

PREFACE

Enzymology lies at the boundary of several disciplines. It has benefitted from much progress: in physics, which has lead in particular to the determination of the three dimensional structures of biological macromolecules and to the study of their dynamics; in chemistry, with the development of analytical methods and processes of synthesis; and in biology, with the potential of genetic and cell biological techniques. The coincidence of these methods with those of molecular modelling today enables us to modify an enzyme in order to make it more stable or to alter its functional properties. These possibilities are of great importance not only for the precise knowledge of the mechanisms involved in catalytic events and in their regulation, but also to meet the need for applications in biotechnology. Furthermore, enzymology is of interest to diverse fields in biology and even in medicine where it contributes, amongst other things, to the development of diagnostics for, and soon the treatment of, genetic and metabolic diseases. Important developments are expected due to the entry of biology into the post-genomic era; it is now vital to process the information contained within genomes i.e. the structure and function of proteins coded for by genes. This is why we felt it necessary to bring together in a single work the ensemble of current knowledge relating to enzymology.

Molecular and Cellular Enzymology addresses not only experienced enzymologists but also all those, e.g. biologists, medical doctors, industrialists, who are confronted by enzymological problems during their fundamental or applied research. Equally, it addresses students who will find herein the basics, as well as the most recent developments in the subject. We hope that this work will be able to stimulate in these readers an interest in this field in which an urgent need for training exists in order to meet both the requirements of research and industrial endeavours. This book consists of several levels: practical aspects and elementary explanations are given for the benefit of non-specialists' understanding; specialists will also find topics more deeply expounded with the principal bibliographic references cited. The bibliography, however, is not exhaustive; the choice includes general books and review articles as well as some specialised articles. In order to facilitate the task of students, two typographies have been adopted. The main text corresponds to basic knowledge, whereas text in a smaller font, indented and indicated by ▼▲, provides more specialised information.

Part I describes the thermodynamics of enzymatic reactions. At the very beginning, in Chap. 1, there is a succinct reminder of the laws of thermodynamics at equilibrium, the experimental methods for determining the energetic parameters of reactions, as well as a study of coupled reactions. Chapter 2 treats protein-ligand association equilibria and their experimental study. It concerns as much enzymologists as biologists confronted with the problem of binding molecules to receptors. The third chapter is devoted to the study of living systems, as open systems far from equilibrium.

Part II concerns kinetic studies of enzymatic reactions in solution. Chapter 4 is a reminder of those elements of chemical kinetics indispensable for the understanding of enzyme kinetics. In Chap. 5, all aspects of the kinetics of enzyme reactions possessing Michaelian behaviour are worked through. The experimental methods for studying these reactions, along with procedures for data processing and interpretation, are presented in Chap. 6.

Part III covers the formation and structure of enzyme active sites. A discussion about the origin of enzymatic function is included (Chap. 7), as well as a presentation of the formation of the functional structure of enzymes (Chap. 8). The diverse approaches used to determine the topology of enzyme active sites are the subject of Chap. 9.

Part IV analyses catalytic function, detailing the mechanisms brought into play in the formation of enzyme-substrate complexes (Chap. 10), the principal catalytic mechanisms and their involvement in enzyme catalysis (Chap. 11). To illustrate these as an ensemble, some specific enzymatic systems are studied in Chap. 12, which represent diverse types of catalytic mechanism. They were chosen based on structural knowledge of the enzyme molecule and on the extent to which the relationship between the structure and functional properties has been determined.

Part V explores the regulation of enzymatic activity. It contains an analysis of the non-covalent regulation of allosteric enzymes, the kinetics of which are treated in Chap. 13 and their covalent regulation forms the focus in Chap. 14. Multi-functional enzymes and multi-enzymatic systems are discussed in Chap. 15.

Part VI is devoted to enzymology in a structured environment, whether it be artificially immobilised enzymes or enzymes linked to well-defined cellular structures. The theory of metabolic pathway control is also included.

This work thus brings together diverse aspects of enzymology, which only exist in separate books or articles. For practical reasons we have had no hesitation in recalling certain basic concepts in the different parts, so that the reader may—thanks to a detailed Index—consult the topic of interest without being obliged to study the preceding chapters. In a similar vein, the indexing will enable precise points of interest to be readily looked up.

ACKNOWLEDGEMENTS

The authors would like to thank deeply Drs Florence LEDERER, Charis GHELIS and Michel DESMADRIL for their careful reading of certain parts of this work and for their constructive suggestions, and in particular Dr Nicolas KELLERSHOHN who took great care in checking all the equations. These thanks also go to Profs Alain COZZONE, Bernard BADET, Christian CAMBILLAU and Jacques HAIECH for the documentation that they provided. The authors thank equally the members of the Reading Committee, Profs G. LAUQUIN, J.P. MAZAT, B. HOUCMANDZADEH, M. VAN DER REST, J. LUNARDI, J. PELMONT and J. RICARD for having carefully read the manuscript and for communicating their constructive remarks and suggestions.

The authors wish also to thank Philip SIMISTER, Lisa WALTER and Katy WOOD for their contributions to the translation of the French version of this book and to Julie RIDARD and Sylvie BORDAGE from Grenoble Sciences for their skilful preparation and shaping of the two versions.

Jeannine Yon-Kahn

September 2009

Guy Hervé