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The Rockefeller University

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CONTENTS OF THE ROCKEFELLER INSTITUTE *Quarterly*

VOLUME 2 NUMBER 4 WINTER · 1959

page

THE NATURE OF THE NERVE IMPULSE AND ITS CONDUCTION

WHAT WE KNOW of the world around us, what we experience within ourselves, and our various physical, emotional and intellectual manifestations are determined by dimly understood processes occurring within and among some million billion nerve cells within our bodies. As Wilder Penfield put it a few years ago: "In them throbs the essential energy of life. Through them the body and the mind alike are controlled, and sensorimotor mechanisms are coordinated and integrated in such a way that conscious thought and direction of human activity are possible."

It is little wonder then that neurobiology, the study of the structure and function of the nervous system, has been an important area of research at The Rockefeller Institute for many years. Something of what is known about the nervous system as a result of work carried on by members of the faculty of the Institute will be set forth in this article—too sketchily, perhaps—but not without interest, we hope, and profit to our readers.

The nervous system is a vastly complex and highly integrated assembly of about 1,000,000,000,000,000 neurons, or nerve cells. Nearly all of them are located in the brain and spinal cord, referred to as the central nervous system, but long fibers from these cells extend into the remotest part of the body. These tiny thread-like fibers from individual neurons are gathered together into bundles or cords which we recognize as nerves. Those extending outside the brain and spinal cord are referred to as the peripheral nerves. Early anatomists misunderstood the function of nerves, thinking them to be cords, perhaps for mechanical purposes. The very word "nerve" reflects their confusion, for it is taken from the Greek word *νευρον*, meaning sinew, tendon, or bow string.

Information flows up and down the peripheral nervous system—from sense receptors of various kinds into the central nervous system and out again, carrying instructions of various sorts. Incoming and outgoing fibers are often in the same nerve. The nerve impulses, whether incoming (sensory), or outgoing (motor), are now known to be essentially similar electrical impulses and much of what we have to write about concerns the discovery and elaboration of this fact.

The Italian physiologist, Galvani, accidentally discovered nearly two centuries ago that an electrical shock to a frog's nerve would cause its muscles to twitch. Later he observed (also accidentally) that decapitated frogs suspended by brass hooks through their spinal marrow, twitched when they were hung over an iron railing around his laboratory balcony. He tried other metals with roughly the same result. Galvani was convinced that the metal only conducted "animal electricity" already present, the flow causing the twitch. Volta, a contemporary Italian physicist, was equally convinced that the electricity arose from the dissimilar metals and stimulated the muscle externally. We now know they were both right, though Volta's purely physical interpretation was more fruitful at the time. Out of the storm of controversy that resulted from Galvani's experiments came Volta's development of the electrical cell composed of two different metals, a profoundly important step in the history of physics and technology. Out of it, too, came techniques in electrophysiological investigations that are being used today. It was a long way from the observation that electrical stimulation caused a muscle to twitch to the highly refined ideas of today about the why and how of nervous function.

It is a common fact of our experience that sense impressions may be strong or weak, and a muscle may be tensed much or little. If these stronger or weaker events are controlled by sensory and motor nerve impulses it is natural to suppose that the impulses must also be stronger or weaker as the case may be. In a sense this is so, but the strength of the impulse varies in a surprising way. The facts are that although a stimulus to a sense organ, a nerve, or a muscle fiber may produce local effects which may vary with the strength of the stimulus, the individual nerve impulse, which travels along the nerve away from the affected region, is not significantly changed in intensity by making the stimulus stronger or weaker. It is rather like the progress of burning in a lighted fuse, which proceeds at the same speed and with the same amount of sputtering as it goes

(continued on page two)

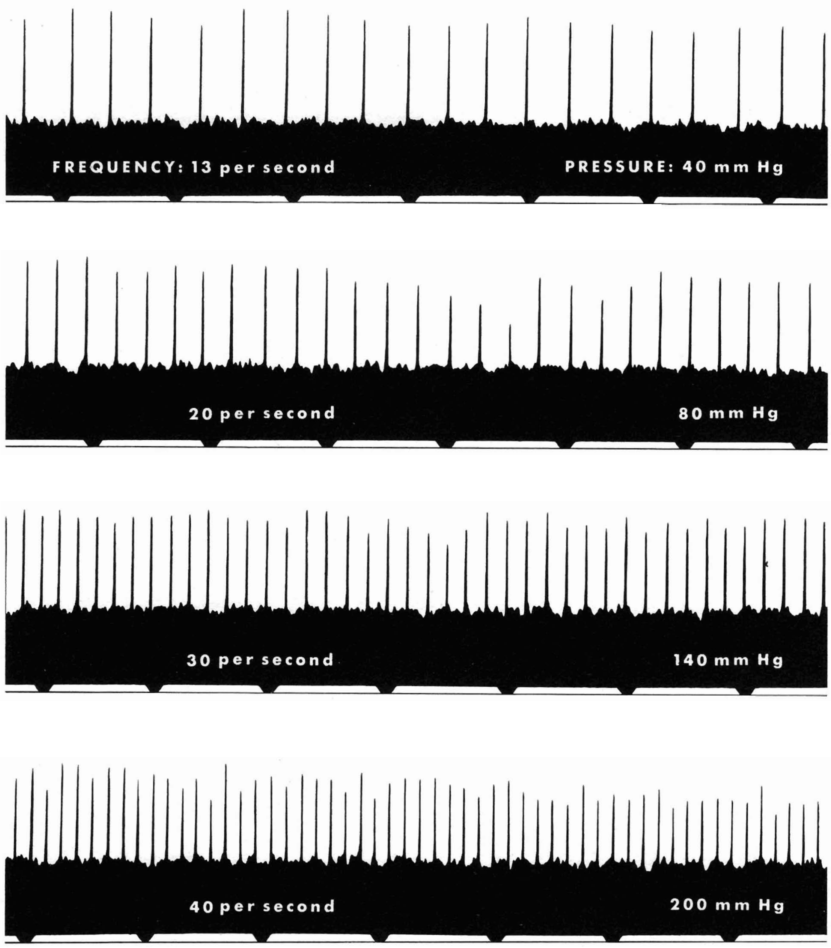
GRADUATE STUDENT RESIDENCE OPENS

A LANDMARK in the Institute's new history as a graduate university of science was reached on December 19, 1958 when the new Graduate Student Residence Hall was opened for occupancy. As part of the complex of new buildings and gracious landscaping of the Institute campus, the Residence Hall will do much to foster the association between students and faculty in a true academic community. Instead of following the original plan to operate a separate students' commons for breakfast and dinner, resident students dine in the faculty refectory of Abby Aldrich Rockefeller Hall in the morning and evening.

No longer need we feel, as was said of the scattered and crowded housing conditions at an ancient university in New England, that our students encounter "a shabby introduction to the much bruited dignity of the academic life." Three of the four floors of the building are devoted to residences, 50 being single rooms. But in keeping with the modern trend in graduate schools, 29 suites for married students are provided. The suites consist of a living room, bedroom, kitchenette, and bath.

Recreational and athletic facilities will be provided on the first floor and basement, where there are squash courts, fencing mats, pool, billiards, and Ping-pong tables with lockers for men and women. There will also be a reading room and social hall.

The Residence Hall was constructed in two stages, and as a result was occupied while the rest is nearing completion. When final construction and landscaping are accomplished this Spring the Institute's 13-acre campus will offer gracious living accommodations as well as superb scientific and educational facilities in a setting of great natural beauty that is unsurpassed in the city of New York.



How stronger stimulus increases the frequency of nerve impulses but not their size is shown in these oscillograms of the impulses in the carotid sinus nerve at four different blood pressures in this large artery. (Bronk and Stella)

THE NERVE IMPULSE *continued from page one*

regardless of how hot the match was that lit it in the first place. In nerve, this is referred to as the "all-or-nothing" principle, and it has been a puzzle of neurophysiology to explain how a nerve which is excited to the maximum, if excited at all, can transmit impressions of varying intensity.

More than 30 years ago, E. D. Adrian (now Baron Adrian of Cambridge, Master of Trinity College and Visiting Professor at the Institute), Yngve Zotterman, now Professor of Physiology at the Royal Veterinary College of Sweden, and President Bronk showed at Cambridge how this happens. The nerve either fires or it does not fire, but a continuing stimulus at a sense organ or a motor nerve cell produces trains of individual impulses. A strong stimulus produces many pulses per second and a weak one produces few. Each individual electrical impulse lasts only about one-thousandth of a second and after a recovery period of a few thousandths of a second the nerve is ready for another stimulus. As a result trains of closely spaced impulses at frequencies varying from a few per second to 1000 or more per second are possible, though most fall in the range of 50 to 200 per second.

Adrian and Zotterman (then a Rockefeller Foundation Fellow) first studied impulses in sensory nerves, using the impulses from the stretch receptors by which the degree of stretching in a given muscle is reported to the central nervous system. Soon they extended their investigations to other sensory systems and finally proposed as was later shown to be true, that all sensory nerve impulses indicate varying stimulus by varying frequency in the trains of nerve impulses that are transmitted.

As we have pointed out, a single nerve may contain hundreds of individual fibers, each carrying an impulse of different character from as many different sense receptors. Adrian and Zotterman were able to minimize the confusion from these many sources of impulses, however, by dissecting away all but one or two of the sensory origins of a nerve, which then would presumably contain only one or two active fibers. They found that stronger stimuli were reported in two ways: not only did the impulse frequency from any one fiber increase, but more fibers responded by conducting impulses, because the sense receptors to which they were connected were of differing sensitivity. In no case was it found that the size of the individual impulses changed, only their frequency and the number of conducting fibers.

The four oscillograms on this page, made several years later, show the frequency effect very clearly. They were made by Dr. Bronk at the Johnson Foundation for Medical Physics of the University of Pennsylvania with Dr. Guido Stella, now Professor of Human Physiology at the University of Padua. The impulses from a single pressure-sensitive ending in the carotid sinus nerve (which reports the blood pressure to the central nervous system) are shown at four different static pressures. As the pressure increased so did the frequency of the impulses, but their size remained essentially unchanged.

Adrian was naturally interested to know whether motor impulses *to* a muscle were signalled in the same way, and with Dr. Bronk, then a National Research Council Fellow, began to study motor impulses in nerves. Here impulses coming *out* of the central nervous system were involved, and it was therefore not possible to eliminate all but one source of impulses as was possible with the sensory nerve. However, Adrian and Bronk managed by remarkable dexterity and dissection to sever all but two or three individual fibers in a branch of the phrenic nerve supplying the diaphragm and observed the impulses in the remaining intact fibers. The trains of impulses they found were very similar to the impulses in the sensory nerves. A weak contraction was shown to be the result of a low frequency of impulses in comparatively few nerve fibers. A strong contraction, on the other hand, was seen to be developed as a result of a high frequency of impulses in many fibers. These experiments at Cambridge showed the similarity in the trains of all nerve impulses, whether sensory or motor.

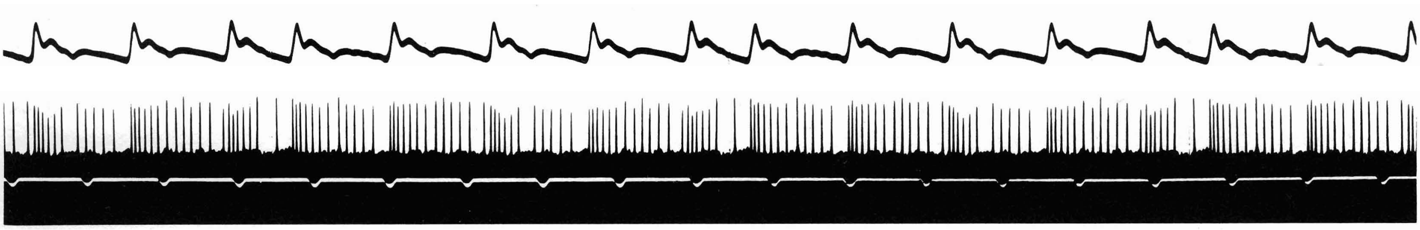
Thirty years ago, when the work just described was completed, measuring and recording techniques were, relatively speaking, so primitive that we marvel today at the precision and refinement of the conclusions that were based on them. It was a time of rapidly advancing techniques, however, and less than five years later Dr. Bronk at the Johnson Foundation had produced the beautifully clear oscillograms of nerve impulses in single fibers, reproduced on these pages, that show how trains of impulses carry sensory information *into* the central nervous system while similar trains of outgoing impulses control motor functions. In the upper of the two figures shown below the carotid sinus nerve impulses are shown under more natural conditions as they vary in frequency with the corresponding variations in blood pressure which the nerve reports. It can be seen that the individual impulses are wider spaced, e.g., of lower frequency, when the pressure is at its lowest; in the lower figure rhythmic bursts of impulses in the phrenic nerve to the intercostal muscles (by which chest breathing is effected) are compared with pneumograms that show the corresponding inspirations produced by each burst of impulses. The frequency of impulses faithfully follows each fluctuation in pressure. Bronk's associate, Professor H. K. Hartline, long before he came to the Institute (where he is still studying the visual system) showed that intensities of light on the retina also give rise to impulses in the optic nerve that vary in frequency and number of fibers conducting. It has been shown that the same principle applies throughout the nervous system.

COMPOSITE IMPULSES

Neurophysiology became an important area of investigation at The Rockefeller Institute in 1935 when Dr. Herbert Gasser, formerly Professor of Physiology at Cornell Medical College, succeeded Dr. Simon Flexner as Director of the Institute. Gasser and Erlanger had already carried out their studies of conduction velocity and fiber size in frog nerve at Washington University School of Medicine in St. Louis where Dr. Gasser began his career as a pharmacologist. When he came to the Institute he soon gathered around him a number of young men interested in neurophysiology. Dr. Harry Grundfest came with him from Cornell, but after the diversions of World War II Grundfest continued his work at Columbia University's College of Physicians and Surgeons. Gasser had met Professor Rafael Lorente de Nó, a student of the great neuroanatomist Ramon y Cajal, in St. Louis at the Central Institute for the Deaf where he came in 1931 from Spain, and in 1936 Lorente joined him at the Institute. Professor David P. C. Lloyd came in 1939 from Oxford where he had gone as a Rhodes Scholar in 1933. Having worked briefly with Sir Charles Sherrington during his last days there, Lloyd's interests have remained largely in the central nervous system, an aspect of neurophysiology which space forces us to save for discussion in a later issue of The Rockefeller Institute Quarterly.

By severing all but a single fiber in a nerve Adrian and Bronk had learned a great deal about the electrical impulse in single fibers. How the individual impulses combine to produce the composite action potential in the intact nerve was the object of studies begun more than 30 years ago at the Washington University School of Medicine by Dr. H. Gasser who is now Director Emeritus of the Institute, and Dr. Joseph Erlanger, for which they shared the Nobel Prize in Medicine and Physiology in 1944.

It is not easy to grasp how difficult such a study could be. More than a hundred years ago the German physiologist, Helmholtz, (later turned physicist) ingeniously but nevertheless crudely deduced the velocity at which the composite action potential is conducted in frog nerve. Helmholtz compared the time it took the impulse to



Trains of nerve impulses of varying frequency carry sensory information into the central nervous system and motor stimuli out. In either case the stronger the stimulus the higher the frequency of the impulses. The sensory impulses in the carotid sinus nerve (above) are compared with the corresponding blood pressure variations as the heart beats (upper saw-toothed line). The motor impulses in a fiber of the phrenic nerve to the intercostal muscles (below) are compared with the corresponding pressure fluctuations in the lungs during two successive inspirations (smooth curve). The broken white line in each figure marks intervals of 1/5 second. (Bronk)

reach the muscle and make it twitch when two points on a nerve at different distances from the muscle were stimulated. But a typical nerve may be a cable of two or three thousand individual fibers of widely varying size, the smallest of which may be less than a ten-thousandth of an inch in diameter. Each fiber conducts with a characteristic velocity depending on its diameter and other factors which will appear later. Moreover, the character of the electrical impulse in the individual fiber is easily altered by changes in the nerve's environment—by too little carbon dioxide, for example, or by dissection to make it accessible.

When Gasser and Erlanger studied the total nerve impulse they found the shape of the impulse to be complicated and to vary with the distance from the point of origin of the impulse. This they concluded to be the result of the fact that different fibers conduct with different velocities. As Dr. Gasser has put it, if a race were started in which athletes, untrained individuals and boys participated, the athletes would shoot out ahead. At a short distance they would be followed by the untrained individuals and the boys would be far behind, the separation of the groups depending upon the length of the course.

THE COMPOSITE IMPULSE

To show how the individual impulses separate as the composite action potential moves away from the stimulus, Dr. Gasser has very kindly prepared two oscillograms, shown on the page opposite, of the composite impulse in the saphenous nerve of a cat at two points along the nerve.

It is truly remarkable that in spite of these difficulties and the even greater difficulties imposed by the primitive nature of their electrical recording apparatus, Gasser and Erlanger were able 30 years ago to reconstruct the observed composite action potential of certain nerves by calculating the velocity and potential contribution from each fiber in the nerve based on microscopic examination.

Over the years and as a result of the work of many, a wide range of conduction velocities has been found in nerve fibers, varying from a maximum of about 120 meters per second (nearly 300 miles per hour) to less than 1 meter per second. At first Gasser and Erlanger based their calculations on the assumption that the speed of conduction of all the fibers varied only according to their physical dimensions. Later, when better amplifiers disclosed more details in the action potentials, Gasser and Erlanger realized that different groups of fibers exist in nerve, each with a distinct set of properties. Within each group the relationship of conduction velocity to physical dimensions was found to hold.

A, B, AND C FIBERS

Nerve fibers are now classified into three broad types—the fastest, called A fibers, conduct at velocities from 120 to 15 meters per second; the intermediate, called B fibers, which conduct at from 15 to 10 meters per second, and the slowest, C fibers, which conduct at from 2 to less than 1 meter per second. Dr. Gasser's most recent work, which we will later describe, has disclosed that there are two distinct types of C fibers. Not all three types of fibers are found in all nerves. The B fibers, for example, are abundant in the frog, but do not seem to appear in the mammalian somatic nerves at all. Gasser and Erlanger very early made a rough correlation of the type of the fibers (and hence their size and speed of conduction) with their function. The A fibers, which are the fastest, control the voluntary muscles. The smallest, the slow-conducting C fibers, carry impulses to the viscera and from the skin, and, in the skin at least, they appear to be the most numerous. The larger fibers are called medullated because they are encased in a sheath of white fatty material somewhat as if insulated. The smaller (non-medullated) fibers are bare. Here we must pause to admire the economy of Nature, for it appears that the largest fibers are used only when their high-speed conduction is necessary. The more numerous, but less urgent problems of managing the automatic functions and action of the senses, are handled by the smaller, slower fibers.

When he came to The Rockefeller Institute in 1935 with Dr. Harry Grundfest, Dr. Gasser began a series of studies of the properties of mammalian nerve fibers. One question which concerned them was how to be sure that the impulses observed in isolated nerves selected for study were indicative of the behavior of the nerve under normal physiological conditions. The earlier studies of frog nerve had raised less question, because the nerves of cold-blooded animals are much less sensitive to changes in their environment. Gasser and Grundfest developed techniques for determining the physiological state of the isolated nerve by comparing its electrical behavior with the same nerve in their animals and this, in turn, enabled them to develop techniques for maintaining the normal physiological functioning of isolated mammalian nerve.

When they began their work, Gasser and Erlanger worked with systems capable of amplifying the weak impulses of nerves only a few hundred times. While their measuring instrument was a great improvement over the twitching muscle attached to Helmholtz's frog nerve, it was capable of indicating the total quantity of the electrical impulse but told almost nothing of its shape. Yet we have seen how important the detailed shape of the impulse as it passes the recording electrode has proved to be.

TECHNICAL PROGRESS

Early in the 1920's when the oscilloscope (then called the Braun Tube) was introduced it must have seemed to Dr. Gasser like giving sight to the blind. Even so, the difficulties were severe. The earliest oscillograms were made by repeated impulses superimposed on a single film until enough exposure had accumulated to be developed. The blurred and distorted results would be regarded as hopeless material for study today, but by patient accumulation and careful analysis of such records Gasser and Erlanger found the evidence of varying velocities of conduction described above. Today high-gain amplifiers, feeding cathode ray oscilloscopes, can make the slightest electrical activity of a nerve readily observable with negligible distortion.

When, in connection with the award of the Kober Medal of the Association of American Physicians in 1954, Dr. Gasser was moved to reflect upon his career, he remarked: "As for myself, I often wonder what the story would have been like, if in 1884 Edison had not observed an electric current flowing between the heated filament of his lamp and a metal plate which he had inserted into the bulb. From these strategically important beginnings each of us can trace developments of better ways for getting answers to our questions, developments still going forward at an accelerated pace, new means for observing events in dimensions progressively smaller, new means of observing events in times progressively shorter; in sum methods for making analyses ever finer and more penetrating."

Recently, Dr. Gasser has pressed his studies of fiber types down to the very finest, the C fibers, and has discovered that they include at least two distinct types. Just before World War II interrupted their work Dr. Gasser and Dr. Grundfest, studying the C fibers in mammals (notably the cat), found that the C fibers to the viscera behaved quite differently from those from the skin.

As soon as he could after the war Dr. Gasser returned to the C fibers, and he has now shown that there are two distinct types among these extremely fine, slowly conducting fibers. One carries impulses to the viscera; the other carries stimuli from the skin (presumably sensations of pain) to the brain and spinal cord. The success of this work is a further example of the importance of developing refined and ever more sensitive techniques of measurement. Tiny variations in the shape of the electrical impulse were studied in bundles of more than 2000 fibers, many of which were only one or two ten-thousandths of an inch in diameter. The microscopic inventory of these fibers (necessary in order to calculate the composite action potential from them) was done by pushing the light microscope to its limit and supplementing it with electron microscope examinations carried out with the help of Professors Porter and Palade at magnifications of 12,000 diameters. Similarly great sensitivity in the recording techniques is demanded, for in order to avoid disruption of the weak C fiber pulses by the strong A fiber pulses, the measurements must be made after the A and C pulses are well separated from each other as they move along the nerve. Unfortunately this also means that because of the various speeds among the C fibers their composite pulse is blurred when it passes, complicating the analysis.

More recently still Dr. Gasser has been studying C fibers in the olfactory nerve. In most animals this is a short nerve and not very accessible. Fortunately, the olfactory nerve of the pike is relatively long and homogeneous enough as to fiber type and size that electrical measurements are relatively simple. The number of olfactory

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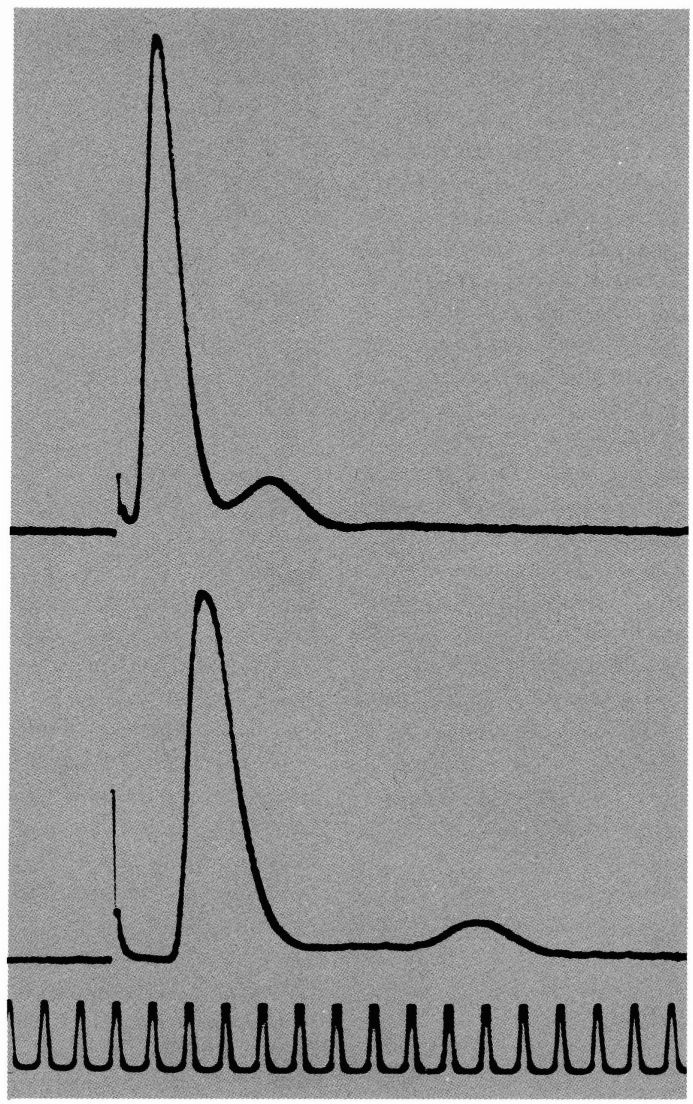


The action potential of the saphenous nerve of the cat after conduction for 13 millimeters (upper trace) and 33 millimeters (lower trace). This nerve includes fibers of many sizes, but two groups predominate, a fast group and a slow one, producing the two peaks in the action potential shown in the oscillograms. Time of arrival of the peaks is measured from left to right, the first break in the line indicating the start. Thus, the smaller elevation, produced by the slower group, arrives after the higher and faster one in both traces, but it is much later in the lower trace (after 33 millimeters of conduction) than in the upper one (after travelling only 13 millimeters). Careful measurement would show that though the height of the two peaks is less in the lower oscillogram their width is greater so that the area under them remains the same. This is exactly what would be expected, since the same amount of energy is presumably being conducted at both points on the nerve, but spread along the nerve more in one case than in the other. Timing pulses at the bottom mark intervals of 2/10,000ths of a second. Courtesy of Dr. H. S. Gasser nerve fibers is astonishing, however, for Dr. Gasser estimates 6,000,000 from one side of the nasal septum of the pig. The properties of the olfactory fibers lead Dr. Gasser to believe that they could be classified among the C fibers.

As we have pointed out, Adrian and Bronk and their co-workers at Cambridge and elsewhere found many years ago that the nervous system does not depend on the *size* of the nerve impulse to indicate the *intensity* of excitation. This is done in part by exciting fibers of different sensitivity and in part by producing in them impulses of varying frequency. The all-or-none principle holds that the impulses, once established, are of maximum size.

None of this proves that a given impulse is conducted through a nerve fiber without losing any of its intensity, however. As a matter of fact this very question was the subject of considerable controversy thirty years ago. The question was supposedly settled once, but during the past year Professor Rafael Lorente de Nó at the Institute discovered evidence to make him believe the controversy was settled in error.

What happened is this. Forty years or so ago Keith Lucas and Adrian, studying conduction of nerve impulses through narcotized segments of nerve, found that for a given degree of narcosis there was a certain maximum length of nerve through which the impulse would pass. The deeper the narcosis the shorter the length of nerve through which an impulse would pass. That was before today's superbly sensitive cathode ray oscillographs or even the only relatively delicate techniques of the string galvanometer were available. It was difficult, therefore, to tell exactly what happened when the impulse succeeded in crossing the affected segment; for the "measuring device" was simply the twitch of the muscle the nerve was attached to.

DECREMENT OR NO DECREMENT?

Lucas and Adrian interpreted these results to mean that the impulse was conducted through the affected segment "with decrement"—that is to say, the further it went the weaker it got—until it was extinguished altogether if the segment were too long (or the decrement too steep because of deep narcosis). In the early 1920's a Japanese physiologist, Genichi Kato, at Keio University in Tokyo, reached the conclusion that Lucas's and Adrian's results were wrong because of experimental errors. After an incredible number of experiments (to which more than 70,000 hapless giant toads were sacrificed) Kato announced his "theory of decrementless conduction." His arguments, backed up by so many toads, were compelling, and so it has been supposed for twenty-five years that nerve conducts without decrement either in the normal state or under narcosis. Kato held that while narcosis may lower the size of the impulse, as long as there is any impulse at all it would travel through any length of narcotized nerve whatever. Dr. Lorente now has demonstrated conduction with

(continued on page eleven)

EDWARD L. TATUM: NOBEL LAUREATE IN MEDICINE AND PHYSIOLOGY

EDWARD L. TATUM, Member and Professor at The Rockefeller Institute, shared the 1958 Nobel Prize in Medicine and Physiology with George W. Beadle, Professor of Biology at the California Institute of Technology, and Joshua Lederberg, Professor of Genetics at the University of Wisconsin. Tatum and Beadle were cited by the Royal Caroline Institute of Medicine, through which the Nobel Awards in medicine and physiology are made, for "their discovery that genes act by regulating specific chemical processes." Lederberg was cited for "his discoveries concerning genetic recombination and the organization of the genetic material of bacteria."

Beadle and Tatum began their work together at Stanford University in the early 1940's using genetically determined biochemical processes of the mold *Neurospora* as their material for investigation. In 1945 Tatum joined the faculty at Yale University and persuaded Joshua Lederberg, who was then at medical school, to take a leave of absence to work with him on the genetic characteristics of bacteria. It was this work which led to their discovery together of the sexual cycle in the bacteria *E. coli.* The readers of the *Quarterly* will find this work described in considerable detail in the article "Biochemical Genetics and Inherited Metabolic Disease" that appeared in the Summer 1958 issue, Volume 2. No. 2.

In 1948 Dr. Tatum returned to Stanford University, and in 1956 he became Professor at The Rockefeller Institute. In 1953 he was awarded the Remsen Award of the American Chemical Society for his contributions to biochemical genetics and for his work with Lederberg. Dr. Tatum is a member of the National Academy of Sciences, the American Philosophical Society, and of the National Science Board of the National Science Foundation.

We asked him how he felt when he heard the news of his great honor. "It is quite an overwhelming feeling, naturally," he said. "It is always gratifying to a scientist to have his work recognized and to feel that his work has contributed to human welfare and knowledge. I am sure I express the feelings of my colleagues when I say that it makes me proud and humble to represent America in the field of international research and understanding."

More than a hundred of Dr. Tatum's friends and colleagues at The Rockefeller Institute and elsewhere in the vicinity of New York gave him a banquet on January 16 in Welch Hall to pay tribute to the honor he had received.

Many Nobel Laureates have been associated with The Rockefeller Institute. In 1912 Dr. Alexis Carrel received the Nobel Prize in Medicine and Physiology, and in 1930 it was awarded to Dr. Karl Landsteiner. In 1934, Dr. George H. Whipple, who is now Vice Chairman of the Board of Trustees of the Institute, shared it with Drs. G. R. Minot and W. P. Murphy for work described elsewhere in this issue. Ten years later Dr. Herbert Gasser shared the prize with Dr. Joseph Erlanger. In 1946 Dr. John Northrop shared the Nobel Prize in Chemistry with Drs. James B. Sumner and Wendell M. Stanley. Professor Fritz Lipmann shared the prize in Medicine and Physiology with Sir Hans Krebs in 1953, and in 1955 Dr. Vincent du Vigneaud, Trustee of the Institute, received the Nobel Prize in Chemistry.

The Trustees

GEORGE H. WHIPPLE, M.D.

George Hoyt Whipple, M.D., Vice Chairman of the Board of Trustees, is emeritus Professor of the School of Medicine and Dentistry of the University of Rochester. The Nobel Prize in Medicine and Physiology which he shared with Drs. George Minot and W. P. Murphy in 1934 was one of his highest scientific honors, but he has also made noteworthy advances in the field of medical education, and he is a seasoned and able administrator as well. He was dean of the School of Medicine and Dentistry at Rochester from 1921 to 1953, and he has been a member of the Board of Trustees of the Institute since 1936.

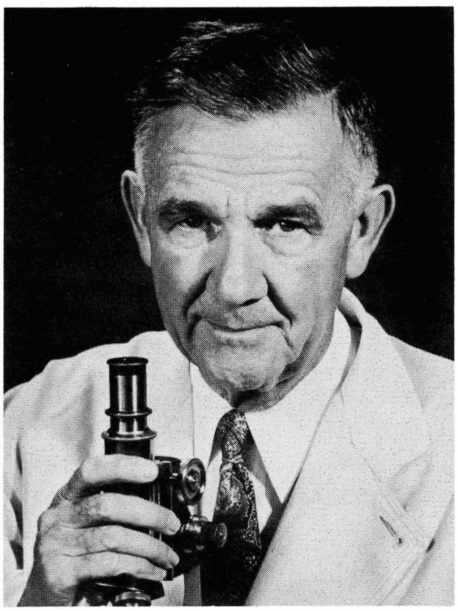
Born in Ashland in northern New Hampshire in 1878, Dr. Whipple congratulates himself today on the good fortune of having discovered very early the lure of the woods, hiking, snowshoeing, canoeing, fishing, hunting—the pleasures of the out-of-doors that remain essential parts of his life today. The portrait that we print here was done by his friend, Ansel Adams, who is best known for his beautiful photographs of high places in the mountains of California.

Like so many distinguished men in American medicine, George Whipple took his undergraduate and graduate training at The Johns Hopkins Medical School where he was under the influence of such men as Osler and Cushing, and of course Dr. William H. Welch. In 1914 Dr. Whipple married Katharine Waring of Charleston, South Carolina, and after a honeymoon in the woods of New Hampshire they moved to San Francisco. Dr. Whipple had been invited by the President of the University of California to establish a new department of research medicine in the medical school and to serve as Director of the newly-endowed Hooper Foundation for Medical Research. By 1920 Dr. Whipple had become Dean of the Medical School, and he regarded himself as a settled Californian.

Word of his research and administrative achievements on the West Coast, however, had reached the East, and in 1921 he was prevailed upon to undertake a new and larger task at the University of Rochester. A new medical school was being established there, generously endowed by The Rockefeller Foundation and Mr. George Eastman; further, one million dollars had been given by the daughters of Mr. and Mrs. Henry Strong for construction of the Strong Memorial Hospital of the University. Dr. Whipple was to be Dean of the Medical School. Four busy years later the first class of medical students started in the new facilities, and the hospital was completed a few months later. The school and its teaching hospital were under one roof, unusual at the time, but the innovation was an important arrangement for the vitality of both.

MEDICINE AND DENTISTRY

Mr. Eastman, whose association with Dr. Whipple in establishing the medical school grew into a close friendship, proposed that the medical school be combined with a school of dentistry that would offer education in dentistry of the highest order. When the medical school opened, applications for dentistry were expected but there were almost none. This led after a few years to a decision to offer scholarships for graduate instruction in dentistry, and with the support of The Rockefeller Foundation and The Carnegie Foundation an experimental program of this sort was established. It was eminently successful. In this way began the School of Medicine and Dentistry of the University of Rochester.



The research on the effects of diet on anemia which ultimately led Dr. Whipple to the Nobel Prize began even before he went to Rochester. In San Francisco he and Dr. Charles Hooper had undertaken studies of liver injuries and bile pigment metabolism which led to interest in hemoglobin production. It was natural that this should have led on to anemia studies, and the results of some of their studies of the influence of diet on hemoglobin production and anemia were published as early as 1918. Dr. Whipple credits Dr. Hooper, his younger colleague, with having wanted to make clinical tests of liver extracts on anemia patients at that time, and his preliminary trials were encouraging. But clinicians discounted the results of the work and the tests were dropped. Dr. Frieda Robbins, a colleague from San Francisco, went to Rochester to continue work there with Dr. Whipple on anemia due to blood loss. Extensive and methodical experiments in dogs with various diets soon showed that bread, milk, fish and grains were poor in hemoglobin producing factors while visceral tissue of beef, sheep, pig and chicken was quite potent. Liver was especially potent.

In alluding to this work, the official presentation of the Nobel Prize stated: "Whipple's experiments were planned exceedingly well and carried out very accurately, and consequently their results can lay claim to absolute reliability." The prize was awarded to Dr. Whipple jointly with Dr. George Minot and Dr. William Murphy of the Harvard Medical School. The relation of the work of these men was set forth in the official presentation: "These investigations and results of Whipple's gave Minot and Murphy the idea that an experiment could be made to see whether favourable results might not also be obtained in the case of pernicious anemia, an anemia of quite a different type, by making use of foods of the kind that Whipple had found to yield favourable results in his experiments regarding anemia from loss of blood."

OTHER HONORS

Dr. Whipple has been a member of the National Academy of Sciences for thirty years and a member of the American Philosophical Society for twenty. The University of Toronto has awarded him its Charles Mickle Fellowship and he holds the Kober Medal and the Rochester Civic Medal. He is a past President of the American Association of Pathology and Bacteriology and was awarded the William Wood Gerhard Gold Medal from the Philadelphia Pathology Society.

Yet in spite of his many honors for achievements in research and administration, Dr. Whipple would be remembered as a teacher. "Perhaps research may give a greater sense of accomplishment," he says, "but teaching carries greater personal happiness."

COLUMBIA UNIVERSITY SCIENCE WRITERS ARE INSTITUTE GUESTS

THE INSTITUTE was host on December 19 to a group of graduate fellows in science writing who are studying at Columbia University under a program sponsored by The Rockefeller Foundation and The Sloan Foundation. After an informal reception and luncheon President Bronk welcomed the guests to the Institute and spoke of the significant importance that scientists must attach to those who seek to make the work of science accessible and understandable to the broad public. Dean Edward Barrett of the Columbia University Graduate School of Journalism responded, citing the importance that Columbia University had attached to the program. He said that the university had made special provisions so that science courses could be taken for credit or audited regardless of usual prerequisites and requirements. He commented upon the selectivity which had reduced approximately 100 applicants to the six who were our guests. Professor John Foster, who is in charge of the program, then introduced the graduate fellows, each of whom is a mature journalist and most of whom are on leave from newspaper offices.

Mr. Earl Ubell of the New York Herald Tribune, who was also a guest at the luncheon, presented President Bronk with a certificate of honorary membership in the National Association of Science Writers. Professors Alfred E. Mirsky and Frank L. Horsfall, Jr., then made brief presentations of the work of their laboratories and its significance to the fields of biochemistry and virology. Following a lively discussion period the group adjourned.

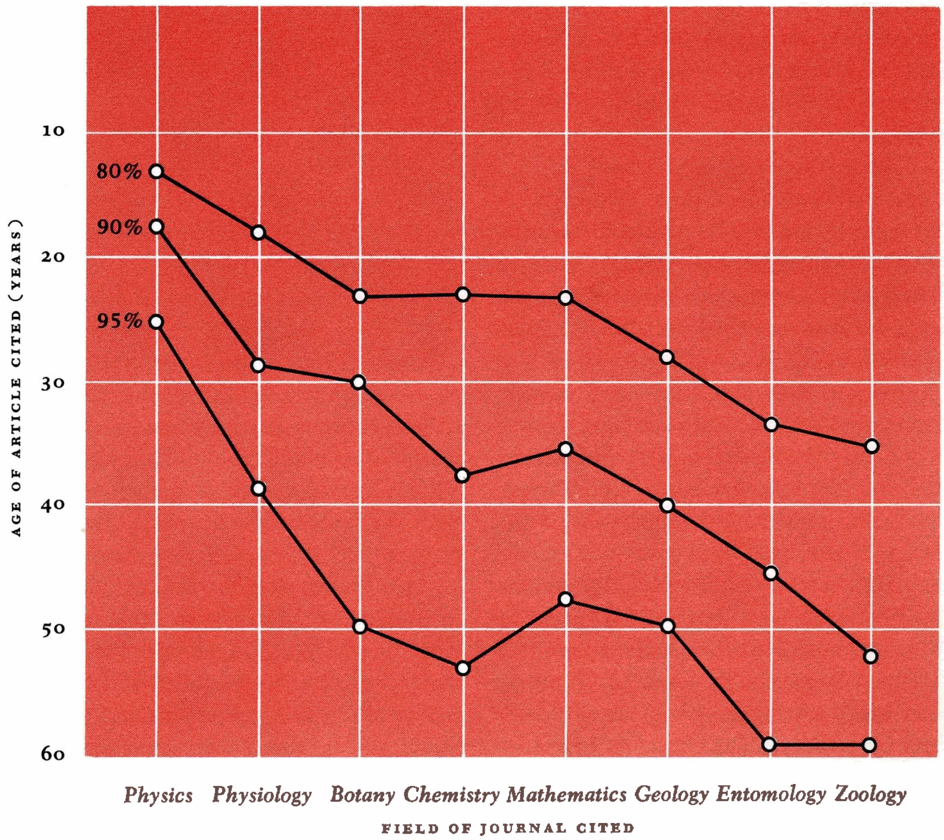
THE QUEST FOR MORE SPACE IN THE ROCKEFELLER INSTITUTE LIBRARY

BOOKS AND JOURNALS are flowing into the Institute's library at an unprecedented rate as the size of the Institute's faculty increases, the scope of its activities widens, and the scale of scientific publication throughout the world rises. This accumulating wealth of information is regarded as a mixed blessing by the Library Committee and the administration who are faced with storing a steadily growing collection in a finite volume and in such a way as to make it as convenient and useful for the Institute's research as possible.

Completion of the new laboratory building this Spring will free considerable space in the lower part of the library that has been devoted to other uses, thus, temporarily at least, averting an explosion. But this, too, raises problems for the additional free space is not in the reading room of the library where we would like it, but in the lower stacks. As a result, much thought is being given to determining the relative use of the various types and ages of the literature in our collection. Since about three-quarters of our entire collection consists of bound volumes of journals, the most effective solution of the space problem appears to be to arrange them by title and date so that the least-used titles and the oldest issues go to the remotest shelves. This is where planning has begun.

As a first approximation a list of journals to be candidates for the basement stacks was compiled with the help of nine senior faculty members and the Library Committee, working with Miss Esther Judkins, the Librarian. This group represents broadly all of the fields of interest at the Institute. Their list of candidates for the basement (212 out of 636 titles considered) is now in the hands of all the faculty as well as the students to be sure that a key journal of daily reference value to someone is not inadvertently consigned to the lower stacks.

It is possible that when the results of this phase of the survey are at hand it will be found that so many journals are used



Age of journal collections to contain various percentages of articles cited frequently by someone that other measures will be needed. One such possibility is to place the older issues of the journals in the basement. The problem then would be what date to use for the division and whether to use the same date for all fields of science.

Meaningful, quantitative data on the useful life of literature in various fields are not easily found or compiled, but some interesting information on this subject was published recently by Charles H. Brown, Librarian Emeritus of Iowa State College (Scientific Serials, Association of College and Research Libraries Monograph Number 16, Chicago, 1956). We cannot go into the details of this study, but statistics pertaining to the use of back issues have been derived from it and summarized in the accompanying figure. The three profiles show the "age" of collections of journals in the various fields that would contain 80%, 90%, and 95% of the articles cited during the year studied (1953). One limitation in applying these figures to our problem is that they are based on published *citations,* not on reading and reference frequency, distribution of which might be very different. It is evident, however, from Dr. Brown's data that no single cut-off date would serve all fields equally. What solution would best suit the needs of those at The Rockefeller Institute is yet to be determined, but it is just possible that with good luck the problem may not have to be faced for some years.

OTHER MEASURES

While we are on the subject of the library's problems we should mention several measures which have been taken or are planned to increase its effectiveness. Over a thousand books are being added to the collection each year and the Library Committee has devised a system for increasing this number. Each week as newly-published scientific books are announced they are secured on approval for display in the library if they seem to lie within fields of interest. Faculty and students are invited to indicate their interest in having a copy in the library, whereupon either the book is purchased, or, if no interest is expressed, the book is returned. To keep the faculty and students abreast of this growing collection of books, a bimonthly accessions list has been initiated by the library for general distribution.

For many years the books in the library have been arranged on the shelves alphabetically by author, an excellent system for those who know precisely what they want, but frustrating to one who wishes to browse. It has now been decided to arrange the books on the shelves according to Library of Congress subject classification. This task of thousands of trying, intellectual decisions has been boldly undertaken by the librarians and is now well under way. In the meantime rearrangement on the shelves will not be possible until the entire job is done, perhaps a year or more from now.

Study rooms and working space have been insufficient in the past few years, but a part of the rearrangement of the basement stacks will include provision of two quiet, air-conditioned rooms overlooking the East River that will be used as seminar rooms and for study. Moreover, at various places throughout the library small study-carrels will be located. Three experimental units of this kind have been in heavy use on the balcony above the main reading room.

A number of other plans for improving the library's service are being considered, but they have not reached a state where they could be reported as more than the bright vision of the future.

THE FIRST SIGMA XI INITIATION

THE ROCKEFELLER INSTITUTE Chapter of the Society of the Sigma Xi held its first initiation ceremony in connection with a banquet and a lecture by Dr. Peter Debye on Tuesday, November 25, 1958, at 6:00 p.m. The initiation was attended by over a hundred Chapter members and initiates and also by Mr. David Rockefeller, the Chairman of the Board of Trustees, Dr. Frank M. Carpenter, President of Sigma Xi, and Dr. Peter Debye, Professor Emeritus of Chemistry at Cornell University.

The initiates numbered forty-three; all were members of the faculty of The Rockefeller Institute or The Rockefeller Foundation Virus Laboratory. Besides four members emeriti, Dr. P. K. Olitsky, Dr. W. J. V. Osterhout, Dr. T. M. Rivers and Dr. D. D. Van Slyke, nine full Professors and two Nobel Prize winners were initiated. As Dr. Carpenter stated, "This is probably the most distinguished group of initiates in the history of Sigma Xi."

A full list of the new initiates and of the Associate Members who were promoted to full membership will be found under Institute Mention on page fourteen.

The speakers at the dinner, which was presided over by Dr. N. R. Stoll, the President of the Chapter, included Dr. Detlev W. Bronk, Mr. Rockefeller and Dr. Carpenter. Dr. Stoll's presidential address highlighted the growing realization of the importance of personal communication among scientists and the significant role that Sigma Xi plays in this phase of scientific life. Following the formal promotion of four Associate Members to full membership, the initiation ceremony was conducted by Dr. Stoll. Next, President Bronk introduced Mr. Rockefeller who presented the Chapter with a magnificent Initiates Book containing the Constitution and By-Laws of the Chapter, with pages for the initiates' signatures for well over fifty years to come. In his presentation, Mr. Rockefeller emphasized his belief in the importance of friendship and easy communication among scientists and congratulated Dr. Bronk on the important changes which he has effected at The Rockefeller Institute. After a brief word of greeting from Dr. Carpenter, the ceremony was adjourned.

At 8:00 p.m. in Caspary Auditorium Dr. Theodore Shedlovsky introduced Dr. Peter Debye, the Sigma Xi lecturer. Dr. Debye's talk was entitled "Tales of Science and Scientists" and included several deeply penetrating descriptions of the atmosphere and work patterns of individuals and groups of individuals that he had known who were, at the time, making highly significant contributions in physics. In conclusion, Dr. Debye stressed the importance of informal conversation in a relaxed atmosphere for the generation of important ideas.

The Sigma Xi Chapter plans to have three more meetings this year, each selected to be of special interest. The Chapter Initiates Book will be on display shortly in the Commons Room in Welch Hall.

MARAMOROSCH GIVEN AAAS-CAMPBELL AWARD

DR. KARL MARAMOROSCH, Assistant Professor at The Rockefeller Institute, was honored in December by being selected as the 1958 recipient of the American Association for the Advancement of Science-Campbell Award for Vegetable Research. The award, established last year by the Campbell Soup Company, consists of a bronze medal and $1500. It is given for "an outstanding single research contribution, of either fundamental or practical significance, relative to the production of vegetables, ...in the fields of horticulture, genetics, soil science, plant pathology, entomology, plant physiology, or other appropriate scientific areas."

Award of the medal to Dr. Maramorosch was based on his work with the corn stunt virus which resulted in showing that one strain of the virus inhibits the transmission of a related strain through the insect which is one of the vectors transmitting the disease. Dr. L. O. Kunkel, working with strains of aster yellows virus which are also transmitted by leaf-hoppers, had shown earlier that one strain of this virus which multiplies in its insect vector, protects against infection by a related strain of virus. Dr. Maramorosch's work with corn stunt confirms this finding but he has shown that the cross-protection between the two strains of corn stunt virus is unilateral, e.g., one will protect the insect against the other, but protection does not occur in the reverse order. This is believed to be the first demonstration of unilateral cross-protection by a plant virus in an insect host.

LEE D. PEACHEY AWARDED LEITZ FELLOWSHIP FOR GRADUATE STUDY

LEE D. PEACHEY has been selected as the first recipient of the Leitz Fellowship for graduate study at The Rockefeller Institute. The Leitz Fellowship was created last year by the E. Leitz Company in recognition of the contributions The Rockefeller Institute is making through its new program of graduate study. Mr. Peachey, who is completing his work in preparation for the degree of Doctor of Philosophy from the Institute, holds a B.S. in engineering physics from Lehigh University. He came to The Rockefeller Institute in 1956 after beginning graduate study at The University of Rochester.

The Fellowship is awarded annually to a student in the later years of his graduate program so that he may continue his studies for a longer time than usual.

Cytological investigations attempting to correlate structure and function are Mr. Peachey's chief research interest. While at the Institute he has concentrated on muscle cells, studying impulse conduction and related structural elements in cells of various species. As is customary for graduate fellows at the Institute, Peachey has spent several months studying abroad. He has just returned from England where he studied for 6 months with A. F. Huxley in the Physiological Laboratory at Cambridge University. Mr. Peachey has carried on his work at the Institute under Professor Keith R. Porter.

FIFTY YEARS AGO AT THE ROCKEFELLER INSTITUTE

Appointment of the First Director of The Rockefeller Institute Hospital

ON OCTOBER 10, 1908, the Board of Scientific Directors elected Dr. Rufus I. Cole to be director of the new hospital to be built at the Institute, for which Mr. Rockefeller had provided a special gift of $500,000. Dr. Cole, 36 years old, had been resident physician of The Johns Hopkins Hospital, where he had done notable work in clinical bacteriology, especially in developing a method of cultivating the typhoid bacillus from the patients' blood. Plans for the organization of the hospital staff, which he began at once to draw up, were very influential in establishing The Rockefeller Institute Hospital as a research department whose members were scientific investigators of disease.

ZIMBLER SINFONIETTA

A DOZEN STRING PLAYERS, consisting of seven violins, two violas, two cellos and a double bass, from the Zimbler Sinfonietta, presented a concert in Caspary Auditorium on Sunday, December 14, for members of The Rockefeller Institute faculty, students, and staff and their guests. These artists, all members of the Boston Symphony Orchestra, played works by Vivaldi, Rossini, Barber, Tansman, Bach and Mozart. The concert was enthusiastically received by a large and appreciative audience.

Dr. Shedlovsky, who had been instrumental in arranging the concert, introduced the ensemble. One of the violinists, Mr. Harry Dickson, introduced the program and offered some engaging remarks about the works played, the instruments of some of the players, and music in general.

Mr. Zimbler, leader of the group (which prides itself on being able to play together without a conductor), was joined by others in the ensemble in praise of Caspary Auditorium as a place for musical performances. Mr. Dickson remarked to the audience: "The acoustics for us were magnificent; I hope it sounded well out there." In response to the enthusiasm of the audience, the ensemble played as an encore a charming excerpt from a suite for strings by Corelli.

HOLIDAY FESTIVITIES

CONTINUING A CUSTOM they began several years ago President and Mrs. Bronk invited the faculty, students, and staff of the Institute, and their families, to join them in singing Christmas Carols on the afternoon of December 23rd. More than six hundred were led in the carols by a group of our best singers, fortified by the return of their former leader, Dr. Smillie, and our organist, Mr. George Morgan, Head of the Music Department of the Taft School. After singing Christmas classics for more than an hour, tea was served and Christmas greetings were exchanged.

As part of their efforts to provide more opportunities for the families of the Institute faculty to meet each other and the students, Dr. and Mrs. Bronk were at home in the President's House on New Year's Day to all of the faculty and students who reside in New York City.

decrement in frog nerve, and he has also been able to explain to his own satisfaction why Kato found contrary results. This old controversy will no doubt not be settled (or re-settled) in a single season, but Dr. Lorente is convinced that when others bring modern measuring techniques to this old but significant problem in neurophysiology, they will confirm his findings.

NERVE METABOLISM

We have written much about the electrical behavior of the nerve cell, but have as yet said nothing about the source of its electrical energy. Study of this question in recent years has yielded significant results, thanks to highly refined biophysical and biochemical techniques developed at the Institute and elsewhere. Like all of the cells in our bodies, the neurons require food and oxygen which they consume, eliminating carbon dioxide and other waste products. These are the processes that enable most living cells to maintain themselves and to carry out their various highly specialized functions: the growth and division of embryonic cells, the contraction of muscle cells, the secretion of glandular cells, etc. The specialized function of the neuron is conduction of electrical impulses, and study of the relationship between the energy-providing processes of metabolism in nerve cells and their energy-consuming electrical activity has provided greater understanding of the cellular basis of the nervous control of the body. For many years, questions of this kind have occupied President Bronk and his colleague, Professor Frank Brink, Jr., who came to the Institute in 1954 from The Johns Hopkins University so that he could continue their collaboration.

The electrical characteristics of nerve cells are associated with a difference in the concentration of electrically-charged ions (particularly sodium and potassium ions), between the interior of the cell and the exterior body fluids. Such a difference is characteristic of many, and perhaps all cells, but in nerve the difference is functionally of especial importance.

It seems to be one of the properties of the universe that everything tends more or less quickly toward uniformity—differences in temperature are difficult to maintain, for example; buildings decay and fall, and, more to the point, ions quickly diffuse uniformly throughout a solution so that it becomes electrically neutral. The living cell is able to oppose this diffusion and to maintain a difference in concentration of ions between its surface and interior. In nerve cells the difference is recognizable as a rather considerable electrical potential, e.g., the nerve is said to be polarized. When a nerve impulse is initiated, the mechanism for maintaining the ion concentrations breaks down locally, and we measure the depolarizing effect as a local drop in the electrical potential of the surface membrane of the nerve. This local breakdown causes adjacent points on the nerve fiber to be depolarized and the effect spreads like a wave. But almost at the instant the local depolarization occurs, the cell sets about to do the work necessary to sort out the ions again, thus restoring the original ionic content. Part of the refractory period of a few thousandths of a second during which the nerve will not conduct is accounted for by this re-sorting process. Like the nerve impulse itself, the restoration occurs locally, so that we measure a drop in polarity of only very short duration which spreads along the nerve fiber (in both directions, incidentally, unless the fiber is stimulated at its end).

A helpful analogy for visualizing this local disturbance which appears to move down the nerve is to consider the nerve fiber to be like a long row of dominoes stood on end. If one is pushed down, it will knock over its neighbors and the disturbance will pass along the row. Now if our imagination will provide each domino with a little man to set it upright again as quickly as possible after it falls, we will see that the disturbance will flow down the row as a local and temporary tumbling over of dominoes which spring upright again. Until the first domino is set right again (e.g., until after the refractory period) no new impulse can be sent down the row of dominoes and hence there is a maximum frequency at which impulses will pass. Moreover, we can see that the impulse would proceed in much the same way, re-

(continued on page twelve)

THOMAS MCELRATH DEBEVOISE

For understanding of Mr. Thomas M. Debevoise it is necessary to understand the old English legal verb "to attorn". At the feudal law one attorned when he appointed another to act in his place; and the one appointed was then called an attorney—as he is to this day.

Gradually, through the centuries, men learned in the law of England came to be divided into two groups: barristers-at-law who are those who practice as advocates in the superior courts of justice, and attorneys-at-law who are the counsellors—standing in the place of their principals and acting for those principals in all sorts of matters, both weighty and small.

In the oldest and best sense of the word—almost in its feudal sense—Mr. Debevoise was an attorney. The flamboyant arts of the advocate in court were not for him. He counselled, he persuaded, he advised, he encouraged, he mediated, he dissuaded—and he found no reason ever to raise his voice.

Mr. Debevoise was Counsel to The Rockefeller Institute for 34 years. He was moral, grave, and judicious—indeed, he was *sublime* in the poise he brought to a discussion. Among all those who know what it is "to attorn", Tom Debevoise is cherished as a counsellor of unrivalled decorum, judgment and taste. This is his best valediction.

He died at the age of 84 on December 20, 1958. Mr. Debevoise is survived by his son, Eli Whitney Debevoise, a Trustee of The Rockefeller Institute; a brother, Colonel Paul Debevoise; two sisters, Mrs. Ronald K. Brown and Mrs. William F. Decker; two grandchildren and 4 great grandchildren.

HENRY ALLEN MOE

gardless of how hard the first domino is struck.

Our imaginary little man who sets things right after each impulse is obviously an important part of the scheme. He, and the ways he uses to restore the system to the conducting state, are essential determinants of its behavior. In nerve, they correspond to the oxygen metabolism and the enzymatic processes by which the energy of metabolism is converted into the electrical potential of the cell membrane. Techniques have been developed whereby the oxygen consumption of a nerve can be measured as the impulse is conducted along its fibers. One such device, capable of very quick response to changes in the nerve's respiration, was developed a few years ago by Dr. C. M. Connelly, who is now at the Institute.

RESPIRATION OF NEURONS

It can be shown that the active nerve "breathes harder", so to speak, as it conducts pulses at a higher rate. From careful study of exactly how much more oxygen it requires as the rate increases, how soon it requires it, and for how long after the work ceases, etc., some idea of the nature of the connection between oxygen consumption and impulse transmission can be formed. Even more information can be learned from similar experiments in which different steps in the metabolic chain are interfered with by drugs and various other chemicals.

Hodgkin and Huxley at Cambridge have shown during the past ten years or so that when the nerve impulse passes, sodium ions seem to move into the nerve and potassium ions move outward towards its surface. This connection between the ion movements and nerve processes affords a basis for studying the connection between oxygen consumption and electrical action in nerve. Connelly has shown recently at the Institute that the effect of prolonged stimulation at high frequency seems to be that the ion re-sorting processes are set in motion with such intensity that when the stimulus ceases an abnormally great extrusion of sodium ions from the cell interior occurs. As a result the nerve membrane becomes electrically polarized more than normally. This is seen as a momentary positive potential following termination of the train of impulses, falling back to normal as the sodium ions quickly diffuse. As might be expected, the metabolic rate of the cell is higher during this time. During the past year radioactive potassium has been used by Paul Hurlbut to study the movement of potassium ions into and out of nerve in the presence of various inhibitors of metabolism. Thus the relation of ion movement to oxygen metabolism is revealed.

FIRE-FLY TAILS

By varying the biophysical and biochemical conditions, many modifications in nerve cell function and metabolism occur that give some clue as to the great complexity of the detailed processes in the nerve. Recent investigations by Dr. Cheng have suggested that though oxygen respiration is essential to healthy function, nerve cells can call upon energy sources other than oxygen metabolism. They can maintain their electrical function for several hours when oxygen metabolism is inhibited by chemicals. Incidentally, readers who have wondered all this time what became of the great quantities of firefly tails being sought by our Purchasing Department (see "Questing for Research", Volume 1, No. 3, September 1957) will find the answer here. One of the enzymes in the firefly's light-producing reactions is used as a detector for certain components of the nerve cell's metabolism.

SODIUM SUBSTITUTES

Precise understanding of the role of sodium and potassium ions in nerve function has been the object of neurophysiologists for decades, and for the past several years this has been a particular interest of Dr. Lorente and his colleagues at the Institute. Recently, he has been able to show that sodium can evidently be replaced by a number of other chemical substances. Nerves that have become non-conductive because of sodium deficiency are restored to activity by such ions as ammonium, hydroxylammonium, hydrazinium and guanidinium ions. In just what way these ions act as substitutes for sodium is not clear. Dr. Lorente suspects that certain of the metabolic processes, even in sodium-deficient nerve, must continue to function with residual sodium while the substitute ions only facilitate an otherwise impaired but not altogether obliterated ability to conduct.

Almost incidentally, Dr. Lorente's work with sodium substitutes in nerve function has led him to discover that sodium is also necessary to maintain the filtering ability of the walls of the capillary blood vessels. If colloidal albumin or dextran is supplied to the hind legs of a bullfrog in a solution closely resembling the blood, it is retained inside the blood vessels and does not escape into the tissues. In sodium-free solution, however, the colloidal matter quickly diffuses through the walls of the blood vessels and swells the tissues. None of the sodium substitutes which restore conduction in sodium-deficient nerve will prevent this loss of filtering ability in capillaries.

Johns W. Hopkins, III, Graduate Fellow of the Institute who is now working in the laboratory of Dr. Mirsky undertook to determine whether any of the sodium substitutes that Dr. Lorente found to work in nerve would also work in the cell nucleus. They do not, which further complicates the question of the precise role of sodium in the two different cell-functions.

CONCLUSION AND PROLOGUE

But to pursue such experiments here would lead us far from the nerve impulse, for to understand one thing thoroughly we are often confronted by the necessity to understand all. The nerve cell is after all basically like every other cell in our body; all that is being done to understand the cell generally, applies, therefore, more or less directly to the nerve as well. We shall leave these tempting by-ways unexplored, however, perhaps to return to them another time.

But much remains to be said about the nervous system, itself, and the work of those at the Institute to understand it—studies by Drs. Lloyd, Brooks, and Wilson of reflex mechanisms; work by Drs. Hartline, Ratliff, and Miller on the visual systems of invertebrates and their implications for man; and we shall return to Dr. Lorente to mention his work on the brain and spinal cord. The intricate but intriguing question of the inter-relations among nerves and nerve impulses, which they and others are studying, will be the subject of the next article in this series on important fields of science as they are pursued at The Rockefeller Institute.

FACULTY ACTIVITIES

Academic Honors

DETLEV W. BRONK
L.H.D., Oberlin College

Lectures, Conferences and Symposia

ALEXANDER G. BEARN
Lowell Lecture, Massachusetts General Hospital, Boston.
Lecture, Royal Society of Medicine.
Participant, Symposium on Genetics in Medicine, Harveian Society of London.

LUDWIG BERGMANN
Participant, Symposium on Viruses in Tissue Culture, New York Academy of Sciences.

DETLEV W. BRONK
Dedication Address, Millikan and Seaver Science Laboratories, Pomona College.
Address, International Conference on Scientific Information Banquet.

MERRILL W. CHASE
Participant, Symposium II on the Physicochemical Properties of Allergic Antibodies, Third International Congress of Allergology, Paris.

ARPAD I. CSAPO
Participant, Lecture Series on Recent Advances in Endocrinology and Intermediary Metabolism, University of Chicago.

RENÉ J. DUBOS
Lowell Lecture, Massachusetts General Hospital, Boston.

MARILYN G. FARQUHAR
Participant, Tenth Annual Conference on the Nephrotic Syndrome, Columbia University.

THOMAS D. C. GRACE
Participant, Symposium on Viruses in Tissue Culture, New York Academy of Sciences.

MAN-CHIANG NIU
The Lilly Research Laboratories Lecture, Indianapolis.

HOWARD A. SCHNEIDER
Address before New York Regional Group, Medical Library Association, The Rockefeller Institute.
Participant, Arden House Conference on Nutrition.

RICHARD E. SHOPE
Hanau W. Loeb Lecture, St. Louis University School of Medicine.

IRA SINGER
Participant, International Colloquium on Resistant Infections, New York, under the auspices of The World Medical Association.

EDWARD L. TATUM
Nobel Lecture, "A Case History in Biological Research", Karolinska Institute, Stockholm.

A. CECIL TAYLOR
Chairman, Conference on Hypothermia, New York Academy of Sciences.

PAUL A. WEISS
Marshall Woods Lecture, Brown University.
Lowell Lecture, Massachusetts General Hospital, Boston.

VICTOR H. WITTEN
Symposium on A Decade of Anti-Inflammatory Steroids, from Cortisone to Dexamethasone, New York Academy of Sciences.

Society Elections

FRANK L. HORSFALL, JR.
Affiliate, Royal Society of Medicine, London.

KARL MARAMOROSCH
Vice Chairman, Section on Insect Vectors, Entomological Society of America, Salt Lake City.
Chairman, Division of Mycology, New York Academy of Sciences.

ALFRED E. MIRSKY
Member, Deutsche Akademie der Naturforscher Leopoldina, Halle.

EDWARD L. TATUM
Member of the Council, New York Academy of Sciences.

Other Appointments and Distinctions

DETLEV W. BRONK
Trustee, Protein Foundation.
Honorary President, Tenth Pacific Science Congress.
Member, American Committee of the Heart Foundation-Princess Liliane.
Member, Electoral College of the Hall of Fame, New York University.
Member, National Advisory Council for International Medical Research.

VINCENT P. DOLE
Member, Editorial Board, *Circulation Research.*

RENÉ J. DUBOS
Member, Panel on Biological and Medical Sciences, Committee on Polar Research, National Academy of Sciences—National Research Council.

D. DZIEWIATKOWSKI
Editorial Advisory Board, *Archives of Oral Biology.*

H. KEFFER HARTLINE
Chairman, Committee on Biological Sciences of the Space Science Board, National Academy of Sciences—National Research Council.

FRANK L. HORSFALL, JR.
International Board of Editors, *Excerpta Medica Foundation.*

ROLLIN D. HOTCHKISS
Trustee, Foundation for Microbiology, New Brunswick.

HENRY G. KUNKEL
Member, Committee on Blood and Related Problems, National Academy of Sciences—National Research Council.

DAVID P. C. LLOYD
Board of Advisory Editors, *The Journal of Neurophysiology.*
Research Advisory Board, The United Cerebral Palsy Research and Educational Foundation.

FACULTY ACTIVITIES

(continued from page thirteen)

DUNCAN A. MAC INNES

Member of Research Committee, American Philosophical Society.

Honorary Editorial Advisory Board for the Collected Works of Irving Langmuir.

KARL MARAMOROSCH

Campbell Award and Bronze Medal, American Association for Advancement of Science.

JOHN B. NELSON

Member, Committee on Gnotobiotics and Specific Pathogen-Free Animals, Institute of Laboratory Animal Resources, National Academy of Sciences—National Research Council.

Griffin Award, Animal Care Panel, Chicago.

RICHARD E. SHOPE

Member, Aftosa Technical Advisory Group, Pan American Sanitary Bureau, Rio de Janeiro.

Member, Technical Advisory Group on Zoönoses in the Americas, Pan American Sanitary Bureau, Azul.

Member, Panel on Biological and Chemical Warfare, President's Science Advisory Group.

EDWARD L. TATUM

Nobel Prize in Medicine and Physiology.

PAUL A. WEISS

Second Annual Honorary Lecture Award, Albany Medical College of Union University.

INSTITUTE MENTION

New Members of the Society of the Sigma Xi

INITIATES

GEORGE ACS
ALEXANDER GORDON BEARN
DIETHELM HARTMUT BOEHME
CARLO BRUNI
SONJA MAREID BUCKLEY
JORDI CASALS-ARIET
PURNELL WHITTINGTON CHOPPIN
DELPHINE HARRIET CLARKE
ZANVIL ALEXANDER COHN
ARPAD ISTVAN CSAPO
VINCENT PAUL DOLE
EARL HOWARD FREIMER
JULES HIRSCH
HALSTED REID HOLMAN
FRANK LAPPIN HORSFALL, JR.
MARGERIS ADOMAS JESAITIS
SEYMOUR JOSEPH KLEBANOFF
RICHARD MICHAEL KRAUSE
HENRY GEORGE KUNKEL
FRITZ ALBERT LIPMANN
DAVID MILLARD LOCKE
ALEXANDER GEDEON MATOLTSY
MACLYN MCCARTY
ALFRED EZRA MIRSKY
MARJORIE MARY NEMES
PETER KOSCIUSKO OLITSKY
WINTHROP JOHN VANLEUVEN OSTERHOUT
GEORGE EMIL PALADE
GERTRUDE ERIKA PERLMANN
CLAYTON RICH
THOMAS MILTON RIVERS
ALEXANDRE ROTHEN
MARIA ANNA RUDZINSKA
RUSSELL WILLIAM SCHAEDLER
THEODORE SHEDLOVSKY
FABIO SPARATORE
JOHN MORROW STEWART
WILHELM STOFFEL
TOM TED STONIER
IGOR TAMM
MAX THEILER
DONALD DEXTER VAN SLYKE
FREDERICK D. VIDAL

ASSOCIATE MEMBERS PROMOTED TO MEMBERS

JAMES GERALD HIRSCH
BENJAMIN LOWENHAUPT
WILLIAM HENRY MILLER
RODES TRAUTMAN

New Appointments to the Faculty

DR. LUDWIG BERGMANN, of the Max Planck Institute for Biology, Melchers Division, at Tübingen, has been appointed a Research Associate in the Laboratory of Dr. Maramorosch.

DR. JOSEPH B. BIRDSELL, Professor of Anthropology, Department of Anthropology and Sociology, University of California at Los Angeles, has been appointed a Visiting Professor of the Institute.

DR. CARLO BRUNI, who has been an Affiliate of The Rockefeller Institute, has been appointed a Guest Investigator and Fellow beginning January 1, 1959, to work in association with Dr. Porter.

DR. AIDA TRAVERSO CORI, an Assistant in the Department of Biochemistry, School of Chemistry and Pharmacy at the University of Chile in Santiago, was appointed Guest Investigator on November 25, 1958, and will work with Dr. Perlmann in her Laboratory.

DR. FRANCIS H. C. CRICK, of the Medical Research Council Unit for Molecular Biology in the Cavendish Laboratory, Cambridge University, has been appointed a Visiting Professor of the Institute.

DR. FRIEDRICH P. DIECKE, Professor in the Department of Physiology at the University of Tennessee, has been appointed a Guest Investigator beginning January 1, 1959, and will work in association with Drs. Wilson and Lloyd in the Laboratory of Neurophysiology.

DR. SETSURO EBASHI, an Assistant in the Department of Pharmacology of the University of Tokyo, has been appointed a Guest Investigator in the laboratory of Dr. Lipmann, effective January 1, 1959.

DR. MARILYN G. FARQUHAR, a Guest Investigator in Dr. Palade's Laboratory, has been appointed a Research Associate.

DR. ANTONIO GALLEGO, Director of Fundacion Marques de Urquijo in Madrid, worked for a month during October-November, 1958, as a Guest Investigator in Dr. Lorente's Laboratory.

DR. ERHARD GROSS, a Visiting Scientist at the National Institutes of Health in Bethesda, was appointed Guest Investigator in Dr. Craig's Laboratory, beginning January 19, 1959.

DR. WILLEM C. HÜLSMANN, of the Laboratory of Physiological Chemistry at the University of Amsterdam, has been appointed a Guest Investigator to work in association with Dr. Lipmann, beginning January 1, 1959.

DR. HAR G. KHORANA, Head of the Organic Chemistry Section, British Columbia Research Council, University of British Columbia, has been appointed a Visiting Professor of the Institute.

DR. S. PETER MARFEY, formerly a Guest Investigator in Dr. Craig's Laboratory, has been appointed a Research Associate.

DR. HIROTO NAORA, formerly an Assistant in Research of the Cancer Institute, Tokyo, has been appointed a Research Associate in Dr. Mirsky's Laboratory.

DR. THEODORE T. PUCK, of the Department of Biophysics, University of Colorado Medical Center, has been appointed a Visiting Professor of the Institute.

DR. BETTY SAMS ROOF, of the Department of Pathology, Massachusetts General Hospital, has been appointed a Research Associate to work in Dr. Rous's Laboratory.

DR. MURRAY D. ROSENBERG, formerly a Consultant for the Biophysics and Biophysical Chemistry Study Section of the National Institutes of Health, has been appointed a Research Associate in Dr. Weiss's Laboratory.

DR. JANUSZ S. SKUPIN, formerly of the Department of Agriculture, Institute of Biochemistry, University of Adannickiewicz, in Posnan, Poland, has been appointed a Guest Investigator to work with Dr. Stein, beginning November 14, 1958.

DR. DAVID S. SMITH, of the Department of Zoology, Sub-Department of Entomology, Cambridge University, has been appointed Guest Investigator and Fellow of the Institute, beginning November 1, 1958, and will work in Dr. Porter's Laboratory.

DR. WALTHER STOECKENIUS, of the Physiologische Institut, Universität Hamburg, has been appointed a Research Associate in Dr. Porter's Laboratory.

DR. ROBERT S. STONE, of the Department of Pathology, the School of Medicine, University of California at Los Angeles, has been appointed a Guest Investigator and Fellow, beginning January 1, 1959, and he will work in association with Dr. Dan Moore.

Faculty Terminations

DR. DIETHELM H. BOEHME, a Research Associate in the Laboratory of Dr. Dubos, left the Institute December 31, 1958, to work in the Department of Pathology of The New York Hospital.

DR. LAWRENCE S. FRISHKOPF, formerly a Guest Investigator in Dr. Hartline's Laboratory, left the Institute on October 1st, 1958.

DR. HANS GERD GUNDLACH, Guest Investigator in the Laboratory of Drs. Moore and Stein, left on November 21, 1958, and is now at the Physiologie-Chemisches Institut, Universität Würzburg.

DR. JEAN-PAUL MEYER, appointed as a Guest Investigator to work with Dr. Weiss, resigned as of December 3, 1958, because of illness.

DR. BELA F. P. NAGY, who worked in Dr. Csapo's Laboratory as a Research Associate, left on October 1, 1958, and is now in the Department of Biochemistry at Columbia University.

DR. MARJORIE M. NEMES, who was a Research Associate in Dr. Horsfall's Laboratory, left the Institute on November 30, 1958, and is now a Virologist with Merck, Sharp and Dohme Research Laboratories in West Point, Pennsylvania.

DR. ALFRED R. PRAY, who worked as a Research Associate in Dr. MacInnes's Laboratory, left the Institute on December 1, 1958.

MR. SIDNEY ROSEN, a Guest Investigator in Dr. Dan Moore's Laboratory, left on December 31, 1958, and is now with the Psychiatric Department of the College of Physicians and Surgeons, Columbia University.

Visiting Professors in Residence

DR. THEODORE T. PUCK, Professor of Biophysics, University of Colorado Medical Center, October 5-16, 1958.

DR. DAVID R. GODDARD, Professor of Botany, University of Pennsylvania, Philadelphia, October 13-17, 1958.

DR. JOSEPH B. BIRDSELL, Professor of Anthropology, University of California, Los Angeles, December 15-19, 1958.

Guest Speakers

BORIS MAGASANIK, Associate Professor of Bacteriology and Immunology, Harvard Medical School, October 14, 1958.

JOHN T. RANDALL, University of London King's College, October 21, 1958.

JACQUES MONOD, Head of the Department of Cellular Biochemistry, Institut Pasteur, Paris, October 28, 1958.

GERHARD SCHRAMM, Max-Planck-Institut für Virusforschung, Tübingen, Germany, November 4, 1958.

J. D. BOYD, Professor of Anatomy, Cambridge University, Fellow of Clare College, November 14, 1958.

INSTITUTE MENTION

(continued from page fifteen)

THEODOSIUS DOBZHANSKY, Professor of Zoology, Columbia University, November 18, 1958.

PETER DEBYE, Emeritus Professor of Chemistry, Cornell University, November 25, 1958.

ANDRZEJ BAJER, Docent of the Jagellonian University, Cracow, Poland, December 2, 1958.

Guest Seminar in Medicine

M. G. P. STOKER, Professor of Virology, University of Glasgow, November 12, 1958.

New Grants and Contracts

From the United States Public Health Service for the following work:

For studies by Dr. S. William Pelletier on the chemistry of the aconitum and delphinium alkaloids $21,164

For the first year of an 8-year study by Dr. Keith R. Porter on response of cells, in terms of fine structures, to common carcinogenic agents $11,270

From the National Science Foundation for the following work:

For studies on the chemical nature and mode of action of a specific inducer of the male sex organ in certain plant species by Dr. Armin C. Braun $30,000

For studies by Dr. Lyman C. Craig on the isolation and chemical composition of cypridina luciferin $9,000

For a lecture series on science to young people $24,150

For a two-year study on anatomical pathway of various substances across the wall of glomerular capillaries, by Dr. George E. Palade $15,000

From The Rockefeller Foundation towards the cost of scientific illustrations for a joint research publication on mammalian cytology in the *Journal of Biophysical and Biochemistry Cytology* $200

From the National Foundation for an 18-months' study by Dr. Margeris A. Jesaitis on the manner in which the chemical markers of the nucleic acids of the even-numbered T. bacteriophages $52,965

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