

BIOTECHNOLOGY

26 – 30 June 2006

Advanced Course on Downstream Processing

Aim

The challenge for biochemical engineers is to design compact and clean processes to efficiently separate instable products, such as recombinant proteins, from the dilute concentrations in complex fermentation broths to the required pharmaceutical degree of purity. Therefore, the design of integrated downstream processes is the general theme of the Advanced Course.

The Advanced Course presents the state of the art in downstream processing of biotechnological products. It provides knowledge of different techniques for the solid-liquid separation, product release, concentration and purification of precious biotechnology products. An international group of experts from industry and university will lecture to assure an optimal balance of practical knowledge and theoretical insight which will be trained by exercises, into the quantitative engineering aspects of bioseparations. At the end of the course, the participants should be able to estimate main equipment dimensions, know qualitative constraints to the integrated bioprocess, and have a quantitative insight in process streams, structure and economics.

Course description

The course will start with an overview of possibilities and problems typically associated with the recovery of bioproducts. Physico-chemical characteristics of the products, as well as those of the fermentation broth with its multiple contaminants, are discussed in relation to possibilities for selective separation. Using this information, the general structure of large scale industrial processes will be outlined.

The basics of thermodynamics and biochemical engineering will be introduced and developed during the course. Special attention will be paid to the unit operations typically used in this field of industry. Firstly, various solid-liquid separation techniques and cell disruption will be treated. Particular consideration will be given to the application of major concentration techniques such as extraction, adsorption and membrane separation. Furthermore, the scientific and industrial aspects of purification by means of precipitation and chromatography will be discussed. In addition, the release of intracellular products as well as protein folding in industrial protein processes will be discussed.

Process integration is the binding element in the course. During the course, a case study on the design of an integrated purification process for a recombinant protein will offer the participants the opportunity to practice on the individual unit operations as well as on the integrated process. Finally, possibilities of computer-aided, rational design of integrated separation processes, will be demonstrated.

This intensive course consists of lectures, exercises, case studies and computer simulations. Course notes and lectures will be in English. Before the start of the course, the participants will receive preparatory texts. For the exercises during the course, a pocket calculator is required.

Who should attend?

The course is aimed at postgraduates (M.Sc., Ph.D., Dutch “doctoraal” or “ingenieursexamen” or equivalent experience) in (bio)chemical engineering, or in microbiology or biochemistry with a basic knowledge in chemical engineering. The course is primarily aimed at those already employed in industry who are interested in the separation of biotechnological products. In addition, this Advanced Course is an option in the two-year postgraduate program in Biotechnology and Bioprocess Engineering given by BODL.

Duration / Location

The course will be given from
Monday June 26th - Friday June 30th, 2006

The course will be held at the
Department of Biotechnology
Delft University of Technology
Julianalaan 67, 2628 BC Delft
The Netherlands
Phone: 31 15 2781922
Fax: 31 15 2782355
E-mail: bodl@tudelft.nl

Accommodation

Lunches, the buffet on Monday June 26th and the course dinner on Thursday June 29th, will be provided. For the other meals, a variety of restaurants may be found in the center of the city. Hotel accommodation can be arranged at your request addressed to Ms. Ger Aggenbach.

Program, 26 – 30 June, 2006

Monday, June 26th

Themes: Today's bioseparation processes
Mechanical separation and concentration

08.45 Registration

09.00 Introduction to the separation processes

Pitfalls and challenges in bioseparation processes

Luuk van der Wielen

10.00 Engineering fundamentals

Mass balances: from batch to continuous counter current processes

Luuk van der Wielen

11.15 Case study: industrial protein production (I)

Introduction to the case study

Mass balances

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

13.30 Centrifugation in industry

Design considerations of sedimentation and centrifugation processes:
from biomass removal to centrifugal extraction

Karl-Heinz Brunner

14.30 Solid-liquid separation: filtration

Luuk van der Wielen

15.00 Exercises

Design of filtration and centrifugation equipment

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

16.00 Case study: industrial protein production (II)

Getting familiar with the case study and investigating options for
improvement of a protein purification process

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

18.00 Social event / Buffet

Tuesday, June 27th

Theme: Concentration and formulation

09.00 Predicting molecular properties

Molecular properties and selection of separation conditions

Equilibrium calculations

Luuk van der Wielen

10.30 Bulk crystallization

Unit operation design for the crystallization of small and large biomolecules

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

13.30 Industrial crystallization

Real life examples

Eric Grolman

15.15 Formulation of proteins and enzymes

Gabrie Meesters

16.30 Case study: industrial protein production (III)

Engineering and design of unit operations

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

Wednesday, June 28th

Theme: Concentration and purification processes

09.00 Extractive separation

Solvent selection and equipment design in extraction processes

Marcel Ottens

10.15 Extraction exercises

Marcel Ottens / Xiaonan Li / Tangir Ahamed

11.15 Aqueous two-phase extraction

Fundamental aspects and applications of aqueous two-phase separations

Maria-Regina Kula

13.30 Membrane technology

Design of membrane configurations

Jos Keurentjes

15.00 Membrane separations: an example case

Jos Keurentjes

16.00 Case study: industrial protein production (IV)

Engineering and design of unit operations

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

18.00 Inclusion Body processing and refolding

Michel Eppink

Thursday, June 29th

Theme: Purification processes

09.00 Design of chromatographic separations

Equilibrium theory and column design

Non-linear and mass transfer effects

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

10.30 Simulated Moving Bed chromatography for pharmaceutical proteins

Practical aspects and implementation for large scale chromatography in industry

Marc Bisschops

13.30 Chromatography in industrial practice

Column design and operation from theory and practice

Jan-Christer Janson

15.15 Case study: industrial protein production (V)

Process design: sequencing and interfacing of unit operations

Luuk van der Wielen / Marcel Ottens / Xiaonan Li / Tangir Ahamed

19.00 Course dinner

Friday, June 30th

Theme: Process integration

09.00 Process integration (I)

Downstream processing: overall strategy

Juan Asenjo

10.15 Process integration (II)

Downstream processing case studies: large scale separation and purification of *E. coli*, yeast and mammalian proteins

Juan Asenjo

14.00 Case study: industrial protein production (VI)

Reflection on the case

15.00 Evaluation of the course

Luuk van der Wielen

15.15 Farewell drink

Admission

Although there will be no selection procedure, the candidates are asked to submit information about their scientific background and experience. In special cases, a candidate may be advised to take other BODL Advanced Courses first, or to participate in introductory courses in order to obtain the necessary background.

Fee and registration

If you are interested, please fill in and return the attached form. Applications will be handled in order of the date of receipt.

The subsidized fee is:

€ 2500.- if the payment is received before **1 May 2006** or

€ 2750.- if the payment is received after this date.

To facilitate enrollment of young Ph.D. students from universities, a limited number of fellowships is available covering part of the course fee. In that case the reduced fee is € 1200.-. For application, please include a curriculum vitae and a copy of your university registration as a Ph.D. student.

Enterprises in The Netherlands can apply for the “Extra belastingaftrek (120%) van bedrijfsinvesteringen in scholing” (www.belastingdienst.nl) or in English: Additional tax deduction (120%) for company investment in education.

The fee includes course materials, lunches, the buffet on Monday, June 26th and the course dinner on Thursday, June 29th. The fee does not cover other meals and lodging.

Hotel accommodation can be arranged at your request.

In the event of cancellation before **1 May 2006**, a full refund will be granted. After this date, a 25% fee charge will be made.

Preparatory texts will be sent after receipt of the course fee. The complete course book will be supplied at the start of the course.

Board of the course

Prof. L.A.M. van der Wielen

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

Prof. G.W.K. van Dedem

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

I. Møllerup, M.Sc.

NOVO Nordisk A/S, Bagsvaerd, Denmark

Dr. E.J.A.X. van de Sandt

DSM Anti-Infectives / Innovation, Delft, The Netherlands

Lecturers

T. Ahamed, PDEng.

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

Prof. J.A. Asenjo

Universidad de Chile, Centre for Biochemical Engineering and Biotechnology, Santiago, Chile

Dr. M.A.T. Bisschops

Xendo Pharma Services B.V., Leiden, The Netherlands

Dr. K.-H. Brunner

Dr. Frische GmbH, Alzenau, Germany

Dr. M.H.M. Eppink

Diosynth BV, Oss, The Netherlands

Dr. E. Grolman

DSM-Research, Geleen, The Netherlands

Prof. J.-C. Janson

Uppsala Biomedical Centre, Department of Surface Biotechnology, Uppsala, Sweden

Prof. J.T.F. Keurentjes

Eindhoven University of Technology, Department of Chemical Process Technology, Eindhoven, The Netherlands

Prof. M.R. Kula

Formerly Heinrich-Heine Universität, Institut für Enzymtechnologie, Jülich, Germany

X. Li, PDEng.

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

Dr. G.M.H. Meesters

DSM Food Specialties, Delft, The Netherlands

Dr. M. Ottens

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

Prof. L.A.M. van der Wielen

Delft University of Technology, Department of Biotechnology, Delft, The Netherlands

Course coordinators

Dr. L.A. van der Meer-Lerk

Ms. G.W.J.O. Aggenbach

Biotechnological Sciences Delft Leiden (BSDL) is a graduate school that started as a joint initiative in biotechnological research and education of Delft University of Technology and Leiden University. It is supported by special funds supplied by the two universities, the Dutch government and the European Union. The BSDL postgraduate educational program features Ph.D. studies and special two-year courses for those who wish to tailor their own specialization to the needs of multidisciplinary biotechnological research and design. The latter programs are offered by Biotechnology Studies Delft Leiden (in Dutch: “Biotechnologie Opleidingen Delft Leiden”, BODL) and lead to the degree of "Master of Biotechnology" and the degree of “Professional Doctorate in Engineering”. It also includes participation in a series of Advanced Courses covering the multidisciplinary spectrum of biotechnology:

MICROBIAL PHYSIOLOGY AND FERMENTATION TECHNOLOGY

DOWNSTREAM PROCESSING

ENVIRONMENTAL BIOTECHNOLOGY

BIOCATALYSIS

APPLIED GENOMICS OF INDUSTRIAL FERMENTATION

STRATEGIC COMMUNICATION IN BIOTECHNOLOGY

QUALITY MANAGEMENT IN PHARMA AND BIOTECH

Further information

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Ms. Ger Aggenbach
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The address

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