BP 17: Physics of Cells

Time: Wednesday 14:00–15:45 Location: PC 203

BP 17.1 Wed 14:00 PC 203

Collective Dynamics of Endocytic Vesicles in Membrane Trafficking — •Mirko Birbaumer[1], Markus Kalisch[2], Frank Schweitzer[3], Peter Bühlmann[2], and Lucas Pelkmans[1] — [1]Institute of Systems Biology, Swiss Federal Institute of Technology, ETH Hönggerberg, CH-8093 Zurich — [2]Seminar for Statistics, Swiss Federal Institute of Technology, Leonhardstrasse 27, CH-8092 Zurich — [3]Chair of Systems Design, Swiss Federal Institute of Technology, Kreuzplatz 5, CH-8032 Zurich

Spatial organization and compartmentalization of intracellular organelles such as endocytic vesicles play an essential role for many cellular processes. A variety of different vesicle patterns can result from a systematic perturbation of the cell, as e.g. by RNA interference in mammalian cells. By silencing a large set of genes in a mammalian cell numerous well distinguishable patterns arise and we are therefore dealing with a clustering problem. In order to cluster vesicle patterns, we first need to extract as much relevant information about intracellular organelles as possible, such as intensity distribution, location with respect to the cell center, shape, their spatial distribution and quantity. A new clustering approach enables us to distinguish between different patterns and group these according to their properties. These patterns should also result as steady states from a macroscopic theory of intracellular transport. Here we present a modeling approach of intracellular trafficking based on Brownian Agents.

BP 17.2 Wed 14:15 PC 203

Particle tracking and microscopy of the intracellular transport of polyethyleneimine based gene carriers — •Ralf Bausinger[1] and Andreas Zumbusch[2] — [1]Fachbereich Physik, Universität Konstanz, Fach M684, 78457 Konstanz — [2]Fachbereich Chemie, Universität Konstanz, Fach M722, 78457 Konstanz

Polyethyleneimine (PEI) based gene carriers are among the most efficient synthetic vectors for the delivery of DNA into the cell nucleus. We use highly sensitive fluorescence microscopy and single particle tracking methods for the investigation of the particles' paths from the plasma membrane to the nucleus. Active actin polymerization around the particle supports its cell entry and Rab protein accumulation initiates the fast vesicular transport on microtubules. Trajectories of this bidirectional transport process are segmented by a numerical algorithm separating different modes of motion. Diffusion analysis of these segments allows the unravelling of the distribution of intracellular transport velocities. We further investigated the role of mitosis on the particle distribution of the daughter cells and the subsequent expression of the transgene.

BP 17.3 Wed 14:30 PC 203

Actin-membrane interactions in a biomimetic systems studied by a novel, high precision optical method — •Timo Betz, Léa Laetitia Pontani, and Cécile Sykes — Institut Curie, UMR CNRS 168, 11 rue Pierre et Marie Curie, 75248 Paris, France

The lethal potential of cancer results from abnormal cell division and aggressive metastatic activity that turns resting cancer cells into motile structures which spread through an organism, resulting in numerous and often uncontrollable growing subpopulations. It is well known that both cell motility and cell division depend crucially on cell mechanics, namely on the actin cortex which is a dense biopolymer network that is steadily contracted by myosin motors. A key to understand the abnormal motility and proliferation of cancer cells is the quantification of the physical properties of the actin cortex. Of special interest is the activity of the acto-myosin network and its interaction with the plasma membrane that contributes to the physical properties of the cell. To investigate these interactions we combine a novel optical technique that detects the edge fluctuations of a biomimetic cell with high spatial and temporal resolution. The investigated system mimics the actin cortex by polymerizing an actin network under the membrane of a lipid vesicle. Analyzing the membrane fluctuation with and without the actin cortex allows the quantification of physical parameters like bending rigidity and viscoelastic properties of the actin membrane system.

BP 17.4 Wed 14:45 PC 203

Stem Cell Fate Directed by Matrix Elasticity and Ligands — •Florian Rehfeldt, Shenshen Cai, and Dennis E. Discher — University of Pennsylvania, Biophysical Engineering Lab, Philadelphia, USA

Mesenchymal stem cells (MSCs) from adult bone marrow have recently been found responsive to matrix elasticity in their differentiation. Collagen-I coated hydrogels induce MSCs to express neurogenic, myogenic, and osteogenic markers depending on the Young's modulus E (ranging from 1 to 34 kPa) of the substrate that is used to approximate the physiological elasticity of native tissue. While collagen is the most abundant protein in mammals, hyaluronic acid (HA) is the major non-protein factor in the marrow and is a widely distributed load-bearing matrix polysaccharide that promotes proliferation and migration during embryonic development and other processes. We show that MSCs dynamically express an HA-receptor, and we use the tunable elasticity of novel HA hydrogels to understand the morphology, motility, and fate choices of MSCs as they depend on matrix elasticity and adhesive ligands. Marrow-derived hematopoietic stem cells (HSCs) are also studied, and the results amplify the influence of matrix elasticity in stem cell fate choices.

BP 17.5 Wed 15:00 PC 203

Dynamics of different probe particles to study local microenvironments inside living cells — •Michael Duits, Yixuan Li, Siva Vanapalli, and Frieder Mugele — MESA+ institute, University of Twente, PO Box 217, 7500 AE The Netherlands

To understand the dynamics of particles inside living cells in relation to intracellular rheology, we examined living endothelial cells in untreated form, and after (chemical) interventions, aimed at revealing specific contributions to particle motions via driving forces or passive mechanical resistances. Endogenous granules (EG) and ballistically injected particles (BIP) were used as tracers. At 37 C the mean-squared displacement (MSD) showed different time dependence for the two probes. While EGs showed only a linear dependence, for BIPs also a transition to a plateau at small lagtimes was observed. Moreover, the (normalized) MSDs were much larger for the EGs. This suggests different local micro-environments for EGs and BIPs. Also the sets of individual trajectories were analyzed. Here, both the magnitude and the power-law exponent showed distributions that suggest heterogeneity in the environment for both probes. Depletion of intracellular ATP resulted in opposite effects on the MSDs of EGs and BIPs. While for EGs the MSD and the fraction of trajectories with superdiffusive exponents were reduced, for BIPs an increase in MSD was found. It thus seems that ATP depletion not only annihilates active processes, but also alters the cytoskeleton. These observations of cytoskeletal network heterogeneities have profound implications for the quantification of global mechanical behavior in living cells.

BP 17.6 Wed 15:15 PC 203

A new approach in Ca^{2+} modeling — •Alexander Skupin and Martin Falcke — Hahn Meitner Institut, Glienicker Straße 100, 14109 Berlin, Germany

Ca^{2+} is the most important second messenger in living cells serving as a critical link between a variety of physiological stimuli and their intra and intercellular response. In our recent study we have demonstrated the stochastic character of Ca^{2+} oscillations, which are caused by the stochastic opening of ion channels releasing Ca^{2+} from internal stores into the cytosol. This liberated Ca^{2+} can activate adjoining channels resulting in a global Ca^{2+} wave within the cell, i.e. that microscopic fluctuations determine the global behavior of cells.

Thus modeling has to take the spatial character of this phenomenon into account, since oscillation are orchestrated on that level. The describing system of coupled reaction diffusion equations exhibits huge gradients which slow down the simulation speed of straight forward methods. Therefor we linearized the equations and developed an analytical solution in terms of coupled Greens function which are driven by the stochastic behavior of the ion channels acting as source terms in the equations. We will compare the results of the interplay of our analytical solution and the stochastic driving modeled by a Gillespie algorithm with our experimental results.

BP 17.7 Wed 15:30 PC 203

Transmembrane Potential and Proton Buffering Capacity of

a Small Vesicle — •Tihamér Geyer and Sarah Blass — Zentrum für Bioinformatik, Universität des Saarlandes, D 66041–Saarbrücken

The dynamic behavior of a metabolic network is determined both by the reaction rates and by the buffering capacities of the reservoirs. While a lot of effort goes into determining rate constants, much less emphasis is put on the capacities. Consequently, for setting up a dynamic simulation of a part of the metabolism of a cell, it is much easier to gather the necessary rates than to find reliable information on how to describe, e.g., a proton buffering capacity in a typical *in vivo* geometry like a small vesicle.

To shed some more light onto how to incorporate a specific biological setup into a simulation, we used stochastic molecular simulations of a photosynthetic vesicle of the purple bacterium *Rhodobacter sphaeroides* to investigate how the transmembrane potential $\Delta\Phi$ has to be described in order to reproduce the measured time course after a short flash of light. By treating the small vesicle as a spherical capacitor, both the biphasic rise and the exponential decay of $\Delta\Phi$ are reproduced, while a Nernst-like model based on the pH gradient leads to a different signature in time. The simulation also reproduces the simultaneously measured cytochrome *c* oxidation state.

We also discuss how the findings from the vesicle apply to other confined geometries as, e.g., the cristae of the mitochondria.