

CONTENTS

Preface	xiii
Acknowledgments	xix
1 Inorganic Chemistry Essentials	1
1.1 Introduction, 1	
1.2 Essential Chemical Elements, 1	
1.3 Metals in Biological Systems: A Survey, 3	
1.4 Inorganic Chemistry Basics, 6	
1.5 Biological Metal Ion Complexation, 8	
1.5.1 Thermodynamics, 8	
1.5.2 Kinetics, 9	
1.6 Electronic and Geometric Structures of Metals in Biological Systems, 13	
1.7 Bioorganometallic Chemistry, 19	
1.8 Electron Transfer, 22	
1.9 Conclusions, 26	
References, 27	
2 Biochemistry Fundamentals	29
2.1 Introduction, 29	
2.2 Proteins, 30	
2.2.1 Amino Acid Building Blocks, 30	
2.2.2 Protein Structure, 33	

- 2.2.3 Protein Sequencing and Proteomics, 39
- 2.2.4 Protein Function, Enzymes, and Enzyme Kinetics, 43
- 2.3 Nucleic Acids, 47
 - 2.3.1 DNA and RNA Building Blocks, 47
 - 2.3.2 DNA and RNA Molecular Structures, 47
 - 2.3.3 Transmission of Genetic Information, 53
 - 2.3.4 Genetic Mutations and Site-Directed Mutagenesis, 56
 - 2.3.5 Genes and Cloning, 58
 - 2.3.6 Genomics and the Human Genome, 61
- 2.4 Zinc-Finger Proteins, 63
 - 2.4.1 Descriptive Examples, 67
- 2.5 Summary and Conclusions, 73
 - References, 74

3 Instrumental Methods

76

- 3.1 Introduction, 76
 - 3.1.1 Analytical Instrument-Based Methods, 76
 - 3.1.2 Spectroscopy, 77
- 3.2 X-Ray Absorption Spectroscopy (XAS) and Extended X-Ray Absorption Fine Structure (EXAFS), 78
 - 3.2.1 Theoretical Aspects and Hardware, 78
 - 3.2.2 Descriptive Examples, 81
- 3.3 X-Ray Crystallography, 83
 - 3.3.1 Introduction, 83
 - 3.3.2 Crystallization and Crystal Habits, 84
 - 3.3.3 Theory and Hardware, 88
 - 3.3.4 Descriptive Examples, 95
- 3.4 Nuclear Magnetic Resonance, 98
 - 3.4.1 Theoretical Aspects, 98
 - 3.4.2 Nuclear Screening and the Chemical Shift, 101
 - 3.4.3 Spin-Spin Coupling, 104
 - 3.4.4 Techniques of Spectral Integration and Spin-Spin Decoupling, 106
 - 3.4.5 Nuclear Magnetic Relaxation, 107
 - 3.4.6 The Nuclear Overhauser Effect (NOE), 108
 - 3.4.7 Obtaining the NMR Spectrum, 110
 - 3.4.8 Two-Dimensional (2D) NMR Spectroscopy, 111
 - 3.4.9 Two-Dimensional Correlation Spectroscopy (COSY) and Total Correlation Spectroscopy (TOCSY), 112
 - 3.4.10 Nuclear Overhauser Effect Spectroscopy (NOESY), 115
 - 3.4.11 Multidimensional NMR, 116
 - 3.4.12 Descriptive Examples, 117
- 3.5 Electron Paramagnetic Resonance, 122
 - 3.5.1 Theory and Determination of g-Values, 122

- 3.5.2 Hyperfine and Superhyperfine Interactions, 127
- 3.5.3 Electron Nuclear Double Resonance (ENDOR) and Electron Spin-Echo Envelope Modulation (ESEEM), 129
- 3.5.4 Descriptive Examples, 129
- 3.6 Mössbauer Spectroscopy, 132
 - 3.6.1 Theoretical Aspects, 132
 - 3.6.2 Quadrupole Splitting and the Isomer Shift, 134
 - 3.6.3 Magnetic Hyperfine Interactions, 136
 - 3.6.4 Descriptive Examples, 137
- 3.7 Other Instrumental Methods, 139
 - 3.7.1 Atomic Force Microscopy, 139
 - 3.7.2 Fast and Time-Resolved Methods, 143
 - 3.7.2.1 Stopped-Flow Kinetic Methods, 143
 - 3.7.2.2 Flash Photolysis, 144
 - 3.7.2.3 Time-Resolved Crystallography, 146
 - 3.7.3 Mass Spectrometry, 148
- 3.8 Summary and Conclusions, 153
- References, 154

4 Computer Hardware, Software, and Computational Chemistry Methods

157

- 4.1 Introduction to Computer-Based Methods, 157
- 4.2 Computer Hardware, 157
- 4.3 Molecular Modeling and Molecular Mechanics, 160
 - 4.3.1 Introduction to MM, 160
 - 4.3.2 Molecular Modeling, Molecular Mechanics, and Molecular Dynamics, 161
 - 4.3.3 Biomolecule Modeling, 166
 - 4.3.4 A Molecular Modeling Descriptive Example, 167
- 4.4 Quantum Mechanics-Based Computational Methods, 170
 - 4.4.1 Introduction, 170
 - 4.4.2 Ab Initio Methods, 170
 - 4.4.3 Density Function Theory, 171
 - 4.4.4 Semiempirical Methods, 173
- 4.5 Computer Software for Chemistry, 174
 - 4.5.1 Mathematical Software, 180
- 4.6 World Wide Web Online Resources, 181
 - 4.6.1 Nomenclature and Visualization Resources, 181
 - 4.6.2 Online Societies, Online Literature Searching, and Materials and Equipment Websites, 183
- 4.7 Summary and Conclusions, 185
- References, 185

5 Group I and II Metals in Biological Systems: Homeostasis and Group I Biomolecules	189
5.1 Introduction, 189	
5.2 Homeostasis of Metals (and Some Nonmetals), 192	
5.2.1 Phosphorus as Phosphate, 192	
5.2.2 Potassium, Sodium, and Chloride Ions, 193	
5.2.3 Calcium Homeostasis, 194	
5.3 Movement of Molecules and Ions Across Membranes, 195	
5.3.1 Passive Diffusion, 195	
5.3.2 Facilitated Diffusion, 197	
5.3.2.1 Gated Channels, 197	
5.3.3 Active Transport—Ion Pumps, 197	
5.4 Potassium-Dependent Molecules, 199	
5.4.1 Na ⁺ /K ⁺ ATPase: The Sodium Pump, 199	
5.4.2 Potassium (K ⁺) Ion Channels, 203	
5.4.2.1 Introduction, 203	
5.4.2.2 X-Ray Crystallographic Studies, 205	
5.5 Conclusions, 235	
References, 235	
 6 Group I and II Metals in Biological Systems: Group II	 238
6.1 Introduction, 238	
6.2 Magnesium and Catalytic RNA, 238	
6.2.1 Introduction, 238	
6.2.2 Analyzing the Role of the Metal Ion, 241	
6.2.3 The Group I Intron Ribozyme, 244	
6.2.4 The Hammerhead Ribozyme, 261	
6.3 Calcium-Dependent Molecules, 301	
6.3.1 Introduction, 301	
6.3.2 Calmodulin, 302	
6.3.2.1 Introduction, 302	
6.3.2.2 Calmodulin Structure by X-Ray and NMR, 303	
6.3.2.3 Calmodulin Interactions with Drug Molecules, 308	
6.3.2.4 Calmodulin–Peptide Binding, 313	
6.3.2.5 Conclusions, 326	
6.4 Phosphoryl Transfer: P-Type ATPases, 327	
6.4.1 Introduction, 327	
6.4.2 Calcium P-Type ATPases, 327	
6.4.2.1 Ca ²⁺ -ATPase Protein SERCA1a and the Ca ²⁺ -ATPase Cycle, 329	
6.5 Conclusions, 337	
References, 338	

7 Iron-Containing Proteins and Enzymes**343**

- 7.1 Introduction: Iron-Containing Proteins with Porphyrin Ligand Systems, 343
- 7.2 Myoglobin and Hemoglobin, 343
 - 7.2.1 Myoglobin and Hemoglobin Basics, 345
 - 7.2.2 Structure of the Heme Prosthetic Group, 347
 - 7.2.3 Behavior of Dioxygen Bound to Metals, 348
 - 7.2.4 Structure of the Active Site in Myoglobin and Hemoglobin: Comparison to Model Compounds, 349
 - 7.2.5 Some Notes on Model Compounds, 352
 - 7.2.6 Iron-Containing Model Compounds, 353
 - 7.2.7 Binding of CO to Myoglobin, Hemoglobin, and Model Compounds, 356
 - 7.2.8 Conclusions, 359
- 7.3 Introduction to Cytochromes, 359
- 7.4 Cytochrome P450: A Monooxygenase, 361
 - 7.4.1 Introduction, 361
 - 7.4.2 Cytochrome P450: Structure and Function, 363
 - 7.4.3 Cytochrome P450: Mechanism of Activity, 365
 - 7.4.4 Analytical Methods: X-Ray Crystallography, 369
 - 7.4.5 Cytochrome P450 Model Compounds, 372
 - 7.4.5.1 Introduction, 372
 - 7.4.5.2 A Cytochrome P450 Model Compound: Structural, 372
 - 7.4.5.3 Cytochrome P450 Model Compounds: Functional, 374
 - 7.4.6 Cytochrome P450 Conclusions, 382
- 7.5 Cytochrome b(6)f: A Green Plant Cytochrome, 382
 - 7.5.1 Introduction, 382
 - 7.5.2 Cytochrome b(6)f Metal Cofactor Specifics, 386
- 7.6 Cytochrome bc₁: A Bacterial Cytochrome, 388
 - 7.6.1 Introduction, 388
 - 7.6.2 Cytochrome bc₁ Structure, 389
 - 7.6.3 Cytochrome bc₁ Metal Cofactor Specifics, 391
 - 7.6.4 The Cytochrome bc₁ Q Cycle, 395
 - 7.6.5 Cytochrome bc₁ Inhibitors, 397
 - 7.6.6 Cytochrome bc₁ Conclusions, 408
- 7.7 Cytochromes c, 408
 - 7.7.1 Introduction, 408
 - 7.7.2 Mitochondrial Cytochrome c (Yeast), 411
 - 7.7.3 Mitochondrial Cytochrome c (Horse), 416
 - 7.7.4 Cytochrome c Folding, Electron Transfer, and Cell Apoptosis, 422
 - 7.7.4.1 Cytochrome c Folding, 422

- 7.7.4.2 Electron Transfer in Cytochrome c and Its Redox Partners, 424
- 7.7.4.3 Apoptosis, 427
- 7.7.5 Cytochrome c Conclusions, 429
- 7.8 Cytochrome c Oxidase, 429
 - 7.8.1 Introduction, 429
 - 7.8.2 Metal-Binding Sites in Cytochrome c Oxidase, 432
 - 7.8.3 Dioxygen Binding, Proton Translocation, and Electron Transport, 434
 - 7.8.4 Cytochrome c Oxidase Model Compounds and Associated Analytical Techniques, 440
 - 7.8.5 Cytochrome c Oxidase Conclusions, 453
- 7.9 Non-Heme Iron-Containing Proteins, 454
 - 7.9.1 Introduction, 454
 - 7.9.2 Proteins with Iron–Sulfur Clusters, 454
 - 7.9.2.1 The Enzyme Aconitase 455
 - 7.9.3 Iron–Oxo Proteins, 458
 - 7.9.3.1 Methane Monooxygenases 459
- 7.10 Conclusions, 465
- References, 466