
Book reviews

Computational Cell Biology

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Interdisciplinary Applied
Mathematics, Springer-Verlag,
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'Computational Cell Biology' is a textbook that provides an introduction to dynamic modelling in cell biology. It is designed to introduce mathematical modelling in cell biology to advanced undergraduate and beginning graduate students in applied mathematics and engineering science. The book was originally begun by Professor Joel Keizer. However, after his untimely death in 1999, the book was expanded and finished by his former students and colleagues: it has 4 editors and 17 authors.

The book consists of 13 chapters and 3 appendices. It is divided in two parts: Introductory Course (Chapters 1–6) and Advanced Material (Chapters 7–13). The Introductory Course covers the basic elements of intercellular communication and compartmental modelling. Chapter 1 Dynamic Phenomena in Cells gives an outline of the book and an introduction to the subject. The interplay of experiment, theory and computational and mathematical modelling is briefly discussed. The electrical activity of excitable cells is studied in Chapter 2 Voltage Gated Ion Currents. Phase plane analysis and linear stability analysis are introduced in this chapter and Appendix A. In Chapter 3 Transporters and Pumps, models for the transport of ions and molecules across the cell membrane are discussed. Chapter 4 Fast and Slow Time Scales introduces two methods for timescale analysis, the

equilibrium and quasi-steady-state approximations, which are used to eliminate variables and simplify the analysis of differential equations. In Chapter 5 Whole-Cell Models, three cell systems are investigated: the bullfrog sympathetic neuron, the pituitary gonadotroph and the pancreatic β -cell. These models integrate plasma membrane and endoplasmic reticulum membrane fluxes into a system for the control of membrane potential and Ca^{2+} concentrations. Chapter 6 Intracellular Communication focuses on the transmission of signals of electrically active cells. The remaining chapters cover more specialised material such as spatial modelling on physiology (Chapter 7), which includes diffusion theory, exact and numerical solutions of partial differential equations. The theory is applied to the FitzHugh–Nagumo equations. In Chapter 8 some models of intracellular calcium waves and sparks are studied. Chapters 9 and 10 discuss a variety of biochemical cycles with emphasis on biochemical reactions with negative and positive feedbacks, activator–inhibitor oscillators, time–delay feedbacks, circadian rhythms, cell cycle and mitosis regulation. Chapter 11 models stochastic gating of ion channels. The book ends with two excellent chapters on molecular motors, devoted to theory and examples, respectively. Finally, Appendix B presents a very good introduction to the XPPAUT package.

The stated mathematical prerequisite is a full-year calculus course. Since this prerequisite will not suffice for a thorough understanding of the material in the book, an appendix (Appendix A) is provided that covers further mathematical requirements. The mathematical techniques employed in the text are phase plane analysis, bifurcation theory and

perturbation analysis. The book shows how these modelling techniques can be used to study cell biology phenomena with two or three variables, which could not been done without a quantitative description. Furthermore, it demonstrates that mathematics is an appropriate tool for testing assumptions, definitions and hypotheses. Hence, the book illustrates ways in which mathematical theory may be used to give insights into cell biology.

In terms of difficulty, the chapters are written so that the first sections are either elementary or intermediate in mathematical content, while the later sections are somewhat more advanced. The chapters are of varying degrees of difficulty. At the end of each chapter, references in the area and standard textbook problems are given. An attempt has been made to include problems from the research literature. However, solutions to the exercises are not available: availability of solutions would improve the book's usefulness.

The book has its own web site, <http://www.compcell.appstate.edu>, which contains a variety of resources, such as contact information about the contributing authors, computer codes and software, and a list of known mistakes and typos. The web site was created before the publication of the text but does not appear to have been updated to date (9th January 2003).

The first printing of a book with 4 editors and 17 contributing authors is almost certain to contain typos and minor errors, and the book under review is no exception. The contents of the book are homogenised to a reasonable level, but the project would have benefited from much stronger editing. In general the figures do not have sufficient captions and are not always well integrated into the text. The terminology differs among the chapters and the way in which physiological units have been introduced in some chapters can be confusing for readers unfamiliar with the subject. Certainly, readers' corrections, comments

and suggestions will improve future editions.

In this book, the editors interpret the term 'computational biology' to mean using numerical computation on small deterministic models to gain insight into biological issues. This interpretation is different from the increasingly recognised definition of the phrase, which is the production of sophisticated computer simulations against which biological phenomena, data or patterns are compared. Therefore, the title of the book could be misinterpreted, as it gives the impression that it deals with computational techniques required to model complex biological phenomena with computer simulations employed in bioinformatics or computational biology. It also gives the impression that it is a general textbook for modelling cell biology phenomena. Instead, the main subject of the book is an introduction to mathematical cell physiology modelling using computers to find numerical solutions to differential equations. A more appropriate title might be 'Topics in Mathematical Cell Physiology'. Also at the chapter and section level, there are disparities between headings and contents. Chapter titles such as 'Whole-Cell Models' and 'Intercellular Communication' are much more general than the actual contents of the corresponding chapters. One reason for this may be that since 1999 there have been huge strides in modelling and computation in biology so that these phrases have taken on new meanings.

Although the title makes the book appear up to date, the choice of topics made by the editors does not include current hot topics in cell biology, such as control of gene expression, signalling pathways and intracellular metabolism regulation. Recent work by Denis Bray on the stochastic control of the flagellar motor would have fitted well with the topics of Chapters 11–13. Similarly, research by Adam Arkin and others on the stochastic modelling of genetic networks is of increasing relevance, but is

not mentioned. There is overlap with 'Mathematical Physiology' by James Keener and James Sneyd (Interdisciplinary Applied Mathematics, Springer-Verlag, 1998) but topics are covered with less mathematical detail in this book as it focuses on software packages, such as XPPAUT (introduced in Appendix B), to find numerical solutions to differential equations. The topics of the 'Advanced Material' can be found in other mathematical biology textbooks, although some are less easily found than others. However, it is an attractive feature of the book to have this collection of cell biology topics under one cover.

While the idea of applying mathematical and computational techniques to construct models of biological systems is not a new one, in recent years it has become a very important tool, leading to fundamental insights and discoveries in neurophysiology and cell biology. Despite our criticisms, the textbook is a good starting point for students as well as researchers who wish to learn how to build and analyse mathematical models and to become familiar with new areas of application in cell biology. This book is a good reference, is easy to browse and is written in a friendly style. Overall, the authors have done an admirable job of completing Joel Keizer's project and of providing a mathematically inclined readership with a concise introduction to a very large subject. We have no doubt that with further suggestions and contributions of additional material and topics for future editions, this book will serve to develop the field of mathematical and computational modelling in cell biology.

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Instant Notes: Bioinformatics

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The publication of a bioinformatics book in the Instant Notes series of concise undergraduate level textbooks is a sign that bioinformatics is now seen as an essential part of basic studies in molecular biology. These books are systematic, well-structured guides that provide essential information for students of the chemical and life sciences in a compact, but accessible, fashion. This is a worthy addition to this series, as well as to the relatively small list of bioinformatics books that are suitable for beginners. For such a slim volume, it is astonishingly comprehensive: its coverage of fairly complex topics including microarrays and proteome analysis is unrivalled in an introductory book.

The book is laid out in the pattern that is common to all the *Instant Notes* series. The material is divided into 15 sections, A–O, with each section further subdivided into topics. For example, Section D, covering the retrieval of biological data, is divided into D1: Entrez and DBGET and D2: SRS. Section I, on structural bioinformatics, runs from I1: Conceptual models of protein structure to I10: Advanced protein structure prediction. The book starts with a general overview of bioinformatics. This is followed by sections on data acquisition, storage and retrieval, the principles of sequence analysis, structural bioinformatics, genomic and proteomic level techniques, and bioinformatics applications. It ends with a useful glossary.

This is an extremely useful book. It is well written, accessible and very clearly illustrated. Although designed as an undergraduate text, it deserves a place on the reading list of every MSc bioinformatics course, and it is bound to be well thumbed by more senior students and researchers.

