ENGINEERING AND SCIENCE

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MAY, 1947

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FOREWORD

Two men not pictured in this issue, who have done the lion's or perhaps the Beaver's share of both the writing and arranging are Drs. George W. Beadle and Norman H. Horowitz. Dr. Beadle has been chairman of the Division of the Biological Sciences for a year. It was he who introduced to Kerckhoff the Neurospora research which now fills almost half of one floor. Dr. Horowitz, formerly senior fellow in research, now associate professor of biology, is also working with Neurospora, tending towards things chemical. The interrelation between Biology and Chemistry at the Institute is typified by Dr. Horowitz's laboratory, in which he works with Nutrition Fellow Dr. Marguerite Fling, an organic chemist.

Dr. Beadle graduated from the University of Nebraska in 1926 and took his M.S. there in 1927. He received his Ph.D. at Cornell in 1930. Next he was a National Research Fellow and an instructor at the California Institute. After serving as associate professor of biology at Harvard University from 1936 to 1937, he was called to Stanford University as professor of biology, which position he held until the summer of 1946.

Dr. Horowitz received his B.S. from the University of Pittsburgh in 1936, his Ph.D. from CalTech in 1939. He then traveled up and down California, holding a National Research Council Fellowship at Stanford in 1939-40, and a research fellowship at the Institute from 1940 to 1942. Dr. Horowitz returned to Stanford as a research associate in 1942 and remained there until last summer.

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COVER CAPTION

A pink-eye-hooded rat surveys the situation. Inbred by brother-sister matings for more than 30 generations, this line of rats is probably almost homogeneous genetically. Five such inbred lines are at present in use at the California Institute for the study of inherent blood-cell characteristics. Five gene-controlled cellular antigens, each found in all individuals of certain of the lines and not at all in other lines have so far been identified. These studies parallel in some respects other current work on "blood types" in human beings, and in other animals, now gaining recognition as an important segment of modern biology. Much of this work is being aided by the Gosney Fund.

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Monthly

The Truth Shall Make You Free

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Not in the Books

By GEORGE W. BEADLE

SOME YEARS ago the director of a Division of one of the four Regional Research Laboratories of the U. S. Department of Agriculture was called upon to defend before a congressional committee the budget request for his laboratory. Among the items in the proposed budget was a not inconsiderable one for books and periodicals for the library. Pouncing upon this with great vigor a member of the committee pounded the table and shouted: "Doctor, I thought we were paying you fellows to put stuff in books, not to get it out!"

While it is no doubt true that the congressman responsible for this utterance underestimated the importance of a firm foundation in the knowledge of the past as a basis for future discovery, there is a certain justice in his contention. Those of us working in Biology at the Institute are more interested in "putting stuff in books" than we are in getting old stuff out of them. By this I do not mean we are in any way unappreciative of past accomplishment or that we are inclined to decry the importance of an adequate library—quite the contrary. But we do see the many unsolved problems of biology ahead of us and we are impatient to get at them.

What are these problems of biology whose answers we cannot yet find in books? There are many, some of which lie so far in the future that we perhaps cannot yet formulate them in a manner sufficiently clear to make it obvious how we should go about attacking them. Others stand out more boldly.

Many of modern biology's enigmas—some of the profoundest perhaps—center around the gene. As our knowledge of this unit of heredity increases it becomes more and more apparent that it is an irreducible and indispensable unit of all living systems. It appears to be the simplest component of the organism capable of self-duplication. In this it is like the virus. It differs from simpler non-living self-duplicating systems such as crystals in being capable of becoming permanently modified without losing the property of self-multiplication. It is this mutability that has made possible all evolutionary change in living organisms.

While we have learned a great deal about the mechanism by which higher organisms transmit genes from one generation to another with an almost uncanny precision and while much of the mystery surrounding the difference between the living and the non-living has disappeared as a result of our recently acquired knowledge of genes and viruses, there remains much to be learned. We do not know with any certainty what a gene is chemically. We do not know how it produces replicas of itself. Nor do we know how it plays its essential part in the development and functioning of a complex organism. This is a part of the knowledge that biologists will put in the books that are yet to be written.

Gene-duplication involves protein synthesis. It is therefore obvious that we cannot hope to understand this process until we know how proteins are made in the living cell. This, too, is a problem of the future although we are now getting gratifyingly close to it. We can hope soon to know how peptide linkages are formed and once we know this it should be possible to get ahead with the problem of how amino acids are combined to form the essential proteins out of which genes, enzymes and other protoplasmic constituents are built.

Just as advance in basic knowledge at the biological level depends on prior knowledge at the chemical, physical and mathematical levels, so sound medical progress can come only after problems in biology have been formulated and solved. Unfortunately much of present day medical knowledge is empirical and superficial. To illustrate, consider what we know about penicillin, one of Medicine's most remarkable recent discoveries. It is true that at the cost of tremendous labor, which probably could not have been brought to focus on the problem had it not been for the war, we know the chemical structure of the penicillin molecule. But regarding its biological action, our ignorance is indeed profound. Its action on the bacterium whose growth it so effectively stops is a complete unknown.

What is true of penicillin is equally true of most of Medicine's vast array of drugs. Almost nothing is known at a basic level about the action of these substances. Modern chemistry is just now in a position from which it can profitably tackle the problem of molecular structure and biological activity—a position from which it can hope, for example, to tell us why sulfanilamide inhibits the growth of a pathogenic bacterium but a closely related compound does not.

It may be said about the cancer problem, too, that all our knowledge lies close to the surface. Before we can hope to understand in any but a very small way a problem as complex as this, we must solve a basic biological problem about which we now know very little. This is the problem of differentiation. How is it that one group of cells forms an eye while another group, supposedly genetically identical, gives rise to a hand? If we can learn the answer to this, perhaps we will then be in a position to say why in cancer a group of cells suddenly embarks upon an uninhibited growth spree.

These examples serve as a very small sample of the vast unknown in biology. They are a little of the stuff that is not yet in books. They are a part of the challenge to this and future generations of those scientists who are interested in following all possible approaches to a more complete understanding of the ways of living things.

Maximum speed in solving these many problems depends on our bringing to bear on them as soon as we possibly can all the known techniques of the physical and biological sciences. This is exactly what the Institute is attempting to do in the long-term research program in physical chemical biology now well under way. In the Physics laboratory is a modern electron microscope available for use on materials of biological interest. In Chemistry X-ray and electron diffraction techniques determining molecular

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CHEMICAL GENETICS

By NORMAN H. HOROWITZ

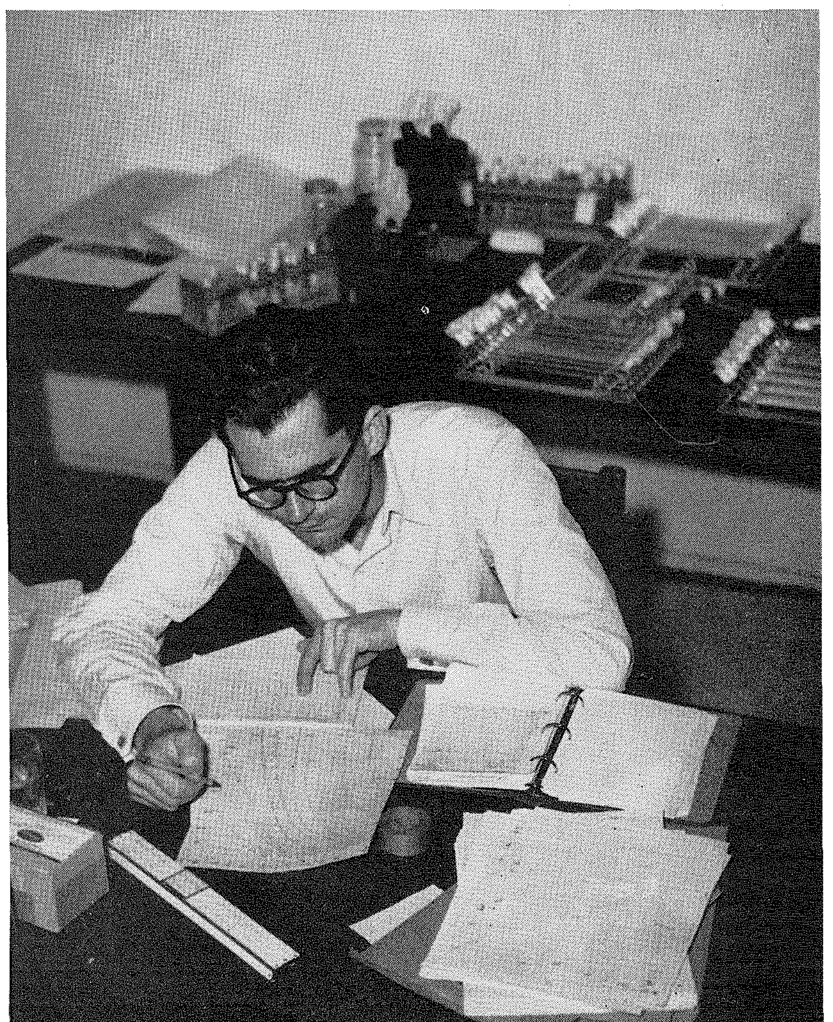
HISTORICAL SKETCH

As ALMOST everyone knows, the science of genetics was founded in his spare time by a monk named Gregor Mendel, who raised peas as a hobby in the monastery garden at Brünn, Austria (now Czechoslovakia). Mendel's great discovery, which went unnoticed for 35 years after it was first published, was, like most other important ideas, radical and simple. It was that the individual is made up of distinct hereditary qualities, and that these qualities, or characters, are transmitted independently of one another to future generations. In other words, hereditary characters are passed on as units, and they are distributed in families and populations according to the laws of independent events,—**i.e.,** the laws of probability.

Mendel's findings were published in 1865 and were promptly forgotten until their rediscovery in 1900. Subsequent research (since 1900) showed that for many characters the rule of independent inheritance is at best a first approximation. That is, when certain characters occur together in one parent—such as colorblindness and hemophilia in man—they tend to be transmitted to the progeny together, rather than independently. This finding, together with other evidence, led to the chromosome theory of inheritance and eventually to the theory of the gene. According to these theories, now universally accepted, the agents which are actually transmitted in the germ cells and which determine the inheritance of the individual are material elements in the chromosomes, called genes. Genes which lie in the same chromosome tend to be inherited together; the closer together they lie the more frequently they go together. Genes which are located on different chromosomes, or far apart on the same chromosome, are transmitted independently of one another. This generalization, which successfully correlated large amounts of biological data, was chiefly the creation of T. H. Morgan, A. H. Sturtevant, C. B. Bridges, and H. J. Muller of the **Drosophila** school of genetics. With the establishment of the gene concept, a new and more fundamental approach to the study of inheritance and evolution was opened—the investigation of the gene itself. Furthermore, by placing the whole problem on a physical basis, the gene theory made possible — or rather, invited — the introduction of chemistry and physics into the picture.

PROPERTIES OF THE GENE

The problem of chemical genetics is twofold: to describe the chemical nature of the gene and to investigate its relationship to the other components of



Researcher Dr. Marco Zalokar plotting the growth rates of Neurospora inhibited by sulfanilamide (SA) in the presence of varying amounts of p-aminobenzoic acid (PAB). Rates are measured in the double-ended tubes in background. This research is attempting to determine the relations between SA and PAB in Neurospora.

the cell. In a number of ways the gene is unique and without a counterpart in the physical universe. After considering the known properties of the gene in a recent book, the eminent physicist Erwin Schrodinger was led to remark that the science of genetics is "easily the most interesting of our day." Most geneticists concur in this opinion.

The genes are the basic self-reproducing units of the body. That is to say, every gene arises from a preceding gene through a process which insures that it will be an exact copy of its predecessor. With rare exceptions, the precision of the copying process is such that not more than once in a million duplications, at the outside, is there a detectable slip. Certain genes are known, such as those determining the blood groups in man, which have not changed perceptibly in centuries. Genes can and do change, however, and this is important, because it is these infrequent changes, or mutations, which make evolution possible. The essential point is that once the gene has mutated it reproduces itself in the new form. It is this property which distinguishes it from all simpler self-duplicating systems.

Indirect measurements of the size of the gene indicate it to be of the order of a large protein molecule. Spectral analysis as well as direct chemical isolation has shown that chromosomes contain nucleic acid. That the nucleic acid is contained in, or at least closely associated with, the genes is shown by the fact that maximum absorption of ultraviolet light by genes (as measured by its efficiency in causing mutations) occurs around 2600 Angstrom units.

THE GENE AND THE METABOLISM OF THE CELL

The gene is also unique in the position it occupies in the economy of the cell. The cell, in the last analysis, is a highly complex chemical system adapted to the production of more cells like itself. It has a means for releasing the stored chemical energy of organic compounds and for utilizing the energy so liberated in the synthesis of new cell substance from simpler materials. To carry on its work, the cell is equipped with a large array of highly specific catalysts, called enzymes, which determine the course and the rate of these transformations. In a sense, there is nothing very novel in these arrangements, although nothing approaching the cell in complexity has ever been created in the laboratory. Catalysis is well known outside of living systems, and even in the cell mass and energy are conserved, and the second law of thermodynamics prevails. The distinctive feature of the cell as a chemical system lies in the fact that it contains certain key molecules, the alteration of a single one of which can radically change the course of the reactions which take place, or can even destroy the cell. The essential, irreplaceable molecules are the genes.

Consider a cell which in the course of its metabolism produces a characteristic pigment. It is possible, by the alteration or destruction of single gene, so to befuddle the cell that it can no longer synthesize the pigment, and all its descendants will be albinos. Restoration of the missing molecule also restores the missing synthesis, and from then on the line is normally pigmented. If, instead of a gene controlling pigment synthesis, we destroy a gene which controls the production of a substance essential to the operation of the cellular machinery—a vitamin, for example—then the cell cannot function and will die unless the vitamin is supplied from the outside. Again, restoration of the gene restores the capacity of the cell to carry on the synthesis.

The extraordinary thing here, from the chemist's point of view, is that we have a system whose structure rests on individual molecules. Yet the laws of physics and chemistry were not designed to describe the behavior of individual molecules, but only of statistical populations of molecules. They do not hold for small numbers. It is for this reason that physicists have concluded that life is not ultimately explainable in terms of ordinary physics and chemistry.

CHEMICAL GENETICS OF NEUROSPORA

The work in chemical genetics being carried on in the Biology Division is concerned with the role of genes in controlling cellular chemistry. To what extent and by what means do the genes govern the rate and direction of biochemical reactions? The research centers around a mold, **Neurospora,** which has been found to be extraordinarily convenient for both genetical and biochemical investigations. As found in nature, **Neurospora** is capable of synthesizing all of its cell constituents, with the exception of one vitamin (biotin) from sugar and inorganic salts. Given carbohydrate, inorganic salts, and biotin, the organism grows without further assistance. By subjecting it to high energy radiations or mustard gas —agents known to produce gene mutations—it has been possible to obtain mutant types which are unable to carry on certain of the normal chemical activities of the wild strain. Mutant forms have been found which require the addition of a particular vitamin, amino acid, purine, or pyrimidine to the ordinary medium before growth can occur, showing that

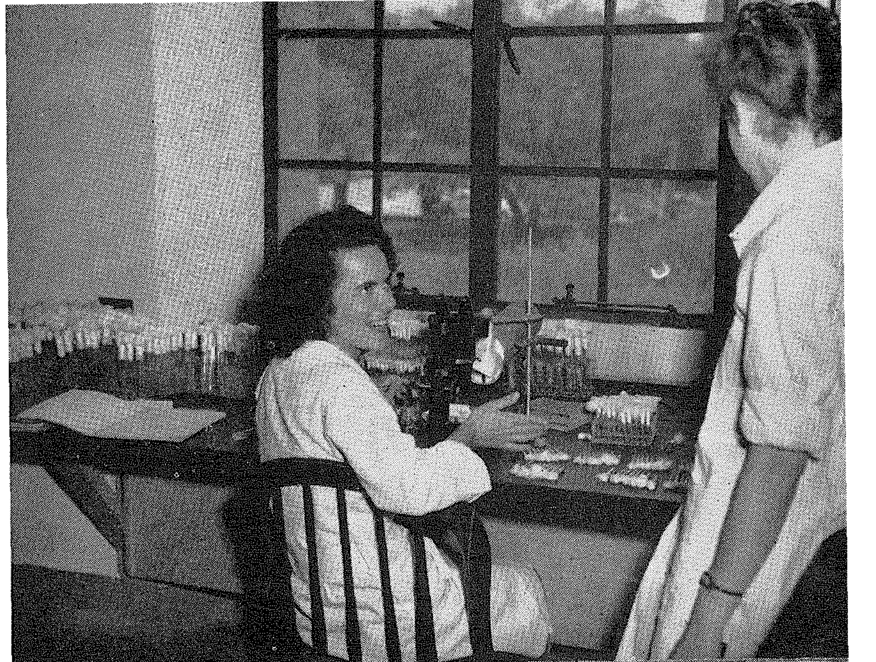
Large scale cultures of Neurospora for the production and isolation of precursors and other metabolic products are maintained in Fernbach flasks and aerated carboys. These are being examined by David Regnery, graduate student in Genetics.

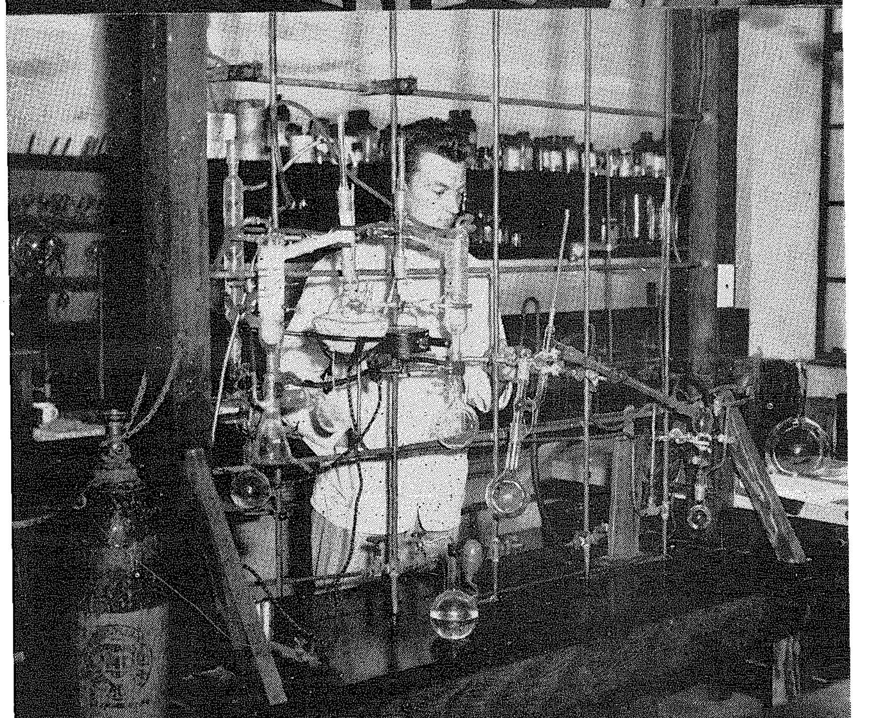
the mutants have lost the ability to synthesize these substances. In every case the loss of synthetic ability has been found to be inherited.

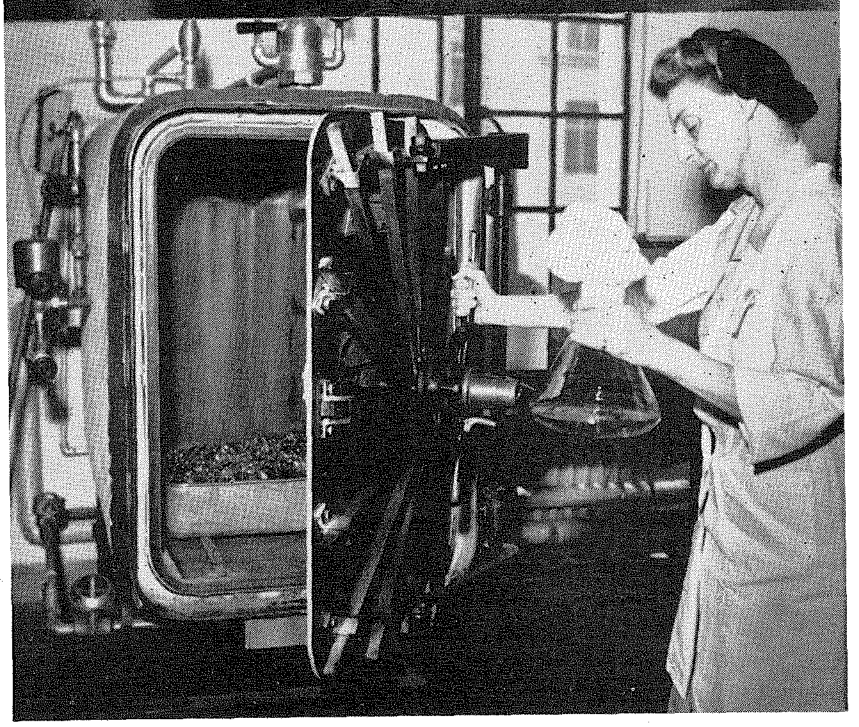
Closer study of the mutants has revealed that the synthesis of each vital substance is governed by a number of single genes, the mutation of any one of which abolishes the synthesis. It has been found that each gene controls a different step in the synthesis, and in numerous instances it has been possible to assign particular genes to particular biochemical reactions.

Aside from its genetic implications, the **Neurospora** work has a number of interesting biochemical aspects. The specific blocking of single reactions through gene mutations offers an unusually delicate method for probing the metabolic machinery of the cell. Through the use of **Neurospora** mutants it has been possible to ascertain the course of certain biological syntheses —**e.g.,** tryptophane, arginine, choline, methionine. One of the surprising results of these studies is the finding that the metabolic pathways so far uncovered in **Neurospora** are closely similar to, if not identical with, those of animals. This increases our confidence that findings made with this organism will have general application to living things. Another biochemical application of the mutants has been in the field of biological assay. The growth rate of mutants which have lost the ability to carry out a particular synthesis is a function of the concentration of the required growth factor. By measuring the growth rate of a mutant on an unknown material the amount of the particular growth substance contained therein can be determined. In this way, it is now possible by the use of **Neurospora** mutants to assay complex mixtures for such biologically important substances as leucine, lysine, choline, p-aminobenzoic acid, inositol, and pyridoxine.

While the lines of investigation described above have proven very fruitful of both fundamental and practical results, and are being actively pursued in the Biology Division, there is no doubt that the most interesting and exacting part of the road is still ahead. A number of basic questions remain to be answered. By what means do genes control the chemical activity of the cell, and how do they utilize cell materials for their reproduction? In answer to the first question it has been suggested that the genes act as templates, or patterns, on which the enzymes and other specific proteins of the cell are formed. Possible answers to the second question cannot be formulated in a few words, but the problem seems at least approachable in terms of quantum mechanics. Whatever the solutions to these problems may be, it is certain that they will be of the greatest consequence for biology and medicine.







UPPER: Suzanne McLean, research assistant in Genetics explains the genetics of the red bread mold Neurspora to Margaret Campbell, research assistant in Embryology. The test tubes contain an agar medium on which the mold grows.

CENTER: Joseph Nyc, research fellow in Chemical Geneitcs, checking apparatus in which chemical compounds of biological importance are synthesized. In collaboration with Dr. H. K. Mitchell and Dr. G. W. Beadle, Dr. Nyc is attempting to determine how Neurospora converts the amino acid tryptophane into the vitamin niacin. Such a transformation, which apparently can be made by man, is of obvious importance in relation to pellagra, a deficiency disease that develops in the absence of sufficient niacin. LOWER: A large steam autoclave in which material is sterilized. For culturing various microorganisms such as Neurospora, it is necessary that all culture media be freed of extraneous bacteria and molds.

CALTECH'S DIVISION OF BIOLOGY

Is Nineteen Years Old

By ALFRED H. STURTEVANT

THE "FIRST Annual Announcement of Throop University" was issued for the academic year 1892-1893; since Throop University ultimately became the California Institute of Technology, this bulletin represents the beginning of the Institute. Listed in it are a "Professor of Zoology" (C. F. Holder) and a "Professor of Biology and Instructor in Physics and Chemistry" (A. J. McClatchie). The college courses listed cover only the Freshman and Sophomore years; Science in the Freshman year was Botany (though Physics of Geology might be substituted), and in the Sophomore year it was Zoology (with Organic Chemistry or Mineralogy as a possible substitute). Biology remained in the curriculum for about twenty years—though not for long in such a preferred position. From 1905 to 1908 the Professor of Biology was Joseph Grinnell, who had taken his A. B. at Throop in 1897, and who left the Institute to become the distinguished Director of the Museum of Vertebrate Zoology at the University of California. His successor at the Institute was Carl S. Milliken, Professor of Biology from 1908 to 1910. Mr. Milliken is now a well-known breeder and grower of Iris in Southern California. For the five academic years from 1910-1911 through 1914-1915 courses in Biology were listed in the Annual Bulletins, with the note that these courses are not to be given in the current year; then Biology ceases to be even mentioned, until 1928.

The character of the Institute was greatly changed in these years when Biology was not represented, and it is therefore not surprising that the new Division of Biology, organized in 1928, was different in kind from the earlier department. In that year Dr. Thomas Hunt Morgan, then Professor of Experimental Zoology at Columbia University, was made Professor of Biology at the Institute, and was charged with the development of the new Division. The first (west) unit of the Kerckhoff building was erected, and work began in September, 1928. The staff members were four geneticists: T. H. Morgan, A. H. Sturtevant, E. G. Anderson, and S. Emerson; the three latter are still in the Division. An undergraduate course, Biology 1, was given, replacing a course in Ethics as a required subject in the Science options. Graduate work was offered from the beginning, and at the end of the first academic year the Ph.D. degree was given to Albert Tyler, who was then appointed to the staff, of which he is still a member.

Thomas Hunt Morgan
1866-1945

The stated object of the organization of the Division of Biology was the development of instruction and research in the experimental and physiological aspects of Biology, with special emphasis on the relations to Physics, Chemistry, and Mathematics, already so well represented at the Institute. Accordingly additions to the staff were made in Biochemistry, Embryology, Plant Physiology, Biophysics, and Animal Physiology, these being the subjects that seemed most appropriate for such a program. Work in General Zoology and Botany has also been developed, as a necessary background for these subjects.

Dr. Morgan remained Chairman of the Division until 1941, and was Emeritus Professor of Biology, in residence at the Institute, until his death in 1945. The present Division is largely of his creation, and its aims are still not far from those he expressed in the 1928 Institute Catalogue:

"Emphasis is placed primarily on research and graduate study; and, even in these directions, no attempt is made to cover at once the whole science of Biology, but rather efforts are concentrated on the development of those of its branches that seem to offer the greatest promise as fields of research. It is proposed to organize groups of investigators in General Physiology, Biophysics, Biochemistry, Genetics, and Developmental Mechanics. The choice of these fields of modern research implies that emphasis will be laid on the intimate relations of Biology to the Physical sciences. A closer relation of these sciences with Biology is imperative."

The physical resources of the Division of Biology have been increased by the acquisition of the experimental farm at Arcadia (1929), the Kerckhoff Marine Laboratory at Corona del Mar (1930), and the greenhouse on Orlando Road in San Marino (1944); and by the erection of laboratories and greenhouse for Plant Physiology (1930 and later), and of the second (east) wing of the Kerckhoff building (1938).

The administration of the Division was under a council (A. H. Sturtevant, H. Borsook, A. J. Haagen-Smit, F. W. Went) from 1941 until 1946; in that year Dr. G. W. Beadle, then of Stanford University, become Professor of Biology and Chairman of the Division of Biology.

A living "library" on heredity of the vinegar fly. This specially constructed constant temperature room houses the largest collection in the world of hereditary variations in Drosophila melongaster. Each bottle contains a population of several hundred flies which breed true for some hereditary abnormality. These range from strains of wingless or eyeless flies to those having differences which can be seen only under the microscope.

DROSOPHILA

By ALFRED H. STURTEVANT

WHEN DR. MORGAN came to the California Institute of Technology in 1928 he brought with him the work on the Genetics of **Drosophila** that had been going on in his laboratory at Columbia University since 1910. This work was supported in part by a grant from the Carnegie Institution of Washington from 1915 through 1946, and this grant at one time supported two full-time investigators (C. B. Bridges and J. Schultz) at the Institute.

The collection of living material of this small fly at the Institute is the basic one in the world, and strains from it are constantly being sent to research laboratories in this country and abroad. Two full-time staff members (A. H. Sturtevant and E. B. Lewis) are devoting their energies to the study of this material, and others of the present staff (G. W. Beadle, E. G. Anderson, S. Emerson) have studied it and published on it in the past.

Drosophila is a small fly, about 2½ mm long, that is to be found about fermenting fruit. The properties that first recommended it to students of heredity are that large numbers may be reared in a short time at little expense and in a small space. A single pair will produce hundreds of offspring in two weeks' time, in a single half-pint bottle, on a medium that consists of corn meal and molasses (often slightly stiffened with agar), seeded with yeast. When one compares this fly with laboratory rodents (with their relatively small numbers of offspring per pair, and the greater expense and space required per individual), or with most higher plants (that have one or occasionally two generations per year), it becomes understandable that most of the framework of modern Theoretical Genetics rests on work done with **Drosophila.**

We are sometimes asked if the material is still worth working with. After 35 years of intensive study by many investigators, hasn't the law of diminishing returns set in? Isn't it now more worthwhile

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The giant chromosomes of the salivary glands of Drosophila robusta — a species of vinegar fly that has been used in the study of heredity and evolution. Individual chromosomes can be seen as long ribbon-like bodies, which have a highly characteristic pattern of cross bands along their length. It is thought that these cross bands, which number in the thousands, may correspond to the genes — the ultimate units of life. Research is in progress at the California Institute to learn more about the genes through a study of these chromosomes. (The scale of the photograph is shown in microns, one micron being equal to about 1/25,400 in.)

ANIMAL BIOCHEMISTRY

By HENRY BORSOOK

THE DYNAMIC STEADY STATE OF THE BODY

UNTIL RECENTLY, the physiological chemist described the animal organism as an engine with a relatively static structure, in which the food was the fuel. The view was that a small fraction of the food was used to replace the wear and tear losses of the engine's structure. The working parts of the engine were composed of what was called "protoplasm."

This concept was typical of the era in which thermodynamics with its satellite, Newtonian statistical mechanics, reigned as the newly enthroned queen of the physical and chemical sciences. It was the era of combustion engines, the era of Helmholtz.

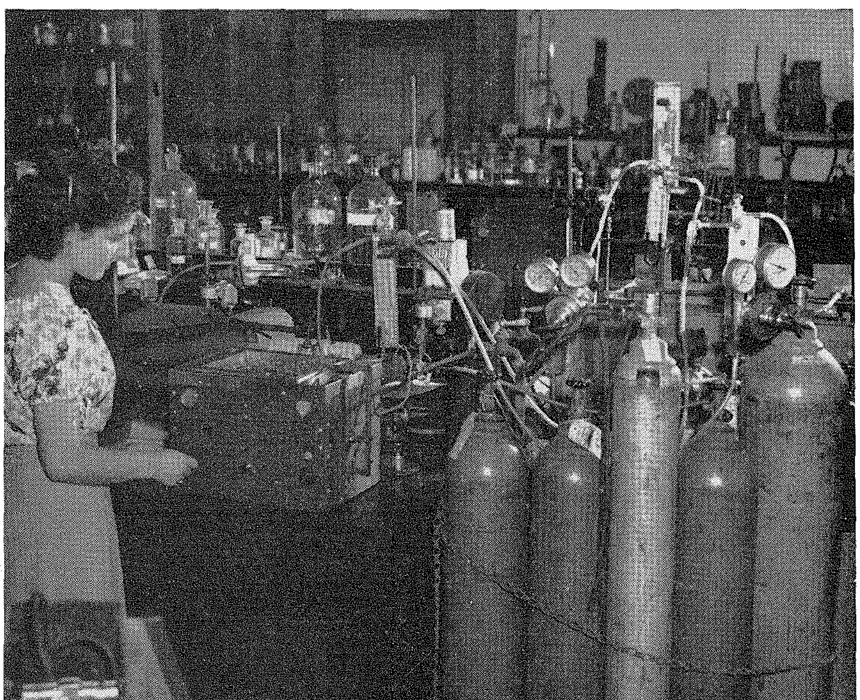
The simplicity of the concept of the organism as a combustion engine was, no doubt, one of its attractions. Another was that it helped the physiologists and physicians who were its devotees to feel respectable in the company of chemists and especially the physicists who were the rigorous pukka sahibs of natural philosophy of the nineteenth century.

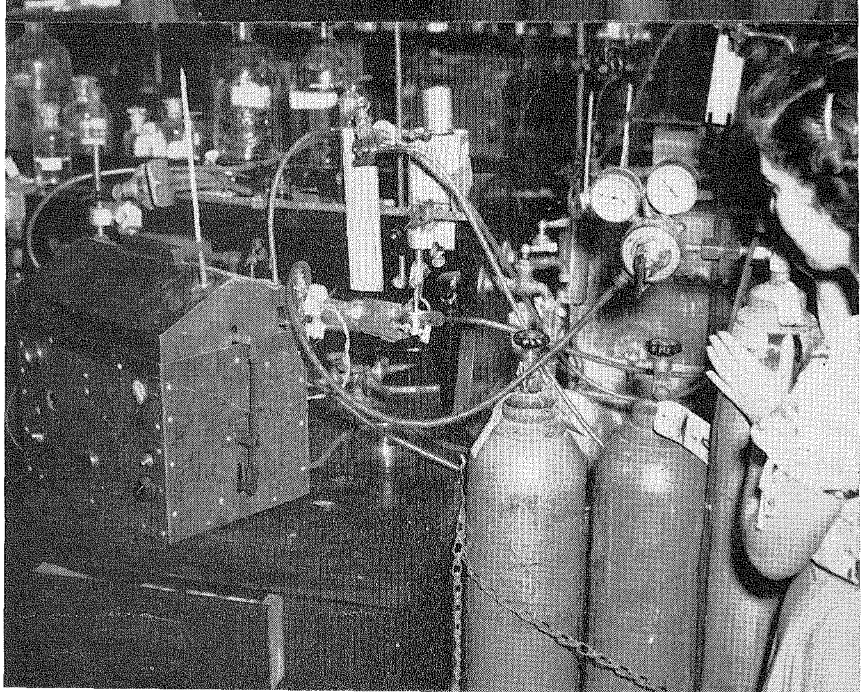
The concept of the organism as a machine was not a biological concept at all; and we now see that it is not in accord with the facts. The organism is a dynamic steady state. Structural substance and fuel substance are continually interchanging on a large scale and very rapidly. There is in many instances little utility in attempting to distinguish between the chemical changes in the structure of the biological engine and its fuel. The animal organism is a chemical system in which protein, fat, carbohydrate, minerals, vitamins, and water are continually and rapidly interacting and yet maintain the chemical composition of the body nearly constant. A small shift in the steady state marks the difference between growth and old age, between health and disease.

The group in Animal Biochemistry is studying this chemical steady state with special reference to proteins and their derivatives and to those reactions in which one component gains free energy from an oxidation; in other words, building-up processes. The formation of protein, creatine, and urea are representative.

These reactions can be viewed as a class of organic syntheses peculiar to living organisms. The mechanisms familiar to the organic chemist rarely operate in the body. Biological catalysts (enzymes) promote reactions which otherwise require high temperatures and pressures, strong acids or alkalies; and the yields are often higher than the latter conditions.

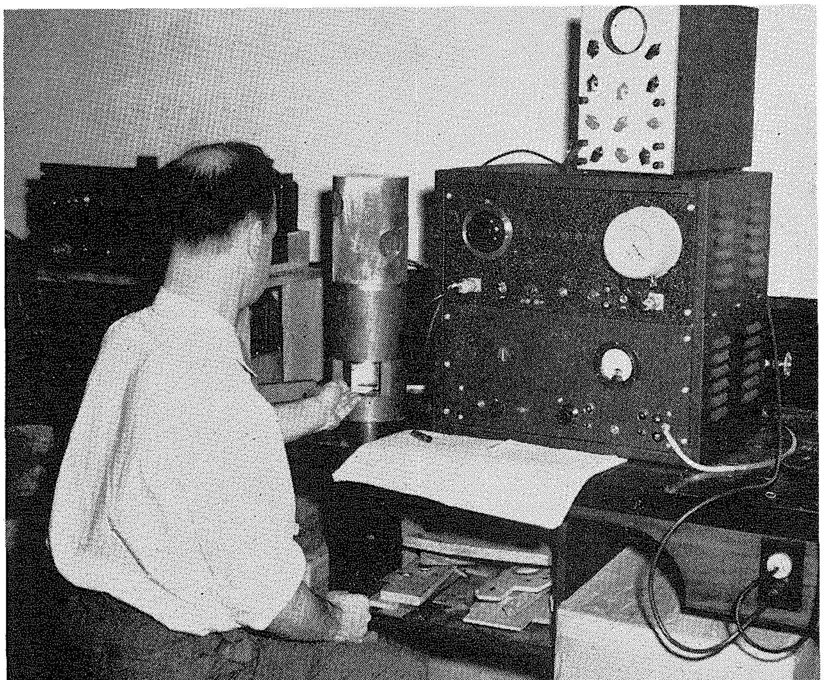
We are accustomed now in biochemistry to the transfer from one molecule to another of large radicals such as $—C(:NH)NH_2$, PO_4, and $—CH_3$. Knowledge gained in recent years on the mechanisms of methyl transfer reactions has elucidated some of the chemical aspects of growth and some diseases of the liver, muscle and heart. For example, cirrhosis of the liver is the result of a cumulative deficiency over years of labile methyl groups. Although many food components contain methyl groups, in only a few are the methyl groups physiologically labile **i.e.,** transferable from one compound to another. The

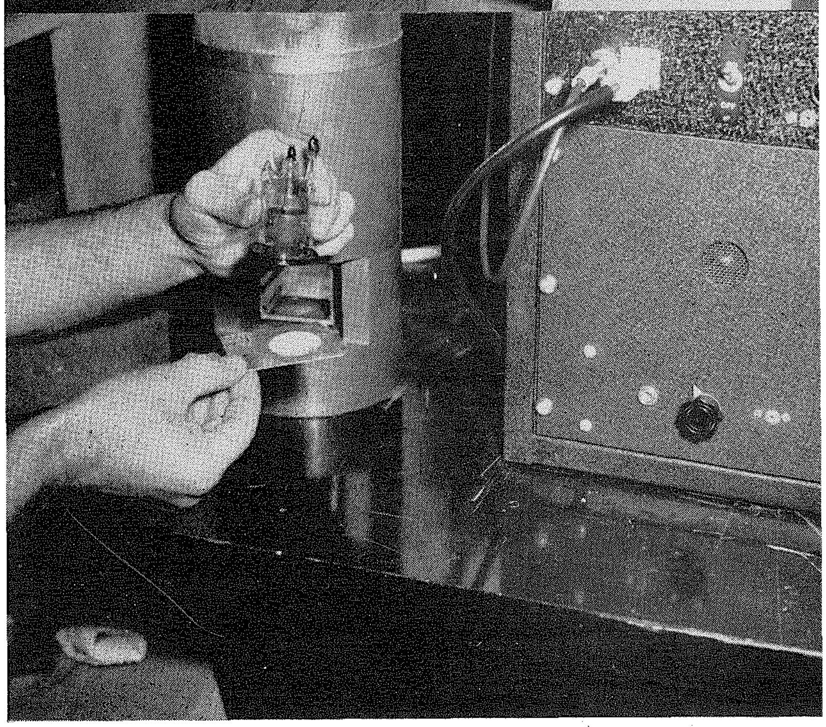




This tissue culture apparatus, designed by Dr. J. W. Dubnoff and demonstrated by assistant Ingelore Silberbach, maintains up to 30 tissue slices or homogenate samples in equilibrium with a physiological gas mixture at constant temperature. The apparatus, shown uncovered in the top picture, and in action in the lower, consists of a thermostatically controlled water bath, a shaking mechanism, and a removable vessel container. Individual handling is obviated since the container with its vessels is brought to temperature and equilibrated with gas as a single unit.

UPPER: Dr. Geoffrey Keighley with some of the apparatus for measuring the activity of radioactive materials used in physiological and biochemical experiments. Material containing the active tracer isotope is placed on a shelf in the lead shield, under the Geiger counter tube. On the right is the apparatus for counting the impulses from the counter. LOWER: Aluminum shelf bearing a sample of radioactive C^{14}. Above it is an end-window Geiger counter. The window is of mica thin enough to pass the weak radiations from the C^{14}. When in use both shelf and counter are held in similar relationship inside the lead shield.





most important food constituents with labile methyl groups are the amino acid methionine and the nitrogenous base choline. The methyl group of methionine is used in the body to make creatine which is essential for muscular contraction. Choline participates in the transfer of fatty acids from the liver to other tissues. The methyl radicals of methionine and of choline are interchangeable. Both substances are essential for growth principally because of their labile methyl groups.

Many reactions participate in the dynamic steady state; their participation is coordinated or there would be no steady state. As food supply and bodily activity vary, some reactions slow down, others become faster. When there is an abundance of carbohydrate in the diet, some is converted to fat; when muscular activity is increased, some protein is converted to carbohydrate.

ISOTOPES AS TRACERS

In a system so complicated and consisting of so many reactions, it has been extremely difficult to follow the course of any one compound through its transformations and disintegration. This study has been greatly helped by the availability of isotopes and their use as tracers. A molecule can be labelled by incorporating an isotope into its structure, N^{15}, for example, in place of normal N^{14}, or C^{14} instead of C^{12}, or H^2 instead of H^1. An isotope is identical in its chemical behavior with its normal counterpart; i.e., N^{15} behaves chemically the same as N^{14}, C^{14} the same as C^{12}, H^2 the same as H^1. It is possible, however, by physical methods to locate and measure isotopes. By following the label (the isotope) one can thus follow the molecule to which it is attached; by identifying the compound in which the isotope is found one learns what has happened to the compound into which the isotope was originally incorporated.

The Biochemistry Department is using isotopes as tracers. Large organic molecules are synthesized, incorporating as a tag the isotope C^{14} in place of the normal C^{12}. The whole molecule can then be followed into and out of protein molecules. And when it is disintegrated, identification of the fragment in which the C^{14} is found tells the manner of its disintegration. The C^{14} is measured by a Geiger-Müller counter, and by this method as little as 0.005 milligrams of an isotope-labeled amino acid can be located and measured.

In studies such as the foregoing it is rarely possible, and always cumbersome and inconvenient, to use a whole, living animal. Much more, and more precise, information is gained by using small amounts of tissue, 1 gram or less, or extracts of tissues. Consequently, it was necessary to develop specific and accurate micro methods for the determination of milligrams or even micrograms of specific substances. One of the most useful general methods for this purpose is chromotography, which is essentially separation of compounds by specific adsorption on selected adsorbents. By this means 2 milligrams of protein have been fractionated semi-quantitatively into 18 different amino acid fractions and each of the fractions identified.

The foregoing uses of physical and chemical methods in our biochemical work are characteristic of contemporary biological research. Spectrophotometers, electrophoresis and ultra-centrifuge equipment are commonplace now in biological laboratories.

The use of physico-chemical methods in Biology carries with it an implication of fundamental importance. It is the preference for physico-chemical and quantitative interpretations of biological phenomena. This trend in Biology may be said to have begun at about the middle of the nineteenth century. Now it is in full flood and dominates the field.

Variations on a Theme -- PLANT GROWTH

By JAMES F. BONNER

THE STUDY of plant sciences at the Institute was initiated in 1930 by the first chairman of the Biology Division, Thomas Hunt Morgan. Professor Morgan was particularly interested in developing the study of the mechanisms by which organisms grow and develop, and for this reason he chose to initiate work in the plant sciences, not with botanical work in general as is done at many other institutions, but rather by confining the development to a few carefully chosen aspects of plant biology. Three principal approaches to the study were started: first, the study of plant heredity; second, the study of photosynthesis; and third, the study of plant growth.

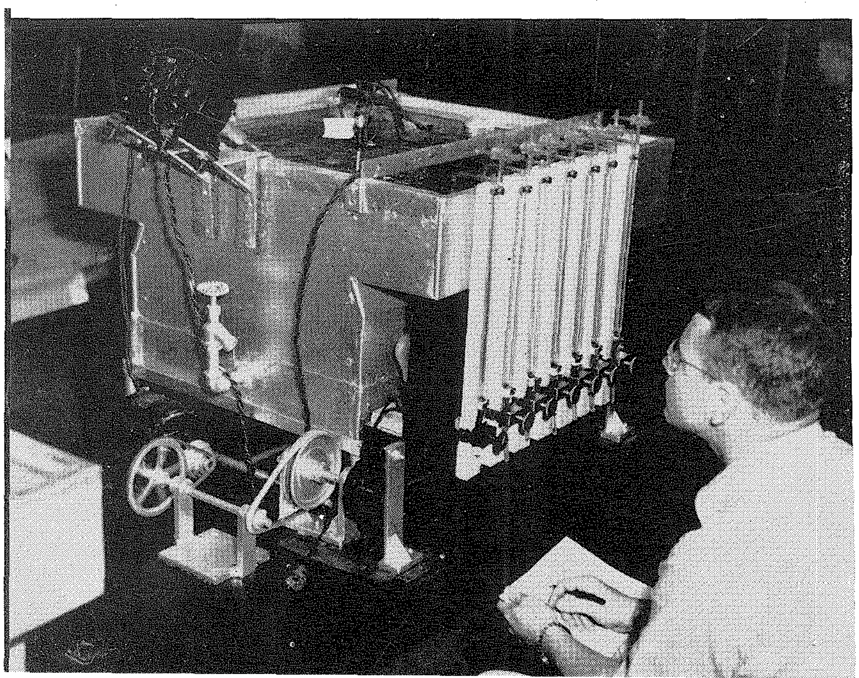
INDOLE ACETIC ACID

The work on plant growth was undertaken by Dr. Herman Dolk of the University of Utrecht, Holland, who became the first professor of plant physiology at the Institute. At that time it was known from work done in Holland by Dr. Dolk, F. W. Went (later a member of the Institute staff) and others that the growth of stems and stem-like organs of the plant is controlled by a particular chemical substance which is produced in the growing tip and which is transported through the stem to lower regions where it is essential for elongation. Dolk and K. V. Thimann, now professor of plant physiology at Harvard, undertook to isolate and identify the chemical nature of this growth promoting compound or growth substance. Their work, together with that af A. J. Haagen-Smit (now professor of bio-organic chemistry at the Institute) and others, established that the activity of the plant growth substance is possessed by a relatively simple organic substance, indole acetic acid. This and other related substances are produced in minute amounts in the tip of the growing plant, but are completely essential to growth of the stem, flower stalks, and other portions of the plant. In plants from which the growth substance producing tip has been severed, application of as little as 5×10^{-6} micrograms (5×10^{-12} grams) of indole acetic acid per plant suffices to bring about a clearly detectable increase in growth.

Within a short time it was discovered that the plant growth substance indole acetic acid regulates a wide variety of processes in the plant in addition to growth in length of stems, etc. Thus Thimann and Folke Skoog (now associate professor of Botany at the University of Wisconsin) found that the phenomenon of apical dominance by which the terminal or main bud of a shoot suppresses the growth of side buds is due to the same growth substance. In plants which had had their terminal buds removed, the side buds which normally grow out rapidly could be completely suppressed by application of indole acetic acid to the stump from which the main bud had been removed. The growth substance which is normally produced in the plant has then not only the property of regulating growth in size but also of regulating the branching or form of the plant. Professor F. W. Went, who joined the staff of the Institute in 1933 after the death of Dr. Dolk in an automobile accident in 1932, discovered a further and more important role of indole acetic acid in 1935 when he found that the application of this substance to cut stems of plants causes the formation of roots at the base of such material. This finding was translated into practical application by Went and W. C. Cooper (now with the U. S. Department of Agriculture) and treatment with indole acetic acid or related compounds has become the worldwide standard for the induction of roots on cuttings or slips of plants which are to be propagated in this way. Treatment with root forming chemicals is used by nursery men on a wide variety of ornamentals such as **Camellia, Chrysanthemum,** etc., and also on economic plants such as fruit trees. Dr. Cooper, now one of the U. S. authorities in this field of plant physiology, was called on during the war to treat cuttings of quinine, **Derris** and other strategic plant materials in connection with the greatly increased need for these products, and carried on work in Puerto Rico and in Peru as well as in the U. S.

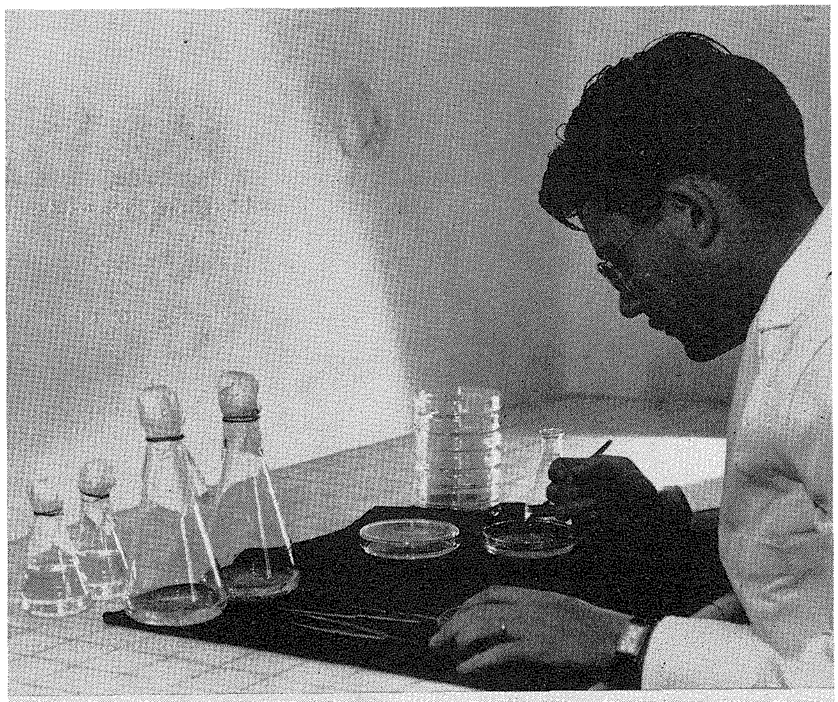
NAPHTHALENE ACETIC ACID AND 2-4-D

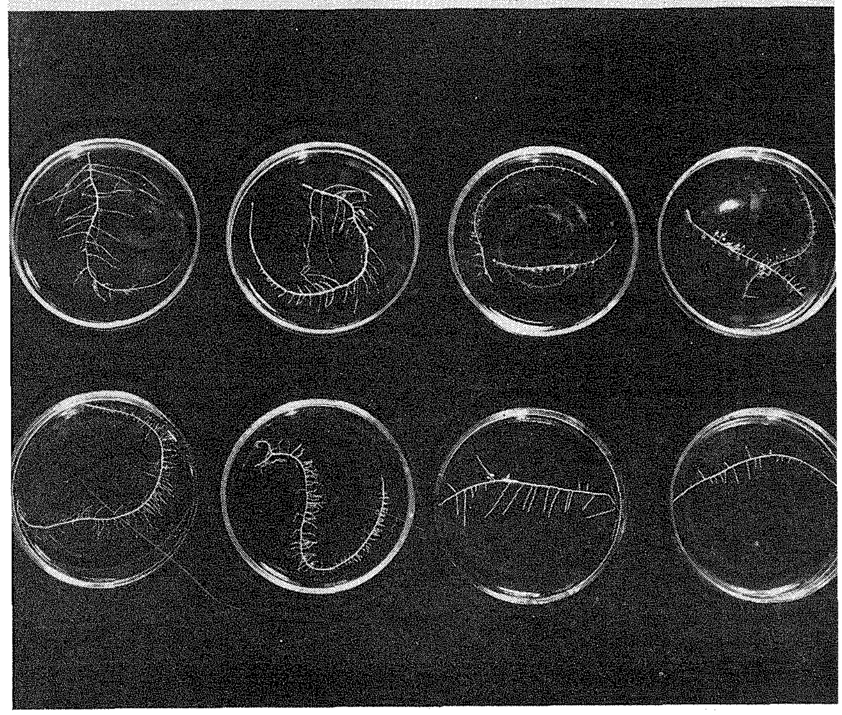
The study of the plant growth substance indole acetic acid initiated in this country at the Institute has been taken up by a great number of individuals and organizations, and steadily increasing numbers of applications in this and related compounds have been found in agriculture. Thus application of naphthalene acetic acid, a compound related to indole acetic acid and possessing growth substance activity, has been found to inhibit preharvest fruit drop, which has been a severe problem in certain apple growing areas. Application of the compound by sprays to apple orchards has now become an important agricultural practice. Similar sprays inhibit fruit drop of grapefruit and other citrus, as has been shown by William S. Stewart, a former student at the Institute,



Undergraduate John Thomas preparing to measure the rate of photo-synthesis of leaves in the Warburg Manometric apparatus.

UPPER: James Bonner culturing isolated plant roots. These roots are cut from the plants and are grown in nutrient solution for the purpose of finding which chemical substances are required in root growth. Here the roots are being cut into small fragments, each one of which will produce a new root. The flasks in the foreground contain flaxroots which have grown into pieces one meter or more long. The whole operation is carried out in an aseptic operating room. LOWER: Isolated roots grown in culture in nutrient solution. Upper left two dishes-tomato roots; upper right two dishes-alfalfa roots; lower left two dishes-clover roots; lower right two dishes-pea roots. All roots have grown for one week, and have increased 10-15 cm in length.





now assistant professor at the University of California. The compound 2-4 dichlorphenoxy acetic acid or 2-4-D, discovered as a product of work on plant growth substances, is highly toxic to some plants and is widely used as a weed killer. Dr. J. van Overbeek, formerly assistant professor at the Institute, now assistant director of the Institute for Tropical Agriculture at Mayaguez, Puerto Rico, has made an important application of this compound in combating weeds in sugar cane fields at a fraction of the cost required by hand weeding. Dr. Gladys King, now of the U. S. Department of Agriculture in New Orleans, has also made successful application of 2-4-D to the control of water hyacinth in the Mississippi River. The agricultural applications of this basic work carried on at the Institute are thus quite large and it should be clear that basic advances in agricultural technique can be expected as a result of work on the fundamental aspects of plant growth.

ROOT GROWTH SUBSTANCES

One of the phases of plant development which have been much investigated at the Institute is the growth of the root system. This has been studied particularly by Professor James Bonner and by F. T. Addicott, assistant professor at the University of California. The root normally grows at the expense of substances formed in the leaves which are transported to the roots and which there take part in the increase of the root system. This problem has been studied by the technique of isolated root culture, in which short pieces of aseptic root are transferred to aseptic nutrient solution and there allowed to grow. The root fragment will grow normally and produce a branched and vigorous root system, provided that the usual inorganic salts (which would ordinarily be taken from the soil), sugar (as a source of energy) and certain root growth substances are all present. These root growth substances, like the stem growth substance, are needed in minute amounts, concentrations of the order of 0.1 mg per liter of nutrient. The root growth substances differ fundamentally from the indole acetic acid of the stem, however, and have in fact been identified as vitamins of the B group. Thus, thiamin, the antineuritic vitamin, is required for the normal growth of all species of roots thus far investigated. This compound which is formed in the leaves of plants and translocated to the roots, here it is used in root growth, is also an essential component of the plant food eaten by the animal. The same is true of pyridoxin and niacin, two other vitamins, both formed in the leaf and essential for root growth but also essential dietary components for the animal. The root lives then at the expense of the leaves, both as to food supply (sugar) and as to essential root growth substances. Through its supplying of these materials to the root, the leaf can in turn regulate the growth of the root and can in this way adjust the root system to the demands of the aboveground portion of the plant. Practical applications of our knowledge of the root growth substances have been found in the promotion of root growth of plants or cuttings in particular instances.

LEAF GROWTH SUBSTANCES

Still another group of plant growth substances is represented by the factors which influence leaf growth. David Bonner, now assistant professor of Botany at Yale University, has studied leaf growth, using portions of excised immature leaves which were found to grow when placed in solutions containing sugar and extracts of leaves or seeds. The leaf or seed extracts contain a specific leaf growth promoting material which was identified as the compounds adenine

Research assistant Jean Campbell is carrying out a surgical operation on an excised plant embryo. The embryo is to be grown under aseptic conditions on antiseptic nutrient solution for the purpose of determining the nutritive requirement of the young plant.

and hypoxanthine. These substances are produced in mature leaves and appear to act in regulating leaf growth in much the same way that the stem and root growth substances regulate their respective organs.

WOUND HEALING AND PLANT TUMORS

Wound healing is an important process in plants as it is in animals, and it has long been known that when plant cells are cut or otherwise injured they liberate substances which tend to promote the proliferation of adjoining uninjured cells. The chemistry of plant wound healing was taken up at the Institute by J. Bonner and A. J. Haagen-Smit, and by James English, Jr., now associate professor of chemistry at Yale University. A powerful wound substance was isolated in pure form and found to be decene dicarboxylic acid, a compound new to organic chemistry. Practical applications of this interesting substance still remain to be made.

The study of the cancer of animals has its counterpart in certain tumor-like growths of plants and it appears from work of Skoog and others that the growth of these plant tumors is closely related to indole acetic acid. Plant tumors, which develop on stems under certain conditions, can grow in aseptic culture in the absence of any added growth substance and can in fact produce indole acetic acid. Non-tumorous normal stem also can grow in culture but apparently only if supplied with indole acetic acid. Thus the tumorous condition might appear to be connected with the ability of the tumor tissue to form its own supply of this growth substance, so that it grows independently rather than dependently and harmoniously with normal tissues. This apparent relation of the tumorous condition in plants to plant growth substances is a field of active investigation at the present time.

A picture of plant growth as controlled and integrated by internal secretions of the plant has begun to emerge as a result of the work discussed briefly above. Each part of the plant depends for its growth on particular compounds which it cannot synthesize but which it obtains from other organs. In this way integration of the growth of the several organs appears to be brought about. It would be of great interest to know in similar detail the physiology of the formation of flowers and fruits, and obviously such knowledge, together with the implied ability to influence and regulate flowering and fruit production, would be potentially of agricultural significance. Only a small beginning in the study of these complicated problems, however, has been made and the study of the growth substances involved in flowering and fruiting remains a challenging problem to plant physiology.

MODE OF ACTION OF GROWTH SUBSTANCES

We have thus far taken up the growth of the plant from the standpoint of the relation of particular natural plant compounds to the expression of plant growth. Work actively under way at the Institute concerns the biochemistry of the growth substances, the way in which they carry out their striking growth effects. The growth substances thus far studied appear to enter into basic cellular reactions as components of enzyme systems. Thus thiamin, nicotinic acid, adenine, and pyridoxin all are known to be components of plant respiratory enzymes. The mode of action of indole acetic acid, on the contrary, has remained a mystery despite long continued study of the matter at the Institute and elsewhere. Recently enzyme systems, in which indole acetic acid participates in the plant, have been studied by James Bonner and S. G. Wildman. Enzyme systems for both the production and destruction of the growth substance have been separated and characterized. In addition a protein which appears to contain indole acetic acid as a constituent has been isolated from the plant and characterized as an enzyme. The study of the plant enzyme systems involved in growth may be expected to lead us to a new and deeper understanding of plant development and this biochemical phase of plant biology is being stressed at the Institute. Modern equipment and the best of facilities for plant enzyme and protein work are making it possible to make rapid progress in this new field.

GUAYULE

This discussion of Plant Physiology and Biochemistry at the Institute would be incomplete without some discussion of the work carried on by the Institute group and their past students during the war. The facilities of the plant physiology group were used during the war for the study of natural rubber production. This work was started by the Institute in 1940 and was continued during the war under contract with the Emergency Rubber Project of the U. S. Department of Agriculture. Work at the Institute involved determination of optimum conditions for production of rubber by rubber forming plants. Thus it was found with the aid of the air-conditioned greenhouses described elsewhere that in the guayule rubber accumulation takes place best under conditions of warm days and cold nights. The exact temperature data obtained permit ready selection of regions for guayule production which will have suitable climate for rubber accumulation. This work, together with basic investigations on the physiology of rubber formation, was carried out primarily by James Bonner, Arthur Galston, who will shortly return to the Institute after having been agricultural officer for the Naval Military Government Unit for Okinawa, and H. K. Pratt, now assistant professor of truck crops at the University of California (Davis). The oils and resins of rubber and rubber plant were investigated at the same time by Haagen-Smit and by Ralph Siu, now director of the Quartermaster Corps Biological Laboratory in Philadelphia. A basically new method for extracting rubber of highest quality from guayule was developed at the Institute by Professor Robert Emerson, now at the University of Illinois. As a result of the intensive work on natural rubber production carried on during the war, small but vitally needed quantities of natural rubber were produced for blending with synthetic rubber, and in addition, the guayule plant was established as a practicable source of domestic natural rubber.

Varied as are the above described research problems carried on in plant physiology and biochemistry, there are still others subjects which have been or are under investigation. Active investigations carried on at the present time by graduate students also include substances given off by plants and toxic to other plants, the biochemical explanation of genetically controlled dwarf structure, the mechanism of formation of organic acids in leaves, the production of carotenes, and others. This wide multiplicity of problems has its common ground in the fact that they apply to the varied aspects of plant growth. As has been shown above, the results of this type of study find their application not only in the better understanding of a general biological problem but also in rather direct ways to the bettering of agricultural procedures. That the training given in Plant Physiology and Biochemistry prepares the student not only for academic work but also for work in agriculture is attested by the success of the graduates of the Biology Division in the most varied phases of agricultural endeavor.

Research fellow Dr. Barbarin Arrengúin-Lozano studying cultures of isolated bark which he has made of the rubber plant Guayule. Dr. Arregúin-Lozano is using these bark cultures in the study of rubber formation.

Animal Physiology

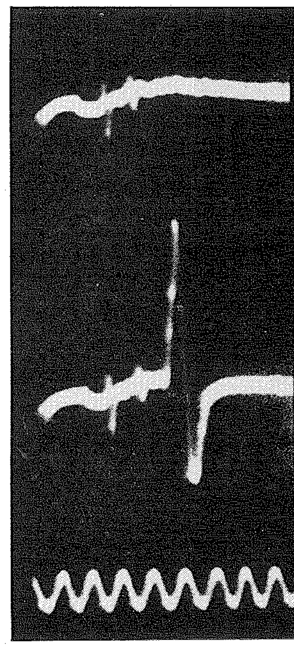
Combines Muscles, Nerves, and Electrons

By A. H. VAN HARREVELD

THE CRUSTACEAN NERVE-MUSCLE SYSTEM

1. Fast and slow contractions

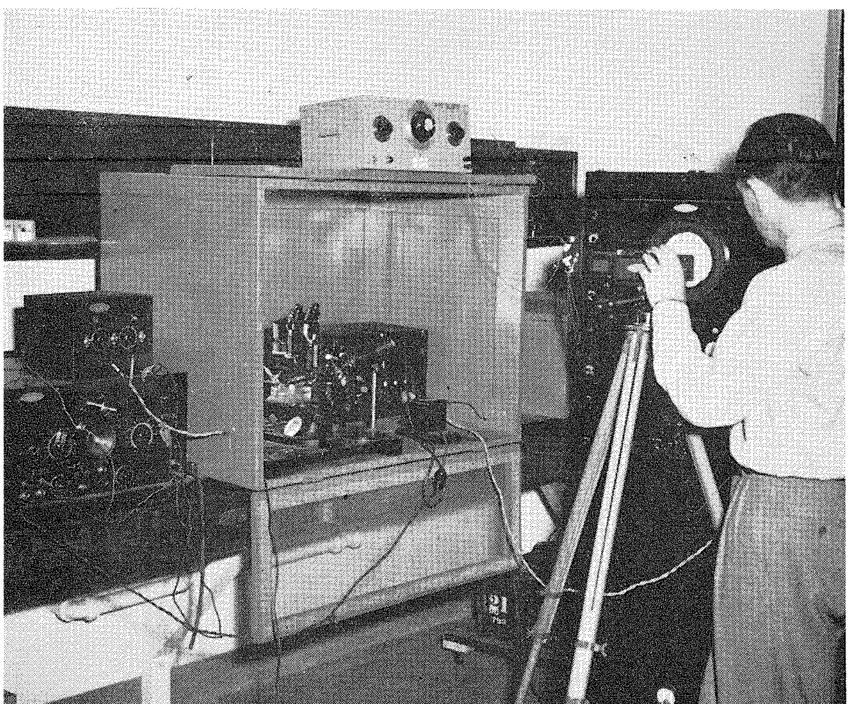
ANIMAL Physiology is represented at the Institute by comparative and vertebrate neurophysiology, a combination which has been found very advantageous for the development of several research problems. Special attention has been paid to the nerve-muscle system of the crustaceans (crayfish, crabs, lobsters, etc.). The functioning of the nerves and muscles of this group of animals has certain remarkable features, the study of which is important for the understanding of nerve-muscle systems in general. For instance, it was found that the muscle fibers of these animals can contract in two different ways. One contraction is fast and serves for the quick movements of the animal; the other contraction is slow and is used for sustained contractions. Both contractions take place in the same muscle fibers, but are brought about by different nerve fibers. The differences between these two types of contraction were further studied by the determination of the heat production and of the chemical changes in the muscle. Further investigations are planned to elucidate the mechanisms underlying these two types of muscle contraction and to investigate their presence in other invertebrates.

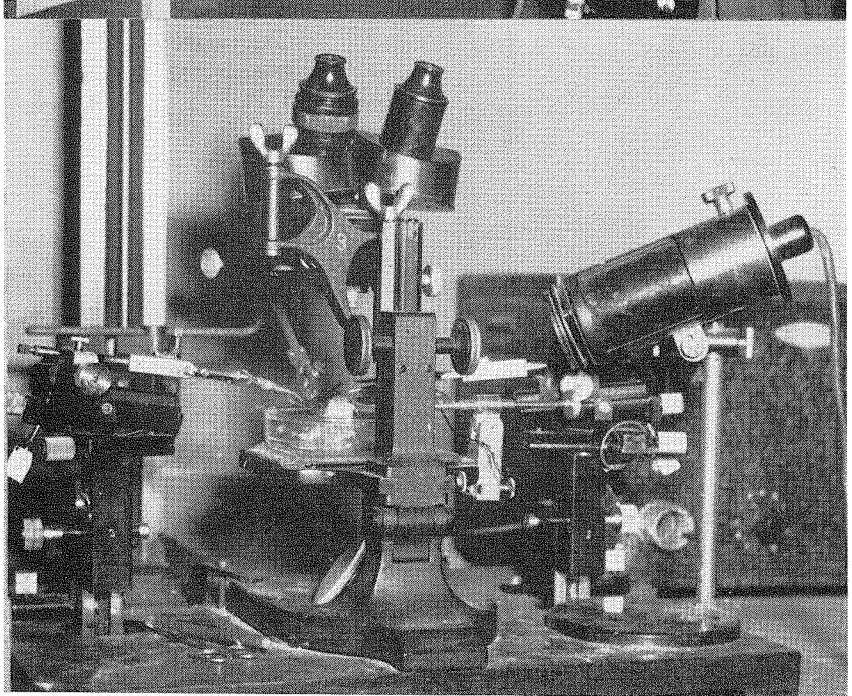


Tracings obtained from the central nervous system of the crayfish when two central fibers are stimulated with two shocks separated by short time intervals. In upper record the interval is 0.8 milliseconds, the two small tops indicate the activity of the two central fibers. In the middle record the interval is lengthened to 1.0 millisecond, and a large diphasic potential results, which is the response of the peripheral fibers, which are now brought into action. In the lower record each complete cycle represents 1.0 millisecond.

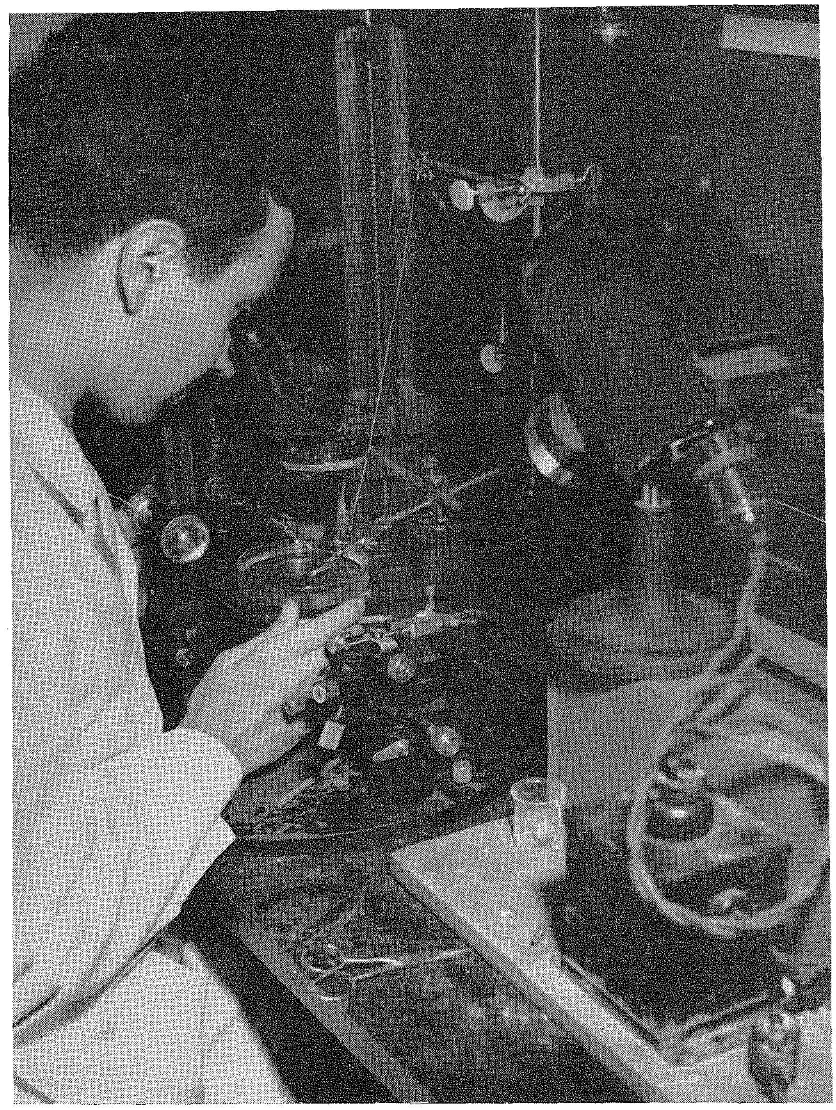
2. Peripheral inhibition.

Another outstanding mechanism present in the





UPPER: A general view of the apparatus used in studying synaptic transmission in the crayfish. The instrument on lower left is a square wave generator able to produce shocks of variable duration, frequency and strength. With the apparatus on top of it, each square wave can be used to produce two short shocks of variable interval to study the effect of summation. In the cage is the set-up with the preparation and the pre-amplifier for recording action potentials, which become visible on the cathode-ray tube at right. Dr. Wiersma is at the camera. On top of the cage shielding the preparation, a timer. LOWER: Closeup of preparation with stimulating and leadingoff electrodes adjusted. The instruments on left and right side of the baseboard are micromanipulators with which the stimulating electrodes are brought in contact with single isolated fibers of the central nervous system in the head region. The leading-off electrodes are attached to the object table of the binocular and are applied to the freed part of the central nervous system in the tail. All parts not in contact with electrodes are submerged in perfusion fluid contained in the Petri dish.

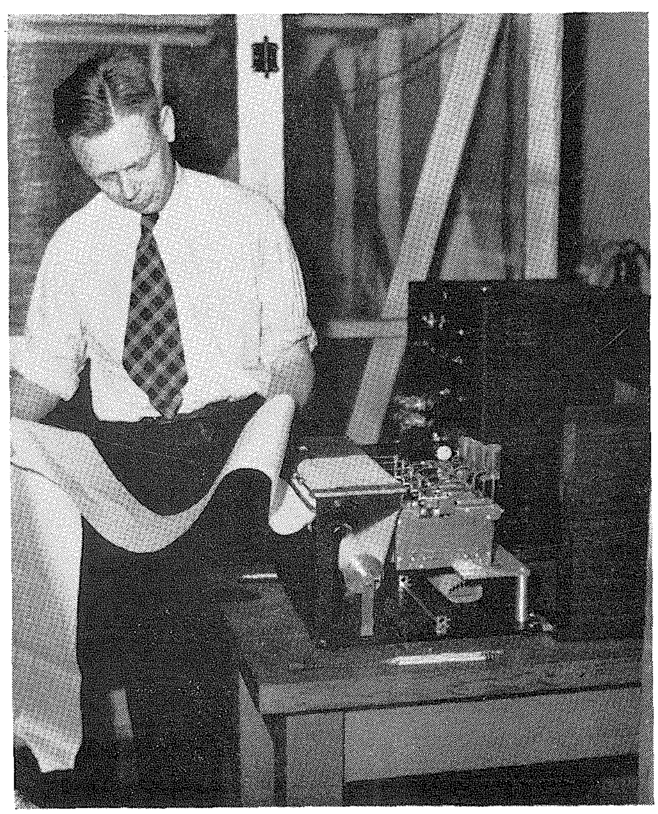


Dr. William Shallek preparing single nerve fibers in a crayfish claw. The nerve is exposed and just submerged in perfusion fluid. With a needle it is carefully divided into bundles which are then tested with the electrodes. The result of the stimulation of each bundle is noted and the ones not wanted are discarded, until only single nerve fibers (30 to 60 microns in diameter) remain. To obtain inhibitory fibers two micromanipulators must be used.

crustacean nerve-muscle system is that of peripheral inhibition. By the stimulation of a single inhibitory nerve fiber, the contraction caused by the stimulation of the motor fibers can be diminished or even completely suppressed. Certain muscles were found to receive a special inhibitory fiber, but, in general, inhibition seems to be a much less selective process. In crabs, for instance, one inhibitory fiber was found to serve no less than five different muscles. Whereas in the muscles with special inhibitory innervation this will have a function during normal movements, it is believed that general inhibition is of importance during moulting, which in these animals is almost as great an event as birth, but is repeatedly performed during growth.

3. Re-innervation of paralysed muscle

It was established that in the crustaceans a single motor nerve fiber innervates the thousands of muscle fibers forming muscles as large as, for instance, the big closer muscles of the claw of crabs and lobsters. In vertebrates, on the other hand, one nerve fiber innervates only a small part of a muscle, and the innervation of a large muscle is thus accomplished by a large number of motor nerve fibers. Each nerve fiber divides in the muscle into a number of branches each of which innervates one single muscle fiber. In this way 100 to 150 muscle fibers may be innervated by one motor nerve fiber. The observation was made that after the destruction of part of the nerve supply of a muscle, the muscle fibers which lost their innervation could be re-innervated spontaneously from the remaining motor nerve fibers. The mechanism involved in this re-innervation is an increase in the terminal branching of the motor nerve fibers which escaped destruction. In this way a muscle which was robbed of most of its muscle power by the destruction of a large part of its nerve supply can in a few months show a considerable return to its former strength. It is likely that this is one of the mechanisms responsible for the improvement of the paralysis observed after the acute phase of poliomyelitis in man. An attempt was made to re-activate the process, causing the increase of the terminal branching, in poliomyelitis patients who had stopped improving spontaneously. Definite though limited improvements were obtained.

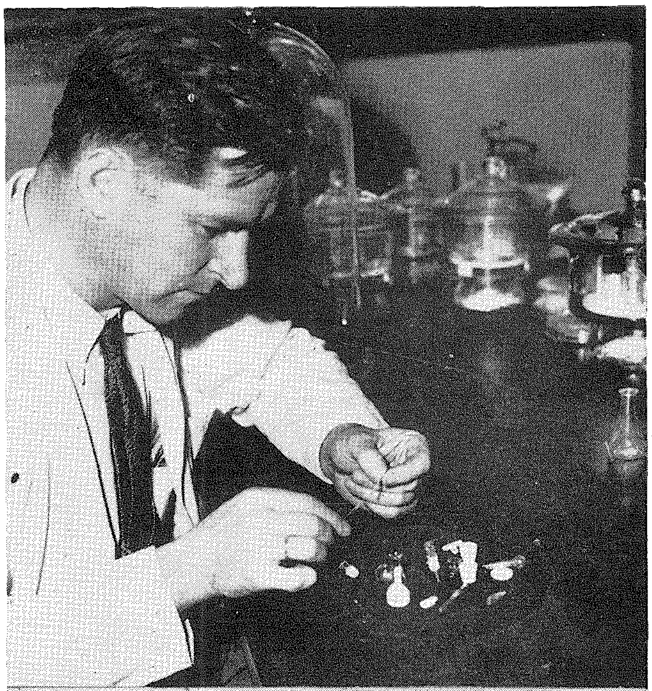


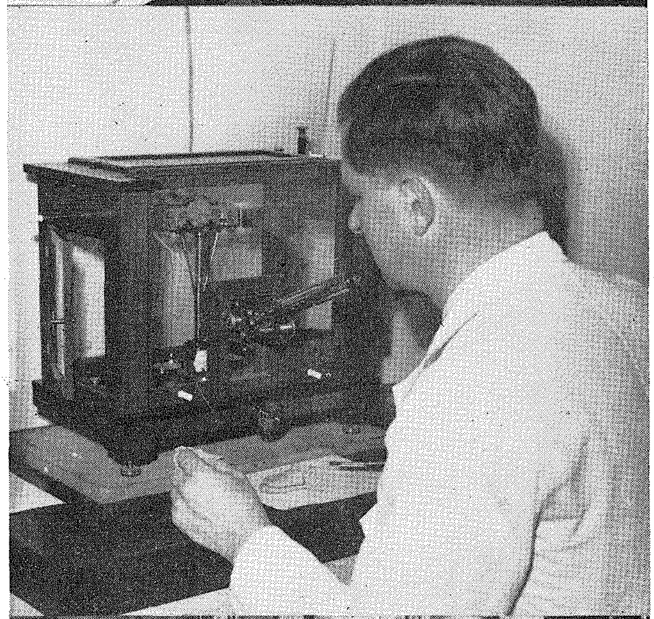
Dr. van Harreveld and the electroencephalograph. This instrument, a recent gift of Mr. and Mrs. Fred S. Markham of Altadena, is used to record small potentials produced by the brain. Four channels of amplification are available which allow the leading off from four different spots on the skull.

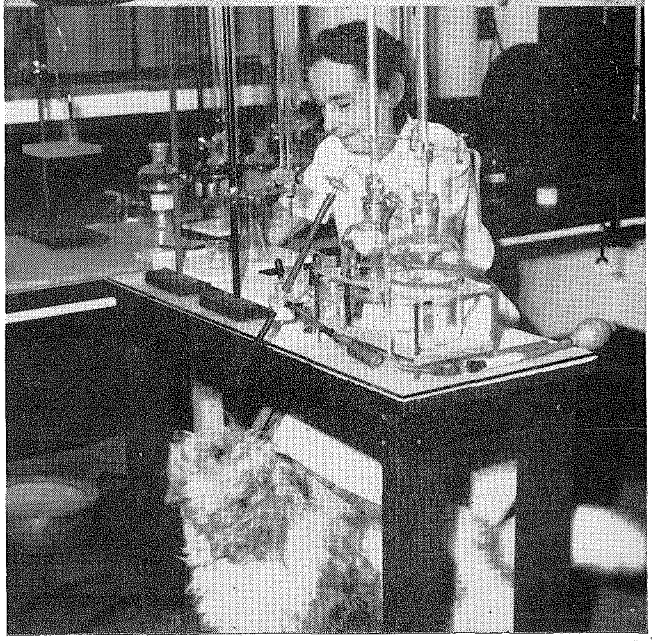
The small potentials (between 30 and 100 microvolts) are amplified in the unit to the left. The unit to the right contains the power supply and a loudspeaker which makes it possible to make the electroencephalogram audible. In the middle is the recording device.

The amplification channels drive four crystographs which making inklines on a long paper strip, usually moved at the rate of an inch per second. The crystograph can follow frequencies up to the vicinity of 100 per second. This is ample since frequencies of the electroencehpalogram are usually between one and 30 per second.

For the investigation of certain aspects of the physiology of the central nervous system, crustaceans have been found to have definite advantages. As in the peripheral nerves of these animals, it has been possible to isolate and stimulate single nerve fibers in their central nervous system. This preparation has been provisorily surveyed only, and it is hoped that many further points may be developed. At present the main interest is centered on the function of the so-called giant fibers, very thick nerve fibers which are responsible for the coordination of swimming movements of the animal. They run the entire length of the central nervous system and transmit their excitation to the motor nerve fibers supplying the muscles involved in the swimming movements.







EFFECTS OF ASPHYXIATION OF CENTRAL NERVOUS TISSUE

In a series of experiments the effects of asphyxiation of central nervous tissue in vertebrates were investigated. When the asphyxiation is prolonged sufficiently to produce damage to the nerve cells, but not long enough to destroy them, there may result a highly increased reflex activity after the tissue has recovered from the acute effects of the oxygen lack. In many respects the state of hyperactivity of the reflexes is comparable with the effects of convulsive drugs like strychnine. It is hoped that it will be possible to ascertain by further study the nature of the changes produced by asphyxiation.

Many of the electrical phenomena observed in living tissues are believed to depend on the presence of membranes permeable to certain ions but impermeable to others. In the presence of suitable concentration gradients such membranes can give rise to ionic double layers which represent electrical potentials. Studies on such membrances in the nervous system have been carried out. Asphyxiation has been shown to destroy the double layer. In the most sensitive parts (nerve cells) the deterioration of the double layer starts within 10 seconds after the beginning of asphyxiation. The effect of drugs is now being investigated.

ELECTROSHOCK THERAPY AND ELECTRONARCOSIS

For a number of years the Physiology group has cooperated with the Department of Institutions of the State of California in introducing in the State Hospitals some of the shock treatments for mental ailments. During this time physiological aspects of electroshock therapy were studied. An improved shock apparatus was constructed which made it possible to apply a preset current independently of the resistance of the patient's tissues.

As an outgrowth of this cooperation, another form of electrical treatment for mental diseases was developed. Whereas in shock therapy the current application lasts but for part of a second, in electronarcosis, as this new form of current application is called, the current is passed throught the patient's head for several minutes, producing unconsciousness. The physiology of this procedure has been worked out in some detail. The effects of electronarcosis on the blood pressure, on the metabolism of the brain and on the anatomy of the central nervous system have been studied. The relation of various forms of current to electronarcosis was investigated. Finally the Physiology group has assisted in the application of this treatment to a group of patients afflicted with schizophrenia. The results were encouraging.

Precision With Carbon -- **Bio-Organic Chemistry**

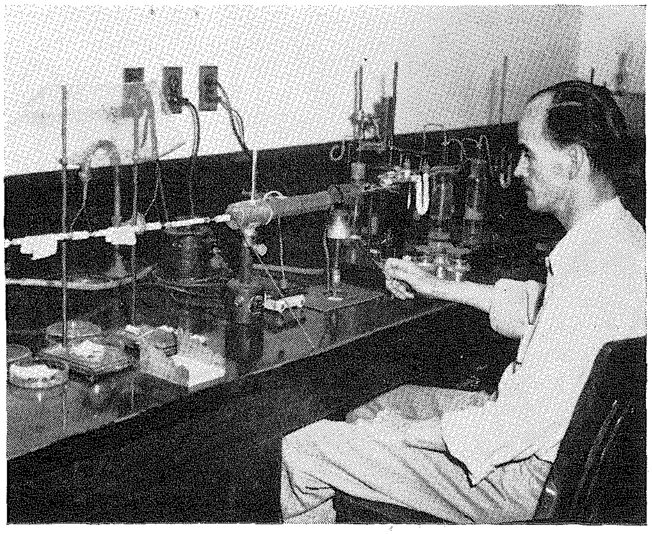
By A. J. HAAGEN-SMIT

ORGANIC Chemistry received its impetus from the study of natural products. The discovery of the constitution and synthesis of urea opened the way for the 300,000 - 400,000 organic compounds now known. While the name "Organic Chemistry" at first indicated the chemistry of the organized world, in later years it became synonymous with the chemistry of carbon.

In the more limited field of Bio-Organic Chemistry we are not concerned with all of the these compounds, which are for the most part synthetics. The number of well characterized compounds known to occur in the living organism is only about 8000 and increases at a rate of less than 100 per year. These figures are astonishingly low when we remember that about a million species of plants and animals have been classified by taxonomists, and that the total number of known seed-bearing plant species alone is estimated at a quarter million and before the war used to increase at the rate of approximately 2000 new species per year.

In any study of biological material the prerequisite for a satisfactory explanation of biochemical phenomena is a knowledge of the variety of compounds taking part in the reaction. The bio-organic chemist has set himself the task of increasing the knowledge of these building stones of the organism. In doing so, he provides the basic requirement for the studies of his fellow worker, the bio-chemist and the physiologist.

Much work remains to be done in this field. A glance through the list of chemically investigated plants shows immediately that only a few species of each family have been investigated and that for many plant families not even one member of the family has found its way into a chemical laboratory. Our chemical knowledge of the investigated species, too, is highly inadequate. Usually, published information consists of mentioning the presence of proteins, amino acids, fats, carbohydrates, rubber, essential oils and alkaloids. As these are all only group names for substances with roughly similar properties, a knowledge of their presence is but of limited use to the biochemist, to the physiologist and frequently to the industrialist.



Since the most numerous compounds found in biological material are compounds containing carbon and hydrogen, the combustion analysis of carbon and hydrogen is highly important to the organic chemist and biologist. Assistant Swinehart is carrying out such a combustion analysis.

While often, as for example in the field of essential oils and alkaloids, the quantities involved are not a special problem, in the case of most physiologically active substances micro-analytical procedures have to be applied to solve the problem. This is also true of the field of flavor substances, which shows in its treatment a certain resemblance to that of the vitamins and hormones. In both cases a physiological assay method is used during the isolation process. For the flavors it is the smell and taste which serve as a guide; for the vitamins and hormones their effects, such as growth, are measured. In both cases the methods used are dictated by the occurrence in extremely low concentrations in the starting material. Even when thousands of pounds of material are worked with, the amounts finally obtained weigh often only a few milligrams. In this way several plant hormones, flavor-substances of pineapple and onions and differentiation factors for certain protozoa were isolated in our laboratory. Together with the U. S. Forestry Service, contributions are being made towards a more complete knowledge of the rosins and essential oils of the genus **Pinus**, and with the Huntington Library a campaign is being carried on to give us a better understanding of the alkaloids in the cacti.

This analytical work is, when possible, followed by synthesis of the compounds and the way is opened for the preparation of a large number of analogues, which might be helpful in explaining the mechanism of biochemical reactions. In the last few years the bio-organic chemist has extended this synthetic work to the incorporation of isotopes of carbon, nitrogen and other elements in these products.

UPPER: Often the quantity of pure chemical compound obtainable from living organisms is very small. Chemical reactions involving such minute quantities of material must be carried out in tiny apparatus in order to minimize losses. Here Dr. Haagen-Smit is shown with some micro chemical laboratory ware. CENTER: Before a chemical compound can be analyzed as a first step in its identification, a sample must be weighed. Dr. Haagen-Smit is shown at one of the micro analytical balances with which it is possible to weigh to the nearest two-millionth of a gram. LOWER: Dr. Gertrud Oppenheimer, research assistant, with several of the micro analytical laboratory burettes. "Patchi" is not an experimental animal.

Dredging. Two dredges are shown and one is being dragged along the bottom. The dredge is towed at a rate of about 2 mph. The size of the boat is such that if the dredge fouls, the boat is held and the line does not not break. A winch powered from the motor hauls up the dredge from depths of 5 to 500 ft. Deeper hauls could be made by using a bronze cable instead of rope. The dredge on the stern of the boat is the one most commonly used. Other dredges not shown are used for amphioxus and other small forms, and another type for rocky bottoms.

First Collect the Specimens -- The Marine Lab

By GEORGE E. MACGINITIE

MARINE animal and plant forms are of great interest to the biologist, chiefly for two reasons. Much experimental biological research is carried on with marine material because it is usually easily available, can be easily handled experimentally, and provides large numbers of eggs. This last characteristic permits experiments with large quantities under controlled laboratory conditions, and provides an excellent supply of raw material for embryologists. The second reason for biological study of marine organisms is the desire for knowledge of the natural history of these forms. The ecology, or relationship between these plants and animals and their environment is a field which has drawn the interest of many biologists in the past and today.

However, detailed study, both for experimental purposes and for ecological information, must be conducted in the laboratory. Collection of marine organisms is therefore necessary.

The William G. Kerckhoff Marine Laboratory of the California Institute's Biology Division, located in Corona Del Mar, on the east side of Newport Bay about one-half mile from the entrance, is ideally situated for the study of marine life. The flora and fauna of the region are abundant and encompass a great diversity of forms. Seaweeds grow profusely on the jetties and on the rocky shores toward Laguna Beach. The region supplies all types of marine habitats for animals: rocky shores, rock jetties, mud flats, sandy beaches, the ocean bottom, and the open water of the ocean. Mud flats, rocky shores and sandy beaches are all within walking distance of the Laboratory. It is possible to collect members of all of the major groups of marine animals for experimental purposes. To mention a few, there are ample supplies of sponges, hydroids, jelly fishes, sea anemones, sea pens, flatworms, annelid worms, echiuroid worms, sea urchins, sand dollars, star fishes, mollusks, crabs, lobsters, tunicates, balanoglossus, amphioxus and fishes.

Good boating facilities are a necessary adjunct to the activities carried on at a marine laboratory in order to obtain the material needed for biological research. The Kerckhoff Marine Laboratory is very fortunate in this respect. Newport Harbor is out of the belt of northwest winds which prevail farther north along the California coast, and the channel islands have something of a dampening effect on large ground swells from the open ocean expanse, so that it is possible to engage in towing or dredging operations almost any day of the year.

The Laboratory owns a 26 foot boat, equipped with a 40 hp engine, which is used for making plankton tows and for dredging operations. There is also a skiff that can be used for collecting in the vicinity of the Laboratory within the entrance of the bay. An ample wharf extends from the Laboratory into the bay.

Diatoms and Dinoflagellates, tiny microscopic plants which float on or near the surface of the ocean in great quantities, sometimes tons per acre, furnish food for a great variety of species of animals. The surface waters of the ocean therefore are very rich in living forms. To obtain these, open ended, cone-

The Haul. These specimens were obtained near the harbor's east jetty in from 10 to 20 ft of water. The haul included sea urchins, sea cucumbers, and cushion stars that can be used for experimental embryology. In addition, there is a lobster used for problems in immunology and for protein studies and a moon shell snail used for physiological studies, interesting because it has pink nerves. Dozens of new species have been found near the Laboratory.

shaped nets are towed through the water with the open end toward the boat. Plants and animals are thus strained out and collect in a glass contained securely fastened in the small end of the net. This material is brought to the Laboratory where that to be used for research purposes is separated out.

Perhaps the greater amount of material obtained with the boat is from the ocean bottom. Many types of dredges and collecting mechanisms have been devised for obtaining particular specimens for study. Some animals live in the rough rocky regions and others live upon or burrow within the smooth muddy floor of the ocean. The surface-dwelling forms on the smooth floor of the ocean are easily obtained, but for the burrowing forms, which are very numerous and of many diverse species, some type of dredge must be used which will dig into the ocean floor and bring the animals to the surface where they are caught in a net that either follows behind or is a part of the digging apparatus.

Collectors have found that the best type for obtaining animals from the rocky bottom is a small, heavily-built, three-cornered dredge. This type of dredge scrapes animals or seaweeds from the crevices and is much less likely to foul and become fast in the rocks. Rough animals like certain star fishes and spiny sea urchins may be obtained by entangling them in an old piece of fish net which is dragged over the rocks. When animals are dredged they are placed in a live-tank aboard the boat through which a stream of ocean water is pumped so that the animals remain fresh and suitable for use when they arrive at the Laboratory.

The Laboratory is a two-story, cement, Spanish-type building containing four large rooms and several smaller ones. It was purchased in 1929 and soon thereafter equipped with a salt water system, and a road was built so that cars could reach the laboratory grounds. The large laboratories and one of the small laboratories are equipped with aquarium tables and aquaria. Salt water, which is pumped daily at high tide to a 5000 gallon tank on the roof of the Labora-

(Continued on page 25)

Laboratory Scene. Right foreground: Opening sea urchins to obtain sex products for respiratory experiments. Background: Sorting the dredge haul for unusual specimens, which are sent to specialists all over the world. Left foreground: A typical salt water table with its aquaria. The small aquarium is for photographic work. The larger aquaria and jars contain certain animals which are being kept for feeding problems and growth rate records, and others for solving problems in natural histories and life histories.

ENGINEERING The Air-Conditioned Greenhouse

By F. W. WENT and H. O. EVERSOLE

AGRICULTURE can be defined as the controlled growing of plants, and therefore it is of paramount importance to know the principles of plant growth and the conditions under which this growth takes place. The Plant Physiology Department of the California Institute of Technology is especially equipped to study both these sides of the problem of plant growth. Others have described the basic contributions made by investigators of the problem of internal chemical control of growth. In this work a very close cooperation between botanists and chemists has brought significant results in the field of biological chemistry.

Another approach to the plant growth problem has been carried out at the Institute to the present advanced stage through the use of the air-conditioned greenhouses built in 1939. This approach is a study of the climatic requirements of plants. Such a study requires complete control over the environment of the plant. This environment can be divided into two parts: 1) the soil in which the roots grow, and 2) the air. The soil is an incredibly complex system, which fortunately we can replace by a well-aerated solution of the inorganic salts necessary for plant growth. With such a simplified root medium, much information concerning plant nutrition has been obtained.

LIGHT VERSUS AIR

But there are no substitutes for air and light in growing the above-ground parts of a plant. The difficulty in controlling this air lies mainly in the need for high light intensities to make plants grow normally. In general, plants require intensities as high as or not less than 1/10 sunlight. Such intensities can be reproduced with difficulty by artificial light sources. But whichever the light source, intense light causes strong heating. This throws off the temperature control of the surrounding air, so that in experiments usually either the temperature of the air around the plants is controlled at a low light intensity, or the plants receive full light at uncontrolled temperature.

To achieve air temperature control at high light intensities it is necessary to install an air-conditioning system differing in many respects from the principles established for human comfort air-conditioning.

The first deviation is obvious: a much larger volume of air has to be passed through the greenhouses to counteract the temperature increase due to light absorption. Depending on how close a temperature control is desired, the air-conditioning system has to renew the air one to four times per minute in the greenhouse. This requires both heavy blowers and wide air ducts. Although such a requirement seems obvious, in many systems which were installed in greenhouses between the years 1926 and 1940 the ducts were entirely insufficient to deliver the volume of air needed to maintain temperatures reasonably close to the setting of the thermostat. This experience led to a wide-spread belief that greenhouses could not be air-conditioned.

The second deviation lies in the air distribution. To move such a large volume of air through a greenhouse without strong air currents and without channelling, it must be introduced from many points and through many openings. The air must move past the surfaces absorbing the light to carry away the heat and the water vapor produced. This means that in a greenhouse the air must move past all leaves. When the plants in a greenhouse are all of the same size, this can be accomplished by providing horizontal currents just over the plants, and having an adequate air supply from below. The heated air will then be carried off as it rises in the horizontal sheet of moving air.

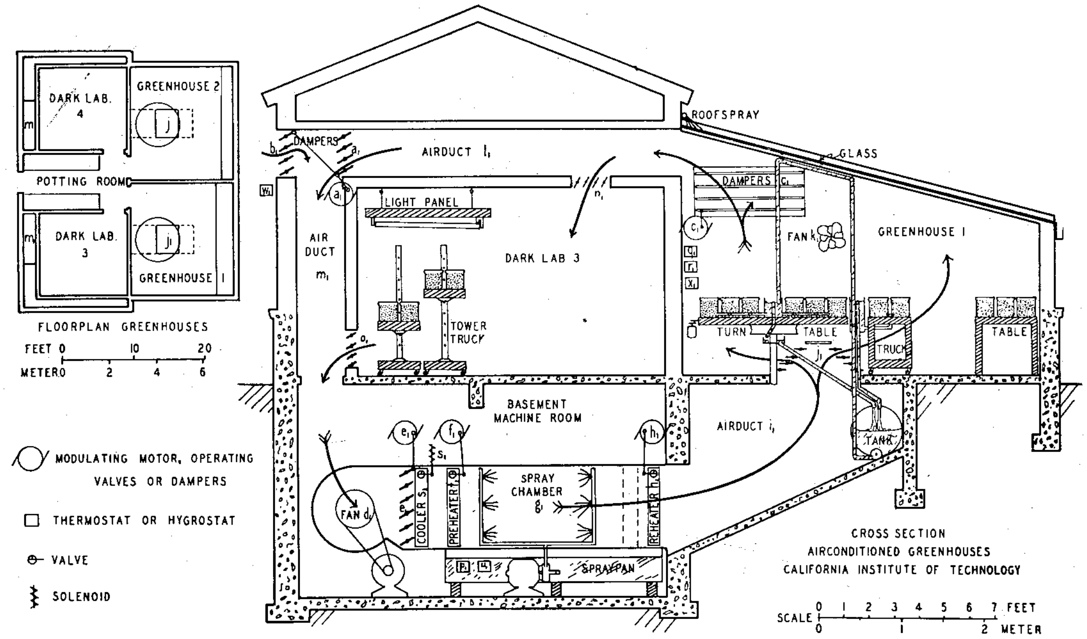
THE WORKING MODEL

In the present air-conditioned greenhouses, plants of different sizes are being and will have to be grown; hence the system of a horizontal sheet of moving air is not very good.

A number of tests have been carried out with different methods of introducing air into greenhouses. For this purpose a model was built of sufficient size to measure air currents around plants of the size used in most experiments. A blower delivered 600 ft^3/min to a plenum under the greenhouse floor. The floor consisted of wooden slats of four in. width, which could be spaced according to need, to let the air pass between them. It was found that if the air was injected through slits of 1/3 in. between the boards, it mixed with the room air almost immediately, and then rose at a rate of about 20 ft/min evenly upward, unimpeded by three ft tall tomato plants, growing in four in. pots, four per square foot. There was

The air-conditioned greenhouses at the California Institute. The sloping glass roof towards the left covers the greenhouses, the tile roof covers the adjoining darkrooms.

Floor plan of the present greenhouses (left side faces north) and cross median section through house "1" and room "3".



little tendency for the air to move sideways towards the exhaust slits before it had reached the ceiling. It was found essential to have the air in the plenum back up against a dead air-space before rising through the slits in the floor.

Another requirement in order to obtain good air distribution with this system is large exhaust openings and wide exhaust ducts. For the main air resistance must be located in the floor slits, when an evenly rising mass of air is desired.

The air-distribution thus obtained in greenhouses is ideal for experimental purposes, where plants are grown in individual containers, but the vertically rising air cannot be used in greenhouses where continuous bench space is required.

If we ask now what the first small air-conditioned greenhouses built in 1939 have contributed to botanical knowledge, an amazing story can be told.

EXPERIMENTATION IN THE AIR-CONDITIONED GREENHOUSES

Whereas usually any first new machine or apparatus has to be rebuilt and improved before it is generally useful, the foresight and care in planning of the present air-conditioned greenhouses made them eminently useful, even though many improvements can be suggested now as a result of eight years of experimentation in these houses.

The primary achievement is reproducibility of experiments with full grown plants. Tomatoes, tobacco and many other plants receive even in winter in Pasadena enough light for optimal growth, and therefore their development is controlled by factors other than light. These other factors, especially temperature, can be controlled, and therefore the whole development of the tomato plant is under control. In this way comparable tomato plants can be grown at any time of the year, so that experiments can be run throughout the year without interruption during summer or winter. The difference between such standardized plants and tomato plants grown in an ordinary greenhouse has become very apparent in our recent experiments with sugar application to plants. Whereas tomatoes grown in ordinary greenhouses sometimes grow better, and sometimes poorer, after being sprayed with a sugar solution, plants grown under rigidly controlled conditions responded in the same way when they had been subjected to the same conditions. This fact is really self-evident as a necessary corollary of the causality principle. The amazing thing is that research workers with plants had so long been satisfied with lack of reproducibility in their experiments.

The second achievement of the air-conditioned greenhouses is theoretically far more important. By disassociating the various climatic factors influencing the development of the plants, the exact role of each factor by itself can be assessed.

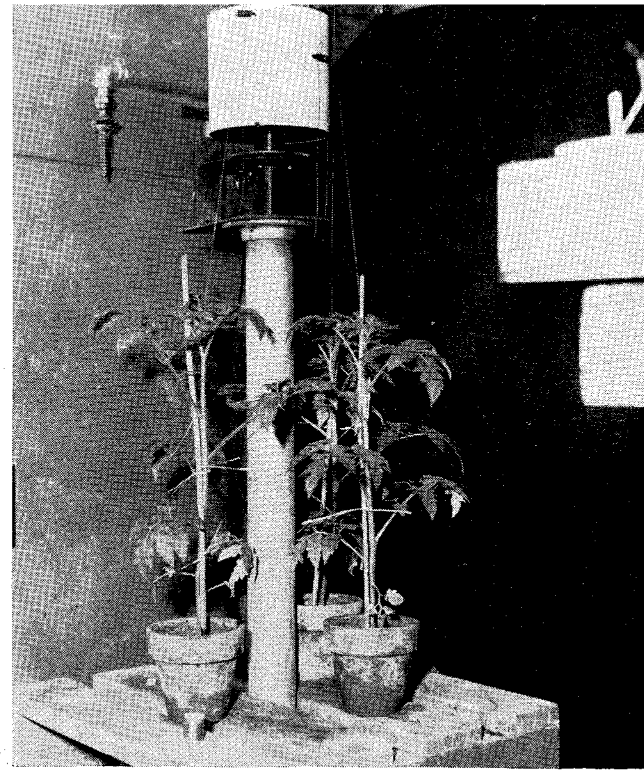
In field experiments stronger light is associated with higher temperature and lower humidity, so that the effects of each factor by itself cannot be deduced from experiments. Separating temperature, humidity and light, it was discovered that the night conditions determine whether a tomato or pepper plant sets fruit. It also seems that the old saying that corn needs very warm nights for best growth is not entirely correct. It needs warm days and fairly cool nights. The beneficial effect of the warm day may overshadow the less favorable effect of a hot night. Thus it becomes possible to assess accurately the effect of individual factors and their interaction for each plant variety. In this way it becomes possible to choose the proper climatic data for judging the fitness of a local climate for the growing of a particular plant or crop.

The study of the interaction between the environmental factors makes this work of particular value for agriculture. If, for instance, it is stated that the optimal night temperature for tomatoes in 65°F, this holds only for a certain variety when the plants have reached a certain size and for a certain light intensity. Therefore in the field we have to know all qualifications before we can apply knowledge gained in the laboratory. A complete set of air-conditioned rooms and greenhouses can supply this information necessary for aplication in the field. This will make plant physiological knowledge much more useful for agriculture.

The accurate and complete knowledge of the reaction of plants to the individual components of the climate will gain special significance in connection with long-range weather forecasting. Then the farmer can plant the varieties of annual crop plants which will respond best to the climate to be expected in any growing season. In this development meteorologists and plant physiologists will have to work in close association, the latter determining which factors are of most significance for particular crops, and the meteorologist making the forecasts for such particular factors.

Perhaps the most important function of the air-conditioned greenhouses is that they furnish the physical conditions to study specific processes in plants, such as water uptake, water loss, transport of water, salts and sugar, hormone production, synthesis of organic components, etc. Many of these processes

Recording the growth of tomato plants. A silk thread is attached to the tip of the plant, runs over a small pulley, and at its other other end carries a pen. This marks a drum, which turns at the rate of one revolution every eight days. The setup is mounted on a truck, which can be moved to different conditions, so that growth can be recorded under different day and night temperatures, in light or darkness.

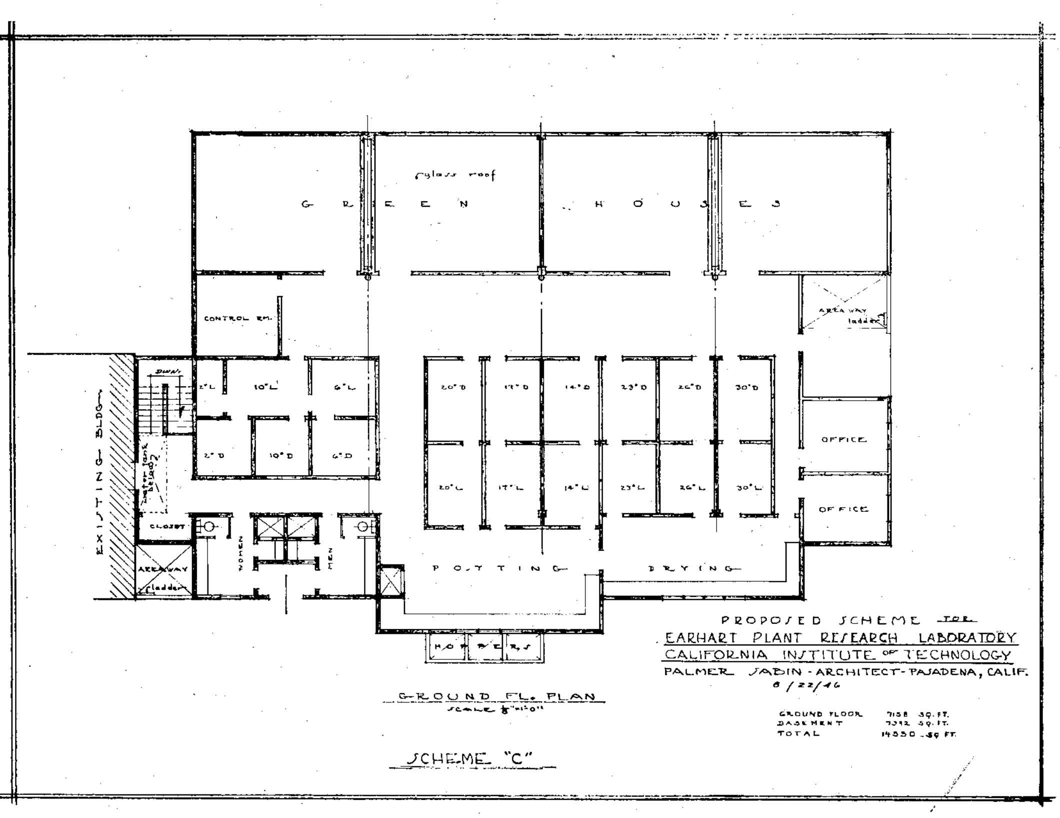


are only slightly known, because most experiments on them have been carried out under uncontrolled or inadequate conditions. With the physical set-up of air-conditioned greenhouses, and the presence of so many eminent physicists and chemists, it is possible to probe much deeper into problems concerning plants. It is very likely that this work will give a powerful stimulus to making Botany a science as exact as Physics and Chemistry are at present.

Considering the very poorly defined and practically uncontrolled conditions under which plants have been generally grown, it is not surprising that physicists especially were reluctant to assist botanists in solving the physical problems connected with the life activities of plants. Now that we are able to work under strictly defined conditions, it must be possible for botanists and physicists to attack problems of hormone, food and water movement, etc., jointly. Thus the greater accuracy obtained not only improves the research but will tend to expand it into the borderfield between Botany and Physics, a practically virgin field.

The present air-conditioned greenhouses were built as an experiment, but they have long since passed the experimental stage. They are now an absolute necessity for further plant physiological work, just as much as the thermostat and pH meter have become essential for physico-chemical work. However, the limit of what can be accomplished in the present air-conditioned greenhouses has been reached. Space limitation and the limited number of different conditions make it impossible to expand the work now being carried out; such expansion is essential, however, if the results are to be applicable in agricultural work.

These considerations led the Earhart Foundation to make a gift to the Institute, enabling it to construct a complete set of air-conditioned greenhouses, darkrooms and artificial light rooms, which will cover practically the whole range of climates on earth. If the present air-conditioned greenhouses have already been so productive, it can be conjectured how important the projected greenhouses will be for the advancement of the Botanical Sciences and of Agriculture. And with these new Earhart Greenhouses, botanical work at the California Institute of Technology can be expected to yield the utmost in results. It is hoped that many guests will come to avail themselves of these facilities, thus making them useful far beyond the boundaries of our own interests and establishing the Earhart Greenhouses as a center of botanical research.



Floor plan of the projected Earhart Plant Research Laboratories at the Institute. Illustrated is the arrangement around a central hallway of four separate greenhouses and 18 light and dark rooms for controlled temperatures ranging from 2° to 30°C.

A number of service rooms, such as the potting room, drying and harvesting room, and control room are on the same floor: a shop, laboratory, more offices and more controlled temperature rooms are projected in the basement, together with the air-conditioning equipment. The entrance of the building is through the washrooms, which act as a quarantine station to prevent as much as possible the introduction of pests and diseases. To the south the new building is connected with the present air-conditioned greenhouses.

Pre-Medical Training at the Institute

By HENRY BORSOOK

THE IMPACT OF PHYSICS AND CHEMISTRY ON MEDICINE

THE DISCOVERIES of Pasteur, Koch and Bernard turned Medicine to view health and disease as physico-chemical biological phenomena. Bacterial invasion and resistance to it are described in chemical terms, an interplay of antigen and antibody. Diabetes means a lack of the specific protein substance, insulin. Viruses, the causes of, for example, influenza, infantile paralysis, some forms of experimental cancer, are complex but nevertheless well defined chemical entities. Similarly the course of a disease process is described, whenever possible, in chemical terms—as a change in hydrogen ion concentration (acidosis), or, in the case of sugar in the blood (diabetes), as too little production of acetylcholine at the locus between the end of a nerve and the muscle fibre it innervates (myastheniargravis). Food is considered as a source of essential nutrients—calories, special nitrogenous substances, minerals and vitamins, and not simply as fuel. Immunological research led to the discovery of the blood groups, and thereby greatly reduced deaths and sickness after transfusions. The blood type of a person was shown to be hereditary. It was then found that one of the causes of death of the new-born is a genetical immunological phenomenon; when the cause was recognized, means were found to avert it.

The great contributions of Physics to Medicine are commonplace. Everybody knows of the medical uses of X-rays and radium. A technician makes a diagnosis of tuberculosis today in a few minutes in cases where 40 years ago the skill, experience and judgment of an Osler were required. Isotopes and the electron microscope are powerful new tools for the study of disease as of other biological processes.

Mathematics, especially statistics, is indispensable to the Public Health officer, epidemiologist, geneticist, and in the anthropological study of populations.

The foregoings were some of the considerations which led to the establishment in 1928 of a Division of Biology at the California Institute of Technology. They were not, of course, the only considerations. The elucidation of biological phenomena, wherever possible in physico-chemical terms and by physico-chemical means, is important in itself; and as appropriate at the Institute as Physics and Chemistry and their applications.

THE BIOLOGY OPTION AS A PRE-MEDICAL COURSE

The Biology Division offers an undergraduate course designated Biology Option. It begins in the last semester of the sophomore year and continues through the remaining two and a quarter years to the B.S. degree. The subjects taught are physics, chemistry, mathematics, zoology, botany, embryology, comparative anatomy, genetics, animal and plant physiology and biochemistry, immunology, English literature, American and European history, and foreign languages.

A relatively advanced knowledge of the basic sciences of Physics, Chemistry, and Mathematics is essential for the student of modern Biology. In the biological courses the point of view is toward the fundamentals; emphasis is on general unifying principles. Applications to Medicine, Agriculture and Industry may be cited as illustrative examples, but they are not taught as subjects in themselves. In a word the objective is to teach Biology and not Medicine, Agriculture or Technology. Students who wish to become proficient in one of the latter subjects are recommended to attend, after they have had a thorough grounding in the basic sciences of Physics, Chemistry, Mathematics and Biology, schools especially devoted to that purpose.

The undergraduate Biology Option serves well as a pre-medical course. It is acceptable to leading medican schools. About half the students who have taken our Biology Option have later studied Medicine. Most have gone into medical practice, the others into academic work, medical, biological, biochemical and industrial research work. The reports we have received from our students and their teachers in medical schools testify to the value of an intensive pre-medical training in the fundamental Physical and Biological Sciences.

The first impact in the applications of Physics and Chemistry to Medicine is, of course, in research. It could be said that abnormal physiology, much of modern pathology and bacteriology, chemotherapy, medical radiology, to name only some of the fields in which important advances are being made now, are essentially extensions of Chemistry and Physics fusing with Biology. The great new powers at our disposal through advances in these basic sciences may be likened to the bow of Ulysses. The strength to bend it comes from a sound working knowledge of the ideas and methods of the basic sciences. A research worker in Medicine today is at a disadvantage without it.

The practising physician and surgeon needs to know the basic sciences in order to apprehend the significance of new advances in medical research and to use them intelligently. Otherwise, he is likely to be slow in taking them up or uncritical in their use. He is dependent on other better trained doctors in their use, and then can use them only in a routine manner as a technician. The advances to be made by their proper, critical use and in extending their usefulness he must leave to colleagues. Leadership in medical practice as in research is taken by doctors better trained in Medicine and in the basic sciences.

The Egg in Kerckhoff

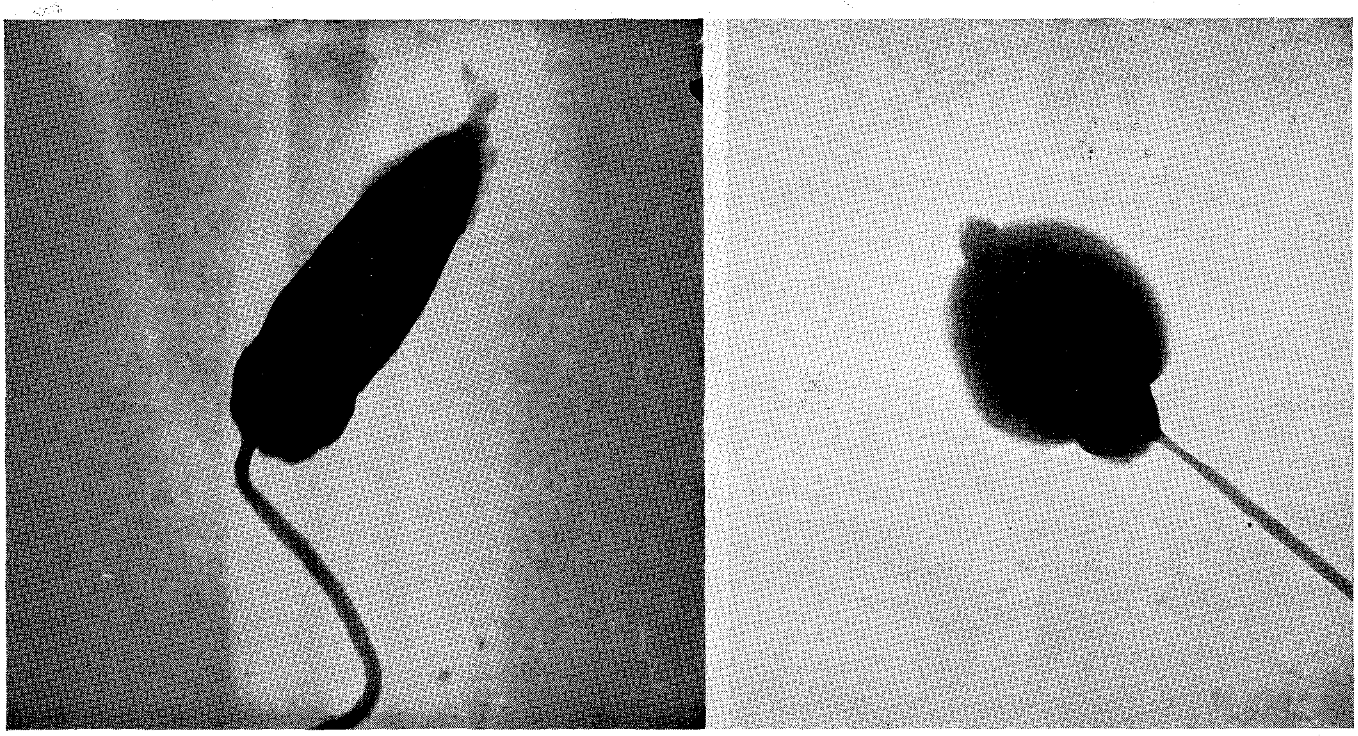
By ALBERT TYLER

RESEARCH in Embryology is directed toward finding the basic causes of the transformations involved in the development of an adult organism from the egg. It is now well established that the main principles and features of development are the same in most multicellular animals; so that discoveries made with eggs and embryos of one kind of animal apply in general to practically all others. This, then, means that the main problems of development may be studied in species that are most suitable for the particular process under investigation, that are most easily handled experimentally, and that provide large numbers of eggs. These characteristics are particularly true of various marine animals. Since the Division of Biology has a Marine Laboratory within a short distance of Pasadena, we are in an especially advantageous position for carrying on such research.

IMMUNO-EMBRYOLOGY

Various kinds of embryological problems have been investigated by the staff and students at the Marine Laboratory and at the main laboratories in Pasadena. These deal mainly with the early stages of development, and for the most part the research is along the line now known at Chemical Embryology, which seeks to identify the chemical reactions responsible for various embryological processes. At present much of the work is concerned with problems of fertilization, which comprise the all-important initial steps in development. Studies in this field have shown the processes of fertilization to be very largely analogous to those encountered in the field of Immunology, and the investigations have proceeded on that basis. Thus, for example, not only does the engulfment of the sperm by the egg in fertilization resemble the phagocytic processes studied by immunologists, but there are specific substances obtained from eggs and sperm that interact in the manner of antigen and antibody. One kind of substance obtained from sperm is an enzyme that dissolves certain membrane barriers surrounding the egg and this same agent is also found in various pathogenic bacteria, in venoms, etc., where it evidently acts by enabling the toxic material to invade the tissues of an animal. So, it may be seen that studies of fertilization are related to those of infection. To implement this approach, immunological laboratories were set up jointly by the embryologists and Professor Sterling Emerson, who found similar relations of Immunology to his problems in Genetics. These immuno-genetics and immuno-embryological laboratories have been equipped and supported largely by grants from the Rockefeller Foundation.

As part of the students' general biological training, a course in Embryology is included in the undergraduate Biology Curriculum. This course includes some experimental work along with the more standard descriptive studies. Along with this a course in Microscopical Technique and Histology is given by the Department. These subjects serve as preparation for advanced work in Embryology, for the work in related fields such as Genetics and Physiology, and as part of the pre-medical requirements for students pre-

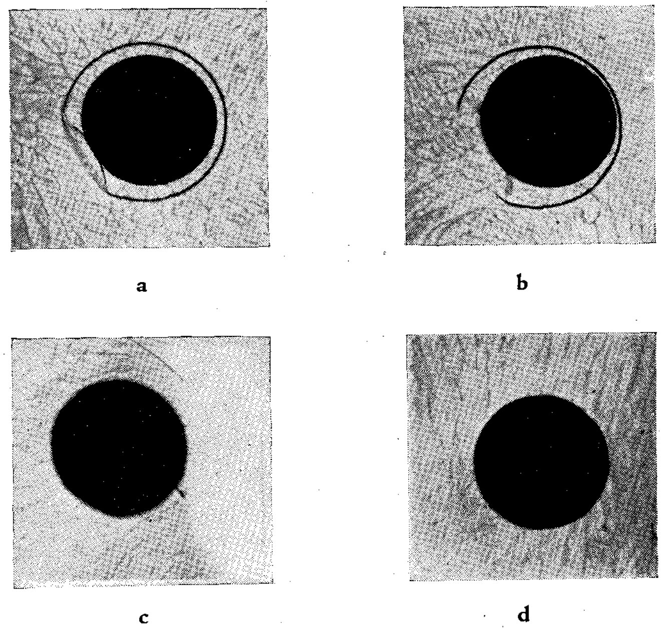


The head and part of the tail of the spermatozoon of a sea urchin taken with the electron microscope at a magnification of 30,000X. These two pictures illustrate the effect of extracting from the spermatozoon one of the specific substances involved in fertilization. On the left is the normal and on the right the extracted spermatozoon. They show that the active material is evidently derived from the nuclear region of the head, which becomes rounded, swollen, and less dense after extraction, while the acrosome, midpiece, and tail remain relatively unaffected.

paring for Medicine. Graduate students majoring in Embryology pursue advanced courses, seminars, and research in Experimental Embryology along with advanced studies in other departments of the Division of Biology, in Chemistry, or in Physics.

OPPORTUNITIES FOR EMBRYOLOGISTS

There has been a gradually increasing demand for embryologists from various sources apart from the universities. Mention may be made of a few such opportunities for non-academic work. In laboratories engaged in production of vaccines, trained embryologists are often employed in connection with the cultivation of viruses on the membranes of chick embryos. Openings for embryologists may be found in fishery stations, in the fish industry, in laboratories and farms engaged in Animal Husbandry (including artificial insemination and poultry raising), in laboratories and enterprises concerned with Endocrinology (production of, or testing for, hormones), in control work in industries involved in radiation work, and even in the paint industry in connection with such things as development of anti-fouling agents. As in other biological fields, completion of advanced work beyond the bachelors' degree and broad training in Chemistry and Physics as well as in Biology are of advantage to men seeking a career in teaching, research, or industry.



Photomicrographs of an egg of a marine mollusk, the keyhole limpet, showing the dissolution of the egg membrane by means of an enzyme derived from sperm of the same species. Pictures taken at a, 1 minute; b, $1\frac{3}{4}$ minutes; c, $2\frac{1}{2}$ minutes; and d, $3\frac{1}{4}$ minutes after addition of the enzyme solution. (From Tyler, 1939).

First Collect the Specimens

(Continued from page 19)

tory, flows by gravity through lead pipes to the aquaria in the laboratories. With the type of installation in use, and its proximity to the entrance of the bay, the salt water system is very efficient, making it easy to culture marine larval forms or maintain adult animals. The temperature of the water in the aquaria in the laboratory is never more than one degree above that of the ocean water.

During 1932, 1933 and 1934 a rather complete survey of the animal population was made, both of the bay animals and the outside ocean fauna. Now when a particular animal is needed for experimental work, a suitable type of dredge is selected and dredging is carried on over the type of bottom that that particular organism inhabits. With few exceptions, however, towing or dredging for a particular animal cannot be done without obtaining a sample of animals of the region. So many new and interesting specimens are still being brought in.

This availability of material means that by towing, or dredging, or collecting on mud flats or rocky shores, living marine material for almost any type of experimental biological research may be supplied. Visiting professors usually come to the Laboratory with a definite problem in view, and so know what organisms they need to carry on their research.

A great deal of work has been done on the respiratory requirements of fertilized eggs and the developing larvae. Another embryological study is based on the fact that most marine animals discharge their sex products directly into the sea water, where fertilization takes place. To prevent waste, nature has provided such animals with an enzyme called fertilizin. When one animal spawns the fertilizin released at the same time causes all other individuals of the same species in the near vicinity to spawn. The determination of the chemical nature and the function of fertilizin has been a problem receiving much attention at the Laboratory.

Many life histories of marine animals are being solved because it is easy to raise larvae in the laboratory. And, because of the ease of simulating natural conditions within the laboratory, much information is being added to our knowledge of the natural history of marine forms.

Marine animals have great powers of regeneration. In some forms, a small piece of an adult will grow into a new animal, in other a new leg grows when one is lost. A star fish that is being used in regeneration experiments grows an entire body from a piece of an arm.

The crustacea of the region furnish material for experimental nerve physiology, and from them a great deal has already been learned about the inhibitory portion of the nervous system. Some of the fishes also afford excellent material for nerve study. The blood of star fishes and of lobsters is being used for studies in immunology, and for protein and amino acid investigations.

Until his death in late 1945, Dr. Thomas Hunt Morgan made use of the Marine Laboratory. where he carried on experiments on the genetics and development of the tunicate **Ciona.** This tunicate is hermaphroditic, that is it is functional both as a male and a female. However, it will not fertilize its own eggs. By treatment with dilute acids or by other means, it is possible to fertilize an individual's eggs with its own sperm. Because of the salt water system, the resulting offspring can be raised to maturity, and thus successive generations from a single parent can be obtained.

The Laboratory is open to biology students of the Institute, members of the Division of Biology, and visiting research workers from other divisions or from other institutions. Undergraduate biologists are required to take a month's work at the Laboratory in the summer following their sophomore year.

FELLOWSHIPS IN BIOLOGY AT THE INSTITUTE

NEVER BEFORE have the opportunities for fellowship aid in higher education been so numerous. This is as it should be, for never has the need been so great. Except for certain special fields such as medicine, almost no men were given an opportunity for advanced training during the five-year period of the war. We are not only left with a large deficit in terms of normal manpower requirements, but because of the tremendous post-war growth of colleges, universities, and industrial laboratories, the need has increased far beyond that of pre-war years.

Biology is no exception—the need for men with post-A.B. and post-Ph.D. training in this field is great and the opportunities for obtaining this training are many.

Men interested in obtaining advanced training in modern Biology at the Institute will find numerous possibilities for financial assistance if this is needed. The Institute itself administers a number of Graduate Fellowships for which Biology majors are eligible. In addition, a number of Graduate Assistantships are ordinarily available. Recipients of such appointments are expected to register and carry on graduate work as well as to assist in instruction or research. Graduate Assistants in Biology for 1947-48 who assist to the extent of approximately 12 hours per week may, on the basis of scholarly achievement and promise, receive a tax-free tuition grant of $500 and in addition a stipend, subject to normal taxation, of $875 for the academic year.

From the time of its establishment in 1928 the Division of Biology of the Institute has had on its staff many post-doctoral fellows engaged in extending our knowledge of the living world. Some thirteen Fellows of the Rockefeller Foundation have carried on research in the William G. Kerckhoff Laboratories of the Biological Sciences of the Institute. These outstanding biologists of many countries include: Hans G. Bauer, D. G. Catcheside, C. D. Darlington, Max Delbrück, Boris Ephrussi, G. H. M. Gottschewski, H. M. Kalckar, G. Karpechenko, P. C. Koller, K. Linderstrom-Lang, K. Mather, Curt Stern, and M. Westergaard.

Professor A. C. Giese of Stanford University is now a Guggenheim Fellow in Biology at the Institute.

Sixteen National Research Council Fellows in the Natural and Medical Sciences have carried on work in Biology at the Institute. They are: G. W. Beadle, J. B. Buck, C. R. Burnham, A. E. Clarke, B. P. Kaufmann, W. E. Lammerts, Barbara McClintock, Eileen Erlanson MacFarlane, J. R. Raper, J. I. Shafer, Jr., A. M. Srb, M. P. Starr, R. D. Stichler, R. P. Wagner, A. H. Whiteley and M. Whittinghill.

Dr. E. L. R. Stokstad, now with the Lederle Laboratories, worked at the Institute as a Lalor Fellow.

The Institute administers a number of post-doctoral research fellowships. At present there are four Senior Research Fellows in Biology: J. W. Dubnoff, G. L. Keighley, H. K. Mitchell, and S. G. Wildman. There are two Nutrition Foundation Fellows: Marguerite Fling and B. O. Phinney. The Eli Lilly Company has made available to the Institute funds for a post-doctoral fellowship in Biology. This is currently held by D. L. Harris.

In 1945 the Human Betterment Foundation, founded by E. S. Gosney, was dissolved and its assets given to the Institute for the establishment of the "Gosney Research Fund, the income from which will be devoted **in perpetuity** to the promotion of research into the biological bases of human qualities, and for making known the results of such research for the public interest." Currently the income from the Gosney Fund is used to support post-doctoral research fellows in Biology. At present, Ray D. Owen, Werner Maas and Herschel K. Roman, are Gosney Fellows.

From its regular budget the Biology Division supports a number of post-doctoral fellows; at present there are ten such Research Fellows in the several branches of Biology represented at the Institute.

Inquiries concerning undergraduate fellowships and scholarships in Biology at the Institute should be addressed to the Registrar's Office. Graduate Fellowships and Assistantships are administered through the Office of the Dean of Graduate Studies, while information regarding post-doctoral fellowships can be had from the Chairman of the Division of Biology.

G. W. B.

Drosophila

(Continued from page 7)

to study other material? There are several reasons why the prospects for profitable work with **Drosophila** are still good. One such reason is that the large body of knowledge now available — incomparably more than that concerning any other organism—has made it possible to develop new techniques. Another point is that the chromosomes, which are the bearers of the genes (**i.e.,** the hereditary units), show an unusual amount of structural detail in Drosophila. This special property, shared by most of the flies, was wholly unknown when the material was selected for study; but in the salivary-gland cells the chromosome structure can be analyzed in a detailed fashion not approached in any organism outside of this one order of insects. This property makes it possible to attack a series of problems for which no other material is available. The problems that can be studied because of these two circumstances are fundamental and general ones, not merely special things pertaining to **Drosophila** alone.

It is clear that the genetic properties of higher animals and plants are very similar—the same general principles apply to all of them. Accordingly, the study of **Drosophila**, which lends itself easily to laboratory work in beginning classes and in advanced research, is useful as a basis for work in Applied Genetics as well as on the theoretical side. In Applied Genetics there is a demand for well-trained men in agricultural colleges and experiment stations, and there is a growing realization of the need for such men in the field of human heredity—a need coming to be recognized by the medical schools.

The Gosney Research Fund

IN 1929 Mr. E. S. Gosney founded and endowed a non-profit organization, known at the Human Betterment Foundation, for the purpose of fostering and aiding constructive and educational forces for the protection and betterment of the human family. In collaboration with Dr. Paul Popenoe and other scientists Mr. Gosney carried on an extensive study in the field of eugenic sterilization, including particularly its medical, legal and social aspects. In 1929 and 1930 an exhaustive survey was made of 6000 cases of sterilization of eugenically unfit. Eight years later a second similar survey of 10,000 cases was made.

Following the death of Mr. Gosney in 1942, the Trustees of the Human Betterment Foundation agreed that the best interests of the Foundation would be served by transferring its activities to the California Institute of Technology. As a consequence in October 1943 an agreement was drawn up according to which the Human Betterment Foundation was to be dissolved as such and its assets turned over to the Institute. The Institute agreed to use these assets "and the proceeds thereof to establish the Gosney Research Fund, the income from which will be devoted in perpetuity to the promotion of research into the biological bases of human qualities and for making known the results of such research for the public interest."

At the present time the income of the Gosney Research Fund is used in support of post-doctoral fellowships in those branches of biological science basic to our understanding of human welfare. Gosney Research Fellowships are available to qualified investigators who hold the Ph.D. degree or its equivalent and who have demonstrated exceptional ability in original research. Preference is given to candidates who desire to carry on research in the general field of heredity. The Gosney Research Fund is currently administered by a Gosney Fund Committee made up of Professors A. H. Sturtevant, chairman, E. G. Anderson, Max Mason, and A. H. van Harreveld.

In effecting the transfer of the material assets of the Human Betterment Foundation to the Gosney Research Fund of the Institute special credit is due Mrs. Lois Gosney Castle, daughter of Mr. E. S. Gosney. Mrs. Castle spent approximately a year in putting the affairs of the Foundation in good order and in converting properties and other assets into fluid form. In addition she has maintained a keen interest in the research activities supported by the Gosney Research Fund.

G. W. B.

The Hixon Fund

IN 1938 A FUND was established at the Institute by the Estate of Frank P. Hixon to support researches in science which offered promise of increased understanding of human behavior. Up to the present the income of the fund has been applied to a series of individual projects of limited duration.

In the first of these Dr. R. Larente de Nó, on leave of absence from the Rockefeller Institute of Medical Research, spent a half year at the Institute continuing his work on nerve action currents, with opportunity for consultation with the Institute staffs in physics and mathematics, and in particular with Dr. Leverett Davis of the Physics Department, who gave analytical formulation to the results. Dr. Larente is now publishing a comprehensive treatise on nerve action currents, and considers that his experience at the Institute was of primary importance for the five years of research which is being reported in the treatise.

The next project aided by the Hixon Fund was started as a cooperative study between members of the Institute staff under the leadership of Drs. Wiersma and van Harreveld and representatives of the State Department of Institutions, on the effects of electroshock as a means of psychotherapy. The work was carried on later in cooperation with the Department of Psychiatry at the Los Angeles County Hospital. Important clinical experience was obtained and reported on electronarcosis as a treatment in mental disorder.

During the war Dr. David B. Tyler, Hixon Research Fellow, at first independently, and later under O.S.R.D. auspices, made valuable studies which resulted in means of treatment for cases of battle shock, fatigue, and motion sickness.

The Hixon Fund is at present administered by a Committee consisting of Professors Max Mason, A. H. Sturtevant, Henry Borsook, and Linus Pauling.

Max Mason

Not in the Books

(Continued from page 2)

structure are focused on chemical compounds that make up living systems. Radioactive isotopes of various elements are being used to determine the fates of specific molecules in the organism. In a similar way the latest methods of electrophoresis, chromatography, and spectroscopy are being made use of. Physicists, Chemists and Biologists are pooling their knowledge and their resources to find the answers. But it is not enough that the attack be made with the techniques and skills that now exist—there must be a constant search for new and improved techniques and, even more important, for fresh imaginations to use them.

PERSONALS

1928

RICHARD ARMSTRONG (Aussieker) returned to Pasadena in August after serving in the Army Medical Corps, and started medical practice limited to the eye.

1929

ALBERT TYLER, Ph.D., has remained at C.I.T., and is now associate professor of embryology.

1930

EMORY L. ELLIS, Ph.D. '34, is working at the U. S. Naval Ordnance Test Station at Inyokern, Calif. His work for the last six years has led him away from the field of his doctorate, biochemistry, as he is now chiefly concerned with physical chemistry and chemical engineering.

1931

RUSSELL LEE BIDDLE, Ph.D., is assistant professor of biology at the College of the City of New York. He is teaching many pre-medical and pre-dental students, and is college advisor to students majoring in pre-med and pre-dent and biology. He spends ten hours a week in this capacity, and regrets that it leaves him little time for research. Dr. Biddle lives in New Jersey with his wife, son Russel Lee, Jr., five, and two daughters, Virginia Ruth, twelve, and Valerie Ann, one.

1932

WILLIAM R. BERGREN, B.S. in Chemistry '32, Ph.D. in Biology '41, is acting as research associate in U.S.C. Medical School's Biochemistry Department. During his more than four years in the Army Sanitary Corps, he served at nutrition officer. The last three years before his discharge last October, Bill was chief nutrition officer for the Pacific Theater, serving at General Headquarters. In addition to his scientific work, which includes the publishing of several papers, Dr. Bergren is keeping up with his music and is conducting a private orchestral society in Los Angeles. He married Miss Marguerite Searle in 1941, and prior to the war was director of research at Truesdall Laboratories in Los Angeles.

1933

DONALD F. POULSON, Ph.D. '36, is associate professor of biology at Yale, working at the Osborn Zoological Laboratory. He spent part of the past summer at the Marine Biological Laboratory, Woods Hole, Massachusetts, collaborating in the study of cholinesterase activity in the well-known fly, **Drosophila melanogaster.** Dr. Poulson and associates are planning a series of investigations on relations between genes and the development of enzyme systems in **Drosophila** embryogenesis. Don has two sons, Donald B., six-and-a-half, and Christian F., four.

1934

GEORGE H. MARMONT, B.S. in mathematics '34, Ph.D. in biology '40, is assistant professor of physiology at the University of Chicago's Institute of Radiobiology and Biophysics. George was formerly section head-electronics in the Bendix Aviation Corporation's research laboratories in Detroit.

HAROLD D. MICHENER, Ph.D. '37, is working on antibiotics of microbial origin at the Western Regional Research Laboratory of the U. S. Department of Agriculture at Albany, Calif. The Microbiological Section in the Laboratory, a group of about ten, is at present occupied principally with problems in this field. Dave's interest is in the production, isolation, and bioassay of antibiotics which are active against fungi. The immediate objective is to get antibiotics which are active against fungi pathogenic to plants. Dr. Michener was married in 1939 to Miss Edna Caney in Honolulu. They have three children, Rose Patricia, four, Elizabeth Ann, two, and Robert Charles, seven months.

1935

RALPH E. HOMAN, JR., spends half his time in the practice of internal medicine in Los Angeles and half as instructor in pathology at U.S.C. Medical School, where he received his M.D. first in his class in 1939. With the latter Ralph is chiefly concerned with the application of pathology to medicine, and the mechanics of disease. In addition, he acts as preceptor to a ward at the Los Angeles County Hospital, serving to coordinate the attending staff and residents, acting as supervisor of the ward. With another doctor, Ralph is giving a postgraduate course in recent advances in diagnosis and treatment for the returning veterans one night a week. At present Dr. Homan is starting a hobby of model railroading in his spare time. He was married in 1942 to Miss Noradeane Hamilton. The Homans have two children, Nancy Jane, three, and Ralph E., Jr., one.

1936

CLARENCE W. CLANCY, who did three years of graduate work between 1933 and 1936, is now assistant professor of biology at the University of Oregon. He married in the summer of 1939, and now has two daughters, Angharad Jean and Patricia Ellen, born in 1943 and last March, respectively. Prior to his appointment at Eugene, Oregon, Clancy was a captain in the Army Air Corps.

1937

HARRY H. MILLER has been assistant surgical resident at Boston City Hospital since his discharge from the Army Medical Corps as a major last August. Following his graduation, he spent four years at the Harvard Medical School, graduating in 1941. For the next year and a half he was at the Boston City Hospital as an intern and surgical resident. From there he went into the Army. While in Service, Harry attended the School of Aviation Medicine, and was with the Air Forces as a flight surgeon, 22 months of which were spent in Italy. He anticipates about two more years' hospital training in surgery. Harry married Miss Ruth Macfadden in 1940. The Millers have one son, Harry H., Jr., three and one-half.

1938

PHILIP T. IVES, Ph.D., is now research associate in biology at Amherst College, Massachusetts. He is back on the farm where he was raised, living with his father, older brother, wife Dorothy Ann whom he married in June 1940, and three children, Richard Truman, four, Elinor Gage, two, and a two-months old baby. The Ives raise most of their meat and vegetables, supply eggs for the Department of Biology wives, newts for embryologists, fruit flies for Drosophilists, and recently hens for a new addition to the Department, a student of animal behavior. Phil's major extra curricular interest is his family, but he reports the community and cultural life of Amherst and Northhampton have their places, too. Recreation in addition to these is afforded by fishing in a little trout stream "a stone's throw away," tending a large garden, and working up seven to ten cords of wood each year from the Ives' wood lot.

Dr. Ives' professional interests center around the problem of evolution, with studies of population genetics and mutation (spontaneous) phenomena of **Drosophila** as the points of attack. As a secondary line of work, he is making a study of factors influencing the sex-ratio in human beings, in which work Phil has the collaboration of two former Amherst faculty and student associates. Some of their data will be published eventually. Dr. Ives describes it as nothing startling, but some interesting stuff.

GEORGE T. RUDKIN, Ph.D. '42, is a research fellow at the Lankenau Hospital Research Institute in Philadelphia. His present interest is **Drosophila** nutrition, and nutrition and synthetic media for micro-organisms in general. George was discharged from the Army Air Corps as a first lieutenant in December, 1945, and married the former Diana Lianos last October.

1939

WILLIAM E. BERG is now a research fellow in the Division of Medical Physics at the University of California. He received his Ph.D. at Stanford in 1946, and was present at Test Baker at Bikini Atoll last July. Bill plans to continue with research and teaching in the biological field.

1940

SHELDON CYR CRANE left his position as chemistry research assistant with a Navy project at CalTech last summer to become a research assistant at Scripps Institute of Oeanography at La Jolla. He was married in 1941 to Miss Aleta Smith of Los Angeles, and became the father of a son, Sheldon Cyr III, last November. Sheldon plans to work for his Ph.D. at Scripps Institute and U.C.L.A.

FRANK W. DESSEL, JR., since his discharge as a lieutenant from the Navy where he was an aerologist, is working as a pharmacist. He plans to take graduate work at the University of California for his secondary teaching credential. Frank was married while a senior to Mary Catherine Troutman. The Dessels have two sons, Frank William III, four, and John David, almost one.

1941

JOHN D. SPIKES, since his discharge from the Medical Corps as a staff sergeant, has been a teaching fellow in embryology at the Institute. He plans to continue toward his Ph.D. John was married to Anne Dorland in 1942.

1942

ERIK V. HEEGAARD, M.S. in Chemistry '40, Ph.D. in Biology '42, has very recently been promoted to chief development chemist in charge of all unit processes, analytical and physical chemistry laboratory activities of the Development Department of the Amino Products Division, International Minerals and Chemicals Corp., San Jose, California. His two previous posts have been senior project chemist with the Corporation, and research associate in Chemistry at Stanford.

In April 1947 the Amino Products Division's new San Jose plant started operating to produce two and a half million pounds of monosodium glutamate per year. Erik's work in the Development Department is connected with devising new or improved industrial processes for the isolation of amino acids from natural products. He reports that the work is very interesting and a challenge, since new ideas have to be evolved to carry out these projects on an industrial scale. The Department hopes soon to put in a laboratory for microbiological determinations of amino acids, using **Neurospora** and other organisms.

Dr. Heegaard and his wife, Lilli, have two children, Ingrid Christina, three, and Carl Linus, four months.

ADRIAN S. MAYER is a senior medical student at Northwestern, and will graduate in August. For a year after graduation he worked as a mathematician for the Douglas Aircraft Co. He is currently engaged in research concerning the effects of procaine hydrochloride on traumatic edema. While the results so far have been negative, they are interesting enough to publish. After receiving his M.D. degree, Adrian plans to work for a master's degree in basic science to fulfill a requirement for specializing.

1943

WILLIAM HOVANITZ teaches genetics and evolution mechanisms as part of his duties as assistant professor of botany and assistant biologist in the Laboratory of Vertebrate Biology at the University of Michigan. Bill is also research associate in the University's Botanical Gardens. His current research **consists of investigations** on macromolecular chromosome structures and the genetics of **Peromyscus** and **Colias.**

RALPH G. H. SIU, Ph.D., director of the Philadelphia Quartermaster Depot Biological Laboratories, is interested in biochemical mechanisms, specifically the microbiological degradation of cellulose, wool and oils.

1944

THOMAS C. FLEMING, ex. '44, is working in a Veterans' Administration hospital at Tuscaloosa, Alabama, on detached duty with the Army Medical Corps. Prior to this service he was resident physician at St. Luke's Hospital in New York. Tom married Miss Sarah McGraw last summer. He expects to remain on active military duty until the summer of 1948, after which he plans to return to the Institute to work for a Ph.D. in biophysics or physiology.

ROBERT P. HOLMES, ex '45, who received his senior certificate under the Navy V-12 Pre-Medical Program at the Institute, is a senior at the Louisiana State University Medical School.

F. HARLAN LEWIS, special student from 1942 to 1944, is an instructor in botany at U.C.L.A. Harlan completed work for his Ph.D. at that school in 1946, after discharge from the Army's Chemical Warfare Service. He was married in 1945 to Miss Margaret Ensign of San Marino. Harlan plans to spend 1947-48 as a National Research Council Fellow at the John Innes Horticultural Institute, London, England, working on the cytology of **Godetia** as the initial step in studying problems of speciation in that genus.

MAX L. PANZER, teaching assistant at the Institute, has biochemical research in progress toward his Ph.D.

1945

CLYDE A. DUBBS, B.S. in chemistry '43, Ph.D. in biology '45, is a research associate in bacteriology at U.S.C. Medical School. His chief interests lie in the study of polio virus in tissue culture, especially with labelled C^{14} compounds; the biosynthesis of some variety of labelled C^{14} compounds using **Chlorella;** and the biochemistry of essential oils.

1946

WALTER D. BONNER writes that he is trying to convert himself into a better plant biochemist at Harvard University. Dr. Bonner is studying the growth process of the **avena coleoptile** by observing the effects of various enzyme inhibitors on growth and on respiration, how these effects may be overcome, and what chemical changes, if any, take place in the plant tissue. By this type of study, he hopes to find out something about the growth process and the nature of the effect of auxins on growth. In particular he is interested in studying the role of the organic acids which seem to play such an important part in plant respiration and growth.

On the non-scientific side he is trying to take advantage of living in Boston where there is lots of good music, theater, etc. After a serious study of clarinet playing, during the winter he did as much skiing as possible, and in late spring took up rock climbing. Another of Dr. Bonner's activities is looking for a place where he and his wife, Josephine, can live.

DAVID R. ESNER is a research assistant in Pasadena. He plans to return to the Institute to work for his Ph.D. in embryology.

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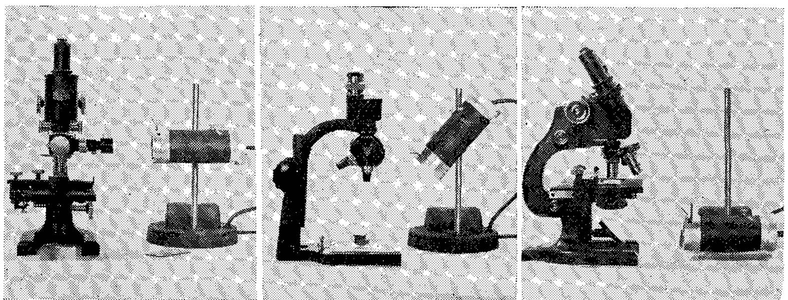

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