
PREFACE

Computation is an essential part of the cell biologist's toolbox. The value of computation in analyzing systems involving numerous, interconnected mechanisms has long been appreciated. Computational models provide a framework not only to formally represent and simulate the mechanisms, but also predict the response of an integrated system to new perturbations and thereby lead to testable hypotheses. In this way, computational modeling and analysis can suggest new experiments that challenge and help revise our mechanistic understanding of the cell system.

Prediction and hypothesis-generation, however, tells only part of the story. The need for computation is now far more pervasive in cell biology. Cell biological data is increasingly gathered with high bandwidth, often exploiting heterotypic measurement modalities. This flood of data includes changes in gene expression, post-translational modifications, and the subcellular location of key regulatory events. The 'omic' scale *in vivo* imaging of spatiotemporal patterns in gene expression during the development of model organisms is a compelling example. Extracting meaningful data from such images is a key challenge and involves reliable segmentation, annotation, storage and data management, bioinformatics, and data mining.

Having acquired the data, one seeks to infer salient mechanistic relationships and models. Deriving a model of how a system works based on experimental data is, of course, not new. The challenge now is that the volume, the spatiotemporal resolution, and the heterotypic nature of the data make such inferences difficult to execute by intuition alone. Computational algorithms to sift through the data and extract models consistent with the data are essential. Furthermore, model schematics, whether derived by computation or intuition, are conceptual until they are used to generate concrete, testable predictions. Making such predictions, however, is encumbered by a dearth of information regarding parameter values and by the fact that cellular mechanisms often operate over multiple time and spatial scales, in many cases combining biochemical and mechanical elements. Thus, inferring *computable* models that are amenable to simulation requires inference not only of the mechanistic connections, but also the parameters that describe the strength of those connections and interactions.

This remarkable breadth of applications of computation in cell biology impresses the fact that computation is more than a module in a multi-step process that involves iterative feedback between model and experiment. It is also increasingly integral to how data is gathered and interpreted, how mechanistic models are inferred, and how new mechanisms are hypothesized and uncovered. This volume captures this broad integration of computation in experimental cell biology. The volume covers the role of computation in the extraction of quantitative information from raw data; inference

of mechanistic computable (i.e., parameterized) models from large, heterotypic datasets; and prediction and hypothesis-generation to drive new experiments.

The contributors to this volume were presented with a difficult challenge: to tailor each chapter in a way that provides both high-level and in-depth tutorials of key computational methods, while also communicating the biological question that inspired the computational approach and the biological insights that were uncovered. The contributors have, in our opinion, succeeded admirably in tackling this challenge. The chapters are organized into three parts that focus on (1) molecular regulatory networks, (2) spatial and biophysical aspects of cell regulation, and finally (3) multicellular systems. Each part of the volume contains chapters that deal with the different applications of computation in cell biology: measurements and data extraction, model development and inference, and prediction and hypothesis generation.

With acknowledgment and deepest gratitude to the tremendous efforts of the contributors and to the many anonymous peer reviewers, we are pleased to present this volume and trust that it will provide inspiration and instructive tutorial in your search for the right computational tool for your cell biology quest.

Anand R. Asthagiri

Department of Chemical Engineering,
Northeastern University, Boston,
Massachusetts, USA

Adam P. Arkin

Department of Bioengineering,
University of California, Berkeley,
California, USA

September 30, 2011