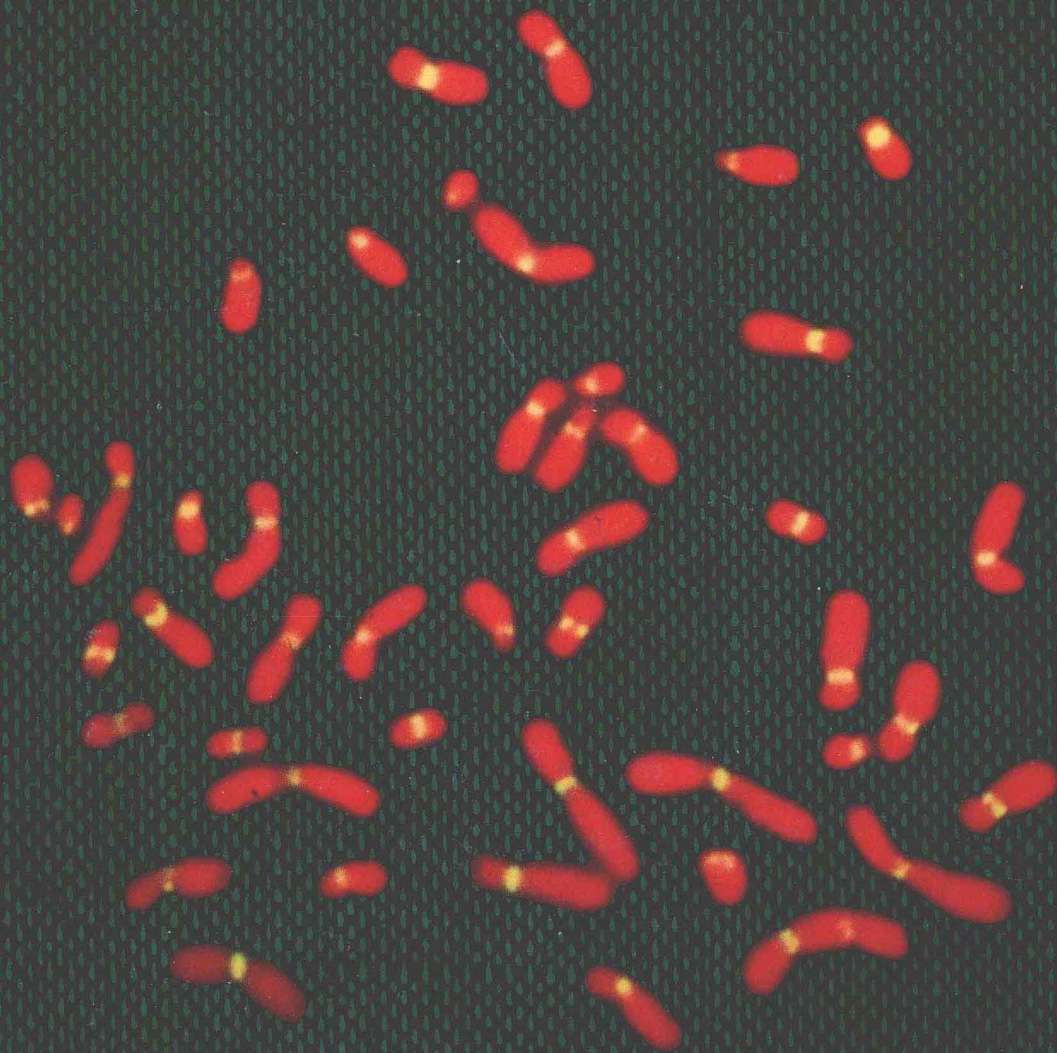


MOLECULAR BIOLOGY OF THE CELL

SECOND EDITION



Bruce Alberts • Dennis Bray • Julian Lewis
Martin Raff • Keith Roberts • James D. Watson

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Garland Publishing, Inc.
New York & London

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Library of Congress Cataloging-in-Publication Data

Molecular biology of the cell / Bruce Alberts . . . [et al.].—2nd ed.
p. cm.

Includes bibliographies and index.

ISBN 0-8240-3695-6.—ISBN 0-8240-3696-4 (pbk.)

1. Cytology. 2. Molecular biology. I. Alberts, Bruce.

[DNLN: 1. Cells. 2. Molecular Biology. QH 581.2 M718]

QH581.2.M64 1989

574.87—dc19

DNLN/DLC

for Library of Congress

88-38275

CIP

Published by Garland Publishing, Inc.
136 Madison Avenue, New York, NY 10016

Printed in the United States of America

15 14 13 12 11 10 9 8 7 6 5 4 3

Preface to the Second Edition

More than 50 years ago, E.B. Wilson wrote that “the key to every biological problem must finally be sought in the cell.” Yet, until very recently, cell biology was usually taught to biology majors as a specialized upper-level course based largely on electron microscopy. And in most medical schools, many cell-biological topics, such as the mechanisms of endocytosis, chemotaxis, cell movement, and cell adhesion, were hardly taught at all—being regarded as too cellular for biochemistry and too molecular for histology. With the recent dramatic advances in our understanding of cells, however, cell biology is beginning to take its rightful place at the center of biological and medical teaching. In an increasing number of universities, it is a required full-year course for all undergraduate biology and biochemistry majors and is becoming the organizing theme for much of the first-year medical curriculum. The first edition of *Molecular Biology of the Cell* was written in anticipation of these much needed curriculum reforms and in the hope of catalyzing them. We will be gratified if the second edition helps to accelerate and spread these reforms.

In revising the book, we have found few cases where recent discoveries have proved old conclusions wrong. But in the six years since the first edition appeared, a fantastically rich harvest of new information about cells has uncovered new connections and in many places forced a radical change of emphasis. The present revision, therefore, goes deep: every chapter has undergone substantial changes, many have been almost entirely rewritten, and two new chapters—on the control of gene expression and on cancer—have been added.

Some commentators on the first edition, especially teachers, wanted more detailed discussion of the experimental evidence that supports the concepts discussed. We did not wish to disrupt the conceptual flow or to enlarge an already very large book; but we agree that it is crucial to give students a sense of how advances are made. To this end, John Wilson and Tim Hunt have written a Problems Book to accompany the central portion of the main text (Chapters 5–14). As explained in the Note to the Reader on page xxxv, each section of *The Problems Book* covers a section of *Molecular Biology of the Cell* and takes as its principal focus a set of experiments drawn from the relevant research literature. These are the basis for a series of questions—some easy and some hard—that are meant to involve the reader actively in the reasoning that underlies the process of discovery.

The second edition, like the first, has been a long time in the making. As before, each chapter has been passed back and forth between the author who wrote the first draft and the other authors for criticism and extensive revision, so that every part of the book represents a joint composition; Tim Hunt and John Wilson often helped in this process. In addition, outside experts were invited to make suggestions for revision and, in a few cases, to contribute material for the text, which the authors reworked to fit with the rest of the book. We are especially indebted to James Rothman (Princeton University) for his contribution to Chapter 8 and to Jeremy Hyams (University College London), Tim Mitchison (University of California, San Francisco), and Paul Nurse (University of Oxford) for their contributions to Chapter 13. All sections of the revised text were read by outside experts, whose comments and suggestions were invaluable; a list of acknowledgments is on page xxxiii.

Miranda Robertson again played a major part in the creation of a readable book, by insisting that every page be lucid and coherent and rewriting many pages that were not. We are also indebted to the staff at Garland Publishing, and in particular to Ruth Adams, Alison Walker, and Gavin Borden, for their kindness, good humour, efficiency, and unfailingly generous support during the four years that it has taken to prepare this edition. Special thanks go to Carol Winter, for her painstaking care in typing the entire book and preparing the disks for the printer.

Finally, to our wives, families, colleagues, and students we again offer our gratitude and apologies for several years of impositions and neglect; without their help and tolerance this book could not have been written.

Preface to the First Edition

There is a paradox in the growth of scientific knowledge. As information accumulates in ever more intimidating quantities, disconnected facts and impenetrable mysteries give way to rational explanations, and simplicity emerges from chaos. Gradually the essential principles of a subject come into focus. This is true of cell biology today. New techniques of analysis at the molecular level are revealing an astonishing elegance and economy in the living cell and a gratifying unity in the principles by which cells function. This book is concerned with those principles. It is not an encyclopedia but a guide to understanding. Admittedly, there are still large areas of ignorance in cell biology and many facts that cannot yet be explained. But these unsolved problems provide much of the excitement, and we have tried to point them out in a way that will stimulate readers to join in the enterprise of discovery. Thus, rather than simply present disjointed facts in areas that are poorly understood, we have often ventured hypotheses for the reader to consider and, we hope, to criticize.

Molecular Biology of the Cell is chiefly concerned with eucaryotic cells, as opposed to bacteria, and its title reflects the prime importance of the insights that have come from the molecular approach. Part I and Part II of the book analyze cells from this perspective and cover the traditional material of cell biology courses. But molecular biology by itself is not enough. The eucaryotic cells that form multicellular animals and plants are social organisms to an extreme degree: they live by cooperation and specialization. To understand how they function, one must study the ways of cells in multicellular communities, as well as the internal workings of cells in isolation. These are two very different levels of investigation, but each depends on the other for focus and direction. We have therefore devoted Part III of the book to the behavior of cells in multicellular animals and plants. Thus developmental biology, histology, immunobiology, and neurobiology are discussed at much greater length than in other cell biology textbooks. While this material may be omitted from a basic cell biology course, serving as optional or supplementary reading, it represents an essential part of our knowledge about cells and should be especially useful to those who decide to continue with biological or medical studies. The broad coverage expresses our conviction that cell biology should be at the center of a modern biological education.

This book is principally for students taking a first course in cell biology, be they undergraduates, graduate students, or medical students. Although we assume that most readers have had at least an introductory biology course, we have attempted to write the book so that even a stranger to biology could follow it by starting at the beginning. On the other hand, we hope that it will also be useful to working scientists in search of a guide to help them pick their way through a vast field of knowledge. For this reason, we have provided a much more thorough list of references than the average undergraduate is likely to require, at the same time making an effort to select mainly those that should be available in most libraries.

This is a large book, and it has been a long time in gestation—three times longer than an elephant, five times longer than a whale. Many people have had a hand in it. Each chapter has been passed back and forth between the author who wrote the first draft and the other authors for criticism and revision, so that each chapter represents a joint composition. In addition, a small number of outside experts contributed written material, which the authors reworked to fit with the rest of the book, and all the chapters were read by experts, whose comments and corrections were invaluable. A full list of acknowledgments to these contributors and readers for their help with specific chapters is appended. Paul R. Burton (University of Kansas), Douglas Chandler (Arizona State University), Ursula Goodenough (Washington University), Robert E. Pollack (Columbia University), Robert E. Savage (Swarthmore College), and Charles F. Yocum (University of Michigan) read through all or some of the manuscript and made many helpful suggestions.

The manuscript was also read by undergraduate students, who helped to identify passages that were obscure or difficult.

Most of the advice obtained from students and outside experts was collated and digested by Miranda Robertson. By insisting that every page be lucid and coherent, and by rewriting many of those that were not, she has played a major part in the creation of a textbook that undergraduates will read with ease. Lydia Malim drew many of the figures for Chapters 15 and 16, and a large number of scientists very generously provided us with photographs: their names are given in the figure credits. To our families, colleagues, and students we offer thanks for forbearance and apologies for several years of imposition and neglect. Finally, we owe a special debt of gratitude to our editors and publisher. Tony Adams played a large part in improving the clarity of the exposition, and Ruth Adams, with a degree of good-humored efficiency that put the authors to shame, organized the entire production of the book. Gavin Borden undertook to publish it, and his generosity and hospitality throughout have made the enterprise of writing a pleasure as well as an education for us.

Acknowledgments

In writing this book we have benefited greatly from the advice of many biologists. In addition to those who advised us by telephone and those who helped with the first edition, we would like to thank the following for their written advice in preparing this edition:

Chapter 1 Hans Bode (University of California, Irvine), Tom Cavalier-Smith (Kings College, London), Elaine Robson (University of Reading, U.K.).

Chapter 2 Efraim Racker (Cornell University), Harry van der Westen (Wageningen, The Netherlands), Richard Wolfenden (University of North Carolina).

Chapter 3 Charles Cantor (Columbia University), Russell Doolittle (University of California, San Diego), Steven Harrison (Harvard University), Richard Wolfenden (University of North Carolina).

Chapter 4 Charles Cantor (Columbia University), Steven Harrison (Harvard University), Richard Henderson (MRC Laboratory of Molecular Biology, Cambridge, U.K.), George Ratcliffe (Oxford University), Peter Shaw (John Innes Institute, Norwich, U.K.).

Chapter 5 Tim Hunt (Cambridge University), Marilyn Kozak (University of Pittsburgh), Thomas Lindahl (Imperial Cancer Research Fund, South Mimms, U.K.), Harold Varmus (University of California, San Francisco).

Chapter 6 Mark Bretscher (MRC Laboratory of Molecular Biology, Cambridge, U.K.), Lewis Cantley (Harvard University), Stuart Cull-Candy (University College London), Anthony Gardner-Medwin (University College London), Walter Gratzer (Kings College London), Ari Helenius (Yale University), Richard Henderson (MRC Laboratory of Molecular Biology, Cambridge, U.K.), Regis Kelly (University of California, San Francisco), Mark Marsh (Institute of Cancer Research, London), Samuel Silverstein (Columbia University), Wilfred Stein (Hebrew University), Peter Walter (University of California, San Francisco), Judy White (University of California, San Francisco).

Chapter 7 Martin Brand (Cambridge University), Leslie Grivell (University of Amsterdam), Richard McCarty (Cornell University), David Nicholls (University of Dundee), Gottfried Schatz (University of Basel), Alison Smith (John Innes Institute, Norwich, U.K.).

Chapter 8 Regis Kelly (University of California, San Francisco), Stuart Kornfeld (Washington University, St. Louis), Paul Lazarow (Rockefeller University), Vishu Lingappa (University of California, San Francisco), George Palade (Yale University), James Rothman (Princeton University), Gottfried Schatz (University of Basel), Kai Simons (EMBO Laboratory, Heidelberg), Alex Varshavsky (Massachusetts Institute of Technology), Peter Walter (University of California, San Francisco), William Wickner (University of California, Los Angeles).

Chapter 9 Pierre Chambon (University of Strasbourg), Sarah Elgin (Washington University, St. Louis), Gary Felsenfeld (National Institutes of Health, Bethesda), Christine Guthrie (University of California, San Francisco), Harold Weintraub (Hutchinson Cancer Center, Seattle), Keith Yamamoto (University of California, San Francisco).

Chapter 10 Pierre Chambon (University of Strasbourg), Enrico Coen (John Innes Institute, Norwich, U.K.), Gary Felsenfeld (National Institutes of Health, Bethesda), Ira Herskowitz (University of California, San Francisco), Tim Hunt (Cambridge University),

Robert Roeder (Rockefeller University), Harold Weintraub (Hutchinson Cancer Center, Seattle), John Wilson (Baylor University), Keith Yamamoto (University of California, San Francisco).

Chapter 11 Roger Cooke (University of California, San Francisco), Marc Kirschner (University of California, San Francisco), Michael Klymkowsky (University of Colorado, Boulder), Mark Mooseker (Yale University), Tom Pollard (Johns Hopkins University), Joel Rosenbaum (Yale University), Lewis Tilney (University of Pennsylvania), Klaus Weber (Max Planck Institute for Biophysical Chemistry, Göttingen).

Chapter 12 Henry Bourne (University of California, San Francisco), Philip Cohen (University of Dundee), Graham Hardie (University of Dundee), Daniel Koshland (University of California, Berkeley), Alex Levitzki (Hebrew University), Robert Mishell (University of Birmingham, U.K.), Anne Mudge (University College London), Michael Schramm (Hebrew University), Zvi Sellinger (Hebrew University), Tom Vanaman (University of Kentucky).

Chapter 13 Robert Brooks (King's College London), Leland Hartwell (University of Washington, Seattle), John Heath (Oxford University), Tim Hunt (Cambridge University), Jeremy Hyams (University College London), Marc Kirschner (University of California, San Francisco), Tim Mitchison (University of California, San Francisco), Andrew Murray (University of California, San Francisco), Paul Nurse (Oxford University).

Chapter 14 Michael Bennett (Albert Einstein College of Medicine), Benny Geiger (Weizmann Institute), Daniel Goodenough (Harvard Medical School), Barry Gumbiner (University of California, San Francisco), Richard Hynes (Massachusetts Institute of Technology), Tom Jessell (Columbia University), Louis Reichardt (University of California, San Francisco), Erkki Ruoslahti (La Jolla Cancer Research Foundation), Masatoshi Takeichi (Kyoto University), Robert Trelstad (UMDNJ—Robert Wood Johnson Medical School), Anne Warner (University College London).

Chapter 15 Adelaide Carpenter (University of California, San Diego), James Crow (University of Wisconsin, Madison), David Epel (Stanford University), Tim Hunt (Cambridge University), James Maller (University of Colorado Medical School), John Maynard Smith (University of Sussex), Anne McLaren (University College London), Montrose Moses (Duke University), Lewis Tilney (University of Pennsylvania), Victor Vacquier (University of California, San Diego).

Chapter 16 Marianne Bronner-Fraser (University of California, Irvine), Robert Horvitz (Massachusetts Institute of Technology), James Hudspeth (University of California, San Francisco), Philip Ingham (Imperial Cancer Research Fund, Oxford), Ray Keller (University of California, Berkeley), Cynthia Kenyon (University of California, San Francisco), Judith Kimble (University of Wisconsin, Madison), Tom Kornberg (University of California, San Francisco), Mark Krasnow (Stanford University), Peter Lawrence (MRC Laboratory of Molecular Biology, Cambridge, U.K.), Gail Martin (University of California, San Francisco), Patrick O'Farrell (University of California, San Francisco), Jonathan Slack (Imperial Cancer Research Fund, Oxford).

Chapter 17 Michael Banda (University of California, San Francisco), Alan Boyde (University College London), Michael Dexter (Paterson Institute for Cancer Research, Manchester, U.K.), Charles Emerson (University of Virginia), Howard Green (Harvard University), David Housman (Massachusetts Institute of Technology), Norman Iscove (Ontario Cancer Institute, Toronto), Anne Mudge (University College London), Michael Solursh (University of Iowa), Jim Till (Ontario Cancer Institute, Toronto), Fiona Watt (Imperial Cancer Research Fund, London).

Chapter 18 Fred Alt (Columbia University), Peter Lachmann (MRC Center, Cambridge, U.K.), Avron Mitchison (University College London), William Paul (National Institutes of Health, Bethesda), Ronald Schwartz (National Institutes of Health, Bethesda), David Strandring (University of California, San Francisco).

Chapter 19 Tim Bliss (National Institute for Medical Research, London), Michael Brown (Oxford University), Steven Burden (Massachusetts Institute of Technology), Gerald Fischbach (Washington University, St. Louis), James Hudspeth (University of

California, San Francisco), Trevor Lamb (Cambridge University), Dale Purves (Washington University, St. Louis), James Schwartz (Columbia University), Charles Stevens (Yale University), Michael Stryker (University of California, San Francisco).

Chapter 20 Brian Gunning (Australian National University, Canberra), Andy Johnston (John Innes Institute, Norwich, U.K.), Clive Lloyd (John Innes Institute, Norwich, U.K.), Freiderick Meins (Freiderich Miescher Institut, Basel), Scott Stachel (University of California, Berkeley), Andrew Staehelin (University of Colorado, Boulder), Anthony Trewavas (Edinburgh University), Virginia Walbot (Stanford University), Patricia Zambryski (University of California, Berkeley).

Chapter 21 Michael Bishop (University of California, San Francisco), John Cairns (Harvard School of Public Health), Ruth Ellman (Institute of Cancer Research, Sutton, U.K.), Hartmut Land (Imperial Cancer Research Fund, London), Bruce Ponder (Institute of Cancer Research, Sutton, U.K.).

The cover photograph shows a set of human chromosomes at metaphase. Chromatin is shown red, fluorescently stained with propidium iodide, while the centromeres are revealed with an anti-kinetochore antiserum. The photograph was supplied by Bill Brinkley and is taken from Merry, D.E., Pathak, S., Hsu, T.C. and Brinkley, B.R. *Am. J. Hum. Genet.* 37:425–430, 1985.

A Note to the Reader

Although the chapters of this book can be read independently of one another, they are arranged in a logical sequence of three parts. The first three chapters of **Part I** cover elementary principles and basic biochemistry. They can serve either as an introduction for those who have not studied biochemistry or as a refresher course for those who have. Chapter 4, which concludes Part I, deals with the principles of the main experimental methods for investigating cells. It is not necessary to read this chapter in order to understand the later chapters, but a reader will find it a useful reference.

Part II represents the central core of cell biology and is concerned mainly with those properties that are common to most eucaryotic cells, beginning with the fundamental molecular mechanisms of heredity and concluding with cell adhesion and the extracellular matrix.

Part III follows the behavior of cells in the construction of multicellular organisms, starting with the formation of eggs and sperm and ending with the disruption of multicellular organization that occurs in cancer.

Chapter 4 includes several tables giving the dates of crucial developments along with the names of the scientists involved. Elsewhere in the book the policy has been to avoid naming individual scientists. The authors of major discoveries, however, can usually be identified by consulting the **lists of references** at the end of each chapter. These references frequently include the original papers in which important discoveries were first reported. **Superscript numbers** that accompany the text headings refer to the numbered citations in the reference lists, providing a convenient means of following up specific topics.

Throughout the book, **boldface type** has been used to highlight key terms at the point in a chapter where the main discussion of them occurs. This may or may not coincide with the first appearance of the term in the text. *Italics* are used to set off important terms with a lesser degree of emphasis.

The Problems Book is designed as a companion volume that will help the reader appreciate the elegance, the ingenuity, and the surprises of research. It provides problems to accompany the central portion of this book (Chapters 5-14). Each chapter of problems is divided into sections that correspond to the sections of the main textbook, the principal focus of each section being a set of research-oriented problems derived from the scientific literature.

Most of the research problems illustrate points in the main text and are flagged with a symbol in the margin next to the relevant concept heading. Thus 5-4 in the margin of this text refers to Problem 4 in Chapter 5 of *The Problems Book*. In addition, each section of *The Problems Book* begins with a set of short fill-in-the-blank and true-false questions intended to help the reader review the vocabulary and main concepts of the relevant topic. *The Problems Book* should be useful for homework assignments and as a basis for class discussion. It could even provide ideas for exam questions.

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A sense of scale. These scanning
electron micrographs, taken at
progressively higher magnifications,
show bacterial cells on the point of an
ordinary domestic pin. (Courtesy of
Tony Brain and the Science Photo
Library.) ►

Contents in Brief

<i>List of Topics</i>	<i>xi</i>
<i>Special Features</i>	<i>xxxv</i>
<i>Acknowledgments</i>	<i>xxxvii</i>
<i>A Note to the Reader</i>	<i>xxxix</i>

Introduction to the Cell

PART

1. The Evolution of the Cell	3
2. Small Molecules, Energy, and Biosynthesis	41
3. Macromolecules: Structure, Shape, and Information	87
4. How Cells Are Studied	135

The Molecular Organization of Cells

PART

5. Basic Genetic Mechanisms	201
6. The Plasma Membrane	275
7. Energy Conversion: Mitochondria and Chloroplasts	341
8. Intracellular Sorting and the Maintenance of Cellular Compartments	405
9. The Cell Nucleus	481
10. Control of Gene Expression	551
11. The Cytoskeleton	613
12. Cell Signaling	681
13. Cell Growth and Division	727
14. Cell Adhesion, Cell Junctions, and the Extracellular Matrix	791

From Cells to Multicellular Organisms

PART

15. Germ Cells and Fertilization	839
16. Cellular Mechanisms of Development	879
17. Differentiated Cells and the Maintenance of Tissues	951
18. The Immune System	1001
19. The Nervous System	1059
20. Special Features of Plant Cells	1137
21. Cancer	1187

<i>List of Tables</i>	<i>1219</i>
<i>Index</i>	<i>I-1</i>

List of Topics

Introduction to the Cell

PART I

CHAPTER 1		From Single Cells to Multicellular Organisms	27
The Evolution of the Cell		Single Cells Can Associate to Form Colonies	27
From Molecules to the First Cell		The Cells of a Higher Organism Become Specialized and Cooperate	28
Simple Biological Molecules Can Form Under Prebiotic Conditions		Multicellular Organization Depends on Cohesion Between Cells	28
Polynucleotides Are Capable of Directing Their Own Synthesis		Epithelial Sheets of Cells Enclose a Sheltered Internal Environment	29
Self-replicating Molecules Undergo Natural Selection		Cell-Cell Communication Controls the Spatial Pattern of Multicellular Organisms	30
Specialized RNA Molecules Can Catalyze Biochemical Reactions		Cell Memory Permits the Development of Complex Patterns	31
Information Flows from Polynucleotides to Polypeptides		Basic Developmental Programs Tend to Be Conserved in Evolution	31
Membranes Defined the First Cell		Eucaryotic Organisms Possess a Complex Machinery for Reproduction	32
All Present-Day Cells Use DNA as Their Hereditary Material		The Cells of the Vertebrate Body Exhibit More Than 200 Different Modes of Specialization	32
Summary		Cells of the Immune System Are Specialized for the Task of Chemical Recognition	33
From Procaryotes to Eucaryotes		Nerve Cells Allow Rapid Adaptation to a Changing World	34
Procaryotic Cells Are Structurally Simple but Biochemically Diverse		Nerve Cell Connections Determine Patterns of Behavior	35
Metabolic Reactions Evolve		Summary	37
Cyanobacteria Can Fix CO ₂ and N ₂		References	39
Bacteria Can Carry Out the Aerobic Oxidation of Food Molecules			
Eucaryotic Cells Contain Several Distinctive Organelles			
Eucaryotic Cells Depend on Mitochondria for Their Oxidative Metabolism			
Chloroplasts Are the Descendants of an Engulfed Procaryotic Cell			
Eucaryotic Cells Contain a Rich Array of Internal Membranes			
Eucaryotic Cells Have a Cytoskeleton			
Protozoa Include the Most Complex Cells Known			
Genes Can Be Switched On and Off			
Eucaryotic Cells Have Vastly More DNA Than They Need for the Specification of Proteins			
In Eucaryotic Cells the Genetic Material Is Packaged in Complex Ways			
Summary			

Biological Order and Energy

Biological Order Is Made Possible by the Release of Heat Energy from Cells

Photosynthetic Organisms Use Sunlight to Synthesize Organic Compounds

Chemical Energy Passes from Plants to Animals

Cells Obtain Energy by the Oxidation of Biological Molecules

The Breakdown of Organic Molecules Takes Place in Sequences of Enzyme-catalyzed Reactions

Part of the Energy Released in Oxidation Reactions Is Coupled to the Formation of ATP

The Hydrolysis of ATP Generates Order in Cells

Summary

Food and the Derivation of Cellular Energy

Food Molecules Are Broken Down in Three Stages to Give ATP

Glycolysis Can Produce ATP Even in the Absence of Oxygen

Oxidative Catabolism Yields a Much Greater Amount of Usable Energy

Metabolism Is Dominated by the Citric Acid Cycle

In Oxidative Phosphorylation, the Transfer of Electrons to Oxygen Drives ATP Formation

Amino Acids and Nucleotides Are Part of the Nitrogen Cycle

Summary

Biosynthesis and the Creation of Order

The Free-Energy Change for a Reaction Determines Whether It Can Occur

Biosynthetic Reactions Are Often Directly Coupled to ATP Hydrolysis

Coenzymes Are Involved in the Transfer of Specific Chemical Groups

Biosynthesis Requires Reducing Power

Biological Polymers Are Synthesized by Repetition of Elementary Dehydration Reactions

Summary

The Coordination of Catabolism and Biosynthesis

Metabolism Is Organized and Regulated

Metabolic Pathways Are Regulated by Changes in Enzyme Activity

Catabolic Reactions Can Be Reversed by an Input of Energy

Enzymes Can Be Switched On and Off by Covalent Modification

Reactions Are Compartmentalized Both Within Cells and Within Organisms

Summary

References

45

58

59

59

60

60

61

61

62

62

63

64

64

65

67

67

69

70

70

71

71

71

75

77

78

78

80

80

80

80

84

84

85

86

Macromolecules: Structure, Shape, and Information**Molecular Recognition Processes**

87

The Specific Interactions of a Macromolecule Depend on Weak Noncovalent Bonds

88

A Helix Is a Common Structural Motif in Biological Structures Made from Repeated Subunits

89

Diffusion Is the First Step to Molecular Recognition

92

Thermal Motions Bring Molecules Together and Then Pull Them Apart

93

Atoms and Molecules Are in Constant Motion

93

Molecular Recognition Processes Can Never Be Perfect

94

Summary

95

Nucleic Acids

95

Genes Are Made of DNA

95

DNA Molecules Consist of Two Long Chains Held Together by Complementary Base Pairs

95

The Structure of DNA Provides an Explanation for Heredity

96

Errors in DNA Replication Cause Mutations

97

The Nucleotide Sequence of a Gene Determines the Amino Acid Sequence of a Protein

100

Portions of DNA Sequence Are Copied into RNA to Make Protein

101

Eucaryotic RNA Molecules Are Spliced to Remove Intron Sequences

102

Sequences of Nucleotides in mRNA Are "Read" in Sets of Three and Translated into Amino Acids

102

tRNA Molecules Match Amino Acids to Groups of Nucleotides

103

The RNA Message Is Read from One End to the Other by a Ribosome

104

Some RNA Molecules Function as Catalysts

105

Summary

106

Protein Structure

107

The Shape of a Protein Molecule Is Determined by Its Amino Acid Sequence

107

Common Folding Patterns Recur in Different Protein Chains

109

Proteins Are Amazingly Versatile Molecules

110

Proteins Have Different Levels of Structural Organization

112

Relatively Few of the Many Possible Polypeptide Chains Would Be Useful

112

New Proteins Usually Evolve by Minor Alterations of Old Ones

115

New Proteins Can Evolve by Recombining Preexisting Polypeptide Domains

116

Structural Homologies Can Help Assign Functions to Newly Discovered Proteins

117

Protein Subunits Can Self-assemble into Large Structures

118

A Single Type of Protein Subunit Can Interact with Itself to Form Geometrically Regular Assemblies

118

Some Self-assembling Structures Include Protein Subunits and Nucleic Acids

Not All Biological Structures Form by Self-assembly

Summary

Protein Function

A Protein's Conformation Determines Its Chemistry

Substrate Binding Is the First Step in Enzyme Catalysis

Enzymes Accelerate Chemical Reactions but Cannot Make Them Energetically More Favorable

Many Enzymes Make Reactions Proceed Preferentially in One Direction by Coupling Them to ATP Hydrolysis

Multienzyme Complexes Help to Increase the Rate of Cell Metabolism

Intracellular Membranes Increase the Rates of Diffusion-limited Reactions

Protein Molecules Can Reversibly Change Their Shape

Allosteric Proteins Help Regulate Metabolism

Allosteric Proteins Are Vital for Cell Signaling

Proteins Can Be Pushed or Pulled into Different Shapes

Energy-driven Changes in Protein Conformations Can Do Useful Work

ATP-driven Membrane-bound Allosteric Proteins Can Act as Pumps

Membrane-bound Allosteric Proteins Can Harness the Energy Stored in Ion Gradients to Do Useful Work

Protein Machines Play Central Roles in Many Biological Processes

Summary

References

How Cells Are Studied

Microscopy

The Light Microscope Can Resolve Details 0.2 μm Apart

Tissues Are Usually Fixed and Sectioned for Microscopy

Different Components of Cells Can Be Selectively Stained

Specific Molecules Can Be Located in Cells by Fluorescence Microscopy

Living Cells Are Seen Clearly in a Phase-Contrast or a Differential-Interference-Contrast Microscope

Images Can Be Enhanced and Analyzed by Electronic Techniques

The Electron Microscope Resolves the Fine Structure of the Cell

Biological Specimens Require Special Preparation for the Electron Microscope

Three-dimensional Images of Surfaces Can Be Obtained by Scanning Electron Microscopy

119	Metal Shadowing Allows Surface Features to Be Examined at High Resolution by Transmission Electron Microscopy	147
122	Freeze-Fracture and Freeze-Etch Electron Microscopy Provide Unique Views of the Cell Interior	147
122	Negative Staining and Cryoelectron Microscopy Allow Macromolecules to Be Viewed at High Resolution	148
123	The Structure of an Object in a Crystalline Array Can Be Deduced from the Diffraction Pattern It Creates	150
124	X-ray Diffraction Reveals the Three-dimensional Arrangement of the Atoms in a Molecule	151
125	<i>Summary</i>	153

Probing Chemical Conditions in the Interior of Living Cells

126	Nuclear Magnetic Resonance (NMR) Can Be Used to Assay the Chemistry of Populations of Living Cells	153
126	Ion Concentrations Can Be Measured with Intracellular Electrodes	155
127	Rapidly Changing Intracellular Ion Concentrations Can Be Measured with Light-emitting Indicators	156
128	There are Several Ways of Introducing Membrane-impermeant Molecules into Cells	157
129	<i>Summary</i>	158

Cell Separation and Culture

130	Cells Can Be Isolated from a Tissue and Separated into Different Types	159
131	Cells Can Be Grown in a Culture Dish	160
131	Chemically Defined Media Permit Identification of Specific Growth Factors	161
131	Eucaryotic Cell Lines Are a Widely Used Source of Homogeneous Cells	162
131	Cells Can Be Fused Together to Form Hybrid Cells	162
132	<i>Summary</i>	163

Fractionation of Cell Contents

	Organelles and Macromolecules Can Be Separated by Ultracentrifugation	163
	The Molecular Details of Complex Cellular Processes Can Be Deciphered in Cell-free Systems	166
	Proteins Can Be Separated by Chromatography	167
	The Size and Subunit Composition of a Protein Can Be Determined by SDS Polyacrylamide-Gel Electrophoresis	169
	More Than 1000 Proteins Can Be Resolved on a Single Gel by Two-dimensional Polyacrylamide-Gel Electrophoresis	169
	Selective Cleavage of a Protein Generates a Distinctive Set of Peptide Fragments	172
	Short Amino Acid Sequences Can Be Analyzed by Automated Machines	172
	<i>Summary</i>	174

Tracing Cellular Molecules with Radioactive Isotopes and Antibodies

	Radioactive Atoms Can Be Detected with Great Sensitivity	175
	Radioisotopes Are Used to Trace Molecules in Cells and Organisms	175

CHAPTER

4

135

Antibodies Can Be Used to Detect and Isolate Specific Molecules	177	Northern and Southern Blotting Facilitate Hybridization with Electrophoretically Separated Nucleic Acid Molecules	189
Hybridoma Cell Lines Provide a Permanent Source of Monoclonal Antibodies	178	Synthetic DNA Molecules Facilitate the Prenatal Diagnosis of Genetic Diseases	191
Antibodies and Other Macromolecules Can Be Injected into Living Cells	180	Hybridization at Reduced Stringency Allows Distantly Related Genes to Be Identified	191
<i>Summary</i>	180	<i>In Situ</i> Hybridization Techniques Locate Specific Nucleic Acid Sequences in Chromosomes and Cells	192
Recombinant DNA Technology	180	Recombinant DNA Techniques Allow Even the Minor Proteins of a Cell to Be Studied	193
Recombinant DNA Technology Has Revolutionized Cell Biology	180	Mutant Organisms Best Reveal the Function of a Gene	193
Restriction Nucleases Hydrolyze DNA Molecules at Specific Nucleotide Sequences	182	Cells and Organisms Containing Altered Genes Can Be Made to Order	194
Any DNA Sequence Can Be Produced in Large Amounts by DNA Cloning	182	Engineered Genes Encoding Antisense RNA Can Create Specific Dominant Mutations	195
Gel Electrophoresis Rapidly Separates DNA Molecules of Different Sizes	184	<i>Summary</i>	196
Purified DNA Molecules Can Be Labeled with Radioisotopes <i>in Vitro</i>	185	References	196
Isolated DNA Fragments Can Be Rapidly Sequenced	185		
Nucleic Acid Hybridization Reactions Provide a Sensitive Way of Detecting Specific Nucleotide Sequences	188		

The Molecular Organization of Cells

PART



Basic Genetic Mechanisms

CHAPTER

5
201

RNA and Protein Synthesis

RNA Polymerase Copies DNA into RNA: The Process of DNA Transcription	202	In Eucaryotes Only One Species of Polypeptide Chain Is Usually Synthesized from Each mRNA Molecule	214
The Promoter Sequence Defines Which DNA Strand Is to Be Transcribed	204	The Binding of Many Ribosomes to an Individual mRNA Molecule Generates Polyribosomes	214
Transfer RNA Molecules Act as Adaptors That Translate Nucleotide Sequences into Protein Sequences	205	The Overall Rate of Protein Synthesis in Eucaryotes is Controlled by Initiation Factors	215
Specific Enzymes Couple Each Amino Acid to its Appropriate tRNA Molecule	207	The Fidelity of Protein Synthesis Is Improved by Two Separate Proofreading Processes	215
Amino Acids Are Added to the Carboxyl-Terminal End of a Growing Polypeptide Chain	208	Many Inhibitors of Prokaryotic Protein Synthesis Are Useful as Antibiotics	218
The Genetic Code Is Degenerate	209	How Did Protein Synthesis Evolve?	219
The Events in Protein Synthesis Are Catalyzed on the Ribosome	210	<i>Summary</i>	219
A Ribosome Moves Stepwise Along the mRNA Chain	210	DNA Repair Mechanisms	220
A Protein Chain Is Released from the Ribosome When One of Three Different Stop Codons Is Reached	212	DNA Sequences Are Maintained with Very High Fidelity	220
The Initiation Process Sets the Reading Frame for Protein Synthesis	213	The Observed Mutation Rates in Proliferating Cells Are Consistent with Evolutionary Estimates	220
		Most Mutations in Proteins Are Deleterious and Are Eliminated by Natural Selection	221
		Low Mutation Rates Are Necessary for Life as We Know It	221