Biosimulation

This practical guide to biosimulation provides the hands-on experience needed to devise, design, and analyze simulations of biophysical processes for applications in biological and biomedical sciences. Through real-world case studies and worked examples, students will develop and apply basic operations through to advanced concepts, covering a wide range of biophysical topics, including chemical kinetics and thermodynamics, transport phenomena, and cellular electrophysiology. Each chapter is built around case studies in a given application area, with simulations of real biological systems developed to analyze and interpret data. Open-ended project-based exercises are provided at the end of each chapter, and with all data and computer codes available online (www.cambridge.org/biosim) students can quickly and easily run, manipulate, explore, and expand on the examples inside. This hands-on guide is ideal for use on senior undergraduate/graduate courses, and also as a self-study guide for anyone who needs to develop computational models of biological systems.

Daniel A. Beard is a Professor in the Biotechnology and Bioengineering Center and the Department of Physiology at the Medical College of Wisconsin. Research in his laboratory is focused on systems engineering approaches to understanding the operation of physiological systems in health and disease. A recent major effort in his group has been on theoretical and experimental characterization of the thermodynamics, kinetics, and electrophysiology of cardiac mitochondria. Additional research interests include nonequilibrium thermodynamics in biochemical networks, mass transport and microvascular exchange in physiological systems, and drug metabolism and physiologically based pharmacokinetics.

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Biosimulation

Simulation of Living Systems

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Preface

Research, development, and design in bioengineering, biomedical engineering, biophysics, physiology, and related fields rely increasingly on mathematical modeling and computational simulation of biological systems. Simulation is required to analyze data, design experiments, develop new technology, and simply to attempt to understand the complexity inherent in biological systems.

This book focuses on practical implementation of techniques to study real biological systems. Indeed, whenever possible, specific applications are developed, starting with a study of the basic operation of the underlying biological, biochemical, or physiological system and, critically, the available data. It is hoped that this data-rich exposition will yield a practical text for engineering students and other readers interested primarily in earthy real-world applications such as analyzing data, estimating parameter values, etc. Thus for the examples developed here, important details of underlying biological systems are described along with a complete step-by-step development of model assumptions, the resulting equations, and (when necessary) computer code. As a result, readers have the opportunity, by working through the examples, to become truly proficient in *biosimulation*.

In this spirit of soup-to-nuts practicality, the book is organized around biological and engineering application areas rather than based on mathematical and computational techniques. Where specific mathematical or computational techniques can be conveniently and effective separated from the exposition, they have been and can be found in the Appendices. Computer codes implemented in MATLAB® (The MathWorks, Natick, MA, USA) for all of the examples in the text can be found online at the URL http://www.cambridge.org/biosim.

I am particularly grateful to a number of individuals who provided critical feedback on the text, including Edmund Crampin, Peter Hunter, Muriel Mescam, Gary Raymond, Nic Smith, Matt Thompson, Kalyan Vinnakota, and Fan Wu. Andy Salmon graciously provided the data from his experiments presented in Section 2.2.2. Tom O'Hara provided some guidance on the model analyzed in Section 8.3. Jim Bassingthwaighte's guidance and advice over many years, as well as specific criticism of the text, are gratefully acknowledged.

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More information

Extracts

"All is in flux."

Heraclitus (540–480 BCE)

"This application of mathematics to natural phenomena is the aim of all science, because the expression of the laws of phenomena should always be mathematical."

Claude Bernard, Introduction a l'étude de la médecine expérimentale *1865 Flammarion, Paris (English translation from Noble,* Exp. Physiol. *93: 16–26, 2008)*

"Of physiology from top to toe I sing."

Walt Whitman, Leaves of Grass*, 1883*

"The human body is a chemical and physical problem, and these sciences must advance before we can conquer disease."

Henry A. Rowland, The Highest Aims of the Physicist*, Address to the American Physical Society, 1899, published in* Science *10: 825–833, 1899*

"We are seeing the cells of plants and animals more and more clearly as chemical factories, where the various products are manufactured in separate workshops. The enzymes act as the overseers. Our acquaintance with these most important agents of living things is constantly increasing. Even though we may still be a long way from our goal, we are approaching it step by step. Everything is justifying our hopes. We must never, therefore, let ourselves fall into the way of thinking 'ignorabimus' ('We shall never know'), but must have every confidence that the day will dawn when even those processes of life which are still a puzzle today will cease to be inaccessible to us natural scientists."

Eduard Buchner, Nobel Lecture, 1907

"To a physician or physiologist at the present day a man's body is a machine, or rather a factory full of machines, all working harmoniously together for the good of the organism."

Ernest N. Starling, The Linacre Lecture on the Law of the Heart*, 1915, published by Longmans, Green and Co., London, 1918*

"The mathematical box is a beautiful way of wrapping up a problem, but it will not hold the phenomena unless they have been caught in a logical box to begin with."

John R. Platt, Strong inference. Science*, 146: 347–353, 1964*

"People who wish to analyze nature without using mathematics must settle for a reduced understanding."

Richard Feynman

"[This book] is aimed at 'non-believers', that is to say the 90% or so of biochemistry students, and indeed of practicing biochemists, who place enzyme kinetics in the same category as Latin and cold showers, character-building perhaps, but otherwise to be forgotten as quickly as possible."

Paul C. Engel, Enzyme Kinetics: The Steady-State Approach *1977, Chapman & Hall, London*

"Why make models? To think (and calculate) logically about what components and interactions are important in a complex system."

James E. Bailey, Mathematical modeling and analysis in biochemical engineering: past accomplishments and future opportunities. Biotechnol. Prog.*, 14: p. 8–20, 1998*

"Without data, there is nothing to model; and without models, there is no source of deep predictive understanding."

James B. Bassingthwaighte, The Physiome Project: The macroethics of engineering toward health. The Bridge*, 32: 24–29, 2002*

"Over the last half century, we have proceeded by breaking living systems down into their smallest components, the individual genes and molecules. Humpty Dumpty has been smashed into billions of fragments . . . Can we put Humpty Dumpty back together again?"

Denis Noble, The Music of Life: Biology beyond the Genome. *2006, Oxford, New York*