
Contents

Preface	vii
1 Introductory Concepts	1
1.1 Systems biology: Modeling, analysis and role of feedback	1
1.2 The cell as a system	8
1.3 Control and dynamical systems tools	11
1.4 Input/output modeling	18
1.5 From systems to synthetic biology	22
1.6 Further reading	28
2 Dynamic Modeling of Core Processes	29
2.1 Modeling chemical reactions	29
2.2 Transcription and translation	44
2.3 Transcriptional regulation	55
2.4 Post-transcriptional regulation	70
2.5 Cellular subsystems	81
Exercises	86
3 Analysis of Dynamic Behavior	89
3.1 Analysis near equilibria	89
3.2 Robustness	103
3.3 Oscillatory behavior	113
3.4 Bifurcations	124
3.5 Model reduction techniques	127
Exercises	133
4 Stochastic Modeling and Analysis	139
4.1 Stochastic modeling of biochemical systems	139
4.2 Simulation of stochastic systems	154
4.3 Input/output linear stochastic systems	157
Exercises	164

5 Biological Circuit Components	169
5.1 Introduction to biological circuit design	169
5.2 Negative autoregulation	171
5.3 The toggle switch	177
5.4 The repressilator	180
5.5 Activator-repressor clock	184
5.6 An incoherent feedforward loop (IFFL)	189
5.7 Bacterial chemotaxis	191
Exercises	203
6 Interconnecting Components	205
6.1 Input/output modeling and the modularity assumption	205
6.2 Introduction to retroactivity	206
6.3 Retroactivity in gene circuits	209
6.4 Retroactivity in signaling systems	214
6.5 Insulation devices: Retroactivity attenuation	219
6.6 A case study on the use of insulation devices	236
Exercises	239
7 Design Tradeoffs	243
7.1 Competition for shared cellular resources	243
7.2 Stochastic effects: Design tradeoffs in systems with large gains	253
Exercises	257
Bibliography	259
Index	267