

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.





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 lifelines
- 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

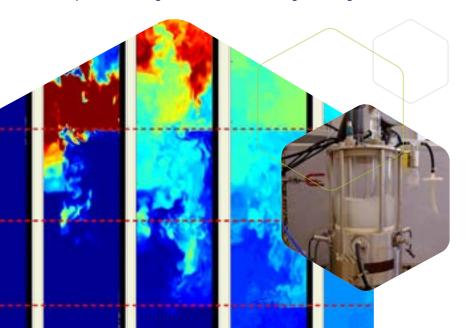
The theory presented in lectures will be applied in exercises in the afternoon sessions. The participants will receive hands-on experience with state-of-the-art computational tools implemented in Ansys/Fluent, Comsol Multiphysics and MATLAB.

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-firmenich 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

Djordje Bajic Industrial Microbiology Department of Biotechnology Delft University of Technology Delft, the Netherlands

PROGRAM

MONDAY 2 MARCH 2026

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 MARCH 2026

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 tbd tbd

12:15 Exercise on Time & Length scale Cees Haringa

12:45 Flow and reaction modelling/computation *Cees Haringa*

13.15 Lunch

14:00 Exercise: fermentor computation using Fluent Cees Haringa

17:00 40 years of Process Technology Matthias Reuss

WEDNESDAY 4 MARCH 2026

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 scaledown 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 Up- and down-scaling in practice Ralf Takors

18:00 End of day

THURSDAY 5 MARCH 2026

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 MARCH 2026

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 Mixed culture modelling: *Djordje Bajic*

13.00 Lunch

14:00 Impact of single cell heterogeneity on population dynamics

Frank Delvigne

15:00 Directing cell population : switching cost and Burden-Entropy compensation effect 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 of Biotechnology Van der Maasweg 9 2629 HZ Delft, The Netherlands



COURSE REGISTRATION

Please register via the website to attend the course. Applicants 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)
- 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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