The Enzymes

CHEMISTRY AND MECHANISM OF ACTION

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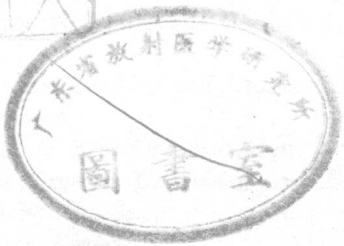
VOLUME I, PART I



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Foreword

Recent years have seen a remarkable advance in every phase of enzymology. Indeed, research in this field has progressed to such an extent that a survey of its findings in comprehensive form has become increasingly imperative. Enzymology has become the central province of biochemistry. Enzymes are the principal tools of the living cell; non-enzymatic substances and conditions known to be important for the functioning of living matter in an ever-increasing number of cases have been shown to exert their action by means of enzymes, sometimes as components of enzyme systems, and in other instances by regulating the rate or mode of action of an existent enzyme. It is therefore self-evident that enzymology must form an essential part of all biological sciences. Equally, the problem of the chemical nature of enzymes and its relation to their catalytic activity is one of the most intriguing questions of organic and physical chemistry. Enzymes have been prepared in a pure state, but we cannot yet explain how they exert their enormous and highly specific catalytic action. All that can be done at the present time is to gather and sift available knowledge, present it in an orderly fashion, and try to utilize it for the advancement of enzymology. It is our aim, therefore, to present systematically the accumulated knowledge in the various phases of enzymology as a comprehensive survey which will be of the most efficient service both to those already working in the field and to those preparing to enter it. In order to accomplish this purpose adequately a great number of our colleagues—each of them an authority on certain aspects of the subjects—have been invited to cooperate in this undertaking. In all, seventy-eight scientists in the United States, Europe, and Australia have united in this endeavor, and it is their sustained interest and effort which has made our project possible.

It is understandable that a treatise by different authors should be less homogeneous than a book written by one, were such a work on enzymology possible in our times. However, the editors have thought it better to give the authors considerable liberty in the composition of their chapters than to try achieve a uniformity which could in any case be only superficial. The editors are well aware that a certain amount of overlapping is inevitable between certain chapters, but they deemed it more helpful to the reader to have the individual chapters as complete as possible without too many cross-references.

In the treatise, an introduction into the special chemistry of the various enzymes is given in a section consisting of eight chapters on general questions of enzymology, such as the formation of enzymes, their role in adapta-

tion, their cytological foundation, their relation to other biologically active substances and to immunochemistry. Sections dealing with the physical chemistry of enzymes, the kinetics of enzyme reactions and the inhibition of enzymes by chemical reagents have also been included here. In a special part of the work chapters have been devoted to all enzymes which can be said with any certainty to possess an individual existence and which are reasonably well known. The editors are aware that reactions, said to be enzymatic, have been reported which have not been mentioned here. The reason for the omission is, in the majority of cases, that the enzymatic nature of the reactions seems very doubtful.

Our general idea has been that this work should be a treatise of enzymology; we did not intend to present to the initiated reader recent developments in the chemistry of certain enzymes, or of certain enzymatic processes, but to present, to any reader, the chemistry of the enzyme or the mechanism of a process as a whole—in other words, to present as far as possible, every fact, either old or new, which has a bearing upon the general understanding of the problem in question. In order to achieve this object, it has not been considered necessary or even appropriate to include a comprehensive survey of practical methods used in enzymology. Therefore, methods have been described in these volumes only to the extent that they are required for a complete understanding of the subject.

When trying to systematize the special chemistry of enzymes, one is confronted with various difficulties. The basis of the classification of enzymes is their specificity, and on the principle of reaction and substrate specificity hydrolytic enzymes and certain others can be classified fairly well. However, in other cases it does not seem possible or suitable to adhere strictly to this scheme. In a few instances, the nature of the prosthetic group of an enzyme can be used as the basis of classification, for example, with enzymes containing iron, copper, etc. But with many enzymes, especially those involved in dissimilations known as fermentation, respiration, etc. it has appeared desirable not only to describe the individual enzymes but also to give comprehensive chapters on the mechanisms as such. In a few cases, so very little is known about the participating enzymes that only an overall description of the complex reactions has been presented. The closing chapters of the work are devoted to tumor enzymology and to enzyme technology.

It must be recognized that a very considerable expenditure of time is involved in the preparation of a work of this kind, and that new material will have inevitably appeared in the literature before the release of the subsequent parts of the work. We hope, however, that most of the pertinent information available at the time of publication will be contained in each volume.

The publication of a work of this scope represents a somewhat venturesome enterprise on the part of the Publishers, and the Editors wish to acknowledge the service which the Publishers are rendering to the cause of our science.

An Author and Subject Index will be included at the end of Volume I, Part 2 and Volume II, Part 2. The Subject Indexes will be prepared by Dr. Martha Sinai.

We regret to report that one of our most illustrious associates, Professor Leonor Michaelis, died a short time ago. This is not the proper place to enter upon an evaluation of his work and its importance for enzymology. May it suffice to state that many of his investigations form a lasting part of the fundamentals of biochemistry—of which the reader will find ample evidence in the subsequent pages. Perhaps the chapter written by Michaelis for this treatise may be considered his last contribution to science.

JAMES B. SUMNER
KARL MYRBÄCK

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Author and Subject Indexes for both parts of Volume I will appear at the end of Volume I, Part 2.

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Chapter 1

Introduction

By JAMES B. SUMNER and KARL MYRBÄCK

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I. The Role of Enzymes

One way of defining life is as an orderly functioning of enzymes. Disease manifests itself as a disorder, inhibition, or hyperfunction of enzymes. All sorts of chemical changes take place in living matter; most of these changes do not occur spontaneously. On the contrary, these reactions are so slow that many of them by themselves would not take place at all. The reason why the living cell can bring about these reactions is that it possesses an equipment of catalysts, the enzymes. Practically all reactions which occur in organisms can be attributed to the action of enzymes and enzymes and genes can be called the fundamental units of life.

Only within the past fifty years has the significance and importance of enzymes in biology been fully realized. At the present time the enzyme

field has become greatly broadened, and it now interests the bacteriologist and the researcher in natural sciences as well as the biochemist and the physiologist. Enzymic reactions and the quantitative determination of enzymes are acquiring more and more importance in clinical medicine. Enzymic reactions are of immense value in industrial chemistry.

New enzymes are being discovered every year, and there is little doubt that a great many others await detection. Enzyme chemistry and its application in science and technology is in a state of continuous and rapid evolution.

Enzymes are present in all organisms, both in the cells and in such fluids as plant sap, blood plasma, saliva, gastric juice, urine, and milk. Some enzymes seem to occur dissolved in the cytoplasm; many appear to be bound somehow to cell structures such as mitochondria and different types of granules.

Since hundreds of chemical reactions are necessary for the existence, growth and reproduction of organisms it is readily seen that the enzymes which catalyze these reactions must possess a high degree of efficiency in order that they may all be packed into cells. Enzymes are effective in bringing about chemical reactions at relatively low temperatures and in approximately neutral solutions in water, whereas the catalysts frequently employed by the organic or industrial chemist to bring about the same reactions, i.e., strong sulfuric acid, potassium hydroxide, chlorine, are violently corrosive and often require a temperature of 100° or more.

II. Definitions

An *enzyme* or *ferment* is defined as a catalyst of biological origin, possessing a high molecular weight. The term ferment (Latin, *fermentum*) has been used for centuries; the name enzyme (from Greek $\epsilon\nu\zeta\upsilon\mu\eta$, literally "in yeast" was introduced by Kühne in 1878.

In the light of our modern conception of the chemical nature of enzymes it seems extremely probable that all enzymes are proteins or contain a protein component. Therefore the definition above can be written: "Enzymes are specific, catalytically active proteins, simple or conjugated." It was supposed earlier, as for instance by Willstätter, that all enzymes are composed of an "active prosthetic group" and a "colloidal carrier." However, it seems clear by now that many enzymes are proteins without any detectable prosthetic groups.

A *catalyst* (Berzelius, Mitscherlich, W. Ostwald) is a substance which influences the velocity of a chemical reaction without being used up in the reaction. The statement, that catalysts act "by their mere presence" is certainly not correct. Catalysts take part in reactions, but they reappear in their original form. They change during the reaction, but they describe a cycle and theoretically a catalyst can convert an unlimited amount of