



CELL BIOLOGY

SECOND EDITION

A SHORT COURSE

STEPHEN R. BOLSOVER
JEREMY S. HYAMS
ELIZABETH A. SHEPHARD
HUGH A. WHITE
CLAUDIA G. WIEDEMANN

CONTENTS

PREFACE, xv

ACKNOWLEDGMENTS, xvii

INSTRUCTOR NOTES, xix

* 1 CELLS AND TISSUES, 1

Principles of Microscopy, 2

The Light Microscope, 3

The Electron Microscope, 8

The Scanning Electron Microscope, 9

Only Two Types of Cell, 9

Special Properties of Plant Cells, 11

Viruses, 11

Origin of Eukaryotic Cells, 12

Cell Specialization, 12

Epithelia, 12

Connective Tissue, 13

Nervous Tissue, 13

Muscle, 14

Plants, 15

Summary, 16

Review Questions, 16

Answers to Review Questions, 17

* 2 FROM WATER TO DNA: THE CHEMISTRY OF LIFE, 19

The Chemical Bond: Sharing
Electrons, 19

Interactions with Water: Solutions, 21

Ionic Compounds Will Dissolve Only in
Polar Solvents, 21

Acids Are Molecules That Give H^+ to
Water, 21

Bases Are Molecules That Take H^+ from
Water, 25

Isoelectric Point, 25

A Hydrogen Bond Forms When a
Hydrogen Atom Is Shared, 25

Biological Macromolecules, 27

Carbohydrates: Candy and Canes, 27

An Assortment of Sweets, 27

Disaccharides, 28

Out of the Sweet Comes Forth
Strength, 30

Modified Sugars, 31

Nucleosides, Phosphate, and
Nucleotides, 35

Amino Acids, Polypeptides, and Proteins, 37

Lipids, 39

Hydrolysis, 44

Summary, 46

Further Reading, 47

Review Questions, 47

Answers to Review Questions, 48

* 3 MEMBRANES AND ORGANELLES, 51

Basic Properties of Cell Membranes, 51

Straight Through the Membrane:

Diffusion Through the Bilayer, 53

Beyond the Cell Membrane:

The Extracellular Matrix, 53

Cell Junctions, 54

Organelles Bounded by Double-Membrane
Envelopes, 56

The Nucleus, 56

Mitochondria and Chloroplasts, 58

Organelles Bounded by Single-Membrane Envelopes, 58
 Peroxisomes, 59
 Endoplasmic Reticulum, 60
 Golgi Apparatus, 60
 Lysosomes, 61
 Summary, 61
 Review Questions, 62
 Answers to Review Questions, 63

* 4 DNA STRUCTURE AND THE GENETIC CODE, 65

Introduction, 65
 The Structure of DNA, 65
 The DNA Molecule Is a Double Helix, 68
 The Two DNA Chains Are Complementary, 69
 Different Forms of DNA, 71
 DNA as the Genetic Material, 71
 Packaging of DNA Molecules into Chromosomes, 71
 Eukaryotic Chromosomes and Chromatin Structure, 71
 Prokaryotic Chromosomes, 73
 Plasmids, 74
 Viruses, 74
 The Genetic Code, 75
 Amino Acid Names Are Abbreviated, 79
 The Code Is Degenerate But Unambiguous, 79
 Start and Stop Codons and the Reading Frame, 79
 The Code Is Nearly Universal, 80
 Missense Mutations, 80
 Summary, 81
 Further Reading, 84
 Review Questions, 84
 Answers to Review Questions, 85

* 5 DNA AS A DATA STORAGE MEDIUM, 87

Introduction, 87

DNA Replication, 87
 The DNA Replication Fork, 88
 Proteins Open up the DNA Double Helix During Replication, 88
 DnaA Protein, 88
 DnaB and DnaC Proteins, 90
 Single-Strand Binding Proteins, 90
 Biochemistry of DNA Replication, 90
 DNA Synthesis Requires an RNA Primer, 90
 RNA Primers Are Removed, 92
 The Self-Correcting DNA Polymerase, 92
 DNA Repair, 94
 Spontaneous and Chemically Induced Base Changes, 94
 Repair Processes, 94
 Gene Structure and Organization in Eukaryotes, 98
 Introns and Exons—Additional Complexity in Eukaryotic Genes, 98
 The Major Classes of Eukaryotic DNA, 99
 Gene Nomenclature, 101
 Summary, 101
 Further Reading, 102
 Review Questions, 102
 Answers to Review Questions, 103

* 6 TRANSCRIPTION AND THE CONTROL OF GENE EXPRESSION, 105

Structure of RNA, 105
 RNA Polymerase, 106
 Gene Notation, 106
 Bacterial RNA Synthesis, 106
 Control of Bacterial Gene Expression, 109
 lac, an Inducible Operon, 111
 trp, a Repressible Operon, 116
 Eukaryotic RNA Synthesis, 118
 Messenger RNA Processing, 118
 Control of Eukaryotic Gene Expression, 119

Glucocorticoids Cross the Cell Membrane
to Activate Transcription, 121

Summary, 125

Further Reading, 125

Review Questions, 126

Answers to Review Questions, 127

* 7 RECOMBINANT DNA AND GENETIC ENGINEERING, 129

DNA Cloning, 129

Creating the Clone, 130

Introduction of Foreign DNA Molecules
into Bacteria, 130

Selection of cDNA Clones, 134

Genomic DNA Clones, 139

Uses of DNA Clones, 143

DNA Sequencing, 143

Southern Blotting, 146

In situ Hybridization, 147

Northern Blotting, 148

Production of Mammalian Proteins in
Bacteria, 149

Protein Engineering, 149

Polymerase Chain Reaction, 150

Identifying the Gene Responsible for a
Disease, 152

Reverse Genetics, 152

Transgenic Animals, 157

Ethics of DNA Testing for Inherited
Disease, 157

Summary, 158

Further Reading, 159

Review Questions, 159

Answers to Review Questions, 160

* 8 MANUFACTURING PROTEIN, 163

Attachment of an Amino Acid to Its
tRNA, 163

Transfer RNA, the Anticodon, and the
Wobble, 164

The Ribosome, 165

Bacterial Protein Synthesis, 168

Ribosome-Binding Site, 168

Chain Initiation, 169

The 70S Initiation Complex, 171

Elongation of the Protein Chain, 171

The Polyribosome, 173

Termination of Protein Synthesis, 174

The Ribosome Is Recycled, 175

Eukaryotic Protein Synthesis Is a Little
More Complex, 175

Antibiotics and Protein Synthesis, 176

Summary, 178

Further Reading, 179

Review Questions, 179

Answers to Review Questions, 180

* 9 PROTEIN STRUCTURE, 183

Naming Proteins, 184

Polymers of Amino Acids, 184

The Amino Acid Building Blocks, 184

The Unique Properties of Each Amino
Acid, 188

Other Amino Acids Are Found in
Nature, 191

The Three-Dimensional Structures of
Proteins, 192

Hydrogen Bonds, 195

Electrostatic Interactions, 199

van der Waals Forces, 199

Hydrophobic Interactions, 199

Disulfide Bonds, 199

Tertiary Structure: Domains and
Motifs, 200

Quaternary Structure: Assemblies of Protein
Subunits, 204

Prosthetic Groups, 205

The Primary Structure Contains all the
Information Necessary to Specify
Higher-Level Structures, 206

Summary, 209

Further Reading, 209

Review Questions, 210

Answers to Review Questions, 211

* 10 INTRACELLULAR PROTEIN TRAFFICKING, 213

- Three Modes of Intracellular Protein Transport, 213
 - Targeting Sequences, 215
 - Retention, 215
- Transport to and from the Nucleus, 215
 - The Nuclear Pore Complex, 216
 - Gated Transport Through the Nuclear Pore, 216
 - GTPases and the GDP/GTP Cycle, 218
 - GTPases in Nuclear Transport, 218
- Transport Across Membranes, 221
 - Transport to Mitochondria, 221
 - Chaperones and Protein Folding, 221
 - Transport to Peroxisomes, 221
 - Synthesis on the Rough Endoplasmic Reticulum, 223
 - Glycosylation: The Endoplasmic Reticulum and Golgi System, 225
- Vesicular Trafficking Between Intracellular Compartments, 226
 - The Principle of Fission and Fusion, 226
 - Vesicle Formation, 228
 - Coatomer-Coated Vesicles, 228
 - Clathrin-Coated Vesicles, 229
 - The Trans-Golgi Network and Protein Secretion, 229
 - Targeting Proteins to the Lysosome, 230
 - Fusion, 231
- Summary, 232
- Further Reading, 233
- Review Questions, 233
- Answers to Review Questions, 234

* 11 HOW PROTEINS WORK, 237

- How Proteins Bind Other Molecules, 237
- Dynamic Protein Structures, 238
- Allosteric Effects, 238
- Chemical Changes That Shift the Preferred Shape of a Protein, 240
- Enzymes Are Protein Catalysts, 241

- The Initial Velocity of an Enzyme Reaction, 242
- Effect of Substrate Concentration on Initial Velocity, 244
- The Effect of Enzyme Concentration, 245
- The Specificity Constant, 247
- Enzyme Catalysis, 247
- Cofactors and Prosthetic Groups, 249
- Enzymes Can Be Regulated, 251
- Summary, 254
- Further Reading, 254
- Review Questions, 255
- Answers to Review Questions, 256

* 12 ENERGY TRADING WITHIN THE CELL, 257

- Cellular Energy Currencies, 258
 - Reduced Nicotinamide Adenine Dinucleotide (NADH), 259
 - Nucleoside Triphosphates (ATP plus GTP, CTP, TTP, and UTP), 259
 - The Hydrogen Ion Gradient Across the Mitochondrial Membrane, 261
 - The Sodium Gradient Across the Plasma Membrane, 262
- Energy Currencies Are Interconvertible, 263
 - Exchange Mechanisms Convert Between the Four Energy Currencies, 263
 - Electron Transport Chain, 265
 - ATP Synthase, 269
 - Sodium/Potassium ATPase, 270
 - ADP/ATP Exchanger, 271
 - Photosynthesis, 271
 - All Carriers Can Change Direction, 275
- Summary, 278
- Further Reading, 278
- Review Questions, 278
- Answers to Review Questions, 279

* 13 METABOLISM, 281

- The Krebs Cycle: The Central Switching Yard of Metabolism, 283

- From Glucose to Pyruvate: Glycolysis, 284
 - Glycolysis Without Oxygen, 286
 - Glycogen Can Provide Glucose for Glycolysis, 288
 - Glucose May Be Oxidized to Produce Pentose Sugars, 289
 - From Fats to Acetyl-CoA: β Oxidation, 290
 - Amino Acids as Another Source of Metabolic Energy, 292
 - Making Glucose: Gluconeogenesis, 295
 - Making Glycogen: Glycogenesis, 298
 - Making Fatty Acids and Glycerides, 300
 - Synthesis of Amino Acids, 300
 - Carbon Fixation in Plants, 302
 - Control of Energy Production, 303
 - Feedback and Feedforward, 303
 - Negative Feedback Control of Glycolysis, 304
 - Feedforward Control in Muscle Cells, 304
 - Summary, 306
 - Further Reading, 306
 - Review Questions, 307
 - Answers to Review Questions, 308
- * 14 IONS AND VOLTAGES, 309**
- The Potassium Gradient and the Resting Voltage, 309
 - Potassium Channels Make the Plasma Membrane Permeable to Potassium Ions, 310
 - Concentration Gradients and Electrical Voltage Can Balance, 311
 - The Chloride Gradient, 314
 - General Properties of Channels, 314
 - General Properties of Carriers, 316
 - The Glucose Carrier, 316
 - The Sodium–Calcium Exchanger, 317
 - Carriers with an Enzymatic Action: The Calcium ATPase, 318
 - Summary, 322
 - Further Reading, 322
 - Review Questions, 322
 - Answers to Review Questions, 324
- * 15 THE ACTION POTENTIAL, 325**
- The Calcium Action Potential in Sea Urchin Eggs, 325
 - Effect of Egg Transmembrane Voltage on Sperm Fusion, 325
 - The Voltage-Gated Calcium Channel, 327
 - The Calcium Action Potential, 328
 - The Voltage-Gated Sodium Channel in Nerve Cells, 330
 - The Voltage-Gated Sodium Channel, 330
 - Electrical Transmission down a Nerve Cell Axon, 332
 - Myelination and Rapid Action Potential Transmission, 334
 - Summary, 337
 - Further Reading, 338
 - Review Questions, 338
 - Answers to Review Questions, 339
- * 16 INTRACELLULAR SIGNALING, 341**
- Calcium, 341
 - Calcium Can Enter from the Extracellular Medium, 341
 - Calcium Can Be Released from the Endoplasmic Reticulum, 344
 - Processes Activated by Cytosolic Calcium Are Extremely Diverse, 348
 - Return of Calcium to Resting Levels, 350
 - Cyclic Adenosine Monophosphate, 350
 - Cyclic Guanosine Monophosphate, 353
 - Multiple Messengers, 353
 - Biochemical Signaling, 353
 - Receptor Tyrosine Kinases and the MAP Kinase Cascade, 353
 - Growth Factors Can Trigger a Calcium Signal, 356
 - Protein Kinase B and the Glucose Transporter: How Insulin Works, 356

Crosstalk—Signaling Pathways or Signaling Webs?, 357

Summary, 359

Further Reading, 360

Review Questions, 360

Answers to Review Questions, 361

* 17 INTERCELLULAR COMMUNICATION, 363

Classifying Transmitters and Receptors, 363

Ionotropic Cell Surface Receptors, 364

Metabotropic Cell Surface Receptors, 365

Intracellular Receptors, 365

Intercellular Communication in Action:

The Gastrocnemius Muscle, 365

Telling the Muscle to Contract:

The Action of Motoneurons, 367

Controlling the Blood Supply: Paracrine Transmitters, 368

New Blood Vessels in Growing Muscle, 371

Synapses Between Neurons, 372

Summary, 376

Further Reading, 377

Review Questions, 377

Answers to Review Questions, 378

* 18 MECHANICAL MOLECULES, 381

The Cytoskeleton is Both Strong and Motile, 381

Microtubules, 381

Microtubule-Based Motility, 386

Cilia and Flagella, 386

Intracellular Transport, 389

Microfilaments, 390

Muscle Contraction, 393

Cell Locomotion, 395

Cytoplasmic Streaming, 395

Intermediate Filaments, 396

Anchoring Cell Junctions, 396

Summary, 398

Further Reading, 398

Review Questions, 398

Answers to Review Questions, 400

* 19 CELL CYCLE AND CONTROL OF CELL NUMBER, 401

Stages of Mitosis, 402

Meiosis and Fertilization, 404

Meiosis, 405

Fertilization and Inheritance, 406

Dominant Genetic Disease, 408

Crossing Over and Linkage, 408

Control of the Cell Division Cycle, 408

Molecular Regulation of the G₂/M (Interphase/Mitosis) Cell Cycle Control Point, 410

What About the G₁/S Control Point?, 412

Apoptosis, 415

Instructed Death: Death Domain Receptors, 416

Default Death: Absence of Growth Factors, 416

The Sick Are Left to Die:

Stress-Activated Apoptosis, 417

Summary, 419

Further Reading, 420

Review Questions, 420

Answers to Review Questions, 421

* 20 CASE STUDY: CYSTIC FIBROSIS, 423

Introduction, 423

Cystic Fibrosis is a Severe Genetic Disease, 423

The Fundamental Lesion in Cystic Fibrosis Lies in Chloride Transport, 424

Homing in on the *CF* Gene, 425

Cloning the Gene for *CF*, 426

The *CFTR* Gene Codes for a Chloride Ion Channel, 426

Gene Therapy for *CF*, 427

Diagnostic Tests for *CF*, 431

CONTENTS

xiii

The Future, 432

Summary, 433

Further Reading, 433

Review Questions, 434

Answers to Review Questions, 435

APPENDIX: CHANNELS AND
CARRIERS, 437

GLOSSARY, 441

INDEX, 501