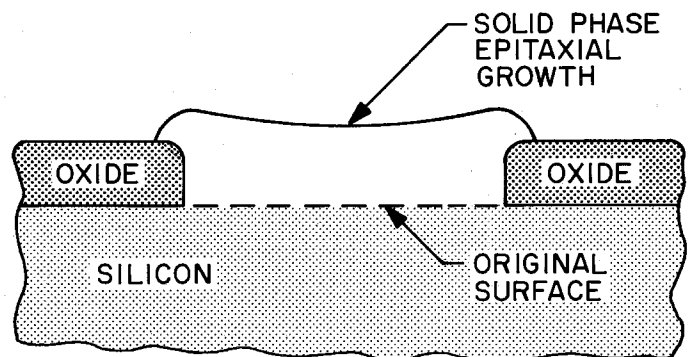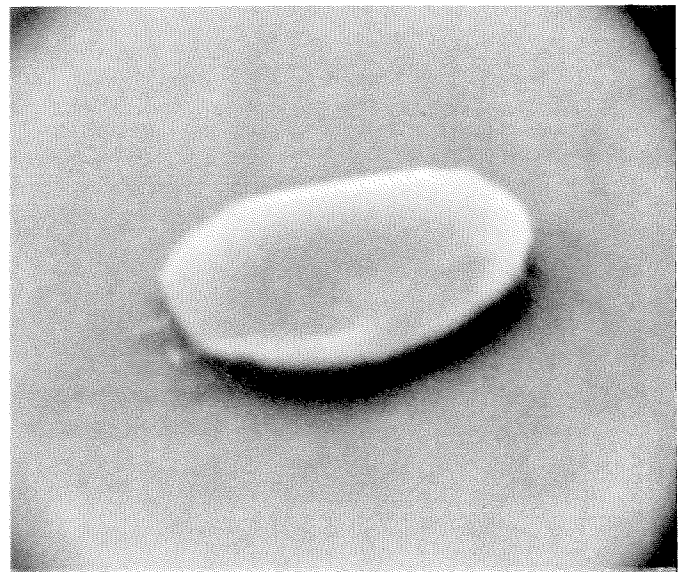
The silicon mesa in the scanning electron micrograph (top) is only 12 millionths of an inch high and 16 hundred-thousandths of an inch wide. It was grown from a solid aluminum film by the process illustrated below. An oxide mask is placed on the silicon where epitaxial growth is not supposed to occur. Over it is evaporated a thin layer of aluminum containing silicon. Where the metal touches the original surface of the silicon, crystal growth occurs by silicon atoms depositing onto the crystal substrate. This grown structure is just the form necessary for transistor action. The process is called solid phase epitaxial growth.

Pioneer Women

Stephanie Charles, Deborah Chung, Sharon Long, and Flora Wu are the first women undergraduates to receive BS degrees from Caltech.

The girls have only a few things in common—most of them academic. They all wanted to come to Caltech because of its research atmosphere, and because they wanted to be around intelligent students with interests like theirs. They all wanted to come to Caltech as freshmen—but though they were ready for Caltech in the fall of 1969, the Institute wasn't ready for them. Girls were not accepted as undergraduates until September 1970.

They have all had excellent grades—in fact, they all graduated with honors—and they all intend to go to graduate school.

Stephanie Charles

Stephanie Charles went through high school in Falls Church, Virginia, in three years, and enrolled for a year at the University of Maryland before coming to Caltech. The Institute's reputation in physics was the magnet that drew her to the West Coast, because her interests lie in applied physics.

Stephanie completed her graduation requirements before the third term of her senior year and took a part-time job at the Jet Propulsion Laboratory working for Dr. John Anderson. Dr. Anderson supervises a planetary ephemerides and relativity group which furnishes computed material on planetary positions to space missions. It also deals in experimental relativity, using spacecraft data to test relativity problems. Stephanie has been working specifically on the orbital effects of general relativity and how they might affect spacecraft orbits. She is also calculating earth tides.

Stephanie will do graduate work in electrical engineering at Stanford.

Deborah Chung

Deborah Chung entered Wellesley after graduating from King's College in Hong Kong. After a year she transferred to Caltech because of what she had heard of its academic and engineering standing.

She immediately took advantage of the campus research atmosphere and went to work for Professor Gerry Neugebauer on infrared measurements obtained from Mariner 9. Since June of last year she has worked for Professor Pol Duwez and Dr. Chang-Chyi Tsuei on x-ray diffraction. She has been particularly absorbed in studying the structure and properties of amorphous solids by computer simulation.

Deborah graduated from Caltech with a BS in engineering and applied science and an MS in engineering science, and will go to MIT for further graduate work.

When she arrived at Caltech, Deborah moved into Lloyd House, but eventually opted for the available kitchens and relative quiet of Marks Graduate House. She also discovered the best-tuned piano on campus in the glee club practice room and managed to keep up her practicing. She has studied the piano since she was five and in April 1970 won the Brahms Intermezzo Piano Solo Competition in the Hong Kong Music Festival. In 1971 she became a diplomate of the Royal Schools of Music in England.

Sharon Long

Sharon Long went to George Washington High School in Denver, whose challenging academic atmosphere—mostly in the mathematics course—prepared her for Caltech. She spent a year at Harvey Mudd College before transferring here. She started out in the chemistry option, then went into the Institute's new Independent Studies Program, with a double major in biochemistry and French literature. Her program included both course work and research done with Daniel McMahon, assistant professor of biology.

She has been deeply involved in student government since her sophomore year, and on the side she has played oboe in the Caltech Woodwind Quintet and pursued her interests in films, cooking, and needlework. Although she was accepted in medical school at UC Irvine, she has decided to wait a year before continuing her studies. She will go to Europe this summer—to start breathing again after her three years at Caltech.

Flora Wu

Flora Wu, also a native of Hong Kong, came to Caltech for her last two years by way of Pasadena City College, where she was class valedictorian at her graduation. Flora followed the same path blazed by her older sister Bessie, who is now a third-year medical student at USC.

Flora arrived in the U.S. in August 1969 with little more than "a coat and my violin." She got a part-time job doing light housekeeping for one of Pasadena's little old ladies, which helped her learn English conversation and American customs.

Flora, a chemistry major, is following her sister into medicine, and will enroll at the University of California, San Diego, medical school in the fall.

While she was amassing many more units than she needed for graduation from Caltech, Flora also worked on non-histone chromosomal proteins under Dr. Sarah Elgin, a research fellow in biology in Professor Leroy Hood's group.

She has lived in Page House and considers that an important part of her Caltech experience. She still has her violin, though she's afraid to play it because she hasn't had time to practice. If she can just hold off until she finishes her medical education, she'll get back to it eventually.

"Being a woman at Caltech has its own special

Of all the prizes bestowed on exceptional Caltech students at commencement time, none quite has the flavor of the Hinrichs Award, which goes "to the senior who throughout the undergraduate years at the Institute has made the greatest contribution to the welfare of the student body and whose qualities of character, leadership, and responsibility have been outstanding."

This year Sharon Long shared the award with classmate Russ McDuff; both of them fill the bill admirably.

During her three years at Caltech Sharon was a highly visible, vocal, and effective participant in student and academic affairs. As a sophomore—in her first year here—she served on both the freshman and upperclass admissions committees. In her junior and seniors years she was director of academic affairs and one of the strongest and most active members of the board of directors of the ASCIT. She also served as a student member of the faculty committees on academic policies and curriculum.

Winning the Hinrichs Award was a double honor for Sharon because she is also one of the first undergraduate women to receive a BS degree from Caltech, along with Stephanie Charles, Deborah Chung, and Flora Wu.

What's it like—being a woman undergraduate at Caltech? If you ask Sharon Long, she'll answer you something like this:

The girls are probably more academically insecure than the guys when they come here, and they have a little more on the line as to whether they'll succeed or fail. With me, it took the form of feeling I couldn't go to anybody and talk about anything that was bothering me. As freshmen, male students learn pretty quickly to ask for help from other students. I was afraid to, because I didn't want people saying "Dumb girl!"

I felt a strange ambivalence. At the same time that I thought I must be really special, I was convinced that I wasn't nearly as good as the other students, and was special only because I was a girl. I didn't want to use my being a female as an excuse for anything, and yet I sometimes did it without knowing it.

The man-woman relationship here makes for some difficulties. The way I handled it was to stay essentially paired off with one man almost all the time, and I got married at the end of my sophomore year. This made it possible to have casual friendships with men because it was understood that only friendship was implied. But being married during a period when you are still developing your life and your goals can get to be unworkable if the two people realize that they have taken different forks in the road—which is what happened to us.

Being a woman at Caltech has its special set of challenges —and it presents some challenges to the faculty too. There aren't many women professors to act as models for you, and there are male professors here who definitely let their prejudices show. I have a good friend who almost always dresses grubby. One day she went to class in a dress, and the professor was really extra nice to her. He leaped down to her chair to light her cigarette, and she was so embarrassed she never dressed up for class again.

When I was on faculty committees where I was the only female, I always felt a lot of ambiguity. I enjoy looking good. It makes me feel more comfortable. But I kept wondering if things wouldn't get complicated if I went in there and really looked pretty. I felt I'd be in a double bind by calling attention to my being feminine—and thus categorized—plus my being a student and therefore already on one of the lower rungs of the ladder.

When I came here I had all the qualities of the average freshman—not socially very adept, having a lot of insecurities about my intellectual capabilities, afraid of other people. After you're here awhile you have all your worst fears realized. You think, I'm really not as smart as people have told me I am. I'm fooling everybody. What if I really blow it?

But the first time you can look somebody in the eye and expose yourself to the potential humiliation of admitting you aren't doing well, and they look at you and say, "Me too," the sense of relief is awesome.

There is a lot of anti-intellectualism on campus of course. I think it has something to do with people seeing the gap between what they're doing and what they would like to be doing, and feeling guilty because of it. Most students really expect a lot from themselves, inside. I've never been able to forgive myself for not working beyond my capacity.

I think most people come here with big goal orientations. But the work here is so hard that you can't do it if all you have pushing you is goals. You have to be doing it because you basically like it. You have to enjoy the process.

A lot of professors have reinforced this idea in me by talking about their research. You can't do research if all

set of challenges."

you want is an answer. You have to enjoy working in a lab and performing endless repetitive tests and reading endless journals to be a good researcher. I'm not sure I have all those qualities. But no goal, no matter how strong, is going to be able to get you through the work here otherwise.

One important factor that contributed to my intellectual growth at Caltech was tackling work that was difficult. You have to get it done, in spite of your frustration. You have to be able to have ideas even when you're confused, even when you're exhausted.

I think the work here is too hard, but I accepted it and eventually developed methods for ignoring enough of it so I could survive. You look for the essentials that are going to get you by. You have to learn to balance one class against another. You can't learn everything in depth. You're lucky if you learn one thing well here and there.

You can't talk about Caltech without talking about the honor system. Its effect on me was closely linked to the process of coming to accept myself.

Working under the honor system makes people become very intellectually honest with themselves. It gets them to know their limitations. That's important—not to live with fantasies about what you're capable of doing. Another thing that makes it work is that, even if you get a test back and you've done poorly, you realize that there is that firm little center core inside yourself that's starting to build up.

I came to grips with myself at Caltech because I had to, and maybe I wouldn't have had to if I had been someplace else. I have no way of knowing.

I went into the Independent Studies Program mostly because of the humanities courses I took here in my sophomore year. Annette Smith's course in French literature and Will Jones's course in philosophy opened up a new world for me. I had always been interested enough in humanities to read broadly, but until I took the courses here, I didn't connect literature with life; I treated it abstractly—as a scientist, if you will.

In joining the ISP I was dedicating myself to looking at life and the world on more than one level. I know what it is to look at the world as a scientist, whose basic philosophy is that effects can be traced to causes, and that reproducible order is meaningful. But life doesn't seem to me to be completely rational; poetry in particular, with its use of image and metaphor, seems to be an equally powerful approach to reality, and one whose beauty is complementary to the beauty of order that I have always loved in science.

Being in ISP made me feel more responsible for my education, in several ways. First of all, I quite literally chose what I thought was important to study— and that was what I studied.

As a result, my attitude toward the difficulties I encountered was healthier than before, because I realized I was there by my own choice. And there was a deeper sense in which I felt responsible, which is that, floating as I did between scientific and metaphorical descriptions of reality, I began to feel responsible for what I thought, and for what I believed. There are a lot of equally valid ways of looking at the world; I am the one who chooses the way in which I myself perceive.

Last summer I got a chance to supplement my education when I was chosen as one of the two Caltech students to attend the Institute for Humanistic Studies at Aspen. It's mainly a program for executives to broaden their horizons on social and philosophical issues. They also invite people with different points of view, from other countries, from universities, government, business, and the media. I found I had more in common with people from the academic world in Germany, say, than I did with people from Denver or Los Angeles who were in business. I found that social classes transcend national barriers.

At present I would like to head for a university career, because that seems to be the best way to get paid for thinking and writing and teaching. I think I would prefer being a professor to just about anything; but in the next year I'll have to decide what field or combination of fields I want to pursue. I would specialize, although reluctantly, if that were the only way to become part of the academic world—a world which, I must add, sometimes seems to be only dreamed. But if many people have the same dream, then we can share it. I guess that's as much as I feel I can expect. ◗

The Making of a Mahatma
—Gandhi's South African Years

by Robert A. Huttenback

In 1900 Mohandas Karamchand Gandhi was a dapper young lawyer, just beginning those "experiments with truth" that led to his becoming the revered Mahatma of hundreds of millions of Indians.

The troubles Asians are encountering in East Africa today were foreshadowed by those experienced by Indians in South Africa at the turn of the century. The Uganda Indians are (or perhaps "were" is more accurate) essentially leaderless, whereas those in South Africa were fortunate enough to fall under the spell of one of the modern era's most charismatic leaders—a man who sought to alter the existing order not through appeals to man's darker side but rather to his better nature.

Mohandas Karamchand Gandhi is properly remembered as the father of India's independence, uniquely achieved through the practice of nonviolence. It is too frequently forgotten, however, that the *satyagraha*, or militant nonviolence, was forged as a political technique not in India but during the 21 years Gandhi lived in South Africa—years which saw the development of philosophical precepts that were to guide him throughout the rest of his life.

Gandhi was born on October 2, 1869, in the tiny princely state of Porbander on the west coast of India. The Gandhi family was of the Vaisya caste, and the future Mahatma's father, Ota, rose to the dignity of *dewan*, or prime minister, of the principality. The young Gandhi gave no signs of greatness in his youth. He was an undistinguished student, and when his family sent him to England in 1888 to study law, it could not have been with much confidence in his abilities. Gandhi returned to India after two and a half years in London with the uncertain intent of practicing law. From the first he was ineffectual. In one of the few cases in which he became involved, he was virtually struck dumb while cross-examining a witness. Finally, frustration forced him to accept a year's contract in South Africa in connection with a £40,000 civil suit.

The case involved litigation between Indians, and there were in fact some 43,000 Indians as opposed to 40,000

Gandhi is properly remembered as the father of India's independence, but his political technique of nonviolence was forged during the 21 years he lived in South Africa

whites in the colony of Natal when Gandhi landed in Durban in 1893. Indians had first started arriving in Natal in 1860. They came as indentured laborers to work in the sugar fields of the colony. It had been fully expected by the white colonists that the Indians would return to their native land at the end of the five-year period of indenture. This, however, they failed to do; and when they were joined—starting in the 1880's—by free Indians who entered the retail business to the detriment of white merchants, anti-Indian feeling in Natal became intense.

There was more to Gandhi than his early years had promised, and when he encountered the wall of anti-Indian sentiment in Natal, he fought back. On his first day in court he wore a *pugri* (turban) and was ordered to remove it by the judge. He refused to do so and left the chamber in protest. But worse was to come. He bought a first-class train ticket to Pretoria, only to be forced out of his compartment by a constable who wanted him to sit in the baggage car. Rather than accede, Gandhi spent the night in the unlit, ice-cold station at Pietermaritzburg. The next day, at Charlestown, he boarded a stage for Standerton and was first given a seat next to the driver. He was, however, soon ordered to move to the footboard; but again he would not comply and was roughly handled as a consequence of not submitting to an "insult [which] was more than I could bear." Gandhi was in South Africa for purely professional reasons and could easily have returned to India. But these indignities forced him to consider his position more deeply.

In Natal, the real Gandhi began to emerge; as it turned out, he was not just another canny Gujerati lawyer bearing the credentials of a British legal education. He was deeply introspective—a moralist and ideologue who all his life wrestled with conscience and the spirit, Truth and Right. These preoccupations spawned a complex mentality which allowed Gandhi to think little of personal discomfort, to eschew the shackles of ego and ambition, and, concomitantly, rarely to harbor resentment or rancor against others.

Not that Gandhi developed his personal philosophy and code of ethics easily, or ever saw the process as complete; truth to him was never monolithic or simple, and he spent his life in what he called "experiments with truth." His metaphysical probings led him often from one extreme to another. Upon encountering Gandhi in Piccadilly Circus, Sachchidanand Sinha, a fellow Indian, described the 21-year-old fledgling barrister:

> He was wearing a high silk hat burnished bright, a Gladstonian collar, stiff and starched, a rather flashy tie displaying almost all the colours of the rainbow under which there was a fine striped silk shirt. He wore as his outer clothing a morning coat, a double-breasted vest, and dark striped trousers to match and not only leather boots but spats over them. He carried leather gloves and a silver-mounted stick.

What a far cry from the more familiar figure, garbed only in the abbreviated *dhoti* of the poorest Indian cultivator.

As in dress, likewise in food, philosophy, and religion; a short period of meat eating gave way to devout vegetarianism and the realization that control of the palate and carnal appetites in general led to the sublimation of materialism and the physical self and the attainment of real freedom. Gandhi's dietary experiments, which were at first dictated by imperatives of health and economy, later became part of his religious and spiritual evolution. It is not hard to see the connection of vegetarianism to the Hindu concept of *ahimsa* (literally nonhurting, nonviolence) which became the basis of so much of Gandhi's thinking.

Gandhi arrived in South Africa just at a time when he was most needed by his Indian confreres not only in Natal but in Cape Colony and the Afrikaner republics of the interior. In Natal, where the vast majority of the Indian population resided, the government determined that if the Indians were to remain in their midst they should at least do so only as hewers of wood and drawers of water. The Colonial Legislature consequently passed three highly discriminatory acts.

Natal's main objective was to inhibit the ease of entry into the colony enjoyed by free Indians. Initially the legislative assembly wanted to pass an act specifically

Gandhi's method was singularly law abiding, and his goal was not one of total victory. He fought for triumphs of principle rather than sweeping reform.

excluding all but indentured Indians from the colony, but the Colonial Office would not permit it. As a result, Act 14 of 1897, "to place certain restrictions on Immigration," was technically nonracial. Qualifications for entry into Natal were based on property (£25) and knowledge of a European language.

The Immigration Restriction Act of 1897 was administered in such a manner that most Europeans were judged eligible to enter Natal while virtually all Indians were not. As the prime minister of Natal told the legislature, "It never occurred to me for a single minute that [the act] should ever be applied to English immigrants."

The removal of all Indians from the colonial voters' rolls was considered a matter of no less urgency than immigration restriction. In the first instance, a bill making all Indians ineligible to vote in Natal parliamentary elections was passed by the legislative assembly, but the Colonial Office, as guardian of the imperial philosophy of the equality of all British subjects regardless of race, informed the government of Natal that "to assent to this measure would be to put an affront upon the people of India as no British government could be a party to."

In a second version of the franchise act, the colonists were able to disenfranchise for the future all Indians, regardless of qualifications, who were not at that time on the voters' rolls. The colonial legislators merely stipulated that those "who (not being of European origin) are Natives or descendants in the male line of Natives of countries which have not hitherto possessed elective institutions," unless exempted by the governor in council, could not vote in parliamentary elections. Again, once the specific racial terminology was removed from the franchise law and despite the clarity of its objective, the Colonial Office's opposition essentially evaporated.

Objectionable as were the immigration restriction and franchise acts, by far the most insidious piece of legislation passed by the Colony was the Natal Act of 1897, which made all applicants for trading licenses or renewals of trading licenses subject to municipal licensing officers to be appointed by the corporations. The act stipulated that all books were to be kept in English and that com-

mercial premises should be maintained in a sanitary condition. The licensing officer was to determine whether these conditions were being met or not. Appeals were to be allowed to a board made up of municipal officials (those very merchants who were determined to drive the Indians out of business) but not to the courts of the land.

The position of the British government must be viewed with some sympathy. On the one hand, if the Empire stood for equality, any attack on a particular group of the Queen's subjects by other members of the British family struck at the very roots of the imperial policy of equality. On the other hand, it must have been difficult for Englishmen of the 19th century, not the most tolerant of ages, to feel in their hearts that Africans and Indians were really the equals of white men. Embarrassed and frustrated, the government compromised. It insisted that the letter of any particular law be nondiscriminatory but cared little about the spirit.

All of this must have been immensely discouraging to Gandhi. He fought against anti-Indian legislation, and although he riveted world attention on the situation in Natal, he inevitably failed. Yet, Gandhi was a passionate believer in the British Empire. He felt that much of the antipathy that the white colonists of South Africa felt toward the Indians was based on misunderstanding and on doubts about the Indians' commitment to the Empire. Consequently, when the Anglo-Boer War broke out in 1899, Gandhi organized a corps of stretcher bearers to serve with the British troops in the field.

But Gandhi was disappointed in his conviction that loyal Indian service would change settler attitudes. In fact, the situation, as far as Indians were concerned, deteriorated even more rapidly after the British victory in the Anglo-Boer War than before. In the Transvaal, which became the main arena of the future Mahatma's postwar activities, Gandhi fought the situation as well as he could; but it is worthy of note that he did not lead his followers into the streets but rather conducted his battle through the established courts. Not only was Gandhi's method singularly law abiding, but his goal was not one of total victory. He fought for triumphs of principle rather than sweeping reform. For example, he demanded the *right* of Indians to enter the Transvaal. But he would have deemed honor vindicated if administrative practice had restricted the actual immigration to no more than six.

It is significant in this context that the birth of *satyagraha* is again associated with a conflict over principle rather than more pragmatic realities. In 1906 the Trans-

vaal government sought to implement an ordinance which would have required the registration of Indians and the issuance of residence permits to them. As Indians alone were singled out for such treatment and as they had submitted to special registration already twice before, Gandhi was prepared, this time, to lead his followers to the metaphoric barricades.

The Transvaal Indians deluged the governor and the secretary of state with telegrams and other protests, and on September 11 they held a mass meeting at which for the first time the use of *satyagraha* as a political weapon was proposed. Gandhi moved the relevant resolution:

> In the event of the Legislative Council, the local Government and the Imperial Authorities rejecting the humble prayer of the British Indian community of the Transvaal in connection with the Draft Asiatic Ordinance, this mass meeting of British Indians here assembled solemnly and regretfully resolves that, rather than submit to the galling, tyrannous and Un-British requirements laid down in the above Draft Ordinance, every British Indian in the Transvaal shall submit himself to imprisonment and shall continue to do so until it shall please His Most Gracious Majesty the King Emperor to grant relief.

When another speaker passionately declared that in the name of God he would never submit to the law, it appeared to Gandhi that the scales had been taken from his eyes, and he wondered how he had not before seen that the pledge to initiate *satyagraha* must be taken in the form of a solemn oath.

Clearly *satyagraha* could not be undertaken lightly. The situation to be fought had to be massively and manifestly wrong, a determination which could only be made after the soul had been leeched of all hate, passion, and prejudice through the practice of nonviolence of the mind. Insight, when combined with the spirit of love, could light the path to the Truth. Once the Truth had been discovered, the *satyagrahi* could boldly assert his opposition to the wrong and refuse to cooperate with those attempting to implement it. The *satyagrahi* might indulge in public acts of dissent and disobedience but he could never act violently, for to do so would cloud his insight and set him on a path as misguided as that of his adversary. If physically assaulted, the *satyagrahi* might never defend himself. He had willingly to go to prison and even to his death. He would win his adversary to his side through love, patience, purity, and humility—would convert him through the eloquence of his suffering.

Gandhi warned his listeners of all the possible consequences they faced if they pledged themselves.

> We might have to go to gaol, where we might be insulted. We might have to go hungry and suffer extreme heat or cold. Hard labour might be imposed on us. We might be flogged by rude warders. We might be fined heavily and our property might be attached and held up to auction. . . . Opulent today, we might be reduced to abject poverty tomorrow. We might be deported. Suffering from starvation and similar hardships in gaol, some of us might fall ill and die. In short, therefore, it is not at all impossible that we might have to endure every hardship that we can imagine, and wisdom lies in pledging ourselves on the understanding that we shall have to suffer all that is worst.

Gandhi emphasized that "going to gaol is a unique step, a sacred step, and only by doing so can the Indian community maintain its honour." Optimistically, he concluded: "I can boldly declare, and with certainty, that as long as there is even a handful of men true to their pledge, there can be only one end to the struggle, and that is victory." With a roar of enthusiasm the Transvaal Indians rose to take the pledge as *satyagrahis*, and a new political technique was born.

On August 16, 1907, the Indians formally commenced their struggle. At a meeting held outside the Hamidia Mosque in Johannesburg, some 3,000 Indians from all over the Transvaal gathered to hear their leaders. The *Transvaal Leader* described what happened at the close of the session:

> A large three-legged pot was filled with the registration certificates, about 1,000 in all, and about 500 trading licenses. Paraffin was then poured in, and the certificates set on fire amid a scene of wildest enthusiasm. The crowd hurrahed and shouted themselves hoarse; hats were thrown in the air, and whistles blown. One Indian . . . walked onto the platform and setting alight his certificate held it aloft. The Chinese then mounted the platform and put their certificates in with the others. For a considerable time it was impossible for any leaders on the platform to make themselves heard.

The battle was now fully joined, and during its eight years duration, other issues merged with the registration question. Immigration continued to be a burning issue, as did the annual £3 tax Natal levied on all former indentured Indian laborers and legal attacks levied on the vested interests of the Indian community. As more and more Indians refused their cooperation to the government, they were tried, convicted, and sent to prison. In keeping with the principles of *satyagraha* they did not try to evade punishment but rather demanded the maximum penalty. Gandhi himself was arrested on October 7, 1908, for refusing to produce his registration certificate and was

In 1914 Gandhi—with his wife, Kasturbai—for the first time adopted Indian dress. This was his way of identifying with the indentured laborers of Natal who were fighting against the annual £3 tax on them.

sentenced to two months at hard labor.

The creation of the Union of South Africa in 1910 did little to alter the context of the Indian question in South Africa. It did, however, concentrate the struggle as it had existed in four separate colonies into a single arena.

With so many of the Indians incarcerated and out of work, Gandhi needed the support of sympathetic Europeans. One of these, Hermann Kallenbach, a German-Jewish architect, purchased a 1,100-acre farm 21 miles from Johannesburg and offered it to Gandhi, rent free, for the use of the *satyagrahis*. Gandhi named the estate the "Tolstoy Farm" in honor of Alexei Tolstoy, whose philosophy he greatly admired. There, Gandhi, always the experimentalist, was able to pursue his theories on health, education, and the virtuous life. He even tried to work out the implications of *ahimsa* (nonviolence) as they applied to snakes.

Gandhi's tendency toward puritan ethics, food fadism, and metaphysical experimentation of course extended beyond Tolstoy Farm. His family of three children and his wife, Kasturbai, were constant victims. As history has shown many times before and since, great men tend to make difficult husbands and fathers.

The final phase of Gandhi's sojourn in South Africa

was ushered in by an intensification of the *satyagraha* campaign prompted by a court decision invalidating virtually all Indian marriages and the passage of a Union immigration act which totally excluded Indians from South Africa. Gandhi traveled to Natal and brought the Indians in the collieries and sugar fields out on strike. Next he led a column of over 2,000 *satyagrahis* on an illegal march from Natal to the Transvaal. Again Gandhi and hundreds of his followers filled the South African jails. It was the kind of dissent with which a government drawn on British lines did not know how to deal.

Pressed by the Indian community, the government of India, and liberals throughout the British Empire, the Union government capitulated. Indian marriages were recognized as legal. The measure empowering Natal to collect an annual £3 tax on all formerly indentured Indians was repealed. The administration of the immigration act was relaxed slightly, and the registration issue was finally settled to the Indians' satisfaction.

Gandhi now felt he could at last return to India. One wonders what he would have been like without the South African experience. He had landed in Natal as the junior counsel for a commercial firm, earning a salary of £105 per annum. Within a few short years he was receiving £5,000 a year in legal fees, all of which he was to contribute to a cause in which he deeply believed. Operating in a sphere where he really had no rivals, Gandhi was able to rid himself of the uncertainty which had caused him to fail as a lawyer in Bombay, and to emerge not only as a skilled attorney, respected throughout Natal, the Transvaal, and later the Union, but as a political leader of great maturity, flexibility, and imagination. On the other hand, it is much too easy to confuse what Gandhi accomplished as a human being—his stature as the prophet of a devastating new philosophy of dissent—with what his presence in South Africa meant in changing imperial policy and attitudes and the actual fabric of Indian life. He had returned to the Indians their honor but little else. And in spite of everything, Gandhi still remained enamored of the British constitution and the principles he thought stood in back of it.

As he sailed away from South Africa in July 1914, Gandhi knew not what great task lay ahead of him in India. Wistfully he wrote from shipboard: "I have been so often prevented from reaching India that it seems hardly real that I am sitting in a ship bound for India. And having reached that what shall I do with myself? However, 'Lead Kindly Light, amid the encircling gloom. Lead Thou me on.' That thought is my solace." □
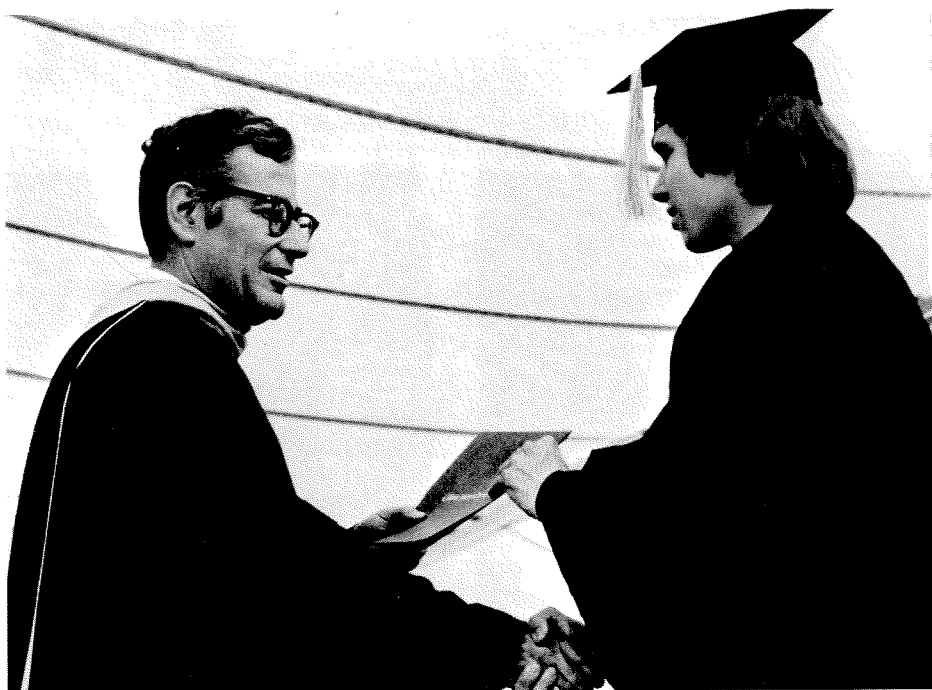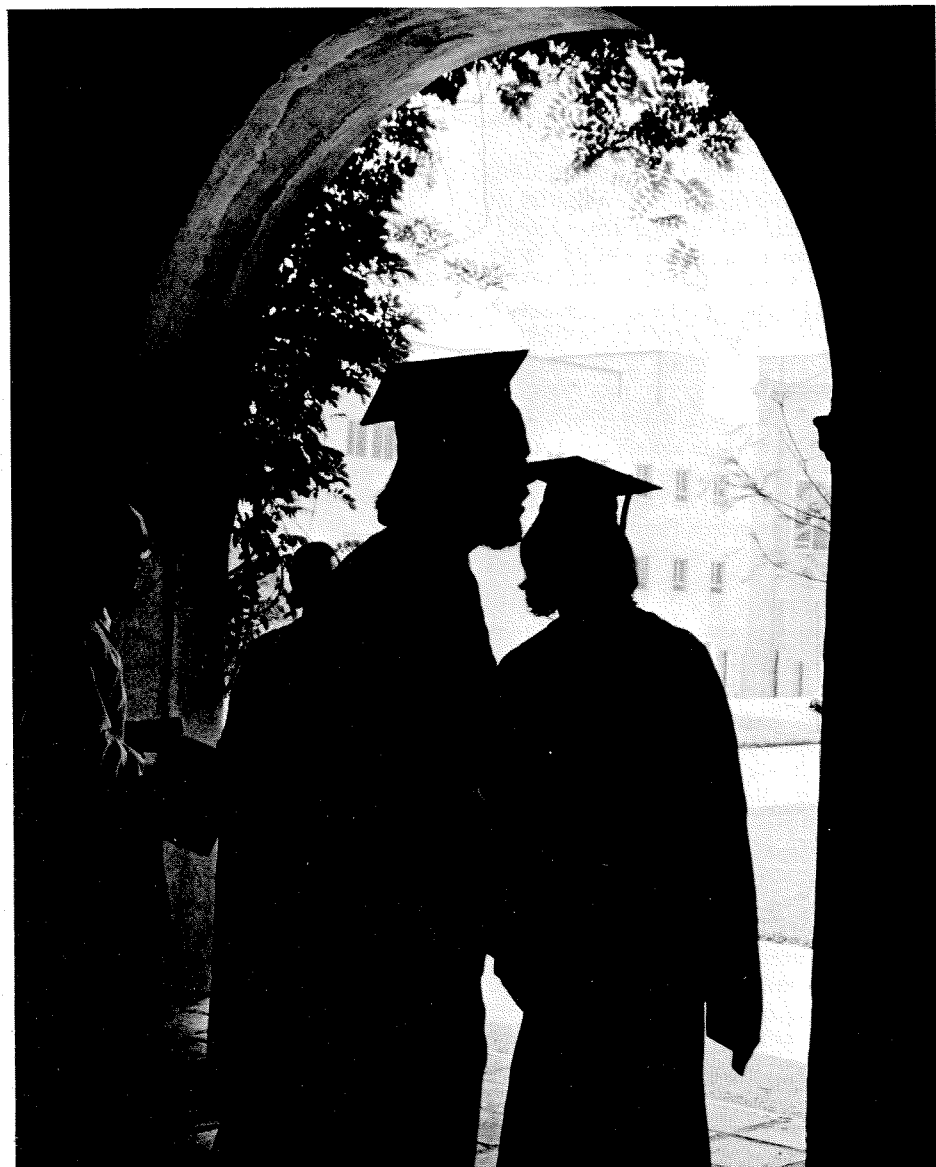
The Month at Caltech

Ringing the Changes

If you've been holding commencements for 79 years, it's a little hard to come up with something new. Even so, the ceremonies on Beckman Mall on June 8 had a few firsts.

The most noticeable was the awarding of the first BS degrees to women (page 20). Another was the absence of a special commencement speaker. This idea was suggested by the faculty committee on convocations so that more time could be devoted to honoring the graduates—and, in line with this policy, thesis titles were read off as PhD candidates received their hoods.

Arnold O. Beckman, chairman of the board of trustees, presided; and President Harold Brown concluded the event with brief remarks and good wishes to the 387 men and women on whom he had conferred 111 PhD, 104 MS, 8 Engineer, and 164 BS degrees.

Vetlesen Prize

William A. Fowler, Institute Professor of Physics, received Columbia University's 1972 Vetlesen Prize last month for "contributions toward our understanding of the origin and evolution of the earth and its place in the universe."

The prize—a gold medal and $25,000—is open to scientists of all nations and is given for "outstanding achievements in the sciences resulting in a clearer understanding of the earth, its history, or its relation to the universe." It has been called the Nobel Prize of the earth sciences.

Fowler's principal contributions to science have been in nuclear physics and its application to astrophysics and geophysics. His research into the interactions of matter and energy in the physics laboratory has made possible determinations of the processes of stellar evolution. "Almost all of our quantitative information about the basic nuclear processes that enter into stellar energy generation and element synthesis is due to Dr. Fowler or to work directly instigated by him," said the Vetlesen citation.

Fowler came to Caltech as a graduate student in 1933, receiving his PhD in 1936. He has been a member of the faculty ever since. He became a full professor in 1946 and the first Institute Professor in 1970.

William A. Fowler
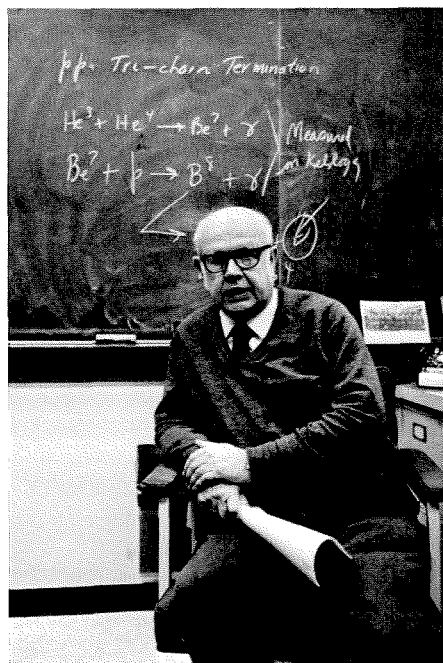
Alumni Honors

Last month *E&S* reported a shower of honors to the faculty. Honors have also been pouring on alumni this spring. For example: In addition to four faculty members who are also Caltech alumni (*E&S*, May), the National Academy of Sciences elected four other alumni to membership this year. They are Andrew A. Benson (PhD'42), director of the physiological research laboratory and professor of biology at the Scripps Institution of Oceanography at La Jolla; Arthur E. Bryson Jr. (MS'49, PhD'51), professor of applied mechanics, aeronautics, and astronautics and chairman of the department of aeronautics and astronautics at Stanford University; William B. McLean (BS'35, MS'37, PhD'39), technical director of the Naval Undersea Research and Development Center in San Diego; and H. Guyford Stever (PhD'41), director of the National Science Foundation.

These new members bring to 74 the number of Caltech alumni memberships out of NAS's current roster of approximately 1,000.

The recent election of 70 engineers to the National Academy of Engineering brings its total membership to 429, of whom 45 are Caltech alumni. Ten of these were elected this year. Two of the ten were faculty (*E&S*, May), and the other eight are: William F. Ballhaus (PhD'47), Beckman Instruments, Inc.; Joseph V. Charyk (MS'43, PhD'46), Communications Satellite Corporation; George C. Dacey (PhD'51), Bell Telephone Laboratories, Inc.; John F. Kennedy (MS'56, PhD'60), University of Iowa; Daniel A. Okun (MS'38), University of North Carolina; Robert J. Parks (BS'44), Caltech's Jet Propulsion Laboratory; Harold A. Rosen (MS'48, PhD'51), Hughes Aircraft Company; and Ivan E. Sutherland (MS'60), University of Utah.

Marshall Hall Jr.

Cross Medal

Marshall Hall Jr., professor of mathematics, received the Wilbur Lucius Cross Medal at the Yale University commencement services in New Haven this month. The medal honors the late Wilbur Lucius Cross, who was dean of Yale's graduate school for many years and governor of Connecticut for four terms. Recipients of the medal are graduates of the school who have achieved excellence in an area in which Dean Cross excelled—scholarship, writing, teaching, editing, administration, or government.

Hall is an authority on combinatorial theory, which has to do with finding the most effective solution among a limited number of approaches. This area of mathematics has applications ranging from counting molecules to discovering the most efficient management systems. He is also noted for his work in group theory, which describes the symmetry of objects—particularly useful in molecular physics and chemistry in defining the symmetry of elementary molecules.

A professor of mathematics at Ohio State University before coming to Caltech in 1959, Hall received his PhD and BA degrees from Yale and was an instructor and assistant professor on the Yale faculty.

Retiring Coach

After 24 years as a coach at Caltech, Bert LaBrucherie is retiring. He came to the Institute in 1949 with a record of playing varsity football at Los Angeles High School and UCLA and 20 years of coaching at the same schools.

A 1929 graduate of UCLA, LaBrucherie's first coaching job was at his high school alma mater—Los Angeles High. He was there for 16 years, and his teams won three "B" team league titles and seven "A" championships. He also coached varsity track for six years. In 1945 he became head football coach at UCLA, and his 1946 team won the Pacific Coast Conference and played in the Rose Bowl. His four-year record at UCLA was 23 wins and 16 losses, but 7 of the 16 were in the 1948 season and some disappointed alumni expressed dissatisfaction. LaBrucherie resigned. After a brief stint as a used-car salesman while he considered other coaching jobs, he accepted Caltech's offer. This gave him a chance to get back to doing the thing he most enjoyed—and made it possible to stay in California.

For his first 19 years at the Institute, LaBrucherie's fall activity was to coach football, and his teams rolled up an impressive—but lopsided—tally of 121 losses, 19 wins, and 2 ties. Not a single alumni hackle even quivered. In fact, early this month more than 200 alumni and other LaBrucherie friends honored him with a farewell dinner at the Athenaeum.

Each spring he coached track, and by a

narrow margin the record was a winning one —107 wins and 105 losses. About ten years ago LaBrucherie started teaching golf, and in 1968 he dropped football and became cross-country coach.

Bert LaBrucherie doesn't have any long-range plans for retirement, except perhaps to see more of his family. But in the near future he and his wife will be taking a trip to Europe—thanks to the gifts and good wishes of 227 LaBrucherie admirers.

Drs. Stewart Harrison and Richard Webb

Health Director

Gregory Ketabgian, MD, has been appointed director of health services at the Institute, beginning July 1. He replaces Richard F. Webb, who has been director since 1953. Dr. Webb will continue to serve in a consulting capacity.

Dr. Ketabgian did his undergraduate work at UCLA, graduating in 1959. He received his MD from USC in 1963, and was first an intern and then a resident at Los Angeles County General Hospital. From 1967 to 1969 he served in the U. S. Army, after which he returned to Pasadena to set up a private practice in internal medicine—and to join the staff at Caltech's Young Health Center as attending physician. In 1972 he was appointed assistant director.

Retiring Doctors

Drs. Stewart Harrison and Richard Webb are retiring from the staff of Caltech's Health Center, and 75 of their friends and colleagues came to the Athenaeum on May 29 to honor them. Provost Robert Christy presented the men with certificates of appreciation for their long service to the Institute —a combined total of 58 years.

Stewart Harrison came to Caltech in 1935 as an assistant professor of radiation therapy. He was active in the early development of the treatment of cancer with high voltage x-rays, participated in the creation of a health center on the campus, and has been a medical consultant in radiation safety and diagnostic radiology.

Richard Webb has headed Caltech's health services program for 20 years. He worked on the design of the Young Health Center, helped inaugurate counseling services for the students, and has promoted wide use of Pasadena specialists as consultants.

Gregory Ketabgian, MD

Conversation Pieces

Technically intriguing items from TRW, guaranteed to add luster to your conversation and amaze your friends.

Disarming a Virus You, a teenager with mononucleosis, and an African girl with a cancer called Burkitt's lymphoma have one thing in common. Your cells very likely contain a "living molecule" called the Epstein-Barr virus (EBV). But you are in no danger, the teenager will recover from a long and exhausting illness, and the African child may die. Why?

Viruses and cancer are frequently associated, but we don't know much about their exact relationship. Is cancer caused by the virus or by a combination of factors? What makes people react differently to the same virus?

We know that when an organism fights disease it produces antibodies which travel through its bloodstream combining with and deactivating the foreign chemicals, called antigens. But antigens are not only viruses or virus products. The virus-transformed cells themselves make antigens which can cause or contribute to their destruction. When cells are invaded by EBV, five different antigens may be formed.

To best study the properties of antigens, we must separate them from all the other materials found in cells. One way is to use immunoadsorbents, long-chain molecules to which EBV antibodies have been chemically attached. EBV-infected cells are homogenized and the immunoadsorbent is immersed in the mixture. The antigens cling to the antibodies and when the immunoadsorbent is removed, the antigens come with it. The antigens are then freed from the immunoadsorbent and concentrated.
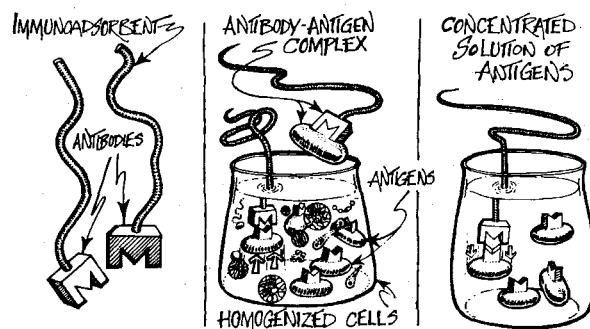
Scientists at the National Cancer Institute hope to isolate EBV antigens and those of other cancer-associated viruses. These antigens could be used to produce serums which would be catalogued and stored in a serum bank. Each serum would contain the antibody to one specific antigen.

TRW researcher Dr. Norman Weliky has been perfecting the immunoadsorbent technique for the National Cancer Institute. His group has prepared a highly purified serum against a mouse leukemia virus, and is now working on EBV-associated antigens. Their work is a small but important step toward the solution of the cancer-virus mystery.

Boomerang Have you ever considered how many hazardous chemicals get into our environment via their containers alone? Paint residues left in the cans and carted to your local dump add 32,700 pounds of mercury, 4.4 million pounds of lead, and 1 million pounds of chromium to the earth and water each year. And what about the packages that held pesticides like dieldrin and herbicides like 2,4-D? How do you clean the solvent that washed the can that contained the powder that killed the bugs that ate the wheat that farmer Jack grew?

The Environmental Protection Agency realized that we don't know enough about hazardous chemicals and their disposal. For instance, mankind has been using the oceans as an ultimate disposal site for centuries without knowing the effects of waste materials on the ocean environment.

TRW Systems was asked to help. In a year of investigation we have compiled and studied a rouges' gallery of over 500 chemicals which are highly toxic, persistent, extremely flammable or explosive, or radioactive. We have also recommended ways of dealing with these ecological menaces, usually by breaking them down completely or isolating them from the environment.

Waste can be like a boomerang; you think you've thrown it away, but it returns, sometimes with destructive force. TRW is working with the EPA to improve waste management techniques in the United States. You should go to the dump, but the dump shouldn't come back to you.

For further information, write on your company letterhead to:

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Attention: Marketing Communications, E2/9043
One Space Park Redondo Beach, California 90278

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HOW CAN A SHINY PIECE OF CRYSTAL HELP GIVE LIFE TO A DYING MAN?

That's no ordinary crystal. It's ultra-pure germanium. The purest substance on earth.

General Electric researchers and engineers first figured out how to refine germanium to such a pure level. (Less than one atom of impurity in a trillion.)

That was a major technical achievement. But that's not the reason it's important.

Ultra-pure germanium is very sensitive to certain radioisotopes. So it's making possible a revolutionary new sensing device for studying the brain. Conceived at the NYU Medical Center's Institute of Rehabilitation Medicine, this system is intended to give doctors their first 3-dimensional look at the entire brain.

A patient, wearing a helmet containing germanium sensors, will be given a radioisotope. As the isotope flows through the brain, the sensors will feed signals to a computer, resulting in a complete mathematical picture of the brain's blood-flow rates.

That information could be invaluable in treating hundreds of thousands of people with brain damage resulting from strokes or accidents.

For example, take an auto-accident victim with critical head injuries. Without fast treatment he could easily be a dead man.

Within 15 minutes this new system could pinpoint the size and location of trauma in his brain. That's something no existing system can do in any amount of time.

It's a pretty clear example of how a technological innovation can help solve a human problem.

That's why, at General Electric, we judge innovations more by the impact they'll have on people's lives than by their sheer technical wizardry.

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