



Program for the NORA Summer School 2 - the Marie Skłodowska-Curie ITN NORA

Systems biology and biochemistry of N₂O producing bacteria; Waste water treatment technologies

Location: Technische Universiteit Delft (TUD), Biotechnology building: *Julianalaan 67* ([map](#)).

Themes: Biochemistry, kinetics, energetics, systems biology, wastewater technology

Work load: *NORA Summer School 2* will give **3 credits (ECTS)**, including preparatory tasks and a written assignment to work on afterwards. Course literature is available on the NORA intranet, [here](#).

Purpose

To obtain a basic understanding of the functioning of living cells at the molecular level, and introduction to qualitative and quantitative methods applicable inside and outside the living cell. To learn to design and execute studies where these methods are applied, and to interpret the results. Specifically, the students will be trained in:

- The use and interpretation of information about cellular processes such as energy metabolism, regulation of gene expression, make up and function of respiratory networks, biochemistry and kinetics of denitrification enzymes, quantification of fluxes.
- Exploring the metabolic potential of selected organisms, model their respiratory systems, and predicting growth parameters such as ATP yield.
- Application of Metabolic Control Analysis to quantify distribution of control and regulation of cellular processes by individual cellular reactions.
- The use of existing computer models of molecular systems in the cell to explore the behavior of these systems.

Content

- Introduction to Metabolic Control Analysis and its basis in enzyme kinetics.
- Laws and practical applications of Metabolic Control Analysis, and extension of this method to include gene expression.
- Modular kinetic analysis of cellular networks.
- Structure and function of respiratory networks, with *Paracoccus denitrificans* as example.
- Biochemistry, kinetics and bioenergetics of respiration and denitrification
- Use of a depository of mathematical models to explore reaction systems in the cell.

Set up

Lectures and exercises in systems biology of denitrifying bacteria and communities, including microbial physiology, microbial ecology and relevance to kinetic modelling, regulation analysis and multivariate analysis. Lectures (eight contact hours); workgroups (eight contact hours); computer practical (four contact hours). PDFs of the lectures will be uploaded on the NORA website on Friday 14th of November. Homework-exercises will be uploaded on the day of the lectures.

Homework:

1. **Ahead of the School:** Reading and understanding the **literature** listed below and that is uploaded on the NORA site.
2. **After the School:** Do **exercises** that will be offered to you by the teachers on their respective days and mail the answers to the responsible teacher before November 30th 2014. You will be evaluated, get feedback and explanations before December 15th.

Literature

Reading list with PDFs that are available on the NORA website. NB! External participants will receive the literature via e-mail. The literature is to be read and understood prior to the accompanying lectures. If one does not understand certain parts of it please contact colleague students for help.

PDFs Andy gates:

To be announced

PDFs Rob van Spanning:

Simon J, van Spanning RJ, Richardson DJ (2008) The organisation of proton motive and non-proton motive redox loops in prokaryotic respiratory systems. *Biochim Biophys Acta* 1777: 1480-1490.

Simon J, Klotz MG (2013) Diversity and evolution of bioenergetic systems involved in microbial nitrogen compound transformations. *Biochim Biophys Acta* 1827: 114-135.

Al-Attar S, de Vries S (2013) Energy transduction by respiratory metallo-enzymes: From molecular mechanism to cell physiology. *Coordination Chemistry Reviews* 257 (2013) 64– 80

PDFs Lars Bakken:

Lesley A.H. Bowman, Samantha McLean, Robert K. Poole and Jon M. Fukuto (2009) The Diversity of Microbial Responses to Nitric Oxide and Agents of Nitrosative Stress: Close Cousins but Not Identical Twins. *ADVANCES IN MICROBIAL PHYSIOLOGY, VOL. 59: 135-219*

Petra Girsch, Simon de Vries (1997) Purification and initial kinetic and spectroscopic characterization of NO reductase from *Paracoccus denitrificans*. *Biochimica et Biophysica Acta* 1318 : 202–216

Stephen Spiro (2007) Regulators of bacterial responses to nitric oxide. *FEMS Microbiol Rev* 31: 193–211

PDFs Wilfred Roling:

Bruggeman FJ, Westerhoff HV (2006) The nature of systems biology. *TRENDS in Microbiology* Vol.15 No.1: 45-50

Homework exercises:

Homework-exercises will be uploaded on the day of the lectures.

Andy Gates; the task will be to analyse enzyme assays and plot and determine K_M and V_{max} values and possibly modes of inhibition from real data.

Total time: 2-4 hours.

Details on the NORA web site on Saturday November 15th

Rob van Spanning; the task will be to figure out denitrification schemes of selected organisms based on blasting and to predict the bioenergetics. Also two small exercises on stoichiometries of denitrification.

Total time: 2-4 hours.

Details on the NORA web site on Saturday November 15th

Lars Bakken; the task will be to identify kinetic functions and estimate parameters by the “solver” in Excel. Data for these exercises will be provided. Present the results in plenum at the end of the day

Total time: 2-4 hours

Details on the NORA web site on Sunday November 16th

Wilfred Roling; the task will be to write a short essay on how each ESR/ER could implement systems biology into his/her research (\approx 500 words).

Total time: 4 hours.

Details on the NORA web site on Monday November 17th

Participating students

NORA PhD students (Early Stage Researchers):

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NORA post doc.'s (Experienced Researchers):

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External participants:

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Eveline van den Berg- **TUD** <E.M.vandenBerg@tudelft.nl>

Lucas Fillinger- **VUA** <l.fillinger@vu.nl>

Ulisses Nunes Da Rocha- **VUA** <u.nunesdarocho@vu.nl>

Programme for school 2

	Time	Topic	Teacher
Saturday 15/11	9.00-12.30	Biochemistry of denitrification, lectures and exercises	Andy Gates
	12.30-13.30	Lunch	
	13.30-17.00	Bioenergetics of denitrification, lectures and exercises	Rob van Spanning
Sunday 16/11	10.00-12.30	Kinetics of denitrification, lectures	Lars Bakken
	12.30-13.30	Lunch	
	13.30-16.30	Kinetics of denitrification, exercises	Lars Bakken
Monday 17/11	10.00-12.30	Systems bioinformatics of metabolic networks, lectures	Wilfred Roling
	12.30-13.30	Lunch	
	13.30-16.30	Systems bioinformatics of metabolic networks, exercises	Wilfred Roling

Venue: “Old library” computer room of the TU Delft Biotechnology building: Julianalaan 67 – we can all meet 15 minutes before the course starts at the main entrance since we need a card to get into the building during the weekend.