BP 5: Cell Adhesion

Time: Monday 10:30–13:00 Location: H44

Invited Talk BP 5.1 Mon 10:30 H44

Force induced strengthening of binding domains in specifically adhered vesicles — •Ana-Suncana Smith — II. Institutut für Theoretische Physik,Universität Stuttgart

Specific adhesion between ligand-containing vesicles and receptor-functionalized substrates is an established model system for studying the initial stages of the cell recognition process and its control mechanisms. In order to provide a better understanding of the underlying physics emerging from recent experiments, and to allow for quantitative exploitation of this system, we develop a theoretical framework that accounts for the equilibrium state of adhesion. Therein, the macroscopic and microscopic aspects of the problem are successfully merged. Several mechanisms that control adhesion or induce deadhesion are studied at the same level of theory. Particular attention is given to the problem of an externally applied force. In response to pulling, we predict passive strengthening of the adhesion, with the latter effect being significantly enhanced by the mobility of both binding partners.

BP 5.2 Mon 11:00 H44

Efficiency of Initiating Cell Adhesion in Hydrodynamic Flow — •Christian Korn[1,2] and Ulrich Schwarz[1] — [1]University of Heidelberg, Im Neuenheimer Feld 293, D-69120 Heidelberg, Germany — [2]Max Planck Institute of Colloids and Interfaces, D-14424 Potsdam, Germany

Motivated by the importance of cell adhesion under flow for various biological and biotechnological applications, we theoretically investigate the efficiency of initial binding between a receptor-coated sphere and a ligand-coated wall in linear shear flow. Using a Langevin equation that accounts for both hydrodynamic interactions and Browian motion, we numerically calculate the mean first passage time (MFPT) for receptor-ligand encounter. We study the influence of flow rate, receptor and ligand coverage, as well as receptor patch geometry on the MFPT. With increasing shear rate, the MFPT always decreases monotonically. Above a threshold value of a few hundreds, binding efficiency is enhanced only weakly upon increasing the number of receptor patches. Regarding receptor geometry, increasing height increases binding efficiency much stronger than increasing lateral size. This explains why white blood cells adhere to the vessel walls through receptor patches localized to the tips of microvilli, and why malaria-infected red blood cells form elevated receptor patches (*knobs*).

[1] C. Korn and U. S. Schwarz, *Phys. Rev. Lett.* **97**: 138103, 2006.

BP 5.3 Mon 11:15 H44

Adhesion of Membranes with Active Stickers — •Bartosz Rozycki, Thomas Weikl, and Reinhard Lipowsky — Max Planck Institute of Colloids and Interfaces, Science Park Golm, 14424 Potsdam, Germany

The adhesion of biological membranes has been theoretically studied for some time but primarily for equilibrium systems. Some of the adhesion proteins like integrins, however, are active molecules, which means that their conformational transitions are driven by external sources of energy such as ATP hydrolysis. These active, externally driven conformational transitions lead to local perturbations in interactions between membranes and keep the system away from equilibrium. We study the influence of these active processes on membrane adhesion in the framework of stochastic lattice models [1-3]. We show that the membrane adhesiveness exhibits a resonance as the rate of switching of the active adhesion molecules is varied [1,3].

[1] "Adhesion of Membranes with Active Stickers", Bartosz Rozycki, Reinhard Lipowsky, Thomas R. Weikl, Phys. Rev. Lett. 96, 048101 (2006). [2] "Adhesion of Membranes via Switchable Molecules", Bartosz Rozycki, Thomas R. Weikl, Reinhard Lipowsky, Phys. Rev. E 73, 061908 (2006). [3] "Stochastic Resonance for Adhesion of Membranes with Active Stickers", Bartosz Rozycki, Thomas R. Weikl, Reinhard Lipowsky, submitted to European Physical Journal E.

BP 5.4 Mon 11:30 H44

Investigation of erythrocytes cell-cell adhesion using holographic optical tweezers — •Achim Jung[1], Ingolf Bernhardt[2], Lyubomira Ivanova[2], Lars Kaestner[3], Peter Lipp[3], and Christian Wagner[1] — [1]Department of Physics, Saarland University, 66041 Saarbrücken, Germany — [2]Laboratory of Biophysics, Saarland University, 66041 Saarbrücken, Germany — [3]Institute for Molecular Cell Biology, Saarland University, 66424 Homburg, Germany

Prostaglandin E_2 (PGE_2) and lysophosphatidic acid (LPA) are released from activated platelets. Using fluorescence imaging, spectral imaging and the patch-clamp technique, we recently provided evidence that these lipid-mediators at physiological concentrations activate a non-selective cation-channel in human red blood cells (RBCs). This results in a Ca^{2+} influx and the consecutive intracellular Ca^{2+} concentration increase. Ca^{2+} increases elicits the Ca^{2+}-activated K^+ channel (Gardos channel) in the RBC membrane resulting in K^+ efflux and shrinkage of the cells. Therefore we have postulated that the PGE_2 and LPA responses of RBCs reveal a direct and active participation of these cells in blood clot formation. In order to test this hypothesis we set out to measure whether the intracellular Ca^{2+} increase leads to an adhesion force between individual RBCs. These measurements are making use of holographic optical tweezers based on a conventional fluorescence microscope. Experimentally the increase of the intracellular Ca^{2+} concentration was induced by the Ca^{2+} ionophore $A23187$.

15 min. break.

BP 5.5 Mon 12:00 H44

Quantification of Cell Adhesion Forces on Elastic Nanopattern Substrates — •Ilia Louban[1,2], Christine Selhuber[1,2], Stefan Gräter[1,2], and Joachim Spatz[1,2] — [1]Max-Planck-Institute for Metals Research, Dept. of New Materials and Biosystems, Heisenbergstr. 3, D-70569 Stuttgart — [2]University of Heidelberg, Biophysical Chemistry, INF 253, 69120 Heidelberg, Germany

Rigidity of the extracellular matrix (ECM) is one of the key properties in cell adhesion and cell migration. Its influence on cell adhesion forces is not quantitatively evaluated by biophysical means. Hydrogels, based on Poly(ethylene glycol) Diacrylate (PEG-DA), have been developed and tailored as synthetic ECM analog the last years. By changing the molecular weight of the PEG-DA macromolecules a variety of hydrogel elasticity are achieved. The Young's moduli (E) of available hydrogels span more than three orders of magnitude: from Petri-dish-like, stiff PEG-DA 700 (E = 6 MPa) to soft, gelatinous PEG-DA 20000 (E = 1 kPa). To promote cell adhesion, c(-RGDfK-) peptide functionalized, extended gold-nanopatterns are anchored on the surface of PEG-DA hydrogel. For adhesion experiments rat embryonic fibroblast are plated five to six hours on nanostructured hydrogel substrates. Cell adhesion forces are measured by detaching cells from the PEG-DA surface with tipless, biofunctionalized cantilever driven by an atomic force microscope. Forces are determined as a function of hydrogel stiffness and ligand patterning. The latter enables the quantification of cooperative processes on the molecular scale which govern cell adhesion phenomena.

BP 5.6 Mon 12:15 H44

Dynamic force spectroscopy on multiple bonds: evaluating rupture force histograms with a master equation model — •Thorsten Erdmann[1,3], Sebastien Pierrat[2], Pierre Nassoy[2], and Ulrich Schwarz[1] — [1]Center for Modelling and Simulation in the Biosciences (BIOMS),Universität Heidelberg, Im Neuenheimer Feld 293, 69120 Heidelberg, Germany — [2]Institut Curie, UMR 168, 26 rue d'Ulm, 75248 Paris Cedex 05, France — [3]Fom Institute for Atomic and Molecular Physics (AMOLF), Kruislaan 407, 1098 SJ Amsterdam, The Netherlands

We probe the dynamic strength of multiple parallel biotin-streptavidin adhesion bonds under linear loading using the biomembrane force probe setup for dynamic force spectroscopy. Using multiple rather than single bonds allows a more efficient evaluation of the experimental data. Measured rupture force histograms are compared to results from a master equation model for the stochastic dynamics of bond rupture under load. We extract the average number of bonds ruptured in each experiment as well as characteristic parameters of the adhesion bonds. The analysis shows that the peaks in the measured histograms are not simple multiples of the single bond values, but follow from a convolution procedure which generates different peak positions.

BP 5.7 Mon 12:30 H44

Vinculin head and tail fragments control adhesion forces and cell mechanics — •Claudia Tanja Mierke, Philip Kollmannsberger, Gerold Diez, Daniel Paranhos Zitterbart, Ben Fabry, and Wolfgang Goldmann — Biophysics, University of Erlangen, Germany

The focal adhesion protein vinculin consists of a head-domain and a tail-domain. Our aim was to quantify cell mechanics and the strength of cytoskeleton, focal adhesion complex and integrin receptor bonds in F9wt mouse embryonic carcinoma cells, vinculin knock-out, vinculin re-transfected and two vinculin-mutants: vinculin-knock-out cells transfected with head-fragment (vin-head) and tail-fragment (vin-tail). We measured rupture forces and creep responses by applying a staircase-like sequence of step forces between 0.5-10 nN to fibronectin-coated magnetic beads attached to the cells. All cells displayed power-law creep responses, J(t)=J0 (t/t0)b, and in most cases linear stress stiffening. The power-law exponent b was taken as a measure of molecular bond stability, with lower values corresponding to more stable bonds. The inverse creep modulus 1/J0 was taken as a measure of cell stiffness. Our results show a significant reduction in bond strength and bond number in vinculin knock-out cells and vin-tail cells. Cell stiffness was reduced in vinculin knock-out cells and vin-head cells. The effect of vin knock-out is more prominently in MEF than in F9 cells indicating cell-type specific differences. Our results show that the head-domain of vinculin is involved in adhesion strength and tail-domain in whole cell mechanics.

BP 5.8 Mon 12:45 H44

Directed cytoskeletal remodeling in response to integrin activation — •Carina Raupach, Claudia Tanja Mierke, Claus Metzner, and Ben Fabry — Zentrum für medizinische Physik und Technik, Universität Erlangen-Nürnberg

Binding of fibronectin-coated beads to the cell surface has been previously shown to trigger integrin clustering, recruitment of focal adhesion proteins, and directed cytoskeletal (CSK) remodeling (Galbraith *et al.* JCB (2002)). Moreover, these events have been shown to depend on bead size and bead binding time. To quantify CSK remodeling triggered by integrin activation, we measured the spontaneous motion of fibronectin-coated beads bound to carcinoma cells. We analyzed bead binding times ranging from 15 min to 7 h, and used beads with diameters of 0.5, 1, 2 and 4.5 μm. From the bead trajectories we computed the mean square displacement (MSD) and the persistence of motion, $p_\phi \in [-1, 1]$. For all bead sizes and binding times, the MSD followed a power law, $\Delta r^2(\Delta t) = D \cdot \Delta t^\beta + c$, with a motion that was superdiffusive ($\beta > 1$) and directionally persistent ($p_\phi > 0$ for $\Delta t > 3$ s). Persistence p_ϕ (for $\Delta t = 3$s) and β decreased monotonically with increasing bead binding time from a highly persistent and nearly ballistic behavior (at 15 min) to a more undirected and random behavior (at 7 h). With increasing bead size, persistence p_ϕ and β increased monotonically. These data show that directionally persistent CSK remodeling is highly dependent on bead size, and continues, although with declining persistence p_ϕ, for several hours after the initial integrin receptor activation through bead binding.