BP 15: Physics of Cells II

Time: Tuesday 14:30–17:00 Location: H43

BP 15.1 Tue 14:30 H43

Formation of long lived local protein kinase C clusters after short Calcium puffs — •Mike Bonny[1], Martin Peglow[1], Lars Kaestner[2], Peter Lipp[2], Heiko Rieger[1], and Karsten Kruse[1] — [1]Department of Theoretical Physics, Saarland University, D-66041 Saarbrücken, Germany — [2]Institute for Molecular Cell Biology, Medical Faculty of the Saarland University, D-66421 Homburg/Saar, Germany

Conventional protein kinases C (cPKCs) play an important role in signal transduction and in gene regulation. PKCα, a member of the cPKC-family, translocates to the plasma membrane after activation via cytosolic Ca^{2+} ions. In particular, there exist local translocation events, when PKCα forms clusters on the membrane with limited spatial spreads ($< 4\mu$m). The lifetime of brief events is 400-1500ms, while long lasting events have a lifetime larger than 5s, which markedly exceeds the duration of a Calcium puff [1].
We show theoretically that allosteric effects together with interactions between membrane-bound PKCα can lead to the observed behaviour. Using fluorescence resonance energy transfer (FRET) measurements we support our assumption of so far unknown interactions between PKCα molecules.

[1] Reither, G., Schaefer, M., Lipp, P. (2006). PKCα: a versatile key for decoding the cellular calcium toolkit. JCB 174: 521-533

BP 15.2 Tue 14:45 H43

Sensitisation waves in a bidomain fire-diffuse-fire model of intracellular Ca^{2+} dynamics — •Rüdiger Thul[1], Steven Coombes[1], and Greg D Smith[2] — [1]School of Mathematical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK — [2]Department of Applied Mathematics, The College of William and Mary, Williamsburg, VA 23187, USA

We present a bidomain threshold model of intracellular calcium (Ca^{2+}) dynamics in which, as suggested by recent experiments, the cytosolic threshold for Ca^{2+} liberation is modulated by the Ca^{2+} concentration in the releasing compartment. We explicitly construct stationary fronts and determine their stability using an Evans function approach. Our results show that a biologically motivated choice of a dynamic threshold, as opposed to a constant threshold, can pin stationary fronts that would otherwise be unstable. This illustrates a novel mechanism to stabilise pinned interfaces in continuous excitable systems. Our framework also allows us to compute travelling pulse solutions in closed form and systematically probe the wave speed as a function of physiologically important parameters. We find that the existence of travelling wave solutions depends on the time scale of the threshold dynamics, and that facilitating release by lowering the cytosolic threshold increases the wave speed.

BP 15.3 Tue 15:00 H43

Bifurcations and Chaos in the MAPK Signaling Cascade — •Martin Zumsande and Thilo Gross — Max-Planck-Institut für Physik komplexer Systeme, Dresden, Deutschland

The mitogen-activated protein kinase (MAPK) cascade is an important signaling pathway in eukaryotic cells. It is involved in the regulation of a large number of cell functions. Many molecular details of the cascade that consists of multiple phosphorylation cycles are known today. However, many aspects of the dynamics are still unknown, most importantly how exactly the different cell functions can be triggered. We apply the method of generalized modelling [Gross, Feudel: PRE 73, 2006] to a model of the MAPK cascade. We describe how external parameters are correlated with stability of the steady states. Furthermore, we report complex oscillations and potentially chaotic behavior caused by a sequestration-based feedback mechanism. We also investigate the interplay between sequestration and external feedback loops. Our analysis thereby confirms, extends and generalizes previous results obtained by conventional modeling and points out the diversity of dynamics that sequestration can bring about.

BP 15.4 Tue 15:15 H43

Generating alternating bidirectional gradient fields for dynamic measurement of chemotactic response in living cells — •Börn Meier, Christoph Weber, Simon Youssef, Thomas Franosch, Joachim Rädler, and Doris Heinrich — Fakultät für Physik und CeNS, LMU München, Germany

Chemotactic response in eucaryotic cells is inherently probabilistic and measurements of single cell responses and population distributions help to advance quantitative understanding of underlying signalling pathways. Therefore we have designed a microfluidic function generator, creating time-varying but spatially homogenous chemical gradients of opposing direction. In a first step we monitored the migratory response of Dictyostelium discoideum cells to alternating cAMP-gradients with decreasing switching frequency. At low switching rates directed cell migration according to the applied chemotactic sequence appears. At frequencies above 0.01 Hz cellular motility is stalled, leading to trapped cells. We monitored the actin reorganization, underlying the cell response, identified by the Lim-Gfp fluorescence distribution in the cell. Cell polarization, reflected by the dipolar moment of the fluorescence distribution, expresses a delayed cell response, where two phases of opposing actin polymerization are intercepted by a phase of decreased actin polymerization.

BP 15.5 Tue 15:30 H43

Does Molecular Crowding affect DNA Hybridization in vivo? — Ingmar Schoen, Hubert Krammer, and •Dieter Braun — Systems Biophysics, Center for Nanoscience, Ludwig Maximilians University, Munich, Germany

Molecules in a cell are subject to significant crowding from their sister molecules. While measurements of anomalous diffusion inside cells point towards a marked effect of molecular crowding, its impact on the rate of reactions is hard to assess.

We have developed a novel technique to image kinetics in living cells using an optical lock-in approach[1]. The reaction time constant is resolved in frequency space with optical resolution under a moderate temperature oscillation and sinusoidal illumination.

DNA hybridization kinetics in living cells is strongly length selective: 16 base pair DNA has a seven-fold faster on-rate as compared to the in vitro situation, whereas 12bp DNA has a five-fold slower on-rate in vivo as compared to in vitro. Evidence points towards a catalytic acceleration for longer DNA and a slowing down by DNA binding proteins.

Above results are not expected from molecular crowding. We assessed molecular crowding with Dextran and Ficoll at high concentrations [20% (w/v)] and find no significant changes in the hybridization kinetics, indicating a minor role of molecular crowding for bi-molecular DNA hybridization.

[1] Schoen, Krammer and Braun, PNAS, in press

15 min. break

BP 15.6 Tue 16:00 H43

Correlation of protein density with cell morphology both in motile mouse fibroblasts and slime molds — •Erik Bernitt, Christina Oettmeier, Siddharth Deshpande, and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen

We have characterized cell motility as temporal sequences of distinct dynamic phases. Transitions between these phases are indicated by a number of cellular observables including adhesion area, membrane front velocity, topological markers, and special characteristics of internal density fields. In this talk, we present examples of two species from different evolutionary kingdoms. Under environmental stress, the slime mold *Physarum polycephalum* exhibits a transition from a globular phase to an extended network with an increasing number of holes. This change in topology is coupled to a pronounced variation in the frequency of area oscillations and internal density waves. We calculate multidimensional cross correlations of these phase indicators. Mouse embryonic fibroblasts show distinct phases of spreading. We correlate front velocity with actin distribution in these phases.

BP 15.7 Tue 16:15 H43

The role of the G protein-coupled receptor CXCR4 in angiogenesis - a single-molecule approach — •Susanne Fenz[1], Cassandra Verheul[1], Ewa Snaar-Jagalska[2], and Thomas Schmidt[1] — [1]Leiden Institute of Physics, Leiden, The Netherlands — [2]Institute

of Biology, Leiden, The Netherlands

Directed cell movement in a chemical gradient, chemotaxis, is a prerequisite for many vital processes like the immune response, but it is also the basis for cancer metastasis. Chemotaxis is governed by extracellular gradients of small molecules, the chemokines. While their receptors in the cell membrane are identified, it is still unknown how the cell subsequently builds up an asymmetric phenotype with defined front and rear edge, necessary for directed movement. This polarization is triggered by tiny gradients and is robust in noisy environment. Thus, we propose that universal physical mechanisms underlie the first steps towards polarity.

Two potential ordering parameters, the receptor mobility and cytoskeleton-induced membrane domains, were investigated on a molecular level in living mouse fibroblasts and human vascular endothelial cells. We applied single-molecule fluorescence microscopy to characterize the diffusion behaviour of CXCR4-eYFP upon stimulation with its chemokine SDF and to probe for potential association with CCR5. Since it is known that tumor cells expressing CXCR4 perform metastasis not only by direct migration to organs expressing SDF, but additionally promote angiogenesis towards the tumor our model system will yields insights into both mechanisms.

BP 15.8 Tue 16:30 H43

A model for thickness oscillations in protoplasmic droplets of Physarum polycephalum — Markus Radszuweit[1], Harald Engel[2], and •Markus Bär[1] — [1]Physikalisch Technische Bundesanstalt, Berlin — [2]Technische Universität Berlin

A model for explaining thickness oscillations in protoplasmic droplets in true slime mold physarum polycephalum is proposed and numerical simulations are presented. An autonomous Ca^{2+}-oscillator based on the regulation of myosin binding to actin is combined with a two phase mechanical model for a polymer gel. Using Darcy's law of porous media for the endoplasmic flow field and theory of active elastic gels a full description of the flow, pressure and deformation field is obtained. The nonlocal feedback of this quantities on the reaction-diffusion-advection system of the chemical oscillator leads to the formation of various dynamical patterns like targets, standing or spiral waves.

BP 15.9 Tue 16:45 H43

Impact of microscopic motility on overall swimming behaviour of parasites — Sravanti Uppaluri[1], Jan Nagler[1], •Eric Stellamanns[1], Niko Heddergott[2], Stephan Herminghaus[1], Markus Engstler[2], and Thomas Pfohl[1,3] — [1]Max Planck Institute for Dynamics and Self Organization, Göttingen — [2]Biocenter, University of Würzburg — [3]Chemistry Department, University of Basel

Trypanosomes, causative agents of sleeping sickness and Chagas disease, exhibit complex flagellum mediated motility. In trypanosomes this flagellum mediated motility has been shown to be essential for cell division, viability, and immunological escape from the host. Trypanosomes swim in one of three distinct motility modes: random walk, directional persistence, and an intermediate class in which they exhibit a combination of both. Using high-speed microscopy with a frame rate of 1000 Hz, we investigate the microscopic origin of these macroscopic motility modes. The experimentally observed motility modes correspond to distinct physical movements and can be attributed to distinct cell shape conferred mainly by flagellum dynamics. We find that directional persistence arises only with stretched cells implying that there are significant energy or stiffness differences within a single population. We report our findings on the dependence of cell shape on the cell cycle in which the flagellum plays a key role.