

Principles of
**Cell and
Molecular
Biology**

Second Edition

Lewis J. Kleinsmith
Valerie M. Rish

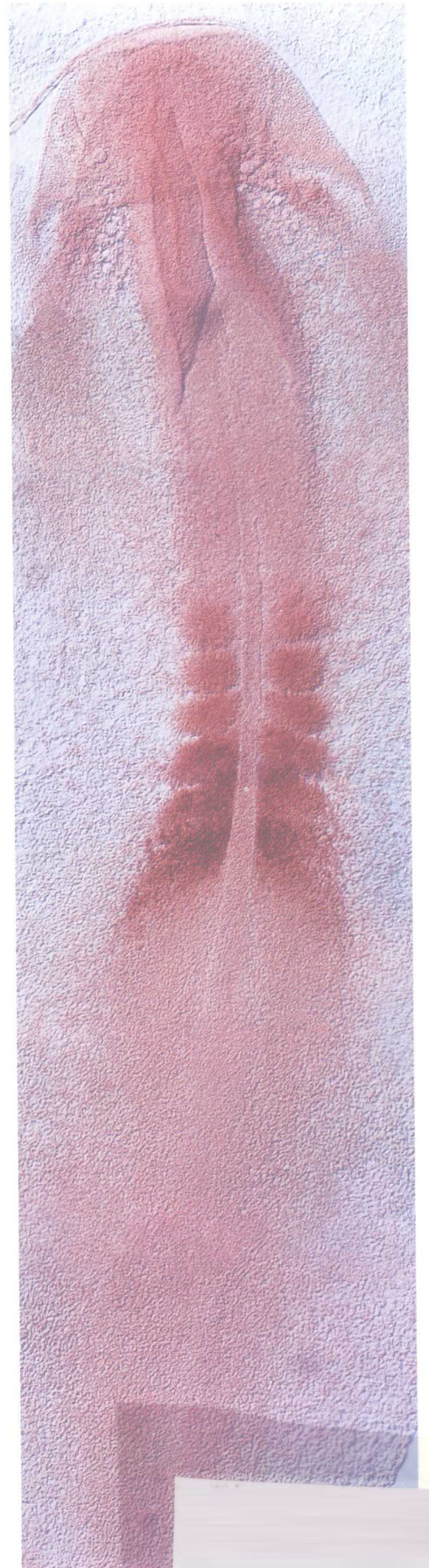
Developmental Biology

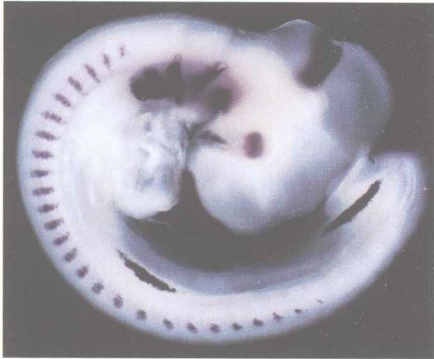
FIFTH EDITION

Scott F. Gilbert
Swarthmore College



SINAUER ASSOCIATES, INC.
PUBLISHERS
Sunderland, Massachusetts





The cover

COVER PHOTOGRAPH: The mRNA for Fibroblast Growth Factor-8 can be detected by wholemount in situ hybridization using chemically labeled RNA that is complementary to this message. In this 3-day chick embryo, the *Fgf8* message is found in the most distal ectoderm of the limb buds, in the boundary between the midbrain and hindbrain, in the somites, in the branchial arches of the neck, and in the developing tail. FGF8 is important for several developmental processes, and it plays critical roles in the outgrowth of the limbs and the patterning of the developing brain. Chapters 3, 7 and 18. (Photograph courtesy of E. Laufer, C.-Y. Yeo and C. Tabin.)

BACK COVER PHOTOGRAPH: Photograph of a Day 20–21 chicken embryo at the pipping and prehatching stage. Note the prominent peridermal covering at the tip of the beak (egg-tooth), used by the chick to make holes in the egg-shell, which has become thinner and more brittle as a consequence of mineral utilization by the embryo for its growing skeleton. This developmental stage marks the transition of the embryo into an air-breathing chick. Chapters 1 and 5. (Photograph from the *International Poultry Journal*, courtesy of R. Tuan.)

The title pages

LEFT PAGE: Gene expression generates boundaries in *Drosophila* imaginal discs. The large and small discs within the fly larva form the adult wing and haltere, respectively. At this stage, Apterous protein (red) is expressed only in the dorsal compartments; the Cubitus interruptus protein (blue) marks the anterior (but not the posterior) compartments (a line forming this boundary can be seen). The green staining (from the Vestigial protein) in the interior demarcates the boundary between the free limb and the hinge linking it to the thoracic wall. Chapter 19. (Photograph courtesy of J. Williams, S. Paddock and S. Carroll.)

RIGHT PAGE: Expression of the *paraxis* gene in the 6-somite chick embryo. Wholemount in situ hybridization using a digoxigenin-labeled RNA complementary to a portion of the chick *paraxis* message shows the expression of this gene during somite formation. The Paraxis protein is important in establishing the structure of these mesodermal clusters. Chapters 2 and 9. (Photographic montage courtesy of R. Tuan.)

Developmental Biology, FIFTH EDITION

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Sinauer Associates, Inc., P. O. Box 407,
Sunderland, Massachusetts 01375-0407
U.S.A.

Fax: 413-549-1118

E-mail: publish@sinauer.com

Library of Congress

Cataloging-in-Publication Data

Gilbert, Scott F., 1949–
Developmental biology / by Scott F. Gilbert.
—5th ed.

p. cm.

Includes bibliographical references and index.

ISBN 0-87893-244-5 (hc)

1. Embryology. 2. Developmental biology.

I. Title.

QL955.G48 1997

97-6182

571.8—dc21

CIP

Printed in U.S.A.

6 5 4 3

To Daniel, Sarah, and David

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Preface

The last years of the twentieth century find developmental biology returning to the position it held a century earlier: the discipline that unifies the studies of heredity, evolution, and physiology. In 1896, E. B. Wilson's first edition of *The Cell in Development and Inheritance* announced "the wonderful truth that a single cell may contain within its microscopic compass the sum-total of the heritage of the species." Today, developmental biology is in the forefront of this study of our natural heritage. In its *molecular* aspects, it touches physical chemistry in its probing of the biochemical mechanisms by which different proteins are made in different cells from the same genome. It is also at the lead of *evolutionary* studies that seek to understand how macroevolutionary changes have occurred. It has recently opened a new area of *ecological* developmental biology wherein environmental changes are seen to create alterations in organismal development. During the past three years, developmental biology has also expanded into *medicine*, merging with clinical genetics to create a revitalized science of human embryology, a science that has already become important in explaining congenital malformations.

The fifth edition of *Developmental Biology* has been revised and rewritten to reflect these ongoing revolutions. There have been four major changes in the structure of the book since the last edition. First, it has become impossible to discuss the fundamental principles of embryology without knowledge of *gene activity* or *signal transduction* pathways. Therefore, this information has been brought into the introductory section of the book so that cellular interactions such as fertilization and induction can be appreciated on the molecular as well as on the morphological levels.

Second, new interest in the effects of the environment on normal and abnormal development has led to a new chapter. Chapter 21, "Environmental Regulation of Animal Development," concerns the ways by which the environment effects the phenotype of the organism. Interest in environmental protection and in controversies surrounding possibly teratogenic pollutants has forced a new awareness of the influences that the environment plays in normal and abnormal development. Indeed, developmental biologists may soon find themselves at the forefront of ecological conservation movements. The first four editions of this book sought to integrate the molecular, cellu-

lar, and organismal approaches to developmental biology; this edition adds the ecological dimension.

Third, this edition places new emphasis on the roles of paracrine factors in development. Not only are the signal transduction studies placed in the introductory section of the book, but Part V of the Fifth Edition begins with an overview of the fibroblast growth factor, TGF- β , Wnt, and Hedgehog families of growth and differentiation factors.

Fourth, this book is connected to a website wherein students and faculty can find more material on many selected topics. Such material includes (1) details of experiments that are too specialized to put into the textbook, (2) historical information about particular areas of developmental biology and the personalities involved, (3) medical implications of particular developmental phenomena, (4) debates or commentaries on issues relevant to the field, and (5) updates of the text material in this increasingly rapidly growing area of biology. Movies and taped interviews are included and this feature will be expanded as the technology makes them easier to use. This website is also connected to other websites and can be used to enrich one's perspective about what is happening in animal development. The presence of a website allows me to keep directing this book to the people for whom it was originally intended: upper-level undergraduates and introductory graduate students. It also has helped me keep the book from becoming a substitute for standing weights.

It was Roux's vision that developmental biology would "sometime constitute the common basis of all other biological disciplines and, in continued symbiosis with these disciplines, play a prominent part in the solutions of the problems of life." These were bold, even arrogant words one hundred years ago; today, they express a widely held assumption. Development integrates all areas of biology and plays the crucial role of relating genotype to phenotype. Development can be studied using any organism and at any level of organization, from molecules to phyla.

As the field continues to expand and deepen, a word of warning is called for: developmental biology cannot be taught or learned in a single semester. This text is an attempt to provide each person with sufficient material for their course, but an instructor need not feel guilty for not assigning every chapter, and students need not feel deprived if they have not read every chapter. This is the beginning of the path, not its conclusion.

How to use the website

One can enter the website through its homepage [<http://zygote.swarthmore.edu/index.html>] or through its table of chapter files located at [<http://zygote.swarthmore.edu/info.html>]. Alternatively, we have placed specific access addresses throughout the book wherever a relevant entry exists at the time of publication. These addresses all begin with [<http://zygote.swarthmore.edu/>] and are followed by the code given in the textbook. Thus, the location specified on page 20 of the textbook is:

<http://zygote.swarthmore.edu/intro2.html>

More locations are being added to the website, and these can be accessed by entering the chapter files. In addition, by clicking on the "Other Files" button on the bottom of each chapter file, connections to other websites will be facilitated. Have fun.

Acknowledgments

This edition, like its earlier incarnations, owes a great deal to the suggestions and criticisms of the students in my developmental biology and developmental genetics classes. The extremely supportive staff and faculty of Swarthmore College have also played major roles in producing this book, and science librarians E. Horikawa and M. Spencer are due special thanks for keeping recent volumes from being sent to the bindery while I was writing the book. The scientists who reviewed these chapters provided enormous help in both the technical accuracy of the chapters and in suggestions for further work. These investigators include S. Carroll, J. Cebra-Thomas, E. M. De Robertis, S. DiNardo, E. Eicher, C. Emerson, D. J. Grunwald, G. Grunwald, M. Hollyday, L. A. Jaffe, W. Katz, R. Keller, K. Kempfues, D. Kirk, G. Martin, H. F. Nijhout, D. Page, R. Raff, R. Schultz, C. Stern, S. Tilghman, R. Tuan, and M. Wickens. I also want to thank several scientists who went out of their way to help make this edition better by reading specific portions of the chapters. They include M. Bronner-Fraser, J. Fallon, N. M. Le Douarin, E. McCloud, J. Opitz, K. Sainio, H. Sariola, I. Thesleff, and T. Valente. If I left anyone out, please forgive me. Needless to say, the final editorial judgments were my responsibility. My special thanks to Judy Cebra-Thomas who not only advised me on certain chapters but whose excellent help during my sabbatical leave allowed me to finish this book. Thanks also to the scientists and philosophers, especially C. van der Weele, R. Amundson, L. Nyhart, R. Burian, H. F. Nijhout, A. F. Sterling, K. Smith, and A. I. Tauber, who participated in the developmental biology workshops of the International Society for the History, Philosophy, and Social Studies of Biology. Some of the best constructive critiques of this textbook have come from these people.

Andy Sinauer has yet again managed to gather the same remarkable people around this project, and it has been a privilege to work with them. My thanks to him and to editors Nan Sinauer and Carol Wigg, production coordinator Chris Small, artists John Woolsey and Gary Welch, designer Susan Schmidler, copy editor Janet Greenblatt, and layout artist Janice Holabird. The editorial skills of Tinsley Davis are greatly appreciated. Because publishing deadlines must be met and other work gets put aside, I have to thank my family for once again allowing me to get away with this. In particular, this book could never have been completed were it not for the encouragement of my wife, Anne Raunio, who, as an obstetrician, enjoys the more practical side of developmental biology. My thanks to you all.

SCOTT F. GILBERT

MARCH 1, 1997

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