

# Advanced Course Microbial Physiology and Fermentation Technology

11 – 22 January 2016

## **Aim**

The advanced course “Microbial Physiology and Fermentation Technology” aims to familiarize participants with the integrated, interdisciplinary approach required in modern biotechnology. Microbial physiologists, enzymologists and (bio)chemical engineers from the faculty staff, together with invited (inter)national experts from other universities and industry, will offer a combination of theoretical (lectures, tutorials, mathematical modelling) and practical work (demonstrations, data collection and interpretation of results). In this way, the course will present an intensive and in-depth treatment of the state of the art. At the same time, the course provides the necessary link between, on one hand, fundamental subjects (e.g. biochemistry / enzymology) and, on the other hand, practical applications in large-scale biotechnological processes.

## **Course description**

For a better understanding of the lectures and to enhance active participation by those attending, this intensive two-weeks course consists of lectures, practical demo's, computer simulations, exercises and case studies.

## **Morning and evening**

The lectures are mainly scheduled in the mornings and the early evenings.

In the lectures, attention will be paid to the following themes:

- Energy transduction and growth 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

## **Afternoon**

Demo's in fed-batch fermentation. Discussions and interpretation of results. On- and off-line measurements in the gas and liquid phase of reaction parameters and determination of the kinetics of biological conversions. Statistical data processing using mass balances. Tutorials in setting-up and simulating computer models of metabolic networks. Introduction to rate based design. Possibilities to visit the research projects of the Department of Biotechnology of Delft University of Technology.

The course will be given in English.

A pocket calculator is required.

## **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 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.

## **Duration/Location**

This Advanced Course will be given on  
Monday, 11 January – Friday, 22 January 2016

The course will be held at the  
Department of Biotechnology  
Delft University of Technology  
Julianalaan 67  
2628 BC Delft  
The Netherlands  
P +31 15 278 1922  
F +31 15 278 2355  
E [bsdl-edu@tudelft.nl](mailto:bsdl-edu@tudelft.nl)  
W [www.biotechnologycourses.nl](http://www.biotechnologycourses.nl)

## **Accommodation**

Hotel accommodation can be arranged at your request addressed to [bsdl-edu@tudelft.nl](mailto:bsdl-edu@tudelft.nl). Lunches, the buffets on Monday, 11th and Thursday, 14th and the course dinner on Thursday, 21st will be provided. For the other meals a variety of restaurants may be found in the centre of the city.

## **Program 11 – 22 January 2016**

### **Monday, 11 January 2016**

Theme: Energy transduction and growth thermodynamics

- 08.45 Registration
- 09.00 Outline of the course  
Jack Pronk
- 09.30 Basic energetics of microbial metabolism  
Ton van Maris
- 10.30 Solute transport: mechanisms and energetics  
Jack Pronk
- 11.15 Balances  
Sef Heijnen
- 13.30 q-rates  
Sef Heijnen
- 14.00 Batch, fed-batch and continuous cultivation  
Ton van Maris
- 15.15 Parallel sessions:  
Exercises on energetics of microbial metabolism  
Exercises on balances and q-rates
- 18.00 Social drink and buffet

### **Tuesday, 12 January 2016**

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

- 09.00 Transport reactions and energy coupling: implications for industrial product formation  
Jack Pronk
- 10.15 Black box model: kinetics  
Sef Heijnen
- 11.30 Black box model: stoichiometry  
Sef Heijnen
- 13.45 Introduction to bioprocess design  
Sef Heijnen
- 14.30 Exercises on bioprocess design

### **Wednesday, 13 January 2016**

Themes: Regulation of metabolism by environmental parameters  
High-cell-density fermentation

- 09.00 Primary metabolism and its regulation  
Pascale Daran-Lapujade
- 10.00 Carbohydrate metabolism in yeasts: respiration versus alcoholic fermentation  
Jack Pronk
- 11.00 Physiological aspects of high cell density fermentation  
Jack Pronk
- 13.00 Fed-batch fermentation and transport phenomena  
Sef Heijnen
- 15.30 Microbial growth with mixtures of carbon substrates  
Jack Pronk
- 16.45 Optional: Visit tour research projects

### **Thursday, 14 January 2016**

Theme: Metabolic networks: stoichiometry and fluxes

- 09.00 Metabolic network analysis  
Sef Heijnen
- 11.45 Redox balances in microbial sugar metabolism: consequences for industrial product formation  
Ton van Maris
- 13.30 Bioenergetics of microbial growth and the cost of adaptation  
Joost Teixeira de Mattos
- 15.30 Fed-batch demo (1): design of the feed profiles
- 17:15 Fed-batch demo (2): measurements why and how
- 18.15 Buffet

### **Friday, 15 January 2016**

Theme: Metabolic networks: stoichiometry and fluxes

- 09.00 Metabolic flux balancing: theory and applications  
Walter van Gulik
- 10.15 Computer exercises on metabolic network analysis
- 13.45 Metabolic studies in the industrial contexts  
Ralf Takors
- 14:45 Exercises on high-cell density fed-batch cultivation
- 17.30 Social drink

### **Monday, 18 January 2016**

Theme: Rate based design

- 09.00 Rate based design of biosystems  
Sef Heijnen
- 10.00 Case study introduction: feedstock and stoichiometry variants, mass and energy balances  
Henk Noorman
- 10.30 Case study: rate based design
- 14.00 Reactor types, rate limiting transport steps and reactor sizing  
Henk Noorman
- 14.30 Continuation case study
- 17.30 Large scale reactors: mixing and scale-up problems  
Henk Noorman

### **Tuesday, 19 January 2016**

Theme: Regulation and control of metabolic fluxes

- 09.00 Multi-scale modelling of process dynamics in large-scale bioreactors  
Matthias Reuss
- 10.15 Multi-level regulation of metabolic fluxes, transcripts versus fluxes  
Pascale Daran-Lapujade
- 11.00 Through Van Leeuwenhoek's Eyes  
Lesley Robertson
- 11.30 Van Leeuwenhoek and Delft: A microbiological pilgrimage (social / cultural event)
- 14.30 Analysis of in vivo kinetics: rapid sampling and metabolite analysis  
Walter van Gulik
- 15.45 Fed-batch (3): practising fed-batch calculations on the batch phase

**Wednesday, 20 January 2016**

Theme: Metabolic engineering

- 09.00 Metabolic engineering strategies for reducing costs  
Sef Heijnen
- 10.30 Design and engineering of industrial microorganisms  
Christoph Wittmann
- 11.45 Engineering, fermentation and scale-up of fungi for protein  
Rutger Douma
- 14.15 Evolutionary and reverse engineering  
Jack Pronk
- 15.30 Exercises on metabolic engineering strategies for reducing costs
- 17.15 Metabolic engineering of thermophiles  
Lee Lynd

**Thursday, 21 January 2016**

Theme: Heterogeneity and mixed cultures

- 09.00 Microbial community engineering for production of chemicals and bioenergy  
Robbert Kleerebezem
- 10.15 Spatio-temporal single-cell analysis in picoliter reactors  
Dietrich Kohlheyer
- 11.30 Responsive diversification – an explanation for lag phases?  
Matthias Heinemann
- 13.30 Fed-batch (4): calculations on mass balances of a fed-batch fermentation and evaluation
- 19.00 Course dinner, downtown Delft

**Friday, 22 January 2016**

Theme: Capita Selecta

- 09.30 Low-pH fermentation to succinic acid, the basis for efficient recovery  
Mickel Jansen
- 10.45 High-throughput strain construction and phenotypic screening  
Stefan de Kok
- 13.45 Transcription factor-based biosensors for strain development  
Jan Marienhagen
- 14.45 Keynote lecture  
Lee Lynd
- 15.45 Evaluation of the course
- 16.00 Farewell drink

## Fees and registration

Please complete and return the form below, or register via the website, if you are interested to attend the course or would like to receive information on other courses. Applicants will be handled in order of the date of receipt.

The course fee is:

Early bird fee: € 3650 in case of payment received on or before **30 November 2015** or  
Regular fee: € 3900 in case of payment received after this date.

In the event of cancellation before 30 November 2015, a full refund will be granted, after this date, a 25% fee charge will be made.

To facilitate enrolment of young PhD-students from universities, a limited number of fellowships is available. The course fee with fellowship is € 1825. To apply, please include a copy of your registration as a PhD-student from your university.

The fee includes course materials, lunches, the buffets on Monday, 11th and Thursday, 14th and the course dinner on Thursday, 21st. The fee does not cover other meals and lodging.

When the number of participants is too low to have a fruitful course, the Institute BSDL 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, BSDL will arrange an equivalent replacement.

Hotel accommodation can be arranged at your request.

Preparatory texts will be sent after receipt of the course fee. The complete set of course books will be supplied at the start of the course.

## Advanced Course Microbial Physiology and Fermentation Technology

- I wish to attend the course of 11 – 22 January 2016
- I would like to receive information of the other courses of the Institute BSDL
- Please, send me announcements of the future Advanced Course Microbial Physiology and Fermentation Technology

Family name, title, Mr / Ms .....First name .....

Organisation / Company .....

Address .....

.....

Phone .....

E-mail address .....

Educational background .....

Diet wishes .....

Date / Signature .....

## **Board of the course**

**Prof. J.J. Heijnen**

Bioprocess Technology

**Prof. J.T. Pronk**

Physiology of Industrial Microorganisms

## **Faculty staff**

**Dr. P.A.S. Daran-Lapujade**

Systems Biology

**Dr. W.M. van Gulik**

Metabolic Engineering

**Ir. R. Mans**

Metabolic Engineering

**Dr. R. Kleerebezem**

Environmental Biotechnology

**Dr. A.J.A. van Maris**

Metabolic Engineering

**Dr. L.A. Robertson**

Curator of the Beijerinck Museum

**Dr. S.A. Wahl**

Systems Biology

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## **Coordinators Fed-batch demo**

**Ing. D.J.M. Geerts**

**Ing. R. Kerste**

**Yi Song**

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## **Guest lecturers**

**Dr. R. Douma**

Novozymes

Copenhagen, Denmark

**Prof. M. Heinemann**

Molecular Systems Biology

Rijksuniversiteit Groningen

the Netherlands

**Dr. M. Jansen**

DSM Biotechnology Center

Delft, the Netherlands

**Dr. D. Kohlheyer**

Research Centre Jülich

Germany

**Dr. S. de Kok**

Zymergen

Emeryville, USA

**Prof. L.R. Lynd**

Dartmouth College, Thayer School of

Engineering, Hannover, NH

USA

**Dr. J. Marienhagen**

Research Centre Jülich

Germany

**Prof. H.J. Noorman**

DSM Biotechnology Center and

Delft University of Technology

Delft, the Netherlands

**Prof. M. Reuss**

Institut für Bioverfahrenstechnik

University Stuttgart

Germany

**Prof. R. Takors**

Institut für Bioverfahrenstechnik

University of Stuttgart

Germany

**Prof. M.J. Teixeira de Mattos**

Swammerdam Institute for Life

Sciences, SILS, University of Amsterdam

the Netherlands

**Prof. C. Wittmann**

Institut für Bioverfahrenstechnik

Braunschweig

Germany

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## **Course coordinator**

**Ms. Jenny Boks-Zondervan**

Delft University of Technology

Department of Biotechnology

Delft, the Netherlands

**Institute Biotechnology Studies Delft Leiden**  
**Department of Biotechnology**  
**Julianalaan 67**  
**2628 BC Delft**  
**The Netherlands**

The institute **Biotechnology Sciences Delft Leiden** (BSDL-EDU) constitutes a joint initiative in biotechnological post-graduate education of Delft University of Technology and Leiden University and is coordinated from the department of Biotechnology of Delft University of Technology.

BSDL-EDU was founded in 1987 and has since then very successfully organised various types of postdoctoral education: the Advanced Course Quality Management in Pharma and Biotech, the PDEng programmes and the Advanced Courses in biotechnology. The Advanced Course Quality Management in Pharma and Biotech was developed by BSDL-EDU and is currently organised by PAO Farmacie. The PDEng programmes are special two-year postgraduate programmes that are aimed at those who wish to tailor their own specialisation to the needs of multidisciplinary biotechnological research and design, and lead to the degree of 'Professional Doctorate in Engineering'. Originally developed by BSDL-EDU, these programmes are now hosted by the 3TU School for Technological Design / Stan Ackermans Institute.

Currently BSDL-EDU offers various Advanced Courses covering the multidisciplinary spectrum of biotechnology:

**BIOCATALYSIS AND PROTEIN ENGINEERING**  
**BIOPROCESS DESIGN**  
**DOWNSTREAM PROCESSING**  
**ENVIRONMENTAL BIOTECHNOLOGY**  
**GENOMICS IN INDUSTRIAL BIOTECHNOLOGY**  
**METABOLOMICS FOR MICROBIAL SYSTEMS BIOLOGY**

**Further information**

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