Preface

This volume presents what may well be the most impressive achievements of macromolecular analysis by X-ray diffraction methods, the structures of the viruses. Represented here are examples of icosahedral or spherical plant viruses, helical plant viruses, filamentous phages, and initial investigations of the more complex icosahedral animal viruses. In addition to studies of the intact viruses, two examples are included of high resolution analyses of the structures of proteins found on the surfaces of an adenovirus and the influenza virus. These lend significant new insights into the architectural principles involved in the design and assembly of viral particles and interactions with their hosts. The investigations described here establish a sound structural basis for interpretation of the vast accumulation of data involving viruses from other sources of biochemical, physical, and physiological research. They provide the most convincing confirmation of now widely accepted virus structure theory but at the same time make evident the likelihood that these principles will see substantial alteration and refinement as larger and more complex structures become available. A not insignificant feature of these achievements is that they serve as inspiring testament to the perseverance and ingenuity of diffractionists working at the leading edge of their science with success never assured, methods marginally adequate to the task, and specimens possessing the most complex and elusive properties.

Chapter 1 is an overview of the chemical and physical properties of the spherical plant viruses and their implications for general virus structure. As such, it establishes conditions and standards by which the structure analyses must be measured. Chapters 2 and 3 focus on two small icosahedral plant viruses whose structures have now been determined in near atomic detail, southern bean mosaic virus and satellite tobacco ne-

crosis virus. These two structures, along with that of tomato bushy stunt virus, elegantly illustrate the principles of virus construction postulated by Caspar and Klug but at the same time suggest alternative bonding mechanisms by which the postulated quasi-equivalence might be achieved. Further, they beautifully illustrate the integration of protein structural principles into larger macromolecular assemblies, the economy of structure and function, and the consistency of design.

Tobacco mosaic virus, described in Chapters 4 and 5, represents a different class entirely, the viruses constructed according to precise helical symmetry. The structure of tobacco mosaic virus, the most exhaustively studied of all the viruses, illustrates the means by which small, identical protein subunits of relatively uncomplicated structure have encoded within their three-dimensional array of amino acids, the ability to recognize and bind their genomic nucleic acid, to order and protect it, and to organize themselves into a complete viral assembly with new and sophisticated properties.

In Chapter 6, the traditional crystallographic technique of isomorphous replacement is by necessity abandoned in the study of the filamentous bacteriophages. Using primarily physical constraints in conjunction with fiber diffraction data, visual images have been achieved that reveal the interaction between small α-helical subunits and the DNA genome at the core of the virus. Unlike the icosahedral and helical viruses, these bacteriophages are designed according to subtly different principles of symmetry and nonequivalence of interaction. They suggest that there may exist many variations or entirely new patterns of self-assembly in viruses.

Chapter 7 describes the low resolution analysis of an animal virus, the polyoma virus. Unexpectedly—perhaps because it so faithfully assumed the principles of Casper and Klug regarding icosahedral symmetry—the results of this study have suggested the most radical departure from those principles. Once again, the methodology was somewhat unorthodox in that it did not employ isomorphous replacement; nevertheless, it appears valid by current criteria. If the results are confirmed by other investigations or by higher resolution analyses of the polyoma virus itself, they will certainly require a reconsideration of our expectations for capsid structure and assembly in the $T = 7$ and larger virus particles.

Chapters 8 and 9 are elegant and impressive examples of traditional isomorphous replacement methods coupled with the clever application of molecular replacement and symmetry constraints. The structures emerg-

ing from these investigations, the capsid protein hexon from adenovirus and the influenza virus hemagglutinin, are striking in the manner by which recognized protein secondary structural patterns are extended and reorganized to produce unusual and unique protein molecules. These are molecules that not only contribute to our understanding of general protein structure but bring to light new principles and mechanisms for macromolecular interaction, assembly, and physiological activity.

The nine chapters presented here illustrate and describe in a reasonably comprehensive fashion what is currently known of virus structure at the atomic and near atomic level. The structures were derived principally by X-ray diffraction and the perspectives primarily are those of scientists versed in that technique. This should in no way be interpreted as ignoring the extensive achievements resulting from the many other methods that have been applied to virus structure analysis. Indeed, it should be noted that immediately following or closely entwined with the description of any structure is the correlation or rationalization of each feature in terms of benchmarks derived from biochemical and physical analyses. Perhaps the crystallographers may here repay their debt to the scientific community at large by suggesting new approaches and new experiments and at the same time provide a structural basis for their design and interpretation.

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