

Preface

All life is problem solving

Sir Karl R. Popper

Cellular signal processing, often called signal transduction, is a subject that ranks among the most rapidly developing fields in biomedical sciences. Diseases such as cancer, diabetes, dementia, psychoses, and cardiovascular disorders are caused in part by disturbances in cellular signal processing, and the majority of therapeutic drugs as well as many narcotics target corresponding cellular pathways.

This book is intended for undergraduate and graduate students in biology, biochemistry, bioinformatics, and pharmacology as well as for medical students. It 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, presented 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 that currently provided by available textbooks and monographs.

The most serious obstacle we faced in developing this book is the rapidly increasing amount of data that is still more or less in a preliminary form. In order to address this problem and keep the reader from losing the thread of the narrative, we decided to organize the content in a way that is different from that in other textbooks. To this end, the discussion is guided by three major principles that dominate cellular signal processing, namely the protein network, its energy supply, and its evolution.

These principles are introduced in the first three chapters. 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 aiming at 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. An essential condition of survival in prokaryotes in an unpredictable environment is the ability to process signals, a function that must have evolved in parallel with metabolism and reproduction at the dawn of life. As discussed in Chapter 3, the biochemistry of cellular signal transduction that was initiated billions of years ago has been conserved during evolution, thus rivaling the conservatism of metabolic and genetic mechanisms. Chapters 4 through 16 then examine variations of these basic themes in terms of signal transduction in eukaryotic cells. The final chapter places cellular signal processing in context with systems biology and describes the formation and function of networks.

One of the hallmarks of the book is its presentation of a unifying concept of signal transduction that traces cell signaling to a few simple biochemical switch-

ing reactions that link protein-protein interactions with energy-delivering processes. To this end, the book devotes attention to important aspects that play a major role in these processes and that, in many textbooks, are either treated in a cursory manner or not at all. These topics include prokaryotic signal transduction, lipid signaling, hedgehog and Wnt signaling, Toll-like receptors and innate immunity, small G-proteins, steroid hormones and nuclear receptors, signals controlling mRNA translation, the role of ubiquitylation in signal processing, sensory signaling, ion channels, and neurotransmitter signaling. Presently the genome – considered to be the innate memory store of the “cellular brain,” is emerging as a highly complex and dynamic system, which forms a regulatory network of its own. Since the exploration of this matter is just in the very beginning, we confined ourselves to a discussion of those interactions between the genome and the protein network that are sufficiently understood today.

The highly visual illustration program and features such as sidebars, which highlight complementary perspectives to the main discussion, help to strengthen the student's understanding of the essential concepts. The figures in the book are available in both PowerPoint® and JPEG formats on the book's Website, which can be accessed at www.garlandscience.com.

Academic lecturing is a process of giving and receiving. Therefore, we are grateful to our students for their attentive and critical interest and many helpful suggestions. We are particularly indebted to Ingrid Hofmann, Peter Krammer, Frank Rösl (all, German Cancer Research Center Heidelberg), Stefan Rose-John (University of Kiel), and Felix Wieland (University of Heidelberg) for reviewing individual chapters and providing critical comments. We would also like to express our appreciation to the following for their valuable critiques of the manuscript: Joseph Eichberg (University of Houston), Mark A. Lemmon (University of Pennsylvania School of Medicine), Shigeki Miyamoto (University of Wisconsin, Madison), Bradley J. Stith (University of Colorado, Denver), Wei-Jen Tang (University of Chicago), and Alexey Veraksa (University of Massachusetts). Thanks also to our colleague Martin Frank for his support in the preparation of figures showing three-dimensional protein structures. Finally, we would like to thank Heather Whirlow Cammarn, our copyeditor, and the editorial staff at Garland Science, in particular Janet Foltin and Katherine Ghezzi. Their never-ending patience, support, and encouragement were an invaluable experience and indispensable condition for the preparation of this book.

Factual errors are, of course, inexcusable but, unfortunately, not unavoidable. In this respect, we ask our readers for forbearance and welcome suggestions for improvement. We are aware of the fact that, in such a rapidly developing field, ideas, concepts, conclusions and the latest “facts” are highly perishable goods. Many of the questions raised today will certainly be answered in the near future, whereas other problems not yet recognized will become apparent. Nevertheless, we hope that the book serves as 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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