PREFACE

When I began teaching a bioinorganic course in the mid-1980s, Robert Hay's short text (Hay, R. W. *Bio-Inorganic Chemistry*, Ellis Horwood Limited, Halsted Press, New York, 1984, 210 pp.) addressed most topics in the area. Coverage of the entire bioinorganic field in such a text now would be impossible because the number of topics and their complexity have grown tremendously. In all recent iterations of my bioinorganic courses, I have followed a philosophy upon which this "short" text is based:

1. Review enough introductory material in inorganic (Chapter 1: Inorganic Chemistry Essentials) and biochemistry (Chapter 2: Biochemistry Fundamentals) to bring all students to more or less the same level. I try to take the students' backgrounds into account: Are their principal knowledge and interest areas chemistry, biology, biochemistry, physics, spectroscopy, pharmaceuticals, and so on? Do they intend to become synthetic chemists, theoretical chemists, molecular biologists, physicians, pharmacologists, neuroscientists, and so on?

2. Introduce instrumental techniques used in analysis of the bioinorganic systems I will lecture on (Chapter 3: Instrumental and Computer-Based Methods). Typically, these would be electron paramagnetic resonance (EPR) and Mössbauer spectroscopies not often covered in undergraduate instrumental analysis courses plus X-ray diffraction and NMR techniques used for structural analyses of metalloproteins and their small molecule model compounds.

3. Present one or two bioinorganic topics of my choice. I follow the paradigms the reader will note in Chapters 4, 5, and 6: Use the structural information gained through X-ray crystallographic and NMR solution studies to try to understand the metalloprotein's function and mechanism of activity and then design small

molecule compounds to confirm mechanism, extend the catalytic activity for industrial purposes, or diagnose and cure the disease states caused by the metalloprotein's malfunction.

4. Encourage students to choose their own bioinorganic topics for individual study and class discussion in the remaining course time. I find that undergraduate and graduate student fascination and enthusiasm for the subject area always energizes them (and me) for the study of diverse and interesting bioinorganic topics. Certainly the subject area provides great opportunities for introducing the use of primary literature sources and the application of computer- and internet-based searching, visualization, and modeling techniques.

In keeping with this philosophy I believe the text is appropriate for a one-semester bioinorganic chemistry course offered to fourth-year undergraduate chemistry, biochemistry, and biology majors and first-year graduate students concentrating in inorganic and biochemical subject areas. The text presents review chapters on inorganic chemistry (Chapter 1: Inorganic Chemistry Essentials) and biochemistry (Chapter 2: Biochemistry Fundamentals), although ideally students will have previously taken undergraduate one-semester advanced inorganic and biochemistry courses. Chapter 3 (Instrumental and Computer-Based Methods) provides an introduction to some important instrumental techniques for bioinorganic chemistry; the computer section includes basic information about computer hardware and software available in late 2001. I hope I have passed along my enthusiasm for computer-aided modeling and visualization programs with an emphasis on free software and databases available via the World Wide Web. The bioinorganic subjects covered in Chapter 4 (Iron-Containing Oxygen Carriers and Their Synthetic Models), Chapter 5 (Copper Enzymes), and Chapter 6 (The Enzyme Nitrogenase) emphasize the use of primary sources. Every effort has been made to include up-to-date references in each subject area. Following (or instead of) presentation of these chapters, teachers and learners are encouraged to find bioinorganic subject areas of special interest to them. My special interest area is introduced in Chapter 7 (Metals in Medicine).

Some important bioinorganic areas not discussed in this text are mentioned in the following paragraphs, hopefully to jump-start student investigations of areas of interest to them. Other texts and sources—references 3–7 in Chapter 1, for instance—will be helpful in choosing bioinorganic topics for further discussion.

The use of alkali and alkaline earth group metal ions, especially those of sodium, potassium, magnesium, and calcium, for maintenance of electrolyte balance and for signaling and promotion of enzyme activity and protein function are not discussed in this text. Many of these ions, used for signaling purposes in the exciting area of neuroscience, are of great interest. In ribozymes, RNAs with catalytic activity, solvated magnesium ions stabilize complex secondary and tertiary molecular structure. Telomeres, sequences of DNA at the ends of chromosomes that are implicated in cell death or immortalization, require potassium ions for structural stabilization.

Hemoglobin's protoporphyrin IX, discussed in Chapter 4, is only one of many important porphyrin hemes involved in bioinorganic and catalytic science.

Cytochromes, catalases, and peroxidases all contain iron–heme centers. Nitrite and sulfite reductases, involved in N–O and S–O reductive cleavage reactions to NH_3 and HS^-, contain iron–heme centers coupled to $[Fe_4S_4]$ iron–sulfur clusters. Photosynthetic reaction center complexes contain porphyrins that are implicated in the photoinitiated electron transfers carried out by the complexes.

To access information about the structure and function of metalloproteins and enzymes, I recommend a visit to the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data Bank (PDB) website at www.rcsb.org/pdb. Begin by entering the enzyme's name into the search routine. If an X-ray crystallographic or NMR structural study has been published, the hits displayed will provide journal references. A recent PDB search on the term *cytochrome* yielded 478 hits including 22 referring to cytochrome P-450, a membrane-bound monooxygenase that catalyzes incorporation of one oxygen atom from O_2 into substrate molecules. Sixteen citations described cytochrome c oxidase, a membrane-bound electron transfer protein that couples electron donor NADH with electron acceptor O_2, releasing large amounts of energy. Fifteen citations result from a search on aconitase, an enzyme that contains an $[Fe_4S_4]^{2+}$ cluster and catalyzes the isomerization of citrate and isocitrate. The isomerization is a key reaction in the Kreb's cycle. In aconitase, one cluster iron binds citrate at the active site during the catalytic cycle. Liver alcohol dehydrogenase (LADH) and carbonic anyhydrase are two interesting zinc-containing metalloenzymes. The growing zinc-finger family of similarly shaped metalloproteins constitutes an important motif for binding nucleic acids. This last topic is discussed in Section 2.4 (Zinc-Finger Proteins) of Chapter 2.

A very brief introduction to the important topic of bioinorganic electron transfer mechanisms has been included in Section 1.8 (Electron Transfer) of Chapter 1. Discussions of Marcus theory for protein–protein electron transfer and electron or nuclear tunneling are included in the texts mentioned in Chapter 1 (references 3–7). A definitive explanation of the underlying theory is found in the article entitled "Electron-Transfer in Chemistry and Biology," written by R. A. Marcus and N. Sutin and published in *Biochem. Biophys. Acta*, 1985, **811**, 265–322.

Bioinorganic chemical knowledge grows more interesting and more complex with each passing year. As more details about the usage and utility of metals in biological species and more mechanistic and structural information becomes available about bioinorganic molecules, more biologists, chemists, and physicists will become interested in the field. Senior-level undergraduates in chemistry, biology, and physics, as well as beginning graduate students, will do well to educate themselves in this diverse and fascinating chemical area. I hope this introductory text will be catalytic for students, whetting their appetites for more information and encouraging them to join research groups engaged in the search for new knowledge in the continually expanding bioinorganic field.

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