

Cell and Molecular Biology

E. D. P. De ROBERTIS, M.D.

E. M. F. De ROBERTIS, JR., M.D., Ph.D.

EIGHTH EDITION

2
Q 7 11878
8

Cell and Molecular Biology

E.D.P. De ROBERTIS, M.D.

*Emeritus Professor of Cell Biology
University of Buenos Aires
Buenos Aires, Argentina*

E.M.F. De ROBERTIS, JR., M.D., Ph.D.

*Norman Sprague Professor of Molecular Oncology
University of California
Los Angeles, California*

EIGHTH EDITION



Lea & Febiger

1987

Philadelphia

857811
Lea & Febiger
600 Washington Square
Philadelphia, PA 19106-4198
U.S.A.
(215) 922-1330

Q7
8

Library of Congress Cataloging-in-Publication Data

De Robertis, Eduardo D. P., 1913-
Cell and molecular biology.

Includes bibliographies and index.

1. Cytology. 2. Molecular biology. I. De Robertis,
E. M. F. II. Title. [DNLM: 1. Cells. 2. Molecular
Biology. QH 581 D437c]

QH581.2.R613 1987 574.87 86-123
ISBN 0-8121-1012-9

Copyright © 1987 by Lea & Febiger. Copyright under the International Copyright Union.
All Rights Reserved. This book is protected by copyright. No part of it may be reproduced
in any manner or by any means without written permission from the publisher.

PRINTED IN THE UNITED STATES OF AMERICA

Print number: 5 4 3 2 1

PREFACE

Life has an immense variety of forms that arose by the process of biological evolution, but all living organisms share a master plan of structural and functional organization. This book is about the building blocks—*cells* and *molecules*—that constitute the unity of the living world.

Progress in our field of science has been so rapid that during the lifetime of this book, first published in 1946, we have witnessed the most revolutionary discoveries, such as those involving the recognition of the ultrastructure and macromolecular organization of cell components, the uncovering of the DNA helix, and the molecular basis of the genetic code and gene expression. This tremendous progress necessitated making extensive revisions every five years and changing the original title, *General Cytology*, to *Cell Biology* in 1965 and to *Cell and Molecular Biology* in 1980.

The present, eighth, edition should be seen as a new book rather than as a revision because the changes have been so profound that the text has been entirely rewritten and more than half of the illustrations have been changed or added. We have tried to integrate the most recent advances in molecular biology with our knowledge of the structure and function of cells, while taking into account the work of classical cytologists—often forgotten these days—which laid the foundations of our understanding of the living cell.

The book has been organized to facilitate learning by proceeding from simple to more complex matters. For example, the first three chapters give an overview of the cell and its main

structural components, a general introduction to the biochemistry of the cell, and an account of some of the current methods used in the study of cell biology.

Each of the following twenty-one chapters contains an introduction, stating the main objectives; sectional summaries that provide a synopsis of the essential points; and for further information and study, a list of numbered references and additional readings.

The specific fields of cell and molecular biology are presented dynamically, based on experimental data from which the student can draw his own conclusions. All the figures, many of them original drawings that represent classic experiments, are integrated in the text. A special feature of this edition is a glossary that defines words and concepts.

Cell and molecular biology have become the basic pillars on which all biological and medical sciences are based. Although primarily intended for courses at the college level, the book may be useful in more advanced courses, because of the wealth of up-to-date information contained in it. Much of the text should be of interest to those in the applied sciences such as medicine, veterinary, agronomy, and biotechnology.

By emphasizing that cell and molecular biology are in constant progress and much remains to be discovered, we hope to stimulate research among young scientists who want to dedicate their efforts to uncovering the basis of life on our planet.

Buenos Aires, Argentina
Los Angeles, California

E. De Robertis
E.M. De Robertis, Jr.

ACKNOWLEDGMENTS

We have been stimulated in our task by the good reception the book has received in previous English-language editions, as well as in the Spanish, Portuguese, Italian, French, Hungarian, Polish, Russian, Chinese, and Japanese translations. We especially want to recognize the contributions of Professors Richard Shivers, R. E. Hausman, James C. Tan, Ernest R. Vyse, Brower R. Burchill, Joseph F. Gennaro, Gerald Schatten, and William H. Beers, who have read the manuscript and have contributed valuable suggestions and criticisms.

Among the illustrations, we have included the original micrographs and designs of many experiments that led to major discoveries in cell

and molecular biology. We hope that these experiments help the students to recognize the avenues by which scientific progress is made. We especially wish to express our gratitude to our colleagues who have contributed so generously to the illustrations of the present and past editions and whose names are acknowledged at each special instance.

We would like to thank the staff of Lea & Febiger who have contributed immensely to improving the presentation of this textbook.

We also want to acknowledge the collaboration of the staff of EL ATENEO, publishers of the Spanish edition, for their contribution of many valuable drawings to this book.

CONTENTS

Chapter 1 THE CELL—STRUCTURAL ORGANIZATION	1
1-1 Levels of Organization in Biology	3
Levels of Organization and Instrumental Resolving Power	3
Summary: Levels of Organization	5
1-2 History of Cell and Molecular Biology	5
The Development of the Cell Theory	5
The Development of Submicroscopic and Molecular Biology	6
Summary: Modern Cell Biology	6
1-3 General Organization of Prokaryotic Cells	7
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
1-4 Mycoplasmas, Viruses, and Viroids	11
Summary: Mycoplasmas, Viruses, and Viroids	12
1-5 General Organization of Eukaryotic Cells	12
Morphological Diversity of Eukaryotic Cells	15
The Cell Membrane	15
1-6 The Nucleus and the Cell Cycle	16
Mitosis and Meiosis—Essentials	18
Summary: Essentials about Nucleus and Chromosomes	20
1-7 The Ultrastructure of the Cytoplasm	21
The Cytoskeleton—Microtubules, Microtubular Organelles, Microfilaments, and Intermediate Filaments	21
The Endomembrane System—Nuclear Envelope, Endoplasmic Reticulum, 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

Additional Readings	71
Chapter 3 TECHNIQUES IN CELL BIOLOGY	73
3-1 Various Types of Light Microscopy	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
3-2 Electron Microscopy	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
3-3 Study of the Living Cell	84
3-4 Fixation and Staining	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
3-5 Cytochemical Methods	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
3-6 Immunocytochemistry	94
3-7 Radioautography	96
3-8 Cell Fractionation	98
Differential or Gradient Centrifugation	99
Flow-sorting Cytometry	101
Summary: Cytochemistry	101
Additional Readings	102
Chapter 4 CELL MEMBRANE AND PERMEABILITY	103
4-1 Molecular Organization of the Cell Membrane	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
4-2	Molecular Models of the Cell Membrane	112
	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
4-3	Cell Permeability	120
	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 $\text{Na}^+\text{K}^+\text{ATPase}$ and Sodium Transport	124
	Transport Proteins—Carrier and Fixed Pore Mechanisms	126
	Summary: Cell Permeability	128
	References	128
	Additional Readings	129
Chapter 5	CELLULAR INTERACTIONS	130
5-1	Differentiations of the Cell Membrane	130
	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
5-2	Intercellular Communications and Gap Junctions	135
	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
5-3	Cell Coat and Cell Recognition	141
	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

5-4	The Cell Surface of Cancer Cells	147
	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
	References	152
	Additional Readings	153
Chapter 6	THE CYTOSKELETON AND CELL MOTILITY—MICROTUBULES, MICROFILAMENTS, AND INTERMEDIATE FILAMENTS	154
6-1	Cytosol, Ergastoplasm, and Cytoskeleton	155
	Summary: The Cytoskeleton	157
6-2	Microtubules	158
	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
6-3	Microtubular Organelles—Cilia, Flagella, and Centrioles	163
	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
6-4	Microfilaments	174
	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
6-5	Microfilaments and Cell Motility	181
	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
6-6	Intermediate Filaments—Mechanical Integrators of Cellular Compartments	194
	Intermediate Filaments During Mitosis	195
	Summary: Intermediate Filaments	196
	References	196
	Additional Readings	197
Chapter 7	CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE	199
7-1	Structure of the Striated Muscle Fiber	200
	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 α -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
7-2	Molecular Organization of the Contractile System	205
	The Thick Myofilament—Myosin Molecules; The Cross-Bridges— S_1 Subunits	205
	Actin, Tropomyosin, and the Troponins Constitute the Thin Myofilament Structural Proteins	207
7-3	The Sliding Mechanism of Muscle Contraction	208
	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
7-4	Regulation and Energetics of Contraction	210
	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
7-5	Excitation-Contraction Coupling	212
	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

References	216
Additional Readings	216
Chapter 8 ENDOPLASMIC RETICULUM AND PROTEIN SEGREGATION	218
8-1 General Morphology of the Endomembrane System	219
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
8-2 Microsomes—Biochemical Studies	224
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
8-3 Biogenesis and Functions of the ER	228
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
8-4 The ER and Synthesis of Exportable Proteins	230
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
8-5 Protein Segregation	235
Cotranslational and Posttranslational Translocation of Proteins— Segregation Sequences	237
Synthesis and Assembly of Membrane Proteins—Stop Transfer Sequences	237
Summary: Protein Segregation	239
References	240
Additional Readings	240
Chapter 9 GOLGI COMPLEX AND CELL SECRETION	241
9-1. Morphology of the Golgi Complex (Dictyosomes)	242
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

9-2	Cytochemistry of the Golgi Complex	246
	Chemical Composition of the Golgi Complex—Intermediate Between Those of the ER and the Plasma Membrane	246
	Glycosyl Transferases are Concentrated in the Golgi	247
	Summary: Cytochemistry of the Golgi Complex	248
9-3	Functions of the Golgi Complex	248
	Synthesis of Glycosphingolipids and Glycoproteins—A Major Role of the Golgi	249
	Cancer Cells—Changes in Glycosidation of Lipids and Proteins	251
9-4	Secretion—The Main Function of the Golgi Complex	252
	The Secretory Cycle—Continuous or Discontinuous	252
	The Secretory Process in the Pancreas—Six Consecutive Steps	254
	Endocytosis and Recycling of Membranes of Secretory Granules	259
	The GERL Region and Lysosome Formation	259
	Compartments of the Golgi Apparatus	259
	Insulin Biosynthesis—A Good Example of the Molecular Processing of Secretion	262
	Summary: Functions of the Golgi Complex	264
	References	265
	Additional Readings	265
Chapter 10	LYSOSOMES, ENDOCYTOSIS, COATED VESICLES, ENDOSOMES, AND PEROXISOMES	267
10-1	Major Characteristics of Lysosomes	268
	Various Cytochemical Procedures for Identifying Lysosomes	268
	Lysosomes are Very Polymorphic	269
	Primary Lysosomes and Three Types of Secondary Lysosomes	269
	Lysosomal Enzymes—Synthesized in the ER, Packaged in the Golgi— The Mannose-6-Phosphate Receptor	272
	Summary: Lysosomal Morphology and Cytochemistry	273
10-2	Functions of Lysosomes—Intracellular Digestion	274
	Autophagy by Lysosomes—The Renovation and Turnover of Cell Components	274
	Lysosomal Removal of Cells and Extracellular Material and Develop- mental Processes	274
	Release of Lysosomal Enzymes to the Medium for Extracellular Action	274
	Lysosomal Enzyme Involvement in Thyroid Hormone Release and in Crinophagy	275
	Leukocyte Granules Are of a Lysosomal Nature	275
	Lysosomes Are Important in Germ Cells and Fertilization	275
	Lysosomal Involvement in Human Diseases and Syndromes	275
	Storage Diseases—Caused by Mutations That Affect Lysosomal Enzymes	275
	Lysosomes in Plant Cells and Their Role in Seed Germination	276
	Summary: Functions of Lysosomes	277
10-3	Endocytosis	277
	Phagocytosis—The Process of Cellular Ingestion of Solid Material	277
	Pinocytosis—The Ingestion of Fluids	277

Micropinocytosis and the Ingestion and Transport of Fluids	278
Endocytosis—An Active Mechanism Involving the Contraction of Microfilaments	278
Summary: Endocytosis and Lysosomes	279
10-4 Coated Vesicles and Receptor-Mediated Selective Transport	279
The Coat is Made of Clathrin	279
Functions of Coated Vesicles—Receptor-Mediated Endocytosis	280
Coated Vesicles and Intracellular Traffic	283
The Endosome and the Sorting of Ligands and Receptors	284
Summary: Coated Vesicles and Selective Transport	285
10-5 Peroxisomes	285
Morphology of Peroxisomes and Microperoxisomes	286
Biogenesis of Peroxisomes—A Mixed Model	286
Peroxisomes Contain Enzymes Related to the Metabolisms of H_2O_2 and β -Oxidation	287
Plant Peroxisomes Are Involved in Photorespiration	288
Summary: Peroxisomes	289
References	289
Additional Readings	289
Chapter 11 MITOCHONDRIA AND OXIDATIVE PHOSPHORYLATION	291
11-1 Morphology of Mitochondria	293
Summary: Mitochondrial Morphology	294
11-2 Mitochondrial Structure	294
F_1 Particles—On the M Side of the Inner Mitochondrial Membrane	295
Mitochondrial Structural Variations in Different Cell Types	296
Mitochondrial Sensitivity to Cell Injury and Resultant Degeneration	298
Summary: Structure of Mitochondria	298
11-3 Isolation of Mitochondrial Membranes	298
Outer and Inner Membranes—Structural and Chemical Differences	298
Mitochondrial Enzymes Are Highly Compartmentalized	299
The Inner Membrane—Regional Structural and Enzymatic Differences	300
Summary: Isolation of Mitochondrial Membranes	301
11-4 Bioenergetics: Molecular Organization and Function of Mitochondria	301
Entropy is Related to the Degree of Molecular Order	302
Chemical Energy and ATP	302
Glycolysis—First Step in the Release of Energy	303
Coenzymes Play a Central Role in Mitochondria	303
The Krebs Cycle—A Common Pathway in the Degradation of Fuel Molecules	305
Electrons Flow Along a Cytochrome Chain Having a Gradient of Redox Potential	306
The Respiratory Chain—Four Molecular Complexes	308
Electron Transport—Coupled to the Phosphorylation at Three Points	311
Mitochondrial ATPase—A Structurally Complex Proton Pump	311
Topological Organization of the Respiratory Chain and the Phosphoryl- ation System	312

	The Chemiosmotic Theory—An Electrochemical Link Between Respiration and Phosphorylation	313
	The Chemical-Conformational Hypothesis Involves Short-Range Interactions	314
	Overall Energy Balance—Glucose and the P:O Ratio	314
	Summary: Molecular Organization and Function	314
11-5	Permeability of Mitochondria	315
	ADP, ATP, and Pi—Transport by Specific Carriers	316
	Mitochondrial Conformation—Changes with Stages of Oxidative Phosphorylation	316
	Mitochondrial Swelling and Contraction—Agent-Induced	318
	Mitochondrial Accumulation of Ca ⁺⁺ and Phosphate	318
	Summary: Mitochondrial Permeability	318
11-6	Biogenesis of Mitochondria	319
	Mitochondria are Semiautonomous Organelles	319
	Mitochondrial DNA—Circular and Localized in the Matrix	319
	Mitochondrial Ribosomes—Smaller than Cytoplasmic Ribosomes	320
	Mitochondria Synthesize Mainly Hydrophobic Proteins	320
	The Symbiont Hypothesis—Mitochondria and Chloroplasts are Intracellular Prokaryotic Parasites	322
	Summary: Mitochondrial Biogenesis	323
	References	323
	Additional Readings	323
Chapter 12	PLANT CELL—CHLOROPLAST AND PHOTOSYNTHESIS	325
12-1	The Cell Wall of Plant Cells	325
	The Cell Wall—A Network of Cellulose Microfibrils and a Matrix	326
	Development of Primary and Secondary Walls and Plant Cell Differentiation	326
	Cell Wall Components—Synthesis Associated with the Golgi or the Plasma Membrane	327
	Plasmodesmata Establish Communication Between Adjacent Cells	327
	Summary: The Plant Cell Wall	329
12-2	Plant Cell Cytoplasm	329
	Mitochondria Can be Distinguished from Proplastids	330
	Seed Development—Cell Division, Cell Expansion, and a Drying Phase	331
	Seed Germination Involves Synthesis of Hydrolytic Enzymes	331
	Glyoxysomes—Organelles Related to Triglyceride Metabolism	331
	Summary: Plant Cell Cytoplasm	331
12-3	The Chloroplast and Other Plastids	333
	Chloroplast Morphology Varies in Different Cells	333
	Chloroplast Structure—Envelope, Stroma, and Thylakoids	334
12-4	Molecular Organization of Thylakoids	336
	Several Chlorophyll-Protein Complexes in Thylakoid Membranes	337
	Freeze-Fracturing Best Reveals the Fine Structure of the Thylakoid Membrane	338
	Summary: Structure and Molecular Organization of Chloroplasts	341

12-5	Photosynthesis	342
	Pigment Molecules are Photoexcited	343
	Primary Reaction of Photosynthesis—Photochemical Reaction	343
	Electron Transport Chain—Cytochromes, Plastoquinone, and Ferredoxin	344
	Topology of the Electron Transport and Photosystems	344
	Photophosphorylation Involves a CF ₁ ATPase—The Chemiosmotic Coupling	345
	The Photosynthetic Carbon-Reduction (PCR) Cycle—Dark Reactions ..	346
	The C ₄ -Pathway in Angiosperms	347
	Ion Fluxes and Conformational Changes—Caused by Light and Darkness	348
	Summary: Photosynthesis and the Chloroplast	349
12-6	Biogenesis of Chloroplasts	349
	Chloroplasts as Semiautonomous Organelles	350
	Summary: Biogenesis of Chloroplasts	353
	References	353
	Additional Readings	354
Chapter 13	THE INTERPHASE NUCLEUS, CHROMATIN, AND THE CHROMOSOME	355
13-1	The Interphase Nucleus	356
	Ultrastructure of the Interphase Nucleus	356
13-2	The Nuclear Envelope	358
	Nuclear Pores Are Not Wide-Open Channels	359
	Annulated Lamellae—Cytoplasmic Stores of Pore Complexes	360
	The Nuclear Lamina Depolymerizes During Mitosis	360
	Interphase Nuclei Can Be Assembled from Bacteriophage λ DNA	363
	Nuclear Pores Are a Selective Diffusion Barrier Between Nucleus and Cytoplasm	363
	Nuclear Proteins Accumulate Selectively in the Nucleus	365
	Cells Use Multiple Mechanisms to Segregate Proteins into Cellular Compartments	369
	Summary: The Nuclear Envelope	370
13-3	Chromatin	370
	The C-Value Paradox	370
	Chromatin Is a Complex of DNA and Histones	371
	Electron Microscopy of Chromatin Spreads Revealed a Beaded Structure	371
	The Nucleosome—An Octamer of Four Histones (H2A, H2B, H3, and H4) Complexed with 200 Base Pairs of DNA	372
	The 30 nm Fiber—A Nucleosome Solenoid	373
	Bacterial Chromosomes Are Not Complexed with Histones	376
	Chromatin Structure of Active Genes	376
	Summary: Chromatin	377
13-4	The Chromosomes	378
	Chromosomal Shape is Determined by the Position of the Centromere ..	378
	Chromosomal Nomenclature—Chromatid, Centromere, Telomere, Satellite, Secondary Constriction, Nucleolar Organizer	378

Karyotype—All the Characteristics of a Particular Chromosomal Set . . .	379
Each Chromatid Has a Single DNA Molecule	380
Metaphase Chromosomes are Symmetrical	380
Centromeric DNA Has Conserved Sequences	380
Chromosome Ends Can Be Cloned in Linear DNA Vectors in Yeast . . .	381
Interphase Chromosomal Arrangement—Random or Non-random? . . .	382
Chromosomes Are Made of Radial Loops of 30 nm Chromatin Fibers . .	383
13-5 Heterochromatin	387
Heterochromatin—Chromosomal Regions That Do Not Decondense	
During Interphase	387
Heterochromatin Can Be Facultative or Constitutive	387
Heterochromatin is Genetically Inactive	387
Constitutive Heterochromatin Contains Repetitive DNA Sequences . .	389
Summary: The Chromosomes and Heterochromatin	390
References	391
Additional Readings	392
Chapter 14 THE CELL CYCLE	394
14-1 The Cell Cycle	394
Interphase—The G ₁ , S, and G ₂ Phases	395
G ₁ —The Most Variable Period of the Cell Cycle	395
Visualization of Chromosomes During G ₁ , S, and G ₂ by Premature	
Condensation	397
Condensed Chromosomes do not Synthesize RNA	397
Several Molecular Events Occur at Defined Stages of the Cell Cycle . .	397
A Cytoplasmic Clock Times the Cell Cycle in Early Embryogenesis . .	399
Polypeptide Growth Factors Control Cell Proliferation	401
Summary: The Cell Cycle	403
14-2 DNA Replication	403
DNA Replication is Semiconservative	404
DNA Synthesis is Discontinuous on One Strand	405
Okasaki Fragments Start with an RNA Primer	406
Helix-Destabilizing Proteins and DNA Topoisomerases are Required for	
Replication	407
Reverse Transcriptase Can Copy RNA into DNA	408
Replication of the <i>E. coli</i> Chromosome is Bidirectional	408
Eukaryotic Chromosomes Have Multiple Origins of Replication	409
Eukaryotic DNA Synthesis is Bidirectional	410
The Number of Replicons is Developmentally Regulated	410
Eukaryotic Origins of Replication and the ARSes of Yeast	411
Reinitiation Within the Same Cycle is Prevented in Eukaryotic Cells . .	411
New Nucleosomes are Assembled Simultaneously with DNA	
Replication	412
RNA Synthesis Continues During DNA Replication	413
DNA Repair Enzymes Remove Thymine Dimers Induced by Ultraviolet	
Light— <i>Xeroderma Pigmentosum</i>	415
Summary: DNA Replication	416