

DYNAMIC ASPECTS OF BIOCHEMISTRY

BY

ERNEST BALDWIN, B.A., PH.D.

*Professor of Biochemistry at University College in the
University of London, formerly Fellow of
St John's College, Cambridge*

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PREFACE TO THE THIRD EDITION

There has been no diminution in the rate of progress of biochemistry during the five years since the last edition of this book appeared. In preparing this new edition it has often been difficult to decide what new material to include and what to leave out. The book was originally planned rather as an elementary than as a reference work and, in the new edition, I have tried to retain its original flavour; to give broad cover rather than a welter of detail.

A considerable number of new discoveries of fundamental and general importance, e.g. those of transketolation, and transaldolation, the new work on photosynthesis, oxidative decarboxylation, purine synthesis and the like, deserve a place in any work of this kind. On the other hand there are fields no less important but in which the available information is very complex and in which even the experts differ, e.g. in the chemistry of nucleic acids and nucleoproteins. While these must be studied by every advanced student they cannot be dealt with at more than a superficial level in such a book as this. I accept full responsibility, therefore, for what may seem to some to be errors of judgement in deciding what to include and what to leave out.

To find space for new material without sacrificing some of the old is manifestly impossible unless the size of the book is to be increased and this, I think, is undesirable. A good deal of drastic pruning has therefore been necessary. Some passages of a mainly historical interest have been removed bodily, others have been abbreviated or condensed. The remainder of the text I have done my best to bring up to date.

I owe much to many friends and colleagues who have brought to my attention a considerable number of papers that had escaped my own notice, and in this connexion I am especially grateful to Drs D. J. Bell and K. R. Rees. The latter also undertook what is surely the most difficult and certainly the most tedious part of the whole task; the preparation of the index.

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Drs E. M. Crook and B. Rabin read large sections of the copy and to them I am grateful for many suggestions and criticisms. If the thermodynamic ideas expressed here are any less exasperating to pure chemists than they were formerly, the credit is due to the influence of these last-named colleagues. To my wife, who helped and supported me in every way and at every stage of this revision, I owe more than I can say.

The Cambridge University Press, which exerted every effort to produce this new edition at high speed and co-operated in every way, deserves my warmest thanks. At times their task has been a difficult one, for the proof reading and type setting operations were separated by some 6,000 miles.

E. B.

LA JOLLA, CALIFORNIA

14 July 1957

PREFACE TO THE FIRST EDITION

IN spite of war-time difficulties and restrictions, Biochemistry has continued to expand more and more rapidly each year, in stature as well as in scope. It has been impossible for many years past for any one worker to read more than a small fraction of the new output, even when foreign journals were available. Without the invaluable aid of the *Annual Reviews of Biochemistry*, to whose authors and editors I and every other biochemist must pay high tribute, the preparation of this new book would have been impossible. Even with their help, some sections of the book will probably be out of date by the time it appears in print, and may well be out of date already in certain respects. But the last few decades have seen the establishment of a considerable body of information which, though it may change considerably in detail, will perhaps not change significantly in substance during the next few years. I venture to hope that a new edition may be called for before the present contents have become wholly archaic, so that there will be opportunity to correct the many faults which have doubtless escaped notice and to bring the whole volume up to date.

The subject-matter of biological chemistry, like that of biology itself, can be roughly divided into two parts; the static, or morphological, and the dynamic, or physiological. Knowledge of the latter demands as an essential pre-requisite a knowledge of the former, and it is therefore a matter for rejoicing that many organic chemists of the present day are devoting their attention to the chemical constitution and configuration of the organic *Bausteine* that form the material basis of living cells. In some fields, notably in that of protein chemistry, the interdependence and collaboration between the organic and the biochemist are so intimate that it is impossible to say which is the organic chemist and which the biochemist. If any differentiation were necessary it could best be made, probably, in terms of their respective attitudes towards the *Bausteine*. For the organic chemist the main focus of attention is the structure and

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configuration of these materials while, for the biochemist, the main problems are those of the behaviour and function of these substances in organized, biological systems.

The more static aspects of these *Bausteine* are already fairly well covered by monographs and review articles, some of which I have indicated in the bibliography; the essentially dynamic aspects, on the other hand, have hitherto been but inadequately described and, in view of their wide importance and interest, I believe that a real demand exists at the present time for a book of this kind.

Elementary Biochemistry is taught in this University in two courses. The first and older of these, Chemical Physiology, forms part of the course in mammalian Physiology, and caters primarily for the needs of medical and veterinary students. For these there already exists a wealth of text-books, which the present volume neither hopes nor desires to supplant. In the second course, much more recently introduced, Biochemistry is taught as an independent scientific discipline, and without that emphasis on clinical problems with which it has usually been associated in the past, and which properly finds a place in Chemical Physiology. For students taking this second course there exists no suitable text-book, and it is primarily with their needs in mind that the present book has been written. I hope, however, that it will also help to open up new horizons to those whose interest in Biochemistry is primarily that of the organic chemist or the clinician in training. Perhaps it will serve too as an introduction to others who, wishing to take an advanced degree course here or elsewhere, find it difficult at the present time to discover suitable elementary reading. With the needs of such students as these in mind I have included a short bibliography of review articles and books, mostly of recent date and written by experts in their respective fields.

In Biochemistry, as in any young but rapidly expanding branch of science, there are fields in which facts are scanty, evidence contradictory and speculation rife. I have tried to avoid such topics, but where this has not been possible I have attempted to give a critical account of the facts but, at the same time, to speculate a little. I cannot wholly subscribe to the doctrine that speculation is out of place in an elementary text-

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book, for there are many gaps in the subject, and unless these can in some way be bridged it is difficult or impossible to give a coherent account. My experience as a teacher has been that coherence is essential in an elementary exposition. Speculation plays and has always played an important part in the advancement of scientific knowledge, for no research worker gropes blindly after he knows not what; he invariably begins with certain reasonable possibilities in mind. In short, he speculates. To speculate unreasonably is worse than not to speculate at all, but providing certain tests of reasonableness and compatibility are applied beforehand, speculation is a valuable tool, and one which finds a place in every scientific workshop. The danger is that speculation is not always recognized as what it is, and I have, therefore, tried to distinguish clearly between fact and fantasy, hoping in this way to steer a middle course between unbridled imagination on the one hand, and an equally undesirable hypertrophy of the critical faculty on the other.

A word of explanation is perhaps necessary for the use in these pages of somewhat novel and certainly unorthodox methods of writing the equations of certain chemical reactions and groups or sequences of reactions. I have adopted them only after a long period of trial. They give a distinctively pictorial representation of chemical events, and many students find such a picture more easily comprehended and remembered than the more formal representations usually adopted. I trust that the reader will exercise the little patience necessary to become familiar with these 'whirligigs', for they have great advantages in cases where a long chain of successive chemical events has to be described briefly and as a whole.

The writing of this book has been largely a spare-time occupation, and there has been little enough spare time during the war years. Progress has often been slow, therefore, and the task has nearly been abandoned more than once. I owe the fact of its eventual completion to the kind encouragement given to me by my friends and colleagues. Particular thanks are due to Dr D. J. Bell and Dr E. Watchorn, who have read the whole of the manuscript, and to Prof. A. C. Chibnall, who read the proofs. I am glad also to acknowledge the help I have had from Miss V. Moyle. These, and others who have read particular

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sections and chapters, have all given precious advice and valuable criticisms. My task has been simplified in many ways by Prof. J. B. S. Haldane's *Enzymes* and by Dr D. E. Green's *Mechanisms of Biological Oxidations*, and particular thanks are due to Dr Malcolm Dixon, who has given me much from his great personal store of information.

I should also like to record my thanks to Dr J. C. Bournsell, who heroically undertook the preparation of the index, to Mr H. Mowl, who prepared the drawings for Fig. 14, and to members of the Cambridge Part I Biochemistry Class of 1945-6, who have allowed me to make use of some of their experimental data in the preparation of Figs. 1, 3 and 7.

To my wife, who prepared the work for publication, and to all departments of the Cambridge University Press I wish to express my humble and hearty thanks for their patience, consideration and expert workmanship.

E. B.

CAMBRIDGE
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PART I

ENZYMES

CHAPTER I

THE GENERAL BEHAVIOUR AND PROPERTIES OF ENZYMES

INTRODUCTION

WHEREVER we turn in the world of living things we find chemical changes taking place. Green plants, together with certain bacteria, are capable of fixing solar energy and synthesizing complex organic substances of high-energy content from very simple starting materials, namely, water, carbon dioxide and small amounts of inorganic substances such as nitrates and phosphates. Other living organisms possess the ability to decompose these complex materials and to exploit for their own purposes the energy that is locked up within them, and it is in this way that animals, for instance, obtain the energy they expend in the discharge of their bodily functions; reproduction, growth, locomotion and so on. Now it is a significant fact that nearly all the chemical changes that go on in living tissues are changes which, in themselves, proceed too slowly to be measurable or even, in many cases, detectable. How, then, does it happen that living animals can obtain energy and expend it as fast as they do? The answer is that living organisms possess numerous catalysts which speed up chemical reactions to the rates achieved in biological systems. Whether we consider digestion, metabolism, locomotion, fermentation or putrefaction, chemical changes are going on, and these chemical changes are catalysed. It is the purpose of this book to give some account of these changes and of the various mechanisms at present known to participate in their catalysis.

A catalyst, in the classical definition of Ostwald, is 'an agent