

# Advanced Course

## Downstream Processing

4 - 8 July, 2016

### **Aim of the course**

The aim of the course is to provide and explain the tools to quantitatively and systematically design integrated downstream processes. Biotechnological engineers need to design compact and clean processes to efficiently separate bioproducts, such as proteins, from dilute complex fermentation broths to the required pharmaceutical degree of purity. Therefore, the general theme of this Advanced Course is the quantitative systematic design of integrated downstream processes.

The course presents the state of the art in downstream processing of biotechnological products. It provides knowledge of different techniques for solid-liquid separation, product release, refolding, concentration and purification of precious biotechnology products with a focus on the total integrated process. An international group of experts from both industry and academia will lecture to assure an optimal balance of practical knowledge and theoretical insight. Subsequently participants 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.

The course starts with an overview of possibilities and problems typically associated with the recovery of bioproducts. Physico-chemical characteristics of the products, as well as 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.

### **Course description**

This one-week course is intensive and has long days. To ensure active participation by those attending, a combination of theoretical (lectures) and practical (exercises, computer simulations and case study) work is offered. Some online preparatory materials will be given to ensure all have the same basic knowledge.

### **Lectures**

The thermodynamical basics and bioseparation principles will be introduced and developed during the course. Special attention will be paid to the unit operations typically used in this field of industry. Every day will be focused around a central theme.

The following subjects will be addressed:

Various solid-liquid separation techniques and cell disruption  
application of major concentration techniques such as extraction, adsorption and membrane separation  
scientific and industrial aspects of purification by means of precipitation and chromatography  
release of intracellular products as well as protein folding in industrial protein processes.

### **Exercises and case study**

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. The course will be given in English.

## **Who should attend?**

This Advanced Course is aimed at professionals (MSc or PhD level) 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 and who are interested in the separation of biotechnological products. In addition, this Advanced Course is an option in the two-year postgraduate programs of Delft University of Technology.

## **Location**

The course will be held at:  
Department of Biotechnology  
Delft University of Technology  
Van der Maasweg 9  
2629 HZ Delft, the Netherlands  
<http://bt.tudelft.nl>

## **Accommodation**

Hotel accommodation can be arranged at your request addressed to [biotechdelft@tudelft.nl](mailto:biotechdelft@tudelft.nl).

## Program, 4 – 8 July, 2016

### Monday 3 July 2017

Theme: Today's bioseparation processes.

Mechanical separations: solid-liquid separation

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)

Marcel Ottens and Exercise Assistances

12.30 Lunch

13:30 Solid-liquid separation: filtration and centrifugation

*Marcel Ottens*

14:15 Assignment: design of filtration equipment

15:15 Predicting molecular properties. Molecular properties and selection of separation conditions:  
Equilibrium calculations

*Luuk van der Wielen*

16:15 Case study: industrial protein production (II)

18:00 Social drink and buffet

### Tuesday 4 July 2017

Theme: Mechanical separations: solid liquid separation.

Concentration and design

09:00 Centrifugation in the biopharmaceutical industry

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

*Joe Shultz*

10:30 Assignment: centrifugation

11:30 Extractive separation: Solvent selection and equipment design in extraction processes

*Marcel Ottens*

12.30 Lunch

13:30 Assignment: extraction

14:30 Membrane technology: theory, design & industrial application

*Reinoud Noordman*

13:30 Assignment: membrane separation

14:30 Case study: industrial protein production (III)

18:00 End of the day

### Wednesday 5 July 2017

Theme: Purification processes

09:00 Design of chromatographic separations. Equilibrium theory and column design: Non-linear and mass transfer effects

*Marcel Ottens*

10:15 Chromatography in industrial practice

*Jan-Christer Janson*

11:45 Industrial cases and applications of chromatography

Column design and operation from theory and practice

*Jeroen den Hollander*

12.30 Lunch

14:00 Assignment: chromatography

15:15 Quality by Design

*Danielle Horneman*

16:30 Case study: industrial protein production (IV)

17:45 End of the day

18:00 Lab tour: High Throughput facilities (optional)

## **Thursday 6 July 2017**

Theme: Purification & formulation processes

- 9:00 Continuous chromatography and Simulated Moving Bed (SMB) Technology: Practical aspects and implementation for large scale chromatography in industry  
*Marc Bisschops*
- 10:15 Bulk crystallization: Unit operation design for the crystallization of small and large biomolecules  
*Geert-Jan Witkamp*
- 11:30 Assignment: crystallization
- 12.15 Lunch
- 13:15 Industrial crystallization: Real life examples  
*Rob Geertman*
- 14:45 The use of continuous operations to enable next generation production economics  
*Joe Shultz*
- 16:00 Design of an industrial process for purification of biologicals  
*Michel Eppink*
- 17:15 Case study: industrial protein production (V)
- 18:15 End of the day
- 19:00 Course dinner

## **Friday 7 July 2017**

Theme: Process development & process integration

- 9:00 Rational methodology for protein purification  
*Beckley Nfor*
- 10:15 High Throughput techniques in downstream process  
*Jürgen Hubbuch*
- 11:30 Process integration in industry  
*Matthias Wiendahl*
- 12.15 Lunch
- 14:15 Case study: industrial protein production (VI)  
Presentations of the three winning teams: the strategy DSP award ceremony
- 14:45 Evaluation of the course
- 15:00 Farewell drinks

## **Course Board**

### **Dr. Marcel Ottens**

Bioprocess Engineering  
Delft University of Technology  
Delft, the Netherlands

### **Prof. Luuk A.M. van der Wielen**

Bioprocess Engineering  
Delft University of Technology  
Delft, the Netherlands

## **Course coordination**

### **Vincent Renken, MSc, MSc(Ed)**

#### **Claudia Westhoff**

BioTech Delft  
Delft University of Technology  
Delft, the Netherlands

## **Lecturers**

### **Dr. Marc A.T. Bisschops**

Pall Life Sciences  
the Netherlands

### **Prof. Michel H.M. Eppink**

Synthon BV, Nijmegen and  
Bioprocess Engineering  
Wageningen University,  
Wageningen, the Netherlands

### **Dr. Rob Geertman**

DSM Fibre Intermediates BV  
Geleen, the Netherlands

### **Dr. Jeroen L. den Hollander**

DSM Biotechnology Center  
Delft, the Netherlands

### **Dr. Danielle Horneman**

Bataviabiosciences  
Leiden, the Netherlands

### **Prof. Jürgen Hubbuch**

Karlsruhe Institute for Technology  
Karlsruhe, Germany

### **Prof. Jan-Christer Janson**

Uppsala Biomedical Centre  
Department of Surface Biotechnology  
Uppsala, Sweden

### **Dr. Beckley Kungah Nfor**

Crucell  
Leiden, the Netherlands

### **Dr. Reinoud Noordman**

Pentair X-Flow  
Enschede, the Netherlands

### **Dr. Joe Shultz**

Novartis  
Basel, Switzerland

### **Dr. Matthias Wiendahl**

NOVO Nordisk A/S  
Gentofte, Denmark

### **Prof. Geert-Jan Witkamp**

Bioprocess Engineering  
Delft University of Technology  
Delft, the Netherlands

## **Exercises assistance**

### **Debora Gernat**

### **Victor Koppejan**

### **Silvia Pirrung**

### **Marcelo Silva**

Delft University of Technology  
Bioprocess Engineering  
Delft, the Netherlands

## Course registration

Please register via the website to attend the course. Deadline for application is 19 June 2017. Applicants will be handled in order of the date of receipt.

## Course fee

€ 2.750 in case of payment received before **22 May 2017** or

€ 3.000 in case of payment received after this date. In the event of cancellation before **22 May 2017**, a full refund will be granted, after this date, a 25% fee charge can be made.

To facilitate enrolment of young PhD-students from universities, a limited number of fellowships is available. The course fee with fellowship is € 1.375. To apply, please include a copy of your registration as a PhD-student from your university.

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

When the number of participants is too low to have a fruitful course, BioTech Delft will cancel the event no later than six weeks before the start of the course. The course fee will be reimbursed within three weeks after cancellation.

In case a speaker will not be able to present his/her lecture due to unforeseen circumstances, BioTech Delft will arrange an equivalent replacement.

Hotel accommodation can be arranged at your request.

Preparatory texts will be sent after receipt of the course fee, a month before the start of the course. The complete digital course book will be supplied at the start of the course.

BioTech Delft organises biotechnology education at postgraduate level. BioTech Delft closely cooperates with the department of Biotechnology of Delft University of Technology. Since its foundation, in 1987, BioTech Delft has very successfully organised various types of postdoctoral education.

Currently BioTech Delft offers given each year various Advanced Courses covering the multidisciplinary spectrum of biotechnology. The courses have a long track-record dating back to 1988.

- Microbial Physiology and Fermentation Technology (1988)
- Downstream Processing (1989)
- Biocatalysis and Protein Engineering (1999)
- Environmental Biotechnology (1993)
- Genomics in Industrial Biotechnology (2005)
- Metabolomics for Microbial Systems Biology (2010)
- Bioprocess Design (2014)

### **Further information**

Claudia Westhoff

Vincent Renken, MSc, MSc(Ed)

Course coordination

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