



Q.55  
E601

HENRY FORD HOSPITAL  
International Symposium

8201924  
外文书库

# ENZYMES: Units of Biological Structure and Function

Edited by  
**OLIVER H. GAEBLER**  
Head, Biochemistry Department  
Edsel B. Ford Institute for Medical Research,  
Detroit



1956

ACADEMIC PRESS INC. • PUBLISHERS • NEW YORK

Copyright ©, 1956,

by

ACADEMIC PRESS INC.

125 EAST 23RD STREET

NEW YORK, 10, N. Y.

*All Rights Reserved*

NO PART OF THIS BOOK MAY BE REPRODUCED  
IN ANY FORM, PHOTOSTAT, MICROFILM, OR ANY  
OTHER MEANS, WITHOUT WRITTEN PERMISSION  
FROM THE PUBLISHERS.

*Library of Congress Catalog Card Number: 56-8683*

## Participants

Arnon, Daniel I.	Berkeley, California
Ball, Eric G.	Boston, Massachusetts
Chance, Britton	Philadelphia, Pennsylvania
Cohn, Melvin	St. Louis, Missouri
Cori, Carl F.	St. Louis, Missouri
Davis, Bernard D.	New York, New York
Demerec, M.	Long Island, New York
Ephrussi, Boris	Paris, France
Gale, Ernest F.	Cambridge, England
Green, David E.	Madison, Wisconsin
Hastings, A. Baird	Boston, Massachusetts
Hershey, A. D.	Long Island, New York
Hogeboom, George H.	Bethesda, Maryland
Horowitz, Norman H.	Pasadena, California
Hotchkiss, Rollin D.	New York, New York
Kamen, Martin D.	St. Louis, Missouri
Kuff, Edward L.	Bethesda, Maryland
Lardy, Henry A.	Madison, Wisconsin
Lederberg, Joshua	Madison, Wisconsin
Lehninger, Albert L.	Baltimore, Maryland
Lipmann, Fritz	Boston, Massachusetts
McElroy, William D.	Baltimore, Maryland
Mazia, Daniel	Berkeley, California
Mommaerts, W. F. H. M.	Cleveland, Ohio
Monod, Jacques	Paris, France
Morales, Manuel F.	Bethesda, Maryland
Mudge, Gilbert H.	Baltimore, Maryland

Ochoa, Severo	New York, New York
Palade, George E.	New York, New York
Pauling, Linus	Pasadena, California
Potter, Van R.	Madison, Wisconsin
Quastel, J. H.	Montreal, Canada
Singer, Thomas P.	Detroit, Michigan
Spiegelman, Sol	Urbana, Illinois
Stotz, Elmer H.	Rochester, New York
Strehler, Bernard L.	Chicago, Illinois
Sutherland, Jr., Earl W.	Cleveland, Ohio
Szent-Györgyi, Albert	Woods Hole, Massachusetts
Taggart, John V.	New York, New York
Tatum, Edward L.	Stanford, California
Velick, Sidney F.	St. Louis, Missouri
Wald, George	Cambridge, Massachusetts
Welch, Arnold D.	New Haven, Connecticut
Yanofsky, Charles	Cleveland, Ohio

## PREFACE

Recorded in this volume are the proceedings of an International Symposium on *Enzymes: Units of Biological Structure and Function*, held at Henry Ford Hospital, Detroit, November 1-3, 1955.

There is a recurrent need for symposia in which representatives of many different scientific disciplines are brought together to discuss topics of common interest. The present Symposium was an event of this type. Among the participants were representatives of the basic sciences of the medical curriculum, as well as of many nonmedical departments interested in enzymes as structural and functional units. Devotees of another "unit," the gene, were also well represented. The proceedings should, therefore, be of interest in many fields, notably microbiology, biology, genetics, physiology, pharmacology, pathology, nutrition, biochemistry, and biophysics. It is also significant that this review of typical current enzyme studies was suggested by members of the clinical staff of the Hospital, who noted the growing impact of this field of investigation on medicine in the broader sense.

The "Introduction to the Purpose and Scope of the Symposium" includes a preview of the six sessions and two evening lectures, and there is an extensive review of the meeting [*Science* **123**, 149 (1955)] containing brief comments on the individual contributions; it therefore seems unnecessary to repeat what has been said elsewhere.

Acknowledgments for initiative and effort are due to many. The idea of sponsoring a series of symposia was presented to the Medical Board of Henry Ford Hospital by Dr. Robin C. Buerki, Executive Director of the Hospital, on May 19, 1952. Consideration of enzymes as a future topic was suggested by Dr. R. H. Durham in July 1953. A year later, this emergent idea was presented in more specific form by Dr. C. E. Rupe and adopted.

The Advisory Program Committee, whose names appear on a following page, devoted a great deal of time to selection of topics and speakers. It is a pleasure to acknowledge their splendid services, and to voice the mutual satisfaction of the Advisory and Local Committees with the high scientific standards maintained by the participants, who ultimately contributed the Symposium itself.

Particular recognition is due to Dr. C. E. Rupe of the Local Committee for efficient handling of all matters pertaining to invitations, accommoda-

tions, and registration, which reached a total of 605. Not to be forgotten are other decidedly endergonic aspects of such meetings: administrative ones, to which Mr. William Nye, Mr. David L. Everhart, and Dr. J. T. Howell devoted a great deal of time; dietetic ones, for which acknowledgments are due to Miss Margaret King and her staff; secretarial ones, cheerfully and efficiently borne by Miss Dorothy Reid and Mrs. Eleanore Lugosky; and numerous well-rendered photographic, purchasing, and maintenance services.

*Detroit, Michigan*  
*February, 1956*

O. H. GAEBLER

The Symposium was jointly sponsored by the Henry Ford Hospital and the Edsel B. Ford Institute for Medical Research, Detroit, Michigan, and held at the Hospital, November 1, 2, 3, 1955.

### Program Committee

#### Advisory:

CARL F. CORI

DAVID E. GREEN

ALBERT L. LEHNINGER

ELMER H. STOTZ

ARNOLD D. WELCH

#### Local:

BROCK E. BRUSH

PAUL R. DUMKE

OLIVER H. GAEBLER

DONALD G. REMP

CLARENCE E. RUPE

THOMAS P. SINGER



# Contents

Preface.....	
Introduction: Purpose and Scope of the Symposium .....	I
BERNARD D. DAVIS	
Part I: The Origin of Enzymes	
Chairman: Bernard D. Davis	
1. Remarks on the Mechanism of Enzyme Induction .....	7
JACQUES MONOD	
2. Enzymes in Cellular Differentiation .....	29
BORIS EPHRUSSI	
Added Comment .....	41
MELVIN COHN	
General Discussion .....	46
BERNARD D. DAVIS, JACQUES MONOD, SOL SPIEGELMAN, CARL C. LINDEGREN, BORIS EPHRUSSI	
3. Nucleic Acids and Enzyme Synthesis .....	49
ERNEST F. GALE	
4. On the Nature of the Enzyme-Forming System .....	67
SOL SPIEGELMAN	
Added Comment .....	90
SIDNEY F. VELICK	
General Discussion .....	93
BERNARD D. DAVIS, SOL SPIEGELMAN, JACQUES MONOD, BORIS ROTMAN, ERNEST F. GALE, ARTHUR B. PARDEE, EDWARD L. TATUM, A. D. HERSHEY, MELVIN COHN, MAHLON B. HOAGLAND, ALVIN MARKOVITZ	
Part II: The Status of the Gene-Enzyme Relationship	
Chairman: Edward L. Tatum	
Chairman's Comments .....	107
EDWARD L. TATUM	
5. Genetic Structure and Function in Bacteriophage T2 .....	109
A. D. HERSHEY	

6. The Genetic Organization of the Deoxyribonucleate Units Functioning in Bacterial Transformations .....	119
ROLLIN D. HOTCHKISS	
Added Comment .....	131
M. DEMEREC	
General Discussion .....	134
NORMAN H. HOROWITZ, JACQUES MONOD, EDWARD L. TATUM, BERNARD D. DAVIS, CHARLES YANOFSKY, M. DEMEREC, A. D. HERSHEY, SOL SPIEGELMAN	
7. The Role of the Genes in the Synthesis of Enzymes .....	139
NORMAN H. HOROWITZ AND MARGUERITE FLING	
8. Gene Interactions in Enzyme Synthesis .....	147
CHARLES YANOFSKY	
Comments on Gene-Enzyme Relationship .....	161
JOSHUA LEDERBERG	
General Discussion .....	170
STUART MUDD, SOL SPIEGELMAN, RUTH SAGER, NORMAN H. HOROWITZ, EDWARD L. TATUM, ROBERT J. RUTMAN, HARRY EAGLE, CYRUS LEVINthal, NATHAN O. KAPLAN, JACQUES MONOD	

### Evening Lecture

9. The Future of Enzyme Research .....	177
LINUS PAULING	

### Part III: Enzymes and Cell Structure

Chairman: George H. Hogeboom

9. Electron Microscopy of Mitochondria and Other Cytoplasmic Structures .....	185
GEORGE E. PALADE	
10. Physiology of Mitochondria .....	217
ALBERT L. LEHNINGER	
11. Sedimentation and Biochemical Characteristics of Cytoplasmic Particles .....	235
EDWARD L. KUFF AND GEORGE H. HOGEBOOM	
Added Comment .....	252
VAN R. POTTER	

<b>General Discussion</b> .....	<b>257</b>
FRITZ LIPMANN, ALBERT L. LEHNINGER, DANIEL I. ARNON, HERRICK BALTSCHIEFFSKY, BRITTON CHANCE, GEORGE E. PALADE	
<b>12. Nuclear Products and Nuclear Reproduction</b> .....	<b>261</b>
DANIEL MAZIA	
<b>13. Localization of Photosynthesis in Chloroplasts</b> .....	<b>279</b>
DANIEL I. ARNON	
<b>General Discussion</b> .....	<b>306</b>
CYRUS LEVINTHAL, DANIEL MAZIA, SEVERO OCHOA, DANIEL I. ARNON, NATHAN O. KAPLAN, VERNON CHELDELIN, GEORGE E. PALADE, HENRY A. LARDY, ALBERT L. LEHNINGER, DAVID E. GREEN, FRITZ LIPMANN	
<b>Part IV: Enzymatic Basis of Some Physiological Functions</b>	
Chairman: A. Baird Hastings	
<b>14. The Actomyosin System and its Participation in Organized Enzyme Reactions</b> .....	<b>317</b>
W. F. H. M. MOMMAERTS	
<b>15. Is Energy Transferred from ATP to Myosin at the Moment that ATP is Split?</b> .....	<b>325</b>
MANUEL F. MORALES	
<b>16. Enzymatic Aspects of Excretory Mechanisms</b> .....	<b>337</b>
JOHN V. TAGGART	
<b>Added Comment</b> .....	<b>347</b>
GILBERT H. MUDGE	
<b>General Discussion</b> .....	<b>349</b>
A. BAIRD HASTINGS, JOHN GERGELY, MANUEL F. MORALES, W. F. H. M. MOMMAERTS, SIDNEY BERNHARD	
<b>17. The Biochemistry of Visual Excitation</b> .....	<b>355</b>
GEORGE WALD	
<b>18. The Enzymatic Basis of Light Emission</b> .....	<b>369</b>
WILLIAM D. MCELROY AND ARDA GREEN	
<b>Added Comment</b> .....	<b>381</b>
BERNARD L. STREHLER	
<b>General Discussion</b> .....	<b>383</b>
GEORGE WALD, MANUEL F. MORALES, WILLIAM D. MCELROY, W. F. H. M. MOMMAERTS, DANIEL I. ARNON, BERNARD L. STREHLER, J. J. WOLKEN	

## Evening Lecture

Mechano-chemical Coupling in Muscle .....	393
ALBERT SZENT-GYÖRGYI	

## Part V. Cellular Energy Sources

Chairman: Fritz Lipmann

19. Components of the Cytochrome System .....	401
ELMER H. STOTZ, MARTIN MORRISON, AND GUIDO MARINETTI	
20. Succinic Dehydrogenase .....	417
THOMAS P. SINGER, EDNA B. KEARNEY, AND VINCENT MASSEY	
Added Comment .....	433
ERIC G. BALL	
General Discussion .....	440
VAN R. POTTER, THOMAS P. SINGER, FRITZ LIPMANN, RICHARD J. WINZLER, HAROLD A. NEUFELD	
Chairman's Comments .....	444
FRITZ LIPMANN	
21. Interaction of Adenosinediphosphate with the Respiratory Chain ....	447
BRITTON CHANCE	
22. Structural and Enzymatic Pattern of the Electron Transfer System ..	465
DAVID E. GREEN	
23. Hematin Compounds in the Metabolism of Photosynthetic Tissues ..	483
MARTIN D. KAMEN	
General Discussion .....	498
W. F. H. M. MOMMAERTS, BRITTON CHANCE, DANIEL I. ARNON, FRITZ LIPMANN, DAVID E. GREEN, GEORGE E. PALADE, J. A. BASSHAM, MANUEL F. MORALES, ALVIN NASON, RALPH W. MCKEE, RONALD ESTABROOK, EDWARD L. TATUM	

## Part VI: Regulation of Enzyme Activity

Chairman: Severo Ochoa

Chairman's Comments .....	507
24. Relations between Enzymes and Permeability (Membrane Transport) in Bacteria .....	509
BERNARD D. DAVIS	

25. Action of Drugs on Enzyme Systems .....	523
J. H. QUASTEL	
Added Comment .....	536
EARL W. SUTHERLAND, JR.	
General Discussion .....	541
SEVERO OCHOA, BERNARD D. DAVIS, CYRUS LEVINTHAL, JACQUES MONOD, STUART MUDD, OLOV LINDBERG, ARTHUR B. PARDEE	
26. Interference with Nucleic Acid Metabolism .....	547
ARNOLD D. WELCH	
27. Regulation of Enzyme Activity in Muscle During Work .....	573
CARL F. CORI	
Added Comment .....	584
HENRY A. LARDY AND R. E. PARKS, JR.	
Chairman's Comments .....	588
SEVERO OCHOA, ROBIN C. BUERKI	
Author Index .....	589
Subject Index .....	604

# Introduction: Purpose and Scope of the Symposium

BERNARD D. DAVIS

Department of Pharmacology, New York University  
College of Medicine, New York, New York

For at least two decades a large fraction of research on enzymes has been concerned with their role in intermediary metabolism, and this work has marched forward pretty much in a straight line. Biochemists have learned how to prepare extracts that will carry out many of the same chemical reactions as the intact cells. The enzymes involved have then been separated, purified often to the point of crystallization, and individually characterized in terms that are now quite standardized. This approach has brought biochemistry to a new level of precision, and it is still both necessary and highly rewarding. However, enzyme research has of late been tending to spread in a number of other directions. It is with these newer approaches that the present Symposium is concerned.

One reason for this shift of emphasis, it seems to me, is the following: the classical enzymatic approach to problems of intermediary metabolism has become so efficient and has attracted so many students that it is now rapidly consuming its own substrate. Thus simple and versatile methods (gasometric, spectrophotometric, and chromatographic) for chemical microanalysis have been developed; isotopically labeled compounds have been of great value in a number of ways; and genetic changes have been used to block metabolic paths at a single reaction with a cleanness and versatility that inhibitors could not reach. With the help of these methods investigators in literally hundreds of laboratories throughout the world have managed to organize an extraordinary amount of cosmos from the chaos of biochemical processes.

As an index of the extent of this progress, I estimate that roughly half the intermediates involved in the biosynthesis of the common amino acids have already been defined, and many of the corresponding enzymes have been studied in more or less detail. And as an index of the biological significance of this work it should be emphasized that the results obtained with extracts have for the most part been concordant with those furnished by isotopic and genetic studies on intact cells. There is, therefore,

good reason to believe that, in general, the reactions observed in isolated enzyme systems do reflect physiological events and are not artifacts of isolation.

A few years ago there seemed to be no visible limit to the number, variety, and complexity of the reactions to which one could apply the well-developed methodology of intermediary metabolism. It had become a mature discipline, analogous to organic chemistry. But meanwhile the picture has changed. For there has been a growing suspicion that highly specific macromolecules—proteins, DNA, and presumably RNA—do not attain their complexity through a summation of simple enzyme-controlled reactions, each adding one building block at a time, but rather are formed through some quite different mechanism, involving a multiheaded template. If this be so, then the number of simple reactions that are carried out by enzymes is finite after all; and of these the number that are widely distributed in biological systems may be surprisingly small. Indeed, I suspect that this limitation in the number of available enzymes, combined with the standardization of approach, is largely responsible for the competitiveness and duplication of effort that are so striking in contemporary biochemistry. I refer to this state of affairs because I am convinced, from having worked in other fields such as microbial genetics, that it is not an inevitable state in science. The obvious cure for such crowding in our community is, of course, further suburban development; and this is one reason for exploring in this Symposium the more outlying territories of enzyme research.

But I do not wish to emphasize too much the importance of such a negative reason. For clearly an enormous amount of work remains to be done before the reservoir of simple enzyme-controlled reactions is exhausted. A much more important reason for our orientation is the inherent interest of recent studies on other aspects of enzymes, and the exciting prospects they offer for the future. The techniques now available make it possible to tackle at a molecular level of organization certain problems that until lately could be studied exclusively by physiologists or geneticists, at quite a different level. It is the purpose of this Symposium to gather together a group of people to discuss such attempts, groping in some cases and well advanced in others, to relate enzymes to some of the more complex aspects of cell physiology.

These aspects are clearly revealed in the program of Symposium. The first day will be concerned with the mechanism of enzyme formation. This problem converges with that of the form and function of DNA and RNA, and with the essentially identical problem, approached from another angle, of gene action.

In addition, since we tend, erroneously, to think of the mutable units of the geneticist as being the only factors that determine the inheritable properties of a cell, it has been considered advisable to include a discussion of the other large class of heredity-determining mechanisms. These are the environmentally directed changes in the inheritable properties of cells that go variously under the name of differentiation, morphogenesis, or epigenetics. This process is at present as mysterious to the biologist as to the biochemist, and the importance of giving it much more attention is underscored by the likelihood that the origin of neoplasms lies in aberrations of differentiation.

A second major area of interest concerns the mechanisms that regulate metabolic activities. These mechanisms include the action of various hormones, the adaptive aspects of enzyme formation, and the relation of enzymes to the structural organization of the cell. The most prominent of these structural features at present are two: the grouping of enzymes into particles, and the presence of membranes exhibiting selective permeability and concentrating power. This development might be summed up by saying that biochemists, having found useful the simplified model of the cell as a bag of enzymes, are now increasingly inquiring into the nature of the bag. And where a few years ago many investigators were careful to avoid making further acquaintance with an enzyme unless it could be purified of the taint of its former associations, the tide is now turning and the trick is to get multienzyme systems out of the cell with a minimum of disorganization. These topics of regulation and organization will come up repeatedly during the second and third days.

Also spread through these two days will be a third major topic: transduction between the chemical energy of enzymatic reactions and other forms of energy. These include mechanical work, the osmotic work of excretory processes and intracellular concentration, emission of light, the uptake of light in photosynthesis and in vision, and electrical activity, especially of nerve cells.

In the time available it will not be possible to provide complete coverage of the stated subject of the Symposium, enzymes in relation to biological structure and function. It will therefore be necessary to forego detailed discussion of the more chemical aspect of enzyme research, which probably has the widest interest of all, since it aims at elucidating the intimate mechanism of enzyme action. However, I am sure we shall hear some provocative suggestions on this subject when Dr. Pauling conducts us on an excursion into the future.

I have already emphasized that this Symposium is particularly concerned with bringing into prominence the newer directions of enzyme



research. Accordingly, the participants have been encouraged to engage in judicious projection of stimulating hypotheses, even where the experimental support may be scant. At the same time, to die by drowning in a flood of loose talk is hardly more pleasant than to die of thirst in a desert of facts. I hope we will be able to maintain a nice, comfortable, middle range of humidity!