

Preface

There has been a lot of excitement surrounding the science of biology in recent years. The human genome of three billion letters has been sequenced, as have the genomes of thousands of other organisms. With unprecedented resolution, the rush of *omics* technologies is allowing us to peek into the world of genes, biomolecules, and cells – and flooding us with data of immense complexity that we are just barely beginning to understand. A huge gap separates our knowledge of the molecular components of a cell and what is known from our observations of its physiology – how these cellular components interact and function together to enable the cell to sense and respond to its environment, to grow and divide, to differentiate, to age, or to die. We have written this book to explore what has been done to close this gap of understanding between the realms of molecules and biological processes. We put together illustrative examples from the literature of mechanisms and models of gene-regulatory networks, DNA replication, the cell-division cycle, cell death, differentiation, cell senescence, and the abnormal state of cancer cells. The mechanisms are biomolecular in detail, and the models are mathematical in nature. We consciously strived for an interdisciplinary presentation that would be of interest to both biologists and mathematicians, and perhaps every discipline in between. As a teaching textbook, our objective is to demonstrate the details of the process of formulating and analyzing quantitative models that are firmly based on molecular biology. There was no attempt to be comprehensive in our account of existing models, and we sincerely apologize to colleagues whose models were not included in the book.

The mechanisms of cellular regulation discussed here are mediated by DNA (deoxyribonucleic acid). This DNA-centric view and the availability of sequenced genomes are fuelling the present excitement in biology – perhaps because one can now advance the tantalizing hypothesis that the linear DNA sequence contains the ultimate clues for predicting cellular physiology. Examples of mechanisms that explicitly relate genome structure and DNA sequence to cellular physiology are illustrated in some chapters (on gene expression and initiation of DNA replication in a bacterium); however, the majority deals with known or putative mechanisms involving pathways and networks of biochemical interactions, mainly at the level of proteins (the so-called workhorses of the cell). The quantitative analysis of these complex networks poses significant challenges. We expect that new mathematics will be developed to sort through the complexity, and to link the many spatiotemporal scales that these networks operate in. Although no new mathematics is developed in this book, we hope that the detailed networks presented here will make significant contributions to the inspiration of mathematical innovations. Another important goal is to show biologists with non-mathematical backgrounds how the dynamics of these networks are modelled, and,

more importantly, to convince them that these quantitative and computational treatments are critical for progress. The collaboration between biologists and mathematical modellers is crucial in furthering our understanding of complex biological networks.

There are currently hundreds of molecular interaction and pathways databases that proliferate on the internet. In principle, these bioinformatics resources should be tapped for building or extracting models; but the sheer complexity of these datasets and the lack of automatic model-extraction algorithms are preventing modellers from using them. Although an overview of these databases is provided, almost all of the models in this book are based on current biological hypotheses on what the central molecular mechanisms of the cellular processes are.

One of us was trained as a physical-theoretical chemist, and the other as a pure mathematician. Individually, each has undergone many years of re-education and re-focusing of his research towards biology. We hope that this work will help in bringing together biologists, mathematicians, physical scientists and other non-biologists who seriously want to gain an understanding of the inner workings of life.

It is our pleasure to thank Shoumita Dasgupta for reading and generously commenting on some of the biology sections (but let it be known that lapses in biology are certainly all ours). We gratefully acknowledge the support provided by the Mathematical Biosciences Institute that is funded by the National Science Foundation USA under agreement no. 0112050.

B. D. Aguda & A. Friedman
Columbus, Ohio, USA
12 November 2007