# MEMBRANE STRUCTURAL BIOLOGY

## WITH BIOCHEMICAL AND BIOPHYSICAL FOUNDATIONS

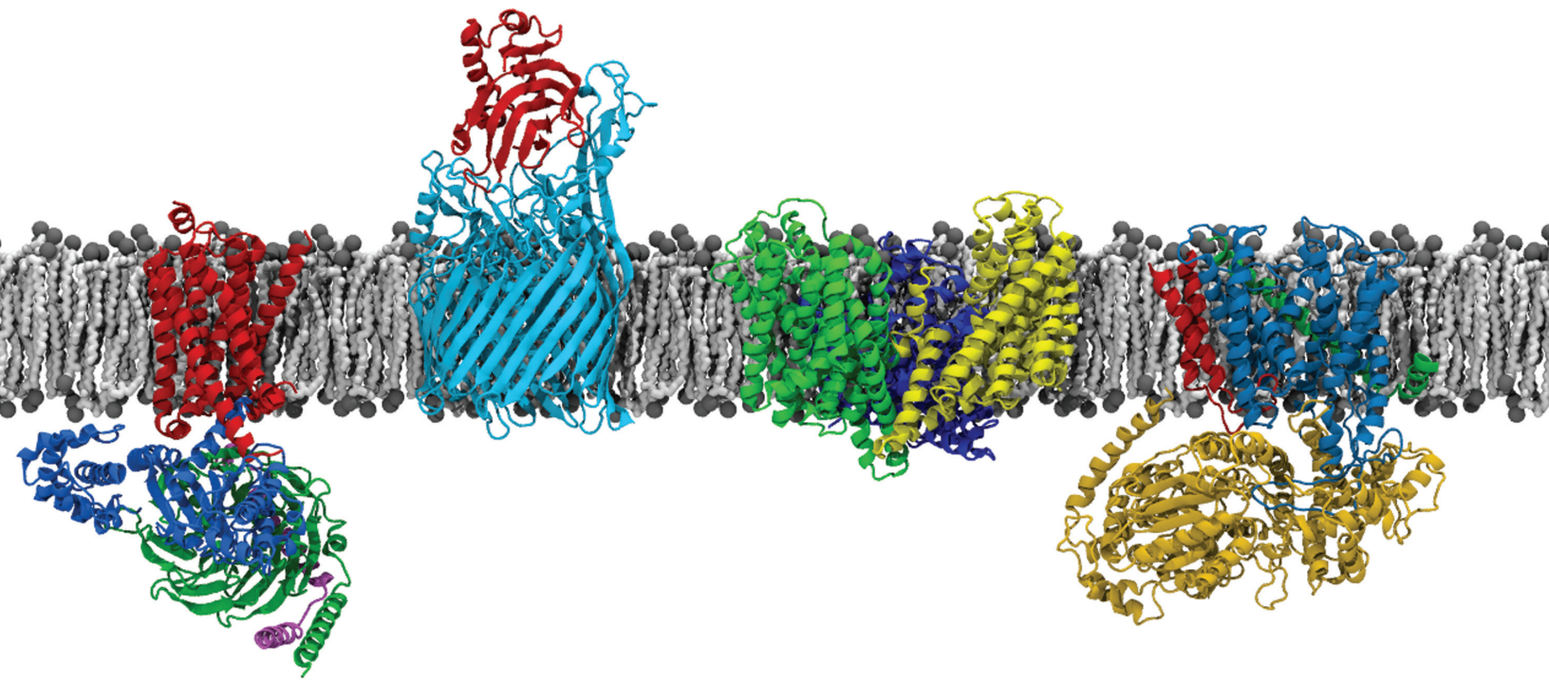
**Second Edition**

This textbook provides a strong foundation and a clear overview for students of membrane biology and an invaluable synthesis of cutting-edge research for working scientists. The text retains its clear and engaging style, providing a solid background in membrane biochemistry, while also incorporating the approaches of biophysics, genetics, and cell biology to investigations of membrane structure, function, and biogenesis to provide a unique overview of this fast-moving field.

A wealth of new high-resolution structures of membrane proteins are presented, including the $Na^+$-$K^+$ pump and a receptor G protein complex, offering exciting insights into how they function. All key tools of current membrane research are described, including detergents and model systems, bioinformatics, protein-folding methodology, crystallography and diffraction, EPR and NMR spectroscopy, and molecular modeling.

This comprehensive and up-to-date text, emphasizing the correlations between membrane research and human health, provides a solid foundation for all those working in this field.

**Mary Luckey** is Professor Emerita in the Department of Chemistry and Biochemistry at San Francisco State University. She earned her Ph.D. in Biochemistry at the 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 over 25 years, including the graduate-level membrane biochemistry course that provided the impetus for this book.



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MARY LUCKEY

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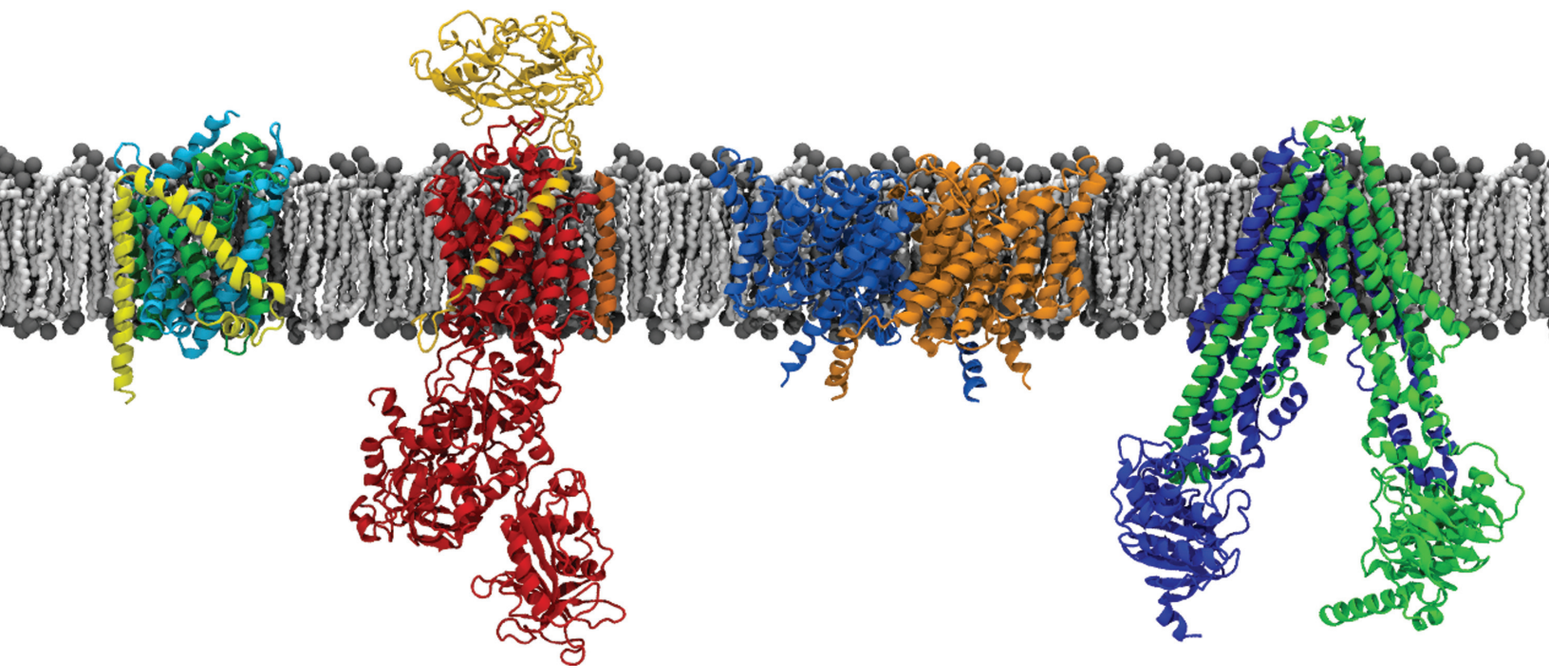

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Cover image:

The title page shows high-resolution structures of membrane proteins incorporated into a simulated lipid bilayer. The proteins are, from left to right, $\beta$2A in complex with an agonist and a trimeric G-protein, the heme receptor HasR in complex with the heme-binding protein HasA, the trimeric aspartate transporter GltPh that is a homolog for neurotransmitter transporters, the SecYEG translocon in complex with the energizing subunit SecA, the amino acid transporter LeuT that is another homolog for neurotransmitter transporters, the $Na^+$, $K^+$ ATPase, the dimeric chloride transporter ClC, and P-glycoprotein, a dimeric transporter that extrudes drugs.

Kindly provided by J. C. Gumbart, Georgia Institute of Technology, and E. Tajkhorshid, University of Illinois.

In memory of Amy L. Davidson, 1958–2013, insightful scientist,
meticulous experimentalist, gracious colleague, and good friend.

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# LIST OF BOXES

# PREFACE

The first edition of *Membrane Structural Biology* met a need for a comprehensive presentation of the explosion of information about the structure and organization of biological membranes. It also acknowledged how new techniques and whole new methodologies had changed both how we acquired knowledge of the membrane and how we viewed it. With a foundation derived from basic physical and life sciences, advances in structural biology were depicted through the molecular details of membrane components provided by sophisticated diffraction analysis of fluid lipid bilayers and by high-resolution structures of a variety of membrane proteins. As the book moved from basic membrane biochemistry to detailed examples, it covered a wide range of material at a level appropriate for both students and scientists in the field. I am gratified with the responses from membrane scientists all over the world.

This new edition has been expanded to include over 20 additional membrane proteins visualized in atomic detail. Discovery of superfamilies based on the protein folds shows relationships among membrane proteins, while capture of multiple states begins to disclose mechanisms. Some new topics have been introduced, other topics updated, and yes, sadly, some interesting new findings had to be left out. I hope readers will jump into the literature from the key references provided to learn about the exciting new findings, to study these topics in more detail, and to tackle the larger and more complex systems at the frontiers of membrane research.

While I am responsible for the omissions and any errors, I am indebted to many people who have been generous with their time, reviewing new parts of this edition, as well as those who did so for the first edition. I was assisted when I started writing the book by my former students, Dr. Aram Krauson and Dr. Andréa Dosé. For their comments on specific topics in the first edition I thank Professors Scott Feller, Steve White, Sam Hess, Rosemary Cornell, Ehud Landau, David Hackney, Paula Booth, Bill Plachy, and Hiroshi Nikaido. For comments on new sections of the second edition I thank Poul Nissen, Maike Bublitz, Satinder Singh, Merritt Maduke, Brian Kobilke, Chuck Sanders, Jörg Standfuss, Bill Cramer, Reinhard Krämer, Christine Ziegler, Shelagh Ferguson-Miller, and Eduardo Perozo. I am especially grateful to those who reviewed the entire original manuscript: Professors Lin Randall and Stanley Parsons, and my former students Shyam Bhaskaran, Marla Melnick, and Jared Matt Greenberg. Lin Randall and my former student Chris Chin also read all the new chapters for the second edition.

With much appreciation I thank Professors J. C. Gumbart and Emad Tajkhorshid for the cover figures. In addition I want to thank the many individual scientists who shared their figures of beautiful membrane protein structures, particularly those who prepared figures for this edition: Shelagh Ferguson-Miller, Rosemary Comell, Krzyszt of Palzewski, and Tivadar Orban. 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 affection and encouragement I received from my family, Ariel, SAM, Ryan, donna, Kesa, Amanda, and Dana, with profound gratitude for steadfast love, patience, and support from my husband Paul.

Mary Luckey