MEMBRANE STRUCTURAL BIOLOGY

Membrane Structural Biology provides a solid background in membrane biochemistry that also incorporates the approaches of biophysics, genetics, and cell biology to investigations of membrane structure, function, and genesis. It describes the many tools of current membrane research, including detergents and model systems, bioinformatics, protein-folding methodology, crystallography and diffraction, and molecular modeling. The beautifully detailed structures of membrane components are presented in the context of the classes of families of molecules they represent. Many correlations between membrane research and human health are discussed, and key themes for future work in membrane structural biology are identified.

Written with remarkable clarity, this book appears at a time when membranes have moved back into the scientific spotlight and provides a unique foundation for advanced students and working scientists. The new high-resolution structures of membrane proteins generate exciting insights into how they function. The prediction that up to a third of the proteins encoded in the genome are membrane proteins has spurred the development of high-throughput tools for their structural analysis, as well as powerful computational approaches for proteomics and modeling. Research in membrane structural biology is poised to answer many basic and applied questions, and this cutting-edge text will provide a solid foundation for all those working in this field.

Mary Luckey is a professor in the Department of Chemistry and Biochemistry at San Francisco State University. She earned her Ph.D. in Biochemistry at University of California Berkeley with the first identification of an iron transport protein in the bacterial outer membrane. Her postdoctoral work demonstrated the specificity of the *E. coli* maltoporin in proteoliposomes. While continuing research on maltoporin structure and function, she has taught biochemistry for 25 years, including the graduate-level membrane biochemistry course that provided the impetus for this book.

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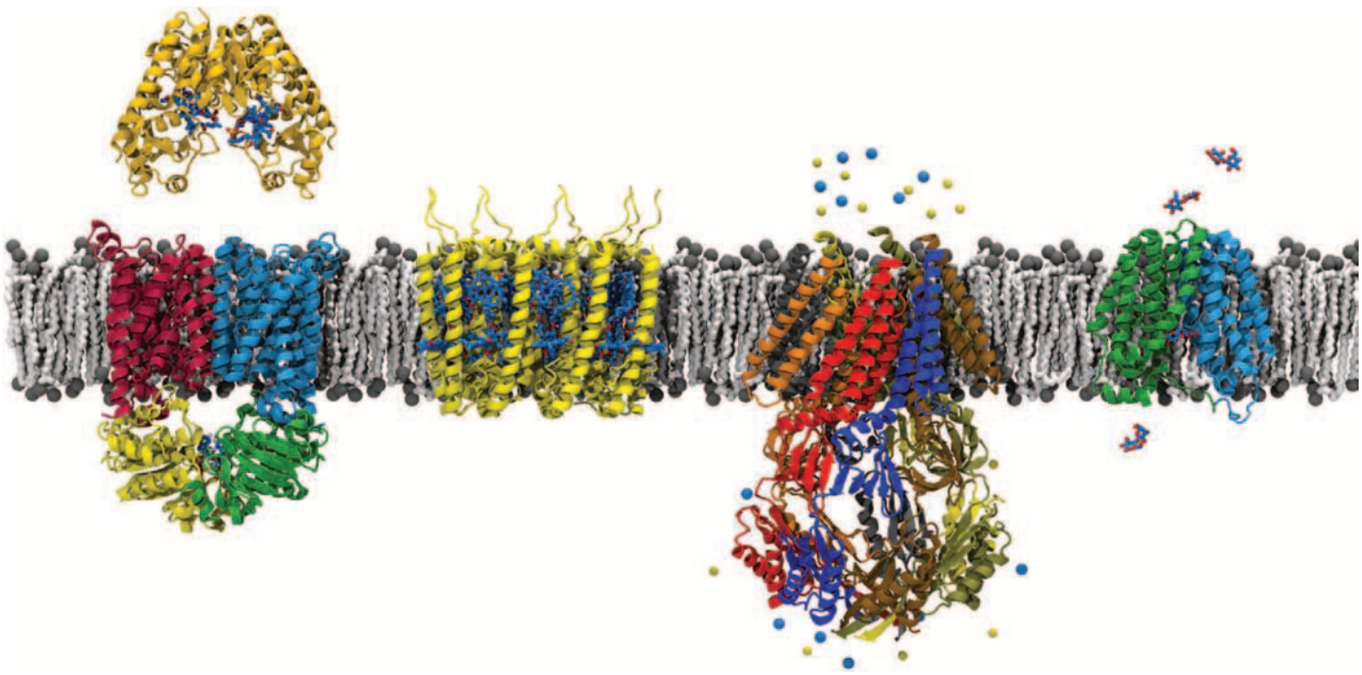

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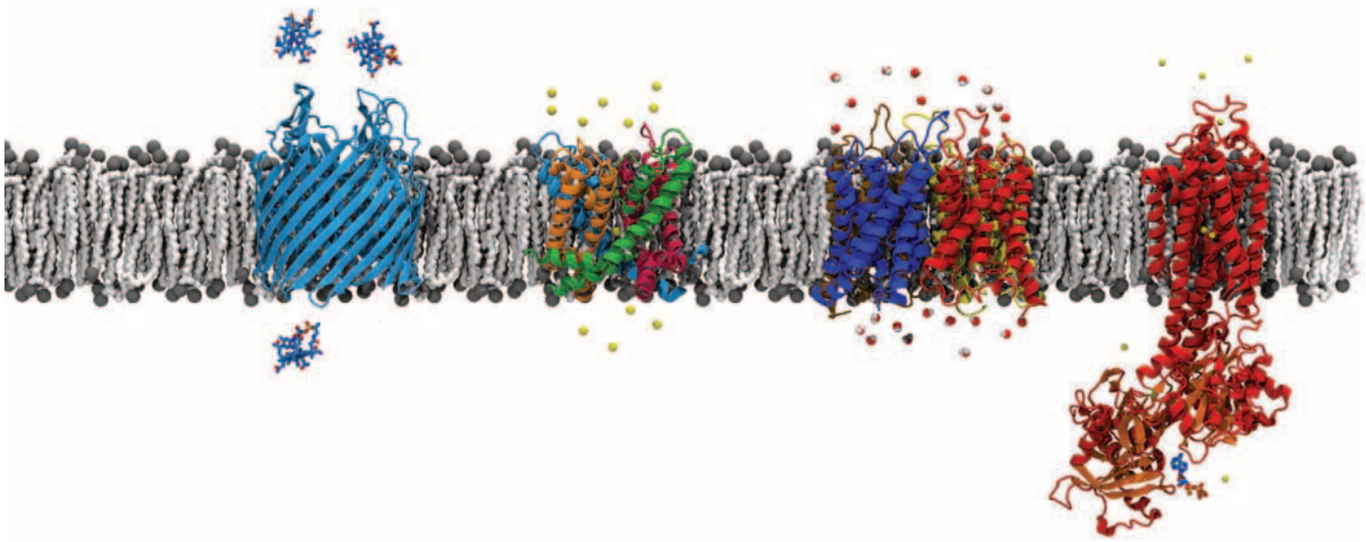

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The title page shows high-resolution structures of membrane proteins incorporated into a simulated lipid bilayer. The proteins are, from left to right: vitamin B_{12} transporters BtuCD with BtuF, the light harvester LH2 with some chlorophylls, the mechanosensitive channel MscS, lactose permease, BtuB from the outer membrane, the pore domain of Kv1.2, aquaporin, and Ca^{2+}-ATPase. Substrates, including ions and water molecules, are indicated.

Kindly provided by J. Gumbart, Y. Wang, A. Aksimentiev, E. Tajkhorshid, and K. Schulten, Theoretical and Computational Biophysics Group at the University of Illinois, Urbana-Champaign.

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Preface

The tremendous progress made over the last decade in our understanding of biomembranes calls for a new gestalt in a book about their structure and function. The need for such a book was apparent as I labored to capture the explosion of information about the structure and organization of biological membranes for my course on membrane biochemistry. Applications of new techniques and whole new methodologies have changed both how we acquire knowledge of the membrane and how we view it. For many years, the difficulties in crystallization of membrane proteins caused a scarcity of structural detail. Now sophisticated diffraction analysis allows description of fluid lipid bilayers, and high-resolution structures have been determined for a variety of membrane proteins. Each new high-resolution structure of a membrane protein that graces a journal cover offers new insights into membrane functions. And yet, a full understanding of each new structure and its lipid environment is built on foundations of membrane biochemistry that derive from basic physical and life sciences.

This book combines a physicochemical analysis of the membrane milieu with the latest structural biology on membrane lipids and proteins to give an exciting portrayal of biomembranes. The book's title, *Membrane Structural Biology*, emphasizes the successes of structural biology in revealing exciting details of many membrane components. To see the impact of structural biology on biochemistry textbooks, one need only compare a biochemistry book from 25 years ago with a current textbook, in which colorful and detailed molecular structures illustrate the functions of biomolecules and mechanisms of complex biochemical processes. A textbook on membrane biochemistry can only now approach that transformation to molecular detail, drawing from x-ray crystal structures, lipid diffraction and liquid crystallography, and computational modeling.

To cover these advances and their foundations in one comprehensive volume, this book moves from basic membrane biochemistry to detailed examples of membrane structural biology. It includes numerous new topics, such as phase diagrams of lipid raft mixtures, reconstitution using bicelles and nanodiscs, binding domains of amphitropic proteins, effects of elasticity on folding of membrane proteins, a biological scale for identification of transmembrane helices, bioinformatics and proteomics of membrane proteins, and joint refinement of x-ray and neutron diffraction data for lipid bilayers. It offers explanations of techniques as varied as statistical methods for prediction of transmembrane sequences, surface effects in binding and kinetics, protein folding studies, liquid crystal theory, and molecular dynamics simulations.

Written at a level appropriate for advanced students and scientists new to the field, *Membrane Structural Biology* assumes a background familiarity with the concepts covered in an undergraduate biochemistry course. Although it includes a wide range of material in a broad and rapidly moving field, the book is not encyclopedic. Nor does it provide the thousands of references to the scientific papers on which it is based. That literature is vast, but fortunately it is readily accessible with the search engines now available. Readers who want to learn more can get started with the key references to seminal papers and reviews provided for each chapter. They can study the papers cited in the figure captions and can easily search for other contributions from those authors. A thorough familiarity with the examples described in the book will provide the reader with a solid foundation for further studies, including the exploration of other important topics, such as membrane fusion, chemotaxis, endocytosis, and membrane recycling.

It is a challenge to cover the full scope of this burgeoning field, including new methodologies and latest developments. Though it is my hope that the number of typographical and/or factual errors in this text will be small, I welcome the readers of this first edition to send me their corrections so that they may be incorporated into the next edition.

I want to acknowledge assistance when I started writing the book from my student, Aram Krauson, along with early feedback I received from Professor Jurg Rosenbusch. For their comments on specific topics I thank Professors Scott Feller, Steve White, Sam Hess, Rosemary Cornell, Ehud Landau, David Hackney, Paula Booth, Bill Plachy, and Hiroshi Nikaido. I am especially grateful to those who reviewed the entire manuscript: Professors Lin Randall and Stanley Parsons, and former students Shyam Basharam, Marla Melnick, and Jared Matt Greenberg. I thank Andréa Dosé for library help, J. C. Gumbart for the model membrane figures and graphic artist Diane Fenster of SFSU for the design of the publicity postcard, which led to the cover design. I appreciate how diligently Mary Paden and her staff worked on the production. For her unflagging enthusiasm and wise editorial help, I thank Dr. Katrina Halliday. Thanks as well to my colleagues and friends who supported my progress writing the book. Finally, I deeply appreciate the patience and encouragement I received from my family, Paul, Ariel, Amanda, SAM, and Ryan.

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