MOLECULAR BIOLOGY OF THE CELL

ALBERTS JOHNSON LEWIS RAFF ROBERTS WALTER

FOURTH EDITION

MOLECULAR BIOLOGY OF THE CELL

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Front cover Human Genome: Reprinted by permission from *Nature,* International Human Genome Sequencing Consortium, 409:860–921, 2001 © Macmillan Magazines Ltd. Adapted from an image by Francis Collins, NHGRI; Jim Kent, UCSC; Ewan Birney, EBI; and Darryl Leja, NHGRI; showing a portion of Chromosome 1 from the initial sequencing of the human genome.

Chapter opener Portion of chromosome 2 from the genome of the fruit fly *Drosophila melanogaster.* (Reprinted with permission from M.D. Adams et al., *Science* 287:2185–2195, 2000. © AAAS.)

Back cover In 1967, the British artist Peter Blake created a design classic. Nearly 35 years later Nigel Orme (illustrator), Richard Denyer (photographer), and the authors have together produced an affectionate tribute to Mr Blake's image. With its gallery of icons and influences, its assembly created almost as much complexity, intrigue and mystery as the original. *Drosophila, Arabidopsis,* Dolly and the assembled company tempt you to dip inside where, as in the original, "a splendid time is guaranteed for all."
(Gunter Blobel, courtesy of The Rockefeller University; Marie Curie, Keystone Press Agency Inc; Darwin bust, by permission of the President and Council of the Royal Society; Rosalind Franklin, courtesy of Cold Spring Harbor Laboratory Archives; Dorothy Hodgkin, © The Nobel Foundation, 1964; James Joyce, etching by Peter Blake; Robert Johnson, photo booth self-portrait early 1930s, © 1986 Delta Haze Corporation all rights reserved, used by permission; Albert L. Lehninger, (unidentified photographer) courtesy of The Alan Mason Chesney Medical Archives of The Johns Hopkins Medical Institutions; Linus Pauling, from Ava Helen and Linus Pauling Papers, Special Collections, Oregon State University; Nicholas Poussin, courtesy of ArtToday.com; Barbara McClintock, © David Micklos, 1983; Andrei Sakharov, courtesy of Elena Bonner; Frederick Sanger, © The Nobel Foundation, 1958.)

Preface

"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."

Thus began the preface of our first edition, written 18 years ago. Much of what we wrote in that preface holds for the present edition too. Our goals have not changed: we want to make cell biology comprehensible. We aim, as before, to give readers a perspective both on what is known, and on what is unknown. We have written the book for a wide range of students, but it should also prove useful for scientists wishing to follow progress outside their own specialized fields. As in past editions, each chapter is a joint composition of multiple authors and has been reviewed by a number of experts. This helps to explain why this edition, like the first, has been "a long time in gestation—three times longer than an elephant, five times longer than a whale."

Although information in the life sciences is expanding rapidly, human brain capacity is not. This discrepancy creates an increasing challenge for textbook writers, teachers, and especially students. We have been forced to think harder than ever in deciding what facts and concepts are essential. We have had to summarize—omitting much detail that, in overabundance, can prevent understanding. But specific examples are still needed to bring the subject to life. Thus, the most difficult part of the revision has been deciding what to leave out, while the most rewarding has been the opportunity that new discoveries provide to strengthen the conceptual framework.

What is new in the 4th edition?

Genomics has given us a new perspective that has demanded a complete recasting and expansion of the material on molecular genetics (Chapter 1 and Chapters 4 through 8). These six chapters can now be used as a stand-alone text in molecular biology. As before, the book ends with a major section on Cells in Their Social Context, but we have added a new chapter on Pathogens, Infection, and Innate Immunity. This reflects the remarkable advances in the understanding of the cell biology of infection, as well as the renewed awareness that infectious disease remains one of the greatest unconquered dangers in our world.

As our book makes clear, the complete sequencing of the genomes of hundreds of organisms, from bacteria to humans, has revolutionized our understanding of living things and the relationships between them. At last we can see what is there: the set of genes and proteins is finite, and we can list them. But we also recognize that these components are combined for use in marvelously subtle and complex ways, even in the simplest of organisms. Therefore, the traditional explanatory cartoons that we show on nearly every page of the book generally represent only the primitive first step toward an explanation. These drawings cannot capture the enormous complexity of the networks of protein–protein interactions that are responsible for most intracellular processes, whose understanding will require new and more quantitative forms of analysis. Thus, we are no longer as confident as we were 18 years ago that simplicity will eventually

emerge from the complexity. The extreme sophistication of cellular mechanisms will challenge cell biologists throughout the new century, which is very good news for the many young scientists who will succeed us.

As never before, new imaging and computer technologies have changed the ways we can observe the inner workings of living cells. We have tried to capture some of the excitement of these observations in *Cell Biology Interactive,* a CD-ROM disk that is included with each book. It contains dozens of video clips, animations, molecular structures, and high-resolution micrographs, which complement the static material in individual book chapters. One cannot watch cells crawling, dividing, segregating their chromosomes, or rearranging their surface without feeling curious about the molecular mechanisms that underlie these processes. We hope that *Cell Biology Interactive* will stimulate this curiosity in students and thereby make the learning of cell biology easier and more rewarding. We also hope that instructors will use these visual resources in the classroom for the same purpose.

We are deeply indebted to the many people who have helped us with this revision. The experts who critically reviewed specific chapters are acknowledged separately on p. xxix. We are especially grateful to Julie Theriot, who largely wrote both Chapter 16 and Chapter 25; we have all benefited from her wisdom. We are also grateful to the other experts who made major contributions to individual chapters: Nancy Craig helped to revise part of Chapter 5; Maynard Olson drafted the section on genome evolution in Chapter 7; Peter Shaw helped to revise Chapter 9; David Morgan largely wrote Chapter 17; Lisa Satterwhite prepared initial drafts of Chapter 18; Robert Kypta largely revised Chapter 19; Cori Bargmann helped us to restructure Chapter 21; and Paul Edwards played a central part in the revision of Chapter 23. Karen Hopkin drafted large parts of Chapters 8 and 23. We are also very grateful to the many scientists who generously provided micrographs for the book and materials for the CD-ROM.

Finally we are indebted to the outstanding staff of Garland Publishing. Nigel Orme oversaw the production of the final artwork with remarkable skill and speed. Mike Morales put in endless hours tackling the diverse challenges of developing the CD-ROM. Emma Hunt skillfully and artfully set the entire text and figures into pages. Sarah Gibbs and Kirsten Jenner kept us organized. Adam Sendroff and Nasreen Arain connected us to our customers. Eleanor Lawrence prepared the Glossary, and Mary Purton collected many of the references. Through it all, Denise Schanck calmly directed the whole effort with great skill. Last, but not least, Tim Hunt and John Wilson once again created a masterful Problems Book that supplements the main text; they worked side-by-side with us and were a constant source of wise advice. Their clever problems illustrate how discoveries are made and provide a unique way of learning cell biology.

It goes without saying that our book could not have been written without the strong support of our families and the forbearance of our friends, colleagues, and students. For decades, they have had to put up with our absences at frequent and lengthy book meetings, where most of the writing was done. They have helped us in innumerable ways, and we are grateful to them all.

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A Note to the Reader

Structure

Although the chapters of this book can be read independently of one another, they are arranged in a logical sequence of five 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.

Part II represents the central core of cell biology and is concerned mainly with those properties that are common to most eucaryotic cells. It deals with the expression and transmission of genetic information.

Part III deals with the principles of the main experimental methods for investigating cells. It is not necessary to read these two chapters in order to understand the later chapters, but a reader will find it a useful reference.

Part IV discusses the internal organization of the cell. **Part V** follows the behavior of cells in multicellular organisms, starting with cell–cell junctions and extracellular matrix and concluding with a new chapter on pathogens and infection.

References

A concise list of selected references is included at the end of each chapter. These are arranged in alphabetical order under the chapter section headings. These references frequently include the original papers in which important discoveries were first reported. Chapters 8 and 9 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.

Full references for each chapter arranged by concept headings can be found on the Garland Science website at: http://www.garlandscience.com

Glossary terms

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. *Italic* is used to set off important terms with a lesser degree of emphasis. At the end of the book is the expanded **glossary**, covering technical terms that are part of the common currency of cell biology; it is intended as a first resort for a reader who encounters an unfamiliar term used without explanation.

Nomenclature

Each species has its own conventions for naming genes, proteins, and mutant phenotypes. In this book, for names of genes, we follow the established conventions when referring to a gene in a particular species (see the table below). When we refer to a gene or gene family generically, without intending restriction to a particular species, we use the same convention as for the mouse: italics, with first letter upper-case and subsequent letters lower-case (for example, *Engrailed, Wnt*); the corresponding protein, if it takes its name from the gene, is then given the same name, with the first letter upper-case, but not in italics (Engrailed, Wnt). For proteins not named after genes but given names in their own right (such as actin, tubulin), the initial letter is generally not capitalized.

ORGANISM	GENE	PROTEIN
Mouse	*Hoxa4*	Hoxa4
Human	*HOXA4*	HOXA4
Zebrafish	*cyclops, cyc*	Cyclops, Cyc
Caenorhabditis	*unc-6*	UNC-6
Drosophila	*sevenless, sev* (named after recessive mutant phenotype)	Sevenless, SEV
	Deformed, Dfd (named after dominant mutant phenotype, or named by homology with another species)	Deformed, DFD
Yeast		
Saccharomyces cerevisiae (budding yeast)	*CDC28*	Cdc28, Cdc28p
Schizosaccharomyces pombe (fission yeast)	*Cdc2*	Cdc2, Cdc2p
Arabidopsis	*GAI*	GAI
E. coli	*uvrA*	UvrA

Cell Biology Interactive

The *Cell Biology Interactive* CD-ROM is packaged with every copy of the book. Created by the *Molecular Biology of the Cell* author team, the CD-ROM contains over 90 video clips, animations, molecular structures and high-resolution micrographs. The authors have chosen to include material that not only reinforces basic concepts but also expands the content and scope of the book. A complete table of contents and overview of all electronic resources is contained in the *Viewing Guide,* located in the Appendix of the CD-ROM. For instructors, there is also a *Teaching Guide for Cell Biology Interactive,* which reviews the electronic resources from a pedagogical perspective, and provides practical suggestions for successfully incorporating multimedia in the classroom.

Molecular Biology of the Cell, Fourth Edition: A Problems Approach

Molecular Biology of the Cell, Fourth Edition: A Problems Approach is designed to help students appreciate the ways in which experiments and simple calculations can lead to an understanding of how cells work. It provides problems to accompany Chapters 1–8 and 10–18 of *Molecular Biology of the Cell.* Each chapter of problems is divided into sections that correspond to those of the main textbook and review key terms, test for understanding basic concepts, and pose research-based problems. *Molecular Biology of the Cell, Fourth Edition: A Problems Approach* should be useful for homework assignments and as a basis for class discussion. It could even provide ideas for exam questions. Answers for half of the problems are provided in the back of the book and the balance are available to instructors upon request.

The Art of MBoC4

A CD-ROM containing all the figures in the book for presentation purposes.

Teaching Supplements

Upon request, teaching supplements for *Molecular Biology of the Cell* are available to instructors.

MBoC4 Transparency Set

250 full-color overhead acetate transparencies of the most important figures from the book.

Garland Science Classwire™

Located at http://www.classwire.com/garlandscience offers instructional resources and course management tools (*Classwire* is a trademark of Chalkfree, Inc).

Tables

The Genetic Code

1st position (5′ end)	2nd Position U	2nd Position C	2nd Position A	2nd Position G	3rd Position (3′ end)
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	**STOP**	**STOP**	A
	Leu	Ser	**STOP**	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Amino Acids Codons

A	Ala	Alanine	GCA GCC GCG GCU
C	Cys	Cysteine	UGC UGU
D	Asp	Aspartic acid	GAC GAU
E	Glu	Glutamic acid	GAA GAG
F	Phe	Phenylalanine	UUC UUU
G	Gly	Glycine	GGA GGC GGG GGU
H	His	Histidine	CAC CAU
I	Ile	Isoleucine	AUA AUC AUU
K	Lys	Lysine	AAA AAG
L	Leu	Leucine	UUA UUG CUA CUC CUG CUU
M	Met	Methionine	AUG
N	Asn	Asparagine	AAC AAU
P	Pro	Proline	CCA CCC CCG CCU
Q	Gln	Glutamine	CAA CAG
R	Arg	Arginine	AGA AGG CGA CGC CGG CGU
S	Ser	Serine	AGC AGU UCA UCC UCG UCU
T	Thr	Threonine	ACA ACC ACG ACU
V	Val	Valine	GUA GUC GUG GUU
W	Trp	Tryptophan	UGG
Y	Tyr	Tyrosine	UAC UAU

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