

ADVANCED COURSE

Downstream Processing

3 - 7 July 2023

Course board:
Marcel Ottens
Luuk van der Wielen

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 via 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.

COURSE BOARD

Prof. Marcel Ottens
Bioprocess Engineering
Delft University of Technology
Delft, The Netherlands

Prof. Luuk A.M. van der Wielen
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Bernal Institute and Chair of Biosystems
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University of Limerick
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COURSE COORDINATION

Jenifer Baptiste, BA
BioTech Delft
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LECTURERS

Prof. Raquel Aires Barros
Instituto Superior Tecnico
Lisboa, Portugal

Dr. Marc A.T. Bisschops
Pall BioTech
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Dr. Matthias Wiendahl
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Gentofte, Denmark

COURSE ASSISTANTS

Roxana Disela, Msc
Daphne Keulen, MSc
Delft University of Technology
Bioprocess Engineering
Delft, The Netherlands



PROGRAM

MONDAY 3 JULY 2023

Theme: Today's bioseparation processes.

Mechanical separations: solid-liquid separation

- 08:30 Registration
- 09:00 Opening
- 09:10 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 Course Assistants
- 12:30 Group picture and lunch
- 13:30 Solid-liquid separation: filtration and centrifugation
Marcel Ottens
- 14:15 Assignment: design of filtration equipment
Marcel Ottens and Course Assistants
- 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)
Marcel Ottens and Course Assistants
- 18:00 Social drink and buffet

TUESDAY 4 JULY 2023

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
Eduardo Lau
- 10:30 Assignment: centrifugation
Marcel Ottens and Course Assistants
- 11:30 Liquid-Liquid Extraction & Aqueous two phase
extraction
Raquel Aires Barros
- 12:45 Lunch
- 13:45 Assignment: extraction
Marcel Ottens and Course Assistants
- 14:45 Membrane technology: theory, design & industrial
application
Reinoud Noordman
- 16:15 Case study: industrial protein production (III)
Marcel Ottens and Course Assistants
- 18:05 Lab tour: High Throughput Facilities
- 19:00 Social Drink

WEDNESDAY 5 JULY 2023

Theme: Purification processes

- 09:00 Design of chromatographic separations.
Equilibrium theory and column design
Non-linear and mass transfer effects
Marcel Ottens
- 10:15 Assignment: ultrafiltration
Marcel Ottens and Course Assistants
- 11:15 Large-scale Continuous Chromatography and
Simulated Moving Bed (SMB) technology for
biotechnological products
Marc Bisschops
- 12:30 Lunch
- 13:30 Industrial cases and applications of chromatography
Column design and operation from theory and
practice
Alexander Hanke
- 14:15 Assignment: chromatography
Marcel Ottens and Course Assistants
- 15:45 Quality by Design
Danielle Horneman
- 17:00 Case study: industrial protein production (IV)
Marcel Ottens and Course Assistants
- 18:00 End of the day

THURSDAY 6 JULY 2023

Theme: Purification & formulation processes

- 9:00 Bulk crystallization: Unit operation design for the
crystallization of small and large biomolecules
Marcel Ottens
- 10:15 Assignment: crystallization
Marcel Ottens and Course Assistants
- 11:15 Industrial crystallization: Real life examples
Rob Geertman
- 12:15 Lunch
- 13:15 Inclusion body processing
Michel Eppink
- 14:45 Panel discussion
- 15:30 Case study: industrial protein production (V)
Marcel Ottens and Course Assistants
- 19:00 Course dinner

FRIDAY 7 JULY 2023

Theme: Process development & process integration

- 9:00 Rational methodology for vaccine purification process
development
Beckley Nfor
- 10:15 Design of an industrial process for purification of
biologicals
Michel Eppink
- 11:30 Process integration in industry
Matthias Wiendahl
- 12:30 Lunch
- 13:30 Case study: industrial protein production (VI)
Presentations of the three winning teams:
the strategy & DSP award ceremony
Marcel Ottens and Course Assistants
- 14:00 Closure of the course
Marcel Ottens
- 14:30 Farewell drink



LOCATION

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

ACCOMMODATION

For more information check our website or
email us at biotechdelft@tudelft.nl.

COURSE REGISTRATION

Please register via the website to attend the course. Deadline for application is **12 June 2023**. Applicants will be handled in order of the date of receipt.

COURSE FEE

€ 2.750 in case of payment received before **24 April 2023** or € 3.000 in case of payment received after this date. In the event of cancellation before **8 May 2023**, 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 Advanced Courses given each year, 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)*
- *Bioprocess Design (2014)*
- *Multiscale Computational Methods in Bioprocesses (2018)*
- *Integrated Multi-Omics approaches for Improvement of Industrial Microbes (2020)*

FURTHER INFORMATION

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Course coordination

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Advanced
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