

# *Contents in Brief*

|                                       |   |
|---------------------------------------|---|
| Introduction                          |   |
| The History of Molecular Cell Biology | 1 |

|  |    |
|--|----|
| <i>PART I</i>  |    |
| <b>Molecules, Cells, Proteins, and<br/>Experimental Techniques: A Primer</b> | 17 |

|   |   |     |
|---|---|-----|
| 1 | Chemical Foundations  | 19  |
| 2 | Molecules in Cells  | 43  |
| 3 | Synthesis of Proteins and Nucleic<br>Acids                  | 85  |
| 4 | The Study of Cell Organization and<br>Subcellular Structure | 109 |
| 5 | Growing and Manipulating Cells and<br>Viruses               | 151 |
| 6 | Manipulating Macromolecules                                 | 189 |

|  |     |
|--|-----|
| <i>PART II</i>   |     |
| <b>Gene Expression, Structure, and<br/>Replication</b> | 227 |

|   |  |     |
|---|--|-----|
| 7 | RNA Synthesis and Gene Control in<br>Prokaryotes | 229 |
| 8 | RNA Synthesis and Processing in<br>Eukaryotes    | 261 |

|                                    |   |     |  |   |  |     |
|------------------------------------|---|-----|--|---|--|-----|
| 9                                  | The Structure of Eukaryotic Chromosomes                                     | 317 | 18   | Organelle Biogenesis: The Nucleus, Chloroplast, and Mitochondrion         | 681  |     |
| 10                                 | Eukaryotic Chromosomes and Genes: Molecular Anatomy                         | 347 | 19   | Cell-to-Cell Signaling: Hormones and Receptors                            | 709  |     |
| 11                                 | Gene Control and the Molecular Genetics of Development in Eukaryotes        | 391 | 20   | Nerve Cells and the Electric Properties of Cell Membranes                 | 763  |     |
| 12                                 | DNA Replication, Repair, and Recombination                                  | 449 | 21   | Microtubules and Cellular Movements                                       | 815  |     |
| <b>PART III</b>                    |   |     | 22   | Actin, Myosin, and Intermediate Filaments: Cell Movements and Cell Shapes | 859  |     |
| <b>Cell Structure and Function</b> |   |     | 489  | 23  | Multicellularity: Cell-Cell and Cell-Matrix Interactions | 903 |
| 13                                 | The Plasma Membrane   | 491 | <b>PART IV</b>   |   |  |     |
| 14                                 | Transport across Cell Membranes   | 531 | <b>The New Biology: Facing Classic Questions at the Frontier</b> |   |  |     |
| 15                                 | Energy Conversion: The Formation of ATP in Mitochondria and Bacteria        | 583 | 24   | Cancer  | 955  |     |
| 16                                 | Photosynthesis  | 617 | 25   | Immunity  | 1003   |     |
| 17                                 | Plasma-membrane, Secretory, and Lysosome Proteins: Biosynthesis and Sorting | 639 | 26   | Evolution of Cells  | 1049   |     |
|                                    |   |     |  | Index   | 1077   |     |

# Contents

|   |       |
|---|-------|
| <i>Chapter-opening Illustrations</i>  | xxxix |
| <i>INTRODUCTION The History of Molecular Cell Biology</i>   | 1     |
| <i>Evolution and the Cell Theory</i>  | 2     |
| The Theory of Evolution Arises from Naturalistic Studies  | 2     |
| The Cell Theory Comes to Prominence through Improved Microscopic Techniques and Recognition That Single Cells Can Grow and Divide       | 3     |
| <i>Classical Biochemistry and Genetics</i>  | 4     |
| Biochemistry Begins with the Demonstration That Chemical Transformations Can Take Place in Cell Extracts                                | 4     |
| Classical Genetics Begins with the Controlled Breeding Studies of Gregor Mendel   | 5     |
| Chromosomes Are Identified as the Carriers of the Mendelian Theory of Heredity  | 7     |
| The Reduction of Chromosome Numbers in Meiosis That Forms Germ Cells Is Crucial to the Development of the Chromosome Theory of Heredity | 7     |
| Chromosomes Are Shown to Contain Linear Arrays of Genes That Can Undergo Reordering   | 8     |

|   |    |  |    |
|---|----|--|----|
| <i>The Merging of Genetics and Biochemistry</i>   | 9  | Acids Release Hydrogen Ions and Bases<br>Combine with Hydrogen Ions  | 29 |
| <i>Drosophila</i> Studies Establish the Connection<br>between Gene Activity and Biochemical<br>Action; <i>Neurospora</i> Experiments Confirm<br>That One Gene Controls One Enzyme | 9  | Many Biological Molecules Contain Multiple<br>Acidic or Basic Groups   | 29 |
| DNA Is Identified as the Genetic Material,<br>Paving the Way for the Study of the<br>Molecular Basis of Gene Structure and<br>Function  | 10 | <i>The Direction of Chemical Reactions</i>   | 31 |
| <i>The Birth of Molecular Biology</i>   | 11 | The Change in Free Energy $\Delta G$ Determines<br>the Direction of a Chemical Reaction                      | 31 |
| Watson and Crick Deduce the Double-helical<br>Structure of DNA  | 11 | The Generation of a Concentration Gradient<br>Requires an Expenditure of Energy                              | 33 |
| X-ray Crystallography Facilitates the<br>Construction of Three-dimensional Models of<br>Complex Biological Molecules  | 11 | Many Cellular Processes Involve the Transfer<br>of Electrons in Oxidation-Reduction<br>Reactions             | 34 |
| Biochemical Experiments Have Elucidated the<br>Relationship between Enzymes and Metabolic<br>Pathways   | 12 | An Unfavorable Chemical Reaction Can<br>Proceed if It Is Coupled with an Energetically<br>Favorable Reaction | 35 |
| <i>A Modern View of Cell Structure</i>  | 12 | Hydrolysis of the Phosphoanhydride Bonds in<br>ATP Releases Substantial Free Energy                          | 35 |
| Advances in Electron Microscopy Reveal the<br>Commonality of Structures within Eukaryotic<br>Cells  | 12 | ATP Is Used to Fuel Many Cellular Processes  | 37 |
| Biochemical Activities Can Be Assigned to<br>Specific Subcellular Structures  | 13 | <i>Activation Energy and Reaction Rate</i>   | 38 |
| The Activity of Genes Is Highly Regulated by<br>the Protein Products of Other Genes   | 13 | Energy Is Required to Initiate a Reaction  | 39 |
| The Molecular Approach Is Applied to<br>Eukaryotic Cells  | 13 | Enzymes Catalyze Biochemical Reactions   | 39 |
| <i>References</i>   | 14 | <i>Summary</i>   | 41 |
|   |    | <i>References</i>  | 41 |
|   |    | <b>CHAPTER 2 <i>Molecules in Cells</i></b>   | 43 |
|   |    | <i>Proteins</i>  | 44 |
|   |    | Amino Acids—the Building Blocks of<br>Proteins—Differ Only in Their Side Chains                              | 44 |
|   |    | Polypeptides Are Polymers Composed of<br>Amino Acids Connected by Peptide Bonds                              | 46 |
|   |    | Three-dimensional Protein Structure Is<br>Determined through X-ray Crystallography                           | 46 |
|   | 17 | The Structure of a Polypeptide Can Be<br>Described at Four Levels  | 47 |
|   | 19 | Two Regular Secondary Structures Are<br>Particularly Important   | 48 |
|   | 20 | Many Proteins Are Organized into Domains   | 50 |
|   | 20 | Regions of Similar Architecture Often Have<br>Similar Sequences  | 51 |
|   | 20 | Many Proteins Contain Tightly Bound<br>Prosthetic Groups   | 52 |
|   | 23 | Covalent Modifications Affect the Structures<br>and Functions of Proteins                                    | 53 |
|   | 27 | The Native Conformation of a Protein Can<br>Be Denatured by Heat or Chemicals                                | 54 |
|   | 28 | Many Denatured Proteins Can Renature into<br>Their Native State  | 54 |
|   | 28 |  |    |



## **PART I** **Molecules, Cells, Proteins, and Experimental Techniques: A Primer**

### **CHAPTER 1 *Chemical Foundations***

#### *Energy*

#### *Chemical Bonds*

The Most Stable Bonds between Atoms Are  
Covalent

Noncovalent Bonds Stabilize the Structures of  
Biological Molecules

#### *Chemical Equilibrium*

#### *pH and the Concentration of Hydrogen Ions*

Water Dissociates into Hydronium and  
Hydroxyl Ions

|  |    |  |     |
|--|----|--|-----|
| <b>Enzymes</b>   | 55 | Glycolipids of Various Structures Are Found in the Cell Surface Membrane                   | 81  |
| Certain Amino Acids in Enzymes Bind Substrates: Others Catalyze Reactions on the Bound Substrates            | 56 | <b>The Primacy of Proteins</b>   | 82  |
| Trypsin and Chymotrypsin Are Well-characterized Proteolytic Enzymes  | 56 | <b>Summary</b>   | 82  |
| Coenzymes Are Essential for Certain Enzymatically Catalyzed Reactions  | 59 | <b>References</b>  | 83  |
| Substrate Binding May Induce a Conformational Change in the Enzyme   | 60 | <b>CHAPTER 3 Synthesis of Proteins and Nucleic Acids</b>                                   | 85  |
| The Catalytic Activity of an Enzyme Can Be Characterized by a Few Numbers                                    | 61 | <b>Rules for the Synthesis of Proteins and Nucleic Acids</b>                               | 86  |
| The Actions of Most Enzymes Are Regulated  | 62 | <b>Protein Synthesis: The Three Roles of RNA</b>   | 87  |
| <b>Antibodies</b>  | 65 | Messenger RNA Carries Information from DNA in a Three-Letter Genetic Code                  | 88  |
| Antibodies Can Distinguish among Closely Similar Molecules   | 65 | Synthetic mRNA and Trinucleotides Break the Code   | 89  |
| Antibodies Are Valuable Tools for Identifying and Purifying Proteins   | 66 | The Anticodon of Transfer RNA Decodes mRNA by Base Pairing with Its Codon                  | 91  |
| <b>Nucleic Acids</b>   | 66 | Aminoacyl-tRNA Synthetases Activate tRNA   | 93  |
| Nucleic Acids Are Linear Polymers of Nucleotides Connected by Phosphodiester Bonds                           | 66 | Each tRNA Molecule Must Be Identifiable by a Specific tRNA Synthetase                      | 94  |
| <b>DNA</b>   | 68 | Ribosomes Are Protein-synthesizing Machines  | 95  |
| The Native State of DNA Is a Double Helix of Two Antiparallel Chains with Complementary Nucleotide Sequences | 69 | <b>The Steps in Protein Synthesis</b>  | 99  |
| DNA Is Denatured When the Two Strands Are Made to Separate   | 71 | AUG Is the Initiation Signal in mRNA   | 99  |
| Many DNA Molecules Are Circular  | 72 | Initiation Factors, tRNA, mRNA, and the Small Ribosomal Subunit Form an Initiation Complex | 100 |
| Many Closed Circular DNA Molecules Are Supercoiled   | 72 | Ribosomes Use Two tRNA-binding Sites (A and P) during Protein Elongation                   | 100 |
| RNA Is Usually Single-stranded and Serves Many Different Functions   | 73 | UAA, UGA, and UAG Are the Termination Codons   | 101 |
| <b>Lipids and Biomembranes</b>   | 75 | Rare tRNAs Suppress Nonsense Mutations   | 101 |
| Fatty Acids Are the Principal Components of Membranes and Lipids   | 75 | <b>Nucleic Acid Synthesis</b>  | 101 |
| Phospholipids Are Key Components of Biomembranes   | 76 | Nucleic Acid Synthesis Can Be Described by Five Rules                                      | 101 |
| Certain Steroids Are Components of Biomembranes  | 76 | Chemical Differences between RNA and DNA Provide Functional Properties                     | 106 |
| Phospholipids Spontaneously Form Micelles or Bilayers in Aqueous Solutions                                   | 77 | <b>Summary</b>   | 107 |
| <b>Carbohydrates</b>   | 77 | <b>References</b>  | 107 |
| Many Important Sugars Are Hexoses  | 77 | <b>CHAPTER 4 The Study of Cell Organization and Subcellular Structure</b>                  | 109 |
| Polymers of Glucose Serve as Storage Reservoirs  | 79 | <b>Prokaryotic and Eukaryotic Cells</b>  | 111 |
| Glycoproteins Are Composed of Proteins Covalently Bound to Sugars  | 80 | Prokaryotes Have a Simpler Structure Than Eukaryotes                                       | 111 |
|  |    | Eukaryotic Cells Have Complex Systems of Internal Membranes and Fibers                     | 113 |

|  |     |  |     |
|--|-----|--|-----|
| Prokaryotes and Eukaryotes Contain Similar Macromolecules                                      | 114 | Proteins Are Secreted by the Fusion of an Intracellular Vesicle with the Plasma Membrane               | 139 |
| Prokaryotes and Eukaryotes Differ in the Amount of DNA per Cell                                | 116 | Small Vesicles May Shuttle Membrane Constituents from One Organelle to Another                         | 140 |
| The Organization of DNA Differs in Prokaryotic and Eukaryotic Cells                            | 116 | Lysosomes Contain a Battery of Degradative Enzymes That Function at pH 5                               | 140 |
| <b>Light Microscopy and Cell Architecture</b>  | 117 | Vacuoles in Plant Cells Store Small Molecules and Enable the Cell to Elongate Rapidly                  | 142 |
| Standard Light (Bright-field) Microscopy Utilizes Fixed, Stained Specimens                     | 118 | Contractile Vacuoles in Certain Protozoans Function in Osmotic Regulation                              | 143 |
| Immunofluorescence Microscopy Reveals Specific Proteins and Organelles within a Cell           | 120 | Peroxisomes Produce and Degrade Hydrogen Peroxide  | 144 |
| The Confocal Scanning Microscope Produces Vastly Improved Fluorescent Images                   | 122 | The Mitochondrion Is the Principal Site of ATP Production in Aerobic Cells                             | 144 |
| Dark-field Microscopy Allows Detection of Small Refractile Objects                             | 123 | Chloroplasts Are the Sites of Photosynthesis   | 145 |
| Phase-contrast and Nomarski Interference Microscopy Visualize Living Cells                     | 125 | The Plasma Membrane Has Many Varied and Essential Roles  | 145 |
| <b>Electron Microscopy</b>   | 126 | Cilia and Flagella Are Motile Extensions of the Eukaryotic Plasma Membrane                             | 145 |
| Transmission Electron Microscopy Depends on the Differential Scattering of a Beam of Electrons | 126 | Microvilli Enhance the Absorption of Nutrients   | 146 |
| Minute Details Can Be Visualized on Viruses and Subcellular Particles                          | 127 | The Plasma Membrane Binds to the Cell Wall or the Extracellular Matrix                                 | 146 |
| Scanning Electron Microscopy Visualizes Detail on the Surface of Cells or Particles            | 128 | <b>Summary</b>   | 148 |
| <b>Sorting Cells and Their Parts</b>   | 129 | <b>References</b>  | 148 |
| Flow Cytometry Is Used to Sort Cells   | 129 |  |     |
| Fractionation Methods Isolate Subcellular Structures   | 130 | <b>CHAPTER 5 Growing and Manipulating Cells and Viruses</b>  | 151 |
| Velocity Centrifugation Separates on the Basis of Size and Density                             | 132 | <b>Types of Cell Division</b>  | 152 |
| Equilibrium Density-gradient Centrifugation Separates Materials by Density Alone               | 133 | <b>The Cell Cycle in Prokaryotes Consists of DNA Replication Followed Immediately by Cell Division</b> | 152 |
| Immunological Techniques Can Yield Pure Preparations of Certain Organelles                     | 133 | <b>Eukaryotic DNA Synthesis Occurs in a Special Phase of the Cell Cycle</b>                            | 152 |
| <b>The Organelles of the Eukaryotic Cells</b>  | 134 | Mitosis Is the Complex Process That Apportions the New Chromosomes Equally to Daughter Cells           | 154 |
| The Eukaryotic Nucleus Is Bound by a Double Membrane   | 134 | Meiosis Is the Form of Cell Division in Which Haploid Cells Are Produced from Diploid Cells            | 156 |
| The Nucleus Contains the Nucleolus, A Fibrous Matrix, And DNA-Protein Complexes                | 134 | <b>The Growth of Microorganisms and Cells in Culture</b>   | 159 |
| The Cytosol Contains Many Cytoskeletal Elements and Particles                                  | 136 | <i>Escherichia coli</i> Is a Favorite Organism of Molecular Biologists                                 | 159 |
| The Endoplasmic Reticulum Is an Interconnected Network of Internal Membranes                   | 138 | Genes Can Be Transferred between Bacteria in Three Ways  | 161 |
| Golgi Vesicles Process Secretory Proteins and Partition Cellular Proteins and Membranes        | 139 |  |     |

|   |     |   |     |
|---|-----|---|-----|
| The Yeast Life Cycle Includes Haploid and Diploid Phases  | 164 | Labeled Precursors Can Trace the Assembly of Macromolecules and Their Distribution in a Cell    | 193 |
| Cultured Animal Cells Share Certain Growth Requirements and Capacities  | 166 | <i>Determining the Size of Nucleic Acids and Proteins</i>                                       | 194 |
| <i>Cell Fusion: An Important Technique in Somatic-Cell Genetics</i>   | 170 | Centrifugation Is Used to Separate Particles and Molecules that Differ in Mass or Density       | 195 |
| Hybrid Cells Containing Chromosomes from Different Mammals Assist in Gene-mapping Studies                             | 170 | Electrophoresis Separates Molecules According to Their Charge-Mass Ratio                        | 198 |
| Mutants in Salvage Pathways of Purine and Pyrimidine Synthesis Are Good Selective Markers                             | 171 | Gel Electrophoresis Can Separate Most Proteins in a Cell  | 200 |
| Hybridomas Are Fused Lymphoid Cells That Make Monoclonal Antibodies   | 172 | In Vitro Protein Synthesis and Gel Electrophoresis Provide an Assay for Messenger RNA           | 201 |
| <i>DNA Transfer into Eukaryotic Cells</i>   | 173 | <i>Examining the Sequences of Nucleic Acids and Proteins</i>                                    | 202 |
| Yeast Cells Exhibit Homologous Recombination of Foreign DNA in Contrast to Nonspecific Integration in Mammalian Cells | 173 | Molecular Hybridization of Two Nucleic Acid Strands Can Be Detected in Several Ways             | 202 |
| Foreign DNA Can Be Introduced into the Germ Line of Animals to Produce Transgenic Strains                             | 174 | Fingerprinting (Partial Sequence Analysis) Allows Quick Comparisons of Macromolecules           | 206 |
| Plants Can Be Regenerated from Plant Cell Cultures  | 175 | Restriction Enzymes Allow the Precise Mapping of Specific Sites in DNA                          | 206 |
| <i>Viruses: Structures and Function</i>   | 176 | The Sequence of Nucleotides in Long Stretches of DNA Can Be Rapidly Determined                  | 212 |
| Most Viral Host Ranges Are Narrow   | 178 | Proteins Can Be Sequenced Automatically   | 213 |
| Viruses Can Be Accurately Counted   | 179 | <i>Recombinant DNA: Selection and Production of Specific DNA</i>                                | 214 |
| Viral Growth Cycles Can Be Divided into Stages  | 179 | cDNA Clones Are Whole or Partial Copies of mRNA   | 215 |
| Bacterial Viruses Are Widely Used to Investigate Biochemical and Genetic Events                                       | 180 | Genomic Clones Are Copies of DNA from Chromosomes   | 217 |
| Plant Viruses Proved That RNA Can Act as a Genetic Material   | 181 | Vectors for Recombining DNA Exist in Many Cell Types  | 218 |
| Animal Viruses Are Very Diverse   | 181 | The Polymerase Chain Reaction Amplifies Specific DNA Sequences in a Mixture                     | 219 |
| <i>Summary</i>  | 186 | <i>Controlled Deletions and Base-specific Mutagenesis of DNA</i>                                | 219 |
| <i>References</i>   | 186 | <i>Synthetic Peptide and Nucleotide Sequences: Their Use in Isolating and Identifying Genes</i> | 220 |
| <b>CHAPTER 6 Manipulating Macromolecules</b>  | 189 | <i>Summary</i>  | 222 |
| <i>Radioisotopes: The Indispensable Modern Means of Following Biological Activity</i>                                 | 190 | <i>References</i>   | 223 |
| Radioisotopes Are Detected by Autoradiology or by Quantitative Assays   | 191 |   |     |
| Pulse-chase Experiments Must Be Designed with Knowledge of the Cell's Pool of Amino Acids and Nucleotides             | 192 |   |     |