## Preface

Chapt	er 1 Biological Macromolecules	1
1.1	General Principles	1
	1.1.1 Macromolecules	2
	1.1.2 Configuration and Conformation	5
1.2	Molecular Interactions in Macromolecular Structures	8
	1.2.1 Weak Interactions	8
1.3	The Environment in the Cell	10
	1.3.1 Water Structure	11
	1.3.2 The Interaction of Molecules with Water	15
	1.3.3 Nonaqueous Environment of Biological Molecules	16
1.4	Symmetry Relationships of Molecules	19
	1.4.1 Mirror Symmetry	21
	1.4.2 Rotational Symmetry	22
	1.4.3 Multiple Symmetry Relationships and Point Groups	25
	1.4.4 Screw Symmetry	26
1.5	The Structure of Proteins	27
	1.5.1 Amino Acids	27
	1.5.2 The Unique Protein Sequence	31
	Application 1.1: Musical Sequences	33
	1.5.3 Secondary Structures of Proteins	34
	Application 1.2: Engineering a New Fold	35
	1.5.4 Helical Symmetry	36
	1.5.5 Effect of the Peptide Bond on Protein Conformations	40
	1.5.6 The Structure of Globular Proteins	42
1.6	The Structure of Nucleic Acids	52
	1.6.1 Torsion Angles in the Polynucleotide Chain	54
	1.6.2 The Helical Structures of Polynucleic Acids	55
	1.6.3 Higher-Order Structures in Polynucleotides	61
	Application 1.3: Embracing RNA Differences	64
	Exercises	68
	References	70

v

xiii

(	Co	or	nt	e	nt	s

Chapt	ter 2	Thermodynamics and Biochemistry	72
2.1	Heat.V	Work, and Energy—First Law of Thermodynamics	73
2.2	Moleci	ular Interpretation of Thermodynamic Ouantities	76
2.3	Entrop	by, Free Energy, and Equilibrium—Second Law	
	of The	rmodynamics	80
2.4	The St	andard State	91
2.5	Experi	mental Thermochemistry	93
	2.5.1	The van't Hoff Relationship	93
	2.5.2	Calorimetry	94
	Applic	ation 2.1: Competition Is a Good Thing	102
	Exerci	ses	104
	Refere	ences	105
Chapt	ter 3 I	Molecular Thermodynamics	107
3.1	Compl	exities in Modeling Macromolecular Structure	107
	3.1.1	Simplifying Assumptions	108
3.2	Molect	ular Mechanics	109
	3.2.1	Basic Principles	109
	3.2.2	Molecular Potentials	111
	3.2.3	Bonding Potentials	112
	3.2.4	Nonbonding Potentials	115
	3.2.5	Electrostatic Interactions	115
	3.2.6	Dipole-Dipole Interactions	117
	3.2.7	van der Waals Interactions	118
21	3.2.8	Hydrogen Bonds	120
3.3	Stabiliz	zing Interactions in Macromolecules	124
	3.3.1	Protein Structure	125
	3.3.2	Dipole Interactions	129
	3.3.3	Side Chain Interactions	131
	3.3.4	Electrostatic Interactions	131
	3.3.5	Nucleic Acid Structure	133
	3.3.6	Base-Pairing	137
	3.3.7	Base-Stacking	139
35	3.3.8	Electrostatic Interactions	141 Idag
3.4	Simula	ting Macromolecular Structure	145
	3.4.1	Energy Minimization	146
	3.4.2	Molecular Dynamics	147
	3.4.3	Entropy	149
	3.4.4	Hydration and the Hydrophobic Effect	153
	3.4.5	Free Energy Methods	159
	Exercis	ses	161
	Refere	ences	163

Chap	ter 4	Statistical Thermodynamics	166
4.1	Gene	ral Principles	166
	4.1.1	Statistical Weights and the Partition Function	167
	4.1.2	Models for Structural Transitions in Biopolymers	169
4.2	Struct	tural Transitions in Polypeptides and Proteins	175
	4.2.1	Coil-Helix Transitions	175
	4.2.2	Statistical Methods for Predicting Protein	fet Struc
		Secondary Structures	181
4.3	Struct	tural Transitions in Polynucleic Acids and DNA	184
	4.3.1	Melting and Annealing of Polynucleotide Duplexes	184
	4.3.2	Helical Transitions in Double-Stranded DNA	189
	4.3.3	Supercoil-Dependent DNA Transitions	190
	4.3.4	Predicting Helical Structures in Genomic DNA	197
4.4	Nonre	egular Structures	198
	4.4.1	Random Walk	199
	4.4.2	Average Linear Dimension of a Biopolymer	201
	Appli	ication 4.1: LINUS: A Hierarchic Procedure to	
	Predie	ct the Fold of a Protein	202
	4.4.3	Simple Exact Models for Compact Structures	204
	Appli	cation 4.2: Folding Funnels: Focusing Down to the Essentials	208
	Exerc	vises	209
	Refer	ences	211
Chap	ter 5	Methods for the Separation and Characterization	
338		of Macromolecules	213
5.1	Gene	ral Principles	213
5.2	Diffus	sion	214
	5.2.1	Description of Diffusion	215
	5.2.2	The Diffusion Coefficient and the Frictional Coefficient	220
	5.2.3	Diffusion Within Cells	221
	Appli	cation 5.1: Measuring Diffusion of Small DNA Molecules in Cell	is 222
5.3	Sedim	nentation	223
	5.3.1	Moving Boundary Sedimentation	225
	5.3.2	Zonal Sedimentation	237
	5.3.3	Sedimentation Equilibrium	241
	5.3.4	Sedimentation Equilibrium in a Density Gradient	246
5.4	Electi	rophoresis and Isoelectric Focusing	248
	5.4.1	Electrophoresis: General Principles	249
	5.4.2	Electrophoresis of Nucleic Acids	253
	Appli	cation 5.2: Locating Bends in DNA by Gel Electrophoresis	257
	5.4.3	SDS-Gel Electrophoresis of Proteins	259
	5.4.4	Methods for Detecting and Analyzing Components on Gels	264
		Washington CD	

vii

	$\sim$	-	-	1.20	-	-	1	-
100.3		O	П	IT	е	n	E	S
	-	-		-	-		-	_

	<ul> <li>5.4.5 Capillary Electrophoresis</li> <li>5.4.6 Isoelectric Focusing</li> <li>Exercises</li> <li>References</li> </ul>	266 266 270 274
Chapt	er 6 X-Ray Diffraction	276
6.1	Structures at Atomic Resolution	277
6.2	Crystals	279
	6.2.1 What Is a Crystal?	279
	6.2.2 Growing Crystals	285
	6.2.3 Conditions for Macromolecular Crystallization	286
	Application 6.1: Crystals in Space!	289
6.3	Theory of X-Ray Diffraction	290
	6.3.1 Bragg's Law	292
	6.3.2 von Laue Conditions for Diffraction	294
	6.3.3 Reciprocal Space and Diffraction Patterns	299
6.4	Determining the Crystal Morphology	304
6.5	Solving Macromolecular Structures by X-Ray Diffraction	308
	6.5.1 The Structure Factor	309
	6.5.2 The Phase Problem	317
	Application 6.2: The Crystal Structure of an Old	
	and Distinguished Enzyme	327
	6.5.3 Resolution in X-Ray Diffraction	334
6.6	Fiber Diffraction	338
	6.6.1 The Fiber Unit Cell	338
	6.6.2 Fiber Diffraction of Continuous Helices	340
	6.6.3 Fiber Diffraction of Discontinuous Helices	343
	Exercises	347
	References	349
	3.2.2 The Diffusion Coolicient and the Prictional Coefficient	
Chapt	er 7 Scattering from Solutions of Macromolecules	351
7.1	Light Scattering	351
205	7.1.1 Fundamental Concepts	351
	7.1.2 Scattering from a Number of Small Particles:	
	Rayleigh Scattering	355
	7.1.3 Scattering from Particles That Are Not Small	000
	Compared to Wavelength of Radiation	358
7.2	Dynamic Light Scattering: Measurements of Diffusion	363
7.3	Small-Angle X-Ray Scattering	365
7.4	Small-Angle Neutron Scattering	370
025	Application 71: Using a Combination of Physical Methods	510
	to Determine the Conformation of the Nucleosome	377
7.5	Summary	376

Contents
Contents

	Exercises	376
	References	379
<b>C1</b>	Applications of the Chemical/Durile and provide and Relationship (C)	200
Chapt	ter 8 Quantum Mechanics and Spectroscopy	380
8.1	Light and Transitions	381
8.2	Postulate Approach to Quantum Mechanics	382
8.3	Transition Energies	386
	8.3.1 The Quantum Mechanics of Simple Systems	386
	8.3.2 Approximating Solutions to Quantum Chemistry Problems	392
	8.3.3 The Hydrogen Molecule as the Model for a Bond	400
8.4	Transition Intensities	408
8.5	Transition Dipole Directions	415
	Exercises	418
	References	419
Chapt	ter 9 Absorption Spectroscopy	421
9.1	Electronic Absorption	421
	9.1.1 Energy of Electronic Absorption Bands	422
	9.1.2 Transition Dipoles	433
	9.1.3 Proteins	435
	9.1.4 Nucleic Acids	443
	9.1.5 Applications of Electronic Absorption Spectroscopy	447
9.2	Vibrational Absorption	449
	9.2.1 Energy of Vibrational Absorption Bands	450
	9.2.2 Transition Dipoles	451
	9.2.3 Instrumentation for Vibrational Spectroscopy	453
	9.2.4 Applications to Biological Molecules	453
	Application 9.1: Analyzing IR Spectra of Proteins for Secondary Structure	456
9.3	Raman Scattering	457
	Application 9.2: Using Resonance Raman Spectroscopy	
	to Determine the Mode of Oxygen Binding to Oxygen-Transport Proteins	461
	Exercises	463
	References	464
Chapt	ter 10 Linear and Circular Dichroism	465
10.1	Linear Dichroism of Biological Polymers	466
10.1	Application 10.1 Measuring the Base Inclinations	400
	in dAdT Polynucleotides	471
10.2	Circular Dichroism of Biological Molecules	471
	10.2.1 Electronic CD of Nucleic Acids	476
	Application 10.2: The First Observation of Z-form	
	DNA Was by Use of CD	478

	10.2.2 Electronic CD of Proteins	481
	10.2.3 Singular Value Decomposition and Analyzing the	
	CD of Proteins for Secondary Structure	485
	10.2.4 Vibrational CD	496
	Exercises	498
	References	499
Chapt	er 11 Emission Spectroscopy	501
11.1	The Phenomenon	501
11.2	Emission Lifetime	502
11.3	Fluorescence Spectroscopy	504
11.4	Fluorescence Instrumentation	506
11.5	Analytical Applications	507
11.6	Solvent Effects	509
11.7	Fluorescence Decay	513
11.8	Fluorescence Resonance Energy Transfer	516
11.9	Linear Polarization of Fluorescence	517
	Application 11.1: Visualizing c-AMP with Fluorescence	517
11.10	Fluorescence Applied to Protein	524
	Application 11.2: Investigation of the Polymerization of G-Actin	528
11.11	Fluorescence Applied to Nucleic Acids	530
	Application 11.3: The Helical Geometry of Double-Stranded	
	DNA in Solution	532
	Exercises	533
	References	534
1CH	2.2.2 Fiber Enteraction of Coolinguous Fieldes saloring notification	
Chapt	er 12 Nuclear Magnetic Resonance Spectroscopy	535
12.1	The Phenomenon	535
12.2	The Measurable	537
12.3	Spin-Spin Interaction	540
12.4	Relaxation and the Nuclear Overhauser Effect	542
12.5	Measuring the Spectrum	544
12.6	One-Dimensional NMR of Macromolecules	549
	Application 12.1: Investigating Base Stacking with NMR	553
12.7	Two-Dimensional Fourier Transform NMR	555
12.8	Two-Dimensional FT NMR Applied to Macromolecules	560
	Exercises	575
	References	577
ETRA	in dAdT Polynacleotides	
Chapt	er 13 Macromolecules in Solution: Thermodynamics and Equilibria	579
13.1	Some Fundamentals of Solution Thermodynamics	580
	13.1.1 Partial Molar Quantities: The Chemical Potential	580

x

	13.1.2	The Chemical Potential and Concentration:		504
12.0	A 1'	Ideal and Nonideal Solutions	Application 10.2: 5	584
13.2	Applic	Mambrana Equilibria	lioria	500
	13.2.1	Memorane Equilibria		507
	13.2.2	Sedimentation Equilibrium		597
	13.2.3	Steady-State Electrophoresis		598
	Exercis	ses		600
	Refere	nces		603
Chap	ter 14 (	Chemical Equilibria Involving Macromolecules		605
14.1	Therm	odynamics of Chemical Reactions in Solution: A	Review	605
14.2	Interac	tions Between Macromolecules		610
14.2	Rindin	a of Small Ligands by Macromolecules		615
14.3	1/21	General Principles and Mathada		615
	14.5.1	Multiple Equilibrie		622
	14.5.2	Multiple Equilibria		022
	Applic	ation 14.1: Thermodynamic Analysis of the		(11
	Bindin	g of Oxygen by Hemoglobin		641
	14.3.3	Ion Binding to Macromolecules		644
14.4	Bindin	g to Nucleic Acids		648
	14.4.1	General Principles		648
	14.4.2	Special Aspects of Nonspecific Binding	Iniversity of the Sciel	648
	14.4.3	Electrostatic Effects on Binding to Nucleic Acid	15	651
	Exercis	ses		654
	Refere	nces		658
Chap	ter 15 N	Mass Spectrometry of Macromolecules		660
15.1	Genera	al Principles: The Problem		661
15.2	Resolv	ing Molecular Weights by Mass Spectrometry		664
15.3	Determ	nining Molecular Weights of Biomolecules		670
15.4	Identif	ication of Biomolecules by Molecular Weights		673
15.5	Sequer	ncing by Mass Spectrometry		676
15.6	Probin	g Three-Dimensional Structure by Mass Spectron	netry	684
	Applic	ation 15.1: Finding Disorder in Order	ical kinetics mother.	686
	Applic	ation 15.2: When a Crystal Structure Is Not Enou	ugh	687
	Exerci	ses	0	690
	Refere	nces		691
Chap	ter 16	Single-Molecule Methods		693
16.1	Why S	tudy Single Molecules?		693
	Applic	ation 16.1: RNA Folding and Unfolding Observe	d at	
	the Sin	gle-Molecule Level		694
16.2	Observ	vation of Single Macromolecules by Fluorescence		695

Atomic Force Microscopy 699 16.3 Application 16.2: Single-Molecule Studies of Active Transcription by RNA Polymerase 701 703 **Optical Tweezers** 16.4 707 Magnetic Beads 16.5 708 Exercises 709 References A-1 **Answers to Odd-Numbered Problems** hapter 14 Chemical Equilibria Involving Macromolecules I-1 Index

xii