# ADVANCED COURSE

# Microbial Physiology and Fermentation Technology

13 - 24 January 2025

Course board:
Pascale Daran-Lapujade
Henk Noorman

#### 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, (13°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
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
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**LECTURERS**Wouter van Winden dsm-firmenich Delft, the Netherlands

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

Ruud Weusthuis 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

oordinator Pascale Daran-Lapujade

**08.45** Registration **09.00** Outline of the course

Pascale Daran-Lapujade
Microbial Physiology vs. Fermentation Technology
Jack Pronk / Henk Noorman
Developing scalable bioprocesses: Lessons and examples from industry
Chris Mehrer

Balances and rates 11.30

Sef Heijnen Lunch & Picture

q: Biomass specific conversion rates Sef Heijnen 13.30

14.15 Excercises on balances and biomass specific conversion rates

Sef Heijnen

16.45 Balances and modes of fermentation operation

Marieke Kliin

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

13.15 Thermodynamics

Mark Bisschops
Black Box model: kinetics/parametrization 14:15

15.30 Black Box model: stoichiometry/process reaction for design Sef Heiinen

Engineering yeast for 1st and 2nd generation bioethanol production Jack Pronk 17:00

18.00 End of the day

#### **WEDNESDAY 15 JANUARY 2025**

Theme: Fermentation: design, transport and data analysis Coordinator Sef Heijnen

Introduction to bioprocess design using the process reaction Sef Heijnen

10:00

Excercises on bioprocess reactions in design Sef Heijnen

13.30 Fermentor O2/CO2 transport and fed-batch design

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

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

Exercise: Stoichiometry pathway model for glutamate fed-batch demo Djordje Bajić /Wouter van Winden / Sef Heijnen

12.30 Lunch

11.10

Continuation Exercise

Interactive exercise: Design calculation of glutamate fed-batch demo Wouter van Winden 14.00

16.10

Simulation exercise: Introducing the fed-batch simulator and carrying out the designed fed-batch fermentation *in silico* 

Wouter van Winden

17.20 Interactive exercise: Discussion on measurements

Sef Heijnen End of the day 18.30

#### FRIDAY 17 JANUARY 2025

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

Coordinator Wouter van Winden

Fermentation feedstocks: beyond (pure) carbohydrates Wouter van Winden

10.00 Metabolic Engineering in industrial contexts

Ruud Weusthuis

Simulation exercise: Use simulated fed-batch data to calculate performance 11.15

Wouter van Winden Interactive exercise: Batch phase: quantification of knowledge for microorganism and fermentor using balance calculations with only online data

Sef Heijnen

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

18.30 Social drink

#### **MONDAY 20 JANUARY 2025**

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

Sef Heijnei

Case study: Ethanol from syngas 09.30 Henk Noorman / Sef Heijnen

12.45 Lunch

13.25 (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

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 Metabolic Engineering: from bench to business
Irina Borodina 13.30

Evolutionary Engineering highlighting Adaptive Laboratory Evolution Jack Pronk 14.45

Engineering membrane transport Jack Pronk 15.30

Fermentation intensification Henk Noorman 16.30

17.30 End of the day

#### **WEDNESDAY 22 JANUARY 2025**

Theme: Scale down: Single cell studies and heterogeneity, physiology in the

screening stage 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 11.15 Scale-down for understanding large-scale performance and robust bioprocessing Cees Haringa / Anna-Lena Heins

(optional) Visit fermentation lab Transcription factor-based biosensors for strain development Jan Marienhagen
Single cell studies of micro-organisms / Microfluidics
Frank Bruggeman
High Throughput Strain Phenotype Testing
Sarah Lieder 13.15

14.15

15.30

Advances and developments in microbial proteomics

Martin Pabst 16.30

17.30 End of the day

#### **THURSDAY 23 JANUARY 2025**

Theme: Microbial protein production: excretion and intracellular accumulation

Coordinator Henk Noorman

09.00 Why is biology so difficult to engineer?

Microbial production of therapeutic proteins
Nico Callewaert
Microbial proteins for food applications 10.15

11.30 Katelijne Bekers

12.30 Lunch

13.30 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 Microbial community engineering for production of chemicals

and bioenergy Robbert Kleerebezem 10.15

Synthetic consortia: new options for industrial biotechnology Djordje Bajić Electrobiotechnology: production of chemicals using renewable

electricity as energy source Ludovic Jourdin

Lunch Microscope modification and use by Antoni van Leeuwenhoek Lesley Robertson 13.15

Verdezyne: A Case Study in Beginning with the End in Mind 14.15

Brett Schreyer 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

#### **COURSE REGISTRATION**

Please register via the website to attend the course. Applications will be handled in order of the date of receipt.

#### **COURSE FEE**

The course fee can be found on the <u>website</u>. 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)
- 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)
- EPS for resource recovery (2025)
- Biopharmaceutical Bioprocessing (2025)

#### **FURTHER INFORMATION**

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