

Contents

<i>Preface</i>	<i>page xi</i>
1 Introduction	1
1.1 Biological networks	1
1.2 Why build and study models?	5
1.3 Characterizing dynamic states	6
1.4 Formulating dynamic network models	7
1.5 The basic information is in a matrix format	11
1.6 Studying dynamic models	13
1.7 Summary	16
2 Basic concepts	17
2.1 Properties of dynamic states	17
2.2 Primer on rate laws	20
2.3 More on aggregate variables	25
2.4 Time-scale decomposition	28
2.5 Network structure versus dynamics	31
2.6 Physico-chemical effects	34
2.7 Summary	36
PART I. SIMULATION OF DYNAMIC STATES	
3 Dynamic simulation: the basic procedure	41
3.1 Numerical solutions	41
3.2 Graphically displaying the solution	43
3.3 Post-processing the solution	49
3.4 Demonstration of the simulation procedure	51
3.5 Summary	56
4 Chemical reactions	58
4.1 Basic properties of reactions	58
4.2 The reversible linear reaction	60
4.3 The reversible bilinear reaction	62

4.4	Connected reversible linear reactions	66
4.5	Connected reversible bilinear reactions	70
4.6	Summary	75
5	Enzyme kinetics	76
5.1	Enzyme catalysis	76
5.2	Deriving enzymatic rate laws	78
5.3	Michaelis–Menten kinetics	80
5.4	Hill kinetics for enzyme regulation	85
5.5	The symmetry model	90
5.6	Scaling dynamic descriptions	94
5.7	Summary	96
6	Open systems	97
6.1	Basic concepts	97
6.2	Reversible reaction in an open environment	100
6.3	Michaelis–Menten kinetics in an open environment	104
6.4	Summary	107

PART II. BIOLOGICAL CHARACTERISTICS

7	Orders of magnitude	111
7.1	Cellular composition and ultra-structure	111
7.2	Metabolism	116
7.3	Macromolecules	124
7.4	Cell growth and phenotypic functions	128
7.5	Summary	131
8	Stoichiometric structure	132
8.1	Bilinear biochemical reactions	132
8.2	Bilinearity leads to a tangle of cycles	134
8.3	Trafficking of high-energy phosphate bonds	137
8.4	Charging and recovering high-energy bonds	145
8.5	Summary	149
9	Regulation as elementary phenomena	150
9.1	Regulation of enzymes	150
9.2	Regulatory signals: phenomenology	152
9.3	The effects of regulation on dynamic states	153
9.4	Local regulation with Hill kinetics	156
9.5	Feedback inhibition of pathways	161
9.6	Increasing network complexity	165
9.7	Summary	169

PART III. METABOLISM

10	Glycolysis	173
10.1	Glycolysis as a system	173
10.2	The stoichiometric matrix	175

10.3	Defining the steady state	181
10.4	Simulating mass balances: biochemistry	185
10.5	Pooling: towards systems biology	189
10.6	Ratios: towards physiology	199
10.7	Assumptions	202
10.8	Summary	203
11	Coupling pathways	204
11.1	The pentose pathway	204
11.2	The combined stoichiometric matrix	210
11.3	Defining the steady state	214
11.4	Simulating the dynamic mass balances	216
11.5	Pooling: towards systems biology	218
11.6	Ratios: towards physiology	219
11.7	Summary	222
12	Building networks	224
12.1	AMP metabolism	224
12.2	Network integration	231
12.3	Whole-cell models	240
12.4	Summary	241
PART IV. MACROMOLECULES		
13	Hemoglobin	245
13.1	Hemoglobin: the carrier of oxygen	245
13.2	Describing the states of hemoglobin	248
13.3	Integration with glycolysis	253
13.4	Summary	257
14	Regulated enzymes	259
14.1	Phosphofructokinase	259
14.2	The steady state	265
14.3	Integration of PFK with glycolysis	269
14.4	Summary	274
15	Epilogue	275
15.1	Building dynamic models in the omics era	275
15.2	Going forward	280
APPENDIX A. Nomenclature		285
APPENDIX B. Homework problems		288
<i>References</i>		306
<i>Index</i>		314