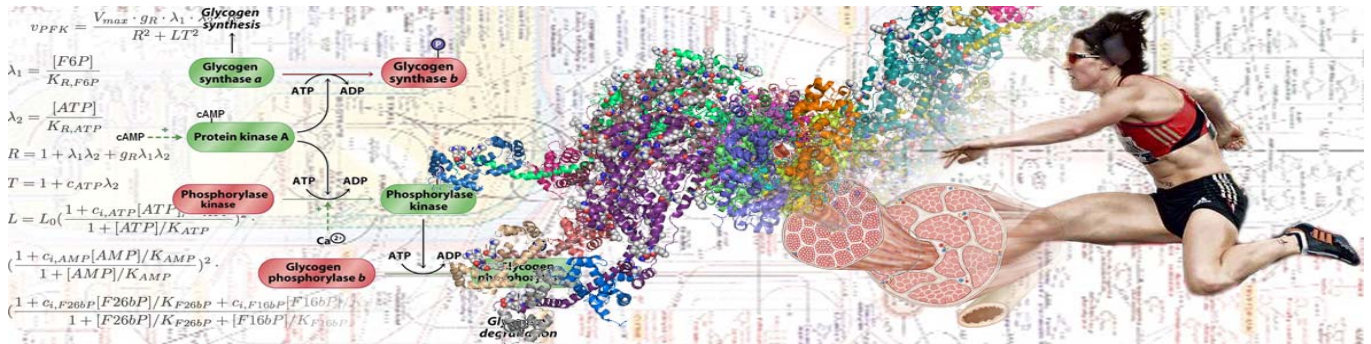


Joint 4th FEBS and 1st Systems X Advanced Lecture Course on
Systems Biology:

From Molecules to Function

Innsbruck, Austria, EU, February 26-March 4, 2011



Organizers

Anneke (J.G.) Koster (course secretary)
 Institute for Systems Biology Amsterdam

Edda Klipp (poster co-chair)
 Humboldt University Berlin
 Institute for Biology
 Theoretical Biophysics

Ursula Kummer (black board chair)
 Modeling of Biological Processes
 Institute for Zoology
 Heidelberg, Germany

Frank Bruggeman (IT)
 Netherlands Institute for Systems Biology
 Life Sciences, Centre for Mathematics and
 Computer Science Amsterdam

Karl Kuchler
 Medical University Vienna
 Max F. Perutz Laboratories
 Campus Vienna Biocenter

Uwe Sauer (program co-chair)
 Institute for Molecular Systems Biology
 ETH Zürich

Jacky L. Snoep

Triple-J Group for Molecular Cell Physiology
Department of Biochemistry
University of Stellenbosch

Hans V. Westerhoff (program chair)

AstraZeneca Chair for Systems Biology,
Manchester Centre of Integrative Systems Biology,
The University of Manchester and
Molecular Cell Physiology,
Netherlands Institute for Systems Biology,
VU University Amsterdam



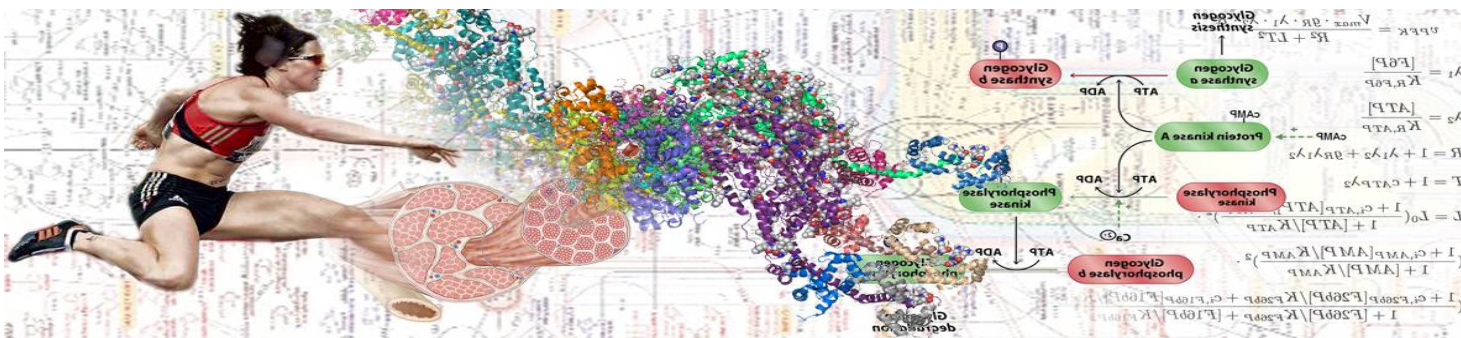
SystemsX.ch
The Swiss Initiative in Systems Biology

Teachers

Ruedi Aebersold
Rudi Balling
Philippe Bastiaens
Angela Brand
Frank Bruggeman
Carsten Carlberg
Saso Dzeroski
Johan Elf
Heinz Engl
David Fell
Akira Funahashi
Jeff Hasty

Mathias Heinemann
Adriano Henney
Dagmar Iber
Jeroen Jeneson
Ursula Klingmüller
Edda Klipp
Karl Kuchler
Ursula Kummer
Joseph Lehar
Hans Lehrach
Pedro Mendes
Andrew Millar
Maria Nardelli

Jens Nielsen
Uwe Sauer
Marcel Schilling
Birgit Schöberl
Luis Serrano
Jacky Snoep
Irina Surovtsova
Bas Teusink
Jens Timmer
Natal Van Riel
Hans Westerhoff



Scientific Program



Saturday, February 26

08.30 – 09.00	<i>Pre-course registration</i>		<i>L</i>
09.00 – 10.30	4 parallel pre-courses part I		Rooms C, H, I and J
	David Fell <i>(Oxford, UK)</i>	Pre-1	Mathematical Biochemistry in a Nutshell Room H
	Ursula Kummer <i>(Heidelberg, DE)</i>	Pre-2	Computing in a Nutshell Room I
	Maria Nardelli and Ursula Klingmüller <i>(Manchester, UK, Heidelberg, DE)</i>	Pre-3	Cell Biology in a Nutshell Room J
	Karl Kuchler <i>(Vienna, AT)</i>	Pre-4	Molecular Genetics in a nutshell Room C
10.30 – 11.00	<i>Coffee break</i>		<i>R</i>
11.00 – 12.30	4 parallel pre-courses part II		Rooms C, H, I and J
12.30 – 13.30	<i>Lunch</i>		<i>Restaurant upstairs</i>
13.30 – 15.00	4 parallel pre-courses part III		Rooms C, H, I and J
15.00 – 15.30	<i>Tea break</i>		<i>R</i>
15.30 – 17.00	4 parallel pre-courses part IV		Rooms C, H, I and J
17.30 – 18.30	<i>Reception; getting to know each other</i>		<i>R / Bar</i>

Saturday, February 26 – Opening Session

16.30 – 18.30	Course Registration	L In lobby
17.30 – 18.30	<i>Reception; getting to know each other</i>	<i>R / Bar</i>
17.30 – 19.00	Poster mounting	D, E, and F
19.00 – 20.25	<i>Welcome Dinner</i>	<i>Restaurant</i>
20.30 – 21.15	Opening Session <i>Chair: Heinz Engl</i> (Vice Rector, University Vienna)	Lecture Hall
20.30 – 20.35	Welcome address <i>Karl Kuchler, Hans Westerhoff</i>	
20.35 – 21.15	L-D1 Hans R. Lehrach The 1010 \$ model for all and then?	
20.30 – 22.00	Late Course Registration <i>(late arrivals call one of the FEBSX-SysBio2011 Hotlines)</i>	Office (O)

Sunday, February 27

07.00 – 08.30	<i>Breakfast</i>	<i>Restaurant</i>
08.30 – 12.30	Symposium D: Discovery of components, interactions and network inference <i>Chair: Edda Klipp</i>	
08.30 – 09.45	Methodology Lectures	Plenary
08.30 – 08.35	Chair's Introduction	
08.35 – 09.05	L-D1 Carsten Carlberg Finding gene functions through systems biology	Lecture hall
09.05 – 09.25	L-D2 Philippe Bastiaens Spatial organization in growth factor signaling	Lecture hall
09.25 – 09.45	L-D3 Jeff Hasty Genetic clocks from engineered oscillators	Lecture hall
09.45 – 10.00	<i>Mini coffee break</i>	
10.00 – 10.45	Tutorials corresponding to Lectures	3 in parallel
	L-D1 Tutorial Carsten Carlberg	Lecture hall
	L-D2 Tutorial Philippe Bastiaens	Room C
	L-D3 Tutorial Jeff Hasty	Room J
10.45 – 11.10	<i>Macro coffeebreak with pastries</i>	
11.10 – 12.30	Results Lectures	Plenary
11.10 – 11.30	L-D1 Results Carsten Carlberg	Lecture hall
11.35 – 11.55	L-D2 Results Philippe Bastiaens	Lecture hall
12.00 – 12.20	L-D3 Results Jeff Hasty	Lecture hall
12.25 – 12.30	Chair's summary and awarding of best student question prize	Lecture hall
12.30 – 16.00	<i>Lunch (package) and ski break</i>	<i>Bar (S)</i>

16.00 – 16.30	Tea	
16.30 – 18.45	Black Board Teaching (BB) and Computer Practicals (CP)	
16.30 – 17.30	Session I (parts 1)	Parallel
BB-1	Frank Bruggeman Modelling of molecular stochasticity in cell biology (<i>intermediate/advanced</i>)	room C
BB-2	Saso Dzeroski Machine learning for systems biology (<i>intermediate/advanced</i>)	room J
BB-3	Bas Teusink & Matthias Heinemann Genome-scale metabolic models, their construction (basic/intermediate)	room M
CP-1	Akira Funahashi CellDesigner4.1: A process diagram editor for gene-regulatory and biochemical networks (basic/intermediate)	room H
CP-2	Ursula Kummer & Pedro Mendes Introduction to modeling (using Copasi) and analysis (basic/intermediate)	room I
17.30 – 17.45	Mini coffee break	
17.45 – 18.45	Session II (parts 1)	Parallel
BB-4	Dagmar Iber Computational analysis of developmental patterning processes (basic/intermediate)	room C
BB-5	Jeroen Jeneson & Natal van Riel Physiological modeling (basic/intermediate)	room J
BB-6	Edda Klipp Introduction to sensitivity analysis (basic/intermediate)	room M
BB-7	Marcel Schilling Advanced Parameter Estimation (<i>intermediate/advanced</i>)	Lecture hall
CP-3	Jacky Snoep Standards for Computational Modeling (basic/intermediate)	room I
CP-4	Irina Surovtsova Dynamical simulation of multiscale nonlinear biochemical networks (<i>intermediate/advanced</i>)	room H

18.50 – 19.50	<i>Dinner</i>	<i>Restaurant (upstairs)</i>
20.00 – 20.40	Short talks	Plenary
	<i>Chair: Edda Klipp</i>	
20.00 – 20.20	D-23 Kristina Gruden SegMine: a tool for semantic microarray data analysis	Lecture hall
20.20 – 20.30	E-15 Alexey Kolodkin Blueprint modelling of nuclear receptor signaling: discovering design principles	Lecture hall
20.30 – 20.40	T-23 Berend Snijder Cell-to-cell variability modelling reveals complex RNAi phenotypes in virus infection	Lecture hall
20.40 – 21.15	<i>Macro coffeebreak with pastries</i>	
21.00 – 23.30	Poster Session 1	rooms DEF
21.00 – 21.45	Viewing posters; presentation of posters 3n-2	
21.45 – 22.30	Free poster wandering	
22.30 – 23.30	Bar poster discussions of posters 3n-2	
21.15 - 23.30	<i>Bar: 1 free drink (using coupons)</i>	

Sunday's Poster Presentations

Rooms D, E, and F

Discovery

- D-01 Use of the Reconstruction, Analysis and Visualization of Metabolic Networks (RAVEN) Toolbox for generating the genome-scale metabolic network for *Penicillium chrysogenum*
Rasmus Agren, Liming Liu, Wanwipa Vongsangnak, Intawat Nookaew, Jens Nielsen
- D-04 Metabolic Modeling of the Gut Microbiota
Fredrik Karlsson, Intawat Nookaew, Dina Petranovic, Jens Nielsen
- D-07 Systems Biology reveals a novel mechanism regulating glucocorticoid action
David Morgan, Namshik Han, Laura Matthews, Andy Brass, David Ray
- D-10 Long-term effects of high-fat diet on metabolic pathways in 129Sv and C57B6/J mouse livers: A proteomics approach
Eduard Sabidó, Thomas Porstmann, Veavi Chang, Tim Clough, Olga Vitek, Markus Stoffel, Ruedi Aebersold
- D-13 Adrenal gland hormone deprivation as a modulator of synaptic plasticity in amyloid-induced model of Alzheimer's disease
Harutyun Y. Stepanyan, Vergine A. Chavushyan, Irina B. Meliksetyan, John S. Sarkissian
- D-16 Glucose-tolerant subpopulations in *tps1*Δ cultures – a result of phenotypic plasticity?
Johan H. van Heerden, Jan Berkhout, Meike Wortel, Bas Teusink
- D-19 Accounting for extrinsic variability in the estimation of stochastic rate constants
Christoph Zechner, Heinz Koepl, Arnab Ganguly
- D-22 NO ABSTRACT SUBMITTED
Bernhard P. Steiert
- D-25 NO ABSTRACT SUBMITTED
Andre Wegner

Top-down systems biology

- T-01 Regulation of MtlR, the transcription activator of the *Bacillus subtilis* mannitol operon via phosphorylation by and interaction with PTS components
Houda Bouraoui, Meriem Derkaoui, Marie-Françoise Noirot-Gros, Sandrine Poncet, Philippe Joyet, Josef Deutscher
- T-04 Regulation of lipid metabolism in eukaryotic cells
Pramote Chumnanpuen, Nookaew Intawat, Nielsen Jens
- T-07 Mitochondrial concept of leukemogenesis: key role of oxygen-peroxide effects
Tatyana Engel, Sanzhar Ismailov, Marcel Schilling
- T-10 Mathematical modelling of mammalian TCA cycle metabolism
Amar Ghaisas, David Fell
- T-13 Short chain fatty acid induced transcriptional regulation in mice intestine and liver
Katja Lange, Danielle Haenen, Guido JEJ Hooiveld, Michael Müller
- T-16 NO ABSTRACT SUBMITTED
Violeta Madjarova
- T-19 Thermodynamic analysis of yeast
Caroline Paget, Daniela Delneri, Jean-Marc Schwartz
- T-22 Developing models of the mammalian cell S-phase
Alex Shaw
- T-25 A computational framework for protein-protein interactions in yeast
Kwanjeera Wanichthanarak, Marija Cvijovic, Dina Petranovic, Jen Nielsen

Bottom-up systems biology

- B-01 Computational analysis of the cell growth regulatory network of fission yeast cells.
Archana Bajpai, Federico Vaggi, Attila Csikász-Nagy
- B-04 Multi-level regulation of IL-6 signaling during the priming phase of liver regeneration
Svantje Braun, Andreas Kowarsch, Sebastian Bohl, Andreas Raue, Ruth Merkle, Ute Albrecht, Johannes Bode, Jens Timmer, Fabian Theis, Ursula Klingmüller
- B-07 HGF-driven PI3 kinase and MAP kinase crosstalk in primary mouse hepatocytes
Lorenza A. D'Alessandro, Regina Samaga, Seong-Hwan Rho, Steffen Klamt, Jens Timmer, Ursula Klingmüller
- B-10 Metabolic network reconstruction of the pathogen *Enterococcus faecalis*.
Carla Portela, Isabel Rocha, Silas G. Villas-Boas, Eugenio C. Ferreira
- B-13 Exploring carbon use efficiency of *Arabidopsis thaliana* using a genome-scale metabolic model
Aliah H. Hawari, Mark G. Poolman, David A. Fell, R. George Ratcliffe, Lee J. Sweetlove
- B-16 Mechanisms for liver size regulation
Nadine Hohmann, Anja Voß-Böhme, Andreas Deutsch
- B-19 Dealing with input signals in systems biology models
Max Schelker, Andreas Raue, Clemens Kreutz, Jens Timmer
- B-22 Metabolic Engineering Approaches for Strain Optimization using Evolutionary Computation Techniques
Pedro Tiago Evangelista, Isabel Rocha, Miguel Rocha
- B-25 Exploring the effects of snare proteins on insulin signaling cascade in skeletal muscle via computational modeling.
Ceylan Colmekci Oncu, Haili Liu, Peter A.J. Hilbers, Natal A.W. van Riel

Evolutionary design

- E-01 Exploring protein expression levels in optimal networks
Jan Berkhout, Emrah Nikerel, Evert Bosdriez, Dick de Ridder, Bas Teusink, Frank Bruggeman
- E-04 Happy Model Maker: creating, editing, running and visualizing constraint-based stoichiometric models
Joost Boele, Brett Olivier
- E-07 Feedback regulation of integrin signaling
Georgios Fengos, Florian Geier, Dagmar Iber
- E-10 The temporal coordination of cellular metabolism: an in-silico approach
Willi Gottstein, Hanspeter Herzel, Ralf Steuer
- E-13 Stoichiometric network analysis for microbial communities.
Ruchir A. Khandelwal, Brett G. Olivier, Wilfred F. M. Röling, Bas Teusink, Frank J. Bruggeman
- E-16 Branch point selection during lung branching morphogenesis
Denis Menshykau, Dagmar Iber
- E-19 Elucidating transcriptional regulatory networks from heterogeneous gene expression compendia
Andrea Pinna, Nicola Soranzo, Vincenzo de Leo, Alberto de la Fuente
- E-22 New developments in the diurnal changes of nitrogen metabolism in *Chlamydomonas reinhardtii*
Sascha Schäuble, Ines Heiland, Stefan Schuster
- E-25 Understanding the Crabtree effect from cellular economics
Meike Wortel, Douwe Molenaar, Bas Teusink

Making systems biology **W**ork

- W-01 A tool for constructing kinetic models for metabolic pathways
Monica Abrudan
- W-04 Therapy-induced cancer cell adaptation captured by data-driven fuzzy logic modelling of mapk signalling rearrangements
Marti Bernardo Faura, Stefan Massen, Anne Hamacher-Brady, Roland Eils, Christine Falk, Nathan R. Brady
- W-07 Modeling circadian transcriptional feedback loops in mouse liver with delay differential equations
Anja Korencic, Grigory Bordyugov, Marko Golcnik, Jure Acimovic, Rok Kosir, Martina Perse, Damjana Rozman, Hanspeter Herzel
- W-10 Bioprocess monitoring and prediction using mobile devices
Martins Mednis, Jurijs Meitalovs, Sandis Vilums, Vytautas Galvanauskas
- W-13 A system-based approach for biopolymer production by an extremophilic bacteria, *Halomonas* strain CRSS DSM 15686
Gonca Özdemir, Ebru Toksoy Öner, Kazim Yalcin Arga
- W-16 NO ABSTRACT SUBMITTED
Clarissa Riegert
- W-19 Differential networking studies of microRNA regulation
Nicola Soranzo, Andrea Pinna, Alberto de la Fuente
- W-22 Global Silicon Human(GSH) using volunteer computing
Chengkun Wu, Hans Westerhoff
- W-25 Network biology @ Pfizer
Glyn Bradley, Daniel Ziemek, Bryn Williams-Jones

Monday, February 28

07.00 – 08.30	<i>Breakfast</i>	<i>Restaurant</i>
08.30 – 12.30	Symposium T: Top-down (Generating biological insights from Top-down systems biology) <i>Chair: Ursula Kummer</i>	
08.30 – 09.45	Methodology Lectures	Plenary
08.30 – 08.35	Chair's Introduction	
08.35 – 09.05	L-T1 Edda Klipp Information integration in signaling	Lecture hall
09.05 – 09.25	L-T2 Ruedi Aebersold Quantitative proteomics and systems biology	Lecture hall
09.25 – 09.45	L-T3 Hans V. Westerhoff Looking down and back-up: The systems biology workflow from genes to discovery	Lecture hall
09.45 – 10.00	<i>Mini coffee break</i>	
10.00 – 10.45	Tutorials corresponding to Lectures	3 in parallel
	L-T1 Tutorial Edda Klipp	Lecture hall
	L-T2 Tutorial Ruedi Aebersold	Room C
	L-T3 Tutorial Hans V. Westerhoff	Room J
10.45 – 11.10	<i>Macro coffeebreak with pastries</i>	
11.10 – 12.30	Results Lectures	Plenary
11.10 – 11.30	L-T1 Results Edda Klipp	Lecture hall
11.35 – 11.55	L-T2 Results Ruedi Aebersold	Lecture hall
12.00 – 12.20	L-T3 Results Hans V. Westerhoff	Lecture hall
12.25 – 12.30	Chair's summary and awarding of best student question prize	Lecture hall
12.30 – 16.00	<i>Lunch (package) and ski break</i>	<i>Bar (S)</i>

16.00 – 16.30	Tea	
16.30 – 18.45	Black Board Teaching (BB) and Computer Practicals (CP)	
16.30 – 17.30	Session I (parts 2)	Parallel
BB-1	Frank Bruggeman Modelling of molecular stochasticity in cell biology (<i>intermediate/advanced</i>)	room C
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CP-2	Ursula Kummer & Pedro Mendes Introduction to modeling (using Copasi) and analysis (basic/intermediate)	room I
17.30 – 17.45	Mini coffee break	
17.45 – 18.45	Session II (parts 2)	Parallel
BB-4	Dagmar Iber Computational analysis of developmental patterning processes (basic/intermediate)	room C
BB-5	Jeroen Jeneson & Natal van Riel Physiological modeling (basic/intermediate)	room J
BB-6	Edda Klipp Introduction to sensitivity analysis (basic/intermediate)	room M
BB-7	Marcel Schilling Advanced Parameter Estimation (<i>intermediate/advanced</i>)	Lecture hall
CP-3	Jacky Snoep Standards for Computational Modeling (basic/intermediate)	room I
CP-4	Irina Surovtsova Dynamical simulation of multiscale nonlinear biochemical networks (<i>intermediate/advanced</i>)	room H

18.50 – 19.50	<i>Dinner</i>	<i>Restaurant (upstairs)</i>
20.00 – 20.40	Short talks	Plenary
	<i>Chair: Ursula Kummer</i>	
20.00 – 20.20	B-28 Rafael Moreno-Sanchez Modeling glycolysis in cancer and parasitic cells	Lecture hall
20.20 – 20.30	E-01 Jan Berkhout Exploring protein expression levels in optimal networks	Lecture hall
20.30 – 20.40	E-11 Ines Heiland Temperature compensation and temperature entrainment - amity or enmity?	Lecture hall
20.40 – 21.15	<i>Macro coffeebreak with pastries</i>	
21.00 – 23.30	Poster Session 2	rooms DEF
21.00 – 21.45	Viewing posters; presentation of posters 3n-1	
21.45 – 22.30	Free poster wandering	
22.30 – 23.30	Bar poster discussions of posters 3n-1	
21.15 - 23.30	<i>Bar: 1 free drink (using coupons)</i>	

Monday's Poster Presentations

Rooms D, E and F

Discovery

- D-02 Metabolic cross-engineering of lactic acid bacteria, and with yeast: Surgical engineering *in silico*
Malgorzata Adamczyk, Ettore Murabito, Hans Westerhoff
- D-05 Identification of marker genes involving obesity and insulin resistance based on transcriptome and clinical data
Kanthida Kusonmano, Intawat Nookaew, Armin Graber, Klaus Liedl, Jens Nielsen
- D-08 Analysis of the human protein UBB+1 and UCH-L1 in the proteasome impairment and cell death in the yeast *Saccharomyces cerevisiae*
Ana Joyce Muñoz, Andrea Neiss, Dina Petranovic
- D-11 Modelling of *E. coli* metabolism in salt stress conditions: application to the overproduction of succinate and L-carnitine
Guido Santos, José Hormiga, Hugo Velazco, Carlos González, Paula Areense, Manuel Cánovas, Néstor Torres
- D-14 Single cell level analysis of TGF- β signaling pathway in hepatocytes
Tibor Szekeres, Philippe Lucarelli, Antony D. Adamson, Stefan Legewie, Marcel Schilling, Ursula Klingmüller
- D-17 Towards 'domino' systems biology and an integrated ATP-centric model of regulation in *Saccharomyces cerevisiae*
Malkhey Verma, Maksim Zhakhartsev, Martin Valachovic, Ana Kitanovic, Hanan Messiha, Karl Kuchler, Femke Mensonides, Stefan Wölfl, Matthias Reuss, Fred Boogerd, Pedro Mendes, Walter Glaser, Jacky Snoep, Hans Westerhoff
- D-20 The alterations in human lymphocytes under the influence of carbon nanotubes
Alena Zhornik, Ludmila Baranova, Valentina Emelyanova, Igor Volotovskii
- D-23 SegMine: a tool for semantic microarray data analysis
Kristina Gruden, Vid Podpecan, Nada Lavrac, Igor Mozetic, Petra Kralj-Novak, Laura Langohr, Kimmo Kulovesi, Hannu Toivonen, Marko Petek, Helena Motaln
- D-26 Cancer and Energetics: Comparative Hierarchical Regulation Analysis and Dynamic Modelling of the "Warburg effect"
Kathryn Blount

Top-down systems biology

- T-02 *In silico* simulations of heterologously expressed glycerol dehydrogenase in yeast *Saccharomyces cerevisiae*
Valters Brusbardis, Janis Liepins
- T-05 Why *Saccharomyces cerevisiae* exhibit variability in the ability of growth?
Lucie Crépin, Cécile Cadoux, Isabelle Sanchez, Sylvie Dequin, Carole Camarasa
- T-08 Metabolomics as a functional assay for active transcriptional regulation in yeast
Laura Falter, Nicola Zamboni, Uwe Sauer
- T-11 Gut microbiomics of SCFA metabolism
Floor Hugenholtz, Michiel Kleerebezem, Hauke Smidt
- T-14 Modeling of mitochondrial modulation of Ca²⁺ handling in skeletal muscle
Haili Liu, Natal van Riel, Peter Hilbers
- T-17 The control by glucose transport: cells toggling between life and death
Maria Nardelli, Malkhey Verma, David Morgan, Malgorzata Adamczyk, Hans V. Westerhoff
- T-20 Using MapMan to facilitate biological interpretation of transcriptomic data analysis: its use and implementation to new plant species
Ana Rotter, Špela Baebler, Matjaž Hren, Björn Usadel, Kristina Gruden
- T-23 Cell-to-cell variability modelling reveals complex RNAi phenotypes in virus infection
Berend Snijder, Raphael Sacher, Pauli Ramo, Lucas Pelkmans
- T-26 A quantitative proteomic analysis of the heat stress response in *Clostridium difficile* strain 630
Shailesh Jain, Robert Graham, Ciaren Graham, Geoff McMullan, Nigel Ternan

Bottom-up systems biology

- B-02 Forkhead (Fkh) transcription factors influence timing of *CLB3,4* expression regulating the pattern of mitotic cyclins in cell cycle progression
Matteo Barberis, Christian Linke, Alberto Gonzalez-Novo, Hans Lehrach, Francesc Posas, Sylvia Krobitsch, Edda Klipp
- B-05 Hydrocarbonoclastic bacteria: from bioremediation to bioenergy feedstock
A. Rita Castro Carvalho, Alcina Pereira, Madalena Alves, Isabel Rocha
- B-08 The impact of short-chain fatty acids on mouse metabolism
Gijs den Besten, Karen van Eunen, Barbara Bakker, Dirk-Jan Reijngoud
- B-11 Vertebrate limb bud development - Towards a comprehensive, spatiotemporal mathematical model of organogenesis
Philipp Germann, Conradin Kraemer, Dagmar Iber
- B-14 Metabolic regulation and channelling: flux and flux control
Fei He, Hans Westerhoff
- B-17 An updated genome-scale metabolic model for *Saccharomyces cerevisiae* including regulatory information
Tobias Österlund, Intawat Nookaew, Jens Nielsen
- B-20 An automated approach to assigning subcellular localization in genome-scale metabolic network reconstructions
Saeed Sheykhshoai, Rasmus Agren, Jens Nielsen
- B-23 Novel carbon wasting profiles and metabolic flux dynamics in *Escherichia coli* are dependent on specific growth rate
Kaspar Valgepea, Kaarel Adamberg, Raivo Vilu
- B-26 Control analysis of the action potential and its propagation in the Hodgkin-Huxley model
Francois du Toit, Riaan Conradie, Jacky Snoep

Evolutionary design

- E-02 The role of transcriptional fidelity and processivity on the noise of transcription, and its consequences on phenotypic bistability in *Streptococcus pneumoniae*
Prasanna Bhogale, Johannes Berg
- E-05 The cost and benefit of enzyme expression
Evert Bosdriesz, Jan Berkhout, Frank Bruggeman, Douwe Molenaar
- E-08 Population-based modeling of Bar1 activity via finite elements
Wolfgang Giese, Christian Diener, Edda Klipp
- E-11 Temperature compensation and temperature entrainment — amity or enmity?
Ines Heiland, Christian Bodenstein, Stefan Schuster
- E-14 Delineating cellular expression machinery effects from transcriptional regulation of gene expression in *Escherichia coli*
Karl Andreas Kochanowski, Luca Gerosa, Bart R. B. Haverkorn van Rijsewijk, Matthias Heinemann, Uwe Sauer
- E-17 The state trajectory of a cell
Tomáš Náhlík, Dalibor Štys, Jan Urban, Petr Císař
- E-20 Adaptive evolution of *Lactococcus lactis* to stable environments
Filipe Santos, Douwe Molenaar, Bas Teusink
- E-23 What influences DNA replication rate in budding yeast?
Thomas W. Spiesser, Christian Diener, Matteo Barberis, Edda Klipp
- E-26 Epigenetic gene regulation of the eukaryotic genome: systems biology approaches using mammalian synthetic cell systems
Pernette J. Verschure, Lisette C.M. Anink, Diewertje G.E. Piebes, Maartje C. Brink, Julio Mateos-Langerak, Anne Schwabe, Frank J. Bruggeman

Making systems biology **W**ork

- W-02 Circadian rhythm of post-squalene cholesterol synthesis intermediates in mice liver, a statistical modelling approach
Jure Acimovic, Rok Kosir, Marko Golcnik, Damjana Rozman, Martina Perse, Gregor Majdic, Katarina Kosmelj
- W-05 Stochastic reaction-diffusion kinetics in the microscopic limit
David Fange, Otto G. Berg, Paul Sjöberg, Johan Elf
- W-08 Systems theories and systems biology
Andrei Lapitski, Jan Urban, Jan Vanek, Dalibor Stys, Petr Cesar, Aliaksandr Pautsina, Tomas Nahlik
- W-11 High-content siRNA screening for host factors required for rhinovirus infection
Daria Mudrak, Andreas Jurgeit, Urs F Greber
- W-14 Biological systems state variable identification using joint analysis of biological and technical hypothesis in the time-lapse tissue culture development experiment
Aliaksandr Pautsina, Jan Urban, Dalibor Stys, Jan Vanek, Petr Cisar, Tomas Nahlik, Andrei Lapitski
- W-17 *In silico* design and modeling of new biosynthetic pathways: curcumin production in *Escherichia coli*
Simão Soares, Isabel Rocha, Lígia Rodrigues
- W-20 Systems theories and systems biology
Jan Urban, Jan Vanek, Tomas Nahlik, Petr Cisar, Aliaksandr Pautsina, Andrei Lapitski, Dalibor Stys
- W-23 Comparative systems biology: Experimental and protein structure-based analysis of L-lactate dehydrogenases from different Lactic acid bacteria
Araz Zeyniyev, Tomas Fiedler, Bernd Kreikemeyer, Vlad Cojocar, Omarou Samna, Rebecca Wade
- W-26 Control loop based engineering approach of cellular processes
Egils Stalidzans

Tuesday, March 1

07.00 – 08.30	<i>Breakfast</i>	<i>Restaurant</i>
08.30 – 12.30	Symposium B: Bottom-up systems biology <i>Chair: Frank Bruggeman</i>	
08.30 – 09.45	Methodology Lectures	Plenary
08.30 – 08.35	Chair's Introduction	
08.35 – 09.05	L-B1 Jens Timmer The Physics of Systems Biology	Lecture hall
09.05 – 09.25	L-B2 Johan Elf Stochastic kinetics in time and space	Lecture hall
09.25 – 09.45	L-B3 Andrew Millar Rhythms in Life	Lecture hall
09.45 – 10.00	<i>Mini coffee break</i>	
10.00 – 10.45	Tutorials corresponding to Lectures	3 in parallel
	L-B1 Tutorial Jens Timmer	Lecture hall
	L-B2 Tutorial Johan Elf	Room C
	L-B3 Tutorial Andrew Millar	Room J
10.45 – 11.10	<i>Macro coffeebreak with pastries</i>	
11.10 – 12.30	Results Lectures	Plenary
11.10 – 11.30	L-B1 Results Jens Timmer	Lecture hall
11.35 – 11.55	L-B2 Results Johan Elf	Lecture hall
12.00 – 12.20	L-B3 Results Andrew Millar	Lecture hall
12.25 – 12.30	Chair's summary and awarding of best student question prize	Lecture hall
12.30 – 13.30	<i>Lunch</i>	<i>Restaurant</i>
14.00 – 23.30	Excursion	

Wednesday, March 2

07.00 – 08.30	<i>Breakfast</i>	<i>Restaurant</i>
08.30 – 12.30	Symposium E: Evolutionary design <i>Chair: Jacky Snoep</i>	
08.30 – 09.45	Methodology Lectures	Plenary
08.30 – 08.35	Chair's Introduction	
08.35 – 09.05	L-E1 Frank Bruggeman How cells convey a message: regulation of stochastic transcription dynamics	Lecture hall
09.05 – 09.25	L-E2 Bas Teusink Purpose in life: a functional perspective to the evolution of metabolic regulation	Lecture hall
09.25 – 09.45	L-E3 Matthias Heinemann How cells respond to nutrient changes	Lecture hall
09.45 – 10.00	<i>Mini coffee break</i>	
10.00 – 10.45	Tutorials corresponding to Lectures	3 in parallel
	L-E1 Tutorial Frank Bruggeman	Lecture hall
	L-E2 Tutorial Bas Teusink	Room C
	L-E3 Tutorial Matthias Heinemann	Room J
10.45 – 11.10	<i>Macro coffeebreak with pastries</i>	
11.10 – 12.30	Results Lectures	Plenary
11.10 – 11.30	L-E1 Results Frank Bruggeman	Lecture hall
11.35 – 11.55	L-E2 Results Bas Teusink	Lecture hall
12.00 – 12.20	L-E3 Results Matthias Heinemann	Lecture hall
12.25 – 12.30	Chair's summary and awarding of best student question prize	Lecture hall
12.30 – 16.00	<i>Lunch (package) and ski break</i>	<i>Bar (S)</i>

16.00 – 16.30	Tea	
16.30 – 18.45	Black Board Teaching (BB) and Computer Practicals (CP)	
16.30 – 17.30	Session I (parts 3)	Parallel
BB-1	Frank Bruggeman Modelling of molecular stochasticity in cell biology (<i>intermediate/advanced</i>)	room C
BB-2	Saso Dzeroski Machine learning for systems biology (<i>intermediate/advanced</i>)	room J
BB-3	Bas Teusink & Matthias Heinemann Genome-scale metabolic models, their construction (<i>basic/intermediate</i>)	room M
CP-1	Akira Funahashi CellDesigner4.1: A process diagram editor for gene-regulatory and biochemical networks (<i>basic/intermediate</i>)	room H
CP-2	Ursula Kummer & Pedro Mendes Introduction to modeling (using Copasi) and analysis (<i>basic/intermediate</i>)	room I
17.30 – 17.45	Mini coffee break	
17.45 – 18.45	Session II (parts 3)	Parallel
BB-4	Dagmar Iber Computational analysis of developmental patterning processes (<i>basic/intermediate</i>)	room C
BB-5	Jeroen Jeneson & Natal van Riel Physiological modeling (<i>basic/intermediate</i>)	room J
BB-6	Edda Klipp Introduction to sensitivity analysis (<i>basic/intermediate</i>)	room M
BB-7	Marcel Schilling Advanced Parameter Estimation (<i>intermediate/advanced</i>)	Lecture hall
CP-3	Jacky Snoep Standards for Computational Modeling (<i>basic/intermediate</i>)	room I
CP-4	Irina Surovtsova Dynamical simulation of multiscale nonlinear biochemical networks (<i>intermediate/advanced</i>)	room H

18.50 – 19.50	<i>Dinner</i>	<i>Restaurant (upstairs)</i>
20.00 – 20.40	Short talks	Plenary
	<i>Chair: Jacky Snoep</i>	
20.00 – 20.20	E-26 Pernette J. Verschure	Lecture hall
	Epigenetic gene regulation of the eukaryotic genome: systems biology approaches using mammalian synthetic cell systems	
20.20 – 20.30	B-02 Matteo Barberis	Lecture hall
	Forkhead (Fkh) transcription factors influence timing of <i>CLB3,4</i> expression regulating the pattern of mitotic cyclins in cell cycle progression	
20.30 – 20.40	E-28 Andrew Hufton	Lecture hall
	Scientific publishing in systems biology	
20.40 – 21.15	<i>Macro coffeebreak with pastries</i>	
21.00 – 23.30	Poster Session 3	rooms DEF
21.00 – 21.45	Viewing posters; presentation of posters 3n	
21.45 – 22.30	Free poster wandering	
22.30 – 23.30	Bar poster discussions of posters 3n	
21.15 - 23.30	<i>Bar: 1 free drink (using coupons)</i>	

Wednesday's Poster Presentations

Rooms D, E and F

Discovery

- D-03 Data-based mathematical modeling reveals distributive ERK phosphorylation as a general systems property
Nao Iwamoto, Lorenza D'Alessandro, Bettina Hahn, Sofia Depner, Margareta M. Mueller, Wolf D. Lehmann, Ursula Klingmüller, Marcel Schilling
- D-06 Regulation of EpoR signaling by microRNAs in lung cancer
Ruth Merkle, Julie Bachmann, Andreas Kowarsch, Agustin Rodriguez, Jie Bao, Hauke Busch, Fabian J. Theis, Ursula Klingmüller
- D-09 Inferring the metabolic and transcriptional networks specific to Dupuytren's disease tumours
Samrina Rehman, Warwick B Dunn, Magnus Rattray, Ardeshir Bayat, Roy Goodacre, Philip J Day, Hans V Westerhoff
- D-12 Retrieval, alignment, and clustering of computational models based on semantic annotations
Marvin Schulz, Falko Krause, Nicolas Le Novere, Edda Klipp, Wolfram Liebermeister
- D-15 Inferring dynamic networks of cell signaling from high throughput data
Camille D. A. Terfve, Julio Saez-Rodriguez
- D-18 Time-resolved integrative multiplex analysis of inflammatory responses in the liver.
Katharina Waldow, Lorenza D'Alessandro, Annette Schneider, Tim Mailwald, Ursula Kummer, Ursula Klingmüller
- D-21 Enrichment for polypharmacology in metabolic pathways
Florian Nigsch, Eugen Lounkine, Ben Cornett, Roy Kishony, Jeremy Jenkins
- D-24 Quantitative and qualitative inverse analysis of mathematical models from systems biology
Clemens A. Zarzer, Philipp Kügler, James Lu, Gottfried Köhler, Martin Puchinger

Top-down systems biology

- T-03 Applied metabolomics for placental-focused research in pregnancy related diseases
Emanuela Filipa Cabral Monteiro, Alexander E. Heazell, Warwick B. Dunn
- T-06 A translational network of RNA binding proteins derived from the identification of phylogenetic footprints in 3' untranslated regions
Erik Dassi, Toma Tebaldi, Paola Zuccotti, Paola Riva, Alessandro Quattrone
- T-09 Incorporating cell-to-cell variability into Bayesian estimation of chemical reaction systems
Arnab Ganguly, Heinz Koepl, Cristoph Zechner
- T-12 Comparison of TEAFS and NP analysis: integration of interactome and time course transcriptome data to reveal dynamic response to C-pulse in *S. cerevisiae*
M.Erkan Karabekmez, Duygu Dikicioglu, Bharat Rash, Andy Hayes, Steve G. Oliver, Betul Kirdar
- T-15 Linking a bottom-up and top-down approach to investigate the translation of TGF β signaling and its modulator SnoN in primary mouse hepatocytes to target gene activation
Philippe Lucarelli, Stefan Legewie, Tibor Szekeres, Lorenza Alice D'Alessandro, Jens Timmer, Marcel Schilling, Ursula Klingmüller
- T-18 An optimization approach for prediction of microbial growth strategies
Pinar Ozturk, Douwe Molenaar, Bas Teusink
- T-21 Cell-sorting at the A/P-compartment boundary in the *Drosophila* wing primordium: a computational model to consolidate observed non-local effects of Hedgehog signaling
Sabine Schilling, Maria Willecke, Tinri Aegerter-Wilmsen, Olaf A. Cirpka, Basler Konrad, von Mering Christian
- T-24 Contact specificity in protein-DNA complex
Ludmila Voronova

Bottom-up systems biology

- B-03 The Just Enough Results Model (JERM): Standardising and Exchanging Experimental Data in Systems Biology
Olga Krebs, Katy Wolstencroft, Stuart Owen, Isabel Rojas, Carole Goble, Wolfgang Müller, Jacky Snoep
- B-06 NO ABSTRACT SUBMITTED
Frédéric G. E. Cremazy
- B-09 PottersWheel Matlab Toolbox - A software tool for mathematical modeling and parameter fitting of multiple experiments
Oliver Eberhardt, Thomas Maiwald, Andreas Raue, Julie Blumberg, David Liffmann, Peter Sorger, Jens Timmer
- B-12 Construction and analysis of a *Salmonella typhimurium* genome scale metabolic model
Hassan Hartman, Mark Poolman, David Fell
- B-15 Quantifying FRAP data using reaction-diffusion models
Tim Heinemann, Katharina Müller, Elan Gin, Karsten Rippe, Thomas Höfer
- B-18 Agent-based modeling of endocytosis and intracellular trafficking
Martin Sander
- B-21 Mathematical modeling of the HCV drugs combinations effect
Anna Shindova
- B-24 Harmonographic signal visualization
Michal Wittner

Evolutionary design

- E-03 Circadian rhythms: Temperature entrainment and influence of molecular noise
Christian Bodenstein, Ines Heiland, Stefan Schuster
- E-06 Dynamic Optimization in computational systems biology
Gundian M. De Hijas-Liste, Eva Balsa-Canto, Julio R. Banga
- E-09 *In-vivo*-like maximum enzyme activities for *Lactococcus lactis* at varying growth rates: Purely metabolic regulation?
Anisha Goel, Douwe Molenaar, Willem deVos, Bas Teusink
- E-12 Importance of compartmentalisation for Akt signaling
Felix Jonas, Mariko Okada
- E-15 Blueprint modelling of nuclear receptor signaling: discovering design principles
Alexey Kolodkin, Frank Bruggeman, Nick Plant, Nilgun Yilmaz, Hans Westerhoff
- E-18 Towards the mechanistic relationship of the rate/efficiency trade-off in yeast metabolism
Bastian Niebel, Matthias Heinemann
- E-21 Small RNA, big effect: co-regulating mRNAs
Jörn Schmiedel, Ilka Axmann, Nils Blüthgen, Stefan Legewie
- E-24 NO ABSTRACT SUBMITTED
Michael Unger
- E-27 Inferring biochemical regulation sites from metabolomics covariance data-a mathematical framework
Wei Yang, Xiaoliang Sun, Matthias Steinfath, Dirk Walther, Wolfram Weckwerth, Philipp Kuegler

Making systems biology **W**ork

- W-03 Tools to quantify yeast sex pheromone transduction in vivo
Alvaro Banderas, Gabriele Malengo, Victor Sourjik
- W-06 NO ABSTRACT SUBMITTED
Steven Geinitz
- W-09 What dynamic metabolite profiles tell about allosteric regulation
Hannes Link, Uwe Sauer
- W-12 High-throughput sequencing proves heterogeneity of stock cultures and no evolution in short term continuous cultures
Ranno Nahku, Karl Peebo, Kaspar Valgepea, Jeffrey E Barrick, Kaarel Adamberg, Raivo Vilu
- W-15 Comprehensive database for human genome scale metabolic modeling
Natapol Pornputtpong, Adil Mardinoglu, Rasmus Ågren, Intawat Nookaew, Sergio Velasco, Jens B Nielsen
- W-18 Selection of thermodynamically feasible and active pathways
Zita Soons, Eugénio Ferreira, Isabel Rocha
- W-21 Designing a storage lipids-free *Saccharomyces cerevisiae* cell
Juan O. Valle-Rodríguez, Verena Siewers, Shuobo Shi, Jens Nielsen
- W-24 Combining theoretical analysis and experimental data generation reveals IRF9 as crucial factor for accelerating interferon alpha induced early antiviral signalling
Tim Maiwald, Annette Schneider, Hauke Busch, Ursula Kummer, Ursula Klingmüller

Thursday, March 3

07.00 – 08.30	<i>Breakfast</i>	<i>Restaurant</i>
08.30 – 12.30	Symposium W: Making Systems Biology Work <i>Chair: Uwe Sauer</i>	
08.30 – 09.45	Methodology Lectures	Plenary
08.30 – 08.35	Chair's Introduction	
08.35 – 09.05	L-W1 Jens Nielsen Systems biology of the cell factory <i>Saccharomyces cerevisiae</i>	Lecture hall
09.05 – 09.25	L-W2 Joseph Lehar Systems biology from chemical combinations	Lecture hall
09.25 – 09.45	L-W3 Birgit Schöberl Applying engineering principles to the development of novel cancer therapies	Lecture hall
09.45 – 10.00	<i>Mini coffee break</i>	
10.00 – 10.45	Tutorials corresponding to Lectures	3 in parallel
	L-W1 Tutorial Jens Nielsen	Lecture hall
	L-W2 Tutorial Joseph Lehar	Room C
	L-W3 Tutorial Birgit Schöberl	Room J
10.45 – 11.10	<i>Macro coffeebreak with pastries</i>	
11.10 – 12.30	Results Lectures	Plenary
11.10 – 11.30	L-W1 Results Jens Nielsen	Lecture hall
11.35 – 11.55	L-W2 Results Joseph Lehar	Lecture hall
12.00 – 12.20	L-W3 Results Birgit Schöberl	Lecture hall
12.25 – 12.30	Chair's summary and awarding of best student question prize	Lecture hall
12.30 – 16.00	<i>Lunch (package) and ski break</i>	<i>Bar (S)</i>

16.00 – 16.30	Tea	
16.30 – 19.45	Systems Biology and its contexts	Plenary
	<i>Chairs: Adriano Henney and Uwe Sauer</i>	
16.30 – 17.35	Systems biology at work: the real life (discussion session)	Lecture hall
C-01	Adriano Henney The virtual liver	
C-02	Rudi Balling Systems Biomedicine Luxembourg/Seattle	
C-03	Luis Serrano CRG-EMBL Systems Biology	
C-04	Uwe Sauer SystemsX	
17.35 – 17.50	<i>Mini coffee break</i>	
17.50 – 18.30	Systems Biology and Society	Lecture hall
C-05	Angela Brand Systems Biology for Public Health	
18.30 – 19.00	<i>Wine break with presentation of FEBSXSysBio young investigator award</i>	Bar (S)
19.00 – 19.45	Closing lecture	Lecture hall
C-06	Luis Serrano Absolute quantification and integration of mRNA, protein and turnover in a bacterium	
20.00 – 21.00	<i>Banquet</i>	<i>Restaurant upstairs</i>
21.30 – 25.00	<i>Farewell party</i>	<i>Disco: Lecture hall</i>

Friday, March 4

- | | |
|---------------|---------------------------------------------------------------|
| 09.00 – 12.00 | Restaurant open |
| 07.00 – 10.00 | Check-out (accomodation) and departure |
| 07.00 – 12.00 | Shuttle from Hotel to Airport and Train Station (bus or taxi) |

Abstracts Pre-courses

Pre-1 Mathematical biochemistry in a nutshell

David A. Fell

Life Sciences, Oxford Brookes University, Headington, Oxford, OX3 0BP, UK

The aim of the course is to illustrate how mathematical models of biochemical systems are formulated and solved, and it is directed principally at those with a background in biological sciences who have had little formal training in the mathematical techniques used in systems biology. The emphasis will be on explaining the mathematical vocabulary and giving insight into the strategies used to compute solutions so that the mathematical aspects of the subsequent symposia and blackboard sessions are not a complete mystery. Obviously a one day course cannot turn you into trained mathematicians, nor will the practical exercises demand much mathematical technique. Rather, we will use spreadsheets and graphs to illustrate the approaches to getting solutions by analogy. We will start by going from the kinetics of a single enzyme to the time course of an enzyme reaction, and then generalize that to systems of several reactions. The mathematical symbolism used to represent such systems in a compact form will be explained, and then the different types of solutions that can be obtained, depending on the information available. Other topics that will be explained qualitatively, or with the aid of spreadsheets, will be parameter estimation and sensitivity analysis.

Pre-2 Computing in a nutshell

Ursula Kummer

BioQuant, Ins Neunheimer Feld 267, D-69120 Heidelberg, Germany, EU

This course will introduce computational resources and how to set models up with their aid. Modelling approaches are explained. Common databases, tools and standards used for these will be discussed in detail.

The course is aimed at participants with little mathematical training and new to the field, but also at people with a more formal training, but new to systems biology and interested in getting to know the different resources available to help with setting up models etc.

Like the other precourses, the course aims to provide the complete newcomers in the field with important concepts and knowledge, useful for following the rest of the course.

Pre-3 Cell Biology in a Nutshell

Maria Nardelli¹ and Ursula Klingmüller²

¹Doctoral Training Centre for Integrative Systems Biology from Molecules to Life, MIB, the University of Manchester, 131 Princess Street, M1 7DN, Manchester, UK, EU

²Deutsches KrebsForschungsZentrum, Ins Neuenheimer Feldn 280, D 66120 Heidelberg, Germany, EU

The cells as building blocks of life are the results of combinations of organic and inorganic components. The results of these combinations are the cellular processes which are deeply analysed in Systems Biology. For this reason a system biologist should approach his research project having knowledge of them. An overview of living organisms and their distinctive features will be the starting point. The components as well as the processes of living organisms will then be described. Particular attention will be paid to molecules such as carbohydrates, proteins and nucleic acids, as well as to ATP and NADH. Processes such as nucleic acid and protein synthesis as well as cell division and respiration, which have as results synthesis or degradation of these molecules, will be illustrated.

For Systems Biology approaches, knowledge regarding the advantages and disadvantages of selected cellular model systems are essential. A basic concept of differences in time and spatial scales will be introduced. An overview of technologies and their specific advancements to be used for quantitative data generation specifically for modeling purposes, will be provided. Furthermore, mechanisms of intracellular signal transduction as well as a link to physiological responses will be addressed. Strategies to link measurements at different levels and connection to responses in the organ/tissue context will be discussed.

Pre-4 Molecular Genetics in a nutshell

Karl Kuchler

Medical University of Vienna, Christian Doppler Laboratory for Infection Biology, Max F. Perutz Laboratories, Campus Vienna Biocenter, Dr. Bohr-Gasse 9/2, A-1030 Vienna, Austria. *Phone: +431-4277-61812; FAX: +431-4277-9618; e-mail: karl.kuchler@meduniwien.ac.at*

Systems biology (SysBio) aims to gain a systems-level understanding of organismic, cellular or even subcellular pathway behaviour to identify novel as well as emerging principles of a living system. The long-term hope is to be able to better predict and cure diseases of complex genetic origin. One of the key features of SysBio is the integration of a multitude of quantitative biological data (deep-sequencing, SNP and mutations, genetic interactions, microarrays, proteomics, metabolomics, etc.) with various applicable mathematical modelling approaches. While modelling and the use of proper algorithms depends on the question and hypothesis to be addressed, the generation of quantitative biological data often poses unsurmountable technical problems or are even impossible with the current methodologies. This is especially true for measuring the dynamics and time-scale of biological processes from transcription, translation to post-translational modification as well as the kinetics of intracellular biomolecule trafficking. Likewise, pathway architectures and features often result from complex genetic interactions, which respond to various types of input, making parameter estimation for modeling a difficult task. In this pre-course teaching on molecular genetics for theoreticians and modellers, I will try to use simple model systems such as yeast as an example to explain how and which kind of experimental (genetic) data can be obtained from eukaryotic cells in a (near)-quantitative manner and which technical issues and pitfalls apply to the some of the current state-of-the-art technologies to study the dynamics of biological processes related to signal transduction.

Black Board and Computer Practical Abstracts

BB-1 Modeling of molecular stochasticity in cell biology

Frank Bruggeman

Netherlands Institute for Systems Biology (NISB)
Life Sciences, Centre for Mathematics and Computer Science, Amsterdam, The Netherlands
Molecular cell physiology, VU University, Amsterdam, The Netherlands

Population of isogenic cells can display remarkable cell-to-cell heterogeneity in physiological behaviors. The origins of this heterogeneity (so-called noise) can often be traced back to the stochasticity inherent to transcription. In this small course, some experimental results on prokaryotic and eukaryotic stochasticity will be discussed and explained in terms of a few mathematical models that describe molecular stochasticity. A number of theoretical concepts and approaches will be illustrated that are useful in understanding molecular stochasticity and its effects on cellular physiology. After this course, most of the concepts and models in the field of single-cell analyses will be clear to you.

BB-2 Machine Learning for Systems Biology

Saso Dzeroski

Dept. of Knowledge Technologies, Jozef Stefan Institute, Jamova cesta 39, Ljubljana, SI-1000, Slovenia

In systems biology, a flood of information is being produced through a variety of “-omics” approaches. Genomics, transcriptomics, proteomics and metabolomics, are devoted respectively to the examination of the entire systems of genes, transcripts, proteins and metabolites present in a given cell or tissue type. Taking advantage of this wealth of information has become a *conditio sine qua non* for the practitioners of systems biology. Machine learning naturally appears as one of the main drivers of progress in this context, where of most interest are techniques that deal with complex structured objects: sequences, 2D and 3D structures, or interaction networks. The lectures will introduce the machine learning approaches that are most relevant for applications in systems biology. These include methods for analyzing structured data, and in particular structured output prediction, and methods for learning the full dynamics of biological networks, including both network structure and the kinetics of the corresponding reactions. Example applications will be presented, which include gene function prediction, predicting the response of genes to stress and analyzing image data from genome screens, as well as reconstructing the dynamics of endocytosis (more specifically endosome maturation).

BB-3 Genome-scale metabolic models, their construction and analysis

Bas Teusink and Matthias Heinemann

The post-genomics revolution has confronted mainstream biologists with the need of models for data integration, analysis, and - ultimately - understanding of the complexity of biological systems. Hence, if we want to make optimal use of functional genomics data, we need models of genome scale. Such genome-scale metabolic models are based on bioinformatics, comparison with other genome-scale models, literature, and experimental evidence for the activity of specific pathways. These models are now an important tool in the lab for data integration and visualisation, but also for predictions of metabolic phenotypes. In this blackboard course we will first discuss the metabolic reconstruction process, *i.e.* issues related to the construction of a genome-scale model. Then we will explain and discuss several so-called constraint-based modelling techniques applied to such models. These modelling techniques all aim to predict or interpret flux distributions through the metabolic network. The most important ones are flux balance and flux variability analysis. In the last session we will discuss applications of stoichiometric analysis, including ^{13}C analysis, thermodynamic constraints and sensitivity analysis.

BB-4 Computational Analysis of Developmental Patterning Processes

Dagmar Iber

D-BSE, ETH Zurich, Mattenstrasse 26, Basel, 4058, Switzerland

Morphogen gradients are key to the patterning of organisms during development. They define the body axes and direct the patterning of tissues and organs. Mathematical models can help to understand how gradients emerge and how they are read out. Previous models have largely focused on steady-state gradients, yet experimental data suggest that gradients change in time and can be read out while they emerge. I will present dynamic models for two patterning problems: the patterning of the dorso-ventral axis during embryogenesis and the limb bud axes during development. An important problem with regard to dorso-ventral patterning concerns the issue of scaling. Speman showed almost 100 years ago that also a halved frog embryo can grow into a normal adult. How gradients can define a relative position (e.g. the middle) on very differently sized domains is largely unclear. I will present a mechanism that is consistent with available mutants and which provides an explanation as to how dynamic scaling can be achieved. By example of the limb bud I will illustrate how the definition of different axes (i.e. proximo-distal and anterior-posterior) can be coordinated.

BB-5 Physiological Modeling Blackboard Teaching

Natal A.W. van Riel and Jeroen A.L. Jeneson

Biomedical Engineering, Eindhoven University of Technology, Den Dolech 2, Eindhoven, 5612 AZ, The Netherlands

Where the objectives of Systems Biology are grandiose – i.e., to gain a comprehensive understanding of a biological system at all levels including the genomic level, Systems Physiology seeks to gain a model-based understanding of the performance and homeostasis of a biological system phenotype by taking a reverse engineering approach. Central in this approach is: 1) experimental observations on the intact system, and 2) ‘constraint-based modeling’. Specifically, fundamental principles like thermodynamics together with information on the in vivo performance (including limits) of the intact biological system under investigation are exploited to generate hard and tractable constraints guiding model development. This blackboard teaching course seeks to introduce the participant to the various practical aspects of Physiological Modeling, involving the use of both ‘wet’ (experimental observation) as well as ‘dry’ (computational modeling and advanced computational analysis) approaches. As a teaching vehicle, an enigmatic problem in eukaryotic energy balance has been selected: the regulation of mitochondrial function in the mammalian cell. The course will include a computer practical using Copasi. Participants will be briefly introduced to the mitochondrial ATP synthetic pathway and (ongoing debate of) its regulation, and to various computational models of this pathway that have been proposed in the literature. Concrete problems, including computational challenges, that are typically encountered in physiological modeling as well as solutions viz. strategies to overcome these problems will be identified and discussed. The use of computational parameter sensitivity analysis to identify key processes and gain new mechanistic insight is illustrated as well as how models with many uncertain parameters can be parameterized by making use of the desired physiological behavior.

BB-6 Introduction to sensitivity analysis

Edda Klipp

Theoretical Biophysics, Humboldt-Universität zu Berlin, Invalidenstr. 42, Berlin, 10407, Germany

Computational models of biological systems and biochemical networks in the form of ordinary differential equations comprise variables and parameters. The behaviour of the variables in steady state or over time depends on the parameter values and on the structure of the biochemical network. In many studies it is important to know how much the values of variables change, if we perturb individual parameters.

In this black board session, we present basic sensitivity measures. As special cases for metabolic and biochemical networks, global sensitivity measures for the dependence of steady state rates or concentrations, so-called flux and concentration control coefficients, will be introduced together with the local elasticity coefficients. It will be demonstrated how these coefficients can be calculated. Extensions for other variables or dynamic regimes or stochastic systems will be provided.

BB-7 Black Board Teaching: Advanced Parameter Estimation

Marcel Schilling

Systems Biology of Signal Transduction, German Cancer Research Center, Im Neuenheimer Feld 280, Heidelberg, 69120, Germany

Mathematical modeling of biological systems has become a powerful approach to investigate complex dynamic, non-linear interaction mechanisms in cellular systems. As the kinetic parameters of a model are often unknown, an increasing interest in Systems Biology is focused on deriving these parameters directly from experimental data by parameter estimation. However, this is both numerically and methodologically challenging, as the solution is often not unique, resulting in non-identifiabilities. One reason for non-identifiability are parameters that can compensate each other leading to the same goodness of fit. However, by exploring the parameter space, these dependencies can be detected. Furthermore, novel developments allow improved calculation of confidence intervals of the estimated parameters, giving a measure of the predictive power of a mathematical model. In this tutorial, experimental time-course data will be used to parameterize simple kinetic models of signaling pathways. The concepts of over-parameterization, identifiability and observability will be introduced with specific examples and model reduction will be demonstrated. It will be shown how identifiability and confidence intervals of model parameters depend on the model structure and the nature and quality of experimental data. As this tutorial will be based on experimental data and most concepts are visualized by examples, it should appeal to both students without a strong mathematical background as well as to the ones with experience in modeling.

CP-1 CellDesigner4.1: A process diagram editor for gene-regulatory and biochemical networks

Akira Funahashi

Dept. of Biosciences and Informatics, Keio University, 3-14-1 Hiyoshi Kouhoku-ku, Yokohama, 223-8522, Japan

CellDesigner is software for modeling and simulation of biochemical and gene regulatory networks, originally developed by the Systems Biology Institute in Japan. While CellDesigner itself is a sophisticated structured diagram editor, it enables users to directly integrate various tools, such as built-in SBML ODE Solver and SBW-powered simulation/analysis modules. CellDesigner runs on various platforms such as Windows, MacOS X and Linux, and is freely available from our website at <http://celldesigner.org/>. In this course, I will explain how CellDesigner can be used from both modeling and software development perspectives. The first topic will feature network modeling using CellDesigner, and will show how she/he could build a model from scratch, and examine simulations. This topic also includes an explanation on how we build a biochemical network as a "map" which includes links to several existing databases, and how we build a mathematical model by the aspect of process-diagram based modeling. Once a model is described with appropriate mathematical equations and parameters, running a simulation on CellDesigner is quite straight forward. I will also explain how to easily tweak your model from CellDesigner's user-interface and observe some changes in the dynamics. Not just building a model from scratch, this course also introduces how we can "import" an existing model from several third-party databases (ex. BioModels.net, PANTHER database). This might be useful for users who actually read a paper and got interested in the model, but does not have enough experience on building a mathematical model by hand. The second topic will feature plugin development of CellDesigner, which allows users to manipulate network diagram in many ways (for example changing the color/size of node, reflecting experimental data etc.). This tutorial will cover both modeling and software development topics, and mainly focuses on modeling part. Both CellDesigner users and software developers are encouraged to join. Bringing your notebook PC is highly recommended.

CP-2 Introduction to modeling (using COPASI)

Ursula Kummer¹, Pedro Mendes²

¹ Modeling of Biological Processes, University of Heidelberg, INF 267, Heidelberg, 69120, Germany

² University of Manchester

This computer practical introduces basic modeling approaches as setting up models, simulating them, parameter fitting and sensitivity analysis. The course will make use of the commonly used software COPASI to learn the topics in a hand-on and applied way.

CP-3 Standards for computational modeling

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Mathematical modeling might be considered some sort of art in the sense that it is not possible to define a set of rules that need to be followed to construct a model. However, modeling is also a scientific process that should be transparent and reproducible. Thus, if a model is based on experimental data, such links should be made explicit and it should be clear what data was used for model construction and what data was used for model validation. As part of a good modeling practice the process that was used to construct the model should be described such that it can be reproduced. Although no standard procedure for generic model construction is available/possible; a number of standards have been defined for model description and model annotation. In this computer practical we have selected a set of standards that are important for model description and annotation; SBML (Systems Biology Markup Language), SBGN (Systems Biology Graphical Notation), and MIRIAM (Minimal Information Required In the Annotation of Models). These standards will be discussed and then an easy to use web interface will be introduced to define a mathematical model according to these standards. Students can bring their own model, define a new model or adapt an existing model. SEDML and SBRML, markup languages to define model simulations and their results will be introduced. Time permitting, the Silicon Cell strategy for modeling will be illustrated for a detailed kinetic model, showing how experimental data can be linked to individual processes for model construction, and to the complete system for model validation.

CP-4 Dynamical simplification of multiscale nonlinear biochemical networks.

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Motivation: Understanding the functioning of large existing biochemical models asks for means to rationally dissect the networks into meaningful and rather independent subnetworks. On the other hand, there is a strong need for general reduction techniques for the use during the modeling process itself allowing the derivation of several manageable models displaying distinct properties of the large systems. *Contents:* During this computer practical we present the methodology for simplification of biochemical reaction networks. The technique is based on elimination of fast metabolites and reactions. The set of fast species and near equilibrium reactions is detected by dynamical time scale decomposition methods implemented within the software COPASI. We propose the "practical recipes" for reducing and analyzing the multiscale biochemical models displaying different dynamical regimes (also with strong oscillatory behavior).

