Introduction: Bioinorganic Enzymology II

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Editorial

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Introduction: Bioinorganic Enzymology II

To contribute to the research and teaching pedagogics of the multidisciplinary subject that is Bioinorganic Chemistry—also denoted as Inorganic Biochemistry or Metallobiochemistry—we organized and served as coeditors of two thematic issues. The first of these, now designated Bioinorganic Enzymology I (Volume 96, Number 7, 1996; Figure 1, left), contains a detailed account of the structural and functional aspects of enzyme sites as they were understood at the time, includes electron transfer with and without enzymatic catalysis, and describes selected enzyme systems implicated in hydrogen, carbon, oxygen, and nitrogen metabolism. The second issue, Biomimetic Inorganic Chemistry (Volume 104, Number 2, 2004; Figure 1, middle) recognizes the essential role of abiological systems in interpreting the structure and function of native sites. The principal components of such systems are designed molecular representations of these sites and are often termed models or synthetic analogues. This issue largely deals with ligand design and implementation, the classic systems of iron−sulfur clusters, heme-dioxygen and electron-transfer centers (Fe, Cu), and nonredox (Zn) and redox-active (V, Mn, Fe, Cu, Mo) site analogues.

Over the nearly twenty-year period encompassed by the two thematic issues, but especially in the past decade, bioinorganic chemistry as a discipline has evolved an identity that does not merely maintain the currency of earlier subjects but expands the field well beyond the purview of the preceding issues. Consequently, we have organized a third thematic issue, Bioinorganic Enzymology II (Figure 1, right), to summarize certain consequential advances whose origins can be found in the five significant areas of investigation emphasized on the front cover. As will become evident, the contents of this issue subsume a broader array of subjects than the title implies. Enzymology continues to refine known catalytic mechanisms and reveal new ones for investigation. Molecular biology presents an array of powerful experimental methodologies applicable to proteins and nucleic acids. Among these, site-directed protein variants are particularly incisive in bioinorganic research. Inorganic synthesis is the foundation of biomimetic inorganic chemistry. Spectroscopy and associated magnetism investigations define ground and excited electronic states, details of chemical bonding including bond covalency and pathways of electron transfer, and magnetic coupling of metal sites. Computational methods provide geometrical and electronic metal site structures, approximate global protein architecture, and formulate reaction coordinates. Superimposed on these endeavors are the structural insights gained from continually expanding crystallographic databases, including protein structures at atomic resolution. Results from all of these subjects lead to a molecular level understanding of function as detailed in Bioinorganic Enzymology II. In addition, contributions in the burgeoning fields of metalloimaging, medicinal inorganic chemistry, and metallosensors are included. It is anticipated that Bioinorganic Enzymology II will contribute significantly to the foundation for future studies in this rapidly evolving and expanding field.

With the publication of Bioinorganic Enzymology II, appearing consecutively in two parts (issues 7 and 8), the triad of issues under our joint guest editorship is complete. We trust that the latest addition and its predecessors provide a useful resource in the teaching and research of bioinorganic chemistry. We acknowledge the editorial support of *Chemical Reviews* and are much indebted to all authors for their authoritative and scholarly contributions, without which this series would not have been possible.

COVER ART EXPLANATION

Crystallographically defined structures of metalloenzyme active sites provide the foundation for studies using enzymology, molecular biology, inorganic synthesis, and spectroscopic and computational methods that elucidate mechanisms and describe function on a molecular level. Topical crystallographic structures for enzyme classes covered in this thematic issue are featured in the top row, showing each active site structure and the tertiary structure of the protein subunit containing the active site. These include, from left to right, the ferryl form of *Pseudomonas putida* cytochrome P450cam (Protein Data Bank identification code

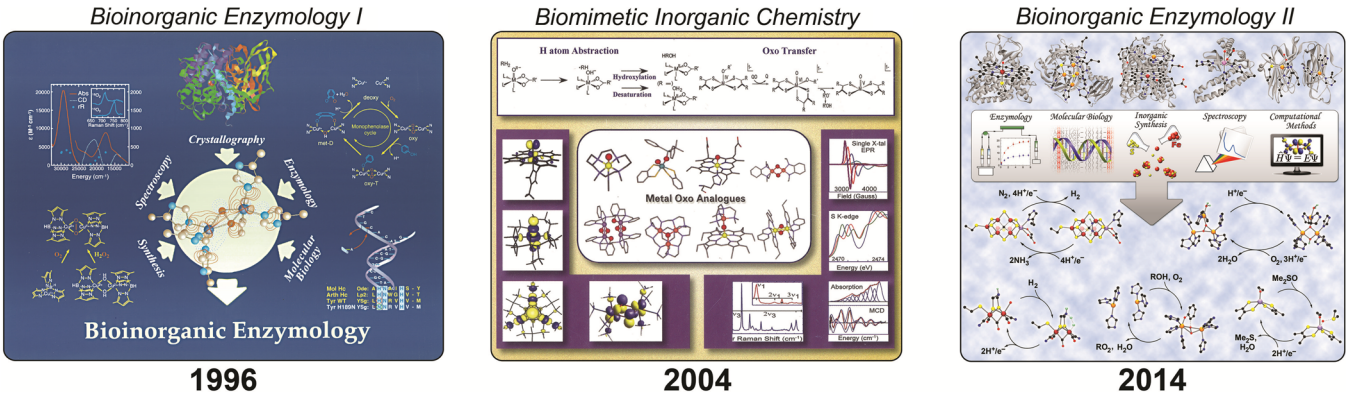

Figure 1. Covers of the triad of *Chemical Reviews* thematic issues on Bioinorganic Chemistry (1996, 2004, 2014).

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1DZ9), the tetranuclear Cu_Z cluster in *P. stutzeri* nitrous oxide reductase (3SBR), the binuclear heme-copper site in bovine cytochrome *c* oxidase (2Y69), human manganese superoxide dismutase (2P4K), and the dioxygen-bound form of the non-coupled binuclear copper site in the catalytic core of peptidylglycine α-hydroxylating monooxygenase (1SDW).

Five methods are emphasized in the middle: *enzymology*, which is represented by comparative steady-state enzyme kinetics and stopped-flow spectroscopy; *molecular biology*, represented by a genetic sequence alignment of several cytochrome *c* oxidases (the 3 histidine ligands to Cu are highlighted in red) and by a DNA strand enabling site-directed mutagenesis; *inorganic synthesis*, represented by the self-assembly of iron−sulfur site analogues; *spectroscopy*, represented by the visible absorption spectrum of as-isolated laccase featuring low energy (S_{Cys} → type I Cu) and high energy (μ_2-OH → type III Cu) charge transfer bands; and computational methods, represented by the occupied π^*_σ molecular orbital in a computational model of the μ-η^2:η^2-peroxo intermediate of tyrosinase. Finally, five molecular mechanisms are highlighted in the bottom panel for topical areas in bioinorganic chemistry. Clockwise from the top left: *nitrogenase*, showing the resting Fe_7S_9CMo cofactor (PDB 3U7Q) and a proposed N_2H_2 intermediate; the trinuclear copper cluster in the multicopper oxidase *laccase*, highlighting the O−O cleavage step (structures based on 1GYC); the molybdenum site in *DMSO reductase*, showing the desoxo form (1EU1) and a transition state for S−O cleavage (based on 4DMR); the coupled binuclear copper site in *tyrosinase*, showing the deoxy form and a proposed transition state for electrophilic attack on the aromatic ring (structure based on 1WX2); and the diiron active site in *[FeFe]-hydrogenase*, showing the reduced form and a proposed transition state for H−H cleavage (based on 3C8Y). The details of these molecular mechanisms are the focus of ongoing research efforts and are included here to highlight several important areas of active research in the bioinorganic chemistry community. (Artwork by Ryan Cowley, Stanford University.)

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AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

Biographies

Richard H. Holm was born in Boston, Massachusetts. He spent his early years on Nantucket Island and in Falmouth, Massachusetts, where he received his secondary school education. He is a graduate of the University of Massachusetts (B.S.) and Massachusetts Institute of Technology (Ph.D. in Chemistry). His graduate advisor was Professor F. A. Cotton. He has served on the faculties of the University of Wisconsin, the Massachusetts Institute of Technology, and Stanford University. Since 1980, he has been at Harvard University, where he has been Chair of the Department of Chemistry and, from 1983, Higgins Professor of Chemistry. As of 2006, he has been Higgins Research Professor of Chemistry. His research interests are centered in inorganic and bioinorganic chemistry, with particular reference to the synthesis and properties of molecules whose structures and reactivity are relevant to biological processes. With Professor Edward I. Solomon, he has been coeditor of three thematic issues in *Chemical Reviews*: Bioinorganic Enzymology I (1996), Biomimetic Inorganic Chemistry (2004), and Bioinorganic Enzymology II (issues 7 and 8 of 2014).

Edward I. Solomon grew up in North Miami Beach, Florida, received his Ph.D. at Princeton (with D. S. McClure), and was a postdoctoral fellow at The Ørsted Institute (with C. J. Ballhausen) and then at Caltech (with H. B. Gray). He was a Professor at the Massachusetts Institute of Technology until 1982, when he joined the faculty at Stanford University, where he is now the Monroe E. Spaght Professor of Humanities and Sciences and Professor of Photon Science at SLAC National Accelerator Lab. He has been an Invited Professor in Argentina, Australia, Brazil, China, France, India, and Japan. Professor Solomon's research is in the fields of Physical-Inorganic and Bioinorganic Chemistry with emphasis on the application of a wide range of spectroscopic methods combined with QM calculations to elucidate the electronic structure of transition metal sites and its contribution to physical properties and reactivity. With Professor Richard H. Holm, he has been co-editor of three thematic issues in *Chemical Reviews*: Bioinorganic Enzymology I (1996), Biomimetic Inorganic Chemistry (2004), and Bioinorganic Enzymology II (issues 7 and 8 of 2014).

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