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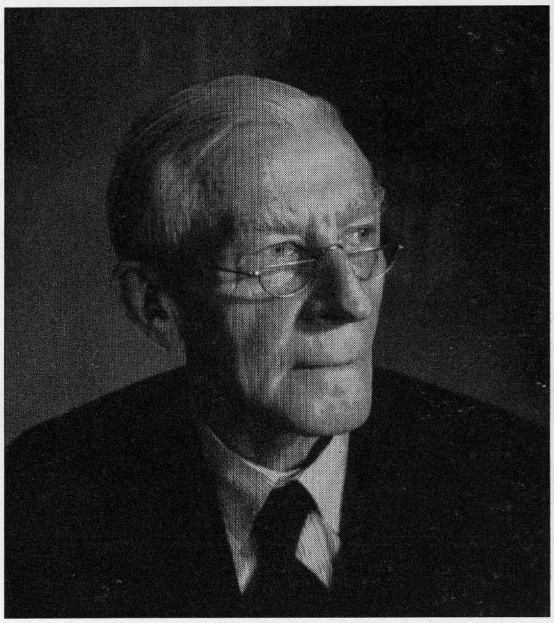
NEUROPHYSIOLOGY IN THE NINETEEN TWENTIES

BY YNGVE ZOTTERMAN

These recollections were given by Professor Zotterman of the Royal Veterinary College, Stockholm, at a dinner in honor of Lord Edgar Douglas Adrian, Master of Trinity College and Trustee of The Rockefeller Institute, in Kings College, Cambridge, 18 March 1964.



LORD ADRIAN

ONE DAY early in 1919 my teacher in physiology Professor Johansson put in my hand the 1908 volume of the *Journal of Physiology* and asked me to read a paper by Keith Lucas on the cutaneous dorsi muscle of the frog. In this classical paper Lucas very elegantly proved that striated skeletal muscle followed the all-or-none principle first established for cardiac muscle by Bowditch. Naturally I wanted to read more by him and so found the papers by Lucas and Adrian between 1910 and 1916 on summation of stimuli, and Adrian's papers on the recovery of conductivity and excitability in nerve fibers. They appealed immensely to me and when in early October 1919 I had passed my first MB exam I sent a cable to the Registrary of Cambridge University asking for permission to visit the Physiological Lab, and received a favorable answer. So on a foggy October day in 1919 my classmate Åke Berglund and I stepped up to the Registrary in his office in the tower of the University Press. He was an old, small gentleman, Dr. Keynes, the father of Lord Keynes and Mrs. A. V. Hill, and grandfather to Dr. Richard Keynes. He put on his cap and gown and took us up through Pembroke Street to the lab. He introduced us to Professor Langley who received us very kindly, and to whom we presented the greetings of Professor Johansson, his colleague in the international physiology congress committee. Langley advised us to join the advanced class, which we did the next morning.

The class appeared to consist of only two undergraduates — one of them was Jack Roughton. I wonder if so few ever were taught physiology by such a galaxy of stars as Langley had collected in his new building.

Thus we were given lectures in the morning and a practical class in the afternoon by Joseph Barcroft, Sir William Bate Hardy, H. Hartridge, A. V. Hill, and E. D. Adrian, who all let us repeat most of their previously published experiments using their original set-up of apparatus. Under Adrian's guidance we did experiments on the sciatic nerve in the ebonite

LORD ADRIAN OF CAMBRIDGE

Lord Adrian is one of the world's great scientists and educators: one-time Professor of Physiology in Cambridge University, Past President of the Royal Society of London, Nobel Laureate, Master of Trinity College, Cambridge. In proposing the toast at the dinner held this spring in honor of Adrian's approaching 75th birthday, President Bronk spoke of his friend of 35 years in the words of an earlier Master of Trinity. "Adrian 'is one whose mind has been trained in the splendid discipline of a natural science, but whose heart and eyes also take delight in the triumphs of art, the history of man, and the beauties of nature. Such a man is about the best thing that our modern civilization can produce.'" Photograph shows Lord Adrian at right, with President Bronk and Professor Uhlenbeck, at the dedication of Sophie Fricke Hall last February.

trough, recording the height of the twitch of the gastrocnemius muscle. We used Lucas' pendulum or his bandspring release for sending in two break shocks at variable intervals into the nerve. Hence we were allowed to convince ourselves of the existence of the absolute refractory period followed by a relative refractory period. We felt very proud and rich when we were able to produce the smooth features of Lucas' and Adrian's now classic "recovery curve" even when it took quite some hours to plot what today is produced within a fraction of a second and demonstrated on a screen with a good afterglow.

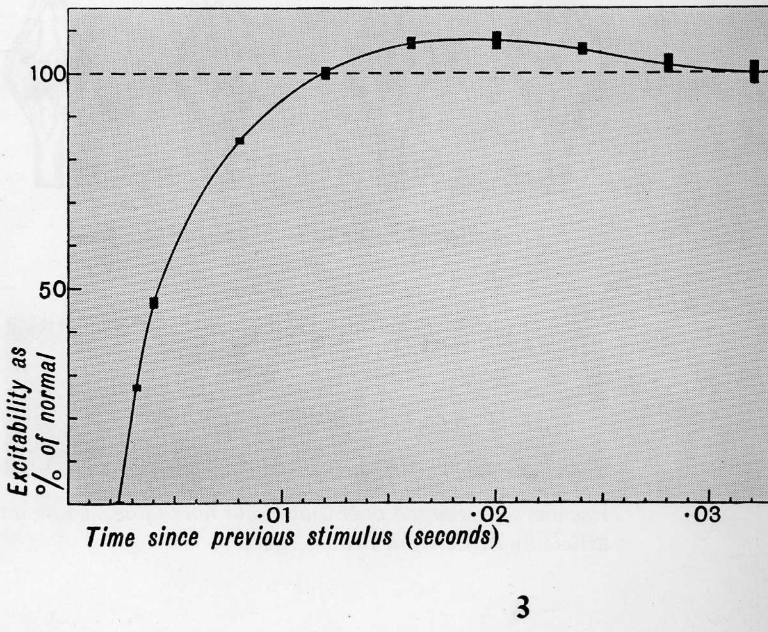
Back to Cambridge

Having attended the advanced class for six weeks, I returned to start my clinical studies at Uppsala firmly determined to go back to Cambridge as soon as possible. In June 1920 I was there, and Adrian kindly let me work in his room in the basement and helped me to start a bit of research on the conductivity of the motor endplates using the double-stimulus technique. Adrian's method of plotting the recovery curve of the nerve proved very useful in studying the effect of various agents on the endplates and represented in those days a new and very advanced approach. The use of this fairly simple technique had as a matter of fact led to the establishment of some quite fundamental concepts about the conductivity of the nervous impulse. Thus we owe to Keith Lucas and to Adrian the discovery of the all-or-none character of the propagated disturbance in motor and sensory nerve fibers, the recovery curve of nerve, and the phenomenon which Lucas and Adrian called "summation of local excitation."

All this was achieved from experiments on peripheral nerves using induction coils, Lucas' pendulum, and a smoked drum recording the height of the muscle twitch. Consequently the evidence was only indirect from experiments in which the twitch of the muscle was used as an indication of what had happened in the nerve. In the early twenties direct evidence was very scarce. The capillary electrometer used by Keith Lucas, and particularly Einthoven's string galvanometer, had been of very great value and had been used outside electrocardiography to record the electric disturbance from peripheral nerves, and even responses from sensory nerves elicited by adequate stimuli, as by Einthoven and Jolly in 1911, by Buytendyk in 1910; in 1924 Alexander Forbes recorded from afferent fibers from the muscles. These experiments gave a first clear indication of the nature of the electric response, but they could not be expected to give any information as to the duration or frequency of the electric response in each fiber. They gave, however, the first clear indication that the activity of a sensory nerve evoked by the natural stimulus to its end-organ is of the same nature as the activity of a motor nerve stimulated artificially. The use of Lucas' capillary electrometer and Einthoven's string galvanometer gave, as Adrian himself expressed it in 1932, "valuable results of the kind needed to consolidate a position already won and there was no hope of further advance without a fresh development on the instrumental side."

That development occurred very rapidly after the First World War and was due to the invention of vacuum tube amplification. In England de Burgh Daly had already in 1920 introduced such an amplifier connected to a string galvanometer, and in America Gasser and Newcomer in 1921 used an amplifier for recording the electric response of the phrenic nerve. Herbert Gasser, with Erlanger, was then the first to use a three-valve amplifier in connection with a cathode-ray oscillograph in 1924—which led to their discovery of the relation between velocity of the nerve impulse and fiber diameter.

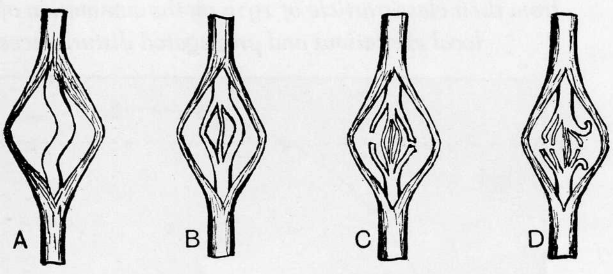
One of the Adrian and Lucas recovery curves from their classic article of 1912 on the summation of local excitations and propagated disturbances



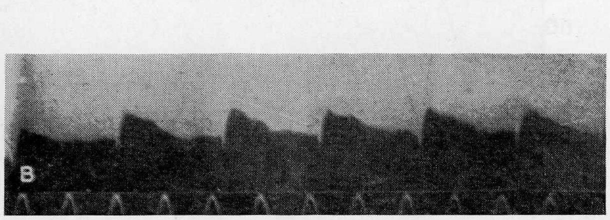
After completion of my clinical studies I wanted to return to Cambridge, and Adrian said I was welcome as he had just obtained a three-valve amplifier and was anxious to look at sensory fibers. Thus in October 1925 I came back to Adrian's room in the basement. There Adrian had the amplifier in a neat wooden box, connected to Lucas' capillary electrometer, with its camera, in the darkroom. With this set-up Adrian had recorded the afferent inflow in the sciatic nerve when the gastrocnemius muscle was stretched and further obtained records from the depressor and vagus nerve.

Meccano Set and Plasticine

When I arrived Adrian wanted to start with the cutaneous dorsi muscle of the frog as its nerve only contained about ten fibers of which one or two might be afferent. However, it gave no afferent response at all, so we looked into the cutaneous sterni muscle which had 12 – 25 fibers in its nerve, and here we got a very nice afferent response which obviously derived from a number of sensory fibers. However, a preparation which only retained one spindle was at last obtained, by successively cutting off small strips of the muscle. Adrian, of course, immediately grasped the opportunity which this preparation offered. Thanks to an extraordinary manual dexterity he improvised devices such as one for pulling the muscle at different speeds, using only parts from a Meccano set and, of course, plasticine, "the physiologist's little friend," as he used to call it. Thus he was able to collect most of the essential data for which he had been looking so long. In that very afternoon and evening he got the direct evidence of what he had previously suggested.



Dissection of nerve to divide all but one fiber.



Impulses discharged over that motor nerve fiber. From an article by Adrian and Bronk, 1928.

I can assure you that we had a fine day. We had started in the morning and we went on until late in the evening, having no time either for lunch or tea; but Adrian later in the evening offered some bits of chocolate which he always kept in the laboratory.

Returning home to our flat at 27 Bridge Street in the late evening in a very happy mood indeed, I was met by a wife in tears – "the chicken is all burnt and destroyed," she cried – and it did not help when I tried consoling her by saying that what we had done that afternoon would be in every textbook of physiology within five years. It was a very happy period indeed. We had unusually cold weather that November in 1925 which indirectly affected our endeavors. The very keen sportsman in Adrian took an upper hand; he could not resist the opportunity to skate which was offered by the frozen sewage ponds outside Cambridge. In the midst of our exciting experiments Adrian disappeared for nearly a whole week to practice skating. He was not the only one. On our landlord's second-hand furniture shop at 27 Bridge Street we read the sign "Closed because of skating."

Next Adrian put the eye and optic nerve on the program. We started on the cat's eye but we could not split up the optic nerve so we had to give it up and went to cutaneous nerves. Later in 1926, however, Adrian returned to the eye of the frog and the eel – which resulted in two brilliant papers by Adrian and Rachel Matthews in 1927. The following year Detlev Bronk joined Adrian, which resulted in the classical work on single motor nerve fibers in the phrenic nerve. Then Bryan Matthews constructed his iron-tongue oscillograph which provided very much better records until the cathode-ray tube was improved and better adapted for use by neurophysiologists.

Well, these are in short my recollections from the twenties limited to the horizon of Cambridge neurophysiology. They contain, I would say, the small overture to the grand opera of the present electronic era of neurophysiology.

CONVOCATION FOR CONFERRING DEGREES

12 JUNE 1964

On June 12, 1964, The Rockefeller Institute, at its sixth annual convocation, awarded thirteen advanced degrees: twelve Doctorates in Philosophy to the young scientists whose work is described in the following pages, and the thirteenth, the degree of Doctor of Science honoris causa, *to James Bryant Conant, whose richly creative career as scientist, educator, and statesman, so exemplifies the ideals of the Institute as an educational force. The degrees were conferred by President Detlev W. Bronk.*

It was just one decade ago in 1954, on the fiftieth anniversary of the opening of the first laboratory of the Institute, that the Charter was amended to make The Rockefeller Institute a graduate university, with authority to grant advanced degrees. The Institute's purpose could be stated simply: the preparation of young people for careers as professor, teacher, and investigator, the first being a combination of the second and third.

In Dr. Bronk's remarks on the occasion of the first commencement, on June 18, 1959, he stated movingly: "We are grateful to you students for many things: for your friendship, for your gay, enthusiastic zest for living, for your willingness to adventure with us in our new undertaking. You have enabled us to make the greatest contribution of a scholar, which is the inspiration and preparation of a younger colleague to carry forward the love of learning."

And in speaking of the objectives of the Institute he had concluded, "We will devote our resources, time, and effort to the furtherance of excellence, not numbers. As I have said before, in the words of Ellery Sedgwick, we will seek to influence many by inoculating the influential few." There was little doubt among those who watched the twelve tall young men step forward to receive their degrees on June 12th that they too will take their places among the influential few.

James Bryant Conant

BY DETLEV W. BRONK

University commencements are suitable occasions at which to honor some who have served their fellow men in high degree. Universities thus express our nation's gratitude and admiration for loyal servants as kings and queens of other countries do.

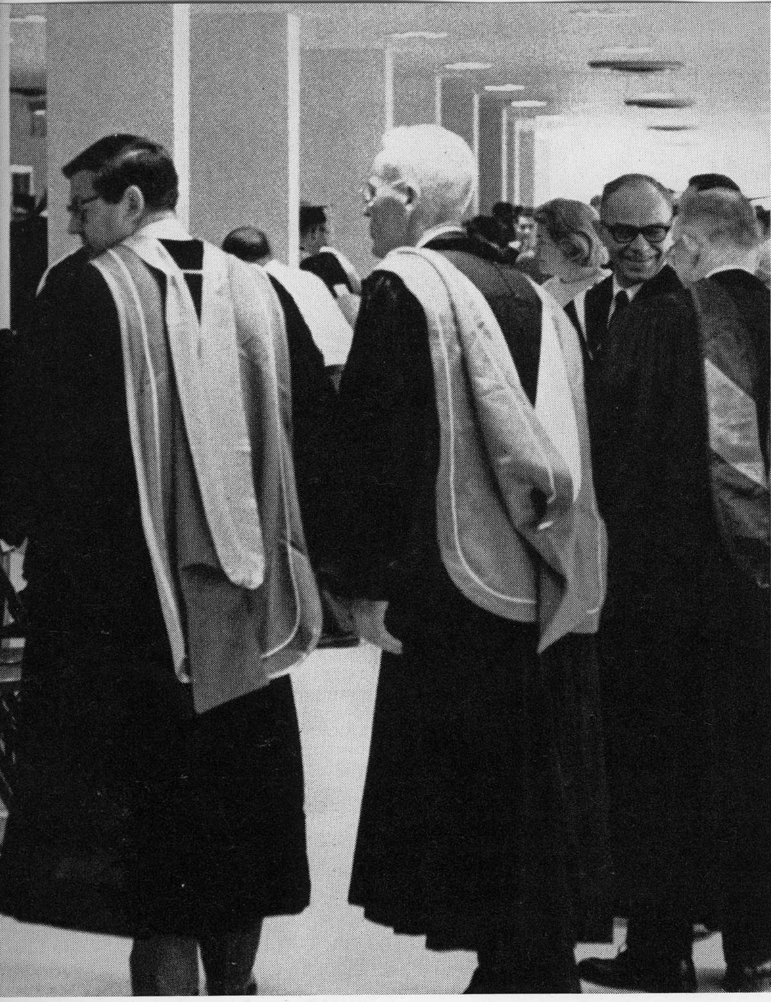
For an institution such as this the custom has deeper significance than that. It has a purpose uniquely appropriate to the day that is memorable and meaningful in the lives of young scholars as each begins a new epoch of his career. We thus associate with the graduates one whose ideals and achievements are worthy of the graduates' emulation.

James Bryant Conant is unique even among the distinguished few we have chosen in earlier years as our scholarly exemplars. Few men have served mankind in so many ways; few have had such broad competence for that service. Few with great talents have used those talents in so many worthy ways. To recount them would exceed the span of this Convocation; rather, I would speak of qualities that characterize the man who is admired with affection by all who know him well.

Never was it said of James Conant that he "darkeneth counsel without thought and knowledge." He thinks before he speaks.

Judgments matured in thought are a sure foundation for his moral courage, and that he has in abundant measure.

Deep regard for the needs and rights of others has been the motive for his life of public service during momentous years.



In five careers — but always as a scientist in mind and spirit — James Bryant Conant has been benefactor of mankind: as imaginative, creative chemist; eminent President of Harvard University for two decades; leader of scientists in wartime defense of free nations; ambassadorial healer of the scars of war in a vanquished country; catalyst of reform in elementary and secondary education.

For twenty years he was a wise trustee of The Rockefeller Institute which now confers upon him the degree of Doctor of Science, *honoris causa*, with gratitude and admiration.

David Baltimore

B.A. SWARTHMORE COLLEGE

BY IGOR TAMM

There are times in the development of a field of knowledge when the ground for the next major development is laid, but the actual advance is not likely to be made unless an investigator comes forward who clearly understands the nature of the problem and can conceive of workable approaches to its solution. It is very much to David Baltimore's credit that about two years ago he clearly understood the nature of two major problems in the biology of animal viruses: first, how viruses such as polio damage cells; and second, how their genetic material, the viral ribonucleic acid, is manufactured in the infected cell. His original and exciting work has shed new light on both of these questions.

David's interest in science was awakened early and developed through association with enthusiastic and dedicated scholars at Swarthmore — which was his own college — and at Bar Harbor and Cold Spring Harbor. During this early period his interests already had begun to focus on biosynthetic processes and control mechanisms in animal cells. Then, in 1961, after a year's graduate study in biochemistry, genetics, and biophysics at the Massachusetts Institute of Technology, David was introduced to animal viruses, first in the laboratory of Dr. Philip Marcus at Albert Einstein College of Medicine, and then through a course given at Cold Spring Harbor by Dr. Richard Franklin, at that time a member of our faculty. David found his work and study with Dr. Franklin so interesting and rewarding that in the fall of 1961, instead of returning to M.I.T., he came to our laboratory. Under the friendly guidance of Dr. Franklin, David moved forward with remarkable vigor and penetration.

The sinuous path of scientific progress is not always easy to trace, but I think in David's case the stepping stones he used and the steps he so successfully took can be readily identified.

He knew from the previous work of Franklin and Rosner that Mengovirus, an agent similar to the well-known poliovirus, rapidly stops the production in the infected cell of vitally important cellular constituents, in particular of cellular ribonucleic acid, RNA. Instead of making any more cellular ribonucleic acid, the infected cell makes viral ribonucleic acid. David also knew through the work of Reich, Franklin, and associates, that actinomycin, an anti-tumor compound which stops cellular RNA synthesis, does not interfere with the synthesis of the RNA of Mengovirus.

David asked himself how the infecting virus succeeded in stopping the production of cellular RNA, and then in making its own RNA independently of the host cell mechanism for RNA synthesis. Through

well-conceived experiments with isolated cell fractions, he was able to demonstrate two enzymatic changes that explain the metabolic changes in RNA biosynthesis in virus-infected cells. David showed that infection of cells with Mengovirus results in the inactivation of the cellular enzyme which catalyzes the synthesis of the ribonucleic acid of the cell. This inactivation appears to be mediated through a protein synthesized under the direction of the virus.

He next obtained evidence that the mechanism whereby the ribonucleic acid of the virus is manufactured involves a new enzyme capable of making viral RNA. This enzyme is normally not present in the cell, and after infection of cells with virus, the time sequence of its appearance parallels that of viral growth.

These discoveries made by David have allowed us, for the first time, to understand in enzymatic terms some of the profound metabolic changes which occur in animal cells infected with such a virulent virus as Mengo.

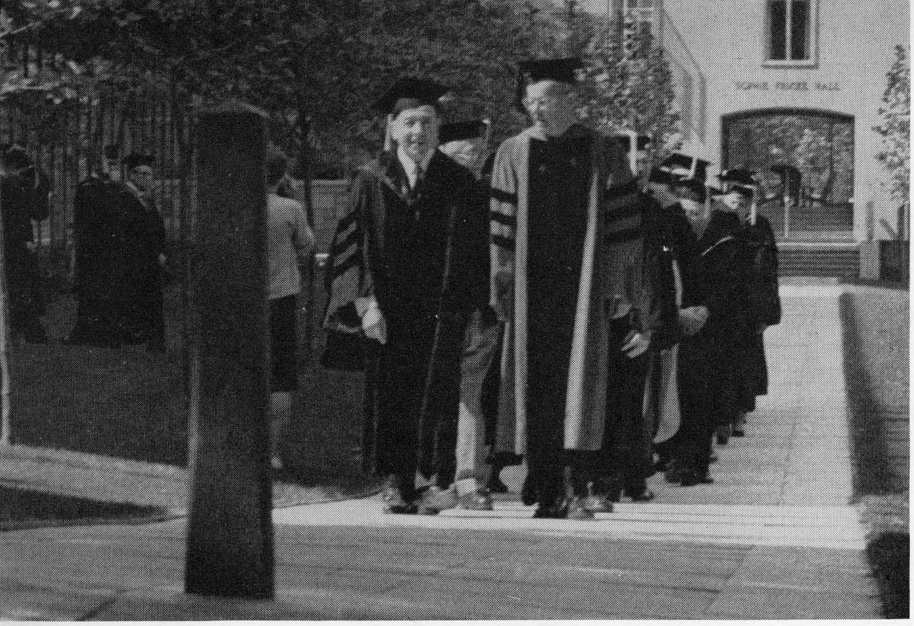
Many have come to know David as a prolific thinker searching for ever-deeper insights into the molecular mechanisms of biological phenomena, and as an experimenter who is able to subject ideas to the critical test in the laboratory. His contacts both within the Institute and outside have been wide. His wide interests encompass the humanities. David's teachers and associates have all been impressed with his broad grasp of concepts and the integrative quality of his mind. I therefore think that David has ample qualifications not only for a productive life in research but also for a rewarding life in teaching. I expect that his lively interests in science will fire enthusiasm in others; that his insights will illuminate many.

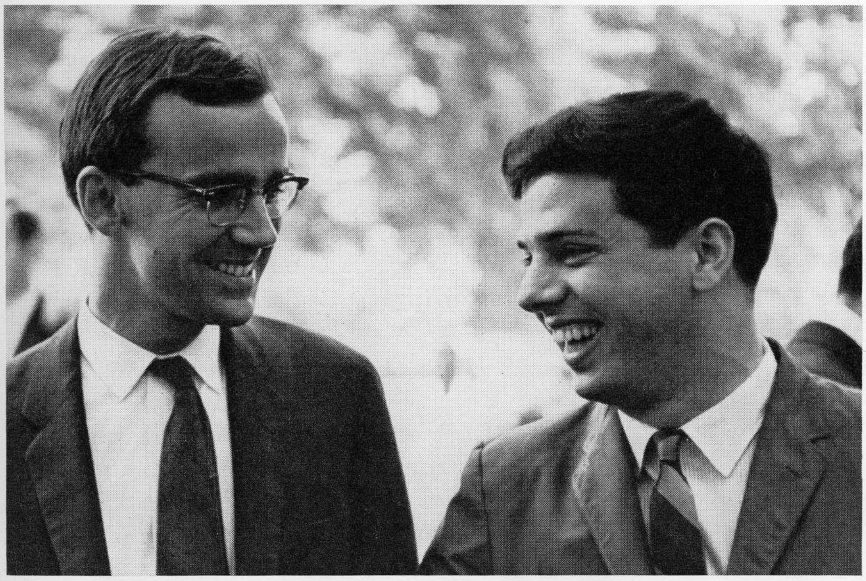
James William Fristrom

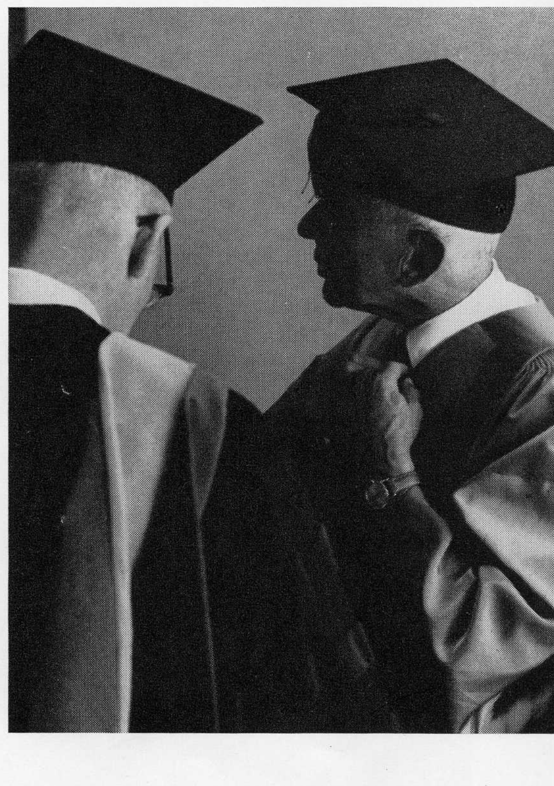
B.A. REED COLLEGE

BY EDWARD L. TATUM

One of the primary goals of the Graduate Program of The Rockefeller Institute is to train scientists in the basic disciplines, concepts, and techniques of modern biology and to equip and encourage them to explore and push back the frontiers of knowledge in new fields. In these days of almost overwhelming emphasis on molecular biology and on nucleic acid metabolism and functioning, particularly in microorganisms, it is refreshing to see one of our students devote his research interest and attention to a less







popular area, that of morphological differentiation and development in the fruit-fly, *Drosophila melanogaster.* It has been even more gratifying to follow the scientific development both of this student and of his research problem and to find that it has been possible to apply fruitfully to the fruit-fly a wide variety of modern experimental techniques, so as to add to our basic knowledge and concepts of the interrelations of genes, biochemistry, and morphology.

Mr. James W. Fristrom received his B.A. from Reed College in 1959 and entered the Institute program later that year. He soon selected as his area of research the development of *Drosophila.* Specifically, he elected to study the development of the head of this fly, using a strain in which head development was abnormal as a consequence of the mutant gene, *cryptocephal.* As the name indicates, this gene leads in the extreme case to the production of an adult fly with its head hidden within the body cavity. In his exploration of this condition of "having no head," Mr. Fristrom first inquired how the normal head is formed and how the development of the *cryptocephal* head differs from the normal. He found the critical difference to be at the stage of head emergence, a process in which the head, developing inside-out within the thorax, is turned right-side out as one blows out the indented finger tip of a rubber glove. In an ingenious series of experiments which involved exposure of the developing flies to partial vacuum, he was able to obtain normal head emergence in the mutants, and to correlate the required reduced pressure with the expression of the gene. This and other related evidence rather clearly implicated an increased structural rigidity of the head integument, or covering layer, as the important factor involved in the mutant.

Mr. Fristrom then inquired what this increased rigidity was due to, and how the gene *cryptocephal* caused the increase.

Drawing upon his knowledge that the major constituent of insect integument is chitin, a polymer of N-acetyl glucosamine, synthesized biologically from glucose and glutamine, Mr. Fristrom conducted a detailed examination of the pertinent biological reactants and reactions in the mutant and in wild-type *Drosophila.* In this he successfully developed and applied various radioactive tracer and chromatographic techniques.

He established first that the mutant indeed has a higher content of chitin glucosamine than the wild type, and that this content is correlated with the expression of the gene in the mutant population. He also established that feeding glucosamine to the wild type produced a phenocopy with more chitin than normal and greater resistance to head eversion. He then showed that glucose is more rapidly converted to chitin in the mutant. Combining this information with the detection of various phosphorylated intermediates, and with the demonstrated lower levels of glutamine and higher levels of glutamic acid in the mutant, it seemed clear that *Drosophila* chitin is synthesized from glucose phosphate by the "classical" pathway established in other organisms, and that the *cryptocephal* gene increases the effectiveness of this synthesis. It thus leads to the typical morphological character of the mutant.

Surprisingly, Fristrom found that glucosamine is less effectively converted to chitin in the mutant, and that N-acetyl glucosamine counteracts the effects of glucosamine in the wild type, but has little effect on the mutant. With ingenious insight, Fristrom has proposed an interesting hypothesis in which these latter findings represent the action of modifier genes which increase the viability of the mutant by counteracting the primary effect of the *cryptocephal* gene in increasing chitin synthesis.

In summary, then, Mr. Fristrom's work has resulted in a better understanding of the molecular events underlying the action of a gene affecting and controlling morphological differentiation. Even more significantly his work has demonstrated an understanding of the concepts and problems of the frontiers of biology and an ability to apply biochemical techniques toward pushing back these frontiers. He has thus admirably fulfilled the goals for which the Institute Graduate Program stands.

Joseph Anthony Gally

B.A. POMONA COLLEGE

BY GERALD M. EDELMAN

Every student of medicine worth his salt knows that the presence of so-called Bence-Jones proteins in the urine of a patient points to a diagnosis of the malignant disease, multiple myeloma. Not every medical student yet knows that an understanding of the struc-

ture of these proteins is essential to an understanding of antibodies and immunity, although undoubtedly this notion will soon be a commonplace of medical texts.

Mr. Joseph Gally has played a major role in establishing this concept by helping to show that Bence-Jones proteins are in fact polypeptide chains that contribute to the formation of antibodies. In doing so, he has helped to solve a major medical mystery that was noted in 1845 when two British practitioners, MacIntyre and Watson, attended a grocer afflicted with multiple myeloma. They found that his urine contained a substance which became insoluble when heated to moderate temperatures. Watson sent a note to Dr. Henry Bence-Jones, an eminent chemical pathologist, asking, "What is it?" The answer is now at hand. Bence-Jones proteins are the so-called light polypeptide chains of antibody molecules.

But it is not only as puzzle-solving that this accomplishment is outstanding. It has unified a welter of hitherto unconnected facts in immunology, pathology and protein chemistry, as even a brief survey of Mr. Gally's specific accomplishments will show. From his refined analysis of the interaction of Bence-Jones proteins with each other, he has developed the first working model of the molecule. It consists of two light polypeptide chains linked by a single disulfide bond, and it provides the starting point for further chemical studies in this field.

Turning his interest to the peculiar insolubility of heated Bence-Jones proteins, he proceeded to devise new optical methods of analysis. The methods follow the thermally induced unfolding of the protein by measuring accompanying changes in its natural fluorescence. These delicate physical techniques will become generally useful; indeed Mr. Gally has already shown that they may be applied to a variety of proteins in addition to Bence-Jones proteins.

A word should be said about the unpredictable paths of scientific inquiry, for Joseph Gally is a physical chemist, but he interested himself in a medical problem. As a result of his curiosity, this problem was solved, new methods in the physical chemistry of proteins were developed and immunologic concepts have been expanded. Here is a resounding rebuttal of the position of narrow specialization and technology. It is not impertinent to note that Dr. Henry Bence-Jones the biologist was Michael Faraday's friend and biographer. Mr. Gally stands in this tradition.

These days, the word argument has unfortunately taken on a pejorative flavor. To argue a scientific problem with Joseph Gally is on the contrary an enlarging experience for he knows how to explore an idea. His broad studies here have strengthened this gift. It is a privilege, Mr. President, to recommend him to you as a fellow scholar.

Bruce Sherman McEwen

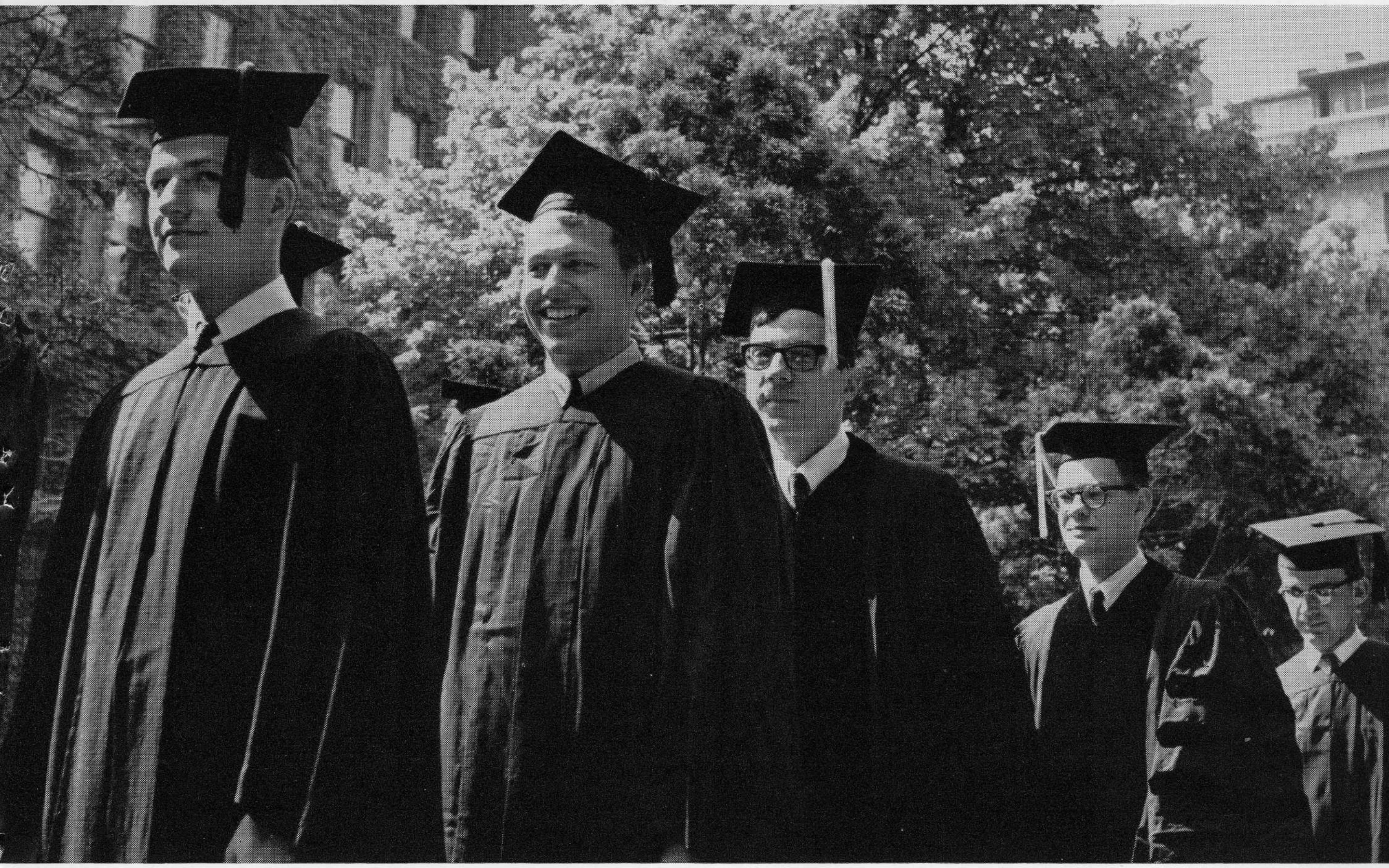
A.B. OBERLIN COLLEGE

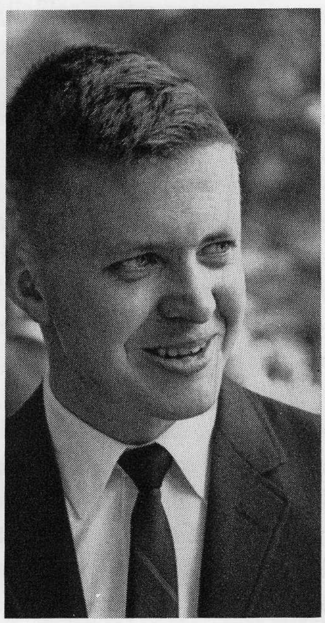
BY VINCENT G. ALLFREY

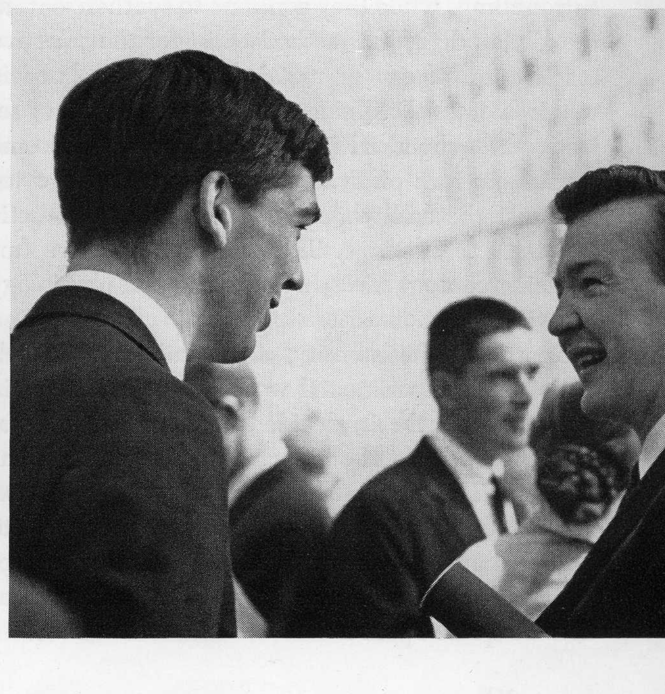
Bruce McEwen came to The Rockefeller Institute in 1959. He was a graduate of Oberlin College, where he had taken a major interest in Chemistry. During his first year at the Institute he discovered that a fellow graduate student, Johns W. Hopkins, was in the midst of an exciting problem – on how the cell nucleus synthesizes its proteins. It was clear at that time that synthetic reactions in the nucleus did not proceed spontaneously but required a constant input of chemical energy; this was usually required in the form of adenosine triphosphate (ATP). Bruce McEwen immediately became interested in the source of this nuclear energy; energy which must, in the last analysis, power the genetic control centers which regulate the life of the cell.

A more promising fundamental research opportunity could hardly be imagined, and yet there were good reasons for caution and hesitation. It was widely believed that virtually all of the ATP required for cell function was synthesized in the cytoplasm, by specialized particles (the mitochondria). Indeed, the mitochondrion had long been referred to as the "powerhouse of the cell." What Bruce McEwen did was to show conclusively that the nucleus did not depend on these distant dynamos for its ATP-energy supply. On the contrary, the nucleus seemed to have its own cascades and fires which could operate independently of the rest of the cell.

Naturally, such a view of independent nuclear respiration and ATP generation required sound experimental proof. It must be said to Bruce McEwen's credit that, even after the difficulties were made clear







to him, he did not hesitate to attack this formidable problem which required continuous critical evaluation.

It was hard and demanding work; often nuclei had to be isolated by four different methods to verify the results obtained using any single procedure. He learned many new techniques and learned them well. For a time there was a very fruitful contact and exchange of information with Dr. Britton Chance and his coworkers. This led to electronic measurements of respiration in isolated nuclei. Under the generous and able guidance of Dr. Maria Rudzinska, he learned the cytological techniques of electron microscopy and began to examine nuclear and mitochondrial preparations for purity as well as biochemical function. As time went on, he made extensive use of radioactive tracer techniques to follow the oxidation of sugars and other metabolites in isolated nuclei.

His work now appears in his thesis and in four major publications, any one of which reflects credit on his knowledge, ability, and critical perception. He has scored a number of important "firsts," among them 1) the discovery that nuclei have a complete, functional cycle for the oxidation of tricarboxylic acids, 2) that nuclei have enzymes which transfer electrons from pyridine nucleotides to flavin nucleotides, 3) that basic proteins (histones) derived from the nucleus can inhibit the function of mitochondria, 4) that nuclei reject and degrade ATP added to their surroundings while they continue to synthesize it internally, and 5) that methods exist for the selective inactivation of energy metabolism in mitochondria within living cells. Using the latter technique of selective mitochondrial inhibition it has now become possible to turn off synthetic reactions in the cytoplasm of the cell while allowing nuclear synthetic processes to continue. This finding may have far-reaching consequences in studies of cell physiology and viral infection.

Apart from the intensity, scope, and general excellence of his experimental work, Bruce McEwen, in preparing his thesis, decided to include a general review of the field of energy metabolism and nuclear function. This account is a work of scholarship and understanding which can be highly recommended to the graduate fellows and faculty both as a source of information and as a model of training and preparation. To quote Spenser:

"So double was his pains; so double be his praise."

Bruce McEwen has now set out with a new problem; that of understanding the biochemical processes underlying the function of nerve cells. For the past half year he has been working with Dr. Holger Hydén at the Institute for Neurobiology in Göteborg, Sweden. I know that Dr. Hydén, if he were here, would agree with me that Bruce McEwen is a credit to The Rockefeller Institute, both as a scientist and as a fine and sensitive human being.

Donald Edward Olins

A.B. THE UNIVERSITY OF ROCHESTER

BY GERALD M. EDELMAN

In the course of his scientific studies, Donald Olins has been constantly concerned with chemical specificity, a problem that pervades all of biological research. In no field is this problem more exquisitely framed than in immunology, and in no branch of immunology is it more accessible to attack than in the study of humoral antibodies. These are large protein molecules which appear in animal blood after the injection of various chemicals known as antigens.

It was particularly through the achievements of Karl Landsteiner at The Rockefeller Institute that the enormous specificity of antibodies was first fully appreciated. By specificity we mean the capacity of antibodies to recognize and interact with just that type of chemical structure present on the injected antigen, and with no other. What properties of antibody molecules endow them with this capacity?

Mr. Olins realized that the answer to this question depended largely on the chemical analysis of antibody molecules. Guided by the hypothesis that specificity resulted from the spatial arrangement of polypeptide chains of which the antibody molecule is composed, he devised a variety of techniques for their separation and characterization. He reasoned that if antibodies could be reformed in the test tube by mixing their separate polypeptide chains, particularly those of different origin, then their specificity might be altered. He succeeded in his first task and showed that an active antibody molecule could be rebuilt from its separated subunits. Encouraged, he went on to build new molecules composed of polypeptide chains from different antibodies and even

from antibodies of two different animal species.

By applying delicate tests of function to these newly formed molecules, he provided direct support for the notion that specificity results from the interaction of different polypeptide chains in space. Thus, he showed that only those molecules reformed from chains originally derived from the same antibodies were capable of interacting well with the corresponding antigen. This is a remarkable accomplishment and will provide a rich harvest for immunologists of the future. It has technical implications that will extend the range of his chosen discipline.

Science is not the sum of its techniques, however, nor even of its disciplines, and it is a mark of his growth at The Rockefeller Institute that Donald Olins has recognized this. He has studied broadly, discussed with others and tried to understand. At the same time he has appreciated the importance of details and the dangers of glib generalization. His concern with generalities buttressed by detail is reflected in his present plans to study chemical specificity in other biological domains, notably in growth and development.

His enthusiasm and great skill are now guided by a growing wisdom. It is with confidence that his continuing interest will expand and illumine the sciences of biology that I propose him to you as a scholar, Mr. President.

Richard La Mott Purple

A.B. HAMILTON COLLEGE

BY H. KEFFER HARTLINE

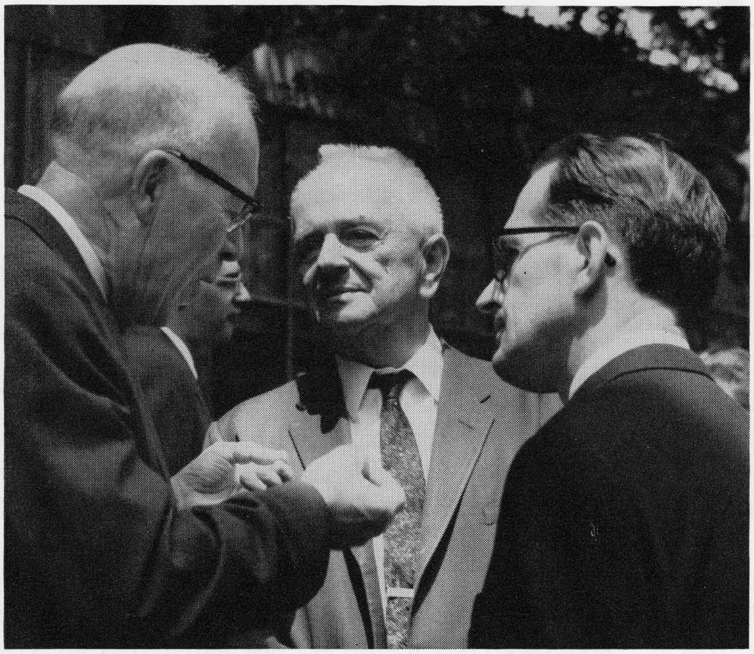
The cell is the basic unit — structural and functional — of the living organism. Its molecular mechanisms are studied to elucidate its actions; its actions and its interactions with other cells constitute the integrated activity of the organism. Mr. Richard Purple in his thesis research undertook the study of a nerve cell in the eye. Nerve cells have a special responsibility in the integration of the activity of the entire organism; those in receptor organs stand at the boundary between the organism and the world it lives in.

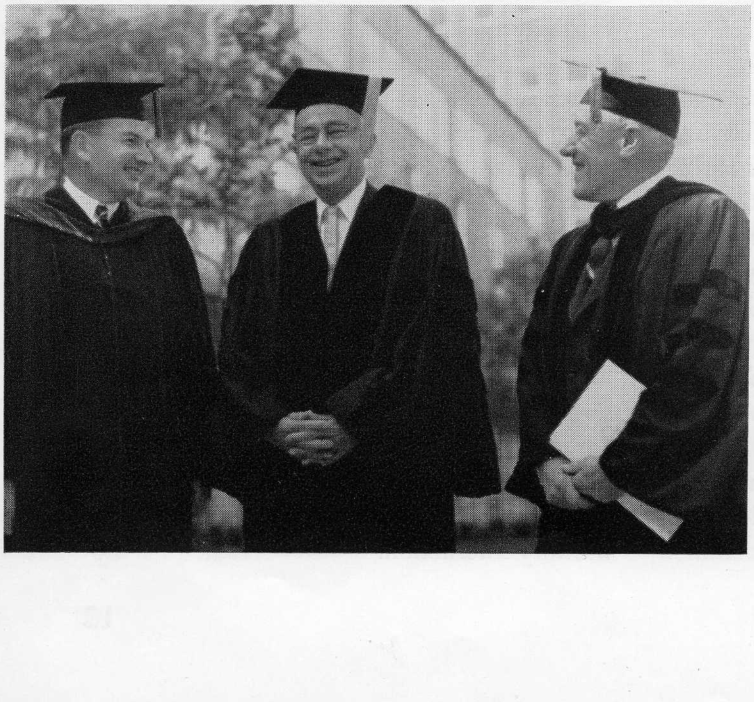
In all nerve cells, electrical phenomena are an essential concomitant of action. Mr. Purple's research concerned the electrical activity of a special kind of nerve cell found in the compound eye of our common horseshoe crab, *Limulus*. Behind each facet in this eye is a cluster of light-sensitive receptor cells; associated with each such cluster is one of these special neurons, which when excited by illumination of the receptors discharges a train of nerve impulses in the optic nerve fiber to which it gives rise.

In *Limulus* the facets of the eye are coarse, and the sensory cells large and especially suitable for electrophysiological study. A fine glass pipette electrode — that ubiquitous instrument of modern electrophysiology — may be thrust into them without causing serious damage, and with its aid a detailed analysis may be made of the electrical properties of the cells, both at rest and during illumination of the eye. By measuring voltages, by passing electric currents of known strength, Mr. Purple showed that light, acting by the mediation of the receptor cells that surround the outer end of the neuron, causes an increase in the ease with which the common inorganic ions pass across that part of the cell's membrane. As is well known for other neurons, such a partial short circuit, by depolarizing the entire cell membrane, can generate trains of impulses in the neuron's nerve fiber. Mr. Purple's analysis provides an explicit quantitative formulation of part of the excitatory process whereby light, absorbed by the photosensitive substance of the receptors, elicits the sensory nerve message.

The retina, even in a primitive animal, is a complex nervous center. Receptor units in the retina interact with one another — a first step in the interpretation of the visual image by the nervous system. In the *Limulus* eye, the interaction is no more than a simple inhibition of near neighbors by one another, but it is the basis for contrast effects in vision, for sharpening of contours and for the emphasis of movement in the patterns of light and shade in the visual image. Mr. Purple has elucidated the mechanism of the inhibitory process in the visual neuron in *Limulus*. He has shown that it is a typical instance of synaptic inhibition in nerve cells in general. As in other neurons, specific ionic mechanisms act to restore the electrical polarization of the cell membrane, thus antagonizing the depolarizing effects of excitation. Mr. Purple's results provide us with an explicit quantitative formulation of the inhibitory mechanisms in the *Limulus* retina, on which to base a theory of inhibitory interaction.







It is not the primary function of the doctoral thesis research to add to the store of highly specialized knowledge. Rather it is to serve as a focus for the education of a beginning scholar in diverse fields. Diversity of experience Mr. Purple has certainly had, in both physical and biological specialties. The list is long; it even includes a little field zoology, with a trip to collect animals – and get stopped by the police for unwitting trespass on a private beach. Rick Purple's thesis research, I think, has served him well. And if some new and valuable understanding of cellular physiology has been a by-product – and it most certainly has – that is not only an added reward, but is undeniable proof of the success of the educational process.

James Harris Schwartz

A.B. COLUMBIA UNIVERSITY

BY FRITZ LIPMANN

James Schwartz had just finished medical school at New York University when he came to us. During his later medical years he had already spent much time in the laboratory; now he could wholeheartedly become involved in the adventurous chemical exploration of genetic events.

I much admired his courage when he grasped a promising but difficult opportunity, that of connecting enzyme chemistry with genetics. The object of his study was the alkaline phosphatase of the much-explored microbe, *Escherichia coli*. The genetic background for production of this enzyme was well known, and from work with analogous phosphatases, a way had already been suggested of marking its active center by incubation with inorganic phosphate. He easily demonstrated an esterification of P^{32}-phosphate with a particular serine, and succeeded in obtaining by acid hydrolysis several small peptides containing serine P^{32}-phosphate. Then, a characteristic tetradecapeptide was isolated from pepsin-trypsin digests and the amino acid sequence around the serine was elaborated in this large enzyme fragment. The successful resolution of this problem was possible only through the interest and active collaboration of Drs. Crestfield and Stein. The amino acid sequence in part of the active center, thus is now available for studying mutational effects on enzyme action.

By now, Jim Schwartz had become an accomplished protein chemist. His skill in the art of fingerprinting proteins by chromatographic spreading of a tryptic digest into characteristic patterns found many applications.

To mention only one example, he collaborated with Nathans, Notani, and Zinder on the *in vitro* synthesis of the coat protein of f2 phage with phage RNA as the template.

Through his analysis of the phosphatase he penetrated into the inner sanctum of an enzyme. He discovered a striking similarity between the functional part of phosphatase and that of other hydrolases such as choline esterase or chymotrypsin. And further exploration of the mechanism of reaction between enzyme molecule and phosphate has led him to propose an interesting interpretation of enzymatic hydrolysis.

Jim Schwartz's enthusiasm and capacity to explore and understand is enormous and he will, I am sure, find out a great deal that is new about the mechanisms of enzyme action and genetics at N.Y.U. where he has returned in a new capacity. He was a spirited and wonderful companion in the laboratory and we miss him.

Charles Franklin Stevens

A.B. HARVARD COLLEGE

M.D. YALE UNIVERSITY SCHOOL OF MEDICINE

BY FLOYD RATLIFF

Charles Stevens and I first met about 10 years ago when he was an undergraduate at Harvard College. He came to me then for some advice about his course of study and research and, as I recall, I recommended that – among other things – he study the integrative neural mechanisms that underlie the behavior of organisms. This seemed to be such good advice that I took it myself, and when the opportunity arose a short time later I came to The Rockefeller Institute to work with Dr. Hartline. Dr. Stevens did the same, after he graduated from Yale Medical School in 1960, and as a result of all this I now have the pleasant duty of giving this brief account of his work here.

Artists have known for centuries that the apparent color and brightness of one object may be greatly modified by placing another object of a different

color and brightness next to it. Nearly 100 years ago, Ernst Mach — the well-known Austrian physicist — suggested that these and other contrast effects might result from inhibitory influences which spread laterally in the retinal network and oppose the excitatory influences generated in neighboring regions. The results of modern electrophysiological experiments, in which the electrical signs of these opposed influences can be recorded directly from some elements in the retina, lend much support to this view.

The aim of Dr. Stevens' research was to develop a precise quantitative theory to describe the algebraic summation of opposed excitatory and inhibitory influences, for this now appears to be one of the fundamental processes by means of which neurons in all parts of the nervous system integrate the information that they receive, and by means of which they generate information to be passed on to other neurons. In order to make his theory generally applicable, Dr. Stevens based it on a wide variety of relevant experimental observations that had been made on many different species and in many parts of the nervous system. But once the general theory had been formulated he put it to a direct and specific test by comparing calculated results with actual observations of neural responses in a particular system — the retina of the horseshoe crab, *Limulus*.

Dr. Stevens is an able mathematician and we were not much surprised when he showed that the behavior of his theoretical neural network and that of the real neural network seemed to be exactly equivalent in the steady state. But I think that he was a little surprised, later on, when he found that the two networks did not respond in the same way to abrupt changes. Where he expected the frequency of discharge of impulses to be uniform he found instead a high initial frequency which gradually declined to a steady frequency. Happily, this apparent disaster was turned to good account. After carrying out a number of ingenious experiments and theoretical computations Dr. Stevens concluded that the decline in frequency could be produced by "self-inhibition." That is, each nerve impulse generated in the neuron under observation gives rise to a small inhibitory potential which acts on that neuron itself. This immediate negative feedback results in a gradual slowing of the discharge until a steady state is reached. This interpretation has recently been reinforced by the observation of minute changes in membrane potential associated with the production of each nerve impulse in the *Limulus* eye. These local potentials appear to be electrical signs of the very self-inhibition that Dr. Stevens predicted. Thus for Dr. Stevens' work the value of the mathematical account was to be found not only in the compactness with which it could describe complex neural interactions, it also enabled him to gain insight into the nature of certain neural processes that had not been previously observed in experiments. In short, Dr. Stevens used his mathematical theory as a tool of investigation as well as a mere descriptive device.

Research on special topics is but one part of graduate study, and I would give a false impression of Dr. Stevens' breadth of interest and knowledge if I did not mention his general studies. They have ranged from the physical and chemical bases of the behavior of single cells to the physiological and psychological bases of the behavior of organisms, and from pure mathematics to theoretical and experimental physics. I can say with confidence that he is well prepared for a career as an investigator and a teacher in the field of biophysics.

Dr. Stevens completed his thesis research and general studies last summer and has since been Assistant Professor of Physiology and Biophysics at the University of Washington Medical School. We therefore do not have to speculate about what he might accomplish in his first year away from The Rockefeller Institute. I can tell you now that he has had a successful year in teaching and research; that he is now working on the final chapters of a textbook on neurophysiology; and — most important for the events today — that he completed the final version of his thesis — yesterday.

Also, we do not have to speculate about what things will be like in our laboratory after Chuck leaves. I know — after a year of experience — that I will miss his willing help in straightening me out when I get entangled in mathematical problems; we will miss the stimulus of his insatiable curiosity about everything and everybody; we will miss his arguments with Rick Purple about self-inhibition; but — above all — we will miss him as anyone misses a close friend who is on the other side of the continent.

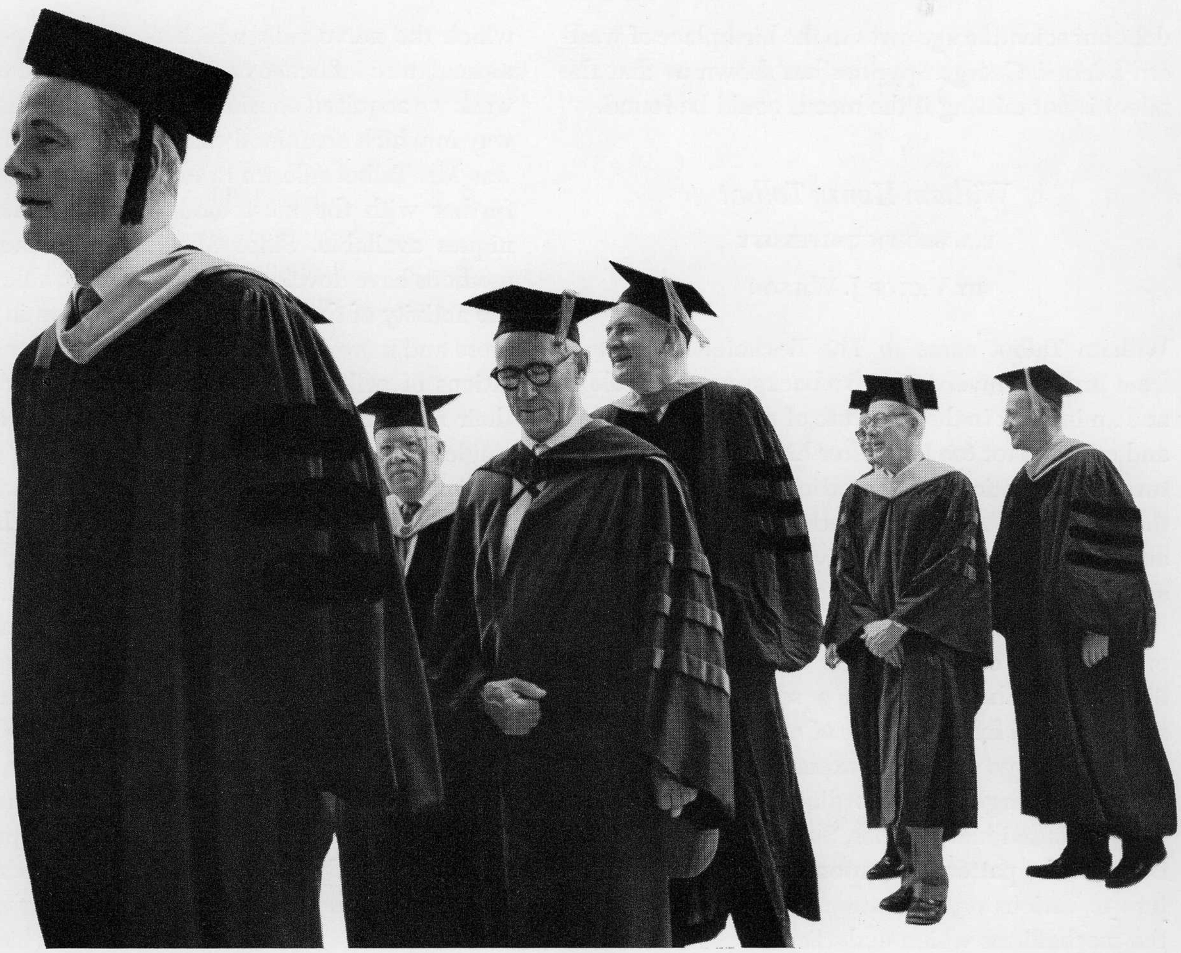
George John Spyrides

A.B. DARTMOUTH COLLEGE

BY FRITZ LIPMANN

When George Spyrides came to us, he was already seasoned by having worked in a number of fine laboratories. With us he quickly became absorbed in protein synthesis as part of genetochemistry. His early work was concerned with whether, as some thought, the information contained in messenger ribonucleic acid was expressed only once in a microbial protein and was destroyed then, or if it was used repeatedly. Although in fast-growing bacteria, the message is indeed destroyed relatively rapidly, with cell-free systems of *E. coli* and a simplified messenger nucleic acid, polyuridylic acid, Spyrides could show that the message can be used many times for specific synthesis of polyphenylalanine. The RNA, therefore, acting as a catalyst, is "read" several times before destruction. He then continued studies with the system and made one of the earliest observations on the manner in which the message-carrying RNA connects a number of intracellular particles, the ribosomes, to form the polyribosome complex that is the active center of protein synthesis.

George Spyrides is very good at putting results together and visualizing their significance. His work here soon caught the attention of other groups and he is now continuing it at the Harvard Biological Laboratories. I know he dreams of returning at some time in the future to Greece, his home, to help create there a renaissance of science. I wish the western world could help Greece by honoring the immense



debt our scientific age owes to the birthplace of western science. George Spyrides has shown us that the talent is not missing if the means could be found.

William Henry Talbot

B.A. BROWN UNIVERSITY

BY VICTOR J. WILSON

William Talbot came to The Rockefeller Institute from Brown University with a background in biology and an interest in the structure of mammalian tissues and organs. Not too long after his arrival his interest turned to functional organization and particularly to the integrative action of the central nervous system and to that aspect of its activity which controls an animal's movement.

The complex organized activity of which the mammalian spinal cord is capable was first analyzed by Sir Charles Sherrington in a series of pioneering studies which form the basis of modern central nervous physiology. From his experiments, which were carried out largely by recording the mechanical activity of individual muscles, Sherrington was able to describe the pattern of response of the leg musculature to various types of stimuli, to explain many of the mechanisms which underlie this pattern, and to suggest the nature of the synaptic phenomena by which the nerve cells which control the peripheral musculature influence one another. From this kind of work we acquired considerable understanding of the way in which an animal can stand, walk, and run. It was Mr. Talbot's desire to explore these phenomena further with the most modern experimental techniques available. Since Sherrington's time, as our methods have developed, we have been able to study the activity of the central nervous system in terms of more and more discrete units. The behavior of populations of cells has been investigated by recording their mass discharge in nerve trunks. The action of single cells has been analyzed by recording their potentials in axons isolated by dissection. Finally, the introduction of the ultrafine microelectrode has made it possible to study the electrical activity taking place inside single cells within the brain and spinal cord. By means of this approach, a large body of knowledge has been accumulated concerning the properties of nerve cells and the manner in which they interact. Much of this work has been carried out by means of electrical stimulation of nerves, a technique of immense usefulness, but nevertheless one which applies a distorted and artificial input to the cell under study. It has been Mr. Talbot's goal to apply the latest techniques of recording and data analysis to a study of the manner in which spinal motoneurons respond to stimuli more closely related

to those to which an animal is normally exposed, such as touch and pressure applied to the skin. The results of his thesis work show the value of the combination of natural stimulation and intracellular recording.

Mr. Talbot's studies have added significant information to our previous knowledge of the behavior of nerve cells. In throwing new light on the discharge properties of cells, they have emphasized the close correspondence of these properties of motoneurons to the properties of the muscles they innervate and have demonstrated that many of the unusual discharge patterns that can be observed are not artifacts due to electrical stimulation. Furthermore, it has been possible to correlate the behavior of individual cells with that of the complex reflex responses originally described by Sherrington and to show the great similarity of the responses of single units and the responses of whole populations. Finally, this work points to a program of research which may lead eventually to a proper understanding of the production of long-lasting reflex discharge in spinal motoneurons and of the generation and control of rhythmical activity, in other words to a better understanding of the phenomena which make coordinated movement possible.

In carrying out his work Mr. Talbot has acquired a broad competence in many areas of knowledge, some close and some peripheral to his main field of interest. He has also demonstrated a great ability to communicate his knowledge to others. It has been a stimulating as well as a pleasant experience having Mr. Talbot in our laboratory and I look forward with anticipation to his future accomplishments in teaching and research.

Richard Vance Wolfenden

A.B. PRINCETON UNIVERSITY

BY LEONARD B. SPECTOR

The putting together of protein molecules from their component amino acids is one of the major chemical activities of the living cell, and the study of this phenomenon is in turn the major activity of a large number of the world's biological laboratories. It has engaged, and continues to engage, the attention of some of our best minds. As we presently know it, the process of protein synthesis is an intricate one, with many stages following one on another in ordered sequence. We think we understand some few of these stages, but we also know clearly that the rest of them are currently outside our knowledge and comprehension.

One of these stages, formerly outside of our knowledge, has lately been illuminated through the perceptive use of chemical methods by our candidate, Richard Wolfenden. Amino acids, subsequent to their necessary activation, are transferred to what is called soluble ribonucleic acid, the point of chemical attachment being at one extremity of the molecule, which is to say, at one or the other of two adjacent oxygen atoms. Ever since the discovery of this fact some years ago, investigators have striven to learn which of these oxygen atoms represents the actual point of linkage to the activated amino acid. It fell to Richard to reveal that, with the methods now available, it is quite impossible to state surely which is the true site of attachment, because the amino acid appears to jump back and forth from one oxygen atom to the other; and the rate of this movement is altogether too rapid for the investigator to securely ascertain which oxygen the amino acid is on at any given moment. This astonishing result, while clarifying much, has also created new problems, but then the appearance of new problems is often a consequence of good research.

Telling you thus briefly of the nature of Richard's work here leaves untold the manner of its doing. The indispensable element in the successful prosecution of this investigation was the highly professional use of the methods of physical organic chemistry. The acquisition of facility in this exacting discipline was for Richard a feat of self-education, but he had early in life heard the call of chemistry and chemistry came easy to him. The union of chemistry and biochemistry in our candidate has already yielded notable progeny and promises more for the future.

Although he is zealous in the pursuit of his professional goals, Richard enlivens his zeal with a fresh and beguiling style of humor, which has cheered many a dreary day for his associates and has refreshed me personally with many happy laughs. If for no other reason than this, his departure from us will be felt.

It is idle to attempt to predict what a man will or will not achieve in his future career; the best one can

do is to make a judgment of his capabilities on the basis of what you know of him now. And what we know of him now impels us to affirm with pride that Richard Wolfenden is capable of the very best.

Coleman Peter Wolk

S.B., S.M. MASSACHUSETTS INSTITUTE OF TECHNOLOGY

BY ALFRED E. MIRSKY

What is it that takes hold of a person and draws him into biology? Some of our colleagues were in their childhood bird watchers or collectors of beetles and butterflies. For them the pathway into biology was simple and direct, even if they have ended up working with oscilloscopes or scintillation counters.

Peter Wolk's route was very different, indeed. I do not know about his childhood, but I cannot help believing that he did chase an occasional butterfly. I do know that before coming to the Institute he studied mathematics and physics at the Massachusetts Institute of Technology and that he did not study either biology or chemistry. Now, six years later, he has his mind on cell differentiation and talks about such things as calcium glucuronate.

When we see someone turning from physics to biology we are somewhat surprised because, as biologists, we admire the magnificent achievements of physicists. We should, however, not forget that in the past three centuries some of the greatest physicists have taken an active interest in biology. It is always a delight to look into Galileo's *Dialogues Concerning Two New Sciences,* published in 1638, and see how he often chooses examples in living organisms to illustrate his discoveries in mechanics. When, for example, he proved that the strength of a hollow tube exceeds that of a solid cylinder for the same weight of material, he gave examples in engineering of course, but he was also intent to show that in the long bone of a bird's wing, tubular construction is manifested in its perfection and that the thin tube of the wheat-straw bearing its heavy burden in the ear also illustrates this mechanical principle.

One hundred and fifty years later Laplace and Lavoisier published their celebrated memoir on heat in the course of which they describe their experiments on the respiration of guinea pigs. This work, one of the foundations of physiology, was done in the same years in which Laplace and Lagrange pursued their enquiries concerning the stability of the solar system.

So in moving about, from physics to biology, Peter Wolk is in very good company.

In their first year at the Institute all of our students have important decisions to make. I do not know what was going on in Peter's mind, but I can say something about the thoughts that some of us were having about him. Would he become a theoretical biologist, or would he work in the physicochemical borderlands of biology, or would he put his hands right into the stuff of life? Peter's decision was characteristically forthright. He decided to study development, surely no borderline problem in biology.

At this time Peter came under the wing of Professor Armin Braun. He was taught the elements of Botany and Plant Physiology by Dr. Braun and others in the laboratory. Later he carried on his research under the supervision of Dr. Braun. I am very sorry that Armin Braun is not well enough to be here today.

The problem which Peter chose for his thesis was the nature of the effect which one cell type has upon other cell types in the course of differentiation and development. Recognition of the importance of changes induced in cells by contiguous cells has come mainly from experiments on animals, especially amphibians and echinoderms. Choice of material is of the first importance in biology and, recognizing this, Peter decided that he could simplify the problem by going far down in the scale of living creatures; and so he chose to work with the blue-green algae.

The alga he chose has three types of cells: vegetative cells, heterocysts, and spores. Sporulation generally takes place adjacent to heterocysts. Is this indeed an inductive process and, if so, what is the underlying metabolic system? In a systematic study the conditions promoting active sporulation were worked out and an insight was gained concerning the role of certain metabolites.

At this point we are interested in Peter as well as in the alga. I shall therefore conclude with Professor Braun's opinion —"I feel that Peter has a very promising future in the biological sciences since he possesses many, if not all, of the attributes necessary to make a productive and creative scientist."

NEWS AND NOTES

MAX PLANCK MEDAL

Professors George E. Uhlenbeck and Visiting Professor Samuel A. Goudsmit have been awarded the Max Planck Medal of the German Physical Society. In 1925, Professors Uhlenbeck and Goudsmit, both of whom received their education in the Netherlands, discovered the "spin of the electron," a cornerstone of present atomic theory. They came to this country in 1927 and joined the faculty of the University of Michigan. During World War II both were connected with radar research at the Massachusetts Institute of Technology. Professor Uhlenbeck has been at The Rockefeller Institute since 1961. Professor Goudsmit, who is also Deputy Chairman of the Department of Physics at the Brookhaven National Laboratory, has been a Visiting Professor at The Rockefeller Institute since 1956. Albert Einstein, Niels Bohr, Lise Meitner, Enrico Fermi, Wolfgang Pauli, Lev D. Landau, and Eugene P. Wigner have been among the previous recipients of the Medal.

HONORARY DEGREES

To Theodosius Dobzhansky, from Columbia University, on June 2, the degree of Doctor of Science, "you disclose with clarity solutions long sought by man in his unending survey of his nature."

To Theodosius Dobzhansky, from Oxford University, on June 24, the degree of Doctor of Science, "praesento vobis virum musicae, picturae, equestris disciplinae studio insignem, doctrinam plurimas per terras et consecutum et largitum, cuius nomen stabit dum avi numerantur avorum."

To Loren C. Eiseley, from Pace College, on June 7, the degree of Doctor of Humane Letters, "to this scholar who has contributed much to our understanding of ourselves, who has preserved a place of wonder and reverie in the laboratory."

To Rafael Lorente de Nó, from Clark University, on June 7, the degree of Doctor of Science, as a "surgeon, scientist, sensitive interpreter of life, his long and distinguished career has had an international scope for over 45 years."

To Edward Lawrie Tatum, from Rutgers, The State University, on June 2, the degree of Doctor of Science, "a leader in opening new areas of scientific endeavor."

To Edward Lawrie Tatum, from the University of Wisconsin, on June 8, the degree of Doctor of Science, for "distinguished and original contributions as a thinker and a research worker in the fields of microbiology, biochemistry and genetics."

To Donald K. David, Trustee, from the University of California, at Los Angeles, on June 11, the degree of Doctor of Laws for the "encouragement of the discovery and application of knowledge in many fields and in many nations."

BOARDS AND COMMITTEES

President Bronk has been elected to the Board of Trustees of the Rensselaer Polytechnic Institute. This spring Dr. Bronk was also re-elected to the Board of Trustees of the University of Pennsylvania, and continues as a trustee of The Johns Hopkins and Bucknell University.

Professor D. D. Van Slyke, Member Emeritus of The Rockefeller Institute, has been appointed one of the four members of the Committee of Scientific Advisors of the Biochemical Research Institute of the American Medical Association's Education and Research Foundation. The Institute will begin functioning next year when laboratories are completed in Chicago.

SEDGWICK LECTURE

The second Ellery Sedgwick Memorial Lecture in Literature was given in the Caspary Auditorium on May 25 by Charles E. Wyzanski, Jr., District Judge of the United States Court in Boston. Judge Wyzanski's address was entitled "Both the Saying and the Thinking."

Judge Wyzanski was presented by Edward Weeks, present Editor of *The Atlantic Monthly,* who described with humor his own affectionate recollections of his predecessor, Ellery Sedgwick. Mr. Weeks was introduced by President Bronk.

Judge Wyzanski engaged his listeners both by the lively content of his address and its delivery. His lecture was enriched by a great variety of quotations, all of which were given, to the great admiration of the audience, without any recourse to notes. His talk concluded with a passage from the poem of William Butler Yeats, "A Dialogue of Self and Soul." The text of Judge Wyzanski's address will appear in a future issue of the *Review*.

In addition to his position as United States District Judge, which he has held since 1941, Judge Wyzanski has served as a lecturer on government at Harvard College, a Visiting Professor at the Massachusetts Institute of Technology, and is a trustee of the Ford Foundation, a member of the International Labor Organization, and a Fellow of the American Academy of Arts and Sciences.

The first Sedgwick Memorial Lecture, held in 1963, was given by Professor Marjorie Hope Nicolson.

FACULTY ABROAD

In March Professor George E. Palade gave an invited paper at the Third European Microcirculatory Conference in Jerusalem.

Also in the Middle East this spring was Professor Walther Goebel who attended a Biological Conference on Antigens and Antibodies at Oholo on the Sea of Galilee in Israel. In the course of the same trip, Professor Goebel gave an invited paper at a colloquium on immunochemistry held by the German Society for Physiological Chemistry in the town of Mosbach. Professor Goebel spoke on "The Capsular Antigen of Mucoid Strains of *Escherichia coli.*"

In May, in Paris, Ronald Hinsdill, Research Associate at the Institute, and Professor Goebel gave an invited paper at a colloquium on the bacteriocines. The paper, "The Chemical Nature of the Bacteriocines," was presented by Dr. Hinsdill.

Dr. Curtis Williams helped to organize and participated in a symposium on the phylogeny of proteins at the Twelfth Colloquium on Proteins of Biological Fluids. The symposium was held at the St. Jans Hospital in Bruges, Belgium.

Dr. Gerald M. Edelman presented papers at the World Health Organization Nomenclature Conference held in Prague from May 28 to May 30, and the following week at a conference sponsored by the Czechoslovakian Academy of Sciences.

Professor E. G. D. Cohen is teaching at a NATO-sponsored summer school in theoretical physics at Cargèse, Corsica, from June 22 to July 11. His series of lectures will be attended by James Foch, Graduate Fellow of the Institute, among others.

ACHIEVEMENT AWARD

Professor René J. Dubos has received the Scientific Achievement Award of the American Medical Association. The Award is given on special occasions to scientists in recognition of a body of distinguished and outstanding work. Professor Dubos accepted the Award in San Francisco on June 23.

PASSANO AWARD

The Passano Foundation Award for 1964 was given jointly to Professor George E. Palade of The Rockefeller Institute and Professor Keith R. Porter, now Professor of Biology at Harvard University and for many years Professor in the Institute. The Award, which was presented on June 22 during the convention of the American Medical Association in San Francisco, was made to Professors Palade and Porter "in recognition of their original work in developing the use of the electron microscope in cytological research and the subsequent importance of their work in the field of genetics."

The Passano Foundation was formed in 1943 to encourage medical science and research; it is supported by The Williams and Wilkins Company, publishers. Past award winners from the Institute include Oswald T. Avery, Vincent du Vigneaud, George W. Corner, and René J. Dubos.

SCIENCE WRITERS

On May 14, the Institute was host, as it has been in previous years, to the Sloan-Rockefeller Advanced Science Writing Fellows of the Graduate School of Journalism of Columbia University. The subject of the day-long seminar was "Biochemical Genetics."

President Bronk extended an informal welcome to the group and traced for them the history of the Institute, with particular emphasis on the Institute's new role in graduate education. The first speaker, Norton Zinder, described the discovery of the f2 phage and some of his trials and tribulations with this small RNA-containing virus. The f2 is of particular interest because it is believed to contain only three genes and therefore it should be possible, theoretically, to identify its entire genome. Dr. Alexander G. Bearn who followed presented recent work on chromosome aberrations and human diseases, such as leukemia, mongolism, and various other congenital syndromes, as well as the "supermales" and "superfemales."

Professor Edward L. Tatum spoke informally at the luncheon for the group reviewing the history of genetics from the classical era into the present stages of molecular biology. In the afternoon session, Dr. Igor Tamm outlined some of the new data on the morphology and action of the animal viruses and described how chemotherapeutic agents such as HBB can interfere with biosynthetic steps necessary to viral multiplication and so produce elective inhibition. The final speaker of the day was Vincent G. Allfrey who described experiments showing the effects of histones in modulating the transcription of the DNA to messenger RNA in isolated cell nuclei. Dr. Allfrey presented data that suggested that the histones, and perhaps also methyl and acetyl groups, may provide the off-on switches for DNA expression.

The Columbia Science Writing Program is directed by Professor John Foster of the School of Journalism. All of the Fellows have had considerable writing experience as well as a special interest in science; about half of the group were on leave from newspapers, some from cities as far distant as San Antonio. In addition to Professor Foster and the nine Fellows, the seminar was also attended by Mr. John Osmundsen of *The New York Times,* a frequent visitor to the Institute. The purpose of the seminar, which is also the purpose of the fellowship program as a whole, was to provide background information and to indicate probable new developments in science so as to help these writers in interpreting and evaluating the material they will encounter in their difficult and demanding profession of presenting science to the general public.

DR. WHITAKER RETIRES

At the close of this academic year, Dr. Douglas M. Whitaker retired as Vice President for Academic Administration of The Rockefeller Institute. In his capacity, in which he has served since 1955, Dr. Whitaker gave invaluable assistance, based on his many years of experience, to the organization and administration of the Institute's education and research program.

Dr. Whitaker was born in Stanford, California, and received both his A.B. and Ph.D. degrees from Stanford University. He taught at Harvard and Columbia before returning to Stanford in 1931 where he became Associate Professor and then Professor of Biology. In 1946, he was appointed Dean of the School of Biological Science, and he served as Acting Vice President and Dean of Graduate Study before being named Provost in 1952.

Dr. Whitaker's first major area of research interest concerned differentiation and embryonal growth of *Fucus*, a marine brown alga; his investigations of the effects of temperature and chemical gradients on the polarity of the eggs are still considered classics in this field. Because of his vast knowledge of marine forms, he was called upon to participate in the Bikini Science Resurvey in 1947.

His editorships have included *The Biology Bulletin, Journal of Experimental Zoology, Journal of Morphology,* and *Acta Anatomica.*

Dr. Whitaker also conducted a series of important experiments on the mechanisms of bubble formation in the bloodstreams of animals, a subject of great interest to submarine and aviation medicine. A third principal investigative pursuit, according to intimates, was wine, both foreign and domestic, another field in which Dr. Whitaker became both expert and connoisseur.

It was to education and educational administration, however, that Dr. Whitaker made perhaps his greatest and most highly individual contribution. In addition to his services to Stanford in this regard and his work at the Institute, Dr. Whitaker served in various educational capacities for the National Science Foundation, the United States Army, the United States Department of State, The Rockefeller Foundation, and other private and public organizations.

In announcing his retirement, President Bronk stated: "We will miss and long remember the services rendered to us by Douglas Whitaker. It is difficult to imagine how the Institute could have changed and grown as it has over the last decade without the benefit of his wise, warm, and quiet counsel."

DEPARTURES

As is always necessary at this time of year, the Institute this spring has had to bid good-bye to several members of its faculty and research staff who are leaving to pursue their careers at other universities and research centers.

Three of last year's graduates have recently accepted new appointments. Dr. Joan Kent will join the Department of Molecular Biology at the Albert Einstein College of Medicine. Dr. Peter Gomatos is going to Scotland where he will be a Special Fellow in the Institute of Virology of the University of Glasgow. Dr. Cecil Yip has accepted an appointment as Assistant Professor at the Charles H. Best Institute at the University of Toronto.

Nancy Alcock, Research Associate, has been appointed Senior Research Officer at the Kanematsu Memorial Institute, Sydney Hospital, New South Wales, Australia. Two Guest Investigators, Dr. Paul G. Quie and Dr. Bella S. Strauss, have been at the Institute for two years and will be departing this summer. Dr. Quie, who was a John and Mary L. Markle Scholar and a USPHS Career Development Awardee, returned to the University of Minnesota

Medical School where he is Assistant Professor of Pediatrics, and Dr. Strauss, who was an Investigator for the Health Research Council of the City of New York, returned to an Assistant Professorship at New York University Medical School. Both Dr. Quie and Dr. Strauss worked in the laboratory of Dr. James G. Hirsch.

Dr. Roy S. Dombro, Research Associate in Dr. Woolley's laboratory since 1958, has been appointed Research Associate in the Division of Protein Chemistry at the Institute for Muscle Disease in New York.

BERLIN GARDEN

On the afternoon of June 12, following the Commencement Convocation, a simple ceremony was held to dedicate the Theodore Berlin Memorial Garden. President Bronk, Professors Samuel A. Goudsmit and Mark Kac, and Dr. Charles Stevens each spoke briefly to the group of friends assembled in the Students Residence Hall adjoining the garden. Tea was served after the ceremony.

Dr. Bronk paid tribute to Dr. Berlin's unusual ability to influence and inspire the minds of the students with whom he came in contact. In reflecting on moments of his own personal experience with the Berlins, he recalled in particular their love of art and Dr. Berlin's admiration and appreciation of the Institute's landscape. It was for this reason, Dr. Bronk stated, that the Garden came to be chosen as his memorial. The President also spoke warmly of Mrs. Berlin's continuing association with the Institute as a Special Assistant and of her many contributions to the beauty of the campus.

Charles Stevens, a former student of Dr. Berlin's, who had received his degree of Doctor of Philosophy earlier that same day, spoke movingly of his personal memories of Dr. Berlin, as did Professor Kac, a longtime personal friend as well as a colleague.

The feeling of the occasion was summarized by Dr. Goudsmit, who was instrumental in bringing Dr. Berlin to The Rockefeller Institute, where, as he said, "He influenced and guided our thoughts and thus improved our achievement, not merely our research." Dr. Goudsmit concluded: "Though we miss him this is no moment for sorrow. For this beautiful garden represents the future and growth. It is encouraging for us to see that when we do good it is not forgotten. In fact, this garden symbolizes that what Berlin has done for us has not disappeared. We still feel his influence. We are better for what he has given us. We cannot forget him."

ILLUSTRATIONS

THE COVER PHOTOGRAPH shows the academic procession for the sixth annual Convocation for Conferring Degrees approaching Caspary Auditorium; photograph by Richard Carter. PAGE 1 Lotte Meitner-Graf, London; PAGE 2 Sam Vandivert; PAGES 3 and 4 *The Journal of Physiology*, 1912 and 1928; other photographs by Heka and The Rockefeller Institute Illustration Service.