COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY

VOLUME XXVII

Basic Mechanisms in Animal Virus Biology

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VOLUME XXVII

COLD SPRING HARBOR SYMPOSIA
ON QUANTITATIVE BIOLOGY

Founded in 1933

by

REGINALD G. HARRIS

Director of the Biological Laboratory

1924 to 1936

The Symposia were organized and managed by Dr. Harris until his death. Their continued usefulness is a tribute to the soundness of his vision.

The Symposium Volumes
are published by the Long Island Biological Association
as a part of the work of the Biological Laboratory
Cold Spring Harbor, L.I., New York

FOREWORD

Viruses as agents of disease have elicited extensive research activity for many years. In recent years, there has been vigorous growth of interest in the basic biology of animal viruses. Utilizing the tools and methodology of modern molecular biology, such investigative approach promises to contribute much to our understanding of basic mechanisms in normal biological systems as well as in virus-infected systems.

The program, this year, was organized by Renato Dulbecco, with the assistance of John Cairns, George Hirst, André Lwoff, Harry Rubin, and Michael Stoker. Chairmen of the various sessions were: R. Williams, H. Ginsberg, S. Cohen, J. S. Colter, F. Fenner, K. Sanders, H. Koprowski, W. Schlesinger, R. E. Shope, W. B. Bryan, G. Hirst, and H. Rubin. To all of these gentlemen, I wish to express our gratitude for their generous and thoughtful advice and assistance.

There were a few departures from the program this year, and some last-minute additions. At a special session of the Symposium, Drs. Lwoff, Horne, and Tournier presented "A System of Viruses," an attempt at a general classification of viruses. Drs. Caspar, Dulbecco, Klug, Lwoff, Stoker, Tournier and Wildy collaborated on a short paper entitled "Proposals," an attempt at nomenclature and a schematic on the structure of viruses. Another addition to the volume is the paper by Dr. P. Marcus. Finally, it had been hoped that Dr. L. Zilber of the Gamaleya Institute of Moscow would be able to participate in the meetings. Although other commitments made it impossible for him to attend, his paper is included in the volume.

The meetings this year were held from June 7th to June 13th and were attended by approximately 220 virologists and workers in allied areas of research. Our editor was assisted in the preparation of the volume by Marge Sundgaard.

In addition to the support of the Long Island Biological Association, I am pleased to acknowledge the support of this program by the National Institutes of Health, U.S. Public Health Service, The Rockefeller Foundation, The National Science Foundation, The United States Atomic Energy Commission, and The United States Air Force under Grant AF-AFOSR-62-276; monitored by the Air Force Office of Scientific Research of the Air Research and Development Command.

Arthur Chovnick,
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Editor: Leonora Frisch

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(Photographs by N. Messik and Dr. G. K. Hirst.)

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Physical Principles in the Construction of Regular Viruses

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THE FUNCTIONAL ORGANIZATION OF VIRUS PARTICLES

There are two key facts about viruses from which all consideration of their structure and functional organization must proceed. The first is that the essential infective agent of all viruses is a high molecular weight nucleic acid component—either deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). Second, the nucleic acid molecule is contained in a protective package which serves to transmit this infectious agent in a functionally intact state through space and time to a susceptible host.

The virus nucleic acid has the capacity of redirecting the synthetic machinery of its host cell to the production of more virus. It is becoming increasingly clear that this control over the cell metabolism can be exerted at a number of different stages of normal biosynthesis. The DNA of large bacteriophages, for example, may pertinently be regarded as a transmissible piece of bacterial chromosome (Luria, 1959). In contrast, the RNA of tobacco mosaic virus and presumably of other RNA viruses, appears to be homologous to the normal messenger RNA of the cell (Matthaei et al., 1962). Indeed, the ultimate classification of many viruses may be primarily in terms of their relation to normal cell constituents.

It is not merely a matter of labeling viruses as DNA- or RNA-containing, but also of distinguishing them in terms of the amount of information carried by the nucleic acid. A complex DNA virus may be able to direct the synthesis of many new enzymes, as well as its own structure protein, whereas a simpler DNA virus may be able to specify only a small number of proteins. On the assumption of a universal coding ratio (Crick, Barnett, Brenner, and Watts-Tobin, 1961) between nucleic acid and protein, the amount of information transmitted by a virus would depend on the size of its nucleic acid moiety. Large DNA viruses contain several hundred times as much nucleic acid as the very small DNA and RNA viruses. The RNA of a small bacterial virus (Loeb and Zinder, 1961) consists of only about 1,600 nucleotides (molecular weight 500,000) which, if the coding ratio is 3:1, could specify at most only two or three different protein molecules. The comparably small tobacco necrosis virus particles (Kassanis and Nixon, 1960, 1961) do not appear to carry complete enough information for their own multiplication, and can only reproduce in association with another, larger tobacco necrosis virus. The molecular weight of the DNA content of vaccinia (Smadel and Hoagland, 1942) and *Tipula* iridescent virus (Thomas, 1961) are both about 150×10^6, which is considerably greater than the DNA content of the small living cells of pleuro-pneumonia-like organisms (PPLO) (Morowitz et al., 1962).

The infectivity of a virus must persist in a latent state outside the host cell. Isolated nucleic acid molecules are very labile, particularly in an intercellular environment containing nucleases. If the virus is to succeed in propagating itself, its nucleic acid must be contained in a protective package. This is achieved by the provision of a protein coat or framework which contains the nucleic acid. It may appear, at first sight, that there is an enormous variety in the ways in which this could be done, judging, for instance, only by the range of morphological variation found in viruses. On the contrary, it is the main thesis of this paper that this is not so. The important point is that there are only a limited number of efficient designs possible for a biological container which can be constructed from a large number of identical protein molecules (Caspar and Klug, 1963). The two basic designs are helical tubes and icosahedral shells. For this reason, the same kind of molecular architecture may turn up in RNA or DNA viruses infecting animals, plants, and bacteria.

The structure of biologically completely unrelated viruses—for example, poliovirus and turnip yellow mosaic virus—may be based on very similar designs. Thus, the use of morphology or symmetry as a basis for classifying biological interrelationship must be regarded with caution. Although it is quite likely that closely related viruses will be morphologically similar, the converse is not true. A firmer basis for classification of biological relationship between viruses might be based on the more peripheral aspects of their structure (cf.