

Dynamic Models In Biology

Biological and biomedical research are increasingly driven by experimental techniques that challenge our ability to analyse, process and extract meaningful knowledge from the underlying data. The impressive capabilities of next generation sequencing technologies, together with novel and ever evolving distinct types of omics data technologies, have put an increasingly complex set of challenges for the growing fields of Bioinformatics and Computational Biology. The analysis of the datasets produced and their integration call for new algorithms and approaches from fields such as Databases, Statistics, Data Mining, Machine Learning, Optimization, Computer Science and Artificial Intelligence. Clearly, Biology is more and more a science of information requiring tools from the computational sciences. In the last few years, we have seen the surge of a new generation of interdisciplinary scientists that have a strong background in the biological and computational sciences. In this context, the interaction of researchers from different scientific fields is, more than ever, of foremost importance boosting the research efforts in the field and contributing to the education of a new generation of Bioinformatics scientists. PACBB'14 contributes to this effort promoting this fruitful interaction. PACBB'14 technical program included 34 papers spanning many different sub-fields in Bioinformatics and Computational Biology. Therefore, the conference promotes the interaction of scientists from diverse research groups and with a distinct background such as computer scientists, mathematicians or biologists.

From controlling disease outbreaks to predicting heart attacks, dynamic models are increasingly crucial for understanding biological processes. Many universities are starting undergraduate programs in computational biology to introduce students to this rapidly growing field. In *Dynamic Models in Biology*, the first text on dynamic models specifically written for undergraduate students in the biological sciences, ecologist Stephen Ellner and mathematician John Guckenheimer teach students how to understand, build, and use dynamic models in biology. Developed from a course taught by Ellner and Guckenheimer at Cornell University, the book is organized around biological applications, with mathematics and computing developed through case studies at the molecular, cellular, and population levels. The authors cover both simple analytic models--the sort usually found in mathematical biology texts--and the complex computational models now used by both biologists and mathematicians. Linked to a Web site with computer-lab materials and exercises, *Dynamic Models in Biology* is a major new introduction to dynamic models for students in the biological sciences, mathematics, and engineering.

Dynamic Models in Biology Princeton University Press

Mathematical and computational modeling approaches in biological and medical research are experiencing rapid growth

globally. This Special Issue Book intends to scratch the surface of this exciting phenomenon. The subject areas covered involve general mathematical methods and their applications in biology and medicine, with an emphasis on work related to mathematical and computational modeling of the complex dynamics observed in biological and medical research. Fourteen rigorously reviewed papers were included in this Special Issue. These papers cover several timely topics relating to classical population biology, fundamental biology, and modern medicine. While the authors of these papers dealt with very different modeling questions, they were all motivated by specific applications in biology and medicine and employed innovative mathematical and computational methods to study the complex dynamics of their models. We hope that these papers detail case studies that will inspire many additional mathematical modeling efforts in biology and medicine

Despite great advances in public health worldwide, insect vector-borne infectious diseases remain a leading cause of morbidity and mortality. Diseases that are transmitted by arthropods such as mosquitoes, sand flies, fleas, and ticks affect hundreds of millions of people and account for nearly three million deaths all over the world. In the past there was very little hope of controlling the epidemics caused by these diseases, but modern advancements in science and technology are providing a variety of ways in which these diseases can be handled. Clearly, the process of transmission of an infectious disease is a nonlinear (not necessarily linear) dynamic process which can be understood only by appropriately quantifying the vital parameters that govern these dynamics.

Biology is incredibly complex -- at the molecular, cellular, tissue, and population level, there exists a tremendous number of discrete interacting components tightly regulating the processes that sustain life. Biological systems have traditionally been viewed in a reductionist manner often literally (and metaphorically) through a magnifying glass, leading to insight into how the individual parts work. Network theory, on the other hand, can be used to put the pieces together, to understand how complex and emergent behaviors arise from the totality of interactions in complex systems, such as those seen in biology. Network theory is the study of systems of discrete interacting components and provides a framework for understanding complex systems. A network-focused investigation of a complex biological system allows for the understanding of the system's emergent properties, for example its function and dynamics. Network dynamics are of particular interest biologically because biological systems are not static but are constantly changing in response to perturbations and environmental stimuli in space and time. Systems level biological analysis has been aided by the recent explosion of high throughput data. This has led to an abundance of quantitative and qualitative information related to the activation of biological systems, but frequently there is still a paucity of kinetic and temporal information. Discrete dynamic modeling provides a means to create predictive models of biological systems by integrating fragmentary and

qualitative interaction information. Using discrete dynamic modeling, a structural (static) network of biological regulatory relationships can be translated into a mathematical model without the use of kinetic parameters. This model can describe the dynamics of a biological system (i.e. how it changes over time), both in normal and in perturbation (e.g. disease) scenarios. In this dissertation we present the application of network theory and discrete dynamic modeling integrated with experimental laboratory analysis to understand biological diseases in three contexts. The first is the construction of a network model of epidermal derived growth factor receptor (EGFR) signaling in cancer. We translate this model into two types of discrete models: a Boolean model and a three-state model. We show how the effects of an EGFR inhibitor (such as the drug gefitinib) can suppress tumor growth, and we model how genomic variants can augment the effect of EGFR inhibition in tumor growth. Importantly, we compare discrete modeling outcomes to an alternative modeling framework, which relies on detailed kinetic information, called ordinary differential equation (ODE) modeling and show that both models achieve similar findings. Our results demonstrate that discrete dynamic model can accurately model biomedical systems and make important predictions about the effect a drug will have on a disease (e.g. tumor growth) in the context of various perturbations. Importantly, discrete dynamic models can be employed in the absence of kinetic parameters, making this modeling approach suitable for the many biological systems in which detailed kinetic information is not available. Second, we construct a network model of epithelial-to-mesenchymal transition (EMT), a developmental process hijacked by cancer cells to leave the primary tumor site, invade surrounding tissue, and establish distant metastases. We demonstrate that the EMT network model recapitulates known dysregulations during the induction of EMT and predicts the activation of the Wnt and Sonic hedgehog (SHH) signaling pathways during this process. We confirm the cross-talk between TGF[β], Wnt and SHH signaling in vitro in multiple human liver cancer cell lines and tumor samples. Next, we use the EMT network model to systematically explore perturbations that suppress EMT, with the ultimate goal of identifying therapeutic interventions that suppress tumor invasion. We computationally explore close to half a million individual and combination perturbations to the EMT network and identify that only a dozen suppress EMT. We test these interventions experimentally and our findings suggest that many predicted interventions suppress the EMT process. Lastly, we construct a model of the enormous ecological community of bacteria that live in our intestines, collectively called the gut microbiome. This model is used to understand the effect of antibiotic treatment and opportunistic *C. difficile* infection (a devastating and highly prevalent disease entity) on the native microbiome and predict therapeutic probiotic interventions to suppress *C. difficile* infection. We integrate this modeling with another type of modeling, genome scale metabolic network reconstructions, to understand metabolic differences between community members and to identify the role of metabolism in the observed microbial interactions. In vitro experimental data validate

a key result of my computational model, that *Barnesiella intestinihominis* can in fact suppress *C. difficile* growth. This novel result suggests that *Barnesiella* could potentially be used as a probiotic to suppress *C. difficile* growth. Taken together, the studies presented in this thesis demonstrate the tremendous capacity of network modeling to elucidate biomedical systems. We build networks, construct mathematical models, study network dynamics, and use network-directed insight to guide experiments in critical biomedical areas. The ultimate goal of this work has been to translate network-directed insight into actionable biomedical findings that lead to improved understanding of human disease, enhanced patient care, and a betterment of the human condition.

Covering the major topics of evolutionary game theory, *Game-Theoretical Models in Biology* presents both abstract and practical mathematical models of real biological situations. It discusses the static aspects of game theory in a mathematically rigorous way that is appealing to mathematicians. In addition, the authors explore many applications of game theory to biology, making the text useful to biologists as well. The book describes a wide range of topics in evolutionary games, including matrix games, replicator dynamics, the hawk-dove game, and the prisoner's dilemma. It covers the evolutionarily stable strategy, a key concept in biological games, and offers in-depth details of the mathematical models. Most chapters illustrate how to use MATLAB® to solve various games. Important biological phenomena, such as the sex ratio of so many species being close to a half, the evolution of cooperative behavior, and the existence of adornments (for example, the peacock's tail), have been explained using ideas underpinned by game theoretical modeling. Suitable for readers studying and working at the interface of mathematics and the life sciences, this book shows how evolutionary game theory is used in the modeling of these diverse biological phenomena.

Biophysical models have been used in biology for decades, but they have been limited in scope and size. In this book, Bernhard Ø. Palsson shows how network reconstructions that are based on genomic and bibliomic data, and take the form of established stoichiometric matrices, can be converted into dynamic models using metabolomic and fluxomic data. The Mass Action Stoichiometric Simulation (MASS) procedure can be used for any cellular process for which data is available and allows a scalable step-by-step approach to the practical construction of network models. Specifically, it can treat integrated processes that need explicit accounting of small molecules and protein, which allows simulation at the molecular level. The material has been class-tested by the author at both the undergraduate and graduate level. All computations in the text are available online in MATLAB and MATHEMATICA® workbooks, allowing hands-on practice with the material.

Through a series of examples from physics, engineering, biology and economics, this book illustrates the enormous potential for application of ideas and concepts from nonlinear dynamics and chaos theory. The overlap with examples

published in other books is virtually equal to zero. The book takes the reader from detailed studies of bifurcation structures of relatively simple models to pattern formation in spatially extended systems. The book also discusses the different perspectives that nonlinear dynamics brings to different fields of science. Contents: Deterministic Approach to Die Tossing Bifurcation Analysis of Simple Nonlinear Systems Coupled Period-Doubling Systems Chaos in Technical Control Systems Ecological and Microbiological Population Dynamics Physiological Control Systems Chaos and Hyperchaos in Economic and Managerial Systems Spatiotemporal Phenomena in Extended Systems Readership: Nonlinear scientists. keywords:

This book is intended as a text for a first course on creating and analyzing computer simulation models of biological systems. The expected audience for this book are students wishing to use dynamic models to interpret real data much as they would use standard statistical techniques. It is meant to provide both the essential principles as well as the details and equations applicable to a few particular systems and subdisciplines. Biological systems, however, encompass a vast, diverse array of topics and problems. This book discusses only a select number of these that I have found to be useful and interesting to biologists just beginning their appreciation of computer simulation. The examples chosen span classical mathematical models of well-studied systems to state-of-the-art topics such as cellular automata and artificial life. I have stressed the relationship between the models and the biology over mathematical analysis in order to give the reader a sense that mathematical models really are useful to biologists. In this light, I have sought examples that address fundamental and, I think, interesting biological questions. Almost all of the models are directly compared to quantitative data to provide at least a partial demonstration that some biological models can accurately predict.

This book studies and applies modern flexible regression models for survival data with a special focus on extensions of the Cox model and alternative models with the aim of describing time-varying effects of explanatory variables. Use of the suggested models and methods is illustrated on real data examples, using the R-package `timereg` developed by the authors, which is applied throughout the book with worked examples for the data sets.

Mathematical Biology has grown at an astonishing rate and has established itself as a distinct discipline. Mathematical modeling is now being applied in every major discipline in the biological sciences. Though the field has become increasingly large and specialized, this book remains important as a text that introduces some of the exciting problems which arise in the biological sciences and gives some indication of the wide spectrum of questions that modeling can address.

The development of a proper description of the living world today stands as one of the most significant challenges to physics. A variety of new experimental techniques in molecular biology, microbiology, physiology and other fields of

biological research constantly expand our knowledge and enable us to make increasingly more detailed functional and structural descriptions. Over the past decades, the amount and complexity of available information have multiplied dramatically, while at the same time our basic understanding of the nature of regulation, behavior, morphogenesis and evolution in the living world has made only modest progress. A key obstacle is clearly the proper handling of the available data. This requires a stronger emphasis on mathematical modeling through which the consistency of the adopted explanations can be checked, and general principles may be extracted. As an even more serious problem, however, it appears that the proper physical concepts for the development of a theoretically oriented biology have not hitherto been available. Classical mechanics and equilibrium thermodynamics, for instance, are inappropriate and useless in some of the most essential biological contexts. Fortunately, there is now convincing evidence that the concepts and methods of the newly developed fields of nonlinear dynamics and complex systems theory, combined with irreversible thermodynamics and far-from-equilibrium statistical mechanics will enable us to move ahead with many of these problems.

Dynamic Models in Biology offers an introduction to modern mathematical biology. This book provides a short introduction to modern mathematical methods in modeling dynamical phenomena and treats the broad topics of population dynamics, epidemiology, evolution, immunology, morphogenesis, and pattern formation. Primarily employing differential equations, the author presents accessible descriptions of difficult mathematical models. Recent mathematical results are included, but the author's presentation gives intuitive meaning to all the main formulae. Besides mathematicians who want to get acquainted with this relatively new field of applications, this book is useful for physicians, biologists, agricultural engineers, and environmentalists. Key Topics Include: Chaotic dynamics of populations The spread of sexually transmitted diseases Problems of the origin of life Models of immunology Formation of animal hide patterns The intuitive meaning of mathematical formulae explained with many figures Applying new mathematical results in modeling biological phenomena Miklos Farkas is a professor at Budapest University of Technology where he has researched and instructed mathematics for over thirty years. He has taught at universities in the former Soviet Union, Canada, Australia, Venezuela, Nigeria, India, and Columbia. Prof. Farkas received the 1999 Bolyai Award of the Hungarian Academy of Science and the 2001 Albert Szentgyorgyi Award of the Hungarian Ministry of Education. A 'down-to-earth' introduction to the growing field of modern mathematical biology Also includes appendices which provide background material that goes beyond advanced calculus and linear algebra

Complex artificial dynamic systems require advanced modeling techniques that can accommodate their asynchronous, concurrent, and highly non-linear nature. Discrete Event systems Specification (DEVS) provides a formal framework for hierarchical

construction of discrete-event models in a modular manner, allowing for model re-use and reduced development time. Discrete Event Modeling and Simulation presents a practical approach focused on the creation of discrete-event applications. The book introduces the CD++ tool, an open-source framework that enables the simulation of discrete-event models. After setting up the basic theory of DEVS and Cell-DEVS, the author focuses on how to use the CD++ tool to define a variety of models in biology, physics, chemistry, and artificial systems. They also demonstrate how to map different modeling techniques, such as Finite State Machines and VHDL, to DEVS. The in-depth coverage elaborates on the creation of simulation software for DEVS models and the 3D visualization environments associated with these tools. A much-needed practical approach to creating discrete-event applications, this book offers world-class instruction on the field's most useful modeling tools.

Abstract: Due to the high complexity of biological data it is difficult to disentangle cellular processes relying only on intuitive interpretation of measurements. A Systems Biology approach that combines quantitative experimental data with dynamic mathematical modeling promises to yield deeper insights into these processes. Nevertheless, with growing complexity and increasing amount of quantitative experimental data, building realistic and reliable mathematical models can become a challenging task: the quality of experimental data has to be assessed objectively, unknown model parameters need to be estimated from the experimental data, and numerical calculations need to be precise and efficient. Here, we discuss, compare and characterize the performance of computational methods throughout the process of quantitative dynamic modeling using two previously established examples, for which quantitative, dose- and time-resolved experimental data are available. In particular, we present an approach that allows to determine the quality of experimental data in an efficient, objective and automated manner. Using this approach data generated by different measurement techniques and even in single replicates can be reliably used for mathematical modeling. For the estimation of unknown model parameters, the performance of different optimization algorithms was compared systematically. Our results show that deterministic derivative-based optimization employing the sensitivity equations in combination with a multi-start strategy based on latin hypercube sampling outperforms the other methods by orders of magnitude in accuracy and speed. Finally, we investigated transformations that yield a more efficient parameterization of the model and therefore lead to a further enhancement in optimization performance. We provide a freely available open source software package that implements the algorithms and examples compared here

Modern biology is rapidly becoming a study of large sets of data. Understanding these data sets is a major challenge for most life sciences, including the medical, environmental, and bioprocess fields. Computational biology approaches are essential for leveraging this ongoing revolution in omics data. A primary goal of this Special Issue, entitled "Methods in Computational Biology", is the communication of computational biology methods, which can extract biological design principles from complex data sets, described in enough detail to permit the reproduction of the results. This issue integrates interdisciplinary researchers such as biologists, computer scientists, engineers, and mathematicians to advance biological systems analysis. The Special Issue contains the following sections: • Reviews of Computational Methods • Computational Analysis of Biological Dynamics: From Molecular to

Cellular to Tissue/Consortia Levels • The Interface of Biotic and Abiotic Processes • Processing of Large Data Sets for Enhanced Analysis • Parameter Optimization and Measurement

Mathematical and statistical network modeling is an important step toward uncovering the organizational principles and dynamic behavior of biological networks. This chapter focuses on methods to construct discrete dynamic models of gene regulatory networks from experimental data sets, also sometimes referred to as top-down modeling or reverse engineering. Time-discrete dynamical systems models have long been used in biology, particularly in population dynamics. The models mainly focused on here are also assumed to have a finite set of possible states for each variable. That is, the modeling framework discussed in this chapter is that of time-discrete dynamical systems over a finite state set.

System Biology encompasses the knowledge from diverse fields such as Molecular Biology, Immunology, Genetics, Computational Biology, Mathematical Biology, etc. not only to address key questions that are not answerable by individual fields alone, but also to help in our understanding of the complexities of biological systems. Whole genome expression studies have provided us the means of studying the expression of thousands of genes under a particular condition and this technique had been widely used to find out the role of key macromolecules that are involved in biological signaling pathways. However, making sense of the underlying complexity is only possible if we interconnect various signaling pathways into human and computer readable network maps. These maps can then be used to classify and study individual components involved in a particular phenomenon. Apart from transcriptomics, several individual gene studies have resulted in adding to our knowledge of key components that are involved in a signaling pathway. It therefore becomes imperative to take into account of these studies also, while constructing our network maps to highlight the interconnectedness of the entire signaling pathways and the role of that particular individual protein in the pathway. This collection of articles will contain a collection of pioneering work done by scientists working in regulatory signaling networks and the use of large scale gene expression and omics data. The distinctive features of this book would be: Act a single source of information to understand the various components of different signaling network (roadmap of biochemical pathways, the nature of a molecule of interest in a particular pathway, etc.), Serve as a platform to highlight the key findings in this highly volatile and evolving field, and Provide answers to various techniques both related to microarray and cell signaling to the readers.

This text provides an introduction to the use of mathematical models in biology, the statistical techniques for fitting and testing them, and associated computing methods. The properties of models, and methods of fitting and testing, are demonstrated by computer simulation illustrations.

The dynamic development of various processes is a central problem of biology and indeed of all the sciences. The mathematics describing that development is, in general, complicated, because the models that are realistic are usually nonlinear. Consequently many biologists may not notice a possible application of theory. They may be unable to decide whether a particular model captures the essence of a system, or to appreciate that analysis of a model can reveal important aspects of biological problems

and may even describe in detail how a system works. The aim of this textbook is to remedy the situation by adopting a general approach to model analysis and applying it several times to problems (drawn primarily from molecular and cellular biology) of gradually increasing biological and mathematical complexity. Although material of considerable sophistication is included, little mathematical background is required - only some exposure to elementary calculus; appendixes supply the necessary mathematics and the author concentrates on concepts rather than techniques. He also emphasizes the role of computers in giving a full picture of model behavior and complementing more qualitative analysis. Some problems suitable for computer analysis are also included. This is a class-tested textbook suitable for a one-semester course for advanced undergraduate and beginning graduate students in biology or applied mathematics. It can also be used as a source book for teachers and a reference for specialists.

This is the only book that teaches all aspects of modern mathematical modeling and that is specifically designed to introduce undergraduate students to problem solving in the context of biology. Included is an integrated package of theoretical modeling and analysis tools, computational modeling techniques, and parameter estimation and model validation methods, with a focus on integrating analytical and computational tools in the modeling of biological processes. Divided into three parts, it covers basic analytical modeling techniques; introduces computational tools used in the modeling of biological problems; and includes various problems from epidemiology, ecology, and physiology. All chapters include realistic biological examples, including many exercises related to biological questions. In addition, 25 open-ended research projects are provided, suitable for students. An accompanying Web site contains solutions and a tutorial for the implementation of the computational modeling techniques. Calculations can be done in modern computing languages such as Maple, Mathematica, and MATLAB?

Linear and non-linear models of populations, molecular evolution, phylogenetic tree construction, genetics, and infectious diseases are presented with minimal prerequisites.

Contains topics including modelling the dynamics of signalling pathways, modelling metabolic networks using power-laws and S-systems, modelling reaction kinetics in cells, the regulatory design of cellular processes, metabolomics and fluxomics, modelling cellular signalling systems, and systems analysis of MAPK signal transduction.

The theme of this book is the self-generation of information by the self-modification of systems. The author explains why biological and cognitive processes exhibit identity changes in the mathematical and logical sense. This concept is the basis of a new organizational principle which utilizes shifts of the internal semantic relations in systems. There are mathematical discussions of various classes of systems (Turing machines, input-output systems, synergetic systems, non-linear dynamics etc), which are contrasted with the author's new principle. The most important implications of this include a new conception on the nature of information and which also provides a new and coherent conceptual view of a wide class of natural systems. This book merits the attention of all philosophers and scientists concerned with the way we create reality in our mathematical representations of the world and the connection those representations have with the way things really are.

This book is an introduction for readers interested in biological applications of mathematics and modeling in biology, showing how

relatively simple mathematics can be applied to a variety of models. Despite the great advances that have taken place, the simple lessons described in the text are still important and informative.

Role of ruminants in human food production; Why an animal scientist would choose to model animal systems; Basic organization of this book; Modeling principles and terminology; Classification of models; Objectives in modeling; The modeling process I objective statements, block diagrams, equation forms and parameterization; Steps in modeling; Setting the modeling objective; Block diagrams; Formulation of mathematical statements; Development of numerical inputs; The modeling process II - solution algorithms, model evaluations and parameter estimation; Model solution algorithms; Evaluation of management and research models; Evaluation and use of analytical models for parameter estimation; Decision support software; Animal energetic models; Thermodynamic concepts in nutrition; Historical development of bases for feeding system models; Energy requirements for maintenance and production; Equations used to estimate maintenance and costs of production; Components of maintenance; Protein and amino acid models; Current protein and amino acid systems; Analytic models of amino acid and protein metabolism; Dynamic modeling; Biology and algebraic models of ruminant digestion; The rumen microbes and their metabolism; Balance models of ruminant digestion; An analytical model of rumen digestion; Microbial growth elements; Biology and algebraic models of growth; Classical equations for growth; Nutritional models of growth; Concepts of the basic biology of growth used in mechanistic models; Biology of lactation; Recent evolution of feeding systems for lactating dairy cattle; An analytical model of nutrient transactions during lactation; Dynamic models of ruminant digestion; Early dynamic models; Current dynamic models; Dynamic models of ruminant adipose tissue metabolism; Evolution of steady-state balance model; Radioisotope tracer elements; Dynamic models of ruminant mammary metabolism; Development of model inputs and initial parameters; Descriptions of a model of mammary gland metabolism; Dynamic models of liver and viscera metabolism; Overall structure and notation; Mechanistic, dynamic models of growth; Beef growth models; Sheep growth and metabolism model; Lactation Background on MOLL Y. CSL; The program MOLL Y. CSL; Evaluation and use of a growth and lactation model; Behavioral analyses; Sensitivity analyses; Bioeconomic analysis.

Many biologists and ecologists have developed models that find widespread use in theoretical investigations and in applications to organism behavior, disease control, population and metapopulation theory, ecosystem dynamics, and environmental management. This book captures and extends the process of model development by concentrating on the dynamic aspects of these processes and by providing the tools such that virtually anyone with basic knowledge in the Life Sciences can develop meaningful dynamic models. Examples of the systems modeled in the book range from models of cell development, the beating heart, the growth and spread of insects, spatial competition and extinction, to the spread and control of epidemics, including the conditions for the development of chaos. Key features: - easy-to-learn and easy-to-use software - examples from many subdisciplines of biology, covering models of cells, organisms, populations, and metapopulations - no prior computer or programming experience required Key benefits: - learn how to develop modeling skills and system thinking on your own rather

than use models developed by others - be able to easily run models under alternative assumptions and investigate the implications of these assumptions for the dynamics of the biological system being modeled - develop skills to assess the dynamics of biological systems

This book constitutes the proceedings of the 11th International Conference on Computational Methods in Systems Biology, CMSB 2013, held in Klosterneuburg, Austria, in September 2013. The 15 regular papers included in this volume were carefully reviewed and selected from 27 submissions. They deal with computational models for all levels, from molecular and cellular, to organs and entire organisms.

Dynamic Systems Biology Modeling and Simulation consolidates and unifies classical and contemporary multiscale methodologies for mathematical modeling and computer simulation of dynamic biological systems - from molecular/cellular, organ-system, on up to population levels. The book pedagogy is developed as a well-annotated, systematic tutorial - with clearly spelled-out and unified nomenclature - derived from the author's own modeling efforts, publications and teaching over half a century. Ambiguities in some concepts and tools are clarified and others are rendered more accessible and practical. The latter include novel qualitative theory and methodologies for recognizing dynamical signatures in data using structural (multicompartmental and network) models and graph theory; and analyzing structural and measurement (data) models for quantification feasibility. The level is basic-to-intermediate, with much emphasis on biomodeling from real biodata, for use in real applications. Introductory coverage of core mathematical concepts such as linear and nonlinear differential and difference equations, Laplace transforms, linear algebra, probability, statistics and stochastics topics; PLUS ... The pertinent biology, biochemistry, biophysics or pharmacology for modeling are provided, to support understanding the amalgam of "math modeling" with life sciences. Strong emphasis on quantifying as well as building and analyzing biomodels: includes methodology and computational tools for parameter identifiability and sensitivity analysis; parameter estimation from real data; model distinguishability and simplification; and practical bioexperiment design and optimization. Companion website provides solutions and program code for examples and exercises using Matlab, Simulink, VisSim, SimBiology, SAAMII, AMIGO, Copasi and SBML-coded models.

Biology education, like science education in general, is in the midst of a revolution that is worldwide in scope. The changes in the ways science education researchers think about learning and understanding represent a major paradigm shift. In this book, international leaders in the field of biology education research give summaries of problems and solutions in biology learning and teaching at various grade levels. Based on a NATO workshop in the Special Programme on Advanced Educational Technology, it provides practical information for teachers, especially in using new interactive, constructivist teaching methods. For science education researchers, it offers a concise summary of a number of research

issues in biology education.

Exploring Mathematical Modeling in Biology through Case Studies and Experimental Activities provides supporting materials for courses taken by students majoring in mathematics, computer science or in the life sciences. The book's cases and lab exercises focus on hypothesis testing and model development in the context of real data. The supporting mathematical, coding and biological background permit readers to explore a problem, understand assumptions, and the meaning of their results. The experiential components provide hands-on learning both in the lab and on the computer. As a beginning text in modeling, readers will learn to value the approach and apply competencies in other settings. Included case studies focus on building a model to solve a particular biological problem from concept and translation into a mathematical form, to validating the parameters, testing the quality of the model and finally interpreting the outcome in biological terms. The book also shows how particular mathematical approaches are adapted to a variety of problems at multiple biological scales. Finally, the labs bring the biological problems and the practical issues of collecting data to actually test the model and/or adapting the mathematics to the data that can be collected. Presents a single volume on mathematics and biological examples, with data and wet lab experiences suitable for non-experts Contains three real-world biological case studies and one wet lab for application of the mathematical models Includes R code templates throughout the text, which are also available through an online repository, along with the necessary data files to complete all projects and labs

This book provides an introduction to the analysis of stochastic dynamic models in biology and medicine. The main aim is to offer a coherent set of probabilistic techniques and mathematical tools which can be used for the simulation and analysis of various biological phenomena. These tools are illustrated on a number of examples. For each example, the biological background is described, and mathematical models are developed following a unified set of principles. These models are then analyzed and, finally, the biological implications of the mathematical results are interpreted. The biological topics covered include gene expression, biochemistry, cellular regulation, and cancer biology. The book will be accessible to graduate students who have a strong background in differential equations, the theory of nonlinear dynamical systems, Markovian stochastic processes, and both discrete and continuous state spaces, and who are familiar with the basic concepts of probability theory.

A one-of-a-kind guide to using deterministic and probabilistic methods for solving problems in the biological sciences Highlighting the growing relevance of quantitative techniques in scientific research, Mathematical Methods in Biology provides an accessible presentation of the broad range of important mathematical methods for solving problems in the biological sciences. The book reveals the growing connections between mathematics and biology through clear

explanations and specific, interesting problems from areas such as population dynamics, foraging theory, and life history theory. The authors begin with an introduction and review of mathematical tools that are employed in subsequent chapters, including biological modeling, calculus, differential equations, dimensionless variables, and descriptive statistics. The following chapters examine standard discrete and continuous models using matrix algebra as well as difference and differential equations. Finally, the book outlines probability, statistics, and stochastic methods as well as material on bootstrapping and stochastic differential equations, which is a unique approach that is not offered in other literature on the topic. In order to demonstrate the application of mathematical methods to the biological sciences, the authors provide focused examples from the field of theoretical ecology, which serve as an accessible context for study while also demonstrating mathematical skills that are applicable to many other areas in the life sciences. The book's algorithms are illustrated using MATLAB®, but can also be replicated using other software packages, including R, Mathematica®, and Maple; however, the text does not require any single computer algebra package. Each chapter contains numerous exercises and problems that range in difficulty, from the basic to more challenging, to assist readers with building their problem-solving skills. Selected solutions are included at the back of the book, and a related Web site features supplemental material for further study. Extensively class-tested to ensure an easy-to-follow format, *Mathematical Methods in Biology* is an excellent book for mathematics and biology courses at the upper-undergraduate and graduate levels. It also serves as a valuable reference for researchers and professionals working in the fields of biology, ecology, and biomathematics.

An introduction to the mathematical concepts and techniques needed for the construction and analysis of models in molecular systems biology. Systems techniques are integral to current research in molecular cell biology, and system-level investigations are often accompanied by mathematical models. These models serve as working hypotheses: they help us to understand and predict the behavior of complex systems. This book offers an introduction to mathematical concepts and techniques needed for the construction and interpretation of models in molecular systems biology. It is accessible to upper-level undergraduate or graduate students in life science or engineering who have some familiarity with calculus, and will be a useful reference for researchers at all levels. The first four chapters cover the basics of mathematical modeling in molecular systems biology. The last four chapters address specific biological domains, treating modeling of metabolic networks, of signal transduction pathways, of gene regulatory networks, and of electrophysiology and neuronal action potentials. Chapters 3–8 end with optional sections that address more specialized modeling topics. Exercises, solvable with pen-and-paper calculations, appear throughout the text to encourage interaction with the mathematical techniques. More involved end-of-chapter problem sets require computational software. Appendixes

provide a review of basic concepts of molecular biology, additional mathematical background material, and tutorials for two computational software packages (XPPAUT and MATLAB) that can be used for model simulation and analysis.

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