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# BIOSEPARATIONS ENGINEERING

## Principles, Practice, and Economics

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**MICHAEL R. LADISCH, Ph.D.**  
Purdue University



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Published simultaneously in Canada.

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For ordering and customer service, call 1-800-CALL WILEY.

## *Library of Congress Cataloging-in-Publication Data:*

Ladisch, Michael R., 1950-

Bioseparations engineering : principles, practice, and economics / Michael R. Ladisch.  
p. cm.

Includes bibliographical references and index.

ISBN 0-471-24476-7 (alk. paper)

1. Biomolecules—Separation. 2. Biochemical engineering. 3. Separation (Technology)

I. Title.

TP248.25.S47 L33 2000

660'.2842—dc21

00-043606

Printed in the United States of America.

10 9 8 7 6 5 4 3 2 1

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## PREFACE

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Bioseparations has grown in importance and changed in emphasis. The first book on the topic, *Bioseparations* by Belter, Cussler, and Hu was published in 1988 and set the stage for recognition of bioseparations as an important chemical engineering unit operation. This was a pioneering effort, in my opinion, since it organized and introduced a new discipline. The applications were primarily for products derived from microorganisms that had not been genetically modified, and whose products were principally small to intermediate molecular weight molecules. This first book introduced engineering principles to the purification of biochemicals.

The next major contribution to the bioseparations literature was by Wheelwright in a book entitled *Protein Purification: Design and Scale-up of Downstream Processing*. This book was published in 1991, when the new biotechnology industry was just beginning to enter a dramatic new growth phase in protein biopharmaceuticals. It introduced engineers to the world of separations applied to biotherapeutic proteins whose production was made possible through rDNA technology. These proteins, including bovine growth hormone, interferon, tissue plasminogen activator, and insulin, would be difficult if not impossible to generate by any other means. The new biology, that is, the genetic engineering applied to microorganisms to make protein biopharmaceuticals—required an understanding of “the fundamentals of engineering and their practice as applied to large scale engineering.” This was another pioneering book, both due to its fresh content, and its message that “the hybridization of the biochemist or protein chemist and the chemical engineer or process engineer creates a new discipline.”

*Bioseparations Engineering: Principle, Practice and Economics* attempts to carry this message forward. This book is being completed at the beginning of what is predicted to be the century of biotechnology, as well as an era of multidisciplinary approaches to solving problems in engineering, science, and society. The industry has evolved from one based on fermentations involving recombinant bacteria and mammalian cells, to one where the human genome will be deciphered by the time that this book is in print. The technologies that have made sequencing of the human genome possible are being applied to numerous, and less complex, organisms. The knowledge of the genetic basis of biological functioning is growing at an astronomical rate. With this knowledge comes the challenges and opportunities of applying information derived from genomes to the production of therapeutic compounds, specialty biochemicals, functional food ingredients, environmentally friendly biocatalysts, and new bioproducts from renewable



resources. The directed application of cellular metabolism to produce large quantities of bio-products is impressive. However, without the ability to recover and purify these products at relatively large scales, it would be impossible to provide them in quantities that will benefit society. Bioseparations will be an important factor for fulfilling biotechnology's promise as the new engine of growth and benefits for the global economy.

*Bioseparations Engineering* attempts to convey the principles of bioseparations in a manner that will apply to bioproducts not yet invented, and biological molecules not yet produced on a large scale, as well as the molecules that form the basis of the current industry. Existing products and processes are used to teach the principles. As described here, bioseparations engineering is the multidisciplinary application of fundamental engineering and biological principles to the design of adsorbents, systems, and processes for the separation of biological molecules. Where possible, mechanistic analysis of key phenomena at a microscopic scale are presented. Examples and case studies are intended to assist the reader in extrapolating principles to his or her needs in practicing specific types of bioseparation whether they are for food, pharmaceutical, or biochemical products. Footnotes are provided to give a short background of the economic impact of the product and/or process being considered.

The book is the result of 10 years of teaching and developing this subject matter starting in a mezzanine level course (graduate students and last semester seniors). Since then it has developed to a graduate level course entitled *Bioseparations Engineering*. The student's enthusiasm contributed to my motivation for completing this book. To the students and alumni of ABE 580 and my graduate students at Purdue University, I thank you for your encouragement, contributions, and interest. To the readers of *Bioseparations Engineering*, I hope you find our efforts worthwhile.

Michael Ladisch  
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West Lafayette, Indiana

## ACKNOWLEDGMENTS

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I wish to thank my family, colleagues, and Purdue University for enabling me to transform my vision for bioseparations engineering from lecture notes into a book. Special thanks go to Carla Carie who worked diligently in converting the drafts of manuscripts into legible documents with beautiful schematic diagrams and was involved in all phases of this project; Dr. Ayda Sarikaya for assisting with the proofing process; Craig Keim, Nathan Mosier, Ayda Sarikaya and Cheng-hong Li for their inputs on organizing these materials in order to improve clarity of presentations; and Karie Johnson who assisted with preliminary edits of the organization of the book. Many others contributed to the review and critiques of the materials presented here. These people are acknowledged at the beginning of each chapter.

I wish to thank Professor George Tsao, Professor and founding Director of the Laboratory of Renewable Resources Engineering for providing the environment in which development of the book concept was made possible. The support of Dr. Larry Huggins (Department Head of Agricultural Engineering, and now Associate Dean of Engineering) along the entire course of this project was a major factor in undertaking and then completing the working manuscript. I thank the Schools of Agriculture and Engineering, and Dr. Vince Bralts, head of Agricultural and Biological Engineering for granting me a sabbatical to pursue the completion of this project, and providing encouragement as well. I also wish to acknowledge the memory of Carolyn Wasson, who made many contributions to the early manuscript, as well as Norma Leuck whose encouragement and help was most appreciated.

The computer-based problems were inspired by Henry Bungay's (of Rensselaer Polytechnic Institute) pioneering approach in the book entitled *Basic Biochemical Engineering*. Other sections were modeled after parts of books of Professor Arthur Humphrey (Penn State), Professor Daniel I. C. Wang (MIT), and Professor Munir Cheryan (U. Illinois). I thank these professors for providing role models. I also wish to express my appreciation to Professors Ed Cussler and Wei-Shou Hu, at the University of Minnesota, and Doug Cameron (now at Cargill, formerly at University of Wisconsin), Peter Prescott when at Hanser publishers, and Scott Wheelwright for their suggestions during the course of this project.

I appreciate the patience of the editors who worked with me as I developed the book. Greg Franklin of Butterworths, who suggested an early outline, Betty Sun of John Wiley, who took this project through its first draft manuscript and revisions, and Bob Esposito of John Wiley, who completed the project. Thank you also to Danielle Lacourciere of John Wiley who coor-



minated conversion of the manuscript into typeset form. In addition, I wish to acknowledge the patience and encouragement of my friends and training associates during several marathons: Ron Ellis, Wayne Ramsey, and in particular, Professor and Coach, Howie Zelaznik of the Elite Runner's Association.

Most of all, I wish to convey my appreciation and gratitude to my family for their patience, understanding, and support during the long process of writing "the book."

Michael Ladisch

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