Preface

The modern study of the membranes of cells from a biochemical and structural point of view is only about four decades old. The first phase was the age of lipids, commencing with definitive evidence for the lipid bilayer as the fundamental structural element of all biological membranes. In the decades of the 1970s and 1980s, an explosion of data burst forth on the fascinating properties of lipid bilayers, along with enormous speculation on the potential roles in biology for the variety of physical behaviors that had been observed. Much was discovered about this two-dimensional, highly anisotropic world that resembles no other biological structure.

Partly because of the lack of adequate analogy, the lipid bilayer was, and is today, widely misunderstood, which forms part of the rationale for the preparation of this book. Some of what was learned in that first age of lipid studies is not part of the current view on membrane structure. We would do well to review such studies, to rediscover the unique properties of the lipid bilayer that must inform our contemporary interpretation of membrane structure and function. For that reason, much fundamental lipid lore is included in this volume, most of it updated, but all of it critical to an adequate understanding of this most fundamental of biological structures.

This understanding begins with lipid structure (Chapter 1), which determines the chemistry and the thermodynamics of the collision of lipid properties with water properties. Biological lipids, because they are not soluble in water, form separate phases with behaviors directly relevant to biological function and interesting phases that are not yet related to biological function (Chapter 2, Chapter 3, and Chapter 5). Understanding this phase behavior would obviate the too common treatment of membranes as analogous to soluble components in an experimental system and help the student to appreciate that the biological membrane is one of the largest biological structures that is held together by *non*covalent forces. The multiple phase behavior of lipid bilayers is also critical to a correct understanding of "rafts," as described in Chapter 9. Chapter 4 takes us inside the lipid bilayer to explore the highly anisotropic structure and dynamics of this system. We come away with a view that the interior of a membrane is quite unlike liquid hydrocarbon, to which it has been compared, and that recourse to such inappropriate models will lead to incorrect conclusions. Chapter 6 explores the interaction between membranes at their surfaces, an interaction critical to a variety of cellular phenomena, including nonlamellar lipid phases (Chapter 5), lipid fusion (Chapter 8), and viral fusion (Chapter 16). Cholesterol has long fascinated those who study biological membranes, initially because of the interesting physical chemical phenomena exhibited by cholesterol in a bilayer, and subsequently because of the varied roles cholesterol plays in membrane function. Chapter 7 attempts to synthesize all the kinds of data on cholesterol generated over the past several decades into a unified view of several distinct functions of this molecule. One of the important functions exhibited by cell membranes is membrane fusion. Membrane lipids clearly have a role to play in this phenomenon, and much has been learned from studies on lipid fusion systems, as described in Chapter 8. This section of the book ends with a look at a topic of intense interest at the time this book is being prepared: lipid rafts (Chapter 9). Understanding this model for nonuniform lipid behavior in the plasma membrane requires virtually all the material in the previous chapters and thus is an appropriate way to close Part I.

Part II takes us into the other major component of biological membranes: membrane proteins. The study of membrane proteins has lagged seriously behind both the study of the lipid components of membranes and the study of soluble protein structure and function. This is partly a result of the historical difficulty researchers have experienced in obtaining crystals of membrane proteins suitable for X-ray diffraction experiments. As a result, membrane protein studies have in the past focused more on function than on structure. Thus, much of this section is devoted to function, in particular transport (Chapter 10 through Chapter 13). Because membranes of cells form barriers to transport, separating organelles from the cytoplasm and the cytoplasm from the exterior of the cell, movement of specific materials across membranes requires specific transport systems. Much progress has been made, which has been enhanced recently by the solution of a limited number of structures of membrane transport proteins. Chapter 14 shows an example of membrane proteins for which three-dimensional structural information is now available. Although it is not possible in this book to review exhaustively all the structural information on membrane proteins that has been developed, mostly in just the past few years, this chapter will illustrate, with one protein, how the structural information can be obtained and how it can be used to understand function.

In general, membranes are the location for linking of three functions: lipid–lipid, lipid–protein, and protein–protein interactions. These three sets of interactions are not independent; perturbation in one will affect one or both of the others. Therefore the study of lipid–protein interactions has attracted great interest over the years. Chapter 15 brings together the protein and lipid components to see how one affects the other. Finally, in the chapter on viral fusion, the influence of proteins on the mixing of membrane components, initially lipid, can lead to the fusion of two membranes into one.

This series of topics offers the student of membrane structure and function in-depth insight into a number of the topics necessary to appreciate fully biological membranes in today's research climate. With the development of new structural information on membrane proteins, we can expect a new burst of research activity and understanding in the first part of this new millennium.

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