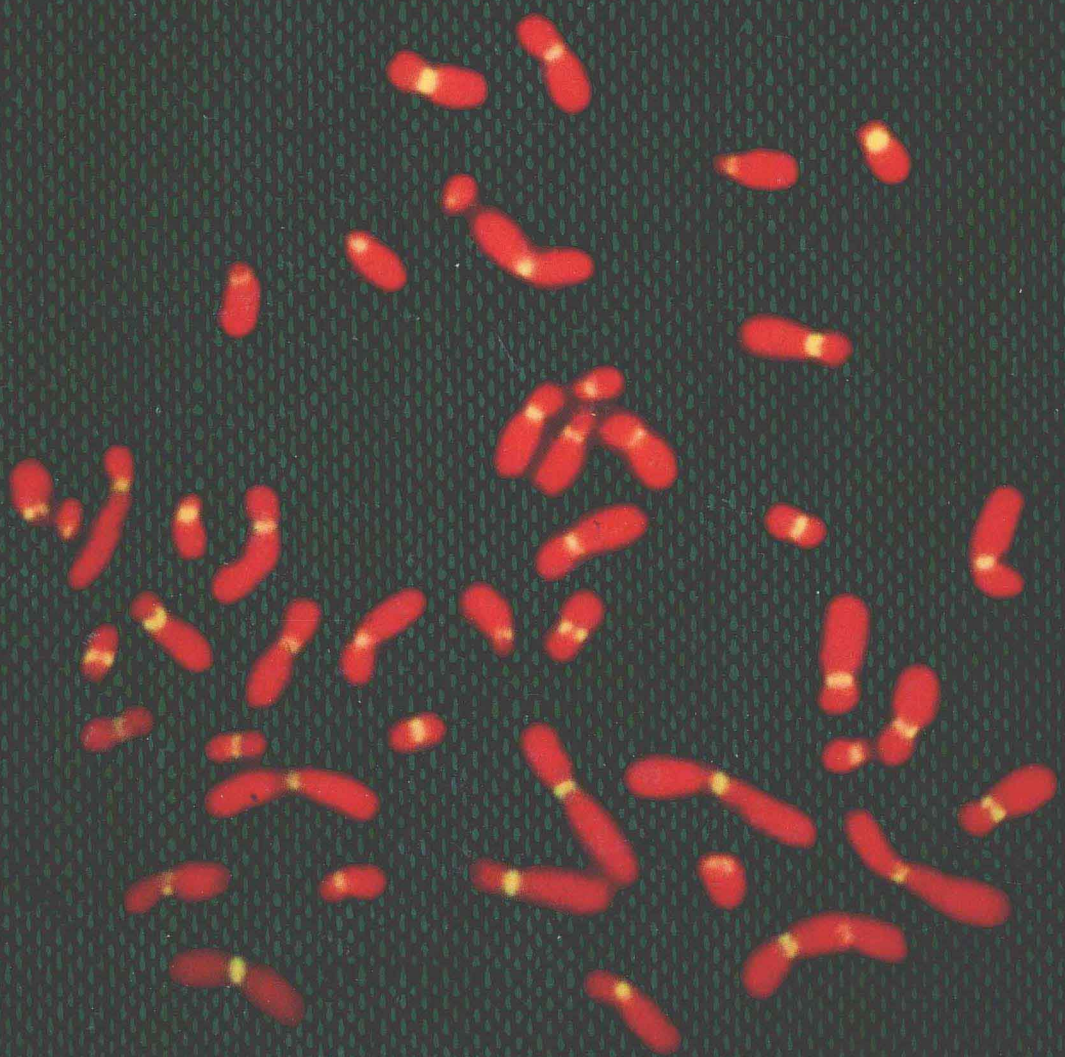
MOLECULAR BIOLOGY OF THE CELL

SECOND EDITION



Bruce Alberts · Dennis Bray · Julian Lewis
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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 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.

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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.) ▶

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