

---

# Contents

|                                                                                          |           |
|------------------------------------------------------------------------------------------|-----------|
| Preface                                                                                  | vii       |
| <b>I GENERAL CONCEPTS</b>                                                                | <b>1</b>  |
| 1 The Role of Modeling in Systems Biology                                                | 3         |
| <i>Douglas B. Kell and Joshua D. Knowles</i>                                             |           |
| 2 Complexity and Robustness of Cellular Systems                                          | 19        |
| <i>Jörg Stelling, Uwe Sauer, Francis J. Doyle III,<br/>and John Doyle</i>                |           |
| 3 On Modules and Modularity                                                              | 41        |
| <i>Zoltan Szallasi, Vipul Periwal, and Jörg Stelling</i>                                 |           |
| <b>II MODELING APPROACHES</b>                                                            | <b>51</b> |
| 4 Bayesian Inference of Biological Systems: The Logic of Biology                         | 53        |
| <i>Vipul Periwal</i>                                                                     |           |
| 5 Stoichiometric and Constraint-based Modeling                                           | 73        |
| <i>Steffen Klamt and Jörg Stelling</i>                                                   |           |
| 6 Modeling Molecular Interaction Networks with Nonlinear Ordinary Differential Equations | 97        |
| <i>Emery D. Conrad and John J. Tyson</i>                                                 |           |
| 7 Qualitative Approaches to the Analysis of Genetic Regulatory Networks                  | 125       |
| <i>Hidde de Jong and Delphine Ropers</i>                                                 |           |
| 8 Stochastic Modeling of Intracellular Kinetics                                          | 149       |
| <i>Johan Paulsson and Johan Elf</i>                                                      |           |
| 9 Kinetics in Spatially Extended Systems                                                 | 177       |
| <i>Karsten Kruse and Johan Elf</i>                                                       |           |

## III MODELS AND REALITY

|                           |                                                                                                                                                                                                                 |     |
|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| 10                        | Biological Data Acquisition for System Level Modeling—<br>An Exercise in the Art of Compromise . . . . .                                                                                                        | 201 |
|                           | <i>Zoltan Szallasi</i>                                                                                                                                                                                          |     |
| 11                        | Methods to Identify Cellular Architecture and Dynamics from<br>Experimental Data . . . . .                                                                                                                      | 221 |
|                           | <i>Rudiyanto Gunawan, Kapil G. Gadkar,<br/>and Francis J. Doyle III</i>                                                                                                                                         |     |
| 12                        | Using Control Theory to Study Biology . . . . .                                                                                                                                                                 | 243 |
|                           | <i>Brian P. Ingalls, Tau-Mu Yi, and Pablo A. Iglesias</i>                                                                                                                                                       |     |
| 13                        | Synthetic Gene Regulatory Systems . . . . .                                                                                                                                                                     | 269 |
|                           | <i>Mads Kærn and Ron Weiss</i>                                                                                                                                                                                  |     |
| 14                        | Multilevel Modeling in Systems Biology: From Cells to Whole<br>Organs . . . . .                                                                                                                                 | 297 |
|                           | <i>Denis Noble</i>                                                                                                                                                                                              |     |
| IV COMPUTATIONAL MODELING |                                                                                                                                                                                                                 | 313 |
| 15                        | Computational Constraints on Modeling in Systems Biology .                                                                                                                                                      | 315 |
|                           | <i>Vipul Periwal</i>                                                                                                                                                                                            |     |
| 16                        | Numerical Simulation for Biochemical Kinetics . . . . .                                                                                                                                                         | 331 |
|                           | <i>Daniel T. Gillespie and Linda R. Petzold</i>                                                                                                                                                                 |     |
| 17                        | Software Infrastructure for Effective Communication and Reuse<br>of Computational Models . . . . .                                                                                                              | 355 |
|                           | <i>Andrew Finney, Michael Hucka, Benjamin J. Bornstein,<br/>Sarah M. Keating, Bruce E. Shapiro, Joanne Matthews,<br/>Ben L. Kovitz, Maria J. Schilstra, Akira Funahashi,<br/>John Doyle, and Hiroaki Kitano</i> |     |
| A                         | Software Tools for Biological Modeling . . . . .                                                                                                                                                                | 379 |
|                           | References . . . . .                                                                                                                                                                                            | 385 |
|                           | Contributors . . . . .                                                                                                                                                                                          | 435 |
|                           | Index . . . . .                                                                                                                                                                                                 | 439 |