BP 31: Cell adhesion and migration, multicellular systems II

Time: Friday 9:30–12:00 Location: H10

Invited Talk BP 31.1 Fri 9:30 H10

Mechano-chemical self-organization determines search pattern in migratory cells — •Milos Galic — Institute of Medical Physics and Biophysics, University of Muenster, Germany

Efficient signal detection is fundamental for motile cells. To optimize their search strategy, cells seeking signal inputs employ non-Brownian motion pattern. Combining experimental and theoretical analysis, we identify a self-organizing system for super-diffusive two-state motion. We demonstrate that nanoscale plasma membrane deformations at the leading edge nucleate a mechano-chemical feedback loop that mediates polarization longevity and in consequence migration persistence. The resulting two-state motion, defined by continuous transitions between random and persistent phases, reduces oversampling to expand the search area. Collectively, the findings establish a mechanism for optimized search efficiency of vertebrate cells in the absence of polarized signal inputs.

BP 31.2 Fri 10:00 H10

Entropic DNA swelling drives complex cellular behavior — •Sebastian Kruss — Universität Göttingen, Göttingen, Germany

Neutrophilic granulocytes are able to release their own DNA as neutrophil extracellular traps (NETs) to capture and eliminate pathogens. DNA expulsion (NETosis) has also been documented for other cells and organisms, thus highlighting the evolutionary conservation of this process. Moreover, dysregulated NETosis has been implicated in many diseases, including cancer and inflammatory disorders. During NETosis, neutrophils undergo dynamic and dramatic alterations of their cellular as well as sub-cellular morphology whose biophysical basis is poorly understood. Here we investigate NETosis in real-time on the single-cell level using fluorescence and atomic force microscopy. Our results show that NETosis is highly organized into three distinct phases with a clear point of no return defined by chromatin status. Entropic chromatin swelling is the major physical driving force that causes cell morphology changes and the rupture of both nuclear envelope and plasma membrane. Through its material properties, chromatin thus directly orchestrates this complex biological process.

BP 31.3 Fri 10:15 H10

Stochastic Nonlinear Dynamics of Confined Cell Migration — •David Brückner[1], Alexandra Fink[2], Christoph Schreiber[2], Joachim Rädler[2], and Chase Broedersz[1] — [1]Arnold-Sommerfeld-Center For Theoretical Physics and Center for NanoScience, LMU Munich — [2]Faculty of Physics and Center for NanoScience, LMU Munich

In many biological phenomena, cells migrate through confining structured environments. We study how migrating cells overcome physical obstacles in the form of a thin constriction. Specifically, we ask whether such confined migration exhibits emergent stochastic dynamical laws. To this end, we develop two-state micropatterns, consisting of two adhesive sites connected by a thin constriction, allowing the cells to perform repeated stochastic transitions between the sites. For this minimal system, we obtain a large data set of single cell trajectories, enabling us to infer an equation of cell motion, which decomposes the dynamics into deterministic and stochastic contributions. Our data-driven approach reveals that these cells exhibit intricate non-linear migratory dynamics, with qualitatively similar features for cancerous (MDA-MB-231) and non-cancerous (MCF10A) cells. In both cases, the cells drive themselves deterministically into the thin constriction, a process that is sped up by noise. Interestingly, the deterministic dynamics of the cancerous cells exhibits a limit cycle, while the non-cancerous cells show excitable bistable dynamics. Our approach yields a conceptual framework that may be extended to describe active motility on different scales, and in more complex confining environments.

BP 31.4 Fri 10:30 H10

Rotating lamellipodium waves prior to cell polarization — Cody Reeves[1,2], Benjamin Winkler[3], Igor S. Aranson[2,4], and •Falko Ziebert[5] — [1]Engineering Sciences and Applied Mathematics, Northwestern University, Evanston, USA — [2]Materials Science Division, Argonne National Laboratory, USA — [3]Physikalisches Institut, Albert-Ludwigs-Universität Freiburg, Germany — [4]Department of Biomedical Engineering, Pennsylvania State University, University Park, USA — [5]Institute for Theoretical Physics, Heidelberg University, Germany

Cellular protrusion and lamellipodium waves are widespread and observed for many cell types. They are involved in the cells' exploration of the substrate, their internal organization, as well as for the establishment of self-polarization prior to the onset of motion. Here we apply a recently developed phase field approach to model shape waves and their competition on the level of a whole cell. We derive analytic descriptions for the emergence of a single wave deformation. Further we develop an amplitude equation approach to study competition of multiple waves, describing how cells can transition from a non-moving state towards a polarized, steady moving state. Reference: C. Reeves et al., Comms. Phys. 1,73 (2018).

BP 31.5 Fri 10:45 H10

Placing the power plants: functional crosstalk between mitochondrial homeostasis and active cellular dynamics — •Sufi O. Raja and Christoph F. Schmidt — Third Institute of Physics-Biophysics, Georg-August University of Gottingen, Friedrich-Hund-Platz 1, Gottingen-37077, Germany

Dynamic actomyosin organization is an energy dependent active process and the key to several cellular processes related to shape change and movement. But our knowledge regarding how living cells spatiotemporally control such dynamic organization is still limited. In this context studying the functional role of mitochondrial homeostasis can be a potential target as mitochondria are the cellular energy (Adenosine Tri-Phosphate, ATP) hub and directly regulate the homeostasis of Ca+2 and reactive oxygen species which in turn can potentially regulate actomyosin dynamics locally. On the other hand the mobility of mitochondria is solely determined by the cytoskeleton elements. So, the question is if and how a functional feedback circuit does exists or not. In this context, we are trying to revisit cellular processes like cell adhesion spreading kinetics in the context of mitochondrial homeostasis. How dynamics of the mitochondria (activity/mobility) gets coupled with actomyosin dynamics locally through modulation of local supply of energy and level of small signaling molecules. Lastly, we are also trying to study the response of mitochondrial dynamics during mechanical perturbation of cell to establish a direct connection between cellular energetics and dynamics.

BP 31.6 Fri 11:00 H10

Cortical Actin Contractility of Single Suspended Cells Might Determine Tissue Surface Tension — •Enrico Warmt, Steffen Grosser, Erik Morawetz, and Josef Käs — University of Leipzig, Faculty of Physics and Earth Sciences, Peter Debye Institute, Soft Matter Physics Division, Linnéstr. 5, 04103 Leipzig, Germany

Here, we investigate suspended cells regarding active contractility, lacking stress fibers and adhesion points. Epithelial cells assemble a strong actomyosin cortex providing pretension forming round cells and exhibiting more contractile behavior. Contrastly, mesenchymal cells behave much less contractile. In tissue development experiments, epithelial suspended cells rapidly form stable cell-cell contacts, which is accompanied with rearrangement of their actomyosin cortices building up a collective actomyosin rim. This collective actomyosin rim envelops whole cell clusters visible in round shaped cell spheroids suggesting high tissue surface tension. In contrast, suspended mesenchymal cells do not form stable cell-cell contacts. No collective actomyosin rim forms and envelops cell clusters, resulting in rough cell spheroid surfaces, suggesting low tissue surface tension. Demixing experiments, where we observe segregation behavior of epithelial and mesenchymal cells, show that epithelial cells form always a compact inner core, supporting the theory of expressing higher tissue surface tension. Altogether we hypothesize, that the contractile potential, in particular of epithelial cells, is highly correlated with the ability to rearrange actomyosin assembly. Furthermore, cells contractile potential is thus a driving force in tissue development and essential in tissue integrity.

BP 31.7 Fri 11:15 H10

Efficient outgrowth of primordia is mechanically driven — •Jason Khadka, Jean-Daniel Julien, and Karen Alim — Max Planck Institute for Dynamics and Self-Organization, Göttingen, Germany

Morphogenesis of plants and animal often emerges from mechanical

moulding and deformations. Yet, how precisely cells as individual mechanical entities can act to shape a tissue reliably and efficiently in three dimensions is still puzzling. In plants, the mechanics of cells within a tissue is particularly well defined as individual cell growth is essentially mechanical yielding of cell-wall in response to internal turgor pressure. Most intriguingly, cell-wall stiffness is controlled by biological signalling and is observed to respond to mechanical stresses building up within a tissue. What is the role of such a mechanical feedback during morphing in three dimensions? Here, we propose a three dimensional vertex model to investigate tissue mechanics at the onset of organ outgrowth at the tip of a plant shoot. We find that organ height is primarily governed by the ratio of growth rates of faster growing cells initiating the organ to slower growing tissue cells surrounding them. Remarkably, the outgrowth rate is more efficient when cells can remodel their cell-wall stiffness in response to the tissue-wide mechanical stresses. Our quantitative analysis of simulation data shows that the feedback acts by not only modulating cell growth by reorganising walls but also by changing the stress pattern within the tissue promoting organ outgrowth.

BP 31.8 Fri 11:30 H10

Visualization of intracellular calcium levels in Dictyostelium discoideum with a genetically encoded reporter — •Manuel Frey, Sven Flemming, Serena Cucinotta, and Carsten Beta — University of Potsdam, Potsdam, Germany

Calcium is an important second messenger in eukaryotic cells and is crucial for several signaling pathways related to cellular functions such as chemotaxis and cell motility. To visualize calcium in the social amoeba Dictyostelium discoideum, we expressed a genetically encoded GFP based calcium reporter at the plasma membrane. This enabled us to monitor spatiotemporal changes in the intracellular Ca2+ levels.

We could detect global increases in Ca2+ levels after chemotactic stimulation with cAMP. Mechanical stimulation of cells led to a local Ca2+ response. Furthermore, we could detect short, focal increases of Ca2+ at the basal plasma membrane, which coincided with the appearance of F-actin foci at the same location. In cells exposed to continuous shear flow, we observed periodic oscillations of the intracellular Ca2+ levels. Interestingly, once excited these oscillations continued for several minutes even after the shear flow was stopped. In contrast, application of a short pulse of shear flow induced only single responses.

Inhibitor experiments suggested that the observed Ca2+ response at the plasma membrane is caused by an influx of Ca2+ needed to replenish the internal stores for Ca2+. Our results show that localized increases in calcium can be visualized with our new reporter in live cell imaging experiments and revealed interesting oscillatory behavior under shear flow.

BP 31.9 Fri 11:45 H10

Coiled coils as molecular force sensors for the extracellular matrix — •Melis Goktas, Chuanfu Luo, Ruby May Arana Sullan, Ana Elisa Bergues-Pupo, Reinhard Lipowsky, Ana Vila Verde, and Kerstin Blank — Max Planck Institute of Colloids and Interfaces, Science Park Potsdam-Golm, 14424 Potsdam, Germany.

Cells sense the mechanical properties of the extracellular matrix (ECM) and use this information for regulating a wide range of cellular functions. Even though it is well understood that mechanical signals play a crucial role in directing cell fate, surprisingly little is known about the range of forces that define cell-ECM interactions at the molecular level. To determine the single molecular forces required to maintain initial cell adhesion, we developed a library of coiled coil (CC)-based molecular force sensors (MFSs). Using AFM-based SMFS, we have calibrated the rupture forces of a series of short heterodimeric CCs (3-5 heptad repeats) under shear geometry. We show that the rupture forces lie in the range of 20-50 pN and depend on CC length (i.e. number of heptads). Using these mechanically calibrated CCs as molecular building blocks, we developed a two-component MFS approach. Proof-of-concept experiments performed with fibroblasts and endothelial cells revealed that single integrin-ligand bonds transmit forces lower than 40 pN during initial cell adhesion and that cells with endothelial lineage exert lower cell-ECM forces compared to fibroblasts. These results aid the future design of 2D and 3D CC-based MFS platforms for investigating cellular mechanosensing processes at the single molecule level.