

# Contents

## Part I Principles of Biophysical Inquiry

<b>1</b>	<b>Introduction: To the Student – First Edition . . . . .</b>	<b>3</b>
<b>2</b>	<b>Philosophy and Practice of Biophysical Study . . . . .</b>	<b>5</b>
2.1	What Is Biophysical Chemistry and Why Study It? . . . . .	5
2.2	Science Is Not Content but a Unique Method of Discovery . . . . .	6
2.3	The Progression of Inquiry Guides the Scientific Modeling Process . . . . .	8
2.4	A Brief History of Human Methods of Inquiry Reveals Important Aspects of the Scientific Method . . . . .	9
2.5	The Gedanken Experiment Is a Thought Experiment . . . . .	12
2.6	The Beginnings of Modern Science– Kepler and Galileo . . . . .	14
2.7	Modern Biophysical Studies Still Follow the Paradigm of Kepler and Galileo . . . . .	16
2.7.1	Describe the Phenomenon – What Is happening Here? What Are the Emergent Properties of the System? . . . . .	16
2.7.2	Reduce the Phenomenon to a Systems Description: Identify the Components of a System – Who and What Is Involved? (What Are the Elements?) . . . . .	17
2.7.3	Analysis of Structure – What Does it Look Like? What Are the Relationships Between the Components? (What Are the Interaction Rules and What Is the Context of the System?) . . . . .	17
2.7.4	Analysis of Dynamic Function – What Is the Mechanistic or Explanatory Cause of That? . . . . .	18
	Further Reading . . . . .	20
	Problem Sets . . . . .	22

<b>3 Overview of the Biological System Under Study</b> . . . . .	<b>23</b>
3.1 Hierarchies of Abstraction Are Essential in the Study of Biophysical Chemistry . . . . .	24
3.2 An Overview of the Cell: The Essential Building Block of Life . . . . .	25
3.2.1 The Cell Membrane Is a Physical Boundary Between the Cell System and Its Surroundings but This Membrane Is Also Part of the Biological System . . . . .	26
3.2.2 The Cytoplasmic Space Is the Matrix of the Intracellular System . . . . .	26
3.2.3 The Organelles Are Subsystems that Are Found Within the Cytoplasmic Space but Have Unique Environments and Are Therefore Complex Physical Systems . . . . .	28
3.2.4 The Nuclear Space Is an Intracellular Space that Is Separated from the Cytoplasmic Space Because of the Systems Interactions . . . . .	31
3.3 Control Mechanisms Are Essential Process Elements of the Biological State Space . . . . .	33
3.4 Biological Energy Transduction Is an Essential Process that Provides Energy to Ensure the High Degree of Organization Necessary for Life . . . . .	34
3.5 The Cell Is a Building Block of Chemical and Biological Organization and Also a Key to the Study of Biological Complexity . . . . .	44
3.6 A Brief History of Life . . . . .	45
3.7 Evolution Can Be Modeled as a Dynamic Process with Many Bifurcations in the State Space of Life . . . . .	46
3.7.1 The Scarcity of Energy and Chemical Resources Is a Fundamental Challenge Encountered in Biological Evolution . . . . .	47
3.7.2 The Biochemical Solution to the Energy Limitations Created a New Waste Problem: Global Oxygenation . . . . .	48
3.7.3 The Response to the New Biochemical Environment Resulted in a Biological Bifurcation: The Appearance of the Eukaryotic Cell . . . . .	49
3.7.4 Compartmentalization Is an Important Reordering of Physiochemical Relationships that Changes the Physical Environment from Solution Dominated to Surface Dominated . . . . .	52
Further Reading . . . . .	54
Problem Sets . . . . .	55

<b>4</b>	<b>Physical Thoughts, Biological Systems – The Application of Modeling Principles to Understanding Biological Systems . . .</b>	<b>57</b>
4.1	The Interaction Between Formal Models and Natural Systems Is the Essence of Physical and Biophysical Science . . .	57
4.2	Observables Are the Link Between Observer and Reality . . .	58
4.3	Systems Science Guides the Linkage of Natural and Formal Models . . . . .	60
4.4	Abstraction and Approximation May Be Useful but Are Not Always Correct . . . . .	61
4.5	The Choices Made in Observables and Measurement Influence What Can Be Known About a System . . . . .	62
4.6	The Simplifying Concept of Abstraction Is Central to Both Scientific Understanding and Misconception . . . . .	64
4.7	Equations of State Capture the System Behavior or “Systemness” . . . . .	65
4.8	Equivalent Descriptions Contain the Same Information . . . . .	67
4.9	Symmetry and Symmetry Operations Allow Molecules to Be Placed in Groups . . . . .	69
4.10	The Goodness of the Model Depends on Where You Look with Bifurcation Leading to New Discovery . . . . .	71
4.11	Bifurcations in State Space Characterize Complex Systems . . . . .	72
4.12	Catastrophes and Chaos Are Examples of Formal Mathematical Systems That May Capture Important Behaviors of Natural Systems . . . . .	74
	Further Reading . . . . .	78
	Problem Sets . . . . .	80
<b>5</b>	<b>Probability and Statistics . . . . .</b>	<b>81</b>
5.1	An Overview of Probability and Statistics . . . . .	82
5.2	Discrete Probability Counts the Number of Ways Things Can Happen . . . . .	82
5.3	Specific Techniques Are Needed for Discrete Counting . . . . .	84
5.3.1	Multiplication Counts Possible Outcomes of Successive Events . . . . .	85
5.3.2	Permutations Are Counts of Lineups . . . . .	86
5.3.3	Combinations Are Counts of Committees . . . . .	86
5.3.4	Counting Indistinguishable Versus Distinguishable Entities Require Different Techniques . . . . .	87
5.4	Counting Conditional and Independent Events That Occur in Multistage Experiments Require Special Considerations . . . . .	87
5.5	Discrete Distributions Come from Counting Up the Outcomes of Repeated Experiments . . . . .	89
5.5.1	The Multinomial Coefficient . . . . .	89

- 5.5.2 The Binomial Distribution Captures the Probability of Success in the Case of Two Possible Outcomes . . . . . 91
- 5.5.3 The Poisson Distribution Requires Fewer Parameters for Calculation Than the Binomial Distribution . . . . . 91
- 5.6 Continuous Probability Is Represented as a Density of Likelihood Rather Than by Counting Events . . . . . 94
  - 5.6.1 Some Mathematical Properties of Probability Density Functions . . . . . 95
  - 5.6.2 The Exponential Density Function Is Useful for Lifetime Analysis . . . . . 98
  - 5.6.3 The Gaussian Distribution Is a Bell-Shaped Curve . . . . . 99
  - 5.6.4 Stirling’s Formula Can Be Used to Approximate the Factorials of Large Numbers . . . . . 101
  - 5.6.5 The Boltzmann Distribution Finds the Most Probable Distribution of Particles in Thermal Equilibrium . . . . . 102
- Further Reading . . . . . 105
- Problem Sets . . . . . 105

**Part II Foundations**

- 6 Energy and Force – The Prime Observables . . . . . 109**
  - 6.1 Experimental Models Are a Careful Abstraction of Either Descriptive or Explanatory Models . . . . . 109
  - 6.2 Potential Energy Surfaces Are Tools that Help Find Structure Through the Measurement of Energy . . . . . 110
  - 6.3 Conservative Systems Find Maximal Choice by Balancing Kinetic and Potential Energies Over Time . . . . . 113
  - 6.4 Forces in Biological Systems Do the Work That Influences Structure and Function . . . . . 115
    - 6.4.1 The Concept of Forces and Fields Is Derived from Newton’s Laws of Motion . . . . . 115
    - 6.4.2 Force and Mass Are Related Through Acceleration . . . . . 116
    - 6.4.3 The Principle of Conservation Leads to the Concept of a Force Field . . . . . 117
    - 6.4.4 Energy Is a Measure of the Capacity to Do Work . . . . . 118
  - Further Reading . . . . . 122
  - Problem Sets . . . . . 123
- 7 Biophysical Forces in Molecular Systems . . . . . 125**
  - 7.1 Form and Function in Biomolecular Systems Are Governed by a Limited Number of Forces . . . . . 126

7.2	Mechanical Motions Can Describe the Behavior of Gases and the Migration of Cells . . . . .	127
7.2.1	Motion in One and Two Dimensions . . . . .	127
7.2.2	Motion Under Constant Acceleration . . . . .	128
7.2.3	Projectile Motion in a Constant Potential Energy Field . . . . .	129
7.3	The Kinetic Theory of Gases Explains the Properties of Gases Based on Mechanical Interactions of Molecules . . . . .	129
7.3.1	Collisions Are Impacts in Which Objects Exchange Momentum . . . . .	130
7.3.2	Reviewing the Phenomenology of Dilute Gases Sheds Light on Molecular Mechanics . . . . .	131
7.3.3	The Pressure of a Gas Is Derived from the Transfer of an Extremely Small Amount of Momentum from an Atom to the Wall of a Vessel . . . . .	134
7.3.4	The Law of Equipartition of Energy Is a Classical Treatment of Energy Distribution . . . . .	138
7.3.5	The Real Behavior of Gases Can Be Better Modeled by Accounting for Attractive and Repulsive Forces Between Molecules . . . . .	141
7.4	The Electric Force Is the Essential Interaction that Leads to the Chemical Nature of the Universe . . . . .	144
7.4.1	Electrostatics Define Electrical Forces Between Stationary Charges . . . . .	144
7.4.2	The Electric Field Is Associated with a Charged Object . . . . .	147
7.4.3	Electric Dipoles Are Opposite Charges that Are Separated in Space . . . . .	151
7.4.4	The Electric Flux Is a Property of the Electric Field . . . . .	152
7.4.5	Gauss' Law Relates the Electric Field to an Electric Charge . . . . .	153
7.4.6	A Point Charge Will Accelerate in an Electric Field . . . . .	154
7.4.7	The Electric Potential Is the Capacity to Do Electrical Work . . . . .	155
7.4.8	Equipotential Surfaces Are Comprised of Lines of Constant Potential . . . . .	158
7.4.9	Calculating Potential Fields . . . . .	158
7.4.10	Capacitors Store Electrostatic Field Energy . . . . .	160
7.5	Wave Motion Is Important in Electromagnetic and Mechanical Interactions in Biological Systems . . . . .	162
7.5.1	Pulses Are the Starting Point for Understanding Wave Motion . . . . .	163
7.5.2	The Wavefunction Is a Mathematical Expression for Wave Motion in Terms of Space and Time . . . . .	164

7.5.3	Superposition and Interference Are Fundamental Properties of Wave Interaction . . . . .	165
7.5.4	The Velocity of a Wave Pulse Is a Function of the Transmission Medium . . . . .	166
7.5.5	Reflection and Transmission of a Wave Depends on the Interface Between Two Phases of Different Speeds of Propagation . . . . .	167
7.6	Harmonic Waves Are the Result of a Sinusoidal Oscillation . . . . .	167
7.6.1	Wavelength, Frequency, and Velocity . . . . .	168
7.6.2	Polarization . . . . .	169
7.6.3	Superposition and Interference – Waves of the Same Frequency . . . . .	171
7.7	Energy and Intensity of Waves . . . . .	174
7.7.1	Sound and Human Ear . . . . .	175
7.8	Standing Waves . . . . .	176
7.9	Superposition and Interference – Waves of Different Frequencies . . . . .	179
7.10	Complex Waveforms . . . . .	181
7.11	Wave Packets . . . . .	182
7.12	Dispersion . . . . .	184
7.13	The Wave Equation . . . . .	185
7.14	Waves in Two and Three Dimensions . . . . .	186
	Further Reading . . . . .	189
	Problem Sets . . . . .	189
<b>8</b>	<b>Physical Principles: Quantum Mechanics . . . . .</b>	<b>191</b>
8.1	The Story of the Discovery of Quantum Mechanics Is an Instructive History of How Scientific Ideas Are Modified . . . . .	192
8.2	From the Standpoint of the Philosophy of Epistemological Science, the Quantum Revolution Ended an Age of Certainty . . . . .	192
8.3	The Ultraviolet Catastrophe Is a Term That Refers to a Historical Failure of Classical Theory . . . . .	194
8.3.1	Thermal Radiation . . . . .	195
8.3.2	Blackbody Radiation . . . . .	195
8.3.3	Classical Theory of Cavity Radiation . . . . .	197
8.3.4	Planck’s Theory of Cavity Radiation . . . . .	199
8.3.5	Quantum Model Making – Epistemological Reflections on the Model . . . . .	200
8.4	The Concept of Heat Capacity Was Modified by Quantum Mechanical Considerations . . . . .	202
8.5	The Photoelectric Effect and the Photon-Particle Properties of Radiation Could Be Understood Using Planck’s Quanta . . . . .	203
8.6	Electromagnetic Radiation Has a Dual Nature . . . . .	205

8.7	de Broglie's Postulate Defines the Wavelike Properties of Particles . . . . .	206
8.8	The Electron Microscope Employs Particles as Waves to Form Images . . . . .	207
8.9	The Uncertainty Principle Is an Essential Conclusion of the Quantum Viewpoint . . . . .	209
8.10	An Historical Approach to Understanding Atomic Structure and the Atom . . . . .	210
	8.10.1 Atomic Spectra . . . . .	213
	8.10.2 Bohr's Model . . . . .	215
8.11	Quantum Mechanics Requires the Classical Trajectory Across a Potential Energy Surface to be Replaced by the Wavefunction . . . . .	218
	8.11.1 The Schrödinger Equation . . . . .	220
8.12	Solutions to the Time-Independent Schrödinger Theory . . . . .	224
	8.12.1 Linear Motion – Zero Potential Field . . . . .	224
	8.12.2 The Step Potential . . . . .	226
	8.12.3 The Barrier Potential . . . . .	227
	8.12.4 The Square Well Potential . . . . .	229
	8.12.5 The Harmonic Oscillator . . . . .	232
	8.12.6 Rotational and Angular Motion . . . . .	233
8.13	Building the Atomic Model – One-Electron Atoms . . . . .	235
8.14	Building the Atomic Model – Multi-electron Atoms . . . . .	238
	8.14.1 Fermions and Bosons . . . . .	238
	8.14.2 Self-Consistent Field Theory Finds Approximate Wavefunctions for Multi-electron Atoms . . . . .	239
	Further Reading . . . . .	240
	Problem Sets . . . . .	241
<b>9</b>	<b>Chemical Principles . . . . .</b>	<b>243</b>
9.1	Knowing the Distribution of Electrons in Molecules Is Essential for Understanding Chemical Structure and Behavior . . . . .	243
9.2	The Nature of Chemical Interactions . . . . .	244
9.3	Electrostatic Forces Describe the Interactions from Salt Crystals to van der Waals Attraction . . . . .	244
	9.3.1 Ion–Ion Interactions . . . . .	244
	9.3.2 Ion–Dipole Interactions . . . . .	245
	9.3.3 Ion-Induced Dipole Interactions . . . . .	246
	9.3.4 van der Waals Interactions . . . . .	246
9.4	Covalent Bonds Involve a True Sharing of Electrons Between Atoms . . . . .	249
	9.4.1 Lewis Structures Are a Formal Shorthand that Describe Covalent Bonds . . . . .	250

9.4.2	VSEPR Theory Predicts Molecular Structure . . . . .	250
9.4.3	Molecular Orbital Theory Is an Approximation to a Full Quantum Mechanical Treatment of Covalent Interactions . . . . .	251
9.5	Hydrogen Bonds Are a Unique Hybrid of Interactions and Play a Fundamental Role in the Behavior of Biological Systems . . . . .	262
9.6	Biological Systems Are Made from a Limited Number of Elements . . . . .	264
	Further Reading . . . . .	266
	Problem Sets . . . . .	267
<b>10</b>	<b>Measuring the Energy of a System: Energetics and the First Law of Thermodynamics . . . . .</b>	<b>269</b>
10.1	Historically Heat Was Thought to Be a Fluid or “the Caloric”	269
10.2	The Thermodynamic Modeling Space Is a Systemic Approach to Describing the World . . . . .	271
10.2.1	Systems, Surroundings, and Boundaries . . . . .	272
10.2.2	Properties of a Thermodynamic System . . . . .	272
10.2.3	Extensive and Intensive Variables . . . . .	273
10.2.4	The State of a System . . . . .	274
10.2.5	How Many Properties Are Required to Define the State of a System? . . . . .	275
10.2.6	Changes in State . . . . .	276
10.3	The First Law States that “The Energy of the Universe Is Conserved” . . . . .	276
10.3.1	Specialized Boundaries Are Important Tools for Defining Thermodynamic Systems . . . . .	278
10.3.2	Evaluating the Energy of a System Requires Measuring Work and Heat Transfer . . . . .	280
10.4	The Heat Capacity Is a Property that Can Reflect the Internal Energy of a System . . . . .	283
10.5	Enthalpy Is Defined When a System Is Held at Constant Pressure . . . . .	285
	Thought Questions . . . . .	289
	Further Reading . . . . .	289
	Problem Sets . . . . .	290
<b>11</b>	<b>Entropy and the Second Law of Thermodynamics . . . . .</b>	<b>293</b>
11.1	The Arrow of Time and Impossible Existence of Perpetual Motion Machines Are Both Manifestations of the Second Law of Thermodynamics . . . . .	294
11.1.1	The Movement of a System Toward Equilibrium Is the Natural Direction . . . . .	295
11.2	The Design of a Perfect Heat Engine Is an Important Thought Experiment . . . . .	295



11.2.1	Reversible Paths Have Unique Properties Compared to Irreversible Paths . . . . .	296
11.2.2	A Carnot Cycle Is a Reversible Path Heat Engine . .	301
11.2.3	Entropy Is the Result of the Consideration of a Carnot Cycle . . . . .	305
11.3	A Mechanical/Kinetic Approach to Entropy . . . . .	307
11.3.1	The Statistical Basis of a Mechanistic Theory Is Reflected by System Properties . . . . .	308
11.3.2	Fluctuations Can Be Measured Statistically . . . . .	309
11.4	Statistical Thermodynamics Yields the Same Conclusions as Classical Treatment of Thermodynamics . . .	310
11.4.1	The Ensemble Method Is a Thought Experiment Involving Many Probability Experiments . . . . .	310
11.4.2	The Canonical Ensemble Is an Example of the Ensemble Method . . . . .	312
11.4.3	The Distribution of Energy Among Energy States Is an Important Description of a System . . .	316
11.4.4	Heat Flow Can Be Described Statistically . . . . .	317
11.4.5	Internal Molecular Motions, Energy and Statistical Mechanics Are Related by a Partition Function . . . . .	320
11.5	Entropy Can Be Described and Understood on a Statistical Basis . . . . .	321
11.5.1	Different Statistical Distributions Are Needed for Different Conditions . . . . .	321
11.5.2	Phenomenological Entropy Can Be Linked to Statistical Entropy . . . . .	323
11.6	The Third Law of Thermodynamics Defines an Absolute Measure of Entropy . . . . .	324
	Further Reading . . . . .	324
	Problem Sets . . . . .	325
<b>12</b>	<b>Which Way Is That System Going? The Gibbs Free Energy . . .</b>	<b>327</b>
12.1	The Gibbs Free Energy Is a State Function that Indicates the Direction and Position of a System's Equilibrium . . . . .	327
12.2	The Gibbs Free Energy Has Specific Properties . . . . .	329
12.3	The Free Energy Per Mole, $\mu$ , Is an Important Thermodynamic Quantity . . . . .	333
12.4	The Concept of Activity Relates an Ideal System to a Real System . . . . .	333
12.5	The Application of Free Energy Considerations to Multiple-Component Systems . . . . .	334

12.6	The Chemical Potential Is an Important Driving Force in Biochemical Systems . . . . .	335
12.6.1	Characteristics of $\mu$ . . . . .	336
12.7	Entropy and Enthalpy Contribute to Calculations of the Free Energy of Mixing . . . . .	337
12.8	Finding the Chemical Equilibrium of a System Is Possible by Making Free Energy Calculations . . . . .	340
12.8.1	Derivation of the Activity . . . . .	340
12.8.2	Activity of the Standard State . . . . .	341
12.8.3	The Equilibrium Expression . . . . .	342
12.9	The Thermodynamics of Galvanic Cells Is Directly Related to the Gibbs Free Energy . . . . .	345
12.10	Free Energy Changes Relate the Equilibrium Position of Biochemical Reactions . . . . .	348
	Further Reading . . . . .	348
	Problem Sets . . . . .	349
<b>13</b>	<b>The Thermodynamics of Phase Equilibria . . . . .</b>	<b>351</b>
13.1	The Concept of Phase Equilibrium Is Important in Biochemical Systems . . . . .	351
13.2	Thermodynamics of Transfer Between Phases . . . . .	353
13.3	The Phase Rule Relates the Number of Variables of State to the Number of Components and Phases at Equilibrium . . . . .	353
13.4	The Equilibrium Between Different Phases Is Given by the Clapeyron Equation . . . . .	355
13.4.1	Colligative Properties Vary with Solute Concentration . . . . .	358
13.4.2	The Activity Coefficient Can Be Measured by Changes in the Colligative Properties . . . . .	361
13.5	Surface Phenomena Are an Important Example of Phase Interaction . . . . .	362
13.6	Binding Equilibria Relate Small Molecule Binding to Larger Arrays . . . . .	364
13.6.1	Binding at a Single Site . . . . .	366
13.6.2	Multiple Binding Sites . . . . .	367
13.6.3	Binding When Sites Are Equivalent and Independent . . . . .	368
13.6.4	Equilibrium Dialysis and Scatchard Plots . . . . .	370
13.6.5	Binding in the Case of Non-equivalent Sites . . . . .	373
13.6.6	Cooperativity Is a Measure of Non-independent Binding . . . . .	374
13.6.7	The Acid–Base Behavior of Biomolecules Reflects Proton Binding . . . . .	379
	Further Reading . . . . .	383
	Problem Sets . . . . .	383

**Part III Building a Model of Biomolecular Structure**

<b>14</b>	<b>Water: A Unique Solvent and Vital Component of Life . . . . .</b>	<b>389</b>
14.1	An Introduction to the Most Familiar of All Liquids . . . . .	389
14.2	The Physical Properties of Water Are Consistent with a High Degree of Intermolecular Interaction . . . . .	391
14.3	Considering the Properties of Water as a Liquid . . . . .	392
14.4	The Structure of Monomolecular Water Can Be Described Using a Variety of Models . . . . .	394
14.5	The Capacity of Water to Form Hydrogen Bonds Underlies Its Unusual Properties . . . . .	398
14.6	The Structure and Dynamics of Liquid Water Results in “Ordered Diversity” That Is Probably Distinct from Ice . .	402
14.7	Hydrophobic Forces Reference Interactions Between Water and Other Molecules . . . . .	405
	Further Reading . . . . .	407
	Problem Sets . . . . .	408
<b>15</b>	<b>Ion–Solvent Interactions . . . . .</b>	<b>409</b>
15.1	The Nature of Ion–Solvent Interactions Can Be Discovered Through the Progression of Inquiry . . . . .	409
15.2	The Born Model Is a Thermodynamic Cycle That Treats the Interaction Energy Between a Simplified Ion and a Structureless Solvent . . . . .	410
15.2.1	Building the Model . . . . .	411
15.2.2	Choosing an Experimental Observable to Test the Model . . . . .	414
15.3	Adding Water Structure to the Solvent Continuum . . . . .	418
15.3.1	The Energy of Ion–Dipole Interactions Depends on Geometry . . . . .	419
15.3.2	Dipoles in an Electric Field: A Molecular Picture of the Dielectric Constants . . . . .	420
15.3.3	What Happens When the Dielectric Is Liquid Water? . . . . .	426
15.4	Extending the Ion–Solvent Model Beyond the Born Model . .	429
15.4.1	Recalculating the New Model . . . . .	430
15.5	Solutions of Inorganic Ions . . . . .	435
15.6	Ion–Solvent Interactions in Biological Systems . . . . .	437
	Further Reading . . . . .	438
	Problem Sets . . . . .	438
<b>16</b>	<b>Ion–Ion Interactions . . . . .</b>	<b>441</b>
16.1	Ion–Ion Interactions Can Be Modeled and These Models Can Be Experimentally Validated and Refined . . . .	441
16.2	The Debye–Hückel Model Is a Continuum Model That Relates a Distribution of Nearby Ions to a Central Reference Ion . . . . .	444

16.3	The Predictions Generated by the Debye–Hückel Model Can Be Experimentally Evaluated . . . . .	453
16.4	More Rigorous Treatment of Assumptions Leads to an Improved Performance of the Debye–Hückel Model . . . . .	455
16.5	Consideration of Other Interactions Is Necessary to Account for the Limits of the Debye–Hückel Model . . . . .	457
16.5.1	Bjerrum Suggested That Ion Pairing Could Affect the Calculation of Ion–Ion Interactions . . . . .	457
	Further Reading . . . . .	458
	Problem Sets . . . . .	459
<b>17</b>	<b>Lipids in Aqueous Solution . . . . .</b>	<b>461</b>
17.1	Biological Membranes Form at the Interface Between Aqueous and Lipid Phases . . . . .	461
17.2	Aqueous Solutions Can Be Formed with Small Nonpolar Molecules . . . . .	462
17.3	Aqueous Solutions of Organic Ions Are an Amalgam of Ion-Solvent and Nonpolar Solute Interaction . . . . .	465
17.3.1	Solutions of Small Organic Ions . . . . .	465
17.3.2	Solutions of Large Organic Ions . . . . .	466
17.4	Lipids Can Be Placed into Several Major Classes . . . . .	468
17.5	The Organization of Lipids into Membranes Occurs When Aqueous and Lipid Phases Come in Contact . . . . .	474
17.6	The Physical Properties of Lipid Membranes . . . . .	478
17.6.1	Phase Transitions in Lipid Membranes . . . . .	478
17.6.2	There Are Specific and Limited Motions and Mobilities Found in Membranes . . . . .	479
17.7	Biological Membranes: A More Complete Picture . . . . .	482
	Further Reading . . . . .	483
<b>18</b>	<b>Macromolecules in Solution . . . . .</b>	<b>485</b>
18.1	The Physical Interactions of Polymers in Solution Are Not Unique but Modeling the Interactions Will Require Different Considerations Than Those of Smaller Molecules . . . . .	486
18.2	Thermodynamics of Solutions of Polymers . . . . .	487
18.2.1	The Entropy of Mixing for a Polymer Solution Requires a Statistical Approach . . . . .	489
18.2.2	The Enthalpy of Mixing in a Polymer Solution Is Dominated by van der Waals Interactions . . . . .	493
18.2.3	The Free Energy of Mixing Relates Enthalpy and Entropy in the Standard Manner . . . . .	498
18.2.4	Calculation of the Partial Specific Volume and Chemical Potential . . . . .	499

18.2.5	Vapor Pressure Measurements Can Experimentally Be Used to Indicate Interaction Energies . . . . .	504
18.3	The Conformation of Simple Polymers Can Be Modeled by a Random Walk and a Markov Process . . . . .	505
18.4	The Major Classes of Biochemical Species Form Macromolecular Structures . . . . .	506
18.4.1	Nucleic Acids Are the Basis for Genetic Information Storage and Processing . . . . .	506
18.4.2	Carbohydrate Polymers Are Dominated by Hydrophilic Interactions with Water . . . . .	513
18.4.3	The Polymers of Amino Acids, Proteins Are by Far the Most Diverse and Complex of All Biological Polymer Families . . . . .	515
18.5	Nonpolar Polypeptides in Solution . . . . .	523
18.6	Polar Polypeptides in Solution . . . . .	527
18.7	Transitions of State . . . . .	531
18.8	The Protein Folding Problem . . . . .	538
18.9	Pathological Protein Folding . . . . .	542
18.9.1	Alzheimer's Disease . . . . .	544
18.9.2	Familial Amyloidotic Polyneuropathy . . . . .	545
18.9.3	Spongiform Encephalopathies . . . . .	546
	Further Reading . . . . .	549
	Problem Sets . . . . .	551
<b>19</b>	<b>Molecular Modeling – Mapping Biochemical State Space . . . . .</b>	<b>553</b>
19.1	The Prediction of Macromolecular Structure and Function Is a Goal of Molecular Modeling . . . . .	553
19.2	Molecular Modeling Is Built on Familiar Principles . . . . .	554
19.3	Empirical Methods Use Carefully Constructed Physical Models . . . . .	555
19.3.1	Sticks and Stones . . . . .	555
19.3.2	The Ramachandran Plot Is the “Art of the Possible” . . . . .	557
19.3.3	Secondary Structure Prediction in Proteins Is an Important Challenge in Molecular Modeling . . . . .	563
19.4	Computational Methods Are the Ultimate Gedanken Experiments . . . . .	569
19.5	Molecular Mechanics Is a Newtonian or Classical Mechanical Modeling Approach . . . . .	571
19.5.1	Bond Stretching . . . . .	574
19.5.2	Bond Bending . . . . .	576
19.5.3	Torsional or Dihedral Potential Functions . . . . .	576
19.5.4	van der Waals Interactions . . . . .	577
19.5.5	Electrostatic Interactions . . . . .	578

19.6	Quantum Mechanical Methods Are Computational Difficult but Theoretically “Pure” . . . . .	579
	Further Reading . . . . .	581
	Problem Sets . . . . .	582
<b>20</b>	<b>The Electrified Interphase . . . . .</b>	<b>583</b>
20.1	The Interphase Is Formed When Phases Meet . . . . .	583
20.2	A Detailed Structural Description of the Interphase Is a Task for Physical Study . . . . .	587
20.3	The Simplest Picture of the Interphase Is the Helmholtz–Perrin Model . . . . .	589
20.4	The Balance Between Thermal and Electrical Forces Is Seen as Competition Between Diffuse-Layer Versus Double-Layer Interphase Structures . . . . .	590
20.5	The Stern Model Is a Combination of the Capacitor and Diffuse Layer Models . . . . .	591
20.6	A More Complete Picture of the Double-Layer Forms with Added Detail . . . . .	593
20.7	Colloidal Systems and the Electrified Interface Give Rise to the Lyophilic Series . . . . .	595
20.8	Salting Out Can Be Understood in Terms of Electrified Interphase Behavior . . . . .	599
	Further Reading . . . . .	600
	Problem Sets . . . . .	600
 <b>Part IV Function and Action Biological State Space</b>		
<b>21</b>	<b>Transport – A Non-equilibrium Process . . . . .</b>	<b>605</b>
21.1	Transport Is an Irreversible Process and Does Not Occur at Equilibrium . . . . .	605
21.2	The Principles of Non-equilibrium Thermodynamics Can Be Related to the More Familiar Equilibrium Treatment with the Idea of Local Equilibrium . . . . .	606
	Further Reading . . . . .	610
<b>22</b>	<b>Flow in a Chemical Potential Field: Diffusion . . . . .</b>	<b>611</b>
22.1	Transport in Chemical, Electrical, Pressure, and Thermal Gradients Are All Treated with the Same Mathematics . . . . .	611
22.2	Diffusion or the Flow of Particles Down a Concentration Gradient Can Be Described Phenomenologically . . . . .	612
22.3	The Random Walk Forms the Basis for a Molecular Picture of Flux . . . . .	616
	Further Reading . . . . .	622
	Problem Sets . . . . .	622

<b>23</b>	<b>Flow in an Electric Field: Conduction</b>	625
23.1	Transport of Charge Occurs in an Electric Field	625
23.1.1	Ionic Species Can Be Classified as True or Potential Electrolytes	626
23.2	Describing a System of Ionic Conduction Includes Electronic, Electrode, and Ionic Elements	627
23.3	The Flow of Ions Down a Electrical Gradient Can Be Described Phenomenologically	631
23.4	A Molecular View of Ionic Conduction	637
23.5	Interionic Forces Affect Conductivity	640
23.6	Proton Conduction Is a Special Case that Has a Mixed Mechanism	643
	Further Reading	646
	Problem Sets	647
<b>24</b>	<b>Forces Across Membranes</b>	649
24.1	Energetics and Force in Membranes	649
24.2	The Donnan Equilibrium Is Determined by a Balance Between Chemical and Electrical Potential in a Two-Phase System	650
24.3	Electric Fields Across Membranes Are of Substantial Magnitude	653
24.3.1	Diffusion and Concentration Potentials Are Components of the Transmembrane Potential	653
24.3.2	The Goldman Constant Field Equation Is an Expression Useful for Quantitative Description of the Biological Electrochemical Potential	656
24.4	Electrostatic Profiles of the Membrane Are Potential Energy Surfaces Describing Forces in the Vicinity of Membranes	657
24.5	The Electrochemical Potential Is a Thermodynamic Treatment of the Gradients Across a Cellular Membrane	661
24.6	Transport Through the Lipid Bilayer of Different Molecules Requires Various Mechanisms	661
24.6.1	Modes of Transport Include Passive, Facilitated, and Active Processes	661
24.6.2	Water Transport Through a Lipid Phase Involves Passive and Pore Specific Mechanisms	663
	Further Reading	666
	Problem Sets	667
<b>25</b>	<b>Kinetics – Chemical Kinetics</b>	669
25.1	The Equilibrium State Is Found by Chemical Thermodynamics but Chemical Kinetics Tells the Story of Getting There	670

25.2	A Historical Perspective on the Development of Chemical Kinetics . . . . .	671
25.3	Kinetics Has a Specific and Systemic Language . . . . .	675
25.3.1	Mechanism and Order . . . . .	675
25.4	Order of a Reaction Relates the Concentration of Reactants to the Reaction Velocity . . . . .	676
25.5	Expressions of the Rate Laws Are Important	
	Properties of a Reaction . . . . .	677
25.5.1	Zero Order Reactions . . . . .	677
25.5.2	First-Order Reactions . . . . .	679
25.5.3	Second-Order Reactions . . . . .	680
25.5.4	Experimental Determination of a Rate Law Requires Measurement of Two Observables, Time and Concentration . . . . .	681
25.6	Elementary Reactions Are the Elements of the System That Defines a Chemical Mechanism . . . . .	681
25.7	Reaction Mechanisms Are a System of Interacting Elements (Molecules) in the Context of a Potential Energy Surface . . . . .	682
25.7.1	Collision Theory . . . . .	682
25.7.2	Surprises in the Collision Theory State Space Require Re-evaluation of the Abstraction . . . . .	686
25.7.3	Transition-State Theory Is a Quantum Mechanical Extension of the Classical Flavor of Collision Theory . . . . .	687
25.7.4	The Potential Energy Surface Unifies the Models . . . . .	691
25.8	Solution Kinetics Are More Complicated Than the Simple Kinetic Behavior of Gases . . . . .	699
25.9	Enzymes Are Macromolecular Catalysts with Enormous Efficiency . . . . .	699
25.9.1	Enzyme Kinetics . . . . .	702
25.9.2	Enzymes Can Be Characterized by Kinetic Properties . . . . .	704
25.9.3	Enzymes Are Complex Systems Subject to Biophysical Control . . . . .	707
	Further Reading . . . . .	710
	Problem Sets . . . . .	710
<b>26</b>	<b>Dynamic Bioelectrochemistry – Charge Transfer in Biological Systems . . . . .</b>	<b>713</b>
26.1	Electrokinetics and Electron Charge Transfer Depend on Electrical Current Flow in Biochemical Systems . . . . .	713
26.2	Electrokinetic Phenomena Occur When the Elements of the Biological Electrical Double Layer Experience Either Mechanical or Electrical Transport . . . . .	714



26.2.1	The Zeta Potential Is Measured at the Outer Helmholtz Plane of the Electrical Double Layer . . .	714
26.2.2	A Streaming Potential Results When Fluid Flows in a Cylinder . . . . .	715
26.2.3	Electro-osmosis Is the Transport of Solvent Coincident with Electrical Induced Flux of Electrolytes . . . . .	716
26.2.4	Electrophoresis Describes the Motion of Particles with an Electrical Double Layer in an Electrical Field . . . . .	717
26.2.5	A Sedimentation Potential Arises When with the Movement of a Particle Relative to a Stationary Solvent . . . . .	721
26.2.6	Electrokinetic Phenomena Can Have a Role in Biological Systems . . . . .	721
26.3	Electron Transfer Is an Essential Form of Biological Charge Transfer . . . . .	722
26.3.1	Dynamic Electrochemistry Is the Study of Electron Transfer and Their Kinetics . . . . .	722
26.3.2	Electron Transfer Is a Quantum Mechanical Phenomenon . . . . .	726
26.3.3	Electron Charge Transfer Can Occur in Proteins . . .	730
	Further Reading . . . . .	736
	Problem Sets . . . . .	737

**Part V Methods for the Measuring Structure and Function**

<b>27</b>	<b>Separation and Characterization of Biomolecules Based on Macroscopic Properties . . . . .</b>	<b>741</b>
27.1	Introduction: Mechanical Motion Interacts with Mass, Shape, Charge, and Phase to Allow Analysis of Macromolecular Structure . . . . .	742
27.2	Buoyant Forces Are the Result of Displacement of the Medium by an Object . . . . .	742
27.2.1	Motion Through a Medium Results in a Retarding Force Proportional to Speed . . . . .	743
27.2.2	Frictional Coefficients Can Be Used in the Analysis of Macromolecular Structure . . . . .	744
27.2.3	The Centrifuge Is a Device that Produces Motion by Generating Circular Motion with Constant Speed . . . . .	745
27.2.4	Sedimentation Occurs When Particles Experience Motion Caused by Gravitational or Equivalent Fields . . . . .	748

27.2.5	Drag Forces on Molecules in Motion Are Proportional to the Velocity of the Particle . . . . .	755
27.2.6	Fluids Will Move and Be Transported When Placed Under a Shearing Stress Force . . . . .	756
27.3	Systems Study in the Biological Science Requires Methods of Separation and Identification to Describe the “State of a Biological System” . . . . .	760
27.4	Electrophoresis Is a Practical Application of Molecular Motion in an Electrical Field Based on Charge and Modified by Conformation and Size . . . . .	760
27.5	Chromatographic Techniques Are Based on the Differential Partitioning of Molecules Between Two Phases in Relative Motion . . . . .	763
27.6	The Motion Induced by a Magnetic Interaction Is Essential for Determination of Molecular Mass in Modern Biological Investigations . . . . .	767
27.6.1	Magnetic Fields Are Vector Fields of Magnetic Force that Can Be Found Throughout Space . . . . .	768
27.6.2	Magnets Interact with One Another Through the Magnetic Field . . . . .	770
27.6.3	Current Loops in <b>B</b> Fields Experience Torque . . . . .	771
27.6.4	The Path of Moving Point Charges in a <b>B</b> Field Is Altered by the Interaction . . . . .	771
27.6.5	The Mass Spectrometer Is Widely Used Following Various Separation Techniques to Characterize Biological Samples . . . . .	772
	Further Reading . . . . .	775
	Problem Sets . . . . .	775
<b>28</b>	<b>Analysis of Molecular Structure with Electronic Spectroscopy . . . . .</b>	<b>779</b>
28.1	The Interaction of Light with Matter Allows Investigation of Biochemical Properties . . . . .	780
28.2	The Motion of a Dipole Radiator Generates Electromagnetic Radiation . . . . .	780
28.3	Optical Interactions Can Be Treated at Varying Levels of Abstraction . . . . .	780
28.4	Atomic and Molecular Energy levels Are a Quantum Phenomenon That Provide a Window on Molecular Structure . . . . .	782
28.4.1	There Are Points of Maximum Inflection Occurring at Particular Wavelengths . . . . .	783
28.4.2	Each Maximum Has a Different Intensity . . . . .	786
28.4.3	The Maxima Are Spread to Some Degree and Are Not Sharp . . . . .	787

28.5	Absorption Spectroscopy Has Important Applications to Biochemical Analysis . . . . .	789
28.5.1	Absorption Spectroscopy Is a Powerful Tool in the Examination of Dilute Solutions . . . . .	793
28.6	Fluorescence and Phosphorescence Occur When Trapped Photon Energy Is Re-radiated After a Finite Lifetime . . . . .	794
28.7	Electron Paramagnetic Resonance (EPR) and Nuclear Magnetic Resonance (NMR) Depend on Interactions Between Photons and Molecules in a Magnetic Field . . . . .	797
28.7.1	The Solenoid Shapes the Magnetic Field in a Manner Similar to the Parallel-Plate Capacitor . . . . .	798
28.7.2	Magnetism in Matter Has Distinct Properties . . . . .	798
28.7.3	Atoms Can Have Magnetic Moments . . . . .	800
28.7.4	EPR Spectroscopy Allows Exploration of Molecular Structure by Interaction with the Magnetic Moment of an Electron . . . . .	803
28.7.5	NMR Spectroscopy Employs the Magnetic Properties of Certain Nuclei for Determining Structure . . . . .	804
28.7.6	Further Structural Information Can Be Found by NMR Studies of Nuclei Other Than Protons . . . . .	809
	Further Reading . . . . .	812
	Problem Sets . . . . .	813
<b>29</b>	<b>Molecular Structure from Scattering Phenomena . . . . .</b>	<b>815</b>
29.1	The Interference Patterns Generated by the Interaction of Waves with Point Sources Is a Valuable Tool in the Analysis of Structure . . . . .	815
29.2	Diffraction Is the Result of the Repropagation of a Wave . . . . .	819
29.3	X-Ray Diffraction Is a Powerful Fool for Structure Determination . . . . .	822
29.4	Scattering of Light Rather Than Its Absorption Can Be Used to Probe Molecular Structure and Interaction . . . . .	831
29.4.1	Rayleigh Scattering . . . . .	831
29.4.2	Raman Scattering . . . . .	833
29.4.3	Circular Dichroism and Optical Rotation . . . . .	834
	Further Reading . . . . .	835
<b>30</b>	<b>Analysis of Structure – Microscopy . . . . .</b>	<b>837</b>
30.1	Seeing Is Believing . . . . .	837
30.2	The Light Microscope Allows Visualization of Structures on the Dimensional Scale of the Wavelength of a Photon . . . . .	839
30.3	Visualization Requires Solving the Problem of Contrast . . . . .	843

30.3.1	Dark Field Microscopy . . . . .	843
30.3.2	Phase Microscopy . . . . .	843
30.3.3	Polarization Microscopy . . . . .	845
30.3.4	Histochemistry . . . . .	847
30.3.5	Fluorescence Microscopy . . . . .	848
30.4	Scanning Probe Microscopy Creates an Image of a Structures by Interactions on a Molecular Scale . . . . .	849
30.4.1	Scanning Tunneling Microscopy . . . . .	850
30.4.2	Scanning Force Microscopy . . . . .	852
30.4.3	Near-Field Optical Microscopy, Outside the Classical Limits . . . . .	854
	Further Reading . . . . .	854
	Problem Sets . . . . .	855
<b>31</b>	<b>Epilogue . . . . .</b>	<b>857</b>
	Now Try . . . . .	857
<b>32</b>	<b>Physical Constants . . . . .</b>	<b>859</b>
	Conversions . . . . .	859
	<b>Appendix A: Mathematical Methods . . . . .</b>	<b>861</b>
A.1	Units and Measurement . . . . .	861
A.2	Exponents and Logarithms . . . . .	862
A.3	Trigonometric Functions . . . . .	865
A.4	Expansion Series . . . . .	869
A.5	Differential and Integral Calculus . . . . .	870
A.6	Partial Differentiation . . . . .	870
A.7	Vectors . . . . .	872
A.7.1	Addition and Subtraction . . . . .	872
A.7.2	Magnitude of a Vector . . . . .	873
A.7.3	Multiplication . . . . .	873
	<b>Appendix B: Quantum Electrodynamics . . . . .</b>	<b>875</b>
	<b>Appendix C: The Pre-Socratic Roots of Modern Science . . . . .</b>	<b>877</b>
	<b>Appendix D: The Poisson Function . . . . .</b>	<b>879</b>
	<b>Appendix E: Assumptions of a Theoretical Treatment of the Ideal Gas Law . . . . .</b>	<b>881</b>
	<b>Appendix F: The Determination of the Field from the Potential in Cartesian Coordinates . . . . .</b>	<b>883</b>
	<b>Appendix G: Geometrical Optics . . . . .</b>	<b>885</b>
G.1	Reflection and Refraction of Light . . . . .	885
G.2	Mirrors . . . . .	886
G.2.1	The Plane Mirror . . . . .	886
G.2.2	The Concave Mirror . . . . .	887

G.3	Image Formation by Refraction . . . . .	889
G.4	Prisms and Total Internal Reflection . . . . .	891
<b>Appendix H:</b>	<b>The Compton Effect . . . . .</b>	<b>893</b>
<b>Appendix I:</b>	<b>Hamilton’s Principle of Least Action/Fermat’s Principle of Least Time . . . . .</b>	<b>895</b>
<b>Appendix J:</b>	<b>Derivation of the Energy of Interaction Between Two Ions . . . . .</b>	<b>897</b>
<b>Appendix K:</b>	<b>Derivation of the Statement, <math>q_{\text{rev}} &gt; q_{\text{irrev}}</math> . . . . .</b>	<b>899</b>
<b>Appendix L:</b>	<b>Derivation of the Clausius–Clapeyron Equation . . . . .</b>	<b>901</b>
<b>Appendix M:</b>	<b>Derivation of the van’t Hoff Equation for Osmotic Pressure . . . . .</b>	<b>903</b>
<b>Appendix N:</b>	<b>Fictitious and Pseudoforces – The Centrifugal Force . . . . .</b>	<b>905</b>
<b>Appendix O:</b>	<b>Derivation of the Work to Charge and Discharge a Rigid Sphere . . . . .</b>	<b>907</b>
<b>Appendix P:</b>	<b>Review of Circuits and Electric Current . . . . .</b>	<b>909</b>
P.1	Current Density and Flux . . . . .	909
P.1.1	Ohm’s Law . . . . .	910
P.2	Circuits . . . . .	911
P.2.1	Useful Legal Relations . . . . .	911
P.2.2	Kirchoff’s Rules . . . . .	911
P.2.3	Capacitors in Series and Parallel . . . . .	912
P.2.4	Resistors in Series and Parallel . . . . .	913
P.2.5	RC Circuits and Relations . . . . .	913
P.3	Measuring Instruments . . . . .	916
P.3.1	Ammeters, Voltmeters, Ohmmeters . . . . .	917
<b>Appendix Q:</b>	<b>Fermi’s Golden Rule . . . . .</b>	<b>919</b>
<b>Appendix R:</b>	<b>The Transition from Reactant to Product: Adiabatic and Non-adiabatic Transitions . . . . .</b>	<b>921</b>
<b>Index . . . . .</b>		<b>923</b>



<http://www.springer.com/978-1-4419-6323-9>

The Physical Basis of Biochemistry  
The Foundations of Molecular Biophysics  
Bergethon, P.R.  
2010, XXX, 950 p. 200 illus., Hardcover  
ISBN: 978-1-4419-6323-9