
Preface

Metalloproteins play essential critical functional roles in enzymatically catalyzing reactions difficult to achieve without metals, in signal transduction, and in storage and transport of proteins constituting over 1/3 of the proteome of living organisms. Recent breakthroughs in crystallography have provided insights into understanding their mechanisms, but challenges remain in identifying the particularly redox states of the metals and in the chemical mechanisms for the complex reactions they catalyze. With these advances in structural information, theory and computation are starting to play a more significant role, particularly in identifying the reaction mechanism. This volume summarizes some of the recent progresses in both experiment and theory/computation showing the synergy that is now developing.

Two papers review the progress in understanding the Oxygen Evolution Reaction (OER) accomplished by Photosystem II (PSII), where four thrusts have converged to provide something close to an atomistically based mechanism:

- X-ray structures of some (but unfortunately not all) of the intermediate states in the catalytic reactions and characterization of the active sites through techniques such as EXAFS and XANES
- Model systems synthesized to reproduce the active states to enable clear-cut experimental studies of the details of the structures and redox states of the metals
- EPR and NMR studies of many of the active states to clarify the steps
- Quantum mechanical calculations of the active states to determine the structures and reaction barriers

This remarkable progress is summarized in the papers from the Britt and Agapie groups.

A driving force in trying to understand the mechanisms of the metalloenzymes is to use them as a model for developing biomimics that catalyze such important reactions as CH₄ activation and the OER. The paper by Chan and coworkers describes the Odyssey from characterizing the complex structures and chemistry in methane monooxygenase (pMMO) to determining its unique structure involving three distinct Cu sites and then to developing a functioning biomimic catalyst that is very effective for selective oxidation of CH₄ and alkanes.

A particularly important class of metalloenzymes is the radical S-adenosyl-l-methionine (SAM) superfamily in which 4Fe-4S complexes carry out important anaerobic transformations as explained in the paper by Betz, Shepard, and Broderick.

With the development of accurate structural models, it has become possible to use first principle quantum mechanics (DFT) to develop an understanding of the electron processes of the catalytic and electron transfer reactions involved as summarized by the Klein group. Cho then shows how to model the binding of ligands to metalloproteins by including the role of the more remote parts of the protein on these

electronic processes through coupling of QM with a force field description (QM/MM).

The advances in our understanding of the electrochemical processes essential to metalloproteins through protein film electrolysis (PFE) are summarized by Armstrong, showing how this provides detailed mechanisms underlying how these proteins play essential roles in life.

Ferritins play an essential role in storing iron in bioavailable assembly, providing an example of the interplay between metal transport and storage of well-characterized structural detail as explained in the paper by Kim and Kim showing the unique characteristics that are important in the functioning of *Helicobacter pylori*.

At the heart of essentially all metalloenzymes is the role of electron transfer in controlling the rates of their reactions. The elucidation of how these electron transfer processes are mediated by the structures of the metalloenzymes involves a combination of theory and experiment as explained by the Gray group.

We hope that this volume will ignite further collaborations between experiment and theory in elucidating and exploiting the metalloproteins. We envision that the volume will be valuable to researchers in the general field of bioinorganic chemistry and also as a sourcebook for courses at the biology/chemistry interface.

We hope that this comprehensive collection of the recent research by top researchers will stimulate accelerated developments in combining experimental and theoretical studies of metalloproteins.

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