

Contents in Brief

	Preface	xi
1	Introduction	1
2	The Diversity of Membrane Lipids	13
3	Tools for Studying Membrane Components: Detergents and Model Systems	42
4	Proteins in or at the Bilayer	68
5	Bundles and Barrels	102
6	Functions and Families	127
7	Protein Folding and Biogenesis	160
8	Diffraction and Simulation	191
9	Membrane Enzymes and Transducers	213
10	Transporters and Channels	241
11	Membrane Protein Assemblies	271
12	Themes and Future Directions	309
	Appendix I: Abbreviations	315
	Appendix II: Single-Letter Codes for Amino Acids	318
	Index	319

Contents

Preface	<i>page xi</i>	3 Tools for Studying Membrane Components: Detergents and Model Systems	42
1 Introduction	1	Detergents	43
General Features of Membranes	1	Types of Detergents	43
Paradigm 1: The Amphiphilic Molecules in Membranes Assemble Spontaneously due to the Hydrophobic Effect	4	BOX 3.1 Surfactants and surface tension	43
Paradigm 2: The Fluid Mosaic Model Describes the Membrane Structure	5	Mechanism of Detergent Action	45
A Shift in the Paradigm: Biomembranes Have Lateral Domains that Form "Rafts"	8	Membrane Solubilization	48
A View for the Future: Dynamic Protein Complexes Crowd the Membrane Interior and Extend Its Borders	9	Lipid Removal	50
2 The Diversity of Membrane Lipids	13	Model Membranes	50
The Acyl Chains	13	Monolayers	50
Complex Lipids	17	Planar Bilayers	53
Phospholipids	17	BOX 3.2 Electrophysiology	53
Sphingolipids	20	Patch Clamps	55
Sterols and Linear Isoprenoids	20	Supported Bilayers	57
The Lipid Bilayer Matrix	23	Liposomes from SUVs to GUVs	60
Structure of Bilayer Lipids	24	Mixed Micelles and Bicelles	63
Diffusion of Bilayer Lipids	24	Blebs and Blisters	63
BOX 2.1 Fluorescence techniques	26	Nanodiscs	66
Lipid Asymmetry and Membrane Thickness	26	4 Proteins in or at the Bilayer	68
Lipid Polymorphism	28	Classes of Proteins that Interact with the Membrane	68
Lamellar Phase	28	Proteins at the Bilayer Surface	69
Hexagonal Phase and the Amphiphile Shape Hypothesis	29	Extrinsic/Peripheral Membrane Proteins	69
Cubic Phase	31	Reversible Interactions of Peripheral Proteins with the Lipid Bilayer	76
Miscibility of Bilayer Lipids	31	BOX 4.1 Binding of ligands to surfaces	79
BOX 2.2 Phase diagrams	31	Proteins and Peptides that Insert into the Membrane	84
Lateral Domains and Lipid Rafts	33	Toxins	84
Detergent-Resistant Membranes	36	Colicins	85
Diversity of Lipids	37	Peptides	87
BOX 2.3 Nonlamellar phase lipids and growth of <i>E. coli</i>	40	SecA: Protein Acrobatics	88
		Proteins Embedded in the Membrane	90
		Monotopic Proteins	90
		Integral Membrane Proteins	90
		Protein-Lipid Interactions	94
		BOX 4.2 Electron paramagnetic resonance	97
		Hydrophobic Mismatch	98

5 Bundles and Barrels	102	Biogenesis of Membrane Proteins	170
Helical Bundles	102	Export from the Cytoplasm	170
Bacteriorhodopsin	102	BOX 7.2 Evidence for cleavable signal sequences involved in protein translocation	171
Photosynthetic Reaction Center	107	BOX 7.3 Import of mitochondrial proteins	177
β-Barrels	113	Integration of Nascent Proteins into the Membrane	178
BOX 5.1 NMR determination of membrane protein structure	116	BOX 7.4 Cross-linking traces nascent peptides through the translocon into the bilayer	179
Porins	118	Topogenesis in Membrane Proteins	184
Specific Porins	120	Misfolding Diseases	187
Iron Receptors	123		
6 Functions and Families	127	8 Diffraction and Simulation	191
Membrane Enzymes	127	Back to the Bilayer	191
BOX 6.1 Surface dilution effects	128	Liquid Crystallography	192
Diacylglycerol Kinase	129	BOX 8.1 X-ray and neutron scattering	193
P450 Cytochromes	130	Liquid Crystal Theory	193
Transport Proteins	131	Joint Refinement of X-Ray and Neutron Diffraction Data	194
Transport Classification System	132	Modeling the Bilayer	196
Superfamilies of ATPases	134	Simulations of Lipid Bilayers	196
ABC Transporter Superfamily	134	Molecular Dynamics	197
Group Translocation	135	BOX 8.2 Molecular dynamics calculations	198
Symporters	137	Monte Carlo	202
Antiporters	138	Lipids Observed in X-Ray Structures of Membrane Proteins	203
Ion Channels	138	The Crystallographer's Art	207
Membrane Receptors	139	Membrane Simulations	210
Nicotinic Acetylcholine Receptor	139		
G-Protein Coupled Receptors	140	9 Membrane Enzymes and Transducers	213
Bioinformatics Tools for Membrane Protein Families	141	Enzymes	214
Predicting TM Segments	141	OMPLA	214
BOX 6.2 Bioinformatics basics	142	Prostaglandin H ₂ Synthase	216
Hydrophobicity Plots	143	BOX 9.1 Mechanism of action of prostaglandin H ₂ synthase	218
Orientation of Membrane Proteins	143	Formate Dehydrogenase	222
The Positive-Inside Rule	144	Transducers	226
BOX 6.3 Making and testing hydrophobicity plots	144	Rhodopsin, a GPCR	227
Genomic Analysis of Membrane Proteins	145	BOX 9.2 Efficiency of light-induced signal transduction	229
BOX 6.4 Statistical methods for TM prediction	148	BOX 9.3 Numbering TM helices	231
Helix-Helix Interactions	154	Mechanosensitive Ion Channels	235
Proteomics of Membrane Proteins	156		
β -Barrels	157	10 Transporters and Channels	241
7 Protein Folding and Biogenesis	160	Transporters	241
Protein Folding	161	LacY and GltT	242
Folding α -Helical Membrane Proteins	162	Mitochondrial ADP/ATP Carrier	249
BOX 7.1 Energetics of folding and insertion a hydrophobic α -helix into the bilayer	164	Channels	253
Folding Studies of β -Barrel Membrane Proteins	167	Aquaporins and Glyceroaquaporins	253
Other Folding Studies	169	Potassium Channels	258
		Calcium ATPase	264

11 Membrane Protein Assemblies	271	Tripartite Drug Efflux via a Membrane Vacuum Cleaner	300
F_1F_0 -ATPase/ATP Synthase	272	AcrB, a Peristaltic Pump	300
Subunit Structure and Function	273	AcrA, a Membrane Fusion Protein	302
Regulation of the F_1F_0 -ATPase	276	TolC, the Channel-Tunnel	304
Catalytic Mechanism of a Rotary Motor	277		
Complexes of the Respiratory Chain	279	12 Themes and Future Directions	309
Cytochrome bc_1	279	Oligomerization	309
Cytochrome- c Oxidase	284	Conformational Changes	310
The Translocon	286	Motifs and Patterns	311
The <i>M. jannaschii</i> Translocon		Conclusions	312
Structure	286		
The Translocon-Ribosome Complex	288	Appendix I: Abbreviations	315
ABC Transporters and Beyond	290		
The Vitamin B ₁₂ Uptake System	291	Appendix II: Single Letter Codes for Amino Acids	318
Transport across the Inner Membrane	291		
Transport across the Outer Membrane	294		
Drug Efflux Systems	296	Index	319
Sav1866, an ABC Multidrug Transporter	297		
EmrE, Small but Powerful	299		