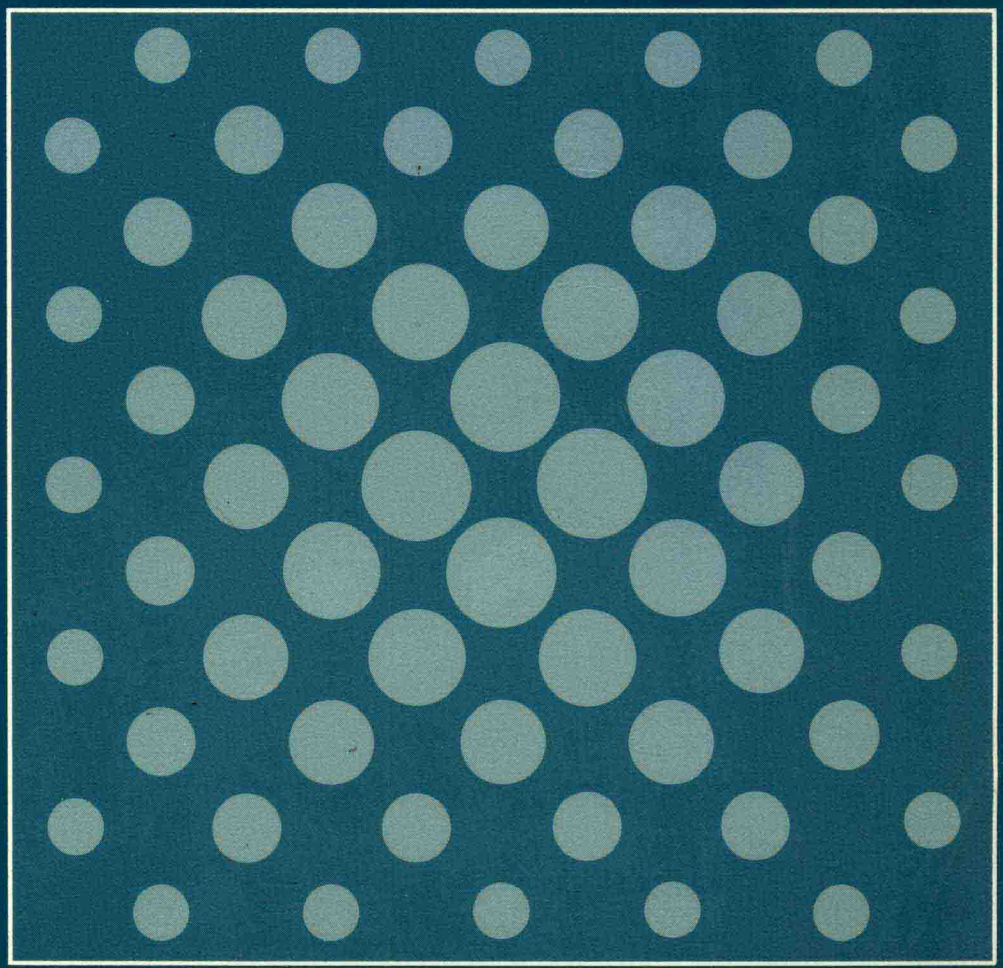
BIOTOL

BIOTECHNOLOGY BY OPEN LEARNING

Bioreactor Design and Product Yield



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Bioreactor Design and Product Yield

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BIOTECHNOLOGY BY OPEN LEARNING

Bioreactor Design and Product Yield

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This series of books has been developed through a collaboration between the Open universiteit of the Netherlands and Thames Polytechnic to provide a whole library of advanced level flexible learning materials including books, computer and video programmes. The series will be of particular value to those working in the chemical, pharmaceutical, health care, food and drinks, agriculture, and environmental, manufacturing and service industries. These industries will be increasingly faced with training problems as the use of biologically based techniques replaces or enhances chemical ones or indeed allows the development of products previously impossible.

The BIOTOL books may be studied privately, but specifically they provide a cost-effective major resource for in-house company training and are the basis for a wider range of courses (open, distance or traditional) from universities which, with practical and tutorial support, lead to recognised qualifications. There is a developing network of institutions throughout Europe to offer tutorial and practical support and courses based on BIOTOL both for those newly entering the field of biotechnology and for graduates looking for more advanced training. BIOTOL is for any one wishing to know about and use the principles and techniques of modern biotechnology whether they are technicians needing further education, new graduates wishing to extend their knowledge, mature staff faced with changing work or a new career, managers unfamiliar with the new technology or those returning to work after a career break.

Our learning texts, written in an informal and friendly style, embody the best characteristics of both open and distance learning to provide a flexible resource for individuals, training organisations, polytechnics and universities, and professional bodies. The content of each book has been carefully worked out between teachers and industry to lead students through a programme of work so that they may achieve clearly stated learning objectives. There are activities and exercises throughout the books, and self assessment questions that allow students to check their own progress and receive any necessary remedial help.

The books, within the series, are modular allowing students to select their own entry point depending on their knowledge and previous experience. These texts therefore remove the necessity for students to attend institution based lectures at specific times and places, bringing a new freedom to study their chosen subject at the time they need and a pace and place to suit them. This same freedom is highly beneficial to industry since staff can receive training without spending significant periods away from the workplace attending lectures and courses, and without altering work patterns.

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Project Manager: Dr J. W. James

How to use an open learning text

An open learning text presents to you a very carefully thought out programme of study to achieve stated learning objectives, just as a lecturer does. Rather than just listening to a lecture once, and trying to make notes at the same time, you can with a BIOTOL text study it at your own pace, go back over bits you are unsure about and study wherever you choose. Of great importance are the self assessment questions (SAQs) which challenge your understanding and progress and the responses which provide some help if you have had difficulty. These SAQs are carefully thought out to check that you are indeed achieving the set objectives and therefore are a very important part of your study. Every so often in the text you will find the symbol Π , our open door to learning, which indicates an activity for you to do. You will probably find that this participation is a great help to learning so it is important not to skip it.

Whilst you can, as a open learner, study where and when you want, do try to find a place where you can work without disturbance. Most students aim to study a certain number of hours each day or each weekend. If you decide to study for several hours at once, take short breaks of five to ten minutes regularly as it helps to maintain a higher level of overall concentration.

Before you begin a detailed reading of the text, familiarise yourself with the general layout of the material. Have a look at the contents of the various chapters and flip through the pages to get a general impression of the way the subject is dealt with. Forget the old taboo of not writing in books. There is room for your comments, notes and answers; use it and make the book your own personal study record for future revision and reference.

At intervals you will find a summary and list of objectives. The summary will emphasise the important points covered by the material that you have read and the objectives will give you a check list of the things you should then be able to achieve. There are notes in the left hand margin, to help orientate you and emphasise new and important messages.

BIOTOL will be used by universities, polytechnics and colleges as well as industrial training organisations and professional bodies. The texts will form a basis for flexible courses of all types leading to certificates, diplomas and degrees often through credit accumulation and transfer arrangements. In future there will be additional resources available including videos and computer based training programmes.

Preface

The popular misconceptions that biotechnology is synonymous with genetic manipulation and cell cloning belittles the importance of process technology to the successful development of biotechnology. Biotechnology is much more than a sub-discipline of biology. Although it is true that new knowledge emerging from the relevant biological sciences, has provided a fresh impetus to biotechnological exploitation over the past few decades, the key to successful exploitation lies in developments in the associated process technology. The integration of process engineering strategies with the possibilities made available by scientific research is essential if the desired goals of improved health care, food manufacture, agriculture and environmental protection are to be realised. Recent years have seen much progress made in the relevant engineering practices and we are rapidly moving away from using the empirical techniques of the past to a rationally developed technology much more fitted to exploit the biological possibilities.

This text is one of four BIOTOL texts designed especially to develop the knowledge and understanding of the principles and practices of contemporary bioprocess technology. These four texts are:

- Bioprocess Technology: Modelling and Transport Phenomena
- Operational Modes of Bioreactors
- Bioreactor Design and Product Yield
- Product Recovery in Bioprocess Technology

The first two of these texts deal with the fundamental principles which underpin bioreactor performance. This text extends this development to examine the issues of scale up and product yield and also includes a short introduction to process control. The final text in the series explains the processes and strategies that can be used for the recovery of products from bioreactors.

In this text, the authors have provided a brief orientating chapter which explain what pre-knowledge is assumed of the reader and to more fully explain the layout of the text. This is followed by a section dealing with the strategies that can be used to scale up laboratory scale processes to production scale. This section mainly examines the selection of scale up criteria and the advantages and limitations inherent in using such criteria. It also introduces the newly developing technique referred to as scale down. This section leads on to consider the performance of bioreactors of different design and configuration. The main focus is on the yields of biomass and other bioproducts and their relationships with process parameters and variables. The final part of the text introduces aspects of process control. The main focus here is on simple linear control systems.

The contributors have made an excellent job of integrating logically developed technical themes with sound educational practice. This text is a learning resource of distinction. It has made accessible to the reader, much of the current thinking in bioprocess technology, a reflection of the status of authors and advisors and the care they took in

selecting and developing material. Our thanks to all who have contributed. It is up to the reader to take full advantage of the opportunities this text offers. We encourage you to attempt the in text activities which have been designed to facilitate your learning and to use the self assessed questions to check your progress. In this way you will maximise the benefit you may gain from the text.

Scientific and Course Advisors: Prof M. C. E. van Dam-Mieras

Dr C. K. Leach

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An introduction to bioreactor design and product yield

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An introduction to bioreactor design and product yield

1.1 Sectors in the biotechnology industry

Increased knowledge of how biological systems function has undoubtedly increased mankind's ability to manipulate these systems. Key to this manipulation has been the development of the techniques which enable us to transfer genes from one organism to another and to modify the expression of genes within organisms. These techniques, commonly referred to as gene manipulation or genetic engineering are not simply confined to re-arranging existing, naturally occurring genes. Increasingly, through the use of molecular biological approaches, genes themselves are being modified to make more desirable products. For example by making the product made by the gene easier to purify or more stable and, therefore, longer-lived in use.

importance of bioprocess technology

The advances in biotechnology are not, however, solely a consequence of increase in biological knowledge and expertise. Of equal importance has been the progress made in process engineering. Industrial biotechnology, in essence, makes use of biological systems to catalyse chemical changes. The types of chemical changes that are of interest are very diverse. In some cases the value to mankind is to remove undesired components from a system. Waste water treatment is a good example of this. In such a process we seek to remove organic (and other) materials in the water to generate a non-toxic, usable product (clean water). In other cases we are interested in the chemical products made by the biological system. These may be bulk products like ethanol, citric acid or biomass itself or they may be fine chemicals including pharmaceutical compounds such as antibiotics and hormones. The diversity of biotechnological products and processes is described in Table 1.1.

diversity of products

Π Examine Table 1.1 carefully and estimate (or guess) for each product, the volume produced per year.

Industrial sector		Examples of products and processes
Pharmaceuticals		vaccines antibiotics diagnostics steroids alkaloids protein hormones and blood factors
Food		dairy meat and fish products beverages (alcohol, coffee, tea, etc) bread, bakers yeast food additives (antioxidants, colours, flavours) food supplements (amino acids, vitamins) starch products glucose and high fructose syrups enzymes novel foods, fungi
Agriculture		plant cell and tissue culture for quality assured stock genetically improved varieties biopesticides ensilaging and composting animal feedstuff manufacture vaccines
Chemicals	(bulk)	ethanol, butanol organic acids metal extraction
	(fine)	enzymes polymers (gums,agars) perfumes
Energy		ethanol methane biomass
Service		efficient treatment water re-claimation oil recovery analysis

Table 1.1 Industrial sectors and biotechnology products and processes.

We would anticipate that you would not have very accurate figures for each but you probably have placed each in the categories of fairly small, medium and large. In practice high priced, low volume products such as some of the specialised pharmaceuticals are produced in the range of $0.1\text{-}10^2$ kg y^{-1}. In the service sector, volumes of effluent treated is in the range of $10^6\text{-}10^{10}$ m^3 y^{-1}. There is, in fact, an enormous range in the scales of biotechnological processes.

We can identify three quite distinct scales of operation. Table 1.2 describes the broad characteristics of these three sectors.

Although we have divided these into three groups, you should realise that there are some areas of overlap. For example the use of recombinant DNA (genetically engineered) organisms are not included under sector III, but there is no inherent reason why they should not be used on this scale.

Characteristic	Sector I	Sector II	Sector III
Volumes	0.1-10^2 kg y^{-1}	10^3-10^5 kg y^{-1}	10^6-10^9 kg y^{-1}
Organism	rDNA	partly rDNA	natural producers
Product purity	very high	high/very high	relatively low
Recovery yield	subordinate importance	of minor importance	highly important
Cost price	fraction	20-50% determined by raw materials	50-90% determined by raw materials

Table 1.2 Characteristics of the three sectors of biotechnology based on the volume of annual output (rDNA = recombinant DNA, ie genetically engineered strains).

Π Examine Tables 1.1 and 1.2 carefully and mark on the tables those products and processes which involve the application of process technology be it for primary production, downstream processing or product transport and packaging.

You may not have been familiar with some of the products listed in Table 1.1. Nevertheless, a moments thought will have enabled you to realise that virtually all biological products will require the application of process technology. In most cases, the requirements of the market, the nature of the product and the need to retain commercial viability, results in the application of process technology to processes carried out on a large scale. Examination of Table 1.1 could not fail to have impressed you not only by the great diversity and value of bioproducts, but also by the importance of process technology in enabling us to produce these bioproducts.

Bioprocess technology essentially turns biological possibilities into practical propositions.

1.2 The components of bioprocess technology and the BIOTOL texts

Process biotechnology has its origins in chemical engineering. In both areas we are predominantly concerned with transforming one set of chemicals into another. The fundamental difference is that when we are using biological agents to carry out the catalysis, we can bring about more complex chemical changes with greater precision and yield. This advantage is, however, partially counterbalanced by the very specific demands that biological systems make on the environment in which they operate.