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BOOK REVIEWS

Metal Ions in Biological Systems. Volume 39. Molybdenum and Tungsten: Their Roles in Biological Processes. Edited by Astrid Sigel and Helmut Sigel (University of Basel). 2002. ix + 810 pp. $250.00. ISBN 0-8247-0765-6.

Molybdenum and tungsten are both group VI transition metals, the only 4d and 5d metals known to be involved in biological catalysis. Organisms that utilize Mo enzymes are ubiquitous in nature and are required by archaea, bacteria, fungi, plants, animals, and humans. Over 50 different molybdenum enzymes are now known, and these enzymes play vital roles in the global carbon, nitrogen, and sulfur cycles. Although the bioavailability of tungsten is considerably less than that of molybdenum, the number of enzymes known to require tungsten continues to increase. This volume of *Metal Ions in Biological Systems*, which is devoted solely to the bioinorganic chemistry of Mo and W enzymes, is timely, following on the heels of the first two Gordon Conferences on these enzymes. It represents the most comprehensive overview of the field since Hille's oft-cited 1996 *Chem. Rev.* article and the review of tungstoenzymes in the same issue.

This volume is an extensive 22 chapter work that contains 810 pages of text, including a very well-organized and useful subject index. Over two-thirds of the volume is devoted to the pyranopterin Mo and W enzymes, indicating rapid growth in what has previously been perceived as a nascent field. The book starts with a very touching memorial to the contributions of the late Prof. R. C. Bray, who was a true pioneer in the pterin-containing Mo enzyme field. Lowe does a fine job of detailing Bray's career, including his background, achievements, and contributions to the field. The book proper begins with a well-written overview of the roles Mo and W play in biogeochemical cycles and an opening chapter on the biologically important transport and regulation of molybdate and tungstate. Chapter 2 does a fine job of highlighting Mo- and W-transport in addition to providing a very detailed description of the structural chemistry of cytoplasmic molybdate-binding proteins.

Chapters 3−5 discuss various aspects of the molybdenum nitrogenases. The first half of Chapter 3 focuses on crystallographic studies of the protein and provides a framework for a discussion of the mechanism of nitrogen fixation. The latter half is very well written and effectively melds electron-transfer reactivity and redox chemistry, spectroscopic and reactivity studies, and theoretical calculations with what has been gleaned from the structural work. The coordination chemistry of Mo and W dinitrogen complexes is presented in Chapter 4 with a specific emphasis on their reactivity. This chapter illuminates the remarkable chemistry of Mo and W with respect to activating coordinated dinitrogen for conversion to various nitrogen-containing species. The last chapter on the molybdenum nitrogenases represents a succinct account of the state-of-the-art regarding the biosynthesis of the FeMo cofactor.

A very comprehensive collection of the recent work being undertaken on pyranopterin Mo and W enzymes is presented in Chapters 6−20. Hille in Chapter 6 provides a very nice overview of the body of work on pyranopterin Mo enzymes. This includes a description of the various reactions catalyzed by the three principal families of molybdenum enzymes and the rationale behind their classification. A timely discussion of current ideas regarding the mechanism of the molybdenum hydroxylases is also found in this chapter. A very clear presentation of various X-ray structures representing members of the three pyranopterin Mo enzyme families and the W-containing aldehyde oxidoreductase family is detailed in Chapter 7. Of particular interest is the lucid presentation of the structures of active sites, specifically that of the CODH from *O. carboxidovorans*, which represents a unique active-site structure within the Mo hydroxylase enzyme family. A brief discussion of series-termination effects and their effect on the interpretation of the crystallographic model concludes the chapter.

Chapter 8 discusses model chemistry for understanding various aspects of pyranopterin Mo and W active sites. The goals of the synthetic model approach are clearly delineated in this chapter, and these are followed by a historical account of relevant model chemistry and newer work that focuses on the redox synergy between the metal, the ene-1,2-dithiolate, and the pterin. A particularly attractive aspect of this contribution is the discussion of electroactive metal-dithiolate and metal-pterin complexes. The molecular biology of the molybdenum cofactor as presented in Chapter 9 is clear and is digestible by the nonexpert. A particularly interesting section discusses some open questions in eukaryotic systems, including the role of the Cnx4 protein, subcellular localization of molybdenum cofactor biosynthesis, the nature and function of molybdenum cofactor binding proteins, and how the cofactor is inserted into the enzymes. The dissimilatory and assimilatory nitrate reductases are presented in Chapter 10. This chapter also includes a discussion of bacterial respiratory chains and a brief presentation of nitrite oxidoreductase.

Chapters 11−15 primarily focus on the molybdenum hydoxylases, which are of interest because the oxygen atom incorporated into the substrate is derived from water and not dioxygen, and these enzymes generate rather than consume reducing equivalents. Together, these chapters present some of the most exciting work in the field and provide discussion of the fundamental distinction between monooxygenase and molybdenum hydroxylase reactivity.

The hydroxylation of nicotine, nicotinate, and isonicotinate, and their derivatives, is presented in Chapter 11. The chapter includes a brief presentation of medical and biotech aspects of these enzymes, which catalyze substrate specific and regioselective hydroxylations. Chapter 12 provides an account of the crystal structures obtained for the xanthine oxidase and dehydrogenase forms of bovine xanthine oxidoreductase. The chapter is concise and well written, concluding with a brief description of picolinate dehydrogenase, a new member of the xanthine oxidase family. Chapter 13 has a different approach, in that the primary focus is on spectroscopic and theoretical investigations aimed at elucidating the mechanism of xanthine oxidase-mediated hydroxylations. The spectroscopic section is very well written, detailing powerful electronic absorption, MCD, XAS, and EPR methodologies aimed at resolving various controversial aspects concerning specific details regarding the mechanism of action of the enzyme and the structure of the active site. A clear discussion of recent theoretical and ENDOR experiments related to the nature of the "very rapid" intermediate, and arguments for and against tetrahedral and Mo-carbon bound intermediates, are presented. A thorough description of the xanthine oxidase-related quinoline, isoquinoline, and quinaldine hydroxylases is the subject of Chapter 14. The partial overlap with the material presented in the prior chapter is constructive rather than repetitive. Specifically, the relevant biochemical and EPR data for these enzymes are compared to those of the more extensively studied xanthine oxidoreductases. The EPR, ENDOR, and redox properties of these hydroxylases are presented in detail and will be of interest to researchers interested in the mechanism of Mo-catalyzed hydroxylations. The molybdenum hydroxylase contributions conclude in Chapter 15 with a discussion of various aldehyde oxidases. The chapter begins with a discussion of the members of the xanthine oxidase family and provides a very nice comparison of their three-dimensional structures and the remarkable similarity in how the endogenous redox cofactors are arranged to facilitate electron-transfer regeneration via a common pathway. Other notable aspects of this contribution include a summary of spectroscopic data for the molybdenum aldehyde oxidases and an overview of members of the tungsten aldehyde oxidoreductase family.

Chapter 16 provides an up-to-date review on the structure and function of bacterial and archaeal Mo and W enzymes involved in C1 metabolism. The Mo enzymes sulfite oxidase, DMSO reductase, and biotin sulfoxide reductase are discussed in Chapter 17. The section on EPR, ESEEM, and HYSCORE studies of sulfite oxidase is particularly nice and provides new details regarding the structures of high- and low-pH forms of sulfite oxidase. Of particular note are the various references to bioinspired model compounds interspersed throughout the text. There are six known Se–Mo enzymes, and these are compared in Chapter 18. The chapter illustrates the unique role of selenium in the catalytic cycles of these enzymes. Members of the tungstoenzyme family are classified in Chapter 19. The chapter presents the molecular, catalytic, and physical properties for each class of tungstoenzyme, in addition to providing detailed information on their structure and mechanism. Interestingly, certain molybdenum enzymes, including nitrogenase, can be substituted with tungsten, and this work is detailed in Chapter 20. The chapter discusses differences in Mo and W bioavailability, reduction potentials, metal-oxo bond enthalpies, and rates of oxygen atom transfer reactions. The book concludes with chapters on the requirement and metabolism of molybdenum and the metabolism and toxicity of tungsten in humans, respectively.

In summary, the volume is comprehensive and thoughtfully organized and is required reading for any scientist whose research focuses on Mo and W enzymes. It should find its way onto all research library stacks as another fine addition to the *Metal Ions in Biological Systems* series.

Martin L. Kirk, *The University of New Mexico*

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