Contents

Preface *xvi*
Acknowledgments *xx*
About the Companion Website *xxi*

Part I Scientific Overview, Biological and Biochemical Surveys *1*

1 Background Notions, Histories, and Fundamental Issues in Physics and Biophysics *3*
1.1 The Evolution of Scientific Thought *3*
1.1.1 Error in the Laboratory *6*
1.1.2 Error Versus Approximation *6*
1.2 Historical Sketch of Atomic Theory and Evolutionary and Genetic Thought *7*
1.2.1 Historical Sketch of Atomic Theory *7*
1.2.2 Evolutionary Thought *9*
1.2.3 Genetics and Molecular Biology *13*
1.3 Historical Developments in Biophysics *15*
1.3.1 Electrophysiology *15*
1.3.2 Hermann von Helmholtz *15*
1.3.3 Osmosis and Diffusion *16*
1.3.4 X-rays *17*
1.3.5 Imaging Methods *18*
1.3.6 Radiation Biophysics *18*
1.4 Subfields in Biophysics *19*
1.4.1 Molecular Biophysics *19*
1.4.2 Cellular Level and Integrative Biophysics *19*
1.4.3 Macroscopic Biophysics *19*
1.4.4 Theoretical Biophysics *19*
1.4.5 Instrumental and Medical Biophysics *20*
1.5 Interdisciplinarity *20*
1.5.1 A Simplified Net of Scientific Knowledge *20*
1.5.2 Engineering Vis-à-vis Science *23*
1.6 Disciplinary Physics *23*
1.6.1 Fundamental Forces *24*
1.6.2 The Standard Model *24*
1.6.3 Cosmology *25*
1.7 Are Currently Known Physical Laws Adequate for Understanding Living State Phenomena? *28*
1.8 Unifying Characteristics of the Living State *29*
1.9 Summary *30*

2 Overview of Biological Cell Structure *34*
2.1 The Prokaryotic Cell *34*
2.2 The Eukaryotic Cell *36*
2.3 Plant Cell *37*
2.4 Where Do Viruses Fit in? *37*
2.5 Overview of Cell Functions *39*
2.5.1 Energy Production *39*
2.5.2 Gene Expression *39*
2.5.3 Motion *39*
2.5.4 Cell Reproduction *40*
2.5.5 Chemical Sensing and Signaling *41*
2.5.6 Excitable Cells and Receptors *42*
2.5.7 Self-defense *43*
2.6 Specialized Cell Types and Structures *44*
2.6.1 Nerve Cells *44*
2.6.2 Bone *47*
2.6.3 Blood Cells *48*
2.6.4 Muscle Cells *49*
2.6.5 Skin *50*
2.7 Molecular Biology Methods *50*
2.7.1 DNA Polymerase Chain Reaction *50*
2.7.2 Gel Electrophoresis *50*
2.7.3 Ion Exchange Chromatography *51*
2.7.4 Affinity Chromatography *51*
2.7.5 Radioactive Tracer Techniques *51*
2.7.6 Nucleic Acid Hybridization *51*
2.7.7 Chromosome Conformation Capture *52*
2.8 Summary *52*

3 Biochemistry Survey *53*
3.1 Amino Acids and Proteins *53*
3.1.1 The Peptide Bond and the Amino Acids *54*
3.1.2 Protein Isoelectric Point *55*
3.1.3 Levels of Protein Organization *56*
3.1.4 Multidomain Proteins *57*
3.2 Nucleic Acids *58*
3.2.1 Nucleobases, Nucleosides, and Nucleotides *58*
3.2.2 Nucleotides for Energy Currency *59*
3.2.3 Nucleotides for Reducing Power: ATP, FAD, and NAD *61*
3.2.4 Polynucleic Acids, DNA, and RNA *62*
3.3 Carbohydrates *62*
3.3.1 Mono- and Disaccharides *63*
3.3.2 Oxidation of Carbohydrates *63*
3.3.3 Polysaccharides *63*
3.4 Lipids *64*
3.4.1 Classification of Lipids *64*
3.4.2 Membrane Formation from Lipids *65*
3.5 Metabolism *67*
3.5.1 Oxidation–Reduction Reactions (Redox Reactions) *68*
3.5.2 Principle Catabolic Pathways *71*
3.6 Summary *73*

Part II Physical Processes Underlying the Living State *75*

4 Thermodynamics, Reaction Kinetics, and Information Theory *77*
4.1 Thermodynamically Based Forces *77*
4.2 Thermodynamic Laws *78*
4.2.1 "Zeroeth" Law *79*
4.2.2 First Law *79*
4.2.3 Second Law *79*
4.2.4 Third Law *81*
4.2.5 Free Energy *81*
4.3 Thermodynamic Processes Involving Ideal Gases *82*
4.3.1 Reversible Isothermal Expansion of an Ideal Gas *82*
4.3.2 Reversible Adiabatic Expansion of an Ideal Gas *83*
4.3.3 Irreversible, Adiabatic Free Expansion of an Ideal Gas *83*
4.3.4 The Carnot Cycle *83*
4.4 Connection Between Ideal Gas Law and Molecular Kinetic Energy *84*
4.4.1 Ideal Gas Specific Heats Derived from Relation of $<KE>$ to T *86*
4.4.2 Thermal Energy, k_BT *86*
4.5 The Boltzmann Distribution *86*
4.5.1 Continuous Probability Distributions *87*
4.5.2 The Maxwell–Boltzmann Speed Distribution for Atomic Gases *88*
4.5.3 Equipartition Principle *89*
4.6 The Partition Function *91*
4.7 Statistical Interpretation of Entropy *93*
4.8 Ideal Osmotic Solutions *94*
4.8.1 Macroscopic Manifestations of Osmotic Pressure in the Living State *97*
4.9 Working Substances and Bioenergetics Cycles *99*
4.10 The Hydrophobic Effect *99*
4.11 Surface Tension *99*
4.11.1 Young's Equation for Contact Angle of a Drop on a Solid Surface *100*
4.11.2 Capillary Action *101*
4.12 Thermodynamics of Multicomponent Solutions *102*
4.12.1 Chemical Potential *102*
4.12.2 Chemical Potential μ_i for an Ideal Solution *105*
4.13 Chemical Potential for Nonideal Solutions *107*
4.13.1 Osmotic Pressure and Relation to Chemical Potential *108*
4.13.2 Measurement of Number Average Molar Mass and Average A_2 by Osmometry *110*
4.13.3 Dialysis *111*
4.14 Excluded Volume Approach to Nonideal Solutions *112*
4.14.1 General Form for Excluded Volume *115*
4.14.2 Depletion Forces *117*
4.15 Chemical Equilibrium *117*
4.15.1 Ionic Dissociation of Water as an Example of Equilibrium: pH and pK_a *118*
4.15.2 Le Chatelier's Principle *119*
4.15.3 Micellization of Surfactant Molecules in Solution *120*
4.16 Reaction Kinetics *122*
4.16.1 Order of Reactions *124*
4.17 Phase Transitions *125*
4.18 Nonequilibrium Thermodynamics *126*
4.19 Information Theory *126*
4.19.1 The Geometric Distribution and the Binomial Distribution *128*

4.19.2 Information and Biomolecules *129*
4.19.3 Information and Entropy *130*
4.19.4 Information, Shannon Entropy, and Communication Theory *131*
4.20 Summary *132*

5 Electrostatics in Solution *137*
5.1 Review of Electrostatics (in MKSA Units) *137*
5.1.1 The Electric Field, $\vec{E}$ *138*
5.1.2 The Electrostatic Potential, ϕ *138*
5.1.3 Capacitance, C *140*
5.1.4 The Electric Dipole Moment, $\vec{p}$ *142*
5.2 Covalent Bonds in the Living State are Stable Against Thermal Energy *144*
5.2.1 Useful Conversions for Energy Units *144*
5.3 "Weak Electrostatic Forces" Allow for Self-organization and Rapid Dynamic Processes *144*
5.3.1 Ion–Ion Interactions *144*
5.3.2 Ion–Dipole Interactions *145*
5.3.3 Dipole–Dipole Interactions: Van Der Waals Forces *145*
5.3.4 Lennard–Jones Potential *145*
5.3.5 London Forces and Mutually Induced Dipoles *145*
5.4 Hydrogen Bonds *147*
5.5 Electrically Charged Macromolecules and Colloids in Solution *148*
5.6 Poisson–Boltzmann Equation *148*
5.6.1 Boundary Conditions for a Sphere and Resulting Potential and Charge Distribution Around It *152*
5.6.2 Capacitance with a Screened Potential *153*
5.6.3 Ionic Strength *154*
5.6.4 Asymmetric Electrolytes Show Clear Deviations Due to the Nonlinearity of the PBE *156*
5.7 Osmotic Pressure of an Ideal Polyelectrolyte Solution with a Semi-Permeable Membrane: Donnan Equilibrium *158*
5.8 Self-energy of a Hydrated Ion *161*
5.9 Force on an Ion near an Interface of Two Media with Different Dielectric Constants *162*
5.10 Bjerrum Length and Counterion Condensation *163*
5.11 Summary *163*

6 Fluid Mechanics and Transport Processes *167*
6.1 Conceptual Approach to Viscosity *168*
6.1.1 The Relationship of Shear Rate to Viscosity and Shear Stress *168*
6.2 The Stress Tensor *170*
6.3 Navier–Stokes Equation of Motion for Incompressible, Viscous Fluids *170*
6.3.1 Reynolds Number *172*
6.3.2 Steady Flow and Stokes Approximation *172*
6.4 Applications of Navier–Stokes for Steady Flow *173*
6.4.1 Steady State Flow of Fluid in a Tube with Pressure Difference ΔP *173*
6.4.2 Viscometers *174*
6.4.3 Hydrodynamic Resistance *175*
6.4.4 Frictional Coefficient for a Sphere in a Viscous Liquid *175*
6.5 Hemodynamics *177*
6.6 The Intrinsic Viscosity $[\eta]$ of Particles in a Fluid *177*
6.7 Force–Flux Relations *180*
6.7.1 Conserved Quantities and the Continuity Equation *182*
6.7.2 Electrophoretic Mobility and Zeta Potential *183*
6.8 Diffusion *184*
6.8.1 Nonideal Effects in Diffusion *189*
6.9 The Nernst–Planck Equation *189*
6.9.1 Electrostatic Potential Across a Cell Membrane *190*

6.10 Fluctuation–Dissipation and a Qualitative Overview of Its Consequences *191*
6.10.1 Electrical Noise from Fluctuation–Dissipation *191*
6.10.2 Blackbody Radiation and Fluctuation–Dissipation *192*
6.10.3 Fluctuation–Dissipation in the Living State *193*
6.10.4 Fluctuation–Dissipation and the Time Autocorrelation Function *193*
6.10.5 Time Course of a Charge Density Fluctuation *195*
6.11 Coupled Forces and Flows: Onsager's Reciprocal Relationships *195*
6.12 Fluid Transport in Plants *196*
6.13 Diffusional Versus Directed Motion *197*
6.14 Time Reversal Symmetry and Its Breaking *198*
6.15 Techniques for Determining Transport Properties *198*
6.16 Summary *199*

Part III Polymer Science *205*

7 Overview of Polymer Science *207*
7.1 Biological and Synthetic Polymers *207*
7.2 Brief Overview of Classes of Organic Molecules *208*
7.2.1 Hydrocarbons *208*
7.2.2 Organic Molecules Containing Halogens *210*
7.2.3 Organic Molecules Containing Oxygen *211*
7.2.4 Organic Molecules Containing Nitrogen *213*
7.2.5 Hybrid Orbitals and Molecular Geometry *214*
7.3 Synthetic Polymers *215*
7.3.1 Glass Transition Temperature, Chirality, and Tacticity *215*
7.3.2 Specific Types of Synthetic Polymers *216*
7.3.3 Natural Products from Biological Macromolecules *219*
7.3.4 Stimuli-responsive Polymers and Highly Architected Polymers *219*
7.3.5 Biomimetics *221*
7.4 Polymerization Reactions *221*
7.4.1 Methods of Performing Polymerization Reactions *222*
7.4.2 Monitoring Polymerization Reactions *223*
7.5 Free Radicals and Chain Reactions *224*
7.5.1 Free Radicals and the Vinylic Bond *225*
7.6 Free Radical Polymerization Kinetics *225*
7.6.1 Quasi-steady State Approximation, QSSA *226*
7.6.2 Effect of Chain Transfer on Molar Mass *229*
7.7 Ideal Living Polymerization *232*
7.7.1 Controlled Radical Polymerization *233*
7.8 Chain Growth Copolymerization Kinetics *234*
7.8.1 Mayo–Lewis Approach to Free Radical Copolymerization *234*
7.8.2 Living Copolymerization *237*
7.8.3 The Sequence Length Distribution *237*
7.9 Cumulative and Instantaneous Polymer Characteristics During Free Radical Reactions *238*
7.10 Fully Automatic Feedback Control of Molar Mass and Conversion During Chain Growth Polymerization *239*
7.11 Linear Step Growth Reactions *243*
7.12 Molar Mass Distributions (MMD) and Averages *244*
7.12.1 Molar Mass Averages of the Geometric Distribution *247*
7.12.2 Molar Mass Averages of the Log-Normal Distribution *248*
7.12.3 Poisson Distribution for "Living" Type Reactions *249*
7.13 Experimental Methods for Determining Molar Mass Distributions *251*
7.13.1 Size Exclusion Chromatography *251*

7.13.2 Other Fractionation Methods *254*
7.13.3 Chromatography-free Determination of MMD *255*
7.14 Summary *256*

8 Polymer Physics *260*
8.1 Polymer Conformations and Dimensions *260*
8.1.1 Rotational Isomeric Model *260*
8.1.2 Polymer Conformations *261*
8.1.3 Ideal Random Coil Polymer Statistics Obey the Diffusion Equation *262*
8.1.4 Entropic Origin of Polymeric Elasticity *265*
8.1.5 Estimate of Young's Modulus and the Effect of Cross-linking *266*
8.1.6 Polymer Dimensions for Random Coils: Relation Between Radius of Gyration and End-to-end Length *268*
8.1.7 Effect on Polymer Dimensions of Restricted Bond Angles *269*
8.1.8 Rotational Isomeric States and Their Effect on Bond Angle *271*
8.1.9 Persistence Lengths of Semiflexible Polymers *271*
8.1.10 Branching and Cross-linking *275*
8.2 Polymer Excluded Volume (EV) *276*
8.2.1 A_2 for Coil Polymers *277*
8.2.2 Third and Higher Virial Coefficients *278*
8.3 Hydrodynamic Characteristics of Polymers in Solution *278*
8.3.1 Diffusion *279*
8.3.2 Polymer Intrinsic Viscosity *279*
8.3.3 Dilute, Semidilute, and Concentrated Polymer Solution Regimes *280*
8.4 Electrically Charged Polymers: Polyelectrolytes *281*
8.4.1 Electrostatic Persistence Lengths and Electrostatic Excluded Volume *282*
8.5 Case Study of Polystyrene Characteristics in Tetrahydrofuran *285*
8.6 Thermodynamics of Polymer Solutions *285*
8.6.1 Flory–Huggins Mean-field Theory *285*
8.6.2 Phase Behavior *287*
8.7 Rheology *288*
8.7.1 Newtonian and Non-Newtonian Polymer Liquids *289*
8.7.2 Dynamic Mechanical Analysis and Other Viscoelastic Analyses *289*
8.8 Solid-state Properties *290*
8.9 Summary *290*

9 Light Scattering and Cognate Methods *295*
9.1 Overview of Light Scattering *295*
9.2 The Maxwell Electromagnetic Equations and the Prediction of Electromagnetic Waves and Their Properties, in Gaussian (CGS) Units *297*
9.2.1 The First Maxwell Equation *297*
9.2.2 The Second Maxwell Equation *298*
9.2.3 The Third Maxwell Equation *298*
9.2.4 The Fourth Maxwell Equation *299*
9.2.5 Electromagnetic Force Law *299*
9.2.6 The Solar Wind, Cosmic Rays, and Possible Implications for the Living State *300*
9.2.7 The Continuity Equation for Electric Charge *301*
9.2.8 The Wave Equation and Electromagnetic Waves in Vacuum *301*
9.2.9 Electromagnetic Units, the Discovery of the Speed of Light, and Einstein's Special Relativity *303*
9.3 Radiation Emitted by an Accelerated Charge *304*
9.4 Basic Scattering Theory: Light Emitted from an Oscillating Electric Dipole *305*
9.4.1 Rayleigh Scattering by a Single Particle *305*

9.4.2 Rayleigh Scattering by Dilute, Noninteracting Particles *307*
9.4.3 The Rayleigh Scattering Ratio *308*
9.4.4 The Clausius–Mossotti Equation and the Differential Refractive Index $\partial n / \partial c$ *310*
9.5 Relation of Light Scattering by Pure Liquids to Thermodynamic Fluctuations *311*
9.5.1 Extension of the Fluctuation Theory to Liquids Containing Polymers or Colloids *314*
9.6 The Angular Dependence of Scattered Light: Intramolecular Interference Effects on Scattering *315*
9.6.1 The Rayleigh–Debye Approximation (RDA) *317*
9.6.2 Computation of the Spatial Average of $e^{-i\vec{q}\cdot\vec{r}_{ij}}$ for Uniform Mass Density *321*
9.6.3 The Limit of $P(q)$ at Small qr_{ij} *322*
9.6.4 The Zimm Approximation for Polymers *323*
9.6.5 Zimm Equation for a Disperse Polymer Solution *324*
9.7 The Angular Dependence of Scattered Light: Intermolecular Interference Effects on Scattering: The structure factor $S(q,c)$ *326*
9.8 Mie Scattering *328*
9.9 Scattering Model for Index of Refraction *330*
9.10 Scattering at Interfaces *331*
9.10.1 The Fresnel Equations *331*
9.10.2 The Evanescent Wave in Total Internal Reflection *334*
9.10.3 Scattering at Metal Surfaces *335*
9.10.4 The Phase Contrast Microscope *336*
9.11 Single Photon Scattering *337*
9.12 Dynamic Light Scattering *338*
9.12.1 Depolarized Scattering and Rotational Diffusion *341*
9.12.2 Electrophoretic Light Scattering *341*
9.13 X-ray Diffraction and Crystallography *342*
9.14 Raman Scattering *342*
9.15 Optical Activity *343*
9.16 Superconducting Quantum Interference Devices (SQUIDs) *344*
9.17 Antimatter and PET Imaging *345*
9.18 Electron Microscopy *346*
9.19 Summary *347*

Part IV Examples of Specific Living State Phenomena *353*

10 Proteins: Structure, Folding, Enzyme Kinetics, and Cooperativity *355*
10.1 The Protein Folding Problem *355*
10.1.1 More on Chaperones *358*
10.1.2 Is Nothing Spontaneous in the Living State? *359*
10.2 Protein Aggregation *360*
10.2.1 Aggregation of Therapeutic Proteins and Light Scattering Analysis *360*
10.2.2 On the Reproducibility of Protein Aggregation: Deterministic, Stochastic, or Chaotic? *363*
10.2.3 Cooperativity and Other Effects in Protein Aggregation *365*
10.2.4 Temperature Ramps Can Muddle Protein Aggregation Behavior *367*
10.2.5 Equilibrium Properties of Native Proteins *367*
10.2.6 Protein Aggregation under Denaturing Conditions *369*
10.2.7 Blood Clotting Via the Fibrinogen Coagulation Cascade *370*
10.2.8 mRNA Delivery in Lipid Nanoparticles Versus Therapeutic Protein Injection *370*
10.3 Enzyme Kinetics *370*
10.3.1 Simple Enzyme Model: Michaelis–Menten–Henri Kinetics *371*
10.3.2 Enzymatic Depolymerization Kinetics Determined by Light Scattering *373*

10.3.3 Presteady-state Kinetics *375*
10.3.4 Michaelis–Menten–Henri Kinetics with an Intermediate Enzyme Complex, EI *375*
10.3.5 Kinetics of Reversible Product Formation *376*
10.4 Cooperative Binding in Proteins *377*
10.4.1 Effect of Cooperative Binding on Kinetics *380*
10.5 Cooperativity in the Helix–Coil Transition *381*
10.6 Histones and Other Chromosomal Proteins *383*
10.7 The Action of Proteins Often Depends on Correlated Internal Motions *383*
10.8 Directed Protein Motion and Protein Motors *384*
10.9 Allostery and Feedback Regulation *385*
10.10 Energetics of Iscosahedral Viral Self-assembly *385*
10.11 Summary *387*

11 DNA and RNA Properties and Structures: The Genetic Code *391*
11.1 Structure and Macromolecular Properties of RNA and DNA *391*
11.1.1 Mechanical Properties of Isolated DNA *391*
11.2 The Genetic Code *393*
11.3 Brief Description of Gene Expression with a Focus on Protein Synthesis *395*
11.3.1 Transcription *396*
11.3.2 Properties of RNA Polymerase (RNAP) *396*
11.3.3 Transcription Factors and Mediator Complexes *396*
11.3.4 Translation and Ribosomes *397*
11.3.5 Mitochondrial DNA and Ribosomes *397*
11.4 Chromatin and DNA Mechanics *397*
11.4.1 Telomeres *399*
11.5 Summary *399*

12 Some Polysaccharide Phenomena *403*
12.1 Polymer and Polyelectrolyte Properties of Polysaccharides *403*
12.1.1 Profile of a Polyfunctional Polysaccharide, Gum Arabic *403*
12.2 Proteoglycans and Extracellular Matrix Functions *404*
12.2.1 Cartilage Dynamics *405*
12.2.2 Cartilage Electrokinetics *407*
12.3 Proteoglycan Degradation Mechanisms Found by Light Scattering *408*
12.4 Summary *411*

13 Phospholipids Membranes: Channels and Nerve Impulses *413*
13.1 General Properties of Membranes *413*
13.2 Membrane Potentials *413*
13.2.1 Circuit Model for Transmembrane Electric Potential *416*
13.3 The Voltage Clamp and Patch Clamp *418*
13.4 Membrane Current–Voltage Curves *419*
13.5 Membrane Channel Proteins *420*
13.6 Passive Propagation of Potentials Along an Axon *421*
13.7 Action Potentials and Nerve Impulse Propagation *423*
13.7.1 The Hodgkin–Huxley Equations *424*
13.7.2 Trains of Action Potential Spikes *428*
13.8 Summary *428*

14 Integrated Biological Systems *430*
14.1 Light and Life *430*
14.1.1 Archaea *430*
14.1.2 Absorption and Emission of Light in the Living State *431*
14.2 Vision *432*
14.2.1 Geometrical Optics and Image Formation *432*
14.2.2 Structure and Optics of the Human Eye *434*
14.2.3 Transduction Events in Vision *438*
14.3 Cilial and Flagellar Biomotion *439*
14.4 Theoretical Biology: Cycles, Instabilities, and Attractors *439*
14.4.1 Elementary Time-dependent Processes Leading to Cycles, Instability, and Chaos *439*
14.5 Dissipative, Far from Equilibrium Spatially Self-organizing Systems *444*
14.5.1 Example of Stability and Instability in Simple Coupled Reaction–Diffusion Equations *445*
14.5.2 Turing Patterns *445*
14.5.3 Fibonacci Sequence and Patterns in Nature *447*
14.6 Summary *448*

15 On the Frontier *450*
15.1 Prebiotic Origins of Life *450*
15.1.1 The "RNA World Hypothesis" *451*
15.1.2 Alternate Prebiotic Paths *452*
15.1.3 Origin of Homochirality *452*
15.1.4 Information Theory Objections to a Strictly Physics/Chemistry Origin of the Genetic Code *453*
15.1.5 The Entscheidungsproblem and Relationship to the Origin of Life and the Genetic Code *454*
15.2 Quantum Biology *454*
15.2.1 Spin Radicals as a Possible Quantum Mechanical Origin of Magnetoreception *455*
15.3 Neuroscience and the Question of Consciousness *456*
15.3.1 A Short Tour of the Human Brain *457*
15.3.2 The Question of Consciousness *458*
15.3.3 Further Considerations Regarding Consciousness *459*
15.4 Artificial Intelligence *460*
15.4.1 Neural Networks and Parallel Computing *461*
15.5 Astrobiology and Exoplanets *463*
15.5.1 Types of Exoplanets *464*
15.5.2 Exoplanetary Atmospheres and Conditions for Life *465*
15.5.3 The James Webb Space Telescope *466*
15.6 Summary *467*

Afterword *472*
Appendix I: Probability Distributions and Their Averages *473*
Appendix II: Review of Vector Calculus and Notation Used *479*
Index *483*