# MOTOTAR CETTOLOGY

# MOLECULAR CELL BIOLOGY

Charlotte J. Avers



Sponsoring editor: Bruce Spatz
Art development editor: James Funston
Production supervisor: Margaret Pinette

Copy editor: Connie Day
Text designer: Catherine Dorin
Illustrators: Oxford Illustrators
Art consultant: Loretta Bailey

Production coordinator: Janet Davis Castro Manufacturing supervisor: Ann DeLacey

On the cover: A schematic dissection of globin into the product of the separate exons, with color added for effect. Copyright by the Nobel Foundation, Stockholm, Sweden.

Library of Congress Cataloging in Publication Data

Avers, Charlotte J. Molecular cell biology.

Includes bibliographies and index.
1. Cytology. 2. Molecular biology. 1. Title.
QH581.2.A96 1985 574.87 85-3908
ISBN 0-201-10307-9

Copyright © 1986 by Addison-Wesley Publishing Company, Inc.
All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher. Printed in the United States of America. Published simultaneously in Canada.

BCDEFGHIJK-MU-89876

# **Preface**

We are in the midst of a revolution in biological studies due mainly to the development of precise methods of analysis at the molecular level. The growing excitement in molecular cell biology stems from important new information and insights concerning the elegant and sophisticated worlds within worlds that make up the living cell. The dynamic nature of the cell is evident from its varied responses to many kinds of stimuli, its repertory of regulation mechanisms for coping with a constantly changing internal and external environment, its ability to manage alone or in accommodation with other cells in the test tube or organism, and its properties of repair, growth, reproduction, and flexibility to evolve.

Biology itself is undergoing unification as cell biologists, developmental biologists, geneticists, biochemists, immunologists, and others direct and focus their efforts toward common objectives and the solutions of basic problems. In this book I have tried to convey the ongoing challenge and excitement of current research, the debts we owe to seminal studies of the recent past in paving the way to present-day understanding, and the convergence of ideas, methods, and intellectual approaches of different life sciences.

#### **About This Book**

I have written *Molecular Cell Biology* for students with a college-level background in biology and chemistry who are taking a first, one-term course in modern cell biology. In my writing I made every effort to provide discussions and explanations of complex phenomena, data, and processes. In collaboration with members of the publishing staff I assembled an extensive set of photographs and illustrations to provide graphic accompaniment to the written word, and the electron micrographs have been reproduced in their original size for full pedagogical effect. Other aids for the student and the instructor include summaries and extensive sets of readings and references for each chapter, and a glossary of more than 800 terms, all of which are highlighted in boldface type in the text.

#### A Flexible Organization \_\_

To permit the greatest flexibility I have designed the chapter contents to allow for alternative sequences of instruction. The book is subdivided into six parts. Part I contains chapters on cellular structures and molecules and the major biochemical and genetic processes and units of life. With these four chapters as an introduction, the remaining fourteen chapters can be rearranged to suit individual preferences and course organizations. For example, Part IV (Organization of the Genome) and Part V (Reproduction and Development) could be covered prior to Part II (Cell Boundaries and Surfaces) and Part III (Organization of the Cytoplasm) if that order is preferred. Some may wish to assign Chapter 4, Genetic Processes, in conjunction with Part IV, Organization of the Genome. Part VI (Evolution), however, was deliberately written as a summarizing evolutionary perspective of molecular cell biology. I believe this perspective to be the one that brings together any or all of biology in its most basic content and highly recommend that this material be the final, capstone section of the course.

#### Topic Coverage \_

Given the massive amounts of information required in an up-to-date text in modern cell biology, a key challenge facing the author of such a book is to keep it to a length that is suitable for an undergraduate first course. I have answered this challenge by setting as my goal the need to avoid overwhelming introductory students with excessive detail or material that should come in a later course. Thus, I have discussed some topics more briefly than is done in other texts, but in all cases I have given at least the flavor and major significance of the subject in sketching the picture of the living cell in all its varied features. I am comfortable with the decisions that I have made in allocating more space to some topics than to others, but I welcome comments and suggestions from the readers.

#### Acknowledgments

It is a pleasure to acknowledge my debt to many friends and colleagues who generously provided excellent photographs, offered useful comments and suggestions to improve the book, and reviewed all or part of the text and art manuscripts. In particular I wish to thank the following reviewers for their helpful comments:

William Bradshaw Brigham Young University

Robert P. Donaldson George Washington University Gideon Dreyfuss Northwestern University

Edwin V. Gaffney The Pennsylvania State University Mary Lee S. Ledbetter College of the Holy Cross

Sara McCowen Virginia Commonwealth University Albert P. Torzilli George Mason University

Margaret Waterman Emory University

I could not have managed the many phases of preparation and production of this book without the cheerful encouragement of my editor, Bruce Spatz; the efficiency of the production staff, Margaret Pinette and Judy Ullman in particular; and the prodigious efforts of James Funston and Dr. Mary Lee S. Ledbetter in writing and revising the summaries and carefully developing and editing the entire set of illustrations. I believe the book has benefited greatly by all these inputs and that the students will be as enthusiastic as I am about the story now emerging in molecular cell biology—a story of the cell as a dynamic and elegant unit of life.

New Brunswick, New Jersey

C. J. A.

# Abridged Contents

PA	Introduction to the Cell	
СНАР	TER 1 Cells in Perspective	3
СНАР	TER 2 Organic Molecules	31
CHAP	G.	67
СНАР	TER 4 Genetic Processes	101
PAR	Cell Boundaries and Surfaces	
СНАР	Membrane Structure and Function	141
CHAP	The Cell Surface	183
PART	Organization of the Cytoplasm	
СНАРТ	TER 7 Endoplasmic Reticulum and Golgi Apparatus	227
СНАРТ		267
СНАРТ		305
СНАРТ	TER 10 Chloroplasts	363
CHAPI	TER IT Cytoskeletal Systems and Movement	413
PART	Organization of the Genome	
СНАР	TER 12 Molecular Nature of the Genome	479
CHAP'	TER 13 Gene Expression: Transcription and Translation	529
CHAP	TER 14 Regulation of Gene Expression	585
СНАР	TER 15 The Nucleus	621
PAF	Reproduction and Development	. `
СНАР	TER 16 Cell Growth and Division	671
CHAP	TER 17 Meiosis and Crossing Over	. 723
PART	Evolution	
СНАР	TER 18 Cellular and Molecular Evolution	765

## **Contents**

#### PART

#### Introduction to the Cell

## CHAPTER 1

Cells in Perspective 3

Historical Highlights 3

1.1 Microscopy and the Cell Theory 4

1.2 Genetic and Biochemical

Aspects of the Cell 7

Structural Organization of the Cell 9

1.3 Prokaryotic Cell Organization 11

1.4 Eukaryotic Cell Organization 14

1.5 Evolutionary Relationships 21

Viruses 24

**Summary 27** 

Readings and References 28

## CHAPTER 2

#### Organic Molecules 31

Basic Features of Organic Molecules 31

2.2 The Chemistry of Carbon Atoms 33 2.1 Chemical Bonds 31

2.4 Biologically Important Carbon Compounds 34 2.3 Isomers 34

Carbohydrates 35

2.5 Monosaccharides 35 2.6 Polysaccharides 38

Lipids 42

2.9 Phospholipids 45 2.8 Neutral Fats 43 2.7 Fatty Acids 42

2.11 Steroids and Terpenes 47 2.10 Sphingolipids and Glycolipids 46

Proteins 48

2.12 Amino Acids 48

2.13 Polypeptides 51

2.14 Protein Structure 52

Nucleic Acids 56

2.15 Nucleotides 56

2.16 The Double Helix 58

Water 60

2.17 Properties of Water 60

2.18 The pH Scale 61

Summary 63

Readings and References 65

## CHAPTER 3

#### Energy and Enzymes 67

**Bioenergetics 67** 

3.1 Free Energy 67 3.2 Change in Free Energy 68

3.3 Open Systems and Steady States 70

**Energy Transfer in Coupled Metabolic Reactions 71** 

3.4 Phosphoryl Group Transfer and ATP 71
3.5 Electron Transfer and Oxidation–Reductions 74
3.6 Energy Transfer by Electron Carriers 76
Enzymes: Catalysts of Life 78

**3.7** Enzyme Activity 79 **3.8** Substrate Specificity 82

3.9 Enzyme Kinetics 85 3.10 Inhibition of Enzyme Activity 86

**3.11** Regulation of Enzyme Activity 87 **3.12** Isozymes 90

3.13 Multienzyme Systems 91

Glycolysis: A Metabolic Pathway 92

**3.14** An Overview of Glycolysis 92 **3.15** The Fate of Pyruvate 95

3.16 Regulation of the Rate of Glycolysis 96

Summary 97

Readings and References 99

## CHAPTER 4

#### Genetic Processes 101

The Genetic Material 101

**4.1 DNA Is the Genetic Material 101 4.2 DNA Replication 104** 

4.3 Mutation 107

Information Storage and Flow 111

**4.4** The Genetic Code 112 **4.5** Transcription and Translation of Stored Information 115 **4.6** Gene Organization and Transcript Processing 119

4.7 Recombinant DNA Technology 121

4.8 Regulation of Information Flow 126

Packaging of the Genome in Chromosomes 128

**4.9** Structural Organization of the Chromosome 129

**4.10** Synthesis of New Chromosomes and Their Distribution to Progeny Cells 131

Summary 135

Readings and References 137

#### PART

#### Cell Boundaries and Surfaces

## CHAPTER 5

#### Membrane Structure and Function 141

Molecular Organization of Membranes 141

**5.1** The Fluid Mosaic Membrane 142 **5.2** Membrane Lipids 146

**5.3** Membrane Proteins 151 **5.4** Membrane Asymmetry 154

**5.5** Molecular Mobility Within the Membrane 156 **5.6** Restraints on Membrane Protein Mobility 159

CONTENTS - XV

Transport of Molecules Across Membranes 163

**5.7** Passive Transport 163 **5.8** Active Transport 167

5.9 Endocrtosis and Exocytosis 170 5.10 Receptor Mediated

Endocytosis 174

Summary 179

Readings and References 180

## CHAPTER 6

The Cell Surface 183

Cell Junctions 183

**6.1** Desmosomes 184 **6.2** Tight Junctions 187 **6.3** Gap Junctions 190

**6.4** Septate functions 193

Extracellular Matrix 194

6.5 Extracellular Matrix in Animal Tissues 195
6.6 Collagen Chemistry and Biosynthesis 196
6.7 Glycosaminoglycans and Proteoglycans 200

**6.8** Other Structural Matrix Proteins 202 **6.9** Plant Cell Walls 205

Intercellular Aggregation, Recognition, and Communication 208

6.10 Cell Recognition and Aggregation 209
 6.11 Chemical Signals in Intercellular Communication 213
 6.12 Intracellular Receptors and Steroid Hormone Action 215
 6.13 Cell-Surface Receptors and Second Messengers 217
 6.14 Ca<sup>2+</sup> as a Second Messenger 219

Summary 220

Readings and References 222

## PART

#### Organization of the Cytoplasm

## CHAPTER 7

Endoplasmic Reticulum and Golgi Apparatus 227

**Endoplasmic Reticulum 227** 

7.1 Rough ER and Smooth ER 228 7.2 The Signal Hypothesis 233

7.3 Glycosylation of Proteins in the ER 236

7.4 Cotranslational Insertion of Integral Membrane Proteins 238

7.5 Intracellular Sorting of Protein Traffic from the ER 241

**7.6** Protein Transfer from the Cytosol to Mitochondria and Chloroplasts 243 The Golgi Apparatus 246

7.7 Ultrastructural Organization of Golgi Membranes 246

7.8 Functions of the Golgi Apparatus 250

7.9 Carbohydrate Processing in the Golgi Apparatus 255

7.10 Membrane Recycling via the Secretory Pathway 257

Summary 261

Readings and References 263

### CHAPTER 8

#### Lysosomes and Microbodies 267

Lysosomes 267

**8.1** General Nature of Lysosomes 268 **8.2** Intracellular Digestion 269

**8.3** Lysosome Formation 273 **8.4** Protein Traffic to the Lysosomes 275

8.5 Sorting Out of Receptors in Membrane Recycling 279

8.6 Lysosomes and Disease 282

Microbodies 286

8.7 Microbody Morphology and Metabolism 286
8.8 Peroxisomes and Glyoxysomes 290
8.9 Leaf Peroxisomes, Hydrogenosomes, and Glycosomes 296
8.10 An Overview of Microbody Formation

Glycosomes 296 **8.10** An Overview of Microbody Forma and Functions 299

Summary 301

Readings and References 303

## CHAPTER 9

#### Mitochondria 305

Mitochondrial Structure and Form 305

**9.1** Mitochondrial Ultrastructure 306 **9.2** Mitochondrial Shape and Numbers 308

Aerobic Respiration 310

9.3 Fermentation 312 9.4 The Krebs Cycle 313 9.5 Electron Transport

Toward Oxygen 317 9.6 ATP Synthesis During Respiratory

Electron Transport 323 9.7 Chemiosmotic Coupling of

Oxidative Phosphorylation and Electron Transport 325

9.8 ATP Synthetase in Chemiosmotic Coupling Membranes 331

Mitochondrial Compartmentation 334

**9.9** Communication by Carriers 336 **9.10** Communication by Shuttles 337 Mitochondrial Biogenesis 340

9.11 Growth and Division of Pre-existing Mitochondria 341 9.12 Import of

Proteins Synthesized in the Cytosol 344 9.13 The Mitochondrial

Genetic System 345 9.14 Protein Synthesis in Mitochondria 351

9.15 Evolutionary Origins of Mitochondria 354

Summary 358

Readings and References 360

## CHAPTER 10

#### Chloroplasts 363

Structure and Chemistry of Photosynthetic Systems 363

10.1 Chloroplast Structure 364 10.2 Thylakoids in Prokaryotes 368

10.3 Photosynthetic Pigments 371 10.4 General Features of

Photosynthesis 375 10.5 Photoexcitation 376

10.6 Separability of Light and Dark Reactions 377

The Light Reactions of Photosynthesis 378

10.7 Photosystems I and II 379 10.8 Electron Flow in Chloroplasts 380

10.9 Photophosphorylation 383 10.10 Chemiosmotic Coupling of

Electron Flow and Photophosphorylation 385

10.11 Molecular Organization of Thylakoid Membranes 387

CONTENTS

The Dark Reactions of Photosynthesis 390

10.12 CO<sub>2</sub> Fixation by the C<sub>3</sub> Cycle in Chloroplasts 391

10.13 CO<sub>2</sub> Fixation by the C<sub>1</sub> Cycle in Chloroplasts 393

10.14 Photorespiration 396

Chloroplast Biogenesis 399

10.15 Proplastid Multiplication and Differentiation 399

10.16 The Chloroplast Genetic System 400 10.17 Evolutionary

Origins of Chloroplasts 405

Summary 408

Readings and References 410

## CHAPTER 11

Cytoskeletal Systems and Movement 413

Cytoskeletal Protein Fibers 414

11.1 Microtubules 414 11.2 Microfilaments 415

11.3 Intermediate Filaments 416 11.4 Myosin Filaments 418

**Muscle Contraction 420** 

11.5 Muscle Fibers 420 11.6 The Sliding Filament Model of Muscle

Contraction 425 11.7 Coupled Excitation and Contraction 428

11.8 Troponin and Tropomyosin: Regulatory Proteins 431

**Ciliary Movement 432** 

11.9 Ciliary Ultrastructure and Chemistry 434 11.10 The Sliding

11.11 Modified Cilia Microtubule Mechanism of Ciliary Movement 437

XVII

and Flagella 442 11.12 Bacterial Flagella 443

**Anaphase Movement of Chromosomes 445** 

11.13 Organization and Dynamics of the Spindle 445

11.14 Mechanism of Anaphase Movements 447

11.15 Microtubule Organizing Centers 450

Nonmuscle Contractile Systems 453

11.17 Ameboid Movement 455 11.16 Cytoplasmic Streaming 454

11.18 Ruffled Membrane Movement of Cells in Culture 456

11.19 The Role of Calcium and Actin-Binding Proteins in

Nonmuscle Contractility 461

Organization of the Cytoskeleton 463

11.20 Architecture of the Cytoskeleton 463 11.21 Cytoskeletal

Assemblies and Cell Shape 466

Summary 471

Readings and References 474

### PART

### Organization of the Genome

## CHAPTER 12

Molecular Nature of the Genome 479

**DNA Replication 479** 

12.1 The DNA Double Helix 479 12.2 Origin and Direction of Strand 12.3 Synthesis of New Strands 486 12.4 Replication in Synthesis 484

12.5 Replication in Mitochondria and Chloroplasts 499 Viruses 492

Packaging the Genome 500

12.6 Packaging Viral Genomes 501 12.7 The Bacterial Nucleoid 504

12.8 Nucleosomes: Subunits of Chromosome Structure 505

12.9 Looped Domains in Packed Chromatin 508

12.10 Replication of the Chromatin Fiber 510

Organization of the Genome 513

12.11 Genome Size and the C Value Paradox 514

12.12 Genome Analysis by the Use of Renaturation Kinetics 517

12.13 Clustered Genes, Scattered Genes, and Overlapping Genes 520

Summary 525

Readings and References 526

## CHAPTER 13

#### Gene Expression: Transcription and Translation 529

The Genetic Template 529

13.1 The Organization of Gene Sequences 530

13.2 The Organization of the mRNA Template 532

Transcription of DNA into RNA 535

13.3 Composition and Action of RNA Polymerases 535

**13.4** Promoters: Sites of Transcription Initiation 540

13.5 tRNA Transcripts 545 13.6 rRNA Transcripts 551

13.7 Posttranscriptional Processing of mRNA in Eukaryotes 557

Translation of the Genetic Message 562

13.8 Amino Acids, tRNAs, and Aminoacyl-tRNA Synthetases 562

13.9 Ribosomes 564 13.10 Studies of Ribosome Disassembly and

Reassembly 567 13.11 Monosomes and Polysomes 571 13.12 Polypeptide

Chain Initiation 573 13.13 Polypeptide Chain Elongation 574

13.14 Polypeptide Chain Termination 575

13.15 Chemical Inhibitors of Protein Synthesis 577

Summary 580

Readings and References 582

## CHAPTER 14

#### Regulation of Gene Expression 585

Differential Gene Expression 585

14.1 Totipotent Nuclei in Differentiated Cells 586

14.2 Repressor Control of Transcription in Bacteria 588

14.3 Attenuation Control of Transcription in Bacteria 593

14.4 Transcriptional Control in Eukaryotes 597

14.5 Posttrancriptional and Translational Controls in Eukaryotes 601

Genomic Alterations and Gene Expression 604

**14.6** Gene Amplification 604 **14.7** The Generation of

Antibody Diversity 606 14.8 Transposable Genetic Elements 611

Summary 615

Readings and References 617

CONTENTS

## CHAPTER 15

The Nucleus 621

Nuclear Organization 621

**15.2** The Nucleolus 627 15.1 The Nuclear Envelope 622

15.3 The Chromosome Complement 631

Special Features of Chromosome Organization 639

15.5 The Centromere 15.4 Heterochromatin and Euchromatin 639

XIX

Region 644 15.6 The Telomere Region 648

Transcriptionally Active Chromatin 650

15.7 Studies at the Cytological Level 650 15.8 Studies at the Molecular

15.9 DNA Methylation and Level: Sensitivity to DNAase I 654

**Transcriptional Activity 658** 

15.10 Hypersensitive Sites in Active Chromatin 661

Summary 664

Readings and References 666

#### PART 1

#### Reproduction and Development

## CHAPTER 16

Cell Growth and Division 671

Cell Growth 671

**16.1** Cell Renewal 672 16.2 Somatic Cell Cultures 678

16.3 Oncogenes and the Control of Cell Growth 684

The Cell Cycle 693

**16.4** Activities During the Cell Cycle 693 16.5 Variations in Cell Cycles 695

16.6 Genetic Control of the Cell Cycle in Yeast 699

Mitosis 701

16.7 The Stages of Mitosis 702 16.8 Genetic Consequences of

Mitosis 704 16.9 Modifications of Mitosis 705

Cytokinesis 712

16.10 Furrowing in Animal Cells 713 16.11 Cell Plate Formation

in Plants 715

Summary 717

Readings and References 719

## CHAPTER 1

#### Meiosis and Crossing Over 723

The Meiotic Process 724

17.2 Why Two Divisions in Meiosis? 727 17.1 Sexual Life Cycles 724

17.3 The First Meiotic Division 729 17.4 The Second Meiotic

Division 738 17.5 Genetic Consequences of Meiosis 738

Crossing Over and Genetic Recombination 741

17.6 Cytogenetic Evidence for Chromosome Exchanges in Crossing 17.7 Crossing Over Involves Chromosome Breakage and

17.8 Molecular Studies of Recombination **Reunion Events 743** 

Mechanisms 745

Chromosome Synapsis 752
17.9 The Synaptonemal Complex 752
17.10 Recombination Nodules and Chiasmata of Synapsed Chromosomes 755
Summary 758
Readings and References 760

PART V

#### **Evolution**

## CHAPTER 18

Cellular and Molecular Evolution 765

**Prebiotic Evolution 765** 

18.1 The Primeval Earth 765

18.2 Chemical Evolution 768

18.3 Protobiont Models 771

**18.4 Requirements** for Life Forms 774

Cellular Evolution 776

18.5 Origin of the Information System 776
 18.6 The Evolution of Metabolic Diversity 778
 18.7 The Evolution of Photosynthesis and Aerobic Respiration 781
 18.8 Eukaryotes from Prokaryotes 787

18.9 The Appearance of Multicellular Organisms in Evolution 790

**Evolving Genes and Proteins 795** 

**18.10** Relationships Between Genes and Between Gene Products 795 **18.11** Gene Duplication in Evolution 799

Summary 809

Readings and References 811

Glossary G-1

Index I-1

Introduction to the Cell \_\_\_\_