BP 25: Cell Mechanics II

Time: Wednesday 15:00–17:15 Location: HÜL 386

BP 25.1 Wed 15:00 HÜL 386

Chemotherapy interferes with leukocyte deformability in a cancer patient study — Martin Kräter[1,2], Maik Herbig[1,2], Martin Bornhäuser[3], Jochen Guck[1,2], and •Angela Jacobi[1,2,3] — [1]MPL, Erlangen, Germany — [2]BIOTEC, TU Dresden, Dresden, Germany — [3]University Hospital Carl Gustav Carus, TU Dresden, Dresden, Germany

Blood cell mechanics, dictated by the cytoskeleton, is essential for circulation in microcapillary networks, where cells need to deform and squeeze through vascular constrictions. If this deformability is attenuated, blood flow can be impeded, leading to thromboembolic complications. Using real-time deformability cytometry (RT-DC), a high-throughput method that determines cell mechanics, we performed a pilot study on blood samples from a cancer patient undergoing chemotherapy with epirubicin/cyclophosphamide (EC) and paclitaxel (P). Over the course of the treatment, we monitored leukocyte count, size and deformability. During the therapy, granulo-/monocytes exhibited a dramatic decrease in deformability. However, 45 weeks post treatment, leukocyte deformability was restored to normal levels, indicating that blood cell mechanics is tightly regulated in homeostatic conditions. Intriguingly, the treatment did not alter cell size, which emphasises the advantage of measuring blood cell deformability when monitoring poor circulation in chemotherapy patients. Finally, our study suggests that reduced blood cell deformation could favour vascular complications encountered during chemotherapy.

BP 25.2 Wed 15:15 HÜL 386

Investigating the red blood cells (dis)aggregation mechanism using optical tweezers — •Francois Yaya[1,2], Olivera Korculanin[3], Mehrnaz Babaki[3], Kisung Lee[4], Pavlik Lettinga[3,5], and Christian Wagner[1] — [1]1Experimentalphysik, Saarbrücken, Germany — [2]Interdisciplinaire de Physique, Grenoble, France — [3]ICS-3 Forschungszentrum, Jülich, Germany — [4]Korean Institute for Basic Science, Ulsan, South Korea — [5]Laboratory for Soft Matter and Biophysics, KU Leuven, Belgium

Red blood cells (RBC) in our body circulate, while continuously aggregating and disaggregating under low shear rates. RBC aggregation is a reversible process that can only be observed in the presence of macromolecules (i.e. large plasma proteins like fibrinogen or non-ionic polymers). The potential description of the RBC interaction was studied, mainly from the scope of polymer induced aggregation and predominantly with dextran. Despite the favored model based on the depletion forces, one can find that, conclusive experimental affirmations of the model are still lacking. Hence, we aimed to investigate the RBC interaction mechanism utilizing holographic optical tweezers (HOT). We assessed RBC interaction forces in two model solutions, namely dextran and a pure depletant (Fd virus). Aggregation and disaggregation of multiple pairs of RBC, in dextran, revealed that forces differ by more than 3 fold. For Fd virus, interaction forces are in the same order of magnitude. Combining HOT with a microfluidic platform, we finally show that adsorption of macromolecules takes place onto a single RBC membrane.

BP 25.3 Wed 15:30 HÜL 386

Dynamics of Circular Dorsal Ruffles as a Function of Cellular State — •Merthe Schwachenwald, Julia Lange, Malte Ohmstede, and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen

Circular Dorsal Ruffles (CDRs) are dense moving actin structures that play an important role in cell propagation and the uptake of growth factors. The occurrence and propagation of CDRs are controlled by a multitude of different proteins and interconnected signaling pathways, the most prominent and well-understood being Arp2/3-mediated actin branching. Thus the dynamics of CDRs can be manipulated by interfering with actin regulators or actin itself. Further, the kinetics of CDRs are influenced by membrane tension. To quantify the impact of the different players, we investigate the dynamics of CDRs under narrowly-controlled conditions. Experimentally, we ensure even boundary conditions by using microcontact printed substrates to enforce an even cell shape. The influences of different proteins and growth-factor stimulation on CDR dynamics are controlled employing a microfluidic set-up, and examined using light microscopy. The dynamics of the occurring CDRs are analyzed via kymographs or the use of machine-learning alghorithms.

BP 25.4 Wed 15:45 HÜL 386

Stochastic bond dynamics induce optimal alignment of malaria parasite — •Anil Kumar Dasanna, Sebastian Hillringhaus, Gerhard Gompper, and Dmitry Fedosov — Institute of Complex Systems and Institute for Advanced Simulation, Forschungszentrum Jülich, Germany

Malaria parasites invade healthy red blood cells (RBCs) to escape from the immune response and multiply inside the host by utilizing its machinery. The invasion only occurs when the parasite apex is aligned with RBC membrane, which makes the alignment a crucial step. Recent experiments also demonstrated that there is a considerable membrane deformation during the alignment process which are thought to speed up the alignment process. In this work, using mesoscopic simulations we try to assess the exact roles of RBC deformations and parasite adhesion during the alignment. Using deformable RBC and a rigid parasite, we show that both RBC deformation and parasite's adhesion work together to induce an optimal alignment. By calibrating our parasite's movement with experiments, we show that our alignment times match quantitatively with the experimental alignment times. Here we stress that the stochastic nature of our adhesion bond kinetics is the key for inducing optimal alignment times rather than too fast times such as in case of smooth potentials or too slow such as in case of purely rotational diffusion. We also show that alignment times increase drastically for rigid RBC which signifies that parasite invasion is less probable with already infected RBC and signifying the role of membrane deformations during the parasite alignment.

BP 25.5 Wed 16:00 HÜL 386

Unbiased recovery of frequency-dependent mechanical properties from noisy time-dependent data — •Shada Abuhattum[1], Paul Müller[1], Vasily Zaburdaev[2], Jochen Guck[1], and Hui-Shun Kuan[2] — [1]Max Planck Institute for the Science of Light — [2]Department of Biology, FAU-Universität Erlangen-Nürnberg

The mechanical response of materials to dynamic loading has great significance in various applications, ranging from performance and failure of engineered setups to exploring the structure of biological matter. This mechanical response is quantified using the frequency-dependent complex modulus. Probing materials directly in the frequency domain faces technical challenges such as a limited range of frequencies or lengthy measuring times. Therefore, it is common practice to extract frequency-dependent properties by fitting predefined mechanical models to measurements done in time-domain. Fitting these models circumvents problems with noise handling and signal shape imperfections. However, it precludes the probing of unique and unexplored material properties. Here, we demonstrate that the frequency-dependent complex modulus can be properly derived from stress-strain time-domain measurements even in the presence of random noise and systematic offset. We apply signal blurring methods to eliminate the systematic offset and to clean the complex modulus at lower frequencies. We then extend the range of reliable frequencies by employing a local averaging method to the complex modulus data. Finally, we propose an alternative probing procedure to increase the signal-to-noise ratio and further extend the frequency range for a reliable mechanical characterization.

15 min. coffee break

BP 25.6 Wed 16:30 HÜL 386

Mechano-chemical interactions in a one-dimensional description of intracellular reaction-diffusion systems — •Alexander Ziepke and Erwin Frey — Arnold Sommerfeld Center for Theoretical Physics, Ludwig-Maximilians-Universität München, Germany

The understanding of self-organization processes in biological systems represents a key challenge in the field of theoretical biology. There are various studies on reaction-diffusion (RD) models in a single spatial dimension (1D) that give insights on the fundamental behavior of pattern formation in biological systems [1]. However, effects of a spatial confinement, e.g. the cell geometry, are not captured by most of the 1D models. With our new approach we bridge this gap between biological systems in a spatio-temporally varying confinement and simple 1D-

RD equations. On the basis of an asymptotic perturbation analysis, we reduce the dimensionality of the confined system [2]. The resulting description incorporates the effects of mechano-chemical coupling and, therefore, extends significantly the applicability of 1D models beyond free dynamics on straight lines. Studying the derived equation for mass-conserving RD systems with interacting membrane-bound and cytosolic species, we find conditions for geometry induced pattern formation. Moreover, mechano-chemical interactions can lead to a feedback between RD kinetics and a deformation of the cell membrane, giving rise to a variety of interesting phenomena.

[1] J. Halatek and E. Frey, Nat. Phys., 14, 507 (2018)

[2] A. Ziepke, S. Martens, and H. Engel, J. Chem. Phys., 145, 094108 (2016)

BP 25.7 Wed 16:45 HÜL 386

Quantification of size-dependent organelle transport in cells — •Simon Wieland[1], David Gitschier[1], Marius M Kaiser[1], Solange Hoffbauer[1], Magdalena Haaf[1], Adam G Hendricks[2], and Holger Kress[1] — [1]Universität Bayreuth, Arbeitsgruppe Biologische Physik, Bayreuth — [2]McGill University, Department of Bioengineering, Montreal

Intracellular organelle transport is a vital process for a large variety of cellular functions, like exocytosis and endocytosis, including phagocytosis. Recently, it was found that organelle transport during phagocytosis is not only regulated biochemically, but also by the size of the organelle [1]: In macrophages, larger phagosomes are transported very persistently towards the nucleus, whereas smaller phagosomes exhibit highly irregular motion. To unravel the molecular causes of this behavior, we systematically quantified the size-dependence of the intracellular transport of phagosomes. Using magnetic tweezers, we found that intracellular transport forces of organelles strongly depend on the cargo size. Immunofluorescence experiments performed on isolated phagosomes allowed us to identify and partially quantify dynein, kinesin-1, and kinesin-2 on the organelles. The scaling behavior of the numbers of dyneins on the organelles together with the scaling behavior of measured stall forces implies cooperation between the molecular motors. These findings can lead to a more fundamental understanding of intracellular transport and the dynamics of molecular motors.

[1]: Keller, S., Berghoff, K., & Kress, H. (2017). Scientific reports, 7(1), 17068.

BP 25.8 Wed 17:00 HÜL 386

Stochastic model of T Cell repolarization during target elimination — •Ivan Hornak and Heiko Rieger — Saarland University, Dep. Theoretical Physics, Center for Biophysics

Cytotoxic T lymphocytes (T) and natural killer cells are the main cytotoxic killer cells of the human body to eliminate pathogen-infected or tumorigenic cells (target cells). Once T-cell has identified a target cell, they form a tight contact zone, the immunological synapse (IS). One then observes a re-polarization of the cell involving the rotation of the microtubule (MT) half-spindle and a movement of the microtubule organizing center (MTOC) to the IS. Concomitantly a massive relocation of organelles attached to MTs is observed. Since the mechanism of this relocation remains elusive we devise a theoretical model for the molecular motor driven motion of the MT half-spindle confined between membrane and nucleus. We analyze different currently discussed scenarios, the cortical sliding and the capture-shrinkage mechanisms, and compare quantitative predictions about the spatio-temporal evolution of MTOC position and spindle morphology with experiments. Model predicts the experimentally observed biphasic nature of the repositioning and confirms the dominance of the capture-shrinkage over the cortical sliding mechanism when MTOC and IS are initially diametrically opposed. We find that the two mechanisms act synergetically reducing the resources necessary for repositioning. Localization of dyneins in the pSMAC facilitates their interaction with MTs. Model opens a way to infer details of the dynein distribution from the experimentally observed features of the MT half-spindle dynamics.