

Preface

The ability to sense one's environment and respond to it is one of the most fundamental properties common to all living organisms. Single-celled organisms are able to seek out nutrients, avoid toxins, and change their shape, gene expression, and metabolism depending on conditions. In multicellular animals and plants, even more subtle and sophisticated interactions between cells and the outside environment are needed. Individual cells are able to sense and integrate vast amounts of information and use it to make decisions about whether to grow, divide, migrate, adopt a particular shape, or even die. Without these decisions, a multicellular organism could neither develop nor maintain its integrity as a coherent living entity. Cell signaling is everywhere we look.

For most of its relatively brief history, cell signaling (or signal transduction, as it is often termed) was typically taught from the perspective of individual, top-down physiological stories—for example, understanding how a cell responds to a particular type of hormone, such as insulin or epinephrine. However, this approach has become increasingly untenable as we attempt to understand and explain how thousands of signaling proteins interact with each other in vast interconnected networks. Fortunately, it is now apparent that diverse signaling processes are often executed by very similar sets of molecular components, which in turn often interact in common network patterns. We can now consider a more bottom-up view—that there are hierarchical building blocks for signaling often used in archetypical ways to achieve particular classes of cellular behaviors. The overarching theme of this book is that signaling is best understood by focusing on the common design principles, components, and logic that drive all signaling.

We have written this book embracing this new, bottom-up view of cell signaling, and focus on the principles and mechanisms that underlie many, if not all, cell signaling processes. Therefore, we emphasize the commonality of underlying mechanisms rather than the diversity of individual examples. As we enter the postgenomic era, research is shifting away from the discovery of specific signaling molecules and toward understanding how such cellular components can execute nuanced, complex regulatory behaviors. Understanding how simple molecules specifically interact to form a system with emergent response properties is very much at the heart of cellular signaling, as is understanding how such a diversity of response behaviors has evolved. Signaling is a field in

which our understanding is growing exponentially and our viewpoint is constantly changing. While the rapid growth and change in this field makes writing a textbook on cell signaling challenging, it is also a particularly exciting time to try to lay out the core molecular concepts and principles that have emerged in this young field.

Memorizing the details of “who did what to whom and when” for a number of specific pathways, especially where most of the players have similar-sounding three-letter acronyms, can be a recipe for confusion. It is our hope that by focusing on the common themes and concepts that underlie all signaling pathways, students will better see the beauty and logic of the system, and be able to apply this understanding to any signaling problem they encounter. This is particularly relevant in our era of superabundant information where manifold details are readily available at a few keystrokes. We hope the book conveys the deeper principles of the subject that cannot be encapsulated in a Wikipedia entry.

ORGANIZATION OF THE BOOK

The first major section of the book (Chapters 2–9) focuses on the molecular parts and molecular principles used in cell signaling. These chapters introduce the types of molecular players, including catalytic domains, protein interaction domains, and receptor molecules. They also introduce the core currencies that are used to store and transmit signaling information at the molecular level, including molecular conformation, interaction, localization, modification, and degradation. In this section, we hope the reader will gain a deep understanding of how these molecular players can be used to conditionally modulate the core information-storage currencies. The second major section of the book (Chapters 10–12) moves gradually toward understanding cell signaling systems—how these components and currencies can be used to make more complex devices and networks that are capable of executing higher-level physiological decisions. The last chapter of this section (Chapter 12) is organized as a set of exploratory, visual panels. Here, we return to a more classical view of signaling—focusing on four physiologically important pathways (vision, mitogen response, the cell cycle, and T cell activation)—and describe their molecular components from top to bottom. We attempt to illustrate how the components discussed in previous sections of the book are used to solve key physiological problems in

these model pathways. The goal of this unique chapter is to integrate a top-down physiological perspective with a bottom-up perspective of central principles and molecular components. Finally, the last chapter of the book (Chapter 13) is a compendium of experimental methods and approaches used to study cell signaling. It provides an overview of “how we know” what we know and of important tools of the trade.

Although our aim in organizing the book is to provide a conceptual framework for understanding signaling mechanisms, we understand that some readers may also wish to use it to provide an introduction to specific signaling pathways. For this reason, we use many specific examples throughout the book (mostly but not exclusively from multicellular animals) to illustrate the broader principles. In this way, most major signaling pathways and families of signaling molecules are explained and illustrated in some detail. However, we imagine that many instructors using this book may choose to supplement it with readings selected from recent experimental papers, in order to provide greater depth in specific areas of interest.

The end of each chapter includes a set of study questions. These questions are designed to encourage students to think more concretely about the concepts covered in each chapter, to extract and synthesize this information in new ways, and to think about signaling from an experimental perspective. Some questions have one clear answer, whereas others are more open-ended and have multiple possible answers. Answers to the questions are available online from the publisher's Web site. Chapter 12 does not contain end-of-chapter questions,

but rather integrates exploratory questions throughout each panel set.

We also include a short list of references at the end of the chapters. The intent is to provide a starting point for readers who wish to delve more deeply into the topics covered. These references are by no means comprehensive, and in a field as rapidly moving as cell signaling, it would be impossible to cover fully the most recent developments. Therefore we sincerely apologize to the many valued colleagues whose publications deserved to be included, but were omitted due to space constraints or inadvertent oversight.

STUDENT AND INSTRUCTOR RESOURCES

Every copy of the book includes a two-sided “Signal Transduction Pathways” poster created by Cell Signaling Technologies®. The poster details forty important signaling pathways.

Online resources for students and instructors can be found at www.garlandscience.com/cellsignaling.

For qualified instructors:

- Artwork in JPEG and PowerPoint® formats

For students:

- Online flashcards and glossary
- Answers to end-of-chapter questions
- PDF of “Signal Transduction Pathways”