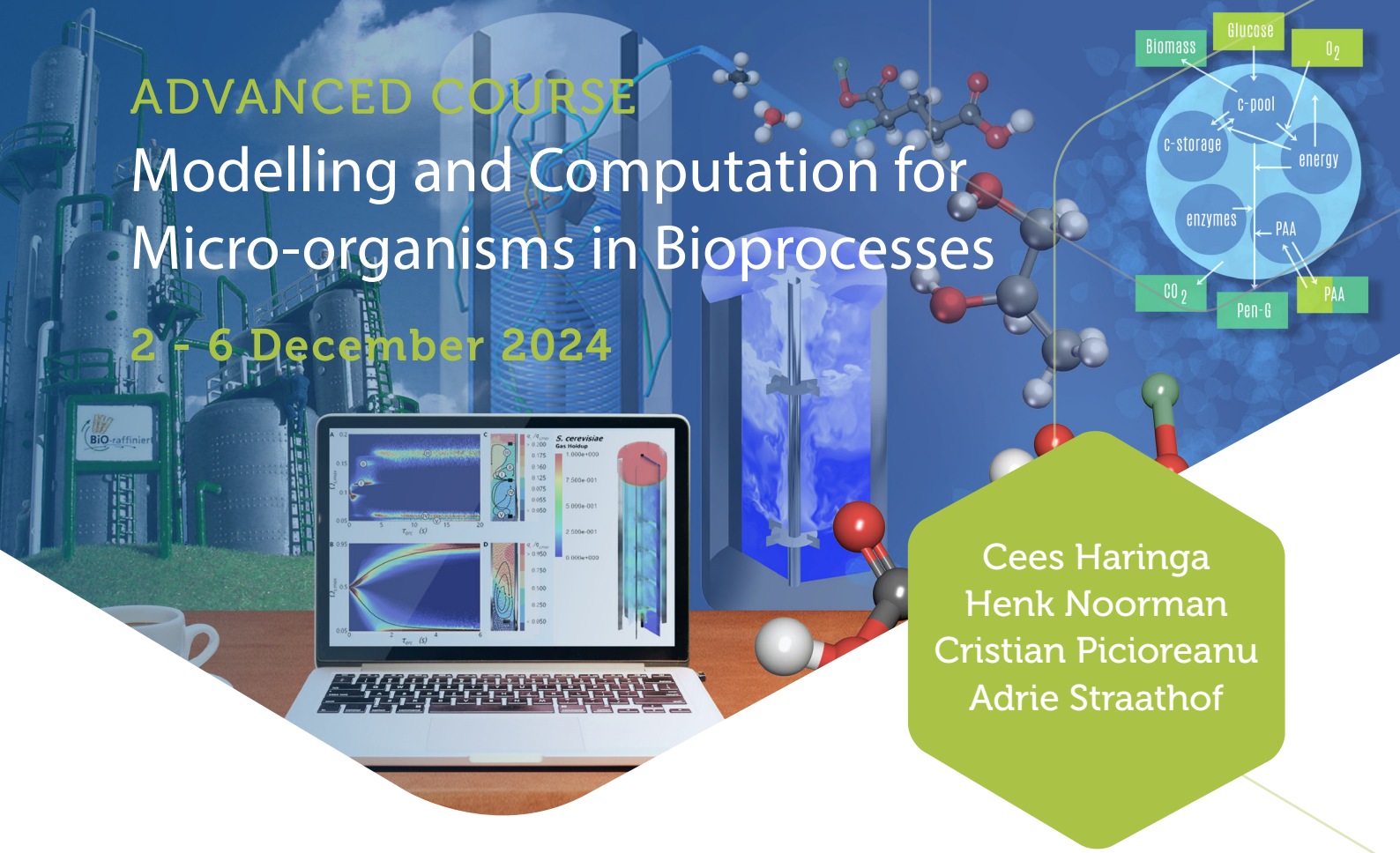
ADVANCED COURSE

Modelling and Computation for Micro-organisms in Bioprocesses

2 - 6 December 2024



Cees Haringa
Henk Noorman
Cristian Picioreanu
Adrie Straathof

AIM OF THE COURSE

This course brings together contributions from different disciplines, i.e. bioprocess technology, applied physics, transport phenomena, molecular biology and biomedical sciences. They all address different elements on the coupling between several time and length scales in the simulation of different bioprocesses (e.g. bioreactor and bioprocess operation, microbial strain improvement, tissue and organ cultivation, plant design and integration). Computational methods will deepen the understanding of the connecting principles between different scales.

The idea of this course is to move from large-scale industrial bioprocesses (hectometers/days) down to the intracellular level (nanometers/microseconds), through several intermediate scales. These intermediate scales describe details inside the bioreactor (meters/hours) and in multicellular aggregates, as e.g. appearing in biofilms or tissues (millimeters/seconds). Top-down approaches allow answering particular questions in a natural way: a quantitative understanding at a higher level will - due to progressing insight or new requirements - be enhanced by details revealed by smaller scales approaches.

A higher resolution description of the system will require a greater experimental effort to identify mechanisms and parameter values, together with considerably larger computational expenses.
With the material presented in the course, the participants will better grasp the complexity of multi-leveled systems based on the underlying mechanisms. The increasing power of computational methods and hardware drastically reduces the need for simplification and thereby enhances the predictive capabilities of numerical models and our level of process understanding. This trend is expected to further develop at high pace in the coming years.

BioTechDelft
POSTGRADUATE EDUCATION

TU Delft

COURSE DESCRIPTION

This intensive one-week course aims at active participation by those attending. A combination of theoretical (lectures) and practical (exercises, case study) work is offered. The course is build up around a few currently relevant biotechnological systems (e.g., lactic acid fermentations, antibiotic production, aerobic/anaerobic processes). Applications will be demonstrated with numerical models at all relevant scales, from factory and bioreactor to cell aggregate and intracellular processes, Particular emphasis will be on the identification of mechanisms and parameters, as well as on integration of scales to maximize complete system insight.

LECTURES

The lectures are mainly scheduled in the mornings and late afternoons and will focus on the following themes:

- Industrial bioprocess design, integration and flowsheeting
- Gradients (concentration, shear rate, temperature) in bioreactors coupled to dynamic microbial response and compartmented kinetic models
- Industrial fermentation models with computational fluid dynamics and reaction dynamics by Euler-Lagrange approach and cell life-lines
- Micro-gradients in multicellular aggregates (biofilms, granules, tissues)
- Single-cell models including membrane transport, metabolic variation, intracellular dynamics and genetic diversity

EXERCISES AND CASE STUDY

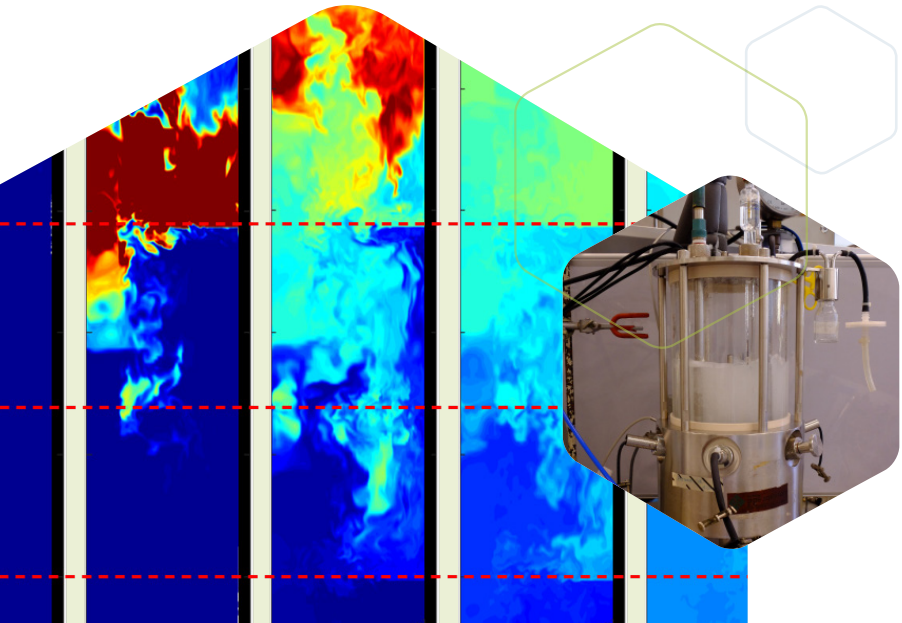
The theory presented in lectures will be applied in exercises in the afternoon sessions. The participants will receive hands-on experience with state-of-the-art computational tools implemented in Ansys/Fluent, Comsol Multiphysics and MATLAB.

WHO SHOULD ATTEND?

The course is primarily aimed at academic and industrial specialists (MSc, PhD or equivalent experience) who seek broadening their knowledge and practical skills in multiscale modelling. Educational background in transport phenomena, basic reaction engineering and biotechnology is strongly advised. Affinity with biological systems is recommended. Preparatory materials will be provided to help participants reaching the basic prerequisite knowledge for this course.

COURSE DETAILS

The course has a workload of 48 hours. 2ECTS can be issued after a passed final assignment. The course will be given in English.



COURSE BOARD

Cees Haringa
Bioprocess Engineering
Delft University of Technology
Delft, the Netherlands

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

Cristian Picioreanu
Environmental Biotechnology
Delft University of Technology
Delft, the Netherlands

Adrie Straathof
Bioprocess Engineering
Delft University of Technology
Delft, the Netherlands

COURSE COORDINATION

Jenifer Baptiste
BioTech Delft
Delft University of Technology
Delft, the Netherlands

INVITED LECTURERS

Frank Delvigne
Gembloux Agro-Bio Tech
University of Liège
Luik, Belgium

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

Wenjun Tang
DSM Biotechnology Center
Delft, the Netherlands

Matthias Reuss
Stuttgart Center Sytems Biology
Stuttgart, Germany

Ralf Takors
Institut für Bioverfahrenstechnik /
Institute of Biochemical Engineering
University of Stuttgart
Germany

Emrah Nikerel
Systems Biology and Bioinformatics Lab
Department of Genetics and
Bioengineering
Yeditepe University.
Istanbul, Turkey

Peter J.T. Verheijen
Department of Biotechnology
Delft University of Technology
Delft, the Netherlands

Frank Bruggeman
Vrije Universiteit Amsterdam
Amsterdam, the Netherlands

PROGRAM

MONDAY 2 DECEMBER 2024

Theme: Process scale (homogeneous)

08:30 Registration
09:00 Course introduction
Henk Noorman
09:15 Black box model of microbes
Sef Heijnen
10:30 Flow sheeting using black box models
Adrie Straathof
11:45 Exercise: plant/full process simulation using SuperPro Designer
Adrie Straathof
13.00 Group picture & Lunch
14:00 Continuation exercise
17:00 Overview of modelling techniques in biotechnology
Peter Verheijen
19:00 Social drink and buffet

TUESDAY 3 DECEMBER 2024

Theme: Fermentor - industrial scale and organism modelling

09:00 Time and length scales in the fermentor
Sef Heijnen
10:00 Characteristics of large scale bioreactors (gradients)
Henk Noorman
11:15 Genetic targeting via organism modelling
Matthias Reuss
12:00 Exercise on Time & Length scale
Cees Haringa
12:30 Flow and reaction modelling/computation
Cees Haringa
13.00 Lunch
14:00 Exercise: fermentor computation using Fluent
Cees Haringa
17:00 Dynamic modelling of regulatory networks
Matthias Reuss

WEDNESDAY 4 DECEMBER 2024

Theme: Fermentor scale-down - lab scale

09:00 Building large scale model for Penicillium by model reduction
Emrah Nikerel
10:15 Use of computational models to design scale-down simulators
Cees Haringa
12:00 Exercise: CFD modelling
Cees Haringa
13.00 Lunch (optional Lab Tour)
14:00 Exercise: CFD modelling
Cees Haringa
17:00 Scale-down in practice
Ralf Takors
18:00 End of day

THURSDAY 5 DECEMBER 2024

Theme: Aggregate scale

09:00 9-pool model
Wenjun Tang
09:45 Models for cell aggregates
Cristian Picioreanu
12:00 Exercises: modelling gradients and microbial growth using COMSOL Multiphysics
Cristian Picioreanu
13.00 Lunch
14:00 Exercises: modelling gradients and microbial growth using COMSOL Multiphysics
Cristian Picioreanu
17:00 Stochastic principles of microbial physiology: origins and consequences of non-genetic phenotypic heterogeneity
Frank Bruggeman
18.30 Course dinner

FRIDAY 6 DECEMBER 2024

Theme: Single cell/molecule scale

09:00 Euler-Langrange/Agent-based cell population modelling
Cees Haringa
10:45 Observability of in vivo kinetic models
Sef Heijnen
12:00 Single Cell Modelling: The impact of cellular architecture on 4D spatial-temporal dynamics in cellular signal transduction processes
Matthias Reuss
13.00 Lunch
14:00 Quantification of single cell performance and population heterogeneity (techniques + case studies)
Frank Delvigne
15:00 Directing cell population heterogeneity
Frank Delvigne
16:00 Models, software, methods and outlook (plenary discussion)
Henk Noorman
16:30 Closing of the course
Henk Noorman

LOCATION

The course will be held at
Delft University of Technology
Department fo Biotechnology
Van der Maasweg 9
2629 HZ Delft, The Netherlands
http://www.bt.tudelft.nl

COURSE REGISTRATION

Please register via the website to attend the course. Deadline for application is **11 November 2024**. Applicants will be handled in order of the date of receipt.

COURSE FEE

€ 2.500 in case of registration before **23 September 2024** or € 2.750 in case of registration after this date. In the event of cancellation before **7 October 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 € 1.250. 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)*
- *Biocatalysis and Protein Engineering (1999)*
- *Environmental Biotechnology (1993)*
- *Bioprocess Design* (2014)*
- *Multiscale Computational Methods in Bioprocesses (2018)*
- *Integrated Multi-Omics approaches for Improvement of Industrial Microbes (2020)*

* in partnership with Wageningen University & Research

FURTHER INFORMATION

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

Advanced Courses in Biotechnology

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