



# CONTENTS

<b>Chapter 1 THE CELL—STRUCTURAL ORGANIZATION</b> .....	<b>1</b>
<b>1-1 Levels of Organization in Biology</b> .....	<b>3</b>
Levels of Organization and Instrumental Resolving Power .....	3
Summary: Levels of Organization .....	5
<b>1-2 History of Cell and Molecular Biology</b> .....	<b>5</b>
The Development of the Cell Theory .....	5
The Development of Submicroscopic and Molecular Biology .....	6
Summary: Modern Cell Biology .....	6
<b>1-3 General Organization of Prokaryotic Cells</b> .....	<b>7</b>
Cell Organization and the Energy Cycle .....	7
<i>Escherichia coli</i> ( <i>E. coli</i> )—The Most Studied Prokaryote .....	8
Summary: General Organization of Prokaryotic Cells .....	10
<b>1-4 Mycoplasmas, Viruses, and Viroids</b> .....	<b>11</b>
Summary: Mycoplasmas, Viruses, and Viroids .....	12
<b>1-5 General Organization of Eukaryotic Cells</b> .....	<b>12</b>
Morphological Diversity of Eukaryotic Cells .....	15
The Cell Membrane .....	15
<b>1-6 The Nucleus and the Cell Cycle</b> .....	<b>16</b>
Mitosis and Meiosis—Essentials .....	18
Summary: Essentials about Nucleus and Chromosomes .....	20
<b>1-7 The Ultrastructure of the Cytoplasm</b> .....	<b>21</b>
The Cytoskeleton—Microtubules, Microtubular Organelles, Microfila- ments, and Intermediate Filaments .....	21
The Endomembrane System—Nuclear Envelope, Endoplasmic Reticu- lum, and Golgi Complex .....	22
Membrane Organelles—Mitochondria, Chloroplasts, Lysosomes, and Peroxisomes .....	22
Summary: Ultrastructure of the Cytoplasm .....	25

1–8	Literary Sources in Cell and Molecular Biology . . . . .	25
	Additional Readings . . . . .	26
Chapter 2	MOLECULAR ORGANIZATION OF THE CELL . . . . .	27
2–1	Water, Salts, Ions, and Trace Elements in Cells . . . . .	28
2–2	Nucleic Acids . . . . .	29
	Nucleic Acids—A Pentose, Phosphate, and Four Bases . . . . .	30
	DNA Base Composition—A = T and G = C . . . . .	31
	DNA Is A Double Helix . . . . .	34
	Right-Handed B- and A-DNA and Left-Handed Z-DNA . . . . .	34
	DNA Strands Can Be Separated and Annealed . . . . .	35
	Circular DNA—Supercoiled Conformation . . . . .	37
	RNA Structure—Classes and Conformation . . . . .	38
	Summary: Nucleic Acids . . . . .	39
2–3	Carbohydrates . . . . .	41
	Glycoproteins—Two-step Carbohydrate Addition . . . . .	41
2–4	Lipids . . . . .	42
	Triglycerides—Three Fatty Acids Bound to Glycerol . . . . .	42
	Phospholipids and Biological Membranes . . . . .	43
2–5	Proteins . . . . .	43
	Proteins—Chains of Amino Acids Linked by Peptide Bonds . . . . .	43
	Four Levels of Structure in Proteins . . . . .	47
	Factors Involved in Determining Protein Structure . . . . .	47
	Electrical Charges of Proteins and the Isoelectric Point . . . . .	49
	Separation of Cell Proteins—Isoelectric Focusing and SDS Electrophoresis . . . . .	50
	Summary: Molecular Components of the Cell . . . . .	51
2–6	Enzymes and Their Regulation . . . . .	54
	Some Enzymes Require Cofactors or Coenzymes . . . . .	54
	Substrates Bind to the Active Site . . . . .	55
	Essentials of Enzyme Kinetics— $K_m$ and $V_{max}$ Define Enzyme Behavior . . . . .	55
	Enzyme Inhibitors Can Be Very Specific . . . . .	56
	Zymogens Are Inactive Forms of Enzymes . . . . .	57
	Isoenzymes . . . . .	57
	The Cell Is Not Simply A Bag Full of Enzymes . . . . .	57
	Some RNAs Have Enzymatic Activity—Ribozymes . . . . .	58
	Cooperativity and Allosterism in Enzyme Kinetics . . . . .	58
	Enzyme Regulation at the Genetic and Catalytic Levels . . . . .	59
	Cyclic AMP—The Second Messenger in Hormone Action . . . . .	60
	Calcium, Calmodulin, and Regulation of Cellular Functions . . . . .	62
	Summary: Enzymes in the Cell . . . . .	64
2–7	The Assembly of Macromolecules and the Origin of Cells . . . . .	66
	Proteins and Nucleic Acid May Self-Assemble . . . . .	66
	The Origin of Cells . . . . .	67
	Summary: Assembly of Macromolecules and the Origin of Life . . . . .	71

<b>Additional Readings</b> .....	71
<b>Chapter 3 TECHNIQUES IN CELL BIOLOGY</b> .....	73
<b>3-1 Various Types of Light Microscopy</b> .....	74
Light Microscope—Resolving Power .....	74
Phase and Interference Microscopy—Detect Small Differences in Refractive Index .....	75
Darkfield Microscopy—Based on Light Scattering at Cell Boundaries ..	76
Polarization Microscopy—Detects Anisotropy with Polarized Light ....	76
<b>3-2 Electron Microscopy</b> .....	77
Thin Specimens—Essential for EM Study .....	78
Shadow Casting, Negative Staining, and Tracers—Increased Contrast ..	78
Freeze-Fracturing—Membranes Split at Cleavage Planes .....	80
Preparation of Thin Sections—Epoxy Resins and Ultramicrotomes .....	80
High Voltage EM—Allows Study of Thicker Specimens .....	80
Scanning EM and Scanning Transmission EM (STEM) .....	82
Image Reconstruction from Electron Micrographs .....	83
Summary: Microscopy .....	83
<b>3-3 Study of the Living Cell</b> .....	84
<b>3-4 Fixation and Staining</b> .....	85
Freeze-drying and Free-substitution .....	85
Microtomes and Embedding .....	85
Chemical Basis of Staining .....	86
Metachromasia—A Change in Original Dye Color .....	87
Summary: Observation of Living and Fixed Cells .....	87
<b>3-5 Cytochemical Methods</b> .....	89
Schiff's Reagent—Detection of Aldehydes—Cytochemistry of Nucleic Acids .....	89
Lipids—Detection by Lipid-soluble Stains .....	91
Enzymes—Detection by Incubation with Substrates .....	91
Cytophotometric Methods .....	93
Fluorescence Microscopy—Autofluorescence and Fluorochrome Dyes ..	93
<b>3-6 Immunocytochemistry</b> .....	94
<b>3-7 Radioautography</b> .....	96
<b>3-8 Cell Fractionation</b> .....	98
Differential or Gradient Centrifugation .....	99
Flow-sorting Cytometry .....	101
Summary: Cytochemistry .....	101
<b>Additional Readings</b> .....	102
<b>Chapter 4 CELL MEMBRANE AND PERMEABILITY</b> .....	103
<b>4-1 Molecular Organization of the Cell Membrane</b> .....	104
The Cell Membrane—Composed of Proteins, Lipids, and Carbohydrates .....	104
Lipids Are Asymmetrically Distributed within the Bilayer .....	104
Carbohydrates—In the Form of Glycolipids and Glycoproteins .....	106
Membrane Proteins—Peripheral or Integral .....	106

	Every Protein of the Cell Membrane Is Distributed Asymmetrically . . .	108
	Major Polypeptides of the Red Cell Membrane and Cytoskeleton . . . . .	108
	Asymmetrical Distribution of Enzymes . . . . .	111
	Summary: Molecular Organization of the Cell Membrane . . . . .	112
<b>4-2</b>	<b>Molecular Models of the Cell Membrane</b> . . . . .	<b>112</b>
	Artificial Model Systems—Liposomes . . . . .	112
	The Unit Membrane Model—Reevaluation of the Electron Microscopic Image . . . . .	114
	The Fluid Mosaic Model—Generally Accepted . . . . .	115
	Membrane Fluidity and Membrane Fusion . . . . .	116
	The Mobile Hypothesis of Receptors . . . . .	118
	Summary: Membrane Molecular Models . . . . .	119
<b>4-3</b>	<b>Cell Permeability</b> . . . . .	<b>120</b>
	Passive Permeability—Concentration Gradient and Partition Coefficient	120
	Passive Ionic Diffusion—Dependent on the Concentration and Electrical Gradients . . . . .	121
	Active Transport—The Sodium Pump . . . . .	122
	Ionic Transport through Charged Pores in the Membrane . . . . .	123
	Anion Transport in Erythrocytes Involves the Special Band-3 Polypeptide . . . . .	124
	Vectorial Function of Na <sup>+</sup> K <sup>+</sup> ATPase and Sodium Transport . . . . .	124
	Transport Proteins—Carrier and Fixed Pore Mechanisms . . . . .	126
	Summary: Cell Permeability . . . . .	128
	<b>References</b> . . . . .	<b>128</b>
	<b>Additional Readings</b> . . . . .	<b>129</b>
<b>Chapter 5</b>	<b>CELLULAR INTERACTIONS</b> . . . . .	<b>130</b>
<b>5-1</b>	<b>Differentiations of the Cell Membrane</b> . . . . .	<b>130</b>
	Microvilli—A Greatly Increased Cell Membrane Surface Area . . . . .	132
	Tight Junctions and the Sealing of Epithelia . . . . .	132
	Belt and Spot Desmosomes—Mechanical Function . . . . .	134
	Summary: Differentiations of the Cell Membrane . . . . .	135
<b>5-2</b>	<b>Intercellular Communications and Gap Junctions</b> . . . . .	<b>135</b>
	Electrical Coupling between Cells Depends on Gap Junctions . . . . .	135
	The Connexon—Opening and Closing of the Channel . . . . .	136
	Gap or Communicating Junctions—Permeability to Ions and Small Molecules . . . . .	138
	Coupling between Cells Enables Metabolic Cooperation . . . . .	139
	Altered Coupling in Cancer Cells . . . . .	139
	Summary: Gap Junctions and Intercellular Communications . . . . .	140
<b>5-3</b>	<b>Cell Coat and Cell Recognition</b> . . . . .	<b>141</b>
	Glycosaminoglycans and Proteoglycans as Extracellular Materials . . . . .	142
	Functions Attributed to the Cell Coat . . . . .	143
	Factors Mediating Cell-Self Recognition—The Aggregation Factor of Sponges . . . . .	143
	Animal Cell—Recognition Molecules . . . . .	145
	Cellular Interactions and Cyclic AMP . . . . .	146
	Summary: Cell Coats and Cell Recognition . . . . .	146

<b>5-4</b>	<b>The Cell Surface of Cancer Cells</b> .....	<b>147</b>
	Surface Changes in Cancer Cells .....	147
	Cancer Cells and Iron Transport .....	148
	Fibronectin and the Cancer Cell .....	148
	Loss of Control of Growth in Cancer Cells .....	149
	Viruses as Oncogenic Agents .....	151
	Summary: Cell Surface in Cancer Cells .....	152
	<b>References</b> .....	<b>152</b>
	<b>Additional Readings</b> .....	<b>153</b>
<b>Chapter 6</b>	<b>THE CYTOSKELETON AND CELL MOTILITY—MICROTUBULES, MICROFILAMENTS, AND INTERMEDIATE FILAMENTS</b> .....	<b>154</b>
<b>6-1</b>	<b>Cytosol, Ergastoplasm, and Cytoskeleton</b> .....	<b>155</b>
	Summary: The Cytoskeleton .....	157
<b>6-2</b>	<b>Microtubules</b> .....	<b>158</b>
	Tubulin—The Main Protein of Microtubules .....	158
	Microtubules—Assembly from Tubulin Dimers and Polarity .....	160
	Detection of Microtubules by Antibodies .....	161
	Functions of Cytoplasmic Microtubules .....	162
	Summary: Properties of Microtubules .....	163
<b>6-3</b>	<b>Microtubular Organelles—Cilia, Flagella, and Centrioles</b> .....	<b>163</b>
	Ciliary and Flagellar Motions in Cells and in Tissues .....	163
	The Ciliary Apparatus—The Cilium, Basal Bodies, and Ciliary Rootlets .....	164
	The Axoneme Contains Microtubular Doublets .....	164
	Basal Bodies (Kinetosomes) and Centrioles Contain Microtubular Triplets .....	165
	Ciliary Movement .....	167
	A Sliding of Microtubular Doublets that Involves Dynein .....	169
	The Immotile Cilia Syndrome .....	170
	Photoreceptors are Derived from Cilia .....	171
	Cilia and Flagella Originate from Basal Bodies .....	171
	Summary: Structure, Motion, and Origin of Cilia and Flagella .....	174
<b>6-4</b>	<b>Microfilaments</b> .....	<b>174</b>
	Microtrabecular Lattice—Revealed by High-Voltage Electron Microscopy .....	175
	Cytochalasin B Impairs Several Cellular Activities Involving Microfilaments .....	176
	Microfilaments Detected by Specific Antibodies—The Cellular Geodome .....	176
	The Contractile Machinery in Nonmuscle Cells .....	176
	Summary: Microfilaments .....	180
<b>6-5</b>	<b>Microfilaments and Cell Motility</b> .....	<b>181</b>
	Cytoplasmic Streaming (Cyclosis)—Observed in Large Plant Cells .....	181
	Ameboid Motion—Characteristic of Amebae and Many Free Cells .....	181
	Interaction of Microfilaments with the Cell Membrane and Surface Receptors .....	185
	Cell Adhesion, Focal Contacts, Stress Fibers, Fibronexus, and Transmembrane Interaction .....	187

	Cell Adhesion and Collagens .....	190
	Microtubules and Microfilaments in Cancer Transformation .....	191
	Summary: Microfilaments and Cell Motility .....	192
<b>6-6</b>	<b>Intermediate Filaments—Mechanical Integrators of Cellular Compartments</b> .....	<b>194</b>
	Intermediate Filaments During Mitosis .....	195
	Summary: Intermediate Filaments .....	196
	<b>References</b> .....	<b>196</b>
	<b>Additional Readings</b> .....	<b>197</b>
<b>Chapter 7</b>	<b>CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE</b> .....	<b>199</b>
<b>7-1</b>	<b>Structure of the Striated Muscle Fiber</b> .....	<b>200</b>
	The Myofibril and Sarcomere are Structures Differentiated for Contraction .....	201
	Thick and Thin Myofilaments Are the Macromolecular Contractile Components .....	202
	The Z-disc Shows a Woven-Basket Lattice and Contains $\alpha$ -Actinin, Desmin, Vimentin, and Synemin .....	202
	The Sarcomere I-Band Shortens and the Banding Inverts During Contraction .....	203
	Smooth Muscles Lack the Z-disc .....	204
	Summary: The Structure of Muscle .....	204
<b>7-2</b>	<b>Molecular Organization of the Contractile System</b> .....	<b>205</b>
	The Thick Myofilament—Myosin Molecules; The Cross-Bridges— $S_1$ Subunits .....	205
	Actin, Tropomyosin, and the Troponins Constitute the Thin Myofilament Structural Proteins .....	207
<b>7-3</b>	<b>The Sliding Mechanism of Muscle Contraction</b> .....	<b>208</b>
	Myosin and Actin Have a Definite Polarization within the Sarcomere ..	208
	Muscle Contraction—A Cyclic Formation and Breakdown of Actin-Myosin Linkages .....	209
	Summary: Molecular Organization and the Sliding Mechanism .....	210
<b>7-4</b>	<b>Regulation and Energetics of Contraction</b> .....	<b>210</b>
	Molecular Regulation—Displacement of Tropomyosin After Binding of $Ca^{++}$ to Troponin-C .....	211
	Energy for Contraction Comes from Oxidative Phosphorylation and Glycolysis .....	211
	Summary: Regulation and Energetics of Contraction .....	212
<b>7-5</b>	<b>Excitation-Contraction Coupling</b> .....	<b>212</b>
	The SR—A Longitudinal Component with Terminal Cisternae that Form Part of the Triad .....	212
	The T-System is in Continuity with the Plasma Membrane and Conducts Impulses Inward .....	212
	Stimulation Releases $Ca^{++}$ from the Terminal Cisternae .....	214
	A $Ca^{++}$ -Activated ATPase is Present in the SR and Acts as a $Ca^{++}$ Pump .....	214
	Summary: Excitation-Contraction Coupling and the SR .....	216

<b>References</b> .....	<b>216</b>
<b>Additional Readings</b> .....	<b>216</b>
<b>Chapter 8 ENDOPLASMIC RETICULUM AND PROTEIN SEGREGATION</b> .....	<b>218</b>
<b>8-1 General Morphology of the Endomembrane System</b> .....	<b>219</b>
The RER—Ribosomes and Protein Synthesis .....	219
Ribosomal Binding to the ER—60S Subunit and Ribophorins Involved .....	223
The SER Lacks Ribosomes-Glycosomes .....	224
Summary: The Endoplasmic Reticulum .....	224
<b>8-2 Microsomes—Biochemical Studies</b> .....	<b>224</b>
Microsomal Membranes—A Complex Lipid and Protein Composition ..	225
Two Microsomal Electron Transport Systems—Flavoproteins and Cytochromes $b_5$ and P-450 Involved .....	227
Microsomal Enzymes—Glycosidation and Hydroxylation of Amino Acids .....	227
Summary: Microsomes .....	228
<b>8-3 Biogenesis and Functions of the ER</b> .....	<b>228</b>
Membrane Biogenesis Involves a Multi-Step Mechanism .....	228
ER-Membrane Fluidity and Flow Through the Cytoplasm .....	229
Ions and Small Molecules—Transport Across ER Membranes .....	229
Special Functions of the SER—Detoxification, Lipid Synthesis, and Glycogenolysis .....	229
Summary: Biogenesis and Functions of the ER .....	230
<b>8-4 The ER and Synthesis of Exportable Proteins</b> .....	<b>230</b>
The Signal for Secretory Proteins Resides in the Nascent Polypeptide: The Signal Theory .....	231
The Hydrophobic Signal Peptide is Removed by a Signal Peptidase ...	231
The Role of the Signal Recognition Particle (SRP) .....	233
Protein Secretion in Bacteria Uses a Signal Peptide .....	234
Summary: Synthesis of Exportable Proteins—The Signal Hypothesis ...	235
<b>8-5 Protein Segregation</b> .....	<b>235</b>
Cotranslational and Postranslational Translocation of Proteins— Segregation Sequences .....	237
Synthesis and Assembly of Membrane Proteins—Stop Transfer Sequences .....	237
Summary: Protein Segregation .....	239
<b>References</b> .....	<b>240</b>
<b>Additional Readings</b> .....	<b>240</b>
<b>Chapter 9 GOLGI COMPLEX AND CELL SECRETION</b> .....	<b>241</b>
<b>9-1. Morphology of the Golgi Complex (Dictyosomes)</b> .....	<b>242</b>
Dictyosomes—A Forming Face, and a Maturing Face Near the GERL	243
Polarization of Dictyosomes and Membrane Differentiation .....	245
Summary: Morphology of the Golgi Complex .....	245