

APPLIED BIOTECHNOLOGY

PROCEEDINGS OF BIOTECH 86 EUROPE HELD IN
LONDON MAY 1986



WORLD BIOTECH
REPORT 1986
VOLUME 1

onTime

APPLIED BIOTECHNOLOGY

PROCEEDINGS OF BIOTECH 86 EUROPE HELD IN
LONDON MAY 1986

WORLD BIOTECH REPORT 1986 VOLUME 1

onTime

London : New York



British Library Cataloguing in Publication Data

Biotech 86 (*London*)

The world biotech report 1986 : proceedings
of Biotech '86 held in London, May 1986.

Vol. 1 Applied biotechnology

1. Biotechnology

I. Title

660'.6 TP248.2

ISBN 0-86353-075-3

© Online 1986

ISBN 0 86353 075 3

Printed in the UK

The papers in this book are presented by the individual authors.
Online, therefore, accepts no liability for any errors or omissions.

No part of this book may be reproduced, stored in any form, by any
means, electronic, mechanical, photocopying, microfilming, recording
or otherwise, without written permission from the publisher.

Online Publications

A Division of Online International Ltd, London : New York



Online International is the world's leading specialist in the design, coordination and management of conferences and exhibitions concerned with the business implications and applications of leading-edge technology. With a schedule spanning some 20 technology areas, many Online events have achieved world forum status. The company was formed in 1971 and now employs more than 100 specialists based in London and New York.

Online International Ltd
Pinner Green House, Ash Hill Drive, Pinner, Middlesex HA5 2AE, UK
Phone: 01-868 4466 Telex: 923498 ONLINE G Fax: 018689933

Introduction

The past decade has witnessed the emergence of biotechnology as a vital commercial force. It now has a place in the business plans of major corporations and underpins a multitude of new companies, joint ventures, acquisitions and research agreements. The benchmark event, still talked about in the evolution of this new industry, was Biotech '83, held in London in May of that year.

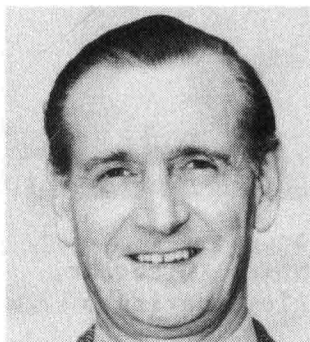
Three years on and both the business and science of biotechnology are stronger. The managers and researchers are more experienced and ambitious, the marketeers have packaged and sold their first products, and the marketplace has high expectations of further progress.

Three years on and **Applied Biotechnology** is the first in Online's 1986 series of Biotech proceedings. Its contents offer more on basic science applied in industry and more in-depth technical coverage. The contributions to this book will keep you informed and updated about the rapid scientific progress and technological innovations in biotechnology today.

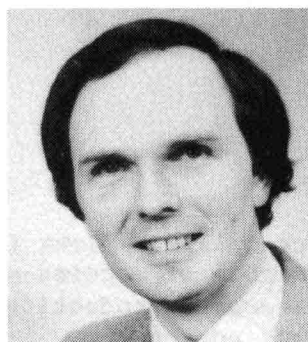
Session Chairmen



Peter Baker
Head, Biotechnology
Research Group, DTI



Fred Brown
Head of Virology R&D,
Wellcome Biotechnology



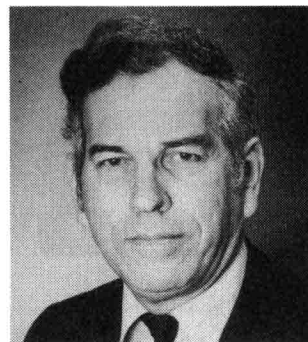
Robert Brown
Principal Scientific
Officer, Royal Signals
& Radar Establishment



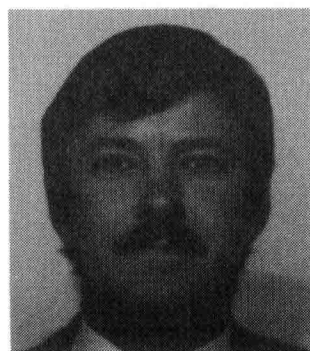
Howard Dalton
Prof. of Biological
Sciences, University
of Warwick



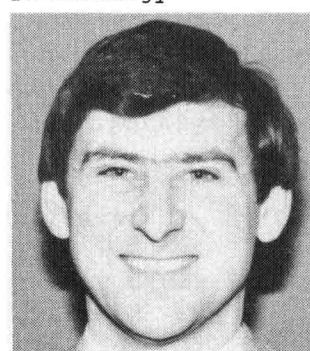
Brian Hartley FRS
Director, Centre for
Biotechnology, Imperial
College of Science &
Technology



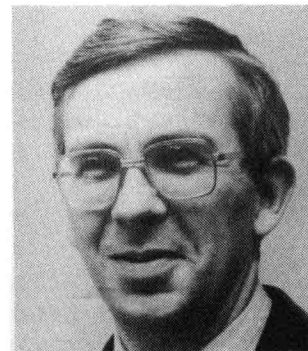
Peter Haskell
Director of the Field
Research Station,
UCW Cardiff



Gwyn Humphreys
Director of
Research, Apcel



Trevor Jarman
Manager, Biotechnology
Group, PA Technology



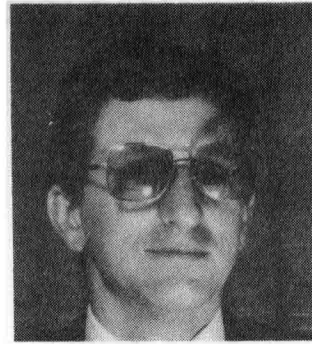
Chris Knowles
Prof., Biotechnology
Group, University of
Kent



Jack Melling
Director of Vaccine
Research & Production,
CAMR, Porton Down



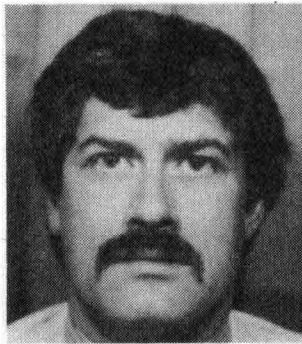
Brian Sagar
Technical Director,
Shirley Institute



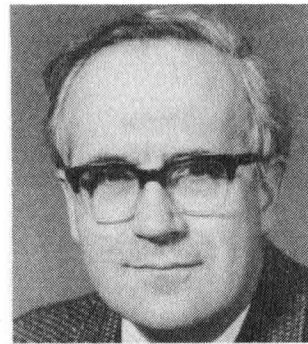
Norman Sawyer
Control Systems Mgr.,
Drew Scientific



Geoffrey Schild
Director, National
Institute for
Biological Standards &
Control



Roger Sherwood
Deputy Director,
Microbial Technology
Laboratory, CAMR,
Porton Down



David Tyrrell
Chairman, MRC Working
Party on AIDS

Contents

Production & processing of fine chemicals

Biotechnology: potential impact on the chemical industry

Sol Barer 1
Chem Systems
USA

Large scale chemistry with enzymes: a new process for a fine chemical

Stephen Taylor 5
ICI
UK

Enzymatic methods for the production of intermediates for organic synthesis

David Crout 13
University of Warwick
UK

Screening for new biocatalysts: general principles & examples

Peter Cheetham 19
PPF International
UK

Crop protection strategies

Breeding disease resistant varieties & strategies for their use

Martin Wolfe 29
Plant Breeding Institute
UK

Commercialisation of microbially produced pesticides

Barry Baldwin 39
Microbial Resources
UK

Strategies for the development of an integrated crop protection package

Dale Shaner 51
American Cyanamid
USA

Toxic and environmental waste

Polyurethane foam, rotating drums & aerobic wastewater treatment

Martin Davies 63
& Iain Sonley
University of York
UK

Microbial inoculants in environmental management	Howard Slater University of Wales Institute of Science & Technology & BioTechnica UK	75
Genetic engineering for dehalogenation & landfill applications	Stanley Sojka Occidental Chemical USA	81
Environmental management: is there a business?	Frank Holt ICI UK	89
Status report on AIDS		
Testing for HTLV-III/LAV antibodies in transfusion centres	Patricia Hewitt North London Blood Transfusion Centre UK	101
The individual at risk	Tony Whitehead The Terrence Higgins Trust UK	107
Formation & recovery of biologicals		
Production requirements of continuous r <u>E.coli</u> fermentations	Malcolm Rhodes Celltech UK	111
Production of human IFN-gamma & IL-2 in r-mammalian cell culture	Masahiko Iizuka et al Toray Industries Japan	117
Key issues in large-scale production of monoclonal antibodies for human health care	Brandon Price Damon Biotech USA/UK	119
New challenges to gel chromatography in bioprocess separations	John Ptak LKB-Produkter Sweden	129
Recombinant healthcare proteins: a route from expression to product	Peter Lowe Celltech UK	137
Future trends in downstream processing for industry	Tony Atkinson CAMR UK	143

Natural 'Biogenic' Materials**Structure & function relationships**

Natural structural materials	Julian Vincent University of Reading UK	149
Engineering aspects of natural composite materials	George Jeronimidis University of Reading UK	153
Biological ceramics	John Currey University of York UK	159
Adhesion in nature	Andrew Yule University College of N Wales UK	165

Novel materials for industry

Polyhydroxybutyrate: a commercial challenge	Nigel Uttley Marlborough Biopolymers UK	171
Chitin as a raw material for product development	Arthur J Hale Genzyme UK/UK	179
Novel protein materials via microbial production	Janice Light & Trevor Jarman PA Technology UK	185

New industrial applications

Hyaluronic acid	Derek Ellwood Fermentech UK	193
Novel medical composites	William Bonfield & John Behiri Queen Mary College UK	253*

Novel routes for the manufacture of polysaccharide fibres	Tom Burrow & Peter Laity Courtaulds Research UK	201
Biopolymers for materials uses: prospects for future innovation	Trevor Jarman & Janice Light PA Technology UK	211
<u>Vaccines</u>		
Enabling technologies		
From Jenner to genes: the new vaccines	Fred Brown Wellcome Biotechnology UK	219
Molecular basis of virus attenuation	David Bishop NERC Institute of Virology UK	225
New vaccine presentation approaches	Duncan Stewart-Tull University of Glasgow UK	231
Commercial perspectives		
Vaccines: scientific developments & commercial prospects	Jack Melling CAMR UK	239
Standardisation & control of vaccines	Ian Furminger Evans Medical UK	247

* To incorporate the most recent material this paper is included out of sequence.

Workshop documentation

Biotransformations: opportunities for the chemical industry

Biotransformations: opportunity for industry?	Peter Baker Department of Trade & Industry UK	A1
Biotechnology & the manufacture of organic chemicals	Christopher Drew SORIS UK	A7
Commercial prospects for biotransformation	Geoff Walker Department of Trade & Industry UK	A13
Biotransformations & bioprocesses for chemicals anticipated advantages & difficulties	Noël Rouy Rhône-Poulenc France	A15

Protein engineering

Protein engineering of industrial enzymes	Brian Hartley Imperial College UK	B1
Computer-aided peptide & protein engineering	Barry Robson Victoria University of Manchester UK	B9
X-ray crystallography & protein structure	Peter Murray-Rust Glaxo Group Research UK	B15
Engineered α_1 -antitrypsin variants of increased stability & altered specificity	Michael Courtney Transgene France	B21

Standardisation of control requirements for biologicals

Standardisation & controls of new generation biologicals	Tony Meager National Institute for Biological Standards & Control	C1
--	--	----

Biosensing systems

Introducing optical biosensors	Elizabeth Hall University of Cambridge UK	D1
Dynamic light scattering in biotechnology	Robert Brown Royal Signals & Radar Establishment UK	D7
Optical sensing of immunochemicals & biochemicals	Martin Smith Unilever Research UK	D9
Laser light scattering applied to biotechnology	David Clarke et al CAMR UK	D15

Computers in processing

Handling fermentation data by computer	Derek Fletcher Glaxo Group Research UK	E1
A practical guide to computer control of fermentation	Norman Sawyer Drew Scientific UK	E7
Digital fermentation control	Jeremy Court CAMR UK	E17
The applicability of future control to biotechnology	James Leigh Polytechnic of Central London UK	E23

Authors

Atkinson T	CAMR	UK	143/D15
Baker P B	Dept of Trade & Industry	UK	A1
Baldwin B	Microbial Resources	UK	39
Barer S J	Chem Systems	USA	1
Behiri J C	Queen Mary College	UK	253
Bishop D H L	NERC Institute of Virology	UK	225
Bonfield W	Queen Mary College	UK	253
Brown F	Wellcome Biotechnology	UK	219
Brown R G W	RSRE	UK	D7
Burrow T R	Courtaulds Research	UK	201
Carr R J G	CAMR	UK	D15
Cheetham P S J	PPF International	UK	19
Clarke D J	CAMR	UK	D15
Court J R	CAMR	UK	E17
Courtney M	Transgene	France	B21
Crout D H G	University of Warwick	UK	13
Currey J D	University of York	UK	159
Davies M	University of York	UK	63
Drew C J	SORIS	UK	A7
Ellwood D C	Fermentech	UK	193
Fletcher D L	Glaxo Group Research	UK	E1
Furminger I G S	Evans Medical	UK	247
Hale A J	Genzyme	UK/USA	179
Hall E A H	University of Cambridge	UK	D1
Hartley B S	Imperial College	UK	B1
Hewitt P E	North London Blood Transfusion Centre	UK	101
Holt F	ICI	UK	89
Iizuka M	Toray Industries	Japan	117
Ito M	Toray Industries	Japan	117
Jarman T	PA Technology	UK	185/211
Jeronimidis G	University of Reading	UK	153

Kobayashi S	Toray Industries	Japan	117
Laity P R	Courtaulds Research	UK	201
Leigh J R	Polytechnic of Central London	UK	E23
Light J	PA Technology	UK	185/211
Lowe P A	Celltech	UK	137
Meager T	National Inst for Biological Standards & Control	UK	C1
Melling J	CAMR	UK	239
Murray-Rust P	Glaxo Group Research	UK	B15
Okano K	Toray Industries	Japan	117
Price B J	Damon Biotech	UK/USA	119
Ptak J	LKB-Produkter	Sweden	129
Rhodes M	Celltech	UK	111
Robson B	Victoria University of Manchester	UK	B9
Rouy N	Rhône-Poulenc	France	A15
Sano E	Toray Industries	Japan	117
Sawyer N H	Drew Scientific	UK	E7
Shaner D L	American Cyanamid	USA	51
Slater J H	University of Wales Institute of Science & Technology & BioTechnica	UK	75
Smith A M	Unilever Research	UK	D9
Sojka S A	Occidental Chemical	USA	81
Sonley R I	University of York	UK	63
Stewart-Tull D E S	University of Glasgow	UK	231
Sudo T	Toray Industries	Japan	117
Tanaka T	Toray Industries	Japan	117
Taylor S C	ICI	UK	5
Uttley N L	Marlborough Biopolymers	UK	171
Vincent J F V	University of Reading	UK	149
Walker G	Dept of Trade & Industry	UK	A13
Whitehead T	The Terrence Higgins Trust	UK	107
Wolfe M S	Plant Breeding Institute	UK	29
Yule A B	University College of N Wales	UK	165

Biotechnology: potential impact on the chemical industry

**Sol J Barer
Director
Process Evaluation and Research Planning
Chem Systems
USA**

The chemical industry has undergone significant change during the past decade. A major aspect of this is the industry's trend to more high value-added materials from the previous commodity orientation. This change is still proceeding, with biotechnology potentially representing a discontinuity within this industry in both process technology and products. This talk will review the major potential advantages of microbial processing to fine chemicals and discuss the economics of specific potential processes including hydroxylated aromatics and amino acids.

Dr Sol J Barer is currently Director of Process Evaluation and Research Planning for Chem Systems, an international consulting firm for the chemical and biotechnology industries. He is involved with evaluation of the impact of biotechnology and other technologies on the chemical industry including techno-economic, strategic and commercial analyses. His clients include both major chemical companies and biotechnology companies.

Previously he was responsible for Celanese's Corporate research in the biotechnology, catalysis and new chemical process technology areas. His experience included the areas of agricultural chemicals, commodity chemicals and fine and specialty materials.

He is the holder of over twenty-five patents, is on the editorial board of Biocatalysis, is editing a book on industrial biotechnology, is on the Board of Directors of Alpha Probe a diagnostic company, is involved with new start-up biotechnology companies, is on the Industrial Overseeing Committee of the Engineering Research Center of Purdue University, and has been recently named a Distinguished Industrial Fellow at North Carolina State University.

The chemical industry has undergone significant change during the past decade. A major aspect of this is the industry's trend to more high value-added materials from the previous commodity orientation. This change is still proceeding, with biotechnology potentially representing a discontinuity within this industry in both process technology and products. This "new" technology arose as a result of a number of contributing factors building on the base of traditional fermentation technology. These factors include the increased knowledge of microbial pathways, the advent of recombinant DNA technology, advances in analytical capabilities, advances in biochemical engineering and the advent of monoclonal antibody technology.

Biotechnology processes are well known to have the potential advantages of selectivity, specificity, use of alternative raw materials, milder operating conditions, non-toxic nature and the ability of catalyst tailoring. The traditional disadvantages have been the requirement of dilute aqueous solutions as well as low rates and sterility. Although some of these disadvantages, e.g. dilute aqueous solutions, are solvable via biological and/or engineering means, they still represent a barrier to successful exploration of this technology.

Although much of the recent exploitation of this technology has been by the pharmaceutical industry, there has also been considerable activity in the chemical industry. Today a number of products are being produced biologically by this industry. These include the amino acids, citric acid, ethanol, polysaccharides, and pharmaceuticals. Newer research is in these areas as well as the specialty areas comprising flavors and fragrances, insecticides, fats and oils and, of course, pharmaceuticals.

Significant resources are being expanded towards the development of bioprocesses both within corporations and in university supported research.

Acrylamide is conventionally produced by the hydrolysis of acrylonitrile, which uses a heterogeneous catalyst. Conversion rates of 90 percent are typical, although a new Dow process is said to have a conversion rate of about 96 percent. Nitto's process involves a microbiological method for carrying out the hydrolysis of acrylonitrile to acrylamide using a variety of organisms.