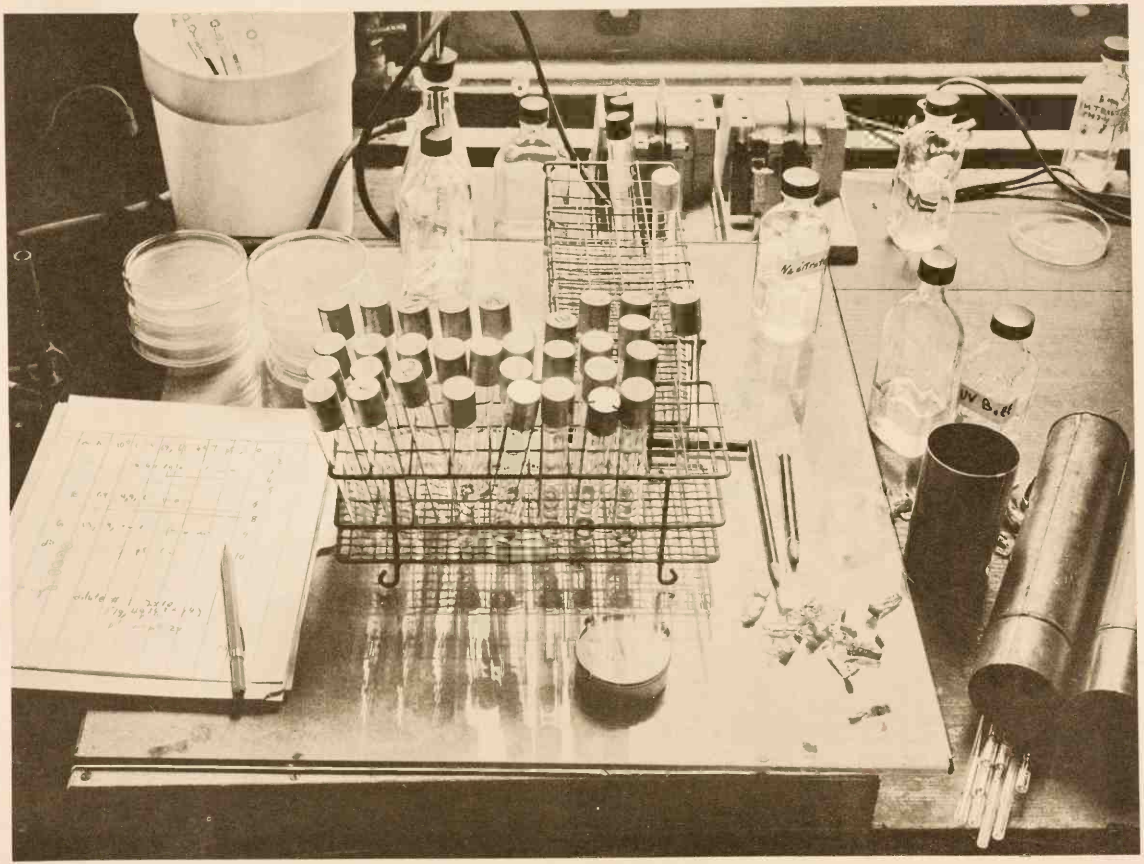
ANNUAL REPORT of the BIOLOGICAL LABORATORY

OF THE LONG ISLAND BIOLOGICAL ASSOCIATION, COLD SPRING HARBOR, NEW YORK



1961-62

The Biological Laboratory was organized in 1890 as a department of the Brooklyn Institute of Arts and Sciences. It was financed and directed by a Board of Managers, consisting mainly of local residents. In 1924 this group incorporated as the Long Island Biological Association and took over the administration of the Laboratory.

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A MESSAGE TO THE MEMBERS:

This year has been one of accomplishment for the Biological Laboratory. The year-round research program has benefited from the completed facilities of the rebuilt Dr. Walter B. James Laboratory. The summer courses at the Laboratory continued on the scale, and of the quality of past years. Our XXVII Symposium, "Basic Mechanisms in Animal Virus Biology" maintained the Cold Spring Harbor reputation as a center of the scientific world for the discussion of most advanced developments in the field of genetics. At the close of the Symposium, an open meeting was held for our members, at which a synopsis of its topics was presented in lay language by three of its leaders, Drs. Renato Dulbecco, Richard M. Franklin, and André Lwoff. The meeting was well attended, and greatly appreciated by the community.

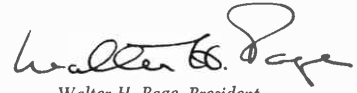
In addition to being a year of accomplishment, this year has been one of impending reorientation for the Cold Spring Harbor laboratories. Early last fall our collaborating organization, the Carnegie Institution of Washington decided to discontinue its Genetics Department at Cold Spring Harbor, but offered to lease its facilities to any organization with satisfactory scientific and financial backing to carry on similar work. Under the leadership of Dr. Edward L. Tatum, Chairman of our Scientific Advisory Committee, a new organization is being formed, called The Cold Spring Harbor Laboratory of Quantitative Biology. It will be controlled and sponsored by a number of the universities and other scientific institutions which have in the past, or will in the future, take an active part in the various programs at Cold Spring Harbor. Your Board of Directors last June reviewed Dr. Tatum's plans and unanimously endorsed them, committing the Long Island Biological Association to lease its facilities to the new body. We understand that the Carnegie Institution and the Wawepex Society will follow this same course. The Long Island Biological Association will continue its legal form, with its membership and directors, and become one of the sponsoring institutions in the new "Cold Spring Harbor Laboratory of Quantitative Biology."

We feel that the new arrangement with the outstanding sponsorship envisaged will attract financial support on an enlarged scale from United States government sources and private foundations. This will ensure continuance and expansion of research, teaching, and the Symposia at Cold Spring Harbor.

With these changes in the offing, we have had some changes in our staff. Dr. Harold Abramson, who has conducted research at the Laboratory for many years and served constructively on our Board of Directors, has found the development of his work divergent to the principal area of interest of the Laboratory and is transferring his work elsewhere. Dr. Arthur Chovnick has resigned as our Director to accept an appointment as head of The Department of Genetics at the University of Connecticut. We wish him well in his enlarged responsibilities and are grateful for his help in our transition period. Dr. H. Edwin Umbarger has been appointed our Director "pro tem." We are happy to report that both he and Dr. Paul Margolin will continue their research this winter and expect to join the new "Cold Spring Harbor Laboratory of Quantitative Biology" when it is established. Also, Dr. Alfred Hershey and Dr. Barbara McClintock of the Carnegie Institution have indicated their wishes to continue work at Cold Spring Harbor.

One of the factors which has influenced Dr. Tatum and his committee to work so hard for the continuance of the Cold Spring Harbor laboratories is the membership support which the Long Island Biological Association has always received from the community and friends. We hope you will renew your membership gift again this year. At this critical period of reorganization, your continued support and participation is particularly important.

Nevil Ford, Chairman



Walter H. Page, President

One of the major activities of the Biological Laboratory is the program of year-round research carried on by several groups of investigators in the areas of genetics, biochemistry, and psychobiology. Following are brief summaries of research completed or in progress, submitted by three of the staff investigators at The Laboratory.

BACTERIAL GENETICS

Paul Margolin

The work of the bacterial genetics group has centered upon three primary topics: 1) Factors affecting recombination; 2) The molecular basis of mutation, and 3) The genetic basis for the regulation of gene function. All of these topics are closely related to each other in that they are concerned with structural and functional relationships within the very small region of the chromosome which governs leucine synthesis in *Salmonella typhimurium*.

Approximately 160 leucine auxotrophic mutants have been mapped by complementation and many of these by the three-point recombination test. Most of these have been found to belong to one of the four cistrons. There appears to be some indication that the cistrons show differing responses to different mutagenic agents. There is evidence which suggests that this is partly due to differing guanine-cytosine to adenine-thymine ratios among the cistrons.

Only three of the leucine auxotrophs appeared to be large deletions involving more than one cistron. One of these was induced by X-rays and affected the entire leucine region, while two were spontaneous and involved cistrons II, III, and IV. The latter two are apparently identical. Demerec, studying cystine mutants, and Hartman, studying histiolinc mutants in *Salmonella*, have found repeated occurrences of deletions having identical endpoints. They suggest that the chromosome breaks which give rise to deletions are not completely random with respect to their location.

Evidence was obtained which indicated that changes in the chromosome which cause leucine auxotrophy also affect the frequency of recombination immediatcly around the site of mutation. The various auxotrophs differ quantitatively in the degree of effect upon recombination near the sites of mutation. This factor must be taken into account when mapping mutant sites by recombination.

Dr. Mukai has continued studies which utilize purine and pyrimidine analogues for the induction of both forward and back mutations. The present evidence indicates that 2-aminopurinc prefcrentially induces transitions of guanine-cytosine to adenine-thymine, while 5-bromuracil preferentially does just the reverse. The mechanism for this mutagenesis is being investigated in terms of how the information carried by the DNA is transferred to the protein synthesizing apparatus of the cell.

One leucine auxotroph when analyzed by complementation studies was determined to have resulted from a mutation of the operator region of the leucine cluster of genes. The position and function of this leucine operator is being investigated. An operator is a portion of the genetic material which controls the functioning of the genes which determine the structure of enzymes, and can turn them on or off.

Dr. Siddiqi continued studies begun by Dr. Falk on the requirement for protein synthesis in the fixation of potential mutations. Dr. Falk had demonstrated that protein synthesis was involved in fixing X-ray induced mutations. Dr. Siddiqi obtained evidence for a similar condition for nitrous acid induced mutations. This may prove to be very important in elucidating the relationship between protein synthesis and the mechanism of mutation since more information is available about the action of chemical mutagens than about irradiation.

MICROBIAL BIOCHEMISTRY

H. Edwin Umbarger

Dr. Christoph Jungwirth continued his studies on the biosynthesis of leucine in *Salmonella typhimurium*. As reported last year after the first reaction had been defined, these biochemical studies were greatly abetted by the fact that Dr. Margolin was able to supply four kinds of genetically distinct, leucine-requiring mutants. More recently, Dr. Jungwirth collaborated closely with Dr. S. R. Gross, of Duke University, who was a summer visitor at our laboratory last year. Dr. Gross employed a series of leucine auxotrophs of *Neurospora crassa* which were comparable to the *leu* mutants of S. *typhimurium*. The work in both laboratories indicates that the pathway leading to leucine consists of four steps:

$$\alpha\text{-ketoisovalerate} \xrightarrow{1} \beta\text{-carboxy-}\beta\text{-hydroxyisocaproate} \xrightarrow{2} \alpha\text{-hydroxy-}\beta\text{-carboxyisocaproate} \xrightarrow{3} \alpha\text{-ketoisocaproate} \xrightarrow{4} \text{leucine.}$$

Dr. Jungwirth's work indicated that the *leu 1* cistron in Dr. Margolin's mutants controlled the structure of the enzyme catalyzing step 1, cistrons III and IV together controlled the structure of the enzyme catalyzing step 2, and cistron II controlled the structure of the enzyme catalyzing step 3. Step 4 is catalyzed by at least a pair of nonspecific transaminases and has not been observed to be affected by any of the mutations studied by Dr. Margolin's group.

Dr. Jungwirth has studied in some detail the first enzyme and found it to be inhibited by the endproduct of the sequence—an interaction that may be looked upon as a negative feedback mechanism preventing oversynthesis of leucine.

The third enzyme has been studied and partially purified by Dr. Richard Burns, who joined our group in the fall of 1961. Dr. Burns has also studied the control of the synthesis of the enzymes of the leucine pathway, and has devised a method for derepressing all the enzymes in the pathway by limiting the amount of leucine without having to employ a leucine auxotroph. The method should be generally useful.

Dr. Martin Freundlich joined our group in the fall of 1961, and has been studying the control of the enzymes responsible for leucine and valine biosynthesis. Dr. Freundlich's observations have considerably clarified the pattern of control in this pathway. He also discovered one organism with an abnormal threonine deaminase which was dependent upon the normal feedback inhibitor, isoleucine, for its stability to storage at 0°C.

Dr. Richard Leavitt continued his study of the first step in the pathway leading to valine, acetolactate formation, obtaining more information on the mechanism of action of the enzyme.

Other efforts in this laboratory were directed toward the biosynthetic pathway leading to serine. Isotope evidence for the first time virtually eliminated the possibility that bacteria had any pathway other than that found earlier in plants and animals:

3-phosphoglycerate $\xrightarrow{1}$ phosphohydroxypyruvate $\xrightarrow{2}$ phosphoserine $\xrightarrow{3}$ serine.

These reactions were all demonstrated in extracts. Proof that this was the only significant pathway in *S. typhimurium* was obtained by examining a series of mutants which had been divided into two genetically distinct classes by Dr. Demerec and his collaborators. One class was unable to perform step 1, and the the other was unable to perform step 3. As yet, no mutants blocked in step 2 have been found, so that the question of whether or not this step is catalyzed by a specific transaminase is unresolved.

Another observation made on this pathway was that the first enzyme in the sequence is inhibited by serine, thus providing another example of regulation of a biosynthetic sequence by endproduct inhibition.

CYTOGENETIC STUDIES

Berwind P. Kaufmann

Much of the work of the past year has been devoted to completion of projects already under way, rather than the initiation of new ones. In continuation of electron-microscope investigations reported last year, Mr. Keizo Maruyama and Dr. Helen Gay, of the Department of Genetics, Carnegie Institution of Washington, have collaborated in studies of the changes that occur in cytoplasmic organelles during the differentiation and growth of two types of cells in *Tradescantia paludosa*, namely stigma cells and pollen grains. At certain stages in growth of the stigma cell, ellipsoidal or irregularly shaped electron-dense bodies appear in the cytoplasm. It has now been ascertained that they develop from cisternae of the endoplasmic reticulum and are precursors of the vacuole. Thus it seems probable that the vacuolar system in plants originates from the endoplasmic reticulum, and consequently that the tonoplast of the stigma cell consists of a single membrane.

In continued studies of fine structure of the *Tradescantia* pollen grain, these workers have observed the developmental changes that occur during the two meiotic divisions leading to formation of the microspore. These cells contain Golgi bodies, similar in structure to those first demonstrated in animal cells, which are composed of stacks of cisternae with associated small vesicles and are usually dispersed at random within the cytoplasm. Most published reports suggest that there are no major modifications of these structures as differentiation proceeds. We find that in the vegetative cells of the *Tradescantia* pollen grain all the Golgi bodies undergo, more or less synchro-

nously, structural changes that can be correlated with well-known nuclear events, thus enabling us to reconstruct a sequence of developmental changes at different stages of cell growth. It is concluded from these studies that the Golgi body arises and develops from a simple structure, which is circular in cross section, into a multilayered structure, and finally into the familiar stacked form.

Findings reported last year, regarding the mutagenic effects of both DNase I and the non-enzymatic protein bovine plasma albumin, led us to undertake, with the assistance of Mrs. Gloria Gillies and of Mrs. Jennie S. Buchanan of the Carnegie Institution, an assay of the mutagenic potential of an agent that can alter DNA by modifying base sequences. The agent tested, 5-bromodeoxyuridine, is selectively incorporated in DNA as a substitute for thymine. When injected into adult males, it induced sex-linked lethals but, in contrast to DNase, no chromosomal rearrangements. A high frequency of damage to germ cells was reflected in low survival and low fertility of the injected individuals and poor viability of the F_1 progney.

As the first step in a combined cytochemical and electron-microscopical study of the chromosomes of *Drosophila melanogaster*, Dr. C. C. Das has made cytochemical determinations of the amounts of DNA and proteins in the chromosomes during early embryonic development. Amounts of DNA were measured spectrophotometrically by the two-wavelength method; and the results indicate clearly that there is no significant change in the amount of DNA per diploid set of chromosomes from the first to the eleventh cleavage mitosis. The amount also corresponds closely, as would be anticipated, with that present in the diploid nucleus of the larval neuroblast. These observations are in harmony with the constancy hypothesis. The distribution of proteins, and changes in this distribution, were determined by staining sections of formalin-fixed eggs with alkaline fast green or acidic bromphenol blue. The results suggest that a type of protein appears during the tenth and eleventh cleavages that was not present at earlier stages, that this protein is a histone (the somatic adult histone), and that its synthesis is not restricted to the nucleus. During the early cleavages another basic protein is apparently present (the so-called cleavage histone), which is neither a protamine nor an arginine-containing protein.

RESEARCH STAFF

Harold A. Abramson, *Investigator*
Russell Bauer, *Technician*
Doris A. Blume, *Research Assistant*
Caroline J. Bradley, *Technician*
Richard Burns, *Research Associate*
Arthur Chovnick, *Laboratory Director*
Stuart Cohen, *Technician*
Chandi Charan Das, *Research Associate*
Gladys G. Dean, *Research Assistant*
John Foulds, *Research Assistant*
Martin Freundlich, *Research Associate*
Henriette Gettner, *Research Assistant*
Gloria Gillies, *Research Assistant*
Christoph Jungwirth, *Research Associate*
Ruth Kellogg, *Technician*
Roy P. Kernaghan, *Research Assistant*
Marian Krauss, *Research Assistant*
Richard Leavitt, *Research Associate*
Paul Margolin, *Investigator*
Keizo Maruyama, *Research Associate*
Kenneth McFall, *Research Assistant*
Bernadine Miller, *Research Assistant*
Frank Mukai, *Research Associate*
Barbara Prokop, *Research Assistant*
Richard Pullen, *Technician*
Alan Ruthig, *Technician*
Abraham Schalet, *Research Associate*
Doris Schoonmaker, *Technician*
Obaid Siddiqi, *Research Associate*
Alexander Sokoloff, *Investigator*
Matthew Taffel, *Technician*
Joy Talsma, *Research Assistant*
Albert Taylor, *Technician*
Harold E. Umbarger, *Investigator*
Merle Umbarger, *Research Assistant*
Donald Wheeler, *Technician*

COLLABORATORS

Berwind P. Kaufmann—*Carnegie Institution of Washington*
Helen Gay—*Carnegie Institution of Washington*
Jennie S. Buchanan—*Carnegie Institution of Washington*
Ilse Schwinck—*Max-Planck Institut für Tierzucht, Mariensee, Germany*

RESEARCH GRANTS

The Association is pleased to recognize the generous support of various agencies which make our research possible. During the past year, year-round research at the Biological Laboratory was supported by the following research grants:

National Institutes of Health, U. S. Public Health Service:
Grants G17285, G19848(O), C4440(C3), RG7464(C1), RG5336(C4), RG7178(C1), RG7842(O), E3501(C2), RG7675(C1), EDP 14374.
National Association for Retarded Children
Association for the Aid of Crippled Children

XXVII COLD SPRING HARBOR SYMPOSIUM

"BASIC MECHANISMS IN ANIMAL VIRUS BIOLOGY"

The XXVII Cold Spring Harbor Symposium on Quantitative Biology was held from June 7th through June 13th, 1962. Approximately 220 virologists and workers in allied areas of research attended the meetings, including 33 from abroad.

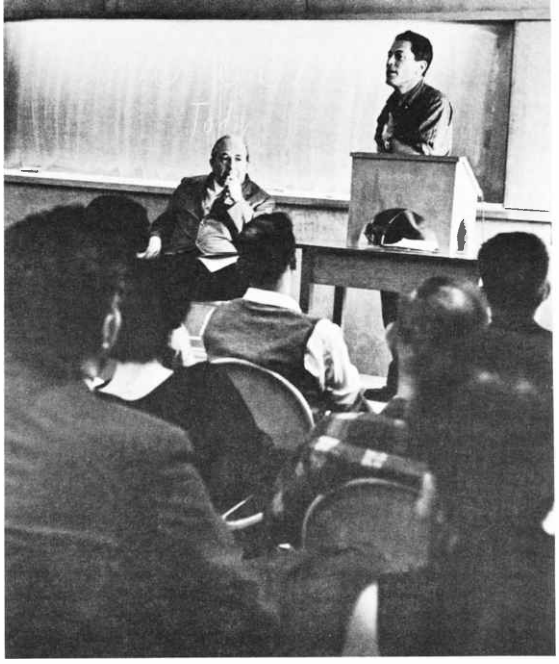
Following is an excerpt from the summary of the proceedings, prepared by Dr. Renato Dulbecco, of the California Institute of Technology, chairman of the organizing committee for this symposium.

"In general, this symposium developed around three main areas. The first was concerned with molecular biology, and had to do with the synthesis of the viral nucleic acids and protein connected with the virus development. This part of the symposium dealt primarily with the molecular biology of the viral RNA. The second point had to do with the transformation of the normal cells into neoplastic cells by viruses, and with the mode of action of the viruses in causing the transformation. The third area of consideration was the problem of the origin and significance of the antigens which have been shown to appear in cells infected by tumor-producing viruses.

"The discussion had been especially constructed in terms of future experimentation in the area of molecular biology. It can be anticipated that this symposium will have a marked effect on future research in this area, because very many new experiments were proposed and discussed; and these will certainly be performed soon.

"A second area in which this symposium will have a marked influence is that concerning animal virus genetics; although the number of reports were relatively few, the demonstration that recombination can be obtained with poliovirus will not fail to stimulate a resurgent interest in this area, which had been somewhat neglected lately. This symposium demonstrated that there is a great deal of interest in problems concerning tumor viruses. In this area of research, the effect of the symposium will be felt in two directions—on one hand, in stimulating entirely new types of approach, such as studies of cell hybridization and, on the other hand, probably, in encouraging a bridging of the molecular biological approach with other biological investigations."

In addition to Dr. Dulbecco, major contributors to the organization of the Symposium for 1962 were: Dr. John Cairns, Australian National University; Dr. George Hirst, The Public Health Research Institute of the City of New York; Dr. André Lwoff, The Pasteur Institute; Dr. Harry Rubin, University of California; and Dr. Michael Stoker, Glasgow University.



In addition to the support of the Long Island Biological Association, the XXVII Cold Spring Harbor Symposium was supported by the following agencies:

The Rockefeller Foundation
National Institutes of Health, U.S. Public Health Service
National Science Foundation
United States Atomic Energy Commission
United States Air Force under Grant AF-AFOSR-61-73; monitored by the Air Force Office of Scientific Research of the Air Research and Development Command.

SUMMER COURSES

These courses are designed to provide, in a very short period of time, the latest methods and tools for research employing bacterial mutants, bacterial viruses, and animal viruses in tissue cell cultures. Selection of a limited number of students has favored biochemists, physical chemists, physicists and mathematicians who are interested in moving into biological research.

Courses given at the Laboratory in the past have been instrumental in the fusion of genetics and biochemistry that has recently resulted in so many great advances in molecular biology. They have furnished the models for experiments presently employed in graduate level courses at many colleges and universities.

In conjunction with these courses, the Laboratory brings about 50 prominent investigators as seminar speakers. These speakers provide an extensive review of the latest research developments in the various areas of the courses.

COURSES FOR THE SUMMER OF 1962

1) **Baterial Genetics:** June 18th to July 7th.
   Staff—M. Fox, Rockefeller Institute
   P. Margolin, Biological Laboratory, LIBA
   N. Zinder, Rockefeller Institute
2) **Bacterial Viruses:** July 9th to July 28th.
   Staff—F. Stahl, Institute for Molecular Biology
   G. Streisinger, University of Oregon
3) **Microbiology of Vertebrate Cells and Quantitative Animal Virology:**
   Staff—R. M. Franklin, Rockefeller Institute
   P. Marcus, Albert Einstein College of Medicine

SEMINAR PROGRAM—SUMMER, 1962

F. H. Mukai—LIBA: "Base pair analysis of leucine auxotrophs."

S. Falkow—Walter Reed Army Inst. for Research: "Episomic elements in bacteria."

B. Ames—National Institutes of Health: "Genes, enzymes, and control mechanisms in histidine biosynthesis."

H. Bernheimer—Downstate Medical Center of Brooklyn: "Genetics and biochemistry of capsule formation of Pneumococcus."

H. Morowitz—Yale University: "Pleuropneumonia-like organisms."

A. Pardee—Princeton University: "Recent studies on metabolic control in bacteria."

F. Ryan—Columbia University: "Molecular basis of mutation."

B. Hall—University of Illinois: "Hybrid formation with phage-specific RNA."

M. Demerec—Brookhaven National Laboratory: "Fine structure of certain Salmonella genes."

R. Hotchkiss—Rockefeller Institute: "Bacterial transformation."

B. McCarthy—Dept. of Terrestrial Magnetism, Carnegie Institute: "Synthesis of ribosomal and DNA-like RNA in bacteria."

F. Stahl—University of Oregon: "The circular basis of heredity"

C. A. Thomas—Johns Hopkins University: "The phage chromosome."

H. Dintzis—Johns Hopkins University: "Biosynthesis of hemoglobin."

S. Spiegelman—University of Illinois: "The use of DNA-RNA hybridization as an analytical tool."

N. Zinder—Rockefeller Institute: "A bacteriophage which contains RNA."

M. Nirenberg—National Institutes of Health: "RNA-Code."

M. Meselson—Harvard University: "Genetic recombination between DNA molecules."

A. H. Doermann—Vanderbilt University: "Phage heterozygosis."

A. Campbell—University of Rochester: "Order of prophage genes."

D. A. Hopwood—The University, Glasgow: "Gene recombination in *Streptomyces coelicolor.*"

H. Eagle—Albert Einstein College of Medicine: "Biochemistry of cultured mammalian cells.""

R. P. Cox—New York University School of Medicine: "Alkaline phosphatase in cultured cells."

D. L. D. Caspar—Children's Hospital of Boston: "The structure of viruses."

S. Dales—Rockefeller Institute: "Electron microscopy of animal viruses and animal virus infected cells—techniques and applications."

O. Maaløe—Copenhagen: "Patterns of macromolecular synthesis in bacteria."

D. Baltimore—Rockefeller Institute: "Biosynthesis of macromolecules in mammalian cells—effects of infection with an RNA virus."

J. E. Darnell, Jr.—Massachusetts Inst. of Technology: "Biochemical and biophysical studies on the reduplication of poliovirus."

M. Green—St. Louis Univ. School of Medicine: "Enzymology and biochemistry of adenovirus infection."

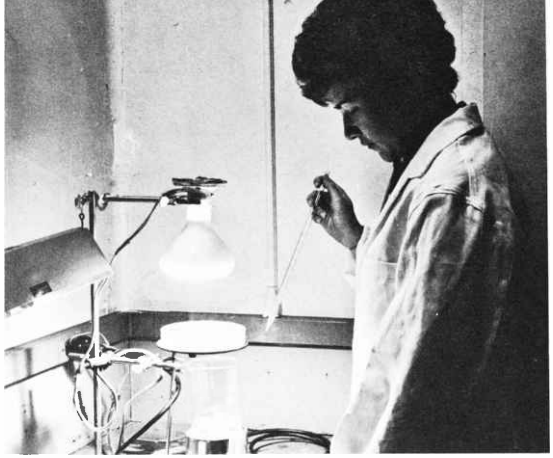
N. Salzman—National Institutes of Health: "Biochemistry of vaccinia multiplication."

G. K. Hirst—Public Health Research Institute of the City of New York: "Genetics of animal viruses."

W. K. Joklik—Australian National University: "Early events in vaccinia reduplication."

W. Szybalski—University of Wisconsin: "DNA-mediated genetic transformation of human cells."

The summer courses and seminars are supported by the following grants: The National Foundation, CPERT 133; and The National Institutes of Health, 2G-890 (C4S1, C5).



SUMMER GUEST INVESTIGATORS

Originally conceived as an informal, summer haven for scientists to meet their colleagues, the Biological Laboratory continues to play host to a group of active workers who spend the summer here. They come to teach the courses, pursue independent projects, write, and collaborate with others in related fields.

In the informal summer atmosphere at Cold Spring Harbor, the scientific activities are enhanced intellectually by the presence of this group.

SUMMER INVESTIGATORS — 1962

Dr. Alan W. Bernheimer	*New York University School of Medicine*
Dr. Maurice Fox	*Rockefeller Institute*
Dr. Richard M. Franklin	*Rockefeller Institute*
Dr. Gabriel Gasic	*University of Pennsylvania*
Dr. Luigi Gorini	*Harvard Medical School*
Dr. Sam Granick	*Rockefeller Institute*
Dr. Rollin D. Hotchkiss	*Rockefeller Institute*
Dr. Philip I. Marcus	*Albert Einstein College of Medicine*
Dr. Harris Moyed	*Harvard Medical School*
Dr. Arthur Pardee	*Princeton University*
Dr. Franklin Stahl	*University of Oregon*
Dr. George Streisinger	*University of Oregon*
Dr. Stephen H. Vessey	*State College of Pennsylvania*
Dr. Norton Zinder	*Rockefeller Institute*

Following are brief reports on the research activities of several of our guest investigators, carried on during the summer of 1961:

SAMSON R. GROSS

Duke University School of Medicine

A series of experiments were performed in the microbial-biochemistry laboratory. Initially, it was demonstrated that the accumulation of β-carboxy-β-hydroxyisocaproate found by Dr. Jungwirth to occur with three of the four classes of *S. typhimurium* auxotroph also occurred with the corresponding *Neurospora crassa* leucine auxotrophs. However, whereas the fourth class of *S. typhimurium* auxotroph could respond to the compound, this was not true of the corresponding *N. crassa* mutant. It was thus necessary to employ the appropriate *S. typhimurium* auxotroph to recognize the compound.

An unexpected dividend of comparing the feeding patterns of the two species was the fact that one of the classes of *N. crassa leu* mutants also accumulated a second compound to which three classes of *S. typhimurium leu* mutants respond. (Only one class of *S. typhimurium leu* mutant respond to β-carboxy-β-hydroxyisocaproate.) Preliminary attempts were made to isolate the newly discovered compound. (The isolation was accomplished later at Duke University and the compound identified as α-hydroxy-β-carboxyisocaproate.)

In collaboration with Dr. Jungwirth, preliminary experiments concerned with the utilization of β-carboxy-β-hydroxyisocaproate with *S. typhimurium* and *N. crassa* extracts were performed.

DARRELL PRATT, *University of Florida*

The alkaline phosphatase activity of the cells of a marine pseudomonad was shown to be inhibited by the concentration of Mg^{++} found in sea water. This inhibition was found to be characteristic of intact, freshly harvested cells; if the cells were damaged by toluene, detergent or osmotic shock, the enzymic activity was no longer inhibited by Mg^{++}. When the concentration of Mg^{++} was reduced by washing the cell suspensions in 0.5 M NaCl, the cells were found to require Mg^{++} for activity; maximal activity occurred in the presence of 0.0025 M Mg^{++}; higher concentrations were inhibitory. Extracts prepared by osmotic shock of such cells also required Mg^{++} for phosphatase activity; the response of cells and extracts to Mg^{++} was equivalent until the concentration became high enough to inhibit the activity of the intact cells.

The inhibition was greatest at the optimum pH (ca. pH 9) but the residual activity exhibited at pH 7 was not affected by high concentrations of Mg^{++}; in fact, increasing the pH had no effect on fully inhibited cells. The Mg^{++} inhibition was thus related to cell structure and not to the enzyme *per se* and, in fact, lysates were always more active than the equivalent quantity of intact cells. This partial crypticity suggested that the enzyme was not freely available to exogenous substrate. Since the marine habitat normally contains only traces of inorganic phosphate, the phosphate economy of marine bacteria is probably critical in regulating their metabolism. This subject is being investigated further in the Bacteriology Laboratories at the University of Florida.

ELLIS ENGLESBERG, PATRICIA HOFFEE, and GAIL CHODER
University of Pittsburgh

The energy requirements of the exit reaction of the glucose permease of *Salmonella typhimurium*, LT 2, as measured by the accumulation of C14 alpha methyl glucoside (αMG), was further characterized. At optimal concentrations of NaN_3 (4×10^{-2}M - 8×10^{-2}M) the internal concentration of αMG is approximately 9-fold greater than that observed in the absence of NaN_3. The maximal internal concentration of αMG in the presence of optimal concentrations of dinitrophenol (4×10^{-3}M - 6×10^{-3}M) was 7-fold that found in the absence of dinitrophenol. Preliminary experiments were conducted on the effect of increasing external αMG concentration on the accumulation process and the specificity of the permease.

A mutant of *Escherichia coli* B/r, in which glucose inhibited growth on mineral acetate medium, was found to be blocked in glucose metabolism prior to the Krebs cycle.

The L-arabinose inhibition (diauxie) of the synthesis of β galactosidase was studied with the aid of various L-arabinose negative mutants of *Escherichia coli* B/r. It was shown that mutants deficient in L-arabinose isomerase, (ara-2) or L-ribulokinase, (ara-23) or both these enzymes and L-arabinose permease, (ara-3) are immune to the L-arabinose effect even though the two former mutants (ara-2, and ara-23) produce large quantities of enzymes involved in L-arabinose metabolism. These experiments offer proof against the competition hypothesis as an explanation of this carbohydrate inhibition.

ALAN W. BERNHEIMER and LOIS L. SCHWARTZ
New York University, School of Medicine

Earlier work from our laboratory showed that pathogenic staphylococci synthesize a series of extracellular substances of high molecular weight that are demonstrable by means of starch gel electrophoresis. These substances are not synthesized by non-pathogenic strains of staphylococcus and they are not identifiable with previously described products of staphylococcal growth.

Two of the substances have been obtained in small amounts in substantially pure form. One of them, a protein, is designated A_{12S}; the other, a carbohydrate-containing macromolecule, is designated 12S. By means of double diffusion in agar, it was shown for the first time that antibodies to the new substances are demonstrable in appropriate samples of serum. Antibody to 12S was found in two samples of commercial staphylococcal (horse) antitoxin, in two samples of human gamma globulin and in the sera of three patients suffering from staphylococcal disease but in none of six samples of normal human serum. Similar results were obtained with A_{442S} except that two of the six normal sera yielded a line of precipitate while one of the pathological sera did not. The results are interpreted as meaning that man forms antibodies to these growth products in the course of staphylococcal disease and that the two substances would bear further scrutiny with respect to their possible significance in pathogenicity.

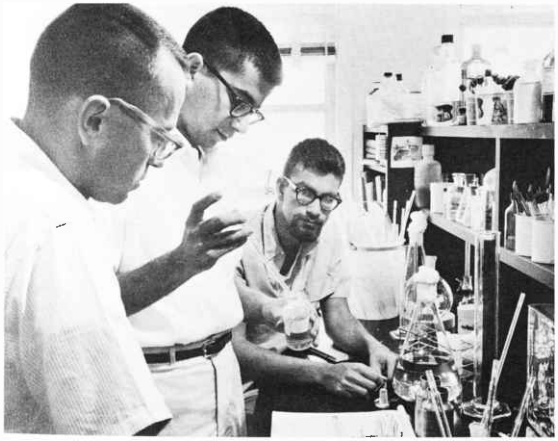
ALLAN CAMPBELL and ALICE DEL CAMPILLO-CAMPBELL
University of Rochester

Campbell spent most of the summer writing a review on "Episomes" to appear in *Advances in Genetics* (1962). He also showed that a mutant of λ (*λind*), which is not inducible by ultraviolet light, is likewise non-inducible by mitomycin C. del Campillo-Campbell studied the properties of the lysozymes produced by a temperature-sensitive and a suppressor-sensitive mutant of phage λ. The lysozyme from the temperature-sensitive mutant proved to differ from the wild type enzyme in several respects, but that from the suppressor-sensitive mutant could not be differentiated from the wild type enzyme.

A SUMMER OF RESEARCH FOR UNDERGRADUATES

For the past four summers, the Biological Laboratory has been privileged to conduct an undergraduate research participation program, sponsored by the National Science Foundation. With the aim of encouraging careers in science for outstanding young students, the year-round and summer staff at Cold Spring Harbor provide unique opportunities for these young people to learn at first-hand what a career in research is like.

In most cases, the student is given a set of orientation exercises performed under the direction of his supervisor. Later the student is channeled into a project which ordinarily is closely associated



with the supervisor's area of interest. For most students, every phase of these projects introduces new concepts and new techniques. It is the aim of every supervisor to choose projects which will give the student the satisfaction of interpreting his own data and revealing previously unknown information.

The following students participated in this program during the summer of 1962:

Barry Rosen, Senior, Massachusetts Institute of Technology: "Genetics of doubly auxotrophic mutants under conditions of continuous culture."
Supervisor: Dr. R. O. Burns

Robert James Pollet, Junior, Columbia University: "The hydrolysis of dipeptides by *Salmonella typhimurium* extracts."
Supervisor: Dr. M. Freundlich

Claire Diane Dryfuss, Sophomore, Douglas College of Rutgers University: "Development of techniques for a microbial genetic course."
Supervisor: Dr. A. Schalet

John Lewis Farber, Junior, Reed College: "Genetic analysis of adenine linkage groups in *Bacillus subtilis.*"
Supervisor: Dr. M. Fox

Jeff Evan David Siegel, Sophomore, Reed College: "Fine structure of the leucine region of the chromosome of *Salmonella typhimurium.*"
Supervisor: Dr. P. Margolin

Linda Jane Brody, Junior, Pembroke College: "Analysis of nucleic acid hydrolyzates by thin-layer chromotography."
Supervisor: Dr. R. M. Franklin

Lawrence Jerome Kadish, Junior, Princeton University: "Photodynamic inactivation of genetic material."
Supervisor: Dr. A. B. Pardee

Agnes Gayler Harford, Junior, Radcliffe College: "The effect of 1-methyl-3 nitro-1 nitroso on the transforming principle of *Bacillus subtilis.*"
Supervisor: Dr. M. Fox

Charles E. Wahl, Junior, Columbia University: "The genetic and environmental control of L-serine biosynthesis in *Salmonella typhimurium.*"
Supervisor: Dr. H. E. Umbarger

Barbara Joan Furman, Sophomore, Cornell University: "Fine structure of the rosy cistron in *Drosophila melanogaster.*"
Supervisor: Dr. A. Chovnick

This program was supported by a grant, G15869, from the National Science Foundation.

Also participating in this program, but sponsored by a NSF grant to Harvard University:

Robert Temple, Senior, Harvard University: "The nature of the 'linear growth' of *E. coli* strain K12 in the presence of valine."
Supervisor: Dr. H. E. Umbarger

NATURE STUDY WORKSHOP FOR TEACHERS

The seventh annual Workshop in Nature Study was offered during the summer of 1962. There were twenty participants, mostly elementary school teachers, three of whom were supported by scholarships sponsored by the Port Washington Chapter of the Audubon Society. Upon satisfactory completion of the requirements of the course, teachers were entitled to two in-service credits awarded by the New York State Department of Education.

A primary objective of the workshop was to acquaint teachers with the remaining natural environment of Long Island. This was accomplished by collecting field trips to each of the following representative types of habitats: a fresh water pond, a salt marsh, a tidal mud flat, a beach for intertidal zone exploration, a field-meadow, and a deciduous woodland. The Laboratory is uniquely situated so as to afford most of the habitats within walking distance. However, car trips were taken to several preserves on Long Island.

After the teachers had become familiar with the variety of life forms in the diverse ecological systems and with the interactions of flora, fauna, and environment, they were encouraged to exploit these areas in their own teaching. Natural history represents a natural interest in children of elementary school age and teachers were therefore encouraged to utilize these interests to teach the value of careful observation, methods of notation, deduction from observation, testing of conclusions, and to stimulate scientific curiosity in their students, so as to foster future careers in science.

STAFF:

Mr. Marvin J. Rosenberg, Assistant Professor of Biology and Education, State University of New York, Long Island Center.

Mr. Otto Heck, Biology Teacher, Island Trees High School, Levittown, N.Y.

NATURE STUDY COURSES FOR CHILDREN OF AGES 6 TO 14

During the summer of 1962, fourteen sections of nine courses in Nature Study were offered in two sessions. The enrollment this year amounted to 314 students. Each class met twice a week on alternate days for a two and one-half hour period; the Advanced Ecology class met on Fridays for an average of five hours per session. The course offerings included:

General Nature Study (6-7)
General Ecology (8-9)
Earth Science (8-9)
Botany-Entomology (9-9)
Fresh Water Biology (10-11)
Entomology (10-11)
Vertebrate Zoology (10-11)
Seashore Life (10-11)
Advanced Ecology (12-14)

INSTRUCTORS:

Mr. Marvin J. Rosenberg, Assistant Professor of Biology and Education, State University of New York, Long Island Center.

Mr. Otto Heck, Biology Teacher, Island Trees High School, Levittown, N.Y.

Miss Barbara Sheehan, Science Teacher, Bellmore Schools, Bellmore, N.Y.

In addition to the above instructors, each class had an assistant to help on the field trips and in laboratory work.

Two films showings highlighted Walt Disney's True Life Adventures series, with showings of "Prowlers of the Everglades" and "Beaver Valley." Both were well attended by overflow audiences.

The Association gratefully acknowledges the third-year contribution of the Huntington Federal Savings and Loan Association. Their contribution provided nature study scholarships for 19 students of the Huntington elementary schools.

BUILDINGS AND GROUNDS

Renovation of Classrooms for Summer Courses

During the past few years it has become apparent that the facilities at Davenport Laboratory were inadequate to support the increasingly complex courses for post-doctoral investigators. In the spring of 1962, these classrooms were redesigned to create more working space, with new lab benches, equipment, kitchen facilities, and additional air-conditioning.

Additional Renovation and Repairs

1. The steep road leading from Bungtown Road to the James Laboratory parking lot was completely repaved in black-top, eliminating the problem of erosion and hazardous driving conditions.
2. Urey Cottage was renovated to become a comfortable year-round residence.
3. The administrative offices in the Nichols Building were furnished with air-conditioning units.
4. The living quarters for dining hall staff, at the lower level in Blackford Hall, were modernized and redecorated.
5. A continuous program of painting, repairs and renovation is being carried on throughout the grounds.

Fire Preventive Measures

1. A new fire-escape was added to the summer residence, The Fire House.
2. A fire-detection system was installed in the Page Motel buildings.
3. Additional fire-preventive devices were installed in the chemical laboratories.

FINANCIAL REPORT

FOR THE PERIOD MAY 1, 1961 - APRIL 30, 1962 —

As of April 30, 1962 our unrestricted assets were as follows:

Cash	$ 36,162.25	
Accounts receivable	23,357.72	
Inventory of books	12,876.87	
Deferred expenses	4,593.03	
Investments (market value $102.75)		
Stocks	99.75	
Land, buildings and equipment	558,481.38	
Total		$635,571.00

Our liabilities were as follows:

Accounts payable and Taxes	$ 29,810.93	
Grants and contracts, unexpended	53,769.51	83,580.44
Leaving unrestricted funds amounting to		551,990.56
Represented by:		
Endowment Fund (Dr. Wm. J. Matheson Bequest)	20,000.00	
Net worth	531,990.56	
Total		$635,571.00

In addition we hold cash and investments in the amount of $20,225.36, representing restricted funds as follows:

Mark H. Adams Memorial Fund	$ 1,619.39
Blackford Memorial Fund	5,000.00
Charles Benedict Davenport Memorial Fund	6,817.51
Charles Benedict Davenport, Junior, Fund	1,491.56
Temple Prime Scholarship Fund	2,744.00
Dorothy Frances Rice Fund	2,552.90
Total	$20,225.36

For the year 1961-1962, our receipts were as follows:

Grants, contracts, research fees	$260,488.20	
Members contributions	16,425.67	
Special contributions	3,355.00	
Interest and dividends	546.62	
Profit on sale of securities	3,299.42	
Operating receipts (rentals, dining hall, booksales, etc.)	115,918.01	
Total		$400,032.92

Our expenditures were as follows:

Research and educational program	$262,606.32	
Administration	41,361.31	
Plant maintenance	57,296.19	
Dining hall, rooms, and apartments	27,826.05	
Total		$389,089.87

Excess Income over Expenditures 1961-1962 ..... $10,943.05

SPECIAL EVENTS

PUBLIC PANEL DISCUSSION—"THE IMPLICATIONS FOR MAN OF BASIC RESEARCH ON ANIMAL VIRUSES"

In conjunction with the XXVII Symposium ,"Basic Mechanisms in Animal Virus Biology," a public panel discussion was presented at the Carnegie Auditorium on June 13th, 1962, following the last session of the Symposium.

Some of the implications for mankind of basic research on animal viruses were explored by three of the Symposium speakers. Drs. Renato Dulbecco of the California Institute of Technology, Richard M. Franklin of the Rockefeller Institute, and André Lwoff of the Pasteur Institute, Paris discussed viruses which cause tumors in animals; speculations about viruses and human cancers; and the applications of present knowledge to cancer therapy.

The Long Island Biological Association wishes to acknowledge the gracious hospitality of the following members who, on the evening of June 13th, arranged dinner parties for many of the scientists participating in the Symposium:

Mr. & Mrs. Walter H. Page
Mr. & Mrs. Bruce Tuttle
Mr. & Mrs. John M. Perkins
Mr. & Mrs. Wm. H. Mathers
Mr. & Mrs.Franz Schneider

Following the termination of the summer programs for 1962, the auditorium and housing facilities of the Biological Laboratory were utilized for the annual phage conference, a four-day meeting attended by most of the active phage workers in the country.

The 38th Annual Meeting of the Long Island Biological Association was held in the auditorium on September 17th, 1961. 75 members and guests were present. The year-round staff members of the Biological Laboratory presented brief reports of their research during the previous year. Following the program and meeting of the officers, tea was served by the Women's Committee, under the chairmanship of Mrs. William S. Smoot.

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