

## Contents

|                                                                                                      |    |
|------------------------------------------------------------------------------------------------------|----|
| A. Stochastic Processes.....                                                                         | 1  |
| 1. Expectation Values, Moments, Variance, Correlations.....                                          | 2  |
| 2. Probabilities.....                                                                                | 4  |
| 2.1 Expectation Values and Probabilities.....                                                        | 5  |
| 3. Binomial, Poisson, Normal Distributions.....                                                      | 7  |
| 4. Stationarity and Ergodicity.....                                                                  | 10 |
| B. Analysis of Stationary Stochastic Processes.....                                                  | 13 |
| 1. Basic Concepts of Noise Analysis.....                                                             | 13 |
| 1.1 Spectral Density.....                                                                            | 13 |
| 1.2 Autocorrelation Function and Wiener-Khintchine Relations.....                                    | 15 |
| 2. Poisson Processes, Carson's Theorem.....                                                          | 17 |
| 2.1 Variance, Autocorrelation Function, Spectral Density.....                                        | 18 |
| 2.2 Special Examples.....                                                                            | 19 |
| 2.3 Ions Crossing Membranes: Shot Noise.....                                                         | 21 |
| 3. The Master Equation Approach to Fluctuations.....                                                 | 24 |
| 3.1 Markov Processes.....                                                                            | 25 |
| 3.2 Master Equation and Phenomenological Equations.....                                              | 26 |
| 3.3 Linearized Phenomenological Equations and Fundamental<br>Solutions.....                          | 29 |
| 3.4 Variances, Correlations, Spectra.....                                                            | 32 |
| 3.5 Correlation and Spectra of Measurable Quantities.....                                            | 35 |
| 3.6 Direct Calculation of Fluctuations from the Fundamental<br>Solutions of the Master Equation..... | 36 |
| 3.7 Current Noise Generated by the Opening and Closing of<br>Channels.....                           | 39 |

|                                                                                                 |    |
|-------------------------------------------------------------------------------------------------|----|
| C. Transport Fluctuations Around Steady States.....                                             | 42 |
| 1. Introductory Remarks on Transport Fluctuations.....                                          | 42 |
| 1.1 Characterization.....                                                                       | 42 |
| 1.2 A simple Example: Channels with one Binding Site....                                        | 44 |
| 2. The Concept of Transport in Discrete Systems.....                                            | 49 |
| 2.1 The Fluxes.....                                                                             | 49 |
| 2.2 Current as a Transport Observable.....                                                      | 52 |
| 2.3 Conservative Systems, Open Systems.....                                                     | 53 |
| 2.4 Interactions Neglected.....                                                                 | 55 |
| 3. Transport Fluctuations at Equilibrium.....                                                   | 58 |
| 3.1 The Nyquist or Fluctuation-Dissipation Theorem.....                                         | 58 |
| 3.2 Voltage Dependence of the Rate Constants.....                                               | 59 |
| 3.3 Linear Response and Complex Admittance.....                                                 | 61 |
| 4. Theory of Transport Fluctuations Around Equilibrium<br>and Nonequilibrium Steady States..... | 64 |
| 4.1 The Flux-Correlation Matrix.....                                                            | 64 |
| 4.2 Autocorrelation Function and Spectral Density of<br>Current Fluctuations.....               | 66 |
| 4.3 More Rigorous Treatment of the Time Correlation<br>Matrix.....                              | 68 |
| 5. Transport Fluctuations in Basic Membrane Transport<br>Systems.....                           | 71 |
| 5.1 Current Noise in Open Channels.....                                                         | 71 |
| 5.2 The Influence of Voltage and Barrier Structure<br>on the Fluctuations.....                  | 76 |
| 5.3 Carrier Noise.....                                                                          | 86 |
| 6. Transport Fluctuations in More Sophisticated Channel<br>Models.....                          | 90 |
| 6.1 Single-File Diffusion Through Narrow Channels.....                                          | 90 |

|                                                                                                                          |     |
|--------------------------------------------------------------------------------------------------------------------------|-----|
| 6.2 Numerical Calculations of Single-File Noise in Open Channels.....                                                    | 96  |
| 6.3 Single-File Noise: Coupling Between Transport and Open-Closed Kinetics of the Channels.....                          | 103 |
| 7. Invalidity of the Fluctuation-Dissipation Theorem for Transport Fluctuations Around Nonequilibrium Steady States..... | 118 |
| 7.1 Special Examples: Channel Noise, Carrier Noise, Noise Generated by Permanently Open Channels.....                    | 120 |
| 7.2 Different Behaviour of Scalar and Vectorial Quantities at Nonequilibrium.....                                        | 126 |
| 8. Current Noise: The Limit of High Applied Voltage.....                                                                 | 130 |
| 8.1 Interactions Neglected: Shot Noise.....                                                                              | 130 |
| 8.2 Reduction of Noise as Consequence of Ionic Interactions in the Single-File Model.....                                | 133 |
| D. Nonstationary Processes, Fluctuations at Transient States...                                                          | 139 |
| 1. A Simple Example: Identical, Independent Channels.....                                                                | 139 |
| 2. Time-Dependent States in Markov Processes.....                                                                        | 141 |
| 2.1 General Equations for the Moments.....                                                                               | 141 |
| 2.2 One-Variable Birth-Death Processes.....                                                                              | 143 |
| 3. Linear Birth-Death Processes With One Variable.....                                                                   | 147 |
| 3.1 Expectation Value and Variance.....                                                                                  | 147 |
| 3.2 Application: Linear Two State Channel Models.....                                                                    | 149 |
| 4. Nonlinear Processes.....                                                                                              | 152 |
| 4.1 Approximation Procedures.....                                                                                        | 152 |
| 4.2 Bilinear One-Variable Birth-Death Processes.....                                                                     | 154 |

|                                             |     |
|---------------------------------------------|-----|
| 4.3 Bimolecular Reactions: The              |     |
| Gramicidin Channel.....                     | 155 |
| 5. Transport Noise at Transient States..... | 159 |
| References.....                             | 161 |
| Subject index.....                          | 166 |