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.
STRUCTURAL BIOLOGY
WITH BIOCHEMICAL AND BIOPHYSICAL FOUNDATIONS

MARY LUCKEY
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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 B₁₂ 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 Ca²⁺-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.
# Contents in Brief

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preface</td>
<td>xi</td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>The Diversity of Membrane Lipids</td>
<td>13</td>
</tr>
<tr>
<td>Tools for Studying Membrane Components:</td>
<td>42</td>
</tr>
<tr>
<td>Detergents and Model Systems</td>
<td></td>
</tr>
<tr>
<td>Proteins in or at the Bilayer</td>
<td>68</td>
</tr>
<tr>
<td>Bundles and Barrels</td>
<td>102</td>
</tr>
<tr>
<td>Functions and Families</td>
<td>127</td>
</tr>
<tr>
<td>Protein Folding and Biogenesis</td>
<td>160</td>
</tr>
<tr>
<td>Diffraction and Simulation</td>
<td>191</td>
</tr>
<tr>
<td>Membrane Enzymes and Transducers</td>
<td>213</td>
</tr>
<tr>
<td>Transporters and Channels</td>
<td>241</td>
</tr>
<tr>
<td>Membrane Protein Assemblies</td>
<td>271</td>
</tr>
<tr>
<td>Themes and Future Directions</td>
<td>309</td>
</tr>
<tr>
<td>Appendix I: Abbreviations</td>
<td>315</td>
</tr>
<tr>
<td>Appendix II: Single-Letter Codes for Amino Acids</td>
<td>318</td>
</tr>
<tr>
<td>Index</td>
<td>319</td>
</tr>
</tbody>
</table>
Contents

Preface page xi

1 Introduction 1
General Features of Membranes 1
Paradigm 1: The Amphiphilic Molecules in Membranes Assemble Spontaneously due to the Hydrophobic Effect 4
Paradigm 2: The Fluid Mosaic Model Describes the Membrane Structure 5
A Shift in the Paradigm: Biomembranes Have Lateral Domains that Form “Rafts” 8
A View for the Future: Dynamic Protein Complexes Crowd the Membrane Interior and Extend Its Borders 9

2 The Diversity of Membrane Lipids 13
The Acyl Chains 13
Complex Lipids 17
Phospholipids 17
Sphingolipids 20
Sterols and Linear Isoprenoids 20
The Lipid Bilayer Matrix 23
Structure of Bilayer Lipids 24
Diffusion of Bilayer Lipids 24
\textit{box} 2.1 Fluorescence techniques 26
Lipid Asymmetry and Membrane Thickness 26
Lipid Polymorphism 28
Lamellar Phase 28
Hexagonal Phase and the Amphiphile Shape Hypothesis 29
Cubic Phase 31
Miscibility of Bilayer Lipids 31
\textit{box} 2.2 Phase diagrams 31
Lateral Domains and Lipid Rafts 33
Detergent-Resistant Membranes 36
Diversity of Lipids 37
\textit{box} 2.3 Nonlamellar phase lipids and growth of \textit{E. coli} 40

3 Tools for Studying Membrane Components: Detergents and Model Systems 42
Detergents 43
Types of Detergents 43
\textit{box} 3.1 Surfactants and surface tension 43
Mechanism of Detergent Action 45
Membrane Solubilization 48
Lipid Removal 50
Model Membranes 50
Monolayers 50
Planar Bilayers 53
\textit{box} 3.2 Electrophysiology 53
Patch Clamps 55
Supported Bilayers 57
Liposomes from SUVs to GUVs 60
Mixed Micelles and Bicelles 63
Blebs and Blisters 63
Nanodiscs 66

4 Proteins in or at the Bilayer 68
Classes of Proteins that Interact with the Membrane 68
Proteins at the Bilayer Surface 69
Extrinsic/Peripheral Membrane Proteins 69
Reversible Interactions of Peripheral Proteins with the Lipid Bilayer 76
\textit{box} 4.1 Binding of ligands to surfaces 79
Proteins and Peptides that Insert into the Membrane 84
Toxins 84
Colicins 85
Peptides 87
SecA: Protein Acrobatics 88
Proteins Embedded in the Membrane 90
Monotopic Proteins 90
Integral Membrane Proteins 90
Protein–Lipid Interactions 94
\textit{box} 4.2 Electron paramagnetic resonance 97
Hydrophobic Mismatch 98
5 Bundles and Barrels

Helical Bundles
- Bacteriorhodopsin 102
- Photosynthetic Reaction Center 107

β-Barrels
- Box 5.1 NMR determination of membrane protein structure 116
- Porins 118
- Specific Porins 120
- Iron Receptors 123

6 Functions and Families

Membrane Enzymes
- Box 6.1 Surface dilution effects 128
- Diacylglycerol Kinase 129
- P450 Cytochromes 130

Transport Proteins
- Transport Classification System 132
- Superfamilies of ATPases 134
- ABC Transporter Superfamily 134
- Group Translocation 135
- Symporters 137
- Antiporters 138
- Ion Channels 138

Membrane Receptors
- Nicotinic Acetylcholine Receptor 139
- G-Protein Coupled Receptors 140

Bioinformatics Tools for Membrane Protein Families
- Predicting TM Segments 141
- Box 6.2 Bioinformatics basics 142
- Hydrophobicity Plots 143
- Orientation of Membrane Proteins 143
- The Positive-Inside Rule 144
- Box 6.3 Making and testing hydrophobicity plots 144
- Genomic Analysis of Membrane Proteins 145
- Box 6.4 Statistical methods for TM prediction 148
- Helix–Helix Interactions 154
- Proteomics of Membrane Proteins 156
- β-Barrels 157

7 Protein Folding and Biogenesis

Protein Folding
- Box 7.1 Energetics of folding and insertion of a hydrophobic α-helix into the bilayer 164
- Folding Studies of β-Barrel Membrane Proteins 167
- Other Folding Studies 169

Biogenesis of Membrane Proteins
- Box 7.2 Evidence for cleavable signal sequences involved in protein translocation 171
- Box 7.3 Import of mitochondrial proteins 177
- Integration of Na+K+Proteins into the Membrane 178
- Box 7.4 Cross-linking traces nascent peptides through the translocon into the bilayer 179
- Topogenisis in Membrane Proteins 184
- Misfolding Diseases 187

8 Diffraction and Simulation

Back to the Bilayer 191
- Liquid Crystallography 192
- Box 8.1 X-ray and neutron scattering 193
- Liquid Crystal Theory 193
- Joint Refinement of X-Ray and Neutron Diffraction Data 194
- Modeling the Bilayer 196
- Simulations of Lipid Bilayers 196
- Molecular Dynamics 197
- Box 8.2 Molecular dynamics calculations 198
- Monte Carlo 202
- Lipids Observed in X-Ray Structures of Membrane Proteins 203
- The Crystallographer's Art 207
- Membrane Simulations 210

9 Membrane Enzymes and Transducers

Enzymes
- OMPLA 214
- Prostaglandin H2 Synthase 216
- Box 9.1 Mechanism of action of prostaglandin H2 synthase 218
- Formate Dehydrogenase 222

Transducers
- Rhodopsin, a GPCR 226
- Box 9.2 Efficiency of light-induced signal transduction 229
- Box 9.3 Numbering TM helices 231
- Mechanosensitive Ion Channels 235

10 Transporters and Channels

Transporters
- LacY and GlpT 241
- Mitochondrial ADP/ATP Carrier 249

Channels
- Aquaporins and Glyceroaquaporins 253
- Potassium Channels 258
- Calcium ATPase 264
## Contents

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td><strong>Membrane Protein Assemblies</strong></td>
<td>271</td>
</tr>
<tr>
<td></td>
<td><strong>F$<em>{1}$F$</em>{0}$-ATPase/ATP Synthase</strong></td>
<td>272</td>
</tr>
<tr>
<td></td>
<td>Subunit Structure and Function</td>
<td>273</td>
</tr>
<tr>
<td></td>
<td>Regulation of the F$<em>{1}$F$</em>{0}$-ATPase</td>
<td>276</td>
</tr>
<tr>
<td></td>
<td>Catalytic Mechanism of a Rotary Motor</td>
<td>277</td>
</tr>
<tr>
<td></td>
<td><strong>Complexes of the Respiratory Chain</strong></td>
<td>279</td>
</tr>
<tr>
<td></td>
<td>Cytochrome b$_{c_1}$</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td>Cytochrome-c Oxidase</td>
<td>284</td>
</tr>
<tr>
<td></td>
<td><strong>The Translocon</strong></td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>The <em>M. jannaschii</em> Translocon</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>Structure</td>
<td>286</td>
</tr>
<tr>
<td></td>
<td>The Translocon–Ribosome Complex</td>
<td>288</td>
</tr>
<tr>
<td></td>
<td><strong>ABC Transporters and Beyond</strong></td>
<td>290</td>
</tr>
<tr>
<td></td>
<td>The Vitamin B$_{12}$ Uptake System</td>
<td>291</td>
</tr>
<tr>
<td></td>
<td>Transport across the Inner Membrane</td>
<td>291</td>
</tr>
<tr>
<td></td>
<td>Transport across the Outer Membrane</td>
<td>294</td>
</tr>
<tr>
<td></td>
<td><strong>Drug Efflux Systems</strong></td>
<td>296</td>
</tr>
<tr>
<td></td>
<td>Sav1866, an ABC Multidrug Transporter</td>
<td>297</td>
</tr>
<tr>
<td></td>
<td>EmrE, Small but Powerful</td>
<td>299</td>
</tr>
<tr>
<td>12</td>
<td><strong>Themes and Future Directions</strong></td>
<td>309</td>
</tr>
<tr>
<td></td>
<td>Tripartite Drug Efflux via a Membrane Vacuum Cleaner</td>
<td>300</td>
</tr>
<tr>
<td></td>
<td>AcrB, a Peristaltic Pump</td>
<td>300</td>
</tr>
<tr>
<td></td>
<td>AcrA, a Membrane Fusion Protein</td>
<td>302</td>
</tr>
<tr>
<td></td>
<td>TolC, the Channel-Tunnel</td>
<td>304</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix I: Abbreviations</strong></td>
<td>315</td>
</tr>
<tr>
<td></td>
<td><strong>Appendix II: Single Letter Codes for Amino Acids</strong></td>
<td>318</td>
</tr>
<tr>
<td></td>
<td><strong>Index</strong></td>
<td>319</td>
</tr>
</tbody>
</table>
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 molecularity and organization of biological membranes for my students Shyam Basharam, Marla Melnick, and Jared Matt Greenberg. I thank Andrea Dosé for library help, J. C. Gumbart for the model membrane figures 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 biconcave 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 Andrea 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 Padern 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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