Preface to the Third Edition

Biological research is in an explosive phase, driven by a new awareness of the basic unity of all life forms. Today, the key to a problem about neurons, plant cells, or cancer may lie in research on yeasts, frogs, or flies. More than ever before, molecular genetics is showing us how to recognize and exploit such connections and is forcing us to reflect on the ancient origins of the components from which we are made. In surveying cell biology, one does not know whether to marvel more at the endless variety of living systems or at the fundamental similarities in the mechanisms by which all cells operate.

The challenge in writing a textbook is to pick out the concepts that are most important for our understanding. The problem in revising it is to see where these concepts have changed or new ones have emerged. This is a very different matter from summarizing the new facts: many new facts may change our view of cells very little, whereas a few can transform the whole picture. Recognizing that it is impossible to be comprehensive, we have struggled to ensure that our book should provide a survey of cell biology that students can readily read and digest. We have therefore devoted as much thought to the problem of what to leave out as to the problem of what to add.

In this third edition, large parts of the text have been radically rewritten to take account of recent advances. Two chapters—those on plants and on neurobiology—have been dismantled and the material from them integrated into other chapters, emphasizing that these topics are not mere side issues for specialists, but belong to the core of cell biology. Several of the central chapters of the book have been subdivided into more manageable parts, and a new chapter devoted to recombinant DNA technology has been added. We have also inserted a new chapter on the principles of protein function, showing how proteins operate as molecules with moving parts to form the dynamic gadgetry of the living cell—a fundamental topic that is only now gaining its rightful prominence, with the rapid growth in knowledge of protein structures. To bring protein molecules to life, we have selected an anthology for inclusion on a computer diskette together with the Kinemage program, which allows one to view the molecular structures three-dimensionally, rotating and manipulating them on the computer screen and watching as they undergo their conformational changes. The diskette is available from the publisher for a small charge. At the end of the book, we have added a glossary of essential technical terms. Tim Hunt and John Wilson have updated and enlarged their problems book to accompany the main text and help students appreciate the experiments and the reasoning on which our understanding of cells is based.

A special acknowledgment is due to four contributors (all from the University of California, San Francisco) who have had a major hand in writing specific chapters: Sandy Johnson (Chapters 8 and 9), Peter Walter (Chapters 12 and 13), Andrew Murray (Chapter 17), and Tim Mitchison (Chapters 16 and 18); also to Michael Klymkowsky (University of Colorado, Boulder) for his contribution to Chapter 16. We once again owe a debt also to the many experts who have generously given advice, comments, and corrections; they are acknowledged individually on pages xxxix–xli. As editor, Miranda Robertson, as always, had a crucial role in making the text clear, coherent, and accessible to students.

With this edition, we have ventured into full color. Nigel Orme converted drawings into printable color artwork with magical promptness and skill. Carol Winter again typed the entire book with painstaking care and prepared the final disks. John M-Roblin wove text and figures together into pages for printing and made the transition to computerized book production seem easy. Brian Rubin helped with references, Fran Dependahl helped with the typing, and Emily Preece fed us in style while we were writing. We give our thanks to all of them, and to many others, especially the staff of Garland Publishing, who contributed in ways too numerous to list. We are particularly indebted to Ruth Adams, who once again oversaw the production of the book with unfailing efficiency and good humor, and to Elizabeth Borden, now head of Garland Publishing, whose warm hospitality, good sense, and friendly encouragement have carried us through to the end of a daunting task for the third time. Thanks, above all, to our long-suffering families, students, and colleagues, who patiently put up with our absences and preoccupations.

Lastly, on a sad note, we record our debt to Gavin Borden, our publisher, who became our close friend and who died of cancer in December 1991. Without him, there would have been no book. We, and the book itself, owe more than we can say to his spirit of adventure, his generosity, his love of life, and his friendship. We dedicate this edition to his memory.

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 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 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 cre-

ation 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.