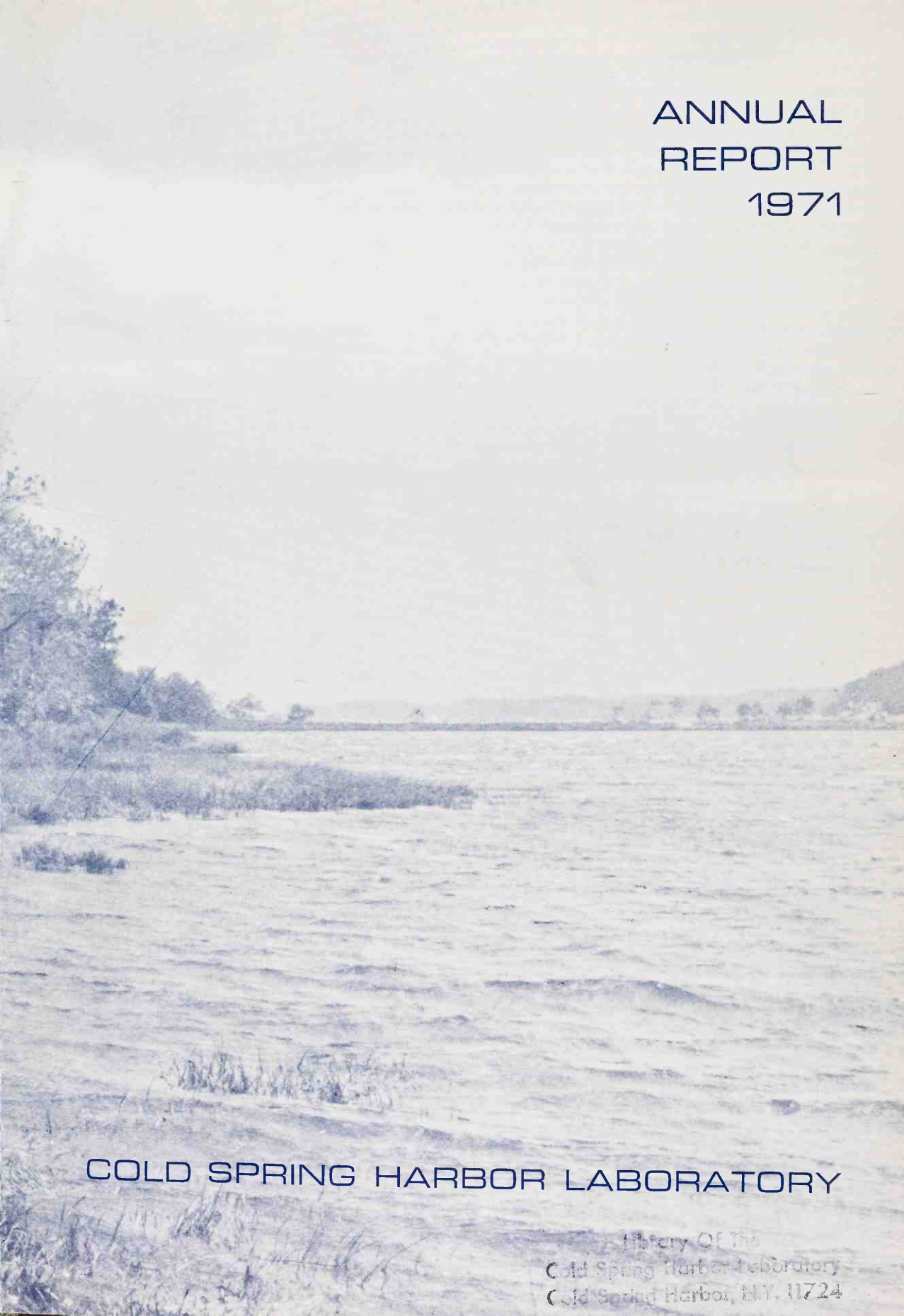
ANNUAL REPORT 1971



COLD SPRING HARBOR LABORATORY

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Cold Spring Harbor, Long Island, New York

ANNUAL REPORT 1971

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COLD SPRING HARBOR, NEW YORK

The distinction between pure and applied science is more easily made by politicians than by practicing scientists. We seize upon a phenomenon because some aspect of it intrigues us, not the least being the possibility that it is not as messy as most people in the past have thought, and that some insight on our part will make it readily explainable in terms of laws of nature that already have wide acceptance. We, of course, worry whether an explanation has wide generality or whether its consequences are so specific as to interest only its discoverer. And we do not relish the thought that we may have tackled a problem so easy that many others will jump in and credit for the discovery will be synonymous with victory at bingo.

Outsiders now witnessing the current dash to enshrine work in cancer research with the fearless computers and chrome-plated environment that marked our past devotion to the moon's surface must wonder what motivates this new breed of public figure. Are they the same people who a few years ago flourished in immaculate Houston suburbs, but now know that our nation is fed up with military and space and that Congress is more than uneasy for being a willing partner in the Vietnam that we masked with the platitudes of national esteem and parochial self-righteousness? For this debacle shows every sign of remaining a malignant sore on our moral fiber with no sign of simple correction. So we must wonder to what extent the current American hysteria to conquer cancer within the next decade arises from the feeling that an infirmity which strikes without respect for social, racial, or economic class must be an easier objective than a moral cancer which grows out of a nation's incapacity to acknowledge the conveniently remote victims of its surgical bombing strikes.

For now, our people are fed up with the catastrophic misuse of their resources by a succession of presidents that their congressional representatives have been unable to control. They would like to strike back and actually see some public good. The question thus becomes, have they seized upon a suitable goal or have they again been sold a bill of unattainable goods, this time by a brand new set of lobbyists who, despite their noble outpourings, are all too easily matched up with a constituency afraid of their future and worrying whether Congress's support of health research will last until their kids are out of college?

Current State of Cancer Research

For an honest answer, we must examine the current state of cancer research and, in particular, look at the origins of the various scientists who have settled for this career. Are they in cancer institutes primarily because of humanitarian feelings, working tirelessly to bring a halt to this most vicious form of human suffering? Or were their career choices the result of the widespread knowledge that cancer money is both the easiest to obtain and the most difficult to choke off and that it is better to do dull science than no science at all? Or are they motivated primarily because cancer is a phenomenon filled with countless intellectual puzzles that must inevitably attract some of the best of our scientific minds?

Without difficulty we can pinpoint individuals who fit each of these pigeonholes, as well as others whose motivations are more complex. The vast majority, however, are in cancer research from a personal desire to alleviate suffering, being supported by various personal and governmental monetary funds specifically created to provide the wherewithal to somehow check cancer. Today most cancer research is carried out by medically trained people who, after becoming frustrated by their inability to alter the course of most cancer cases, have decided that a career in clinical research would be much more satisfying than a lifetime of effectively

impotent ward rounds. To be sure, there also exist many individuals who have chosen cancer research because they smell easy money, and no doubt there will be even more if cancer money explodes in the fashion now predicted. But up until now, this latter group has not been a significant factor in the organization of cancer research, and to a very large degree the people who direct the course of cancer research laboratories are also deeply involved in the life and death aspects of the clinical wards associated with their research institutes.

They are more than aware of their dual constituency composed of the wretchedly sick and their anxious relatives, and so, at times, quietly despair for the emergence of even minor clues that will allow them occasionally to seem optimistic and expectant of real progress. Hampering any rationalization of their effort, however, has been the fact that there has existed no solid intellectual framework around which they could organize any rational attacks on the disease. No possibility existed of a meaningful interaction between the worlds of contemporary biology and clinical cancer research as long as there existed no comprehensive understanding of the fundamental principles that govern the existence of living cells. That is, as long as biology remained a disconnected set of unorganized observations, its knowledge could not be brought to bear on the cancer problem.

Conversion of Biology into a Serious Intellectual Discipline

This was the dominant fact that led, early in the 1950's, to the creation of the National Institutes of Health (NIH). Largely on the advice of perceptive cancer clinicians like Sidney Farber, Congress was convinced that the only rational way to ensure the emergence of new medical advances was a broad support of all aspects of biology. Then it could have the possibility of a spectacular growth of its basic principles similar to that which occurred in physics and chemistry in the interval between the two World Wars. Within a short time after the founding of NIH, large sums of money began to pour out in support of biology, followed soon after by a series of signal advances in the understanding of cell heredity that greatly exceeded the prognostications of even the most rabid promoters of the new biology.

Most of these new insights by themselves, however, have had little direct application to the problem of the clinicians in cancer hospitals. During the past two decades the vast majority of our biochemically inclined biologists focused their efforts on the bacterial cell. They did not want to risk almost certain failure by attacking the much more complicated cells of human beings before they thoroughly understood the fundamental chemical rules that make possible the existence of the bacterial cell.

In finding itself able to understand the heredity of bacteria at the molecular level, biology as an intellectual discipline has begun to acquire a solid professorial status, long the trademark of the apparently more rigorous chemists and physicists. No longer is a biologist arbitrarily thought to be an intellectually inferior breed of scientist. Because of the innumerable remaining major intellectual challenges still facing biology, it attracts for the first time many of the best students who wish to do science. On the whole, most opt for work with the higher cells of vertebrates, not because they know this is where the money lies, but because animal cells now seem intriguingly tractable in much the same way that bacteria looked to me twenty-five years ago when I first began to work in a university laboratory.

For fields of science have their own momentum or nonmomentum, depending on whether the current experimental techniques are capable of moving them forward. Often it is all too obvious that a given key question cannot be answered with the current instrumentation and that, barring some unexpected insight, it is best left for another generation of scientists to take up. This may very well be the case today in the fields of human perception and memory, where the frightful anatomical complexity of the vertebrate brain poses a virtually impenetrable jungle for even the most talented experimentalists.

In contrast, there exists a firm basis for the belief that the essential biochemistry of human

cells can be worked out within the next decade or two. Even though today we still are completely in the dark about how vertebrate chromosomes function and have no good ideas about the detailed architecture of the outside surfaces of cells, there already exist the experimental techniques and machines which, when correctly applied, should quickly lead to important new concepts. This is not to say that further advances will be straightforward. Future progress with mammalian cells will be strongly influenced by the organizational setup within which the individual scientist works.

The most effective laboratories are likely to be those in which large numbers of people with closely related interests work simultaneously. While no doubt many key findings will come from solitary individuals working with total indifference to their neighbors down the hall, in general, I do not believe this approach will be productive. This is because the inherent complexity of the mammalian cell may be several orders of magnitude greater than that of the now familiar bacterial cell. A given experiment with a mamalian cell usually takes some ten times longer and requires a correspondingly greater sum of financial support. Conceivably, someone will come up with a really cheap way to experiment on human cells but now the odds are much against such breakthroughs. Common sense argues that many more people must be involved in establishing a given point than when bacteria are the object of investigation.

We thus must create the organizational framework which not only makes possible, but strongly encourages, the development of research groups of some 10-50 scientists, all of whose research focuses on the fundamental molecular biology of higher cells. Numbers of this size will allow each lab to possess the variety of complex instrumentation often necessary to carry out key experiments. Today it no longer makes sense to regard experimental biology as a cheap science, with high-energy nuclear physics the only big consumer of scientific money. Setting up a minimal lab for higher cell work can easily take more than $100,000—an amount of money far greater than that now usually given to single investigators. But sums this great are likely to be allocated only when the granting agency knows that the equipment it provides is to be used by a number of different people, not when its use is solely the privilege of one person.

Thus, hopefully, those institutions which will be the recipients of much of the largesse coming from the newly-voted cancer research funds will be those which make staff and space commitments that will quickly permit the creation of large labs with a critical personnel mass. Such decisions, however, will not be taken lightly by intelligent university presidents or medical school deans. Already most schools have staffs larger than their real financial resources warrant and another round of expansion of research facilities should necessarily unsettle the equilibrium of any sensible administrator. For he knows that not only is money from a federal pipeline subject to highly unpredictable fluctuations, but even in the best of years, the way federal money is given almost always insures the need for a recipient to raise additional funds to cover the true overhead.

Our nation's medical schools and universities thus cannot afford to increase their commitments to fundamental cancer research unless they receive assurance that Congress appreciates the difficulties that may lie ahead. Serious doubts whether Congress will hold interest in cancer research unless solid new clinical success is soon forthcoming would certainly scare off the sensible and leave the field to a combination of charlatans and fools. Even if the coming decade is marked by virtually unlimited money, observations with real therapeutic consequences may not occur and may only appear after still another decade or two of massive federal aid.

Creation of the Yarborough Citizens Committee

Knowledge of these harsh facts was certainly a key component in the creation two years ago of Senator Yarborough's Citizens Committee to assess the current status of cancer research and treatment within the United States. When it came into existence the aura of financial stagnation that prevailed throughout the scientific community, together with the attendant corollary that

we have more scientists than we can feed, argued strongly against further expansion of cancer research. Had the Yarborough Committee not materialized, the pace of fundamental cancer research within the United States would soon be far less than our national capability.

The recent passage of the Conquest of Cancer legislation is thus an act of major importance. We must not assume, however, that the battle is over. Unless the money is well spent, vast sums will be passed out without visible long-term influence on the treatment of most cancers. This disquieting thought was behind most of the controversy in Congress as to whether a brand new cancer agency, under some super-czar, should be set up independent of the National Institutes of Health, the federal body now responsible for most health-oriented research. Proponents of this scheme argued that the current beaurocratic setup with NIH was ossified and that much forward momentum could be generated by giving more real power to the true cancer researcher, whose freedom for action was often unnecessarily restricted by administrative hurdles.

In contrast, opponents of the superagency argued strongly for keeping cancer research within the domain of NIH. Behind this seemingly conservative approach was the argument that most fundamental cancer research is so interconnected with other forms of medical research that to separate it might so confuse the purpose of NIH as to lead to its essential dismemberment. Also making many scientists and clinicians leery of abandoning the NIH framework was the fear that the creation of a powerful czar would lead toward a monolithic research effort disproportionately influenced by the prejudices of a small number of opinionated operators. One of the greatest virtues of the NIH has been its capacity to give support to all sorts of different ideas. Given the unpredictable nature of research, this approach maximizes the probability that something really new and pertinent will pop up. Given our very incomplete grasp of what cancer cells are like, putting all our eggs into only a few baskets would make sense only if the cancer problem were much more highly defined than is now possible. Conceivably there exists some individual whose ideas are worth ten million or so dollars to test, but I have yet to meet him.

Moreover, the National Cancer Institute (NCI), the component within NIH primarily responsible for cancer research, now utilizes either as direct employees or as active consultants virtually every trained American capable of giving intelligent direction to the cancer area. No group of unused talents now exists that could be brought into the government to supplement the pre-existing advisors. A super-cancer agency, if brought into being, would in essence by the National Cancer Institute renamed, not a brand new entity with its own new ideas.

In addition, cancer research already is, and will become even more, a highly trained discipline requiring many years of professional training in biochemistry, cell biology, immunology, and molecular biology. Thus, newly created cancer programs cannot use the highly trained professional now underemployed because of cutbacks in the aerospace industry. Such people could be utilized only if they were to begin their education anew and acquire new professional degrees. Recruitment of the many new professionals who will be needed for the cancer research of next decade most likely will occur from students already, or soon to be enrolled, in conventional M.D. and Ph.D. programs that are now supported by one or more of the various branches of NIH. At least for some years we must substantially enlarge these NIH-backed training programs, so as to ensure that research of cancer uniformly acquires the high professional standards long associated with the physical sciences.

Decentralized Research: A Wise Decision

So the recent Congressional verdict to keep cancer research decentralized within the NIH framework strikes me as a wise decision. The administrative ball game thus is back where it started, with the NCI still the dominant agency controlling how cancer money is dispensed. And as before, the existence of scores of different advisory bodies will ensure that many fingers are in the pie. Admittedly it is so much a fatter one that its future distribution by the NCI administrators is very much in doubt. They could opt primarily for long-term results by

allocating a significant portion of the money to learning the precise chemical details of human cells. Or they could blanket much more cancer therapy under the umbrella of "clinical research" and construct a series of brand new hospitals, with emphasis on regions now lacking the hospital resources of major medical centers like Boston, New York, and Houston.

Most likely the NCI (as would have the superagency if it had been created) will put their money largely on the short-term option. In doing so, they will optimistically argue that pre-existing methods of therapy might have to be only slightly modified to produce real dividends and that the best way to insure that the right new protocols for treatment are devised is to create new hospital centers specifically designed to decide between alternate methods of therapy. But from cruel experience the leaders of NCI must inwardly fear that, barring the emergence of radically new ways to cure the major cancers, the chief effect of a massive new round of hospital-building will be to provide more cheerful places to die. The main dilemma the clinician lives with is not his failure to keep abreast of new discoveries which could cure his patients but the essential absence, in even the newest cancer hospitals, of effective ways to check virulent cancers like those of the breast and the lung. Setting up of speedy all-inclusive information exchanges to reshuffle current knowledge is likely to enrich only the stockholders of computer companies. But the average citizen, as well as his congressmen, will badly want some short-term result to show for his money and so will be reassured by the sight of a fine new edifice equating glimmer with more effective therapy. We must expect that much, if not most, of the new cancer money will buy patient care, not true research.

Fortunately, the massive funds just voted by Congress mean that even a small share of the pie is a lot of money and most likely sufficient to create a large number of first-rate new research groups whose existence would be impossible without the new money. The real question thus becomes *will this happen or will the NCI leadership just pour out the money without any real plan of action?*

My suspicion is that the answer will largely depend upon the actions of the younger scientists just entering cancer research. It is this group whose research future is still very unclear. All too easily their efforts can be wasted through working under conditions where they have no real chance of pulling off something big. But if they collectively act to insure that they become part of flexible new departments (institutes) that accept the fact that cancer research must be done on a big scale if it is to be done intelligently, then I believe the financial wherewithal will be found within the NCI, and eventually the universities, so as to let them do real jobs. Some may argue this is too important a decision to be left by default in the hands of the young. But I suspect they know better than anyone else where science can go and, all things being equal, will set up the types of research groups that make the most sense. We would be remiss, however, not to leave them with the warning that if they act individually, leaving the important administrative if not scientific decisions to their committee-ridden elders, they may very well have lost their only opportunity to face a wide open frontier.

And the American public will once again wonder where their money has gone.

Highlights of the Year . . .

Receipt of a Center Grant from NIH

Over the past few years several major laboratories, whose research falls largely within the domain of cancer research, have received substantial institutional grants to cover key staff salaries and research costs. In large part, such "center grants" make individual research grants unnecessary and greatly facilitate long-term planning and staff recruitment. Given such support, institutes like ours that lack meaningful endowments are able to attract new staff with firm long-term offers of salary and research fund support. By last May, we believed that our recent building and renovation efforts, together with the many new staff members already appointed, had put us in a position where a center proposal to the National Cancer Institute might meet

with success. We thus put together in one package a series of interconnected research proposals that would not only provide stable support for most of the current staff, but also enable us to make several important new staff appointments.

This application, after going through the normal channels for grant review, came before the Council of the National Cancer Institute in late November and to our great satisfaction was approved in almost the form we initally requested. As a result, for each of the next five years, we shall receive approximately $1,000,000 for support of cancer-related research. This amount, no matter how you view it, is a very large sum of money and provides us with an unparalleled opportunity for research of high distinction.

In the first phase, we plan to finish the re-equipping of Demerec Laboratory. There we will provide Bob Pollack with a modern laboratory for the culture of animal cells, set up new chromographic facilities for protein and nucleic acid structural work, and construct a comprehensive "hot lab" for work with radioactive compounds. Also provided by the center grant will be money to maintain key facilities like our new machine shop in the "Animal House."

Opening of the Annex to the James Laboratory

In the middle of January, construction was completed on the new addition to the James Laboratory, imaginatively designed by the New York architect, Harold Edelman. It was designed primarily for use by our group of scientists whose research activities center on the tumor virus SV40. It also provides us with a spacious new seminar room, as well as allowing me to have my office in a building where I can talk science, not administration. After about a year of occupation, we continue to feel that the building is a great success. Not only is it visually very pleasing, but more importantly, for the first time it gives the tumor virus group a feeling that its facilities are becoming equal to the problem it wishes to solve.

Even with the new space, however, our research area in James is still very crowded and we have just made plans to add a second annex, this time to the west. We would like construction to start in mid-March of this coming year. The new space, which is being designed for the growth of animal viruses and which we expect to cost between $50,000 and $75,000, would then become available by the end of the year.

Publication of the Phage λ Book

The second of our monograph series, *The Bacteriophage Lambda,* came off the press in early October. Edited with great skill and tact by Al Hershey, it provides the most detailed examination of any viral system now in print. Initial outside reactions are very favorable and everyone agrees that it will be hard for subsequent books in this series to maintain the standards set by Al and his many collaborators. As lambda almost always is too difficult for outsiders to understand, the scientific community is much in debt to Al for the almost year-long effort which went into the editing process, a task in which he was ably assisted by his wife Jill and Perch Fisher.

Our next publication, a laboratory manual on bacterial genetics by Jeffrey Miller, is now going into page proof and should be available by late April. It was originally conceived as a short spiral-bound book, based largely on written material already available from our bacterial genetics course. Now with time, it has become much larger and will appear with sixty-three experiments instead of the twelve initially planned. Behind this change in scope was the thought that now was the time for a comprehensive book containing virtually all the key methodology of bacterial genetics that we feel will still be at the center of biology for many years to come.

Still in the middle of seemingly endless revision is our book on animal tumor viruses. Though it was scheduled for publication some months ago, the rapidly changing landscape of the tumor

virus field makes it a hard book to complete. We are constantly tempted to include some new result or to add more background material so that its potential audience can extend down to the student level. Now we aim to have it ready for next fall when we hope it will materially upgrade the teaching of cell biology to students in both medical and graduate schools.

Most sadly, we must report the death on December 24 of Mrs. Leonora Frisch, who for some ten years directed our Publication Department. Lee's remarkably good grasp of the publishing world was an invaluable asset to our well-being. With her sense of what makes a good book, our Publication Department, despite its minuscule size, was a decisive factor in keeping this Laboratory's finances in the black during the several most difficult years following the 1962 reorganization. In particular, I shall remember the cheerful way she combined an excellent head for business and book design with an inherent sense of what was good taste, knowing when she should push a tardy author and when he was best left alone.

Now in charge of our publications is Glen Lyle, formerly the Production Manager of the scientific publishers, W. A. Benjamin, Inc. Glen's broad experience in overseeing the publication of a variety of scientific books should be invaluable as our publication program expands.

Inauguration of the Neurobiology Program

This past summer witnessed the first year of a neurobiology teaching program begun with the help of the Sloan Foundation. In June some twenty-two students of quite diverse backgrounds attended a three-week lecture-demonstration course organized by Regis Kelly of the Neurobiology Department of Harvard Medical School. During the following month, ten of these students stayed on for a laboratory course where they did experiments on the giant sea slug, *Aplysia californica.* Taught by Philip Ascher, JacSue Kehoe, and Roger Thomas, its obvious success makes us confident that total strangers to neurobiology, when bright and motivated, can quickly pick up technical competence in microelectrode recording.

During the coming summer we shall repeat these two courses, and during August, hold one or two workshops on more specialized topics. Their format in large part will depend on our success in obtaining new funds to supplement our Sloan grant. Therefore, we are actively exploring additional neurobiology funding.

Crucial to the success of last summer's program was the extensive, if not almost total, renovation of the "Animal House." Built in 1912, this building had been abandoned as a serious lab since the construction of Demerec Laboratory. Now through the tireless efforts of our Building Superintendent, Jack Richards, it is in effect a new building, with new heating and plumbing as well as air conditioning. On the second floor are a series of five small teaching labs, each designed for one "setup" of electronic equipment; two rooms for biochemical work; a lab for summer research; a large office room for the instructional staff; and a seminar-library room. On the ground floor are two rooms for holding marine invertebrates, cold and dark rooms, more research space, and an electronic machine shop. For visitors who knew the Animal House as it lay in decay, the present status is almost a miracle.

A New Summer Course on Chromosomes

Last winter we came to the conclusion that the Phage Course initiated by Max Delbrück and continuously given since the summer of 1945 was no longer needed. We did not come to this decision because at long last we found phages dull, for they still provide answers to many important problems. Instead, we were motivated by the knowledge that universities throughout the world now feature phage work as a key item of their curriculum, so it is no longer necessary to come to Cold Spring Harbor to learn how to do phage experiments. But just the contrary is now true for work on chromosomes of higher plants an animals. The strong emphasis which biology departments formerly devoted to classical chromosomal cytology no longer exists and many young molecular biologists never learn even the most elementary facts about the behavior

Animal House in its newly remodeled form. The center for our summer neurobiology programs.

of eucaryotic chromosomes. Therefore under the guidance of Charles Thomas, a new course was instituted last August on "Molecular Cytogenetics." Its aim was to bring cytologists, who work with the light microscope, together with the molecular biologists, who are happiest when thinking at the level of molecules only directly observable with the electron microscope (EM).

Because of the limited facilities available in Davenport Laboratory, its activities flowed over into the Animal House as well as Demerec, the site of our EM. Next year, however, the Animal House space no longer will be available owing to the expansion of the neurobiology program, and we shall be forced to restrict the scope of this course until we can come up with funds to make Davenport suitable for EM work.

Continued Support by the Long Island Biological Association

The knowledge that our neighbors stand strongly behind our efforts has always been one of our great assets. Membership in the Long Island Biological Association (LIBA), the local body set up to channel community support, increased at new record levels, thereby generating much-needed unrestricted financial support. Its annual general meeting held on January 24 featured Dr. Roger Payne of The Rockefeller University, telling about how whales communicate with each other and giving us the opportunity to hear his most unique recordings of the songs of individual whales. During the June Symposium a number of LIBA members had dinner parties for our many participants from overseas. For providing most delightful interludes in an otherwise very demanding Symposium schedule, we are most indebted to Mr. & Mrs. Edward Pulling, Mr. & Mrs. David Ingraham, Mrs. Hoffman Nickerson, Mrs. Alex M. White, Dr. & Mrs. Franz Schneider, Mr. & Mrs. George N. Lindsay, Jr., and Dr. & Mrs. Bayard Clarkson.

Wawepex Building—from whaler's storehouse to modern dormitory facility.

Restoration of the Wawepex Building

In the days when Cold Spring Harbor was a tiny whaling port (1835-1860), there stood on its shores a variety of buildings directly connected with outfitting its ships and housing their crews. Our Lab site contains three such buildings: Williams House and Hooper House served as residential dwellings, while Wawepex functioned as a small warehouse. When this Lab came into existence in 1890, Wawepex was converted into the first lecture hall. Then, after Blackford Hall was built, a third story was added and it became a makeshift laboratory. By 1945 its limited facilities no longer were adequate for real experimentation and Wawepex functioned solely as the headquarters for the Children's Summer Nature Program. Because of structural deterioration, even this use, however, was prohibited by 1960 and everyone assumed that the building must be torn down. Fortunately, the Lab was then too broke to put up the money for that purpose.

Wawepex then remained essentially an empty shell until a gift made two years ago by Manny Delbrück let us draw up plans to give it a fourth life, this time as a dormitory guesthouse. Jack Richards and our building crew began work late last fall and, by diligent labor through the winter, had ready by the first of June a handsome year-round dwelling that features air conditioning and very fine views of the harbor. Over the summer it generally housed sixteen students at a given time and so made possible a greater number of summer guests that accompanied the starting of our neurobiology program.

Our Cash Reserves Remain at a Low Level

The accompanying financial statement to this report displays a further increase in our

budget while our cash reserves remain at a minimum level, barely sufficient for the wide fluctuations in cash flow that go with our expanded research and summer programs. Nonetheless, we felt that it was more important to continue our program of capital improvements than to build up a better cash position. This decision could not have been made without the realization that in William Udry the Laboratory has acquired an extremely talented Administrative Director. From the moment of his arrival a year ago, Bill acquired the complete confidence of our Staff and was quickly realized as indispensable. Now he is ably assisted by our new Comptroller, William Keen, who quickly had to master our accounting efforts when his predecessor, Daniel Hayes, most suddenly died of a heart attack in early June. Dan's two years at the Laboratory were marked by great devotion and all here deeply appreciated his efforts on our behalf.

Our Need for Unrestricted Money Continues

A key fact of life for everyone administering research grants is the failure of overhead allotted by the Federal Government to cover all the indirect costs incurred in administering the grants and maintaining the research laboratories. Thus, the great expansion over the past few years in the money that we receive as grants means that we are more dependent than ever upon the help received from local neighbors, our scientific alumni, foundations, industrial sponsors, and participating institutions. Without their support this past year, none of our building renovation programs could have gone forward. The fear that we might once again begin to physically fall apart will always be in our minds. Hopefully, we will continue to receive solid support from our past friends as well as many new ones.

We thus can look forward to the New Year.

December 31, 1971 *J. D. Watson*

DR. BARBARA McCLINTOCK
Medal of Science 1970

A foremost investigator in cytogenetics (the study of chromosome behavior), Dr. Barbara McClintock received the 1970 Medal of Science for her research which resulted in "establishing the relations between inherited characters in plants and the detailed shapes of their chromosomes and for showing that some of the genes are controlled by other genes within chromosomes." She was the first woman to receive the country's highest award for achievement in science and President Nixon made the presentation in a March 1971 ceremony at the White House. Dr. McClintock is a Distinguished Service Member of the Carnegie Institutions of Washington. She has worked at Cold Spring Harbor since 1942.

MOLECULAR BIOLOGY OF TUMOR VIRUS

J. Sambrook
W. Keller
C. Mulder
H. Westphal
P. Sharp
U. Pettersson
B. Ozanne
W. Sugden
A. Jackson
D. Day
I. Wendel
E. van Alphen
N. Sullivan
M. Lurye
J. Maroney
T. Wilson
B. Weiser
N. Aust
B. Root
A. Merrill

During the past year we have continued work on polyoma virus and SV40 and have begun experiments with adenovirus type 2. Several topics are under investigation.

Transcription of viral genomes in vitro

SV40: Henry Westphal, in collaboration with Hajo Delius, has obtained electron micrographs of *in vitro* transcription complexes of SV40 DNA and *E. coli* RNA polymerase. This confirms earlier findings (Westphal, 1970) which indicated that *E. coli* RNA polymerase can pass its own initiation site and proceed into a second round of transcription on the circular DNA, thereby producing RNA of more than unit length. However, no reaction conditions for *in vitro* transcription have yet been found which allow RNA synthesis from unique promotor regions.

Adenovirus: Conditions have been worked out for optimal RNA synthesis by the *E. coli* polymerase with adenovirus type 2 DNA as template. The transcription has been studied by electronmicroscopy (H. Delius) and the synthesized RNA has been analyzed by competition hybridization. Contrary to previous reports the bacterial polymerase has been found to initiate RNA synthesis apparently at random and RNA chains have been identified which correspond in length to the major portion of the adeno-DNA. Competition hybridization studies between "early" and "late" *in vivo* made RNA and RNA synthesized *in vitro* by polymerases from *E. coli* and KB-cells have been started.

RNA polymerase has also been isolated and partially purified from adeno-infected KB-cells and compared to enzymes from uninfected cells. DEAE-chromatography and rate zonal centrifugation did not reveal any differences between polymerases in uninfected KB-cells and cells which were harvested 18 hours after infection.

DNA-protein complexes

From uninfected cells: *In vivo* transcription complexes have been isolated recently from *E. coli* (Stonington and Pettijohn, 1970) and we have developed a way to apply the same method to mammalian cells. When 2 x 10^6 cells are lysed for 10 minutes in 1% Triton-X in 0.2*M* salt and centrifuged at 10K for 20 minutes in a sucrose gradient, a rapidly-sedimenting complex can be isolated which contains most of the RNA polymerase activity of the cell, all of the cell DNA and all of the nascent RNA chains, but only about 1% of the total cell protein. This complex is active in synthesizing RNA *in vitro,* when the appropriate precursors are added. We intend to continue characterization of the properties of this transcription complex by a variety of techniques, including electron microscopy, density gradient centrifugation, sensitivity to actinomycin, alpha amanitin, etc., *in vitro.* Finally, since the complex contains only a few proteins that are detectable on polyacrylamide-SDS gel electrophoresis, it should be possible to search among these proteins for those which are associated with the mammalian RNA polymerases, and which modify their function.

SV40 DNA containing complexes from lytically infected cells: SV40 DNA which is freed by mild detergent treatment of productively infected monkey cells sediments three times faster than naked marker DNA through neutral sucrose gradients. Proteins and RNA are found to cosediment with the DNA. The electron microscope picture shows viral DNA complexed with proteins and seemingly folded to a structure which is much more compact than that of naked DNA. We are presently trying to characterize these proteins and their function. It is thought that these complexes contain elements which are involved in viral DNA processing and/or virus maturation within the host cells.

From adenovirus particles: A protein-DNA complex has been isolated from purified adenovirions after treatment with 10% pyridine. This artificially produced core contains two polypeptides of molecular weight 17000 and 45000. Electronmicroscopy suggests that the DNA is homogeneously covered with protein in this complex. In line with this, it has been found that the RNA polymerase from *E. coli* does not transcribe this entity. Experiments with KB-cell polymerases and the protein-DNA complex have been started.

Isolation and characterization of mammalian RNA polymerases

A procedure has been worked out for the large scale extraction of these enzymes from KB and HeLa cells, grown in culture.

Treatment of homogenized cells with 0.5M ammonium sulfate solubilizes the enzyme activity. After high speed centrifugation and ammonium sulfate precipitation, the RNA polymerase activity can be separated into two types by chromatography on DEAE cellulose. Type II activity differs from type I by a pronounced preference for single stranded DNA as template and its sensitivity for α-amanitin. Both types of enzyme have been further purified by zonal centrifugation, chromatography on DNA cellulose and isoelectric focusing. Their subunit structure is presently being determined.

A study has been begun on the *in vitro* transcription of SV40 and adenovirus DNA by the purified RNA polymerases.

In addition, two proteins from KB cells have been purified which selectively stimulate the transcription of double stranded DNA by type II RNA polymerase. The stimulation occurs at the initiation step of RNA synthesis and could be due either to interaction with the enzyme or to a reversible structural change in the DNA template. This question is currently under investigation.

RNAse H, a nuclease which specifically degrades the RNA strand of DNA-RNA hybrids (Stein and Hausen, 1969) has also been isolated from KB and HeLa cells. The enzyme has been purified by chromatography on DEAE cellulose, phosphocellulose, agarose, DNA cellulose and hydroxyapatite and by isoelectric focusing. It is an endonuclease and the products of its degradative action are currently being characterized with the use of synthetic DNA-RNA hybrids.

Isolation of replicating adenovirus DNA

Procedures for selective extraction and purification of adenovirus DNA from adeno-infected cells have been studied. It has been found that the adenovirus DNA is quantitatively extracted from infected suspension cultures by the Hirt procedure. Cells infected with adenovirus type 2 exhibit after pulse-labeling with ^{3}H-T on sedimentation in neutral sucrose gradients a major peak with the same sedimentation rate as isolated adeno-DNA but also components which sediment faster than unit length DNA. This DNA is purified from host cell contaminants by isopycnic banding in cesium gradients and will later be isolated by electronmicroscopy.

The effect of bacterial restricting enzymes on SV40 DNA

Dana & Nathans reported that restricting enzymes of *E. coli* B and *E. coli* K (P_1) $r_{\overline{K}}$ make one double stranded cut SV40 DNA. These results were confirmed and extended: the purified enzymes make one double stranded cut in 60-70% of plaque purified SV40 DNA. The remaining superhelical DNA has become resistant to cleavage by the homologous enzyme, but its infectivity was unimpaired.

The linear SV40 DNA obtained with the P_1 enzyme appeared to be full length but not to be unique. Denaturation patterns obtained by H. Delius with a DNA-denaturing protein from *E. coli* revealed that the linear SV40 DNA appeared to fall into at least three classes.

Genetics of transformed cells

Transformed cells differ from normal cells primarily in their loss of growth control. This loss may be mediated by changes in the plasma membrane. One difference between normal and transformed cells, probably the result of an alteration in the plasma membrane, is that many transformed cells agglutinate and die after exposure to concanavalin A (con A) a protein isolated from jack beans belonging to a class of proteins (called lectins) which bind to mammalian cell surfaces.

By using con A made radioactive with I^{125} we determined that the number of con A receptor sites on normal 3T3 cells and SV40 transformed 3T3 cells was the same. We also obtained similar results using hamster cells transformed by polyoma virus. This showed that the increased sensitivity for SV40 and polyoma virus transformed cells to the effects of con A was not due to an increase in the number of available con A receptor sites on the surface of transformed cells. Revertants of SV40 transformed cells selected for insensitivity to con A by repeated exposure to con A also had the same number of receptor sites as did the normal and transformed cells.

We also studied the effects of con A on 3T3 cells transformed by RNA tumor viruses. Though these cells did not agglutinate as readily as SV40 transformed cells they had the same number of receptor sites for con A as did normal 3T3 cells and SV40 transformed cells.

Present work concerns further characterizations of the revertant cells mentioned above and selection of new revertants by several different procedures and the characterization of the proteins in the plasma membrane of normal and transformed cells.

MAMMALIAN CELL GENETICS

R. Pollack
J. Watkins
A. Vogel
C. Thomason
B. Mitchell

We arrived at Cold Spring Harbor in late May and have been working since then in the James Laboratory classroom while our new laboratory is being built in Demerec Building A.

Properties of revertants of transformed cell lines

Revertant lines isolated from transformed mouse cells after negative selection with FUdR are increased in chromosome number and size as compared with either their transformed or untransformed ancestors. We are examining the role of this hyperploidy and hypertrophy in reversion by selecting for large and hyperploid lines and then determining whether they have the revertant phenotype. The selection systems are: (a) crossing IPP-transformed mouse lines with TK-transformed mouse lines, and with HAT selective medium, isolating hyperploid hybrid lines; (b) induction of hyperploidy by Velban and colchicine, followed by isolation of large cells by low g sedimentation. We have acquired a Coulter cell counter and cell volume analyzer to assay the volume-distribution of our cultures directly.

In collaboration with J. Sambrook, we are assaying the precise amount of SV40-specific DNA in transformed and revertant cell lines.

To date, revertants of RNA virus-transformed cell lines have not been isolated and, according to Temin (Nature *231*, 117, 1971), such cells are not any more agglutinable by Con-A than their untransformed parents. Therefore, we will test the possibility that such cells, unlike SV40-transformed cells, might yield revertants after selection with FUdR, but not after selection with ConA.

Dr. J. Watkins, Oxford University, spent six months in the laboratory, studying cell fusion between skin fibroblasts from victims of cystic fibrosis, Hurler's syndrome or Hunter's syndrome, and mouse Ehrlich Ascites tumor cells.

Hybrid lines and heterokaryons were made by Sendai virus-induced fusion of fibroblasts from different patients with each other. Preliminary observations showed that metachromasia is suppressed in interspecific heterokaryons and hybrids, at least for the period during which observations were made. Metachromasia seemed not to be suppressed in intraspecific heterokaryons and hybrids.

PROTEIN SYNTHESIS

R. F. Gesteland
B. Allet
M. Anderson
L. V. Crawford
R. Crouch
B. Hirt
P. Jeppessen
C. Kahn
J. Katagiri
A. Rehm
G. Rubin
P. Maloy

Coupled protein synthesis

The work on *in vitro* synthesis of bacteriophage λ proteins has continued, but progress has been hampered by two difficulties: λ DNA is a very poor template compared to T7 and T4 DNAs, and extracts for protein synthesis from λ-induced cells are very inactive. With normal extracts, however, virtually all the λ DNA dependent synthesis is repressor sensitive, which says that most of the transcription initiation is from the expected sites. A comparison of the products made from wild-type DNA and *sex* DNA shows that only about 10% of the synthesis is coming from the *N* promoter, leaving 90% from the rightwards promoter (*x* region). Among the tryptic peptides coming from the *N* promoter there is one that is made by DNA from λ strains that carry distal amber mutations in gene *N* (*N*53, *N*7) and not by DNA from a proximal *N* amber mutation (*N*219). Thus this peptide must be encoded by the *N* gene and does provide a handle for the *N* protein. Further efforts are being made to characterize the products and get induced extracts to function, in order to be able to look for the activities of particular controlling elements (*N*, *Q*, *c*II, *c*III).

We are looking in detail at the proteins made in vitro from T7 DNA. Autoradiograms of high-resolution slab gels show 10-15 bands of varying intensities, with molecular weights ranging from 9000 to 100,000. We have identified four of the proteins by using mutants isolated and characterized by W. Studier. The major in vitro products is the T7 ligase protein (M.W. 40,000). The highest molecular weight species found (100,000) is the gene 1 product, which can also be detected by its specific RNA polymerase activity. A band of molecular weight 9000 is abolished if DNA from the H-1 deletion mutant is used, which agrees with Studier's in vivo experiments and says that the in vitro system is synthesizing this unidentified early protein. We have not yet been able to find the other two known early proteins. A minor band is the product of the lysozyme gene. The band patterns observed for wild-type DNA and a gene 1 amber mutant are identical except, of course, for the gene 1 protein itself. Therefore synthesis of the majority of the products does not require production of the active gene 1 enzyme in the incubation mixture. Surprisingly, amber mutants in each of the other known T7 genes have no effect on the band pattern. We know that the unidentified bands cannot be explained by suppression of the amber mutants used or by substantial transcription and translation of the wrong strand. Apparently many of the bands are fragments of proteins. This is suggested by a comparison of various amber mutants in gene 1. Mutations near the carboxy terminus of the gene alter only the gene 1 protein band on the gel. Those nearer the amino terminus abolish in addition a number of the minor, lower molecular weight species. Thus the extra bands could be due either to premature termination of protein synthesis at specific sites or to specific proteolytic cleavage. If the in vitro system behaved exactly as the infected cells then lysozyme should not be made without the active gene 1 protein, since this gene is situated beyond the termination site for host RNA polymerase. We find that lysozyme is made in vitro even if gene 1 mutant DNA is used. Thus we conclude that either some read-through is occurring or another promoter is active. These results agree with those of others who have measured lysozyme synthesis by its activity. Preliminary results obtained by first synthesizing RNA in vitro from T7 DNA, then adding it to an RNA-dependent protein-synthesizing system, suggest that little lysozyme protein is made and ligase is again the predominant product.

RNA polymerase after λ induction

The detailed structure and biochemical properties of *Escherichia coli* RNA polymerase before and after λ induction might offer clues to the nature of λ controlling functions such as *N*, *Q*, etc. The induced polymerase has salt-dependence properties that are different from normal. Gel electrophoresis and fingerprinting suggest that there is an alteration of at least some of the alpha subunit of the polymerase. Detailed hybridization studies of the RNA made by the normal and induced polymerases, using either linear or circular λ DNA templates, are now being done. This should determine whether or not the observed differences are meaningful. It should be possible then to ascribe such an effect to a particular λ gene by the use of mutants.

Mammalian protein synthesis

A systematic attempt is being made to develop a coupled protein-synthesizing system from mammalian cells in order to study the gene products of SV40 and polyoma viruses. Extracts from

various tissue culture cell lines are first tested under many conditions for their ability to translate a natural messenger RNA such as EMC viral RNA. Extracts from all human (HeLa, KB) and mouse SV3T3, L) lines tested work well with EMC RNA, and synthesize recognizable peptides, whereas extracts from monkey cell lines (BSC-1, MA134, Vero, CV-1) do not respond. When all of these are tested for coupled synthesis by the addition of SV40 RNA and RNA polymerase (usually *E. coli* enzyme), little consistent protein synthesis is observed under any conditions. The RNA synthesis is very efficient but this RNA is not translated. We are now concentrating on extracts from SV40-infected or transformed cells with the hope of finding factors or ribosomes with the proper specificity.

Proteins of tumor viruses–polyoma and SV40

Using the high-resolution gel slabs mentioned above, we are investigating proteins made in SV40-infected cells. Even though SV40 does not shut off host cell functions, it is possible to see specific proteins against the enormous host cell background. Pulse-labeling experiments show that synthesis of at least three of the proteins that make up the virion is turned on at 15-20 hours after infection. These are being fingerprinted to insure identification. We haven't yet found a convincing case of a protein made specifically after infection that does not end up in the virion, though there are two candidates. Various inhibitors are being used to try to prolong and emphasize the early period of synthesis. Also various prefractionation procedures are being tried to increase the chances of finding minor induced proteins.

The virion proteins (labeled with [^{35}S]methionine) from purified polyoma virus have been fractionated on gels and fingerprinted. Each of the six species gives a distinctive pattern of tryptic peptides, which rules out the possibility that the smaller ones are derived from larger ones by degradation. The three smallest virion proteins are histone-like and are thought to be host-cell proteins that are picked up by the virus. This is being verified by fingerprint analysis.

We can use the *E. coli* coupled protein synthesizing system to try to show which proteins are encoded by the SV40 and polyoma viral DNA. Comparison of total tryptic peptide fingerprints of the in vitro products from polyoma DNA and virion proteins suggests that the DNA stimulates synthesis of peptides corresponding to peptides from the major virion proteins. In contrast, SV40 DNA, though it is much more active for protein synthesis in the coupled *E. coli* system, does not make tryptic peptides corresponding to its major coat protein. Acrylamide gel patterns of the polyoma in vitro product show a number of specific bands. One minor one migrates with the major polyoma coat protein, and a second one moves with the second virion protein. Fingerprints are now being done of the proteins eluted from these bands to see if the in vitro and in vivo proteins are the same. If this is the case, it will conclusively prove that these proteins are encoded by the virus. It is hoped that this approach can be extended to ask whether any particular protein found in infected cells is viral coded.

ELECTRON MICROSCOPY

H. Delius
N. Mantell
A. Wilde

DNA unwinding proteins

Proteins which interact strongly and cooperatively with single-stranded DNA are studied by electron microscopy in collaboration with Bruce Alberts (Princeton). Using glutaraldehyde fixation and the Kleinschmidt technique of spreading nucleic acids in a cytochrome film the gene 32-product of bacteriophage T4 could be shown to denature DNA at low temperature in the absence of magnesium. The comparison with the alkaline denaturation map of phage lambda DNA (Inman and Schnös, 1970) leads to the conclusion that it is the same AT-rich regions which are denatured first using either method. No nicks are required for the start of the denaturation by 32-protein.

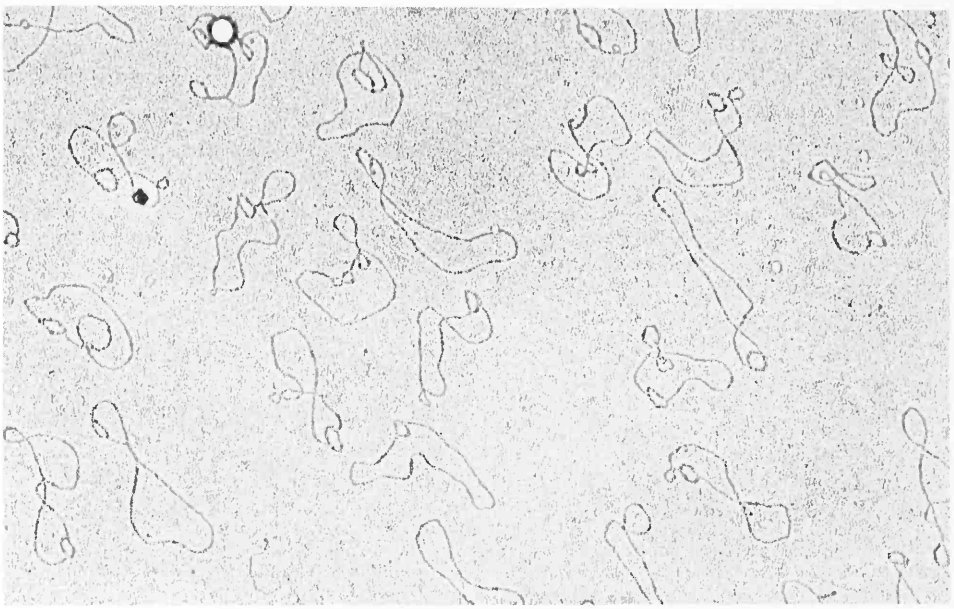
In a mixture of supercoiled and nicked SV40 DNA the supercoiled DNA is denatured preferentially by 32-protein. The extent of the denaturation loop is limited by the closed circular double-stranded structure of the DNA to about 0.1 micron length. The following photograph shows that the partially denatured supercoils assume a relaxed configuration.

DNA unwinding proteins from uninfected *E. coli* and from calf thymus cells form complexes with single-stranded DNA similar to the complexes formed by 32-protein.

Gene 5 product of the bacteriophage fd also binds strongly and cooperatively to single-stranded DNA, but the complex has the appearance of a branched rod when prepared by the Kleinschmidt technique. At high magnification in negatively stained preparations it shows the structure of a helical coil of a diameter of about 100 Å, and longitudinal repeats of 65-70 Å. The nucleoprotein strand has a thickness of 45-50 Å and must contain two chains of single-stranded DNA linked by the protein.

Replicative structures in T4 DNA

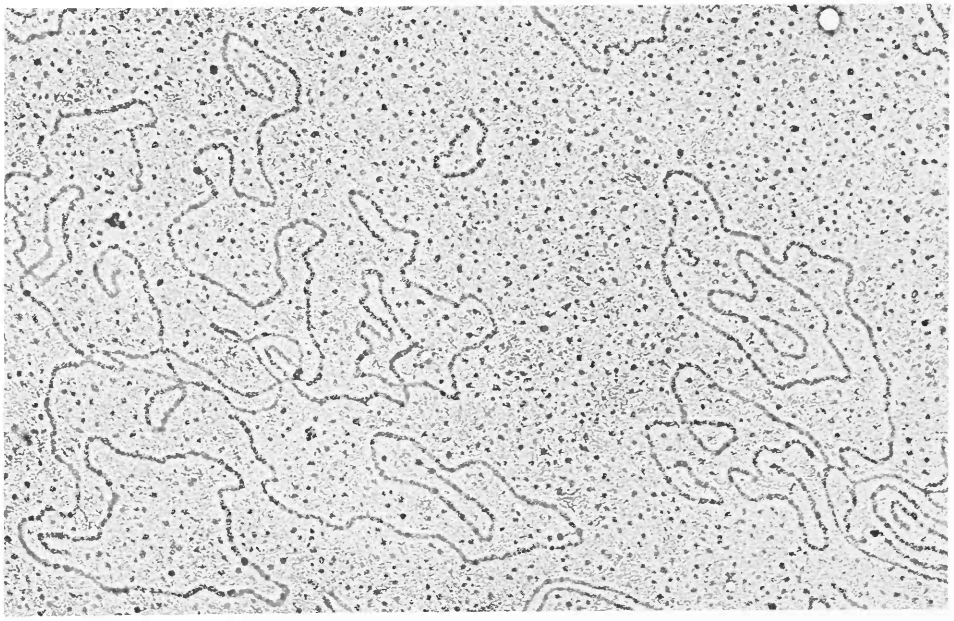
In collaboration with Andrzej Kozinski (Philadelphia) we analyzed replicative DNA isolated from *E. coli* 7-8 min after infection with bromouracil-labeled T4 phage. In contrast to current models of T4 replication these preparations showed some novel features: *1.* The DNA contains loops of double-stranded DNA with whiskers of single-stranded DNA close to the branching points in trans position on the branches. The whiskers are sensitive to exonuclease I, and accordingly have a free 3′-end. *2.* Up to five such loops have been found in a molecule of unit length, suggesting that multiple initiation of DNA replication at several places on the chromosome is possible. *3.* Smaller reinitiation loops were observed within the replicative loops. The location of these loops in the middle of the



branches of the first generation loop suggests that growth of the loops can proceed from the initiation site in both directions.

Visualization of transcription

We found that RNA can be covered and extended by 32-protein. After glutaraldehyde fixation and Kleinschmidt spreading, it is possible to obtain length measurements of the RNA still in position on the DNA template. In experiments with Heiner Westphal it could be directly shown that an incubation of SV40 DNA with *E. coli* RNA polymerase for 2 min at 37° leads to the synthesis of RNA which is longer than the unit size of the SV40 genome. The second photograph shows a circular molecule of SV40 DNA with six strands of RNA attached to it. Studies of RNA synthesis in the presence of rifamycin indicate the presence of at least six possible promotor sites for *E. coli* RNA polymerase on SV40 DNA.



MOLECULAR GENETICS SECTION

D. Zipser
B. Apte
E. Bade
A. Bukhari
J. Caldwell
M. Metlay

Peptidase system

Previous work in our laboratory and others has described a system in *Escherichia coli* that degrades the peptide fragments made by nonsense mutations. This peptidase system has no effect on the nonmutant proteins of the cell.

This year we have isolated mutations in this system which degrade all nonsense fragments at a much lower rate than in the wild type. The properties of the mutants are under active study.

Mu-1 phage

In the past year we have started active study of the mutator phage Mu-1. Our first result has been to show that phage Mu-1 can insert itself into the bacterial chromosome at any site irrespective of base sequence homology. Our objective is to completely define the enzymes used by Mu-1 to recombine one piece of DNA with another without the use of homology.

Lac mRNA

We are using hybridization of mRNA with DNA to measure amounts and size of mRNA produced by polar mutations at different genetic sites within the *z* gene.

In connection with this study a useful technique has been devised using Mu-1 induced *z* mutants with the Mu-1 inserted at different sites in the *z* gene. The mRNA from these strains has been shown to have the *z* gene base sequence only from the operator end to the site of Mu-1 insertion. Clearly, such RNA is ideal for use in competition experiments with mRNA from polar mutants.

Visitors

This summer Dr. A. L. Taylor, the discoverer of Mu-1, visited our laboratory for several weeks and participated in our work with Mu-1. We also had five undergraduates financed by the National Science Foundation working on Mu-1 during the summer.

POST GRADUATE TRAINING COURSES

Summer 1971

From its inception the postgraduate course program at Cold Spring Harbor has aimed to meet the rather special need of training in new interdisciplinary subjects that are either so new or so specialized that they are not adequately treated by universities. The intention is to provide intensive training in the most recent developments and techniques in each of the subjects so that it should be possible for the students to enter directly into research in the particular area.

To do this we bring together a teaching staff from many laboratories around the world. These instructors direct extensive laboratory and lecture programs supplemented with a continuous series of seminar speakers which insures an up-to-date covering of current research work.

For the first time in many years we did not offer a course specifically on bacteriophages. This partly reflects the growing availability of similar courses at universities and partly, the realization that the bacterial genetics course now relies very heavily on phage principles and techniques. In addition to the continuing bacterial genetics, yeast genetics, cell culture and animal virus courses and the tumor virus workshop, we have expanded into two new areas: molecular cytogenetics and neurobiology.

1) BASIC PRINCIPLES OF NEUROBIOLOGY—June 13-July 4, 1971

This was an introductory course in neurobiology for research workers with no previous experience in the field. The course material included the mechanism of nervous conduction; the anatomy and physiology of electrical and chemical synapses; the biosynthesis, release and destruction of neurotransmitters; axonal flow; the electrogenic sodium pump, and the integration of synaptic signals. Other areas covered were the anatomy and development of the C.N.S.; the visual system as a model of C.N.S. function; specificity of nerve regeneration, and higher functions in the brain.

STAFF:

Kelly, Regis, Ph.D., Harvard Medical School
Hubel, David, M.D., Harvard Medical School
Nicholls, John, M.D., Harvard Medical School
Frank, Eric, Harvard Medical School
Hudspeth, Albert James, Harvard Medical School
Van Essen, David, Harvard Medical School

STUDENTS:

Darling, Thomas L., A.B., Yale University
Frankel, Fred R., Ph.D., University of Pennsylvania
Frazier, William A., B.A., Washington University
Goldmark, Peter J., B.A., California at Berkeley
Heinemann, Stephen F., Ph.D., Salk Institute
Hengstenberg, Roland, M.A., Max-Planck-Institut, Tubingen, Germany
Herzberg, Louis P., B.E.E., Brooklyn Polytechnic Institute
Kleinsteuber, Clemens, M.Sc., Konstanz Universität, Germany
Litt, Lawrence, A.M., Harvard University
Pearson, Mark L., Ph.D., University of Toronto, Canada
Peterson, Daniel C., A.M., The Johns Hopkins University
Quinn, William G., Jr., B.A., Princeton University
Reiness, C. Gary, B.A., Columbia University
Schick, Amy M. L., Ph.D., Northeastern University
Seldon, Lee H., B.S., Columbia University
Shainberg, Asher, M.Sc., Columbia University
Sirovich, Lawrence, Ph.D., Brown University
Stavis, Robert L., B.A., Einstein College of Medicine
Stiles, Charles D., B.A., Oak Ridge Graduate School
Ware, Randle W., M.S., Columbia University
Willard, Mark B., B.A., University of Wisconsin

SEMINARS:

Stephen Kuffler, Harvard Medical School, *Introductory lecture.*
John Nicholls, Harvard Medical School, *The ionic basis of resting and action potentials.*
Stephen Kuffler, Harvard Medical School, *Recent research on the septum of the frog heart.*
John Nicholls, Passive electrical properties of nerves.
Eric Frank, Harvard Medical School, *Basic electric elements, Ohm's Law, RC circuitry and an RC cable.*
John Nicholls, Chemical and electrical synapses.

John Nicholls, Permeability changes produced by excitatory and inhibitory transmitters.
John Nicholls, Quantal release of transmitters.
John Nicholls, Physiology of the leech ganglion.
Roger Thomas, Bristol University Medical School, England, *Electrogenic pumps.*
Motoy Kuno, University of Utah, *C.N.S. physiology.*
Jack McMahan, Harvard Medical School, *Microscopic anatomy of the nervous system.*
Zach Hall, Harvard Medical School, *Biosynthesis of transmitters.*
Jack McMahan, Viewing nerve cells, synapses, and neuromuscular junctions in live preparations.
Zach Hall, Release and destruction of transmitters.
Jean-Pierre Changeux, Pasteur Institute, Paris, *acetylcholine receptor I.*
Eric Frank, E.p.s.p. and i.p.s.p.'s in lobster opener muscel. Pre- and post-synaptic inhibition. Facilitation.
David van Essen, Harvard Medical School, *Physiology of the leech ganglion. Action potentials and threshold. Activation of touch receptor cells by stimulation of appropriate receptive field in the skin. Long-lasting hyperpolarization following activity. Electrical coupling between Retzius cells.*
Joav Prives, Columbia University, *Dissection and physiology of the electroplaque of electrophorus. Response to depolarizing drugs.*
J. Rosenbaum, Yale University, *Axoplasmic flow.*
Marshall Nirenberg, National Institutes of Health, *Neuroblastoma.*
David Potter, Harvard Medical School, *Nerve cells in culture.*
Eric Kandel, New York University College of Medicine, *Neuronal plasticity and behavior.*
Max Cowan, Washington University School of Medicine, *Development and general morphology of the vertebrate nervous system.*
Richard Cone, *Johns Hopkins University,* Retinal receptors. Retinal structure. Visual pigment and receptor physiology.
David Hubel, Harvard Medical School, *Physiology of retinal ganglion cells.*
David Hubel, Visual cortex, responses of single cells. Architecture of the striate cortex. The corpus callosum. The effects of visual deprivation.
Roger Sperry, California Institute of Technology, *The split brain.*
Max Cowan, Washington University School of Medicine, *Reaction of neurons to experimental injury, and methods of studying the nervous system.*
Torsten Wiesel, Harvard Medical School, *The visual motor system.*
James Hudspeth, Harvard Medical School, *Single-unit recording in the cat striate cortex. Demonstration of the specificity of single units for different visual stimuli.*
Max Cowan, Washington University School of Medicine, *The cerebellum as a model of neural organization.*
David Hubel, Binocular interactions in vision. Sleep.

2) MOLECULAR BIOLOGY AND GENETICS OF YEAST—June 14-July 4, 1971

This course covered in detail the current techniques for yeast genetic analysis and construction: tetrad analysis, mitotic recombination, and fine structure mapping. New mutants were isolated and characterized. Experiments were also carried out to biochemically characterize cytochrome mutants, specific enzymes, DNA and RNA.

STAFF:

Fink, Gerald, Ph.D., Cornell University
Lawrence, Christopher, Ph.D., University of Rochester
Sherman, Fred, Ph.D., University of Rochester
Vodkin, Michael, B.S., Cornell University

STUDENTS:

Botstein, David, Ph.D., Massachusetts Institute of Technology
Colli, Walter, M.D., Universidade de Sao Paulo, Brazil
Cremona, Terenzio, M.D., International Laboratory for Genetics and Biophysics, Naples, Italy
Ebner, Eberhard, M.D., Cornell University
Herskowitz, Ira, B.S., Massachusetts Institute of Technology
Metzenberg, Robert L., Ph.D., University of Wisconsin
Miller, Donald H., Ph.D., Max Planck Institute, Gottingen, Germany
Neeff, Jurgen A., Biochemisches Institut, Freiburg, Germany
Poralla, Dr. Karl, Institut fur Physiologische Chemie, Munich, Germany
Smith, Gerald R., Ph.D., University of California, Berkeley
Wasserstein, Alan G., B.A., Einstein College of Medicine
Waxman, Michael F., B.A., Brooklyn College

SEMINARS:

Robert K. Mortimer, University of California, Berkeley, *Gene conversion and genetic recombination.*
Michael Esposito, University of Chicago, *Genes controlling meiosis and sporulation in yeast.*
Leland H. Hartwell, University of Washington, *Control of the cell cycle and its integration with the life cycle.*
Calvin S. McLaughlin, University of California, Irvine, *Mutations and antibiotics that affect protein synthesis and RNA synthesis.*
Michael A. Resnick, Oak Ridge National Laboratory, *Radiation repair in yeast.*
Gottfried Schatz, Cornell University, *Structure and genetic modification of mitochondrial membranes.*
Gerald R. Fink, Cornell University, *The organization of biosynthetic pathways in fungi.*
Thomas Orme, Cornell University, *The fatty acid synthetase of yeast.*
Fred Sherman, University of Rochester, *The genetic control of cytochrome C.*
Christopher W. Lawrence, University of Rochester, *Mutagenesis in UV-sensitive mutants of yeast.*

3) QUANTITATIVE MICROBIOLOGY OF ANIMAL CELLS IN CULTURE—June 14-July 4, 1971

The four areas of concentration for this course were growth control of both normal and malignant cells; differentiation and control of expression of specialized differentiated function; radiation biology, and mammalian somatic genetics.

Laboratory exercises demonstrated basic cell growth techniques, primary culture preparation, uses of radio-isotypes, and heterokaryon formation. Other research areas were the selection of viable cell hybrid lines from parents of different genetic constitutions, synchronous culture techniques, assays for differentiated function *in vitro*, and selection for growth in culture of differentiated cells exhibiting such function, cell surface specificity and single cell immune response in culture.

INSTRUCTORS:

Pfeiffer, Steven E., Ph.D., University of Connecticut Health Center
Pollack, Robert E., Ph.D., Cold Spring Harbor Laboratory
Church, Bob, Ph.D., University of Connecticut Health Center
Gross, Tom, B.A., University of Connecticut Health Center
Vogel, Arthur, B.A., New York University School of Medicine

STUDENTS:

Cafferata, Robert L., Ph.D., University of Chicago
Falk, Raphael, Ph.D., Columbia University
Halpern, Barbara, M.D., University of California at Los Angeles
Hill, Ronald J., Ph.D., Harvard University
Hopkins, Nancy H., B.A., Harvard University
Kinzel, Volker, Dr., Institut für Experimentelle Pathologie, Heidelberg, Germany
Liberti, Pietro, M.D., Massachusetts Institute of Technology
Mertz, Janet E., B.S., Stanford University
Monreal, Jaime, M.D., Ph.D., Harvard University
Morel, Carlos M., M.D., Institut Suisse de Recherches Experimentales sur le Cancer, Lausanne, Switzerland
Müller-Hill, Benno A., Dr. Chem., Universität Köln, Germany
Prouty, Walter, Ph.D., Harvard Medical School
Rudiger, Hugo W., M.D., Hamburg University, Germany
Schnierda, Joerg, A.B., Institute of Biochemistry, Freiburg, Germany
Sheiness, Diana K., B.A., Columbia University
Soll, Larry J., A.B., Harvard Medical School
Sugiyama, Tsutomu, Ph.D., Central Research Laboratory, du Pont Co.
Van der Bosch, Jurgen, Dipl. Chem., Konstanz Universitat, Germany
Wechsler, Wolfgang, Priv. Doz., Dr. Med., Max-Planck-Institut, Köln, Germany
Wehrli, Walter E., Ph.D., CIBA-GEIGY, Basel, Switzerland

SEMINARS:

Harry Eagle, Einstein College of Medicine, *The behavior of cells in culture.*
Gordon Sato, University of California, San Diego, *Differentiated cell lines.*
Howard Green, Massachusetts Institute of Technology, *More about hybrid cells.*
Vincent Allfrey, The Rockefeller University, *DNA-associated proteins of the eukaryote.*
Jerome Freed, Institute for Cancer Research, Philadelphia, *Haploid frog cells as material for genetic experiments.*
James Darnell, Columbia University, *The biosynthesis of mRNA in mammalian cells.*
John Watkins, Oxford University, *Sendai virus-mediated cell fusion.*
Sandra Wollman, New York University, *Chromosome staining.*
Robert Phillips, University of Toronto, *In vitro analysis of differentiation in the immune system.*
Steven E. Pfeiffer, University of Connecticut Health Center, *Neurobiology in vitro: glial cell lines.*
Marshall Nirenberg, National Institutes of Health, *Neuroblastoma cell line.*
Gordon Whitmore, University of Toronto, *Isolation and characterization of temperature-sensitive mutants of mammalian cells.*
Robert Perry, Institute for Cancer Research, Philadelphia, *Biosynthesis of eukaryotic ribosomes.*
Howard Holtzer, University of Pennsylvania, *DNA synthesis and myogenesis.*
Elliot Levine, Einstein College of Medicine, *Mycoplasma infection of cultured cells.*
Carl Schildkraut, Einstein College of Medicine, *Mammalian chromosomes: structure and replication.*
Mathew Scharff, Einstein College of Medicine, *Synthesis of immunoglobulines by cultured cells.*
Robert Pollack, Cold Spring Harbor Laboratory, *Safe work in a safe laboratory.*

4) PHYCOMYCES GENETICS WORKSHOP—July 1-September 1, 1971

WORKSHOP MEMBERS:

Cerdá-Olmedo, Enrique, University of Seville, Spain (in charge of the Workshop)
Delbruck, Max, Ph.D., California Institute of Technology
Bergman, Kostia, Ph.D., California Institute of Technology
Hom, William L., Ph.D., University of Pennsylvania
Leighton, Terry J., Ph.D., University of California, Davis
Ootaki, Tamotsu, Ph.D., Carnegie-Mellon University
Reau, Patricia M., Ph.D., California Institute of Technology
Sutter, Richard P., Ph.D., University of West Virginia
Curtin, Paula, Cold Spring Harbor Laboratory

A Phycomyces Genetics Workshop met for two months at the Laboratory this summer. The workshop was centered on genetic problems, particularly the construction and uses of heterokaryons, but the research projects, the daily seminars and discussions were extended to include many subjects.

The heterokaryons of Phycomyces are particularly useful because of their stability and continuous variation in composition. As no anastomosis has ever been found, the construction of heterokaryons requires microsurgical manipulation. Important progress was achieved this summer when Tamotsu Ootaki applied his previous research on sporangiophore regeneration to the development of an elegant and productive technique for construction of heterokaryons, involving the joint regeneration of two cut sporangiophores. By means of this technique, William Hom obtained the first heterokaryon with three different kinds of nuclei, which segregated in the expected way two previously unknown heterokaryons. Hom tried another method, the regeneration of hyphae from the contact zone of two mycelia of different sex, using his dwarf colonial mutant as a marker.

With the hope of developing a parasexual cycle, Enrique Cerdá-Olmedo irradiated spores from a heterokaryon of a white blind strain and a red strain with 150 kilorads of X-rays (courtesy of Brookhaven National Laboratory), and tested the survivors for yellow color and incapacity to segregate the red and white components. Two promising strains were isolated.

Patricia Reau fractionated spores from the same heterokaryon in a sedimenting chamber designed by her, and achieved their separation according to size. The smallest spores tend to be uninucleate. Fractions were obtained containing more than 80% uninucleate spores, as assayed both by Giemsa staining and by determination of the genotypes of the resulting mycelia. The chamber will find application in many genetic problems.

Max Delbrück, with the help of H. Macgregor of the Molecular Cytogenetics Course, used the M85 Vickers Scanning Microdensitometer to estimate the DNA content of Feulgen-stained Phycomyces nuclei at 1.0×10^{-13} grams, or about 10^8 base pairs.

Several lines of research into the sexual reproduction of Phycomyces were pursued by Richard Sutter. He isolated trisporic acids, thought to be sexual hormones, from various types of matings and started the isolation of mutants to clarify the relation of trisporic acids to carotenoids. He examined the sexual reactions between the wild types of *Phycomyces blakesleeanus, Mucor mucedo,* and *Blakeslea trispora,* suggesting the possibility of utilizing Phycomyces in a biological test for trisporic acids. Blakeslea offers the advantage of superproduction of trisporic acids, and the isolation of mutants in this species would be very convenient. Its sporangiospores can be germinated with a low efficiency, and produce colonial growth on acid media, but they seem to have too many nuclei for easy isolation of recessive mutations.

Max Delbrück reexamined the quantitative assay of Phycomyces spores on acid plates, eliminating several supposed irregularities and establishing the procedure for reliable determinations.

Sensory physiology continues as the main focus for studies of this fungus. A new effect of light, discovered by Kostia Bergman, is the control of sporangiophore initiation. This summer Bergman devised a quantitative test of this phenomenon and applied it to several kinds of mutants showing abnormal phototropism. C112, a yellow nonphototropic mutant, which exhibits normal autochemotropism, has been found to lack photoinitation. The albino nonphototropic mutants from Seville show a partial, deranged response, and the mutants affected in both phototropism and autochemotropism are normal in photoinitiation. These results permit the detection of several common parts in the mechanisms for the various inputs and outputs of sensory information. The photoinitiation response, however, is not very clearly localized in the mycelium, as tested by Max Delbrück.

Max Delbrück, with the collaboration of Mark Willard, used the equipment of the Neurobiology laboratory to record intracellular potentials in Phycomyces. They do not seem to be affected by light stimuli.

Enrique Cerdá-Olmedo and Kostia Bergman set up a new procedure for the determination of light-intensity thresholds. Cerdá-Olmedo studied the thresholds of several mutants obtained in Seville, which are simultaneously caroteneless and nonphototropic and which indicate that carotenoids are necessary for vision. Such mutants exhibit some sensitivity to high-intensity light, attributed to the manufacture of very small amounts of β-carotene. Their thresholds have been found to be higher in the presence of diphenylamine, an inhibitor of carotenoid synthesis, and lower in the presence of leucine, an activator, thus supporting the hypothesis.

Terry Leighton obtained crystal violet-resistant mutants to study the relationship of membrane structure to phototropism, and observed the morphological effects of polyoxin D on germinating spores, where it seems to act as a chitin synthetase inhibitor. With the collaboration of Walter Keller he assayed the RNA polymerase of Phycomyces, separating two types of activity, one sensitive and another insensitive to α-amanitin.

All these projects relied on the enthusiasm and know-how of Paula De Lucia Curtin.

The workshop was visited by various workers active in the field, who presented their recent results. Among them were David Allan, David Dennison, William Goodell, Susan Godfrey Hendrix, Walter Shropshire, and Jerome Wolken.

5) EXPERIMENTAL TECHNIQUES IN NEUROBIOLOGY– July 6-August 1, 1971

This laboratory course emphasized the development of experimental techniques. It included intracellular recording of controlled membrane potentials, intracellular injection of ions, ionophoretic application of drugs, and the physiological and electrical stimulation of selected activities.

STAFF:

Ascher, Philippe, Ph.D., Laboratoire de Neurophysiologie Cellulaire du Centre des Etudes de Physiologie Nerveuse du C.N.R.S., Gif-sur-Yvette, France
Kehoe, JacSue, Ph.D., Laboratoire de Neurophysiologie Cellulaire du Centre des Etudes de Physiologie Nerveuse du C.N.R.S., Gif-sur-Yvette, France
Nield, Timothy, Bristol University Medical School, U.K.
Thomas, Roger, Ph.D., Bristol University, U.K.

STUDENTS:

Darling, Thomas L., A.B., Yale University
Hengstenberg, Roland, M.A., Max-Planck-Institut, Tübingen, Germany
Kleinsteuber, Clemens, M.Sc., Konstanz Universität, Germany
Petersen, Daniel C., A.M., The Johns Hopkins University
Quinn, William C., Jr., B.A., Princeton University
Salzberg, Brian M., A.M., Harvard University
Sirovich, Lawrence, Ph.D., Brown University
Stavis, Robert L., Einstein College of Medicine
Ware, Randle W., M.S., Columbia University
Willard, Mark B., B.A., University of Wisconsin

6) BACTERIAL GENETICS–July 12-August 1, 1971

This course was designed to provide specific examples of the current techniques used to map, characterize and construct bacterial mutants. These included analysis of tryptophane minus mutants, induced reversion, suppression of nonsense mutants, analysis of lac mutants, dominance, merodipolids, pleiotropic mutants, and mapping of Hfr crosses. Other analyses were episome mobilization and transfer, transduction with P1, selection of recessive alleles, screening for temperature sensitive lethals and mapping of tryptophane mutants with ϕ80ptrp phages.

STAFF:

Gross, Julian, Ph.D., University of Edinburgh, U.K.
Morse, Daniel, Ph.D., Harvard Medical School
Scaife, John, Ph.D., University of Edinburgh, U.K.
Ehlinger, Sheila, A.B., New York University College of Medicine
Kirschbaum, Joel, B.S., Harvard University

STUDENTS:

Allet, Bernard, Ph.D., Cold Spring Harbor Laboratory
Baess, Inga M., M.D., Statens Seruminstitut, Copenhagen, Denmark
Blumberg, Peter M., A.B., A.M., Harvard University
Bruenn, Jeremy A., Ph.D., Oak Ridge National Laboratory
Chelala, Cesar A., M.D., Foundacion Campomar, Buenos Aires, Argentina
Chesney, Robert H., B.A., University of Virginia
Grunau, John A., Ph.D., University of Missouri
Heere, Leonard J., Ph.D., Medical University of South Carolina
Keller, Walter, Dr. Med., Cold Spring Harbor Laboratory
Landers, Terry A., A.M., Harvard University
Loewen, Peter C., Ph.D., Massachusetts Institute of Technology
Schmitt, Rüdiger W., Ph.D., Erlangen-Nürnberg University, Germany
Shapiro, Herman S., Ph.D., New Jersey College of Medicine and Dentistry
Soper, Thomas S., A.B., Purdue University
Steiner, Kathlyn S., B.A., Pennsylvania State University
Testa, Douglas, B.S., Hunter College
Valenzuela, Manuel S., Brandeis University
Van de Sande, John H., Ph.D., Massachusetts Institute of Technology
Youngs, David, M.S., University of Michigan
Zetter, Bruce, B.A., University of Rhode Island

SEMINARS:

Don Fraenkel, Harvard Medical School, *Glycolysis-deficient mutants of E. coli.*
Jeffrey Miller, University of Cologne, Germany, *Regulation of the lactose operon.*
Michael Malamy, Tufts University School of Medicine, *T7 translation control mechanisms, and their inhibition by F factors.*
Rita Arditti, Harvard Medical School, *Control of gene expression in E. coli and lambdoid phages.*
Robert Weisberg, National Institutes of Health, *Prophage lambda of unusual chromosomal locations.*
Robert Schleif, Brandeis University, *Regulation of the arabinose operon.*
Malcolm Gefter, Columbia University, *New DNA polymerase activities.*
JoAnne deVries, New York University College of Medicine, *F-factor incompatibility mutant analysis.*
Ira Herskowitz, Massachusetts Institute of Technology, *Control of gene expression in phage lambda.*

William Summers, Yale University School of Medicine, *Gene expression in phage T7.*
Bruce Alberts, Princeton University, *Analysis of proteins which interact with DNA.*
Joan Steitz, Yale University School of Medicine, *Nucleotide sequences which punctuate translation of the genetic code.*
Geoffrey Zubay, Columbia University, *In vitro studies of gene expression and its regulation.*

7) ANIMAL VIRUSES—July 12-August 1, 1971

Consisting of lectures, discussions and laboratory exercises, research centered around the following areas: preparation of primary and secondary cell cultures from various tissues; growth in mass cultures of HeLa BHK and L cells; karyotype analysis; DNA and RNA synthesis in the cell life cycle; synthesis of viral RNA; assays for particular viruses; neutralization of viruses with antibody; histochemistry and fluorescent antibody techniques in virus infection; cell transformation, and cell hybridization.

STAFF:

Burge, Boyce W., Ph.D., Massachusetts Institute of Technology
Colby, Clarence, Ph.D., University of Connecticut
Kates, Joseph, Ph.D., University of Colorado
Morgan, Michael, Ph.D., University of Connecticut
Sveda, Michael, University of Connecticut

STUDENTS:

Bendler, John W., Ph.D., University of Pennsylvania
Cole, Patricia, M. Phil., Yale University
Dumont, Raymonde, Candidature in Medicine, Histologisch Instituut, Ghent, Belgium
Gupta, Naba K., Ph.D., University of Nebraska
Hidalgo, Tomal L., Dr., U.N.A.M., Mexico
Hosokawa, Keiichi, M.D., Ph.D., Worcester Foundation
Kolakofsky, Daniel, Ph.D., University of Zurich, Switzerland
Kuehl, Michael W., M.D., Einstein College of Medicine
Lawrence, Charles B., B.S., Washington University
Lewis, James B., M.A., Harvard University
Millette, Robert L., Ph.D., University of Colorado Medical Center
Müller-Hill, Benno A., Dr. Chem., Universität, Köln, Germany
Radke, Kathryn L., Tufts University
Reid, Ted W., Ph.D., Yale School of Medicine
Risser, Rex G., B.S., Harvard University
Silberstein, Harvey A., B.S., Einstein College of Medicine
Silbert, David F., M.D., Washington University
Siler, Jack, Ph.D., Wistar Institute
Stewart-Blair, Margaret L., B.Sc., Einstein College of Medicine
Watson, Bracie, Jr., University of Alabama

SEMINARS:

Philip I. Marcus, University of Connecticut, *Animal cells as micro-organisms.*
Elliott Robbins, Einstein College of Medicine, *Cell ultrastructure and the cell cycle.*
Ellie Ehrenfeld, Einstein College of Medicine, *Poliovirus.*
Al Kapuler, University of Connecticut, *Reovirus.*
Clarence Colby, University of Connecticut, *Induction and action of interferon.*
Tom Benjamin, Department of Public Health, New York City, *DNA tumor viruses.*
Claudio Basillico, New York University College of Medicine, *Animal cell hybrids.*
Richard Compans, The Rockefeller University, *Biochemistry of envelope viruses.*
David Baltimore, Massachusetts Institute of Technology, *RNA tumor viruses.*
Alice Huang, Harvard Medical School, *Vesicular stomatitis virus.*
Joe Kates, University of Colorado, *Poxviruses.*
Michael Bratt, Harvard Medical School, *Newcastle disease virus.*
Harry Ginsberg, University of Pennsylvania School of Medicine, *Adenovirus.*
Dean Engelhardt, University of Connecticut, *Animal cell and animal virus protein synthesis.*
Pat Spear, University of Chicago School of Medicine, *Herpesvirus.*
Brian McAuslan, Roche Institute of Molecular Biology, *Frog virus.*
Boyce Burge, Massachusetts Institute of Technology, *Animal virus genetics.*

8) MOLECULAR CYTOGENETICS—August 3-August 20, 1971

Laboratory exercises and discussions covered lampbrush chromosomes, polytene chromosomes, meiosis, mitosis, *in situ* RNA hybridization, autoradiography, visualization of DNA and transcription complexes with the electron microscope.

STAFF:

Callan, H. G., M.A., D.Sc., F.R.S.E., St. Andrews University, U.K.
Hamkalo, Barbara Ann, Ph.D., Oak Ridge National Laboratory
McClintock, Barbara, Ph.D., Carnegie Institute of Washington
Macgregor, Herbert C., Ph.D., University of Leicester, U.K.
Miller, Oscar L., Jr., Ph.D., Oak Ridge National Laboratory
Pardue, Mary Lou, Ph.D., University of Edinburgh, U.K.
Thomas, C. A., Jr., Ph.D., Harvard Medical School

STUDENTS:

Aufreiter, Eva, Ph.D., Massachusetts Institute of Technology
Crouch, Robert J., Ph.D., Cold Spring Harbor Laboratory
Ducret, Claude G., M.S., University of Geneva, Switzerland
Egel, Richard, Ph.D., University of Freiburg, Germany
Fasy, Thomas M., M.D., Rockefeller University
Franklin, Naomi C., Ph.D., Stanford University
Hill, Ronald J., Ph.D., Harvard University
King, Robert C., Ph.D., Northwestern University
Klotz, Lynn C., Ph.D., Harvard University
Kurnit, David M., B.A., Einstein College of Medicine
Lee, Chong S., Ph.D., Harvard Medical School
Liss, Alan, B.S., University of Rochester
Ostertag, Wolfram, Ph.D., Max-Planck-Institut, Göttingen, Germany
Sugden, William, M.S., Cold Spring Harbor Laboratory
Von Ehrenstein, Gunter, M.D., Ph.D., Max-Planck-Institut, Göttingen, Germany
Werner, Rudolf, Ph.D., University of Miami

SEMINARS:

James Kezer, University of Oregon, *The sex chromosomes of plethodontid salamanders.*
H. G. Callan, St. Andrews University, U.K., *Units involved in the replication of chromosomal DNA.*
H. C. Macgregor, University of Leicester, U.K., *Gene action during oogenesis.*
Charles Laird, University of Washington, *Organization of DNA in Drosophila chromosomes.*
M. L. Pardue, University of Edinburgh, U.K., *Nucleic acid hybridization in cytological preparations.*
C. A. Thomas, Jr., Harvard Medical School, *The cyclization of eukaryotic DNA fragments and its implication to chromosome structure.*
David R. Wolstenholme, University of Utah, *Extranuclear chromosomes.*
R. C. King, Northwestern University, *The synaptonemal complex and chromosome pairing.*
O. L. Miller, Jr., and B. A. Hamkalo, Oak Ridge National Laboratory, *Visualization of transcription.*

9) TUMOR VIRUS WORKSHOP—August 3-August 19, 1971

In-depth coverage of the tumor virus field was the intent of this course which consisted for the most part of lectures. However, there were also experiments to demonstrate transformation, virus rescue from transformed cells and various aspects of the lytic viral cycle. The final three days of the course comprised the 2nd annual Cold Spring Harbor meeting on tumor viruses.

STAFF:

Levinson, Warren, M.D., University of California Medical Center
Martin, Malcolm, Ph.D., National Institutes of Health

STUDENTS:

Anderson, Margaret L. M., Ph.D., Cold Spring Harbor Laboratory
Balizer, Edward, B.A., Syracuse University
Barley, Carolyn L., B.A., New York University
Bond, Sheila B., M.D., George Washington University
Brandner, Gerhard G., Ph.D., Freiburg University, Germany
Bussell, Robert H., Ph.D., University of Kansas
Garfinkle, Barry D., M.S., Pennsylvania State University
Hansen, Christopher B., B.A., University of California at San Francisco
Hayes, Naomi, A.B., University of Vermont
Kaji, Akira, Ph.D., University of Pennsylvania
Kammer, Klaus, University of Heidelberg, Germany
Lewis, James B., B.A., M.A., Harvard University
Maitra, Umadas, Ph.D., Einstein College of Medicine
Mangel, Walter F., Ph.D., University of California at Berkeley
Manteuil, Simone, M.Sc., Institut de Recherches Scientifique sur le Cancer, Villejuif, France
Ptashne, Mark S., Ph.D., Harvard University
Riva, Silvano, Ph.D., Gruppo Lepetit Spa, Milan, Italy
Rogers, Mary Elizabeth, Ph.D., University of Edinburgh, U.K.
Rosenthal, Leonard J., Ph.D., Massachusetts General Hospital
Rouland, Daisy, Ph.D., University of California Medical Center
Tobia, Annette M., M.S., New York University

SEMINARS:

Ray Erickson, University of Colorado, *Nucleic acids of the RNA tumor viruses.*
Michael Bishop, University of California, *Enzymes associated with RNA tumor viruses.*
Peter Duesberg, University of California, *Structure, proteins, and antigens of RNA tumor viruses.*
Lionel Crawford, Imperial Cancer Research Institute, London, *Structure, proteins, and antigens of DNA tumor viruses.*
Tom Kelly, National Institutes of Health, *Replication of viral DNA.*
Jim Rose, National Institutes of Health, *SV40 adenovirus hybrids.*
Robin Weiss, University of Washington, *Defectiveness and variants of Rous Sarcoma Virus.*
J. Sambrook, Cold Spring Harbor Laboratory, *Tumor cell agglutinins.*
W. Eckhart, Salk Institute, *Mutants of DNA tumor viruses.*
Robert Friis, University of Washington, *Mutants of RNA tumor viruses.*
Alan Rabson, National Institutes of Health, *Are herpes viruses tumor viruses?*

COLD SPRING HARBOR SYMPOSIUM ON QUANTITATIVE BIOLOGY

June 3rd to June 10th, 1971

Protein structure analysis is now a field very different from its counterpart of only a few years ago. Then, most inferences about what proteins look like at the three-dimensional level were indirect and most speculations about how they acted were quickly forgotten. But spectacular advances in protein crystallography made during this past decade now present us with precise atomic coordinates for a number of important proteins, thereby allowing the formulation of detailed mechanisms for their manner of function at the molecular level. In this work, important contributions have been made by people of highly diverse backgrounds. Mathematicians, physicists, physical chemists, organic chemists, and biochemists have all played indispensible roles. This year's Symposium thus seemed a good time to bring together these various people to talk about where protein work now stands and to consider which proteins are next ripe for full understanding.

PROGRAM

GENERAL CONSIDERATION OF PROTEIN STRUCTURE AND CATALYSIS

W. P. JENCKS: Structure-Reactivity Correlations and General Acid-Base Catalysis in Enzymic Transacylation Reactions
D. E. KOSHLAND, JR., K. W. CARRAWAY, G. A. DAFFORN, J. D. GASS, and D. R. STORM: The Importance of Orientation Factors in Enzymatic Reactions
T. C. BRUICE: Views on Approximation, Orbital Steering, and Enzymatic and Model Reactions
B. D. SYKES, S. L. PATT, and D. DOLPHIN: The Role of Distortion in the Lysozyme Mechanism
F. M. RICHARDS, H. W. WYCKOFF, W. D. CARLSON, N. M. ALLEWELL, B. LEE, and Y. MITSUI: Protein Structure, Ribonuclease-S and Nucleotide Interactions
G. E. LIENHARD, I. I. SECEMSKI, K. A. KOEHLER, and R. N. LINDQUIST: Enzymatic Catalysis and the Transition State Theory of Reaction Rates: Transition State Analogs
R. J. P. WILLIAMS: The Entatic State

PROTEASES: STRUCTURE, CATALYSIS, INHIBITION

R. HENDERSON, C. S. WRIGHT, G. P. HESS, and D. M. BLOW: α-Chymotrypsin: What Can We Learn about Catalysis from X-Ray Diffraction?
A. R. FERSHT: Conformational Equilibria and the Salt Bridge in Chymotrypsin
S. A. BERNHARD and S.-J. LAU: Spectrophotometric and Structural Evidence as to the Mechanism of Protease Catalysis at Chemical Bonding Resolution
D. M. SEGAL, G. H. COHEN, D. R. DAVIES, J. C. POWERS, and P. E. WILCOX: The Stereochemistry of Substrate Binding to Chymotrypsin Aγ
D. M. SHOTTON, N. J. WHITE, and H. C. WATSON: Conformational Changes and Inhibitor Binding at the Active Site of Elastase
J. DRENTH, W. G. J. HOL, J. N. JANSONIUS, and R. KOEKOEK: A Comparison of the Three-dimensional Structures of Subtilisin BPN' and Subtilisin Novo
J. KRAUT, J. D. ROBERTUS, J. J. BIRKTOFT, R. A. ALDEN, P. E. WILCOX, and J. C. POWERS: The Aromatic Substrate Binding Site in Subtilisin BPN' and Its Resemblance to Chymotrypsin
R. M. STROUD, L. M. KAY, and R. E. DICKERSON: The Crystal and Molecular Structure of DIP-inhibited Bovine Trypsin at 2.7 Å Resolution
R. HUBER, D. KUKLA, A. RUHLMANN, and W. STEIGEMANN: Pancreatic Trypsin Inhibitor (Kunitz) Part I. Structure and Function
A. RUHLMANN, H. J. SCHRAMM, D. KUKLA, and R. HUBER: Pancreatic Trypsin Inhibitor (Kunitz) Part II. Complexes with Proteinases



ENZYMES IN THE GLYCOLYTIC PATHWAY

D. W. BANNER, A. C. BLOOMER, G. A. PETSKO, D. C. PHILLIPS, and C. I. POGSON: Crystallographic Studies of Chicken Triose Phosphate Isomerase

J. R. KNOWLES, P. F. LEADLAY, and S. G. MAISTER: Triosephosphate Isomerase: Isotope Studies on the Mechanistic Pathway

J. W. CAMPBELL, E. DUEE, G. HODGSON, W. D. MERCER, D. K. STAMMERS, P. L. WENDELL, H. MUIRHEAD, and H. C. WATSON: X-Ray Diffraction Studies on Enzymes in the Glycolytic Pathway

DEHYDROGENASES

D. TSERNOGLOU, E. HILL, and L. J. BANASZAK: Structural Studies on Heart Muscle Malate Dehydrogenases

M. G. ROSSMANN, M. J. ADAMS, M. BUEHNER, G. C. FORD, M. L. HACKERT, P. J. LENTZ, JR., A. McPHERSON, JR., R. W. SCHEVITZ, and I. E. SMILEY: Structural Constraints on Possible Mechanisms of Lactate Dehydrogenase as Shown by High Resolution Studies of the Apoenzyme and a Variety of Enzyme Complexes

J. JANIN: Relaxation Studies on an Allosteric Enzyme: Aspartokinase I-Homoserine Dehydrogenase I

D. J. DeROSIER and R. M. OLIVER: A Low Resolution Electron-Density Map of Lipoyl Transsuccinylase, the Core of the α-Ketoglutarate Dehydrogenase Complex

MUSCLE PROTEINS

C. COHEN, D. L. D. CASPAR, D. A. D. PARRY, and R. M. LUCAS: Tropomyosin Crystal Dynamics

R. H. KRETSINGER, C. E. NOCKOLDS, C. J. COFFEE, and R. A. BRADSHAW: The Structure of a Calcium-binding Protein from Carp Muscle

NEW PROTEIN STRUCTURES AND PROGRESS REPORTS

K. K. KANNAN, A. LILJAS, I. WAARA, P.-C. BERGSTEN, S. LOVGREN, B. STRANDBERG, U. BENGTSSON, U. CARLBOM, K. FRIDBORG, L. JARUP, and M. PETEF: Crystal Structure of Human Erythrocyte Carbonic Anhydrase C. VI. The Three-dimensional Structure at High Resolution in Relation to Other Mammalian Carbonic Anhydrases

T. L. BLUNDELL, J. F. CUTFIELD, E. J. DODSON, G. G. DODSON, D. C. HODGKIN, and D. A. MERCOLA: The Crystal Structure of Rhombohedral 2 Zinc Insulin

F. A. COTTON, C. J. BIER, V. W. DAY, E. E. HAZEN, JR., and S. LARSEN: Some Aspects of the Structure of Staphylococcal Nuclease Part I. Crystallographic Studies

C. B. ANFINSEN, A. N. SCHECHTER, and H. TANIUCHI: Part II. Studies in Solution

O. JARDETZKY, J. L. MARKLEY, H. THIELMANN, Y. ARATA, and M. N. WILLIAMS: Tentative Sequential Model for the Unfolding and Refolding of Staphylococcal Nuclease at High pH

H. M. SOBELL, S. C. JAIN, T. D. SAKORE, G. PONTICELLO, and C. E. NORDMAN: Concerning the Stereochemistry of Actinomycin Binding to DNA: An Actinomycin-Deoxyguanosine Crystalline Complex

K. D. HARDMAN, M. K. WOOD, M. SCHIFFER, A. B. EDMUNDSON, and C. F. AINSWORTH: X-Ray Crystallographic Studies of Concanavalin A

G. N. REEKE, J. W. BECKER, and F. A. QUIOCHO: The Structure of Concanavalin A at 4 Å Resolution

D. C. WILEY, D. R. EVANS, S. G. WARREN, C. H. McMURRAY, B. F. P. EDWARDS, W. A. FRANKS, and W. N. LIPSCOMB: The 5.5 Å Resolution Structure of the Regulatory Enzyme, Aspartate Transcarbamylase

D. EISENBERG, E. G. HEIDNER, P. GOODKIN, M. N. DASTOOR, B. H. WEBER, F. WEDLER, and J. D. BELL: Molecular Symmetry and Crystal Packing of *E. coli* Glutamine Synthetase

HEMOGLOBINS: MUTANTS, DERIVATIVES, AND COMPLEXES

M. F. PERUTZ and L. F. TENEYCK: Stereochemistry of Cooperative Effects in Hemoglobin

J. V. KILMARTIN and J. A. HEWITT: The Effect of Removal of C-terminal Residues on Cooperative Interactions in Hemoglobin

J. GREER: Three-dimensional Structure of Abnormal Mutant Human Hemoglobins

R. T. OGATA and H. M. McCONNELL: The Binding of a Spin-labeled Triphosphate to Hemoglobin

R. G. SHULMAN, S. OGAWA, and J. J. HOPFIELD: An Allosteric Model of Hemoglobin

B. M. HOFFMAN, C. A. SPILBURG, and D. H. PETERING: Coboglobins: Cobalt Substitution and the Nature of the Prosthetic Group–Apoprotein Interaction in Hemoglobin and Myoglobin

W. E. LOVE, P. A. KLOCK, E. E. LATTMAN, E. A. PADLAN, K. B. WARD, JR., and W. A. HENDRICKSON: The Structures of Lamprey and Bloodworm Hemoglobins in Relation to Their Evolution and Function

IRON-CONTAINING PROTEINS OTHER THAN HEMOGLOBIN

K. D. WATENPAUGH, L. C. SIEKER, J. R. HERRIOTT, and L. H. JENSEN: The Structure of a Non-Heme Iron Protein: Rubredoxin at 1.5 Å Resolution

M. L. LUDWIG, R. D. ANDERSEN, P. A. APGAR, R. M. BURNETT, M. E. LEQUESNE, and S. G. MAYHEW: The Structure of a Clostridial Flavodoxin, an Electron-transferring Flavoprotein. III. An Interpretation of an Electron-Density Map at a Nominal Resolution of 3.25 Å

C. W. CARTER, JR., S. T. FREER, NG. H. XUONG, R. A. ALDEN, and J. KRAUT: Structure of the Iron-Sulfur Cluster in the *Chromatium* Iron Protein at 2.25 Å Resolution

F. S. MATHEWS, P. ARGOS, and M. LEVINE: The Structure of Cytochrome b_5 at 2.0 Å Resolution

T. TAKANO, R. SWANSON, O. B. KALLAI, and R. E. DICKERSON: Conformational Changes upon Reduction of Cytochrome *c*

A. G. REDFIELD and R. K. GUPTA: Pulsed NMR Study of the Structure of Cytochrome *c*

IMMUNOGLOBULIN STRUCTURE: IgG AND FRAGMENTS

V. R. SARMA, D. R. DAVIES, L. W. LABAW, E. W. SILVERTON and W. D. TERRY: Crystal Structure of an Immunoglobulin Molecule by X-Ray Diffraction and Electron Microscopy

R. J. POLJAK, L. M. AMZEL, H. P. AVEY, L. N. BECKA, D. J. GOLDSTEIN, and R. L. HUMPHREY: X-Ray Crystallographic Studies of the F*ab* and F*c* Fragments of Human Myeloma Immunoglobulins

A. B. EDMUNDSON, M. SCHIFFER, M. K. WOOD, K. D. HARDMAN, K. R. ELY, and C. F. AINSWORTH: Crystallographic Studies of an IgG Immunoglobulin and the Bence-Jones Protein from One Patient

STRUCTURE OF VIRUSES

A. N. BARRETT, J. BARRINGTON LEIGH, K. C. HOLMES, A. KLUG, R. LEBERMAN, E. MANDELKOW, and P. VON SENGBUSCH: An Electron-Density Map of Tobacco Mosaic Virus at 10 Å Resolution

A. KLUG and A. C. H. DURHAM: The Disk of TMV Protein and Its Relation to the Helical and Other Modes of Aggregation

P. J. G. BUTLER: The Mechanism and Control of the Assembly of Tobacco Mosaic Virus from Its RNA and Protein Disks

K. AKERVALL, B. STRANDBERG, M. G. ROSSMANN, U. BENGTSSON, K. FRIDBORG, H. JOHANNISEN, K. K. KANNAN, S. LOVGREN, G. PETEF, B. OBERG, D. EAKER, S. HJERTEN, L. RYDEN, and I. MOKING: X-Ray Diffraction Studies of the Structure of Satellite Tobacco Necrosis Virus

R. A. CROWTHER and L. A. AMOS: Three-dimensional Image Reconstructions of Some Small Spherical Viruses

S. C. HARRISON: Structure of Tomato Bushy Stunt Virus: Three-dimensional X-Ray Diffraction Analysis at 30 Å Resolution

R. M. FRANKLIN, S. C. HARRISON, U. PETTERSSON, C. I. BRANDEN, P.-E. WERNER, and L. PHILIPSON: Structural Studies on the Adenovirus Hexon

SPECTROSCOPY AND SPECTROSCOPIC PROBES

C. F. MEARES and D. G. WESTMORELAND: The Study of Biological Macromolecules Using Perturbed Angular Correlations of Gamma Radiation

B. L. VALLEE, J. F. RIORDAN, J. T. JOHANSEN, and D. M. LIVINGSTON: Spectro-chemical Probes for Protein Conformation and Function

M. COHN, J. S. LEIGH, JR., and G. H. REED: Mapping Active Sites of Phosphoryl-transferring Enzymes by Magnetic Resonance Methods

M. A. RAFTERY, W. H. HUESTIS, and F. MILLETT: Use of ^{19}F-Nuclear Magnetic Resonance Spectroscopy for Detection of Protein Conformation Changes: Application to Lysozyme, Ribonuclease, and Hemoglobin

S. H. KOENIG, R. D. BROWN, and J. STUDEBAKER: On the Interpretation of Solvent Proton Magnetic Relaxation Data with Particular Application to the Structure of the Active Site of Mn-Carboxypeptidase A

F. A. QUIOCHO, P. H. BETHGE, W. N. LIPSCOMB, J. F. STUDEBAKER, R. D. BROWN, and S. H. KOENIG: X-Ray Diffraction and Nuclear Magnetic Resonance Dispersion Studies on Derivatives of Carboxypeptidase A

TECHNIQUES IN DIFFRACTION AND MODEL BUILDING

B. P. SCHOENBORN: A Neutron Diffraction Analysis of Myoglobin. III. Hydrogen-Deuterium Bonding in Side Chains

C. D. BARRY and A. C. T. NORTH: The Use of a Computer-controlled Display System in the Study of Molecular Conformations

J. A. YANKEELOV, JR., and J. R. COGGINS: Construction of Space-filled Models of Proteins Using Dihedral Angles

SUMMARY

D. C. PHILLIPS: Protein Crystallography 1971: Coming of Age

SUMMER MEETINGS

This year the number of meetings increased from five to six in response to the demand for more communication in the just-developing, highly-specialized fields. Joseph Sambrook organized a new meeting on the interaction of lectins with tumor cell surfaces. Carel Mulder organized the Tumor Virus Meeting and Walter Keller arranged the meeting on Eucaryotic RNA Polymerase. The Phage Meetings—one on lysogenic and the other on lytic phages—were arranged by Carl Anderson and Robert Crouch. Bruce Alberts and Noburu Sueoka organized the meeting on DNA Replication which closed the summer session.

Again, we air mailed abstracts of these meetings to all who subscribed to the abstract service.

THE INTERACTION OF LECTINS WITH TUMOR CELL SURFACES

Attended by 47 participants

SUNDAY, MAY 30,—7:30 P.M.

Chairman: R. E. Pollack, New York University Medical Center, N.Y.C.

G. M. Edelman, The Rockefeller University, New York City: "Structure and Function of Concanavalin A."
J. W. Becker, The Rockefeller University, New York City: "Crystallographic Studies on Concanavalin A."
A. Edmundson, Argonne National Laboratories: "X-Ray Crystallographic Studies of Concanavalin A."
A. Palozzo, A. Levy, and W. G. Jaffé, Escuela de Biologia, Universidad Central de Venezuela: "Concanavalin A, A Lipo-Protein."
G. S. Hassing and I. J. Goldstein, The University of Michigan, Ann Arbor, Mich.: "Effects of Chemical Modification on the Activity of Concanavalin A."
H. Markowitz, Mayo Clinic, Rochester, Minnesota: "Isolation and Properties of the Phytohemagglutinin, Robin and its Interaction with Myeloma Proteins."

MONDAY, MAY 31—9:00 A.M.

Chairman: R. Roblin, Massachusetts General Hospital, Boston, Mass.

I. J. Goldstein and R. N. Iyer, The University of Michigan, Ann Arbor, Mich.: "Quantitative Studies on the Interaction of Concanavalin A with Model Carbohydrate-Protein Conjugates."
W. Galbraith and I. J. Goldstein, The University of Michigan, Ann Arbor, Mich.: "Specificity and Some Characteristics of the Lima Bean Lectin-Type A Blood Group Substance Interaction."
Y. Nagata, Princeton University: "Purification of Wheat Germ Agglutinin."
B. Ozanne, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Lectin Mediated Agglutinability of Various Cell Lines."
J. Sambrook, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Binding of Lectins to Virus Transformed, Untransformed, and Mitotic Cells."
B. Ami Sela, H. Lis and L. Sachs, The Weizmann Institute of Science, Rehovot, Israel: "Quantitation of N-acetyl-D-Galactosamine-like Sites on the Surface Membrane of Normal and Transformed Cells."

MONDAY, MAY 31—2:00 P.M.

Chairman: W. Eckhart, Salk Institute, San Diego, California

G. L. Nicolson, University of California at San Diego, La Jolla, Calif.: "Redistribution of Ferritin-Conjugated Concanavalin A Membrane Binding Sites after Trypsinization or SV40 Transformation of 3T3 Cells."
R. Sheinin and I. M. Frohlich, University of Toronto: "Interaction of the Surface Components and the Plasma Membrane of Normal and Virus-Transformed 3T3 Mouse Fibroblasts with Concanavalin A."
W. T. Shier, The Salk Institute, San Diego, Calif.: "Wheat Germ Agglutinin Receptor Sites as Tumor Specific Surface Antigens."
P. Kent, National Institutes of Health, Bethesda, Maryland: "Complex Changes in Carbohydrate Receptor Sites in Cell Transformations."
I. Pastan, National Institutes of Health, Bethesda, Maryland: "The Role of Cyclic AMP and Prostaglandins and the Regulation of Morphology and Growth of Normal and Transformed Fibroblasts."

TUESDAY, JUNE 1—9:00 A.M.

Chairman: R. Sheinin, University of Toronto, Canada

J. A. Forrester and W. J. Smith, Chester Beatty Research Institute, London: "The Use of the Lectin Derived from Wheat Germ in the Detection of Cervical Carcinoma."

W. R. Bruce, H. Lin, M. J. Walcroft, The Ontario Cancer Institute and the Connaught Medical Research Laboratories, Toronto: "Selective Action of Concanavalin A (Con A) on Experimental Tumors."
P. B. Dent, McMaster University, Hamilton, Ontario: "Effect of Phytohemagglutinin on Murine and Human Tumors *in vitro*."
E. Watkins, Jr., Lahey Clinic Foundation, Boston, Mass.: "Target Cell Culture Method (LATCH Culture) for Study of Host Response to Oligovalent Lectin Preparations."
B. G. T. Pogo, The Public Health Research Institute of the City of New York, N.Y.C.: "Early Events in Lymphocytes Transformation by Phytohemoagglutinin."
M. A. Leon and T. Takahashi, St. Luke's Hospital, Cleveland, Ohio: "Suppressive Effect of Antibody to Concanavalin A on Stimulation of Lymphocytes by Concanavalin A."

THIRD TUMOR VIRUS MEETING

Attended by 141 participants

MONDAY, AUGUST 16—7:30 P.M.

Chairman: John Watkins, Oxford University

M. Nonoyama and J. S. Pagano, Department of Bacteriology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, N.C.: "Epstein-Barr Virus Specific C-RNA and EBV DNA Replication in Virus Infected Cells."
A. M. Lewis, Jr., A. S. Levine, C. S. Crumpacker, M. J. Levin, R. Samaha, and P. H. Henry, NIH, Bethesda, Maryland; Children's Hospital, Boston, Mass.; and University of Missouri Medical Center, Columbia, Mo.: "Isolation of Nondefective Ad. 2-SV40 Hybrids which Induce Different SV40 Functions."
A. S. Levine, L. Schnipper, M. Levin, T. Kelly, R. Samaha, M. Oxman, P. Henry, A. M. Lewis, Jr., and C. S. Crumpacker, NIH, Bethesda, Md., Children's Hospital, Boston, Mass., and University of Missouri, Columbia, Mo. "Characterization of SV40 DNA Segments in the Nondefective Adeno 2-SV40 Hybrids, and of the RNA Species Transcribed from these Segments."
S. G. Baum and R. I. Fox, Departments of Medicine and Cell Biology, Albert Einstein College of Medicine, Bronx, N.Y.: "Components of Adenovirus-SV40 Hybrid Viruses."
D. R. Dubbs and S. Kit, Division Biochemical Virology, Baylor College of Medicine, Houston, Texas: "Attempts to Induce Replication of the Resident Nondefective SV40 Genome by Superinfection of SV40-Transformed Human Cells with Mutant SV40 DNA."

TUESDAY, AUGUST 17—9:00 A.M.

Chairman: Thomas Benjamin, Public Health Research Institute of the City of New York

R. Jaenisch and A. J. Levine, Department of Biochemistry, Princeton University, Princeton, N.J.: "The Formation of SV40 Oligomeric DNA in the Presence of Cycloheximide."
T. J. Kelly, Jr., E. D. Sebring, M. M. Thoren and N. P. Salzman, NIH, Bethesda, Md.: "Electron-Microscopy of Replicating SV40 DNA Molecules."
E. D. Sebring, T. J. Kelly, Jr., M. M. Thoren, and N. P. Salzman, NIH, Bethesda, Md.: "Physical Properties of Replicating SV40 DNA Molecules."
D. A. Goldstein and W. Meinke, Department of Microbiology, Scripps Clinic and Research Foundation, La Jolla, Calif.: "Complex Replicative Forms of Polyoma DNA."
W. P. Cheevers, J. Kowalski and K. Yu, Cancer Research Laboratory, University of Western Ontario, London, Canada: "Studies on Cellular DNA Replication in Productive Polyoma Virus Infection."

TUESDAY, AUGUST 17—7:30 P.M.

Chairman: Walter Eckhart, The Salk Institute, San Diego, Calif.

P. M. Frearson and L. V. Crawford, Imperial Cancer Research Fund, London: "Polyoma Virus Basic Proteins."
E.-S. Huang, M. K. Estes, M. Nonoyama, and J. S. Pagano, Department of Bacteriology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, N.C.: "Structural Proteins of SV40: Effect on Transcription *in vitro*."
C. W. Anderson and R. F. Gesteland, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: *In vivo* Synthesis of SV40-Induced Proteins in Lytically Infected Monkey Cells."
J. A. Robb and R. G. Martin, Department of Pathology, University of California, San Diego, La Jolla, Calif., and Laboratory of Molecular Biology, NIAMD, NIH: "Characterization of a Temperature-Sensitive Uncoating Mutant of SV40 During Lytic Infection."
H. L. Ozer, Laboratory of Biochemistry, National Cancer Institute, NIH, Bethesda, Md.: "Synthesis of SV40 Virions."
P. T. Mora, R. O. Brady, and F. A. Cumar, NIH, Bethesda, Md.: "Conjoint Control of Growth and of a Specific Sugar Transferase in SV40 and Polyoma Transformed Cells."

WEDNESDAY, AUGUST 18—9:00 A.M.

Chairman: Malcolm A. Martin, National Institutes of Health, Bethesda, Maryland

M. Haas, M. Vogt, R. Weinberg and R. Dulbecco, The Salk Institute, San Diego, Calif.: "Specific Loss of SV40 DNA-cRNA Hybrids in Hybridization Experiments."
H. S. Smith, L. D. Gelb, and M. A. Martin, Cell Culture Laboratory, University of California, Berkeley, Calif., and NIH, Bethesda, Md.: "Detection and Quantitation of SV40 Genetic Material in Abortively Transformed BALB/3T3 Clones."
N. H. Acheson, E. Buetti, and R. Weil, Department of Molecular Biology, University of Geneva, Switzerland: "Synthesis and Cleavage of Giant Polyoma Virus-Specific RNA."
R. Weil*, E. Buetti*, E. May***, P. May***, C. Salomon*, K. Scherrer**, and N. Acheson*, *Dept. of Molecular Biology, University of Geneva; **Dept. of Molecular Biology, Swiss Cancer Institute, Lausanne; and ***Institut de Recherches Scientifiques sur le Cancer, Villejuif, France: "Studies on SV40 and Polyoma Virus."

P. Lebowitz and S. M. Weissman, Dept. of Internal Medicine, Yale University, New Haven, Conn.: "Discrete RNA Species Transcribed from Virus DNA *in vitro.*"
H. Delius and H. Westphal, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Visualization of the *in vitro* Transcription Complexes of SV40 DNA and *E. coli* RNA Polymerase.

WEDNESDAY, AUGUST 18—2:00 P.M.

Chairman: David Baltimore, Massachusetts Institute of Technology, Cambridge, Mass.

D. B. Rifkin, J. P. Quigley, R. W. Compans, and E. Reich, The Rockefeller University, N.Y.C.: "The Organization of the Proteins of Rous Sarcoma Virus."
H. Bauer, D. P. Bolognesi, H. Gelderblom, and R. Kurth, Max-Planck Institut fur Virusforschung, Tubingen: "Virus Specific Structural and Cell-Surface Antigens of Avian RNA Tumor Viruses."
E. Fleissner, Sloan-Kettering Institute for Cancer Research, NYC: "Comparison of Proteins from Avian Tumor Viruses and from RSV-Transformed, Non-Producing Cells."
R. C. Nowinski, N. Sarkar, L. J. Old, Sloan-Kettering Institute for Cancer Research, NYC: "Proteins and Nucleocapsid Structure of the Oncornaviruses."
J. Hilgers, Department of Biology, The Netherlands Cancer Institute, Amsterdam: "Immunogenetical Studies on the Vertical Transmission of the Group-Specific Antigen of Murine Leukemia Virus."
J. P. Quigley, D. B. Rifkin, and E. Reich, Rockefeller University, N.Y.C.: "Phospholipid Composition of Rous Sarcoma Virus, Host Cell Membranes and Other Enveloped RNA Viruses."

THURSDAY, AUGUST 19—9:00 A.M.

Chairman: Warren Levinson, University of California, San Francisco

D. Baltimore, D. Smoler and I. Verma, Department of Biology, MIT, Cambridge, Mass.: "DNA Polymerase of RNA Tumor Viruses."
J. M. Coffin and H. M. Temin, McArdle Laboratory, University of Wisconsin, Madison, Wisconsin: "Particulate RNA-Directed DNA Polymerase Systems in Cells Infected with Rous Sarcoma Virus."
E. Bromfeld, D. F. Smoler, N. Meuth, K. F. Manly, I. Verma and D. Baltimore, Department of Biology, MIT, Cambridge, Mass.: "An RNA Primer in the Endogenous DNA Polymerase Reaction of Moloney Leukemia Virions."
A. J. Faras, J. M. Taylor, H. E. Varmus, J. P. McDonnell, W. E. Levinson, and J. M. Bishop, Dept. of Microbiology, University of Calif., San Francisco: "Purification and Properties of the RNA-Dependent DNA Polymerase from Rous Sarcoma Virus (RSV)."
N. Tsuchida, M. S. Robin and M. Green, Institute for Molecular Virology, St. Louis University School of Medicine, St. Louis, Mo.: "Virus Specific RNA in Cells Transformed by Murine Sarcoma Viruses (MSV)."
H. E. Varmus, W. E. Levinson, and J. M. Bishop, Department of Microbiology, University of California Medical Center, San Francisco: "Detection of Avian Tumor Virus Sequences in Cell DNA."
J. Leong, A. Garapin, W. Levinson, and M. Bishop, Department of Microbiology, University of California Medical Center, San Francisco: "Virus-Specific RNA in Cells Infected with Rous Sarcoma Virus (RSV)."
N. Biswal, B. McCain, and M. Benyesh-Melnick, Department of Virology and Epidemiology, Baylor College of Medicine, Houston, Texas: "The Replication of Murine Sarcoma-Leukemia Virus (MSV-MLV) RNAs."

THURSDAY, AUGUST 19—2:30 P.M.

Chairman: Boyce Burge, Massachusetts Institute of Technology, Cambridge, Mass.

R. A. Weiss, E. Katz and R. R. Friis, Department of Microbiology, University of Washington, Seattle: "Induction of C Type RNA Viruses in Normal Cells."
W. Levinson, B. Woodson, and J. Jackson, Department of Microbiology, University of California, San Francisco: "Inactivation of Rous Sarcoma Virus upon Contact with N-Substituted Isatin B Thiosemicarbazone (IBT)."
W. A. Carter, W. W. Brockman and E. C. Borden, Departments of Medicine and Microbiology, Johns Hopkins University School of Medicine, Baltimore, Md.: "Effects of Streptovaricins on Functions of Oncogenic RNA Viruses."
Y.-C. Hsu, J. Baskar and S. Leigh, Johns Hopkins University, School of Hygiene and Public Health, Baltimore, Md.: "Host DNA Replication and Viral Gene Expression in Murine Sarcoma Virus Infected Neurons."
K. Somers and S. Kit, Division of Biochemical Virology, Baylor College of Medicine, Houston, Texas: "Properties of Murine Sarcoma Virus (MSV) Cloned in Rat Cells."
H. C. Chopra, J. Hooks, M. J. Walling and C. J. Gibbs, NIH, Bethesda, Md.: "Comparative Study of Simian Foamy Viruses and Monkey Mammary Tumor Derived Virus."
C. W. Boone, P. Brandchaft and R. V. Gilden, NIH, Bethesda, Md.: "Binding of Rat Autoantibody to Surface Antigens of AKR Virus-Induced Rat Tumor Cells."

EUCARYOTIC RNA POLYMERASE MEETING

Attended by 42 participants

FRIDAY, AUGUST 20—7:30 P.M.

M.-J. Tsai and R. S. Criddle, University of California, Davis: "DNA-Dependent RNA Polymerase from Yeast Mitochondria."
P. A. Horgen and D. H. Griffin, Dept. of Forest Botany and Pathology, State University College of Forestry, Syracuse, N.Y.: "RNA Polymerase III of Blastocladiella Emersonii is Mitochondrial."
K. P. Schafer, G. Bugge, M. Grandi, and H. Kuntzel, Max-Planck Institut Fur experimentelle Medizin, Abteilung Chemie, Göttingen, W. Germany: "RNA polymerase from mitochondria of Neurospora crassa and *in vitro* transcription of the mitochondrial DNA with *E. coli* RNA polymerase."
K. P. Mullinix, G. C. Strain, and L. Bogorad, The Biological Laboratories, Harvard University, Cambridge, Mass.: "RNA Polymerases of Maize."

SATURDAY, AUGUST 21—9:30 A.M.

E. DiMauro, R. Adman, and B. D. Hall, Dept. of Genetics, University of Washington, Seattle: "Properties of Yeast RNA Polymerases."
S. Dezélée, Service de Biochimie Cen. Saclay, France: "Yeast RNA Polymerases."
R. G. Roeder, Dept. of Embryology, Carnegie Institution of Washington, Baltimore, Md.: "RNA Polymerases from *Xenopus laevis* and their Fidelity of Transcription *in vitro*."
S. Natori, H. Ristow, and A. Garen, Dept. of Molecular Biophysics and Biochemistry, Yale University, New Haven: "Characteristics of an RNA Polymerase from Drosophila."

SATURDAY, AUGUST 21—7:30 P.M.

R. Weaver, S. Blatti, P. Morris and W. J. Rutter, Dept. of Biochemistry and Biophysics, University of California, San Francisco: "Two Forms of RNA Polymerase II."
J. W. Drysdale, J. C. Bagshaw, and R. A. Malt, Surgical Services, Mass. Gen. Hosp., and Dept. of Surgery, Harvard Medical School, Boston: "Multiple Mammalian RNA Polymerases Displayed on Gel Electrofocusing."
S. T. Jacob and E. M. Sajdel, Massachusetts Institute of Technology, Cambridge, Mass.: "Regulation of Liver RNA Polymerases."
C. J. Chesterton, S. M. Humphrey and P. H. W. Butterworth, Dept. of Virology, Royal Postgraduate Medical School and Dept. of Biochemistry, University College, London: "The DNA-Dependent RNA Polymerases of Whole Rat Liver and of Rat Liver Tumour Cells."

SUNDAY, AUGUST 22—9:30 A.M.

N. Montanaro, F. Novello, and F. Stirpe, Institute of Pharmacology and Institute of General Pathology, University of Bologna, Italy: "RNA Synthesis and RNA Polymerase of Rat Brain Nuclei."
W. I. P. Mainwaring and F. R. Mangan, Imperial Cancer Research Fund, London: "Stimulation of Prostatic RNA Polymerase by Androgenic Steroids both *in vivo* and *in vitro*."
P. H. Butterworth, R. F. Cox and C. J. Chesterton, Dept. of Biochemistry, University College, London: "Transcription of Rat Liver Chromatin by a Specific Rat Liver DNA-Dependent RNA Polymerase."
H. P. Voigt, R. Kaufmann, G. Kreysing, and H. Matthaei, Max-Planck Institut für Experimentelle Medizin, Göttingen, Germany: "Soluble RNA-Polymerase from Human Placenta: Structural and Functional Properties."

SUNDAY, AUGUST 22—7:30 P.M.

SPECIAL SEMINAR

O. L. Miller, Jr., and Barbara A. Hamkalo, Dept. of Biology, Oak Ridge National Laboratory: "Genes *in flagrante transcripto*."

MONDAY, AUGUST 23—9:30 A.M.

W. Sugden and W. Keller, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "RNA Polymerases and Stimulatory Proteins from Cultured Human Cells."
K. H. Seifart and B. J. Benecke, Institut Für Physiologische Chemie, Universität Marburg, West Germany: "Purification and Partial Characterization of Multiple RNA Polymerase Species from Rat Liver Tissue."
M. T. Franze-Fernandez and A. O. Pogo, Dept. of Cell Biology, The New York Blood Center, New York: "Regulation of Nucleolar RNA Polymerase by Amino Acids in Ehrlich Tumor Cells."
G. E. Austin, L. J. Bello, and J. J. Furth, University of Pennsylvania Medical School, Philadelphia, Pa.: "RNA Polymerase from Uninfected and Adenovirus Infected KB Cells."

BACTERIOPHAGE MEETINGS (LYSOGENIC AND LYTIC)

Attended by 274 participants

Lysogenic Section

TUESDAY, AUGUST 24—7:30 P.M.

D. Botstein, R. K. Chan, C. Waddell and M. Osburne, Mass. Inst. of Tech., Cambridge, Mass.: "Gene Order and Gene Function in Phage P22."
V. Israel, H. Rosen and M. Levine, Univ. of Michigan, Ann Arbor, Mich.: "Binding of P22 Base Plate Parts to Cells."
M. Woodworth-Gutai, V. Israel and M. Levine, Univ. of Michigan, Ann Arbor, Mich.: "DNA Exonuclease Activity after Phage P22 Infection."
M. Susskind, A. Wright and D. Botstein, Tufts Medical School, Boston, and M.I.T., Cambridge, Mass.: "Superinfection Exclusion by P22 Prophage."
H. Schmieger, Inst. f. Mikrobiologie der GSF, Gottingen, Germany: "The Formation of Generalized Transducing Particles of Salmonella Phage P22."
R. K. Chan and D. Botstein, Mass. Inst. of Tech., Cambridge, Mass.: "Specialized Transduction of Tetracycline Resistance by Phage P22."
A. I. Bukhari and D. Zipser, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Random Insertion of Prophage MU-1 within a Single Cistron."
M. Howe, Mass. Inst. of Tech., Cambridge, Mass.: "Generalized Transduction Mediated by Phage MU-1."
A. L. Taylor and C. D. Trotter, Univ. of Colorado Med. Center, Denver, Colo.: "Co-Induction of Prophage MU-1 and the Lac Operon in *Escherichia coli*."

WEDNESDAY, AUGUST 25—9:00 A.M.

A. Folkmanis and D. Freifelder, Brandeis Univ., Waltham, Mass.: "Insertion of λ DNA into a Sex Factor Carrying Att^{λ}."
F. Ausubel, P. Voynow and E. Signer, M.I.T., Cambridge, Mass.: "Partial Purification of the λ-Int Protein."
H. A. Nash, Natl. Inst. of Mental Health, Bethesda, Md.: "The Purification of Radiochemically Labeled *int* Protein."
K. Shimada, R. Weisberg and M. Gottesman, NIH, Bethesda, Md.: "Prophage λ at Unusual Chromosomal Locations."
M. Shulman and M. Gottesman, NIH, Bethesda, Md.: *Att* Mutants of Phage Lambda."
D. Freifelder, Grad. Dept. of Biochemistry, Brandeis Univ., Waltham, Mass.: "Physical Studies on Excision of Phage λ."
J. L. Rosner, Lab. of Mol. Biol., NIH, Bethesda, Md.: "Single Lysogens, Double Lysogens, Prophage Substitution and Curing with Bacteriophage P1."
M. Sunshine, Karolinska Inst., Stockholm, Sweden, and B. Kelly, San Diego State College, San Diego, Calif.: "Education of Host Genes by the Temperate Phage P2."
J. F. Lehman, R. W. Davies, W. F. Dove, H. Inokuchi, and R. L. Roehrdanz, McArdle Laboratory, Univ. of Wisconsin, Madison, Wis.: "Transcriptional Stimulation of Prophage Excision."

WEDNESDAY, AUGUST 25—7:30 P.M.

G. Guarneros and H. Echols, Dept. of Molecular Biology, Univ. of Calif., Berkeley: "About the Nature of Site-Specific Recombination by Phage λ."
G. Kayajanian, McArdle Lab., Univ. of Wisconsin, Madison, Wisc.: "Reanalysis of Non-Reciprocal, Red-Mediated Recombination in Bacteriophage λ."
R. White and M. S. Fox, M.I.T., Cambridge, Mass.: "The Structure of Unreplicated λ Recombinants."
K. McMillin, M. Stahl, R. Malone, Y. Nozu and F. Stahl, Inst. of Mol. Biol., Univ. of Oregon, Eugene, Ore.: "Recombination of Phage Lambda under Conditions of Restricted DNA Synthesis."
J. Lutkenhaus and M. Konrad, Univ. of Calif., Los Angeles, Calif.: "A Temperature Sensitive Step in Lambda Phage DNA Replication."
C. Hidalgo and H. Nash, Nat. Inst. of Mental Health, Bethesda, Md.: "Methylation Pattern of Lambda Phage DNA."
V. Simmon and S. Lederberg, Brown University, Providence, R.I.: "Degradation of Host-Restricted Lambda DNA."
J. A. Levy, R. L. Calendar, M. Marsh, and R. N. Goldstein, Dept. of Mol. Biol., Univ. of Calif., Berkeley: "Identification of some P2 Gene Products and Cleavage of the Major Capsid Protein."
H. Murialdo and L. Siminovitch, Univ. of Toronto, Ontario: "Characterization of Proteins of the Morphogenetic Region of Phage λ."
D. P. Harrison and V. C. Bode, Univ. of Maryland Medical School, Baltimore, Md., and Kansas State Univ., Manhattan, Kansas: "A Putrescine Requirement for Head-Tail Joining."

THURSDAY, AUGUST 26—9:00 A.M.

S. Ghosh, A. M. Wu and H. Echols, Dept. of Mol. Biol., Univ. of Calif., Berkeley: "Repression of RNA Synthesis *in vitro* by the cI Protein of Phage λ."
F. R. Blattner, H. A. Lozeron, W. Szybalski, and J. E. Dahlberg, McArdle Lab. and Dept. of Physiol. Chem., Univ. of Wisconsin, Madison, Wisc.: "Promoter and Operator are not Transcribed in Coliphage Lambda."
J. K. Boettiger, G. Kayajanian, and F. R. Blattner, McArdle Laboratory, University of Wisconsin, Madison, Wisc.: "Building a Better Bypass."
K. K. Mark, McArdle Lab., Univ. of Wisconsin, Madison, Wisc.: "Transcriptional Studies on the Effects of the nin5 and byp Mutations in Coliphage Lambda."
N. C. Franklin, Stanford University, Stanford, Calif.: "Fusions of the *TRP* Operon to Lambda in the Region *N-Immunity.*"
K. Krell, M. E. Gottesman and J. S. Parks, NIH, Bethesda, Md., and M. A. Eisenberg, Columbia Univ., N.Y.C.: "Constitutive Synthesis of Desthiobiotin Synthetase in Induced λb2 Lysogens."
H. Drexler, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, N.C.: "Transduction by λ-GAL Hybrid Carried by T1."
M. Thorn, M. Sunshine, W. Gibbs and R. Calendar, Univ. of California, Berkeley, and B. Kelly, San Diego State College, San Diego, Calif.: "Suppression of Polarity Caused by Phage P2 Amber Mutants."
J. Weil, R. Cunningham, E. Mitchell and B. Bolling, Vanderbilt Univ., Nashville, Tenn.: "Characteristics of λp4, a Strain Containing 9% Excess DNA."

THURSDAY, AUGUST 26—2:00 P.M.

J. R. Scott, Emory University, Atlanta, Georgia: "More about P1 Clear Mutants."
M. J. Bronson and M. Levine, Univ. of Mich., Ann Arbor, Mich.: "Virulent Mutants of Phage P22."
D. E. Berg, Stanford University, Stanford, Calif.: "On the Regulation of the Plasmid dv."
S. Hayes and Y. Saturen, McArdle Lab., Univ. of Wisconsin, Madison, Wisc.: "Mutants of λdv with Reduced or Enhanced λ Exclusion Characteristics."
D. Court, L. Green and H. Echols, Dept. of Mol. Biol., Univ. of Calif., Berkeley, Calif.: "Positive and Negative Regulation by the cII and cIII Genes of Phage λ."
S. Hayes and W. Szybalski, McArdle Lab., Univ. of Wisconsin, Madison, Wisc.: "Controls of L-Strand Transcription in the Immunity Region of Coliphage Lambda."
J. S. Hong, G. R. Smith and B. N. Ames, Dept. of Biochem., Univ. of Calif., Berkeley: "Factors Influencing the Phage Decision between Lysis and Lysogeny: cAMP, CRP Protein, RNA Polymerase, and a New Phage Gene, CLY."
L. F. Reichardt and A. D. Kaiser, Stanford University, Stanford, Calif.: "The Control of λ Repressor Synthesis."

FRIDAY, AUGUST 27—9:00 A.M.

S. S. Lee and J. Suit, M.D. Anderson Hospital and Tumor Institute at Houston, Houston, Texas: "Thermal Induction of Bacteriophage Plb in Thermosensitive Mutants of *Escherichia coli* K12."

A. J. Brachet, D. Schwartz and M. Yarmolinsky, Institut de Biologie Moleculaire de la Faculte des Sciences, Paris: "Suppression of the Defects in TS DNA-B Mutants of *E. coli* (unable to continue DNA synthesis at 42°) by Certain Mutants of Prophage P1."
M. Belfort and D. L. Wulff, Univ. of Calif., Irvine, Calif.: "Further Characterization of *E. coli* Mutant hfl-1 which is Lysogenized by Lambda at High Frequency."
L. Hallick, H. Echols* and J. Davies, Dept. of Biochemistry, Univ. of Wisc., and *Dept. of Mol. Biol., Univ. of Calif., Berkeley: "Regulation of the Association of Lambda DNA with the Cell Membrane."
N. Yamamoto, T. Kato and S. Fukuda, Temple University, Philadelphia, Pa.: "Bacterial Functions can Substitute Phage Functions."
S. Kumar and C. R. Fuerst, Dept. of Medical Cell Biology, Univ. of Toronto, Canada: "Control of RNA Transcription of λ DNA by Two *Escherichia coli* Coded Products."
D. I. Friedman, Dept. of Microbiology, The Univ. of Michigan, Ann Arbor, Mich.: "Inhibition of N Gene Expression by a Bacterial Mutation."

Lytic Section

SATURDAY, AUGUST 28—7:30 P.M.

R. D. Camerini-Otero, L. A. Day and R. M. Franklin, Public Health Research Institute, N.Y.C.: "A Simple Turbidimetric Method for Determining the Molecular Weights of Viruses."
S. Marker, R. D. Camerini-Otero, A. Datta and R. M. Franklin, Public Health Research Institute, N.Y.C.: "The Structural Proteins of PM2."
A. Datta and R. M. Franklin, Public Health Research Institute, N.Y.C.: A DNA-Dependent RNA Polymerase Associated with Bacteriophage PM2."
L. A. Goscin and D. H. Hall, Duke University Medical Center, Durham, N. C.: "Hydroxyurea Sensitive Mutants of T4."
G. C. Anderson, H. E. Hendrickson, K. Mizobuchi and D. J. McCorquodale, Univ. of Texas at Dallas: "Genetic Maps of T5 and BF23."

SUNDAY, AUGUST 29—9:00 A.M.

T. Morrison, D. Blumberg and M. H. Malamy, Tufts Univ. School of Medicine, Boston, Mass.: "On the Mechanism of T7 Inhibition by F (Sex) Factors."
W. C. Summers and K. Jakes, Yale University, New Haven, Conn.: "Translation of T7 Lysozyme mRNA *in vivo* and *in vitro.*"
I. Brunovskis, R. W. Hyman and W. C. Summers, Yale University, New Haven, Conn.: "Transcription of Coliphage T7 *in vivo.*"
R. F. Gesteland, C. Kahn and W. Studier, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: *In vitro* Synthesis of T7 Proteins."
L. B. Rothmann-Denes, R. L. Cafferata and R. Haselkorn, Dept. of Biophysics, Univ. of Chicago, Chicago, Ill.: "T4 RNA and Protein Synthesis in *E. coli* B Infected with T7."
N. Axelrod, Harvard University: *"In vitro* Transcription of Phage TX."
J. D. Karam, Division of Genetics, Sloan-Kettering Institute for Cancer Research, N.Y.C.: "Catalytic Functions of T4."
J. H. Wilson and J. S. Kim, Calif. Inst. of Tech., Pasadena, Calif., and J. Abelson, Univ. of Calif., San Diego, La Jolla, Calif.: "Clustering and Function of T4 tRNA."

SUNDAY, AUGUST 29—8:00 P.M.

M. Valee, CNRS, Montpellier, France; H. Bernstein and J. Cornett, College of Medicine, Tucson, Ariz.: "Immunity Towards Ghosts by T4 Infected *E. coli* and the DNA Delay (DD) Genes."
E. Goldman, P. Swerdlow and H. F. Lodish, Mass. Inst. of Tech., Cambridge, Mass.: "Initiation of Protein Synthesis in T4-Infected Extracts."
P. S. Cohen, University of Rhode Island, Kingston, R.I.: "Regulation of T4 Early Enzyme Synthesis."
J. S. Wiberg, S. Mendelsohn, G. Warner, K. Hercules* and J. Munro*, Univ. of Rochester Medical School, Rochester, N.Y., and *Univ. of Colorado Medical School, Denver, Colo.: "A T4 Mutant that Exhibits Altered Regulation of Phage Enzyme Synthesis."
A. R. Price, Univ. of Michigan, Ann Arbor, Mich.: "Enzymology of Uracil-DNA Synthesis by PBS2 Phage in *Bacillus subtilis.*"
C. Stewart, Rice University, Houston, Texas: "Lysis in SP82 Infection."

MONDAY, AUGUST 30—9:00 A.M.

M. Zweig and D. J. Cummings, Univ. of Colorado Medical Center, Denver, Colo.: "The Head Proteins of Bacteriophage T5."
J. King and D. Botstein, Mass. Inst. of Tech., Cambridge, Mass.: "Head Assembly and DNA Encapsulation in P22."
L. W. Black, Univ. of Maryland School of Med., Baltimore, Md.: "Internal Protein Mutants of Bacteriophage T4D."
U. K. Laemmli, Princeton University, Princeton, N.J.: "Intermediates in the Formation of the Head of Phage T4."
D. L. Hamilton and R. B. Luftig, Duke University, Durham, N.C.: "Some Novel Properties of Gene 13 Defective Head Particles."
S. K. Beckendorf, J. H. Wilson, and I. Lielausis, Calif. Inst. of Tech., Pasadena: "T2•T4 Differences in the Tail Fiber Region."
T. Homyk and J. Weil, Vanderbilt University, Nashville, Tenn.: "Long Deletion Mutants in Phage T4."

MONDAY, AUGUST 30—7:30 P.M.

P. V. O'Donnell and J. D. Kabam, Sloan-Kettering Institute for Cancer Research, N.Y.C.: "The Direction of Translation for Bacteriophage T4 Gene 43 (DNA Polymerase-3′-Exonuclease): Counterclockwise."
M. S. Hershfield and N. G. Nossal, National Inst. of Health, Bethesda, Md.: "Nuclease Activity in a Fragment of T4 DNA Polymerase Induced by the Amber Mutant am B22."
C. Majumdar, Univ. of Pa., Philadelphia, Pa.: "Association of DNA Polymerase I with Membrane Following Phage Infection."
A. S. Dion and S. S. Cohen, Univ. of Penna. School of Medicine, Philadelphia, Pa.: "Polyamines and the Synthesis of T-Even Bacterial Viruses."
C. Howe and B. Emanuel, Dept. of Med. Genetics, Univ. of Pa., Philadelphia, Pa.: "Multiple Initiation of Replication in T4 DNA: Characterization of Intermediate Replicative Forms."
H. Delius and A. W. Kozinski, Cold Spring Harbor Laboratory, N.Y., and Dept. of Medical Genetics, Univ. of Penna., Phila., Pa.: "Electron-Microscopic Studies of Partially-Replicated T4 DNA."
P. Serwer, Harvard Medical School, Boston, Mass.: "Intracellular T7 DNA after Gentle Lysis—Two New Structures."

TUESDAY, AUGUST 31—9:00 A.M.

D. R. Bone and C. E. Dowell, Univ. of Calif. at Davis, and Univ. of Mass., Amherst: "Replication of A ϕX174 Mutant in tsDNA Strains of *E. coli.*"
L. B. Dumas and C. A. Miller, Northwestern Univ., Evanston, Ill.: "Phage ϕX174 DNA Replication in a Host Temperature-Sensitive Mutant Defective in DNA Synthesis."
M. Iwaya and D. T. Denhardt, McGill University, Montreal, Quebec, Canada: "Role of the Parental Strand during the Development of the Single-Stranded DNA phage ϕX174."
S. C. Lin and D. Pratt, University of California at Davis: "A Role of M13 Gene 2 in DNA Replication."
D. S. Ray, Molecular Biology Institute and Dept. of Zoology, U.C.L.A., Los Angeles, Calif.: "Pulse-Labeled M13 Supercoils of Low Superhelix Density."
A. K. Dunker, R. Klausner and D. A. Marvin, Yale University, New Haven: "The Structure of Filamentous Phage Strains Carrying Mutations in Gene 3."
H. Smilowitz and J. Carson, Mass. Inst. of Tech., Cambridge, Mass.: "Phage f1 Infection and Host Cell Membrane Synthesis."

TUESDAY, AUGUST 31—7:30 P.M.

R. M. Benbow and R. L. Sinsheimer, Calif. Inst. of Tech., Pasadena, Calif.: "Genetic Recombination of Bacteriophage ϕX174."
C. A. Hutchison III and M. H. Edgell, Univ. of North Carolina, Chapel Hill, N. C.: "A Genetic Assay for Small Fragments of ϕX174 DNA."
C.-Y. Chen, C. A. Hutchison III and M. H. Edgell, Univ. of North Carolina, Chapel Hill, N.C.: "*In vitro* Synthesis of Infective ϕX174 Recombinant DNA."
M. H. Edgell, C. A. Hutchison III and M. H. Sclair, Univ. of North Carolina, Chapel Hill: "Endonuclease R Fragments of ϕX174 Replicative Form DNA."
M. H. Sclair, M. H. Edgell and C. A. Hutchison III, Univ. of North Carolina, Chapel Hill: ϕX174 Mutants Containing New Restriction Sites."
D. Henner, I. Kleber and R. Benzinger, Dept. of Biology, Univ. of Virginia, Charlottesville, Va.: "Transfection of *E. coli* Spheroplasts: V. Specificity and Mechanism of Facilitation of Transfection by Protamine Sulfate."

WEDNESDAY, SEPTEMBER 1—9:00 A.M.

G. Mosig, W. Patrick and R. Ehring, Dept. of Molecular Biology, Vanderbilt University, Nashville, Tenn.: "Reciprocity of Recombination in T4 Revisited."
J. R. Christensen and T. V. Potts, Univ. of Rochester, Rochester, N.Y.: "Recombination in Cooperative Infection."
S. Hattman, Univ. of Rochester, Rochester, N.Y.: "Altered DNA Methylase in Phage T2 gt."
L. A. McNicol and E. B. Goldberg, Tufts Univ. School of Medicine, Boston, Mass.: "Reduced Transformation Efficiency of Non-Glucosylated T4 Phage DNA."
R. Benzinger and I. Kleber, Dept. of Biology, Univ. of Virginia, Charlottesville, Va.: "Transfection of *E. coli* Spheroplasts: IV. Biological Melting Curves of T7, P22, T4, T5 and Lambda Phage DNA's.
R. H. Baltz, Univ. of Illinois, Urbana, Ill.: "Inhibition of T4 Transfection by *E. coli* Endonuclease I."

DNA REPLICATION MEETING

Attended by 123 participants

SATURDAY, SEPTEMBER 4—7:30 P.M.

NEW ENZYMES OF DNA REPLICATION

Chairman: Charles Richardson, Department of Biological Chemistry, Harvard University

M. Gefter and T. Kornberg, Department of Biological Sciences, Columbia University, New York: "Studies on *E. coli* DNA Polymerases."
R. B. Wickner, D. Pisetsky, B. Ginsberg, I. Berkower and J. Hurwitz, Department of Developmental Biology and Cancer, Albert Einstein College of Medicine, Bronx, N.Y.: "DNA Polymerase II and *in vitro* DNA Replication."
J. C. Wang, University of California, Berkeley: "Studies on an *E. coli* Protein Omega."
B. Alberts, G. Herrick, N. Sigal and L. Frey, Department of Biochemical Sciences, Princeton University, Princeton, N.J.: "Proteins that Unwind DNA and Their Role in Genetic Processes."

H. Delius, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Electron Microscopic Studies on Complexes between DNA Unwinding Proteins and Nucleic Acids."
Y. Hotta and H. Stern, Department of Biology, University of California, San Diego: "A DNA Binding Protein in Meiotic Cells."
M. Gellert and M. L. Hicks, National Institutes of Health, Bethesda, Maryland: "Genetics and Physiology of *E. coli* DNA Ligase Mutants."

SUNDAY, SEPTEMBER 5—9:00 A.M.

NEW IN VITRO SYSTEMS

Chairman: Jerome Vinograd, California Institute of Technology, Pasadena, California

J. A. Wechsler and J. Gross, Department of Biological Sciences, Columbia University, and MRC Molecular Genetics Unit, Edinburgh, Scotland: "*E. coli* Mutants Temperature-Sensitive for DNA Synthesis."
H. E. Schaller, B. Otto, B. M. Olivera, V. Nuesslein, A. Klein, R. Herrmann and F. Bonhoeffer, Max-Planck-Institut, Tubingen, and Department of Biology, University of Utah, Salt Lake City, Utah: "*In vitro* DNA Replication."
P. Boerner and D. W. Smith, Department of Biology, University of California, San Diego: "Studies on DNA Synthesis *in vitro* Using Agar-Immobilized *E. coli* W3110 Polal and Pola+ Strains."
R. Moses and C. C. Richardson, Harvard Medical School, Cambridge, Mass.: "DNA Replication in Toluenized Cells."
H. Hoffman-Berling, K. Geider, U. Hess and H. P. Vosberg, Max-Planck-Institut, Heidelberg, Germany: "Structure of Nascent DNA."
M. Kohiyama, E. Milewski and A. Kolber, Institut Biologie Moleculaire, Paris, and Washington University School of Medicine, St. Louis, Missouri: "Purification of Stimulatory Factor for DNA Synthesis in Toluene-Treated DNA-B polA Mutant."
A. T. Ganesan, Department of Genetics, Stanford Medical School, Stanford, California: "Chromosome Replication in Bacillus subtilis."

SUNDAY, SEPTEMBER 5—7:30 P.M.

PRECURSORS, INHIBITORS AND MECHANISMS OF ELONGATION

Chairman: John Cairns, Cold Spring Harbor Laboratory

R. Okazaki, A. Sugino, R. Kainuma-Kuroda and M. Arisawa, Institute of Molecular Biology, Nagoya University, Nagoya, Japan: "Some Recent Observations on the Mechanism of DNA Chain Growth."
D. T. Denhardt, S. Eisenberg, and A. Kato, Department of Biochemistry, McGill University, Montreal, Canada: Gaps and Ends, Repetitious DNA and π Proteins, or How Does DNA Replicate?."
Rudolf Werner, University of Miami School of Medicine, Miami, Florida: "Thymidine Nucleotide Pools in *E. coli* 15 TAMT."
N. H. Mendelson, Department of Microbiology, University of Arizona, Tucson: "Kinetic and Autoradiographic Evidence for Different Utilization of Thymine and Thymidine in Bacillus subtilis."
D. Billen, Laboratory of Radiation Biology, University of Florida, Gainesville: "DNA Synthesis in Freeze-Treated Bacillus subtilis W23."
N. C. Brown, Department of Cell Biology and Pharmacology, University of Maryland School of Medicine, Baltimore: "Inhibition of the Replication of DNA of Staphylococcal Phage P11-M15 by 6(p-Hydroxyphenylazo)-Uracil."
G. J. Bourguignon, J. P. Baird and Rolf Sternglanz, Department of Biochemistry, State University of New York, Stony Brook: "Studies on the Mechanism of Action of Nalidixic Acid."
G. E. Degnen and E. C. Cox, Departments of Biochemical Sciences and Biology, Princeton University, Princeton, New Jersey: "A Conditional Mutator Gene in *E. coli*."

MONDAY, SEPTEMBER 6—9:00 A.M.

CONFIRMATIONAL STUDIES IN BACTERIAL SYSTEMS

Chairman: Ross B. Inman, University of Wisconsin, Madison

D. L. Robberson, H. Kasamatsu, and J. Vinograd, Divisions of Biology and Chemistry, California Institute of Technology, Pasadena, California: "Replication of Mitochondrial DNA in Cultured Mouse Cells. Circular Replicative Structures."
N. P. Salzman, E. D. Sebring, T. J. Kelly, Jr., and M. M. Thoren, N.I.H., Bethesda, Maryland: "SV40 DNA Replication."
R. Jaenisch, A. Mayer and A. Levine, Department of Biochemistry, Princeton University, Princeton, New Jersey: "Replicating SV40 Molecules Containing Closed Circular Template DNA Strands."
R. M. Benbow, M. G. Eisenberg and R. L. Sinsheimer, California Institute of Technology, Pasadena, California: "Multiple Length DNA Molecules of Bacteriophage ϕX174."
G. Ihler and Y. Kawai, Department of Biochemistry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania: "Alternate Fates of the Complementary Strands of Lambda DNA after Infection of *Escherichia coli.*"
A. Skalka, M. Poonian, and P. Bartl, Roche Institute of Molecular Biology and Hoffman-La Roche, Inc., Nutley, New Jersey: "Origin of Concatemers during DNA Replication: Electron Microscopic Studies of Partially Denatured Intracellular Lambda DNA."
J. Wolfson, M. Magazin, and D. Dressler, The Biological Laboratories, Harvard University, Cambridge, Massachusetts: "Actively Replicating T7 DNA."

MONDAY, SEPTEMBER 6—7:30 P.M.

CHROMOSOME REPLICATION AND THE MEMBRANE

Chairman: P. C. Hanawalt, Stanford University, Stanford, California

A. O'Sullivan and N. Sueoka, Department of Biochemical Sciences, Princeton University, Princeton, N.J.: "Membrane Attachment and Chromosome Configuration in Bacillus subtilis."

R. G. Wake, Biochemistry Department, Sydney University, Australia: "Visualization of Reinitiated Chromosomes in B. subtilis."

D. T. Kingsbury, D. J. Sherratt, and D. R. Helinski, Department of Biology, University of California, San Diego: "*Escherichia coli* Mutants Temperature Sensitive for Plasmid Replication."

R. Rownd, C. F. Morris, R. A. Stickgold, C. L. Hershberger, Y. Terawaki, and S, Mickel, Laboratory of Molecular Biology and Department of Biochemistry, University of Wisconsin, Madison: "Replication of Episomes in Proteus Mirabilis."

C. E. Helmstetter, Roswell Park Memorial Institute, Buffalo: "Control of Initiation of Chromosome Replication in *E. coli.*"

C. B. Ward and D. A. Glaser, Virus Laboratory, University of California, Berkeley: "Inhibition of Initiation of DNA Synthesis by Low Concentrations of Penicillin."

M. Inouye, Department of Biochemistry, State University of New York at Stony Brook: "Reversal by NaCl of Envelope Protein Changes Related to DNA Replication and Cell Division of *E. coli.*"

TUESDAY, SEPTEMBER 7—9:00 A.M.

MAMMALIAN CHROMOSOME REPLICATION

Chairman: Joel A. Huberman, Massachusetts Institute of Technology, Cambridge, Mass.

T. Hori and K. G. Lark, Department of Biology, University of Utah, Salt Lake City, Utah: "DNA Synthesis in Chinese Hamster Cells."

H. Weintraub, Department of Anatomy, University of Pennsylvania, Philadelphia: "Bi-Directional Initiation of DNA Synthesis."

J. H. Taylor, Institute of Molecular Biophysics, Florida State University, Tallahassee: "Units of Replication in Mammalian Chromosomes."

L. M. S. Chang and F. J. Bollum, Department of Biochemistry, University of Kentucky Medical School, Lexington: "A Nuclear DNA Polymerase from Mammalian Cells."

J. A. Huberman, A. Tsai, and R. A. Deich, Department of Biology, Massachusetts Institute of Technology, Cambridge: "Studies on the Topology of DNA Replication in Mammalian Cells."

G. P. Tocchini-Valentini, International Institute of Genetics and Biophysics, Naples, and M. Cripps, Laboratory of Molecular Embryology, Naples: "Synthesis of Amplified Ribosomal DNA."

TUESDAY, SEPTEMBER 7—7:30 P.M.

INITIATION I

Chairman: Gisela Mosig, Vanderbilt University, Nashville, Tennessee

W. F. Dove and H. Inokuchi, McArdle Laboratory, University of Wisconsin: "Positive and Negative Control Over Initiation in Lambda DNA Replication."

J. Tomizawa, National Institutes of Health, Bethesda, Maryland: "Bacteriophage Lambda Replication."

K. G. Lark, Department of Biology, University of Utah, Salt Lake City, Utah: "A Direct Role of RNA in DNA Replication?"

R. E. Bird, J. Louarn and L. G. Caro, Department of Molecular Biology, University of Geneva, Switzerland: "Bidirectional Chromosome Replication in *E. coli.*"

A. Worcel and M. Schwartz, Service de Biochimie Cellulaire, Institute Pasteur, Paris: "Reinitiation of Chromosome Replication in a DNA Ts Mutant of *E. coli:* Requirement of recA for Reinitiation."

E. Elizur, Department of Molecular Biology, Hebrew University Hadassah Medical School, Jerusalem: "Studies on Selection and Characterization of Initiation Mutants of Bacillus subtilis."

J. C. Copeland, Division of Biology and Medical Research, Argonne National Laboratory, Argonne, Illinois: "Regulation of Chromosome Replication in Bacillus subtilis."

WEDNESDAY, SEPTEMBER 8—9:00 A.M.

INITIATION II

Chairman: J. Tomizawa, National Institutes of Health, Bethesda, Maryland

G. Mosig, J. Tift, W. Berquist, and S. Brock, Department of Molecular Biology, Vanderbilt University, Nashville, Tennessee: "On Bacteriophage T4 DNA Replication."

J. D. Karam, Division of Genetics, Sloan-Kettering Institute for Cancer Research, New York: "T4 DO Gene 62 Function: Catalytic and Mutagenic."

A. W. Kozinski, Department of Medical Genetics, University of Pennsylvania, Philadelphia: "Multiple Sites of Initiation of Replication in T4 DNA."

B. Francke and D. S. Ray, Molecular Biology Institute and Department of Zoology, University of California, Los Angeles: "Formation of the Parental Replicative Form DNA of Bacteriophage ϕX174 and Initial Events in its Replication."

S. C. Lin and D. Pratt, Department of Bacteriology, University of California, Davis: "M13 Gene 2 in DNA Replication."

G. Lindahl and Y. Hirota, Institut Pasteur, Paris, France: "Replication of *E. coli* Chromosome under the Control of Prophage P2."

A. Jaffe-Brachet, D. Schwartz and M. Yarmolinsky, Institut de Biologie Moleculaire, Paris, France: "Suppression of the Defects in ts DNA-B Mutants of *E. coli* (Unable to Continue DNA Synthesis at 42°) by Certain Mutants of Prophage P1."

UNDERGRADUATE RESEARCH PARTICIPATION PROGRAM

Summer 1971

Supported by the National Science Foundation, the Laboratory hosted 10 undergraduates in the annual Undergraduate Research Participation Program. The program provides increased opportunities for the scholarly development of outstanding undergraduates who may pursue careers in science.

Each participant becomes a member of one of the research teams at the Laboratory and is given a special project to complete. In addition, the students attend the series of summer courses and seminars conducted by the Laboratory.

Members of the 1971 program, supervisors and their areas of research were the following:

Steven Chung, University of Oregon *Supervisor:* David Zipser	Mu phage rec. system
Mitchel Kanter, Duke University *Supervisor:* David Zipser	Mu phage deletion map
Michael Kaplan, Harvard College *Supervisor:* Peter Greenaway	Tumor virus proteins
Ronald Koenig, Yale University *Supervisor:* David Zipser	Mu phage deletion map
Randi Leavitt, Brooklyn College *Supervisor:* David Zipser	Mu-Lac hybrid proteins
Susan Leibenhaut, Massachusetts Institute of Technology *Supervisor:* Joseph Sambrook	Coli-animal cell agglutination
Annamarie Rehm, Duke University *Supervisor:* Ray Gesteland	Coli ribosome binding sites
John Ridge, University of Chicago *Supervisor:* Hajo Delius	DNA renaturation with "gene 32" protein
Gerald Rubin, Massachusetts Institute of Technology *Supervisor:* Ray Gesteland	Lac operator nucleotide sequence
Jerome Zeldis, Brown University *Supervisor:* David Zipser	Orientation of mu prophage

NATURE STUDY COURSES

Children of Ages 6 to 16

Created to stimulate an interest in Nature by observation and the study of flora, fauna and geology in areas surrounding Cold Spring Harbor, the Children's Nature Study Program was attended by more than 420 youngsters in the summer of 1971.

Directed by Otto A. Heck, students canvassed the Laboratory grounds and shoreline, the reserves at St. John's Church, Fox Hollow and Upland Preserves and the Charles T. Church Sanctuary. These areas with freshwater streams, ponds, seashore, tide pools, woodlands and meadowlands are rich in plant and animal life.

The Laboratory provided a headquarters facility (Jones Laboratory) and donated the use of much of the equipment, including microscopes, dissecting instruments, test kits and other instruments useful in attaining an understanding of science and ecology.

The Laboratory gratefully acknowledges the continuing support of the Huntington Federal Savings and Loan Association. The donation, the twelfth contribution by the Association to the program, provided scholarships for 12 students.

INSTRUCTORS

Otto A. Heck, Assistant Professor of Biology, Trenton, N.J., State College.
Alex Pepe, Science Instructor, East Side School, Cold Spring Harbor.
Beth Blauman, Student, University of Colorado.
Robert Budliger, Instructor, Bay Shore Middle School.
Leslee Cattrall, Student, University of Chicago.
Richard Rosenman, Science Instructor, Cold Spring Harbor High School.
Thomas Stock, Instructor, Selden Junior High School, Centereach.

COURSES

General Nature Study (ages 6, 7)
Elementary Geology (ages 8, 9)
Advanced Nature Study (ages 8, 9)
Seashore Life (ages 10, 11)
Bird Study (ages 10, 11)
Plant-Insect relationships (ages 10, 11)
Geology (ages 10, 11)
Plant Ecology (ages 12-16)
Ecology of the Estuary (ages 16-18)
Fresh-water Life (ages 10, 11)
Animals with Backbones (ages 10, 11)
Insect Study (ages 10, 11)
Ichthyology-Herpetology (ages 12-16)
Marine Biology (ages 12-16)
Geology of Long Island (ages 12-16)
Animal Ecology (ages 12-16)

NATURE STUDY WORKSHOP FOR TEACHERS

Twenty-seven Long Island elementary and secondary school teachers attended the annual Laboratory workshop in natural history and ecology of Long Island. Four in-service credits were awarded to those instructors who satisfactorily completed the course.

The workshop is designed to familiarize elementary and secondary school teachers with the natural environment of the Long Island area, including the animals and plants living there and the environment which affects these organisms. The course consisted of field trips, indoor laboratory work-time divided between lectures and practical work and guest lecturers.

Instructors were Otto A. Heck and Robert Budliger.

LABORATORY STAFF

November 1971

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James D. Watson

Administrative Director
William R. Udry

Research Scientists
John Cairns
Hajo Delius
Raymond Gesteland
Walter Keller
Carel Mulder
Robert Pollack
Joseph Sambrook
Henry Westphal
David Zipser

Postdoctoral Fellows
Bernard Allet
Carl Anderson
Margaret Anderson
Bal Apte
Ernesto Bade
Jeremy Bruenn
Ahmad Bukhari
Peter Greenaway
Peter Jeppesen
Ulf Pettersson
Philip Sharp

Graduate Students
Bradford Ozanne
William Sugden
Art Vogel

Research Assistants
Jane Caldwell
Paula Curtin
Arlene Jackson
Clara Kahn
Joe Katagiri
Dreania LeVine
Maria Lurye
Nancy Mantell
Marie Metlay
Bonnie Mitchell
Nabi Sullivan
Carole Thomason
Ingrid Wendell
Annalie Wilde
Elizabeth van Alphen

Genetics Research Unit, Carnegie Institution of Washington
Alfred Hershey, Director
Barbara McClintock

Supporting Staff
Barbara Bankey
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James Stanley
William VanHouten

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GARDEN CITY, NEW YORK 11530

The Board of Trustees
Cold Spring Harbor Laboratory
Cold Spring Harbor, New York:

We have examined the balance sheet of Cold Spring Harbor Laboratory as of October 31, 1971 and the related statements of current income, expenditures and fund balance and of changes in fund balances for the year then ended. 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, except for the absence of recording certain equipment as explained in note 2 to the financial statements, such financial statements present fairly the financial position of Cold Spring Harbor Laboratory at October 31, 1971 and the results of its operations for the year then ended, in conformity with generally accepted accounting principles which, except for the changes of recording and depreciating certain equipment, the accumulating of depreciation on buildings used in research and related activities, and the allocation from current unrestricted funds for the replacement of plant assets as described in notes 2 and 4 to the financial statements, were applied on a basis consistent with that of the preceding year.

Peat, Marwick, Mitchell & Co.

December 10, 1971

Year Ended October 31, 1971 — Exhibit A

ASSETS

Current Funds:	
Unrestricted:	
Cash	$ 52,704
Certificate of deposit	227,798
Accounts receivable (less allowance for doubtful accounts of $6,000)	49,782
Inventory of books at cost (less allowance for obsolescence of $40,679)	72,152
Deferred publication costs (note 3)	3,511
Prepaid expenses	9,686
Total unrestricted	415,633
Restricted:	
Due from other funds	55,249
Grants receivable (note 1)	1,025,028
Total restricted	1,080,277
Total current funds	$ 1,495,910
Plant funds:	
Unexpended–due from other funds	100,677
Invested in plant (note 2):	
Land and improvements	138,297
Buildings:	
Used in research and related activities	715,941
Used in auxiliary activities	301,506
Laboratory equipment	100,841
	1,256,585
Less allowance for depreciation	195,379
Total invested in plant	1,061,206
Total plant funds	$ 1,161,883

LIABILITIES AND FUND BALANCES

Current Funds:	
Unrestricted:	
Accounts payable	$ 68,702
Accrued expenses	33,680
Due to other funds	155,926
Deferred income (note 3)	5,650
Fund balance (Exhibit B)	151,675
Total unrestricted	415,633
Restricted:	
Fund balance (Exhibit C)	1,080,277
Total restricted	1,080,277
Total current funds	$ 1,495,910
Plant funds:	
Unexpended–fund balance (Exhibit D)	100,677
Invested in plant:	
Investment in plant (Exhibit D)	1,061,206
Total invested in plant	1,061,206
Total plant funds	$ 1,161,883

See accompanying notes to financial statements.

STATEMENT OF CURRENT INCOME, EXPENDITURES AND FUND BALANCE

Year Ended October 31, 1971 — **Exhibit B**

Income:	
Expendable grants (Exhibit C)	$ 846,484
Indirect cost allowance on grants	226,235
Contributions	79,958
Symposium registration fees	9,625
Summer programs	94,525
Laboratory rental	27,095
Investment income	10,503
Other sources	674
Auxiliary enterprises:	
Book sales	182,156
Dining hall	64,373
Rooms and apartments	67,970
Total income	1,609,598
Expenditures:	
Research	711,230
Annual symposium	31,315
Summer programs	122,975
Library	14,621
Operation and maintenance of physical plant	216,980
General and administrative	240,732
Scholarships	1,400
Auxiliary enterprises*:	
Book sales	158,090
Dining hall	63,714
Rooms and apartments (excludes depreciation of $20,605 recorded in plant funds)	19,823
Total expenditures	1,580,880
Excess of income over expenditures	28,718
Fund balance at beginning of year	278,213
	306,931
Deduct:	
Appropriation to unexpended plant funds (note 4)	143,326
Appropriation to plant fund	11,930
	155,256
Fund balance at end of year	$ 151,675

See accompanying notes to financial statements.

**The foregoing operations are reported exclusive of an allocation for operation and maintenance of physical plant and general and administrative expenses.*

STATEMENT OF CHANGES IN CURRENT RESTRICTED FUND BALANCES

Year Ended October 31, 1971

Exhibit C

Balance at beginning of year		$ 1,272,076
Add gifts and grants		1,074,722
		2,346,798
Deduct:		
Current expenditures	$ 846,484	
Indirect cost allowance	226,235	
Plant expenditures	194,566	
Unexpended funds returned to grantor	653	
Transfers	(1,417)	
		1,266,521
Balance at end of year		$ 1,080,277

STATEMENT OF CHANGES IN PLANT FUNDS

Year Ended October 31, 1971

Exhibit D

Unexpended Plant Funds		
Balance at beginning of year for plant improvement and renovation		$ 47,572
Add appropriation from current unrestricted funds (note 4)		143,326
		190,898
Deduct expenditures for plant		90,221
Balance at end of year		$ 100,677
Investment in Plant		
Balance at beginning of year		825,166
Add:		
Capital expenditures financed by unrestricted funds	$ 1,930	
Capital expenditures financed by unexpended plant funds	90,221	
Capital expenditures financed by grant awards	194,566	
Donated equipment	10,000	
		296,717
		1,121,883
Deduct depreciation of buildings and equipment (note 2)		60,677
Balance at end of year		$ 1,061,206

See accompanying notes to financial statements.

NOTES TO FINANCIAL STATEMENTS

(1) Grants receivable of the current restricted funds represent amounts pledged to the Laboratory for certain operations and for the completion of designated projects. The grants will be collected as expenditures are made by the Laboratory for the designated projects.

(2) Plant assets are stated on the following bases:

Land, improvements thereon, and buildings are stated at cost or at the May 1, 1963, values as carried on the books of Long Island Biological Association prior to their transfer to Cold Spring Harbor Laboratory.

Equipment acquired prior to the year ended October 31, 1971, is not recorded on the financial statements since the cost of the equipment is not known. In addition, certain Government-owned equipment is utilized by the Laboratory in connection with its performance under agreements with the Government. The Laboratory is, however, accountable to the Government for such equipment. During the year ended October 31, 1971, the Laboratory began recording at cost, (appraisal value for donated equipment) laboratory equipment aggregating $100,841, purchased or acquired with non-federal funds.

Prior to the year ended October 31, 1971, depreciation was only provided on buildings used in auxiliary activities, however, the Laboratory has decided to provide depreciation on all building and recorded equipment over the remaining useful lives of such assets in order to more accurately reflect the indirect operating expenses of the Laboratory. As a result of this accounting change, depreciation for the year ended October 31, 1971, has been increased by $40,072. Depreciation on building and equipment acquired with non-federal funds is an allowable indirect cost in accordance with the Department of Health, Education and Welfare guidelines and accordingly increases the indirect cost recovery for certain Federal grants.

(3) Publication costs aggregating $3,511 and book sales income aggregating $5,650 applicable to future publications have been deferred.

(4) During fiscal 1971 the Laboratory decided to establish a plant replacement fund as part of the unexpended plant fund. This accounting change was adopted to provide funds for the replacement of plant assets as they deteriorate or become obsolete. The charge to the current fund is equal to the depreciation provided on plant assets for the current year, which aggregated $60,677.

(5) The Laboratory employees are covered by Teachers Insurance and Annuity Association of America–College Retirement Equities Fund plan. Total expenditures for this plan amounted to $43,573 for the year ended October 31, 1971. There are no unfunded past service costs.

FINANCIAL SUPPORT OF THE LABORATORY

The Laboratory has been quite fortunate in obtaining a considerable amount of financial support from agencies of the Federal Government and from various national voluntary organizations and foundations. While these "grants" are vital to the work of the Laboratory, they support only direct costs such as salaries of the scientists and their immediate supplies. In most cases these grants do not even provide for all of these costs and in no case do they provide for all supporting costs. Nor do they provide funds for exploratory pilot work–making sure that fresh new ideas are developed to the point where we are "asking the right questions"–for which later major grants may be obtained. And in no case are Federal funds available for "bricks and mortar," the essential building facilities wherein the research can be performed.

Thus we are utterly dependent upon the contributions of our Participating Institutions, our friends and other contributors.

Family Foundations: A New Method Of Contributing

In dealing with private foundations, the Tax Reform Act of 1969 taxes investment income and includes five possible penalty taxes dealing with acts and omissions during operations and a possible penalty tax upon termination of private foundations. Also there are numerous other cumbersome administrative requirements for private or family foundations. In addition a donor is allowed only a charitable deduction of up to twenty percent of his adjusted gross income instead of the higher percentages applying to contributions to other charitable institutions.

Faced with the additional burden of the preparation of complicated annual reports and the payment of a four per cent excise tax on investment income, many small family foundations are planning to terminate their foundation status and exercise the option of becoming a "supporting organization," a conversion made possible under the 1969 Tax Reform Act and proposed Internal Revenue Service regulations.

In becoming a supporting organization, a foundation can *retain its name and continue to carry out the general purposes for which it was formed.* All that must be changed are its articles of incorporation and other governing instruments so as to make it a supporting institution.

A supporting organization, however, is *not* classified as a private foundation and therefore is not subject to the taxes and requirements imposed upon them by law.

A supporting organization operates to benefit a specific charitable organization such as the Cold Spring Harbor Laboratory. The assets of a foundation that becomes a supporting organization and the income therefrom would be devoted to the benefit of the specific charitable organization.

Since a supporting organization benefits a specific charity, the support can be continued while avoiding the tax on investment income and the possibility of penalty taxes. Also, gifts to a supporting organization can qualify for the 30 per cent and 50 per cent charitable income tax deduction.

A board of directors of the governing body controls the supporting organization. A majority of its members must consist of persons who are "disqualified persons" (within the meaning of the Internal Revenue laws) and who are appointed by the specified charitable organization. A minority, however, may consist of those persons who have historically been concerned with the foundation's affairs. Thus, current members could still participate in the affairs of the organization.

The Laboratory would obviously be interested in becoming a beneficiary of such a supporting organization. We would be happy to assist in any way possible the conversion of a private foundation into a supporting organization of the Laboratory. Any of our friends who have a particular interest in, or a knowledge of, such foundations are strongly urged to contact Mr. Udry, at area code 516-692-6660, with such information.

GRANTS

November 1, 1970, to October 31, 1971

Grantor	*Investigator or Program*	*Total Award*	*Duration of Grant*
NEW GRANTS:			
Research Grants			
National Science Foundation	Dr. Gesteland	$ 40,000	9/1/71-2/28/73
National Institutes of Health	General Research Support	93,002	1/1/71-12/31/71
	Dr. Pollack	38,481	6/1/71-5/31/72
American Cancer Society	Dr. Pollack	30,311	5/1/71-6/30/72
Damon Runyon Cancer Fund	Dr. Mulder	15,000	1/1/71-12/31/71
American Cancer Society	Dr. Sambrook	100,000	12/1/70-11/30/75
Jane Coffin Childs Memorial Fund for Cancer Research	Dr. M. Anderson	13,500	5/1/71-4/30/72
	Dr. Bukhari	16,500	7/1/71-6/30/73
	Dr. Jeppesen	16,500	9/1/71-8/31/73
Volkswagen Foundation	Dr. Watson	60,000	1/1/71-12/31/75
Alfred P. Sloan Foundation	Dr. Watson	450,000	1/1/71-6/30/75
CONTINUING GRANTS			
Research Grants			
National Science Foundation	Phycomyces Workshop	20,000	3/15/67-10/1/71
	Dr. Gesteland	163,900	12/1/67-9/30/71
	Dr. Zipser	91,200	3/1/70-2/28/72
	Dr. Cairns	75,000	9/15/70-9/15/72
National Institutes of Health	Dr. Gesteland	126,954	1/1/69-12/31/71
	Dr. Watson	2,100,000	5/1/69-4/30/74
	Dr. Zipser	138,000	1/1/70-12/31/73
Cystic Fibrosis Foundation	Dr. Watson	50,000	9/1/69-6/30/72
American Cancer Society	Dr. Cairns	581,352	1/1/69-life
National Institutes of Health	Dr. Gesteland	80,000	1/1/69-12/31/73
	Dr. Zipser	98,000	5/1/70-4/30/75
Leukemia Society of America	Dr. Westphal	100,000	7/1/70-6/30/75
Training Grants			
National Institutes of Health	Dr. Watson	391,925	1/1/70-12/31/74
National Science Foundation	Undergraduate Research	16,650	1/1/71-10/31/71
Symposium Grants			
National Science Foundation	Symposium Support	5,000	5/1/71-4/30/72
National Institutes of Health	Symposium Support	69,300	4/1/70-3/31/74
Atomic Energy Commission	Symposium Support	8,000	6/1/71-6/11/71

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LONG ISLAND BIOLOGICAL ASSOCIATION

The Laboratory was founded in 1890 by several local philantropists and the Brooklyn Institute of Arts and Sciences. In 1924 when the Institute withdrew from Cold Spring Harbor, the local supporters of the research formalized their efforts by incorporating as the Long Island Biological Association. Jointly with the Carnegie Institution of Washington, LIBA continued to support and direct the research at Cold Spring Harbor Laboratory.

Then in 1962, the Laboratory was reorganized as an operating organization and LIBA relinquished its management responsibilities to concentrate its efforts on continuing financial and community support for the Laboratory's work.

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