

Preface

To the First German Edition

Biotechnology is the technical application of biological systems or parts thereof to provide products and services to meet human needs. It can, besides other techniques, contribute towards doing this in a sustainable manner. Since, in the majority of cases, renewable raw materials and biological systems are used in biotechnological processes, these processes can – and should – be performed practically without waste, as all of the byproducts can be recycled.

The development of natural and engineering science fundamentals for the design of such processes remains a challenge to biotechnology – a field that originated from the overlapping areas of biology, chemistry, and process engineering.

The requisite education for a career in biotechnology consists, in addition to a basic knowledge of each of these fields, of further biotechnological aspects which must provide an overview over the entire field and a deeper insight into different areas of biotechnology. The biotechnological production of various materials is performed either in fermenters using living cells (technical microbiology), or with enzymes – either in an isolated form or contained in cells – as biocatalysts. Indeed, the latter aspect has developed during recent years to form that area of biotechnology known as enzyme technology, or applied biocatalysis.

The aim of the present textbook is to provide a deeper insight into the fundamentals of enzyme technology and applied biocatalysis. It especially stresses the following inter-relationships: A thorough understanding of enzymes as biocatalysts and the integration of knowledge of the natural sciences of biology (especially biochemistry), cell and molecular biology; physico-chemical aspects of catalysis and molecular interactions in solutions; heterogeneous systems and interphase boundaries; and the physics of mass transfer processes. The same applies to the inter-relationships between enzyme technology and chemical and process engineering, which are based on the above natural sciences.

In less than a century since the start of industrial enzyme production, enzyme technology and its products have steadily gained increasing importance. In the industrial production of materials to meet the demands of everyday life, enzymes play an important role – and one which is often barely recognized. Their application ranges from the production of processed foods such as bread, cheese, juice and beer,

to pharmaceuticals and fine chemicals, to the processing of leather and textiles, as process aids in detergents, and also in environmental engineering.

Meeting the demand for these new products – which increasingly include newly developed and/or sterically pure pharmaceuticals and fine chemicals – has become an important incentive for the further development of biocatalysts and enzyme technology. Of similar importance is the development of new sustainable production processes for existing products, and this is detailed in Chapter 1, which forms an Introduction.

Enzymes as catalysts are of key importance in biotechnology, similar to the role of nucleic acids as carriers of genetic information. Their application as isolated catalysts justifies detailed examination of the fundamentals of enzymes as biocatalysts, and this topic is covered in Chapter 2. Enzymes can also be analyzed on a molecular level, and their kinetics described mathematically. This is essential for an analytical description and the rational design of enzyme processes. Enzymes can also catalyze a reaction in both directions – a property which may be applied in enzyme technology to achieve a reaction end-point both rapidly and with a high product yield. The thermodynamics of the catalyzed reaction must also be considered, as well as the properties of the enzyme. The amount of enzyme required for a given conversion of substrate per unit time must be calculated in order to estimate enzyme costs, and in turn the economic feasibility of a process. Thus, the quantitative treatment of biocatalysis is also highlighted in Chapter 2.

When the enzyme costs are too high, they can be reduced by improving the production of enzymes, and this subject is reviewed in Chapter 3 (*Chapter 4 in the present book*).

In Chapter 4 (*here Chapter 5*), applied biocatalysis with free enzymes is described, together with examples of relevant enzyme processes. When single enzyme use is economically unfavorable, the enzymes can be either reused or used for continuous processes in membrane reactors (Chapter 4; *here Chapter 5*) or by immobilization (Chapters 5 and 6; *here Chapters 6 and 7*). The immobilization of isolated enzymes is described in detail in Chapter 5, while the immobilization of microorganisms and cells, with special reference to environmental technology, is detailed in Chapter 6.

In order to describe analytically the processes associated with immobilized biocatalysts that are required for rational process design, the coupling of reaction and diffusion in these systems must be considered. To characterize immobilized biocatalysts, methods which were developed previously for analogous biological and process engineering (heterogeneous catalysis) systems can be used (Chapter 7; *here Chapter 8*).

Details of reactors and process engineering techniques in enzyme technology are provided in Chapter 8 (*here Chapter 9*), while the analytical applications of free and immobilized enzymes is treated in Chapter 10 (*not covered in the present book*).

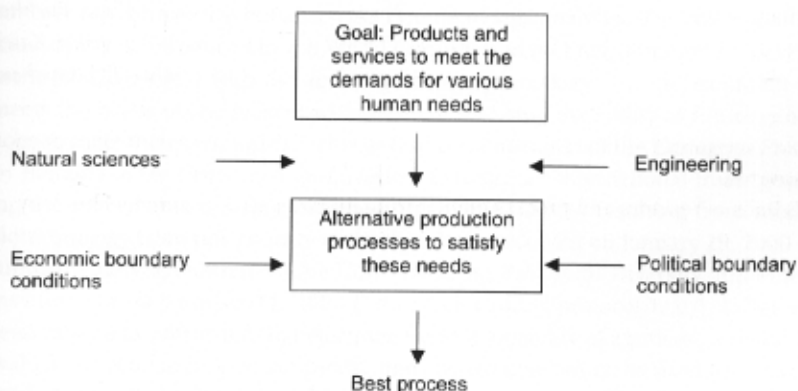
Within each chapter an introductory survey is provided, together with exercises and references to more general literature and original papers citing or relating the content of that chapter.

This textbook is designed to address both advanced and graduate students in biology, chemistry and biochemical, chemical and process engineering, as well as

scientists in industry, research institutes and universities. It should provide a solid foundation that covers all relevant aspects of research and development in applied biocatalysis/enzyme technology. It should be remembered that these topics are not of equal importance in all cases, and therefore selective use of the book – depending on the individual reader's requirements – might be the best approach to its use.

In addition to a balanced methodological basis, we have also tried to present extensive data and examples of new processes, in order to stress the relevance of these in industrial practice.

From our point of view it is also important to stress the interactions, which exist beyond the scientific and engineering context within our society and environment. The importance and necessity of these interactions for a sustainable development has been realized during the past two decades, and this has resulted in new economic and political boundary conditions for scientific and engineering development. Problems such as allergic responses to enzymes in detergents and, more recently, to enzymes produced in recombinant organisms, have direct influences on enzyme technology/applied biocatalysis. Therefore, an integrated process design must also consider its environmental impact, from the supply and efficient use of the raw materials to the minimization and recycling of the byproducts and waste. Political boundary conditions derived from the concept of sustainability, when expressed in laws and other regulations, necessitates due consideration in research and development. The design of sustainable processes is therefore an important challenge for applied biocatalysis/enzyme technology. Ethical aspects must also be considered when gene technology is applied, and this is an increasing consideration in the production of technical and pharmaceutical enzymes. The many interactions between research and development and economic and political boundary conditions must be considered for all applications of natural and engineering sciences. Most importantly, this must be appreciated during the early phases of any development, with subsequent evaluation and selection of the best alternative production processes to meet a variety of human needs, as is illustrated in the following scheme:



This book has been developed from our lecture notes and materials, and we also thank all those who provided valuable help and recommendations for the book's production. In particular, we thank Dipl.-Ing. Klaus Gollembiewsky, Dr. Lieker, Dr. Noll-Borchers, and Dipl. Chem. André Rieks.

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To the First English Edition

The basic philosophy of the previous German edition is retained, but the contents have been revised and updated to account for the considerable development in enzyme technology/applied biocatalysis since the German edition was prepared some 10 years ago. Hence, a new chapter (Chapter 3) has been added to account for the increasing importance of enzymes as biocatalysts in organic chemistry. Recent progress in protein design (by rational means and directed evolution) has been considerably expanded in Chapter 2. The final chapter has been amended with more detailed case studies to illustrate the problems that must be solved in the design of enzyme processes. An appendix on information retrieval using library and internet resources has also been added, and we thank Thomas Hapke (Subject Librarian for Chemical Engineering at the Library of the Technical University Hamburg-Harburg) for help in the preparation of this material. The chapter on enzymes for analytical purposes has been removed in this English edition as it now is beyond the scope of this textbook.

We thank Prof. Dr. L. Jaenicke and Prof. Dr. J.K.P. Weder for their very constructive suggestions for corrections and improvements of the German edition.

The authors of this edition thank Prof. Dr. Andreas Bommarius, Dr. Aurelio Hidalgo, Dr. Janne Kerovuo, Dr. Tanja Kummer, Dr. Dieter Krämer, Dr. Brian Morgan, Sven Pedersen, Poul Poulsen, Prof. Dr. Peter Reilly, Dr. Klaus Sauber, Dr. Wilhelm Tischer, and Dr. David Weiner for valuable discussions, revisions and suggestions while preparing this book.

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Preface to the Second Edition

We have been very pleased by the success of the first English edition of our book. We are especially grateful that it serves as primary source for teaching courses in *Biocatalysis and Enzyme Technology* at many universities around the world. We would also like to thank the readers who pointed out corrections and to those who made useful suggestions for this second edition.

More than 7 years have passed since the first English edition was published and we have observed substantial and exciting developments in all areas of biocatalysis. Hence, we did not simply update the first edition with new references and add singular sentences, but substantially expanded and reorganized the book. For instance, the importance of enzyme discovery and protein engineering is now treated in a separate new section (Chapter 3). Although biocatalysis primarily refers to the use of isolated (and immobilized) enzymes, we decided to cover also the use of designed whole cells for biotransformations in the new Chapter 5 to allow the reader to get a glimpse on the emerging field of metabolic engineering, where the understanding and biochemical characterization of enzymes is of course an important aspect. Furthermore, we have included several new case studies in Chapter 12, to exemplify how biocatalysis can be performed on the large scale and which criteria are important to establish a novel process. These include starch processing and glucose isomerization, biofuels from biomass, and the production of 7-ACA by direct hydrolysis of cephalosporin C as examples for current as well as potential industrial processes. In addition, enzymatic routes for the synthesis of advanced pharmaceutical intermediates for the drug Lipitor are covered.

Furthermore, we have added a few new sections on topics of current interest: process sustainability and ecological considerations, process integration, biofilm catalysis, microbial fuel cells, and regulations that influence the production and use of enzymes.

We have also expanded and updated the exercises and decided that also the solutions be directly given in the book – in Appendix B – so that the students can first try to answer the questions by themselves and then look up the solutions.

Finally, we would like to thank Ulrich Behrendt, Sonja Berensmeier, Matthias Höhne, Zoya Ignatova, Hans-Joachim Jördening, Burghard König, Sven Pedersen,

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