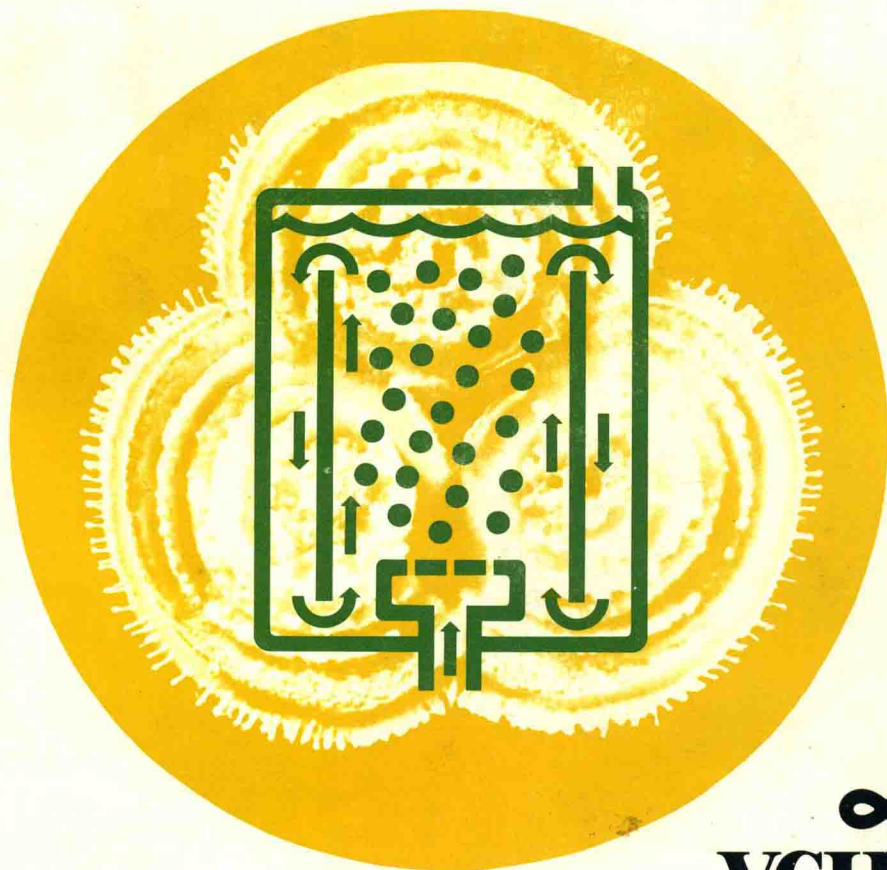


Biotechnology

A Comprehensive Treatise in 8 Volumes
edited by H.-J. Rehm and G. Reed

Volume 7b

Volume Editors:
G.K. Jacobson and S.O. Jolly



VCH 

0-46460

Biotechnology

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Volume 7b
Gene Technology

Volume Editors:
G. K. Jacobson and S. O. Jolly



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Editorial Director: Dr. Hans F. Ebel
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This book contains 60 figures and 58 tables

Deutsche Bibliothek Cataloguing-in Publication-Data

Biotechnology: a comprehensive treatise in 8 volumes / ed. by H.-J. Rehm and G. Reed. –
[Ausg. in 8 Bd.]. – Weinheim; Basel (Switzerland); Cambridge; New York, NY: VCH.
Teilw. mit d. Verl.-Angabe Verl. Chemie, Weinheim, Deerfield Beach, Florida, Basel. –
Teilw. mit d. Erscheinungsorten Weinheim, Deerfield Beach, FL. –
Teilw. mit d. Erscheinungsorten Weinheim, New York
NE: Rehm, Hans J. [Hrsg.]

Gene technology / vol. eds.: G. K. Jacobson and S. O. Jolly. – Weinheim; Basel (Switzerland);
Cambridge; New York, NY: VCH, 1989
(Biotechnology; Vol. 7b)
ISBN 3-527-26517-1 (Weinheim ...) Pp.
ISBN 0-89573-561-X (Cambridge ...) Pp.
NE: Jacobson, Gunnard K. [Hrsg.]
[Ausg. in 8 Bd.]
Vol. 7b. Gene technology. – 1989

© VCH Verlagsgesellschaft mbH, D-6940 Weinheim (Federal Republic of Germany), 1989
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Compositor and Printer: Zechnersche Buchdruckerei, D-6720 Speyer
Bookbinding: Klambt-Druck GmbH, D-6720 Speyer
Printed in the Federal Republic of Germany

Biotechnology

Volume 7b



Biotechnology

A Comprehensive Treatise in 8 Volumes

Volume 1

Microbial Fundamentals

Volume 2

Fundamentals of Biochemical Engineering

Volume 3

Biomass, Microorganisms for Special Applications,
Microbial Products I, Energy from Renewable Resources

Volume 4

Microbial Products II

Volume 5

Food and Feed Production with Microorganisms

Volume 6a

Biotransformations

Volume 6b

Special Microbial Processes

Volume 7a

Enzyme Technology

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Gene Technology

Volume 8

Microbial Degradations

Cumulative Indexes

© VCH Verlagsgesellschaft mbH, D-6940 Weinheim (Federal Republic of Germany), 1989

Distribution

VCH Verlagsgesellschaft, P.O. Box 101161, D-6940 Weinheim (Federal Republic of Germany)

Switzerland: VCH Verlags-AG, P.O. Box, CH-4020 Basel (Switzerland)

United Kingdom and Ireland: VCH Publishers (UK) Ltd., 8 Wellington Court, Wellington Street,
Cambridge CB1 1HW (England)

USA and Canada: VCH Publishers, Suite 909, 220 East 23rd Street, New York, NY 10010-4606 (USA)

ISBN 3-527-26517-1 (VCH Verlagsgesellschaft)

ISBN 0-89573-561-X (VCH Publishers)

Preface

A loose definition of Biotechnology is one that reflects mankind's historical involvement in those biological systems that have both traditionally and recently, affected its well-being. Biotechnology is Applied Biology, and it encompasses the empirical selection of better crop plants and animal husbandry of our ancestors as well as the "cutting edge" development and fermentation of yeasts, fungi, bacteria and other cell cultures for the production of recombinant vaccines. In the preface to the *Biotechnology* series, Drs. Rehm and Reed defined Biotechnology as the inter-disciplinary field of engineering, microbiology, and biochemistry – with "generous assistance from genetics and molecular biology". Their definition emphasizes, as does this series, the technology behind microbial fermentations. Prior to the dramatic advances made in molecular biology, improvements in applied biology relied on what may be called the "old gene technologies" of selective breeding, empirical selection, and especially in the case of microorganisms, mutation and selection. The molecular biology that permits gene cloning, recombinant gene expression, and protein engineering is the basis of the "new gene technology" that is currently applied to these fermentations. This volume in the *Biotechnology* series addresses the techniques and products of the "new gene technology".

The chapters and appendices to Volume 7b "Gene Technology" are organized into sections describing the techniques themselves; the products of these gene technologies; and the evolution and development of

safety measures associated with these techniques and their products. Different from other texts in this series are discussions of topics not usually considered in terms of microbial fermentation technology. These include recombinant plants; transgenic animals; recombinant microorganisms used *per se* for agricultural, food, or other purposes; engineered proteins; and human gene therapy. More traditional products, in the context of fermentation, include the production of industrial commodities such as organic acids, vitamins, and enzymes; also, pharmaceutical proteins, monoclonal antibodies, vaccines, and hormones. Some of these applications, especially those dealing with industrial commodities and food related organisms, are merely elaborations of systems that have been undergoing modification for decades by the "old gene technologies". Many of these systems are discussed in other volumes of this series.

Other applications, however, prior to the development of applied molecular biology, could be envisioned only in the wildest fantasies of scientists and scholars. To the workers of the 1920s who isolated insulin from pancreatic extracts and brought this therapeutic protein to the market, the thought that commercial quantities of *human* insulin would be produced by fermentation in the 1980s could only have been astonishing. And today, more astonishing than this is the prospect of gene therapy in human beings to correct single gene defects responsible for several heritable diseases. The 60 years that spanned the first application of insulin in the treatment of diabetes

and its production by fermentation were due to the lack of tools – tools that not only supply a knowledge base from which ideas can be formed, but also tools that can implement these ideas. Modern molecular biology, the “new gene technology”, is supplying both of these sets of tools. It is the hope of the editors that this volume will demonstrate to the reader that the application of these tools will do much to reduce the span of years traditionally required for the application of biological knowledge to industrial use.

The editors wish to thank the authors, some of whom have demonstrated great patience in waiting for the results of their efforts to appear in print. The help, guidance, and patience of Dr. Reed was instrumental in bringing this volume to press. His efforts on our behalf are greatly appreciated. We would also like to thank Mrs. Christa Schultz whose expertise helped us considerably in this task.

Milwaukee, Wisconsin	Gunnard Jacobson
in May 1989	Setsuko Jolly

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I Methods in Industrial Gene Technology

1 Recombinant DNA

