Michael L. Shuler/Fikret Kargi

Bioprocess Engineering

Basic Concepts

Second Edition

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BIOPROCESS ENGINEERING

Basic Concepts

Second Edition

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For Andy, Kristin, Eric, and Kathy
and for Karen

Preface to the Second Edition

In the decade since the first edition of *Bioprocess Engineering: Basic Concepts*, biotechnology has undergone several revolutions. Currently, the ability to sequence the genome of whole organisms presents opportunities that could be hardly envisioned ten years ago. Many other technological advances have occurred that provide bioprocess engineers with new tools to serve society better. However, the principles of bioprocess engineering stated in the first edition remain sound.

The goals of this revision are threefold. We want to capture for students the excitement created by these advances in biology and biotechnology. We want to inform students about these tools. Most importantly, we want to demonstrate how the principles of bioprocess engineering can be applied in concert with these advances.

This edition contains a new section in the first chapter alerting students to the regulatory issues that constrain bioprocess design and modification. We believe students need to be aware of these industrially critical issues. Part 2, "An Overview of Biological Basics," has been updated throughout and expanded. Greater emphasis is given now to posttranslational processing of proteins, as this is a key issue in choice of bioprocessing strategies to make therapeutic proteins. Basic processes in animal cells are more completely described, since animal cell culture is now an established commercial bioprocess technology. Chapter 5 is made more complete by introduction of a section on noncarbohydrate metabolism. Key concepts in functional genomics have been added to prepare students to understand the impact of these emerging ideas and technologies on bioprocesses.

In Part 3, "Engineering Principles for Bioprocesses," greater attention is given to issues associated with animal cell bioreactors. The discussion of chromatographic processes is expanded. In Part 4, "Applications to Nonconventional Biological Systems," the material has been rearranged and updated and a new chapter added. These changes are evident in the chapters on animal and plant cell culture. Particularly important is the expanded discussion on choice of host-vector systems for production of proteins from recombinant DNA technology. Coverage of two areas of increasing importance to bioprocess engineers, metabolic and protein engineering, has been expanded. A new chapter on biomedical applications illustrates how approaches to bioprocess engineering are relevant to problems typically considered to be biomedical engineering. The chapter on mixed cultures has been extended to cover advanced waste-water treatment processes. An appendix providing descriptive overviews of some traditional bioprocesses is now included.

The suggestions for further reading at the end of each chapter have been updated. We are unable in this book to provide in-depth treatment of many vital topics. These readings give students an easy way to begin to learn more about these topics.

Teaching a subject as broad as bioprocess engineering in the typical one-semester, three-credit class has never been easy. Although some material in the first edition has been removed or condensed, the second edition is longer than the first. For students with no formal background in biology, coverage of all of the material in this book would require a four-credit class. In a three-credit class we suggest that the instructor cover Chapters 1 to 11 (with 7 being optional) and then decide on subsequent chapters based on course goals. A course oriented toward biopharmaceuticals will want to include careful coverage of Chapters 12 and 14 and some coverage of 13 and 15. A course oriented toward utilization of bioresources would emphasize Chapter 16 and the Appendix and selected coverage of topics in Chapters 13 and 14.

Many students now enter a bioprocess engineering course with formal, college-level instruction in biology and biochemistry. For such students Chapters 2, 4, 5, 7, and 8 can be given as reading assignments to refresh their memories and to insure a uniform, minimal level of biological knowledge. Lecture time can be reserved for material in other chapters or for supplementary material. For these five chapters study questions are provided for self-testing. Under these circumstances the instructor should be able to cover the rest of the material in the book.

Once again we have been assisted by comments from many colleagues across the world. These comments have included suggestions for new material to be incorporated and for corrections. While the list is too long to include here, specific contributions deserve special recognition. Mohammad Ataai provided us a summary of IMAC (immobilized metal affinity chromatography) that has been incorporated into the revision. Kelvin Lee provided the paragraph describing 2-D gel electrophoresis. We thank Laura Palomares for an excellent job in updating and revising a first draft of the Appendix on traditional bioprocesses. The first edition of this book was translated into Korean, and Yoon-Mo Koo, Jin Ho Seo, Yong Keun Chang, and Tai Hyun Park provided us an extensive list of corrections, which has been very helpful in preparation of this revision.

We wish to also thank our families for their support during the process of this revision.

Preface to the First Edition

Bioprocess engineering is the application of engineering principles to design, develop, and analyze processes using biocatalysts. These processes may result in the formation of desirable compounds or in the destruction of unwanted or hazardous substances. The tools of the engineer, particularly the chemical engineer, will be essential to the successful exploitation of bioprocesses.

This book's main purpose is to introduce the essential concepts of bioprocessing to traditional chemical engineers. No background in biology is assumed. The material in this book has been used as a basis for a course at Cornell University. Although it was designed primarily for seniors and entering graduate students from chemical engineering, students from agricultural engineering, environmental engineering, food science, soil science, microbiology, and biochemistry have successfully completed this course.

Parts 1 and 2 outline basic biological concepts. These eight chapters are not intended to be a replacement for good courses in microbiology, biochemistry, and genetics. They simply provide sufficient information to make the rest of the book accessible to the reader. A reader who desires a more in-depth understanding of the key biological concepts is referred to the suggested readings at the end of each chapter. Chapters 3 and 6 differ in that they are more detailed and introduce concepts not normally found in the standard biological textbooks.

In Part 3, "Engineering Principles for Bioprocesses," we focus on the generic components of bioprocessing that do not depend on the type of cell used in the process. In

Part 4 we discuss applications to special systems and the particular characteristics of mixed cultures, genetically engineered cells, plant cells, and animal cells. These application chapters reinforce the previous engineering and biological concepts while providing more detailed information about important new biological systems.

This book reflects useful and important suggestions from many people. Students in Chemical Engineering 643 ("Introduction to Bioprocess Engineering") at Cornell University in Fall 1989 provided written critiques on the chapters. This input has been invaluable and is deeply appreciated. The two external reviewers of this text also provided invaluable suggestions. Harvey Blanch, Charles D. Scott, and Octave Levenspiel have provided one of us (FK) with suggested homework problems, which have greatly enhanced the potential usefulness of this book. Finally, the superb technical skills of Bonnie Sisco have been instrumental in converting nearly incomprehensible written scrawls into a readable text.

Finally, both authors wish to thank their families for their patience and support during this process.

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