BP 8: Cell Mechanics I

Time: Tuesday 9:30–13:00 Location: BAR Schö

BP 8.1 Tue 9:30 BAR Schö

Chiral flows can drive pattern formation in viscoelastic surfaces — •Eloy de Kinkelder[1,2], Elisabeth Fischer-Friedrich[3,4], and Sebastian Aland[1,2] — [1]TU Bergakademie Freiberg, Freiberg, Germany — [2]HTW Dresden, Dresden, Germany — [3]TU Dresden, Dresden, Germany — [4]BIOTEC, Dresden, Germany

During division in animal cells, the actomyosin cortex has been found to exhibit counter-rotating cortical flows along the axis of division. These are also known as chiral flows. Notably, the chiral flows were shown to influence cellular rearrangements and drive the left-right symmetry breaking in developing organisms. At the current state, no numerical simulations have been done to study the influence of chiral flows on the cell cortex shape. To deepen the insight on that matter, we present here a numerical study of an axi-symmetric viscoelastic surface embedded in a viscous fluid. On this surface we impose a generic counter rotating force field to investigate its influence on the surface shape and material transport. Notably, we find that a large areal relaxation time results in flows towards the equator of the surface. These flows assist the transport of a surface concentration during the forming of a contractile ring. Accordingly, we show that chiral forces by themselves can drive pattern formation and stabilise contractile rings at the equator.

BP 8.2 Tue 9:45 BAR Schö

Neutrophil mechanotransduction during durotaxis — •Fatemeh Abbasi[1], Matthias Brandt[2], and Timo Betz[1] — [1]Third Institute of Physics,Biophysics, Georg August University Göttingen — [2]Institute of Cell Biology, ZMBE, University of Münster

In Vivo, cells experience complex tissue environments with various chemical and physical features. 3D confinement is one of the major physical obstacles for cells in their natural environment. Neutrophils are among the most abundant immune cells in our body, which have to cope with various physical constrictions on their way from production to the infection site. In addition to confinement, the stiffness of the microenvironment is another mechanical feature these rapidly moving cells are exposed to. Neutrophils experience various tissue stiffness, from 1 kPa (bone marrow) to 20 MPa (bone). Previous studies have demonstrated that these cells are responsive to their microenvironment stiffness by adjusting their adhesion and spreading. Based on this knowledge we decided to combine confinement and stiffness change and investigate the impact of 3D stiffness gradient on cell behaviour and migration, a fact called durotaxis. We hypothesized that stiffness gradient might be a triggering factor of neutrophil migration toward the infection site. We confine neutrophils in between 2 layers of polyacrylamide hydrogels with 2 different stiffness and keep this distance stable for the desired period of time to investigate cell mechanotransduction during durotaxis from different points of view. Our preliminary results regarding the neutrophil durotaxis show a surprising and transient force peak on the soft substrate during cell shifting.

BP 8.3 Tue 10:00 BAR Schö

Red blood cell lingering modulates hematocrit distribution in the microcirculation — •Yazdan Rashidi[1], Greta Simionato[2], Qi Zhou[3], Thomas John[1], Alexander Kihm[1], Mohammed Bendaoud[1], Timm Krueger[3], Miguel o. Bernabeu[3], Lars Kaestner[1], Mattias w. Laschke[2], Michael d. Menger[2], Christian Wagner[1], and Alexis Darras[1] — [1]Experimental Physics, Saarland University, 66123 Saarbruecken, Germany — [2]Institute for Clinical and Experimental Surgery, Saarland University, 66421 Homburg, Germany — [3]School of Engineering, University of Edinburgh, Edinburgh EH9 3FD, United Kingdom

The distribution of red blood cells (RBCs) in the microcirculation determines how oxygen is delivered to tissues and organs. This process relies on the partitioning of RBCs at successive microvascular bifurcations. It is known that RBCs partition disproportionately to the blood flow rate, therefore leading to heterogeneity of the hematocrit in microvessels. Usually, downstream of a bifurcation, the vessel branch with a higher fraction of blood flow receives a higher fraction of RBC flux.

However, deviations from this phase-separation law have been observed in recent works. Here, we quantify how the microscopic behavior of RBCs lingering influences their partitioning, through combined in vivo experiments and in silico simulations. We quantify the cell lingering at capillary-level bifurcations and demonstrate that it correlates with deviations from the phase-separation process from established empirical predictions by Pries et al.

BP 8.4 Tue 10:15 BAR Schö

Mechanical fingerprint of the intra-cellular space — •Till M. Muenker, Bart E. Vos, and Timo Betz — University of Göttingen, Göttingen, Germany

Many important cellular functions such as organelle positioning and internal cargo transport are dependent on the viscoelastic intracellular mechanical properties of cells. A range of different mechanical models has been proposed to describe these properties. Whilst simple models such as Maxwell or Kelvin-Voigt models don't seem sufficient to capture the full complexity of cells, more elaborate models like generalized Kelvin-Voigt models require a huge number of parameters. This hinders the comparison and interpretation of experimental findings. Further, from a physics perspective, cells are systems out of thermodynamic equilibrium, permanently consuming metabolic energy to carry out mechanical work. The level of "non-equilibrium" can be proposed as an indicator for cell type, cell state or even diseases. To determine both, the viscoelastic properties and the cellular activity, we use optical tweezers based active and passive microrheology in a diverse group of 9 different cell-types. Surprisingly, despite differences in origin and function, the complex moduli of all cell types can be described using a 4 parameter based fractional Kelvin-Voigt model. Additionally, the frequency dependent activity can be described with a simple power law. This approach allows to reduce those complex and frequency dependent properties down to a fingerprint of 6 parameter. Further principal component analysis shows that only 2 of them may be sufficient to characterize the mechanical intracellular state.

15 min. break

Invited Talk BP 8.5 Tue 10:45 BAR Schö

Microtubule Lattice Dynamics — Subham Biswas[1], Rahul Grover[2], Cordula Reuther[2], Mona Grünewald[1], Stefan Diez[2], and •Laura Schaedel[1] — [1]Saarland University, Saarbrücken, Germany — [2]TU Dresden, Germany

Microtubules are dynamic cytoskeletal filaments that grow and shrink by subunit addition or removal at their tips. In contrast, the microtubule lattice far from the tips was long considered to be static. The discovery of subunit loss and incorporation along the lattice far from the tips - termed lattice dynamics - led to a paradigm shift and revealed a new dimension of microtubule dynamics.

Microtubule lattice dynamics occur in vitro as well as in living cells and contribute to microtubule organization and resilience to mechanical stress. Yet, it is largely unknown which cellular mechanisms are involved in their regulation. Recent discoveries suggest that microtubule-associated proteins (MAPs), which control a variety of properties of intracellular microtubules, are a key factor in the regulation of lattice dynamics. Here, we take a closer look at MAP-regulated microtubule lattice dynamics.

BP 8.6 Tue 11:15 BAR Schö

Force generation in human blood platelets by filamentous actomyosin structures — •Anna Zelena[1], Johannes Blumberg[2], Ulrich S. Schwarz[2], and Sarah Köster[1] — [1]Institute for X-Ray Physics, Georg-August-University of Göttingen, Germany — [2]Institute for Theoretical Physics, University of Heidelberg, Germany

Blood platelets are central elements of the blood clotting response after wounding. Upon vessel damage, they adhere to the surrounding matrix of the vessel and contract the emerging blood clot, thus helping to restore normal blood flow. The blood clotting function of platelets has been shown to be directly connected to their mechanics and cytoskeletal organization. The reorganization of the platelet cytoskeleton during spreading occurs within minutes and leads to the formation of contractile actomyosin bundles, but it is not known how this structure formation corresponds to force generation. In this study, we combine fluorescence imaging of the actin structures with traction force measurements in a time-resolved manner. We find that force generation is localized in few hotspots, which spatially align very closely with

the visualized end points of the fibrous actin structures and do not change much with time. Moreover we show that force generation is a very robust mechanism independent of changes in the amount of added thrombin in solution or fibrinogen coverage on the substrate, suggesting that force generation after platelet activation is a threshold phenomenon that ensures reliable blood clot contraction in diverse environments.

BP 8.7 Tue 11:30 BAR Schö

How to build muscle? Sarcomeric pattern formation by non-local interactions — •Francine Kolley[1,2], Clara Sidor[3], Frank Schnorrer[3], and Benjamin M. Friedrich[1,2] — [1]Physics of Life, TU Dresden — [2]cfaed, TU Dresden — [3]IBDM,Aix Marseille University

Striated muscles drive all voluntary movements and are highly organized in crystal-like structures, comprising different filament types on a micrometer scale. The specific size of a sarcomere is set by the giant protein titin. Titin links the molecular motor myosin in the middle of a sarcomere to the so-called Z-disc, which is rich in actin crosslinkers at the sarcomere boundary. Despite the importance of the repeated structures of theses sarcomeres for muscle functionality, it is poorly understood how they self-assemble during muscles development.To investigate this question, we introduce theoretical models based on putative mechanism. We can show with a minimal Mean-field model that a non-local interaction between the key proteins is sufficient for the emergence of periodic patterns. Agent-based simulations of this model reveal the influence of small-number fluctuations. We can expand this model to include additional properties, such as different myosin bindings or the catch-bond behavior of the Z-disc crosslinker α-actinin. In addition, from analyzing images of the *Drosophila* flight muscles during early developmental stages, provided by Schnorrer Lab, we are able to identify α-actinin and titin as the first proteins forming periodic patterns with myosin, while actin follows later, constraining possible models.

15 min. break

BP 8.8 Tue 12:00 BAR Schö

Impact of oxidative stress on the mechanical properties of isolated mitochondria — •Yesaswini Komaragiri[1,2], Muzaffar H Panhwar[1,2], Bob Fregin[1,2], Gayatri Jagirdar[3], Carmen Wolke[3], Stefanie Spiegler[1,2], and Oliver Otto[1,2] — [1]Institut für Physik, Universität Greifswald, Friedrich-Ludwig-Jahn-Str. 15a, 17489 Greifswald, Germany — [2]DZHK, Greifswald, Universitätsmedizin Greifswald, Fleischmannstr. 42, 17489 Greifswald, Germany — [3]Universitätsmedizin Greifswald, Ferdinand-Sauerbruch-Strasse, 17475 Greifswald, Germany

Mitochondria are essential in various physiological processes, including the homeostasis of reactive oxygen species (ROS) as key intracellular signaling molecules. While it is already established that mechanical properties are a crucial parameter in characterizing and comprehending biological systems such as cells and tissues, little is known about the significance of organelle mechanics for cell function. Here, we demonstrate the application of real-time fluorescence and deformability cytometry for the label-free and high-throughput analysis of mitochondria isolated from C6 glial cells. Our data on several thousands of viable mitochondria indicate that their deformation is shear stress dependent. We studied the effect of exogenously and endogenously generated ROS on mitochondria mechanics in two proof-of-concept studies. Under both conditions, we observed a decrease in size while the deformation increased relative to a control condition. The results suggest a general biophysical mechanism of how mitochondria respond to oxidative stress.

BP 8.9 Tue 12:15 BAR Schö

New applications for the direct method in 3D traction force microscopy — •Johannes Blumberg[1,2], Simon Brauburger[1,2], and Ulrich Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University — [2]Bioquant, Heidelberg University

Traction force microscopy (TFM) estimates the mechanical forces of cells adhering to an elastic substrate by measuring by the movement of embedded marker beads. It has become a standard tool to study the mechanobiology of single cells or cell monolayers on flat two-dimensional (2D) substrates, but three-dimensional (3D) setups provide new challenges. Although the inverse method of force inference by minimization of a loss function has become the standard method for 2D TFM, for 3D TFM the direct method of directly calculating stress and surface traction from strain becomes an attractive alternative, for example when performing 3D TFM with elastic beads in organisms, tumor spheroids or organoids. We explain how this method works in practice and how it compares to the inverse method.

BP 8.10 Tue 12:30 BAR Schö

Profilin Regulating the Polymerisation Velocity of Actin — •Lina Heydenreich and Jan Kierfeld — TU Dortmund University, 44227 Dortmund, Germany

F-Actin, as a part of the cytoskeleton, drives crucial biological processes like cell motility, where the control of the polymerisation speed is essential. Experiments in [1] show a maximal polymerisation speed of F-actin at high concentrations of profilin and actin.

We present a kinetic model of F-actin growth in the presence of profilin and obtain an exact result for the mean growth velocity which is in agreement with stochastic simulations, and explains the experimental data. The maximal growth speed is limited by the release rate of profilin from filamentous actin. In the limit where nearly all actin monomers are bound to profilin, the polymerisation speed follows the Michaelis-Menten kinetics.

By analysing the presented model, we can examine the influence of an external force and the influence of profilin on the fluctuations and precision of the polymerisation. Additionally we can give constraints on the concentrations to obtain a saturation of the growth velocity.

[1] Johanna Funk et al. "Profilin and formin constitute a pacemaker system for robust actin filament growth". eLife 8 (2019), e50963

BP 8.11 Tue 12:45 BAR Schö

Development of a platform for accessing the membrane tension of cells in microchannels — •Eric Sündermann, Bob Fregin, Doreen Biedenweg, Stefanie Spiegler, and Oliver Otto — ZIK HIKE, University of Greifswald, Greifswald, Germany

The development of high-throughput methods for cell mechanical research is becoming increasingly important in biology, medicine and physics as the analysis of large samples opens up possibilities for basic science and clinical use. Currently, various techniques are available, but hardly any can discriminate between membrane and bulk contributions to the mechanical properties of a cell.

Here, we combined deformability cytometry with fluorescence lifetime imaging microscopy (FLIM) to study the response of membrane tension to hydrodynamic stress. Myeloid precursor cells were first stained with Flipper-TR®, a fluorescent dye with a lifetime proportional to the membrane tension, and then flushed through the constriction of a microfluidic chip, where they deform under a shear stress. Under steady-state conditions, our data shows that the membrane tension of cells increases with increasing hydrodynamic stress, as expected. Exposing cells to methyl-ß-cyclodextrin to reduce the amount of cholesterol in the cell membrane leads to a reduction in membrane tension while the bulk Young's modulus is not affected.

These results highlight the potential of microfluidic technologies to quantify the contribution of different cell components to its overall mechanical phenotype.