Preface

All Life is problem solving
Sir Karl R. Popper

All cells process signals: they associate an exogenous stimulus into a "meaning"—that is, they are able to distinguish between good and bad in order to respond in an adequate manner. Even for most primitive unicellular organisms, signal processing (often called signal transduction) is essential for survival in an unpredictable environment. It is understood that a wide variety of diseases including cancer, diabetes, dementia, psychoses, and cardiovascular disorders are caused or at least promoted by disturbances in cellular signal processing, and most therapeutic drugs, as well as many narcotics, target signaling pathways. Therefore, signal transduction is a subject that ranks among the most rapidly developing fields within biomedical science.

This book deals with the biochemical mechanisms of cellular signal processing. It is intended for undergraduate students with a good knowledge of basic biochemistry and cell biology, and for graduate students in biology, biochemistry, and pharmacology, as well as medical students. The book emerged from our scientific work at the German Cancer Research Center and from a series of lectures we have given at the University of Heidelberg for many years. Although cell biology textbooks provide excellent introductions into the field of signal transduction, our students consistently requested a more comprehensive treatment of the subject that, in particular, addressed evolutionary aspects and questions of medical interest. Moreover, we identified the need for a textbook that would offer a more complete overview of the field than currently provided by available books. As such, it may be useful not only for the student but also for the scientist.

It is currently impossible to depict and describe all the molecular interactions that occur when a cell receives a signal. In an effort to navigate the middle ground between incomprehensibility and superficiality, we have confined ourselves to describing more or less linear signaling cascades that illustrate mechanistic principles of major signaling pathways, although systems biology is currently integrating these cascades into networks. One of the hallmarks of this textbook is its presentation of a unifying concept of signal transduction. Cell signaling is traced to a few simple biochemical switching reactions that link logical operations—mainly performed by protein-protein interactions—with energy-delivering processes of cellular metabolism.

As with the first edition, Chapter 1 deals with the ability of proteins to form a "neural" network that, together with the genome, resembles a cellular brain. In this network, each protein acts as a "molecular neuron" that, according to the laws of chemical thermodynamics and mathematical logic, transforms input signals (environmental and systemic stimuli) into output signals (cellular behavior facilitating adaptation). According to the second law of thermodynamics, a data-processing apparatus needs to be supplied with energy. For the protein network, this energy is derived from a series of exergonic biochemical reactions such as redox processes, GTP and

ATP hydrolysis, protein phosphorylation, and discharge of the membrane potential. This biochemical arsenal is explained in Chapter 2. As discussed in Chapter 3, the biochemistry of cellular signal transduction has a long evolutionary history. It was initiated billions of years ago and, similar to metabolic and genetic mechanisms, has been conserved during evolution. These basic themes are discussed in more detail in Chapters 4 through 16. Finally, Chapter 17 places cellular signal processing in the context of systems biology and describes the formation and function of networks.

In response to our readers, we have updated and reorganized many sections of the text accordingly. New coverage includes intrinsically disordered proteins, signaling by non-coding RNAs, new evolutionary concepts of signal transduction, inflammasomes, regulated necrosis, autophagy, and optogenetics. In addition, the lists of Further Reading found at the end of each chapter have been entirely revised, providing an up-to-date guide for exploring the more specialized literature. To this end, we have focused on the most recent review articles, rather than original publications. Many of the questions raised today will certainly be answered in the near future, whereas other problems not yet recognized will become apparent. Nevertheless, our hope for this new edition of the book, as for the previous one, is that it will be an indispensable resource for students and scientists who are exploring and working in one of the most exciting fields in the life sciences.

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Instructor Resources Website

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