

ADVANCED COURSE

Microbial Physiology and Fermentation Technology

20 - 31 January 2020

Course board:
Sef Heijnen
Han de Winde

AIM OF THE COURSE

The aim of the course is to familiarize participants with the integrated, interdisciplinary approach required in modern biotechnology. The course will cover intensive and in-depth presentations of the state of the art. At the same time, the course provides the necessary link between, on one hand, fundamental subjects (thermodynamics, stoichiometry, kinetics, genetics, system biology, fermentor transport and modeling) and, on the other hand, practical aspects (cultivation, (¹³C-)metabolomics, measurements) and applications in large-scale biotechnological processes.

The course provides lectures in fundamental aspects, followed by extensive exercises, made in groups, to stimulate interdisciplinary teamwork.

Subsequently the integration of biological and engineering concepts will be experienced in a design task and in a fed batch demo.

It will be possible to visit research projects and discuss topics of interest with scientific/technical staff.

At the end of the course you have learned to integrate life science and technology to achieve effective development/optimisation of new and existing fermentation processes.

COURSE DESCRIPTION

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

LECTURES

The lectures are mainly scheduled in the mornings and sometimes the early evenings.

In the lectures, attention will be paid to the following themes:

- Energy transduction and thermodynamics
- Kinetics and stoichiometry of growth and product formation
- Regulation of metabolism by environmental parameters
- High-cell-density fermentation
- Metabolic networks: stoichiometry and fluxes
- Rate based design
- Regulation and control of metabolic fluxes
- Metabolic engineering
- Heterogeneity and mixed cultures
- Capita selecta

EXERCISES, DESIGN CASE STUDY, COMPUTER SIMULATIONS AND FED BATCH DEMO

- The exercises by hand cover thermodynamics, balances, kinetics, stoichiometry analysis of fermentation data, metabolomics pathway stoichiometry and high-density fed batch.
- The case study is on design of a syngas fermentation
- Fed batch demo will focus on the discussions and interpretation of on- and off-line measurements in the gas and liquid phase to establish stoichiometry kinetics of biological conversions. Statistical data processing using mass balances.
- Tutorials in setting-up and simulating computer models of metabolic networks.

CONTACT WITH FACULTY STAFF

- There will be possibilities to visit the research projects of the Department of Biotechnology of Delft University of Technology.
- There will be possibilities to make appointments with faculty staff. Please get into contact with us before hand.

WHO SHOULD ATTEND?

This Advanced Course is aimed at professionals (MSc, PhD or equivalent experience) in microbiology, biochemistry or biochemical engineering with a basic working knowledge of the two other disciplines. Also, molecular biologists with a microbial background may apply. The course is primarily aimed at those already employed in industry and academia who wish to update their theoretical knowledge and practical insight in this field. In addition, this Advanced Course is an option in the two-year postgraduate programs of Delft University of Technology.



COURSE BOARD

Sef Heijnen
Cell Systems Engineering
Delft University of Technology
Delft, the Netherlands

Han de Winde
Molecular and Industrial Biotechnology
Institute for Biology
Leiden University, the Netherlands

FACULTY STAFF

Pascale Daran-Lapujade
Systems Biology
Walter van Gulik
Metabolic Engineering
Robbert Kleerebezem
Environmental Biotechnology
Mark Bisschops
Industrial Microbiology
Lesley Robertson
Curator of the Beijerinck Museum
Aljoscha Wahl
Systems Biology
Martin Pabst
Proteomics

COURSE COORDINATION

Jenifer Baptiste, BA
Vincent Renken, MSc, MSc(Ed)
BioTech Delft, Delft University of Technology
Department of Biotechnology
Delft, the Netherlands

LECTURERS

Matthias Heinemann
Molecular Systems Biology
Rijksuniversiteit Groningen
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MRC-LMB
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Sander Tans
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Technology, and AMOLF institute
Amsterdam, the Netherlands

Prof. Em. Joost Teixeira de Mattos
Swammerdam Institute for Life Sciences, SILS,
University of Amsterdam
the Netherlands

Ruud Weusthuis
Bioprocess Engineering
Wageningen University & Research
Wageningen, the Netherlands

FED BATCH DEMO

Dirk Geerts
Rob Kerste
Cell Systems Engineering
Delft University of Technology
Delft, the Netherlands

PROGRAM

MONDAY 20 JANUARY 2020

Theme: Thermodynamics, balances and q-rates

- 08:45 Registration
09:00 Outline of the course
Han de Winde
09:15 Basic energetics of microbial metabolism
Robbert Kleerebezem
10:30 Balances
Sef Heijnen
11:45 q-rates
Sef Heijnen
12:20 Lunch
13:15 Parallel sessions:
Exercises on energetics of microbial metabolism
Robbert Kleerebezem
Exercises on balances and q-rates
Sef Heijnen
17:45 Social drink and buffet

TUESDAY 21 JANUARY 2020

Theme: Kinetics and stoichiometry of growth, product formation, process design and membranes transport

- 09:00 Batch, fed batch and continuous cultivation
Aljoscha Wahl
10:15 Black box model: kinetics / parameterization
Sef Heijnen
11:30 Black box model: stoichiometry
Sef Heijnen
12:30 Lunch
13:30 Introduction to bioprocess design (batch, continuous)
Sef Heijnen
14:30 Exercises on bioprocess reactions in design
Sef Heijnen
17:45 Transport over biological membranes: mechanisms and thermodynamics
Walter van Gulik
18:30 End of the day

WEDNESDAY 22 JANUARY 2020

Theme: Regulation of metabolism by environmental parameters, fermentation design and data analysis

- 09:00 Primary metabolism and its regulation
Pascale Daran-Lapujade
10:00 Microbial growth with mixtures of carbon substrates
Han de Winde
11:00 Physiological aspects of high cell density fermentation
Han de Winde
12:10 Lunch
13:00 Fed batch fermentation and transport phenomena
Sef Heijnen
14:30 Exercises on data analysis of fermentation processes
Sef Heijnen
17:00 Optional: Visit tour selected research projects department of Biotechnology
18:00 End of the day

THURSDAY 23 JANUARY 2020

Theme: Metabolic networks: stoichiometry, Flash energy and Fed batch demo

- 09:00 Metabolic network analysis
Sef Heijnen
10:15 Exercises : Metabolic pathway stoichiometry
Sef Heijnen
12:30 Lunch
13:30 Fed batch demo: Stoichiometric network calculation
Sef Heijnen
14:00 Fed batch demo: Fed batch fermentation
Sef Heijnen
14:30 Fed batch demo: Design calculation
Rob Kerste
15:15 Fed batch demo: Measurements why and how
Rob Kerste
16:00 Bioenergetics of microbial growth and the cost of adaption, Part I
Joost Teixeira de Mattos
17:00 Bioenergetics of microbial growth and the cost of adaption, Part II
Joost Teixeira de Mattos
18:00 Buffet

FRIDAY 24 JANUARY 2020

Theme: Metabolic networks: stoichiometry, fluxes and high-cell density fed batch

- 09:00 Metabolic flux balancing: theory and applications
Aljoscha Wahl
10:15 Computer exercises on metabolic network analysis
Aljoscha Wahl
12:45 Lunch
13:45 Metabolic studies in the industrial contexts
Ralf Takors
14:45 Exercises on high-cell density fed batch cultivation
Walter van Gulik/Aljoscha Wahl
18:15 Social drink

MONDAY 27 JANUARY 2020

Theme: Case study: Ethanol from syngas

- 09:00 Rate based design of biosystems
Sef Heijnen
09:30 Case study: Ethanol from syngas
Henk Noorman / Sef Heijnen
12:45 Lunch
13:25 (optinal) Visit fermentation lab (max. 10 persons)
Dirk Geerts/Rob Kerste
17:15 Gas Fermentation: a path to low carbon fuel and chemical production with impact
Bjorn Heijstra
18:25 End of the day

TUESDAY 28 JANUARY 2020

Theme: Regulation and control of metabolic fluxes, rapid sampling

- 09:00 Multi-scale modelling of process dynamics in large-scale bioreactors
Matthias Reuss
10:15 Multi-level regulation of metabolic fluxes, transcripts versus fluxes
Pascale Daran-Lapujade
11:00 Analysis of in vivo kinetics: rapid sampling and metabolite analysis
Walter van Gulik
12:15 Lunch
13:15 Fed batch demo: Balance calculations on batch phase data
Sef Heijnen / Dirk Geerts / Rob Kerste / Walter van Gulik
15:15 Through Van Leeuwenhoek's eyes
Lesley Robertson
16:00 Van Leeuwenhoek and Delft: A microbiological pilgrimage (social/cultural event)
Lesley Robertson
18:00 Social drink and small dinner

WEDNESDAY 29 JANUARY 2020

Theme: Metabolic and community engineering

- 09:00 Metabolic engineering strategies for reducing costs
Sef Heijnen
10:30 Exercises on metabolic engineering strategies for reducing costs
Sef Heijnen
12:30 Lunch
13:55 (optinal) Visit fermentation lab (max. 10 persons)
Dirk Geerts/Rob Kerste
13:30 From System Biology to Metabolic Engineering and Industrial Process Development using *Clostridium acetobutylicum* as a Platform Strain
Philippe Soucaille
14:30 *Monascus ruber* as cell factory for lactic acid production at low pH
Ruud Weusthuis
15:45 Zero growth physiology – from biotechnology to brains
Mark Bisschops
17:00 Microbial community engineering for production of chemicals and bioenergy
Robbert Kleerebezem
18:10 End of the day

THURSDAY 30 JANUARY 2020

Theme: Heterogeneity of microbial populations

- 09:00 Single cell studies of micro-organisms / Microfluidics
Sander Tans
10:15 Spatio-temporal single-cell analysis in picoliter reactors
Dietrich Kohlheyer
11:30 The limits to growth: the challenge to dissipate energy
Matthias Heinemann
12:30 Lunch
13:30 Transcription factor-based biosensors for strain development
Jan Marienhagen
14:30 Fed batch demo: Balance calculations on the fed phase data and evaluation
Sef Heijnen / Dirk Geerts / Rob Kerste / Walter van Gulik
17:00 Optional: Practical labtour regarding Chemostat
Dirk Geerts/Rob Kerste
19:00 Course dinner

FRIDAY 31 JANUARY 2020

Theme: Capita Selecta

- 09:30 Microbial protein production in an industrial context
Cees Sagt
10:45 High-throughput strain construction and phenotype testing
Stefan de Kok
11:45 Lunch
13:15 Latest advancements in high-resolution microbial mass spectrometry
Martin Pabst
14:15 The Origin of Life and Metabolism
John Sutherland
15:25 Optional: Practical labtour regarding Chemostat
Dirk Geerts/Rob Kerste
15:25 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

Hotel accommodation can be arranged at your request addressed to biotechdelft@tudelft.nl.



COURSE REGISTRATION

Please register via the website to attend the course. Deadline for application is **30 December 2019**. Applications will be handled in order of the date of receipt.

COURSE FEE

€ 3.650 in case of registration before **11 November 2019** or € 3.900 in case of registration after this date. In the event of cancellation before **25 November 2019**, 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 € 1.825. 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.



 **TU Delft**

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BioTech Delft organises courses in biotechnology 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 various 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)*
- *Genomics in Industrial Biotechnology (2005)*
- *Metabolomics for Microbial Systems Biology* (2010)*
- *Bioprocess Design** (2014)*
- *Multiscale Computational Methods in Bioprocesses (2018)*

* in partnership with Forschungszentrum Jülich

** in partnership with Wageningen University & Research

FURTHER INFORMATION

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