Board of the Course
Dr. Walter van Gulik
Dr. Reza Maleki Seifar
Dr. Aljoscha Wahl
Prof. Sef Heijnen
Delft University of Technology
Department of Biotechnology
Delft, the Netherlands

Course Coordination
Ms. Jenny Boks-Zondervan
Mr. Vincent Renken, MSc MSc(Ed)
Delft University of Technology
Department of Biotechnology
Delft, the Netherlands

Guest Lecturers
Dr. Greg Bokinsky
Delft University of Technology
Department of Bionanoscience
Delft, the Netherlands

Dr. Amit Deshmukh
DSM Biotechnology Center
Delft, the Netherlands

Dr. Peter Droste
Omix Visualization GmbH & Co. KG
Lennestadt, Germany

Prof. Alejandro Cifuentes
National Research Council of Spain (CSIC)
Laboratory of Foodomics, CIAL
Madrid, Spain

Dr. Peter Lankhorst
DSM Biotechnology Center
Delft, the Netherlands

Dr. Liam McDonnell
Leiden University Medical Centre
Center for Proteomics and Metabolomics
Leiden, the Netherlands

Dr. Katharina Nöh
Forschungszentrum Jülich GmbH
Institute of Bio- and Geosciences
Jülich, Germany

Prof. Marco Oldiges
Forschungszentrum Jülich GmbH
Institute of Bio- and Geosciences
Jülich, Germany

Prof. Bas Teusink
Vrije Universiteit Amsterdam
Systems Bioinformatics group (AIMMS)
Amsterdam, 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:

■ MICROBIAL PHYSIOLOGY AND FERMENTATION TECHNOLOGY
■ BIOCATALYSIS AND PROTEIN ENGINEERING
■ BIOPROCESS DESIGN
■ DOWNSTREAM PROCESSING
■ ENVIRONMENTAL BIOTECHNOLOGY
■ GENOMICS IN INDUSTRIAL BIOTECHNOLOGY

Further information
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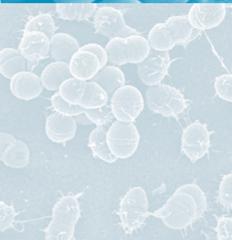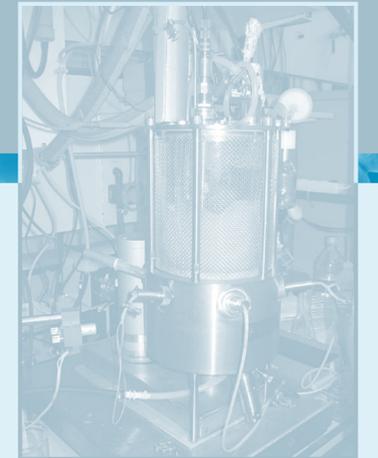**W** www.biotechnologycourses.nl

Address
Institute Biotechnology Studies Delft Leiden
Department of Biotechnology, Delft University of Technology
Julianalaan 67, 2628 BC Delft, the Netherlands

Advanced Course

METABOLOMICS FOR MICROBIAL SYSTEMS BIOLOGY

11 - 15 July 2016

TUDelft

Delft University of Technology

BSDL

Aim

The advanced course "Metabolomics for Microbial Systems Biology" aims at teaching state of the art methods of quantitative metabolomics to industrial and academic research professionals (i.e. MSc, PhD). The focus is to gain insights into the complex metabolic control of central carbon metabolism and connected product formation pathways in industrial micro-organisms.

The course covers recent developments in rapid sampling methods, measurement techniques and modeling approaches for microbial systems. The first two days are mainly dedicated to experimental techniques, from steady-state analysis to stimulus response experiments. Proper sampling and sample handling procedures for reliable and reproducible metabolome analysis will be discussed and exercise calculations are performed. The main measurement techniques addressed are based on liquid and gas chromatographic separation, coupled to mass spectrometry.

The third and fourth day focus on theoretical and modeling aspects of Systems Biology. Approaches from network reconstruction, stoichiometric and thermodynamic network analysis and in-vivo kinetic modeling will be covered. ^{13}C tracer methods will be discussed to extend the information content of stationary state as well as dynamic experiments.

The last day will be dedicated to future developments and advanced applications of quantitative metabolomics to tackle specific biological questions, whereby also other hierarchical levels of the cell will be taken into account.

Course description

This intensive, activating, one-week course aims at providing fundamental and applied knowledge in the field. To this end, the course is set up as an alternating program of expert lectures and exercises.

Lectures
Attention will be on a variety of themes:
• Rapid sampling and quantitative analysis
• Metabolite quantification and validation using Isotope Dilution Mass Spectrometry, IDMS
• Perturbation strategies
• Estimation of extra- and intracellular rates from experimental data
• Kinetic modeling and approaches to handle parameter identification problems
• Outlook and future developments

Exercises
Several exercises will be performed to familiarize the participants with the theory and practice and to illustrate the utility and utilization of quantitative metabolomics in modern biotechnology. IDMS calculations will be carried out using Microsoft Excel. Flux analysis and dynamic simulations are performed using the numerical computing environment MATLAB. Prior knowledge of MATLAB is needed - a tutorial for learning the required (basic) MATLAB knowledge will be sent prior to the course.

The official course language is English.

A laptop and pocket calculator is required.

Who should attend?

This Advanced Course is aimed at participants from industry, universities and research institutions who want to update and extend their theoretical knowledge and practical insight in quantitative metabolomics and modeling.

The course is intended for postgraduates (MSc, PDEng, PhD), with a sound background in microbiology, microbial physiology, biotechnology, biochemistry or biochemical engineering, with a basic working knowledge in some of the other disciplines and an affinity to applied mathematics.

Duration & Location

This Advanced Course will be given on **Monday, 11 July - Friday, 15 July 2016**

The course will be held at the
Department of Biotechnology
Delft University of Technology
Mijnbouwstraat 120
2628 RX Delft
the Netherlands
P +31 15 278 5200
W www.sciencecentre.tudelft.nl

Accommodation

Hotel accommodation can be arranged at your request via bsdl-edu@tudelft.nl. Lunches, the buffet on Monday, July 11th and the course dinner on Thursday, July 14th will be provided. For the other meals, a variety of restaurants may be found in the centre of the city.

Program, 11 - 15 July 2016

Monday, July 11th
Theme: Rapid sampling and quantitative analytics
09.00 **Registration**
09.15 **Outline of the course and introduction of participants**
Walter van Gulik
09.45 **Introduction to microbial metabolomics**
Walter van Gulik
10.45 **Rapid sampling for quantitative metabolomics**
Walter van Gulik
13.30 **MS-technologies**
Reza Seifar
14.15 **Identification of compounds using high-mass-resolution GC-TOF-MS**
Marco Oldiges
15.15 **LC-MS/MS for the quantitative analysis of product pathway intermediates**
Marco Oldiges
16.00 **Application of LC-MS/MS for Penicillin biosynthesis pathway intermediates**
Reza Seifar / Amit Deshmukh
16.45 **NMR for metabolomics**
Peter Lankhorst
17.30 **Social drink and buffet**

Tuesday, July 12th
Theme: Quantification and validation using isotope dilution mass spectrometry
Perturbation and validation strategies
09.00 **Development of quantitative analysis of metabolites using GC isotope dilution mass spectrometry**
Reza Seifar
09.45 **Exercises: calculating concentrations from ID-MS data and validation of sampling and extraction protocols**
Reza Seifar / Walter van Gulik
13.45 **Perturbation strategies for estimation of in-vivo kinetic properties of enzymes**
Walter van Gulik
14.30 **Thermodynamic validation of metabolite data**
Aljoscha Wahl
15.30 **Tackling cellular compartmentalization: application of sensor reactions**
Walter van Gulik
16.15 **Futile cycles during Penicillin production: mimic large scale on the bench using a feast / famine regime**
Aljoscha Wahl
17.15 **Octave introduction / Visit tour**

Wednesday, July 13th
Theme: Estimation of extra- and intracellular rates from experimental data
09.00 **Calculation of net conversion rates from reactor mass balances**
Walter van Gulik
09.45 **Analysis, validation and estimation of rates**
Walter van Gulik
10.45 **Introduction to metabolic flux analysis**
Walter van Gulik
11.30 **Computer exercises on metabolic flux analysis**
Katharina Nöh / Aljoscha Wahl / Walter van Gulik
15.45 **Steady state flux analysis using ^{13}C labeling at isotopic steady state**
Katharina Nöh
17.00 **Computer demonstration/exercises on ^{13}C isotopomer modeling**
Katharina Nöh / Aljoscha Wahl

Thursday, July 14th
Theme: Kinetic modeling, parameter identification and visualization approaches
09.00 **Steady state flux analysis using ^{13}C labeling at isotopic transient states**
Katharina Nöh
10.00 **Setting up a kinetic model using mechanistic enzyme kinetics**
Aljoscha Wahl
11.00 **Computer exercise: kinetic ODE models**
Aljoscha Wahl
14.30 **Hybrid systems modelling approach for efficient dynamic flux estimation**
Aljoscha Wahl
15.30 **Model analysis and visualisation techniques**
Katharina Nöh
16.15 **Computer demonstration on model analysis and visualisation**
Peter Droste
19.00 **Course dinner - Downtown Delft**

Friday, July 15th
Theme: Outlook and future developments
09.00 **Regulation of metabolism: navigating between desired and fatal states**
Bas Teusink
10.45 **Foodomics**
Alejandro Cifuentes
13.30 **How *E. coli* integrates growth rate regulation with amino acid and fatty acid anabolism**
Greg Bokinsky
14.45 **Closing lecture**
Imaging metabolites and metabolic pathways in cancer tissues
Liam McDonnell
15.45 **Evaluation of the course**
Reza Seifar
16.00 **Farewell drink**

Fees & Registration

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

The course fee is:
Early bird fee: € 2500. in case of payment received before **30 May 2016** or regular fee: € 2750.- in case of payment received after this date.
In the event of cancellation before 30 May 2016, a full refund will be granted, after this date, a 25% fee charge will be made.
To facilitate enrolment of PhD-students, a number of fellowships is available. The course fee with fellowship is € 1250.-. To apply, please include a copy of your registration as a PhD-student at your university.

The fee includes course materials, lunches, the buffet on Monday, July 11th and the course dinner on Thursday, July 14th. 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 course book will be supplied at the start of the course.

Advanced Course Metabolomics for Microbial Systems Biology

☐ I wish to attend the course of 11 - 15 July 2016
☐ I would like to receive information of the other courses of **BSDL**
☐ Please, send me announcements of the future **Advanced Course Metabolomics for Microbial Systems Biology**

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

Organisation / Company _____

Address _____

Phone _____

E-mail address _____

Educational background _____

Diet wishes _____

Date / Signature _____