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Convocation for the Conferring of Degrees, 1961

The Rockefeller University

Convocation for the Conferring of Degrees

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THE CONFERRING OF DEGREES

OPENING REMARKS BY DETLEV W. BRONK

It is the purpose of this Convocation, which is held on the sixtieth anniversary of our foundation, to confer degrees upon ten young men and women who have achieved the right to be known as scholars.

Each one of ten members of our faculty will describe a candidate's intellectual progression and the way in which studies in many fields of science ultimately led him or her to seek new knowledge and understanding through research. Each will tell how the graduand's study enabled his or her research, the relevance of that research to other fields of learning, and the significance of the discoveries that were made during the course of the investigations.

We will honor two others for their scholarly achievements and for the noble example they have set for youth such as the youth of whom you now will hear.

PRESENTATION OF

MARY AGNES BONNEVILLE

BY MARIA ANNA RUDZINSKA

Development is one of the outstanding characteristics of life. It assumes its most striking form during metamorphosis, when a butterfly emerges from the pupa or a frog from the tadpole. The adaptive and evolutionary significance of metamorphosis, particularly in Amphibia, has been recognized and stressed long ago and recently supported by biochemical findings. These fascinating problems of amphibian metamorphosis have challenged men of science to extensive experimental work for several decades, and as early as at the beginning of this century it was already known that amphibian metamorphosis is controlled by the potent thyroid hormone.

The great achievements of the past still left a multitude of unresolved problems in this intricate field. One of them, the fate of the larval tissues and the origin of the adult tissues during metamorphosis, attracted the attention of Mary Bonneville. This is an important morphogenetic problem, for it encompasses the question of potency and differentiation of cells. On this point there are still many divergent views among investigators.

Mary realized that an entirely new approach has to be used to solve this controversial problem. The electron microscope seemed the most promising one. This powerful weapon of modern cytology has opened a window into the hitherto inaccessible stratum of reality: the macromolecular structure. A whole host of new information about the molecular organization of the cell originated already from this source. Mary acquired the techniques and skills of electron microscopy and familiarized herself with the ultrastructure of the cell. After a thorough evaluation of organs and tissues based on ex-

tensive reading of the vast literature concerning amphibian metamorphosis, she selected for her problem a comparatively simple tissue of the small intestine, an organ which undergoes drastic anatomical and functional changes during metamorphosis, as the tadpole is a herbivorous and the frog a carnivorous animal.

To analyze and interpret maturely and intelligently the results of her progressing experiments Mary Bonneville had to acquire a broad background not only in related fields but also in a number of basic sciences including mathematics. The unique environment at the Institute provided excellent opportunities for this, as well as for discussions and exchange of ideas with experienced investigators creating a stimulating climate of common adventure in science. Mary was exposed to seminars and lectures of eminent scholars invited to the Institute from all over the world, and the breadth of her thinking and of her knowledge grew extensively and her research problem was deepening and ripening.

Mary Bonneville arrived at significant and clear cut results. Following step by step with patience, devotion, and ingenuity, the stages in development during natural and experimentally induced metamorphosis, she found by means of electron microscopy that the epithelial tissue of the frog represents an entirely new population of cells originating from basal cells under the impact of the thyroid hormone. This is an important contribution, for it shows that the adult epithelial tissue lining the intestine is not formed by dedifferentiation and redifferentiation of larval cells. The latter degenerate. It is quite possible that Mary Bonneville's finding might apply to all other tissues during metamorphosis, and to differentiated cells in general, thus having a broad morphogenetic scope.

It is remarkable that two types of cells within the same tissue react to the same stimulus in a diametrically different manner. The functional larval columnar cells degenerate, while the basal cells proliferate, giving rise to the adult tissue. It is equally remarkable that the same basal cells produce before metamorphosis the larval epithelium and when stimulated by the thyroid hormone develop

into the adult tissue with its own characteristics, which shows that the specific action of the thyroid hormone reaches the molecular level. Particularly significant seems to be the structural difference found by Mary Bonneville between the larval and adult nucleus. It suggests that the thyroid hormone might affect the genetic material of the nucleus which in turn might direct the differentiation of the cell during metamorphosis. This line of research is well worth further exploring. So are the many other avenues opened by her beautiful piece of work.

Let me say at the end that it was a delightful experience for me to watch the metamorphosis of a young candidate of science into a successful investigator. Mary Bonneville today is indeed a person different from the girl who joined us some years ago. Her mind broadened, her intellect sharpened, her scientific judgment matured, she acquired self-confidence and enriched her whole personality. A good case of metamorphosis of a young human mind.

PRESENTATION OF

ROBERT DONALD DEVOE

BY HALDAN KEFFER HARTLINE

Many fields of modern experimental biology require so many specialized physical and chemical techniques, such elaborate equipment needing such sophisticated engineering, that one may sometimes wonder what has become of the biology.

Perhaps Mr. Robert DeVoe had occasional misgivings about this as he worked in his darkened cubicle, crowded with complex apparatus at the center of which was one small creature. For his original interest, if I am not mistaken, was in freely living animals, active in their natural surroundings. But experimental science is also interesting, and the insight into the basic nature of life processes it furnishes, however indirectly it sometimes seems, is known to all of us and is an intellectual reward of high order.

Certainly Mr. DeVoe suffered no attenuation of his interest in animals and their behavior for having developed an enthusiasm for experimental cellular physiology. His choice and treatment of his thesis research problem suggests that his two interests did in fact supplement each other. He chose to study visual receptors; in particular their electrical activity. Of course, the very behavior a naturalist finds so interesting is governed by the information an animal derives from its sensory receptors. But also, the problem of how a receptor cell translates environmental change into nervous action is a basic one in cellular physiology, challenging to the most exacting analytical scientist.

For our interest on this occasion, this problem is one about which a broad program of graduate study could readily be organized. The biochemistry of the visual pigments, the physical chemistry under-

lying bioelectric phenomena, optics, applied electronics, and, as we shall see, the engineering physics and its supporting mathematics required for the analysis of the dynamics of the receptor system are a few of the subjects Mr. DeVoe found relevant to his research.

From his study of comparative physiology Mr. DeVoe could survey the animal kingdom and select that form best suited to his work. He chose the wolf spider, *Lycosa*, because it possesses a relatively simple eye in which the electrical responses probably represent the uncomplicated activity of retinal receptor cells alone. It was a good choice, but I suspect that cold logic alone did not determine it—spiders are interesting animals, and Bob DeVoe cannot resist an interesting animal.

The electrical activity that Mr. DeVoe records from the eyes of his spiders is almost certainly closely related to the discharge of optic nerve impulses by the receptors; it may even be the immediate cause of that discharge. But how this activity arises, as a consequence of the initial photochemical action of the light stimulus, is unknown. For the present, we must be content with an accurate description of some of the properties of this unknown part of the receptor mechanism. It is this description that Mr. DeVoe's research has provided for the restricted but important case of small fluctuations of light intensity about a mean ambient level. Such are the natural stimuli to the individual receptor cells when, for example, images of moving objects sweep across the retinal mosaic.

Because he restricted the light fluctuations to small values, and because the eye he had chosen was indeed a simple one, Mr. DeVoe found that the responses could be dealt with successfully by linear system analysis, now so widely used in engineering physics. The results of this analysis supply a succinct description of the dynamic properties of the receptor mechanism. With the aid of the system function derived from the analysis of relatively few measurements, it is possible to predict the response to any kind of small fluctuation, or to a succession of fluctuations, as in flickering light. In this Mr. DeVoe has made a substantial contribution to the physiology of

the visual receptor. It will be especially valuable in the detailed analysis of the receptor mechanisms. The method can undoubtedly be extended to more complex eyes. And should Mr. DeVoe wish to turn to his earlier interest and study the behavior of his spiders, he will know how to estimate the relative effectiveness, as far as receptor processes are concerned, of many of the visual stimuli to which they react.

Mr. DeVoe has made a significant contribution to a special field of knowledge, but in doing so he has kept and extended his diverse interests in living things, and prepared himself broadly for a career of creative scholarship.

PRESENTATION OF

ALLEN BRODERICK EDMUNDSON

BY CHRISTOPHE HENRI WERNER HIRS

At an early stage in his association with The Rockefeller Institute Allen Edmundson's studies in the fundamental disciplines gave him a strong inclination toward the physical sciences. This found particular expression in his fascination for generalized mathematical approaches and the power of quantitative methods. Contemplating the more recent history of research in biology, Mr. Edmundson was deeply impressed by its repeated demonstration that the most significant advances are made whenever it becomes possible to deal with a complex biological problem at the molecular level and in terms of the concepts and techniques of physics and chemistry. Against this perspective, and with such inclinations, it was inevitable that he should decide to center his attention on one of the most fundamental problems with which molecular biology is faced at the present time: the question of how specificity is expressed at the molecular level. Of central significance in the eventual attainment of an understanding of this basic problem will be a detailed knowledge of the structure of proteins, and especially of the arrangement in space of the atoms that make up the molecules of these, the most complex of all substances that occur in living things.

It is scarcely fifty years since W. H. and W. L. Bragg demonstrated that X-ray diffraction could be used to determine the structures of simple inorganic crystals. W. L. Bragg proceeded to revolutionize our knowledge of the silicate minerals by X-ray analysis; pioneered in the establishment of the science of structural chemistry, which is concerned with the size and shapes of molecules; and ventured as early as 1929 to predict that in time X-ray crystallographic analysis

would even be capable of unravelling the structures of protein molecules. At the time Allen Edmundson began his studies success in the X-ray crystallographic analysis of a globular protein had still to be attained, but encouraging initial results had been obtained at Cambridge by Kendrew in a study of the myoglobin from sperm whales. How far it would be possible to proceed with the X-ray analysis of myoglobin was uncertain at that time, but it was generally agreed that a chemical investigation would have to parallel the X-ray studies if the elucidation of the structure was to be carried to completion. This chemical study was the formidable and ambitious task to which Mr. Edmundson addressed himself.

To gain some perspective against which Mr. Edmundson's achievements are to be viewed we must appreciate that the study of protein structure by chemical means is still at a relatively early stage of development and that, at present, the problems encountered in the investigation of any one particular protein are likely to be highly individual. The study of myoglobin proved to be no exception. Many experimental hurdles had to be overcome before Mr. Edmundson could attempt to answer the key question in any chemical study of the structure of a protein molecule: would it be possible to specifically cleave the protein into smaller, defined fragments, which in sum could be demonstrated to account for all of the parent molecule? The outcome of an outstandingly thorough investigation, to which he brought great skill and indefatigible energy, was that Mr. Edmundson could answer this question affirmatively.

Mr. Edmundson's research has opened the way for a rational chemical study of the myoglobin molecule. The well-defined and accessible degradation products he discovered will serve as relay stations along the road. In the meantime, the results already obtained have been of considerable assistance in furthering the progress of the X-ray studies. Making unprecedented advances in their analysis, Kendrew and his colleagues have been able to calculate a three-dimensional Fourier synthesis of the electron density in sperm whale myoglobin to a resolution of 2 Ångstroms: from it much of the

atomic arrangement in the molecule may be inferred. Indeed along considerable sections of the polypeptide backbone the identity of the amino acid side chains has been ascertained with certainty, and where identification has not been possible the choice has been limited to two or three most probable residues. When Mr. Edmundson's results are added to the X-ray picture, most of the ambiguities vanish and an almost complete representation of the structure of myoglobin appears. There are still some uncertainties in this representation, but it is so close to being accurate that from now on it will be possible to attain further refinement of the structure by direct trial and error calculations. We may look forward with certainty to the day, not far hence, when myoglobin will represent the first protein for which the complete structure is known in all details. In contemplating the advance that such an achievement represents we can all take heart and rejoice; and we can be proud that one of the graduates of this Institute had a part in bringing it about.

PRESENTATION OF

JACK FREDERICK KIRSCH

BY GEORGE EMIL PALADE

Jack Frederick Kirsch joined the student body of this Institute in 1956, soon after graduating as a Bachelor of Science from the University of Michigan. He had majored in physics and mathematics, but during the last year in college he had developed an active interest in biology. He entered this wild field cautiously, through the gate of biochemistry, attracted by the order, logic, and ingenuity of biochemical processes. This encounter with an exciting and promising field, to which he had been introduced by a talented teacher, led him toward graduate studies, and eventually research, in life sciences. Physics and mathematics ceased to be goals—they remained, however, means and examples.

He came to us at a time when electron microscopy was rapidly revealing the complex organization of animal cells; when cell fractionation procedures began to be controlled by the new microscope; when microsomes were finally described in terms of intracellular equivalents; and when ribonucleoprotein particles, or ribosomes, were discovered and characterized by the joint efforts of biochemists, physical chemists, and electron microscopists.

Impressed, he moved a step further in the direction of general biology and became interested in the organization of living matter and in correlations between structure and function at the subcellular level. In so doing he was actually following a major trend in modern biochemistry which concentrates on structurally defined, rather than chemically characterized, entities, on the sensible premise that each structural entity may be related to a distinct function, which can be better analyzed and understood by work on isolated subcellular units.

To this trend we owe, for instance, the unravelling, not yet finished but far advanced, of the process of protein synthesis. The structural entities involved—in this case the microsomes—early attracted Jack Kirsch's interest.

A new exposure to biochemistry at Cambridge in England gave him a better understanding of the initial reactions involved in protein synthesis—the activation of amino acids and their transfer to the site of assembly which at that time was still assumed to be the microsome.

In 1958 Jack Kirsch came back from his year of wandering ready to start working on his thesis. The problem he chose occupies a central position in protein synthesis. It involved a redefinition of the structural unit responsible for the final and crucial step of assembly of amino acids into a protein molecule. At that time, it was already known that the microsomes were complex entities made up of membranes, amorphous material, and ribosomes. There were means of isolating these ribosomes and there was suggestive evidence that they, rather than the other microsomal components, were the site of amino acid assembly. Yet the proof was lacking.

By careful work, Jack Kirsch succeeded in isolating from liver microsomes, ribonucleoprotein particles free of contamination and still able to incorporate, *in vitro*, labeled amino acids into their proteins. Within the limitations of the methods used, his experiments finally identified the ribosomes as the assembly site in the process of protein synthesis. The structural purification he achieved provided, in addition, a better preparation for further analysis, for he showed that the isolated ribosomes were more stable and, at the same time, more dependent than the microsomes on the various co-factors involved in the incorporation process. Finally, his work made available adequate preparative procedures for these ribosomes on which so much interest and so much work is concentrated at present.

Indeed, during the last few years, results similar to those he presented were obtained in many laboratories with ribosomes isolated from a variety of sources. He retains the advantage of having worked out to its natural conclusion the original system—the liver micro-

somes—and of having provided adequate proof that his work was based on ribosomes only.

In his years of study at this Institute, Jack Frederick Kirsch has achieved much more than making a valid contribution to science. For he has learned the trade of scientific research. He has mastered the knowledge of his chosen field. He has distilled a good part of the rush of his youth in judgment and measure. He has learned the vastness of science and the true dimensions—modest yet all important —of the individual working for it. I recommend him as a young scientist fully deserving the title of Doctor of Philosophy of The Rockefeller Institute.

PRESENTATION OF

ELENA ISABELLA RACHELE OTTOLENGHI

BY ROLLIN DOUGLAS HOTCHKISS

Organic nature, in contrast to the biological textbook, or the taxonomic museum, does not oblige living creatures to dwell within the cramping confines of the phylum, class, order, and species to which the mind of man so conveniently relegates them. The animals and plants move or develop in a world containing many sorts of animals and plants—a world in which, to be sure, they are subject to the limitations of those morphological constitutions which have been so carefully tabulated. But how unfortunate is that scholar who forgets that living creatures compete daily in a fantastic tournament, in which there are short races to be won by the swift, longer contests which go to the persistent, and innumerable prizes—prizes which may go for gaudiness or else for unobtrusiveness, for greediness or patience, for watchfulness or maybe for the mere ability to sleep until pleasant weather comes.

The biologist who implies that to understand we must first classify and analyze, is not living up to his text and is furthermore missing most of the adventure if he stops with having analyzed or described and does not press on to understand. He ignores the enormous vitality of ecological existence if he allows himself to think that survival is simply an inevitable result of having superior cervical ganglia or is explained by merely recounting the number and nicety of the vertebral endowment—as if mere rattling of articulated bones in the face of disaster would in itself put a predator to rout, or fend off starvation. Furthermore, the biologist, like the spokesman for the State, must remember all of his citizens, and not honor only the achievements of the heroes who return alive and successful from the

wars. He is doing history a grievous injustice if he forgets the vastly important role played by the starts and trials of evolution during which whole organisms—and morphogenetic and biochemical pathways—appeared which in the end were merely stepping stones for life as we now see it.

What is one to do—how is one to retain the precision of the exact man and yet have the scope of the true scholar? I would like to tell you of the development in our midst of a biologist, Elena Ottolenghi, who has grown up to face these challenges. It is a bright early chapter in a life that I feel will always be in some way devoted to the interactions of living organisms and their impact upon each other.

When she first came to the attention of our faculty, Elena Ottolenghi was studying medicine and becoming impatient with some of the stereotypes of that preoccupation. It has seemed to me that she probably disliked particularly the obligation to direct her thoughts increasingly toward the *deleterious* effects of organisms upon each other—whether it be the pathogen bestrewing the vessels of man with toxins, or man casting chemical volleys at the tender membranes of the pathogen.

In any case, at this Institute Elena chose first to search long and carefully into the possibilities that one mouse could be made, by the precisely limited mechanism of genetic transformation, to contribute its characteristics to the tissues of another mouse. While no such change was destined to be brought about, we have profited from her patient study, for we now know beyond question that mice are protected from genetic change in a way that some bacteria are not.

But as Elena turned to inquire how and in what conditions bacteria can liberate the influential nucleic acids to which other bacteria respond, she continued to study the possibilities for an organism-to-organism interaction. I would like to point out that in doing so she eschewed the easy paths of pursuing a strictly chemical or strictly morphological or genetic study, that is, of instantly assuring a grateful audience for her work by operating on a stage before which an audience was already congregated. Ignoring also all other temptations

to flamboyance for the sake of emphasis, she nevertheless quietly succeeded in turning our concepts the other way about. The important finding of which she has made us forever aware is that growing pneumococcal cells are not only able to receive genes from, but apparently without harm may donate genes to, each other.

This engaging demonstration of unsuspected genetic capabilities in bacteria gives us a new vantage point from which to view bacterial evolution. One group of organisms may while failing, or while prospering, efficiently contribute useful characteristics to organisms of a related but different group. Treasured bacterial information, learned in some rare mutational flash, away in the dim past, can be forever conserved through being passed on to other lines by this natural route. Since bacterial information may accumulate to conclusions important for both man and bacteria, Elena is closely and deeply considering the meanings of this new genetic-ecological fact.

We have witnessed with respect and admiration the careful way in which she has used exacting and precise techniques to safeguard against precocious interpretation, while pressing on to significant biological conclusions.

PRESENTATION OF

PETER GERALD SATIR

BY KEITH ROBERTS PORTER

Over the past few years I have had the pleasure of advising Peter Satir in his studies and research. While in college at Columbia, Peter had majored in biology and on coming to The Rockefeller Institute he was quick to seize the opportunities provided here to improve his knowledge in related sciences. It is my recollection that these first years were somewhat stressful as Peter adjusted to Rockefeller and, to a perceptible degree, Rockefeller adjusted to Peter. But all ended well, and I am happy to report that the Institute is graduating a mature and resourceful young scientist. During this early period also, he spent a year in Copenhagen at the Biological Institute, working with Erik Zeuthen on the relation of growth rate to the weight of single amoebae. From this encounter with Professor Zeuthen and his Cartesian divers Peter acquired a valuable respect for quantitative methods in experimental biology. At some point in his early career Peter became interested in cilia and their motion. In so doing he joined the long line of investigators of these slender cell processes, which began 300 years ago with Antony van Leeuwenhoek. You will recall that this celebrated Dutch microscopist, using simple lenses of his own construction, succeeded in seeing a great number of things previously unobserved by man. Among his observations are a few made on animalicules in rain water, which in his words were "provided with divers incredibly thin little feet, or little legs, which were moved very nimbly and which I was able to discover only after sundry great efforts." Thus is recorded the earliest knowledge of cilia—in this instance on a protozoan.

Since cilia are extremely small—only 0.2 μ in diameter and only a few microns long, it is very remarkable that Leeuwenhoek saw

them and equally remarkable that they have been studied so extensively since. The fascination they have held for biologists lies in part in the often-stated opinion that these tiny extensions of the cell must represent the simplest biological unit capable of motion and therefore valuable for the study of this phenomenon. Over the centuries since Leeuwenhoek's time each new advance in methods of observation has been applied to the study of cilia and each has yielded a wealth of new information. Recently, with the penetrating resolutions provided by electron microscopy, cilia have been found to possess, at the macromolecular level, a relatively simple and ordered pattern of structure, and this fortifies the hope that the study of them will indeed contribute to our understanding of the phenomena of motion in biological systems.

It was against this background of new information that Mr. Satir undertook for the first time, by combined experimentation and electron microscopy, to relate the fine structure of these slender organelles to their motion, in the hope, of course, that he might discover the underlying mechanisms. At the outset he showed a discernment valuable in an investigator by selecting a favorable material—the gills of a fresh-water clam. Then he learned how to control the motion of the cilia on the gill cells and observed and recorded by cinematography every aspect of their beat. And, finally, he discovered how to stop them in various phases of their motion so that they could be sectioned and examined in the electron microscope. In this way he obtained a remarkable series of high resolution pictures of cilia in motion which, when pieced together, gave him the sequence of changes in the normal fine structure associated with movement. This information, as you might guess, has suggested the relative roles of the subunits of ciliary structure in the contraction-conduction phenomena involved. From these observations Mr. Satir has developed an original and plausible hypothesis of ciliary motion which, while too long to recount here, will be studied with interest by his contemporaries. So it is that he has contributed a new chapter to the long history of discovery started by Leeuwenhoek.

PRESENTATION OF

AARON JEFFREY SHATKIN

BY EDWARD LAWRIE TATUM

It has always been true that the future of a society and culture rests on the development of a strong, independent and intellectually mature youth. In these perilous times, in which science is playing an ever increasing role, the training of coming generations of scientists is perhaps more crucial than ever before. To perform this function with imagination and efficiency is at once the goal, the responsibility, and the privilege of our institutions of higher learning. The Rockefeller Institute occupies an enviable and unique position among graduate universities especially in providing its students with maximum freedom in the development of their individual potentialities, along trails which they blaze for themselves in accordance with their needs and their developing insight and experience.

The graduate career of Aaron Shatkin illustrates one of these routes in the training of an investigator and scholar. Starting with a vital interest in biological phenomena, Mr. Shatkin first provided himself with basic experience and training in microbiology, chemistry, biochemistry, and cytology, and then selected as his major research area one of the most challenging and difficult in biology, the analysis of the biochemical bases of morphological differentiation. He selected the ascomycete *Neurospora crassa* as experimental material, and concentrated on the specific morphogenetic function of *m*-inositol as an approach.

Mr. Shatkin has applied to his research problem a wide variety of concepts and techniques stemming from his basic training, and from other investigators' reports. He has developed and improved both old and new lines of approach to his specific research problems.

He has imaginatively developed, mastered, and effectively applied to his research techniques of physiology and nutrition, of electron microscopy and cytology, of cell-fractionation, of isotopic tracers and radioautography, and the concepts of microbiology, of biochemistry, and of genetics.

His work has clearly established that inositol plays a vital role in the cellular ecology of Neurospora as a constituent of all membrane systems, from that of the cell itself to those of the nucleus, of the mitochondria, of the microsomes, and of the endoplasmic reticulum. He has established that a limiting supply of the essential structural component of cell phospholipids, inositol, leads to a progressive and general breakdown of all these membrane systems with the formation of lipid droplets and extensive disorganization of the cell, with consequent distinctive changes in cell and culture morphology, and finally death. He has also obtained experimental evidence that balanced and integrated functioning of cell metabolism is necessary for normal cell morphology, and that this balance is susceptible to alteration through such factors as levels of metabolizable carbon sources and their regulatory control of inositol uptake.

One important aspect of any research career is the stimulation of new ideas and approaches. Mr. Shatkin's contributions have not only significantly clarified our understanding of inositol function in Neurospora, but have already pointed out problems and provided techniques which will be of great value in future work with Neurospora. To mention only a few, these include the electron microscopy of cell walls and other structures, and studies of the development of cross-walls, and of pinocytosis.

Another important aspect of research training and contributions is the broadening of the scientific horizons and abilities of the individual. From this aspect also Mr. Shatkin's training and experience at The Rockefeller Institute has proven most successful. In addition to his dissertation program he has effectively collaborated with Drs. Richard M. Franklin and Edward Reich in a series of investigations on the effects of antibiotics on microbial and mammalian cells,

which have shown that Mitomycin causes a rapid and irreversible degradation of DNA, and that Actinomycin specifically inhibits cellular RNA replication. He is now extending these findings to the philosopher's stone of bacterial genetics, the inducible enzyme β-galactosidase.

PRESENTATION OF

ROGER ELLIOT THIES

BY VERNON BERNARD BROOKS

The traditional purpose of the physiologist is to relate function to structure. During the past decades the emphasis has shifted from the study of whole organs to that of cells and of their parts. The new emphasis has brought with it new ways of thought and of measurement. It is my privilege to present to this Convocation a picture of how Roger Thies absorbed new lines of thinking, made new techniques his own, and how his understanding of nature grew.

Roger Thies was trained as an undergraduate in biology and physiology. He has had a long-standing interest in the relations of plants and animals with their environment, and he has always enjoyed the analysis of the puzzles posed by the workings of their parts. When he came to the Institute he chose as his field of study the borderline of physiology in which insights into cellular events buttress considerations of the economy of the body. Roger Thies became interested in how activity is passed from one cell to another, and he selected as his example the transmission of excitation from motor nerves to muscles. This event is mediated through the release from nerve endings of a hormone called acetylcholine. Some years ago physiologists were presented with the possibility of linking hormone release to histology, when Dr. Palade and Dr. Palay of this Institute discovered in nerve endings a high concentration of very small particles, termed vesicles. These entities, visible only through the electron microscope, were observed almost at the same time by de Robertis and Bennett, and the suggestion was quickly put forth that the vesicles contain the transmitter hormone acetylcholine.

It was this merging between micro-anatomy and physiology that

captured Mr. Thies's attention. He aimed his research initially at relating acetylcholine release to appearance of vesicles. This, he reasoned, might best be done by exhaustion of the acetylcholine content of nerve endings, and subsequent observation of the vesicles. The methods of electron microscopy became part of Mr. Thies's scientific equipment. But he realized quickly that he would have to know the physiological state of individual neuromuscular junctions. To this end he extended his background in the physical sciences, and in due course was able to measure by electrical techniques the acetylcholine release from single junctions. The data presented a challenge in their complexity. Roger Thies studied the rules governing reaction rates, and thus was enabled to create a model for the sequence of events in the release of the transmitter, a model that accommodates the known properties and will guide the study of those still unknown.

Mr. Thies has demonstrated for the neuromuscular hormone what we know to various degrees of certainty for other endocrine secretions: namely, that the amount of hormone available for release is backed up by a reserve store that is at least a thousand times as large. It soon became clear that mobilization of this reserve is a slow process, and that the acetylcholine content of nerve endings could, therefore, not be exhausted by physiological methods. This again provides an illuminating comparison to the economy of other hormones. Mr. Thies explored the operation of the major safety factors that guard transmitter content of nerve endings. Firstly, he found that the amount of transmitter released by each nerve impulse becomes smaller as the frequency of impulses is increased; and secondly, that during very intense neural bombardment nerve branches stop conducting altogether. As Mr. Thies obtained answers to these questions of cellular mechanisms, he related them to natural conditions, in which nerve activity is usually not intense enough to call such effects into play. In this way, confirmation was obtained for the original surmise, made over 30 years ago by Adrian and Bronk, that nerve muscle junctions rarely fail in the natural state; they form a secure link in the chain of transmission from brain to muscle. Thus,

the experiments were with imagination turned to good account, although they had failed so far to satisfy the initial quest.

The problem remained how to exhaust the acetylcholine content experimentally in order to study the micro-anatomy of depleted nerve endings. In the search for means to overcome the natural safety devices, a drug was tested that blocks accumulation of reserve acetylcholine in some other organs. Mr. Thies acquired facility with various pharmacological methods, and was then able to work out the neuromuscular actions of this drug, called Hemicholinium No. 3. Studies by Birks and MacIntosh and subsequent work by Mr. Thies have now revealed that the transmitter content of nerve endings can indeed be almost exhausted in the presence of this drug.

These achievements will form the basis of further work on the vesicle theory. Proof of the theory has so far eluded all laboratories that have attempted it, but Roger Thies, working skillfully on the basic problems, and surmounting difficulties with good cheer, has helped lay the groundwork for future experiments. He has demonstrated insight in his researches, he has broadened his outlook, and he has extracted relations of general interest from the welter of facts.

PRESENTATION OF

BRUCE RAYMOND VOELLER

BY ARMIN CHARLES BRAUN

It has often been said, and truly, that some of the most important concerns of the biological sciences are centered in studies designed to gain insight into the mechanisms that underlie the controlled growth and development of living matter. Many of us here today owe our interest in plants to an aesthetic appeal which derives largely from the almost infinite variety of patterns and forms which they display. To the working scientist, however, an understanding of development and form poses a truly formidable problem, one that is concerned with the very character of life itself.

Mr. Bruce Voeller has, throughout his academic career, been interested in these fundamental problems of growth and development, particularly as they relate to the lower vascular plants. His curiosity concerning natural phenomena doubtless stems in part from his experience as a youth in the gardens, mountain meadows, and forests of his native State of Oregon. There he was first able to observe that a plant is not a static organism but one which displays a continually unfolding series of changes during its growth and development. At Reed College, in Oregon, his interest in plants was formalized under the inspiring leadership of several rather remarkable teachers. It was at Reed that he received the liberal education that prepared him so admirably for the creative effort that he was to undertake during his predoctoral study at The Rockefeller Institute. That he was an outstanding student during his undergraduate days is evidenced by the fact that he was elected to Phi Beta Kappa and was nominated by his College for a Rhodes Scholarship. Nevertheless, his ability to carry out original research at a high level of ex-

cellence had yet to be determined. It was not until he arrived at The Rockefeller Institute that he was confronted with that challenge.

About three years ago Bruce Voeller began work on a thesis which was to determine his competence as a creative scholar. At that time he observed that young fronds of the fern species *Dryopteris* failed to uncoil and thus to develop normally when the two rows of minute leaflets or pinnae that line the frond were removed. This observation led him into a comprehensive study of the growth of the frond and the nature of the physiological regulation underlying its uncoiling. It is clear that problems of this type strike deeply into that territory where many scientific disciplines meet. Mr. Voeller did not hesitate in attacking that problem experimentally to utilize information from peripheral disciplines. He analyzed the uncoiling process mathematically, and from the results of that treatment devised techniques that proved useful to an understanding of the morphogenetic process under investigation. By means of a series of well conceived experiments, he was able to demonstrate that the uncoiling process is under hormonal control and that the growth-regulating hormone is produced by the small leaflets that line the frond. Mr. Voeller not only isolated the hormone from the frond but determined its chemical nature. He applied minute amounts of the pure hormone to coiled fronds from which the pinnae had been removed and found that normal uncoiling resulted. Thus, an intellectually satisfying explanation of this morphogenetic process was achieved. The experimental studies were carried out with ingenuity and precision. Their level of excellence is such that they will doubtless serve as a model for future investigations in the area of plant growth and development.

PRESENTATION OF

EARLE FREDERICK WHEELOCK

BY IGOR TAMM

The body of scientific knowledge exhibits some characteristics of living organisms. By incorporating new facts and new laws it grows in size. But more interestingly, science evolves continuously becoming differentiated as a result of the interplay between the catalytic thoughts of scientists, and the environmental factors which impinge on their work. The growth and evolution of knowledge concerning viruses illustrate well this dual aspect of the history of science.

Studies on viruses became prominent at The Rockefeller Institute almost half a century ago, largely through the efforts of Dr. Thomas M. Rivers who, ever since, has made this field of knowledge so peculiarly his own. At first, virus research was to a large extent just natural history. It was focused on the recognition and description of viruses, as well as on the elucidation of their role in the causation of disease. Very soon however, Dr. Rivers became interested in larger aspects of virology; in particular he called attention to the fact that viruses can have two very different types of action on the living cells they invade. They can cause degenerative changes, leading to the death of the host cells; or in contrast, they can elicit uncontrolled cell division, leading to the formation of tumors.

When Frederick Wheelock came to The Rockefeller Institute four years ago, he was already interested in virology, and for this reason he established headquarters in the department where Dr. Frank L. Horsfall and his associates were continuing and developing the tradition initiated by Dr. Rivers. In this atmosphere, Frederick Wheelock soon realized that the phenomena involved in virus-cell interaction

had become one of the central problems of virology, and that the modern cytological and chemical techniques made it possible, at last, to supplement the descriptive knowledge of this interaction with the analysis of its intimate mechanisms. In other words, Frederick Wheelock found himself in the happy situation where his interests could obtain nourishment, from both the scientific philosophy special to virus research, and the biological and physicochemical sciences represented at The Rockefeller Institute.

While studying cultures of mammalian cells which had been infected with Newcastle disease virus—a typical cytocidal virus which causes degeneration and death of susceptible host cells—Frederick Wheelock observed that some cells containing newly synthesized viral protein were arranged in pairs, as if they had just divided. Subsequently, he saw infected cells in all stages of mitosis, and he demonstrated that cells infected with the cytocidal virus could undergo mitosis and divide, even though they had produced and released new infective viral particles. This discovery enticed him to study mitosis and division in virus-infected cells.

By establishing that reproduction of a cytocidal virus within susceptible host cells does not per se prevent cell division, Frederick Wheelock has shown that viral reproduction does not necessarily disorganize vitally important cellular processes. This awareness made it even more interesting to determine how infection with cytocidal viruses could ultimately bring about cessation of mitotic activity, followed by structural disintegration of the infected cells. Frederick Wheelock's investigations of the biosynthetic capabilities of infected cells led him to the conclusion that cessation of mitotic activity was probably due to inhibition of protein synthesis in virus-infected cells. The late cell damage could be related to general depression of cellular biosynthesis of vitally important macromolecules. In addition to their intrinsic interest, these chemical results explain in part the phenomenon known as viral interference—namely the fact that, at a certain stage of infection, viral production stops, and cells become incapable of supporting the reproduction of another virus.

BY IGOR TAMM

Through his contributions to the study of the interaction between cytocidal viruses and cells, and through his scholarly evaluation of the findings of others, Frederick Wheelock has thus added much to the understanding of the dual action of viruses, first emphasized by Dr. Rivers thirty-three years ago. His findings acquire special significance from the fact that numerous cytocidal viruses cause cellular proliferation before exerting their cell-killing effects, whereas some tumor viruses can cause degeneration and even death of cells, and that there exists a continuous spectrum between these two opposite effects. In the light of such facts, it may become possible in time to formulate a generalized theory accommodating all the apparently incompatible phenomena which are the expression of viral action on cells.

Throughout his studies at the Institute, Frederick Wheelock has shown that he is richly endowed with two qualities which nourish creative scholarship—imagination and perseverance. Furthermore, his scientific accomplishments testify to his acumen in selecting a significant area of research, and to the intellectual and technical breadth that makes it possible to deal with problems by a multidisciplinary approach—one of the most useful assets in the pursuit of science today.

CONFERRING OF THE DEGREE OF DOCTOR OF SCIENCE, *HONORIS CAUSA* ON THOMAS MILTON RIVERS

Director Emeritus

DETLEV W. BRONK: Thomas Milton Rivers, as you journeyed from your native southland, you wisely tarried for a decade at the borders of the north in a university beloved by you and me. As have so many others, you came from the Hopkins to this Institute and thus enriched it. Forty years have passed since then; throughout those years this place has been the site and center of your work and of your wide ranging scientific interests. Here you explored and studied the nature of the viral agents of disease. From your discoveries here you formulated means which have prolonged and made more tolerable the life of man. Here you labored selflessly to make your cherished Hospital and all the Institute a better place for your younger colleagues. To the Institute you have been devoted; those who comprise the Institute have for you deep affection.

The Institute could not contain all your aspirations. But we are proud to think that from the Institute came inspiration which you carried into many fields of humane endeavor. As a leading spirit among those who fought the crippling disease of youth, you will deserve forever the gratitude of countless men and women who grow from childhood into able-bodied adults.

Always willing, always eager to relate your scientific talents and your vast fund of knowledge to the furtherance of human welfare, you have served your city and your country in many ways; I mention only two. For eighteen years you were a member of the New

York City Board of Health. Throughout two wars you aided those who suffered in defense of our country. I have never known an ensign such as I to decorate an admiral such as you. But under the circumstances of this occasion I am emboldened so to do.

CONFERRING OF THE DEGREE OF DOCTOR OF SCIENCE, *HONORIS CAUSA* ON HUGH STOTT TAYLOR

President of the Woodrow Wilson Foundation and
Dean of the Graduate School, Emeritus, of Princeton University

DETLEV W. BRONK: The realms of scholarship are not limited by national boundaries. And so, by tradition, by need and instinct scholars have broad international interests. But even among scholars, Hugh Stott Taylor is almost unique as a friend and counsellor to many nations, and a loyal patriot of two.

Native of England and graduate of the University of Liverpool, he was thereafter a postdoctoral student in Sweden and in Germany. Then, perceptive Princeton lured him to her faculty at the youthful age of twenty-four. They never let him go except to serve his native nation in time of war and to maintain in times of peace affectionate associations between his two countries.

During four and forty years he was a member of the Department of Chemistry in Princeton and the inspiring Chairman of that department for a quarter of a century. While he was thus furthering chemistry in this country, he was President of the Faraday Society of England. He was a wise, dynamic member of the Research Committee of the American Philosophical Society founded by Benjamin Franklin; he was also a Fellow of The Royal Society of London, as was Franklin. He served the United States nobly during World War II, as he served Britain in World War I. Queen Elizabeth the Second conferred knighthood on Sir Hugh about the time he was

elected President of The Society of Sigma Xi of our country. In spirit, Sir Hugh is truly a citizen of two nations; he represents the best of the international qualities of science. This loyal resident of the United States is a double knight, for Elizabeth's knight is also Knight of the Papal Order of St. Gregory the Great.

Sir Hugh has two other claims to our especial, high regard.

We are a graduate university dedicated to the preparation of scholars. The preparation of scholars was the especial concern of Sir Hugh as Dean of the Graduate School of Princeton for thirteen years. To educators throughout the Country he was the Dean of Graduate Deans. Retirement led on to the arduous presidency of the Woodrow Wilson National Fellowship Foundation for support of graduate students.

When our friend first came to this country as a precocious youth, he was invited to The Rockefeller Institute by Jacques Loeb. Princeton won and gained; The Rockefeller Institute lost and suffered. But at last, Sir Hugh, we would claim you among those who hold our degree.