attention to specific concepts or historical facts. The chemistry of ferrocene is summarized well through exhaustive reaction schemes. Topics in catalysis have been dealt with adequately and examples of industrial application of homogeneous catalysis are highly commendable inclusions.

Transition metal-mediated reactions have changed the way we practice organic synthesis today. This book may not come out with such an impression. We hope to soon see an accompanying volume that would directly deal with organometallic reagents, catalysts and transformations leading to intricate molecular architecture with a high degree of selectivity.

The text is pleasantly free of errors though some usage seems peculiarly Indian. Several mistakes in the large body of chemical structures have already been noticed and corrected.

One last thought: organometallic chemistry texts such as these almost always leave out discussion of chemistry involving maingroup metal-carbon bond. In such a case, should we not restrict the title to ‘organotransition metal chemistry’ or ‘organometallic chemistry of transition metals’?

AMITABHA SARKAR

Department of Organic Chemistry,
Indian Association for the Cultivation of Science,
Kolkata 700 032, India
e-mail: ocas@iacs.res.in

Control Theory and Systems Biology.
Pablo A. Iglesias and Brian P. Ingalls (eds). The MIT Press, 55 Hayward Street, Cambridge, MA 02142, USA.

Systems biology is a relatively new research model where the approach of integration, rather than reduction, is employed to analyse biological complexity and understand how biological systems function. By default it requires a multidisciplinary approach with scholars from biology, mathematics, engineering, computer science and physics working in an interactive and collaborative environment. Given this interdisciplinary nature, obviously ‘Systems biology’ acquires different meanings in different contexts and to different researchers. One of the current focuses of systems biology is in understanding biological functions from networks of interactions among the underlying ‘parts’ (genes and proteins) obtained from high-throughput biological experiments. This kind of research requires knowledge of the sophisticated techniques of molecular biology, as well as mathematical and computational tools from engineering and physical sciences, to describe and interpret the results. This also means understanding the culture of unfamiliar research communities. The neck-breaking pace at which molecular data are being generated now far exceeds the rate at which theoretical methods are being developed to analyse and interpret the data. One of the major problems is the gap between disciplines and the unfamiliarity of the communities about each other’s subjects. This book, edited by two engineers and mathematicians, Pablo A. Iglesias and Brian P. Ingalls, is an excellent contribution towards bridging this gap between the disciplines of engineering and biology.

Control theory is an interdisciplinary subfield of science, which was originally a part of engineering and mathematics, having roots in the analysis and understanding of physical and technological systems. But it has gradually revealed its potential as a tool for describing any complex dynamical system, and evolved to have important applications in biological and social sciences. The properties of stability, feedback, controllability, robustness, etc. were used in mathematical models of physical systems with a set of input, output and state variables related by differential equations. The idea is to achieve the desired output of a system (called ‘reference’) by manipulating the inputs using a ‘controller’. Applications are abound in engineering and physics – mechanical systems, electrical circuits, aeronautical processes, etc. Historically, it was Norbert Wiener, a mathematician, who realized the commonality between a physical machine and the ‘animal’ in addressing questions related to communication and regulation1. The development of the area of ‘cybernetics’, based on control theory, fuelled studies on problems related to biological systems, especially systems in physiology, such as respiration, cognition, adaptation, etc. using electrical circuit analogues.

Over the past 25 years, tremendous progress in measurement technologies has advanced our understanding of the workings of biological systems dramatically – especially the molecular processes underlying cellular functions. By the middle of the last century scientists had experimentally shown that specific biochemical reactions inside the cells can be described by small control circuits which possess feedback regulation to optimally adjust the making and breaking of biomolecules. With the present ability of researchers to make hundreds or even thousands of simultaneous experimental measurements for system-wide study of intracellular processes, it has now become apparent that concepts of control theory play a central role in the global performance of these self-regulating biochemical systems, and is one of the active principles by which living systems operate. Thus, the book under review addresses this highly interdisciplinary area and fills an important new niche by presenting control theoretic approaches in the study of cellular mechanisms with surveys of known facts and studies to new applications and developments in
the field. The important feature of this book is that the authors realize the need to address an interdisciplinary community, and so they have developed the control theoretic theme in an accessible manner. Of the 27 expert authors, 18 are from different engineering disciplines—chemical, electrical, mechanical, automation, aerospace, etc. Others are from mathematics, computer and system sciences, biophysics, systems biology and bioinformatics. This points towards the unique situation that biology is in today, where the huge amounts of experimental data generated by the biological experiments require expertise from other disciplines for collation, description, analysis and interpretation.

Even though this is not a textbook, where topics are developed linearly for incremental increase in understanding, the chapters in this book can be grouped into sections dealing with specific areas. There are 14 chapters, of which the first one is an excellent primer on control engineering topics and mathematical tools explaining the differential equation description of biochemical reaction pathways for biologists. It also discusses concepts of stability and bifurcation in linear and nonlinear dynamical systems, and introduces different types of input–output systems which are more common in the realm of engineering. Chapters 2 and 3 contain different modelling methods to address important features of biochemical reactions in cells—the presence of fluctuations in molecular concentrations and spatial heterogeneity. The stochastic analysis of biochemical reactions is mathematical and introduces most of the relevant concepts and methods used in these studies. I particularly liked the article on spatial modelling (chapter 3), as it discusses the issues involved in the control of spatial heterogeneity using partial differential equations—a feature important in many areas in biology where pattern formation occurs. It starts with a simple one-dimensional model, but goes on to show, with more complex models, how controlling diffusion and transport can regulate system behaviour and stability.

Many of the chapters illustrate the application of control theoretic ideas in specific examples of biochemical systems. Understanding the specific design of the MAPK signalling cascade, which transfers environmental signals through intracellular reactions, is discussed using chemical kinetic models in chapter 4. The heat-shock response system in bacteria is studied as a model for stress response mechanisms in chapter 5. The roles played by reaction network topologies and feedbacks are discussed here. Chapter 5 discusses the systems engineering studies of transcriptional regulatory systems (‘gene circuits’), and, based on their similarity with electronic circuits, elaborates the modular nature of these small control systems in biochemical pathways. Chapter 7 introduces the use of graph theory in describing biochemical pathways. It is a common approach today to describe large networks, where less quantitative (reaction rates) and more qualitative (structural) information is available. Chapter 8 develops the established fields of metabolic control analysis and biochemical systems theory, which have been used to model metabolism using parametric sensitivity analysis, from the control engineering perspective. This is a mathematical chapter and highlights the role of stoichiometry in the control of metabolic systems. The next three chapters (chapters 9 to 11) introduce and discuss the commonly used tools in studying the property of robustness in biochemical reaction networks. It is important that biochemical reactions maintain their functionality in the face of internal and external perturbations. Analytic tools from the field of control engineering, such as sensitivity analysis, structured singular value analysis, generalized Nyquist stability, stochastic robustness analysis using a Monte Carlo approach, etc. have been introduced and applied to specific examples of insulin signalling, circadian clocks, population of neurons, MAPK signalling cascade, oscillations in activated neutrophils, and aggregating slime mould cells. Chapter 12 discusses stochastic biochemical processes using a more general method than what is given in the stochastic chemical kinetics formalism in chapter 2. Using a probabilistic approximation method for model comparison and model calibration (‘Wasserstein pseudometric method’) — a tool not so widely known to non-engineers, but seems to have great applicability—the authors study a reaction network derived from gene expression data, which are known to be highly stochastic in nature. The last two chapters are devoted to reaction network reconstruction—an area of immense importance and complexity due to incomplete and insufficient data. Matching the dynamic time series expression data in the face of incomplete information can give rise to multiple possible networks to fit the input–output data. In chapter 13 the authors present a dynamic structure–function approach for designing possible network structure using experimental perturbation data. Chapter 14 discusses a parameter-free coordinate system approach that considers the kinetics of the pathway reactions. Application of the method to the MAPK signalling cascade is shown. The bibliography of all papers referred in the chapters is collated at the end. The subject index is quite extensive. An author index could add more value to this informative book.

This book will be useful for two reasons. For engineers who plan to work in this area, it is a must reference, as it gives, in one place, a large array of methodological and many biological problems where they can be applied. It is also educative to non-engineers who are working in specific areas of pathway modelling, because it gives a wide exposure to other control theoretic tools that can be used. Having both in one place is the uniqueness of this monograph. It certainly is timely, as increasing numbers of workers are entering this interdisciplinary area, and this book is a very useful and excellent educational material covering multiple disciplines. The treatment of the topics in each chapter will be useful not only to beginners in this field, but also to those who are already working in specific areas, and as a companion to multidisciplinary courses in systems biology and engineering. We are only at the beginning of the data deluge that is being generated by high-throughput experiments in biology now. To know how to handle them and to develop algorithms and new hybrid methods will require a large workforce trained in these areas of systems biology. The sooner we start addressing these issues, the better equipped we will be. This book certainly gives direction to the future in systems biology.


SOMADATT SINHA
Centre for Cellular and Molecular Biology,
Uppal Road,
Hyderabad 500 007, India
e-mail: sinha@ccmb.res.in