Methods in Enzymology

Volume 158

Metallobiochemistry

Part A

EDITED BY

James F. Riordan

Bert L. Vallee

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ACADEMIC PRESS, INC.
Harcourt Brace Jovanovich, Publishers
San Diego New York Berkeley Boston
London Sydney Tokyo Toronto

ACADEMIC PRESS, INC.
1250 Sixth Avenue
San Diego, California 92101

United Kingdom Edition published by
ACADEMIC PRESS INC. (LONDON) LTD.
24-28 Oval Road, London NW1 7DX

LIBRARY OF CONGRESS CATALOG CARD NUMBER 54-9110

ISBN 0-12-182059-9 (alk. paper)

PRINTED IN THE UNITED STATES OF AMERICA
88 89 90 91 9 8 7 6 5 4 3 2 1

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Preface

Although it has been suspected since ancient times that metals participate in biological processes, details of the manner in which they might exert a function have until recently remained unknown. It is now appreciated that metals play roles in catalysis, hormone action, gene and other regulatory functions, structural stabilization of macromolecules, muscle contraction, nerve conduction, and transport. The alkali and alkaline earth metals as well as cobalt, copper, iron, manganese, molybdenum, nickel, zinc, and others are known to be essential, many of them in the mechanism of action of specific enzymes.

Most of these elements occur in biological matter in very low concentrations, a fact that long dominated the thinking about the subject and presented not so much intellectual as analytical challenges. The presence or absence of a particular "trace" element in a given biological matrix was the crucial experimental question preoccupying many investigators, and its answer became almost an end in itself; as a consequence, little thought needed to or could be given to how an answer in the affirmative would be pursued. Recent advances in methodology and instrumentation have solved most of the analytical problems that impeded progress. Nevertheless, it is important to realize that the difficulties and frustrations of the past left an imprint on the field that is only slowly giving way to the new realities.

The designation "trace element" has been employed variously to indicate tissue content, the total knowledge of the subject, or—by implication—even its potential importance. Whatever the connotation or viewpoint, this historically conditioned nomenclature has categorized pertinent metals based entirely on once poor detection limits and signal-to-noise ratios of analytical methods which are now so excellent that in this field the very definition of a "trace" has become almost meaningless.

Distinct biological roles for most essential metals are now well recognized, and approaches to the exploration of their functions have become standardized to the point where they have merged with those employed throughout all of biochemistry. As a consequence, what was once the province of the analytical chemist has not only become part of the mainstream of biochemical knowledge and thought but can even be considered a scientific discipline in its own right. "Metallobiochemistry" is a field which has grown and matured rapidly over the past decade to encompass a wide variety of scientific subspecialties but with primary emphasis on the role of a metal or metals in a biochemical system. Metalloenzymes have been the central investigatory targets of this field with most efforts

directed toward the participation of the metal in catalysis. Importantly, the very recognition, purification, and characterization of metalloenzymes have depended as much on progress in the physical chemistry of proteins and the methodology for their isolation and characterization as on advances in spectroscopic, electrochemical, isotopic, and other methods for the detection of metals.

The appropriate analytical method depends, among other things, on the specific metal in question, the nature of the biological matrix, the amount of material available, and whether other metals may be present as well. No method of analysis is helpful unless proper precautions have been taken during the enzyme isolation procedure to avoid either loss of intrinsic metal, addition of extraneous metal, or substitution of the intrinsic by an extraneous metal. Hence a healthy paranoia based on long experience has led to a number of practices generally regarded as safe for avoiding such contamination problems. All of these are detailed in this volume of Metallobiochemistry, Part A, which provides both the emerging and the practicing metallobiochemist with the tools to answer what should be the number one and two questions: Is this enzyme a metalloenzyme? What metal is it? Subsequent volumes will consider the multiplicity of techniques that can be applied to the study of metalloenzymes by virtue of the fact that they contain a metal and to specific classes of metallobiochemicals. In particular, the role of metals in nonenzymatic proteins will be emphasized as will their roles in metalloenzymes other than as components of the catalytic mechanism.

We are deeply indebted to all of the authors who contributed to this volume for their patience, cooperation, and enthusiasm. We also appreciate the advice and suggestions from all those who participated in our initial survey. To those at Academic Press who were so diligent and indulgent we express our sincere thanks.

Finally, we would like to acknowledge both our affection and kindred spirit for the founding editors, Nate Kaplan and Sid Colowick, who will long be remembered for their contributions to science, humanity, and the dignity of man.

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METHODS IN ENZYMOLOGY

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