

ADVANCED COURSE

# Microbial Physiology and Fermentation Technology

21 January - 1 February 2019

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, (<sup>13</sup>C-)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.



**BioTechDelft**  
POSTGRADUATE EDUCATION

**TU**Delft

## 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, the Netherlands

**Han de Winde**  
Industrial Biotechnology  
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

## COURSE COORDINATION

**Vincent Renken**  
BioTech Delft

## LECTURERS

**Matthias Heinemann**  
Molecular Systems Biology  
Rijksuniversiteit Groningen  
Groningen, the Netherlands

**Mickel Jansen**  
DSM Biotechnology Center  
Delft, the Netherlands

**Dietrich Kohltheyer**  
Institute of Bio- and Geosciences  
IBG-1: Biotechnology  
Microscale Bioengineering Group  
Forschungszentrum Jülich GmbH  
Germany

**Stefan de Kok**  
Zymergen  
Emeryville, USA

**Jan Marienhagen**  
Institute of Bio- and Geosciences  
IBG-1: Biotechnology  
Forschungszentrum Jülich GmbH  
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**Henk Noorman**  
DSM Biotechnology Center and  
Delft University of Technology  
Delft, the Netherlands

**Matthias Reuss**  
Institut für Bioverfahrenstechnik  
University Stuttgart  
Germany

**Cees Sagt**  
DSM Biotechnology Center  
Delft, the Netherlands

**Sean Simpson**  
Chief Scientific Officer  
Lanzatech

**Philippe Soucaille**  
LISBP, University of Toulouse,  
Toulouse Cedex, France

**Ralf Takors**  
Institut für Bioverfahrenstechnik  
University of Stuttgart  
Germany

**Sander Tans**  
Kavli Institute of NanoScience, Delft University of  
Technology, and  
FOM-Institute for Atomic and Molecular Physics  
(AMOLF), Amsterdam

**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

**Gilles van Wezel**  
Molecular Biotechnology  
Leiden University  
Leiden, the Netherlands

## FED BATCH DEMO

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



# PROGRAM

## MONDAY 21 JANUARY 2019

Theme: Thermodynamics, balances and q-rates

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

## TUESDAY 22 JANUARY 2019

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 23 JANUARY 2019

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 24 JANUARY 2019

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

- 09:00 Metabolic network analysis  
*Sef Heijnen*
- 10:00 Exercises : Metabolic pathway stoichiometry  
*Sef Heijnen*
- 12:30 Lunch
- 13:30 Bioenergetics of microbial growth and the cost of adaptation  
*Joost Teixeira de Mattos*
- 15:30 Fed batch demo: Stoichiometric network calculation and fed batch fermentation  
*Sef Heijnen*
- 16:15 Fed batch demo: Design calculation and measurements why and how  
*Rob Kerste*
- 18:15 Buffet

## FRIDAY 25 JANUARY 2019

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*
- 18:00 Social drink

## MONDAY 28 JANUARY 2019

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
- 13:30 Continuation of Case study  
*Henk Noorman / Sef Heijnen*
- 17:15 Gas Fermentation: a path to low carbon fuel and chemical production with impact  
*Sean Simpson*
- 18:15 End of the day

## TUESDAY 29 JANUARY 2019

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*
- 11:15 Through Van Leeuwenhoek's eyes  
*Lesley Robertson*
- 12:00 Antonie van Leeuwenhoek: his work and his microorganisms  
*Lesley Robertson*
- 13:00 Lunch
- 14:30 Analysis of in vivo kinetics: rapid sampling and metabolite analysis  
*Walter van Gulik*
- 15:45 Fed batch demo: Balance calculations on batch phase data  
*Sef Heijnen / Dirk Geerts / Rob Kerste / Walter van Gulik*
- 17:45 End of the day

## WEDNESDAY 30 JANUARY 2019

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
- 13:30 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*
- 18:00 End of the day

## THURSDAY 31 JANUARY 2019

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*
- 15:30 Fed batch demo: Balance calculations on the fed phase data and evaluation  
*Sef Heijnen / Dirk Geerts / Rob Kerste / Walter van Gulik*
- 19:00 Course dinner

## FRIDAY 1 FEBRUARY 2019

Theme: Capita Selecta

- 09:30 Microbial protein production in an industrial context  
*Cees Sagt*
- 10:30 High-throughput strain construction and phenotype testing  
*Stefan de Kok*
- 11:45 Lunch
- 13:45 Approaches to discover and develop novel antibiotics from actinobacteria  
*Gilles van Wezel*
- 14:45 Low pH Fermentation to Succinic Acid, the Basis for Efficient Recovery  
*Mickel Jansen*
- 16:00 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](mailto:biotechdelft@tudelft.nl).



## COURSE REGISTRATION

Please register via the website to attend the course. Deadline for application is **7 January 2019**. Applications will be handled in order of the date of receipt.

## COURSE FEE

€ 3.650 in case of registration before **12 November 2018** or € 3.900 in case of registration after this date. In the event of cancellation before **26 November 2018**, 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.



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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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Course coordination

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