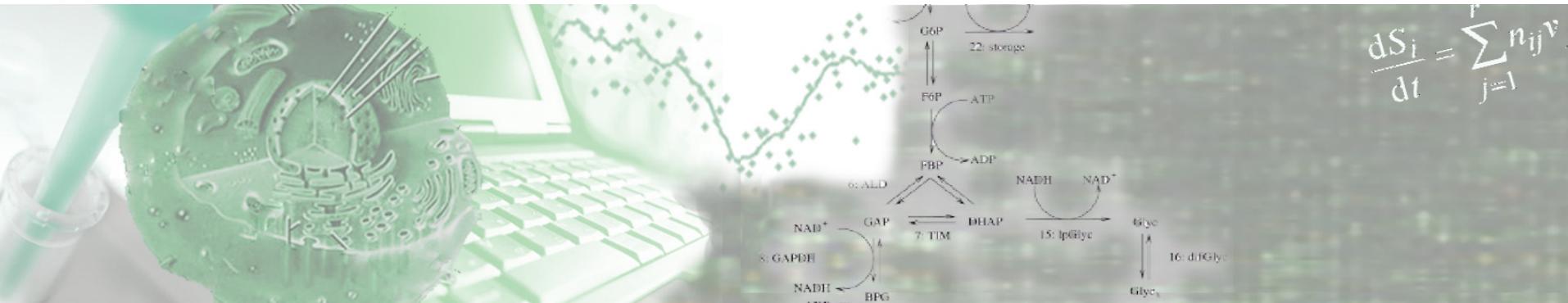


$$\frac{dS_i}{dt} = \sum_{j=1}^r n_{ij} v_j$$



Wintersemester 2016

Fachkurs – Introduction

Edda Klipp

Humboldt-Universität zu Berlin
Institut für Biologie
Theoretische Biophysik



Content

Language?

Script

Time table

Papers to chose

Time Table

Dienstag, 22.11.2016		Dienstag, 29.11.2016			
10.00-11.30	Introduction	Edda	10.00-11.30	How to write	Edda
12.30-14.00	Copasi Intro	Judith/Katja	12.30-14.00	Presentation Techniques	Judith
14.15-15.45	Copasi Exercise	Judith/Katja	14.15-15.45	Project work	-
16.00-17.30	Copasi Exercise	Judith/Katja	16.00-17.30	Project work	-
Mittwoch, 23.11.2016		Mittwoch, 30.11.2016			
10.00-11.30	Copasi: Goldbeter Intro	Judith/Katja	10.00-11.30	Project Work	-
	Copasi: Goldbeter				
12.30-14.00	Implementation	Judith/Katja	12.30-14.00	Project Work	-
14.15-15.45	SBML & Databases	Jannis	14.15-15.45	Project Work	-
16.00-17.30	Python Intro	Jannis/Björn	16.00-17.30	Project Work	-
Donnerstag, 24.11.2016		Donnerstag, 01.12.2016			
10.00-11.30	Python Intro	Jannis/Björn	10.00-11.30	Project Work	-
		Jannis/Wolfgang			
12.30-14.00	Python Numpy/Scipy	Jannis/Wolfgang	12.30-14.00	Project Work	-
		Jannis/Wolfgang			
14.15-15.45	Python Numpy/Scipy	Jannis/Wolfgang	14.15-15.45	Project Work	-
16.00-17.30	Python Plotting	Max	16.00-17.30	Project Work	-
Freitag, 25.11.2016		Freitag, 02.12.2016			
10.00-11.30	Python Datenanalyse	Jannis/Björn	10.00-11.30	Project Presentations	all
12.30-14.00	Python Datenanalyse	Jannis/Björn	12.30-14.00	Project Presentations	all
14.15-15.45	Python ODE	Max/Wolfgang	14.15-15.45	Project Presentations	all
16.00-17.30	Python ODE	Max/Wolfgang	16.00-17.30	Project Presentations	all

Own Contribution

Talk – Presentation of a publication and own simulations

1. Read and understand paper
2. Create the presented model, using SBML/Copasi or Python
3. Reproduce the simulations shown in the publication
4. Analysis and modification of the model
 - Which analyses are made by the authors?
 - Does the model change with parameter changes?
 - Own ideas for model analysis or model improvement?
5. Analysis of model presentation
 - is it possible to reproduce the model from the information given in the paper?
6. Preparation of presentation
 - Summary of the paper
 - Presentation of own results



Own contribution

Talk – Presentation of a publication and own simulations

Form groups of 2 students (in case biophysicists/non-biophysicists)

Time is foreseen in time table

Every paper is connected to a mentor. Contact them!!!



Structure of presentation

Front page – presenters, publication (Title, authors)

Summary of the publication

Summary of open questions and problems

Presentation of own simulations including problems/implementation

Summary and conclusions

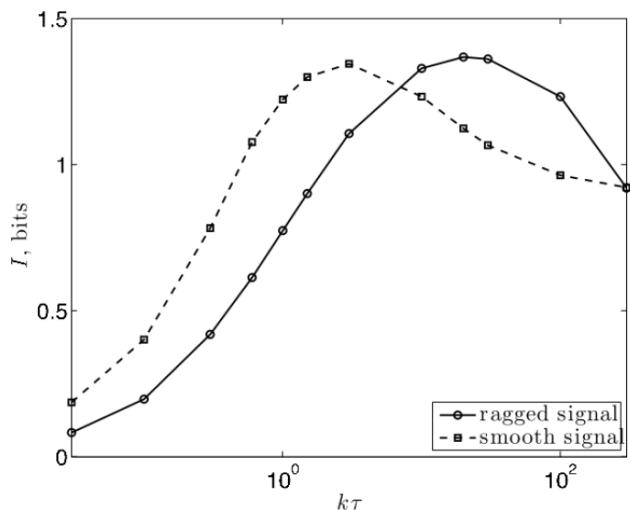
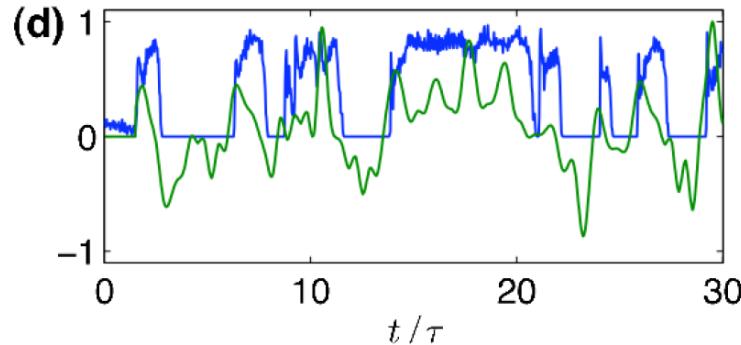
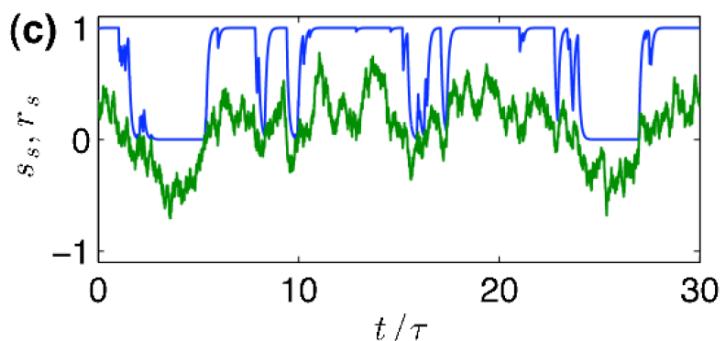
Acknowledgement (to mentor, in case fellow students)

Andrea Auconi

Andrea Auconi (Room 502)

Gain control in molecular information processing: Lessons from neuroscience

Ilya Nemenman

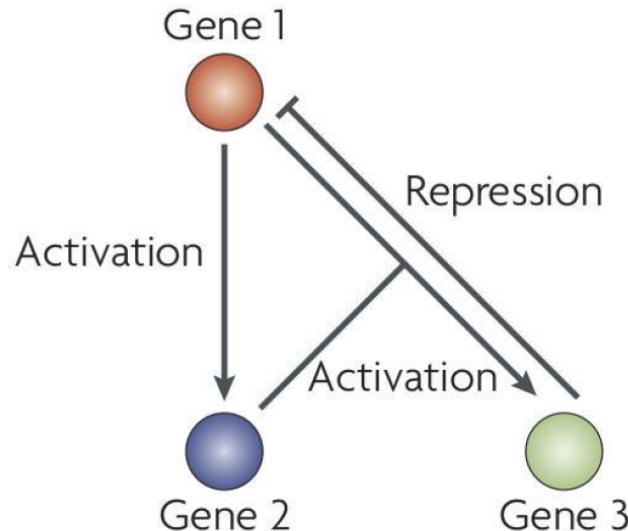


- Read the Paper
- produce a stochastic signal and response
- Compute the time-lagged mutual information
(or the correlation)

Roman Rainer

Modelling and analysis of gene regulatory networks

By Guy Karlebach and Ron Shamir



- Read the paper
- Implement the ODEs
- Evaluate the paper
- Presentation in english

Roman Rainer (505)

Josch Pauling

[Home](#) > Current Issue > vol. 101 no. 30 > Jordi Garcia-Ojalvo, 10955–10960, doi: 10.1073/pnas.0307095101



Modeling a synthetic multicellular clock: Repressors coupled by quorum sensing

Jordi Garcia-Ojalvo * †, Michael B. Elowitz ‡, and Steven H. Strogatz * § ¶

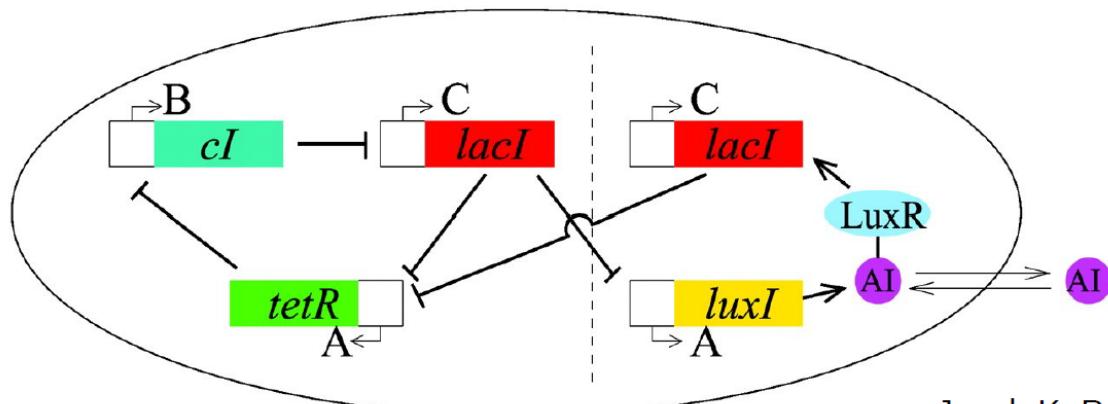
Author Affiliations ▾

Edited by Charles S. Peskin, New York University, New York, NY, and approved June 7, 2004 (received for review October 31, 2003)

Exercise

1. Read and understand the paper
2. Implement an ODE model of the repressor
3. Extend the ODE model by coupling with quorum sensing mechanism
4. Simulate for 10 cells and reproduce results
5. Critically assess the paper

- Quorum sensing is a mechanism for **intercellular signaling**
- **Messenger molecules** diffuse through the cell membrane and affect intracellular regulation, e.g. protein synthesis
- This creates feedback loops and may lead to **multicellular biorhythms/oscillations**
- A simple ODE model is created and then simulated for multiple cells affecting one another



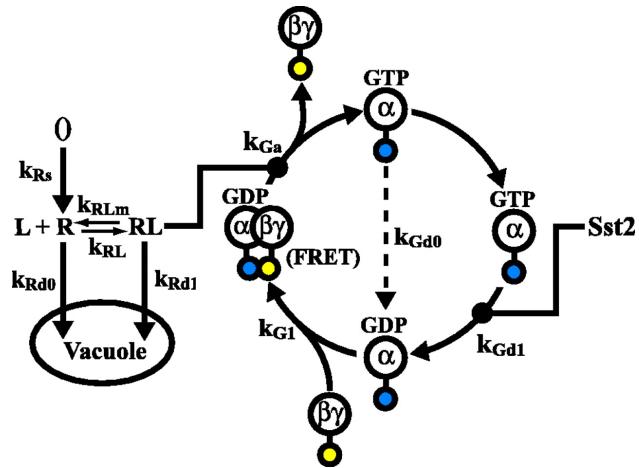
Josch K. Pauling

Wolfgang Giese

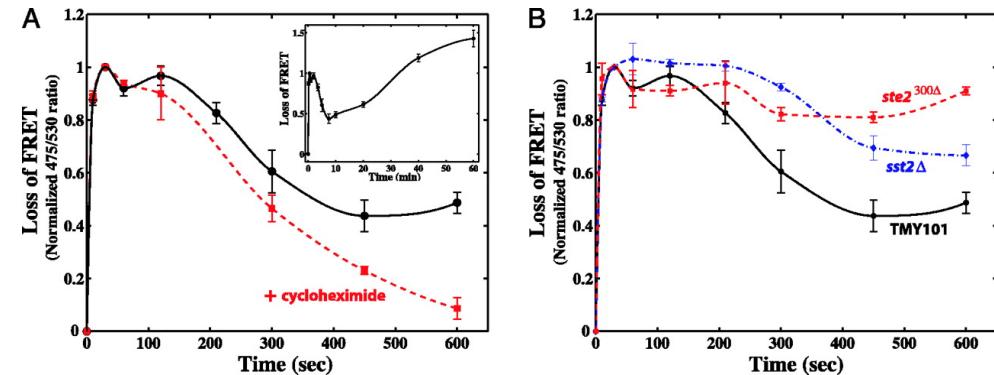


A quantitative characterization of the yeast heterotrimeric G protein cycle

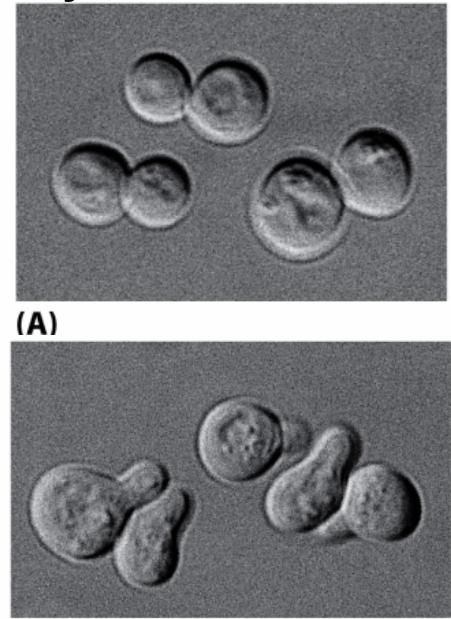
Tau-Mu Yi, Hiroaki Kitano, Melvin Simon – PNAS 2003



Reaction diagram of heterotrimeric G protein cycle.



Kinetics of G protein activation.



(B)

Shmooing yeast cells

ToDo:

- Understand the model of the G-protein cycle and corresponding FRET experiments
- Implement the model based on ODEs in Python/Copasi
- Analyze the model and compare your simulations with experiments

Tutor: Wolfgang, Room 502

wolfgang.giese@biologie.hu-berlin.de

Jannis Uhendorf



Kinkhabwala *et al.* BMC Biophysics 2014, **7**:10
<http://www.biomedcentral.com/2046-1682/7/10>



Jannis Uhendorf

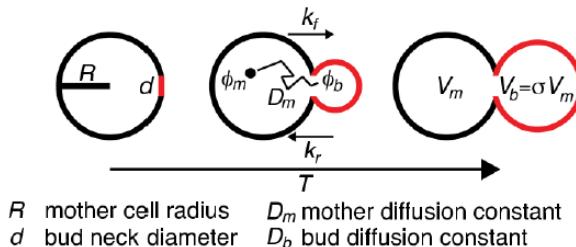
RESEARCH ARTICLE

Open Access

Analytical model for macromolecular partitioning during yeast cell division

Ali Kinkhabwala^{1*}, Anton Khmelinskii² and Michael Knop^{2*}

- Budding yeast divides asymmetrically
 - aging mother, daughter with full lifespan
- Assumption: mother cells retain damaged materials
 - **aging factors** (e.g. misfolded/damaged proteins)
- Different possible mechanisms
 - passive diffusion, localized retention sites, motor-driven transport
- Analytical ODE model to analyze different partitioning schemes in *S. cerevaise*



Tasks

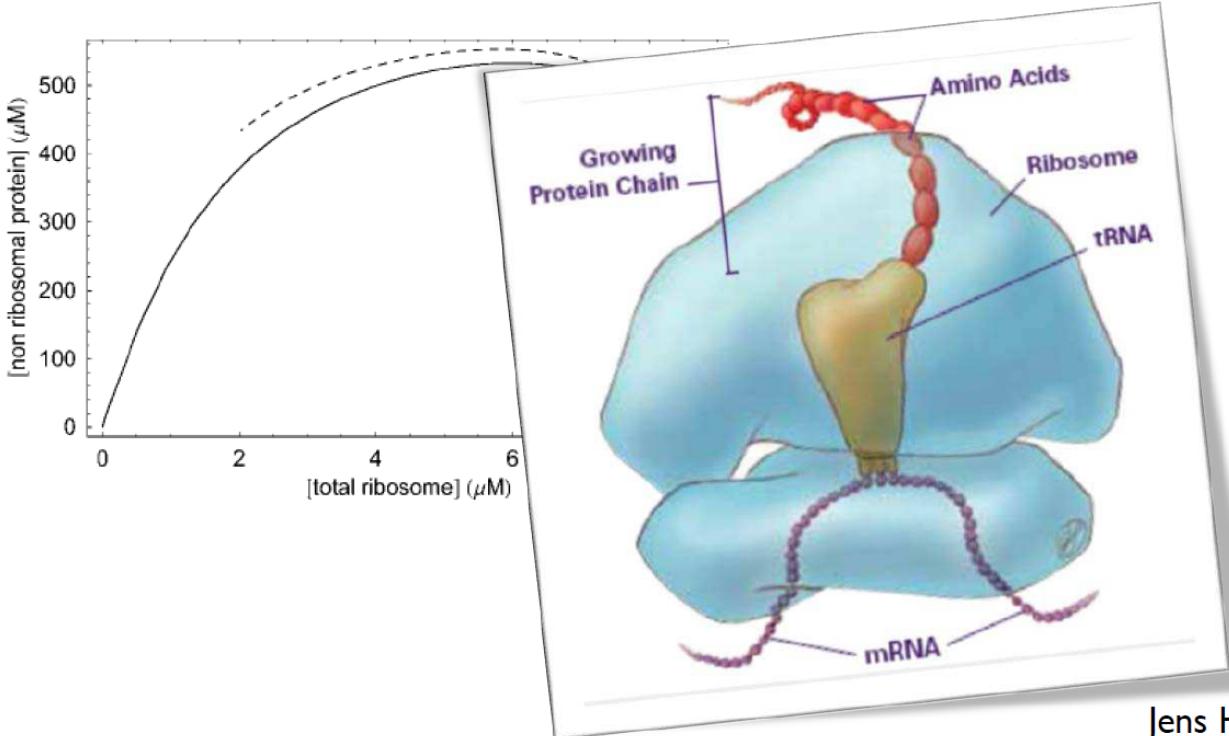
- Understand the paper
- Implement the ODE model
- Reproduce modeling results
- Critic analysis of the results of the paper

Jens Hahn



Is there an optimal ribosome concentration for maximal protein production?

J.L. Snoep, H.V. Westerhoff, J.M. Rohwer and J.-H.S. Hofmeyer



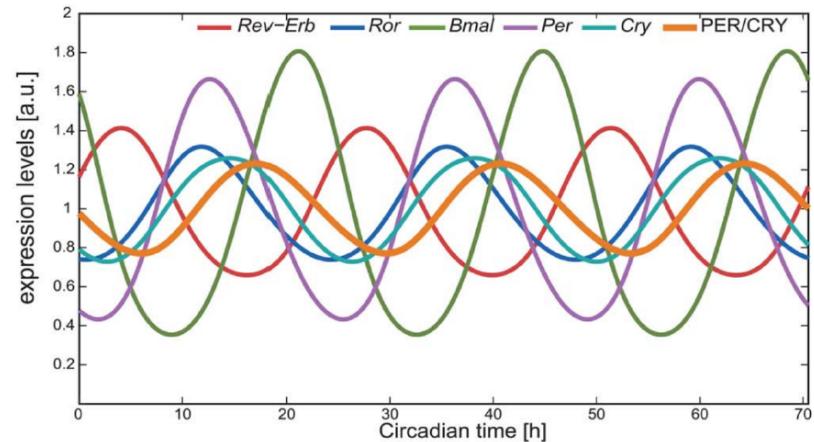
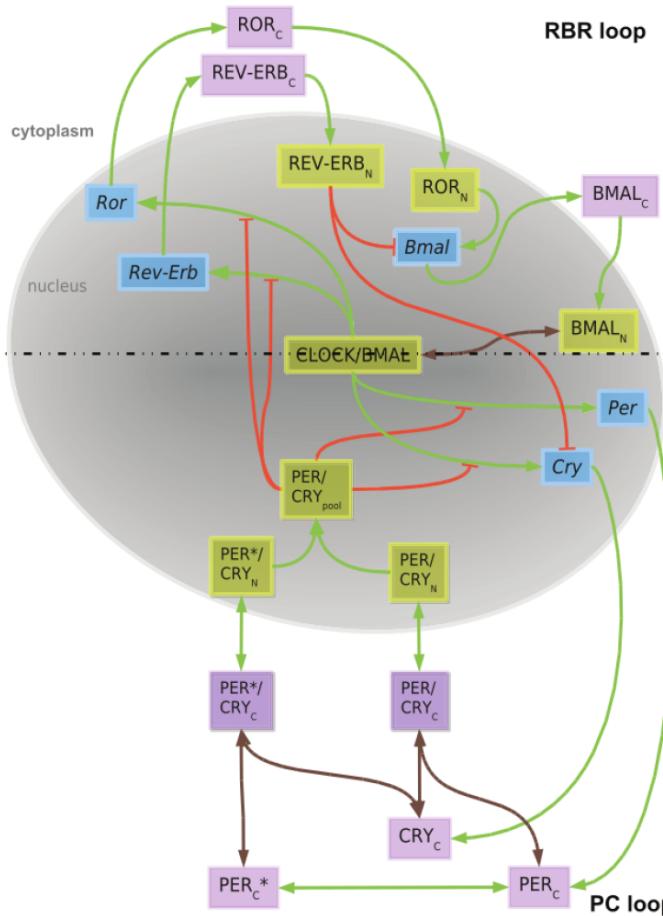
Jens Hahn

Julia Katharina Schlichting

Julia (505)

Tuning the Mammalian Circadian Clock: Robust Synergy of Two Loops

Angela Relógio, Pal O. Westermark, Thomas Wallbach, Katja Schellenberg, Achim Kramer, Hanspeter Herzl



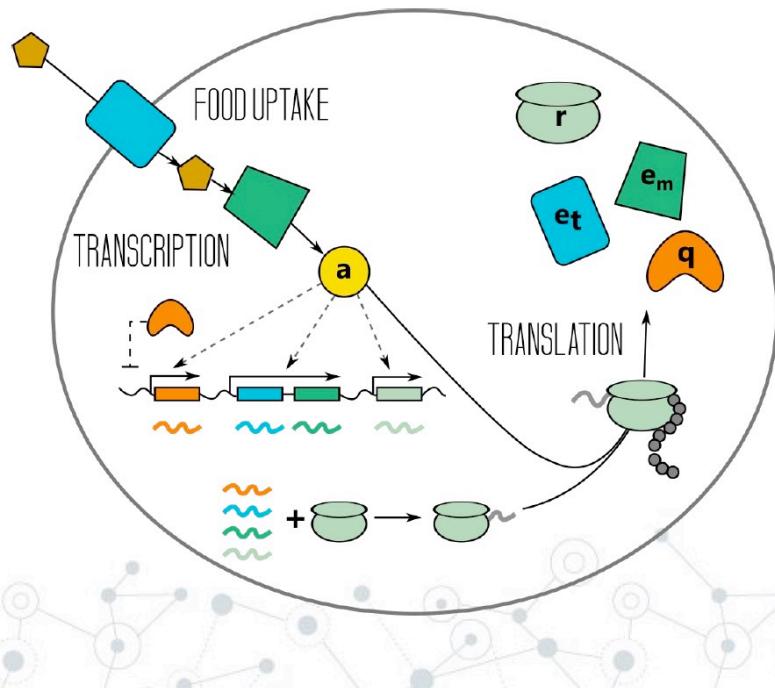
- 1) Become familiar with the circadian clock
(What is the circadian clock? What is the SCN? What are the differences between the core clock and peripheral clocks? ...?)
 - 2) Implement the ODE system in R (19 equations, 71 parameters)
 - 3) Try to simulate the results (at least the expression levels for each component)
 - 4) What do you learn (self-reflection)?



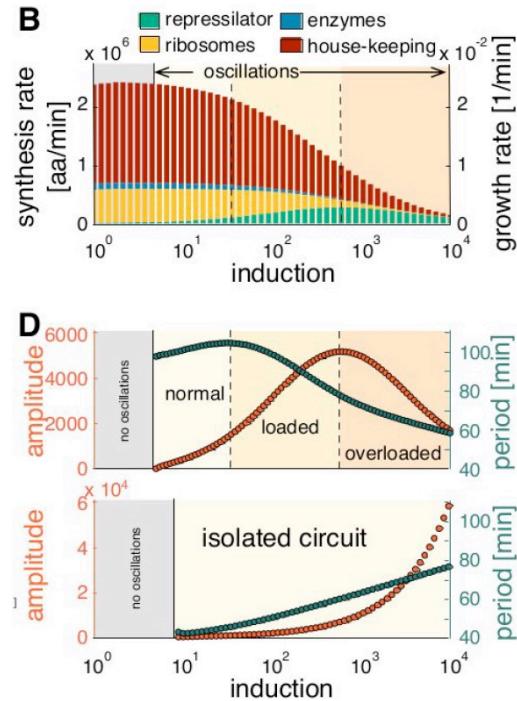
Mechanistic links between cellular trade-offs, gene expression, and growth

Andrea Y. Weiße, Diego A. Oyarzún, Vincent Danos and Peter S. Swain

- Offers simplistic model of nutrient uptake, protein production and cellular growth
- Explores the effect of studying cellular pathways in isolation from the rest of the system
- Connection between cellular trade-offs and empirical laws of microbiology (such as Monod's law)



(Ana Bulovic
Room 510)



Tasks:

- Implement and simulate ODE model in Antimony
- Analyze the effect of cellular trade-offs on a synthetic circuit added to the “cell”
- Discuss high-level considerations of sysbio models



Lost in Transition: Start-Up of Glycolysis Yields Subpopulations of Nongrowing Cells

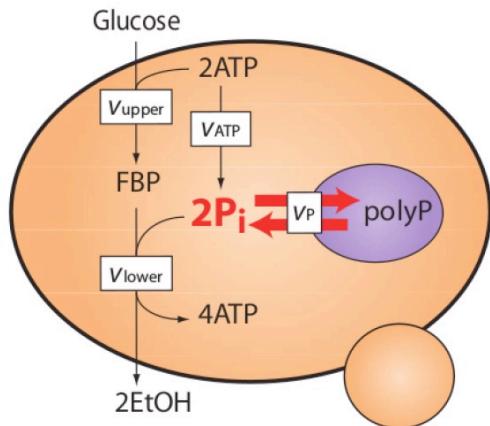
Johan H. van Heerden,^{1,2,3} Meike T. Wortel,^{1,2,3} Frank J. Bruggeman,^{1,3} Joseph J. Heijnen,^{2,4} Yves J. M. Bollen,^{3,5} Robert Planqué,⁶ Josephus Hulshof,⁶ Tom G. O'Toole,⁷ S. Aljoscha Wahl,^{2,4} Bas Teusink^{1,2,3*}

Aufgaben:

- Paper lesen & verstehen
- Implementation & Simulation Minimalmodell
- Paper bewerten
- Zusatzaufgaben

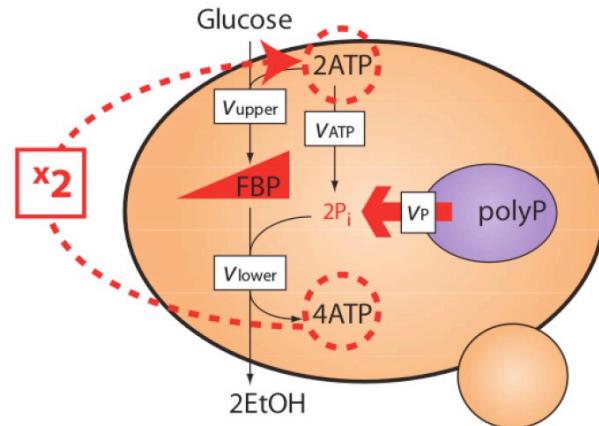
A

Steady state



B

Imbalanced state



Friedemann Uschner

Supervisor: Friedemann Uschner (Raum 502)

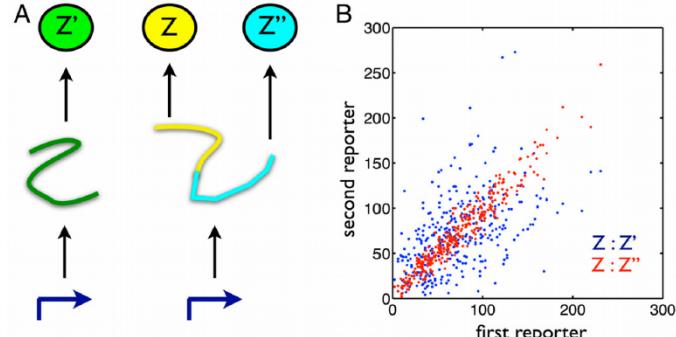
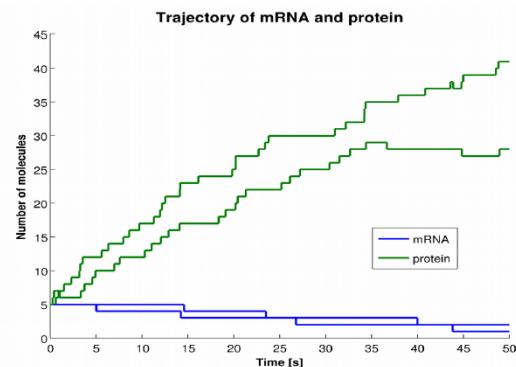
H U M B O L D T - U N I V E R S I T Ä T Z U B E R L I N



Identifying sources of variation and the flow of information in biochemical networks

Clive G. Bowsher^{a,1} and Peter S. Swain^{b,1}

- Investigates a general way to decompose variation in experiment & modeling
 - Sound mathematical interpretation
 - Complete proof of statements
- Applications to various data-sets (gene expression, signal transduction, components of variation, etc.) and different interesting ideas
- Used framework: Stochastics (Conditional probability theory), others depending on detail



$$V[Z(t)] = \overbrace{E\{V[Z(t)|(M, Y_e)^{\mathcal{H}}]\}}^{\text{translational}} + \overbrace{E\{V[E[Z(t)|(M, Y_e)^{\mathcal{H}}]|Y_e^{\mathcal{H}}]\}}^{\text{transcriptional}} + \overbrace{V\{E[Z(t)|Y_e^{\mathcal{H}}]\}}^{\text{from extrinsic effects}}$$

Objectives: [3]

- Studying and understanding the paper - detail will be determined together with the students
- Realization of the Gillespie SSA
- Simulation of a model of gene expression & its application as done in the paper
- Presentation in English

Friedemann Uschner

Supervisor: Friedemann Uschner (Raum 502)

HUMBOLDT-UNIVERSITÄT ZU BERLIN



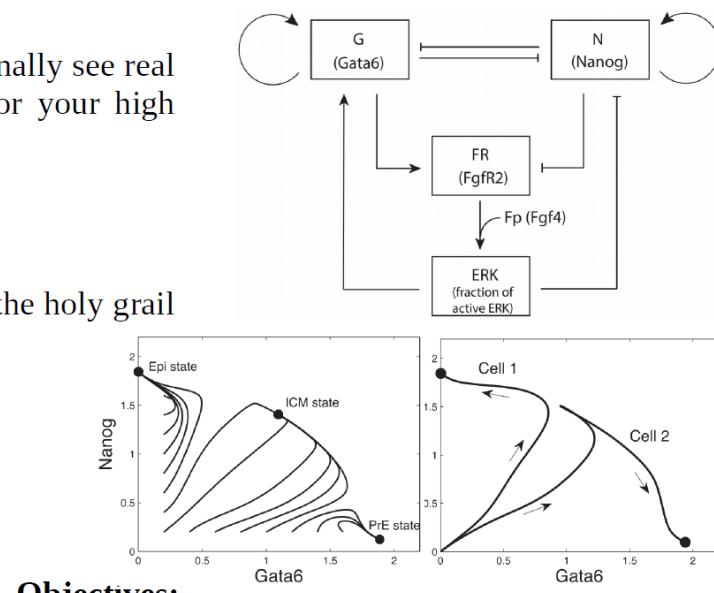
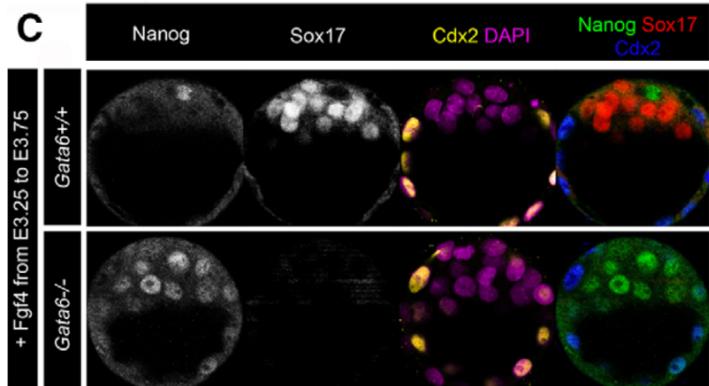
Cell Fate Specification Based on Tristability in the Inner Cell Mass of Mouse Blastocysts

Laurane De Mot,¹ Didier Gonze,¹ Sylvain Bessonnard,^{2,3,4} Claire Chazaud,^{2,3,4} Albert Goldbeter,^{1,5} and Geneviève Dupont^{1,*}

- Fed up with pure theory of Module Bph8? Wanna finally see real bifurcations in action? Bistability is not enough for your high ambitions?

Welcome to the fascinating world of a
TRISTABLE SYSTEM,
 welcome to cell differentiation!!1!

- Embark on an adventure of epic dimensions to find the holy grail of wisdom on how to change a cell's fate forever.



Objectives:

- Studying and understanding the paper
- Simulation and analysis of a GRN model controlling differentiation as done in the paper
- Presentation in English



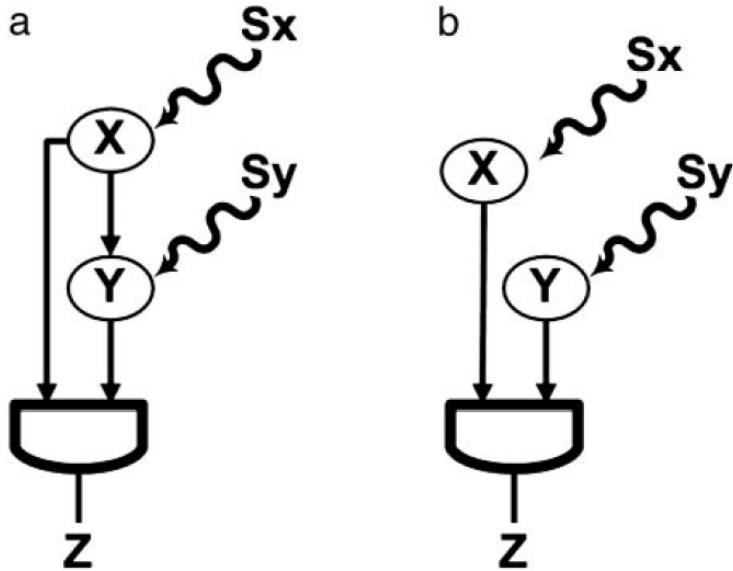
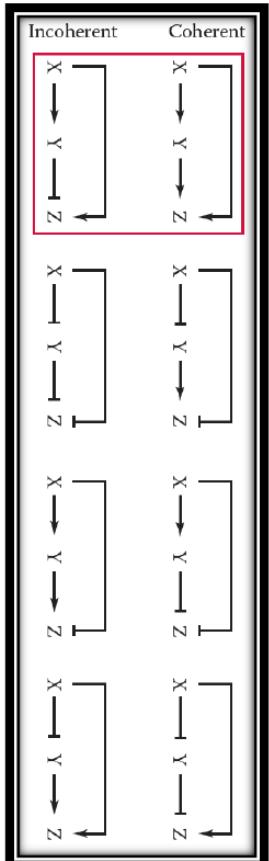
Tasks

- Read and understand the paper
- Implement the model
- Do the perturbation experiments
- Implement different input signal for different mutations – explain the outcome



Structure and Function of the Feed-Forward Loop Network Motif

S. Mangan and U.Alon



$$dY/dt = B_y + \beta_y f(X^*, K_{xy}) - \alpha_y Y$$

$$dZ/dt = B_z + \beta_z G(X^*, K_{xz}, Y^*, K_{yz}) - \alpha_z Z$$