

Contents

| | |
|---|-----------|
| About the Author | xv |
| Preface to the Third Edition | xvii |
| CHAPTER 1 An Overview of the Role of Metals in Biology | 1 |
| Introduction | 1 |
| Essential Elements and Essential Metal Ions for Living Organisms | 5 |
| Why Just These Elements? | 10 |
| An Overview of the Functions of the Essential Metal Ions | 10 |
| Toxic Metals, Metals in Diagnosis and Therapeutics | 13 |
| References | 17 |
| Further Reading | 18 |
| CHAPTER 2 Basic Coordination Chemistry for Biologists | 19 |
| Introduction | 19 |
| Types of Chemical Bonds | 19 |
| Hard and Soft Ligands | 21 |
| The Chelate Effect | 22 |
| Coordination Geometry | 23 |
| Redox Chemistry | 27 |
| Crystal Field Theory and Ligand Field Theory | 28 |
| Further Reading | 34 |
| CHAPTER 3 Structural and Molecular Biology for Chemists | 35 |
| Introduction | 35 |
| The Structural Building Blocks of Proteins | 37 |
| Primary, Secondary, Tertiary and Quaternary Structure of Proteins | 40 |
| The Structural Building Blocks of Nucleic Acids | 52 |
| Secondary and Tertiary Structures of Nucleic Acids | 53 |
| Carbohydrates | 56 |
| Lipids and Biological Membranes | 61 |
| A Brief Overview of Molecular Biology | 64 |
| Replication | 64 |
| Transcription | 67 |
| Translation | 68 |
| Molecular Biology and Molecular Genetics Methods and Tools | 75 |
| References | 78 |
| Further Reading | 79 |

| | | |
|------------------|--|------------|
| CHAPTER 4 | Biological Ligands for Metal Ions | 81 |
| | Introduction..... | 81 |
| | Amino Acid Residues..... | 81 |
| | Low Molecular Weight Inorganic Anions | 84 |
| | Organic Cofactors..... | 87 |
| | Porphyrin-Based Cofactors..... | 87 |
| | Iron–Sulphur Cluster Formation | 92 |
| | MoCo in Mo-Containing Enzymes | 97 |
| | FeMoCo in Nitrogenase | 100 |
| | CuZ in NO Oxidases | 102 |
| | Siderophores | 106 |
| | Insertion of Metal Ions and Metalloclusters into Metalloproteins | 111 |
| | References..... | 116 |
| | Further Reading | 118 |
| CHAPTER 5 | An Overview of Intermediary Metabolism and Bioenergetics | 119 |
| | Introduction..... | 119 |
| | Redox Reactions in Metabolism | 120 |
| | The Central Role of ATP in Metabolism | 121 |
| | There are Only a Few Types of Reactions in Intermediary Metabolism..... | 123 |
| | An Overview of Catabolism..... | 127 |
| | Selected Case Studies – Glycolysis and the Tricarboxylic Acid Cycle..... | 129 |
| | An Overview of Anabolism | 132 |
| | Selected Case Studies: Gluconeogenesis and Fatty Acid Biosynthesis | 135 |
| | Bioenergetics – Generation of Phosphoryl Transfer Potential at the Expense of Proton Gradients..... | 139 |
| | References..... | 147 |
| | Further Reading | 147 |
| CHAPTER 6 | Methods to Study Metals in Biological Systems | 149 |
| | Introduction..... | 149 |
| | Magnetic Properties..... | 150 |
| | Electron Paramagnetic Resonance (EPR) Spectroscopy | 152 |
| | NMR Spectroscopy..... | 154 |
| | Mössbauer Spectroscopy | 156 |
| | Electronic Spectroscopy | 157 |
| | Circular Dichroism and Magnetic Circular Dichroism | 159 |
| | Resonance Raman Spectroscopy..... | 161 |
| | Extended X-Ray Absorption Fine Structure | 162 |
| | X-Ray Diffraction..... | 163 |
| | Concluding Remarks | 165 |

| | |
|--|------------|
| References..... | 168 |
| Further Reading | 169 |
| CHAPTER 7 Metal Assimilation Pathways | 171 |
| Introduction..... | 171 |
| Bio-Geochemistry of Metal Assimilation | 171 |
| Metal Assimilation in Bacteria | 179 |
| Iron..... | 179 |
| Copper, Manganese and Zinc..... | 185 |
| Metal Assimilation in Fungi..... | 189 |
| Copper, Manganese and Zinc..... | 191 |
| Metal Assimilation by Plants | 194 |
| Iron Acquisition by the Roots of Plants..... | 194 |
| Transition Metal Transport in Plants | 199 |
| Metal Assimilation in Mammals..... | 200 |
| Iron..... | 201 |
| Copper, Manganese and Zinc..... | 203 |
| References..... | 204 |
| Further Reading | 206 |
| CHAPTER 8 Intracellular Metabolism and Homeostasis of Metal Ions..... | 207 |
| Introduction..... | 207 |
| Intracellular Metabolism, Storage and Homeostasis of Metals in Bacteria..... | 207 |
| Iron..... | 208 |
| Intracellular Metabolism | 208 |
| Iron Homeostasis | 210 |
| Copper, Manganese, Nickel and Zinc..... | 213 |
| Copper..... | 213 |
| Zinc | 216 |
| Manganese and Nickel | 217 |
| Metal Transport, Storage and Homeostasis in Plants and Fungi | 219 |
| Iron, Copper, Manganese and Zinc Transport and Storage in Plants | 220 |
| Intracellular Transport and Storage..... | 220 |
| Iron, Copper, Manganese and Zinc Homeostasis in Plants..... | 226 |
| Iron, Copper and Zinc Transport and Storage in Fungi | 229 |
| Iron, Copper and Zinc Homeostasis in Fungi..... | 233 |
| Intracellular Metabolism and Homeostasis of Metals in Mammals..... | 237 |
| Intracellular Iron Metabolism in Mammals | 239 |
| Intracellular Cu, Zn and Mn Metabolism in Mammals..... | 241 |
| Iron Homeostasis in Man | 242 |

| | | |
|-------------------|--|------------|
| | Copper, Zinc and Manganese Homeostasis in Mammals | 250 |
| | References..... | 254 |
| | Further Reading | 258 |
| CHAPTER 9 | Sodium and Potassium: Channels and Pumps..... | 261 |
| | Introduction: Transport Across Membranes | 261 |
| | Sodium Versus Potassium | 261 |
| | Potassium Channels..... | 263 |
| | Sodium Channels..... | 271 |
| | The Sodium–Potassium ATPase (NKA)..... | 272 |
| | Active Transport Driven by Na ⁺ Gradients | 277 |
| | Sodium/Proton Exchangers | 281 |
| | Other Roles of Intracellular K ⁺ | 282 |
| | References..... | 286 |
| | Further Reading | 288 |
| CHAPTER 10 | Magnesium–Phosphate Metabolism and Photoreceptors | 289 |
| | Introduction..... | 289 |
| | Magnesium-Dependent Enzymes..... | 290 |
| | Phosphoryl Group Transfer: Kinases..... | 291 |
| | Phosphoryl Group Transfer: Phosphatases | 295 |
| | Stabilization of Enolate Anions: The Enolase Superfamily..... | 299 |
| | Enzymes of Nucleic Acid Metabolism | 302 |
| | Magnesium and Photoreception | 307 |
| | References..... | 312 |
| | Further Reading | 313 |
| CHAPTER 11 | Calcium – Cellular Signalling | 315 |
| | Introduction – Ca ²⁺ Chemistry and Comparison With Mg ²⁺ | 315 |
| | The Discovery of a Role for Ca ²⁺ Other Than as a Structural Component..... | 316 |
| | Overview of Cellular and Tissue Ca ²⁺ | 317 |
| | Membrane-Intrinsic Ca ²⁺ -Transporting Proteins | 319 |
| | Ca ²⁺ Binding and Sensor Proteins..... | 329 |
| | Ca ²⁺ and Cell Signalling | 333 |
| | References..... | 336 |
| | Further Reading | 337 |
| CHAPTER 12 | Zinc – Lewis Acid and Gene Regulator..... | 339 |
| | Introduction..... | 339 |
| | Mononuclear Zinc Enzymes..... | 341 |
| | Carbonic Anhydrase | 343 |
| | Metalloproteinases | 344 |

| | |
|---|------------|
| Alcohol Dehydrogenases | 351 |
| Other Mononuclear Zinc Enzymes | 353 |
| Multinuclear and Cocatalytic Zinc Enzymes | 354 |
| Zinc Fingers DNA and RNA Binding Motifs..... | 360 |
| References..... | 361 |
| Further Reading | 362 |
| CHAPTER 13 Iron: Essential for Almost All Life | 363 |
| Introduction..... | 363 |
| Iron Chemistry | 364 |
| Iron and Oxygen..... | 364 |
| The Biological Importance of Iron | 366 |
| Biological Functions of Iron-Containing Proteins..... | 368 |
| Haemoproteins | 370 |
| Oxygen Transport..... | 370 |
| Activators of Molecular Oxygen..... | 373 |
| Electron Transport Proteins..... | 380 |
| Iron–Sulphur Proteins..... | 385 |
| Other Iron-Containing Proteins | 391 |
| Mononuclear Nonhaem Iron Enzymes..... | 391 |
| Dinuclear Nonhaem Iron Enzymes | 395 |
| References..... | 401 |
| Further Reading | 403 |
| CHAPTER 14 Copper – Coping with Dioxygen | 405 |
| Introduction..... | 405 |
| Copper Chemistry and Biochemistry | 405 |
| Type 1 Blue Copper Proteins – Electron Transport..... | 407 |
| Copper-Containing Enzymes in Oxygen Activation and Reduction..... | 410 |
| Type 2 Copper Proteins..... | 411 |
| Dinuclear Copper Proteins | 414 |
| Multicopper Oxidases..... | 416 |
| The Role of Cu in Cytochrome <i>c</i> Oxidases..... | 419 |
| Superoxide Dismutation in Health and Diseases..... | 422 |
| Copper Enzymes Involved With Other Low-Molecular Substrates..... | 426 |
| Mars and Venus – The Role of Copper in Iron Metabolism | 431 |
| References..... | 431 |
| Further Reading | 433 |
| CHAPTER 15 Nickel and Cobalt: Evolutionary Relics | 435 |
| Introduction..... | 435 |
| Nickel Enzymes..... | 435 |

| | |
|--|------------|
| Urease | 436 |
| Ni–Fe–S Proteins..... | 437 |
| Methyl-Coenzyme M Reductase | 444 |
| Glyoxalase, SOD and Lactate Racemase..... | 445 |
| Cobalamine and Cobalt Proteins..... | 448 |
| B ₁₂ -Dependent Isomerases | 450 |
| B ₁₂ -Dependent Methyltransferases | 451 |
| Noncorrin Co-Containing Enzymes | 452 |
| References..... | 455 |
| Further Reading | 456 |
| CHAPTER 16 Manganese – Oxygen Generation and Detoxification | 459 |
| Introduction: Mn Chemistry and Biochemistry | 459 |
| Photosynthetic Oxidation of Water – Oxygen Evolution..... | 460 |
| Mn ²⁺ and Detoxification of Oxygen Free Radicals..... | 466 |
| Nonredox Di-Mn Enzymes – Arginase..... | 467 |
| References..... | 472 |
| Further Reading | 473 |
| CHAPTER 17 Molybdenum, Tungsten, Vanadium and Chromium | 475 |
| Introduction..... | 475 |
| Mo and W Chemistry and Biochemistry | 475 |
| Molybdenum Enzyme Families..... | 476 |
| The XO Family..... | 478 |
| The Sulphite Oxidases and DMRs | 480 |
| Tungsten Enzymes..... | 484 |
| Nitrogenases..... | 485 |
| Vanadium Biochemistry | 490 |
| Vanadium Biology..... | 493 |
| Chromium in Biology..... | 494 |
| References..... | 496 |
| Further Reading | 497 |
| CHAPTER 18 Nonmetals in Biology..... | 499 |
| Introduction..... | 499 |
| The Major Biogeochemical Cycles..... | 499 |
| Carbon, Hydrogen, Oxygen and Phosphorus..... | 500 |
| The Nitrogen Cycle | 504 |
| Sulphur and Selenium | 506 |
| Chlorine and Iodine | 511 |
| References..... | 516 |
| Further Reading | 516 |

| | | |
|-------------------|--|------------|
| CHAPTER 19 | Biom mineralization | 517 |
| | Introduction..... | 517 |
| | Principles of Solid-State Biological Inorganic Chemistry | 518 |
| | An Overview of the Major Classes of Biom minerals | 519 |
| | Iron Deposition in Ferritin | 520 |
| | Ferritin as a Supramolecular Template in Nanotechnology..... | 526 |
| | Formation of Magnetite in Magnetotactic Bacteria..... | 528 |
| | Calcium-Based Biom minerals – Calcium Carbonates in Ascidians and Molluscs..... | 532 |
| | Biom mineralization in Bone and Enamel Formation | 535 |
| | The Organic Matrix, Mineral Phase and Bone Mineralization | 536 |
| | Silica-Based Biom minerals | 539 |
| | References..... | 543 |
| | Further Reading | 544 |
| CHAPTER 20 | Metals in Brain | 545 |
| | Introduction..... | 545 |
| | The Brain and the Blood–Brain Barrier (BBB)..... | 545 |
| | Sodium, Potassium and Calcium Channels | 552 |
| | Calcium and Signal Transduction | 553 |
| | Zinc, Copper and Iron | 558 |
| | Copper..... | 563 |
| | Iron..... | 565 |
| | Neurons | 567 |
| | Astrocytes | 568 |
| | Microglia..... | 569 |
| | Oligodendrocytes | 569 |
| | Iron, Brain Development and Ageing..... | 569 |
| | References..... | 570 |
| | Further Reading | 571 |
| CHAPTER 21 | Metals and Neurodegeneration | 573 |
| | Introduction..... | 573 |
| | Metal-Based Neurodegeneration | 575 |
| | Metals Associated With Neurodegenerative Diseases..... | 583 |
| | Parkinson’s Disease | 583 |
| | Alzheimer’s Disease | 586 |
| | Huntington’s Disease..... | 589 |
| | Friedreich’s Ataxia | 590 |
| | Amyotrophic Lateral Sclerosis..... | 590 |
| | Creutzfeldt–Jakob and Other Prion Diseases..... | 592 |

| | |
|--|------------|
| Disorders of Copper Metabolism – Wilson’s and Menkes Diseases and Aceruloplasminaemia | 595 |
| References | 596 |
| Further Reading | 598 |
| CHAPTER 22 Metals in Medicine and Metals as Drugs | 599 |
| Introduction | 599 |
| Disorders of Essential Metal Ion Metabolism and Homeostasis | 599 |
| Toxicity Due to Essential Metals | 599 |
| Metal-Based Drugs | 608 |
| Cisplatin, An Anticancer Drug | 609 |
| Metallotherapeutics With Lithium | 615 |
| Contrast Agents for Magnetic Resonance Imaging (MRI) | 617 |
| References | 622 |
| Further Reading | 623 |
| CHAPTER 23 Metals in the Environment | 625 |
| Introduction Environmental Pollution and Heavy Metals | 625 |
| Cadmium | 625 |
| Mercury | 629 |
| Lead | 631 |
| Aluminium | 633 |
| Environmental Metal Toxicity | 638 |
| Metals as Poisons | 639 |
| References | 642 |
| Further Reading | 644 |
| Index | 645 |