

Program

Metabolic Engineering VI:

*From recDNA towards Engineering
Biological Systems*

1-5 October 2006

**NH Leeuwenhorst
Noordwijkerhout, The Netherlands**

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**Sef Heijnen
Kluyver Centre Delft
The Netherlands**

**Roel Bovenberg
DSM Anti Infeetives
The Netherlands**

Conference Co-Chairs

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*Northwestern University, USA***

**Lisa Laffend
*DuPont, USA***

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Sunday, October 1, 2006

- 15.00 – 18.00 Registration
Setup Posters (Session A)
- 17.00 – 17.50 Reception
- 17.50 – 18.05 Opening remarks
Conference Chairs: J.J. (Sef) Heijnen and Roel Bovenberg
- 18.05 – 18.10 Introduction of Jay Keasling by Roel Bovenberg
- 18.10 – 19.00 Keynote lecture
Drugs from bugs: Engineering microorganisms for production of anti-malarial drugs
Jay Keasling, UC Berkeley, California
- 19.00 – 20.30 Dinner
- 20.30 – 23.00 **Poster Session A** including social hour
Chairs: Iman Famili, Genomatica, USA
Wim de Laat, DSM, The Netherlands

Monday, October 2, 2006

- 07.00 – 08.00 Breakfast buffet
- Industrial Applications of Metabolic Engineering***
Chairs: Lisa Laffend, Dupont, USA
John Villadsen, Technical University of Denmark, Denmark
- 08.00 – 08.05 Introduction of Jeff Lievens by Lisa Laffend
- 08.05 – 08.45 Keynote lecture
Metabolic engineering for profit: Know the endgame
Jeff Lievens, Tate and Lyle, USA
- 08.45 – 08.55 Break
- 08.55 – 09.20 **Metabolic engineering of an oleaginous yeast for production of omega-3 fatty acids**
Steve Picataggio, Dupont, USA
- 09.20 – 09.45 **Interscale observation and improvement of guanosine production by restoring the metabolic flux shift**
Siliang Zhang, ECUST, China
- 09.45 – 10.10 **Systems biotechnology of *Corynebacterium glutamicum* for lysine production**
Christoph Wittmann, University of Saarbrücken / BASF, Germany
- 10.10 – 10.40 Coffee Break
- 10.40 – 11.05 **Engineering of a novel protein secretion pathway in *Aspergillus niger***
Herman Pel, DSM, The Netherlands
- 11.05 – 11.30 **Engineering the methylmalonyl-CoA metabolic node of *Saccharopolyspora erythraea* for increased erythromycin production**
Andrew R. Reeves, Fermalogic, Inc., USA
- 11.30 – 11.55 Discussion moderated by chairs
- 11.55 – 13.30 Lunch
- 13.30 – 15.00 Free time
- Metabolic Engineering of Production Organisms***
Chairs: Hermann Sahl, Jülich, Germany
Mariajosé Castellanos, UMBC, USA
- 15.00 – 15.05 Introduction of Sang Yup Lee by Hermann Sahl
- 15.05 – 15.45 Keynote Lecture
Genome-based metabolic engineering of *Mannheimia* for the enhanced production of succinic acid
Sang Yup Lee, KAIST, Korea
- 15.45 – 16.10 **Regulation of the TCA cycle in *Corynebacterium glutamicum***
Michael Bott, Jülich, Germany

Monday, October 2, 2006 (continued)

- 16.10 – 16.35 **Metabolic engineering of an obligate methanotroph**
Pamela L. Sharpe, Dupont, USA
- 16.35 – 17.00 **Improvement of alkaline phosphatase promotor driven product
accumulation in *Escherichia coli* K12**
Susan Leung, Genentech, Inc., USA
- 17.00 – 17.30 Coffee Break
- 17.30 – 17.55 **Optimization of the solvent tolerant *Pseudomonas putida* S12 as
host for the production of aromatics from renewable feedstocks**
Jan Wery, TNO, The Netherlands
- 17.55 – 18.20 **Metabolic engineering of *Saccharomyces cerevisiae* for
isoprenoid production**
Jerome Maury, DTU, Lyngby, Denmark
- 18:20-18:45 **Engineering novel platforms for natural product biosynthesis in
plants**
Anthony Clark, Firmenich SA, Geneva, Switzerland
- 18:45-19:00 Discussion moderated by chairs
- 19:00-20:45 Dinner
- 20.45 – 23.00 **Poster Session A**, social hour
Chairs: Iman Famili, Genomatica, USA
Wim de Laat, DSM, The Netherlands

Tuesday, October 3, 2006

- 07.00 – 08.00 Breakfast buffet
- Strategies for Host Design and Optimization***
Chairs: Nicola Zamboni, ETH Zürich, Switzerland
Christoph Schilling, Genomatica, USA
- 08.00 – 08.05 Introduction of Jack Pronk by Christoph Schilling
- 08.05 – 08.45 Keynote Lecture
Engineering *Saccharomyces cerevisiae* for pentose fermentation
Jack Pronk, Kluyver Centre, Delft, The Netherlands
- 08.45 – 08.55 Break
- 08.55 – 09.20 **Molecular sensors for optimizing alkaloid production in *Saccharomyces cerevisiae***
Christina Smolke, California Institute of Technology, USA
- 09.20 – 09.45 **An integrated platform for model driven strain design**
Stephen van Dien, Genomatica, USA
- 09.45 – 10.10 **Putative regulatory sites unraveled by network embedded thermodynamic analysis of metabolome data**
Matthias Heinemann, ETH, Zurich, Switzerland
- 10.10 – 10.40 Coffee break
- 10.40 – 11.05 **Genome shuffling and genetic engineering of *Bacillus subtilis***
Xue Ming Zhao, Tianjin University, China
- 11.05 – 11.30 **Design construction and performance of the most efficient *Escherichia coli* bacterium and estimation of metabolic fluxes from reaction entropies**
Friedrich Srienc, University of Minnesota, USA
- 11.30 – 11.55 **Strain improvement using metabolomics information**
Mariet van der Werf, TNO, The Netherlands
- 11.55 – 12.15 Discussion moderated by chairs
- 12.15 – 13.30 Lunch
- 13.30 – 14.00 Setup Poster Session B
- 14.00 – 18.00 Optional recreation
Free time
Poster viewing

Tuesday, October 3, 2006 (continued)

14:00 – 15:30

Workshop A

Metabolomics and Fluxomics

Chairs: Silas Villas-Boas, AgResearch, Ltd., New Zealand
Wolfgang Wiechert, University of Siegen, Germany

Identification of metabolic engineering targets from metabolite and enzyme analysis in *Aspergillus niger*

S.L. Meijer, BioCentrum -DTU, Denmark

Evaluation of experimental protocols for metabolome analysis in *Escherichia coli* K-12 MG 1655

Hilal Taymaz, TU Delft, The Netherlands

Metabolic flux analysis applied to human colonic bacterial metabolism

Albert A. de Graaf, Wageningen Center of Food Sciences, The Netherlands

Profiling fluxome shifts in higher cells

Nicola Zamboni, ETH Zürich, Switzerland

Global metabolite and flux analysis in primary human hepatocytes

Klaus Maier, University of Stuttgart, Germany

Metabolic and isotopic instationary experiments: an exploratory simulation study

Aljoscha Wahl, Max-Planck-Institute for Dynamics of Complex Technical Systems, Germany

Workshop B

Microreactors for metabolic engineering studies

Chairs: Dirk Weuster-Botz, Technical University of Munich, Germany
Walter van Gulik, Delft University of Technology, The Netherlands

New experimental techniques on whole cellular systems

Dirk Weuster-Botz, Technical University of Munich, Germany

Metabolome dynamic responses of *Saccharomyces cerevisiae* on simultaneous rapid perturbations in external electron acceptor and electron donor

Mlawule R. Mashego, Technical University of Delft, The Netherlands

***In vitro/in silico* modeling tools for metabolic engineering analysis of adipose tissue function**

Kyongbum Lee, Tufts University, USA

***In vivo* Respiriometric ¹³C metabolic flux analysis - CO₂ The Ubiquitous Metabolic Indicator**

Elmar Heinzle, University of Saarbrücken, Germany

Tuesday, October 3, 2006 (continued)

16:00 – 17:30

Workshop C

Genome Based Reconstruction Of Metabolic And Genetic Regulation Networks

Chairs: Anthony Burgard, Genomatica, USA
Gerald Hofman, DTU, Denmark

Genome-scale reconstruction, validation and analysis of the metabolic network of *Mannheimia succiniciproducens* Mbel55e

Tae Yong Kim; Korea Advanced Institute of Science and Technology, Korea

Optimization based automated curation of metabolic reconstructions

Costas Maranas; Pennsylvania State University, USA

From genomes to increased product flux: the linkage of primary precursors to secondary metabolites

Preben Krabben; University College London, UK

An improved evolutionary algorithm-based framework for identifying *in silico* metabolic engineering targets

Isabel Rocha; Universidade do Minho, Portugal

Identifying gene targets for overexpression and knockout via *in silico* biology: application to tyrosine production in *Escherichia coli*

Curt Fischer; MIT, USA

Transcriptome dynamics-based genome-wide prediction and verification of operons in *Streptomyces coelicolor*

Sarika Mehra; Indian Institute of Technology, India

Workshop D: Evolutionary Approaches In Metabolic Engineering

Chairs: Philippe Soucaille, Metabolic Explorer, France
Patrick Cirino, Pennsylvania State University, USA

Engineering promoter regulation – generation of a yeast promoter induced by oxygen depletion

Elke Nevoigt, University of Technology, Berlin, Germany

Combining forward and reverse metabolic engineering to improve microbial function

Ryan T. Gill, University of Colorado, USA

Use of rational design and *in vivo* molecular evolution for the development of B12 independent biocatalyst converting glucose to 1,3 propanediol and acetate at high yield

Isabelle Meynial-Salles, Laboratoire Biotechnologie Bioprocédés (LBB), INSA

Identification of riboflavin production genes by screening transposon mutants

S. Taennler, Institute for Molecular Systems Biology, ETH Zurich, Switzerland

Metabolic engineering of the thermophilic bacterium *Thermoanaerobacterium saccharolyticum* JW/SL-YS485 for ethanol production

A. Joe Shaw, Dartmouth College, USA

Tuesday, October 3, 2006 (continued)

18.00 – 19.30 Dinner

19.30 – 23.00 **Poster Session B** and social hour
Chairs: Iman Famili, Genomatica, USA
 Wim de Laat, DSM, The Netherlands

Wednesday, October 4, 2006

- 07.00 – 08.00 Breakfast
- Experimental Techniques on X-omics (From Gene to Flux)***
Chairs:Ralph Takors, Degussa, Germany
Maria Klapa, FORTH, Greece
- 08:00 – 08:05 Introduction of Helmut Meyer by Maria Klapa
- 08.05 – 08.45 Keynote Lecture
Proteome research - state of the art
Helmut Meyer, Medical Proteom -Center Ruhr-University of Bochum, Germany
- 08.45 – 08.55 Break
- 08.55 – 09.20 **Design of strain improvement based on DNA-micro-array data analysis of *Saccharomyces cerevisiae***
Hiroshi Shimizu, Osaka, Japan
- 09:20 – 09:45 **Bridging transcriptional regulation and metabolic phenotype**
Michael Jewett, Lyngby, Denmark
- 09:45 – 10.10 **Data correction, normalization and validation for enhanced accuracy of metabolomics analysis using gas chromatography mass spectroscopy**
Maria Klapa, ICEHT, Greece
- 10.10 – 10.40 Coffee break
- 10.40 – 11.05 **Metabolic flux analysis in eukaryotic systems based on LC-MS mass isotopomer distribution of free intracellular metabolites**
Wouter van Winden, Kluyver Centre, Delft, The Netherlands
- 11.05 – 11.30 **Isotopically unstationary ¹³C-metabolic flux analysis in *Escherichia coli*: modeling, experimental design, experiment and data evaluation**
Marco Oldiges, Jülich/Siegen, Germany
- 11.30 – 11.55 **Elementary metabolite units (EMU): a novel framework for modeling isotopic tracer distributions and determining metabolic fluxes**
Maciek Antoniewicz, MIT, USA
- 11.55 – 12.15 Discussion moderated by chairs
- 12.15 – 13.30 Lunch
- Mathematical Modeling for Metabolic Engineering***
Chairs:Jens Nielsen, Technical University of Denmark, Denmark
Costas Maranas, Pennsylvania State University, USA
- 13.30 – 13.35 Introduction of Matthias Reuss by Jens Nielsen
- 13.35 – 14.15 Keynote Lecture
Simulations of 4D-spatial-temporal dynamics in cellular signal transduction processes
Matthias Reuss, Stuttgart, Germany

Wednesday, October 4, 2006 (continued)

- 14.15 – 14.25 Break
- 14.25 – 14.50 **Metabolic engineering under uncertainty**
Vassily Hatzimanikatis, Northwestern University
- 14.50 – 15.15 **Modeling a genetic switch for antibiotic defense: stochasticity and robustness of dynamics**
Sarika Mehra, Indian Institute of Technology, India
- 15.15 – 15.40 **Optimal design of recombination and degenerate oligo based protein combinatorial libraries using pair wise residue scoring matrixes**
Costas Maranas, Pennsylvania State University, USA
- 15:40 – 16.00 Coffee break
- 16.00 – 16.25 **A Boolean approach to reconstruct regulatory and signalling pathways in the yeast *Saccharomyces cerevisiae***
Ana Paula Oliveira, Lyngby, Denmark
- 16.25 – 16.50 **A genome scale model of *Lactobacillus plantarum* WCFS1: useful for omics data integration and exploring metabolic capacities**
Bas Teusink, WCFS/NIZO, The Netherlands
- 16.50 – 17.15 **Metabolomics of recombinant yeast: Gene expression, flux analysis, and a mathematical model for gene regulation of metabolism**
Juan Asenjo, Santiago, Chile
- 17.15 – 17.40 Discussion moderated by chairs
- 17.40 – 18.20 Break
- 18.20 – 18.25 Introduction of Merck Awardee by Barry Buckland and Greg Stephanopoulos
- 18.25 – 19.20 **Merck Award Lecture**

Metabolism: A State Of Flux
James C. Liao, University of California, Los Angeles, USA
- 19.20 – 21.30 Banquet
- 21.30 – 23.00 **Poster Session B**, social hour*
Chairs: Iman Famili, Genomatica, USA
Wim de Laat, DSM, The Netherlands

Thursday, October 5, 2006

- 07.00 – 08.00 Breakfast buffet
- 07.00 – 08.00 Business Breakfast Meeting
- New Frontiers in Metabolic Engineering***
Chairs: Philippe Soucaille, Metabolic Explorer, France
Kristala Jones Prather, Massachusetts Institute of Technology, USA
- 08:00 – 08:05 Introduction of Edwin Cuppen by Kristala Jones Prather
- 08.00 – 08.45 Keynote Lecture
Micro-RNAs in animal development
Edwin Cuppen, Hubrecht Laboratory, Utrecht, The Netherlands
- 08.45 – 08.55 Break
- 08.55 – 09.20 **Controlling cell population heterogeneity through genetic network design**
Nikos Mantzaris, Rice University, USA
- 09.20 – 09.45 **Global transcriptional machinery engineering**
Greg Stephanopoulos, Hal Alper, MIT, USA
- 09.45 – 10.10 **Minimum genome factory – Improvement of basic cellular activity**
Hideo Mori, Kyowa Hakko, Japan
- 10.10 – 10.40 Coffee break
- 10.40 – 11.05 **Development of sugarcane as a biofactory for biopolymers**
Lars Keld Nielsen, The University of Queensland, Australia
- 11.05 – 11.45 **Development challenges for a novel HIV vaccine**
Barry Buckland, Merck and Co., Inc., USA
- 11.45 – 11.50 Introduction of Martin Fussenegger by Philippe Soucaille
- 11.50 – 12.35 Closing Keynote Lecture
Synthetic mammalian transgene control systems
Martin Fussenegger, ETH, Zürich, Switzerland
- 12.35 – 13.00 Closing discussion
- Closing address
Sef Heijnen
Vassily Hatzimanikatis
- 13.00 – 14.00 Lunch and Departure