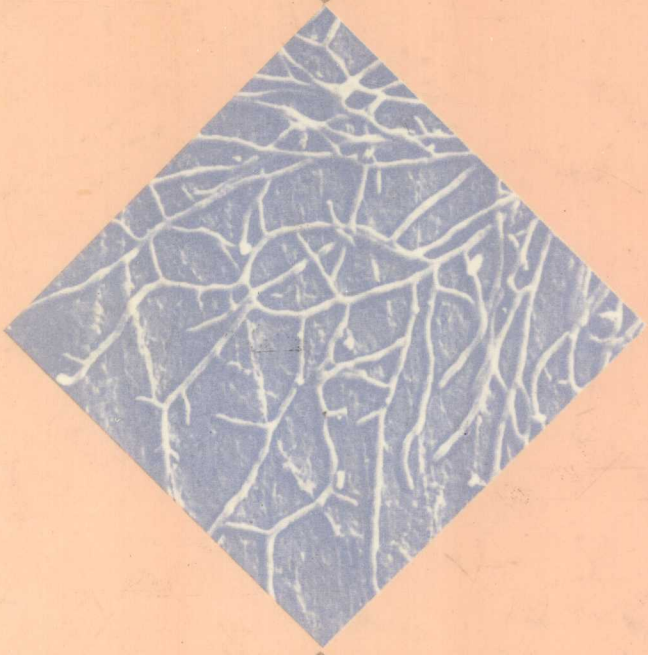
BASIC BIOTECHNOLOGY



JOHN BU'LOCK
BJORN KRISTIANSEN

·BASIC·
BIOTECHNOLOGY

Edited by

JOHN BU'LOCK
Weizmann Microbial Laboratory
Department of Chemistry
University of Manchester
Manchester M13 9PL
England

BJORN KRISTIANSEN
Department of Bioscience and Biotechnology
Applied Microbiology Division
University of Strathclyde
Glasgow G1 1XW
Scotland

1987

ACADEMIC PRESS
Harcourt Brace Jovanovich, Publishers
London Orlando San Diego New York Austin
Boston Sydney Tokyo Toronto

ACADEMIC PRESS INC. (LONDON) LTD.
24/28 Oval Road,
London NW1

United States Edition published by
ACADEMIC PRESS INC.
Orlando, Florida 32887

British Library Cataloguing in Publication Data
Basic Biotechnology.
1. Biotechnology
I. Bu'Lock, J.D. II. Kristiansen, Bjorn
660'.6 TP248.2

ISBN 0–12–140752–7
ISBN 0–12–140753–5 Pbk

Printed in Great Britain by Galliard (Printers) Ltd, Great Yarmouth

Contributors

K. Allermann Institute of Plant Physiology, University of Copenhagen, Ø Farimagsgade 2A, DK-1353 Copenhagen K, Denmark

H. W. Blanch Department of Chemical Engineering, University of California, Berkeley, CA 94720, USA

J. W. Brewer Biotechnology Division, Miles Laboratories Inc, Elkhart, IN 46515, USA

J. D. Bu'Lock Microbial Chemistry Laboratory, University of Manchester, Manchester M13 9PL, UK

K. Corbett Beecham Pharmaceuticals, UK Division, Worthing, West Sussex, BN14 8QH, UK

R. P. Elander Industrial Division, Bristol-Meyers Co, PO Box 4755, Syracuse, NY 13201-4755, USA

M. W. Fowler Wolfson Institute of Biotechnology, Sheffield University, Sheffield S10 2 TN, UK

W. E. Goldstein Research and Development Group, Miles Laboratories Inc, Elkhart, IN 46515, USA

C. F. Gölker Bayer AG, Verfahrensentwicklung Biochemie, Friedrich-Ebert-Strasse 217-333, D-5600 Wuppertal 1, West Germany

D. L. Hawkes Department of Mechanical and Production Engineering, The Polytechnic of Wales, Pontypridd CF37 1DL, UK

F. R. Hawkes Department of Science, The Polytechnic of Wales, Pontypridd CF37 1DL, UK

E. A. Jackman Jackman's Economic and Technical Services Ltd, 244 Highlands Blvd, Leigh-on-Sea S59 3QZ, UK

B. Kristiansen Department of Bioscience & Biotechnology, Applied Microbiology Division, University of Strathclyde, Royal College Building, 204 George Street, Glasgow G1 1XW, UK

J. L. Meers Sturge Biochemicals Ltd, Denison Road, Selby SO8 8EF, UK

P. E. Milsom Sturge Biochemicals Ltd, Denison Road, Selby YO8 8EH, UK

M. Moo-Young Department of Chemical Engineering, University of Waterloo, Waterloo, Ontario N2L 3G1, Canada

K. Murray Department of Molecular Biology, University of Edinburgh, King's Building, Mayfield Road, Edinburgh EH9 3JR, UK
J. Olsen Department of General Microbiology, University of Copenhagen, Solvgarde 83 H, DK-1307 Copenhagen K, Denmark
G. W. Pace Intra-Optics Laboratories Pty Ltd, PO Box 37, St Ives, NSW 2075, Australia
L. B. Quesnel Department of Bacteriology and Virology, University of Manchester, Manchester M13 9PT, UK
C. Ratledge Department of Biochemistry, University of Hull, Hull HU6 7RX, UK
J. A. Roels Gist Brocades, Research and Development, Wateringseweg 1, PO Box 1, 2600 MA Delft, The Netherlands
G. Schmidt-Kastner Bayer AG, Verfahrensentwicklung Biochemie, Friedrich-Ebert-Strasse 217-333, D-5600 Wuppertal 1, West Germany
C. G. Sinclair Department of Chemical Engineering, University of Manchester Institute of Science and Technology, PO Box 88, Manchester M60 1QD, UK
R. E. Spier Department of Microbiology, University of Surrey, Stag Hill, Guildford GU2 5XH, UK
C. Vezina Institut Armand-Frappier, University of Quebec, 531 boulevarde des Prairies, Ville de Laval, Quebec H7N 4Z3, Canada

Preface

Jourdain: Par ma foi! il y a plus de quarante ans que je dis de la prose que j'en suisse rien, et je vois suis le plus obligé du monde de m'avoir appris çela.

Molière, Le Bourgeois Gentilhomme II.iv

And many a Iakke-of-Dover hastow sold
That hath been twyes hoot and twyes cold

Chaucer, The Cook's Tale—Prologue

Why, when there seems to be such a lot of it about, do we need yet another book about biotechnology—and in particular one that claims to deal with *basic* biotechnology? There are real biotechnologists around, who were already doing the same sort of thing they are doing today well before the term became so fashionable; equally there are people who have elected to call what they are doing by this trendy new term because it sells well. So we have headed this preface with quotations that seem to define those two categories; more tediously, we shall follow the worthy but dull definition promulgated by the European Federation of Biotechnology and define our subject as the practical application of biological organisms, or their subcellular components, to manufacturing and service industries and to environmental management.

Above all, through our contributing authors and as editors, we have tried to present biotechnology as something which is already going on. Whereas for some enthusiasts biotechnology has mainly been a matter of promise—and promises—we have tried to introduce it as a productive technology which has real significance now, and even in the not-so-recent past, as well as potentiality for the future, and which can therefore be introduced to students and new researchers in a 'hard-core' way which is not at all superficial. Perhaps for each new generation of entrants into biotechnology it is the future potentialities that provide the motivation, but it must be the past and present realities that provide the machinery through which that drive will work.

In one sense at least, the beginnings of modern biotechnology are exemplified by Weizmann's development of a *practical* acetone–butanol fermentation in 1913–15; prior to this, various 'natural' microbial and enzymic processes had been first used, then interpreted, and—increasingly after Pasteur—controlled and even manipulated, but Weizmann's process was the first *new* productive application of biocatalysis on an industrial scale. Contemporarily, on the other side of the globe and slower to reach industrial significance, the Japanese had been developing both the applications and the production of enzymes. Also contemporary, and by coincidence coming from the same laboratory as Weizmann in Manchester, were the first conscious applications of some (quite crude) microbiology to the large-scale process of sewage treatment, hitherto simply a matter of rather simplistic civil engineering; it is a matter for real regret that some of the aspects of biotechnology arising from this last approach have had to be omitted here because of our over-riding need to present a thorough and self-contained account in quite a small compass.

We have divided our book into two major sections, the first dealing with basic principles and the second with a range of illustrative examples of practical biotechnology and some of its problems. We think that this is the order in which the book itself should be used, but its contents were actually determined by working in reverse order; we started from a range of actual examples of productive biotechnology, by no means exhaustive but hopefully representative, to be dealt with by experts of different kinds, each approaching their own topic in their own way. From these we worked back to define the kinds of basic understanding that would be needed, either to comprehend or to further advance those real processes. As a result our selection of 'basic principles' covers a wide range. However, we believe that no more than a superficial account of biotechnology can be given without taking account of the essential interdisciplinarity of the subject.

It follows that the typical scientist or engineer, and in particular the newly graduated scientist or engineer for whom this book is primarily intended, will find some of the basic principles quite familiar, while others fall quite outside his or her past experience. No matter: even among what is familiar, it will be useful to emphasize what aspects of the known discipline are the most relevant.

The best alternative to superficiality is therefore to try to cope comprehensively with all the relevant (and even partly-relevant) disciplines, and then to append comprehensive 'state-of-the-art' accounts of the equally diverse actual and potential applications. Unfortunately this leads to the assembling of multi-volume compendia, written by experts but edited by committees, meritorious but massive works to be found only in correspond-

ingly well-endowed libraries. Knowing from experience that the task of editing such miscellanies into a coherent account would be beyond our capabilities, we have tried to do something more modest, which we hope will be of real use for a rather larger number of readers.

Sometimes we have been quite ruthless with our authors, despite their individual distinction, and so for the final results of our temerity we must pay by accepting full responsibility for all the errors, inconsistencies, omissions, misplaced emphasis, and plain wrongheadedness that the careful reader will undoubtedly find; *miserere nos*.

For some of the omissions we can make pleas in mitigation. For example, though much of our emphasis is on biotechnology's uses of microorganisms, we have excluded any descriptive microbiology as such, just as we have excluded hydrodynamics, differential calculus, protein chemistry and patent law though all these have their uses and their relevance for biotechnology. It would be possible (and indeed interesting) to compile an account of 'The Organisms of Biotechnology', but the result would probably be neither good biotechnology nor good microbiology. The biotechnologist will need the skills of a microbiologist (or a mathematician or a patent attorney), either personally or as part of the team, for example to understand the requirements of the organism actually being used or to consider what others might fit the application as well or better. Screening, selection, and strain improvement will be the major 'interface' for this, and so we have specifically covered these aspects; perhaps unfortunately, we have not been able to deal with the other interface which is the microbiologists' understanding of the morphology, habit and general life-style of organisms. This is only partly for reasons of space; our present understanding and exploitation of this aspect of biotechnology is actually rather limited. Maybe our omission will stimulate more work in this, as in other under-represented aspects. Thus for microbiology, as for biochemistry and indeed for physics and engineering principles, we have tried simply to indicate what the biotechnologist needs to know in order to ask the microbiologist, or the biochemist or engineer, the right questions—and perhaps to help the microbiologist, biochemist or engineer to understand what they are being asked, and why it matters!

Indeed, if our compilation helps to draw attention to the areas of basic science and engineering in the contributory disciplines that are most relevant to biotechnology, and to promote more research (and more support) for those areas, it will be serving a valuable purpose. In keeping with a narrowly utilitarian age, the fashion for ruthlessly target-oriented research is rapidly leading to a situation in which empirical applications, based on superficial extensions of old understanding, have outstripped the basic knowledge that is needed. Today's shiny edifice of biotechnology is in

serious danger of collapsing into inadequate foundations, and the numerous national and international commissions and committees that exist to 'promote' biotechnology need to have this brought rather urgently to their attention.

This, then, is our plea in mitigation to those who will use our book to make their entry into biotechnology. The enthusiasts who are already there will have different objections; there is little here for flavour-of-the-month fans. By describing a broad selection of process biotechnology as it is, rather than speculating about what it might become, we hope our readers will emerge better-equipped to understand not only what they are doing today, but what they might do tomorrow.

Biotechnology is—or it can be—clean technology, green technology, and human-scale technology. It lends itself more readily to improving the human condition than to terminating it. It will become our major technology if mankind has any future, and today we are only seeing its very beginnings. But even in today's world it can also make good brass-nosed economics—if that is all you care about.

John D. Bu'Lock
Pune, India; November 1986

Contents

Part I | Fundamentals and Principles