BP 20: Cell adhesion, mechanics and migration I

Time: Tuesday 13:00–16:00 Location: HÜL 386

Topical Talk BP 20.1 Tue 13:00 HÜL 386

Catch bond interaction between glycosaminoglycans and cell surface sulfatase Sulf1 — Alexander Harder[1], Ann-Kristin Moeller[1], Fabian Milz[2], Philipp Neuhaus[2], Volker Walhorn[1], Thomas Dierks[2], and •Dario Anselmetti[1] — [1]Experimental Biophysics, Physics Faculty, Bielefeld University, D-33615 Bielefeld, Germany. — [2]Biochemistry I, Faculty of Chemistry, Bielefeld University, D-33615 Bielefeld, Germany.

In biological adhesion, the biophysical mechanism of specific noncovalent biomolecular interaction can be divided in slip- and catch-bonds, respectively. Conceptually, slip bonds exhibit reduced bond lifetime under increased external loads whereas catch-bonds, in contrast, increased lifetime for a certain force interval. Since 2003, a handful of biological systems such as the adhesive proteins P-Selectin and FimH have been identified to display catch bond properties.

Upon investigating the specific interaction between the unique hydrophilic domain (HD) of human cell-surface sulfatase Sulf1 against the native glycosaminoglycan (GAG) target heparan sulfate (HS) by single molecule force spectroscopy (SMFS), we found clear evidence of catch-bond behavior in this system. The HD, about 320 amino acids long and strongly positive charged, and the GAG-polymers, composed of up to 200 disaccharide units, were quantitatively investigated with atomic force microscopy (AFM) based dynamic force spectroscopy (DFS) as well as force clamp spectroscopy (FCS). The observed catch bond character of HD against GAGs was found to be specifically related to the GAG 6-O-sulfation site. Therefore, this behavior can also be found in HS-related GAGs like heparin and (to a lesser extent) dermatan sulfate whereas in contrast, only slip bond binding can be observed in a GAG system where these sites are explicitly lacking. Our observed catch bond binding data can be interpreted within the theoretical framework of a force mediated transition between two slip bond regimes modelled by a switchover within a double-well energy landscape. Interestingly, the transition occurs in a force interval of only 5 Piconewtons while the life-time of the adhesion bond increases approximately 5-fold for heparan sulfate and heparin.

BP 20.2 Tue 13:30 HÜL 386

Migration patterns of dendritic cells in response to chemokines — •Veronika Bierbaum, Eva Kiermaier, Jan Schwarz, Michael Sixt, and Tobias Bollenbach — IST Austria, Am Campus 1, 3400 Klosterneuburg, Austria

Dendritic cells are decisive components of the adaptive immune system. They navigate through tissues by sensing two different chemokines, CCL19 and CCL21. We develop a predictive physical description of dendritic cell migration as a function of the surrounding chemokine concentration fields. We are particularly interested in the role of cell size and shape in sensing and migration. We gain quantitative information about the influence of these parameters on cellular motion from in vitro assays. In these assays, cells are exposed to specific well-controlled combinations of the two different chemokines. We quantify the dynamics of the chemokine profiles and cell motion using time-lapse microscopy. In this way, we obtain ensembles of cell trajectories, which we use to identify the key parameters that control cellular motion in varying environments. Our preliminary results indicate that dendritic cells perform a random walk in the absence of any chemokine gradient. The observed trajectories are generally well captured by Langevin equations, enabling us to separate the stochastic and deterministic contributions to the directionality and velocity of the moving cells. We further find that dendritic cells show qualitatively different migration behaviors for the two types of chemokines. Our combined experimental-theoretical study will enable us to identify general principles of cellular responses to chemokines that ensure robust cell migration.

BP 20.3 Tue 13:45 HÜL 386

Model-based Traction Force Microscopy Reveals Differential Tension in Stress Fibers — •Christoph A. Brand[1,2], Jérôme R. D. Soiné[1,2], Jonathan Stricker[3], Patrick W. Oakes[3], Margaret L. Gardel[3], and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University — [2]Bioquant, Heidelberg University — [3]Gordon Center for Integrative Science, University of Chicago, USA

Adherent tissue cells use self-generated mechanical forces to probe and adapt to their mechanical environment. Traction force microscopy (TFM) has been successfully employed to obtain cellular forces transmitted to elastic substrates via cell-matrix adhesions. However, traction reconstruction represents an ill-posed problem and requires regularization to estimate optimal solutions. Here we introduce a novel technique termed model-based traction force microscopy (MB-TFM) to increase the predictive power of TFM and to reduce the effect of noise. In a first step, image processing of fluorescence microscopy data for focal adhesions and the actin cytoskeleton is used to identify contractile structures and attachement points. In a second step, these data are converted into a mechanical model of the cell using recent advances in modeling whole cell contractility with an actively contracting cable network. In a third step, we optimize the intracellular tension configuration for the best agreement between measured and simulated substrate displacement fields. As a first application, we show that different types of stress fibers are characterized by different tension levels.

BP 20.4 Tue 14:00 HÜL 386

Directional Motors Move on Cell Surface and Give Rise to Gliding Motility and Sporulation in M. xanthus — •Fabian Czerwinski[1], Morgane Wartel[2], Adrien Ducret[2,3], Shashi Thutupalli[1], Anne-Valerie Le Gall[2], Emilia Mauriello[2], Ptissam Bergam[2], Yves Brun[3], Joshua Shaevitz[1], and Tam Mignot[2] — [1]Institute for Integrative Genomics, Princeton University — [2]Institut de Microbiologie de la Méditerranée, CNRS Marseille — [3]Department of Biology, Indiana University, Bloomington

Eukaryotic cells utilize an arsenal of processive transport systems to deliver macromolecules to specific subcellular sites. In prokaryotes, such transport mechanisms have only been shown to mediate gliding motility, a form of microbial surface translocation. Here, we show that the motility function of the Myxococcus xanthus Agl-Glt machinery results from the specialization of a versatile class of bacterial transporters.

Specifically, we used fluorescence microscopy and optical traps to demonstrate that the Agl motility motor is modular and dissociates from the rest of the gliding machinery (the Glt complex) to bind the newly expressed Nfs complex, a close Glt paralogue, during sporulation. Following this association, the Agl system transports Nfs proteins directionally around the spore surface. Since the main spore coat polymer is secreted at discrete sites around the spore surface, its transport by Agl-Nfs ensures its distribution around the spore. Thus, the Agl-Glt/Nfs machineries may constitute a novel class of directional bacterial surface transporters that can be diversified to specific tasks depending on the cognate cargo and machinery-specific accessories.

BP 20.5 Tue 14:15 HÜL 386

Magneto-aerotaxis in different strains of Magnetotactic bacteria — •Livnat Landau[1,2], Christopher T. Lefèvre[1], Mathieu Benneta[1], Peter Vach[1], Dennis A. Bazylinski[3], Richard B. Frankel[4], Stefan Klumpp[2], and Damien Faivre[1] — [1]Department of Biomaterials, Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany — [2]Department of Theory and Bio-Systems, Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany — [3]University of Nevada at Las Vegas, School of Life Sciences, Las Vegas, Nevada 89154-4004 USA — [4]Department of Physics, California Polytechnic State University, San Luis Obispo, California 93407, USA

Magnetotactic bacteria align and swim along magnetic field lines in order to facilitate positioning at an optimal oxygen concentration. Magnetic navigation is accomplished through special magnetic organelles, the magnetosomes, biomineralized, membrane-coated magnetic nanoparticles. We have characterized the magneto-aerotactic behavior of twelve magnetotactic bacteria with various morphologies, phylogenies, physiologies and flagellar apparatus. We have observed five different magneto-aerotactic behaviors that can be described as a combination of distinct mechanisms. Finally, we adapted a model for bacterial aerotaxis to describe magneto-aerotaxis with several different sensing mechanisms. Different sensing mechanisms lead to different behaviors in the presence of conflicting information, i.e. when the magnetic field points in a different direction relative to the oxygen gradient than in the natural environment.

15 min. break

Invited Talk BP 20.6 Tue 14:45 HÜL 386

Synthetic mechanobiology: Dissecting and rewiring force-based signaling — •Sanjay Kumar — University of California, Berkeley, USA

Living cells encounter a variety of mechanical signals encoded within their microenvironment, and these inputs can strongly regulate many fundamental cell and tissue behaviors. Here we present two complementary approaches we have recently created and applied to dissect and genetically manipulate this force-based signaling in living cells. First, we have used laser nanosurgery to spatially map the nanomechanical properties of actomyosin stress fibers. We have combined this approach with advanced molecular imaging tools (FRAP, FRET) to relate intracellular tensile forces to the conformational activation of mechanosensory proteins at the cell-extracellular matrix interface and the activities of specific myosin activators and isoforms. Second, we have used the tools of synthetic biology to precisely control the expression and activation of mechanoregulatory proteins in single cells using multiple mutually orthogonal inducer/repressor systems. This capability has enabled us to quantitatively elucidate relationships between signal activation and phenotype and to deconstruct complex signaling networks. In addition to improving our understanding of force-based signaling, these approaches are enabling us to "rewire" how cells communicate with their physical microenvironment, which we view as an important first step towards instructing cell behavior at interfaces between living and nonliving systems.

BP 20.7 Tue 15:15 HÜL 386

Blood platelet dynamics on structuredsubstrates — •Rabea Sandmann and Sarah Köster — University of Göttingen, Institut for X-Ray Physics, Friedrich-Hund Platz 1, 37077 Göttingen, Germany

Blood platelets are the first cells to interact with implants and build a scaffold into which other cells are embedded. The implant's surface texture plays an important role for platelet behavior and thus for the correct incorporation of implants into the body. We investigate the reaction of platelets to microstructured surfaces by studying their spreading dynamics as well as the formation of cell protrusions (filopodia and lamellipodia). We observe, that on structured substrates, spreading takes more time than on flat substrates. This may be attributed to the decreased number of filopodia and the preference of these filopodia for certain directions. The spread area over time shows a sigmoidal shape and its turning point coincides with the transition from filopodia to lamellipodia. The phase of cellular retraction that follows spreading starts primarily over the holes. This behavior can be explained, since the parts of the cell that span over the holes are probably the mechanically most instable parts. When the spread area has decreased to values close to those at the turning point, new filopodia are formed. This leads us to the conclusion that platelets can detect their area and react to an area decrease by formation of filopodia to start the spreading process anew.

BP 20.8 Tue 15:30 HÜL 386

modulation of t-lymphocyte adhesion forces by activation with tnf — •qian li[1], constanze lamprecht[1], dieter adam[2], and christine selhuber-unkel[1] — [1]Biocompatible Nanomaterials, Institute for Materials Science, University of Kiel, Germany — [2]Institute of Immunology, University of Kiel, Germany

Integrin-mediated T-lymphocyte adhesion to endothelial cells is a crucial step in the mammalian inflammatory response and the elimination of pathogens. In recent years, the outside-in signalling pathway of integrins in response to the proinflammatory cytokine tumor necrosis factor (TNF) was thoroughly studied. In addition, also an inside-out signalling pathway of integrins in lymphocyte activation by TNF has been reported. How this activation modulates T-lymphocyte adhesion strength and dynamics is still not understood at all. We have chosen a biophysical approach to address this question and applied single-cell force spectroscopy (SCFS) to investigate T-lymphocyte (Jurkat E6-1) cell adhesion to fibronectin, which is naturally present on top of endothelial cell layers. In detail, we approached single Jurkat E6-1 cells to fibronectin-coated surfaces and analyzed cell detachment forces. We found that the addition of TNF significantly increased the maximum adhesion force and detachment energy of the cells, even at sub-second timescales.

BP 20.9 Tue 15:45 HÜL 386

Modeling ring formation in cell adhesion — •Daniel Schmidt[1,2], Timo Bihr[1,2], Udo Seifert[2], and Ana-Sunčana Smith[1] — [1]Inst. f. Theor. Physik and Excellence Cluster: Engineering of Advanced Materials, Universität Erlangen-Nürnberg — [2]II. Inst. f. Theor. Physik, Universität Stuttgart

Cellular adhesion is mediated by pairs of adhesion molecules which form bonds. A famous example is the immune synapse where the adhesion of membranes of antigen presenting cells and different cells of the immune system takes place. The key step in this process involves two pairs of binding partners which upon recognition form a ring pattern, in a process that has not yet been fully understood. We study necessary conditions for the formation of rings in a minimal model within a newly developed Monte Carlo scheme. This simulation framework allows us to simulate the entire adhesion process on experimentally observed time and length scales while maintaining the full information about membrane transmitted cooperative effects between individual adhesion molecules. We show that the competition between the recruitment of adhesion molecules into the zone of contact between two cells and the binding kinetics between pairs of binders is sufficient to trigger this particular pattern formation. We find that the ring is transient if one of the binders is immobilized before molecular recognition takes place. However, if both adhesion molecules are mobile, the ring is stabilized through by membrane induced correlations and the ring becomes meta-stable. We compare our results to alternative theoretical models and to experiments in cell-mimetic systems.