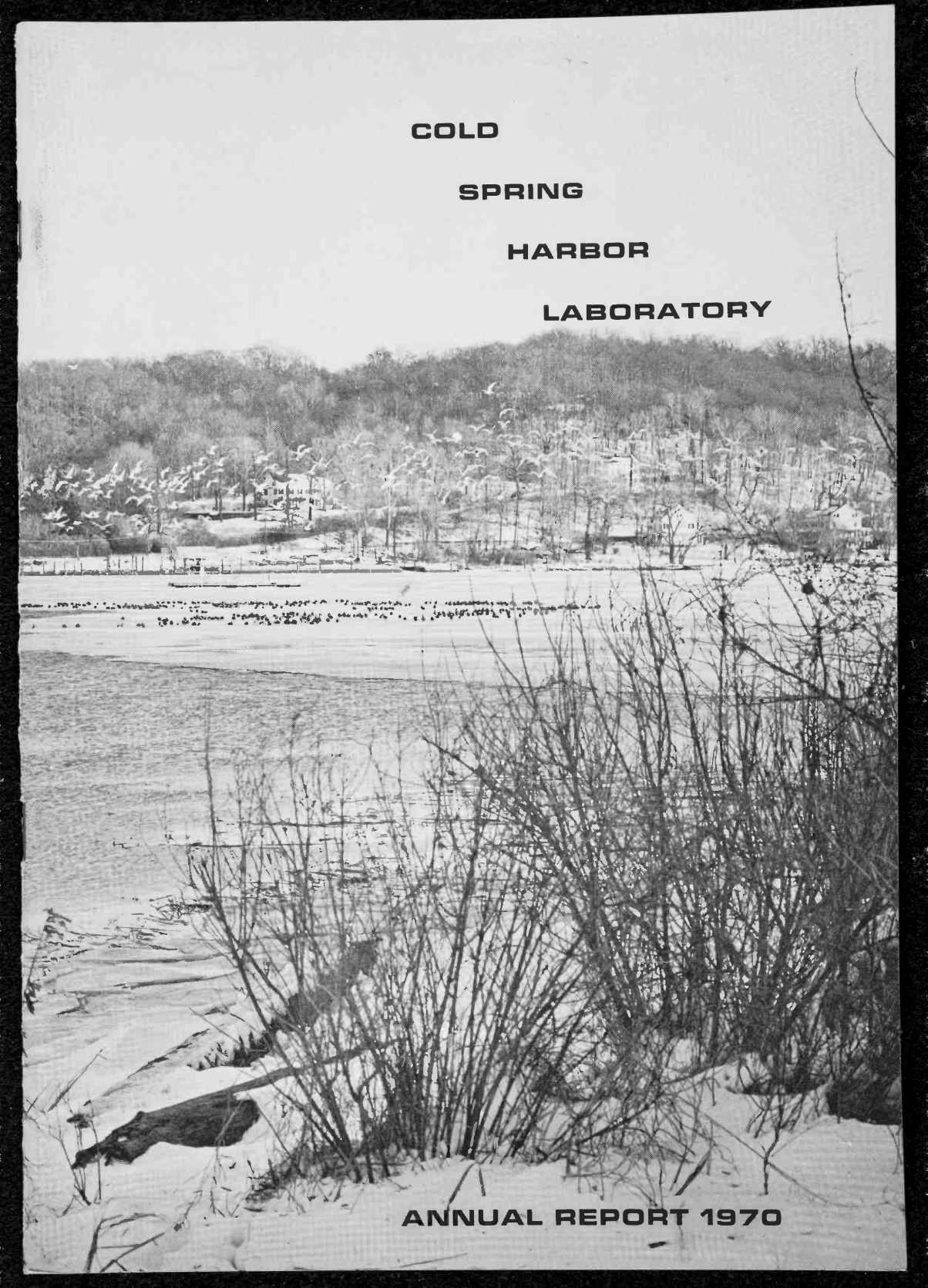
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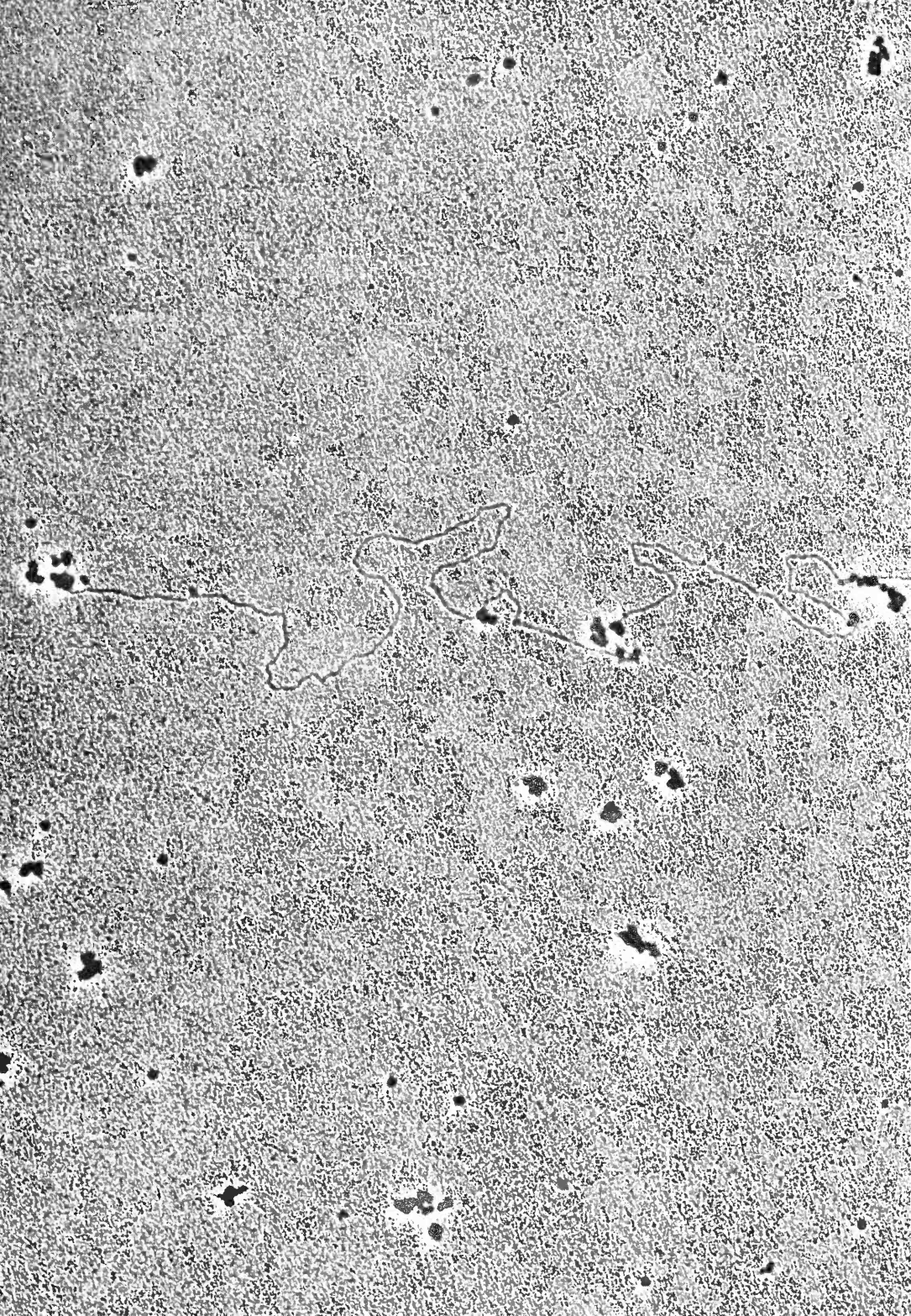

ANNUAL REPORT 1970

COLD SPRING HARBOR LABORATORY

COLD SPRING HARBOR, LONG ISLAND, NEW YORK

COLD SPRING HARBOR LABORATORY

Cold Spring Harbor, Long Island, New York

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DIRECTOR'S REPORT

Today molecular biology is being created much more effectively than it is being assimilated. Whereas ten years ago there were many scientists who knew all the key new facts, today there are at most only a few people who speak with real authority on all the topics we feel we should be on top of. The primary cause of this dilemma is the rapid expansion of molecular biology itself. One way to see this is to look at the size of the *Journal of Molecular Biology*. When it first appeared in 1959, many of us tried to read most of its pages, a not impossible task since there was only one issue appearing every three months. On the average, we needed to read only one article per week to keep abreast. Now, however, a new issue arrives every two weeks, often containing some 10-15 articles. That means that we should be looking over at least one article per day in this journal alone. And, given the existence of other journals which also bring forth decent molecular biology, each new day marks for most of us some four to six unread articles. Yet, if these same papers had appeared a decade ago, I would have read them with concern, if not enthusiasm.

Now, however, we feel lucky if we even seriously peruse the summaries alone. We hope that if something is really important, someone will tell us so, and reluctantly the majority of us decide our most profitable course is to concentrate on a narrow area through which one can move with confidence. In the long run, however, this is a most unsatisfying existence. The real answer to that particular problem which fascinates us may only come through application of a fact from a superficially unrelated area.

Clearly what is needed are intelligent reviews which appear virtually simultaneously with the printed articles. This task is now being seriously attempted only by *Nature* to whom we should be deeply indebted for their efforts in finding first-rate people capable of almost instantaneous journalism. Some people, however, do not like these quick dissections of new ideas, feeling they are cursory, sometimes way off mark, and too frequently overemphasize differences to create a sense of journalistic excitement. A few readers even believe the major effects of such reviews is to make an increasingly competitive science even more unbearable. While the occasional editorial comment makes me temporarily sympathetic to this viewpoint, in the final analysis I think *Nature* is doing the correct thing. The alternative is for most articles to be lost the moment they appear.

But even with extensive high-quality scientific journalism, the long-term future of most scientific articles is still bleak—they are likely to be remembered only if it is given prominent play in a review article of the type that is found in one of the many Annual Reviews or multi-volume series like those given birth to by the late Kurt Jacoby when he guided the fortunes of Academic Press. While Jacoby often subjected grant recipients with an unnecessary, overpriced book, we must still remember him with gratitude. Many, many useful books were the product of his entrepeneurial zeal. The teaching of graduate students in modern biology over the past decade would have been immensely more difficult if we did not have his various products. One cannot give beginning graduate students, much less college undergraduates, random issues of the *Journal of Molecular Biology* and expect them to gain the correct perspectives. Much more likely, they will be so overwhelmed by details they will not have the courage to ask whether a given article really proves something or is merely a holding operation to tell a government agency that a scientist has been in the lab.

This situation is compounded by the virtual absence of intermediate level texts which take the prospective molecular biologist from the cheerful level of a *Scientific American* article to the point where he can differentiate the good from the derivative science which

flows through successive issues of the *Proceedings of the National Academy of Sciences.* Perhaps because most molecular biologists were so busy in creating new ideas they have not, as a whole, been very interested in producing the texts which describe their own experiments. When they do write a review, often it will be for a book filled with unrelated subject matter. As a result there are now vast areas of molecular biology marked by the complete absence of contemporary texts.

Occasionally, our hopes rise that some commercial publishers soon will fill much of this gap. Some, of course, must believe that are in fact doing just that. But in reality I believe that most ventures are guided by the well-tested philosophy that a text should not contain too much material which the teachers themselves do not yet know. Somewhat out-of-date texts are not necessarily commercial disasters—often just the contrary. But in molecular biology the result could be a bad joke if its contents lag too much behind the current mood. So much thought must be given to the current state of the experimental data when the feasibility of a new molecular biology book is being seriously bandied about.

In this respect, this Laboratory has a decided advantage. Many of our meetings and courses represent the extreme frontier of a given area and our guests often tell us when a new idea is unlikely to be overturned by a still newer concept. So we believe we may be in a better position than most commercial concerns to arrange for the publication of advanced books useful to the established research worker as well as the serious student. To test out this possibility, we approached Jon Beckwith and David Zipser, not only to organize a meeting on the Lactose Operon, but also to edit a book on this topic containing specialized research articles as well as general review articles. Vital to our thoughts were the reviews since they were to bring the nonspecialist up to date and thus capable of understanding the more specialized papers. The resulting book is just out and we eagerly await our readers' reactions.

In the meanwhile, two other books based on recent meetings are in preparation for publication in the Spring of 1971. One on Phage λ will contain general reviews as well as specialized research articles. The other, on Tumor Virus Molecular Biology, will contain general articles arising in part from the efforts of the participants of the Tumor Virus Workshops held the past two summers. Also being prepared for publication are Laboratory Manuals containing much of the material presented during our various summer courses. The first two books to appear will feature experiments on the Lactose Operon and on Animal Cell Culture. Generally, most people who take our courses already have their advanced degrees and if not already active teachers, soon will be. Publication of these manuals in a convenient form hopefully will bring about the accelerated introduction of this material into many university and medical school level courses.

Under serious consideration is a project for the quick dissemination of an extended summary of the Symposium, to be available within six to eight weeks after the meeting ends. Behind this thought is the increasingly immense size of each Symposium volume. This year we are trying very hard to bring about its publication by January 15th—2½ to 3 months earlier than is usual. But cutting off any more time, given inevitable delays in receipt of nearly 100 manuscripts, needed corrections, etc., seems virtually impossible. So the best way we can see to impart quickly the tone of a Symposium to those unable to attend would be through an extended critical summary, 50 to 100 pages long containing key tables and illustrations. It thus would be considerably longer than the summaries which appear in *Science* or similar journals, and so in essence would be a small book conceivably very useful in university teaching. But its preparation would be highly expensive, require much effort to find suitable authors, and given the existence of Xerox machines, unlikely to be financially profitable. An annual subsidy would be required. In thinking about high-quality, fast publication, we can easily see why such projects are so

infrequent—they will lose money unless highly subsidized. Yet in the long run, I see no alternative and we shall certainly think about moving in this direction.

Now to look at some of the highlights of the year . . .

Increased level of Long Island Biological Association activities

Crucial to all of the Laboratory objectives has been the support and friendship of our neighboring community. Their support has been expressed for almost fifty years through the Long Island Biological Association (LIBA), a local body whose sole purpose is the advancement of the Laboratory's various activities. Not only have they directly helped us in financing many of our programs, but in an even more important sense, make our existence possible through the long-term lease of its land to the Laboratory. Thus, the increased level of LIBA activities over the past year augurs well for our future. Under LIBA sponsorship two very successful Open Houses were held last Fall, to which some 2,000 people came to hear me explain about the new programs in cancer research and to wander about our various buildings. In addition, LIBA sponsored three lectures arranged for nonscientific audiences—one by Matthew Meselson of Harvard University on "Biological and Chemical Warfare," a second by Professor Hubert N. Alyea of Princeton University on "Lucky Accidents, Great Discoveries, and the Prepared Mind," and a third by Mr. James J. Donegan of the Goddard Space Flight Center on "The Use of Computers in the Apollo Mission." All drew large and enthusiastic audiences. No doubt, partially encouraged by these events, the number of LIBA members rose to 492, in comparison to 214 in the previous year. For all of these activities we are most indebted to our Vice Chariman, Dr. Edward Pulling, who also acts simultaneously as Chariman of the LIBA Board of Trustees.

Staff and its Support

Three new members of the scientific staff were appointed during this year—David Zipser from Columbia University, where he was Associate Professor of Biology; Walter Keller from the National Institutes of Health; and Robert Pollack of the New York University Medical School, where he has been an Assistant Professor of Pathology. Already Dr. Zipser is in residence occupying space in the lower floor of Demerec Laboratory. With his arrival, the Laboratory regains solid strength in bacterial genetics, an area in which it held a commanding presence for over two decades. Dr. Keller, after spending time here in the summer, returns early in November to join the tumor virus group working in James Laboratory. His main interest is eucaryotic RNA polymerases, and he will join in efforts already started by Joe Sambrook and Bill Sugden. Dr. Pollack's appointment does not begin until July 1, 1971, since he is spending this academic year at the Weizmann Institute in Israel. His laboratory also will be located in the Demerec Laboratory, where he shall do experiments in the field of animal cell culture, with particular emphasis on the formation of hybrid cells created through cell fusion techniques.

Much needed financial support in terms of five-year salary grants have been received by Heiner Westphal from the Leukemia Society, David Zipser from the National Institutes of Health, and Joseph Sambrook from the American Cancer Society. Each receipt of such Salary Support Awards greatly strengthens our research potential by allowing the investigators concerned complete freedom to work at whichever research project looks the most promising to them.

Regretfully, we have lost the services of Rudolph Werner, who leaves us after a stay of five years for the Department of Biochemistry at the University of Miami Medical School.

While here, Rudolph did a number of highly ingenious experiments on the replication of T4 DNA and his absence will be keenly felt.

We all also keenly feel the departure of Don Eckels who has guided our Building and Grounds Department for the past five years, presiding over the most difficult task of restoring the many laboratory buildings which he found in a state of seemingly irreparable neglect. The many beautiful new flowers, shrubs and trees which now cover our grounds are the result of Don's efforts and we shall greatly miss the horticultural competence he brought to us. In his new position with the Parks Department of Davis, California, he also will be able to begin work for an advance degree in forestry, the area in which he received his undergraduate degree.

Joining us as the new head of Buildings and Grounds is Mr. Jack Richards, a resident of Huntington for many years. Jack is well known throughout the community for his skill as a general contractor and builder. Already he is managing the construction of the addition to the James Laboratory and the high professional competence he brings augurs well for our building program of the coming years.

Tumor Virus Program

Following very extensive renovations, the Tumor Virus Group was able to move into the James Laboratory early in the year, allowing the arrival in February of Carol Mulder and in April, of Heiner Westphal—both of whom came from the Salk Institute. As it exists now, working space still is very limited and so great relief was felt by all when our fund drive for the addition to James Lab was completed in the middle of February. This allowed construction to begin in early April with completion scheduled for early December of this year. Then we shall have approximately twice our current area to devote to our Animal Cell-Tumor Virus efforts. During the past summer, the coexistence of our year-round effort with our Animal Cell Culture-Animal Virus Courses required much self-restraint on both sides, and the opening of the new research facilities and office space should make for a much more relaxed summer atmosphere.

The total cost of the addition will approach $200,000 and wisely, our trustees insisted that the entire amount be in hand before construction was authorized. But this sum was virtually twice that initally projected when planning began, and for several months last winter, I had anxious moments that we would not be able to start on time. But two very large gifts did the job! One $25,000 gift from the Long Island Biological Association was a most welcome expression of support from our neighbors behind our desire to do serious work in the cancer field. This brought our drive to the halfway point. Then came a $100,000 gift by a kind donor who wishes to remain anonymous. Most interestingly, our donor is someone well-versed in the difficulties of cancer research and his belief in our potential for eventual success gives us great encouragement.

Summer Program

This year marked the introduction of a Yeast Genetics Course taught by Fred Sherman and Jerry Fink. At its conclusion, all ten students were highly enthusiastic about a leading role for yeast in the molecular biology research of the next decade and we look forward to the course being given again next year, hopefully with the number of students increased to fourteen. The Bacterial Genetics Course centered on the Lactose Operon, while λ was the main theme of the Phage Course. Both retained the high intellectual outlook of preceding years.

As in previous summers, all the Animal Cell-oriented courses (Cell Culture, Animal Virus and Tumor Virus Workshop) were heavily oversubscribed and far too many good applicants had to be refused. Some of the students were already committed to work with

animal cells and others wondering whether they should be. Given the increasing potentialities of tissue culture-grown cells, it would be surprising if a large fraction of the previously uncommitted did not decide to make the plunge. But for a few, the main conclusion was that animal cells were not at all like bacteria and retreat was in order.

Next summer, if suitable instructors can be persuaded that the historic charm of Davenport Lab outweighs its primitive facilities, we shall start a small experimental course on the chromosomes of eucaryotic cells. Conceivably the student number will be less than ten but this need not mean it would not be a very good course. However, we shall not be able to offer any such course on the scale we would like until a new laboratory is constructed to accommodate the courses now taught in Davenport. For awhile we were tempted by the posibility of making an addition to Davenport. But when this thought was given a serious architectural look, it did not make long-term sense. So we have been exploring the possibility of constructing an entirely new building somewhere in the vicinity of the Demerec-Animal House complex. Unfortunately, given the bleak prospect of federal financial help, this plan seems destined to be relegated to our list of far distant future projects.

A Sloan Foundation Grant to Support a Summer Program in Neurobiology

Only a few days ago did we learn the exceedingly good news that the Sloan Foundation has approved a five-year grant to us for $450,000 beginning in 1971, to cover a summer-long neurobiology program to be run in renovated Animal House facilities. This grant will come to us in two sections - $250,000 immediately, with $200,000 to be given before January 1973, if we are able to match it with $200,000 from another source. In making this application we received help from an advisory committee consisting of Richard Cone of John Hopkins University, Eric Kandell of New York University Medical School, and John Nicholls and Torsten Wiesel of Harvard Medical School. Soon I hope to bring this group together again to begin formulating definitive plans for our program next summer.

The Need for New Summer Housing Becomes More Acute

During this past summer our housing space was almost 100% utilized and only rarely did we have a free bed for the unexpected visitor. The simultaneous running of two courses, together with the presence of ten undergraduate students, left very few beds available for guests to come here to join in on various research programs, and for the first time in memory, no summertime research went on in the Jones Lab. The housing situation for this coming summer looks even bleaker. The Sloan grant means that we shall be running three courses at the same time and so somehow an additional thirty to thirty-five beds must be available for the instructors and students connected with the new Neurobiology effort. There seems no way to avoid the unpleasant consideration that some of our summer guests may have to be housed outside the Laboratory grounds—a situation which shall certainly reduce the benefits that would accrue to them for being in 24-hour residence.

Thus, we are desperately seeking both short- and long-term remedies. In the short term, we may be able to renovate the now unused Wawepex building to serve temporarily as a dormitory for some twelve to fourteen guests. But a real solution will come only with construction of a new building providing us with a year-round capability of holding advanced courses and workshop-type meetings. While a number of foundations have been approached to so help us, none has given any real encouragement. Most tell us that such living quarters do not fit in with their various objectives. Hopefully our efforts this coming year will prove more successful since the most unique feature of Cold Spring

Harbor is its potential to bring people together for serious discussion.

Financial Picture

A glance at our new financial statement quickly reveals that our 1970 operating budget more than doubled that of 1969. Almost all this increase represents the addition of restricted money (largely federal) given to support specific research and teaching programs. As such support never completely covers the cost of these programs, its effective utilization depends simutaneously on the receipt of unrestricted gifts. Such free money was particularly important in allowing us this past year to make most necessary renovations to various older buildings, some of which are from the days when a small whaling community existed at Cold Spring Harbor. That we have been able to make substantial and very necessary improvements to the Carnegie Dormitory, the Greenhouse, the Library, and James Laboratory is largely due to the generous support from our participating institutions, the industrial sponsors, and many nearby and far-distant friends. Great credit must also be given to our Administrative Director, Mr. James Brainerd, who has been able to greatly expand our various business affairs with the use of a cash reserve amounting to only slightly more than $100,000. But as we project a substantially larger budget for this coming year, we shall have to modestly increase our cash reserves.

Mr. William Udry to replace Mr. James Brainerd as Administrative Director

The skill with which our various business and administrative affairs have been carried out over this year makes it very hard to accept the decision of Jim Brainerd that he and his wife no longer wish to be absent from their family ties in the San Francisco region, where he plans to engage in consulting work in the educational field. As of December 1st of this year, Jim will cease being our Administrative Director. This news, a real shock when first heard, is only acceptable because of the many improvements he initiated during the all-too-brief two years he worked so successfully on our behalf. The multiplicity of tasks facing the Administrative Director is virtually impossible to convey to an outsider and the cheerful, competent way Jim handled them gave great reassurance to all connected with the Lab. Especially important these past two months has been Jim's help with the task of finding a replacement for himself. In this respect we all think we are fortunate in being able to find Mr. William Udry, now Chief Executive Officer of the Eye Research Institute of Bethesda, Maryland. He joins us late this year and we look forward to a continuation of the smooth operation so well established by Jim Brainerd.

. . . Thus, this past year has been pleasantly full and hopeful for our continuation as a site for the accomplishment and communication of difficult science.

J. D. Watson

October 19, 1970

Nobel Laureate Alfred D. Hershey and King Gustav Adolph VI of Sweden,
December 10, 1969

THE REPLICATION OF DNA

Laboratory of
J. Cairns
P. De Lucia
J. Margolskee

Last year, we reported the isolation of a polymeraseless mutant of *E. coli.* Our hope was that if such a mutant could be obtained and was then made generally available, all work on the biochemistry of DNA duplication would become much easier. So, we are pleased to report that five or six research groups, using our mutant, have now found another enzyme, or polymerizing system, in extracts of *E. coli*, which is distinct from the Kornberg polymerase and is present in undiminished amount in the polymeraseless mutant. It is now necessary to show that this new enzyme is indeed involved in normal DNA duplication rather than being used, like its predecessor, for DNA repair.

In the meantime, we have returned to our study, started some years ago, of the kinetics of the labeling of DNA by various precursors in the hope that eventually this should tell us something about the immediate precursors used for normal DNA synthesis. So far, our results have shown only that the situation is much more complex than generally supposed. One by-product of this work has been the finding that the replicating region of the bacterial chromosome does not seem to be associated with the bacterial membrane; thus, the apparent association of newly-made DNA with the membrane (reported by many people) seems to be due to an artifact generated by the procedure used for labeling the newly-made DNA. The association of bacterial nucleus and membrane, which has been observed by electronmicroscopists, is presumably due to the association of the membrane and the origin of replication, which was reported by Sueoka (Princeton).

PROTEIN AND RNA SYNTHESIS

Laboratory of
R. F. Gesteland
M. Anderson
D. Bostrom
L. V. Crawford
R. Crouch
C. Gilbert
B. Hirt
C. Kahn
J. Katagiri
J. Mickelbank
G. Rubin
P. F. Spahr

Bacteriophage R17

In our previous report we described the messenger RNA properties of the two fragments of R17 RNA produced by a single cut in the molecule 40% of the way in from 5' end. The data suggested (though indirectly) that the gene order on the RNA is 5'-A protein-coat protein-synthetase-3'. This has now been confirmed by direct analysis of the RNA sequence. Peter Jeppesen and Joan 'Argetsinger-Steitz, working at M.R.C. in Cambridge, in collaboration with P. F. Spahr and this laboratory, looked for specific, known sequences of nucleotides in the 40% and 60% fragments. The 5' end and the ribosome binding site for the A protein are in the 40% fragment. The proximal part of the coat protein ribosome binding site is in the 40% piece. One oligonucleotide containing the coat initiation sequence is not found in either fragment. The RNAse IV apparently cuts within this sequence to produce the 40% and 60% fragments. The synthetase ribosome binding site and the 3' terminus are found in the 60% fragment. Thus the gene order of A, coat, synthetase can be demonstrated by direct chemical techniques.

RNA synthesis and structure

A thin layer method for separating oligonucleotides generated by pancreatic and T1 ribonuclease digestion of RNA has been developed to the stage where most of the T1 products of 5S RNA can be seen as separate, distinct spots. Some resolution of the pancreatic ribonuclease products is obtained but at the moment not enough to allow for complete separation. The method employs electrophoresis across 20 cmX 20 cm polyethyleneimine (PEI) thin layers on plastic sheets. The buffer used in the first dimension contains 7M urea permitting separation on the basis of phosphate change; the buffer in the second dimension contains no urea and separation is according to base composition and sequence (e.g., AUG and UAG are easily separated in the second dimension).

Using $\gamma^{32}P$ labeled ATP and GTP as labeled nucleoside triphosphates for the in vitro synthesis of RNA with T4 DNA as template, then digesting the product with either pancreatic or T1 ribonuclease, and electrophoresing on PEI, it is possible to separate the oligonucleotides containing the 5' termini into at least three distinct "A" starts and one "G" start–a result previously seen in other laboratories. Similar work is now under way with *E. coli* RNA polymerase and SV40 DNA, as well as RNA polymerases from T4 infected *E. coli.*

Protein synthesis in coupled cell-free systems

Last year we reported some preliminary attempts to use extracts from *E. coli*, supplemented with RNA polymerase, to transcribe and translate various DNAs, with the hope of using this system to investigate viral gene products. T4, T7 and ϕX RF phage DNAs are excellent templates in this coupled system, while λ DNA is five- to ten-fold less active. By using ^{35}S met as label, the products from any of these DNAs can be analyzed by acrylamide gel electrophoresis or by fingerprinting of the tryptic peptides. Each DNA stimulates synthesis of a specific collection of tryptic peptides that is readily differentiable by electrophoresis at pH3.5. Although phage λ DNA works poorly, it is particularly interesting because of the extensive genetics and control mechanisms of the phage. It is expected that the cell-free system which is derived from uninfected *E. coli* will be able to read only the DNA near the immunity region of phage λ, in particular the leftwards (N) and rightwards (tof or Cro) promoters, and not much else in the absence of active N gene product. Since the proteins of this region (with the exception of CI) have been very elusive in infected cells, it was hoped that the system might provide a way to look at the properties of them. Acrylamide gel patterns of the λ in vitro product reveal five to six proteins of 35,000 to 9,000 molecular weight. Comparison of the λ and twenty-one hybrid DNA products shows some specific differences which argue that at least some of the transcription and translation is coming from the immunity region. Upon addition of purified λ repressor, synthesis of virtually all the viral specific material is shut off when λ DNA is used as template but this repression is greatly reduced with 21 hy DNA or λ vir DNA. The in vitro system is at least partially immunity-specific and is under repressor control, and thus mimics the situation in infected cells. We are now using various λ DNA mutants to try to identify the genes being read.

Tumor virus DNA

We are using this same in vitro system from *E. coli* to transcribe and translate SV40 and polyoma DNAs. Again each DNA gives a characteristic and reproducible set of tryptic peptides. With SV40 a careful comparison of the in vitro ^{35}S met peptides with met labeled tryptic peptides from the major structural protein of the SV40 virus (see below) shows that this protein is not made by the coli system to significant extent. .In the case of polyoma there is some correspondence between in vitro tryptic peptides and viral tryptic peptides, and this is being looked at carefully.

Tumor virus proteins

SV40 and polyoma viruses were grown in the presence of ^{35}S labeled methionine. After thorough purification, which did not abolish the infectivity, the virions were disrupted and the resulting polypeptides separated by either SDS-acrylamide electrophoresis or chromatography on agarose in the presence of guanidine-hydrochloride.

Both techniques gave essentially the same results: 80%-90% of the radioactivity was found in one component with a molecular weight of 43,000 for polyoma and 42,000 for SV40. After digestion with trypsin and electrophoresis on thin layer, peptide maps were obtained by autoradiography. No common peptides were observed for the major proteins of SV40 and polyoma. Three to four smaller polypeptides were also observed which gave peptide maps different from that of the major component. No further polypeptides appeared when radioactive leucine or arginine were used instead of methionine.

Protein synthesis in mammalian systems

In order to look in detail at the gene products of SV40 and polyma and of the control of expression of the genes, it is obviously necessary to develop an homologous system.

Preliminary experiments were directed towards obtaining a mammalian cell-free system which would synthesize protein in response to added natural mRNA. In collaboration with A. Smith (M.R.C., Cambridge), we showed that a cell-free system from HeLa cells synthesizes viral specific protein in response to added EMC RNA. Fingerprinting analyses at pH3.5 and 6.5 of a tryptic digest of the products showed that they were identical to the products made in a similar system derived from Krebs II ascites cells (permissive for EMC). Coat protein was not made in the system but as Smith, Marcker and Mathews (Nature *225*:184, 1970) have shown, the tryptic peptides of the product made in the in vitro ascites system are identical to those found in digests of virus-infected cells.

These results suggest that HeLa extracts accurately translate added mRNA. The ability of such extracts to support the coupled synthesis of SV40 RNA and protein from SV40 DNA is being investigated. Using RNA polymerase from *E. coli*, it can be shown that RNA is synthesized in the system, but as yet there is no evidence for viral specific protein synthesis.

TUMOR VIRUS

Laboratory of
H. Delius
C. Mulder
J. Sambrook
H. Westphal
L. Blanding
M. Conant
A. Jackson
D. Levine
B. Mitchell
H. Morrison
B. Ozanne
D. Ratner
B. Sugden
T. Ward
I. Wendel
T. Wilson

Genetics of transformed cells

Transformed cells are principally defined by their changed growth characteristics, primarily the loss of contact inhibition. Increasingly the changes in the outer membrane seem to be directly involved in this release from growth control. One of the changes yields transformed cells susceptible to agglutination by concanavalin A (con A), a glycoprotein isolated from Jack beans.

By repeated exposure of growing 3T3 cells transformed by SV40 to high concentration of con A, we have isolated lines of cells which are no longer agglutinable by con A. These lines arose at a frequency of about one in 10^4 cells.

Of the six lines isolated, two had saturation densities that approached 3T3 cells. The other four had saturation densities ranging from three-fold less than SV3T3 to almost equal to SV3T3. Those lines with the lowest saturation densities were the most resistant to agglutination by con A. Treatment with trypsin rendered the lines as agglutinable as transformed cells. The lines also were able to grow in concentration of con A which inhibited the growth of SV3T3 cells.

The lines resembled transformed cells in their ability to grow in low serum, to plate on 3T3 monolayers, and to yield virus after fusion with BSC-1 cells. Karyotype analysis showed no change in the chromosome number of the revertants compared to SV3T3 cells. T-antigen, as measured by complement-fixation, was the same in both the revertants and SV3T3 cells.

RNA polymerase from mammalian cells

The aim of this laboratory is to understand the transcription of SV40 DNA into messenger RNA in lytically infected and transformed cells.

To this end, we have developed a method to partially purify RNA polymerase from a variety of tissue culture lines, including HeLa, KB, MA134, BSC-1, 3T3 and SV3T3 cells. The extraction procedures consist of lysing either whole cells or isolated nuclei in hypotonic solutions. The RNA polymerase activity appears in the supernatant and is purified by chromatography on DEAE, phosphocellulose and DNA cellulose columns followed by glycerol gradient centrifugation. The final product shows a small number of bands on SDS-polyacrylamide gels.

The purified enzyme has a molecular weight of about 500,000, prefers native DNA to denatured DNAs as a template, and is nuclease free.

Current work centers about determining–(1) the subunit structure of the enzyme, (2) the relationship of the enzyme obtained by hypotonic extraction to the multiple enzyme activities isolated after sonication of cells in high salt solutions (3) changes in enzyme activity and template specificity during lytic infection and transformation, and (4) the characters of the in vitro RNA product synthesized from SV40 DNA.

The in vitro product of SV40 DNA transcription by E. coli RNA polymerase

Transcription of native, superhelical SV40 DNA is asymmetric. In transcribing selectively one of the two DNA strands, the bacterial enzyme apparently recognizes specific signals on the animal virus DNA. A small fraction of the in vitro RNA product is as long or longer in size than the primer DNA strand, indicating that the enzyme can transcribe the entire DNA sequence.

In an effort to obtain unique transcript which could be used for sequence analyses as well as for translation in in vitro protein making systems, we test various assay conditions for their ability to restrict initiation of RNA synthesis to one specific site on the DNA. Direct visualization of the reaction assay in the electron microscope is expected to allow a calculation of the maximal number of RNA chains synthesized per DNA molecule. The RNA product is being characterized by hybridization studies and by analysis of the 5' terminal nucleotide sequences.

Specific hybridization of in vitro SV40 RNA with DNA of SV40-transformed cells

Highly radioactive in vitro RNA has previously been used to detect minute amounts of SV40-homologous DNA sequences in the genome of transformed cells. We have now demonstrated that characteristic melting profiles can be obtained with the RNA-DNA hybrids formed between in vitro RNA and the DNA extracted from SV40-transformed cells. From the amount of SV40 in vitro RNA regained from these hybrids, we expect to arrive at a reliable calculation of the amount of SV40-specific DNA sequences present in the transformed cells. E. D. Kiehn helped with research at the Salk Institute for Biological Science, San Diego, California.

Early proteins of SV40

Virtually nothing is known of SV40-coded proteins that appear in infected cells before viral DNA synthesis occurs. SV40 infection does not shut off host cell protein synthesis. Many enzymes connected with DNA synthesis are enhanced after infection but it has been shown that several of these are identical to the host enzyme and probably all are coded by the host genome. The only new proteins found after infection are a few antigens–T-antigen, U-antigen, S-antigen and transplant rejection antigen. The last two may be identical and are probably host cell coded. The first two are

virus specific and are also found in SV40 transformed cells. These two may be coded by the virus. Therefore, attempts are undertaken to purify T-antigen both to elucidate its function and to compare the peptide pattern with those of the products obtained by R. Gesteland's group in the in vitro protein synthesizing system directed by SV40 DNA.

A comparison of proteins of uninfected and infected monkey kidney cells that stick to DNA-cellulose columns revealed one new protein in infected cells. This protein has a molecular weight of about 40,000 and could be the major component of viral capsids. No early viral proteins were detected by this method.

LACTOSE OPERON

Laboratory of
D. Zipser
J. Arnone
E. Bade
A. Bukhari

Our laboratory arrived at Cold Spring Harbor in February of 1970. We are working on a variety of problems related to the molecular genetics of bacteria using the lactose operon system. Among our main lines of research are:

The code for polypeptide initiation

Mutants have been found within the structural gene for β-galactosidase which code for new polypeptide initiation sites. By comparing peptide fingerprints of the wild-type and mutant proteins we hope to be able to isolate the peptide changed by the re-initiation mutation. Sequencing of these "difference" peptides will add to our knowledge of the nucleotide sequence which codes for polypeptide initiation. So far we have been able to identify a peptide that differs in wild type and mutant but we have not yet purified this peptide.

Specific polypeptide degradation

Work in our laboratory and others has shown that *E. coli* possesses proteolytic enzymes that rapidly degrade incorrectly-made proteins. Thus, the fragments produced by nonsense mutations in the β-galactosidase structural gene are rapidly degraded. We are now studying the mechanism of this degradation and searching for mutants in the enzymes that bring it about.

The mechanism of polarity

Nonsense mutants in one gene affect the amounts of other proteins synthesized by other genes in the same operon. The mechanism of this phenomena, called polarity, is under active study in our laboratory.

Our main thrust at the moment is toward developing methods to accurately study mRNA production in polar mutants.

Other studies

In addition to those described above we also have projects in the fields of mRNA termination, genetic recombination, the mechanism of complementation and some early studies on computer models of molecular genetic systems.

PERSISTENT HETEROZYGOTES IN PHAGE

Laboratory of
A. D. Hershey
E. Burgi
L. Ingraham
S. Makover
D. H. Parma
A. M. Skalka
H. Yamagishi

Parma and Ingraham are studying the genetic structure of phage lines that carry chromosomal duplications.

The *r*II gene of T4 is known from the work of Benzer, who used it in experiments that bridged the gap between the structure of DNA and the structure of genes. The *r*II gene consists of two adjacent DNA segments, A and B, that together comprise about one percent of the DNA of the phage. Except for their cooperative function, A and B behave like separate genes, each subject to mutation from the active (+) to inactive (-) form. Thus Benzer recognized four genotypic classes: A^+B^+, A^+B^-, A^-B^+, and A^-B^-. Only A^+B^+ can perform *r*II function. The three inactive classes are distinguishable both by breeding analysis and by the fact that only the chromosome pair A^+B^- and A^-B^+ can cooperate, when present in the same bacterial cell, to carry out *r*II function. This fact, together with evidence that A^- and B^- mutations occur in adjacent, nonoverlapping segments of the DNA, reveals the bipartite structure of the gene.

The function of the gene is superfluous to phage growth in ordinary bacterial strains but essential for growth in bacterial strains lysogenic for phage λ.

If two phages of genotypes A^+B^- and A^-B^+ are crossed, one gets among the progeny a few percent of A^+B^+ recombinants, and about one percent of A^+B^-/A^-B^+ heterozygotes. Among the heterozygotes some are "internal hets" (two DNA strands of different parental origin) and some are "terminal hets" (repetitions at the ends of the DNA molecule marked by genes of different parental origin). If the particular mutants *r*J101 and *r*1589 are crossed, one gets no internal hets (because the mutants contain mismatching deletions) and no A^+B^+ recombinants (because the two deletions correspond to overlapping nucleotide sequences). Nevertheless, owing to their exceptional structure,

the respective mutants are functionally A^+B^- and A^-B^+ and the cross does generate A^+B^-/A^-B^+ terminal hets. The mutants *r*J101 and *r*1589 are especially useful in genetic experiments, including those described below, that required detection of exceptional events. In principle, though, any functionally equivalent mutants would serve.

Among other things they found that such phage particles could carry out *r*II function in a lysogenic host cell, but yielded progeny that were exclusively of the original mutant types. The prompt segregation identified the particles as heterozygotes rather than recombinants, and the functional complementation was consistent with the expected structure of terminal hets, but not with that of internal hets. (Internal hets would contain part of their genetic information in the unreadable DNA strand, information that could be expressed only after replication.)

Weil, Terzaghi, and Crasemann reported that *r*II crosses of the type $A^+B^- \times A^-B^+$ yielded about one phage particle in 10 million of a special type that could form a plaque on plates seeded with the lysogenic bacterial host. The resulting clones contained physiologically A^+B^+ phage, but proved to segregate with relatively high frequency particles of the ancestral genotypes A^+B^- and A^-B^+. Such particles could be recognized as heterozygotes of the genotype A^+B^-/A^-B^+, concluding that they were stabilized terminal hets, or else carried duplications of another sort.

Duplications of another sort have in fact been revealed by the work of Weil and Terzaghi and of Parma and Ingraham. The experimental results can be appreciated best if the applicable genetic principles are first brought to mind.

The local event that gives rise to recombinant chromosomes is called crossing over. Typically, crossing over is observed between homologous partners and produces no persistent local lesions: parental and recombinant chromosomes differ only with respect to content of genetic markers. The overall process therefore consists, in effect, of interchange of exactly corresponding segments of homologous chromatids. Since crossing over can occur at practically any chromosomal site, one is forced to think of a matching principle based on complementary nucleotide sequences.

In T4, a single crossover involves pairing restricted to the appropriate short segment of DNA. It is, therefore, plausible to imagine occasional local mispairing accompanied by "illegitimate" crossing over. The hypothetical products of single illegitimate crossovers between homologous chromatids are deletions and tandem duplications. A tandem duplication can be exactly defined as one product of a single illegitimate crossover. In terms of DNA structure, it is characterized by a single repeat in a nucleotide sequence containing just one joint of novel origin.

Illegitimate crossing over, like typical crossing over, is known by its products. Neither process is understood in mechanical or chemical terms.

Illegitimate crossing over is unequal in the sense that the reciprocal products are not homologous with respect to each other or their parents. Nevertheless, in chromosomes containing tandem duplications the ancestral genome is not lost and is, in fact, spontaneously regenerated with rather high frequency. The reasons for this were made clear by Sturtevant in experiments with the Bar eye mutants of *Drosophila*. His experiments also provided the criteria for recognizing tandem duplications. Matvienko (*Molekulyarnaya Biologiya*, 1969) verified by density analysis that persistent hets of one line contained only the normal length of DNA per particle.

Weil's persistent hets might be expected to contain tandem duplications of a DNA segment including the *r*II gene, and to have suffered deletions of nonessential DNA elsewhere in the chromosome. This is the hypothesis that Parma and Ingraham have investigated. Their conclusions are summarized below.

1. Persistent hets produce three types of progeny besides particles like themselves: A^+B^- segregants, A^-B^+ segregants, and inviable particles. The segregants comprise 15% to 45% of the viable particles, their proportion being characteristic for each line of hets, depending most likely on the length of the particular duplication. The number of inviable particles is about equal to the number of segregants. The inviable particles therefore can be interpreted as triplications generating a gene set too large to go into a phage particle without loss. Then the segregants and triplications are just reciprocal products of unequal crossing over.

2. The *r* segregants from persistent hets marked by revertible *r*II mutants are themselves revertible to r^+, showing that the revertants are haploid rather than homozygous diploid in structure (Weil et al., 1965). The same inference follows from the fact that crosses between pairs of segregants do not regenerate persistent hets at very high frequency (cf. item 4 below). These facts support the interpretation in terms of tandem duplications as opposed to duplications of other sorts.

3. Crosses of the type $A^+B^- \times A^-B^+$, in which the phages are segregants from persistent hets, generated terminal (nonpersistent) hets at higher than normal frequency, the actual frequency being characteristic for the particular line of persistent hets from which the segregants were derived. This Parma and Ingraham interpret as evidence that the duplications are compensated and often overcompensated by deletions, the net effect being to lengthen terminal repetitions. Weil and Terzaghi have evidence for deletions of known genes in some of their persistent hets.

4. In crosses of the type last mentioned, segregants from persistent hets also regenerate new persistent hets with appreciably higher frequency than do the corresponding ancestral lines. This too may be an indication that the segregants contain deletions, since lengthened terminal repetitions might be expected to favor viability of newly-formed duplications.

5. Parma and Ingraham prepared their persistent hets from stocks containing multiple genetic markers. The distribution of these markers in the hets clearly shows that the duplications arise by a

single crossover in the vicinity of the *r*II gene, and that the resulting duplication is usually not more than a dozen or so recombination units in length.

6. The markers recovered in the persistent hets, as well as other genetic tests, show that the duplications usually have the genetic structure ... $B^+A^-B^-A^+$ ... rather than ... $B^-A^+B^+A^-$ .... This result is expected if short duplications are more likely to survive than long ones. Persistent hets can be recognized only if they contain intact A^+ and B^+ segments. In the first structure this requirement can be met without duplicating the entire *r*II gene, whereas in the second it cannot.

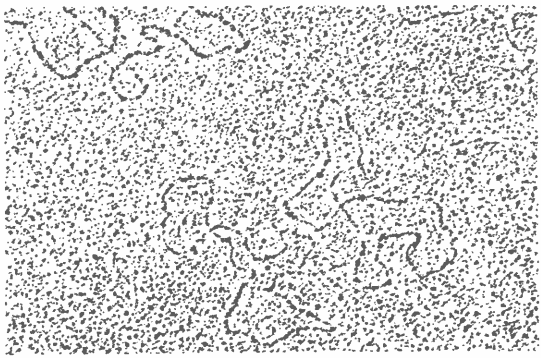
These results are evidently consistent with the hypothesis that persistent hets contain tandem duplications accompanied by compensating deletions. The alternative hypotheses that seem to be excluded are: stabilized terminal repetitions, inverted duplications, and nontandem duplications in general. None of the alternatives can account for the fact that persistent hets sport haploid segregants and inviable particles at similar high frequencies.

ELECTRON MICROSCOPY

Laboratory of
H. Delius
N. Mantell

T4 phage gene 32 product

The gene 32 product is a protein which is necessary for phage DNA replication and recombination (Alberts, in Cold Spring Harbor Symposium, 1968). In collaboration with Bruce Alberts (Princeton) we analyzed complexes formed by binding this protein to the single-stranded circular DNA of phage fd. Preparations obtained by freeze-drying a solution of these complexes directly on a microscope grid showed clearly visible rings, while the free single-stranded DNA under the same conditions is collapsed and hardly visible. With the aid of Martha Simon (Stony Brook) we started to use the Kleinschmidt technique of spreading nucleic acids in a layer of surface denatured protein. When spread with 40% formamide, the fd DNA/32 protein complexes show a 1.3-fold increase in length over the length of the free DNA (2.5 micron as compared to 1.9 micron). The picture shows fd DNA treated with a non-saturating amount of gene 32 protein. The molecules are either completely covered to their full length with the protein or have no protein bound at all. This serves as a nice illustration for the cooperative mode of binding of this protein to DNA as described by Bruce Alberts.



Secondary structure of RNA

The secondary structure of R17 RNA is being studied by the spreading technique. The amount of secondary structure can be varied by the addition of formamide. Under some conditions the middle part of the R17 molecule has the structure of a big loop. It is hoped that the visible patterns of the secondary structure might be used as a tool to characterize different RNA's or specify certain parts of an RNA molecule, like the left- and right-hand ends of the R17 RNA.

λ phage in vitro protein synthesis

Ray Gesteland describes in this Report the in vitro system in which he obtains extensive protein synthesis on λ DNA. Together we have isolated the complexes of DNA, RNA and ribosomes by sucrose gradient centrifugation and can analyze them by the spreading technique. The pictures indicated that consistently one half of the molecule, which we assume to be the left-hand half of λ, is

not transcribed and translated (i.e., does not show polysomes). The right-hand half then shows three regions active in synthesis—one around the b2 region, another one in the immunity region and a rather short one at the right-hand end of the molecule. Currently the changes in this pattern, obtained by using different mutants of λ or by adding repressor to the in vitro system, are being investigated.

DNA REPLICATION IN BACTERIA AND PHAGE

Laboratory of
R. Werner
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D. Margulies

Transfer of TMP from bacterial to phage DNA

When a mixture of α-P-labeled and ^{3}H-labeled TTP is fed to *E. coli* protoplasts, only the ^{3}H-label appears in bacterial DNA. Under conditions of repair synthesis, however, some ^{32}P-label is incorporated into DNA. One possible explanation for these results was that the α-phosphate group of TTP is exchanged during DNA replication but not during repair synthesis. To either prove or disprove this explanation we studied the transfer of BUMP from bacterial DNA to phage DNA after T4 infection. Bacterial labeled with both ^{3}H-BU and ^{32}P-phosphate were infected with phage T4 and incubated in thymine-containing medium. The DNA isolated from the resulting phage particles was hydrolyzed and the 5'-nucleoside monophosphates separated chromatographically. In agreement with the above hypothesis, the phage BUMP had completely exchanged its phosphate and was no longer ^{32}P-labeled. However, when the reverse experiment was done and the transfer of TMP into BU-containing phage DNA studied, between 50%-70% of the TMP retained its original phosphate. This result indicates that 5'-nucleoside monophosphates or derivatives of it (like triphosphates) are at least part of the in vivo precursor of DNA. The exchange of phosphate in BUMP is probably caused by the preference of the nucleoside monophosphate kinase for thymine over BU.

Studies of DNA chain growth under steady state conditions

When bacteria are pulse-labeled with ^{3}H-thymidine most of the radioactivity incorporated into DNA can be recovered as small fragments from alkaline sucrose gradients (Okazaki et al.). Thymidine, however, is not a natural DNA precursor and its incorporation is very different from that of thymine. Thymidine is taken up in the presence of thymine and seems to bypass all intracellular precursor pools so that it is incorporated into DNA at full specific activity. An attempt was made to repeat Okazaki's experiments under steady state conditions using either ^{32}P-phosphate or ^{3}H-thymine as precursors. When T4-infected cells are labeled with ^{32}P-phosphate at 25° for 20 sec, all ^{32}P-counts incorporated into DNA sediment with the bulk of the DNA; there were no Okazaki fragments present. If ^{3}H-thymidine is added to the same culture, ^{3}H-label appears in small fragments.

The same experiment was repeated with ^{3}H-thymine using uninfected bacteria. At 14° C, pulses of 15 sec to 60 sec length produced nearly equal amounts of small and large DNA; after 60 sec, the fraction of large DNA increased. An exact explanation for these results is still missing but it seems that, if Okazaki fragments are intermediates in DNA replication, there can only be one or two small fragments per growing point. Furthermore, at least 50% of the DNA is made continuously and never appears as small fragments.

The effect on DNA replication of T4 gene 32 amber mutants in mixed infection with T4^{+}

Phage T4 containing an amber mutation in gene 32 is defective in the formation of joint "recombinant" molecules (Tonizawa, 1966). In mixed infections of gene 32 mutants with T4 wild type, the overall rate of phage DNA replication is reduced. What is the reason for this reduction of DNA synthesis rate? There could be fewer growing points per infected cell or each growing point could move at a reduced speed or both the number of growing points and the rate of movement have changed. Using the density-labeling techniques (Werner, 1968) we tried to determine the rate of fork movement in cells mixedly infected with mutants and wild type. Preliminary results indicate that the rate of fork movement is not drastically different from that observed in cells solely infected with T4^{+}.

COLD SPRING HARBOR SYMPOSIUM ON QUANTITATIVE BIOLOGY

June 4th to June 11, 1970

There are times in every science when the outline of future progress seems predictable, straightforward, and perhaps a little boring. Inevitably, this leads many of its practitioners to wonder whether they are in the right field and quietly, and occasionally not very quietly, some leave the security of their teachable dogma for the freedom of the confusion surrounding unexplainable phenomena. This state of affairs most certainly held for those people studying the control of gene action. Over several years the newer news seemed merely a confirmation of the ideas of Jacob and Monod. But in November 1968 further molecular characterization of the enzyme RNA polymerase revealed the σ factor and suddenly everyone knew that a vast new field was opening up. An excitement, equal to that which accompanied the discovery of messenger RNA, immediately became apparent. Not only were important new control mechanisms in microbial cells about to be understood but the molecular basis of the embryological development of higher organisms might at last be open to real experimentation.

This year's Symposium marks the beginning of this phase. Clearly much of the data presented will need further refinement. Nonetheless it deserves visible preliminary exposure, if only to speed the day when all the now-proclaimed facts are really facts.

In arranging the program, I gratefully acknowledge the help given by Jim Darnell, Peter Geiduschek, Joe Sambrook and Andrew Travers. The final result was a compromise between a desire to hear everyone with relevant data and the need to restrict the talks to a number ingestible within a week's time. At the end we realized that this year's program was the largest yet and the number of manuscripts appearing in the resulting Symposium volume is 97. Several are last-minute additions. David Baltimore was invited as a chairman, but arrived with news of his very recent experiments showing transcription of DNA upon the RNA chromosomes of certain tumor viruses. So we asked him to close the program with his experiments. At the same time we learned that Howard Temin independently had similar data and we tried to arrange for him also to be present. This proved not possible but in view of the fundamental importance of these results, we asked him also to provide a brief article for publication in this volume.

The date of the meeting was June 4th-11th and some 325 people were in attendance. Financial support, as in past Symposia, was provided by the National Institutes of Health, the National Science Foundation and the United States Atomic Energy Commission. In charge of editing this Symposium has been DeeDee Skiff, ably assisted by Kate Alston, Elspeth Cairns, Deirdre Carson, Patricia Crouch, Robert Crouch, Judy Gordon, Kay Knight and Helen Trilling.

PROGRAM

RNA SEQUENCES

CORY, S., P. F. SPAHR, and J. M. ADAMS: Untranslated Nucleotide Sequences in R17 Bacteriophage RNA

JEPPESEN, P. G. N., J. L. NICHOLS, F. SANGER, and B. G. BARRELL: Nucleotide Sequences from Bacteriophage R17 RNA

SMITH, J. D., K. ANDERSON, A. CASHMORE, M. L. HOOPER, and R. L. RUSSELL: Studies on the Structure and Synthesis of *Escherichia coli* Tyrosine Transfer RNA

FELLNER, P., C. EHRESMANN, and J. P. EBEL: Nucleotide Sequence Analysis of Sections of the 16 S RNA from *E. coli*

LARSEN, C. J., P. LEBOWITZ, S. M. WEISSMAN, and B. DuBUY: Studies of the Primary Structure of Low Molecular Weight Ribonucleic Acid other than tRNA

BACTERIAL RNA POLYMERASE—I

ZILLIG, W., K. ZECHEL, D. RABUSSAY, M. SCHACHNER, V. S. SETHI, P. PALM, A. HEIL, and W. SEIFERT: On the Role of Different Subunits of DNA-Dependent RNA Polymerase from *E. coli* in the Transcription Process

CASSANI, G., R. R. BURGESS, and H. M. GOODMAN: Streptolydigin Inhibition of RNA Polymerase

HINKLE, D. C. and M. CHAMBERLIN: The Role of σ Subunit in Template Site Selection by *E. coli* RNA Polymerase

KRAKOW, J. S., and K. von der HELM: *Azotobacter* RNA Polymerase Transitions and the Release of Sigma

JACOBSON, A., and D. GILLESPIE: An RNA Polymerase Mutant Defective in ATP Initiations
DAVISON, J., K. BROOKMAN, L. PILARSKI, and H. ECHOLS: The Stimulation of RNA Synthesis by M Factor

BACTERIAL POLYMERASE—II

GOFF, C. G. and K. WEBER: A T4-Induced RNA Polymerase α Subunit Modification
BREMER, H.: Influence of KCL on the in vitro Transcription of T4 DNA
ROBERTS, J. W. : The ρ Factor: Termination and Anti-termination in λ
RICHARDSON, J. P.: ρ Factor Function in T4 Transcription
MILLETTE, R. L., C. D. TROTTER, P. HERRLICH, and M. SCHWEIGER: In vitro Synthesis, Termination, and Release of Active Messenger RNA
MAITRA, U., A. H. LOCKWOOD, J. S. DUBNOFF, and A. GUHA: Termination, Release, and Reinitiation of RNA Chains from DNA Templates by *Escherichia coli* RNA Polymerase
GOLDBERG, A. R.: Termination of in vitro RNA Synthesis by ρ Factor

PHAGE TRANSCRIPTION—I

SEDAT, J. W. and R. L. SINSHEIMER: The in vivo ϕX mRNA
HAYASHI, Y. and M. HAYASHI: Fractionation of ϕX/174 RNA Specific Messenger RNA
TAKANAMI, M. T. OKAMOTO, and M. SUGIURA: The Starting Nucleotide Sequences and Size of RNA Transcribed in vitro on Phage DNA Templates
YOUNG, E. T.: Control of Functional T4 Messenger Synthesis
JAYARAMAN, R. and E. B. GOLDBERG: Transcription of Bacteriophage T4 Genome in vivo
BRODY, E., R. SEDEROFF, A. BOLLE, and R. H. EPSTEIN: Early Transcription in T4-Infected Cells

PHAGE TRANSCRIPTION—II

CASCINO, A., S. RIVA, and E. P. GEIDUSCHEK: DNA Ligation and the Coupling of T4 Late Transcription to Replication
GRAU, O., B. M. OHLSSON-WILHELM, and E. P. GEIDUSCHEK: Transcription Specificity in Bacteriophage SPO1 Development
BAUTZ, E. K. F., and F. A. BAUTZ: Studies on the Function of the RNA Polymerase σ Factor in Promoter Selection
HAGER, G., B. D. HALL, and K. L. FIELDS: Transcription Factors from T4-Infected *Escherichia coli*
TRAVERS, A.: RNA Polymerase and T4 Development
SUMMERS, W. C. and R. B. SIEGEL: Regulation of Coliphage T7 RNA Metabolism in vivo and in vitro
CHAMBERLIN, M. and J. McGRATH: Characterization of a T7-Specific RNA Polymerase Isolated from *E. coli* Infected with T7 Phage
LINIAL, M. and M. H. MALAMY: The Effect of F Factors on RNA Synthesis and Degradation after Infection of *E. coli* with Phage ϕII
DAVIS, R. W. and R. W. HYMAN: Physical Locations of the in vitro RNA Initiation Site and Termination Sites of T7M DNA

PHAGE TRANSCRIPTION—III

CHADWICK, P., V. PIRROTTA, R. STEINBERG, N. HOPKINS, and M. PTASHNE: The λ and 434 Phage Repressors
GREEN, M. H., W. S. HAYWARD, and P. GARIGLIO: A Method for the Localization of Active Promoters
KOURILSKY, P., M. F. BOURGUIGNON, M. BOUQUET, and F. GROS: Early Transcription Controls after Induction of Prophage λ
HEINEMANN, S. F. and W. G. SPIEGELMAN: Role of the Gene N Product in Phage λ
CHAMPOUX, J. J.: The Sequence and Orientation of Transcription in Bacteriophage λ
SPIEGELMAN, W. G., S. F. HEINEMANN, P. BRACHET, L. PEREIRA da SILVA, and H. EISEN: Regulation of the Synthesis of Phage λ Repressor
KUMAR, S., E. CALEF, and W. SZYBALSKI: Regulation of the Transcription of *Escherichia coli* Phage λ by its Early Genes N and *tof*
SZYBALSKI, W., K. BϕVRE, M. FIANDT, S. HAYES, Z. HRADECNA, S. KUMAR, H. A. LOZERON, H. J. J. NIJKAMP, and W. F. STEVENS: Transcriptional Units and Their Controls in *Escherichia coli* Phage λ: Operons and Transcriptons
HERSKOWITZ, I., and E. SIGNER: Control of Transcription from the *r* Strand of Bacteriophage λ
SCHLEIF, R. and J. GREENBLATT: Transcription in the λ-*ara* Phage
NAONO, S. and K. TOKUYAMA: On the Mechanism of λ DNA Transcription in vitro

RELAXED VERSUS STRINGENT CONTROL

LAZZARINI, R. A. and R. M. WINSLOW: The Regulation of RNA Synthesis during Growth Rate Transitions and Amino Acid Deprivation in *E. coli*
PRIMAKOFF, P., and P. BERG: Stringent Control of Transcription of Phage $\phi 80psu_3$
GALLANT, J., H. ERLICH, B. HALL, and T. LAFFLER: Analysis of the RC Function
CASHEL, M: Inhibition of RNA Polymerase by ppGpp, a Nucleotide Accumulated during the Stringent Response to Amino Acid Starvation in *E. coli*
TRAVERS, A., R. KAMEN, and M. CASHEL: The in vitro Synthesis of Ribosomal RNA



POSITIVE AND NEGATIVE METHODS FOR CONTROL OF TRANSCRIPTION

PERLMAN, R., B. CHEN, B. deCROMBRUGGHE, M. EMMER, M. GOTTESMAN, H. VARMUS, and I. PASTAN: The Regulation of *lac* Operon Transcription by Cyclic Adenosine 3',5'-Monophosphate

OHSHIMA, Y., T. HORIUCHI, Y. IIDA, and T. KAMEYAMA: Transcription and Repression of the *lac* Operon in vitro

ZUBAY, G., D. SCHWARTZ, and J. BECKWITH: The Mechanism of Activation of Catabolite-Sensitive Genes

ARDITTI, R., L. ERON, G. ZUBAY, G. TOCCHINI-VALENTINI, S. CONNAWAY, and J. BECKWITH: In vitro Transcription of the *lac* Operon Genes

LOSICK, R., A. L. SONENSHEIN, R. G. SHORENSTEIN, and C. HUSSEY: Role of RNA Polymerase in Sporulation

KINETICS OF RNA SYNTHESIS AND DEGRADATION

ADESNIK, M. and C. LEVINTHAL: The Synthesis and Degradation of Lactose Operon Messenger RNA in *E. coli*

MOSTELLER, R. D., J. K. ROSE, and C. YANOFSKY: Transcription Initiation and Degradation of *trp* mRNA

BAKER, R. and C. YANOFSKY: Transcription Initiation Frequency for the Tryptophan Operon of *Escherichia coli*

IMAMOTO, F., Y. KANO, and S. TANI: Transcription of the Tryptophan Operon in Nonsense Mutants of *Escherichia coli*

LAVALLÉ, R. and G. de HAUWER: Repression by Tryptophan at the Level of Transcription and Translation in *E. coli*

MORSE, D. E.: "Delayed-Early" mRNA for the Tryptophan Operon? An Effect of Chloramphenicol

PATO, M. L. and K. von MEYENBURG: Residual RNA Synthesis in *Escherichia coli* after Inhibition of Initiation of Transcription by Rifampicin

EUCARYOTIC RNA

MILLER, O. L., JR., B. R. BEATTY, B. A. HAMKALO, and C. A. THOMAS, JR: Electron Microscopic Visualization of Transcription

DANEHOLT, B., J-E. EDSTRÖM, E. EGYHÁZI, B. LAMBERT, and U. RINGBORG: RNA Synthesis in a Balbiani Ring in *Chironomus tentans*

PELLING, C.: Puff RNA in Polytene Chromosomes

ASHBURNER, M.: A Prodromus to the Genetic Analysis of Puffing in *Drosophila*

SCHERRER, K. and G. SPOHR: Nuclear and Cytoplasmic Messenger-Like RNA and Their Relation to the Active Messenger RNA in Polyribosomes of HeLa Cells

DARNELL, J. E., G. N. PAGOULATOS, U. LINDBERG, and R. BALINT: Studies on the Relationship of mRNA to Heterogeneous Nuclear RNA in Mammalian Cells

PENMAN, S., H. FAN, S. PERLMAN, M. ROSBASH, R. WEINBERG, and E. ZYLBER: Distinct RNA Synthesis Systems of the HeLa Cell

PERRY, R. P., J. R. GREENBERG, and K. D. TARTOF: Transcription of Ribosomal, Heterogeneous Nuclear, and Messenger RNA in Eucaryotes

GRIERSON, D., M. E. ROGERS, M. L. SARTIRANA, and U. E. LOENING: The Synthesis of Ribosomal RNA in Different Organisms: Structure and Evolution of the rRNA Precursor

ATTARDI, G., Y. ALONI, B. ATTARDI, D. OJALA, L. PICA-MATTOCCIA, D. L. ROBBERSON, and B. STORRIE: Transcription of Mitochondrial DNA in HeLa Cells

McCARTHY, B. J. and J. D. DUERKSEN: Fractionation of Mammalian Chromatin

CHETSANGA, C. J., D. L. POCCIA, R. J. HILL, and P. DOTY: Stage-Specific RNA Transcription in Developing Sea Urchins and their Chromatins

TOMKINS, G. M., D. W. MARTIN, JR., R. H. STELLWAGEN, J. D. BAXTER, P. MAMONT and B. B. LEVINSON: Regulation of Specific Protein Synthesis in Eucaryotic Cells

THE RNA POLYMERASE OF MAMMALIAN CELLS

FURTH, J. J. and G. E. AUSTIN: RNA Polymerase of Lymphoid Tissue: A Preliminary Characterization of the Enzyme and the RNA It Synthesizes

BLATTI, S. P., C. J. INGLES, T. J. LINDELL, P. W. MORRIS, R. F. WEAVER, F. WEINBERG, and W. J. RUTTER: Structure and Regulatory Properties of Eucaryotic RNA Polymerase

MONJARDINO, J. P. and L. V. CRAWFORD: RNA Polymerase from Mouse Embryo Cells

SUGDEN, B. and J. SAMBROOK: RNA Polymerase from HeLa Cells

KELLER, W. and R. GOOR: Mammalian RNA Polymerase: Structural and Functional Properties

JACOB, S. T., E. M. SAJDEL, W. MUECKE, and H. N. MUNRO: Soluble RNA Polymerases of Rat Liver Nuclei: Properties, Template Specificity, and Amanitin Responses in vitro and in vivo

CHAMBON, P., F. GISSINGER, J. L. MANDEL, JR., C. KEDINGER, M. GNIAZDOWSKI, and M. MEIHLAC: Purification and Properties of Calf Thymus DNA-Dependent RNA Polymerases A and B

STEIN, H. and P. HAUSEN: Factors Influencing the Activity of Mammalian RNA Polymerase

SEIFART, K. H.: A Factor Stimulating the Transcription on Double-Stranded DNA by Purified RNA Polymerase from Rat Liver Nuclei

ROEDER, R. G., R. H. REEDER, and D. D. BROWN: Multiple Forms of RNA Polymerase in *Xenopus laevis*: Their Relationship to RNA Synthesis in vivo and their Fidelity of Transcription in vitro

TOCCHINI-VALENTINI, G. P. and M. CRIPPA: RNA Polymerases from *Xenopus laevis*

ANIMAL VIRUS GENOMES

KATES, J.: Transcription of the Vaccinia Virus Genome and the Occurrence of Polyriboadenylic Acid Sequences in Messenger RNA

ROIZMAN, B., S. BACHENHEIMER, E. K. WAGNER, and T. SAVAGE: Synthesis and Transport of RNA in Herpesvirus-Infected Mammalian Cells

MILLWARD, S. and M. NONOYAMA: Segmented Structure of the Reovirus Genome

SHATKIN, A. J. and A. K. BANERJEE: In vitro Transcription of Double-Stranded RNA by Reovirus-Associated RNA Polymerase

JOKLIK, W. K., J. J. SKEHEL, and H. J. ZWEERINK: The Transcription of the Reovirus Genome

GREEN, M., J. T. PARSONS, M. PINA, K. FUJINAGA, H. CAFFIER, and I. LANDGRAFLEURS: Transcription of Adenovirus Genes in Productively. Infected and in Transformed Cells

WESTPHAL, H. and E. D. KIEHN: The in vitro Product of SV40 DNA Transcription and its Specific Hybridization with DNA of SV40-Transformed Cells

TONEGAWA, S., G. WALTER, A. BERNARDINI, and R. DULBECCO: Transcription of the SV40 Genome in Transformed Cells and during Lytic Infection

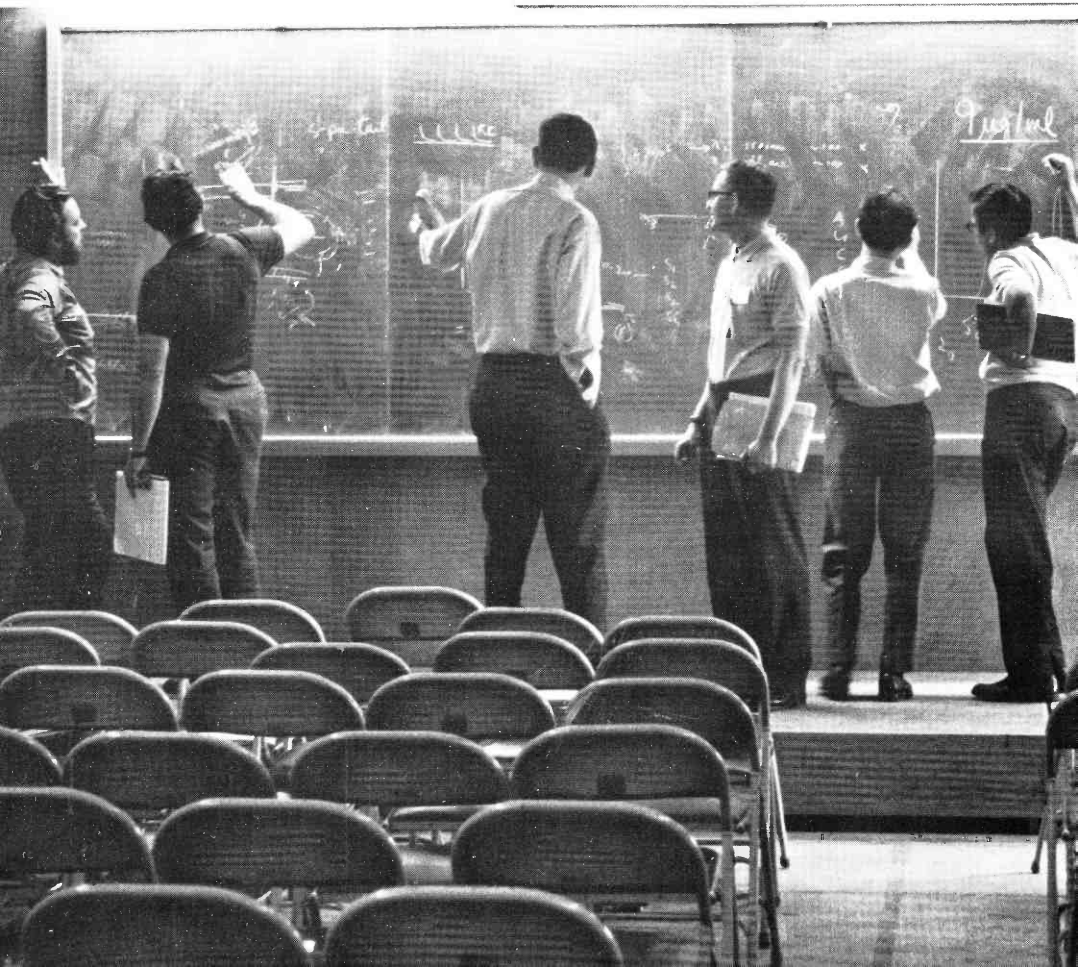
MARTIN, M. A.: Characteristics of SV40 DNA Transcription during Lytic Infection, Abortive Infection, and in Transformed Mouse Cells

BALTIMORE, D.: RNA-Dependent Synthesis of DNA by Virions of Mouse Leukemia Virus

MIZUTANI, S. and H. M. TEMIN: An RNA-dependent DNA Polymerase in Virions of Rous Sarcoma Virus

CHAMBERLIN, M. J.: Transcription 1970: A Summary

Courtesy of LIFE *Magazine, October 30, 1970 issue*



POST GRADUATE TRAINING COURSES

Summer 1970

Many new fields have been developing in biology during the last twenty years that do not fall into any particular subject but equally involve biochemistry, biophysics and genetics. As a result, most research workers have had to enlarge the extent of their professional competence: the biochemist has at last been forced to familiarize himself with genetics, and the geneticist has had to learn some biochemistry. This process of re-education, which could only be carried out with difficulty in most universities, tied as these are to a rigid curriculum, is being accomplished through a series of courses for qualified scientists held each summer at Cold Spring Harbor. The courses are given by a staff drawn from institutions all over the world and have already been attended by many hundreds of scientists from disciplines as far apart as medicine and nuclear physics. In conjunction with these courses, the Laboratory invites many investigators as seminar speakers. This program of seminar speakers provides an extensive review of current research in these fields.

This year the summer courses were expanded (from 5 to 6) to meet the growing interest in yeast as objects for molecular biology research.

1) QUANTITATIVE MICROBIOGLOGY OF ANIMAL CELLS IN CULTURE—June 14-July 4, 1970

Areas examined in the course, included: (1) growth control of both normal and malignant cells, (2) differentiation and control of expression of specialized differentiated function (including examples from neurobiology, immunology, and endocrinology), (3) radiation biology, and (4) mammalian somatic genetics. Laboratory exercises demonstrated basic cell growth techniques, primary culture preparation, uses of radio-isotopes, heterokaryon formation and the selection of viable cell hybrid lines from parents of different genetic constitutions, synchronous culture techniques, assays for differentiated function in vitro and the selection for growth in culture of differentiated cells exhibiting such function, cell surface specificity, and single cell immune response in culture.

INSTRUCTORS:

Pollack, Robert E., Ph. D., New York University
Pfeiffer, Steven E., Ph. D., University of Connecticut Medical School, Farmington, Conn.
Sato, Gordon, Ph. D., Brandeis University
Watkins, J. F., M.D., Oxford University, Oxford, England

ASSISTANT:

Vogel, A., B.S., New York University

KITCHEN STAFF:

Molloy, M.A., Kaplen, M.

STUDENTS:

Adams, Jerry, Institut de Biologie Moleculaire, Genève, Switzerland
Baumal, Reuben, Ph.D., Albert Einstein College of Medicine
Beaudet, Arthur L., M.D., National Institutes of Health
Chetsanga, Chris J., Ph.D., Harvard University
Cory, Suzanne, Ph.D., Institut de Biologie Moleculaire, Genève, Switzerland
Di Cara, Leo, Ph.D., Rockefeller University
Gefter, Malcolm, Ph.D., Columbia University
Goldberg, Alfred L., Ph.D., Harvard Medical School
Greenberg, Jay, Ph.D., Institute for Cancer Research
Guha, Arabinda, D. Phil., Albert Einstein College of Medicine
Hosokawa, Keiichi, Ph.D., Space Sciences Laboratory, University of California
Hutton, John J., M.D., Roche Institute of Molecular Biology
Larsson, Agne, M.D., University of California, San Francisco
Lerner, Stephen, M.D., Stanford University School of Medicine
Massie, Harold R., Jr., Ph.D., Harvard University
McKelvy, Jeffrey F., Ph.D., Roche Institute of Molecular Biology
Messer, Anne, B.S., University of Oregon
Miller, Philip A., Ph.D., Hoffmann-LaRoche Inc.
Sheppard, John R., Ph.D., Princeton University
Sillero, Antonio, Ph.D., New York University Medical Center
Smith, James A., M.Sc., Imperial Cancer Research Fund, Dept. of Hormone Biochemistry, London, England

SEMINARS:

G. Sato, University of California, San Diego, "*Nutrition of Cell Culture.*"
B. Perry, Institute for Cancer Research, Philadelphia "*Transcription in Mammalian Cells.*"
V. Allfrey, Rockefeller University, "*Changes in DNA-Associated Protein at Times of Gene Activation.*"
K. Hirschhorn, Mt. Sinai Hospital, "*Products of Lymphocytes in Continuous Culture.*"
L. Tomach, Washington University, "*Quantitative Cellular Radiation Biology.*"
J. Darnell, Columbia University, "*Relationship of Nuclear and Cytoplasmic RNA in Mammalian Cells.*"
M. Burger, Princeton University, "*Tumor-specific Changes in Transformed Cells as Observed with an Agglutinin.*"
C. Schildkraut, Albert Einstein College of Medicine, "*Mammalian Chromosomes: Structure & Replication.*"
G. Tomkins, University of California, San Francisco Medical School, "*Cell Culture Nutrition; in vitro Differentiated Lines.*"
J. Gall, Yale University, "*Studies on Nucleic Acid Hybridization in vitro.*"
C. Bancroft, Harvard Medical School, "*Clonal Lines of Pituitary and Hepatoma Lines.*"
D. Potter, Harvard Medical School, "*Evidence for the Exchange of Substances of Low Molecular Weight Between the Interior of Cultured Mammalian Cells.*"
D. Osoba, University of Toronto, "*Changes of Immune Reactive Cells in Culture.*"
C. Basilico, New York University, "*Somatic Hybrid Cells: Properties and Responses to Oncogenia Viruses.*"
C. Pierce, National Institute of Health, "*In vitro Antibody Production.*"
F. C. Steward, Cornell University, "*Culture of Free Plant Cells and its Significance.*"
R. Levi-Montalcaini, Washington University, "*In vitro Studies on the Insect Nervous System.*"
H. Koprowski, Wistar Institute, "*Cell Fusion and Virus Rescue.*"
R. Hall, U.S. Dist. Attorney, "*Environmental Law and Basic Research.*"

2) MOLECULAR BIOLOGY AND GENETICS OF YEAST – June 14-July 4, 1970

This course emphasized the major laboratory techniques used in the genetic analysis of yeast: tetrad analysis, mitotic recombination, and x-ray fine structure mapping. Chromosomal and cytoplasmic mutants were isolated and characterized. Biochemical studies were performed with chromosomal and mitochondrial mutants.

INSTRUCTORS:

Sherman, Fred, Ph.D., University of Rochester
Fink, Gerald, Ph.D., Cornell University
Lukins, H. Bruce, Ph.D., University of Rochester

ASSISTANT:

Lowenstein, Robert, Cornell University

STUDENTS:

Ballou, Clinton E., Ph.D., University of California
Brown, Harlan D., M.S., Purdue University
Haber, James E., Ph.D., University of Wisconsin
Marmur, Julius, Ph.D., Albert Einstein College of Medicine
Mayer, Vernon W., Jr., Ph.D., Food and Drug Administration
Rubinstein, Irwin, Ph.D., Carnegie Institution of Washington, Genetics Research Unit, Cold Spring Harbor Laboratory
Schatz, Gottfried, Ph.D., Cornell University
Schweizer, Eckhart, Ph.D., University of Wurzburg, Germany
Wilson, Samuel H., M.D., National Institutes of Health
Womack, Frances C., Ph.D., Vanderbilt University Medical School

SEMINARS:

R. K. Mortimer, University of California, "*A General Introduction to Genetic Mapping in Yeast.*"
"*Gene Conversion and Genetic Recombination.*"
T. R. Manney, Western Reserve University, "*Some Properties of the Tryptophan Synthetase Gene-Enzyme System: Their Physiological Consequences in* Saccharomyces."
R. C. von Borstel, Oak Ridge National Laboratory, "*Mutator Genes in Yeast.*"
L. H. Hartwell, University of Washington, "*Genetic Control of the Cell Division Cycle in Yeast.*"
G. Schatz, Cornell University, "*Differentiation of Yeast Promitochondria During Respiratory Adaptation.*"
C. C. Lindegren, Southern Illinois University, "*Tetrad Analysis.*"
J. H. Parker, State University of New York, "*Selection and Characterization of Yeast Mutants Affecting Oxidative Energy Metabolism.*"
R. A. Gilmore, Southern Illinois University, "*Nonsense Suppressors in Yeast.*"
M. Ogur, Southern Illinois University, "*Gene-Enzyme Relationships in Amino Acid Biosynthetic Pathways.*"
C. Beam, Brooklyn College, "*Radiation Resistance and Repair of Radiation Damage in Yeast.*"
E. W. Jones, Western Reserve University, "*Genetics and Physiological Studies of Mutant Defective in Tetrahydrofolate Metabolism.*"
M. Esposito, University of Chicago, "*Conditional Meiotic Mutants of Yeast.*"

3) ANIMAL VIRUSES—July 8-July 28, 1970

Preparation of primary and secondary chick and mouse embryo cell cultures; chick embryo cultures of heart fibroblast, lung, kidney and iris epithelium; HeLa, BHK, and L-cell growth in mass culture and in clones; isolation of clonal sublines; tests and elimination of PPLO in cell cultures. Spinner cell culture. Karyotype analysis. DNA and RNA synthesis in the cell life cycle—an introduction to quantitative autoradiography. Synthesis of viral RNA: coverslip technique. Growth and purification of Newcastle disease virus (NDV). Assay of NDV by plaque formation, hemagglutination, hemadsorption, and cell-killing. The hemadsorption-negative plaque test and intrinsic interference: detection of noncytopathic viruses. Assay and properties of Sindbis virus, vesicular stomatitis virus and the pox viruses. Quantitative neutralization of viruses with antibody. One-step growth curve. Effect of antimetabolites on viral and cell growth. Preparation, assay and the mechanism of action of interferon. Histochemistry and fluorescent antibody techniques in virus infection. Phenotypic mixing of myxovirus, genetic recombination of pox viruses, complementation with Sindbis virus. Morphologic transformation of cells by Rous sarcoma virus and polyoma. Synchronous growth in cell culture. Hybridization of cells.

INSTRUCTORS:

Marcus, Philip I., Ph.D., The University of Connecticut, Storrs
Black, Paul, M.D., Massachusetts General Hospital, Boston
Colby, Bud, Ph.D., University of California, San Diego

ASSISTANTS:

Sekellick, Margaret, B.S., University of Connecticut
Colby, Diane, B.S., Salk Institute, La Jolla, California

STUDENTS:

Baily, Harvey S., University of California, Berkeley
Brown, Glenn E., B.S., University of California, Irvine
Eisenman, Robert N., B.A., University of Chicago
Fasy, Thomas M., M.D., Columbia Presbyterian Medical Center
Favre, Chantal, Swiss Institute for Experimental Cancer Research, Switzerland
Geissler, Erhard, D., Ph.D., Rostock University, Germany
Hauge, Jens G., Ph.D., Northwestern University
Hunt, John M., B.S., Massachusetts Institute of Technology
Ikeda, Hideo, Ph.D., Harvard University
Klagsbrun, Michael, Ph.D., National Institutes of Health
Knippers, Rolf, Ph.D., F-Miescher-Lab, Max-Planck-Gesellsch, Germany
Laskey, Ronald A., B.A., Oxford University, England
Milman, Gregory, Ph.D., National Institutes of Health
Runge, Lorne A., M.D., Massachusetts General Hospital
Siefert, Wilfried W., Ph.D., Max-Planck-Institut fur Biochemie, Germany
Sorof, Sam, Ph.D., The Institute for Cancer Research, Philadelphia
Stone, Henry O., Jr., Ph.D., St. Jude's Childrens' Hospital
Vogel, Arthur M., New York University Medical Center
Wilhelm, James M., Ph.D., University of Chicago
Zamecnik, Paul, M.D., Massachusetts General Hospital

SEMINARS:

H. Eagle, Albert Einstein College of Medicine, "*Animal Cell Culture.*"
E. Robbins, Albert Einstein College of Medicine, "*Cell Ultrastructure and the Cell Cycle.*"
P. Black, Massachusetts General Hospital, "*DNA Tumor Viruses.*"
P. Choppin, The Rockefeller University, "*Parainfluenza Virus.*"
H. Ginsberg, University of Pennsylvania School of Medicine, "*Adenovirus.*"
D. Baltimore, Massachusetts Institute of Technology, "*Poliovirus.*"
D. Baltimore, Massachusetts Institute of Technology, "*Vesicular Stomatitis Virus. RNA Tumor Virus Polymerase.*"
F. Rapp, Pennsylvania State University College of Medicine, "*Adeno-SV40 Hybrids.*"
C. Colby, University of California, "*Interferon Induction.*"
J. Kates, University of Colorado, "*Poxvirus.*"
A. Kapuler, University of Connecticut, "*Reovirus.*"
J. Sambrook, Cold Spring Harbor Laboratory, "*Animal Virus Genetics.*"
H. Hanafusa, Public Health Research Institute of the City of New York, "*RNA Tumor Viruses.*"
G. Todaro, Viral Carcinogenesis Branch National Cancer Institute, "*Cell Transformation.*"
P. Marcus, University of Connecticut, "*Viral Interference.*"
R. Pollack, New York University School of Medicine, "*Virus-cell Hybrid Interaction.*"

4) BACTERIAL GENETICS—JULY 8-July 28, 1970

Dilution and plating techniques; mode of origin of bacterial variants; induction of mutation; isolation and characterization of auxotrophs, mutagen specificity and reversions; sexual recombination and genetic mapping in *Escherichia coli*; transduction and determination of the linear order of mutational sites in *Salmonella typhimurium*; abortive transductions; characterization of suppressors and reversions by transduction; isolation and characterization of *φpodlac* transforming DNA isolation of *lac* repressor, and special projects on the genetics of the *lac* operon.

INSTRUCTORS:

Gotts, Joseph S., Ph.D., University of Pennsylvania
Gross, Julian, Ph.D., University of Edinburgh, Scotland
Muller-Hill, Benno, Ph.D., University of Cologne, Germany
Miller, Jeffrey, Ph.D., Harvard University

ASSISTANTS:

Gross, Marilyn, Ph.D., University of Edinburgh, Scotland
Ehlinger, Sheila, A.B., New York University

KITCHEN STAFF:

V. Cairns, J. Eisenmon

STUDENTS:

Bade, Ernesto, M.D., Institut de Investigaciones Bioquimicas, Buenos Aires, Argentina
Bloom, Frederic R., M.A., New York University Medical Center
Bodlaender, Peter, Ph.D., Biophysics Research Laboratory, Peter Bent Brigham Hospital
Bollum, Frederick J., B.A., Albert B. Chandler Medical Center, University of Kentucky
Bowman, Barbara G., M.S., University of Utah
Chakraburtty, Kalpana, Ph.D., Marquette School of Medicine
Dumont, Raymonde, M.D., State University of Ghent, Belgium
Eplov, Steen Peter, Ph.D., University of Copenhagen, Denmark
Goodman, Myron F., Ph.D., The Johns Hopkins University
Hershfield, Michael, M.D., National Institutes of Health
Hu, Roger C. Y., M.S., College of Physicians and Surgeons of Columbia University
Keshishian, Nina, M.S., Albert Einstein College of Medicine
Oxender, Dale L., Ph.D., University of Michigan
Ratner, David I., M.S., Cold Spring Harbor Laboratory
Sabol, Steven L., B.S., New York University
Sims, John E., B.S., University of Pennsylvania
Sugden, William, M.S., Cold Spring Harbor Laboratory
Tipper, Donald, University of Wisconsin
Zasloff, Michael A., New York University Medical School
Zeiger, Errol, M.S., Food & Drug Administration
Zeuthen, Jesper, B.S., University of Copenhagen, Denmark

SEMINARS:

G. Zubay, Columbia University, "*Mechanism of Activation of Catabolite-Sensitive Genes–Isolation of a Cyclic AMP-dependent Protein.*"
D. E. Morse, Harvard Medical School, "*Polarity, mRNA Degradation, and Relief by suA.*"
W. Gilbert, Harvard University, "*Repressors and Operators.*"
W. Maas, New York University, "*Genetics of Polyamine Synthesis in E. coli.*"
D. Zipser, Cold Spring Harbor Laboratory, "*Something New About* lac."
J. Cairns and J. Gross, Cold Spring Harbor Laboratory, "*DNA Polymerase Mutants.*"
S. Bourgeois, Salk Institute, "*Super Repressors of the* lac *System.*"

5) BACTERIAL VIRUSES–July 31-August 20, 1970

This course focused on positive control, replicative control, and specific chromosomal recognition as exemplified by bacteriophage λ. Its purpose was to establish competence in the strategies of molecular genetics; mutant selection; functional analysis of mutants to identify the kinds and numbers of genes; mapping; the ways of reversion from the mutant state; biochemical analysis of mutants.

INSTRUCTORS:

Dove, William, Ph.D., University of Wisconsin
Thomas, Rene, Ph.D., Université Libre de Bruxelles

ASSISTANTS:

Purbaiz-Toussaint, Arione, Ph.D.
Lehman, John, B.S., University of Wisconsin
Brockett, Susan, University of Wisconsin

STUDENTS:

Anderson, Margaret, Ph.D., Cold Spring Harbor Laboratory
Bade, Ernesto, M.D., "Fundacion Campomar" Institut de Investigaciones Bioquimicas, Argentina
Berman, Joy, B.A., The City University of New York Graduate Center
Datta, Asis, Ph.D., Public Health Research Institute of the City of New York
Dion, Arnold, S., M.D., University of Pennsylvania, School of Medicine
Dumont, Raymonde, M.D., Laboratory of Histology & Genetics, State University of Ghent, Belgium
Friedman, Emanuel Y., A.B., State University of New York at Stony Brook
Goldstein, Beth A., B.A., Columbia University
Goodman, Myron F., Ph.D., McArdle Memorial Laboratory, University of Wisconsin
Hayes, Sidney J., Ph.D., McArdle Memorial Laboratory, University of Wisconsin

Kamp, Dietmar, Institut für Genetik der Universitat Köln, West Germany
Karam, Jim, Ph.D., Sloan-Kettering Institute for Cancer Research
Karunakaran, Velautham, B.S., McGill University, Canada
Konigsberg, Paula J., State University of New York
Ozanne, Bradford W., B.S., Cold Spring Harbor Laboratory
Prasad, Ishwari, Ph.D., Medical College of Virginia
Ward, Thomas E., B.A., Cold Spring Harbor Laboratory
Waxman, Michael F., M.D. Brooklyn College of the City University of New York
Wright, Peter F., M.D., Laboratory of Infectious Diseases, NIAID, National Institutes of Health
Zeuthen, Jesper, University of Copenhagen, Denmark

SEMINARS:

R. Thomas, University of Brussels, "*The Regulatory Circuit Controlling Viral Growth. I. Trans-cellular elements.*"
R. Losick, Harvard University, "*The Involvement of RNA Polymerase in Changes in Gene Expression During Sporulation.*"
A. Campbell, Stanford University, "*The Regulation of the Integration of Phage Genomes.*"
J. R. Scott, Emory University, "*Phage P1.*"
R. Schleif, Harvard University, "*Dual Control of Arabinose Genes Incorporated in a Phage Genome.*"
J. Cairns, Cold Spring Harbor Laboratory, "*The Replication Apparatus of* E. coli."
R. Gesteland or J. Watson, Cold Spring Harbor Laboratory, "*Controls Over the Translation of R17 Messenger.*"
W. Gilbert, Harvard University, "*The Interaction Between Repressor and Operator*" "*The Structure of Replication Procaryotic Chromosomes.*"
E. Signer, Massachusetts Institute of Technology, "*Viral Integration in Phage and Tumor Viruses.*" "*The λ Integration/Excision Problem in Depth.*"
S. Brenner, MRC Laboratory for Molecular Biology, "*Discussion of Phage and Tumor Viruses.*"
W. Dove, University of Wisconsin, "*The regulatory Circuit Controlling Viral Growth. II. Intra-chromosomal Factors.*"
B. Alberts, Princeton University, "*DNA-binding Proteins Coded by Phage T4: The Initation of Replication.*"
C. Radding, Yale University, "*The Enzymology of Genetic Recombination.*"
H. Eisen, University of California, San Francisco, "*Regulation of the λ Repressor.*"

6) TUMOR VIRUS WORKSHOP—July 31-August 20, 1970

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.

ORGANIZERS:

Benjamin, Tom, Ph.D., Public Health Research Institute of the City of New York
Temin, Howard, Ph.D., University of Wisconsin

STUDENTS:

Anderson, Carl W., B.A., Washington University Medical School
Fluck, Michele M., D.d.Ph., University of California, Los Angeles
Folk, William R., B.A., Stanford University
Goldberg, Seth I., B.S., Downstate Medical Center
Hutchinson, Harrol T., Ph.D., University of Washington
Jaenisch, Rudolf J., Ph.D., Princeton University
Judson, Lynn, B.S., Harvard Medical School
Kobayshi, Sigeyasu, Ph.D., Albert Einstein College of Medicine
Laskey, Ronald A., D. Phil., Oxford University, England
Makover, Shraga, Ph.D., Carnegie Institute of Washington
Mason, William S., B.S., University of Chicago
Moroni, Christoph, M.D., Salk Institute
Phillips, Leo A., Ph.D., National Cancer Institute, National Institutes of Health
Rechler, Matthew M., M.D., NIAMD, National Institutes of Health
Robb, James A., NIAMS, National Institutes of Health
Seifert, Wilfried W., Ph.D., Max-Planck-Institut fur Biochemie, Germany
Stark, George R., Ph.D., Stanford University Medical School

SEMINARS:

T. Benjamin, Public Health Research Institute of the City of New York:
H. M. Temin, University of Wisconsin: *Properties of Transformed Cells; Relationship of Transformation to Malignancy.*
H. M. Temin, University of Wisconsin, *Avian RNA Tumor Viruses (virus-cell states and molecular biology)*
T. Benjamin, Public Health Research Institute of the City of New York, *Papova Viruses (virus-cell interactions and genetics)*
B. Roizman, University of Chicago, *Herpes-like Viruses Associated with Tumors*
W. P. Rowe, National Institute of Health, *Mammalian RNA Tumor Viruses*
P. Black, Massachusetts General Hospital:
M. Baluda, University of California at Los Angeles: *Maintenance of Viral Genome (DNA & RNA viruses) in the Transformed Cell with no Lysis and no Segregation*
G. Marin, Naples, *Integrated Viral Genomes*

E. Signer, Massachusetts Institute of Technology, *Discussion of Viral Integration in Phage and Tumor Viruses*
W. Eckhart, Salk Institute:
Peter Duesberg, Berkeley: *Viral Genes Expressed in Transformed Cells*
S. Brenner, MRC, Cambridge, *Discussion of Phage and Tumor Viruses*
M. Burger, Princeton University:
V. Defendi, Wistar Institute:
R. Nowinski, Sloan-Kettering: *Molecular Mechanisms of Viral Transformation Surface Changes (DNA and RNA viruses)*
E. Reich, Rockefeller Institute, *Molecular Mechanisms of Viral Transformation: Intracellular Mechanisms*
G. Todaro, National Institute of Health, *Relationship of Viruses to Spontaneous X-ray and Chemically-induced Tumors*

Photograph by Jesse W. Knight, Cold Spring Harbor, New York

SUMMER MEETINGS

This year the number of more specialized meetings held during the summer rose to five. Rudolf Werner arranged a highly successful meeting of DNA replication which was held just before the Symposium, while Ray Gesteland was responsible for bringing together a group interested in Mammalian Protein Synthesis. The Tumor Virus Meeting held for the second time grew to almost double last year's size, but was still small enough to allow everyone to meet everyone else. The Phage meeting, originally a two- to three-day affair consumed virtually two weeks with the λ specialists coming together for the week that closed the summer session.

As in the past, we are airmailing abstracts of these meetings to all who wish to subscribe to the Abstract Service.

DNA REPLICATION MEETING

Attended by 64 participants

FRIDAY, MAY 29–7:30 P.M.

DNA REPLICATION MUTANTS

Chairman: J. Drake

W. L. Fangman, Dept. of Genetics, University of Washington, Seattle: "X-Irradiation sensitivity in a DNA replication–defective bacterial mutant."

D. Beyersmann, M. Mikolajczyk, and H. Schuster. Max-Plank-Institut fur Molekulare Genetik, Berlin: "DNA replication in *E. coli* mutants thermosensitive in DNA replication."

R. Novick and E. Feingold, The Public Health Research Institute of the City of New York: "Mutations affecting plasmid replication in *S. aureus.*"

SATURDAY, MAY 30 – 9:30 A.M.

ENZYMOLOGY OF DNA REPLICATION

Chairman: J. Speyer

H. Schaller, D. W. Smith and F. Bonhoeffer, Max-Planck-Institut, Tubingen: "DNA synthesis, a new in vitro system."

R. E. Moses and C. C. Richardson, Dept. of Biological Chemistry, Harvard Medical School, Boston: "Studies on DNA metabolism in a DNA polymerase negative mutant of *E. coli* (Pol Al)."

B. Alberts and L. Frey, Princeton University: "T4 gene 32: a structural protein in the replication and recombination of DNA."

M. Gellert and M. L. Bullock, National Institute of Arthritis and Metabolic Diseases, NIH: "DNA Ligase mutants of *E. coli.*"

SATURDAY, MAY 30 – 7:30 P.M.

INTERMEDIATES IN DNA REPLICATION

Chairman: W. Gilbert

R. Okazaki, T. Okazaki, K. Sugimoto, Y. Imae, N. Iwatsuki, R. Kainuma, A. Sugino, T. Ogawa and N. Kanamori, Institute of Mol. Biology, Faculty of Science, Nagoya University, Nagoya, Japan: "Discontinuous Replication of DNA."

M. P. Deutscher, H. Manor, U. Z. Liffauer, University of Connecticut Health Center, Farmington, Conn.: "Rates of DNA chain growth in *E. coli.*"

C. Pauling and L. Hamm, Dept. of Life Sciences, University of California, Riverside: "Evidence for a hairpin intermediate in DNA replication."

SUNDAY, MAY 31 – 9:30 A.M.

STRUCTURE OF REPLICATING DNA–I

Chairman: J. Cairns

D. B. Clewell, D. J. Sherratt, D. Blair, B. Kline and D. R. Helinski, University of California, San Diego: "Properties of supercoiled DNA relaxation complexes in *E. coli.*"

D. A. Marvin, B. Tseng and B. Hohn, Yale University: "On the mechanism of synthesis of fd DNA."

D. Vapnek and W. D. Rupp, Yale University: "Asymmetric segregation of the complementary sex-factor DNA strands during conjugation in *E. coli.*"

D. Dressler and J. Wolfson, Harvard University: "Opposing Rolling Circles."

SUNDAY, MAY 31 – 2:00 P.M.

STRUCTURE OF REPLICATING DNA–II

Chairman: F. Frankel

A. M. Skalka, Roche Institute of Molecular Biology: "An Investigation into the Role of DNA-Catemers in the Life Cycle of λ Phage."

D. Botstein and M. J. Matz, Mass. Inst. of Technology: "A Recombination Function Essential to growth of Phage P22."

N. Sueoka, R. Bishop and W. G. Quinn, Princeton University: "Replication of the *Bacillus subtilis* chromosome."

MONDAY, JUNE 1 – 9:30 A.M.

CONTROL AND INITIATION OF DNA REPLICATION

Chairman: C. Davern

L. Caro and Y. Nishimura, Oak Ridge National Laboratory: "Control of Chromosome Replication and Cell Division by an Integrated Episome."
T. Kogoma and K. S. Lark, Kansas State University: "DNA replication in *E. coli*: Replication in absence of protein synthesis after replication inhibition."
G. Mosig, R. Marsh and A. Breschkin, Vanderbilt University: "Origin and Direction of Phage T4 DNA Replication."
A. W. Kozinski, University of Pennsylvania: "The Initiation of T4 DNA Replication–Possible Role of Host Enzymes."

TUMOR VIRUS MEETING

Attended by 134 participants

TUESDAY, AUGUST 18 – 7:30 P.M.

PHENOTYPE OF TRANSFORMATION

Chairman: H. Green

C. D. Scher, H. S. Smith, and G. J. Todaro, National Cancer Institute, Bethesda, Maryland, and Mel-Labs, Inc., Springfield, Virginia: "Abortive Transformation of BALB/3T3 by Simian Virus 40."
R. Pollack and S. Wolman, New York University Medical Center, N.Y.: "Increase in Chromosome Number in Phenotypic Revertant Sublines of Transformed Cells."
J. R. Sheppard, A. J. Levine and M. M. Burger, Department of Biochemistry, Princeton University, Princeton, N.J.: "Parameters Influencing the Exposure of an Agglutinin Receptor after Infection by SV40 Virus."
H. Sakiyama and B. W. Burge, Department of Biology, M.I.T., Cambridge, Mass.: "Comparison of Surface Glycoprotein Constituents of 3T3 and SV40-Transformed 3T3 Cells."

VIRAL DNA

K. Danna, S. P. Adler, and D. Nathans, Department of Microbiology, Johns Hopkins University School of Medicine, Baltimore, Maryland: "Cleavage of SV40 DNA by Bacterial Restriction Enzymes."

WEDNESDAY, AUGUST 19 – 9:00 A.M.

POLYOMA AND SV40 MUTANTS AND TRANSFORMATION

Chairman: T. Benjamin

J. A. Robb and R. G. Martin, Lab. of Molecular Biology, NIAMD, NIH, Bethesda, Maryland: "A Temperature-Sensitive Mutant of SV40 Blocked in an Early Function."
S. Kit, S. Tokuno, K. Nakajima, D. Trkula, and D. R. Dubbs, Div. of Biochemical Virology, Baylor College of Medicine, Houston, Texas: "Characterization of a Temperature-Sensitive SV40 Mutant Defective in a Late Function."
W. Eckhart, Salk Institute for Biological Studies, San Diego, California: "Polyoma Virus Gene Functions Required for Transformation."
C. Mulder, J. W. Summers and M. Vogt, The Salk Institute for Biological Studies, San Diego, California: "Recovery of Virus from Polyoma Transformed BHK-21 Cells."
P. Bourgaux and D. Bourgaux-Ramoisy, Department of Microbiology, Centre Hospitalier Universitaire, Universite de Sherbrooke, Quebec, Canada: "The Replicative Intermediate of Polyoma Virus DNA."

WEDNESDAY, AUGUST 19 – 7:30 P.M.

INTEGRATION OF VIRAL DNA

Chairman: L. V. Crawford

W. Doerfler, The Rockefeller University, New York, N.Y.: "Integration of the DNA of Adenovirus Type 12 into the DNA of BHK-21 Cells."
L. D. Gelb and M. A. Martin, Laboratory of Biology of Viruses, NIAID, NIH, Bethesda, Maryland: "Quantitation of Integrated Viral DNA in SV40 Transformed Cell Lines."
K. Hirai, J. Lehman, and V. Defendi, The Wistar Institute, Philadelphia, Pa.: "Evidence for Integration of SV40 DNA with DNA of Chinese Hamster Cells During Primary Infection."
J. Lehman and V. Defendi, The Wistar Institute, Philadelphia, Pa.: "Alternation in DNA Synthesis Regulation in Chinese Hamster Cells Infected by SV40."
A. J. Levine, Department of Biochemistry, Princeton University, Princeton, N.J.: "The Stimulation of Mitochondrial DNA Synthesis by SV40 Infection."

THURSDAY, AUGUST 20 – 9:00 A.M.

PROTEINS OF TUMOR VIRUSES

Chairman: R. O. Roblin

I Polyoma and SV40

B. Hirt and R. Gesteland, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.: "Characterization of the Proteins of SV40 and Polyoma Virus."
M. K. Estes, E-S. Huang and J. S. Pagano, Departments of Bacteriology and Immunology and Medicine, University of North Carolina, Chapel Hill, North Carolina: "Studies of the Structural Polypeptides of Simian Virus 40."
T. Friedmann, The Salk Institute for Biological Studies, San Diego, California: "The In Vitro Reassembly of Shell-Like Particles from Disrupted Polyoma."

II RNA Viruses

R. C. Nowinski and L. J. Old, Division of Immunology, Sloan-Kettering Institute for Cancer Research, New York: "Proteins of Oncogenic RNA Viruses."

J. Hilgers, Sloan-Kettering Institute for Cancer Research, New York: "Identification of Antigens of Oncogenic RNA (Oncorna) Viruses by Immunofluorescence."

THURSDAY, AUGUST 20 – 2:00 P.M.

RNA TUMOR VIRUS – I
TRANSCRIPTION INTO DNA
Chairman: H. M. Temin

S. Mizutani and H. M. Temin, McArdle Laboratory, University of Wisconsin: "An Enzyme that Appears to Make DNA from RNA in Virions of Rous Sarcoma Virus (RSV)."
M. Green, M. Rokutanda, K. Fujinaga, R. K. Ray, H. Rokutanda, and C. Gurgo, Institute for Molecular Virology, Saint Louis University School of Medicine, St. Louis: "Properties of the RNA Dependent DNA Polymerase in Murine Sarcoma Viruses."
S. Spiegelman, A. Burny, J. Keydar, J. Schlom, M. R. Das, M. Travnicek, K. Watson, Institute of Cancer Research, Columbia University, New York City: "Intermediates and Products of DNA Polymerases in Oncogenic RNA Viruses."
J. P. Bader and A. V. Bader, Chemistry and Viral Biology Branches, National Cancer Institute, Bethesda, Maryland: "A DNA Replicative Genome for RNA-Containing Tumor Viruses."
D. Boettiger, McArdle Laboratory, University of Wisconsin, Madison: "The DNA Provirus of Rous Sarcoma Virus: Inactivation of 5-BUDR Labeled Provirus."

FRIDAY, AUGUST 21 – 9:00 A.M.

RNA TUMOR VIRUSES – II
Chairman: R. Erikson

J. M. Bishop, W. E. Levinson and D. Sullivan, Department of Microbiology, University of California Medical Center, San Francisco: "The Low Molecular Weight RNA's of Rous Sarcoma Virus."
B. Brdar, D. B. Rifkin and E. Reich, Rockefeller University, New York City: "Effects of Nucleoside Analogues on Rous Sarcoma Virus RNA Synthesis."
T. Graf and H. Bauer, Max-Planck-Institut fur Virusforschung, Biologisch-medizinische Abteilung, Tubingen, Germany: "Mutants of Rous Sarcoma Virus."
N. H. Sarkar, R. C. Nowinski, and D. H. Moore, Institute for Medical Research, Camden, New Jersey: "The Internal Structure of the Oncogenic RNA Viruses."
D. B. Rifkin and E. Reich, Department of Chemical Biology, The Rockefeller University, New York City: "Selective Lysis of RSV Transformed Cells by Local Anaesthetics."

MAMMALIAN PROTEIN SYNTHESIS MEETING

Attended by 66 participants

SATURDAY, AUGUST 22 – 7:30 P.M.

HETEROLOGOUS SYSTEMS

A. H. Scragg, H. Morimoto, V. Villa, and H. O. Halvorson, Lab. of Molecular Biology, Univ. of Wisconsin: "Cell-Free Protein Synthesizing System from Yeast Mitochondria: A Study of Erythromycin and Chloramphenicol Resistant Mutants."
D. M. Rekosh, H. F. Lodish and D. Baltimore, Dept. of Biology, M. I. T.: "Protein Synthesis in *E. coli* Extracts Programmed by Poliovirus RNA."
R. F. Gesteland, L. V. Crawford, M. L. Anderson, G. M. Rubin, B. Hirt, Cold Spring Harbor Laboratory: "Use of Mammalian DNAs to Direct Coupled Protein Synthesis in Extracts of *E. coli*."

SUNDAY, AUGUST 23 – 9:30 A.M.

HEMOGLOBIN INITIATION

D. Wilson, Dept. of Biochemistry, Cornell University: "Initiation of Hemoglobin Synthesis."
R. J. Jackson and A. R. Hunter, Dept. of Biochemistry, Univ. of Cambridge: "Initiation of Hemoglobin Synthesis by Methionine."
A. Yoshida, Division of Medical Genetics, Univ. of Washington: "N-Terminal Methionine and N-Formylmethionine in Small Nascent Peptides of Rabbit Reticulocytes."
B. Hardesty, W. Culp, J. Morrisey, J. Irvin, and W. Mc Keehan, Clayton Foundation Biochem. Inst., and Dept. Chem., The Univ. of Texas at Austin: "Initiator tRNA for the Synthesis of Globin."
H. F. Lodish, D. Housman, M. Jacobs-Lorena and U. L. Raj Bhandary, Dept. of Biology, M. I. T.: "Initiation of Hemoglobin Synthesis."

MONDAY, AUGUST 24 – 2:00 P.M.

SPECIFICITY

P. Vassalli, B. Lisowska-Bernstein and M. E. Lamm, Dept. of Pathology, University of Geneva: "Cell-Free Synthesis of Rat Immunoglobulin."
S. M. Heywood, Biological Sciences Group, University of Connecticut: "Specificity of mRNA Binding Factor in Eukaryotes."
J. B. Lingrel, R. E. Lockard, R. F. Jones, H. E. Burr, and J. W. Holder, Biological Chemistry Dept., University of Cincinnati College of Medicine: "Cell-Free Hemoglobin Synthesis: Various Systems Programmed with Heterologous Messenger RNA's."
H. Coffier, H. Raskas, and M. Green, Institute for Molecular Virology, St. Louis University: "In Vitro Protein Synthesis of Adeno Virus Proteins."

TUESDAY, AUGUST 25 – 9:00 A.M.

RIBOSOMES, FACTORS AND TERMINATION

B. Mach and B. Mechler, Inst. of Molecular Biology, University of Geneva: "Active Ribosomal Subunits from Mouse Plasmocytoma Tumors."

F. A. Stepheson, M. H. Schreier, and H. Noll, Dept. of Biology, Northwestern University, Evanston: "Primitive Chain Initiation with Ribosomal Subunits from Mouse Liver: the Poly U and $tRNA^{phe}_{OH}$ Dependent Formation of a 70s Initiation Complex."

J. F. Collins, H. M. Moon, and E. S. Maxwell, Laboratory of Molecular Biology, N. I. H.: "Soluble Protein Factors from Rat Liver for in vitro Polypeptide Synthesis."

D. P. Leader, I. G. Wool, and J. J. Castles, Dept. of Physiology, Univ. of Chicago: "A Factor for the Binding of Aminoacyl tRNA to Mammalian 40s Ribosomal Subunits."

B. S. Baliga and H. N. Munro, Dept. of Nutrition and Food Science, M. I. T.: "Site of Attachment of Transferase 11-GTP Complex on Mammalian Ribisomes."

J. L. Goldstein, A. L. Beaudet, and C. T. Caskey, Lab. of Biochemical Genetics, N. I. H.: "Mammalian Peptide Chain Termination."

BACTERIOPHAGE MEETING

Attended by 144 participants

WEDNESDAY, AUGUST 26 – 7:30 P.M.

K. R. Stone & D. J. Cummings, University of Colorado Medical Center, Denver, Colorado: "Internal Proteins of the T-Even Bacteriophages."

C. J. Castillo, Departments of Molecular Biology & Medical Genetics, University of Pennsylvania, Philadelphia, Pa.: "Some Evidence For the Presence of an Endonuclease Within The T4 Capsid."

D. B. Cowie & R. J. Avery, Department of Terrestrial Magnetism, Carnegie Institution of Washington, Wash., D.C.: "T-Even Bacteriophage DNAs."

L. M. Kozloff, M. Lute & L. K. Crosby, University of Colorado Medical Center, Denver, Colorado: "Role of Pteroyl Hexaglutamate In T4D Tail Assembly."

THURSDAY, AUGUST 27 – 9:00 A.M.

B. Dorsett, L. Bernhardt, J. Chu, H. Evans, R. Ziprin & L. S. Jacobson, Brooklyn College of C.U.N.Y. and Long Island University, Brooklyn, N.Y.: "Acid Inactivation of MS2."

R. Dumont, J. Vandekerckhove, C. Meyvisch, H. Teuchy & M. Van Montagu, Univ. of Ghent, Belgium: "Properties of Some Amber Coat Mutants of RNA Bacteriophage MS-2."

N. Fedoroff, Rockefeller University, New York, N.Y.: "In vivo Degradation of Phage f2 RNA."

R. M. Weppelman & C. C. Brinton, JR.: "Infection of *Pseudomonas Aeruginosa* By the RNA Phage PP7."

A. M. Weiner, M. Osborn, & K. Weber, Harvard Biological Laboratories, Cambridge, Mass.: "Large-Scale Purification of the R17 A-Protein And Initial Sequence Studies."

R. Kamen, Harvard University, Cambridge, Mass.: "Subunit Structure of Qβ Replicase."

A. A. Travers & R. I. Kamen, The Biological Laboratories, Harvard University, Cambridge, Mass.: "In vitro Synthesis of Ribosomal RNA Directed By A Host Specific Subunit Of Qβ Replicase."

THURSDAY, AUGUST 27 – 7:30 P.M.

D. H. Duckworth & H. H. Winkler, University of Virginia, Charlottesville, Va.: "Sugar Transport During T4 Phage and Ghost Infection And The Inhibition of Phage Multiplication By Ghosts."

R. Fabricant & D. Kennell, Washington University School of Medicine, St. Louis, Missouri 63130: "Inhibition of Host Protein Synthesis By T2 Ghosts."

R. Swift & J. Wiberg, University of Rochester, Rochester, N.Y.: "Inhibition By T4D Of The Colicin E2-Induced Degradation of *E. Coli* B DNA."

P. Donini, University of California, Berkeley, California: "T4 DNA And Protein Synthesis In Cells Growing At Different Rates."

P. Donini & G. Edlin, University of California, Berkeley and Davis: "The Effect of Amino Acid Starvation On Synthesis Of Late T4 Messenger RNA."

G. W. Notani, Inst. de Biologie Moleculaire, Geneva, Switzerland; "RNA Synthesis during Growth of Phage T4."

I. Brunovskis, R. B. Siegel, & W. C. Summers, Yale University, New Haven, Conn.: "Early Regulatory Controls In T-7 Infected Cells."

T. Burch, W. Gibbs, K. Barrett, E. Six & R. Calendar, University of California, Berkeley, and University of Iowa, Iowa City: "A New RNA Polymerase Activity Induced By Infection With Satellite Phage P4."

FRIDAY, AUGUST 28 – 9:00 A.M.

E. F. Rossomando & J. B. Milstien, National Institutes of Health, Bethesda, Md.: "Electro-optic Studies on the Structure of Bacteriophage fl."

D. J. Zaleske, A. K. Dunker, W. J. Pigram, R. L. Wiseman, & D. A. Marvin, Yale University, New Haven, Conn.: "Model Building and the Structure of Filamentous Viruses."

A. B. Forsheit & D. S. Ray, Molecular Biology Institute and Dept. of Zoology, UCLA, Los Angeles, Calif.: "Conformation of the Single-Stranded DNA of Bacteriophage M13."

J. Beaudoin, T. J. Henry, & D. Pratt, University of Wisconsin, Madison, Wis., and University of Pittsburgh, Pittsburgh, Pa.: "Electrophoretic Separation and Purification of M13 Virions, And A Model For Serum Inactivation Of Ff Bacteriophages."

T. Henry & C. Brinton, Dept. of Biophysics, Univ. of Pittsburgh, Pittsburgh, Pa.: "Fate of the Protein Coat of Coliphage M13 During Infection."

J. Beaudoin & D. Pratt, University of Wisconsin, Madison, Wis.: "Coat Proteins Of Coliphage M13."

J. Salstrom & D. Pratt, University of Wisconsin, Madison, Wis.: "A Role for the M13 Gene 5 Product in the Production of Viral Single-Stranded DNA."

FRIDAY, AUGUST 28 – 7:30 P.M.

R. Benbow, R. Mayol, & R. Sinsheimer, California Institute of Technology, Pasadena, California: "The Genetic Map of Bacteriophage φX174."

B. Francke, Molecular Biology Institute and Dept. of Zoology, UCLA, Los Angeles, Calif.: "Infection of Starved Thymine-Requiring Cells with φX174."

R. W. Schekman, D. T. Denhardt, & D. S. Ray, UCLA and Harvard University: "φX174 Replication in a Temperature-Sensitive DNA Ligase Mutant."

M. Iwaya & D. T. Denhardt, Harvard University, Cambridge, Mass.: "Maturation of Single-Stranded Phage ϕX174."

SATURDAY, AUGUST 29 – 9:00 A.M.

R. H. Baltz, & J. W. Drake, University of Illinois, Urbana: "Infectious T4 DNA."
L. Lawhorne & R. Benzinger, Dept. of Biology, University of Virginia, Charlottesville, Va.: "Transfection of *E. Coli* Spheroplasts: I Infectious T7 And T5 Phage DNA's."
R. Benzinger & I. Kleber, Dept. of Biology, University of Virginia, Charlottesville, Va.: "Transfection of *E. Coli* Spheroplasts: II. Infectious P22 Phage DNA."
R. Benzinger & R. Huskey, Dept. of Biology, University of Virginia, Charlottesville, Va. 22903: "Transfection of *E. Coli* Spheroplasts: III. Highly Infectious λ Phage And Prophage DNA's."
P. J. Weisbeek & J. H. Van de Pol, Institute of Genetics, State University, Utrecht, The Netherlands: "Biological Activity of ϕX174 RF DNA Fragments."
W. E. Borrias & J. H. van de Pol, Institute of Genetics, State University, Utrecht, The Netherlands: "Complementation Between DNA Molecules of Bacteriophage ϕX174 in a Spheroplast System."

SATURDAY, AUGUST 29 – 7:30 P.M.

N. Franklin, Dept. Biological Sciences, Stanford Univ., Stanford, California: "Repression at an Internal Operator Does Not Impede Transcription Through That Operator."
H. Drexler, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, N.C.: "Transduction of λ-Bacterial Hybrids by T1."
R. Calendar & M. Marsh, University of California, Berkeley: "A Temperate-Inducible Mutant of Phage P2."
W. Gibbs, M. Thorn, J. Levy, & Richard Calendar, University of California, Berkeley: "Studies on Satellite Phage P4."
J. Geisselsoder & M. Mandel, University of Hawaii, Honolulu, Hi.: "On the Relationship Between P2 and 299."
J. Schell, S. van den Elsacker, M. Holsters, H. Teuchy, & M. Van Montagu, Univ. of Ghent, Belgium: "Temperate Phages And Bacteriocins of *a. tumefaciens* Their Possible Role as Tumor-Inducing Agents."

SUNDAY, AUGUST 30 – 9:00 A.M.

G. Mosig, R. Ehring, F. C. Womack, & W. Schliewen, Vanderbilt University and C.I.W. Cold Spring Harbor, N.Y.: "Effects of Chromosomal Ends on Recombination in Phage T4."
B. S. Emanuel, Dept. of Med. Genetics University of Pa., Philadelphia, Pa.: "Recombination in T4 am N82."
H. M. Krisch, D. B. Shah, & H. Berger, The Johns Hopkins Univ. Baltimore, Md.: "Replication and Recombination in rII-Ligase T4D Bacteriophage."
K. Carlson, Dept. of Medical Genetics & Dept. of Molecular Biology, University of Pa., Philadelphia, Pa.: "Maturation of T4 Without DNA Replication."
C. Howe, Dept. of Med. Genetics and Molecular Biology, Univ. of Pa., Philadelphia, Pa.: "Partially Replicated Molecules in *E. Coli* B Infected With T4 am B22."
J. D. Karam, Division of Genetics, Sloan-Kettering Institute for Cancer Research, New York, N.Y. 10021: "Expression of the T4 rII Gene."

SUNDAY, AUGUST 30 – 7:30 P.M.

J. Levy, University of Washington, Seattle, Washington: "Effects Of P^{32} Decay on Phage T4D."
R. Wu & Y. C. Yeh, University of Ark., Little Rock, Ark. "Suppression of Defect in Gene 59 of T4 Bacteriophage."
K. Hercules, J. L. Munro, S. Mendelsohn, & J. S. Wiberg, University of Rochester, N.Y. 14620: "*DenA*: A New T4 Gene Controlling Degradation of *E. coli* DNA."
H. R. Warner, D. P. Snustad, & J. F. Koerner, University of Minnesota, St. Paul and Minneapolis, Minn.: "Characterization and Mapping of a T4 Mutant which Induces a Defective Exonuclease A."
H. Rappaport, M. Russel, M. Susman, & J. McLaren, Genetics Dept., University of Wisconsin, Madison, Wis.: "Some Acridine-Resistant Mutants of T4."
G. R. Greenberg, C-s Chiu, P. Tomich, & L. Lu, The University of Michigan, Ann Arbor, Michigan 48104: "Unusual Properties of Temperature-Sensitive Gene 42 Mutants of T4 Phage."

MONDAY, AUGUST 31 – 9:00 A.M.

G. D. Frenkel & C. C. Richardson, Department of Biological Chemistry, Harvard Medical School, Boston, Mass.: "A 5' –Exonuclease of Bacteriophage T5."
P. Grippo, Y. Masamune, & C. C. Richardson, Dept. of Biological Chemistry, Harvard Medical School, Boston, Mass.: "DNA Polymerase and Ligase of Phage T7."
R. A. Schlegel & C. A. Thomas, Jr., Harvard Medical School, Boston, Mass.: "Characterization of Single-chained Regions of Intracellular T7 DNA."
C. F. Earhart, The Univ. of Texas, Austin, Texas: "Studies on the Process of Attachment of T4 DNA to Host Membrane."
R. Marsh, A. Breschkin, & G. Mosig, Dept. of Mol. Biol., Vanderbilt University, Nashville, Tenn: "Origin λ and Direction of Phage T4 DNA Replication."

WORKSHOP ON BACTERIOPHAGE λ

Attended by 127 participants

WEDNESDAY, SEPTEMBER 2 – 7:30 P.M.

Phage λ continues as one of the main vehicles for work on the fundamental problems of molecular genetics. Yet, most outsiders never master the rapidly changing terminology. So a happy consequence of this year's meeting will be the opening of the λ world to non-specialists through the publication of a book devoted exclusively to λ. Twelve introductory general chapters aiming to

explain the phage λ will be followed by some thirty research articles which hopefully, because of the introductory chapters, will be simple reading for all. Now we hope to have it available in June 1971.

MAPPING GENES AND PROTEINS ON λ DNA
Chairman: D. Kaiser

M. N. Simon, R. W. Davis, and N. Davidson, Dept. of Chemistry, Caltech, Pasadena, Calif.: "Electron Microscope Heteroduplex Studies of Sequence Relations of the DNA Molecules of Lambdoid Phages."
M. Fiandt, Z. Hradecna, H. Lozeron, and W. Szybalski, McArdle Lab., University of Wisconsin: "Electron Micrographic Mapping of Deletions, Substitutions, Inversions and Homologies in the λ and φ80 Phage Genomes."
R. Hendrix, Harvard University: "Characterization of λ Proteins."
J. W. Little and M. Gottesman, NIAMD, NIH: "Defective λ Particles Whose DNA Bears One Cohesive End."

THURSDAY, SEPTEMBER 3 – 9:00 A.M.

GENERAL RECOMBINATION
Chairman: E. R. Signer

G. Kellenberger-Gujer, ORNL, Biology Division, Oak Ridge: "General Recombination in Lambda."
C. M. Radding, E. Cassuto, and D. M. Carter, Yale University: "A Model for the Action of λ Exonuclease in Genetic Recombination."
J. F. Zissler and E. R. Signer, Univ. of Minnesota and M.I.T.: "λ Recombination Genes."

THURSDAY, SEPTEMBER 3 – 7:30 P.M.

SPECIAL RECOMBINATION – I
Chairman: A. Campbell

M. Gottesman and M. Shulman, NAIMD, NIH: λ *att*^{2}; A Transducing Phage Capable of Intra-Molecular *Int–Xis* Promoted Recombination."
R. Weisberg and M. Gottesman, NIH: "An In Vivo Assay for Int and Xis Functions."
E. Jordan and H. Echols, University of California, Berkeley: "General and Site-Specific Recombination by λ."
E. R. Signer: Abstract not received.

FRIDAY, SEPTEMBER 4 – 9:00 A.M.

SPECIAL RECOMBINATION – II
Chairman: R. Weisberg

S. Adhya, Bose Institute, Calcutta, India: "Crypticogenicity of λ Bacteriophage."
A. J. D. Bellet, H. G. Busse and R. L. Baldwin, Dept. of Biochemistry, Stanford University School of Medicine: "Genetic Duplications in Tandem in a λ-Related Phage."
J. S. Parkinson, Dept. of Biochemistry, Univ. of Wisconsin: "The Genetic and Physical Structure of the λ Attachment Site."
R. W. Davies, W. F. Dove, H. Inokuchi, J. F. Lehman, and R. L. Roehrdanz, McArdle Laboratory, Univ. of Wisconsin: "Transcriptional Activation of *ATT*λ."

FRIDAY, SEPTEMBER 4 – 7:30 P.M.

DNA REPLICATION – I
Chairman: A. D. Hershey

R. S. Inman and M. Schnos, Dept. of Biophysics, Univ. of Wisconsin: "Replication of λ and P2 Phage DNA."
W. F. Stevens, Y. A. Saturen and W. Szybalski, McArdle Laboratory, Univ. of Wisconsin: "Origin and Orientation of DNA Replication in Coliphage λ."
J. Asaka and J. Tomizawa, Dept. of Biology, Osaka University, Toyonaka: "Transfer of Parental λ DNA Strands to Progeny."
B. J. Carter and M. G. Smith, Otago University, New Zealand: "The Replication of Bacteriophage λ DNA Following Lytic Infection."

SATURDAY, SEPTEMBER 5 – 9:00 A.M.

DNA REPLICATION – II
Chairman: J. Tomizawa

W. F. Dove and H. Inokuchi, McArdle Laboratory, Univ. of Wisconsin: "Replication Control in λ."
Y. Sakakibara and J. Tomizawa, Nat'l. Inst. of Health of Japan, Tokyo, and Faculty of Science, Osaka University, Toyonaka: "Function of Gene N and Membrane Association of λ DNA."
J. Tomizawa, Faculty of Science, Osaka University, Toyonaka: "Functional Cooperation of Genes O and P of Phage λ."
C. P. Georgopoulos and I. Herskowitz, Dept. of Biochemistry, Stanford University, and Dept. of Biology, M.I.T.: "Bacterial Mutants Blocked in the Gene P Step."

SUNDAY, SEPTEMBER 6 – 9:00 A.M.

REPRESSOR AND OPERATORS
Chairman: H. Echols

B. Steinberg and M. Ptashne, The Biological Laboratories, Harvard University, Cambridge: "In Vitro Repression."
P. Chadwick, V. Pirrotta, and M. Ptashne, The Biological Laboratories, Harvard University: "The λ and 434 Phage Repressors."
G. W. Ordal, Dept. of Biochemistry, Stanford Univ.: "Supervirulent Mutants of Bacteriophage λ and the Structure of Operator and Promoter Sites."

W. S. Sly, K. Rabideau, and A. Kolber, Washington University, St. Louis, Mo.: "Regulatory Mutations in Classical λ Virulence."
N. Mantei, S. Ghosh, A. Wu, and H. Echols, Univ. of California, Berkeley: "Negative Regulation of λ Development."

SUNDAY, SEPTEMBER 7 – 7:30 P.M.

CONTROL OF REPRESSOR
Chairman: W. Gilbert

J. Pero, Biological Labs, Harvard University: "Deletion Mapping of the Site of Action of the *TOF* Gene Product of Phage λ."
E. Calef, S. Avitabile, L. Del Giudice, C. Marchelli, T. Menna, Z. Meubauer and A. Soller, International Lab. of Genetics and Biophysics, Naples, Italy: "Genetics of Anti-Immune Phenotype in Defective Lysogens."
H. Eisen, S. Heinemann and W. Spiegelman, Dept. of Biochemistry and Biophysics, Univ. of California Medical Center, San Francisco, and Depts. of Biochemistry and Genetics, Stanford University: "Regulation of Lambda Repressor Synthesis: The Mechanism of *cI* Shut-off."
L. Pereira da Silva, H. Eisen, P. Brachet, W. Spiegelman, and S. Heinemann, Institut Pasteur, Paris; Dept. of Biochemistry and Biophysics, Univ. of Calif., San Francisco; and Depts. of Biochemistry and Genetics, Stanford Univ.: "Regulation of Lambda Repressor Synthesis."

MONDAY, SEPTEMBER 7 – 9:00 A.M.

REGULATION BY N AND Q
Chairman: W. F. Dove

N. Franklin, Biology Dept., Stanford Univ.: "Regulation of Early-Left λ Functions."
C. P. Georgopoulos, Dept. of Biochemistry, Stanford Univ.: "A Bacterial Mutant Unable to Form Active N-Gene Product."
P. Kourilsky, M. F. Bourguignon and F. Gros, Institut de Biologie Moleculaire, Paris: "Cleavage of 1 Strand Transcripts by a Specific Nucleolytic Process."
M. Lieb, Dept. of Microbiology, U.S.C. School of Medicine, Los Angeles: "λ N Mutants: Multiple Plasmids and Prophages."
D. E. Berg, Dept. of Biochemistry, Stanford University: "Regulation of Phages Partially Diploid in the Immunity Region."

MONDAY, SEPTEMBER 7 – 7:30 P.M.

GENERAL PAPERS – I

Chairman: N. Davidson

J. Hedgepeth, D. Roulland-Dussoix, and H. Boyer, Univ. of California, San Francisco: "The Interaction of the Escherichia Coli B Restriction Endonuclease with Specific Regions of DNA."
D. I. Friedman, NIAMD, NIH: "Bacterial Mutants Affecting λ Development."
G. Kayajanian, McArdle Laboratory, Univ. of Wisconsin: "Origin of λ Transducing Genomes."
M. Belfort and D. L. Wulff, Univ. of California, Irvine: "A Mutant of *E. coli* in which λ Lysogenizes with Extremely High Frequency."

TUESDAY, SEPTEMBER 8 – 9:00 A.M.

GENERAL PAPERS – II

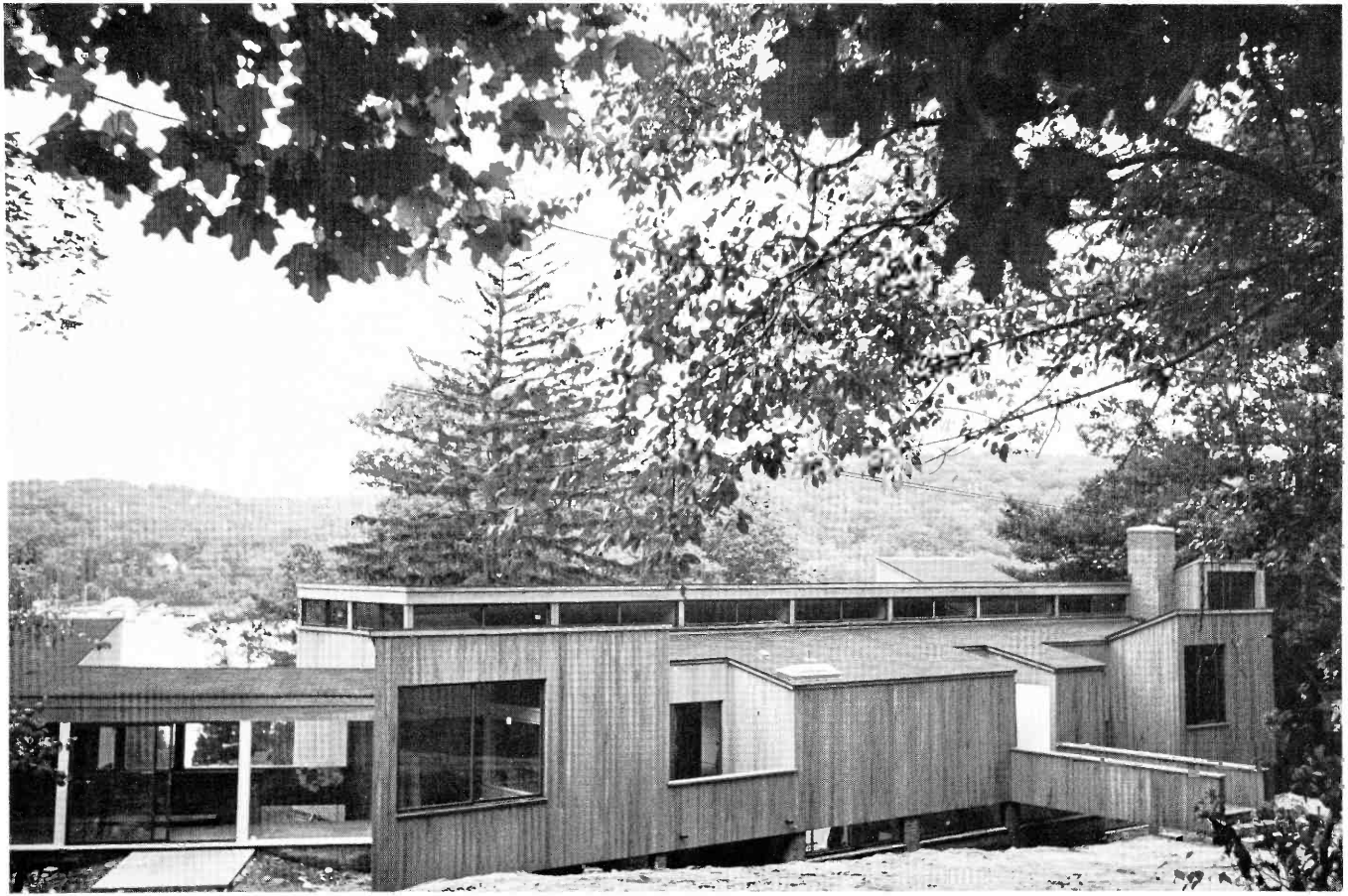
Chairman: M. Gottesman

A. Skalka, Carnegie Institute of Washington, Cold Spring Harbor: "DNA Concatemers and λ growth."
S. Makover, Carnegie Institute of Washington, Cold Spring Harbor: "The Origin and Direction of Replication of λ Phage DNA."
J. D. Sharp, Brandeis University, Waltham: "Lack of Polarity of DNA Injection by Phage λ."

WEDNESDAY, SEPTEMBER 9 – 9:00 A.M.

MORPHOGENESIS
Chairman: R. Edgar

S. Casjens and T. Hohn, Dept. of Biochemistry, Stanford Univ: "The Morphological Proteins of Phage λ."
H. Murialdo, M. Buchwald and L. Siminovitch, Dept. of Medical Cell Biology, Univ. of Toronto: "The Main Structural Proteins of Phage λ."
E. Kellenberger, Lab. Biophysique, Univ. of Geneva: "Special Features of the Form-Inheritance of Phage T4 Head and Head-Related Particles."



James Laboratory Annex nearing completion

Photograph by Jesse W. Knight, Cold Spring Harbor, New York

UNDERGRADUATE RESEARCH PARTICIPATION PROGRAM

Summer 1970

The laboratory was able to take on ten undergraduates for the summer, sponsored by the National Science Foundation's Undergraduate Research Participation Program. The object of this program is to provide increased opportunities for the scholarly development of outstanding undergraduates who may pursue careers in science. Each undergraduate is therefore made a member of one of the research teams working at Cold Spring Harbor during the summer, and is given a particular project. At the same time, he has the opportunity of attending the lectures given in the various courses in microbial genetics, and of joining in the singularly unstratified society that is so characteristic of the place. This program for undergraduates has proved to be very successful in the past, as witness the number of molecular biologists who began their careers as undergraduates at Cold Spring Harbor.

The following students participated in this program during the summer of 1970:

Denise Bostrom, Bennington College *Supervisor*: R. Gesteland	Search for unusual RNA phages
Mark E. Furth, Harvard College *Supervisor*: D. Zipser	The control of operon separation
Charles Gilbert, Amherst College *Supervisor*: R. Crouch	Phage λ DNA attachment in *E. coli* mini cells
David Kaback, S.U.N.Y.-Stony Brook *Supervisor*: D. Zipser	Termination of mRNA synthesis
Ilan Kirsch, University of California *Supervisor*: C. Mulder	Effect of *E. coli* restricting enzyme on SV40 and Polyoma DNA
Jeanne Margolskee, Radcliffe College *Supervisor*: J. Cairns	Membrane attachment of DNA replication fork
David Margulies, Columbia University *Supervisor*: R. Werner	Effect of gene 32 protein on rate of DNA replication in phage T4
Harvey Morrison, Cornell University *Supervisor*: H. Westphal	Number of integrated SV40 genomes in transformed cells
Gerald Rubin, Massachusetts Institute of Technology *Supervisor*: L. Crawford	Translation of mitochondrial DNA in a coupled system
Margaret Tucker, Wellesley College *Supervisor*: J. Sambrook	Isolation of RNA polymerase from HeLa mouse hybrids

Children of Ages 6 to 16

During the summer of 1970, 23 courses in Nature Study were conducted in two monthly sessions. The enrollment this year was 452 students. The course offerings included:

General Nature Study (ages 6,7)
Advanced Nature Study (ages 8,9)
Plant-Insect Relationships (ages 8,9)
Elementary Geology (ages 8,9)
Bird Study (ages 10,11)
Fresh-Water Life (ages 10,11)
Seashore Life (ages 10,11)
Insect Study (ages 10,11)
Animals with Backbones (ages 10,11)
Geology (ages 10,11)
Ichthyology-Herpetology (ages 12-16)
Plant Ecology (ages 12-16)
Advanced Geology (ages 12-16)
Animal Ecology (ages 12-16)
Oceanography (ages 12-16)

NATURE STUDY COURSES

Children of Ages 6 to 16

The Laboratory gratefully acknowledges the eleventh year contribution of the Huntington Federal Savings and Loan Association. This provided nature study scholarships for 12 students of the Huntington elementary schools.

INSTRUCTORS:

Mr. Otto A. Heck, M.S., Assistant Professor of Biology at Trenton State College, Trenton, N.J.
Miss Leslie Cattrall, a college freshman & former student & assistant at the Children's Nature Study Program, Cold Spring Harbor, N.Y.
Mrs. Barbara Church, M.Ed., Science Substitute Teacher at Central High School, Dist. #3, N.Y.
Miss Virginia Jones, M.S., Graduate Student in Nature and Conservation Education, Michigan State University.

Mr. Alex Pepe, M.A., Science Teacher, K-6, East Side School, Cold Spring Harbor, N.Y.
Mr. Richard L. Rosenman, M.A., Chemistry and Biology Teacher, Cold Spring Harbor High School.
Mr. Thomas Stock, M.Ed., Science Teacher, Selden Junior High School, Centereach, N.Y.

NATURE STUDY WORKSHOP FOR TEACHERS

The 15th annual Workshop in Nature Study was offered from June 26th to July 24, 1970. This program was 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 those aspects of the environment which affect these organisms. The course consisted of field trips to ponds, streams, seashore, woodlands, field and other natural habitats, for purposes of collecting specimens and first-hand study, with indoor laboratory worktime divided between lectures and practical work. The experiences of the course were designed to help teachers in their classroom science activities.

Twenty-four teachers attended the Workshop. Upon satisfactory completion of the requirements of the course, teachers were entitled to four points of in-service credit authorized by the New York State Education Department, Division of Higher Education. The instructors for the summer of 1970 were Mr. Otto A. Heck and Miss Virginia Jones.

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FINANCIAL REPORT

Years Ending April 30, 1970 and April 30, 1969

BALANCE SHEET

ASSETS

	April 30, 1970	April 30, 1969
Current Funds:		
General		
Cash	$ 13,019.61	$ 16,734.83
Due from Restricted Fund	221,263.81	–0–
Investments in Government		
Obligation at Cost	57,370.24	70,231.48
Accounts Receivable (net of Reserve)	87,477.73	55,362.51
Inventory of Books (net of Reserve)	62,458.21	63,674.87
Prepaid Expenses	3,003.40	4,589.76
Total General	$ 444,593.00	$ 210,593.45
Restricted:		
Cash and Grants Receivable	$1,717,415.10	$1,403,514.26
Total Current Funds	$2,162,008.10	$1,614,107.71
Plant Funds:		
Unexpended:		
Cash	$ –0–	$ 7,281.48
Invested in Government		
Obligations at Cost	167,075.46	39,758.24
Investment in Plant	681,940.94	567,668.71
	$3,011,024.50	$2,228,816.14

LIABILITIES & FUND BALANCES

Current Funds:		
General		
Accounts Payable and Accrued Expenses	$ 241,129.38	$ 42,641.32
Deferred Income	14,529.52	5,737.50
Fund Balance		
Appropriated for Scientific Salaries	–0–	17,403.61
Unappropriated	188,934.10	144,811.02
Total General	$ 444,593.00	$ 210,593.45
Restricted:		
Due to General Fund	$ 221,263.81	$ $–0–
Fund Balance	1,496,151.29	1,403,514.26
	$1,717,415.10	$1,403,514.26
Total Current Funds	$2,162,008.10	$1,614,107.71
Plant Funds:		
Unexpended:	$ 167,075.46	$ 47,039.72
Invested In Plant	681,940.94	567,668.71
	$3,011,024.50	$2,228,816.14

STATEMENT OF CURRENT INCOME

Years Ending April 30, 1970 and April 30, 1969

	April 30, 1970	April 30, 1969
Income:		
Restricted Grants	$ 832,921.68	$ 191,206.61
Indirect Cost Allowance on Grants	104,476.53	26,630.59
Contributions	121,888.18	123,927.00
Symposium Registration Fees	15,100.00	14,759.50
Summer Programs	53,933.37	33,765.00
Laboratory Rentals	1,500.00	2,500.00
Investment Income	7,425.81	4,139.78
Other Sources	8,427.68	1,804.09
Auxiliary Enterprises:		
Book & Abstract Sales	159,974.45	143,376.25
Dining Hall	51,302.74	47,823.51
Rooms and Apartments	50,914.76	43,302.66
Total Income	$1,407,865.20	$ 633,234.99
Expenditures:		
Research and Education Programs	$ 815,384.15	$ 183,523.62
Annual Symposium	42,895.84	30,169.29
Library	12,959.82	11,182.84
Operation & Maintenance of Plant	178,873.91	158,271.16
General & Administration	128,740.78	104,310.98
Scholarships	2,550.00	250.00
Auxiliary Enterprises:		
Books and Abstracts	100,427.55	59,898.28
Dining Hall	57,298.11	40,845.05
Rooms and Apartments	17,331.39	13,370.71
Total Expenditures	$1,356,461.55	$ 601,821.93
Excess of Income over Expenditures	$ 51,403.65	$ 31,413.06
Deduct: Transfers for Capital Improvements	−24,684.18	−17,502.78
	$ 26,719.47	$ 13,910.28

STATEMENT OF CONTRIBUTIONS RESTRICTED TO:

Capital Improvements:	
Osterhout	$ 1,650.00
Summer Dormitories	40,073.00
James Laboratory Office	171,643.00
	$213,366.00

GRANTS

May 1, 1969 to April 30, 1970

Grantor	*Investigator or Program*	*Total Award*	*Grant Number*	*Duration of Grant*
NEW GRANTS:				
Research Grants				
National Science Foundation	Dr. Zipser	$ 91,200	GB-20714	3/1/70-2/28/72
National Institutes of Health	Dr. Zipser	138,000	GM-17612-01	1/1/70-12/31/73
American Cancer Society	Dr. Sambrook	60,000	E-615	7/1/70-6/30/72
Research Corporation	Dr. Zipser	9,835	BH-463	7/29/70-open
National Science Foundation	Dr. Cairns	75,000	GB-24796	9/15/70-9/15/72
Salary Support Grants				
National Institutes of Health	Dr. Zipser	90,000	GM-10773-01	5/1/70-4/30/75
Leukemia Society of America	Dr. Westphal	100,000	none	7/1/70-6/30/75
Symposium Grants				
National Science Foundation	Phage Lambda Meeting	6,000	GB-21221	4/15/70-4/14/71
National Institutes of Health	Symposium Support	69,300	GA-02809-15	4/1/70-3/31/74
Atomic Energy Commission	Symposium Support	7,000	AT-49-7-3047	6/4/70-6/11/70
National Science Foundation	Symposium Support	5,000	GB-19122	5/1/70-4/30/71
CONTINUING GRANTS:				
Research Grants				
National Science Foundation	Dr. Cairns Phycomycees	20,000	GB-6114	3/15/67-10/1/71
National Science Foundation	Dr. Gesteland	138,900	GB-7209X1	12/1/67-2/28/71
National Institutes of Health	Dr. Gesteland Electron Microscope	126,954	GM-16093-02	1/1/69-12/31/72
National Institutes of Health	Dr. Watson Tumor Virus	1,600,000	CA-11432-02	5/1/69-4/30/74
Cystic Fibrosis Foundation	Dr. Watson	50,000	none	9/1/69-6/31/71
Salary Support Grants				
American Cancer Society	Dr. Cairns	581,352	PRP-37	1/1/69-life
National Institutes of Health	Dr. Gesteland	80,000	GM-18029-02	1/1/69-12/31/73
Training Grants				
National Institutes of Health	Dr. Watson	391,925	GM-00890-14	1/1/70-12/31/74
National Institutes of Health	Undergraduate Research	16,030	GB-7603	1/1/70-10/31/70

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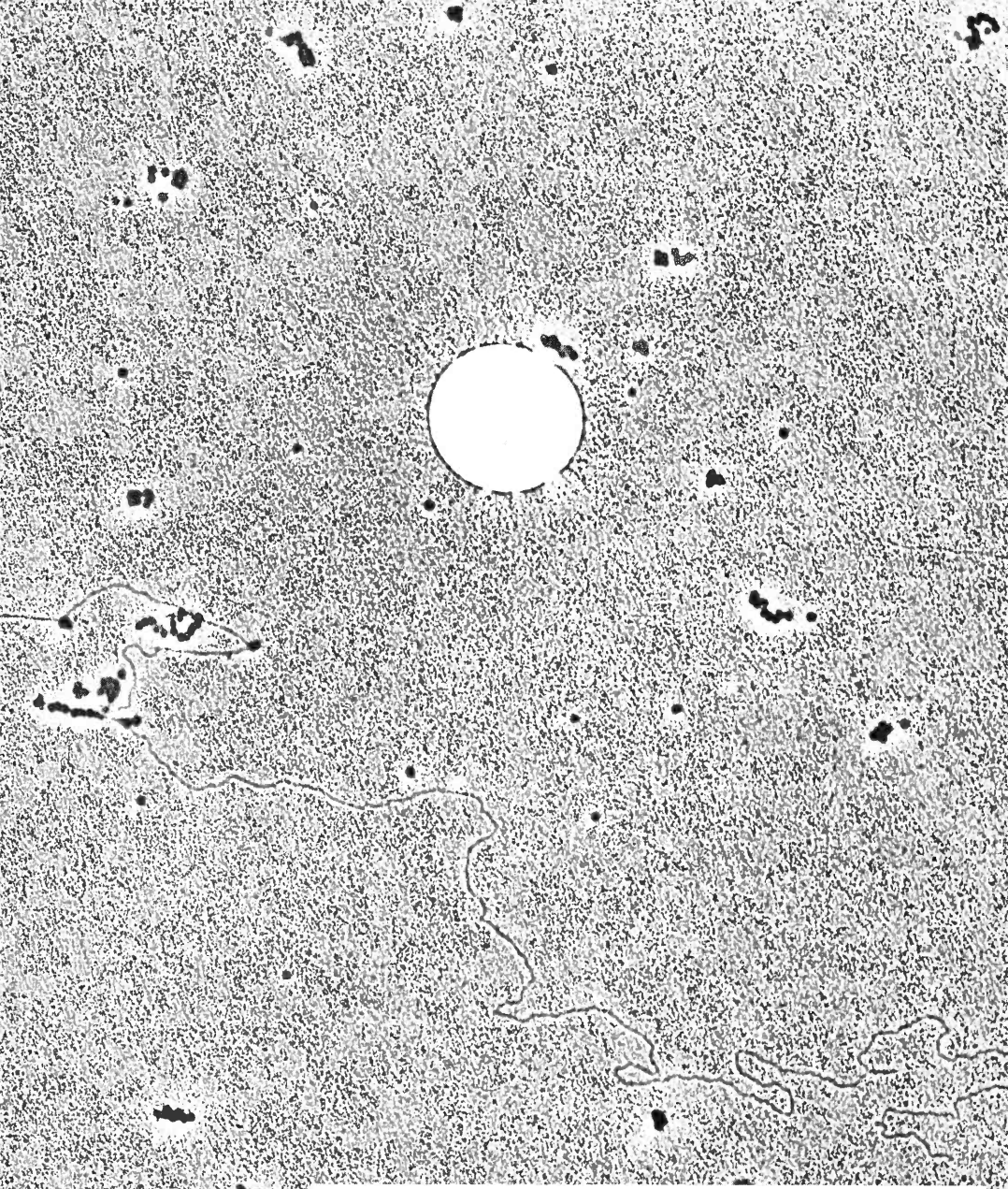

λ DNA with polysomes isolated from a sucrose gradient and spread by Kleinschmidt technique.

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