BP 43: Cell Adhesion

Time: Wednesday 15:00–17:00 Location: H43

Invited Talk BP 43.1 Wed 15:00 H43

Cellular Mechanosensing — •Rudolf Merkel — Forschungszentrum Jülich GmbH, 52425 Jülich, Germany

Throughout the organism almost all tissues experience mechanical strain of sizeable magnitude that often is important to their organization and development. To unravel the underlying signal sensing and processing an in vitro model consisting of cells cultivated on stretchable substrates was introduced. Here, I will show how this system can be used as quantitative tool to unravel the contributions of the different cytoskeletal systems and to quantify the "mechanosensing potential" of individual molecules.

BP 43.2 Wed 15:30 H43

Adhesion of the eukaryotic microalga *Chlamydomonas* to model surfaces — •Christian Kreis, Marcin Makowski, and Oliver Bäumchen — Max Planck Institute for Dynamics and Self-Organization, 37077 Göttingen, Germany

Microorganisms are often found in aqueous environments and complex geometries, where they are likely to come into contact with interfaces. Therefore, their survival and behaviour in confinement depends upon their interaction with and adhesion to surfaces. In these processes, flagella and cilia play a crucial role since they are the source of locomotion and may come into direct contact with an interface. However, their interactions with interfaces are not yet understood. Microalgae represent microorganisms that are omnipresent in bioengineering. Their adhesion to surfaces, however, may obstruct the fluid flow and performance output of, e.g., alga farms and microfluidic devices. The unicellular alga *Chlamydomonas* serves as a biological model organism that entails a high technological relevance in terms of the production of biofuel and drugs. We perform adhesion experiments to study the interaction of *Chlamydomonas* and its flagella to interfaces, as a model for eukaryotic cells, flagella and cilia. We employ a micropipette force sensor technique that enables us to probe dynamic interfacial forces of microscale objects down to the pN range. The optical control enables us to track the adhesion of the cell body and the adhesion of the flagella. We observe that only the flagella and not the cell body adhere to our test substrates and provide precise adhesion force measurements of eukaryotic flagella to different model substrates.

BP 43.3 Wed 15:45 H43

Cytoskeletal dynamics in blood platelets during spreading on fibrinogen — •Ingmar Schön, Sebastian Lickert, and Viola Vogel — Laboratory of Applied Mechanobiology, ETH Zurich, Switzerland

Blood platelets are small anucleate cells that form a thrombus during blood coagulation. The most abundant platelet integrin $\alpha_{\mathrm{IIb}}\beta_3$ specifically binds fibrinogen and thereby enables platelet aggregation. Patients with Glanzmann Thrombasthenia (GT) carry a genetic mutation in integrin $\alpha_{\mathrm{IIb}}\beta_3$ and suffer from defective platelet aggregation and excessive bleeding. Here we investigated the spreading of healthy or GT platelets on fibrinogen-coated surfaces by time-lapse fluorescence imaging, confocal microscopy, and super-resolution microscopy (dSTORM). Healthy platelets re-arranged their cytoskeleton and adhesion complexes during spreading from an early "stellar" arrangement into pronounced bundles spanning the whole cell. GT platelets also adhered and spread on fibrinogen but exclusively exhibited a stellar cytoskeletal arrangement. Based on these findings we hypothesize that cytoskeletal dynamics of GT platelets gets stalled at an early stage of the spreading process. We will present results from experiments with specific inhibitors, knock-out cells, different ligand proteins, and other means that aimed at identifying the crucial step where things went awry.

In general, we suggest that platelets are an interesting biophysical model system to study the autonomous, acto-myosin-driven cytoskeletal dynamics during adhesion formation.

BP 43.4 Wed 16:00 H43

Modelling the adhesion of malaria-infected red blood cells — •Anil Kumar Dasanna[1,2] and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University — [2]BioQuant, Heidelberg University

Clinical symptoms of the malaria disease appear when healthy red blood cells are invaded by the parasites during the blood stage of the malaria lifecylce. An infected red blood cell (iRBC) starts to develop adhesive protrusions, so-called knobs, on its surface. The parasite takes about two days to rebuild the iRBC and during this time, the density of knobs increases whereas their typical size decreases. The knobs cause iRBCs to adhere to endothelial cells in the microvasculature, preventing their clearance by spleen and liver, but also leading to capillary obstruction. To better understand the adhesion of iRBCs under capillary flow, we studied the adhesion of iRBC in shear flow using Stokesian dynamics simulations. The iRBC is assumed to have a spherical shape and the knobs are modelled as cluster of receptors on the spherical surface. The ligands are distributed on the substrate to which receptors on iRBC can make bonds that then can rupture under force. We investigate mainly how the spatial organisation of the receptors on the surface of the iRBC changes its adhesive behavior in shear flow. We discuss the different dynamical states of infected RBC, such as rolling adhesion, transient adhesion, firm adhesion and free motion, as a function of knob density and size. We also will discuss the role of heterogeneous receptor distributions and the role of cell elasticity.

BP 43.5 Wed 16:15 H43

Morpho-dynamics and Mechanics of T lymphocytes — Pierre Dillard[1,2], Astrid Wahl[1], Fuwei Pi[1], Ranime Allameddine[1], Emmanuelle Benard[1], Pierre-Henri Puech[2], Anne Charrier[1], Laurent Limozin[2], and •Kheya Sengupta[1] — [1]CINaM/AMU-CNRS UMR 7325, Marseille, France. — [2]LAI/INSERM UMR 1067 AMU-CNRS UMR 7333, Marseille, France.

We investigate adhesion and membrane organization of T lymphocytes interacting with surrogate antigen presenting cells (sAPCs) carrying the ligand anti-CD3 against the T cell receptor (TCR) complex. The sAPCs comprise supported bilayers with mobile/immobilized ligands (BiophysJ 2014), or ordered arrays of ligand nano-dots in a non-adhesive matrix (NanoLett 2013,2015), or soft elastomers. We show that ligand mobility is an important control parameter in cell spreading: cells adhere but fail to spread on mobile ligands, spreading can be rescued by suppressing myosin activity. We also demonstrate a dual scale of T cell response: locally, the cell responds at the nanoscale and restructures its membrane according to local cues; globally, it integrates the signal and responds to an average dose. Finally, the mechano-response of T cells is very different from connective tissue cells: unlike most previously reported cell types, T-cells spread more on soft than on hard elastomers. These results taken together point to original aspects of TCR-mediated response to mechanical cues which are should be relevant for understanding lymphocyte mechanotransduction.

BP 43.6 Wed 16:30 H43

The membrane as a matchmaker in the cell adhesion process — Timo Bihr[1,2], Susanne Fenz[3,4], •Daniel Schmidt[1,2], Rudolf Merkel[4], Kheya Sengupta[5], Udo Seifert[2], and Ana-Sunčana Smith[1,6] — [1]PULS Group, Inst. f. Theor. Physik and Excellence Cluster "Engineering of Advanced Materials", Universität Erlangen-Nürnberg — [2]II. Inst. f. Theor. Physik, Universität Stuttgart — [3]Department of Cell and Developmental Biology, Universität Würzburg — [4]ICS 7: Biomechanics, Forschungszentrum Jülich — [5]CNRS UPR 3118, CINaM, Aix-Marseille Université — [6]Division of Physical Chemistry, Institute Ruđer Bošković, Zagreb

The integrity of living tissues is maintained by cadherin rich domains. Cadherin molecules form *trans*-dimers bridges between neighbouring cells. The formation of domains of *trans*-bonds is controlled by lateral, /in-plane/*cis*-interactions. The origin of these interactions are still debated. In this presentation, we show that the formation of *cis*-domains is regulated by the membrane via its elasticity and fluctuations. Observations from a cell free system consisting of cadherin-decorated model membranes show that the membrane regulates the *trans*-binding, and is itself a source of *cis*-interactions. We develop a theoretical framework to explicitly show that membrane fluctuations introduce complex cooperative effects that modulate the rates of binding and unbinding of the *trans*-dimers. The regulatory activity of the membrane, quantified here in the context of cadherins, relies purely on physical principles and therefore may be a generic player in the context of formation of any adhesion structures on the plasma membrane and in the cell interior.

BP 43.7 Wed 16:45 H43

Cytoskeletal organization in cells on micropatterns — •Marco Linke[1,2], Felix Frey[1,2], Vytaute Starkuviene-Erfle[2], and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University, Germany — [2]BioQuant, Heidelberg University, Germany

Mammalian cells show large variability in cell shape and cytoskeletal organization when grown on planar cell culture substrates with homogeneous protein coating. Therefore micropatterns are increasingly used to normalize their shape and structure, but a quantitative understanding of the resulting intracellular organization is missing. Here we analyze the cytoskeleton of cells growing on a micropatterned substrate by measuring the local orientation of the microtubule network and calculate a typical orientation field for various micropattern geometries. We then model the microtubule cytoskeleton with two different approaches. First, we simulate individual filaments and take the interaction between the actin and microtubule networks into account by using an effective persistence length of the microtubules. Secondly, we use a continuum model based on the theory of liquid crystals in which we minimize the nematic free energy functional. By considering biologically plausible boundary conditions and the influence of the centrosome and the cell nucleus, in both cases we get predictions for global cell organization that agree well with experimental results.