BP 40: Cell Mechanics II / Cytoskeleton II

Time: Friday 10:00–11:15 Location: BAR/0205

BP 40.1 Fri 10:00 BAR/0205

The keratin network adapts the nucleus to cellular strain — •Ruben Haag[1], Ruth Meyer[1], Sascha Lambert[2], Hajaani Manoharan[3], Ulrike Rölleke[1], Jens Konrad[3], Bernd Hoffman[3], Rudolf Merkel[3], Stefan Klumpp[2], and Sarah Köster[1] — [1]Institute for X-Ray Physics, University of Göttingen, Germany — [2]Institute for the Dynamics of Complex Systems, University of Göttingen, Germany — [3]Institute of Biological Information Processing, Forschungszentrum Jülich, Germany

Intermediate filaments (IFs) comprise one of the cytoskeletal network types and are cell-type specific. In epithelial cells, the keratin IF network connects the desmosomes in the cell membrane with the perinuclear keratin cage, thus forming a mechanical link from the nucleus to the cell membrane. We now ask whether this link transmits mechanical signals from outside the cell to the nucleus. To answer this question, we stretch both epithelial wild type and keratin knockout cells uniaxially and equibiaxially. During stretching, we image cell nuclei and measure their individual deformation to study the influence of the keratin IF network on them. To understand how the keratin network transmits force to the nucleus, we image the keratin network during cell stretching and create a minimal model to mimic how the keratin network deforms the nucleus. Our results suggest that stretching the keratin network is a two-step process: individual keratin bundles are initially pulled straight and are then stretched. Possibly, by this two-step process, the keratin network adapts the nucleus to cellular strain.

BP 40.2 Fri 10:15 BAR/0205

Improving T cell migration and invasion with the Microtubule destabilizing agent Pretubulysin. — •Lukas Schuster[1], Galia Montalvo[1], Reza Shaebani[1], Anna Burgstaller[2], Shweta Nandakumar[1], Rhoda Hawkins[3], Laura Schaedel[1], Bin Qu[4], and Franziska Lautenschläger[1] — [1]Saarland University, Saarbrücken, Germany — [2]Leibniz Institute for New Materials, Saarbrücken, Germany — [3]School of Mathematical and Physical Sciences, University of Sheffield, Sheffield, United Kingdom — [4]Center for Integrative Physiology and Molecular Medicine (CIPMM), Saarland University, Homburg, Germany & Department of Biomedical Sciences, Osnabrück University, Osnabrück, Germany

The immune response depends on the ability of cytotoxic T lymphocytes (CTLs) to migrate and invade into dense 3D environments, such as tumors, and to kill cancer cells. Thus, optimizing the migratory behavior of CTLs is crucial to boost immune response in the treatment against cancer. Here, we focused on the role of destabilized microtubules (MTs) in cell migration. We showed that the disruption of MTs in CTLs with the compound Pretubulysin enhances the infiltration of 3D collagen gels and the killing of target cells. In addition, we confirmed the motile phenotype in 2D and 1D migration assays. We further studied the mechanism of how MT disruption induces cell motility in a theoretical active droplet model. We found enriched actomyosin in the back of CTLs to be linked to a fast and persistent migrating cell.

BP 40.3 Fri 10:30 BAR/0205

Role of mechanics in early immune recognition — •Kheya Sengupta — CINaM, CNRS, Luminy, France.

Our immune system depends on cell scale forces, which are implicated in various phenomena ranging from migration to recognition of pathology or for potentiating diseased cells for killing. Here the focus will be on the first steps of immune recognition which hinges on formation of bonds between specialised receptors and their specific ligands called antigens, where mechanics and forces are thought to be essential to discriminate our own antigens from those indicative of pathology. Intriguingly, unlike for tissue forming cells, the response of T cells is biphasic with the stiffness of their environment when the interaction is mediated through the T-cell receptors (TCRs). However, when the adhesive ligands of integrins are additionally involved, the cellular response becomes monotonic. Based on a mesoscale model, this ligand-specific response can be attributed to molecular properties of a putative link between the ligand/receptor pair and the cytoskeleton. While the molecules linking integrins and actin are known, the equivalent molecules for TCR are yet to be identified. Our model predicts kinetic and mechanical parameters for this putative link, whose existence we prove by mechanical extraction of membrane tubes. We also measure cell scale forces and show that their spatio-temporal patterns depend on chemistry, mechanics and T cell sub-type. Overall, our findings reinforce the proposition that force application provides a general mechanism for immune cells to discriminate mechanosensitive bonds.

BP 40.4 Fri 10:45 BAR/0205

Investigating the interaction between cardiac fibroblasts using ROCS and fluorescence microscopy — •Arash Felekary and Alexander Rohrbach — IMTEK, University of Freiburg, Germany

Cell-cell interaction is essential for cardiac function. Tunneling nanotubes (TNTs), thin actin-based membrane protrusions, mediate long-range interactions by transporting organelles and signaling molecules. To study their role in cardiac fibroblast (FB) interaction, we combined Rotating Coherent Scattering (ROCS) microscopy with fluorescence imaging. ROCS provides label-free, high-contrast recordings at up to 100 Hz and resolves TNTs and lamellipodia across several micrometers above the substrate. Using this approach, we observed a linear correlation between TNT density and lamellipodia motion velocity. Collagen labeling revealed that TNTs frequently align with collagen fibers, suggesting a structural coupling between ECM-linked TNTs and actin-driven protrusions. These observations motivated a spatially resolved simulation of actin filament polymerization and branching, incorporating integrin*collagen interactions and Arp2/3 activation. The model reproduces the experimentally observed increase in lamellipodial velocity with TNT density and supports a mechanism in which TNTs locally amplify integrin-mediated actin remodeling. In this presentation, we discuss how TNTs, lamellipodia, and ECM components cooperatively guide FB interaction, offering new insight into the structural and mechanical coordination underlying cardiac tissue remodeling.

BP 40.5 Fri 11:00 BAR/0205

How to determine cell property distributions from high-throughput experiments via computer simulations — •Stephan Gekle — Biofluid Simulation and Modeling, Theoretische Physik VI, Universität Bayreuth

A central challenge in computer simulations of living cells is the accurate determination of model parameters based on experimental data. This challenge arises since cell properties such as membrane or cytoplasm viscosities are often difficult or impossible to directly measure in an experiment. The current paradigm in the field is to try to find a single "optimal" value for each such property. This approach completely disregards biological heterogeneity and cell-to-cell variability.

Here, we will present a novel inference method which starts from the assumption that *the* optimal value of a cellular property does not exist and that biological reality must rather be reflected by a *distribution* of values for each cell property. We will show how to obtain such property distributions for a realistic and technologically relevant scenario of disease detection via red blood cell membrane alterations.

For this, we will present boundary-integral simulations of red blood cells passing through a microchannel setup corresponding to real-time deformability cytometry (RT-DC) experiments. We will show how the resulting large amounts of scattered experimental data can be combined with our efficient simulations to infer distributions of cytosol and membrane viscosities in a heterogeneous cell population taking full account of cell-to-cell variability.