ADVANCED COURSE Microbial Physiology and Fermentation Technology

> Course board: Pascale Daran-Lapujade Henk Noorman

# AIM OF THE COURSE

13 - 24 January

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.

It will be possible to visit research projects and discuss topics of interest (technical aspects of fermentation, sampling, analytics) 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 10 day course is taught in English and has intensive days. To ensure active participation by those attending, a combination of theoretical (lectures) and practical (exercises, computer simulations, design case study) 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:

- Thermodynamics and balances
- · Kinetics and stoichiometry (process reaction), membrane transport
- Regulation of metabolism by environmental parameters
- High-cell-density fed batch fermentation
- · Metabolic networks: modelling, regulation and stoichiometry
- Case study, Rate based design
- Metabolic engineering, strategy and applications

# EXERCISES, DESIGN CASE STUDY, COMPUTER SIMULATIONS

- The exercises by hand cover thermodynamics, balances, kinetics, stochiometry analysis of fermentation data, metabolomics pathway stoichiometry.
- Tutorials in setting-up and simulating computer models of metabolic networks.
- The case study is on design of a syngas fermentation

## 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 contact 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 Pascale Daran-Lapujade

Pascale Daran-Lapujade Industrial Biotechnology Experimental Systems Biology/Synthetic Biology Henk Noorman Bioprocess Engineering dsm-firmenich

#### FACULTY STAFF Industrial Biotechnology

Industrial Biotechnology Jack Pronk Djordje Bajić Bioprocess Engineering Marieke Klijn Cees Haringa Ludovic Jourdin Environmental Biotechnology Robbert Kleerebezem Martin Pabst Lesley Robertson

Cell Systems Engineering Sef Heijnen

#### COURSE COORDINATION Yvonne van Gameren Jenifer Baptiste BioTech Delft, Delft University of Technology Department of Biotechnology, the Netherlands

**LECTURERS** Wouter van Winden dsm-firmenich

dsm-firmenich Delft, the Netherlands

Bjorn Heijstra LanzaTech B.V. Amsterdam, the Netherlands

Anna-Lena Heins Hamburg University of Technology Institute of Bioprocess and Biosystems Engineering Hamburg, Germany

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

Irina Borodina The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark BioPhero Pheromones, FMC Corporation Copenhagen, Denmark

Jan Marienhagen Institute of Bio- and Geosciences IBG-1: Biotechnology Synthetic Cell Factories Group Forschungszentrum Jülich GmbH Germany

Brett Schreyer Arete BioProcess Consulting LLC Colorado, USA

Nico Callewaert VIB-UGent Center for Medical Biotechnology Zwijnaarde, Belgium

Cees Sagt dsm-firmenich Delft, the Netherlands

Frank Bruggeman Vrije Universiteit Amsterdam Amsterdam, the Netherlands

Katelijne Bekers MicroHarvest Hamburg, Germany

Chris Mehrer Geno San Diego, USA

Sarah Lieder Unilever, R&D Nutrition and Ice Cream Wageningen, the Netherlands

Bas Teusink Systems Biology Lab, AIMMS, Vrije Universiteit Amsterdam Amsterdam, the Netherlands

Mark Bisschops Bioprocess Engineering Wageningen University & Research Wageningen, the Netherlands

# PROGRAM

## MONDAY 13 JANUARY 2025

Theme: Beginning with the end in mind, balances, conversion rates modes of fermenter operation Coordinator Pascale Daran-Lapujade

- 08.45 Registration
- 09.00
- Outline of the course Pascale Daran-Lapujade Microbial Physiology vs. Fermentation Technology Jack Pronk / Henk Noorman 09.15
- 10.30
- Developing scalable bioprocesses: Lessons and examples from industry Chris Mehrer Balances and rates 11.30
- Sef Heijnen Lunch & Picture
- 12.30 13.30
- q: Biomass specific conversion rates Sef Heijnen
- 14.15 Excercises on balances and biomass specific conversion rates Sef Heijnen
- Balances and modes of fermentation operation Marieke Klijn 16.45
- 17.40 Social drink and buffet

#### **TUESDAY 14 JANUARY 2025**

Theme: Thermodynamics, stoichiometry and kinetics of growth, product formation and process design Coordinator Robbert Kleerebezem

- 09:00 Basic energetics of microbial metabolism Robbert Kleerebezem
- Exercises on energetics of microbial metabolism Robbert Kleerebezem 10:00
- 12.30

Lunch Thermodynamics 13.15

- Mark Bisschops Black Box model: kinetics/parametrization 14:15
- Sef Heijnen
- Black Box model: stoichiometry/process reaction for design 15.30 Sef Heijnen
- Engineering yeast for 1st and 2nd generation bioethanol production 17:00
- Jack Pron 18.00 End of the day

## WEDNESDAY 15 JANUARY 2025

#### Theme: Fermentation: design, transport and data analysis

Coordinator Sef Heijnen

- 09.00 Introduction to bioprocess design using the process reaction Sef Heijnen Excercises on bioprocess reactions in design Sef Heijnen 10:00 12.30 13.30 Lunch Fermentor O2/CO2 transport and fed-batch design Sef Heijnen Exercises on data analysis of fermentation processes
- 15.15 Sef Heijnen 17.00 Genomé-scale metabolic networks, proteome constrained models and resource allocation
- **Bas Teusink**

## 18.00 End of the day

#### **THURSDAY 16 JANUARY 2025**

Theme: Pathway stoichiometry, pathway-based models and glutamate fed-batch demo

- Coordinator Wouter van Winden
   09.00 Metabolic pathway stoichiometry: for energy, product, biomass Djordje Bajić
   11.10 Exercise: Stoichiometry pathway model for glutamate fed-batch demo Djordje Bajić /Wouter van Winden / Sef Heijnen
   12.30 Lurch 12.30
- Lunch 13.15 Continuation Exercise
- 14.00 Interactive exercise: Design calculation of glutamete fed-batch demo
- Wouter van Winden Simulation exercise: Introducing the fed-batch simulator and carrying out the designed fed-batch fermentation in silico 16.10 Wouter van Winden
- Interactive exercise: Discussion on measurements 17.20
- Sef Heijnen End of the day 18.30

## FRIDAY 17 JANUARY 2025

Theme: Metabolic networks: model-based fed-batch, modelling of large-scale dynamics

## oordinator Wouter van Winden

- Fermentation feedstocks: beyond (pure) carbohydrates Wouter van Winden 09.00
- Metabolic studies in the industrial contexts 10.00
- thd
- 11.15 Simulation exercise: Use simulated fed-batch data to calculate performance
- Wouter van Winden Interactive exercise: Batch phase: quantification of knowledge for microorganism 12.15 and fermentor using balance calculations with only online data Sef Heijnen
- Lunch
- 12.45 13.30 Interactive exercise: Feed phase: quantification of knowledge for microorganism and fermentor using balance calculations with only online data Sef Heijnen
- Simulation exercise: In silico optimization of the glumate fed-batch Wouter van Winden 15.00
- 16.30 Challenges of large scale fermentation Cees Haringa
- Multi-scale modelling of process dynamics in large-scale bioreactors Cees Haringa 17.15
- Social drink 18.30

#### MONDAY 20 JANUARY 2025

Theme: Case study: Ethanol from syngas Coordinator Henk Noorman 09.00 Rate-based design of biosystems Sef Heijner

- Case study: Ethanol from syngas Henk Noorman / Sef Heijnen 09.30
- 12.45 13.25 Lunch
- (optional) Visit fermentation lab 14 00
- Continuation Case Study Henk Noorman / Sef Heijnen
- 17.15 Gas Fermentation: a path to low carbon fuel and chemical production with impact Bjorn Heijstra
- 18.15 End of the day

#### **TUESDAY 21 JANUARY 2025**

Theme: Metabolic engineering: Strategies and applications

- Coordinator Henk Noorman 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
- 12.55 (optional) Visit fermentation lab 13.30
- Metabolic Engineering: from bench to business Irina Borodina
- Evolutionary Engineering highlighting Adaptive Laboratory Evolution Jack Pronk 14.45
- 15.30 Engineering membrane transport Jack Pronk
- 16.30
- Fermentation Intensification Henk Noorman
- 17.30 End of the day

#### WEDNESDAY 22 JANUARY 2025

Theme: Scale down: Single cell studies and heterogeneity, physiology in the Coordinator Pascale Daran-Lapujade 09.00 Spatio-temporal single-cell analysis in picoliter reactors Dietrich Kohlheyer Population heterogeneity in large-scale bioprocesses Anna-Lena Heins 10.00 Scale-down for understanding large scale performance and robust bioprocessing 11.15 Cees Haringa / Anna-Lena Heins 12.15 Lunch 12.40 (optional) Visit fermentation lab Transcription factor-based biosensors for strain development 13.15 Jan Marienhagen Single cell studies of micro-organisms / Microfluidics 14.15 Frank Bruggema High Throughput Strain Phenotype Testing Sarah Lieder 15.30 Advances and developments in microbial proteomics Martin Pabst End of the day 16.30 17.30

## **THURSDAY 23 JANUARY 2025**

Theme: Microbial protein production: excretion and intracellular accumulation Coordinator Henk Noorman 09.00

- Why is biology so difficult to engineer Cees Sagt
- Microbial production of therapeutic proteins Nico Callewaert 10.15
- 11.30 Microbial proteins for food applications
- Katelijne Bekers
- 12.30 13.30 Lunch Field trip
- 19.00 Course dinner

#### FRIDAY 24 JANUARY 2025

Theme: Looking ahead: Microbial communities, Electrobiotechnology, Megatrends. Looking back: Antonie van Leeuwenhoek, MPFT 2025 Coordinator Pascale Daran-Lapujade

09.00 Microsbial community engineering for production of chemicals

- and bioenergy Robbert Kleerebezem Synthetic consortia: new options for industrial biotechnology 10.15
- Djordje Bajić Electrobiotechnology: production of chemicals using renewable 11.15 electricity as energy source Ludovic Jourdin
- 12.15 Lunch
- 13.15 Microscope modification and use by Antoni van Leeuwenhoek
- Lesley Robertso 14.15
- Verdezyne: A Case Study in Beginning with the End in Mind Brett Schreyer
- 15.15 What have we learned? Jack Pronk / Henk Noorman / Pascale Daran-Lapujade

## 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

tund

## **COURSE REGISTRATION**

Please register via the website to attend the course. Deadline for application is 23 December 2024. Applications will be handled in order of the date of receipt.

## **COURSE FEE**

€ 4.750 in case of registration before 4 November 2024 or
€ 5.000 in case of registration after this date. In the event of cancellation before 18 November 2024, 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  $\in$  2.600. 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.

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)
- Environmental Biotechnology (1993)
- Biocatalysis and Protein Engineering (1999)
- Bioprocess Design (2014)
- Modelling and Computation for Microorganisms in Bioprocesses (2018)
- Integrated Multi-Omics approaches for
   Improvement of Industrial Microbes (2020)
- Cellular Agriculture: Precision fermentation and cultured meat (2024)

## FURTHER INFORMATION

Jenifer Baptiste, BA Course coordination T +31 15 278 1922 / 2342 E biotechdelft@tudelft.nl W biotechdelft.com

**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

Advanced Courses in Biotechnology

biotechdelft.com