



Q67  
Z1

7963681

# BIOLOGICAL MINERALIZATION

EDITED BY

Isadore Zipkin

SCHOOL OF DENTISTRY  
UNIVERSITY OF CALIFORNIA  
SAN FRANCISCO, CALIFORNIA

---



E7963681



A WILEY-INTERSCIENCE PUBLICATION

JOHN WILEY & SONS

New York • London • Sydney • Toronto

Copyright © 1973, by John Wiley & Sons, Inc.

All rights reserved. Published simultaneously in Canada.

No part of this book may be reproduced by any means, nor transmitted, nor translated into a machine language without the written permission of the publisher.

***Library of Congress Cataloging Publication Data:***

Zipkin, Isadore.

Biological mineralization.

Includes bibliographical references.

1. Minerals in the body. 2. Calcification.
3. Bone. 4. Teeth. I. Title.

QP531.Z55            596'.01'8            72-8003  
ISBN 0-471-98381-0

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

# Biological Mineralization

---

This volume is dedicated to the memory of my parents

ABRAHAM and BLUMA

and to my family

LILLIAN, RICHARD, and MICHAEL

---

# Authors

---

- HOWARD J. ARNOTT, The Cell Research Institute and the Department of Botany, The University of Texas, Austin, Texas.
- B. N. BACHRA, Laboratory for Physiological Chemistry, University of Leiden, Leiden, The Netherlands.
- REGINALD R. COOPER, Department of Orthopedic Surgery, The University of Iowa Medical School, Iowa City, Iowa.
- MARCEL J. DALLEMAGNE, \* Institut de Thérapeutique Expérimentale, Université de Liege, Belgium.
- STEPHEN B. DOTY, Division of Orthopedic Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland.
- E. D. EANES, Laboratory of Biological Structure, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland.
- EUGENE EISENBERG, Medical Services, San Francisco General Hospital and School of Medicine, University of California, San Francisco, California.
- J. ENNEVER, Dental Science Institute, The University of Texas, Houston, Texas.
- VERNICE FERGUSON, West Side Veterans Administration Hospital, Chicago, Illinois.
- HERBERT FLEISCH, Department of Pathophysiology, University of Berne, Berne, Switzerland, and Laboratory for Experimental Surgery, Davos, Switzerland.
- ROBERT M. FRANK, Centre de Recherches Odontologiques, Faculté de Chirurgie Dentaire, Strasbourg, France.
- JOAN A. FRIEDLAND, Veterans Administration Hospital, Houston, Texas.
- HAROLD M. FULLMER, Institute of Dental Research, Medical Center, University of Alabama, Birmingham, Alabama.
- GIULIO GABBIANI, Institut de Médecine et de Chirurgie Expérimentales, Université de Montréal, Montréal, Canada.
- D. GASTER, Chicago, Illinois.
- ITZHAK GEDALIA, Laboratory of Oral Chemistry and Fluoride Research, The Hebrew University-Hadassah School of Dental Medicine, Jerusalem, Israel.
- JOHN F. GOGGINS, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland.
- K. GUGGENHEIM, Department of Nutrition, The Hebrew University-Hadassah Medical School, Jerusalem, Israel.

\* Deceased.

- ROBERT PROULX HEANEY, Department of Internal Medicine, Creighton University School of Medicine, Omaha, Nebraska.
- J. W. HEKKELMAN, Laboratory of Cell Biology and Histology, University of Leiden, Leiden, The Netherlands.
- G. M. HERRING, Medical Research Council External Scientific Staff, Bone Research Laboratory, Churchill Hospital, Headington, Oxford, England.
- HENRY D. ISENBERG, The Long Island Jewish Medical Center, New Hyde Park, New York, and The SUNY Downstate Medical Center, Brooklyn, New York.
- JENIFER JOWSEY, Mayo Clinic and Mayo Foundation: Section of Surgical Research (Orthopedics), Rochester, Minnesota.
- LEON KRAINTZ, School of Dentistry, University of British Columbia, Vancouver, B. C., Canada.
- LEROY S. LAVINE, The Long Island Jewish Medical Center, New Hyde Park, New York, and The SUNY Downstate Medical Center, Brooklyn, New York.
- S. A. LEACH, Department of Dental Science, School of Dental Surgery, University of Liverpool, Boundary Place, Liverpool, England.
- ABRAHAM R. LIBOFF, Department of Physics, New York University, New York, New York.
- EDWARD J. MILLER, University of Alabama, Birmingham, Alabama.
- M. W. NEUMAN, Department of Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, New York.
- W. F. NEUMAN, Department of Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, New York.
- ROBERT E. PYKE, 2496 Stone, Northwood V, Ann Arbor, Michigan.
- LEON J. RICHELLE, Institute of Materials Science, University of Connecticut, Storrs, Connecticut.
- WILLIAM G. ROBERTSON, Department of Pathophysiology, University of Berne, Berne, Switzerland and Laboratory for Experimental Surgery, Davos, Switzerland.
- C. ROBINSON, Biological Research Unit, School of Dentistry, University of Leeds, Leeds, England.
- ROBERT A. ROBINSON, Division of Orthopedic Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland.
- R. GRAHAM G. RUSSELL, Department of Pathophysiology, University of Berne, Berne, Switzerland, the Laboratory for Experimental Surgery, Davos, Switzerland, and Nuffield Orthopaedic Centre, University of Oxford, Oxford, England.
- HANS SELYE, Institut de Médecine et de Chirurgie Expérimentales, Université de Montréal, Montréal, Canada.
- MORRIS H. SHAMOS, Department of Physics, New York University, New York, New York.
- IRVING M. SHAPIRO, Department of Biochemistry, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.
- A. C. SMILLIE, Biochemical Research Unit, University of Otago Dental School, Dunedin, New Zealand.
- HERTA SPENCER, Metabolic Section, Veterans Administration Hospital, Hines, Illinois.
- E. STOREY, Department of Conservative Dentistry, University of Melbourne, Melbourne, Victoria, Australia.

I. TAKAZOE, Tokyo Dental College, Tokyo, Japan.

JOHN D. TERMINE, Laboratory of Biological Structure, National Institute of Dental Research, National Institutes of Health, Bethesda, Maryland.

BEATRIZ TUCHWEBER, Institut de Médecine et de Chirurgie Expérimentales, Université de Montréal, Montréal, Canada.

MARSHALL R. URIST, Bone Research Laboratory, School of Medicine, University of California, Los Angeles, California.

J. A. WEATHERELL, Biological Research Unit, School of Dentistry, University of Leeds, Leeds, England.

RALPH W. G. WYCKOFF, Department of Physics, University of Arizona, Tucson, Arizona.

I. ZIPKIN, Division of Periodontology, School of Dentistry, University of California, San Francisco, California.



## Preface

---

A number of reviews and symposia have been written for the scientist with a deep esoteric interest in various phases of biological mineralization. Indeed, specialists have developed specific areas of the anatomy, physiology, biochemistry, and biophysics of the "hard tissues," and learned treatises have been presented as a result of these studies. The major objective of this volume is to present these and related aspects of mineralized tissues in a language and style that would appeal to the student and the academician whose field is not mineralization. It is intended for the scientist who desires to broaden his perspectives to encompass a field foreign to his central interest, but in which he has a reading of peripheral interest. Hence, an attempt has been made to deal with the basic concepts and to minimize the details.

The volume opens with a chapter on apatite as a possible template for life; that is, the primordial material for the evolution of living matter. Part Two deals with the inorganic and organic composition of bones and teeth as well as with the enzymes and hormones concerned with mineralization. Part Three treats the methodologies concerned with the biophysical properties of bones and teeth. Thus the ultrastructure of bones and teeth at the electron microscope level is presented. Such biophysical techniques as x-ray diffraction, infrared and electron spin resonance, as well as autoradiography and microradiography are presented to give some relevance of structure to function. Part Four is concerned with the role that such specific elements as strontium, manganese, copper, zinc, calcium, phosphorus, magnesium, and fluoride may play in the nutritional biochemistry of bone.

Part Five describes some unique mammalian calcification patterns as seen in the fetal hard structures, in fossils, and in dental calculus. In addition, a type of ectopic calcification as seen in calciphylaxis and calcergy is discussed. Calcification in such nonmammalian systems as plants, bacteria, and protozoa is described in Part Six wherein apatite formation may (bacteria and protozoa) or may not (plants) play an important role. In the interests of brevity, such nonapatitic calcification patterns as found in most marine invertebrates are not discussed. "Calcification" involves a specific role of

calcium in the construction of a hard tissue so that "mineralization" would be a more general term. Indeed, the diatom prefers to use silicon rather than calcium for its supporting structure. This particular type of mineralization could then be more specifically called "silicification."

The last three parts deal with more general considerations in the physiology of bone. Thus Part Seven is concerned with balance studies in the human under physiological stress involving elements intrinsically related to mineralization. In a companion chapter, the effect of mechanical stress on clinical growth and development of bone in the experimental animal is presented with relevance to the dental discipline of orthodontia. Part Eight deals with various inducers and inhibitors of calcification, whereas the last part is concerned with the kinetics of calcification as related to both nucleation and to turnover rates.

It is hoped that this volume will appeal to the serious scientist whose field is not calcification (or mineralization), and that he will find a leisurely perusal of the various chapters to be both interesting and enjoyable.

I. ZIPKIN

*San Francisco, California*  
*June 1972*

## Contents



## PART ONE: A HYPOTHESIS FOR THE ORIGIN OF LIFE

1. In the Beginning There Was Apatite. By W. F. NEUMAN and M. W. NEUMAN 3

## PART TWO: PHYSIOLOGICAL CHEMISTRY OF BONES, TEETH, AND OTHER CONNECTIVE TISSUES

2. Inorganic Chemistry of Bone. By MARCEL J. DALLEMAGNE and LEON J. RICHELLE 23
3. The Inorganic Composition of Teeth. By J. A. WEATHERELL and C. ROBINSON 43
4. The Mucosubstances of Bone. By G. M. HERRING 75
5. The Collagen of Bone and Cartilage. By EDWARD J. MILLER 95
6. The Lipids of Skeletal and Dental Tissues: Their Role in Mineralization. By IRVING M. SHAPIRO 117
7. The Chemistry of the Organic Phase of Teeth. By A. C. SMILLIE 139
8. Enzyme Biochemistry of Bone. By J. W. HEKKELMAN 165
9. Enzymes of Connective Tissues. By JOHN F. GOGGINS and HAROLD M. FULLMER 185
10. Hormones in Mineralization: A Brief Survey. By LEON KRAINTZ 207

## PART THREE: BIOPHYSICAL CHEMISTRY OF BONE

11. X-Ray Diffraction of Vertebrate Hard Tissue. By E. D. EANES 227
12. Electron Microscopy of Mammalian Bone. By ROBERT A. ROBINSON, STEPHEN B. DOTY, and REGINALD R. COOPER 257
13. Autoradiographic and Microradiographic Studies of Bone. By JENIFER JOWSEY 297
14. Solid State Physics of Bone. By ABRAHAM R. LIBOFF and MORRIS H. SHAMOS 335

15. Infrared and Electron Spin Resonance Spectroscopy of Hard Tissues. By JOHN D. TERMINE 397
16. Electron Microscopy of the Dental Hard Tissues. By ROBERT M. FRANK 413

PART FOUR: BIOLOGICAL BEHAVIOR OF SELECTED CHEMICAL COMPONENTS OF BONE AND THEIR INTERACTIONS

17. The Biological Metabolism of Strontium. By EUGENE EISENBERG 435
18. The Role of Manganese, Copper, and Zinc in the Physiology of Bones and Teeth. By K. GUGGENHEIM and D. GASTER 443
19. Relationships of Calcium, Phosphorus, Magnesium, and Fluoride in Hard- and Soft-Tissue Calcification. By ROBERT E. PYKE 463
20. Fluoride in the Calcified Structures. By I. ZIPKIN 487

PART FIVE: UNIQUE APATITE MINERALIZATION PATTERNS

21. Fetal Calcification. By ITZHAK GEDALIA 509
22. The Microstructure and Composition of Fossils. By RALPH W. G. WYCKOFF 527
23. Experimental Ectopic Calcification (Calciphyllaxis and Calcergy). By GIULIO GABBIANI, BEATRIZ TUCHWEBER, and HANS SELYE 547
24. Dental Calculus. By S. A. LEACH 587

PART SIX: NONMAMMALIAN MINERALIZATION

25. Plant Calcification. By HOWARD J. ARNOTT 609
26. Bacterial Calcification. By J. ENNEVER and I. TAKAZOE 629
27. Protozoan Calcification. By HENRY D. ISENBERG and LEROY S. LAVINE 649

PART SEVEN: CLINICAL STUDIES

28. Human Balance Studies in Mineral Metabolism. By HERTA SPENCER, JOAN A. FRIEDLAND, and VERNICE FERGUSON 689
29. The Dental Implications of Bone Growth. By E. STOREY 729

PART EIGHT: INITIATORS AND INHIBITORS OF MINERALIZATION

30. Biologic Initiators of Calcification. By MARSHALL R. URIST 757
31. Inhibitors of Mineralization. By R. GRAHAM G. RUSSELL, WILLIAM G. ROBERTSON, and HERBERT FLEISCH 807

## PART NINE: CALCIFICATION KINETICS

32. Calcium Tracers in the Study of Vertebrate Calcium Metabolism.  
By ROBERT PROULX HEANEY 829
33. Nucleation in Biological Systems. By B. N. BACHRA 845
- INDEX 883

A Hypothesis  
for the Origin of Life

---

PART ONE



# ONE In the Beginning There Was Apatite

---

W. F. NEUMAN\* and M. W. NEUMAN\*

I. INTRODUCTION	3
II. HISTORICAL	4
III. THE PROBLEM	6
IV. THE FORMATION OF MONOMERS	7
V. THE PRODUCTION OF POLYMERS	8
VI. THE POSSIBLE ROLE OF CRYSTALS AND TIDES	9
VII. ADSORPTION OF WATER AND SOLUTES BY APATITE CRYSTALS	11
VIII. THE CATALYSIS OF PHOSPHORYLATIONS BY APATITE CRYSTALS	13
IX. THE CATALYSIS OF AMINO ACID POLYMERIZATION	15
X. THE POLYMERIZATION OF NUCLEOTIDES	15
XI. THE FINAL STAGES OF PREBIOTIC EVOLUTION	17
XII. CONCLUSION	
References	19

---

## I. INTRODUCTION

Was there ever a child who, at some troubled moment in his search for selfhood, did not ask, "Mommy, where did I come from?" And was there ever a parent, after stumbling through the story of the "birds and bees," who

\* Department of Radiation Biology and Biophysics, School of Medicine and Dentistry, University of Rochester, Rochester, New York.



himself did not wonder: "Yes, but where did *we* come from?" and continue from there to: "Where and how did life arise?"

The origins of life is one of the ubiquitous questions which have plagued man since he became aware of the transience of life and his own limited mortality. For eons of time, man had to content himself with answers derived from myths and inspired revelation. But today, in our teeming technological world, he is prone to turn to the modern muse, Science, for gratifyingly hard, factual answers to such troubling questions. Unfortunately, as we shall show, Science has no hard, factual answers. Rather, there exist an array of possible answers of underdetermined probability such that the layman and the professional alike can more or less choose what he wishes to believe. Because this situation exists and because this chapter introduces a collection of works on biological mineralization, we choose to believe that: "IN THE BEGINNING THERE WAS APATITE."

This idea, that apatite crystals may have performed a crucial role in prebiotic evolution, requires a contextual setting. However, because the period of scientific thought on the origins of life is very short, so also will be its historical review.

## II. HISTORICAL (1-3)

From ancient times until the late nineteenth century, all great thinkers subscribed to the cult of Spontaneous Generation. It was generally believed that all sorts of living things (insects, worms, frogs, mice, and even crocodiles!) could arise *de novo* from rotting materials (the less attractive, the better!). There even developed recipes for generating life, the most famous being that of van Helmont for making mice from wheat and soiled underwear.

