

LONG ISLAND BIOLOGICAL ASSOCIATION

ANNUAL REPORT

OF

THE BIOLOGICAL LABORATORY

COLD SPRING HARBOR  
LONG ISLAND, NEW YORK  
1951

**LONG ISLAND BIOLOGICAL ASSOCIATION**

**INCORPORATED 1924**

**ANNUAL REPORT**

**OF**

**THE BIOLOGICAL LABORATORY**

**FOUNDED 1890**

**SIXTY-SECOND YEAR**

**1951-1952**

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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# THE LONG ISLAND BIOLOGICAL ASSOCIATION

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Jane N. Page	E. C. MacDowell
Vice-President & Treasurer	Assistant Secretary
Grinnell Morris	B. P. Kaufmann

Director of the Biological Laboratory, M. Demerec

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Mrs. Alexander M. White, Jr.	Oyster Bay, N. Y.
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Caryl P. Haskins	Haskins Laboratory, New York
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Grinnell Morris	Oyster Bay, N. Y.
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Franz Schneider	Oyster Bay, N. Y.
Howland B. Stoddard	Cold Spring Harbor, N. Y.

To serve until 1954

Amyas Ames	Cold Spring Harbor, N. Y.
Robert Chambers	Marine Biological Laboratory
George W. Corner	Carnegie Institution of Washington
Th. Dobzhansky	Columbia University
Helen Kellogg Edey	Brookville, N. Y.
Ernst Mayr	American Museum of Natural History
Mrs. Walter H. Page	Cold Spring Harbor, N. Y.
Willis D. Wood	Huntington, N. Y.

To serve until 1953

H. A. Abramson	Cold Spring Harbor, N. Y.
M. Demerec	The Biological Laboratory
Henry Hicks	Westbury, N. Y.
Dudley H. Mills	Glen Head, N. Y.
Stuart Mudd	University of Pennsylvania Medical School
Robert Cushman Murphy	American Museum of Natural History
John K. Roosevelt	Oyster Bay, N. Y.

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R. C. Leffingwell ..... Oyster Bay, N. Y.  
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Secretary—Mrs. David Ingraham  
Treasurer—Mrs. Walter H. Page  
House Committee Chairman—Mrs. Ashton Hawkins  
Membership Committee Chairman—Mrs. Theodore Streibert  
Entertainment Committee Chairman—Mrs. Philip Wadsworth  
Executive Committee—Mrs. Maitland A. Edey, Mrs. Crispin  
Cooke, Mrs. Franz Schneider

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Grinnell Morris

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Amyas Ames

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Mrs. George S. Franklin, Chairman

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Edwin J. Grace  
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Alfred E. Mirsky

FORMER PRESIDENTS, LABORATORY DIRECTORS, AND  
BOARD MEMBERS

Presidents

Blackford, Eugene 1890-1905	James, Walter B. 1926-27
Matheson, Wm. J. 1905-23	Page, Arthur W. 1927-40
Blum, Edward C. 1923	Murphy, Robert Cushman 1940-1952
Williams, T. S. 1924-26	

Laboratory Directors

Dean, Bashford 1890	Davenport, C. B. 1898-1924
Coon, Herbert H. 1891-98	Harris, Reginald 1924-36

Ponder, Eric 1936-41

Directors

Abbott, Lyman 1896-1901	Flinsch, Rudolph 1909-17
Atkins, C. D. 1915-23	Francis, Mrs. L. W. 1923
Ayer, J. C. 1930-33	Frick, Childs 1924-29
Ayres, H. M. 1892-1900	Gager, C. S. 1915-17
Backus, T. J. 1890-1901	Hall, C. H. 1890-95
Blackford, Eugene 1890-1904	Harris, R. G. 1930-36
Blackford, Mrs. Eugene 1906-17	Harrison, R. G. 1926-51
Bleecker, C. M. 1926-45	Healy, A. A. 1896-1921
Bleecker, T. B. 1946-51	Heckscher, August 1902-17
Blum, E. C. 1923	Hendrix, Joseph 1890-97
Boody, D. A. 1890-1917	Hoagland, C. N. 1890-98
Brackett, G. C. 1904-08	Hooper, F. W. 1890-1924
Brower, G. V. 1899-1917	Hoyt, Colgate 1902-17
Brown, Addison 1890-1913	Hulst, G. D. 1894-1900
Brown, J. S. 1908-17	Huntington, L. D. 1894-1900
Bumpus, H. C. 1903-12; 1927-30.	James, O. B. 1926-41
Butler, N. M. 1903-17	James, W. B. 1902-17; 1924-27
Cochran, D. H. 1890-1902	Jennings, H. S. 1924-27
Cole, K. S. 1940-43	Jennings, Walter 1906-17; 1924-33
Cole, W. H. 1934-52	Levermore, C. H. 1896
Coombs, W. J. 1890-1910	Johnson, D. S. 1924
Crittenden, W. H. 1922-23	Jones, F. S. 1899-1909
Crozier, W. J. 1928-44	Jones, J. D. 1890-95
Davenport, C. B. 1903-44	Jones, O. L. 1890-1913
Davenport, W. B. 1916-17	Jones, Mrs. O. L. 1907
de Forest, H. W. 1912-17; 1924-25	Jones, W. E. 1903-06
de Forest, R. W. 1902-17	Kahn, Mrs. O. H. 1924
Denbigh, J. H. 1923	Leffingwell, R. C. 1924-32
Detwiler, S. R. 1928-42	Lloyd-Smith, Wilton 1928-40
Doubleday, F. N. 1908-11	Low, Seth 1890-1902
Draper, George 1924-32	Lucas, F. A. 1905-17
Field, Marshall 1924-47	Lusk, Graham 1909-17
Fisher, G. C. 1924	MacCracken, H. M. 1890-1905
Fisk, H. D. 1924	

Mather, Frederic 1890-1900  
 Matheson, W. J. 1901-22  
 Mayer, A. G. 1903-17  
 Merle-Smith, Mrs. Van S. 1931-50  
 Mickleborough, John 1890-1917  
 Mills, D. H. 1946-52  
 Montant, A. P. 1902-09  
 Morgan, T. H. 1924-28  
 Newberry, J. S. 1890-93  
 Nichols, Acosta 1927-45  
 Nichols, J. W. T. 1910-17  
 Noyes, H. F. 1902-21  
 Osterhout, W. J. V. 1927-41  
 Overton, Frank 1924  
 Palmer, L. M. 1899-1913  
 Parshley, H. M. 1924-33  
 Peabody, Julian 1911-17  
 Perkins, A. C. 1890-92  
 Ponder, Eric 1937-41  
 Pratt, H. I. 1929-30  
 Prime, Cornelia 1909-17  
 Raymond, J. H. 1890-1900  
 Rumsey, Mary H. 1924  
 Swingle, W. W. 1924-44  
 Schiff, J. M. 1931-50  
 Schiff, M. L. 1924-31  
 Scott, Donald 1911-17  
 Seamans, C. W. 1906-15  
 Shapley, Harlow 1943-51  
 Stimson, H. L. 1925-36  
 Smith, H. C. 1913-17  
 Stewart, J. H. J. 1893-1917; 1924-26  
 Stockard, C. R. 1924-39  
 Stoddard, H. B. 1951-52  
 Stratford, William 1890-1917  
 Straubenmuller, Gustav 1911-17  
 Strauss, Albert 1914-17  
 Stutzer, Herman 1911-23  
 Taylor, H. C. 1926-42  
 Thompson, Edward 1903-17  
 Tiffany, L. C. 1892-1917  
 Urey, H. C. 1934-49  
 Vanderbilt, W. K. 1924-43  
 Walter, H. E. 1924-43  
 Webb, Alexander 1890-1902  
 Weld, F. M. 1914-17  
 Wetmore, C. W. 1902-07  
 White, S. V. 1890-1905  
 Williams, T. S. 1910-30  
 Wilson, E. B. 1903-17  
 Woodbridge, C. L. 1894-1901  
 Woodward, J. B. 1890-96  
 Woodward, R. B. 1890-1914

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Roy A. Waggener  
Bruce Wallace  
William J. Wardall  
Armitage Watkins  
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Mrs. Willis D. Wood  
Sewall Wright  
Stephen Zamenhof

\*Deceased

## MESSAGE FROM THE PRESIDENT

Mr. Amyas Ames's response to his election as President of the Association at a meeting of the Board of Directors, July 15, 1952

It means a great deal to me to have this opportunity to serve as President of the Long Island Biological Association. Since Arthur Page first spoke to me, I have gone back into the history of this organization, and the more I learn about it, the more impressed I am. Perhaps this is partially owing to my own background.

My father was Professor of Botany at Harvard, Director of the Arnold Arboretum, and at one time head of the Biology Department, so that I grew up in a scientific environment. Since my wife's father was Professor of Physics at Trinity, she too has a scientific background. Considering all this, I suppose I am a member of what I think a scientist would call a lost generation, for now my two boys are electing science as their life careers. The older boy, a Harvard senior, is choosing physics and electronics; the second boy, a Harvard sophomore, biology or medicine. He is working this summer as a laboratory assistant at the Biological Laboratory. So, although my chosen field is finance and investment banking in Wall Street, I have been surrounded by scientists.

I have always been greatly impressed by the valuable results of bringing men together to exchange ideas and share thoughts. This, as I analyze it, is one of the great contributions of the Long Island Biological Association—both in research and in its symposia. I think I know how really important this can be because I have had personal experience with it. As a Governor of the Investment Bankers Association and Governor of the New York Stock Exchange, I have had one primary hobby, that of bringing teachers of economics into the financial district to exchange ideas with and get to know the top men in the financial world—a research project in both economics and human nature. On the basis of this experience I believe the Long Island Biological Association, in bringing leading biologists together, is performing a most important function, and I am all the more proud to be associated with it.

I have another reason, which has to do with the nature of our community in Cold Spring Harbor. The really successful town is one where all residents work together to develop the life of the community. Unfortunately, in the average commuters' town, the attention of the residents is divided, part of their focus being on the big city. As a result, a commuters' town is not quite a normal one. But in Cold Spring Harbor we are blessed in having a focus, an activity for which we are known the world over—that is, the Biological Laboratory. Because of this, there is no civic or social position that I prize more than the Presidency of this organization.

And lastly—and this counts very heavily with me—is my admiration for Dr. Demerec and for the caliber of the scientific backing which he represents. Since I am not a scientist, the cornerstone of my policy will be to support Dr. Demerec and his scientific council. As I see it, my function, and that of the nonscientific members of this Board, is to secure for the scientists working at Cold Spring Harbor the understanding and support of the community which surrounds them. I believe that we will succeed, because we have a very able Board; and, as we succeed, we will have the pleasure of feeling that at least in some measure we have contributed to the scientific achievements of the Biological Association.

Amyas Ames, President.

## REPORT OF THE DIRECTOR

After twelve years of service as President of the Long Island Biological Association, Dr. Robert Cushman Murphy submitted his resignation to the Board of Directors at its meeting held on July 15, 1952. Dr. Murphy's action was prompted by the fact that his time in the future will increasingly be spent in the field, and also by his feeling that the affairs of the Association should be placed in younger hands. His resignation was regretfully accepted by the Board. A resolution passed at the Annual Meeting on July 29, 1952, and printed in the Report of the Secretary, eloquently expresses the gratitude of the members of the Association to our past president for his esteemed leadership. During the terms of his office Dr. Murphy was most generous in devoting his time and effort to the affairs of the Association. His advice was particularly valuable in the solution of numerous problems connected with the administration of the Biological Laboratory.

Acting on the recommendation of the Nominating Committee, the Board of Directors elected Mr. Amyas Ames to succeed Dr. Murphy as President. Shortly after he came to live in our neighborhood Mr. Ames became interested in the Biological Laboratory, and in 1950 he was elected a member of the Board of Directors of the Association. Success in the field of banking has apparently not diminished the interest in science which he inherited from his father, Professor Oakes Ames, a distinguished scientist and administrator. The members of the Laboratory staff welcome the new President, and assure him of their full support and cooperation.

This year the question of a building program for the Cold Spring Harbor laboratories, which had been under consideration for some time, was finally settled. In May, 1951, a decision was reached to proceed with the project, which includes two laboratories for the Department of Genetics and a lecture hall for the joint use of both laboratories. Bids for the work were immediately requested, contracts were signed, and the ground was prepared for building. In August the work was begun, and since then has progressed as well as could be expected, considering the season of the year and the intricacies of the construction requirements. Fortunately for us, the steel and copper we need have been allocated to us, and so far we have not experienced any serious inconvenience because of shortages of critical materials. If all goes well, we should be able to use the lecture hall for our Open House gathering in September, 1952. It will represent a greatly needed improvement in the Laboratory's facilities for holding the Symposia and carrying on its lecture program.

With deep regret I record the death this year of three good friends of the Laboratory, Messrs. T. Bache Bleeker, Percy H. Jennings, and J. Southgate Y. Hoyt. As a member and later an officer of the Wawepex Society, Mr. Bleeker took a particular interest in the Laboratory. On many occasions he visited us to discuss our needs and learn about the research that was in progress. In 1946 he was elected to membership in the Board of Directors, to represent the Wawepex Society, and since that time he had taken an active part in the affairs of the Association. Mr. Jennings had been a member of the Association since 1946, and was a par-

ticipant in many of its activities in connection with the Laboratory. Dr. Hoyt will be remembered as the enthusiastic and inspiring teacher of the Nature Study Course. He organized the course in 1941, but when the war started he was taken into the Army and was not able to resume his teaching until 1947. Again in 1949 he was prevented by illness from giving the course; and in 1950 he was with us once more, but unfortunately for the last time. During the four seasons he spent at Cold Spring Harbor he left a lasting impression on the minds of many boys and girls, to whom he communicated some of his own broad knowledge and alert appreciation of the plant and animal life that is part of our environment.

### Research

Bryson and Rosenblum, working on the project supported by the Biological Department, Chemical Corps, Camp Detrick, continued with studies of bacterial mutation and selection, and with correlated investigations of the biochemical influence of mutagenic and bacteriostatic agents. Additional chemical agents were found that favor the growth of radiation-resistant mutants of *E. coli* appearing spontaneously in radiation-sensitive populations, and thus bring about selective elimination of the sensitive type. Ultraviolet induced mutations to phage resistance were shown to differ significantly from spontaneous, both in the types produced and in their relative numbers. In another study, a correlation was established between the ability of cells to take up pyronin B and their viability after exposure to toxic agents. Ultraviolet radiation, which causes little modification of dye-binding capacity, was found in low doses to have an equal and relatively slight effect on oxidative metabolism and adaptive-enzyme formation in both radiation-resistant and radiation-sensitive *E. coli*. The greater sensitivity of strain B to radiation does not, therefore, necessarily extend to certain biochemical activities.

Manometric studies of streptomycin action showed this antibiotic to be more effective in the presence of an energy source for the cells. Additional experiments with the Warburg apparatus suggested that the mutagenic effect of manganous ion may be correlated with inhibited metabolism. By means of paper chromatography, an analysis was made of cell-free filtrates of genetically different *E. coli* strains grown in mixtures. Genetic and environmental factors were examined for ability to influence selection; and a study of the role of environment in selection was initiated with the Selector, an automatic device for providing a changing environment to bacterial populations.

Szybalski completed a study of cross-resistance patterns for thirteen antibiotics. He found that a strain of bacteria developing from a mutant that is resistant to a certain antibiotic generally remains sensitive to other antibiotics, but that occasionally such a strain may be either more or less sensitive than the parent strain to certain other antibiotics. The most interesting feature of this study is the finding that the characteristic cross-resistance pattern is as a rule associated with the antibiotic, and does not vary in different strains of bacteria. By their cross-resistance patterns,



antibiotics may be differentiated from one another; and this may turn out to be a very useful tool for industrial laboratories in the search for new antibiotics. Dr. Szybalski's research is supported by a grant from the National Tuberculosis Association.

Wallace and King, working under contract with the United States Atomic Energy Commission, continued their investigations with experimental populations of *Drosophila melanogaster*, the common fruit fly. They have succeeded in comparing different populations, control and irradiated, and find evidence of slight changes in adaptive values of the populations exposed to chronic gamma radiation. It is interesting that, in those populations with the lowest adaptive values, over 90% of the decreases in adaptive value can be accounted for among the "normal" individuals of the populations; obviously lethal or semilethal characteristics seem to have a very small part in suppressing the adaptive values of populations.

In keeping with the trend that began some seven years ago, a large proportion of our summer guests were interested in research with microorganisms. The group working with bacterial viruses was particularly active. S. E. Luria, of the University of Illinois, studied photoreactivation of phages T2 and T4 treated with ultraviolet light, while his student, George Streisinger, investigated the role of genetic factors in the determination of sensitivity to ultraviolet radiation in the same phages. Nancy Bruce, of the New York University College of Medicine, studied the behavior, in mixed infections and in recombinations, of phages T1 and T8, which are serologically distantly related. M. Delbruck and A. D. Kaiser, of the California Institute of Technology, collaborated with N. Visconti, of the Carnegie Institution, in the development of a comprehensive theory of bacteriophage genetics and growth. Werner Braun, of Camp Detrick, began a series of experiments to determine whether the mutagenic effects of manganous chloride on *E. coli* are associated with alterations of intracellular metabolism. R. D. Hotchkiss, of the Rockefeller Institute, established that penicillin resistance in pneumococcus develops stepwise, as previously determined in staphylococcus. Ruth Sager, also of the Rockefeller Institute, studied chlorophyllless mutants of green algae. E. Caspari and E. Y. Wright, of Wesleyan University, worked on the development of methods for genetic studies with *Bacillus circulans*. Caspari also cooperated with A. W. Bernheimer of the New York University College of Medicine and A. D. Kaiser in injecting larvae and pupae of the Cecropia moth with phage T2, *E. coli*, and streptolysin O. They established that antibodies comparable to those found in mammals are not formed by the moth for any one of the antigens used. Bernheimer tested 46 species of lepidopteran larvae, and found that 10 of them—all moth larvae—were able to agglutinate human erythrocytes. I. A. Tittler, of Brooklyn College, studied the effect of sulfadiazine on the thiamine requirement of a protozoan *Tetrahymena*. H. A. Abramson, in collaboration with R. Goldfarb of the Chicago Medical School, worked on the purification of the material that causes grassweed hay fever.

As in previous summers, several guests were engaged in writing. S. E. Luria worked on the manuscript of his forthcoming book, "Viruses"; R. D. Hotchkiss completed three papers; S. Granick, of the Rockefeller Institute, wrote a review on "Structure and Physiological Actions of Ferritin"; S. Weinhouse and M. A. Spirtes, of the Institute for Cancer Research in Philadelphia, worked on five articles; and D. Shemin of the College of Physicians and Surgeons, spent the summer in writing two papers and organizing material for courses he was to teach during the winter.

### Symposium

During the nine days from June 7 to June 15, a large and enthusiastic group of scientists met from 9:00 in the morning until almost midnight to hear lectures by world-famous geneticists, and to discuss the most recent experiments and theories in this important field. More than 300 in all attended the meetings, and at least 160 were present at each session. Although about half the participants came from laboratories and universities in the New York area, the rest traveled from twenty states and fourteen foreign countries to take part in the Sixteenth Cold Spring Harbor Symposium.

The topic, "Genes and Mutations," was the same as that of the ninth Symposium, held in 1941. Key research workers, active in the rapidly developing branch of genetics that deals with the mechanisms of heredity, again met to exchange results; and their discussions revealed the striking progress made in the decade between these two meetings. The original problem of defining the unit of heredity—which almost fifty years ago was designated the "gene," has not yet been solved. In fact, the large body of information accumulated since 1941 has made geneticists less certain than ever about the physical properties of genes. Ten years ago they were pictured as fixed units with sharply delimited boundaries, strung along the chromosome like beads on a string, very stable and almost immune to external influences. Now, however, they are regarded as much more loosely defined parts of an aggregate, the chromosome, which in itself is a unit and reacts readily to certain changes in the environment. The apparent stability of the gene against outside influences does not reflect the real situation but results from the fact that conditions likely to affect a gene will also produce injurious changes in other parts of a cell, which in most cases will be lethal. Ten years ago only X-rays and ultraviolet rays were known to induce changes in genes; but reports given at this Symposium made it clear that such changes may also be brought about by a great many chemicals.

One of the most striking developments during these ten years of genetics is seen in the organisms used for research. It is well known that Mendel, the discoverer of the basic laws of heredity, used peas for his studies. Other early geneticists also used plants; but some of them soon took up the study of rabbits, rats, and mice, because these are easier to raise and faster to breed. It was an important step forward when the late Professor T. H. Morgan, of Columbia University, began to work with the fruit fly, *Drosophila*, an organism that produces a new generation every two

weeks and can easily be raised in large numbers in a laboratory. Recently, however, geneticists have started to utilize microorganisms, such as molds, bacteria and viruses, in which the equivalent of a generation can be obtained in a few days or a few hours. It has been shown conclusively that fundamental discoveries—regardless of whether they are made on plants, rabbits, flies, bacteria, or viruses—are general and apply to all living organisms.

The number of foreign scientists at this Symposium was larger than usual, since one-third of the thirty-nine speakers on the program were from Europe and twenty-six participants came from outside the United States. The countries represented were Brazil, Denmark, England, France, India, Italy, Japan, Norway, Scotland, Sweden, Switzerland, Turkey, and Yugoslavia.

### Phage Meeting

For the second year, research workers studying bacterial viruses held a meeting at the Laboratory. The conference was organized by Max Delbruck, and was held August 20-22. It was attended by about fifty people, more than half of whom came especially for the meeting.

### Teaching

The Nature Study Course was given by Dr. Pauline James, of the Department of Biology, Texas College of Arts and Industries, Kingsville, Texas. She was assisted by Patricia Moore, of Memphis State College, and Larilee Baty, of Huntington. This course is designed to stimulate interest in nature among the young people of the community, by quickening their observation of the many plants and animals around them, by teaching them how to find the answers to questions raised by their observations, and by helping them realize that careful and accurate study of the smaller incidents we can all observe contributes greatly toward expanding our knowledge of natural phenomena. The course was divided into four sections according to the ages of the pupils, and was attended by forty-eight young people. On the afternoon of the closing day a public exhibition was held to demonstrate the activities of the various classes to parents and friends.

For the seventh consecutive year a three-week course was offered in techniques and problems of research with bacterial viruses. It was taught by Professor Mark H. Adams, of the New York University College of Medicine, and had a capacity enrollment of nineteen students. A series of six special seminars was arranged in connection with the course.

The course in bacterial genetics was given for the second year. It was taught by Evelyn M. Witkin, V. Bryson, M. Demerec, E. J. Beckhorn, and N. Visconti, with Mary I. Bunting of Yale University and E. D. DeLamarter of the University of Pennsylvania as guest instructors. This course emphasizes the newer methods used in the study of heredity in bacteria, and some of the recent results in this field. There was a capacity enrollment of sixteen students.

## Scholarships

The limited number of scholarships available for the summer were used mainly to provide partial tuition for some of the students. The following people held scholarships in the summer of 1951.

Temple Prime: D. Marien, Columbia University.

Dorothy Frances Rice: Dr. Nebahat Yakar, Istanbul University.

John D. Jones: Dr. M. S. Fox, University of Chicago; J. Hurwitz, Western Reserve University; D. Marien, Columbia University; H. Monsees, Biological Laboratory; Dr. G. Montalenti, University of Naples; Dr. M. A. Spirtes, Institute for Cancer Research, Philadelphia; and Dr. Nebahat Yakar, Istanbul University.

## Lectures

Weekly lectures were held throughout the summer in cooperation with the Department of Genetics of the Carnegie Institution. The speakers were members of the two laboratories and special visitors; and Dr. Eugene Rosenblum was in charge of arrangements. The speakers and titles were as follows:

June 28: S. R. Pelc, Hammersmith Hospital, London. Autoradiography as a cytochemical method.

July 5: E. B. Ford, Oxford University. Research in population genetics at Oxford University.

July 12: Werner Braun, Camp Detrick. Effect of metabolites on changes in bacterial populations.

July 19: Program of color-and-sound films of the barrier reef of Australia.

July 26: Alan Bernheimer, New York University. Elaboration and properties of some growth products of Streptococci.

August 2: Max Delbruck, California Institute of Technology. Mutual exclusion between an infecting phage and a carried phage.

August 9: H. A. Abramson, New York City. Revolution in psychiatry?

August 16: Giuseppe Montalenti, University of Naples. Ribonucleic acid supply to germ cells during meiosis.

August 27: E. C. MacDowell, Department of Genetics. Genetics of Cold Spring Harbor.

## Special Events

Two illustrated lectures of general interest were arranged for the members of the Association, their friends, and neighbors. Both were sponsored jointly by the Laboratory and the West Side School Mothers Group, and were held in the West Side School auditorium. In the first of these, on November 30, 1951, the President of the Association, Dr. Robert Cushman Murphy of the American Museum of Natural History, talked about "The Rediscovery of the Bermuda Petrel." He recounted, with the aid of Kodachrome photographs, the fascinating story of his expedition a year before to the Bermuda islands, in search of an "extinct" sea bird. The second lec-

ture in this series, "South Africa: Its Problems and Peoples," was given on April 25, 1952, by Dr. Ronald Singer, professor of anatomy at the Medical College of the University of Capetown in South Africa. He traced the history of that country and of the various racial groups that make up its population, to show how this background has contributed to the present political situation.

On Sunday afternoon, September 23, about two hundred members and friends of the Association attended a demonstration and tea in Blackford Hall. This open-house demonstration, which has become an annual fall event, is held so that members may learn informally about current research at the Laboratory and become more closely acquainted with the work they help to support. The eighteen scientific exhibits included projects of the regular staff of the Laboratory, summer guests, and staff members of the Department of Genetics of the Carnegie Institution. Other events of the afternoon included an informal lecture by Dr. E. C. MacDowell on "The Physical Origins of Long Island, and the Establishment of the Laboratories at Cold Spring Harbor." The serving of tea and refreshments by members of the Women's Committee was efficiently organized by Mrs. Philip Wadsworth, chairman of the Entertainment Committee, with the cooperation of Mrs. Edward S. Blagden, Mrs. Cecil F. Gordon, Mrs. Walter H. Page, and Mrs. John E. Rousmaniere.

### Dining Room

The Blackford Hall dining room was in operation from June 5 to September 5, under the management of Mrs. B. P. Kaufmann. Resident members of the Department of Genetics, as well as guests of the Laboratory, were accommodated there during the summer. During the Symposium period, meals were served to about 150 people, and during the remainder of the summer to a smaller number. A total of 14,908 guest meals were served in the course of the season.

### Laboratories and Equipment

The number of summer guests working with microorganisms has increased so much in the last few years that the Davenport Laboratory is no longer adequate to house all of this work. Since the course in Bacterial Genetics was started, in particular, the two courses given in Davenport occupy the largest part of its space during most of the season. To relieve this situation, space in Jones Laboratory was made available for microbial research by the addition of facilities for washing and sterilizing glassware, preparing culture media, and incubating cultures. Furthermore, the basement floors of the Davenport and Wawepex Laboratories were remodeled for use in connection with two new courses planned for the summer of 1952.

## Buildings and Grounds

The work of modernizing our residence buildings, begun last year, was continued with the funds contributed for that purpose by the Rockefeller Foundation. In addition to the purchase of new equipment for kitchen and dining room, adaptation of the basement floor of Hooper House to year-round use, and construction of four summer cottages—reported last year—a heating system was installed in Cole Cottage to make it usable as a winter residence.

## Finances

The expenses of full-time research are met by grants received from the National Tuberculosis Association, the Army Chemical Corps, and the Atomic Energy Commission. Symposium expenses are partially covered by the Carnegie Corporation grant for that purpose. And during this year the Laboratory still had available for the improvement of buildings and grounds a portion of the grant received from the Rockefeller Foundation. As has been pointed out on several occasions, the Laboratory is doing well with respect to funds for research and the Symposia. In common with many other educational and research institutions, however, we are having some difficulty in connection with funds for the upkeep of grounds and buildings, and for the other general expenses of caring for a plant that includes about 50 acres of land and 18 buildings and cottages. During the last few years these expenses have considerably increased, because of the depreciation of the dollar and the consequent rise in wages and in cost of supplies. As the financial statement shows, the major part of these general expenses is covered by the contribution of the Wawepex Society, the interest on securities, the fees received from students and research workers, and the income from rental of our apartments and rooms. This leaves a relatively small, but very important, amount to be provided by our only other source of income—the contributions of the members of the Long Island Biological Association. In the last few years we have been able to increase our income from research fees and rentals; and if a comparable increase in members' contributions were realized, our Laboratory could be maintained in good physical condition to fulfill its obligation to science and to the community.

## Acknowledgments

It gives me great pleasure to acknowledge the support given the Laboratory by the members of the Association. Their contributions play an important part in providing for the upkeep and overhead expenses, and are most essential for the continued existence of the Laboratory.

The Women's Committee, under the presidency of Mrs. George S. Franklin, made an important contribution toward the support of the scientific work of the Laboratory; and its Entertainment Committee, with Mrs. Philip Wadsworth as chairman, provided the refreshments for the Open House Tea and Exhibit in September.

The Laboratory is grateful to Mrs. Van S. Merle-Smith for her gift of kitchen equipment and bedroom furniture.

Grateful acknowledgment is made of the contribution of the Wawepex Society toward the upkeep of buildings and grounds, of the John D. Jones Scholarship maintained by that Society, and of a special contribution made this year for the upkeep of buildings belonging to the Society.

The Laboratory recognizes with gratitude the research grants made by the National Tuberculosis Association, the Army Chemical Corps, and the Atomic Energy Commission. A grant of the Carnegie Corporation of New York again provided funds for expenses of the Symposium.

With much pleasure I again acknowledge the interest shown by the Carnegie Corporation and the Rockefeller Foundation in the work of the Laboratory, as expressed by their recent grants for construction of the new lecture hall and for improvements to buildings and grounds.

M. Demerec  
Director of the Laboratory

## REPORTS OF LABORATORY STAFF

### Genetic and Biochemical Studies of Bacteria

V. Bryson, E. Rosenblum, S. Kaplan, H. Hershey, H. Cuneo and I. Dittman

Selection of B/r from B by Chemical Methods.—We have previously observed that *Escherichia coli* may be modified morphologically by treatment with toxic chemicals, and made to resemble strain B/r. Braun and Lewis were able to distinguish strain B and B/r very easily by plating bacterial colonies on MacConkey agar, as described in the Annual Report for 1949. The B/r strain develops large numbers of morphologically distinct papillae covering each bacterial colony. Cells from the papillae may be subcultured, with varying further manifestations of instability depending on the type. B/r appears, therefore, to be more unstable genetically; but there is always the possibility that similar mutants arise in colonies of strain B and never become established because of selective disadvantage.

Since radiation-sensitive strain B comes to resemble radiation-resistant strain B/r as a result of consecutive subculture in the presence of certain toxic chemicals, an interesting question at once arises. Are the derived cultures that resemble B/r on MacConkey agar resistant to radiation? In previous experiments this Laboratory has shown the similarity to B/r of strains isolated by exposure to nitrogen mustard. It is now evident that exposure of cells to hydrogen peroxide, crystal violet, safranin, proflavine, sodium selenite, copper chloride, or potassium cyanide will result in the derivation from the sensitive strain B of a radiation-resistant strain resembling B/r.

The process appears to occur by selection. Since the mutation rate of B or B/r is about  $10^{-5}$ , any B population of over one million cells would be almost certain to contain a few spontaneous B/r mutants. If all or some of these mutants were more resistant to specific chemical agents present in the environment, they would have a selective advantage. Under prolonged cultivation, certain B/r mutants would replace the sensitive B parent cells. That this may occur has been verified by observing under the microscope transitional stages of chemically treated populations containing the vanishing B strain and the emerging B/r. The two types may be distinguished by irradiating with ultraviolet and observing the proportion of B/r microcolonies among the long filaments formed by the B strain.

Cross-resistance to chemicals and radiation implies that many B/r strains obtained from irradiated cultures should be resistant to these same chemical agents. Our laboratory strain of B/r is, in fact, relatively more resistant than strain B to hydrogen peroxide, proflavine, crystal violet, and sodium selenite. In the case of potassium cyanide, greater resistance of B/r is not noted by the gradient-plate test of Szybalski, and at least three alternatives exist: that the selection hypothesis does not apply in this case; that selection occurs only under certain restricted experimental conditions, which were not present during the comparative test; or that selective advantage is limited to only a few of the many potential types of B/r mutants. The possibility that cyanide may act indirectly will be discussed. It is



known that B/r mutants of independent origin may differ in their relative resistance to certain chemicals.

It is not possible to make a super-radiation-resistant strain by exposing B/r to repeated selection in media containing copper chloride. Also, there may be more than one apparent pathway in the emergence of resistance to a chemical agent. For example, of two independent proflavine-resistant strains obtained by growing the B strain for at least ten transfers in the presence of the chemical, only one (the more resistant) was a B/r type.

Chemically produced radiation-resistant strains vary in degree of resistance to ultraviolet radiation, but do not approach the high sensitivity of strain B (Figure 1). Radiation resistance remains an all-or-none type of phenomenon, presumably dependent upon an alternative biochemical state of nucleic acid. The work of Morse and Carter, and of Marshak, does not entirely resolve the nature of nucleic acid differences as related to the resistance process, as will be seen.

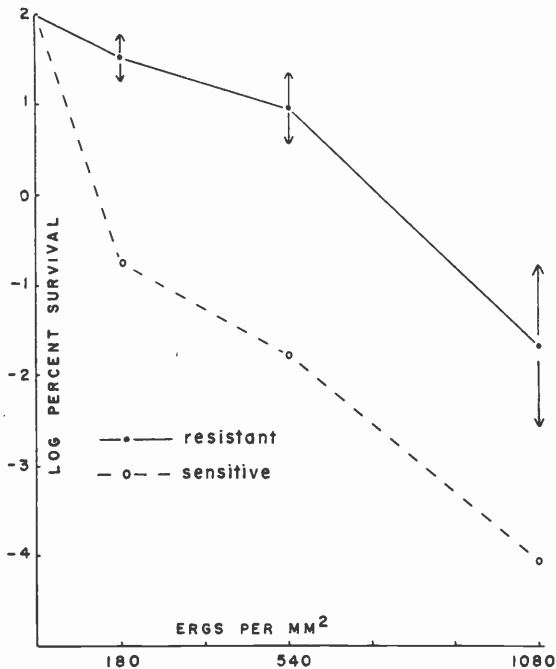


Figure 1. Action of ultraviolet on the radiation-sensitive strain of *E. coli* and derivative strains obtained by exposure to chemicals. Arrows indicate the range of variation.

In what way are the chemicals that appear to select for B/r related, and do they provide a clue to the resistance mechanism? The work of Fricke, Barron, Wyss, and others has directed attention to the role of indirect chemical effects in the radiation of biological material. The apparent selection of radiation-resistant strains by nitrogen mustard and hydrogen peroxide is not unexpected on this basis, since nitrogen mustard is a radio-mimetic agent, duplicating the effects of radiation in many ways, and hydrogen peroxide is one of the group of electron acceptors of great importance in transferring the energy of ionizing or exciting radiation to the biological substrate. As members of the triphenylmethane series of dyes, crystal violet and safranin at low concentrations may act by poisoning the redox potential at a level relatively favorable for the oxidation-resistant strain B/r. It is known from the work of Hoffman and Rahn that the inhibiting effect of crystal violet can be enhanced by adding oxygen to the medium. Investigation of peroxide as a possible intermediary in the selective effects of cyanide may also prove interesting, since Broh-Kahn and Mirsky have shown that if the cytochrome system of *E. coli* is cyanide-inactivated and a suitable dye carrier is present, inhibiting quantities of peroxide are produced. Selenite is another oxidizing agent. It is not known if peroxide is formed during the reduction of selenite by the organism. B/r is relatively more resistant than B to Zephiran, streptomycin, crystal violet, proflavine, safranin, and cupric ion, all of which are basic cations capable of combining with acidic groups of bacterial protein. The significance of charge and ionic state to adsorption by nucleic acid has been widely discussed and leads to the hypothesis that the nucleic acid of B/r may differ from that of strain B. If substantiated, the preliminary evidence of Morse and Carter, and Marshak, suggests the possibility that resistance to oxidation and to dye adsorption may result from a single genetically controlled biochemical alteration of nucleic acid structure.

Differences between Spontaneous and Ultraviolet-induced Mutation.— One of the unresolved problems of genetics is the nature of differences between spontaneous and induced mutation. Although X-rays produce numerous chromosome abnormalities, the effect of ultraviolet radiation is more subtle and has appeared in some experiments to accelerate the process of spontaneous mutation in an unselective manner. Collection of adequate experimental material to analyze the problem, using maize or *Drosophila*, has proved difficult for several investigators. We have begun analysis of the qualitative and quantitative specificity of induced bacterial mutation, using phage resistance as the phenotypic category. The advantage of relative ease in collecting sufficient numbers of mutants for statistical treatment is to some extent offset by inability to classify mutations on the basis of allelism.

The initial experimental technique consisted of irradiating saline suspensions of *E. coli* at 75 cm from a mercury vapor lamp, with sufficient ultraviolet light to inactivate 95% to 99% of the cells. Cells were then spread on nutrient-agar plates and allowed to go through 3 to 6 divisions, with the final population size less than one-tenth of the reciprocal of the

mutation rate to phage  $\cdot$  T1 resistance, insuring a high probability of excluding spontaneous mutants. Plates were phaged with T1 and a single mutant selected from the surviving colony closest to the center of the plate. A possibility of clonal relationship between mutants was eliminated by this technique. Spontaneous mutants were derived from similarly plated non-irradiated cells.

Significant differences are observed when the spontaneous and induced mutants are compared (Figure 2). The first comparison may be drawn between the percentages of mutants resistant only to phage T1. As is well known, many bacteria that resist lysis by phage T1 are also resistant to T5. *E. coli* of strain B/r resistant to T1 alone are conventionally called B/r/1, and those resistant to both T1 and T5 are designated B/r/1,5. Figure 2 shows that the proportion of B/r/1 is much greater in the spontaneous group. In other words, when a mutation is ultraviolet induced, it is more probable that resistance to T1 will be coupled with resistance to T5. We cannot continue inductively to the conclusion that ultraviolet is more likely to produce any pattern of multiple resistance. On the contrary, all the five mutants with unusual patterns of multiple resistance occurred spontaneously. These individuals, having resistance to several types of phages, may be classified as B/r/1,3,4,7,6 and B/r/1,3,4,7. Four of the second type were found in the total of 164 spontaneous mutants, and no similar types were observed in the induced group of 114. Since resistance to T3, T4, and T7 is known to occur characteristically as an independent one-step mutation, B/r/1,3,4,7,6 may be considered as a triple phage-resistant mutant, and B/r/1,3,4,7 as a double. The rates of mutation of the parent strain B/r to B/r/1 and B/r/3, 4, 7 are so low that the occurrence of these two resistance patterns in single individuals must be more than chance coincidence. E. H. Anderson has considered the extensiveness of a resistance pattern as related to the position of genetic interference in a branching chain of interrelated metabolic events. Rare mutations in the main pathways of the branching system would have multiple effects, producing multiple resistance. If nutritional deficiency is included in the pathway, the hypothesis does not explain how both B/r/1 and B/r/1, 5 can be either nutritionally normal or tryptophane deficient. Figure 2 shows that the percentage of nutritionally deficient mutants was much higher in the spontaneous group. This is related to the larger spontaneous population of B/r/1. Considering all mutants of both spontaneous and induced origin, 75% of the nutritionally deficient are B/r/1. All but five of the 72 deficient strains require tryptophane.

It is significant that all of the five nutritionally deficient mutants requiring growth supplements other than tryptophane were in the induced series of 114 mutants. These were methionineless, thiamineless, aromaticless, purineless, and serineless. The aromaticless strains require for growth the presence of three aromatic amino acids — tyrosine, tryptophane, and phenylalanine. The fact that similar phage-resistant *E. coli* mutants have never been found of spontaneous origin leads to the conclusion that they

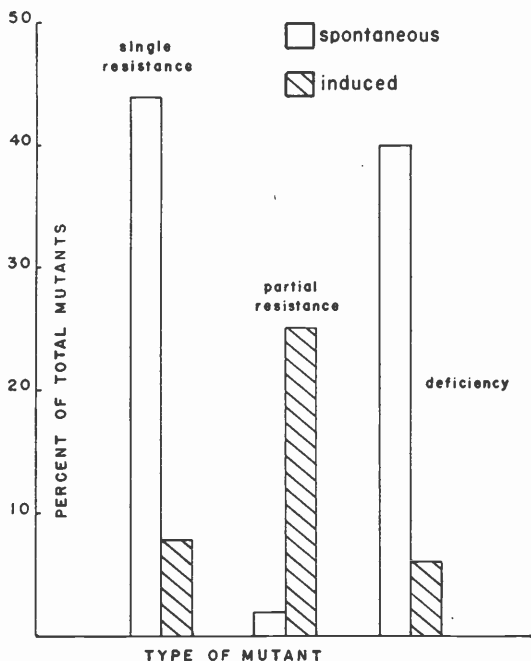


Figure 2. Comparison of two groups of *E. coli* mutants resistant to phage T1. One group is of spontaneous origin; the other was obtained by ultraviolet irradiation.

arise through a different mechanism than mere acceleration of the spontaneous rate.

Another property of the induced series of mutants is a high proportion showing partial resistance to phage T1 (Figure 2). When grown in the presence of high concentrations of phage, mutants with partial resistance have a reduced growth rate. The reduction in growth is not due to selective lysis of phage-sensitive cells within the population, but is a general property of the cells. Partial resistance is lost when cells are isolated from a slow-growing culture and exposed again to phage during subculture. Partial resistance is correlated with low efficiency of plating. If a strain showing partial resistance is plated with enough T1 to give several hundred plaques on a sensitive strain, the plaques found will be cloudy, and their number will be a small fraction of the number observed if a sensitive test strain is used. The reduced efficiency of plating is variable, depending on the identity of the mutant. Through characterization of individual mutants by their efficiency of plating we have begun a study of reverse muta-

tion of nutritionally deficient strains. The correlation of biological changes associated with loss of nutritional requirement in a phage-resistant mutant should provide additional tests for the branching-pathway theory of resistance patterns advanced by E. H. Anderson and elaborated by S. E. Luria.

**Estimation of Cell Inactivation, and Identification of Mutants by Dye Adsorption.**—Knaysi has shown that bacteria will be more heavily stained with neutral red if they are inviable. By an analogous procedure we have used the ability of bacteria to bind pyronin B as an index of inactivation by different toxic agents. Treated cell suspensions and dye buffered at pH 8 are incubated together for 1 hour at 37° C. The cells are then removed from the dye by centrifugation, and the residual pyronin in the supernatant is determined colorimetrically. Although pyronin combines readily with ribonucleic acid, there is no direct proof that a pyronin-ribonucleic acid complex is formed in the bacteria. The binding of pyronin by depolymerized desoxyribonucleic acid is not the cause of the increased dye uptake by damaged cells to be described, since methyl green continues to be adsorbed.

The method employed was to expose *E. coli* cultures to heat (52° C), ultraviolet radiation, or formaldehyde. At successive intervals samples of cells were withdrawn, assayed for the proportion of viable cells, and tested for ability to take up the dye. As sterilization by heat or formaldehyde progresses, the cells lose their dye-binding ability. A correlation can therefore be established. Irradiation with ultraviolet energy in excess of the amount required to inactivate 99.9% of strain B does not give significant changes in pyronin uptake of cells later exposed to the dye. The failure of ultraviolet radiation to produce the same types of change brought about by heat or formaldehyde assumes particular interest in view of the lack of correlation between ultraviolet sterilization and adaptive-enzyme formation, discussed in the following section.

Morse and Carter, and Marshak, have presented some evidence of a difference in the nucleic acid content of B and B/r. In our experiments, B/r did show a significantly higher pyronin adsorption. Other independently derived radiation-resistant strains of *E. coli*, however, either were similar to B or took up significantly less dye than the B strain. It can be demonstrated that the amount of dye taken up by the five independent mutants tested is a specific genetic property, but that no general distinction between B and B/r is possible on this basis. Two analyses were made of the nucleic acid content of several bacterial strains, but differences between radiation-sensitive and radiation-resistant bacteria were not significant.

**Effects of Ultraviolet Radiation on Adaptive-Enzyme Formation.**—We have just seen that, as far as modification of pyronin adsorption by toxic agents is concerned, ultraviolet light falls in the category of a harmless agent producing little effect. It has long been thought that, except when used in high doses, ultraviolet exerts its sterilizing effect by interference with the division mechanism of the cell, without extensive damage to

related systems required for synthesis. Gates showed that continued growth without division is possible in irradiated bacteria, resulting in long filamentous "snakes."

To what extent is the differential effect of ultraviolet on radiation-sensitive strain B and radiation-resistant strain B/r extended into other areas of cellular activity besides division? Study of enzyme activity offers an interesting comparison. B and B/r were compared with respect to the action of constitutive and adaptive-enzyme systems in irradiated populations of B and B/r. While this work was in progress, Brandt, Freeman, and Swenson reported that in yeast X-radiation produced no inhibition of galactozymase production at doses giving 90% inactivation.

Our first experiments compared oxygen uptake of untreated and irradiated *E. coli*. Cells were grown under aeration in M9 medium, centrifuged, resuspended in saline, divided into experimental and control portions (the former irradiated), centrifuged twice in M/15 phosphate buffer at pH 6.8, assayed for viability, and tested in buffer containing .06 M substrate at 37° C in the Warburg. The results indicate that sterilization of about 50% of the cells has no effect on oxidation of glucose, and that if substrates requiring adaptation are used (galactose or arabinose) oxidation proceeds at a slightly lower rate. In contrast, sterilization of 99% of the cells still has no effect on glucose utilization, but the ability of a galactose or arabinose substrate to adapt is lost for the three-hour period of experiment. The remarkable difference in radiation sensitivity of B and B/r, therefore, does not extend to the process of adaptive-enzyme formation, but appears confined to a specific effect on cell division. Since azide, 2, 4-dinitrophenol, and arsenate are known to block adaptive-enzyme formation and interfere with phosphorylation, doses of ultraviolet that interfere equally with the adaptive-enzyme formation of B and B/r should be investigated from the viewpoint of interference with oxidative phosphorylation and esterification of inorganic phosphate.

Experiments on Streptomycin Action.—The familiar observation that penicillin acts most efficiently on actively metabolizing cells can be extended to include streptomycin action. Under conditions permitting little or no metabolism—for example, in saline suspension or in the salt solution of synthetic carbohydrate medium—there is little or no killing action. Streptomycin becomes increasingly effective as a bactericidal agent if glucose is added to the saline. When all the necessary elements are present, as in complete synthetic medium containing glucose and a nitrogen source, the rate of killing is even more rapid. However, when unadapted cells are placed in a complete medium containing an adaptive substrate such as lactose or arabinose, killing action is markedly reduced. The most rapid rate of killing occurs in the presence of broth, a medium that supports the fastest rate of growth. The rapid rate of killing in broth could not be duplicated by the use of synthetic media supplemented with any of 16 different amino acids in 0.2% concentration.

A manometric study was made of streptomycin action in broth, and in synthetic media. It was found that whereas oxygen uptake was reduced

at three hours to about one-third, by the addition of 50 units of streptomycin per ml of broth, less than 10% reduction occurred in synthetic (M9) medium. Similar results were obtained when a peptone medium was compared with synthetic media using fructose as the carbon source. If quantitative platings are made, survival on streptomycin agar is dependent not only on the type of nutrient present in the agar, but also on the nutrient employed in growing the cells for experimental use. Prior growth in glucose permits greater survival on synthetic M9 agar containing streptomycin. Cells grown in broth show reduced survival on the same medium. The differences are not due to random variations in the background of resistant mutants in independent cultures. Streptomycin-resistant mutants are not prevented from exhibiting resistance by the presence of dinitrophenol, indicating that the resistance probably does not depend on the adaptive synthesis of an anti-streptomycin factor.

Effects of a Mutagenic Agent on Metabolism. — Extensive genetic studies by Demerec have revealed that manganous ion is a potent and relatively nontoxic mutagen. On the other hand, magnesium ion does not induce mutations. Braun has observed that the free amino acid concentration of manganous-treated cells is very low, whereas magnesium has a lesser effect. The implied influence of manganous ion on cellular metabolism deserves further study, since there is a possibility that metabolism may be linked to the mutation process.

Twenty-hour broth cultures of cells were prepared for study in the Warburg by centrifuging, washing with 0.3 M NaCl by the method of Demerec, and incubating at 37° C in .04% MnCl<sub>2</sub>, .04% MgCl<sub>2</sub>, or 0.7% saline for four hours. After chemical treatment the cells were again centrifuged, suspended in phosphate buffer, and placed in the Warburg apparatus. Glucose oxidation was presumably influenced by numerous factors, including the osmotic effects of pretreatment with 0.3 M NaCl. The primary effect of manganous ion on oxygen uptake was to reduce activity. Values, in microliters, of oxygen uptake at 80 minutes (37°C) were: magnesium ion, 460; control, 250; and manganous ion, 160. Experiments using gluconate and glycine also showed reduced metabolic activity after the routine mutagenic treatment with manganous ion. At present there is no evidence that would relate the metabolic and genetic effects of manganous ion.

Population Studies.—In 1947, Witkin reported that in mixed populations of *E. coli*, strain B/r would be replaced by strain B where both were present for prolonged periods during the stationary phase. The strains were tagged, for convenience in identification, by the reciprocal use of phage resistance.

Our more recent work with similar bacterial strains indicates that the direction of selection is determined in part by the medium employed in growing the cells. For example, although B/1 will outgrow B/r in broth, the reverse is true if M9 medium is used. In the reciprocal mixture (B + B/r/1), the B strain is favorably selected in both media. Other factors influencing the progress and degree of selection include the relative

initial proportions of the two types of cell, and the length of the experiment, during which the direction of selective pressure may be reversed. The experiments of Braun and his associates on the influence of amino acid metabolites in selection of smooth and nonsmooth *Brucella* suggested similar experiments with *E. coli*. Mixtures of B and B/r, marked with either resistance to phage T1 or inability to ferment lactose, were used in suitable proportions. Samples were collected every five days and the amino acid composition of the broth or synthetic medium was analyzed by paper chromatography. In the broth medium, some variation was noted during the growth in the concentrations of glycine, threonine, alanine, beta-alanine, and hydroxyproline. The major metabolite found in synthetic media was beta-alanine. The results at present available do not present a dominant and inevitable selective effect of any single amino acid in all populations. Attempts to approach the problem indirectly are now in progress, using mixed populations of different genotype in which specific amino acids have been added to the medium at the beginning of the experiment.

Study of Syntrophism in Reverse Mutation.—Many mutants of *E. coli* are known that cannot grow without the addition of amino acids, vitamins, or other growth factors to the simple sugars and inorganic salts of synthetic media. If the deficient mutants (auxotrophs) obtain their essential growth factors from other types of bacteria present in the same culture, the phenomenon is called syntrophism. For example, a histidineless mutant of *E. coli* may grow if provided with an exogenous source of this amino acid, or if it is in proximity to cells secreting the substance or some related precursor into the common environment. Quantitative differences in the growth rate and syntrophism of independent deficient mutants have provided a method for the study of reverse mutation. Demerec has examined the same problem by comparing independent reversions from streptomycin. In either case, the question concerns the direction of reverse mutation. Does it involve an exact restoration of the original genotype, or is it a further novel genetic change, restoring the original phenotype more or less successfully?

The analysis to be described shows that reverse mutations are not identical. Mutational steps involve independent restoration of the ability to dispense with exogenous histidine or methionine in mutants originating from strains requiring these amino acids. Before such experiments can be performed it is therefore necessary to obtain a suitable deficient parent strain. The strains used were Witkin's W-73 methionineless and W-74 histidineless, mutants induced by ultraviolet irradiation of strain B. If the step to deficiency is represented as (a to b), it is obvious that a true reverse mutation restoring the original genotype must produce the change (b to a). The original wild-type strain and all reverse mutations would be alike.

Contrary evidence is easily obtained. If one of the deficient mutants is grown in complete medium, washed, and grown in minimal agar, a few colonies will be found developing among the deficient cells. The colonies represent reverse mutants, able to grow in the absence of added amino acid. Syntrophism soon becomes visible—around certain colonies a halo



of microcolonies may be seen. Microcolonies result from the diffusion of amino acid or other ninhydrin-positive substance into the surrounding agar, giving the numerous deficient cells enough essential nutriment to begin growth and become visible. The significant finding is that the amount of growth surrounding a colony is dependent on the type of colony. Some reverse mutations provide for extensive syntrophism; others are not effective in stimulating the growth of surrounding cells. The differences can be shown to be genetic, proving that reverse mutations are not identical. Further subdivisions can be made on the basis of growth rate in liquid synthetic medium. Obviously, reverse mutations consist of many different types.

A difficulty in interpreting the result arises from inability to estimate the homogeneity of the deficient parent, from which the individual reverse mutations arise. Do reverse mutations represent different genetic changes from a common parent type, or from a parent type already differentiated into diverse genetic elements, which contribute to differences among the reverse mutations? This detail evades direct solution. In either case, it may be seen that the result of "reverse mutation" is predominantly in the direction of the formation of new types, rather than of simple fluctuation between two alternate states. As in the "leaky" gene systems of Horowitz, and the mutants affecting aromatic synthesis of shikimic acid described by Davis, individuals having a resemblance at first observation ultimately are found to be different. The term "reverse mutation" as used in bacterial genetics cannot have more than a descriptive (i. e., phenotypic) meaning until the genetic changes have been defined in terms of allelism.

Use of the Turbidostatic Selector.—For several years we have been interested in the isolation of bacterial mutants resistant to toxic agents. Conventional isolation methods consist in growing cells in the presence of graded doses of the toxic agent. Chemicals may be incorporated directly into the medium, allowing isolation of survivors at the highest tolerable dose. If the survivors possess genetic differences of selective value, resistance may be built up by continuation of the selective process through repeated exposure of bacteria to the chemical, and subculture of survivors.

The familiar example of a gradual increase in resistance during selection has been interpreted by Demerec in a specific instance as due to the accumulation of mutations, each of which reduces the sensitivity of the cell. Large doses of an antibiotic or toxic chemical may eliminate the entire bacterial population, before several mutations have been selectively accumulated in single individuals to permit survival. Small doses of toxic agent may fail to eliminate sensitive elements of the population, preventing the resistant mutants from becoming established. Therefore we may conclude that there is an optimum toxic level for selection at any stage in the progressive development of resistance. The optimum concentration may be missed if several independent concentrations are chosen at random for experimental purpose. Furthermore, the optimum concentration rises as the bacteria become more resistant. An approach to this problem is to provide for a continuously or intermittently increasing concentration gradient. The former is available in the gradient-plate method of Szybalski. Inter-

mittent changes in concentration at a rate determined by the development of resistance are made possible through the use of the Turbidostatic Selector.

The Turbidostatic Selector consists of two essential parts. The first is a proportional-feed, which periodically adds a mixture of nutrient broth and geometrically increasing concentrations of a toxic chemical to the culture. The second part of the device activates a relay when the culture has reached an arbitrarily set turbidity, allowing toxic agent and nutrient to enter the culture from the proportional-feed. Excess fluid from the growth tube overflows into a waste receptacle. The cells are stirred magnetically, aerated from above, and maintained at 37°C in the growth tubes. Samples may be withdrawn at will for tests of sensitivity.

Let us consider the order of events after inoculation of the growth tube with bacteria, with the relay adjusted to operate when the bacterial population reaches a titer of  $10^8$  cells per ml. When the population reaches this density the relay opens a pinch clamp, allowing toxic agent to flow in from the proportional-feed and diluting the culture to a density of about  $9.8 \times 10^7$  cells per ml. The concentration of toxic agent rises each time the population regains the titer required to activate the relay ( $10^8$ ). When inhibition occurs, only resistant mutants or adapted cells will be able to multiply and provide for further selection. Dilution of the toxic substance with plain nutrient may be required, as provided by means of an auxiliary attachment with automatic timer. If the culture cannot grow the addition of toxic nutrient ceases until growth is reinitiated. Evolutionary changes resulting from selective effects of the environment are accelerated at a rate determined by the progress of selection itself, rather than at the discretion of the investigator.

At present time the Selector has been used only to obtain antibiotic-resistant strains. Potential uses include: isolation of strains metabolizing specific foreign materials, by gradual change of substrates through the proportional-feed system; isolation of reverse mutants; test of the effect of metabolites or other chemical agents on selection; analysis of changes in resistance under conditions excluding bacterial growth; measurement of mutation rate; and procurement of cells at the exact level of bacteriostasis for further physiological or biochemical examination.

## Studies of Cross-Resistance of *E. coli* to Thirteen Antibiotics

Waclaw Szybalski

The work reported here was aided by a research grant from the National Tuberculosis Association.

Many people know that certain kinds of bacteria may be prevented from growing by the use of antibiotics in particular concentrations. Microbiologists also know that even in bacterial populations derived from a single cell there may be a few variants, or "black sheep," which can survive at antibiotic concentrations that would wipe out the sensitive parent cells. In the presence of the drug these new resistant variants (mutants) are left to multiply without competition, and may give rise to further drug resistance by producing occasional progeny of even less sensitivity to the drug. Because of the development of resistance, the value of streptomycin in treating tuberculosis has been greatly reduced and some newer drugs may prove to be of value for only a limited period. For this reason it is useful to learn about resistant strains, in order that we may eventually bring the problem under control.

Once bacteria have become resistant to one antibiotic, their sensitivity to other antibiotics may simultaneously be altered. They may now be less, or more, resistant than the parent culture.

Using the "gradient plate" technique, cultures of strains B and B/r of *Escherichia coli* were made resistant to streptothricin, catenulin, neomycin, viomycin, dihydrostreptomycin, aureomycin, chloramphenicol, terramycin, netropsin, penicillin, bacitracin, polymyxin B, and circulin. The sensitivity of each strain was then tested against the entire series of antibiotics, and the factors of resistance calculated. A study of cross-resistance shows that certain resistant strains have similarities that permit placing them in definite groups:

Streptothricin, neomycin, catenulin, and viomycin show a high degree of cross-resistance. Streptomycin is related to this group, but streptomycin-resistant strains show only a rather limited increase in resistance to the foregoing actinomyces antibiotics. Catenulin and neomycin seem to be almost indistinguishable.

Polymyxin B and circulin, two polypeptides of bacterial origin, show almost complete reciprocal cross-resistance; but resistance to these drugs is highly reversible. Strains resistant to these bacterial polypeptides also show a 3- to 10-fold increase in resistance to the above-mentioned group of actinomyces antibiotics, but the reverse does not hold true.

Bacitracin, a third bacterial polypeptide, does not show significant cross-resistance with other antibiotics tested.

Aureomycin-, chloromycetin-, and terramycin-resistant strains are highly cross-resistant. They also show resistance to netropsin and penicillin, but netropsin- and penicillin-resistant strains vary in their resistance to the first three antibiotics.

The radiation-resistant strain B/r shows a slight increase in resistance (1.5 X) to aureomycin, chloromycetin, terramycin, and penicillin, but not to other antibiotics.

There are two ways of obtaining a strain resistant to a given antibiotic: it may be selected in the presence of the antibiotic itself, or through the action of some other toxic agent related by cross-resistance. For example, a strain B with a 50-fold increase in resistance to streptothricin has a 20-fold increase in resistance to viomycin, although it has never been in contact with viomycin. By selection in direct contact with viomycin, the resistance was increased only 10 times.

The phenomenon of "collateral sensitivity" has been observed, wherein a culture resistant to one antibiotic becomes more sensitive to another than is the parent strain. Thus a strain B with a 130-fold increase in resistance to chloromycetin is 40 to 50 times more sensitive to polymyxin B or circulin. The bacitracin-resistant strain behaves similarly. Collateral sensitivity may be of potential clinical importance.

A similar study is in progress using, in addition to Gram-negative *E. coli*, Gram-positive *Micrococcus pyogenes* var. *aureus* and acid-fast *Mycobacterium ranae*.

Systematic studies on cross-resistance are of both theoretical and practical importance. They provide information relevant to the following problems:

- (1) Similarities and dissimilarities in genetic and biochemical mechanisms of resistance development.

- (2) The proper design of programs of multiple chemotherapy. Combinations of antibiotics that show cross-resistance should be avoided; the "collateral sensitivity" phenomenon should be utilized by clinical administration of specific antibiotics in proper sequence.

- (3) Early and simple identification of antibiotics during the screening program for new drugs. This can save much work, and supplement chromatographic methods of analysis. The higher specificity of this cross-resistance identification method makes it more reliable than the comparison of bacterial spectra of inhibition.

## Radiations and Populations

Bruce Wallace and J. C. King

The work reported below was done under contract No. AT-(30-1)-557, United States Atomic Energy Commission. We wish to acknowledge the conscientious assistance of Carol V. Madden, Bobbie R. Kaufmann, Edward McGunnigle, Gloria Cosillo, and Henry Gardner.

The investigations of populations 1, 3, 5, 6, and 7, which have been discussed in previous annual reports (1949, 1950), were continued during the past year. Our chief efforts were spent in attempting to answer two questions: What sort of genetic variants are to be found in the experimental populations? How do the different populations, possessing genetic fabrics of different patterns as they do, compare with one another in adaptive value or "fitness"? Partial answers to these questions have been obtained; the populations differ significantly in frequencies of lethal genes and in other measurable respects, but are remarkably similar in producing individuals of equal fitness. These facts have raised a third question: How can populations that differ greatly in basic genetic material produce such similar end results? It may be more interesting in this report to consider exploratory analyses we have made with regard to this last question than merely to expand the data presented in the two previous reports.

A comparison of adaptive values of populations is difficult to make; we chose a number of physiological traits that are important in the perpetuation of the populations, and measured individuals of the different populations with regard to these traits. In addition to the genetic test described in last year's report, we studied male fertility, longevity, egg hatchability, and larval competition. The results of these studies are summarized in Table 1. The figures show the relative mean longevities, the relative fertilities, and so forth, with population 3 (the control population) represented as 1 in each case. When population 3 was not included in a particular study, population 7 was given a standard value of .98—the adaptive value indicated for this population by the genetic test. On the basis of these data we conclude that the populations produced individuals of nearly equal fitness, despite the diverse frequencies of lethals and "deleterious" genes found within them. The similarity of the end products indicates that populations possess an enormous genetic resilience. In spite of the striking similarities, however, the data are sufficiently extensive to indicate that the adaptive values of the populations can be arranged in the following order: 1—3—7—6—5. The populations with the lowest adaptive values are those that receive continuous radiation at the rate of 2000 r each generation. Of immediate practical importance is the general agreement between the results of the genetic tests and those of the physiological studies; this agreement suggests that refinements of the genetic test necessary for answering specific questions can be used with confidence.

Table 1

Summary of the Adaptive Values Estimated by Various Techniques

Technique	1	3	5	6	7
Genetic test	1.03	1	.93	.95	.98
Male fertility	1.01	1	.89	.90	1.00
Longevity					
Expt. a (males)	—	—	—	.98	.98*
Expt. a (females)	—	—	—	.98	.98*
Expt. b (males)	.91	1	.90	—	—
Expt. b (females)	1.07	1	1.00	—	—
Expt. c (males)	—	—	—	.98	.98*
Egg hatchability					
Sample 41	—	—	—	.83	.98*
Sample 44	1.00	1	—	—	—
Sample 45	—	—	—	.91	.98*
Sample 46	1.00	1	—	—	—
Larval competition (inc. egg hatch.)					
Sample 41	—	—	—	.77	.98*
Sample 44	1.00	1	—	—	—

\* Set at .98 to agree with genetic test, and consequently to make the calculations for 6 comparable to that test.

The chromosomes in a population exhibit a variety of effects when homozygous. One of the questions studied this year was whether chromosomes with given effects when homozygous tend to reflect these effects when heterozygous. Table 2 shows the average viabilities of flies heterozygous for one chromosome that has a given effect when homozygous and a second chromosome chosen at random from the population. There are no obvious correlations between the effects of chromosomes as a group when homozygous and when heterozygous. This does not imply that there is no "semidominance"; the viability of certain combinations was distinctly below the average. Nevertheless, these combinations were compensated for by others of the same group that operated in the opposite direction, and so the averages of the groups are equal.

Table 2

Average Viability of Heterozygous Combinations of Second Chromosomes When the Viability of One When Homozygous Is Known

Viability of known chromosome when homozygous	Population 3	Population 6
0%	35.25	33.18
0%·22.9%	33.65	33.15
23.0%·27.9%	34.36	34.37
28.0%·32.9%	34.76	32.85
33.0%·37.9%	36.03	34.67
38%	36.64	31.20

Another question, related to the first, concerns the viability of heterozygous individuals that have one chromosome in common. If a, b, c, and d are four second chromosomes isolated from four different individuals of a population, the question can be stated as follows: Does the knowledge of the viability of flies carrying chromosomes a and b allow more accurate predictions of the viability of flies carrying b and c than of the viability of flies carrying c and d (or any other unrelated chromosomes)? An analysis of 301 differences between groups carrying a/b and b/c and 312 differences between groups carrying a/b and c/d indicated that, on the average, the two groups of flies having one chromosome in common had viabilities as different as the two groups carrying chromosomes entirely independent of one another.

The adaptive values of the different populations estimated by the genetic test differed slightly from one another, so that the populations could be arranged in order of decreasing fitness. These estimates were based on the total number of "heterozygous" crosses made to test each population, regardless of the viabilities indicated in the individual tests. It is possible to evaluate the importance of individuals of different viabilities in determining the adaptive values of the populations. Table 3 lists the average frequency of wild flies in all heterozygous cultures of each population, and, in addition, the average frequency of wild flies in only those cultures of each population that produced 50% or more of the expected frequency ("normal" cultures). Since the latter value for population 1 was higher than any other figure shown in the table, it was taken as the "ideal" viability. For each of the other populations, the percentage of the total decrease in fitness that was ascribable to the decrease found in "normal" heterozygotes was computed. It is obvious that individuals of drastically lowered vitality are of minor importance in determining the adaptive value of a population; the primary effect resides in the mass of "normal" individuals comprising that population.

Table 3

An Estimation of the Role Played by "Normal" Individuals in the Determination of Adaptive Value

Pop.	Av. viab. of all heterozygous cultures	Av. viab. of normal heterozygous cultures	Diff. between "all" and "normal"		Proportion of difference contributed by normals
1	35.06	35.16	—	—	—
3	34.14	34.19	1.02	.97	95%
5	31.85	32.23	3.31	2.93	89%
6	32.48	32.66	2.68	2.50	93%
7	33.40	33.44	1.76	1.72	98%

A clearer picture of populations emerges as a result of these exploratory studies, although much remains to be done in testing specific hypotheses. It appears that genetic variability increases rapidly in all populations. In the transmission of genetic material from generation to generation, the various genes and chromosomes are continually being shuffled and dealt in a multitude of different combinations. Natural selection operates upon the different adaptive values of heterozygous individuals carrying these different gene combinations. As a result of this selection a population builds up an integrated store of genes that go well with each other, to produce in most cases well adapted individuals. Thus every population acquires within surprisingly few generations a character or personality of its own, reflecting its past, which can be demonstrated by genetic tests and by observation of the physiological traits of the individual members.

The system of interacting and interdependent genes that results from this natural selection has been aptly described as "coadapted." Such a coadapted system embodies two characteristics essential for the continued existence of any population; the system is delicately balanced to respond quickly to the slightest changes in the demands of selection, and, simultaneously, it is extremely stable in resisting those agents that operate contrary to selection. The irradiated populations testify to the stability of this genetic system. The many DDT-resistant populations of insects have already, and too well, attested to the ability of populations to adapt rapidly to meet new requirements of selection.



## REPORTS OF SUMMER INVESTIGATORS

**Abramson, H. A.**, 133 East 58th Street, New York, N.Y., and **Goldfarb, R.**, Chicago Medical School, Chicago, Ill.—Dr. Goldfarb extended the work of previous years and clarified many of the problems connected with the purification of the material that causes ragweed hay fever. Exploratory studies of methods of purification by means of 90% methyl alcohol succeeded in removing most of the pigments, leaving a biologically active residue. Spectrographic studies of the pigments were begun, and it is anticipated that a more basic understanding of the nature of the pigments in ragweed can be achieved by Dr. Goldfarb's contributions along this line. Preliminary electrophoretic analyses of different fractions were carried out.—With Mr. Peter Salkin, attempts were made to devise simplified techniques for the study of the Electrophrenic Respirator. It is hoped that this respirator can eventually be adapted for use in the treatment of severe attacks of asthma.

**Bernheimer, Alan W.**, New York University College of Medicine, New York, N.Y.—The hemolymph of the caterpillar and pupa of the *Cecropia* moth exhibits a relatively powerful agglutinating action when mixed with washed mammalian erythrocytes. The agglutinin was found to be present in titers of 1:25 to 1:625 in a large number of larvae and pupae examined, and appeared to be absent from the adult moth and from the egg. It is a labile substance, its titer being reduced by approximately one-half upon heating, at pH 7.0, to 45° C for one hour. It is largely or completely nondialyzable. In order to see whether agglutinating action is specific for *Samia cecropia*, a total of 46 species of lepidopteran larvae, representing 16 families, were tested for ability to agglutinate human erythrocytes. The results showed that hemagglutinins were present in 10 of the species examined. All 10 were moth larvae; all butterfly larvae tested were negative. Beyond this, little correlation between presence of agglutinins and taxonomic position was evident. The hemolymph of 2 species, *Halisidota caryae* and *Halisidota tessellaris*, can be used to differentiate human O-erythrocytes from A- and B-erythrocytes, a finding of some interest since O-agglutinins are of rare occurrence in nature. In a few instances, *H. caryae* hemolymph caused a relatively weak and delayed agglutination of A- and B-cells, owing apparently to heterozygosity or to antigen A<sub>2</sub>.

**Bernheimer, Alan W.**, New York University College of Medicine, **Caspari, Ernst**, Wesleyan University, and **Kaiser, Armin D.**, California Institute of Technology.—There is a striking difference between vertebrates and insects in the ease with which transplantation experiments can be performed. In vertebrates, it is usually impossible to transplant organs or tissues successfully from one individual to another, even within the same species, unless the organisms belong to the same strain or are genetically identical. In insects, transplantations between organisms of the same spe-

cies can easily be achieved, and in a number of instances successful results have been obtained in experiments involving grafts between different species, genera, and even families. These observations can be explained if insects fail to produce antibodies to materials which are antigenic in vertebrates. We undertook to explore this possibility by injecting larvae and pupae of the Cecropia moth (*Samia cecropia*) with coliphage T2, heat-killed *Escherichia coli*, and streptolysin O. The hemolymphs of injected animals were tested for ability to inactivate coliphage T2, to agglutinate *E. coli*, and to neutralize the hemolytic action of streptolysin O. In these properties, the hemolymphs of injected animals did not differ significantly from those of uninjected animals. The data indicate that antibodies comparable to those found in mammals are not formed by larvae and pupae of *S. cecropia* against any one of the antigens used. Although it may not be justified to generalize from observations made on a single species, the results are consistent with a lack of convincing evidence for antibody formation in other insects. The findings not only explain the success which attends transplantation of tissues and organs among different species and genera of Lepidopteran larvae, but are of interest also in connection with the mechanism of induced immunity in insects to infectious agents.

**Braun, Werner**, Chemical Corps Biological Laboratories, Camp Detrick, Frederick, Md.—During the month of August, 1951, an effort was made to test whether the mutagenic effects of manganous chloride, as described for *E. coli* by Demerec, are associated with alterations of intracellular metabolism, particularly with changes in amino acid levels. This possibility was suggested by the investigator's prior observations with *Brucella*, which had indicated that addition of  $Mn^{++}$  to the growth medium caused accumulation of specific amino acids and simultaneous enhancement of population changes involving the more rapid establishment of amino acid-resistant antigenic mutants. In accordance with the results of Demerec, *E. coli* B/r cells were grown in aerated nutrient-broth cultures, washed with 0.3 M NaCl, suspended in 0.04 per cent  $MnCl_2$  for 40 minutes at 37° C, washed and then stored at 5° C for 12 hours. Control cells were similarly treated except that they were suspended in physiological saline at 37° C for 40 minutes, instead of in  $MnCl_2$ . The washed, stored cells were broken up by freezing and desiccation or by grinding with powdered alumina. Intracellular amino acids were then determined with the help of paper-partition chromatography. Control cells revealed the presence of at least 7 different amino acids, whereas only 1 amino acid (glutamic acid) was recoverable from the cell extracts of  $MnCl_2$ -treated cells. Repeated tests confirmed the validity of these observations; the amino acids missing in the  $MnCl_2$ -treated cells could not be recovered from any of the washings. In contrast,  $Mg^{++}$ -treated cells showed a somewhat similar, but less striking, disappearance of intracellular amino acids, and these missing amino acids could be recovered from the washings—that is, they leaked out of the cells. It remains to be determined whether the shift in intracellular amino acid levels after  $MnCl_2$  treatment is causally related to the mutagenic

effects produced by this treatment.—In addition, studies were made on the efficiency of various methods designed to isolate *E. coli* mutants with multiple antibiotic resistance (streptomycin, chloromycetin, aureomycin, terramycin).

**Bruce, Nancy**, New York University College of Medicine, New York, N.Y.—Preliminary studies were made of coliphage 8, a distant serological relative of T1, with the purpose of carrying out mixed infection with T1 and coliphage 8, and testing for recombination between these two viruses, which differ in host range, latent period, and rate of inactivation by anti-T1 serum. Cullen strain of *E. coli* was used as the common host. It was found that when Cullen was mixedly infected with T1 and coliphage 8, and the first growth tube plated on mixed indicators (B and Cullen/1), about 10 per cent of the plaques were clear, indicating mixed yielders. The results from single cell burst experiments, however, were equivocal.

**Caspari, Ernst, and Wright, Eileen Y.**, Wesleyan University, Middletown, Conn.—Preliminary experiments were carried out to develop methods for genetic studies on aerobic sporeforming bacteria. *Bacillus circulans* was chosen as the test organism, because it does not form chains, occurs singly or at most in pairs, and gives rise in the rough phase to clearly distinguished colonies. It is also a large organism, which may be suitable for cytological studies. Growth curves in glucose broth and in sodium acetate tryptone were established both by viable count and by total count. The nutritional requirements of the organism were investigated. It can synthesize its own purines and pyrimidines, and does not seem to need any vitamins; but it requires the presence of as-yet-undetermined amino acids. The organism is highly sensitive to streptomycin. Streptomycin-resistant strains were developed, but none of them proved to be streptomycin-dependent.—(This work was done for the Chemical Corps Biological Laboratories, Camp Detrick, Frederick, Md., under Contract No. DA-18-064-CML-475 with Wesleyan University, Middletown, Conn.)

**Delbruck, M.**, California Institute of Technology, Pasadena, Calif.—During July and August I collaborated with N. Visconti, of the Carnegie Institution, in the development of a comprehensive theory of bacteriophage genetics. The basic assumptions of this theory are: (1) After infecting the bacterium, the parental phage particles undergo a modification into a non-infective state. In contrast to previous theories, however, this one does not assume that the particles break up into genetic subunits. (2) The non-infective particles multiply. (3) Mating occurs between random pairs of particles. The mating occurs predominantly, if not exclusively, after multiplication. Mating is followed immediately by segregation, with the formation of genetic recombinants. — Our aim was to analyze the implications of these assumptions and to design experiments that enable the experimenter to determine the parameters of the theory (average number of rounds of mating, and the distribution of this number).

**Granick, S.**, The Rockefeller Institute for Medical Research, New York, N.Y.—Part of the summer was spent in writing a review for *Physiological Reviews* on the "Structure and Physiological Functions of Ferritin". Consideration was also given to the question of the comparative efficiency for photosynthesis of the pigments along the biosynthetic chain of chlorophyll. The data available reveal a progressive increase in efficiency for absorption of the quanta of sunlight by the pigments of the biosynthetic chain. If the biosynthetic chain is considered to represent an evolutionary sequence, then the biosynthetic chain of chlorophyll reveals an evolution of pigments each progressively better than the last for carrying out photosynthesis in sunlight.

**Hotchkiss, Rollin, D.**, The Rockefeller Institute for Medical Research, New York, N.Y.—The greater part of the summer was spent in the completion of three manuscripts for publication. Preliminary experiments were also conducted on the course of spontaneous development of penicillin resistance in pneumococci. It was observed that the process is stepwise, as shown by Demerec for staphylococcus and as recently found for the induced transformation to penicillin resistance in pneumococcus.

**Luria, S. E.**, University of Illinois, Urbana, Ill.—Most of my time was devoted to the writing of a book on "Viruses" and to the preparation of lectures given at the Symposium on Biophysics, University of Michigan. I did some preliminary experiments on the following problem. Phages T2 and T4 are inactivated with ultraviolet, adsorbed in buffer on washed bacteria, photoreactivated with visible light, and again irradiated with ultraviolet, either immediately or after addition of nutrients for various times. The number of bacteria that yield phage is measured. Is the ultraviolet sensitivity of the photoreactivated phage-bacterium complexes similar to that of active phage-bacterium complexes immediately after infection, or to that of these complexes at a later stage? The results of such experiments may provide a test of the suggestion (Dulbecco) that photoreactivation of phage T2 may consist in the by-passing of a reaction controlled by a highly ultraviolet-sensitive portion of the phage. The preliminary experiments did not go far enough to allow any conclusion to be drawn.

**Sager, Ruth**, Rockefeller Institute for Medical Research, New York, N.Y.—The production and selection of non-chlorophyll-containing mutants of the green alga, *Chlamydomonas Reinhardi*, was continued, and some of the staining characteristics of this organism were examined. An interesting effect of the Hotchkiss polysaccharide stain was to make clearly visible the two tiny blepharoplasts to which the flagella are attached.

**Streisinger, George**, University of Illinois, Urbana, Ill.—The problem investigated concerned the genetic determination of sensitivity to ultraviolet light in bacteriophage. The related phages T2L and T4 are used for this study; the survival of these phages is an approximately exponential func-

tion of the dose of radiation, but T2L is inactivated at twice the rate of T4. Hybrids between the two phages have either the radiation sensitivity of T2 or that of T4; intermediate levels of sensitivity have not been observed. The level of photoreactivation follows the radiation-sensitivity level.—Phages genetically similar, but differing in ultraviolet sensitivity and in two other marker factors (*r-r<sup>+</sup>* and *h-h<sup>+</sup>*) were obtained by crossing T2L and T4 and repeatedly backcrossing the F<sub>1</sub> hybrids to T2L. Crosses between strains of the seventh backcross indicated that the level of ultraviolet sensitivity is transmitted as a single factor, following the same pattern as the factors studied by Hershey and Rotman in T2H. The ultraviolet locus is not linked to the marker loci used in the backcross, which are in the same relation to each other as T2Hh and T2Hr7.

**Tittler, Irving A.**, Brooklyn College, Brooklyn, N.Y.—It has been shown that in thiamine-deficient medium with glucose, *Tetrahymena* causes an accumulation of pyruvic acid which results in an abnormally early decline of the cultures. Each experiment consisted of control and experimental series. Control cultures contained neither thiamine nor sulphadiazine but were complete in every other respect. To the experimental series the following concentrations of sulphadiazine, with and without added thiamine, were added to the standard culture medium employed: 0.1 mg%, 1.0 mg %, 5.0 mg %, 10.0 mg % and 12 mg %. Determinations of cell numbers per unit volume of culture medium were made on the 10th day following inoculation. At this time a rapid drop in pH occurs in the control cultures. Microscopic examination of these cultures fails to demonstrate the presence of living cells and chemical analysis reveals that an accumulation of pyruvic acid has occurred. A lesser decline is found in cultures containing 0.1 mg% sulphadiazine without added thiamine. Cultures containing 5.0 mg% to 78 mg% sulphadiazine without added thiamine showed no drop in pH and no accumulation of pyruvic acid. Furthermore, growth in these experimental series compared favorably with growth in similar series containing added thiamine. Further studies of this effect are being made with other sulphonamides.

**Weinhouse, Sidney, and Spirtes, Morris A.**, The Institute for Cancer Research, Philadelphia, Pa.—We utilized the facilities of the laboratories and library during July and August in preparing for publication a number of papers representing experimental work carried out at the Institute for Cancer Research. These were: (1) "Metabolism of Neoplastic Tissues. I. The Oxidation of Carbohydrate and Fatty Acids in Transplanted Tumors," by Sidney Weinhouse, Ruth H. Millington, and Charles E. Wenner, to be published in *Cancer Research*. (2) "Metabolism of Neoplastic Tissues. II. A Survey of Enzymes of the Citric Acid Cycle in Transplanted Tumors," by Charles E. Wenner, Morris A. Spirtes, and Sidney Weinhouse, to be published in *Cancer Research*. (3) "The Biosynthesis of Arginine by *Torulopsis Utilis*," by Murray Strassman and Sidney Weinhouse, to be published in the *Journal of the American Chemical Society*. (4)

"The Presence of the Enzymes of the Tricarboxylic Acid Cycle in the Larvae of *Drosophila Melanogaster*," by Morris A. Spirtes, to be submitted to the Archives of Biochemistry. (5) "The Fixation of  $C^{14}O_2$  into Citric Acid by the Mold *Aspergillus Niger* and the Location of the  $C^{14}$  in the Citric Acid Molecule," by Morris A. Spirtes, Benjamin Shapiro, and Severo Ochoa, to be submitted to the Journal of the American Chemical Society.

## COURSE ON BACTERIOPHAGES

June 25 — July 14, 1951

Instructor: Mark H. Adams, New York University College of Medicine.

Assistant: Maryda Swanstrom Colowick, New York University.

For the seventh time an intensive three-week course dealing with techniques and current research problems in the field of bacterial viruses was given. Sixteen students took the course and in addition three auditors attended the lectures and seminars. It is unfortunate that the physical facilities are not adequate to accommodate all who wish to take part in the laboratory work. The following students were enrolled:

W. A. Atchley, M.D., Rockefeller Institute, New York, N.Y.  
G. H. Bornside, Massachusetts Institute of Technology, Cambridge, Mass.  
Helen Bowser, Rockefeller Institute, New York, N.Y.  
F. Marilyn Bozeman, Army Medical School, Washington, D.C.  
R. Britten, Ph.D., Department of Terrestrial Magnetism, Carnegie Institution of Washington, Washington, D.C.  
M. S. Fox, Ph.D., University of Chicago, Institute of Radiobiology and Biophysics, Chicago, Ill.  
Tamara Gotlieb, Ph.D., Hebrew University, Jerusalem, Israel  
S. R. Gross, Columbia University, New York, N. Y.  
J. Hurwitz, Western Reserve University, Cleveland, Ohio  
A. Kohn, Ph.D., Weizmann Institute, Rehovot, Israel  
J. W. McKee, California Institute of Technology, Pasadena, Calif.  
Howard Monsees, Biological Laboratory, Cold Spring Harbor  
G. Montalenti, Ph.D., University of Naples, Naples, Italy  
Kirsten Rosendal, Ph.D., State Serum Institute, Copenhagen, Denmark  
B. N. Siegel, Ph.D., Stanford University, Stanford, Calif.  
B. A. D. Stocker, M.D., London School of Hygiene and Tropical Medicine, London, England  
W. Szybalski, Ph.D., Biological Laboratory, Cold Spring Harbor  
D. Weis, Western Reserve University, Cleveland, Ohio  
J. F. Woessner, Jr., Massachusetts Institute of Technology, Cambridge, Mass.

In connection with the course, a series of lectures was given by students and summer research workers. The speakers and their topics are listed below:

M. H. Adams—Stability of viruses.  
M. H. Adams—Lysogenesis.  
William A. Atchley—Bacterial transformations.  
M. Delbruck—Genetic recombinations in bacteriophage.  
S. E. Luria—Recent work on unusual forms of phage T2.  
B. Stocker—Quantitative aspects of bacterial mutations.

## COURSE ON BACTERIAL GENETICS

July 18 - August 6, 1951

Instructors: Evelyn M. Witkin, V. Bryson, M. Demerec, E. Beckhorn, and N. Visconti, Carnegie Institution and Biological Laboratory.

Guest Instructors: Dr. M. I. Bunting, Yale University; Dr. E. D. DeLamater, University of Pennsylvania.

Assistants: Helen Cuneo and Miriam Schwartz, Biological Laboratory and Carnegie Institution.

Once again, a course on selected methods in bacterial genetics, initiated in the summer of 1950, was offered to advanced graduate and postdoctoral students. The course emphasized the newer methods used in the study of heredity in bacteria, and some of the recent results of work done in this field.

Laboratory sessions, held six mornings a week during the three-week period, were supplemented by lectures and informal discussions every afternoon. The laboratory work covered a wide range of experimental techniques, including the following: the isolation and identification of various bacterial mutants, particularly those resistant to bacteriophages, radiation, and antibiotics, as well as those requiring nutritional supplements; the determination of spontaneous-mutation rates, using several methods; the induction of hereditary changes in bacteria by radiation and by chemicals, and crossing of bacterial strains in which a sexual process occurs. The course was very much enriched this year by the participation of Dr. E. D. DeLamater, who supervised laboratory studies of bacterial cytology, and Dr. M. I. Bunting, who directed the study of color variants in *Serratia marcescens*.

In addition to lectures given by all the course instructors, special lectures were given by some of the distinguished summer visitors at the laboratory, including Dr. R. Hotchkiss, of the Rockefeller Institute, Dr. B. Davis, of the Tuberculosis Research Laboratory, Dr. M. Adams, of New York University, Dr. W. Braun, of Camp Detrick, and Dr. M. Delbruck, of the California Institute of Technology.

Sixteen students were admitted to the course this year, and their diverse training and backgrounds added to the stimulating atmosphere that characterized most of the sessions. The students were:

Louis Baron, Ph.D., University of Illinois, Urbana, Ill.

G. H. Bornside, M.S., Massachusetts Institute of Technology, Cambridge, Mass.

Audrey Evans, B.A., Rockefeller Institute, New York, N.Y.

M. S. Fox, Ph.D., Institute for Radiobiology and Biophysics, University of Chicago, Chicago, Ill.



- E. D. Garber, Ph.D., Naval Biological Laboratory, University of California,  
Oakland, Calif.
- Emily H. Kelly, Ph.D., Camp Detrick, Frederick, Md.
- A. Kohn, Ph.D., Weizmann Institute, Rehovot, Israel
- Grace Leidy, A.B., Columbia University, New York, N.Y.
- Howard Monsees, B.A., Biological Laboratory, Cold Spring Harbor, N.Y.
- Yvonne Posternak, M.S., University of Pennsylvania, Philadelphia, Pa.
- W. B. Schaeffer, M.D., Rockefeller Institute, New York, N.Y.
- B. A. D. Stocker, M.D., London School of Hygiene and Tropical Medicine,  
London, England
- D. Weis, M.S., Yale University, New Haven, Conn.
- J. F. Woessner, Jr., B.A., Massachusetts Institute of Technology,  
Cambridge, Mass.
- Nebahat Yakar, Ph.D., Department of Genetics, Cold Spring Harbor, and  
Istanbul University, Istanbul, Turkey

## PHAGE MEETING

August 20-22, 1951

The fifth annual meeting of phage workers was held this year for the second time at Cold Spring Harbor. The meeting was organized, like the one last year, by Max Delbruck.

S. S. Cohen presented the results of metabolism experiments suggesting that bacterial growth (specifically ribonucleic acid synthesis?) utilizes to a considerable extent an oxidative pathway in the breakdown of glucose, in contrast to virus growth (desoxyribonucleic acid synthesis), which requires a fermentative cycle.

F. W. Putnam summarized the extensive investigations of his group on bacterial precursors of bacteriophage nitrogen, carbon, and phosphorus. He also reported work of O. Maale and G. Stent, on the assimilation of viral phosphorus.

L. M. Kozloff described further experiments aiming to trace materials derived from the parental virus particles in infected bacterial cells. He also summarized a communication from J. D. Watson and O. Maale on the same subject. These workers agree in finding that some material (particularly phosphorus) is transferred from parents to progeny, that some material can be transferred from genetically nonparticipating (e.g., ultraviolet-inactivated) virus to growing virus, and (Watson and Maale) that the parental phosphorus incorporated into progeny enters into all parts of the phage particle that contain phosphorus.

A. F. Graham reported further experiments on the breakdown of virus particles adsorbed to cells already infected with virus (see Annual Report for 1950).

C. D. Prater reported that bacteria suspended in buffer and infected with phage release in about 3 minutes a material that absorbs ultraviolet light and has some of the properties of ribose nucleoprotein. This material is derived from the bacteria.

G. Bertani reported work on a lysogenic strain of *E. coli* which he has found to be host to at least three phages. Only one of these is liberated by any one bacterium at lysis.

R. I. De Mars described experiments on the ultrafilterable substance in phage lysates that is able to combine with antiphage antibody.

S. E. Luria reported that when certain strains of bacteria are infected with T2 or T6, phage progeny are obtained that adsorb normally but possess an abnormal host range with respect to growth. The abnormality is lost when the virus is propagated on another host. The host-virus relations are dependent also on the physiological condition of the bacteria.

T. T. Puck described experiments that reveal two stages in the specific adsorption of phage to bacteria. The first step is reversible, and the two steps are differently affected by electrolytes, temperature, and genetic variation in the host.

A. D. Hershey summarized experiments demonstrating heterozygous particles of phage T2.

N. Visconti and M. Delbruck reported a quantitative theory of successive matings between phage particles that accounts for triparental recombination, for the effect of unequal multiplicities on recombination frequency, and for certain anomalous results in three-factor crosses.

G. T. Barry reported experiments on "receptor gradients" in the adsorption of phages to artificially modified bacterial cells. No evidence has appeared from these experiments that there are independent structures on the bacterial surface responsible for the adsorption of different phages.

Mark Adams reported his experiments on recombination in the T5 group of phages, and also discussed criteria for the classification of viruses, about which he will speak at the conference on taxonomy at the New York Academy of Sciences.

The scientific proceedings were interrupted by a beer-and-pizza party in the evening of the second day.

## NATURE STUDY COURSE

June 25 - July 26, 1951

Dr. Pauline James, Department of Biology, Texas College of Arts and Industries, Kingsville, Texas. Assisted by Patricia Moore, Memphis State College; and Larilee Baty, Huntington, N.Y.

The Nature Study Course was conducted according to the principles set forth in former years, and was guided by the objectives listed in previous annual reports of the course. Every effort was made to acquaint the students with their natural environment and to develop in them an understanding and appreciation of man's dependence on organic resources.

The location of the Laboratory within easy access to many different ecological situations—varying from spring-fed fresh-water streams and lakes to salt-water beaches and brackish swamps, and from open fields to heavily wooded hills—allowed opportunity for unlimited field work. Consequently, all the classes spent a considerable amount of time in the field in addition to working in Wawepex Laboratory, from which the course was directed.

The large number of young students enrolled made it advisable to divide them into a Beginning and a Junior group. The thirteen six- and seven-year-old children met on Mondays and Wednesdays from 9:00 to 11:00 a.m., and the eleven eight-year-olds on Tuesdays and Thursdays from 2:00 to 4:00 p.m. The Intermediate group, aged nine to eleven years, met on Tuesdays and Thursdays from 9:00 to 11:00, and the eleven members of the Advanced class met on Mondays and Wednesdays from 2:00 to 4:00.

The field work of the Beginning group was limited to nearby areas, within walking distance of the Laboratory. An attempt was made to bring the children into contact with as many types of living things as possible and to help them form habits of accurate observation. For instance, a robin's nest with eggs was discovered just outside and beneath one of the laboratory windows at the beginning of the course. This gave the group an excellent opportunity to make daily observations, watching the eggs hatch and the young develop. Frequent occasions for sharing experiences were provided; and each child was encouraged to make individual contributions to all discussions and to participate in every activity.

The members of both the Junior group and the Intermediate group took part in all field work, and showed unusual eagerness and interest in their activities. Collections were made, and more detailed studies were carried on in the field and in the laboratory. In the Intermediate group, some of the children were especially interested in Lepidoptera. One boy made a good collection, including a number of large moths, particularly of the Saturniidae group, which he identified and mounted for display in the final exhibition of the course. This class studied and also prepared for exhibit the life history of the Cecropia moth, *Samia cecropia*, using living specimens to depict each stage from egg—through caterpillar, cocoon, and pupa—to adult. Some members of this class were particularly interested in shells, and studied and collected many of the local forms.

Other activities of the two middle groups included observations of birds, beach life at high and low tide, fresh-water ponds, and woodland habitats. In the study of pond life, the use of the microscope proved extremely valuable as well as fascinating for these two groups, in that it helped to establish the concept of a microscopic world. The setting up of aquaria and terraria indoors brought out the need for an understanding of the interrelationships that exist in the natural habitat, if it is to be duplicated successfully.

In the Advanced group most interests were general, so that many of the fields explored by the Intermediates were also studied by this group. All members of the group were interested in bird study, however, and so a special project in this field was planned and developed. The class decided to build a bird chart, which could be used to check identification of local birds. First the group made a trip to the Trailside Museum of the Roosevelt Bird Sanctuary in Oyster Bay, where Mr. James Callahan, the director of the Sanctuary, very kindly explained and demonstrated for them the various types of electrical charts he has developed and used in the museum. When they had decided to make one of the simpler types and adapt it to suit the purposes of their own group, Mr. Callahan gave them a few practical pointers on construction details. Materials were bought, and parts of two regular class periods were spent in construction. The rest of the work was done outside of class periods by members of the group who voluntarily spent extra time on it. After completion the chart was used by the younger groups also, and it will be kept as part of the permanent equipment of the course—its usefulness being increased by the fact that the bird cards used are interchangeable so that it is possible to check at least 150 different species.

This same group had the experience of observing and inspecting a burrow of young kingfishers when the birds were only a few days old, and again later when they were about two weeks old. Bird banding was discussed, and plans were made to band the young kingfishers as soon as they were mature enough. Unfortunately, the course was over before the birds were large enough, and so the students were not able to participate in the actual banding.

In addition to the bird-study activities, members of the Advanced class successfully established a large aquarium with local fish, plants, and insects. Some of the group also collected and arranged plants to establish woodland terraria, which were then stocked with various local reptiles and amphibians.

As a final activity, members of the group visited the Bronx Zoo, where Mr. Robert McClung, Assistant Curator, took them on a tour of some of the more interesting sections. He told them many fascinating "behind the scenes" stories, and pointed out a number of things that are frequently overlooked by the casual visitor. The trip was climaxed by a very brief visit to the hospital where injured animals are treated and new ones are examined before becoming residents.

On the whole, this Advanced class offers a great opportunity for fur-

ther work, because its members are intensely interested in natural history and plan to return and take the course again.

Staff members of the New York State Fish Hatchery near the Laboratory kindly conducted the various classes on a tour of the hatchery, explaining the activities and the purpose of each. The methods and reasons for restocking streams proved to be of great interest, as did inspection and identification of growing trout.

The two middle groups, as well as the older group, visited the Roosevelt Bird Sanctuary, where Mr. Callahan demonstrated and explained the purposes of the exhibits in the Trailside Museum. He then took the youngsters along the Nature Trail where they were able to see various plantings, baths, and other devices that are used to attract birds to an area.

The Nature Study Course closed on July 26 with a public exhibition of the activities of the different groups during the five-week course. The students had shown great interest in preparing the displays for their parents and friends, and eagerly pointed them out on the day of the demonstration. The bird chart was of especial interest to everyone, as was the exhibit of nature reference materials, which included record albums of bird songs and frog calls and an excellent collection of both recent and classic nature books loaned for the occasion by Hunt's Book Store in Huntington.

At three o'clock the students and visitors were shown two short movies in Blackford Hall: "The Life History of the Monarch Butterfly," and "Life in a Drop of Water." Between the movies, one of the recordings of frog calls was played, with accompanying Kodachrome slides. The program was attended by more than 100 guests. Refreshments were served under the apple tree on Wawepex lawn.

The following students attended the course:

Baty, Larilee	Hewitt, Ned	Radsch, Robert W.
Berry, Roger	Hotchkiss, Paul	Romaine, Gary
Berry, Rosina	Kepler, Ann C.	Ross, Joe
Braun, Renee	Knight, John D., Jr.	Rowe, John
Buckley, Sally	Laverne, Jeremy Joyce	Schier, Susan
Doyle, Howard	Lyon, Stephen	Schneider, Ann
Du Bois, Caroline S.	Munier, Denis	Schneider, Elizabeth
Gerbino, Charis S.	Munier, Quentin	Schneider, Kate
Gillmore, Carol	Myer, Betty	Schneider, Timothea
Gillmore, Lyn	O'Connell, Raymond	Sheshunoff, Alex
Graesser, Gerry	Olmsted, Nancy	Sheshunoff, Billy
Grandjouan, Arabelle	Osborn, John Jay, Jr.	Tittler, Robert B.
Granick, Donna	Page, Jane	Turner, Polly
Granick, Lee	Powell, Robin	Wagner, Edrie
Griffiths, Clare D.	Radsch, Christopher A.	Wagner, Irene
Griffiths, Kathleen	Radsch, Richard T.	West, Gatewood

## COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY

Current volume: XVI. Genes and Mutations. About 550 quarto pages. 1951. Table of contents is listed below:

### THEORY OF THE GENE

- Goldschmidt, R. B.—Chromosomes and genes.  
McClintock, B.—Chromosome organization and genic expression.  
Stadler, L. J.—Spontaneous mutation in maize.  
Horowitz, N. H., and Leupold, U.—Some recent studies bearing on the one gene—one enzyme hypothesis.

### CYTOPLASMIC CONSTITUENTS OF HEREDITY

- Ephrussi, B., and Hottinguer, H.—On an unstable cell state in yeast.  
Spiegelmann, S.—The particulate transmission of enzyme-forming capacity in yeast.  
L'Heritier, P.—The CO<sub>2</sub> sensitivity problem in *Drosophila*.  
Provasoli, L., Hutner, S. H., and Pintner, I. J.—Destruction of chloroplasts by streptomycin.  
Michaelis, P.—Interactions between genes and cytoplasm in *Epilobium*.

### EVOLUTION OF THE GENE

- Stephens, S. G.—Homologous genetic loci in *Gossypium*.  
Bonner, D. M.—Gene-enzyme relationships in *Neurospora*.  
Lewis, E. B.—Pseudoallelism and gene evolution.  
Schultz, J. and Redfield, H.—Interchromosomal effects on crossing over in *Drosophila*.

### INDUCTION OF CHANGES IN GENES AND CHROMOSOMES

- Auerbach, C.—Problems in chemical mutagenesis.  
Demerec, M., and Hanson, J.—Mutagenic action of manganous chloride.  
Roberts, R. B., and Aldous, E.—Manganese metabolism of *Escherichia coli* as related to its mutagenic action.  
Levan, A.—Chemically induced chromosome reactions in *Allium cepa* and *Vicia faba*.  
Jensen, K. A., Kirk, I., Kolmark, G., and Westergaard, M.—Chemically induced mutations in *Neurospora*.  
Gustafsson, A. Mutations, environment and evolution.  
Giles, N. H., Jr.—Studies on the mechanism of reversion in biochemical mutants of *Neurospora crassa*.  
Hollaender, A., Baker, W. K., and Anderson, E. H.—Effect of oxygen tension and certain chemicals on the X-ray sensitivity of mutation production and survival.  
Russell, W. L.—X-ray induced mutations in mice.

### GENETIC MECHANISMS IN BACTERIA AND BACTERIAL VIRUSES

- Novick, A., and Szilard, L.—Experiments on spontaneous and chemically induced mutations of bacteria growing in the chemostat.  
Atwood, K. C., Schneider, L. K., and Ryan, F. J.—Selective mechanisms in bacteria.

- Witkin, E. M.—Nuclear segregation and the delayed appearance of induced mutants in *Escherichia coli*.
- Bisset, K. A.—Genetical implications of bacterial cytology.
- DeLamater, E. D.—A new cytological basis for bacterial genetics.
- Lederberg, J., Lederberg, E. Z., Zinder, N., and Lively, E.—Recombination analysis of bacterial heredity.
- Ephrussi-Taylor, H.—Genetic aspects of transformations of pneumococci.
- Hotchkiss, R. D.—Transfer of penicillin resistance in pneumococci by the desoxyribonucleate derived from resistant cultures.
- Luria, S. E.—The frequency distribution of spontaneous bacteriophage mutants as evidence for the exponential rate of phage reproduction.
- Hershey, A. D., and Chase, M.—Genetic recombination and heterozygosis in bacteriophage.

#### CONCLUDING SESSION

- Mirsky, A. E.—Some enzymes of isolated nuclei.
- Sonneborn, T. M.—Some current problems of genetics in the light of investigations on *Chlamydomonas* and *Paramecium*.

#### APPENDIX

- Flory, L. E.—The television microscope.

#### Previous Volumes

- \* Vol. I (1933) Surface Phenomena, 239 pp.
- \* Vol. II (1934) Growth, 284 pp.
- \* Vol. III (1935) Photochemical reactions, 359 pp.
- \* Vol. IV (1936) Excitations, 376 pp.
- \* Vol. V (1937) Internal Secretions, 433 pp.
- \* Vol. VI (1938) Protein Chemistry, 395 pp.
- \* Vol. VII (1939) Biological Oxidations, 463 pp.
- \* Vol. VIII (1940) Permeability and the Nature of Cell Membranes, 285 pp.
- Vol. IX (1941) Genes and Chromosomes, 315 pp.
- \* Vol. X (1942) The Relations of Hormones to Development, 160 pp.
- Vol. XI (1946) Heredity and Variation in Microorganisms, 314 pp.
- Vol. XII (1947) Nucleic Acids and Nucleoproteins, 279 pp.
- Vol. XIII (1948) Biological Applications of Tracer Elements, 220 pp.
- Vol. XIV (1949) Amino Acids and Proteins, 217 pp.
- Vol. XV (1950) Origin and Evolution of Man, 425 pp.
- \* Out of print.



## LABORATORY STAFF

- \*Brandt, Jane — Research Assistant
- §Bruno, Dominic—Gardener
- Bryson, Vernon—Geneticist
- Corey, Perl Roy — Carpenter
- Cosillo, Gloria—Technical Assistant
- Deiches, Helen Cuneo — Research Assistant
- Demerec, M — Director
- \*Demerec, Vera Rada — Research Assistant
- Dittman, Ilse — Research Assistant
- §Dorsey, Henry — Laborer
- Farrington, Margaret — Technical Assistant
- Fickert, Kurt — Carpenter
- §Forgione, Louis — Research Assistant
- Franzese, Eleanor — Clerical Assistant
- Gardner, Henry — Technical Assistant
- Hershey, Harriet D. — Research Assistant
- §Hsie, Jen-yah — Bacteriologist
- \*James, Ina Pauline — Nature Study Course Instructor
- §Kaplan, Selma — Research Assistant
- Kaufmann, Bobbie — Research Assistant
- \*Kaufmann, Jessie — Dining Hall Manager
- Kern, Charles — Laborer
- King, James C. — Research Associate
- Klem, Dorothy V. — Secretary
- Lowell, Francis — Superintendent of Grounds
- Madden, Carol V. — Research Assistant
- McGunnigle, Edward C. Jr. — Research Assistant
- §Monsees, Howard — Research Assistant
- \*Patricia Moore — Nature Study Course Assistant
- Reddy, William — Laborer
- Rosenblum, Eugene — Bacteriologist
- \*Starr, Elizabeth L. — Technical Assistant
- Szybalski, Waclaw T. — Bacteriologist
- §Valentine, Robert — Electrician
- Wallace, Bruce — Geneticist
- \*Warren, Katherine B. — Editor of Symposium manuscripts.
- \* Summer and Temporary
- §Resigned during the year.

## SUMMER RESEARCH INVESTIGATORS

- Abramson, Harold A.—Cold Spring Harbor, N.Y.  
Adams, Mark H.—New York University College of Medicine, New York, N.Y.  
Bernheimer, Alan W.—New York University College of Medicine, New York, N.Y.  
Braun, Werner—Chemical Corps Biological Laboratories, Camp Detrick, Frederick, Maryland  
Bruce, Nancy Collins—New York University College of Medicine, New York, N.Y.  
Caspari, Ernst—Wesleyan University, Middletown, Connecticut  
Colowick, Maryda Swanstrom—New York University College of Medicine, New York, N.Y.  
Colowick, Sidney—The Johns Hopkins University, Baltimore, Maryland  
DeLamater, Edward D.—University of Pennsylvania, Philadelphia, Pa.  
Delbruck, Max—California Institute of Technology, Pasadena, Calif.  
Goldfarb, A. Roberts—The Chicago Medical School, Chicago, Illinois.  
Gots, Joseph S.—University of Pennsylvania, School of Medicine, Philadelphia, Pa.  
Granick, S.—The Rockefeller Institute for Medical Research, New York, N.Y.  
Kaiser, Armin D.—California Institute of Technology, Pasadena, Calif.  
Levan, Albert—Sveriges Utsadesforening, Svalof, Sweden  
Luria, S. E.—University of Illinois, Urbana, Illinois  
Maramorosch, Karl—The Rockefeller Institute for Medical Research, New York, N.Y.  
Marien, Daniel—Columbia University, New York, N. Y.  
Montalenti, G.—University of Naples, Naples, Italy  
Nason, Alvin—McCollum-Pratt Institute, The Johns Hopkins University, Baltimore, Maryland  
Perlmann, Gertrude—The Rockefeller Institute for Medical Research. New York, N.Y.  
Ratner, Sarah—New York University College of Medicine, New York, N.Y.  
Sager, Ruth—The Rockefeller Institute for Medical Research, New York, N.Y.  
Schaeffer, Morris—U. S. Public Health Service, Communicable Disease Center, Montgomery, Alabama  
Shemin, David—College of Physicians and Surgeons, Columbia University, New York, N.Y.  
Spirtes, Morris A.—The Institute for Cancer Research, Philadelphia, Pa.  
Stocker, B. A. D.—London School of Hygiene and Tropical Medicine, London, England  
Streisinger, George—University of Illinois, Urbana, Illinois  
Tittler, Irving—Brooklyn College, Brooklyn, New York  
Weinhouse, Sidney—The Institute for Cancer Research, Philadelphia, Pa.

## REPORT OF THE SECRETARY

The 61st meeting of the Board of Directors, postponed from January 30, was held on February 20, 1951, at the Down Town Association in New York City. Sixteen members were present. The 212 contributors during 1950 were ratified as Sustaining Members of the Association. The Secretary reported a postal vote of the Executive Committee in December approving the acceptance of the provisions of the Social Security Act for employees of the Biological Laboratory. The Director of the Laboratory reported that as a result of the general economic inflation the funds for building and improvements received last year were no longer adequate, and that therefore the building program was still an open question and the plans for modernization would have to be curtailed. Dr. Demerec then described some interesting results of the current research programs.

Although most of the research is supported by the Army and Atomic Energy Commission, it concerns basic problems of science. However, should the national emergency require the Laboratory's services, the scientific staff will be ready to adapt its programs accordingly. Plans for the Symposium on "Genes and Mutations" and for summer courses were outlined and commented on. The Treasurer, Mr. Morris, in presenting the financial statement, reported that the affairs of the Association were in good condition and running smoothly. He called attention to the change in the financial year to begin May 1. The proposed budget of the Laboratory for the period January 1, 1951 to April 30, 1952 was unanimously approved. President Murphy appointed a Nominating Committee consisting of Dr. Haskins, chairman, Mrs. Franklin, and Mr. Morris; and appointed Mr. Ames a member of the Finance Committee to replace Mr. Wood.

A meeting of the Executive Committee was held on May 31, 1951, at Blackford Hall in Cold Spring Harbor. Dr. Demerec, Director of the Laboratory, reported that additional funds amounting to \$20,000 would be required to complete the program of restoration of the Association's present buildings and property. He presented a statement of estimates, funds available, items of reconstruction already carried out, and those still to be undertaken. After careful consideration of this report, the Committee agreed that a special campaign should be organized to raise the necessary amount.

The 28th Annual Meeting of the Association, held at Blackford Hall on July 31, 1951, was called to order by Mr. Grinnell Morris. The Secretary reviewed the chief acts of the Association during the past year. Copies of the financial statement for the year ending April 30, 1951, were distributed by the Treasurer. The following members were named by the Nominating Committee and elected or re-elected to the Board of Directors: to serve until 1954, Dr. Helen Kellogg Edey; to serve until 1955, Dr. Lloyd V. Berkner, Dr. Caryl P. Haskins, Dr. B. P. Kaufmann, Mr. Grinnell Morris, Mr. Arthur W. Page, Mr. Franz Schneider, and Mr. Howland B. Stoddard. The Director of the Laboratory reported that work was about to

begin on the building program, additional funds for the Lecture Hall having been appropriated by the Carnegie Corporation and the Carnegie Institution. He briefly discussed some of the recent developments in research, described fully in the forthcoming Annual Report, and reported on the exceptional attendance at the Symposium. In conclusion Dr. Demerec summarized the financial situation with regard to support of research and provision for general upkeep, stressing the very important role of membership contributions in the basic economy of the Laboratory.

The 62nd meeting of the Board of Directors, postponed from July 31, was convened on September 23, 1951, at Blackford Hall, with eighteen members present. The Director of the Laboratory, restricting his report to problems of business, summarized in some detail the sources and apportionment of income for the Symposia, research, summer activities, and running expenses. Funds for year-round research are assured; and the Symposia have been so successful that it should not be difficult to obtain future support for them. What the Laboratory requires is an income of about \$10,000 per year from membership contributions, to cover expenditures and upkeep, and a special fund of \$15,000 to \$20,000 to bring the physical plant up to date. This report was discussed and accepted. The Treasurer requested and received approval for the investment of \$10,000 in specified securities. On motion unanimously voted, the Executive Committee was re-elected for the year 1952.

The 63rd meeting of the Board of Directors was held at the Down Town Association in New York on January 29th, 1952, with 16 members present and Dr. Robert Cushman Murphy presiding. The minutes of the previous meeting were approved as distributed. The names of 230 contributors during 1951 were presented by the Secretary and ratified as Sustaining Members for the year.

The report of the Director of the Laboratory announced that ground for the new buildings was broken in August and that allocations of critical metals had been granted. Among the advances made by the various research groups the completion of Dr. Bryson's Turbidostatic Selector was reported. This ingenious instrument automatically controls the unfavorableness of the environment according to the capacity of the bacteria to evolve: the harmful material is increased whenever the population of bacteria begins to enlarge as indicated by the turbidity. The subject of the 1952 Symposium was to be the physiology of nerve fibers. A grant of \$30,000 from the Carnegie Corporation will cover the expenses of the Symposia for the next 5 years. A new special course in Cytology of Microorganisms will be conducted by Prof. E. D. DeLamater of the University of Pennsylvania. An interim Financial report and the budget for 1952-53 were discussed and approved.

The 64th meeting of the Board of Directors was held on July 15th, 1952 at the Down Town Association, New York, with 13 members present, Dr. Robert Cushman Murphy presiding. The minutes of the last meeting were approved as distributed. It was decided to hold the September Open House as usual, postponing the Dedication of the new Lecture Hall until

spring. Mrs. Page reported on the special campaign to increase contributions. Dr. Murphy presented his resignation as President, an office he had held for twelve years. In his place Mr. Amyas Ames of Cold Spring Harbor was elected President and Mrs. Walter H. Page and Mr. Grinnell Morris Vice Presidents. The Executive Committee for the year was elected as follows: Amyas Ames, Mrs. G. S. Franklin, E. C. MacDowell, Grinnell Morris, Wm. B. Nichols, A. W. Page, Mrs. W. H. Page.

In taking the chair, Mr. Ames offered the remarks appearing as the foreword of this pamphlet.

The 29th Annual Meeting of the Association, held at Blackford Hall, Cold Spring Harbor, on July 29th, 1952, was called to order by President Amyas Ames. The secretary reviewed the chief acts of the Annual Meeting and two meetings of the Board of Directors during the past year, including the acceptance of the resignation of Dr. Robert Cushman Murphy as President, and Mr. Arthur W. Page as Vice-President; the election of Mr. Amyas Ames as President and Mrs. W. H. Page and Mr. Grinnell Morris as Vice Presidents.

The following resolution was presented and unanimously adopted:

In regretfully accepting the resignation of Dr. Robert Cushman Murphy as President, the Long Island Biological Association, assembled in its Annual Meeting of 1952, herewith acknowledges its indebtedness to Dr. Murphy for the many important and valuable services he has generously rendered the Association in this office, and its appreciation of the genial spirit of enthusiasm with which he has carried out these services. Throughout the twelve years of his Presidency, 1940-1952—which include the difficult war and post-war periods, Dr. Murphy maintained his vigorous devotion. His good judgment, poise and felicitous phraseology qualified him exceptionally well as Chairman of the meetings of the Board of Directors and the Annual Meetings of the Association.

His acceptance of the nomination to this office was largely prompted by his particular interest, as a native Long Islander, in the growth of cultural institutions in this area. As a direct contribution to the cultural life of the community, his deservedly popular lectures have been received with great enthusiasm and have greatly stimulated interest in Natural History and in our Association.

Under Dr. Murphy's administration, the research work of the Biological Laboratory has increased in quality, significance and volume. Special grants have progressively increased resources and long projected plans for improvements in the physical plant and for the new lecture hall have reached the final stages of realization.

Not only the members of the Board of Directors and of the Association, but all connected with the Biological Laboratory, are grateful to Dr. Murphy.

The following members were named by the Nominating Committee and elected or re-elected to the Board of Directors to serve until 1956: Mark H. Adams, Dr. Crispin Cooke, Mrs. G. S. Franklin, E. Carleton MacDowell, Wm. B. Nichols, Mrs. Alexander M. White, Jr., B. H. Willier.

E. Carleton MacDowell, Secretary

LONG ISLAND BIOLOGICAL ASSOCIATION  
FINANCIAL STATEMENT  
MAIN AND COMPANY

Certified Public Accountants  
New York, U.S.A.

Long Island Biological Association,  
Cold Spring Harbor, L. I., N. Y.

We have made an examination of the accounts of the Long Island Biological Association for the year ended April 30, 1952. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances.

In our opinion, the accompanying balance sheet and statements of income and expense and net worth, and supporting schedule, together with the note thereon, present fairly the position of the Long Island Biological Association at April 30, 1952 and the results of its operations for the year ended on that date.

Main and Company  
Certified Public Accountants

New York, N. Y.  
June 18, 1952.

**LONG ISLAND BIOLOGICAL ASSOCIATION**  
**BALANCE SHEET**

April 30, 1952

**ASSETS**

**General and Endowment Fund**

Cash:

In banks	\$ 26,245.71	
Onhand	100.00	\$ 26,345.71

Investments (market value \$28,048.73)		27,389.19
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Accounts receivable:

Josiah Macy, Jr. Foundation	\$ 219.44	
National Tuberculosis Association	506.64	
United States Department of the Army	9,491.52	
Miscellaneous	1,047.24	11,264.84

Land, buildings and equip-  
ment, at cost or  
appraisal values:

Land	\$ 86,466.52	
Improvements to land	2,898.01	
Buildings	101,265.00	
Land and buildings leased from Wawepex Society	49,700.00	
Equipment	57,940.32	298,269.85
		\$363,269.59

**Special Funds ;**

Cash in bank		\$ 687.12
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Investments (market value \$15,411.83)		15,710.00
		16,397.12

**Total**

**\$379,666.71**

**NOTE:** In accordance with the Association's established practice, the above balance sheet does not include the inventory at April 30, 1952 of the published volumes of the Association's yearly Symposia of Quantitative Biology, nor has any depreciation or amortization on buildings and equipment been recorded on the Association's records. Additions and improvements to buildings and equipment been charged against current operations in conformity with the Association's usual practice.



## LIABILITIES AND NET WORTH

### General and Endowment Fund

#### Liabilities:

Accounts payable	\$	890.43
Accrued payroll		788.25

#### Special grants and contracts:

The Jane Coffin Childs Memorial Fund for Medical Research	\$	405.27
United States Atomic Energy Commission		10,313.80

#### Total liabilities

\$ 12,397.75

Reserve for Scientific Research

3,000.00

#### Endowment Fund:

Dr. William J. Matheson

Bequest

20,000.00

Net Worth

327,871.84    \$363,269.59

### Special Funds

Blackford Memorial Fund:

Principal	\$	5,000.00
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Charles Benedict Davenport

Memorial Fund:

Principal	\$	4,934.75
Unexpected income		535.25

5,470.00

Charles Benedict Davenport

Junior, Fund:

Principal		1,037.12
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Temple Prime Scholarship Fund:

Principal	\$	2,500.00
Unexpected income		80.00

2,580.00

Dorothy Frances Rice Fund:

Principal	\$	2,256.64
Unexpected income		53.36

2,310.00    16,397.12

#### Total

\$379,666.71

## STATEMENT OF NET WORTH

For the Year Ended April 30, 1952

Balance, May 1, 1951	\$320,323.82
<b>Add:</b>	
Excess of income over expense for the year ended April 30, 1952	7,548.02
	\$327,871.84
Balance, April 30, 1952	

## STATEMENT OF INCOME AND EXPENSE

For the Year Ended April 30, 1952

Income:

Contributions:

Dues and contributions	\$ 6,163.94	
Special appeal for buildings and grounds improvements	4,230.00	
Carnegie Corporation (grant for annual Symposia)	6,000.00	
Wawepex Society	1,650.00	
John D. Jones Scholarship	500.00	\$18,543.94

Symposia:

Book sales	\$12,752.56	
Registration fees	208.10	12,960.66

Dining hall

Rooms and apartments		13,019.03
Research fees		12,339.58
		7,215.81

Interest and dividends

on investments		818.85
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Other income:

Summer course tuition	\$ 2,179.00	
Nature study course	35.51	
Beach permits	47.92	
Annual distribution from Walter B. James Fund	150.00	
Miscellaneous	616.12	3,028.55

**Total income**

**\$67,926.42**

Expense:			
Symposia:			
Publication of annual Symposia on Quantitative Biology	\$12,263.90		
Expense of participants and lecturers	5,199.87	\$17,463.77	
Dining hall		10,887.21	
Rooms and apartments		3,223.16	
Research expenses		2,327.61	
Summer course expense		833.44	
Bad debts		348.00	
Distribution of John D. Jones Scholarship		500.00	
Building and grounds maintenance:			
Salaries	\$ 8,524.34		
Materials and supplies	5,303.04		
Heat, light and water	3,025.11	16,852.49	
General and administrative:			
Salaries	\$ 5,120.11		
Insurance	987.35		
Printing and stationery	839.30		
Telephone, telegraph and postage	251.22		
Other	744.74	7,942.72	
Total expense			60,378.40
Excess of income over expense			\$ 7,548.02

# STATEMENT OF GRANTS AND CONTRACTS FOR SPECIAL RESEARCH

For the Year Ended April 30, 1952

From Whom Received	Balance	May 1, 1951	Transactions		May 1, 1951 to	April 30, 1952	Balance	April 30, 1952
	Due to Association (Accounts Receivable)	Unexpended Balance of Grant	Amounts Received	Expenditures Charged Against Grant	Income to Association Charged Against Grant	Due to Association (Accounts Receivable)	Unexpended Balance of Grant	
The Jane Coffin Childs Memorial Fund for Medical Research		\$ 405.27						\$ 405.27
The Commonwealth Fund			\$ 8,000.00	\$ 8,000.00				
Josiah Macy, Jr. Foundation		789.17		858.61	\$ 150.00	\$ 219.44		
National Tuberculosis Association	\$ 608.93		6,346.17	5,784.03	459.85	506.64		
Polio Basic Research Fund of Long Island		540.09		540.09				
Rockefeller Foundation Grant		13,324.68		13,324.68				
United States Atomic Energy Commission		11,935.87	32,107.00	31,125.75	2,603.32			10,313.80
United States Dept. of the Army	8,391.89		24,719.09	22,876.08	2,942.64	9,491.52		
Viking Fund		616.12			616.12			
Wenner-Gren Foundation for Anthropological Research			2,500.00	2,500.00				
<b>Totals</b>	<b>\$9,000.82</b>	<b>\$27,611.20</b>	<b>\$73,672.26</b>	<b>\$85,009.24</b>	<b>\$6,771.93</b>	<b>\$10,217.60</b>		<b>\$10,719.07</b>

