BP 33: Posters - Systems Biology & Gene Expression and Signalling

Time: Tuesday 14:00–16:00 Location: P2-OG1

BP 33.1 Tue 14:00 P2-OG1

Error model estimation by maximum-likelihood methods — •Mirjam Fehling-Kaschek, Daniel Kaschek, and Jens Timmer — Physikalisches Institut, Universität Freiburg

Mathematical modeling has become an established approach in cell biology to gain information about intracellular processes. Especially for dynamic modeling, time-resolved data is required. Depending on the measurement technique, taking data points is time-consuming and expensive. Therefore, the modeler is often confronted with the problem of low number of replicates from which uncertainties need to be estimated reliably.

Error models provide a way to pool replicate measurements from different time-points and conditions to estimate the contributions from different error sources. Here, two complementary maximum-likelihood approaches to identify error model parameters, (1) from mean-variance tuples and (2) from model residuals, are implemented. Advantages and disadvantages of both approaches are discussed and usecases from different applications presented.

BP 33.2 Tue 14:00 P2-OG1

Impact of reparametrization on fitting of ODE models — •Lukas Refisch[1], Jens Timmer[1,2,3], and Clemens Kreutz[1,2] — [1]Institute of Physics, University of Freiburg, Freiburg im Breisgau, Germany — [2]Center for Biosystems Analysis (ZBSA), University of Freiburg, Freiburg im Breisgau, Germany — [3]BIOSS Centre for Biological Signalling Studies, University of Freiburg, Freiburg im Breisgau, Germany

The dynamics of complex biochemical reactions as they occur in living cells can be modeled by ordinary differential equations (ODE). One major task is model calibration, i.e. to estimate parameters like initial concentrations and rate constants based on experimental data. Optimization-based estimation like maximum likelihood is often challenging due to the existence of local minima, the highly nonlinear model responses and the limited precision of numerical ODE solutions.

It has been claimed that parameter transformations are beneficial for fitting of ODE models. Possible parametrizations exploit the model's scaling invariance originating from the free choice of units and the fact, that measurements in molecular cell biology are often taken on a relative scale. However, up to now the impact of reparametrization has not been evaluated in details. For five established models of cellular signaling pathways and infectious diseases with experimental data, we analyze the effect of reparametrization on the performance of optimization. The different influences including the geometry of the likelihood landscape, the choice of initial guesses and the parameter search space are quantified using multivariate statistical analyses.

BP 33.3 Tue 14:00 P2-OG1

Quantitative analysis of the spatial toggle switch that controls Myxococcus xanthus motility — •Manon Wigbers[1], Luis Carreira[2], Filipe Tostevin[1], Dobromir Szadkowski[2], Lotte Søgaard-Andersen[2], and Ulrich Gerland[1] — [1]Department of Physics, Technische Universität München, Garching, Germany — [2]Max Planck Institute for Terrestrial Microbiology, Marburg, Germany

Dynamic control of cell polarity switching is central to the regulation of Myxococcus xanthus motility. Each reversal of the direction of motion of a M. xanthus cell is preceded by a reversal of its cell polarity, which is marked by an asymmetric distribution of signaling proteins. Key components of this system include MglA, which accumulates at the leading cell pole, and MglB, which localizes to the lagging cell pole. The correct localization of the Mgl proteins is also mutually dependent on other proteins, including RomR. Together, these proteins form an intriguing *spatial toggle switch*. Here, we use quantitative data analysis and biophysical modeling to study the working principle of this system. In particular, we study how the asymmetric protein distributions emerge from the involved interactions and reactions, and how the switching of cell polarity could be brought about by the upstream Frz system. We establish a model that has qualitative agreement with the localization patterns of the MglA/MglB/RomR system, for the wild type and all mutants. Furthermore we perform a systematic search to find possible mechanisms to control polarity switching.

BP 33.4 Tue 14:00 P2-OG1

Communication between bacteria and cell-free expression systems within linear chains of emulsion droplets — •Matthaeus Schwarz-Schilling, Lukas Aufinger, Andrea Mückl, and Friedrich C. Simmel — Technical University of Munich, Physics Department E14 and ZNN/WSI, Am Coulombwall 4a, 85748 Garching, Germany.

Position-dependent gene expression in gradients of morphogens is one of the key processes involved in cellular differentiation during development. Here, we study a simple artificial differentiation process, which is based on the diffusion of genetic inducers within one-dimensional arrangements of 50 micrometre large water-in-oil droplets. The droplets are filled with either bacteria or a cell-free gene expression system, both equipped with genetic constructs that produce inducers or respond to them via expression of a fluorescent protein. We quantitatively study the coupled diffusion-gene expression process in gradients of inducers and demonstrate that gene expression can be made position-dependent. The confinement of genetic inducers to diffuse in only one dimension enables strong coupling between neighbouring droplets. Thus, by generating diffusing quorum-sensing signals in situ, we also establish communication between artificial cell-free sender cells and bacterial receivers, and vice versa.

BP 33.5 Tue 14:00 P2-OG1

Deconvolution of luminescence cross-talk in high-throughput gene expression profiling — •Marco Mauri, Stefano Vecchione, and Georg Fritz — LOEWE-Center for Synthetic Microbiology (SYNMIKRO), Philipps-University Marburg, Germany

In recent years, luciferase has become a standard genetic tool to monitor gene expression. It has a high signal-to-noise ratio, which is, in principle, only limited by the sensitivity of the photo detector. However, at the same time luciferase reporters have the drawback of emitting a constant glow upon induction, which can lead to undesired cross-talk between neighbouring wells on a microplate. Indeed, we find that the scattering light from a highly luminescent well affects more than 50% of the wells even in a black plate. In order to overcome this limitation, we developed a computational method to correct for luminescence bleed-through and estimate the "true" luminescence activity for each well of a microplate. As the sole input to our algorithm the signals measured from a calibration plate is needed, in which the light emitted from a single luminescent well serves as an estimate of the light-spread function. From this the algorithm creates a deconvolution matrix, which can be used to correct any other measurement obtained under the same technical conditions. Here, we demonstrate that our correction preserves low level signals that are close to the background and show that it is universally applicable to different kinds of microplate readers and plate types. From our algorithm, we developed a freely available tool to correct the luminescence cross-talk in high-throughput gene expression analyses.

BP 33.6 Tue 14:00 P2-OG1

Quantitative analysis of bacterial growth and starvation at elevated temperatures — •Mariel García Huiman, Severin Schink, Michael Szabo, and Ulrich Gerland — Technical University of Munich, Physics Department, James-Franck-Str. 1. 85748 Garching

Up to now, the temperature dependence of bacterial behavior regarding growth and viability beyond the physiological temperature is poorly understood. We study the effects of temperature stress on E.coli in minimal nutritional environments. At highly elevated temperatures, short-term starvation causes genetically homogeneous bacterial populations to split into two distinct subpopulations, growing and non-growing. This plays a role in bacterial persistence.

BP 33.7 Tue 14:00 P2-OG1

Machine Learning for epigenetic network inference in T cells — •Christoph Kommer[1,2,3], Qin Zhang[1,2], Ahmed Hegazy[4], Max Löhning[4,5], and Thomas Höfer[1,2] — [1]German Cancer Research Center (DKFZ), Heidelberg — [2]BioQuant Center, University of Heidelberg — [3]HGS MathComp, Institute for Scientific Computing, University of Heidelberg — [4]German Rheumatism Research Center, Berlin — [5]Charité-Universitätsmedizin, Berlin

T-helper cells direct the cell- and antibody-based arms of the adaptive

immune system via the secretion of signalling proteins. The classical view of naïve T-helper cells differentiating into a small number of stable steady states has recently been challenged by experimental findings that point towards multistable hybrid states away from a bistable fixed-point solution.

To interrogate the underlying regulatory mechanisms, we identified the epigenetic landscape in naïve and differentiated T-helper cells from histone modification patterns by applying different machine learning approaches and found distinct classes of enhancers and repressors according to their regulation by lineage-specifying transcription factors and/or extrinsic differentiation signals which are also cell-type specific. For mapping epigenetic states to target genes we furthermore developed a novel parametrized multivariable correlation measure model. With this approach, we recovered well-known cis-regulatory elements and predicted new ones with comparable confidence.

We discuss the utility of these data to learn epigenetic regulatory network topologies in order to explain multistability.

BP 33.8 Tue 14:00 P2-OG1

Optimizing Network Models of Nucleosome Configurations at the PHO5 Promoter in Yeast — •Michael Wolff[1], Andrea Schmid[2], Philipp Korber[2], and Ulrich Gerland[1] — [1]Physik-Department TUM and Graduate School of Quantitative Biosciences Munich (QBM), James-Franck-Straße 1, 85748 Garching — [2]Molekularbiologie Biomedizinisches Centrum, LMU, Großhaderner Strasse 9, 82152 Planegg-Martinsried

Nucleosomes are histone DNA complexes densely populating the DNA molecule and their positioning is key to a better understanding of the transcriptional regulation of eukaryotic genes. These positions are influenced by DNA sequence, competition with transcription factors and active reorganization by chromatin remodeling enzymes. A textbook example illustrating the role of nucleosome positioning in promoter regulation is the PHO5 gene in Saccharomyces cerevisiae. The PHO5 promoter is also one of the few cases in which single molecule data describing the probability that a promoter will adopt a given nucleosome configuration in vivo is available, even for different environmental conditions leading to induction or repression of PHO5 transcription. These measured configuration probabilities can be reproduced by Markov processes on nucleosome configuration networks describing remodeler mediated nucleosome assembly, disassembly and sliding along the DNA. Here we explore the space of these Markov models and search for agreement with further experimental data, such as nucleosome turnover rates and nucleosome occupancy after DNA sequence manipulation.