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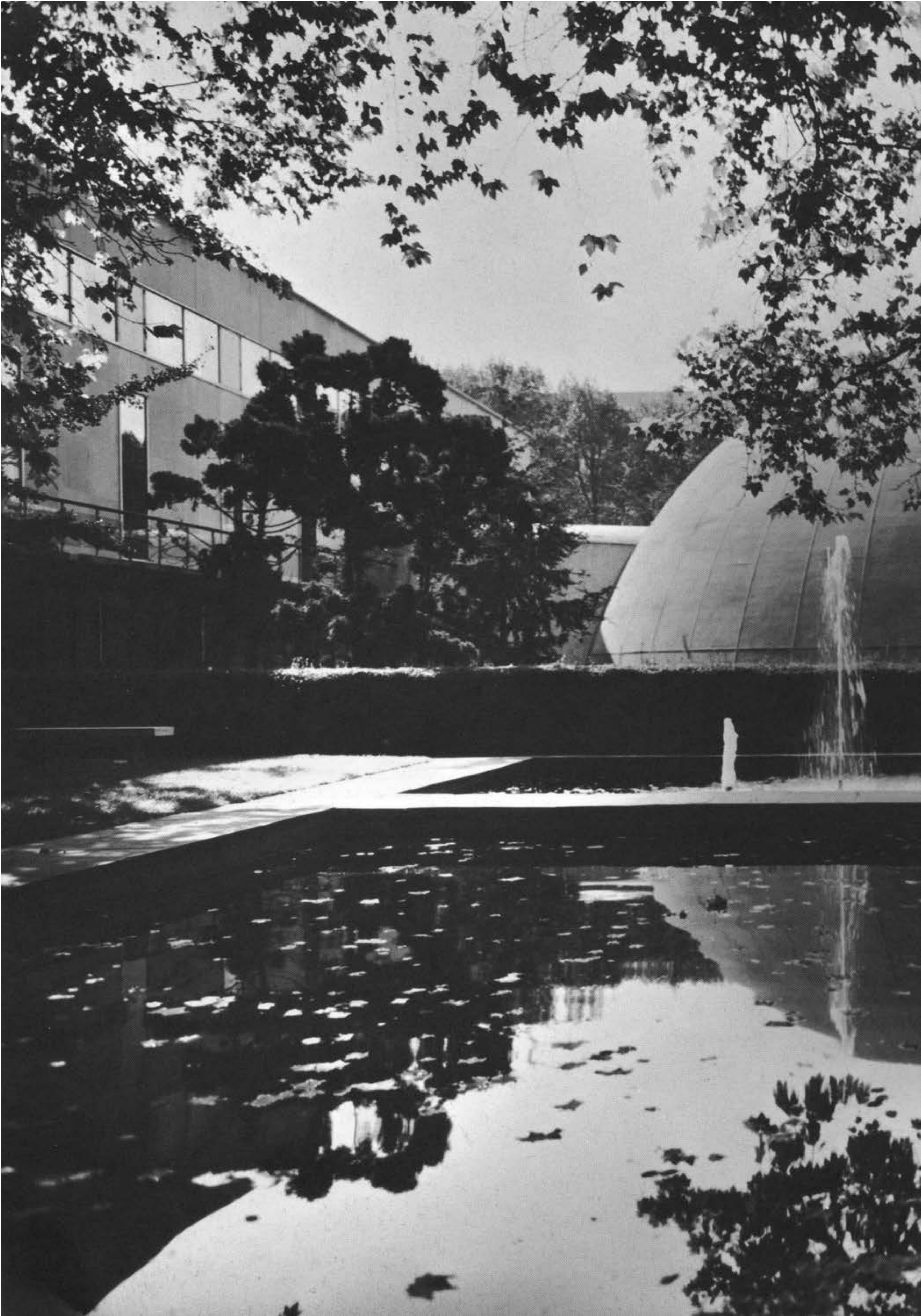

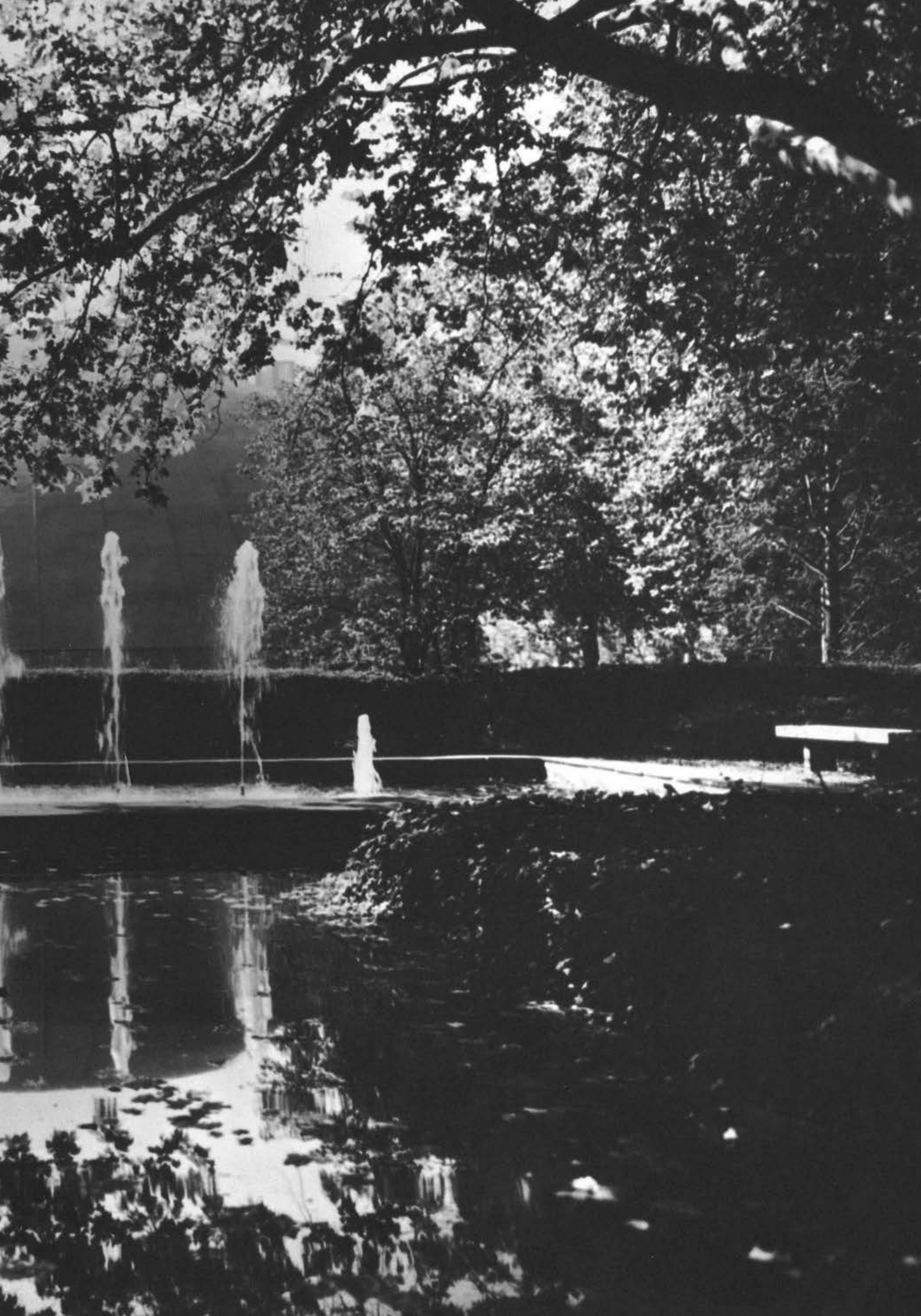

CASPARY AUDITORIUM AND FOUNTAINS

THE ROCKEFELLER UNIVERSITY STORY

THE ROCKEFELLER UNIVERSITY STORY

JOHN KOBLER

PRO·BONO·HUMANI·GENERIS
The Rockefeller University
1901

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INTRODUCTION

The first fifty years of The Rockefeller Institute for Medical Research have been recorded in depth and with keen insight by the medical historian, George W. Corner. His story ends in 1953—a major turning point. That year, the Institute, which from its inception had been deeply involved in post-doctoral education and research, became a graduate university, offering the degree of Doctor of Philosophy to a small number of exceptional pre-doctoral students.

Since 1953, The Rockefeller University's research and education programs have widened. Its achievements would fill a volume at least equal in size to Dr. Corner's history. Pending such a sequel, John Kobler, a journalist and biographer, has written a brief account intended to acquaint the general public with the recent history of The Rockefeller University.

Today, as in the beginning, it is an Institution committed to excellence in research, education, and service to human kind.

FREDERICK SEITZ
President of The Rockefeller University

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. . . the experimental method can meet human needs if it be given its head, wide and free.

PEYTON ROUS

ON JUNE 13, 1969, THE ROCKEFELLER UNIVERSITY celebrated its eleventh commencement, or "Convocation." Compared with traditional graduating ceremonies, the scene that unfolded on the flower-bordered campus hard by New York's East River was a curious one. The academic procession—walking under a green canopy from the flat-roofed, limestone-and-glass Graduate Students Residence Hall to the hemispherical Caspary Auditorium—numbered 378 faculty members and only 27 Graduate Fellows. (The entire student body totaled 143.) No big, blaring band accompanied their steps. Instead, a quintet, the Venetian Brass Ensemble, played sedate selections from the works of an obscure sixteenth century English composer, Antony Holborne.

As soon as the faculty and graduates had taken their places on the platform beneath the domed auditorium ceiling, and a brief invocation had been pronounced, Frederick Seitz, the new President of The Rockefeller University, conferred degrees without any oratory. He followed the example set by his predecessor, Detlev Wulf Bronk, who declared at the first convocation in 1959: "An occasion such as this is fraught with temptations to speak of many things regarding science and education and the objectives of ourselves and our Institute and our nation. But I have vowed that our Commencement should be for those whom we would honor rather than for a speaker to the public which seldom listens."

Each student was formally presented to President Seitz as a doctoral candidate by the faculty member who had stood closest to him during his University career. In a brief citation, this "research adviser" summarized the original work that entitled the candidate to his degree.

Igor Tamm, Professor of Virology and Medicine, cited Nicholas Hill Acheson, saying: "Nicholas Acheson's distinguished work has advanced our understanding of the structure and replication of viruses, which are transmitted by mosquitoes and other arthropods, sometimes causing the disease encephalitis in animals or man. Nick has demonstrated that Semliki Forest virus consists of a core, closely wrapped in an envelope. The envelope is derived from the cell membrane and encloses the viral core as the core is extruded from the cell. Nick has also, for the first time, isolated the viral cores from infected cells."

President Seitz, rising and grasping the graduate's hand, said: "Dr. Acheson, I am pleased to give you your diploma and your hood."

Professor Henry G. Kunkel (biochemistry and immunology), said of Ronald I. Carr: ". . . he gradually focused down on the problem of antibodies to DNA. By rabbit immunization, he was able to produce a variety of such antibodies with specificity for the single-stranded form. These interests naturally turned his attention to the disease called systemic lupus erythematosus, where antibodies to DNA had been known for many years. This disorder is of special current interest because of a rising incidence and because of a relationship to rheumatoid arthritis. Dr. Carr was able to show that certain of the antibodies were more than scientific curiosities, as had been thought, and were very relevant to the disease. In particular, those directed against the native double-helical form were significant because they could react with DNA, appearing in the circulation to produce antigen-antibody complexes. Such protein aggregates were deposited in the kidney, the most vulnerable organ, and played a key role in the malignant nephritis of these patients. Thus, in his thesis work Ronald Carr was able to make a major contribution to our understanding of this disease."

The Rockefeller University is, at present, one of the few exclusively graduate universities in the United States, and the only degrees it confers are doctorates of philosophy and of medical science, and various honorary degrees. It admits fewer students than any other university—so few indeed that senior professors seldom work with more than two students at a time. The physical plant embraces about 14 acres between York Avenue and the East River, and 16 buildings. Its endowment, which currently provides for about two-thirds of the University's income, is based largely on founding gifts made by John D. Rockefeller, Sr. Although the income from the endowment has grown over the years, the University has found it increasingly necessary to turn to other sources of support in order to maintain the high standards of quality and productivity which the institution set from the start, and which have had a profound effect upon the nation as a whole.

From the University's inception 16 years ago, the students have represented virtually every national and ethnic group on earth. In 1968–69 alone, the enrollment of 120 men and 23 women included, in addition to Americans, citizens of Belgium, France, Canada, Switzerland, Argentina, South Africa, and Taiwan. The faculty was equally heterogeneous, with foreigners from 18 countries.

The students pay no tuition. Recommended by the teachers under whom they completed their undergraduate studies, they are paid an annual stipend of $3500 to attend The Rockefeller University.

The Rockefeller University student takes few examinations and no competitive ones. Grading does not exist. "The really important examination comes daily, in the laboratory, in the contacts with the faculty," Bronk points out. "It is only in the laboratory that you learn to live with your uncertainties." The student plans his own curriculum, choosing the professors he finds compatible. At the outset, students and professor are on probation with each other. As the *Graduate Study* booklet notes, the student "presents his tentative study program in an interview with his Faculty Advisory Committee. . . . Thus, each student participates in devising his own curriculum, which may be modified by further consultation with the Dean and other advisers." No professor is obliged to accept students; he remains free to pursue his own line of research to the exclusion of other academic activities. At every level, The Rockefeller University resists categorization. It is flexible and constantly changing, revolving around individuals rather than departments. Indeed, there are no departments, but rather laboratories, and no formal class schedules. Students learn at their own pace through seminars, tutorials, and laboratory experience as well as lectures.

The Rockefeller University has grown in an atmosphere of individual freedom for both students and faculty. In 1903, Simon Flexner, who directed the then recently established Rockefeller Institute for Medical Research, the forerunner of the University, visited the renowned Naples Zoological Station. Deeply impressed by what its founder, Anton Dohrn, told him, he wrote to one of his friends, the pathologist Christian Herter: "The advice he [Dohrn] urged most strongly was freedom. 'Men work here,' he said, 'in a dozen different branches of biological science; can I be an authority on them all? No, no, give them perfect freedom; let them search where and how they will; help them in every way you can, but do not pretend to be master over them.' It was a remarkable pronouncement, and coming from such an authority and one of the most successful research leaders of the world, worthy of the most thoughtful consideration.

And the more I have thought over the subject the more I have come to his point of view."

Flexner upheld this point of view throughout his administration of the Institute, leaving to his colleagues the formulation of their own experimental projects, and one to which the successive heads of the Institute and of the University have adhered to the present day. As the late Professor Emeritus Peyton Rous, one of the Institute's first members, said after Flexner's death, "He had proved that the experimental method can meet human needs if it be given its head, wide and free."

AT THE TURN OF THE CENTURY medicine in the United States was the backward child of the sciences. Few medical research centers existed comparable with those that had been flourishing abroad for decades under such investigators as Pasteur, Koch, and Pavlov. Only Harvard, Johns Hopkins, and two or three other universities had laboratories. Most postgraduates who wanted training in medical research had to go to Europe for it.

Frederick Taylor Gates, the Baptist minister who acted as John D. Rockefeller's adviser in philanthropy, drew the latter's attention to this lack and to the soaring rate of deaths from diseases, especially infectious diseases. In the ten states covered by a 1900 survey, deaths from tuberculosis were 194.4 per 100,000 population; from diphtheria, 40.3; from typhoid and paratyphoid fevers, 31.3. "... medicine," Gates argued, "could hardly hope to become a science until medicine should be endowed and qualified men could be enabled to give themselves to uninterrupted study and investigation, on ample salary, entirely independent of practice."

Rockefeller agreed, and in 1901 incorporated The Rockefeller Institute for Medical Research, the objectives of which, according to its charter, were "to conduct, assist and encourage investigations in the sciences and arts of hygiene, medicine and surgery, and allied subjects, in the nature and causes of disease and the methods of its prevention and treatment, and to make knowledge relating to these various subjects available for the protection of the health of the public and the improved treatment of disease and injury. It shall be within the purposes of said corporation to use any means to those ends which from time to time shall seem to it expedient, including research, publication, education, the establishment and maintenance of charitable or benevolent activities, agencies or institutions appropriate thereto, and the aid of any other such activities, agencies or institutions already established or which may hereafter be established."

An initial grant of $200,000 was referred to a seven-man board headed by William H. Welch, cofounder of The Johns Hopkins Medical School, and including Flexner and Herter. As their first mission, they recruited young university scholars qualified to undertake medical research. The following year Rockefeller added a grant of $1 million to be distributed through the next 10 years. A small building at 127 East 50th Street became the Institute's first headquarters. Soon afterward, most of the acreage now owned along the East River was acquired, and construction was begun on a complex of laboratories, later named Founder's Hall. This was followed by the first research hospital in the United States that admitted only patients with ailments under investigation. Rich or poor, patients pay nothing. In return for unexcelled treatment, service, and nursing, they contribute themselves as case histories.

No single personality, not even one so forceful as Simon Flexner, ever dominated the Institute. But Flexner, who presided until 1935, shaped it and gave it its scientific direction. He was a pathologist and bacteriologist, and he pressed for the application of biochemistry and the physical sciences to research in the life sciences, an approach that typifies the work of the University in those areas today.

Attracted by the promise of unlimited experimental freedom, the finest available laboratory equipment, and generous emoluments, scientists came from all over the world to work at The Rockefeller Institute for Medical Research.

THE LINE BETWEEN BASIC SCIENCE, so-called "pure" science, and applied science is often thin. From the explorations and the dreams of pure scientists emerged practical benefits that placed the United States in the forefront of medical progress. To cite a few:

1905 During an epidemic of cerebrospinal meningitis, Flexner injected a serum, developed jointly by European researchers and the laboratories of the New York City Board of Health, directly into the spinal canal of the victims. Fatalities dropped 50 per cent.

1906 Flexner transmitted poliomyelitis to monkeys.

1906–1939 Alexis Carrel extended his experiments in blood-vessel surgery; cultivated tissues and organs outside the body, including the famous chicken heart, which survived for 34 years. With Henry B. Dakin, he developed a method of treating wounds by irrigation with a solution of chlorinated soda and sodium bicarbonate. With Charles A. Lindbergh, he contrived a perfusion apparatus for further prolonging the lives of organs outside the body.

1908 Samuel J. Meltzer and his son-in-law, John Auer, introduced an improved method of administering anesthesia, which surgeons who operate on the face, throat, or lungs adopted eagerly. In performing face and throat operations and administering anesthesia, the surgeon was hampered by his mask. In thoracic surgery there was the danger of the collapse of a lung. The Meltzer-Auer insufflation tube, inserted in the windpipe as a conduit for a flow of air, permitted the aeration of the blood without requiring breathing movements of the chest, and at the same time the air stream could carry ether or any other anesthetic vapor.

1910 John Auer and Paul A. Lewis published a study of anaphylactic shock in guinea pigs, showing that the cause of death was bronchial spasms. This led Meltzer to formulate the now universally accepted hypothesis that bronchial asthma results from anaphylaxis—that is, hypersensitivity to a foreign protein. It is a vital clue in the study of allergies.

1912 At five o'clock one morning Hideyo Noguchi, greatly excited after sitting up all night at his microscope, roused Flexner. The Japanese bacteriologist had detected, thinly scattered throughout the brain tissue of a paretic, the spirochete of syphilis, which proved that paresis is a late stage of tertiary syphilis.

1917 Peyton Rous and his coworkers Oswald H. Robertson and J. R. Turner, Jr., developed one of the two greatest life-saving techniques ever devised by Rockefeller scientists—the freezing of human blood to preserve it for future transfusion. Not long afterward, close behind the front lines with the British Expeditionary Forces in Belgium, Robertson set up the world's first blood bank.

1919 The second greatest life-saver, a drug called tryparsamide, was developed by Louise Pearce and three of her fellow chemists to combat the sleeping sickness which had been devastating the Belgian Congo.

1930 At great personal risk, Thomas M. Rivers and George P. Berry undertook an investigation of a world-wide epidemic of psittacosis, or parrot fever. Characterized by a virulent pneumonia that killed one out of five victims, it is believed to have been introduced to Europe and North America through the pet and feather trade in South

American parrots. For two years the Rivers-Berry laboratory at the Hospital of The Rockefeller Institute was the only one in the country attempting to contend with the disease. Berry and an assistant, Francis S. Schwenker, both contracted psittacosis, but survived. At length, the researchers concluded that the psittacosis virus was transmitted not by bites or other physical contact with parrots, as the prevalent theory held, but through the human upper respiratory system. They also devised a quick method of diagnosis by injecting a mouse with human sputum.

1931 Donald D. Van Slyke and nine of his colleagues published a monograph on Bright's disease, or chronic nephritis, based on their observations of patients admitted to the Rockefeller Hospital. One valuable result of Van Slyke's work, which included studies of some 600 patients during the next 17 years, was the blood-clearance test. This test measured kidney function by a comparison of the urea excreted with the concentration of the urea in the blood.

1937 René J. Dubos discovered the potent antibiotic gramicidin.

Among the most far-reaching advances in basic science made at the Institute were those of Jacques Loeb, Karl Landsteiner, and Oswald T. Avery. Of the biologist Loeb, who worked here from 1910 to his death 14 years later, George W. Corner wrote in *A History of The Rockefeller Institute:*

> . . . Even before accepting his appointment he had vigorously stated his conviction that the future of medical research and of biology in general depended upon learning how the basic constituents of protoplasm are put together and how they interact. . . . Loeb's questions were directed at the smallest independent elements of the body, the cells. What constitutes them, and what forces hold them together? What sort of boundary surrounds each cell, separating it from its neighbors and from the tissue fluids? . . . What are the effects, in living protoplasm, of changes in temperature, of oxygen supply, of acidity and alkalinity? . . .

His grand discovery of artificial parthenogenesis [the development of an egg without fertilization] suggested a strange new question. The egg cells of all animals, once they are shed from the ovary, are destined to early death unless fertilization gives them continuing life and the impetus to develop. Now that Loeb had induced division of the ovum by chemical stimulation, perhaps he could learn how to save an unfertilized egg from dying. Like many of his apparently specialized inquiries, this one had long-range philosophical implications; Loeb was asking whether death is a necessary consequence of growth and development. . . .

One experiment, done in 1916 with J. H. Northrop, yielded a definite fact, if not about death, at least about the duration of life. . . . Keeping groups of fruit flies . . . at various temperatures, . . . [they] found that the average life span of the flies doubled roughly with every 10° decrease of temperature. This 'temperature coefficient of the duration of life' is of the same order of magnitude as the temperature coefficient of the rate of chemical reactions. The finding obviously suggests that life proceeds by chemical reactions and that death comes when they are completed. . . .

The unending exploratory search of Loeb and his associates frankly involved study of the simplest available living tissues, in experiments designed to avoid the inherent complexities of more highly organized creatures. Yet even this material, the protoplasm of marine eggs and plant cells, was complex beyond the understanding of his time. He was trying to apply laws drawn from the inorganic world of the physicist to living materials of imperfectly known constitution. . . . Naturally, the results were tentative and conjectural, serving largely to raise new questions for further experiment. Loeb's contribution, therefore, was not only his actual discoveries, important though they were, but also his influence upon younger physiologists the world over . . . he did more than any other man in America to bring on the era of physical chemistry in biology and medicine.

The pathologist Landsteiner, who, with Jan Jansky, demonstrated at the University of Vienna that every human being belongs to one of four blood groups, worked at the Institute from 1923 to 1940. There, with Alexander Wiener, he discovered the Rh blood factor. Initially of only academic interest, it was presently shown to be an antigen, which, when present in the blood of a pregnant woman, could cause her to miscarry or her child to develop a serious disease soon after birth. The test for the Rh factor became an indispensable part of prenatal care, enabling physicians to take precautions against misfortunes in childbirth.

Avery Memorial Gateway, two shafts of red granite standing near the corner of York Avenue and 68th Street, commemorates one of the Institute's most creative scientists. Oswald T. Avery started work at the Institute in 1913 as a bacteriologist. When he retired, 35 years later, he had crowned his career with a monumental discovery in genetics. Avery and two young collaborators, Maclyn McCarty, now Vice President and Physician-in-Chief, and Colin MacLeod, mixed nucleic acid from the genetic material of one strain of pneumococcus with pneumococci of another strain, and found that the second strain assumed the inherited characteristics of the first and thereafter "bred true" from cell to descendent cell. Summarized in the statement: "Highly polymerized nucleic acid must be regarded as possessing biological specificity, the chemical basis of which is as yet undetermined," the discovery laid the foundation for all subsequent studies of DNA.

* * *

Under the directorship of Herbert S. Gasser, who succeeded Flexner in 1935, the Institute changed emphasis. During the early decades of its existence, the greatest strides had been made in the study of infectious diseases. Now, Gasser felt, the time was ripe at the Institute, as elsewhere, to explore life processes on the cellular level. In the older-established sciences of pathology and bacteriology he favored new research techniques which would use basic rather than applied medical biology. Gasser's own special field was electrophysiology. He had devised electrical methods for studying nerve conduction and classified nerve fibers according to their electrophysiological characteristics. With his encouragement, the Institute began for the first time to investigate the nervous system. He himself took up such basic questions as what force keeps the living nerve in the polarized state, ready for action when stimulated.

Don't be in a hurry to produce anything practical. If you don't, the next fellow will. You, here, explore and dream.

JOHN D. ROCKEFELLER

FREDERICK T. GATES recalls that he suggested the idea of the Institute to John D. Rockefeller in the summer and fall of 1897:

I remember insisting . . . that even if the proposed institute should fail to discover anything, the mere fact that he, Mr. Rockefeller, had established such an institute of research . . . would result in other institutes of a similar kind . . . until research in this country would be conducted on a great scale and out of the multitude of workers, we might be sure in the end of abundant rewards.

Within four decades Gates's prophecy had come true. The influence of The Rockefeller Institute for Medical Research permeated science both at home and abroad. Regarding its academic standing among European scientists, an officer of the Rockefeller Foundation reported: "Of all the men sufficiently qualified to become Fellows of the Foundation, the largest number desire to work at the Institute." But, whereas the Institute once stood alone, scores of research centers had sprung up, many of them founded and staffed largely by Rockefeller-trained scientists. Every university worthy of the name, moreover, now recognized the importance of laboratory research. In sum, the Institute was no longer unique; it had accomplished what Gates considered its paramount purpose. How, then, justify its continued existence and the expenditure of additional millions?

By 1953, when Herbert Gasser retired, the question was seriously troubling the Board of Trustees and its Chairman, David Rockefeller. Their leadership appreciated what scientific research involves, had a deep sense of public responsibility, and had been the principal guiding force behind the expansion of the Institute's interests. The 15 Trustees included seven scientists, five bankers, an educator, an industrialist, and an attorney. The Vice Chairman of the Board, George H. Whipple, was a Nobel Laureate, cited in 1934 for his investigation of dietary factors in blood formation. In 1955 Vincent du Vigneaud, a Trustee, would also win a Nobel Prize for having isolated the hormones pitressin and oxytocin. David Rockefeller, then Senior Vice President of the Chase Manhattan Bank, received a Ph.D. in economics from the University of Chicago, after postgraduate studies at Harvard and the London School of Economics. An amateur entomologist since boyhood, he had built up one of the world's finest collections of beetles. With his brother John D. Rockefeller, III, he became a Trustee in 1940, and ten years later, when his father, John D. Rockefeller, Jr., retired as President of the Board, he succeeded him.

Concerned about the future of the Institute and convinced that it must seek a new, broader direction, David Rockefeller appointed a committee to review and evaluate its activities. The committee, headed by Detlev W. Bronk, President of The Johns Hopkins University, consulted more than a hundred top-ranking scientists. A number of prestigious members voiced the opinion that the Institute should be liquidated and its funds redistributed among the nation's medical schools. Bronk dissented. The Trustees carefully weighed his views and in the end accepted them. They conceded the need for radical change, but not for liquidation. Although the quality of work performed at the Institute remained as high as ever, its outreach, they agreed, fell short of its potential. The general atmosphere had grown to be too much of the ivory tower, or too monastic. The scientists tended to talk only with one another. What they should be doing, along with their investigations, Bronk argued, was educating promising students and, in turn, being stimulated by them.

The concept of the Institute as both an educational and a research instrument was not entirely novel. The seeds had been present from the beginning. The original charter implied an educational purpose. In fact the early Institute offered one of the few available equivalents of a scientific graduate education in the country, although it was not so called. Relatively few science students took a Ph.D. in those days. One could qualify for excellent academic jobs without it. Those who had determined upon a career in the biomedical sciences and who went to the Institute did so for much the sort of training the graduate fellows receive there today. In the Clinical Research Center, for example, there was an informal "Journal Club" which met semimonthly. Each member reported on any interesting developments in his field. The versatile Dilworth Wayne Woolley, bacteriologist, physiologist, and biochemist, who came to the Institute from the University of Wisconsin in 1939 at the age of 25, called the club "my university."

To Board Chairman Rockefeller, in 1953, it seemed the time had come to stress what was, after all, a traditional concern of the Institute – preparing people for scientific scholarship. The change in prospect, then, was not a sudden revolution, but rather a reaffirmation and an expansion of already existing objectives – "the legitimization [in Bronk's words] of what has always been there in spirit."

The committee concluded: "The Institute should be continued, developed and strengthened, with its research emphasis at the long-range fundamental level in areas of medical research which its independence, resources in men and material, and lack of departmentalization make it uniquely qualified to explore, with the double function of producing trained investigators as well as research publications. To the extent that resources permit, it should support additional selected activities outside the central establishment which will further contribute to the accomplishment of its objectives.

"The present policy of freedom from all programmatic, or project research should be continued. Each individual scientist should be free to shift the direction of his research in accordance with his own best judgment."

As the chief advocate of the proposal to convert the Institute to a university, and as a scientist and educator of vast experience and distinction, Bronk impressed the Trustees as a logical choice to serve as its president. After David Rockefeller so informed him, he (Bronk) notified the committee that if he accepted the nomination, "it must be clearly understood that he [Bronk] does not conceive the Institute to be a haven for a very few outstanding people. It must have a program justifying the expenditure of the income from an endowment which ranks as the third largest for educational purposes in the country, and in his [Bronk's] opinion must have the function of producing trained men as well as new knowledge. He expressed his belief that an enlarged concept of the Institute was possible without disadvantageously affecting the facilities of certain individuals who might work most effectively in relative seclusion."

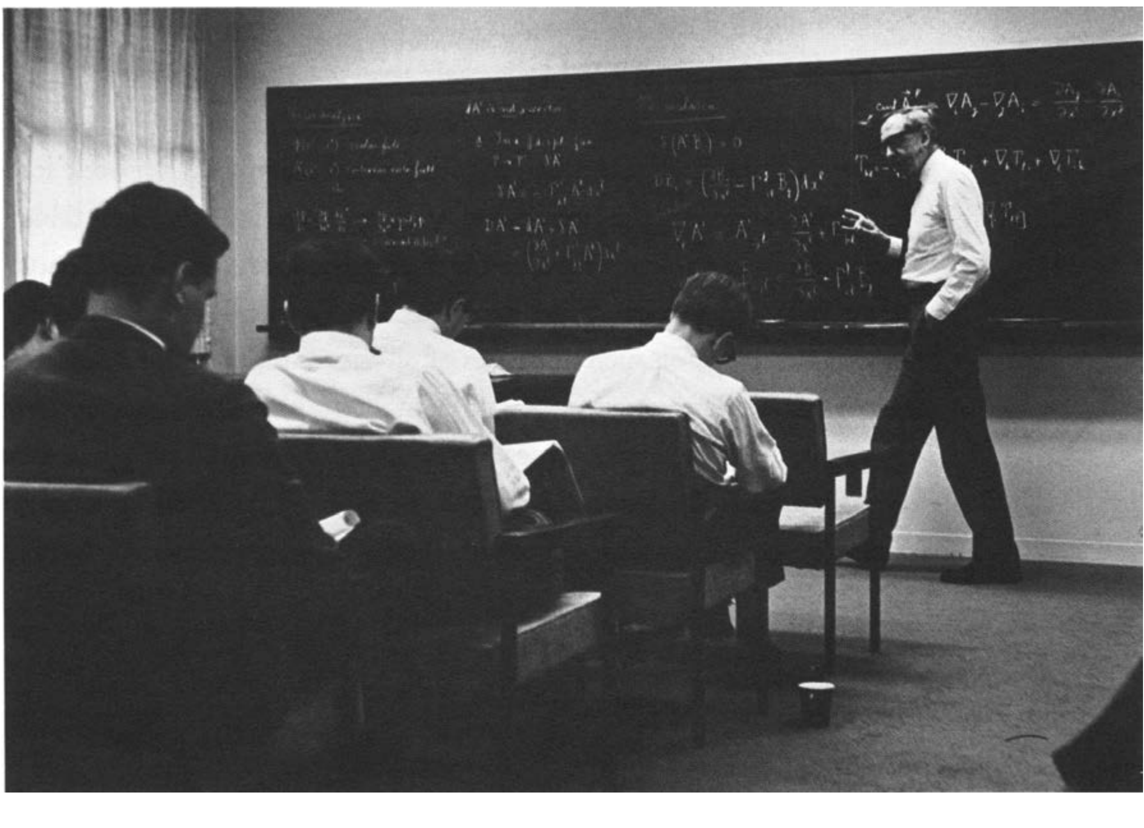
In 1953, the Trustees and the Scientific Directors of The Rockefeller Institute for Medical Research merged into a single board, with David Rockefeller as its Chairman and Bronk as President of the Institute. The following year the Institute amended its charter to become part of the University of the State of New York with the power to grant degrees. The first year it admitted ten students. The total admitted in any year has yet to exceed 30. In 1958 the name was shortened to The Rockefeller Institute and in 1964 the term "University" replaced "Institute."

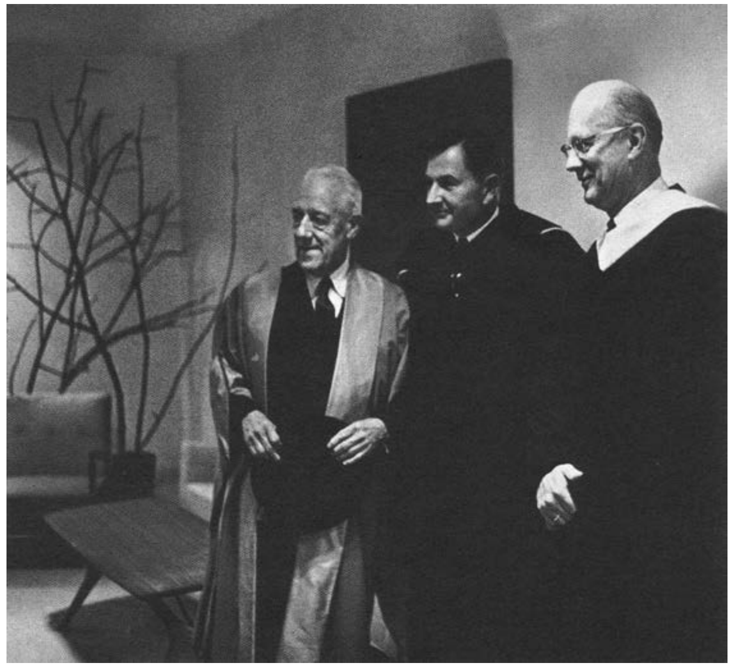
THE MOST STRIKING DIFFERENCE between the original Institute and the University lies in the number and diversity of subjects the latter offers. Although the life sciences remain the predominant area of study and research, involving more faculty and students than any other, three entirely new areas have been introduced and many subdivisions have been added to the old established areas. The *Catalogue* listed physics and mathematics for the first time ten years ago when Professor George E. Uhlenbeck, one of the world's leading theoretical physicists, came to The Rockefeller University from the University of Michigan and Professor Mark Kac, a mathematician preeminent in the field of probability theory, came from Cornell. Five years later, with the arrival of Professor Carl Pfaffmann, a physiological psychologist from Brown University, the life sciences were expanded to include the first laboratory of behavioral sciences. More recently, The Rockefeller University and the New York Zoological Society began to operate jointly an Institute for Research in Animal Behavior, headed by Donald R. Griffin and Peter R. Marler, thereby combining a vast and varied animal collection with the research experience of half a century.

How do all these additional disciplines fit into the general scheme of Rockefeller University? What is their relevance to a program oriented primarily toward biology? Fifty years ago biologists did not need to know much physical chemistry. Today they cannot do without it, for the tools to investigate inanimate matter have become adaptable to investigate living organisms. The more deeply modern biologists delve in their effort to understand the structure and function of cells, the more they must draw upon such resources of physics as the electron microscope, nuclear magnetic resonance, X-ray crystallography, and isotopes. Without physics, for example, James Watson and Francis Crick could never have discovered the structure of DNA. In biology, as in every branch of science from physics to psychology, the investigator sooner or later also

MID-CAMPUS, FLEXNER HALL AND FOUNDER'S HALL

PROFESSOR GEORGE E. UHLENBECK LECTURING IN SOUTH LABORATORY

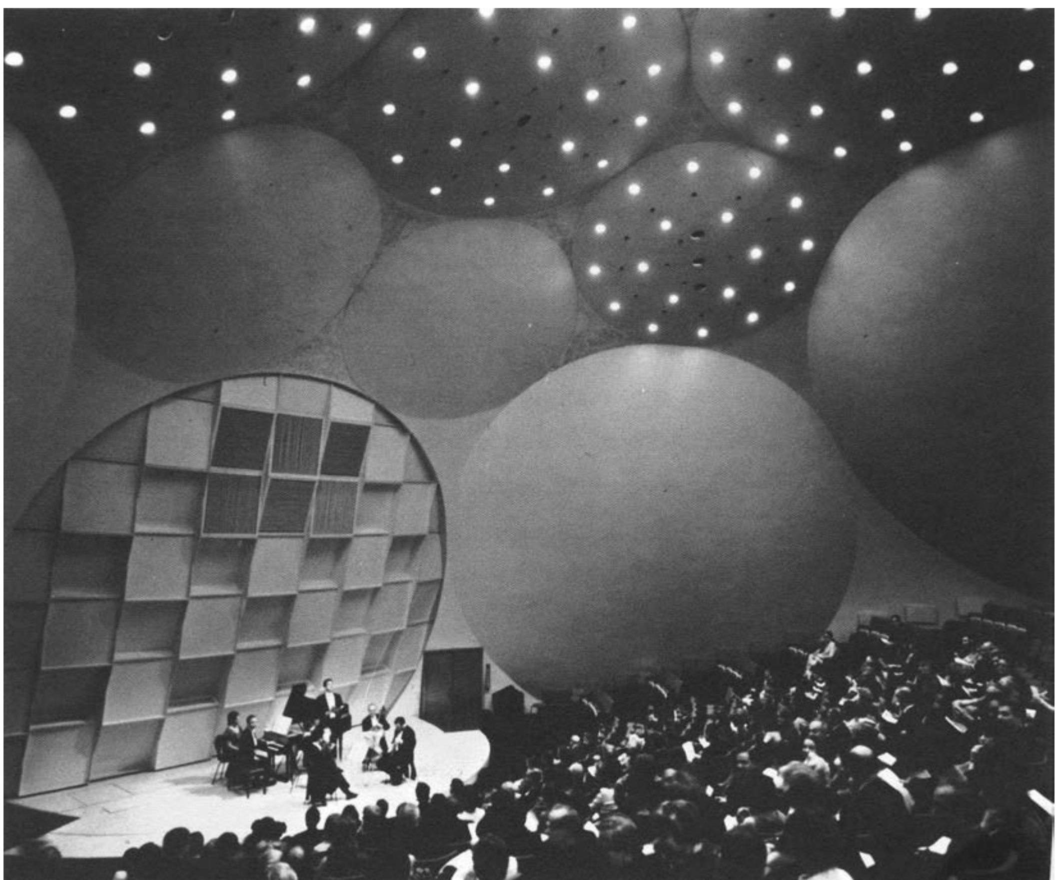




PRESIDENT SEITZ *right* WITH DR. BRONK, PRESIDENT EMERITUS, AND MR. DAVID ROCKEFELLER, CHAIRMAN OF THE BOARD OF TRUSTEES

DINING ROOM, WELCH HALL

CONCERT, CASPARY AUDITORIUM



turns to the computer and probability statistics, so a grasp of mathematical principles is requisite.

Speaking of both physics and mathematics at The Rockefeller University, Kac, who worked as a consultant with Uhlenbeck at the Cambridge Radiation Laboratory during World War II, explains: "The mathematics group here is primarily concerned with probability theory and especially its application to the physical sciences; also, to some extent, to the biological sciences. In taking up mathematics, physics, or any discipline not wholly biological, the University has a two-fold purpose. First of all, because it is a university, it must accommodate many disciplines, particularly mathematics, the oldest one. Mathematics in turn must fulfill two functions: it must be independent, developing on its own, and at the same time it must serve other disciplines.

"For example, the biologist uses chemistry. Chemistry is, in a sense, part of physics. Physics uses all sorts of mathematics. Consequently, anybody working in physical chemistry runs into mathematical problems of varying degrees of sophistication. He may come up with a specific problem which we may or may not be able to help him solve. But above and beyond the direct application of mathematics lies something far more important—the mathematical way of looking at things, a method of approaching a variety of problems. When we teach young people we do not try to drill a fixed inventory of facts into their brains because we do not know what they may have to use later on. We try rather to cue them into mathematics so that they will have a particular dimension available to them as needed. People tend to be pragmatic when struggling with a problem. 'Here it is. Solve it for me.' Sometimes we can. But the main task is to educate the scientist of the future.

"Precisely what should a biologist know about mathematics? I have not the vaguest notion. All I know is that he should know it. He should feel free with it. One should never look at mathematical applications as they exist today. One should simply say, 'The more you know, the broader your vision, the better off you are.' Although my own interests lie close to mathematical physics so that the young people who come to me naturally congregate around this aspect, we will eventually develop into other mathematical areas."

Kac deplores isolationism in scientific education. Young scientists, he fervently believes, need literacy in physics, chemistry, and several other disciplines, but the mathematician needs exposure "to other ways of being clever." Uhlenbeck concurs. A committee of which he is chairman, reporting on the state of the physical sciences at The Rockefeller University, makes this recommendation: ". . . a very high priority should be given to the task of trying to establish a strong and autonomous group of workers in the experimental physical sciences. Such a group would provide a link between the theoretical and mathematical sciences on the one hand and the biological sciences on the other, and thus would strongly improve the intellectual cohesion of the University."

"Interaction" and "interdisciplinary" are key words at The Rockefeller University. Kac cites research in neurophysiology as an instance of interacting disciplines: "Neurofiring – the action of a nerve – is largely a random process and analyzing it calls for probabilistic models. As soon as a nerve fires, it produces a transmissible signal. What finally travels along the nerve fiber is a superimposition of signals emitted at random intervals. Once the element of randomness enters a process, the investigator must refer to probability theory. You can predict the average rate of firing. You cannot do it exactly, you cannot predict the final voltage, but you can fix the probable limits within which the voltage will lie."

A remarkable development in the behavioral sciences, a major breakthrough in scientific method, had already been achieved by Professor William K. Estes and a group of his colleagues at Indiana and Stanford universities before he came to Rockefeller in 1968. It, too, involved mathematical models. The formidable behavioral problem Estes set himself was to obtain a precise, quantitative description of how the human mind learns and how it decides, amasses information, retains it, and retrieves it.

"We work along developing mathematical theory," says Estes, "then check theory against both human and animal performances in experimental tasks. We try to formulate mathematical laws for the limits of the amount of information that can be stored as a result of various types of learning experience, the rate at which it is lost, and the conditions under which it is interfered with."

Among the experimental devices used in the Estes laboratory is the "license-plate simulator," which projects a rapid sequence of numbers such as one would see if standing at a roadside, watching cars flash by. When we receive an item of information, our memory is apt to lose it shortly unless we take steps to retain it. From the recorded, computerized responses of laboratory subjects as they sit before the simulator, the Estes team has reduced some of the mental processes involved to mathematical equations. One equation describes the input, the way the license number is transmitted to a temporary memory-storage system, from which it will be lost if nothing further occurs. Another equation describes the way the information is lost as a function of time. From this a graph can be constructed showing the percentage of information remaining after five, ten, 15 seconds. Still another equation tells how memory is refreshed if the subject has the occasion to rehearse the information just received.

A practical application of this type of mathematical theory would require prediction. If a teacher, say, wished to arrange a training situation enabling his students to accomplish a certain amount of memorizing with the optimum use of a certain amount of time, the theory would be applied to decide how much time to devote to input, how much to rehearsal, and so on. In this fashion, one could predetermine the results.

More sophisticated application might permit engineers to compute the contributions of human operators to complex man-machine systems, as, for example, communications networks.

What Estes considers more important, however, is a problem in basic science. "Before anyone who may discover the biological mechanisms of memory can tell whether he has it right, we must have a mathematical theory. The only way one could verify the theory of genes was to demonstrate that it could account for the observed laws of heredity, notably the Mendelian ratios. To confirm any theory of the biological basis of memory, one must show that the mechanism in question accounts for the observed facts, which means the observed facts must be expressed quantitatively. Otherwise how can one know precisely what requires explanation?

"Just to speculate, suppose someone discovers that memories are stored by a process of forming a type of large molecule. The discoverer must identify the molecules, calculate their number, show what kind of mechanism stores a certain amount of information in the memory and why, in physiological terms, the memory is impermanent. To speculate further, suppose one finds that a DNA molecule is modified by some sort of template to establish a memory or experience the organism has just had. Why is the memory not permanent? Perhaps, as physiological theory might explain it, metabolic processes cause the molecules to disintegrate at a certain rate if they are not renewed. They lose their original properties according to a function of time.

"One would presumably compare the hypothesis concerning the time course of the memory loss that should follow from the molecular interpretation with the time course specified by a mathematical theory of memory developed from experiments.

"The reason one needs a mathematical theory, not just experiments by themselves, is that memory is an abstraction. If one presents an individual with material, then tests him, his performance will be a function of his memory capacity. Many factors will affect that performance—motivation, outside distractions, perceptual errors. The memory must be abstracted. Secondly, let us suppose that one has presented the individual with a string of numbers. What is actually stored in his brain is not numbers, but information. So we must measure the amount of information stored and the amount lost, and these form part of our mathematical theory. The theoretical function, expressing the amount of information retained after various lengths of time, is what the molecular mechanism must explain.

"Our equations establish the facts in suitably significant terms. They enable us to go from the experimental situation, where the individual's performance is a function of many factors, and abstract from it what we infer to be the changes in a particular process—in this case, memory. [Another laboratory might be abstracting the visual process from the same performance.]

"Closely related lines of research in the mathematical psychology laboratory are concerned with the ways in which memory and motivational factors combine to influence human choices and decisions in situations involving uncertainty, e.g., gambling, or processes of bargaining and negotiation which arise in economics and government."

At first, philosophy may seem somewhat peripheral to the University's dominant scientific pursuits. A moment's reflection, however, will show that philosophy and science continually intersect. Throughout man's history the high peaks of philosophy have coincided with the high peaks of scientific discovery. Galileo, Descartes, Darwin, Einstein, each compelled a whole new way of looking at life, of rethinking about accepted values.

When, not long after taking office, President Bronk invited the renowned philosopher Ludwig Edelstein to come to Rockefeller from The Johns Hopkins University, it was with the object of adding not "Philosophy of Science" to the catalogue, but philosophy as such, an autonomous laboratory, yet one that would naturally interact with the autonomous science laboratories. Edelstein was an ideal choice, having taught the history of science as well as philosophy. He and Associate Professor Harry G. Frankfurt, who had also come from The Johns Hopkins, gave courses and seminars from time to time on the history of philosophy, on the theory of knowledge, on ethics, and on the philosophy of Plato and of Kant. Edelstein died in 1966 without having established any formal program. That task fell to Frankfurt. He helped to assemble a faculty of eight philosophers. The first students joined them in 1967.

Frankfurt himself started with a seminar and three students, exploring the status of the problem of free will today. Professor Joel Feinberg, one of the leading moral philosophers in the United States, began a project, before coming to Rockefeller, that he expects will occupy him for his lifetime – a four-volume work entitled *A General Theory of Responsibility*. Other members of the group are engaged in analyzing the fundamental concepts of logic, mathematics, psychology, law, and physics, and in historical studies.

With an assistant professor from the life sciences, Francisco Ayala, a former Dominican friar whose field is population genetics, Frankfurt provided a framework for interdisciplinary reaction, which is available to all faculty members and students. They organized a series of meetings devoted to the general topic "The Biological Future of Man." Each meeting began with a short address by a Rockefeller University scientist regarding the current and probable future state of his discipline. A discussion of the ethical implications followed. The chief concern of the meetings was genetic engineering, a theoretical possibility today, a practical one tomorrow. "It is obvious," says Ayala, "that tampering with the genetic constitution of man cannot be attempted on scientific principles alone."

About 50 people, almost equally divided between faculty and students, attended the meetings. Professor Theodosius Dobzhansky, the world-famous geneticist in whose laboratory Ayala works, introduced the first discussion with a talk on "Natural selection in present-day mankind." Edward L. Tatum, biochemist, geneticist and Nobel Laureate, followed with "The control of gene expression." Next came Rollin D. Hotchkiss, cellular physiologist, on "Directed genetic change," and finally René J. Dubos, whose focus of interest has shifted from microbiology to environmental biology, on "Shaping the biological and mental characteristics of man by environmental manipulation."

Frankfurt and the other members of the group foresee an increasingly important role for philosophy in the future of The Rockefeller University. "Up to about 15 years ago," Frankfurt observes, "philosophical thinking was dominated by the work of a few great figures – Dewey, Whitehead, Russell, and Wittgenstein. Such is no longer the case; fresh philosophical tendencies are beginning to emerge. Although the members of our group have generally been strongly influenced by the so-called 'analytical' tradition in philosophy, we share what is coming to be a widespread sense that the scope, methods, and aims of philosophy need to be redesigned. We expect that those of us at the University will be able to play significant roles in current attempts to revitalize philosophy, and that the work we are doing on a variety of fundamental philosophical problems will, among other things, contribute to a strengthening of the traditionally fruitful relationship between philosophy and the sciences."

There's no use doing anything for anybody until they're healthy.

JOHN D. ROCKEFELLER

ROCKEFELLER CLINICAL RESEARCH CENTER

EVERY YEAR A FOLDER ENTITLED *Conditions Under Study* goes to the physicians in the metropolitan area, explaining: "The Rockefeller University Clinical Research Center provides unusual facilities for the study, care, and treatment of selected patients. Patients who have conditions listed in the inside of this folder may be referred to the Clinical Research Center for possible admission. Care is provided throughout the study without charge to the patient. . . ." The conditions currently listed fall into six main categories – disorders of protein metabolism, lipid metabolism, the glands, the liver and the red corpuscles, rheumatic fever, and obesity – and include some 30 different diseases.

Arteriosclerosis, one of the major medical problems of the age, is the chief target of Edward H. Ahrens, Jr., and his colleagues, who have concentrated on disorders of lipid, or fat, metabolism for 23 years. Usually about a fourth of the 40 beds in the Clinical Research Center are occupied by arteriosclerotic patients; the constant threat of sudden death has motivated them to stay the length of time the study demands – four to eight months. "We tell them we can guarantee no success at all," says Ahrens. "Nevertheless, we have had an extraordinarily good record of helping them. They come here with severe chest pains, which doctors call angina, that has prevented them from leading productive lives. Yet the majority leave feeling enormously better. I do not attribute this to any therapy, to the drugs and diet we prescribe; they could not take effect so quickly. I believe they benefit from the education we give them in the meaning of their disease. We reassure them, not as to the seriousness of it—we never minimize that—but rather as to its real nature. We teach them what their symptoms really amount to, not to be terrified every time they feel a twinge in the chest, not to imagine the end has come. Of course, the mere fact of having an exceptionally good doctor, the same doctor, talk to you about your illness every day for months is, in itself, a great psychological support. When our patients go home, we tell them honestly that we cannot measure the degree of improvement because we cannot measure with any accuracy the little plugs in their blood vessels. But I am convinced that most are healthier when they leave us."

Of the 20 original studies undertaken in the Ahrens laboratory, the most familiar to newspaper readers is the relationship between arteriosclerosis and the finding that diets rich in unsaturated fats lower the concentrations of blood cholesterol. These findings have prompted many doctors to leap to what Ahrens considers an unwarranted conclusion, namely, that causing the cholesterol level to fall will reduce a person's risk of having a heart attack. "It seems to me premature," Ahrens protests, "to recommend in 1969 any sweeping change in dietary habits to the general population. When we know more, we can give advice that the public can more readily accept." The pursuit of this broader knowledge continues to engage faculty and students in the Ahrens laboratory.

Half-a-dozen patients, each weighing more than 300 pounds, are the subjects of Jules Hirsch's study of obesity. Starting 15 years ago with the Ahrens group in its investigation of lipids, Hirsch became interested in man's principal depot of fat – the adipose tissue that lies beneath the skin throughout the entire body. The laboratory had devised a technique for removing slivers of fat by needle aspiration and, to obtain a sufficient supply, it sought obese donors because their fat was so much easier to reach. As an inducement for cooperation, Hirsch offered to reduce their weight, a simple process involving nothing more than a calorie-restricted diet under hospital conditions. What began to fascinate him about his obese patients was that nearly all regained weight after leaving the Hospital until they reached the same point at which they had started. They knew that gross overweight made them unattractive and that it threatened their health. They wanted desperately to reduce, but it seemed as if some regulatory mechanism in their system failed to function. "I realized," Hirsch recalls, "that we had to learn a lot more, not only about the chemical and metabolic changes taking place when these people reduced but about their general behavioral patterns." Accordingly, he recruited as collaborators researchers from various relevant disciplines – biochemistry, biomathematics, nutrition, and psychiatry.

Another phenomenon Hirsch had noted was the profound depression accompanying his patients' weight loss. Instead of the expected elation at shedding a hundred pounds or so, they grew apathetic, complained of cold, and exhibited many of the symptoms of concentration-camp victims. Maintained at their new, lower weight, they felt starved and deprived. Could it be, Hirsch wondered, that the fatty cells in their adipose tissue differed from those of a normal person? When their weight increases, is it because each fatty cell enlarges or because they have more fatty cells?

Hirsch and his colleagues discovered that, whereas the adipose cells in a nonobese person total about 25 billion, in the obese they average 75 billion—a threefold increase. The number is established early in life, and, once established, nothing can alter it. When the obese lose weight, the number of cells remains constant, but the cells become extremely small and shrunken. Examined under a microscope, they resemble those of a person severely starved.

Two burning questions now exercise Hirsch. First, is there any relationship between the larger number of cells and their shrinkage with weight loss and eating behavior? Logically, one might expect that the formerly obese person received from the shrunken cells the command to eat more and refill them. But if he does, through what mechanism is the command transmitted? "If," Hirsch speculates, "we could establish a link connecting those adipose tissue cells with the feeding mechanism in the central nervous system, we might for the first time find a rational method of treating obesity. As it is, we treat it the way we treat alcoholism. We tell the alcoholic that he should not drink and that he is alcoholic because he drinks. He already possesses this superfluous information, just as the obese person knows he eats too much."

Hirsch's second burning question is, How did the number of cells increase in the first place? Are some people born with a larger number or do they increase as they grow older? Does overfeeding in infancy set the framework for adult obesity?

"Such is the main thrust of our present work," says Hirsch. "I think we may differ a bit from other laboratories in the field in that we are more mission-oriented (to use a hackneyed word). We are more concerned with why people get fat and what to do about it, with the relationship of obesity to diabetes, arteriosclerosis, and other disorders, than in elucidating some new nook or cranny of biological lore. On the other hand we realize that we are never going to get useful approaches to obesity without delving deeply into the basic sciences—behavioral psychology and biological subdisciplines such as cytology. . . . What we hope to do here is to gather the relevant information into a meaningful story on the basis of which doctors can really help the obese."

The most controversial experiments in the history of the University have perhaps been those conducted by Vincent P. Dole and his wife, Marie E. Nyswander, with methadone hydrochloride as a maintenance treatment for heroin addicts. In 1963, when Dole, who had been associated with the Rockefeller Hospital (now known as the Clinical Research Center) since 1941, proposed the experiments to Bronk, doctors who dealt with drug addicts at all were subject to harassment by state and federal authorities. In the official view then (and, to a degree, still), addiction was a crime rather than an illness, calling for punishment instead of therapy. As a result, most doctors avoided the problem. But Bronk assured Dole, "If it is too hot for other institutions, then it is our job to take it up."

With tens of thousands of heroin addicts crowding the nation's jails, Dole set out to find a drug that might satisfy their craving without destroying their usefulness to society. He was not thinking in terms of a cure for addiction itself (a goal beyond the present reach of medical knowledge) but of replacing injurious, degrading heroin with a relatively innocuous substitute. Methadone was the fourth drug he tested. Working with the first small groups in the Rockefeller Hospital's metabolic ward, then with larger groups at the Beth Israel Medical Center, he concluded that methadone met the desired conditions. It was nontoxic, acceptable to the patient, could be taken by mouth, and would hold the addict in a stable state all day.

Under the program expanded by Dole and his wife, seven different hospitals and roughly 1400 patients are now involved. The results have so impressed the State Parole Department that it offered to release any imprisoned addict (provided he had committed no serious crime) who volunteered for methadone treatment. The Doles, having kept track of every patient, even those who came for only a single day, could report as of April 1969 that, after five years, 85 per cent had remained in treatment. The rest either left voluntarily, were discharged, or died. Of the 85 per cent three-quarters were at school or employed, the latter supporting families, and without addictive or antisocial behavior.

"To be sure," Dole concedes, "they may need methadone the rest of their lives. Withdrawal from it without reversion to other drugs is a future hope."

The Doles reject the prevalent dogma about narcotics, according to which the addict suffers from a personality defect that compels him to seek euphoria. Methadone confers no euphoria. It only controls the addict's craving. Addiction, the Doles suspect, is a metabolic problem. "Most of the traditional assumptions are probably wrong," Dole argues. "If a man craves water, it merely restates his problem to say that he is thirsty. What makes him thirsty? Certain cells act as monitors when activated. They warn that the blood is too concentrated and needs water. Quite possibly addiction expresses some such chemical drive. Exposure to narcotics may imprint certain cells in a way that permanently alters them. Methadone, then, would restore them to normal function.

" 'We're free. We don't talk about dope all the time. We don't dream about it any more'—are typical comments of methadone patients. One of them told me, 'I bought myself a pair of shoes today.' He meant that he had gone clear across town with money in his pockets, passed drug pushers and did not buy any drugs. Now, that was an enormous thing."

THE GENETICISTS

On the seventh floor of South Laboratory Professor Dobzhansky, seven faculty co-workers, two students, and thousands of bottled fruit flies

(*Drosophila*) are joined in a perennial effort to elucidate the laws of population genetics. Man, not *Drosophila*, is the focus of their attention, but genetic laws exhibit a great degree of generality, and *Drosophila*, which breeds a new generation every two weeks, furnishes cheap, convenient experimental material.

It has been known for about 15 years that the *Drosophila* female prefers the rare male–rare by virtue of a point mutation or perhaps by geographic origin. "Just as in the human species," Dobzhansky observes with a twinkle, "women prefer something new." The sensory basis for this preference is probably olfactory. To the female, the rare male may smell different from the mass of his brothers. One of the three women investigators in the Dobzhansky laboratory, Lee Ehrman, studies the genetic and evolutionary consequences of such preference, which are obviously far-reaching, because heredity confers a sexual advantage and natural selection will favor the rare type as long as it remains rare. In a recent experiment, Ehrman grouped each generation of fruit flies according to the proportions in which they mated during preceding generations. She noted that the frequency of one type grew gradually higher than the other. Starting from the opposite extremes–A-rare mating with B-common and A-common with B-rare–the frequencies gradually converged and became identical. A point was reached when two kinds of males had, on the average, an identical chance of mating success. Dobzhansky enters a word of caution: "Let us not claim that Dr. Madame Ehrman has discovered the laws of love."

Pursuing two other lines of inquiry into genetic behavior, Research Associates Boris A. Spassky and Georges Pasteur have been recording the reactions of *Drosophila* to light and gravity. They use ingenious devices, the phototaxic maze and the geotaxic maze, to measure those reactions. Natural fruit-fly populations are, on the average, neutral to light and gravity. But by breeding, in a series of generations, the flies that choose upward or downward passages in the geotaxic maze, or those choosing light or dark passages in the phototaxic maze, the researchers found it possible to get geopositive and photopositive and negative populations. After 10 to 20 generations, the divergence becomes so great that no doubt whatever remains that genetically different strains exist and behave differently. These observations form the basis for the laboratory's current attempts to build models of the possible genetic processes that may be taking place within various social systems in human populations.

At the opposite end of the campus, in Theobald Smith Hall, another genetics laboratory, headed by Professor Rollin D. Hotchkiss, is extending the possibilities of genetic engineering. Here in 1948 Hotchkiss first found that he could change the hereditary characteristics of bacteria by exposing them to altered DNA. His success was a milestone in man's attempt to control his own destiny, the foreshadowing of a greater power for both good and evil than any scientific advance ever achieved.

THE BEHAVIORAL SCIENTISTS

In 1969 there were 48 of them, 12 students, and seven laboratories. "Mathematical psychology" is the rubric under which the Estes laboratory conducts its studies of human memory and learning.

In a laboratory labeled "Human Behavior and Metabolism" Joel Grinker, a social psychologist, works as a Research Associate with Jules Hirsch on the behavioral aspects of obesity.

A five-man team under under Professor George A. Miller (experimental psychology) is concentrating on the psychological aspects of language and communication. "Mainly," Miller reports, "we are testing the theories growing out of linguistics. There must be something common to all men everywhere, something related to what anthropologists once called the 'psychic unity of mankind,' which underlies the fact that all men have language. Languages are very much alike, each with a phonology, a grammar, a syntax. These similarities suggest to us that genetic factors must be at work. One way to study the phenomenon is to compare all languages and to analyze the features that they share in common. For that, of course, we need to collaborate closely with linguists.

"Linguists draw a distinction between the surface structure and the deep structure of language. Grammar, they say, generates an abstract structure that can be interpreted semantically at the deep level, although realized phonologically at the surface level. At the surface level there can be a great deal of diversity, even when there is uniformity at the deep level. For instance, in English we have at the surface level sentences such as 'John ate the apple' and 'The apple was eaten by John.' The order of the words is quite different, yet each arises from the same basic meaning. Under no condition can one be true and the other false. Various theories have been propounded to explain such language transformations. Donald T. Langendoen, a linguist who has been visiting The Rockefeller University, is educating us in these theories and helping us to understand their psychological implications and how to test them."

Another approach to psycholinguistics, which Associate Professor Thomas Bever is pursuing, involves the study of children as they go from the pre-language to the language phase of their development. Working with children two to three years old, Bever administers various analytic tests in an effort to illuminate the baffling but crucial questions: How does language expression arise? Why do some children handle language better than others? What factors in language learning affect the way they use concepts and language itself?

"Physiological psychology" occupies two large groups, one under Professor Neal E. Miller, the other under Professor Carl Pfaffmann. The University *Catalogue* defines the Miller laboratory's area of study as "Behavioral, physiological, and biochemical analysis of motivation and learning, with current research on hunger, thirst, and fear, behavioral effects of chemical stimulation of the brain, the physical basis for memory, the instrumental learning of glandular and visceral responses, and biochemical and behavioral effects of hormones and monoamines." The Pfaffmann laboratory covers "Electrophysiological and behavioral analysis of the sensory and neural mechanisms of taste and olfaction with particular emphasis on their roles in motivated behavior." A constant interchange of data and observations takes place between the two groups, and both have recourse to the Animal Behavior laboratory ("Physiological basis of orientation behavior, with emphasis on acoustic and visual orientation of flying animals. Developmental basis of physiology of animal communication. Evolution of social behavior in birds and primates").

Typical of the ongoing basic research in the Animal Behavior laboratory are Graduate Fellow Robert Johnston's experiments with Syrian hamsters. A relatively new term of behavioral scientists is "pheromone." It refers to a class of hormonal substances secreted by some animal, and it stimulates a physiological or behavioral response from a member of the same species. What the researchers call "marking" illustrates a probable function of a pheromone. Some mammals apparently use an olfactory signal to mark their own territory. The way a dog urinates against a tree or wall may be a residue of the sort of marking wolves, coyotes, and foxes do in certain terrain—a group or pack signal.

How do animals of different species use pheromones and to what extent? In the control of sexual reactions? In social behavior? Does a particular signal identify a member of the pack as dominant, the leader? Johnston chose the Syrian hamster because it has readily identifiable glands conveniently situated for physiological experiments. They are flank glands on either side of the body. The hamsters, moreover, exhibit a curious form of "marking" behavior. They rub their flanks against the bars of the cages, leaving an odor. What message are they trying to deliver? What prompts them to do a lot of marking or only a little?

To examine the olfactory organs themselves, to see whether this particular scent has a special impetus or a special significance for the olfactory system, Johnston has at his disposal the equipment to implant electrodes in the organs. With this and other devices he is obtaining more and more clues to the puzzle of pheromones.

Another series of animal experiments conducted by Professor Neal E. Miller and his colleagues illuminates a major physiological mystery. Hitherto the autonomic, or involuntary, nervous system, which regulates visceral responses such as heart rate, salivation, and kidney function, has been held inferior to the cerebrospinal, or voluntary, nervous system, which governs muscular activity such as walking, running, and jumping. The organism can learn to control the involuntary responses, so it was believed, only in the primitive fashion known as classical conditioning, whereas it can be taught to control the voluntary responses by the more sophisticated instrumental, or operant, conditioning that calls for reward. The great Russian physiologist Pavlov used classical conditioning as a training technique. He sounded a bell each time before feeding meat to a hungry dog. The salivation produced by the meat was thus conditioned by the bell. After a period of time the bell alone stimulated salivation. To apply the Pavlovian method, the trainer must use a reinforcement that already stimulates the response to be learned. With the alternative method, any reward may be used to produce the learning of any response that immediately precedes that reward. For example, in the Miller laboratory an automatic apparatus recorded the tiny drops of saliva secreted by a thirsty dog. Whenever the period between two drops was slightly shorter, the apparatus immediately rewarded the dog with water. By giving rewards for ever larger quantities of saliva, the experimenters taught a group of dogs to salivate copiously. By reversing the process and rewarding only smaller quantities, they taught another group to stop salivating altogether. The water itself had no effect on salivation.

The implications for human therapy are important. Assistant Professor Jay Weiss is currently exploring one of them. In a cooperative study with the University's next-door neighbor, The New York Hospital—Cornell Medical Center, he is attempting to teach cardiac patients with excessively rapid heart beats to slow them down. The knowledge of success provides the reward. A feedback device that times the intervals between heart beats emits a "beep" whenever they attain a desirable length. This informs the patient that he has done the right thing and motivates him to repeat it. But how, mechanically, does he manage to do so? "The very interesting thing," says Weiss, "is that we do not know. It may be some form of self-hypnosis." In the planning stage are experiments designed to teach patients with high blood pressure to lower it, patients with constipation produced by spastic contractions to resume normal intestinal activity, and epileptics to control their brain-wave irregularities that bring on attacks.

Miller believes that the findings of his laboratory may strongly affect the treatment of psychosomatic disorders. "Evidence of the instrumental learning of visceral responses," he has written, "removes the main basis for assuming that psychosomatic symptoms that involve the autonomic nervous system are fundamentally different from those functional symptoms, such as hysterical ones, that involve the cerebrospinal nervous system. Such evidence allows us to extend to psychosomatic symptoms the type of learning-theory analysis that [we] have applied to other symptoms.

"If the patient who is highly motivated to get rid of a symptom understands that a signal, such as a tone, indicates a change in the therapeutic direction, that tone could serve as a powerful reward. Instruction to produce the tone as often as possible and praise for success should increase the reward. As patients find that they can secure some control of the symptom, their motivation should be strengthened.

"Such a procedure should be well worth trying on any symptom, functional or organic, that is under neural control, can be continuously monitored by modern instrumentation, and for which a given direction of change is clearly indicated medically—for example, cardiac arrhythmias, spastic colitis, and asthma. . . ."

. . . it is our desire to select students who have the will and the qualities of mind that should enable them to become scholarly scientists of distinction. Only to such is it feasible for us to offer intimate association with our distinguished faculty and the exceptional physical resources we make available to our students . . .

DETLEV W. BRONK,
in a letter to John G. Hildebrand, III
accepting him as a Graduate Fellow

JOHN G. HILDEBRAND'S EARLIEST EXPOSURE to life science was at the age of 13. Having volunteered to work after school hours for the Boston Museum of Science, he was entrusted with responsibilities in its live animal center. Working with other youngsters, he kept the cages clean, fed the occupants, and generally saw to their well-being. He also took the museum courses in natural history, insect life, and limnology (the study of fresh-water life). "For four years," he recalls, "my budding interest in life science was nurtured entirely through the museum."

He was born in Belmont, a suburb of Boston, on March 26, 1942, the second of four children, to John G. Hildebrand, Jr., an organic chemist who ran his own prosperous technical consulting firm, and Helen Swedberg, a former high school teacher of English. The public school system of Belmont provided his entire pre-college education from kindergarten through high school.

At about the same time that science first attracted him he began to develop a parallel line of interest in music, which he still pursues passionately. By his freshman year in high school he had become a versatile instrumentalist, having taken lessons on the piano, violin, trombone, tuba, and string bass. In his junior year he was once invited, with several other musically gifted students, to play with the Boston Symphony Orchestra. He then favored the tuba. He has since found time, despite the rigorous demands of scientific research, to play a variety of instruments with such semiprofessional but polished groups as New York's Cosmopolitan Symphony Orchestra, made up chiefly of Juilliard School students and alumni. In addition to performing himself, he collects records and studies music history.

At his graduation in 1960, Hildebrand delivered the class valedictory. Previous academic distinctions included the presidency of the National Honor Society Chapter, the Belmont School Committee Award of Merit, and membership in the Belmont High School Senior Honor Group. The following fall he entered Harvard. At the end of his freshman year he received an honorary scholarship.

When he matriculated, Hildebrand had no idea whether he would major in music or in science. What decided him was a revolutionary new biology course and the influence of the brilliant teacher-scientist who offered it at Harvard for the first time—George Wald (later a Nobel Laureate). Unlike the majority of his research peers, Wald did not teach with reluctance. The challenge excited him. Biology courses then consisted mostly in surveys of the plant and animal kingdoms, the dissection of frogs and worms, and so on. Wald ignored the approved approach. He had designed his course for any students, whatever their central interest (medicine, history, the humanities) who wished to know something about modern life science. "Life—Its Mechanism," Wald called the course. He introduced it at a level for which everybody should have been prepared by the conventional pre-college curriculum; he then developed in integrated fashion the chemistry, physics, and other disciplines necessary for an understanding of modern biology and its physical bases.

Hildebrand, who elected to take the course largely on the strength of Wald's reputation as a stimulating teacher, knew after two weeks that he would not major in music. "The course turned out to be decisive for me from the beginning," he recounts. "If Wald did not determine the details of everything I have done since, he provided the vector under which I have operated."

He took only one music course. He majored in biology, although not of the traditional sort. His curriculum was principally biochemical, with a good deal more chemistry than biology. It embraced organic chemistry, other physical sciences related to mathematics, and the "new biology," that is, modern genetics and cell physiology. During his first year he attained the dean's list and remained there throughout his college career.

Hildebrand, when a freshman at Harvard, had no knowledge whatever of the functioning of The Rockefeller Institute as a university. Awareness came chiefly through a young assistant professor working with Wald, Johns Hopkins (a great-grandson of the university founder). Hopkins was a Rockefeller graduate, class of 1960, and his enthusiasm for the place infected Hildebrand. Toward the end of his freshman year he wrote for further information and received the *Catalogue* of the Institute.

He finished the year convinced that his approach to life science should be biochemical and his fundamental tool chemistry. Shortly after he declared himself a biology "concentrator," the department at Harvard adopted a new program, a variant of the British tutorial system. As an honors student, he qualified for it, so he applied to the undergraduate education committee in biology, requesting a tutor. He specified George Wald, who, to his surprise and delight, consented to take him on. "I was his only tutee, which was very pleasant because during the next three years we had periodic meetings in which we discussed everything from Rembrandt's etchings to the quality of Isaac Newton's research. Through these meetings, which lasted right up to the end of my college career, I learned more about what I wanted to do."

Two other faculty members exerted an important influence on Hildebrand's attitude toward life science, his ultimate choice of a postgraduate career, and the way he himself might one day teach. They were Konrad Bloch, another Nobel Laureate to be, whose introductory lecture course in biochemistry Hildebrand took, and Bloch's young associate, John Law, who taught Hildebrand laboratory biochemistry. As Hildebrand entered his senior year, Bloch, Law, Hopkins, and half a dozen other faculty members whom Hildebrand respected began to explore postgraduate prospects with him. His academic record presented no problem. He was Phi Beta Kappa and would graduate *magna cum laude*. Teachers he trusted, such as Johns Hopkins, III, who had attended The Rockefeller Institute (at the time a university in fact but not in name), described its program with unstinting admiration. "They told me that for somebody who knows what he wants to do, who is committed to it heart and soul, Rockefeller provided the ideal climate." The older, more conservative professors, however, without direct, personal experience of the University, had certain reservations, not about the competence of its faculty nor the value of its research, but about the soundness of its basic concepts. No regular examinations or grading? Could a student function at his full capacity in such a permissive environment? Did he not require a disciplinary kick now and then? They endorsed the traditional system as it had prevailed at Harvard for generations, a system designed to test the student's performance anew at frequent intervals. In their view the lean and hungry look became the burgeoning scholar. "I was not convinced," says Hildebrand. "For one thing, the old ways seemed so much less congenial than the Rockefeller system. Moreover, I had before me people like Johns Hopkins, III, as living, breathing evidence of how brilliantly that system could work."

But even his pro-Rockefeller advisers, who agreed that he scarcely needed the classic kind of university carrot-stick treatment, sounded a note of caution. The time it took to get a Ph.D. at Rockefeller, usually five years as compared with three or four elsewhere, troubled them. And how did the Rockefeller innovations strike the influential figures in his chosen field, those scientific mandarins whose approval would be so important to his postdoctoral career? Would they accept a Ph.D. from Rockefeller as readily as they did one from Harvard, Columbia, or Berkeley? Tradition bounds academe, and the newcomer who departs from it too radically may find the job he desires closed to him. Thus far, by 1964, The Rockefeller Institute had graduated only four classes. Its program was still experimental, still unproved, and to subscribe to it involved a considerable gamble, but at length Hildebrand decided to take that gamble.

"I was drawn by the promise of crossing disciplinary lines. This is hard for a student or junior faculty member to do at most universities. The biologist tends to shut his door to the chemist and vice versa. Each wants to preserve his own little domain intact. Yet it seemed to me that in modern life science the doors must be broken down. We no longer have neat little Leibniz monads. We can no longer work in isolation from everybody else."

Another aspect of the Rockefeller program that irresistibly appealed to him was expressed in the *Guide for Graduate Students* which he received with the *Catalogue:*

> Students must be capable of self-directed study. Although many courses are offered, teaching is done primarily in seminars, in tutorial conferences, and in faculty research laboratories. There is thus considerable freedom for the active process of independent learning.

and in the *Catalogue:*

In this beginning phase of his graduate study, the student deals with the significance and relations of ideas. At the outset of his career he is thus encouraged to develop a broad foundation of competence in many fields of science and to recognize the relations in his special field of interest to other areas of science. He is persuaded to broaden his concepts and become an independent thinker rather than a mere helper in a restricted part of another's highly organized program of research. The student meets and gains inspiration from scores of the faculty who are great scholars and investigators before choosing a few with whom he is most intimately associated.

Having reached his decision by the first semester of his senior year, in October 1963, Hildebrand asked Konrad Bloch to sponsor him, according to the prescribed procedure for a Rockefeller fellowship, and George Wald and John Law to add supporting letters. Allowing time for the reception of these endorsements, Hildebrand then submitted his own petition to President Bronk. "I have been a fortunate undergraduate," he wrote, "in that I have had several years' experience in independent research. This began in my father's laboratory, where I have worked intermittently over the past eight years on several projects in organic chemistry, chiefly dealing with natural products and synthetic polymers. As a sophomore, I undertook research on a problem in the chemistry of (2.2) metacylophane under Dr. Rodger Griffin, then a member of the Harvard Chemistry Department. Finally, for the past year I have done research on bacterial phospholipid biosynthesis under the advice and support of Dr. John Law. We are presently preparing for publication of two papers dealing with these studies. . . .

"I should mention also my strong desire to become a university teacher. An important part of my education has been my close personal relationship with several outstanding faculty members, all of whom are fine researchers and excellent teachers. This has had the effect of strengthening my aspiration to enter a career in both teaching and research. This year I have been given an opportunity to explore my talent for and interest in teaching in the form of a Teaching Fellowship in Biology. . . .

"I find your unique approach to graduate education to be what I would call ideal. I have learned here at Harvard that I function best in a somewhat informal, personal environment, where teaching and learning are constant processes effected at the personal or 'discussion-seminar' level. From all that I know about The Rockefeller Institute, I am certain that I would thrive and be most happy there. . . ."

The response was an invitation to come to the Institute for interviews, and shortly before Christmas Hildebrand boarded a Boston to New York shuttle plane. The Dean of Graduate Studies, Frank Brink, Jr., interviewed him first. At that juncture candidates for admission were not obliged to submit in advance a transcript of their undergraduate record, so that beyond his sponsors' statements Brink knew little about the applicant's Harvard performance. He questioned him closely to determine his competence in the disciplines pertinent to his prospective Rockefeller work, such as mathematics. The faculty hesitated to admit students who still required several courses at the undergraduate level. Satisfied that such was not Hildebrand's case, Brink briefly described the essential nature of the Rockefeller program. "A very candid interview," Hildebrand remembers. "Dr. Brink laid all the cards on the table."

He was then directed to Caspary Hall, a long, low, glass-walled building shaded by a stand of giant sycamores. In a spacious office on the ground floor, its walnut-paneled inner walls bare except for a ship's clock and a life-sized portrait of John D. Rockefeller, Jr., he found a somewhat harassed President Bronk. The New York City engineers had, apparently, proposed to drill a subway tunnel underneath the campus, which would considerable disrupt the academic activities. Bronk was busy formulating a protest, and he let his young visitor in on his arguments against the project. The interview proceeded in a friendly, chatty vein. Bronk appeared far less eager to learn what grades a candidate achieved as an undergraduate than to assess his potential as a creative thinker.* A student, he felt, could produce mediocre work under the conventional curriculum, yet still have a good mind capable of scholarship and originality, given the right stimulus.

The interview lasted two hours. Afterward Bronk led the aspirant across the mall through Founders' Hall, the oldest Institute building, which was built in 1906, to the dining room in Welch Hall. Faculty members and students were lunching together at refectory tables without observing any seating protocol. The traditional lines of academic distinction are blurred at The Rockefeller University. "We are a community of scholars," Bronk remarked, "in which the students are simply the younger scholars." Each table, moreover, seated not only faculty and students but included a wide diversity of disciplines, a biologist next to a mathematician, a philosopher opposite a behavioral psychologist. "When I first came here, the tables were lined up like rows of tombstones in a military cemetery, eight people to a table and usually the same people from the same laboratory at the same table. Nearly everybody had been advised by the head of his laboratory not to talk about his current project lest some outsider get on to it. That kind of insularity was prevalent among research institutes. They were ingrown. They did not perpetuate themselves. They tended to grow selfish. But with young people around the walls have to come down."

An atmosphere that fosters interdisciplinary contacts outside the laboratory, that makes for frequent intellectual collisions and a cross-fertilization of ideas as a heterogeneity of scholars meet during meals, in the lecture auditorium, at campus social affairs, and at private parties typifies the University.

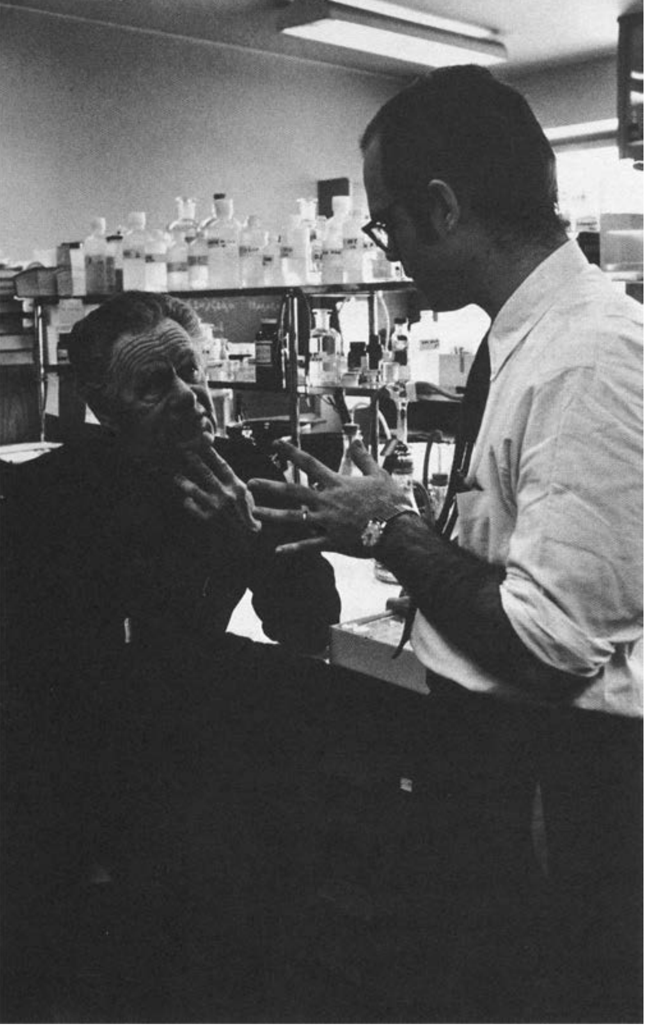
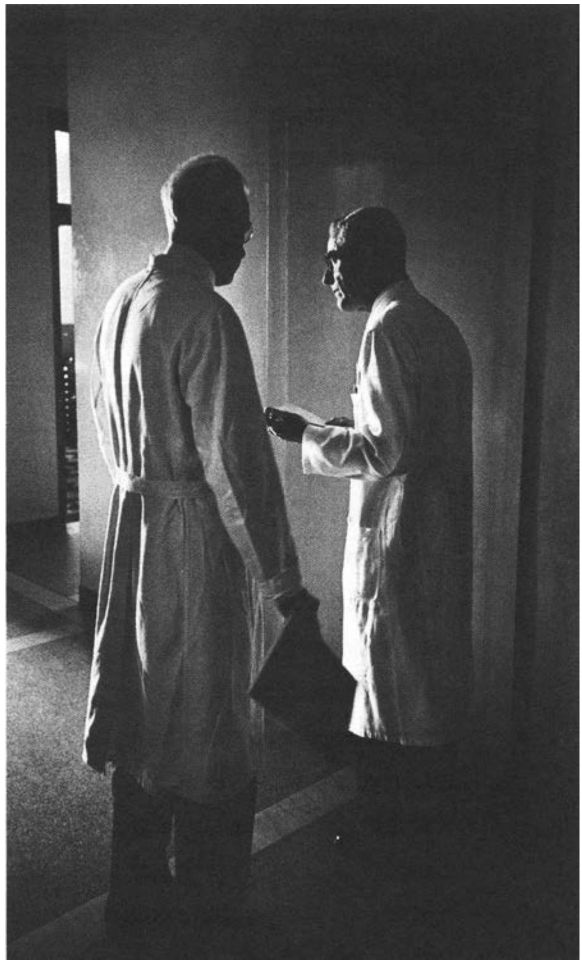
In support of the interdisciplinary spirit President Seitz argues:

* The admissions procedure has since changed. In addition to the letters from his sponsor and supporting endorsers, the candidate must submit a transcript of his undergraduate record. He is then interviewed by various faculty members as well as by the Dean and the President.

"Scientific problems have grown so many-sided and complex, they require techniques so sophisticated, that the researcher undertaking a major investigation can progress only so far without reference to a discipline outside his special competence—mathematics, physics, chemistry. At the same time modern science imposes such stringent intellectual demands on him as to leave him little opportunity to master other disciplines. One can hardly expect a topflight biologist to be an excellent mathematician and a physicist as well. Yet we believe that the biological researcher should at least be aware of how the mathematician or physicist might attack the same problem and that all three should be sensitive to the philosophical implications of what they are doing."

At lunch Hildebrand was awed by the caliber of the scientists whom Bronk pointed out or to whom he was introduced. There were four Nobel Laureates. Fritz Lipmann, who heads the laboratory of biosynthesis and is generally recognized as the father of modern bioenergetics, won the prize in 1953 for his discovery of coenzyme A and his experiments proving that labile phosphate compounds constitute the energy currency of all living matter. Edward L. Tatum, Professor of Biochemical Genetics, shared a Nobel Prize in 1958 with George W. Beadle. Working together at Stanford University 17 years earlier, when Tatum was a graduate student and Beadle a professor, they showed that genes control cell chemistry and that for every chemical reaction in living cells there is a specific controlling gene. In 1966 a Nobel citation went to the late Peyton Rous for demonstrating that a virus could cause cancer. Professor Emeritus of Pathology and Microbiology, Rous had, at the age of 90, embarked upon a completely new line of investigation. In 1967 Haldan Keffer Hartline, the fourth Laureate, Professor of Biophysics, was honored for his work on the primary chemical and physiological visual processes in the eye.

Since The Rockefeller Institute opened its doors 67 years ago, its


". . . I am certain that the independence granted to the students and the informality which characterizes the faculty-student relationship would generate a milieu in which I would thrive both intellectually and socially."

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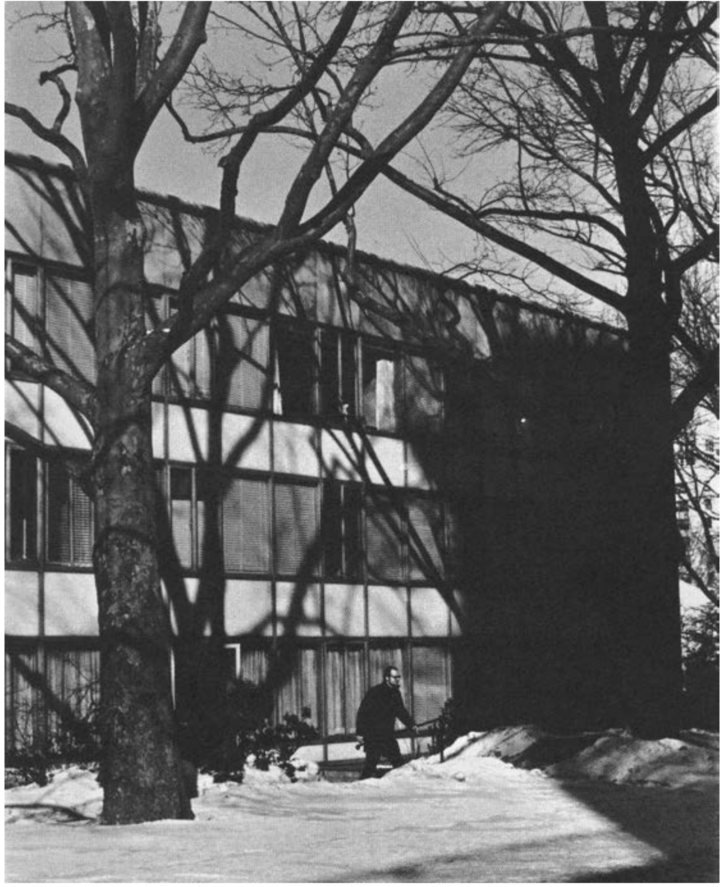

members and associates have included 15 Nobel Laureates, four of them so honored for work performed at the Institute—Rous, Hartline, John H. Northrop, and Wendell M. Stanley, the last two jointly in 1946 for isolating pure enzymes and viruses. In 1912 Alexis Carrel, who had developed his techniques on blood-vessel surgery before joining the Institute, became the first scientist to bring the Nobel Prize in medicine to America. Two other Laureates were Karl Landsteiner (1930) for his blood-group discoveries and Herbert S. Gasser (1944) for his studies of the nature of nerve conduction.

According to a partial list of various major awards to Rockefeller scientists within recent years, 29 of them have received a total of 57. Thirty-nine faculty members belong to the National Academy of Sciences (of which both Bronk and Seitz have been president), a record surpassed only by populous Harvard University, the Massachusetts Institute of Technology, and the University of California.

It excited Hildebrand's imagination to learn how students and faculty worked as colleagues. In April 1969, for example, Gerald M. Edelman, Professor of Biochemistry, announced the completion, after 12 years, of a staggeringly intricate project. It consisted of deciphering the structure of an immunoglobulin, or gamma globulin, an example of one of the antibodies that protects the body against disease. It is formed by 19,966 atoms, assembled in 1320 amino-acid building blocks. When Edelman undertook the Herculean task in 1958, he was himself a Graduate Fellow with an M.D. degree who had been practicing overseas for two years as a Captain in the United States Army Medical Corps. Staying on at the Institute after he received his Ph.D., first as an assistant professor, then as associate professor, and finally as professor, he established a laboratory devoted chiefly to penetrating the mystery of how antibodies work. The investigation eventually involved three faculty members and eight students. "It is no overstatement to say that the students made an enormous contribution," Edelman attests. "All but one received their degree for original work on some aspect of antibody structure."

When bacteria or viruses invade the body, the body manufactures immunoglobulins, or antibodies. If the victim survives, his system retains these antibodies which thereafter defend him against a recurrence of the same disease. Inoculation confers such immunity without causing the disease by stimulating the production of an appropriate antibody. Gamma globulin was formerly thought to consist of a single chain of amino acids, but in 1959 Edelman reported that it had multiple chains chemically bound together—four of them, as it turned out, two light chains of about 210 amino-acid units and two heavy chains of about 440. Two years later, in collaboration with his first student, Joseph A. Gally, he tackled a century-old enigma. In 1847 an English physician and chemist, Henry Bence-Jones, had detected in the urine of people with myeloma (cancer of the bone marrow) massive quantities of a protein which later was given his name. Edelman and Gally showed that the Bence-Jones protein is the light chain of gamma globulin. To advance their investigation, Edelman and his team needed plasma from a myeloma patient. Such a patient was found through medical colleagues in California, who regularly shipped quantities of the plasma to the Edelman laboratory until the fall of 1968, when the patient died.

Having confirmed the hypothesis that the Bence-Jones protein is the gamma-globulin light chain and having analyzed various other aspects of the molecule, the Edelman team proceeded to the awesome challenge of deciphering the entire sequence in which the 1320 amino-acid units are arranged. The most complex molecule ever deciphered had been subtilisin, which had 274 units. At this point, Edelman's collaborators had included two assistant professors, Bruce A. Cunningham and Myron J. Waxdal; an affiliate, William H. Konigsberg, and seven students, Joseph A. Gally, Donald E. Olins, Michel Fougereau (a Frenchman), John J.

Marchalonis, W. Einar Gall, Paul D. Gottlieb, and Urs Rutishauser. Edelman sums up the student contributions as follows:

"The way we operated was to assign a specific job to each of us and at the same time carry on communal functions. Joe Gally's doctoral thesis described some of the physical and chemical properties of the Bence-Jones proteins and the capacity of the chains to pair with each other. Joe thinks of himself primarily as a teacher. He is particularly interested in Negro education and currently holds, in addition to a visiting assistant professorship at Rockefeller, an assistant professorship at Meharry, a Negro medical school in Nashville.

"Donald Olins, my second student, showed that you can take the molecule apart, mix the chains and have them come back together. He is now doing DNA research at the Oak Ridge National Laboratory.

"Michel Fougereau extended Don's findings in the sense that he proved the reconstituted molecule to have the same over-all architecture as the original molecule. After several years of research work at the French National Institute of Agricultural Research, Michel has transferred to the University of Marseilles where he is studying the detailed amino-acid sequence of antibodies from various species.

"Jack Marchalonis, now an assistant professor at Brown University, is continuing the work he started here on the phylogenetic origins of antibodies. He isolated a new protein called hemoglutin from the horseshoe crab and went on to show that lampreys, sharks, frogs, and lungfish all manufacture antibodies. By studying their structure for the first time Jack also traced various evolutionary relationships among them.

"Einar Gall, who graduated in 1969, wrote his thesis on the chemical bonds of the gamma-globulin molecule that weld the amino-acid chains together. Paul Gottlieb deciphered a good part of the light chain, and Urs Rutishauser a good part of the heavy chain. Neither of them has graduated yet."

The joint achievement of those 11 men represents a giant stride toward an understanding of how the human organism marshals its own defenses. Once the process is fully understood, physicians may be able to strengthen it artificially when treating disease and surgeons to repress it and so prevent antibodies from counteracting organ transplants.

To return to young John Hildebrand, President Bronk ended the interview with a characteristically cryptic remark. He suggested that Hildebrand look around a bit more and weigh the matter further, and then, if he wished to attend the Institute, so to inform him. "I thought about that remark all the way back to Boston. It seemed to me that I had already declared myself, but I finally decided that what Dr. Bronk meant was for me just to percolate a while before reaffirming my decision."

He did just that. "Having visited and carefully considered several other graduate schools," he wrote, "I now find myself in a position to state unequivocally that my first choice is the Institute. On the basis of all that you and Dr. Brink told me, I believe that I could not equal nor even approach the opportunities offered by the Institute at any other school. What is more, I am certain that the independence granted to the students and the informality which characterizes the faculty-student relationship would generate a milieu in which I would thrive both intellectually and socially."

Three weeks later, in January 1964, he received a letter of acceptance. The fellowship, Bronk explained, provided $3500 a year, of which $2500 was to cover normal living expenses. The intended use of the remaining $1000 reflected Bronk's concern for the breadth of the student's outlook. Rockefeller offers no courses in the humanities and has no art, drama, or music departments. So "an additional $1000 should enable you to increase the scope of your graduate education by drawing on the rich cultural advantages of New York such as concerts, opera, theater, ballet, and museums, as well as to purchase books, travel to scientific meetings, and to spend as many as twelve months in attendance at universities in Europe during the course of your fellowship when, in the opinion of the Dean and the faculty, this is advantageous."

A Rockefeller fellowship normally starts July 1. The students need not begin work at the University itself on that date but may undertake some scholarly project elsewhere. Their choice of an alternative, however, must have relevance to the Rockefeller program and meet with Dean Brink's approval. Lacking the Dean's approval, they remain on their own until the fall without the material benefits conferred by the fellowship. Between 10 per cent and 20 per cent prefer to enter the University in the fall.

The Dean's office notified Hildebrand that, for anyone planning to study the life sciences, the University's summer biochemistry course was obligatory.* He arrived late in June, one of 29 students matriculating that term. Having chosen to live on campus, he was assigned to the Graduate Students Residence Hall in quarters consisting of a combined living room and bedroom, with bath. The windows open on a vista austere in winter, with gray, leafless trees lining the long stretch of dull, scraggly grass; and along the stone walks the shrubs are dark and stiff with cold, but they turn joyous and giddy with color as spring advances. Then the tree branches, mantled in tender green, invite the birds to sport among them. The shrubs sprout white andromeda blossoms and azalea blossoms in a spectrum from pink to fuchsia. The grass is a clean, glistening green again, bordered by crocuses, daffodils, multihued tulips, blue grape hyacinths. . . .

Rockefeller University has only one required course. Entitled "Seminars in Contemporary Science" and designed to familiarize first-year

* Such is no longer the case Students with adequate prior training in biochemistry may choose other courses.

students with the different laboratories, it consists of a series of lectures and laboratory demonstrations in which faculty members present their current projects. In Hildebrand's first year the seminars started with philosophy, the latest discipline added to the Rockefeller program. The lecturer was the late Ludwig Edelstein. "It was clear to us right away," Hildebrand recalls, "that this wonderful man was not like the philosophy professors we had had in college who were enormously concerned about Plato's letters but could not care less about what we did as science students. Dr. Edelstein was *sui generis.* He was ideally equipped to talk to people in fields other than his own, a believer in and liver of the idea of cross-fertilization, of interdisciplinary communication.

"The burden of his lectures was a personal message to us. He said he hoped we would not bury ourselves in test tubes and lose sight of the humanities and the relevance of our work to the concerns of mankind. 'Do not lose your humanism when you become a scientist,' he told us. 'The more professional you become as a scientist the more important that you retain your element of humanism.' After each lecture he would invite a small group of students to his apartment on campus and over cheese and sherry we would explore issues that transcended science. Here was the Rockefeller University promise really coming through. I think none of us who had the privilege of contact with Dr. Edelstein could ever forget that experience. We felt the loss deeply when he died in 1966."

Delivered at the rate of two a week for four months, these orientation lectures also present a summary view of physics, mathematics, and the life sciences. At the end, each student writes a term paper on a scientific topic of his choice. Hildebrand chose the chemistry of the metabolism of gangliosides (a group of complex glycolipid biochemicals).

Meanwhile, through consultations with the Dean and with faculty members, the student prepares his curriculum. As for his doctoral thesis, two years or more elapse before he settles on his subject.

By January 1965, Hildebrand had enrolled in his first major course, cell biology under Professor George Palade. "Having done a lot of chemistry in college, I felt I needed to go deeper into biology. Dr. Palade's course was a traditional one with lectures, lab work, and all the rest. But what set it apart from such a course elsewhere was its intensiveness. It left you no time for any other study. You did not get just three lectures a week and an hour in the lab. You worked full time five days a week from January to June. About six faculty members were involved at a time, but no more than 12 students were admitted, which followed a Rockefeller University rule of thumb—two students to a professor.

"There was no examination, no pressure, no feeling that you must do homework over the weekend because a paper fell due Monday. And yet most of us did work weekends as well as many nights because, when your mind is that deeply engaged, artificial time distinctions disappear."

By the spring of his first year Hildebrand had begun to wonder whether he might not find his thesis subject in the Palade laboratory. "Commitment to a lab is not a matter of life and death at Rockefeller University the way it is at many universities. You get a reasonable latitude. If a particular lab turns out to be not your cup of tea, you do not have to stay. It is not always easy to move around, of course, but it is possible. In many places it is impossible."

Still uncertain, he started to "ease into," as he puts it, Professor Christian de Duve's laboratory of biochemical cytology. "What moved me in that direction was my long-standing interest in biochemistry plus a growing interest in cytology resulting from Dr. Palade's course. It seemed a logical step. Dr. de Duve's lab combined the two. Furthermore, he used some specialized methods I wanted to learn."

In the tenth grade at Belmont High School, Hildebrand had been attracted to a tall, slender classmate named Zonda Jeanne Mercer who shared his fondness for music. She played the clarinet in the school band.

She too had grown up in Belmont. Her father was an electronics engineer. By the time they graduated, they both felt sure they would eventually marry. Zonda went to Bryn Mawr College and then, having decided to become a doctor, to the State University of New York's Downstate Medical Center in Brooklyn at the same time that Hildebrand entered Rockefeller University. They were married the following June.

Today, if a Rockefeller student's wife earns less than $2000 a year, he receives, in addition to his fellowship stipend, a dependency allowance of $500, and for each child $500 more, but such was not the case in the Hildebrands' day. Couples who prefer to live on campus, as the Hildebrands did, occupy an apartment with a living room, bedroom, bath, and a kitchenette hardly large enough in which to prepare full meals. Most of the young married couples eat in the Rockefeller University dining rooms.

For Zonda Hildebrand three more years of medical school lay ahead. The Rockefeller University allowances barely covered the expense, but neither student would accept financial help from home. "It is just not our philosophy," Hildebrand says. They managed to pay for Zonda's medical schooling at the beginning from her savings and the little that remained from his fellowship and loans. When they established legal residence in New York, Mrs. Hildebrand qualified for free tuition under the state's scholar incentive program and a state loan. She received her degree in 1968 and immediately began an interneship at Downstate in pediatrics. Few young couples ever saw so little of each other. Her duties obliged her to leave home nearly every morning at 6:30 and often to stay at the hospital overnight.

In July 1965, at the beginning of his second year, Hildebrand took a course in general physiology taught by Associate Professor Martin A. Rizack, a biochemist with a medical degree and a Rockefeller University Ph.D. How the course came to be given at that season exemplifies the flexibility of The Rockefeller University system. Rizack normally gives it in midyear. But Hildebrand and four other students gently pressured him into changing his schedule to suit their curriculum, which would have been an unheard-of accommodation at other universities.

Hildebrand was still easing into the de Duve laboratory. At length he asked Professor de Duve, a Belgian of great personal charm and scientific accomplishment, to serve as his research adviser, and under his aegis he started full-time work in the fall of 1966. Six months later he made a third and final change. "I came to the conclusion that, whereas it had been valuable to learn Dr. de Duve's methods and to do some physiologically oriented work in biochemistry, I really wanted to return for my thesis to the kind of biochemistry I had done as an undergrad. In the de Duve lab the primary interest was the biological aspects of the function of intact cells and of their components, the subcellular organelles. We concentrated on cell fractions isolated from whole organs rather than on single cells. But the work I wanted to become professionally competent in involved purifying from a tissue or cell culture many molecules of a single enzyme, then studying the chemical mechanism of the reaction which that enzyme catalyzes."

Since entering The Rockefeller University, Hildebrand had also been attending lectures on enzyme-reaction mechanisms by Associate Professor Leonard B. Spector, the principal coworker of the Nobel Laureate Fritz Lipmann. He found the lectures enthralling. "Dr. Spector is an outstanding teacher. His masterful lectures would do credit to the greatest of orators. His course, in fact, draws the biggest enrollment year after year of any course at Rockefeller University." Hildebrand discussed with him the possibility of switching to his laboratory, which at that time had no Graduate Fellows working in it. He brought with him a suggestion for a doctoral thesis.

The cell machinery has a two-fold primary function: to convert nutrients into energy and simultaneously to create the new molecules needed to synthesize such vital biochemicals as proteins, nucleic acids, lipids, carbohydrates, and hormones. These molecular rearrangements and transformations constitute the metabolic activity of the cell.

A special property of all living organisms is the storing of chemical energy from foodstuffs in specific chemicals. These chemicals possess parts that when transferred to acceptor compounds, so activate the latter as to make possible the reactions they will subsequently undergo. Perhaps the most common transferable chemical group of this sort is the phosphoryl group, and its chief storehouse is adenosine triphosphate (ATP). The chemical energy stored in ATP may be converted into mechanical energy for muscle contraction and electrical energy for nerve impulses and several other forms.

Living cells have six major ATP-yielding reactions. The paramount concern of many biochemists, including those working with Spector in the Lipmann laboratory, was to discover precisely how they worked. To do so, they isolated in pure form, from an appropriate biological source such as rat liver, the individual enzymes that oversee the conversion. They then scrutinized the organic-chemical intermediates produced in the course of the reaction catalyzed by that enzyme. In sum, they sought to learn not only how enzymes catalyze biosynthetic reactions, but how metabolic poisons inhibit the process and how similar transformations occur in widely different species.

At the time Hildebrand approached Spector, the mechanism of only two of the six ATP reactions had been analyzed. Hildebrand proposed for his doctoral thesis a study of a third known as the succinic thiokinase reaction. It was the beginning of a professional association and of a warm friendship.

For the remainder of his career at The Rockefeller University, Hildebrand devoted about 90 per cent of his working hours to the one biochemical phenomenon. Two other students, Christopher Walsh and Robert Anthony, joined the Spector laboratory the same year, and they too were concerned almost exclusively with ATP. Walsh investigated the possible role of citryl phosphate as an intermediate in the reaction catalyzed by the enzyme ATP-citrate lyase, which Lipmann had discovered some 15 years earlier. Anthony studied the enzymatic activation of glutamic acid in the metabolic pathway leading to urea in certain bacteria. It was taxing work, occupying the students ten to 18 hours a day and sometimes two or three days at a stretch without sleep, because, when an enzyme is isolated from its natural source, the successive operations must be carried out quickly and without delay or the enzyme will denature and lose all activity as a catalyst.

While The Rockefeller University dispenses with regular testing and examinations, the student does take a comprehensive examination before his third year and a final examination as part of his thesis presentation. The comprehensive actually consists of three examinations, each in a different area of his major field. They cover subjects previously agreed upon as constituting his range of competence by the student and his Faculty Advisory Committee which was appointed when he proposed his plan of study and research. Hildebrand passed his comprehensive examination in organic chemistry and biochemistry, physiology, and cell biology.

> The purpose of these examinations [the *Guide for Graduate Students* sets forth] is to obtain the information necessary for deciding either that a student has a sufficient understanding of science for continuing his studies self-directed or that specific requirements for further study in particular subjects are necessary. . . . For those students who set high standards of scholarship for themselves, these examinations are merely checkpoints that measure the developing ability of the student to communicate effectively with other scientists.

The comprehensive examination does not determine the student's ultimate success or failure. The Rockefeller University emphasizes "the development of the individuality of the potentially creative scientist" and considers it meaningless to assess such development in terms of comparisons with any group average. Periodic assessments are made, however, by the student's research adviser as well as by members of his Faculty Advisory Committee under whom he has taken courses, seminars, or tutorials. They submit reports to the Dean whenever they believe they have gained insight into the student's progress. Typically, they report that he "participated effectively" in a given research project or that he simply "participated." In addition, at the end of each year the student submits his own account of his progress in study, research, and work toward his doctoral thesis. Final judgments are based largely on this accumulated documentation. An average of one of four students does not graduate. Not all of these, by any means, have fallen below the University's standards. They include married women who are obliged to interrupt their studies because of pregnancy or whose husbands' work takes them to other parts of the country. There are students who come to consider themselves psychologically unsuited to Rockefeller University, and others, having entered a highly specialized field of research, conclude that some other university will offer them greater opportunities to pursue it. Outright academic failure is rare.

By the fall of 1968 Hildebrand had amassed enough data on the succinic thiokinase reaction for his thesis and final examination. The latter falls into two phases—the "thesis defense" under questioning by a four-man committee, and a public lecture followed by questions from the audience. In September Hildebrand took the customary preliminary step of conferring with Associate Dean Clarence M. Connelly, who handles all graduation arrangements. Together they set February 4 as the date for the public lecture and March 15 for submission of the thesis. They then discussed the makeup of the thesis committee. The chairman finally chosen was Professor Robert B. Merrifield, leader of one of two groups of biochemists who that year had synthesized an important enzyme, ribonuclease. The other three committeemen were Spector, de Duve, and Associate Professor John D. Gregory, a biochemist familiar with bio-energetics and biosynthesis.

Hildebrand finished his thesis, entitled *Succinyl Phosphate and the Succinyl-CoA Synthetase Reaction,* in two months. Every year the Federation of American Societies of Experimental Biology selects from among abstracts submitted to it papers that it deems important enough to be read at its spring meeting. One of those selected in 1969 was Hildebrand's. Shortly after the Federation meeting, the findings of Hildebrand's thesis research were further communicated through lectures at other universities and publication in scientific journals.

The term "thesis defense" is somewhat misleading. The thesis committee does not function as a jury, passing or failing the doctoral candidate. If he has progressed as far as submitting his thesis, he is considered ready to graduate. The committee seeks rather to determine the scope of his knowledge in his special field, to purge his thesis of any obscurities of language, possibly to suggest the insertion of material that it believes should not have been omitted, and in general to make recommendations for improving the thesis before it is finally printed, bound, and deposited in the University library.

At commencement Leonard B. Spector declared in his citation of John Hildebrand: "The enzymatic transformation which for three ardent years engrossed the energies of this remarkable young man had long baffled some of the best minds in biochemistry. It may seem strange that John should have succeeded where others failed. But not at all strange is it to those of us who know him. Brains and energy—these form the unconquerable combination. And these our candidate possesses in full measure. Many times have I watched in admiration as flinty problems fused in the heat of his concentration. With this throng as my witness, I here prophesy that the spirit flaming out of John Hildebrand will light him to a lifetime of discovery—to richer, grander exploits that will surely profit us all."

Hildebrand had begun to formulate his postdoctoral plans nearly two years before graduation. "You have to act early in this business," he says, "because desirable positions fill up far in advance." Three main possibilities were open to him. He could turn his technical skills to practical and lucrative use by taking an industrial research job. He could teach. He could continue his training as a postdoctoral fellow. He chose the third. "It seemed the surest road to what I hope ultimately to do, namely, to bring my chemical and biochemical background to bear on the study of the nervous system. For that, of course, I would need to learn a good deal about neurophysiology." Accordingly, he started discussions with the Department of Neurobiology at the Harvard Medical School headed by the eminent Professor Stephen Kuffler. "It's an extremely interesting laboratory because the people there represent so many diverse disciplines—biochemistry, physiology, pharmacology, morphology—all concentrated on problems of neurofunction." The professor with whom he specifically wished to work was Edward Kravitz, a biochemist who directs that section of the department investigating the chemistry of single nerve cells. Hildebrand's financial needs were met by the Helen Hay Whitney Foundation, which awards postdoctoral fellowships to promising biomedical researchers.

The same month that her husband was graduated, Zonda Hildebrand completed her interneship at Downstate Medical Center and became a licensed physician. Within a few weeks they were living in Boston and working in their respective fields. Mrs. Hildebrand, who had also chosen to continue her training, joined the pediatrics department of the Massachusetts General Hospital as a house staff officer. The residency requirement in pediatrics is two years. After that she will study child psychiatry, her ultimate sphere of practice.

Regarding his future, Hildebrand, who will both learn and teach at Harvard and has his sights set on a university chair, once wrote in a biographical sketch requested by the Rockefeller University Public Relations office: "As a teacher I hope to instill in my students a fascination with, and respect for, the order and mechanisms of life, as well as the curiosity and will to seek further elucidation. As a scientist, I hope to have the results of my investigations find some application to the alleviation of nervous diseases."

Il n'y a que le provisoire qui dure (*Only that which is temporary endures*). . . . *Universities are presently struggling to discover how they can adapt their programs to the demands for new kinds of theoretical knowledge and for greater involvement in the practical affairs of society.*

René J. Dubos
in *So Human an Animal*

In 1965 the board of trustees under Chairman David Rockefeller once again entered a period of reappraisal and replanning. It is still going on. Sixteen years earlier, the Trustees had been prey to doubts about the justification of prolonging the existence of the Institute. No such doubts troubled them in 1965. None of them questioned the relevance of the University to American education and science. The major issues did not now concern survival (provided the mounting financial needs were met), but rather size, direction, and change in a world of swiftly increasing technological advance and scientific discovery. What, in sum, should The Rockefeller University do next?

The Chairman divided the Board into three committees, each of which then conferred with some 40 outstanding figures in the worlds of education and science. Frederick Seitz, a physicist and the then President of the National Academy of Sciences, sat on one committee. The deliberations coincided with the search for a new President of the University, for Detlev Bronk would be retiring in three years. Bronk himself, anticipating the need for an academic structure to carry on after his presidency and believing that the faculty should play a greater administrative role, created a Senate, composed of all the senior members. The Senate, in turn, created an Academic Council to function as its steering committee and to advise the President.

One of the most important questions to be reviewed in the period ahead involves the tenure of Graduate Fellows. Hitherto no limit has been placed on the time they might require to produce their doctoral thesis. Of the 27 students who graduated in 1969, for example, one had been at the University eight years, another seven, ten six years and ten five, two four years and two three, and one, who began his graduate work elsewhere, two years. President Seitz questions the continuation of that policy in the present climate in which student attitudes seem to be changing and many students everywhere appear to be restless and uncertain. "There is a big difference between the students of the fifties and those of the sixties," Seitz points out. "I think it safe to say that, although people do not change genetically from one generation to the next, the students of the fifties expected to do their very best professionally, whereas at present some students tend to wonder whether they should not be doing something else, or even if it is not more proper to do something else. I am not sure how much of our limited resources we should devote to such students once it becomes clear that the pursuit of science, or the improvement of society through the use of science, is no longer their main interest. At our last commencement one graduate, a brilliant fellow, whose education in science represents a very large investment by society, announced that he would have nothing further to do with science. This is a highly unusual case, but it is symptomatic of the period through which we are passing."

The great majority of the students, Seitz estimates, do make optimum use of the opportunities the University offers, but a few flounder, partly perhaps because of lack of adequate pressure to finish their studies.

"These few may need either more direction, or at least have somewhat more questions raised with them, once it becomes apparent that they may require substantially more than four years to complete their work.

"Princeton University has evolved a system under which graduate fellows are told in effect: we will give you four years, after that you will have to support yourself. Such a system has worked quite well in Princeton's own framework. We are by no means ready to introduce such a policy now at Rockefeller University, but we will keep the possibility in mind as we watch the way in which student attitudes evolve in the future. Although it is perhaps unrealistic to expect the attitudes toward professional advancement to return to what they were in the decades before 1960, those who guide the University agree that our role in education, as in research, is to advance the welfare of mankind through science and its applications. We all want to encourage most those students who feel sympathetic to this concept in the depth of their minds and souls."

For somewhat related reasons the University may institute an organized "core curriculum." This will be optional in the sense that the student who knows exactly what he wants to do can pass it up. "We do not propose to get in any student's way," Seitz hastens to add, "but if doubts assail him, he will have a formal structure to fall back on."

A number of important changes and additions affecting the different laboratories are also under consideration. In 1969 six committees were formed, each representing a group of related disciplines, a total of 42 professors. They deliberated in frequent meetings over a period of six months, submitting their reports and recommendations to the Academic Council. Agreement was unanimous from the beginning as to what the University should *not* do. It should not expand into nonscientific subjects. The Senate, agreeing in principle with the committees' conclusions, announced: "The Rockefeller University is recognized as a university devoted primarily to the natural sciences; faculty and graduate students do not consider it undesirable that there be such a restriction. Wider intellectual and cultural interests can be satisfied and fostered by a library of broad scope, by such activities as The Rockefeller University concerts and art exhibits, by guest lectures and symposia on a diversity of subjects, by the vast cultural resources of New York, and by interpersonal relations among faculty and students who have many nonscientific interests."

Nor would the University attempt to encompass all fields of science. "The ever-widening scope of modern science and its consequent fragmentation and increasing specialization makes such an attempt virtually impossible in even the largest universities. When institutions endeavor to be all-inclusive, areas of mediocrity develop; it is difficult to maintain the unity of science and cultivate the desirable relations between relevant fields. . . . it is necessary that we be exacting in our selection of the most significant, most fundamental, and most broadly relevant areas of mathematics, physics, chemistry, and biology."

Some of the committeemen favored an increase in the number of students admitted each year, although not by more than half of the present number, or about 60 in all. This would necessitate a corresponding increase in the size of the faculty in order to maintain the student-faculty ratio. But, again, no faculty increase above 50 per cent was desired lest it impede "the ease of association between scholars in immediately related fields and in fields potentially but not obviously related now." (The physical facilities to accommodate this larger community will soon be available with the completion of the 17-story Tower Building, containing 120,000 square feet of space for laboratories, classrooms, faculty studies, and dining rooms.) The selection of new faculty will be limited to those with broad interests and a natural desire to assist others by consultation, advice, and collaboration. "Because of our small size, we cannot afford many who desire the academic life of an isolated recluse." The University will continue to avoid departments, which would restrict its policy of encouraging the interdisciplinary training of its students.

The Behavioral Sciences Committee reported: "The new program... has achieved an excellent foundation which has attracted wide attention in relevant professional circles. In order to capitalize and consolidate this strong beginning, however, certain additional appointments are required." The committee recommended faculty additions in neuroanatomy, neurophysiology, the mathematical aspects of psychology and computer science, population biology, behavioral genetics, the evolution of human behavior, primate behavior, and the development of infantile learning and perception.

The Committee for Biomedical Sciences wrote: "It is clear that there is room for intensive use of new knowledge of basic biology in the study of the major problems of human disease. This opportunity could be exploited . . . by the addition of laboratory groups in the frontiers of modern experimental pathology. These groups would be in a position to derive strength from, as well as to contribute to, the existing programs in cellular and molecular biology, in immunology, and in virology. The general fields of experimental oncology [the branch of medicine dealing with tumors], tissue transplantation, and the degenerative processes of senescence have been suggested for development. . . .

"The possibilities go well beyond the consideration of specific disease processes. There is need for investigation of normal integrative processes in the intact organism and for the study of normal human development. In addition, study is required of those emerging problems of man that might be grouped under the general term of environmental biomedicine."

Professor de Duve entered a special and compelling plea for developing experimental pathology. "Until less than a hundred years ago," he argued, "infectious and nutritional diseases accounted for most of the mortality in the human race. With the discovery of vaccines, immune serums, sulfonamides, antibiotics, and with that of other essential nutrients, these causes of death have now been largely eradicated. . . . As a result, . . . a dramatic change has occurred in the dominant pathology of the Western World. For the first time in the history of humanity, atherosclerosis, cancer, arthritis, and other degenerative diseases, and finally aging itself, have become the main causes of death. The part played in these diseases by infectious, nutritional, or endocrinological factors is undoubtedly still a significant one. Of much greater importance, however, is the manner in which the cells and the tissues themselves react against such environmental factors, or change as a result of their own continuing operation. . . .

". . . Great progress has been made in the realm of cell biology, to the extent that we now have considerable information concerning both the structural and the functional properties of many intracellular organelles, and are beginning to understand how a number of basic cellular processes operate and are regulated. It is remarkable and even disquieting that medical research has so far profited so little from these advances. Except for the developments in surgery and the occasional fruits of empirical drug research, there has been no real breakthrough in practical medicine. In particular, we are as powerless against the major modern diseases as we were 25 years ago.

". . . Few will deny that medicine would progress more rapidly . . . if measures could be taken to bridge the gap . . . between basic biology and pathology, and to overcome the barrier of inertia that prevents a truly fruitful collaboration between the two disciplines. . . . The steps to be taken are obvious. Bring together in a stimulating and propitious environment top-quality biologists and experts in one or more fields of experimental pathology. Let them organize a joint program of teaching and research that will include intensive training in the techniques, concepts, and experimental approaches peculiar to each of the two fields. Provide them with the means of establishing through their trainees a network of truly intimate and interdisciplinary collaborations. . . .

"It must be stressed in support of such a program that the time is really ripe for the launching of a novel and powerful attack on the main cellular mechanisms which underlie the dominant diseases of our time. This would have been unthinkable 20 or even ten years ago. But today we have available new tools, new concepts, and new findings which have actually proved their worth in the study of basic physiological mechanisms. . . . With human health at stake, there can be no excuse for further delay." Such an opportunity should not be lightly disregarded by an institution as intimately identified as is The Rockefeller University with the progress of medicine and the development of modern cell biology."

The committee representing Logic, Mathematics, and Philosophy concluded its appeal for a larger group with a traditionally Rockefellerian long view: "It is almost self-evident that the various disciplines in the University be intellectually autonomous. It would be perilous in the extreme to predicate the development of one discipline on the needs of another. It would be equally perilous for a discipline to become isolated. Fortunately, the University is so constituted that these dangers can be avoided and that we may all look toward a highly cohesive scientific community with a multitude of overlapping interests which by deeds will demonstrate the basic unity of our endeavor.

"And if we cannot do it, our students, hopefully, will."

The Rockefeller University's original endowment came entirely from the Rockefeller family. Today, the annual returns from that endowment contribute approximately 50% of the University's current operating funds; other private sources and the Government supply the balance. The contemplated changes will require larger means—means that in the future economy will lie beyond the scope of any single family. Although the Rockefellers will always maintain a deep interest in the enterprise their forebear launched 70 years ago, and will continue to contribute material and moral support, they believe that the University belongs to society and that the time has come for society to share more broadly in its sustenance *pro bono humani generis.*

ACKNOWLEDGMENTS

TEXT

Quotations not listed were told to the author in writing or interviews

Page 1 epigraph	Peyton Rous: Simon Flexner and medical discovery. *Science*, 1948, *107*, 613.
Page 1 line 17	Detlev Wulf Bronk: Opening remarks, *in* Convocation for the Conferring of Degrees, 18 June 1959. *Occasional Papers of The Rockefeller Institute Press*, 1959, No. 8, p. 1.
Page 2 line 9	Igor Tamm: Presenting Nicholas Hill Acheson. Convocation for Conferring Degrees, 13 June 1969. New York: The Rockefeller University.
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Page 36 line 19	Neal E. Miller: *News from The Rockefeller University*, January 31, 1969, pp. 4–5; *see also Science*, 1969, vol. *163*, no. 3866, pp. 434–445.
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Page 67 line 4	Carl Pfaffmann, chairman: Behavioral Sciences Committee Report, May 1968, p. 1.
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Page 67 line 29	Christian de Duve: The Case for Developing Experimental Pathology at the Rockefeller University, no date, pp. 1–2, 4–6.
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Endleaves	front by Joseph Barnell; back by Fairchild Aerial Surveys
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Two thousand copies of The Rockefeller University Story
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