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BOOK REVIEWS

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Statistical Analysis of Environmental Space-Time Processes
(N. D. Le and J. V. Zidek) *Jon Wakefield*

Applied Mixed Models in Medicine, 2nd edition
(H. Brown and R. Prescott) *Matthew J. Gurka*

Stochastic Modeling for Systems Biology
(D. J. Wilkinson) *Olaf Wolkenhauer*

Knowledge Discovery in Proteomics
(I. Jurisica and D. Wigle) *Zhen Zhang*

Computational Genome Analysis: An Introduction
(R. C. Deonier, S. Tavaré, and
M. S. Waterman) *Marc Suling*

Stochastic Orders
(M. Shaked and J. G. Shantikumar) *Subhash Kochar*

Brief Reports by the Editor

Measurement Error in Nonlinear Models: A Modern Perspective, 2nd edition
(J. Carroll, D. Ruppert, L. A. Stefansky, and C. M. Crainiceanu)

Basic Statistics and Pharmaceutical Statistical Applications, 2nd edition
(J. E. De Muth)

A Handbook of Statistical Analyses Using Stata, 4th edition
(S. Rabe-Hesketh and B. S. Everitt)

Introduction to Randomized Controlled Clinical Trials, 2nd edition
(J. N. S. Matthews)

Introduction to Randomized Controlled Clinical Trials, 2nd edition
(J. N. S. Matthews)

Survival and Event History Analysis
(P. K. Andersen and N. Keiding, editors)

A Pocket Guide to Epidemiology
(D. G. Kleinbaum, K. M. Sullivan, and N. D. Barker)

WILKINSON, D. J. **Stochastic Modeling for Systems Biology.** Chapman & Hall/CRC, London, 2006. 245 pp., US$79.95/£44.99, ISBN 1-58488-540-8.

Systems biology is an area of research that has emerged in the wake of genomics and bioinformatics. While genomics and bioinformatics have focused on an effort to identify and catalogue the components that make up the cell, the signal- and systems-oriented perspective of systems biology focuses on the dynamics of intra and intercellular processes. This shift of focus generates a renewed interest in mathematical modeling at the molecular and cellular level. The majority of models for intracellular processes published to this day are encoded with (ordinary) differential equations—why is that? Are rate equation models more realistic, easier to derive from experimental data, or more powerful in terms of the formal analysis that can be done?

In the preface to his book, Wilkinson writes that his interest in systems biology emerged from an observation about recent experiments in cell biology: "that the kinetics of biological processes at the intracellular level are stochastic [...] cellular function cannot be properly understood without building that stochasticity into *in silico* models." The first chapter of Wilkinson's book is devoted to further arguments why stochastic modeling is important in systems biology. Unfortunately, these very interesting discussions are not further pursued, leaving the reader with shallow statements that "current scientific wisdom views biological systems as essentially deterministic in character" or "In some sense differential equation models are too low level a description..." In fact, I believe that such an argument strongly depends on what process is looked at, the chosen level of description, what technologies are available and what the purpose of the model is. In systems biology, mathematical modeling is the *art* of making appropriate assumptions; a process by which we represent one thing by another because understanding consists of reducing one type of reality to another. But even if "wrong" in this sense, a model can be useful by guiding the wet-lab scientist in the design of his experiments, helping him to decide which variables to measure and when and how. The complexity of intracellular dynamics forces us to ignore numerous details and relevant interactions. The motivation for stochastic models derives, therefore, in most cases from uncertainty induced as a consequence of these reduced representations. An important aspect of systems biology is, therefore, a discussion of alternative conceptual frameworks that could be applied to a given circumstance, helping the student, modeler, or experimentalist to choose an appropriate modeling formalism and develop confidence in the assumptions involved. Although several rate equation models are included, the book obviously focuses on stochastic models.

Wilkinson's book covers in only 238 pages an introduction to biochemical reaction networks, Petri nets, probability theory, stochastic simulation, Markov processes, Bayesian inference and MCMC, as well as computational tools such as **R** and the Systems Biology Markup Language (SBML). SBML is introduced over 12 pages in the second chapter and the Appendix supplies three simple SBML models, including the "obligatory" Lotka–Volterra system and a rather simple biochemical reaction. Over 45 pages, Chapter 3 deals with basic material from probability theory without any reference to systems biology or the examples introduced earlier. Under the heading "Stochastic Simulation," Chapter 4 introduces random number generation and the use of **R**. Chapters 5 to 8 form the central part of the book, covering Markov processes (30 pages), chemical and biochemical kinetics (24 pages), case studies (18 pages), and computational issues related to stochastic simulation. The development of Markov processes is based on a discrete state space rather than developing the discrete model in analogy to the continuous case. Since biochemical reactions are inherently discrete, this approach is intuitive and a positive attribute of this book.

Other key references to stochastic modeling that have been used in molecular biology and chemistry are the books by van Kampen (1992), Gillespie (1992), and Gardiner (2004). While these books are comprehensive mathematical treatments, they lack examples relevant to modern cell biology. Textbooks for the classroom (e.g., Allen, 2003) suffer from a similar problem in that examples are typically about population dynamics rather than gene networks and pathways. Wilkinson has chosen an example for a genetic network (Chapter 1); the Lotka–Volterra system (Chapter 6), which is not really related to molecular biology; dimerization and the enzyme kinetic reaction (in mass action form, incorrectly described by Wilkinson as Michaelis–Menten kinetics), all Chapter 7. This selection of examples could be criticized but the problem any book on systems biology faces is the shortage of practical examples that are sufficiently general. One case study that is notably missing is the MAPK signaling cascade, which is emerging as the systems biologist's equivalent to the Lotka–Volterra system in mathematical biology.

Although the author states that the book is "written with self-study in mind," the text could be used in the classroom (although relatively high prices for such books do not help this cause). The particular selection of topics and examples is not going to match every lecturer's idea for a course in systems biology. It seems impossible, however, to write a book that matches everyone's interest in a field that is rapidly evolving and integrates various disciplines. The likely readership is students in computer science, the engineering, and physical sciences but the material would also be accessible to advanced undergraduates and graduate students in the life sciences.

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