

ADVANCED COURSE

# Microbial Physiology and Fermentation Technology

8 - 17 June 2022

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.

## 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  
**Lesley Robertson**  
Curator of the Beijerinck Museum  
**Jean-Marc Daran**  
Industrial Biotechnology

## COURSE COORDINATION

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

## LECTURERS

**Amit Deshmukh**  
DSM Biotechnology Center  
Delft, the Netherlands

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

**Dietrich Kohlheyer**  
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  
Germany

**Henk Noorman**  
DSM Biotechnology Center and  
Delft University of Technology  
Delft, the Netherlands

**Matthias Reuss**  
Stuttgart Research Center, Systems Biology (SRCB)  
University Stuttgart  
Germany

**Bjorn Heijstra**  
LanzaTech B.V.  
Amsterdam, the Netherlands

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

**John Sutherland**  
MRC-LMB  
Cambridge, United Kingdom

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

**Sander Tans**  
Kavli Institute of NanoScience, Delft University of  
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

**Wouter van Winden**  
DSM - Bioscience and Process Innovation  
Delft, the Netherlands

## FED BATCH DEMO

**Dirk Geerts**  
Environmental Biotechnology  
**Erik de Hulster**  
Industrial Microbiology  
Delft University of Technology  
Delft, the Netherlands



# PROGRAM

## WEDNESDAY 8 JUNE 2022

Theme: Thermodynamics, balances and q-rates

- 08:45 Introduction  
*Vincent Renken*
- 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*
- 17:45 Social drink and buffet

## THURSDAY 9 JUNE 2022

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

- 09:00 Black box model: kinetics / parameterization  
*Walter van Gulik*
- 10:00 Black box model: stoichiometry  
*Walter van Gulik*
- 11:15 Introduction to bioprocess design (batch, continuous)  
*Sef Heijnen*
- 12:00 Exercises on bioprocess reactions in design  
*Sef Heijnen*
- 12:30 Lunch
- 13:30 Continuation: Exercises on bioprocess reactions in design  
*Sef Heijnen*
- 15:45 Plenary discussion exercises  
*Sef Heijnen*
- 16:15 Transport over biological membranes: mechanisms and thermodynamics  
*Walter van Gulik*
- 17:25 End of the day

## FRIDAY 10 JUNE 2022

Theme: Regulation of metabolism by environmental parameters, fed batch fermentation design and fermentation 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*
- 12:00 Lunch
- 13:00 Fed batch fermentation and transport phenomena  
*Sef Heijnen*
- 14:30 Exercises on data analysis of fermentation processes  
*Sef Heijnen*
- 17:00 Plenary discussion exercises  
*Sef Heijnen*
- 17:30 Optional: Fermentation lab facilities tour  
*Dirk Geerts/Erik de Hulster*

## MONDAY 13 JUNE 2022

Theme: Metabolic networks: stoichiometry, energy and application

- 09:00 Metabolic network analysis  
*Walter van Gulik*
- 10:30 Exercises: Metabolic pathway stoichiometry  
*Sef Heijnen*
- 12:30 Lunch
- 14:15 Plenary discussion exercises  
*Sef Heijnen*
- 14:30 Bioenergetics of microbial growth and the cost of adaption, Part I  
*Joost Teixeira de Mattos*
- 15:45 Bioenergetics of microbial growth and the cost of adaption, Part II  
*Joost Teixeira de Mattos*
- 16:45 Metabolic studies in the industrial contexts  
*Ralf Takors*
- 18:00 Social drink and Buffet

## TUESDAY 14 JUNE 2022

Theme: Metabolic networks: modelling, rapid sampling, regulation

- 09:00 Metabolic flux balancing: theory and applications  
*Wouter van Winden*
- 10:15 Computer exercises on metabolic network analysis  
*Wouter van Winden*
- 12:30 Plenary discussion exercises  
*Wouter van Winden*
- 12:45 Lunch
- 13:45 Analysis of in vivo kinetics: rapid sampling and metabolite analysis  
*Matthias Reuß*
- 15:15 Multi-scale modelling of process dynamics in large-scale bioreactors  
*Matthias Reuß*
- 16:15 Multi-level regulation of metabolic fluxes, transcripts versus fluxes  
*Pascale Daran-Lapujade*
- 17:00 Single cell studies of micro-organisms / Microfluidics  
*Sander Tans*
- 18:05 Optional: Lab techniques tour department of Biotechnology

## WEDNESDAY 15 JUNE 2022

Theme: Industrial fermentation: Case study "Ethanol from syngas"

- 09:00 Rate based design of biosystems  
*Sef Heijnen*
- 09:30 Case study: Ethanol from syngas  
*Henk Noorman / Amit Deshmukh*
- 12:45 Lunch
- 13:25 (optional) Visit fermentation lab  
*Dirk Geerts/Erik de Hulster*
- 14:00 Continuation Case Study  
*Henk Noorman / Amit Deshmukh*
- 17:15 Gas Fermentation: a path to low carbon fuel and chemical production with impact  
*Bjorn Heijstra*
- 18:25 End of the day

## THURSDAY 16 JUNE 2022

Theme: Metabolic engineering: Strategies and applications

- 09:00 Metabolic engineering strategies for reducing costs  
*Sef Heijnen*
- 10:30 Exercises on metabolic engineering strategies for reducing costs  
*Sef Heijnen*
- 12:15 Plenary discussion exercises  
*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 Evolutionary and reverse engineering of *S. cerevisiae*  
*Jean-Marc Daran*
- 16:45 Microbial community engineering for production of chemicals and bioenergy  
*Robbert Kleerebezem*
- 18:15 Course dinner

## FRIDAY 17 JUNE 2022

Theme: Capita Selecta: Single cells limits, scale up/down origin

- 09:00 Through Van Leeuwenhoek's eyes  
*Lesley Robertson*
- 10:00 The limits to growth: the challenge to dissipate energy  
*Matthias Heinemann*
- 11:15 Spatio-temporal single-cell analysis in picoliter reactors  
*Dietrich Kohlheyer*
- 12:15 Lunch
- 13:15 Transcription factor-based biosensors for strain development  
*Jan Marienhagen*
- 14:15 Fermentation scale-up and scale-down  
*Stefan de Kok*
- 15:15 The Origin of Life and Metabolism  
*John Sutherland*
- 16:00 Evaluation and certification  
*Han de Winde*
- 16:30 Farewell drinks



### 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 **18 May 2022**. Applications will be handled in order of the date of receipt.

## COURSE FEE

€ 3.650 in case of registration before **30 March 2020** or  
€ 3.900 in case of registration after this date. In the event of cancellation before **13 April 2022**, 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.



Department of Biotechnology, Delft University of Technology  
Van der Maasweg 9, 2629 HZ Delft, The Netherlands

T +31 (0)15 278 1922 E [biotechdelft@tudelft.nl](mailto:biotechdelft@tudelft.nl)

**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)*
- *Modelling and Computation for Microorganisms in Bioprocesses (2018)*
- *Integrated Multi-Omics approaches for Improvement of Industrial Microbes (2020)*

## FURTHER INFORMATION

Jenifer Baptiste, BA

Vincent Renken, MSc, MSc(Ed)

Course coordination

T +31 15 278 1922 / 8311

F +31 15 278 2355

E [biotechdelft@tudelft.nl](mailto:biotechdelft@tudelft.nl)

W [biotechnologycourses.nl](http://biotechnologycourses.nl)

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