

Preface

"You know, the proper method for inquiring after the properties of things is to deduce them from experiments"

Isaac Newton, 1672

The Problems Book aims to provide a running commentary for *Molecular Biology of the Cell, Fifth Edition* by Alberts et al. As we wrote in earlier prefaces, we would like to stimulate our readers to ask questions as well as to accept, digest, and learn the stories that 'the big book' tells. In real life, however, knowledge and understanding come from research, which entails curiosity, puzzlement, doubt, criticism, and debate. Groping one's way through the fog of uncertainty during a research project is a slow and often discouraging process; eureka moments (even if one is lucky) are few and far between. Nevertheless, those moments catch the essence of the drama, and we have tended to focus on them, where we have been able to cast them in the form of a problem. In this way, for student and teacher alike, we hope to encourage a questioning attitude to biology. Without curiosity there would be neither science nor scientists.

We have been making up problems together for more than twenty years, and the revision leading to this new edition of *The Problems Book* has taken us more than three years. There are several new things about this edition. We are proud to say that its 20 chapters now match the first twenty chapters of *Molecular Biology of the Cell*, which means that there are three entirely new chapters: on microscopy (Chapter 8), on the extracellular matrix and cell-cell interactions (Chapter 19) and on cancer (Chapter 20). Elsewhere, the organization of each chapter has undergone major revision besides minor modifications and additions to existing problems. As before, sections start by listing the terms in bold from *MBoC*. As a simple test of memory and comprehension, we have added a new type of problem, which we call **Definitions**, where we ask the reader to identify these terms from a one-sentence description of their meaning. The following **"True/False"** section consists of a set of simple statements, whose truth the reader must judge and justify. Next come short questions we call **"Thought Problems,"** modeled on the kinds of problems presented in *Essential Cell Biology* also by Alberts et al. Some of these are more challenging than others, some are playful, some are serious, but all are designed to make the reader think. After this comes a section called **"Calculations,"** which is designed to help deal with quantitative aspects of cell biology. The calculations in this book are mostly very straightforward, usually involving no more than the interconversion of units, yet they provide a solid framework for thinking about the cell. Are cell-surface receptors sparse in the plasma membrane, or jam-packed? Do molecules diffuse across a cell slowly, or in the blink of an eye? Does chromatin occupy most of the nuclear volume, or just a tiny fraction? Numerical analysis of such questions is very important if one is to gain a feel for the molecular basis of cell biology. Last but not least, the **"Data Handling"** section contains research-based problems, which arguably form the most important part of the book. Our original brief was to compose problems based on experiments so as to allow readers to get a better feel for the way in which biological knowledge is obtained. It is tremendously important to keep asking, "How do we know that? What's the evidence?" or to wonder how one might go about finding something out. Often

it's not at all obvious, often the initial breakthrough was a lucky chance observation, made while investigating some completely different business. In fact, it takes most of us years of research experience to grasp the idea of how one simple fact "can illuminate a distant area, hitherto dark" (Boveri, 1902). Seeing how these tiny shards of evidence give rise to the big picture often involves considerable imagination, as well as a certain discipline, to know how much weight the evidence will bear. We hope we have sometimes, at least, been able to capture the essence of how experiments lead to understanding. To do justice to the authors of the experiments we use in these problems, however, we strongly recommend recourse to the original papers, whose references we always provide.

We hope that the organization and classification of problems will help both student and teacher to find what they are looking for. As far as possible, the order of questions closely follows *Molecular Biology of the Cell*.

Another big change in this edition pleases us very much. For this edition, we have chosen to include the answers to every problem on the CD that comes with this book. We think this is a thoroughly good thing for readers. Many of these problems are difficult to answer, and are not really intended to be set as tests. Rather, we hope that readers will be intrigued (as we were) by the questions we ask, and after thinking a bit will want to see what the answer is, what form the discussion takes, how to get at thinking about this particular kind of a problem. Having used these problems ourselves, we know that even a problem with an answer can serve as the basis for a stimulating discussion in class. And if students are told in advance that a few problems from a larger set will be on an exam, they will be motivated to grapple with the reasoning behind all the answers—a lot of learning.

Another departure from previous editions is that a selection of questions from *The Problems Book* now appears in *Molecular Biology of the Cell* at the end of each chapter. We picked these problems in consultation with the authors of *MBoC* to highlight important issues in the text and to cover the range of problem styles. We are pleased with the final selections; they include some of our all-time favorites. The solutions to all these problems are printed in a separate section at the end of *The Problems Book*. We hope that many more readers of the main textbook will try working problems as a result of this change.

As always, we want to hear from our readers, for despite our best efforts, we do not always get things right. Please email John Wilson at jwilson@bcm.edu or Tim Hunt at tim.hunt@cancer.org.uk with your comments or queries, and we'll do our best to answer them.