Contents

1 Stochastic Kinetics: Why and How? 1
1.1 Chemical Kinetics: A Prototype of Nonlinear Science 1
1.1.1 The Power Law and Mass Action Type Deterministic Model of Homogeneous Reaction Kinetics 3
1.1.2 Stationary States and Their Stability 11
1.2 Applicability of the Deterministic Model 11
1.3 Fluctuation Phenomena 13
1.3.1 Brownian Motion 13
1.3.1.1 Diffusion 14
1.3.1.2 Fluctuation-Dissipation Theorem 16
1.3.1.3 Towards the Theory of Stochastic Processes 17
1.3.1.4 Experimental Determination of the Avogadro Constant 17
1.4 Stochastic Chemical Kinetics 17
1.4.1 Model Framework: Preliminary Remarks 17
1.4.2 Historical Remarks 18
1.4.3 On the Solutions of the Stochastic Kinetic Models: Analytical Calculations Versus Simulations 19
1.4.4 The Renaissance of Stochastic Kinetics: Systems Biology 19
References 20

2 Continuous Time Discrete State Stochastic Models 25
2.1 Model Frameworks 25
2.2 Stochastic Processes 26
2.2.1 Definition 26
2.2.2 Time and State Space 27
2.2.3 Important Types of Stochastic Processes 27
2.2.4 Markov Chains 28

2.2.5 Continuous Time Discrete State Markov Process 31
2.2.6 Semi-Markov Processes 34
2.3 The Standard Stochastic Model of Homogeneous Reaction Kinetics 35
2.3.1 State Space: Size and Enumeration 36
2.3.2 Master Equation 38
2.3.3 Connection Between Deterministic and Stochastic Kinetics: Similarities and Differences 41
2.3.4 Stochastic Maps 44
2.4 Solutions of the Master Equation 45
2.4.1 What Do We Mean by Exact Analytical Solutions? 45
2.4.2 Direct Matrix Operations 45
2.4.3 Time-Independent Q-Functions 47
2.4.4 Laplace Transformation 48
2.4.5 Generating Functions 49
2.4.6 Poisson Representation 50
2.4.7 Mathematical Induction 53
2.4.8 Initial Conditions Given with a Probability Distribution 53
2.4.9 Time Scales 54
2.5 Stationary and Transient Distributions 54
2.5.1 Stationary Distributions 54
2.5.2 Transient Distributions 56
2.5.3 Properties of Stationary and Transient Distributions: Unimodality Versus Multimodality 56
2.6 Simulation Methods 58
2.7 Deterministic Continuation 62
2.8 Continuous State Approximations 63
2.9 Non-Markovian Approaches 66
References 67

3 Applications 71
3.1 Introductory Remarks 71
3.2 Fluctuations Near Instabilities 72
3.2.1 Stochastic Chemical Reaction: A Simple Example 72
3.2.1.1 Keizer's Paradox 73
3.2.2 Stochastic Theory of Bistable Reactions 74
3.2.2.1 Schlögl Reaction of the First-Order Phase Transition 74
3.2.2.2 Time Spent in Each Steady State, and Time Scale of Transitions 75
3.2.2.3 The *lac* Operon Genetic Network 78
3.3 Compartmental Systems 78
3.3.1 Model Frameworks 78
3.3.2 Master Equation and State Space 80
3.3.3 Solutions 81

3.4 Autocatalysis 84
3.4.1 Autocatalytic Extinction 85
3.4.2 Time Dependence of the Crazy Clock Reaction 87
3.4.3 Autocatalytic Cycle Process 88
3.5 Enzyme Kinetics 91
3.5.1 Michaelis–Menten: Scheme and State Space 91
3.5.2 Michaelis–Menten: Solutions 92
3.5.3 Other Enzyme Systems 99
3.6 Signal Processing 101
3.6.1 Signaling with Chemical Networks: General Remarks 101
3.6.2 Signal Processing in Biochemical Networks 102
3.6.2.1 Evaluation of Signal Transfer by Mutual Information 102
3.6.2.2 Impact of Network Structure on the Transmission 104
3.6.2.3 Further Studies 107
3.6.3 Signal Processing in Olfactory Systems 110
3.6.3.1 Fisher Information and Optimal Signal Transmission 110
3.6.3.2 Stochastic Kinetic Models of Odor Intensity Detection 110
3.6.3.3 Estimation of Optimal Olfactory Signals 112
3.6.4 Calcium Signaling 114
3.7 Gene Expression 116
3.7.1 A Very, Very Short Review of Biochemical Background 116
3.7.2 Measurement of Noise in Genetic and Other Biochemical Networks 117
3.7.3 Stochastic Kinetic Models of Gene Expression 118
3.7.3.1 General Remarks 118
3.7.3.2 A Three-Stage Model of Gene Expression 118
3.7.3.3 Separating Intrinsic from Extrinsic Fluctuations 120
3.8 Chiral Symmetry 122
3.8.1 Racemic Mixtures 122
3.8.2 Simple Enantioselective Autocatalysis 125
3.8.3 The Frank Model 129
3.8.4 The Soai Reaction 130
3.9 Parameter Estimation in Stochastic Kinetic Models 132
3.9.1 Estimation of Rate Constants from Equilibrium Fluctuations 132
3.9.2 Parameter Estimation for Stochastic Kinetic Models: Beyond the Fluctuation-Dissipation Theorem 133
3.10 Stochastic Resonance in Chemical Systems 135
3.10.1 General Remarks 135

3.10.2 Stochastic Resonance in One- and Multi-parameter System 135
3.10.3 Stochastic Resonance of Aperiodic Signals 137
3.11 Computation with Small Stochastic Kinetic Systems 137
References 139

4 The Book in Retrospect and Prospect 149
References 156

Index 159