BP 16: Posters: Cell adhesion, mechanics and migration

Time: Monday 17:30–19:30 Location: Poster A

BP 16.1 Mon 17:30 Poster A

Real-time deformability cytometry - a theoretical and experimental analysis — •Alexander Mietke[1,2,3], Oliver Otto[3], Salvatore Girardo[3], Philipp Rosendahl[3], Anna Taubenberger[3], Elke Ulbricht[3], Stefan Golfier[3], Jochen Guck[3], and Elisabeth Fischer-Friedrich[1,2] — [1]Max Planck Institute for the Physics of Complex Systems, Noethnitzer Strasse 38, Dresden, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, Dresden, Germany — [3]Biotechnology Center, TU Dresden, Tatzberg 47/49, 01307 Dresden, Germany

Cell stiffness is a sensitive indicator of physiological and pathological changes in cells with many potential applications in biology and medicine. A new method, Real-Time Deformability Cytometry (RT-DC), probes cell stiffness at high throughput by exposing cells to a shear flow in a microfluidic channel allowing for mechanical phenotyping based on single cell deformability. However, observed deformations of cells in the channel are not only determined by cell stiffness, but also depend on flow speed and cell size relative to channel size. Here, we disentangle mutual contributions of cell size, flow speed and cell stiffness to cell deformation by a theoretical analysis in terms of hydrodynamics and linear elasticity theory. Performing RT-DC experiments on both, model spheres of known elasticity and biological cells, we demonstrate that our analytical model predicts the deformation inside the channel and allows for quantification of cell mechanical parameters making cell stiffness accessible in high-throughput measurements.

BP 16.2 Mon 17:30 Poster A

Dynamics of blood platelet spreading on elastic substrates — •Aishwarya Paknikar[1], Rabea Sandmann[1], Noam Nisenholz[2], Assaf Zemel[2], and Sarah Köster[1] — [1]1Institute for X-Ray Physics, Georg-August-Universität Göttingen, Germany — [2]2Institute of Dental Sciences and Fritz Haber Center for Molecular Dynamics, Hebrew University of Jerusalem, Israel

Platelets, essential for repairing of damaged blood vessels spread at the site of injury and impressively rearrange their acto-myosin cytoskeleton. In vivo, platelets function in a variety of mechanical environments ranging from soft to stiff tissues. The mechanical response of platelets to such different environments is still elusive. Hence, we investigate the spreading dynamics of single platelets on elastic (Esub in the physiological range of 1-100 kPa) polyacrylamide (PAA) gels. We observe that the final platelet spread area increases with increasing values of Esub and the most pronounced sensitivity to stiffness lies below 40 kPa. The time-dependent platelet spread area curves on soft substrates show various irregular spreading profiles, which we classify as monotonic, non-monotonic and damped oscillatory, whereas the spreading profiles on the stiff substrates are majorly regular and monotonic. We present an elastic theory, which predicts that these different spreading profiles of platelets arise due to the different timescales of the myosin activity response. We characterize the spreading by analyzing the temporal evolution of the spread area and perimeter and aim at building a mechanical model for platelet dynamics on a single-cell level.

BP 16.3 Mon 17:30 Poster A

Growth-induced pressure of yeast populations — •Jörn Hartung[1], Morgan Delarue[2], and Oskar Hallatschek[1,2] — [1]MPI DS, Göttingen, Germany — [2]UC Berkeley, CA, USA

Confined cells exert forces onto their surroundings during proliferation [1]. On the one hand these forces can redesign the population's microenvironment. In the case of microbes this can lead for instance to biofouling [2]. On the other hand these growth-induced forces imply a feedback onto the growing cells themselves, which can alter their morphology [3].

We designed a microfluidic device, which enables us to measure the growth-induced pressure confined S. cerevisiae populations exert onto a deformable PDMS membrane. Furthermore, we are able to control the chemical as well as the mechanical conditions the populations experience by employing nutrient channels and passive valves with different degrees of confinement, which we designed. The cells are subject to growth-induced steady state pressures ranging from 0.1 to 1.0 MPa.

[1] Markus Basan, Thomas Risler, Jean-François Joanny, Xavier Sastre-Garau and Jacques Prost, HFSP Journal (2009)

[2] T. Warsheid and J. Braams, Intl. Biodet. And Biodegrad. (2000)

[3] P. S. Stewart and C. R. Robertson, Applied microbiol. and biotech. (1989)

BP 16.4 Mon 17:30 Poster A

Spreading and force generation of blood platelet dynamics on soft and structured substrates — •Jana Hanke, Rabea Sandmann, and Sarah Köster — Institute for X-Ray Physics, University of Göttingen, Germany

Blood platelets play a crucial role in wound closure by attaching to the wounded site and spreading over it to form a temporary seal. Not only do they encounter wounded sites of different stiffness and topography, they also are the first cells to get in contact with (nanostructured) implants. To examine the influences of these cues, we perform live cell experiments on soft substrates and on substrates containing micrometer sized holes. By comparing spreading dynamics on microstructured and on flat substrates, we show that although the final spread area is maintained, platelets show an adaptation of spreading to the underlying substrate. By following cellular protrusions over time, we find that the number of filopodia influences the adaptation to the substrate suggesting that the pathways of spreading (via filopodia/lamellipodia) influences how well the platelets can cope with the underlying substrate. In order to study stiffness dependent force generation, we perform time-resolved Traction Force Microscopy (TFM). As blood platelets are much smaller than other cells that have been studied so far by TFM, it is important adjust both the experimental set-up as well as the analysis. To this end, the imaging resolution has to be enhanced by means of optical set-up, beads size and density. The analysis is performed by a combination of Particle Image Velocimetry, Lagrangian particle tracking and Fourier Transform Traction Cytometry.

BP 16.5 Mon 17:30 Poster A

Migration Behavior of Human Mesenchymal Stem Cells on Biomimetic Elastic Substrates — •Daniel Meyer[1], Felix Segerer[2], Joachim Rädler[2], and Florian Rehfeldt[1] — [1]3rd Institute of Physics - Biophysics, Georg-August University, Göttingen, Germany — [2]Faculty of Physics - Soft Condensed Matter Group, Ludwig-Maximilians-University, Munich, Germany

Cell motility and migration processes are vital during biological development and homeostasis, as they are essential in tissue regeneration, morphogenesis, but also in pathological mechanisms like tumor metastasis. While migration due to biochemical gradients (e.g. chemotaxis) is very well studied, the influence of other parameters of the microenvironment such as topography and stiffness are less understood.

Here, we use polyacrylamide (PA) hydrogels in combination with a novel microcontact printing protocol to generate patterned substrates with well-controlled Young's modulus E. These collagen I coated tracks are used to analyze the migration behavior of human mesenchymal stem cells (hMSC) by parallelized life cell microscopy to achieve sufficient statistics.We demonstrate that both, elasticity as well as width of the track affect the migration velocity and there is a particular optimum that yields a maximal velocity.

BP 16.6 Mon 17:30 Poster A

Analysis of Cell Trajectories with Restricted Boltzmann Machines — •Barbara Feulner, Julian Steinwachs, Christoph Mark, Ben Fabry, and Claus Metzner — Biophysics Group, Univ. of Erlangen-Nürnberg

We report the unsupervised analysis of cell migration trajectories for an automated classification of tumor cells. We track individual cells within collagen gels and on differently coated surfaces and map the cell trajectories to binary time series of forward and backward steps in an arbitrary (x or y) direction. Sections of these binary time series are used as input data vectors for a Restricted Boltzmann Machine (RBM), a generative stochastic neural network. We demonstrate that RBMs are able to extract, or 'learn', the complex underlying probability distribution of the binarized cell trajectories. After training, the RBMs generate surrogate trajectories that reproduce the statistical properties of the training data. Moreover, the RBMs can classify new trajectory segments and determine if they conform to the same statistics as the training data. Strikingly, RBMs are more sensitive to small differences in cell migration behavior than traditional statistical methods, such as the mean squared displacement or the step width dis-

tribution. This finding suggests that RBMs may be used as a tool for assessing the potential malignancy of tumor cells from patient biopsies.

BP 16.7 Mon 17:30 Poster A

Unique mechanical properties of cell nuclei regulated by chromatin — •Chii Jou Chan[1,2], Wenhong Li[2], Jana Scholze[2], Mirjam Schürmann[2], and Jochen Guck[1,2] — [1]Cavendish Laboratory, Department of Physics, University of Cambridge, UK — [2]Biotechnology Center, TU Dresden, Dresden, Germany

Nuclear mechanics could affect gene regulation and gene expression. Chromatin, a major component of cell nuclei, could play an important role in maintaining nuclear integrity and their mechanical properties. Previous studies on nuclear mechanical properties focused largely on the role of the nuclear lamina, using techniques such as AFM and micropipette aspiration. In this work, we explicitly address the contributions of chromatin to nuclear rheology after isolation from the cell using a microfluidic optical stretcher. We find that isolated nuclei swell under uniaxial stress and exhibit significant softening with increased nuclear size, which can be described by a filtration model for the nuclear membrane encasing a cortical layer of chromatin. Changes to the state of chromatin condensation via histone modifications or chromatin remodeling processes (ATP, topoisomerase II) can strongly impact nuclear morphology and compliance. Moreover, isolated nuclear mechanics is sensitive to ionic conditions: nuclei stiffen with increasing ionic strength of the buffer and contract during optical stretching in the presence of multivalent ions. The presented work establishes a quantitative link between nuclear mechanical properties and the compaction state of chromatin, which can be modulated by osmotic stress, chromatin remodeling or electrochemical environment.

BP 16.8 Mon 17:30 Poster A

Traction Force Microscopy during Phagocytosis — •Wolfgang Gross and Holger Kress — Department of Physics, University of Bayreuth, Bayreuth, Germany

In the process of phagocytosis, cells internalize micrometer-sized objects like bacteria and dead cells, thus being a main function of innate immunity. After the detection of foreign particles, the membrane starts to wrap around the phagocytic target. This so-called phagocytic cup is mechanically supported by the polymerization of actin filaments in combination with myosin motors. Even though the molecular players have been identified, there is only few quantitative data describing the dynamics of the major regulators. Using the technique of traction force microscopy (TFM), we measure cellular forces during phagocytosis in a spatially and temporally resolved manner. As a substrate, we use thin polyacrylamide films with a thickness of a few tens of micrometers. To characterize the rheology of these films, we put millimeter sized steel spheres on the surface which are indenting the substrate. Our results suggest linear elasticity and a poisson value close to 0.5 for most gels, depending on the polymerization conditions. The results are consistent for multiple sphere radii and were verified by bulk tensile tests for different elastic moduli from 5 to 20 kPa. TFM allowed us to quantify forces, which J774-A1 macrophages exert when adhering to a fibronectin-coated gel. Preliminary data regarding phagocytosis shows the distribution of contractile forces in direct vicinity of the phagocytic target. We anticipate our results to pave the way for a more quantitative understanding of phagocytosis.

BP 16.9 Mon 17:30 Poster A

Investigation of Cell Adhesion and Motility on Microstructured Substrates — •Daniel Geiger[1], Ulla Nolte[1], Susanne Rappl[1], Michael Beil[2], and Othmar Marti[1] — [1]Institute of Experimental Physics, Ulm University — [2]Department of Internal Medicine, University Hospital Ulm

Interaction between cells and artificial materials is of prime importance for many medical applications like implant technology. An interface can be considered as external stimulus and therefore, for example, affecting differentiation and viability of cells.

For that reason, the behaviour of cells on microstructured substrates is investigated by means of fluorescence microscopy, electron microscopy and common video microscopy. Main emphasis is put on the study of their adhesion properties, e.g. the distribution and formation of focal adhesions. Therefore, immunostaining of specific proteins like vinculin and surface sensitive techniques like total internal reflection microscopy (TIRFM) or electron microscopy of surface sections are used.

Structuring of the substrates is done by UV exposure of a PLL-g-PEG layer on glass through a mask that enables creation of features as small as one micrometer. Subsequent addition of fibronectin creates a strong contrast to the non-illuminated PEG covered sites.

BP 16.10 Mon 17:30 Poster A

Probing the Initial Steps of Bacterial Biofilm Formation: Dynamic and Molecular Principles of Surface Based Cell Motility and Mechano-Sensing — •Nora Sauter[1,2], Matteo Sangermani[3], Urs Jenal[2,3], and Thomas Pfohl[1,2] — [1]Department of Chemistry, Universität Basel — [2]Swiss Nanoscience Institute, Universität Basel — [3]Biozentrum, Universität Basel

We use a microfluidic-based optical tweezers set-up to probe the initial steps of bacterial biofilm formation and to gain further insights into the principles of mechano-sensing. The model bacteria Caulobacter crescentus has two different stages in its life cycle: It starts as a swarmer cell and develops into a stalked cell when it comes into contact with a surface. A single swarmer cell is caught by an optical trap and approached to the surface of a colloidal particle, which is held by a second trap. The set-up allows for studies of the approaching and adhesion characteristics of Caulobacter to different surfaces - colloid particles with different surface coatings - in a controlled manner. Caulobacter swarmer cells adhere to surfaces through their pili followed by irreversibly bonding through the formation of a holdfast. Preliminary studies have led to a model where mechano-sensing occurs by pili-mediated obstruction of the flagellar rotary motor when the bacterium is close to the surface. Our set-up allows for the measurement of forces when the bacterium is approaching the surface, of the obstruction of the flagellar motor and in parallel of the exact distances between cell and surface. The experiments will help to gain further insights into the processes involved in mechano-sensing and adhesion of bacteria.

BP 16.11 Mon 17:30 Poster A

Topography and elasticity measurements on squamous carcinoma cells by AFM — •Tanja Schreyer[1], Susanne Steeger[1], Stefan Hansen[2], Jörg Schipper[2], and Mathias Getzlaff[1] — [1]Heinrich-Heine-Universität Düsseldorf, Deutschland — [2]Univ.-HNO-Klinik Düsseldorf, Deutschland

In this contribution we report on measurements of the mechanoelastic properties of squamous carcinoma cells. This study of single cancer cells in culture medium is carried out by Atomic Force Microscopy. In order to determine the elasticity of the cancer cells by calculating the Youngs modulus in the Hertz model we take force distance curves. We analyse and compare the different stiffnesses dependent on a position within one single cell. Accordingly we are able to avoid interfering effects of the substrate. This strategy is applied to the different densely populated areas of a cell culture. In addition we are interested in the various topography of the cells within a cell culture. In this way we are able to characterise the different cell types of the culture in order to relate their stiffness and their visual appearence.

BP 16.12 Mon 17:30 Poster A

Unbiased analysis of superstatistics in tumor cell migration — •Christoph Mark, Claus Metzner, Julian Steinwachs, and Ben Fabry — FAU University of Erlangen-Nürnberg, Department of Physics, Biophysics Group

We present experimental data showing that migrating tumor cells exhibit highly heterogeneous dynamics - in time as well as across the ensemble. Successive steps $\vec{u}_t$ of the cell's trajectory can locally be described as a discrete persistent random walk, with $\vec{u}_t = q\vec{u}_{t-1} + a\vec{\epsilon}_t$, however, the persistence q and the migratory activity a change over longer timescales. These superstatistical changes can in turn be described by another stochastic process $(q(t), a(t))$, leading to a hierarchical probabilistic model. We describe the superstatistical process as an uncorrelated random walk and infer its parameters from measured cell trajectories with an unbiased Bayesian inference approach using an advanced Hamiltonian Monte Carlo method. This method allows for reliable probabilistic inference without further prior assumptions. We apply our method to data from migrating tumor cells on planar surfaces with and without fibronectin coating, and in 3D collagen matrices. The resulting joint distribution and temporal correlations of the superstatistical parameters show distinct and characteristic features depending on the dimensionality and adhesiveness of the environment.

BP 16.13 Mon 17:30 Poster A

Mechano-sensing of cells on elastic substrates — •Galina Kudryasheva and Florian Rehfeldt — 3rd Institute of Physics Biophysics, Georg-August-University, Göttingen, Germany

It is nowadays well acknowledged that cellular functions, morphology and also differentiation is dependent on the mechanical microenvironment. For example, human mesenchymal stem cells (hMSCs) can be guided to differentiate into various cell types when cultured on appropriate elastic substrates. While the entire differentiation process takes several days up to weeks, the structure and dynamics of the actomyosin fibers can be used as an early morphological marker and modelled using classical mechanics with an active spring model. We use this approach to analyze the mechanical cell-matrix interactions of hMSCs and differentiated cells during their mechano-differentiation process. We use an immunofluorescence approach to label stress fibers and analyze cytoskeletal morphology by fluorescence microscopy. hMSCs and differentiated cells were plated on elastic poly-acrylamide (PA) hydrogels with different Young's moduli E (1-30 kPa). We analyze cell shape and alignment of stress fibers by an order parameter as early morphological marker and extract corresponding material constants that show distinct differences during the differentiation process.

BP 16.14 Mon 17:30 Poster A

Inducing cell mechanical responses using optical tweezers — •Rebecca Michiels and Alexander Rohrbach — Lab for Bio- and Nano-Photonics, University of Freiburg, Georges-Koehler-Allee 102, 79110 Freiburg, Germany

Cells have the ability to both sense mechanical stimuli as well as apply controlled mechanical forces to their environment. Examples are cell migration, the anchoring of the cell on substrates and the uptake of particles in phagocytosis. These processes require complex intracellular remodeling involving reorganization of the actin cytoskeleton in cooperation with molecular motors. Many of the underlying physical principles of how cells tune their reactions to external mechanical stimuli are little understood.

We use a microscope setup in which we combine conventional DIC microscopy together with optical tweezers and particle tracking. Polystyrene beads are held in an optical trap to enable controlled placement in the vicinity of the cells. The motion of the bead in the trap can be tracked in 3D with nanometer precision at a microsecond timescale using back focal plane interferometry. This configuration enables us to induce and analyze cellular responses in a reproducible investigation scheme.

By varying the spatiotemporal pattern and the intensity of stimuli we want to gain deeper insights into the physics governing cell mechanics. We present first results from novel experiments using optical traps to trigger response patterns in cells.

BP 16.15 Mon 17:30 Poster A

Analyzing the influence of external shear stress on cellular force generation with cell traction force microscopy — •Maja Gulic[1], Thomas Kerst[1], Manfred Frick[2], Anita Ignatius[3], and Kay-E. Gottschalk[1] — [1]Institute for Experimental Physics, Ulm, Germany — [2]Institute of General Physiology, Ulm, Germany — [3]Institute of Orthopaedic Research and Biomechanics, Ulm, Germany

External shear stress influences cell properties like cell shape or migration. Important components of the cell migration machinery are integrins, the actin cytoskeleton and messenger proteins. Connection of these components leads to assembly of focal adhesions and thus generation of traction forces. Using cell traction force microscopy we have the possibility to examine these forces under different conditions.

We fabricated polydimethylsiloxane micropost arrays via photolithography. Measuring the deflection of a micropost during cell adhesion made it possible to calculate the cellular force. We examined various cell lines, with and without applied shear stress. The AT I like rat epithelial cell line R3/1 and the adenocarcinomic human alveolar epithelial cell line A549, as an in vitro model for a AT II cell, were used in our experiments. Applying shear stress simulates the negative effects of pulmonary diseases whereupon liquid occlusions in the lung might produce fluid wall shear stress during breathing. In addition we examined the osteocyte-like cell line MLO-Y4. Osteocytes are known to react to fluid shear stress occurring in the canalicular system in bones. In vitro studies showed e.g. upregulation of cell proliferation after inducing shear stress.

BP 16.16 Mon 17:30 Poster A

Early cell adhesion on hydrogels with graded stiffness and ligand affinity — •Christina Müller and Tilo Pompe — Universität Leipzig, Institut für Biochemie, Johannisallee 21-23, 04103 Leipzig

Mechanotransduction is known as one control mechanism for several basic cell functions, like proliferation, differentiation and cell death. For a better understanding of mechanotransduction, we investigated early cell adhesion on hydrogels with an independent variation of substrate stiffness and affinity of adhesion ligands to the hydrogel surface. Thin film coatings of maleic acid copolymers on top of polyacrylamide hydrogel layers were fabricated to tune protein binding to the hydrogel surface. The stiffness of the hydrogel was modulated between 2.5 kPa and 9 kPa. Human umbilical vein endothelial cells were monitored during the first two hours of cell adhesion by time-resolved cell traction force microscopy. Three different regimes of traction force generation were found. In the first regime (R0) cells spread fast, but traction forces were negligibly small. In the second regime (R1) spreading slowed down and traction forces increased until they saturated in the last regime (R2). The force curve characteristics, for instance the slope in R1 and the saturation force in R2 were substrate-dependent. From 2.5 kPa to 5 kPa both parameters showed a tremendous increase and leveled off for 9 kPa hydrogels. For the two polymer coatings an offset in the averaged forces additive to the stiffness dependence could be observed in positive correlation to protein affinity to the substrate surface. These results can be interpreted as a superposition of conservative and dissipative processes in cell adhesion.

BP 16.17 Mon 17:30 Poster A

Examining the influence of size and shape of a particle on phagocytic uptake — Iris Kuntz, •Rebecca Michiels, and Alexander Rohrbach — Lab for Bio- and Nano-Photonics, University of Freiburg, Georges-Köhler-Allee 102, 79110 Freiburg, Germany

Phagocytosis is the process of a cell engulfing and uptaking a particle. This mechanism plays an important role in the functioning of our immune system. However, the influence of the particles'size and shape on the mechanisms and probability to uptake the particle is not clear yet.

We use a high-resolution light microscope equipped with optical tweezers and 3D interferometric particle tracking to induce phagocytic uptake of polystyrene micro-particles of different diameter. Using J774 mouse macrophages, we investigate the influence of variable contacting times and patterns until a defined response of the cell is measurable. First results are presented.

BP 16.18 Mon 17:30 Poster A

Examining the influence of size and shape of a particle on phagocytic uptake — Iris Kuntz, •Rebecca Michiels, and Alexander Rohrbach — Lab for Bio- and Nano-Photonics, University of Freiburg, Georges-Köhler-Allee 102, 79110 Freiburg, Germany

Phagocytosis is the process of a cell engulfing and uptaking a particle. This mechanism plays an important role in the functioning of our immune system. However, the influence of the particles' size and shape on the mechanisms and probability to uptake the particle is not clear yet.

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BP 16.19 Mon 17:30 Poster A

Characterizing the elasticity of fibroblast cell nuclei by atomic force microscopy(AFM) to characterize Lamin and TMEM43 mutations — •Sören Grannemann[1], Ann-Christin Moritzer[1], Helene Schellenberg[1], Astrid Kassner[2], Volker Walhorn[1], Hendrik Milting[2], and Dario Anselmetti[1] — [1]Biophysics, Bielefeld University,Germany — [2]Heart and Diabetes Center NRW, Bad Oeynhausen,Germany

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited heart muscle disease associated with cardiac arrhythmia and sudden cardiac death predominantly of young and athletes [1]. Mutations in the intermediate filament lamin and the protein luma are known to be related to ARVC [2,3]. Both proteins are located at the nuclear envelope. Since the cell nucleus has to resist strong mechanical stress during the contraction phase of the heart muscle, we hypothesized that the mutations affect the functional mechanical properties of the nucleus.

Hence, we explored the elastic modulus of cell nuclei with the AFM. The measurements were performed with skin fibroblasts, which serve as a model system for cardiomyocytes. We analyzed a set of lamin and luma mutated cells and compared them to a control group consisting of wild-type fibroblasts and mutations not associated with ARVC.

The luma mutant showed much higher and widespread elastic moduli, whereas the elasticity of the lamin mutant is similar to the control group [4]. As luma associated ARVC exposes an explicit gender dimorphism we also investigated the impact of testosterone on the elasticity.

BP 16.20 Mon 17:30 Poster A

Model-based traction force microscopy reveals differential tension in cellular actin bundles — •Christoph A Brand[1,2], Jérôme RD Soiné[1,2], Jonathan Stricker[3], Patrick W Oakes[3], Margaret L Gardel[3], and Ulrich S Schwarz[2] — [1]These authors contributed equally — [2]Institute for Theoretical Physics and BioQuant, Heidelberg University, Philosophenweg 19, 69120 Heidelberg, Germany — [3]Institute for Biophysical Dynamics, Department of Physics, and The James Franck Institute, University of Chicago, Chicago, IL 60637, USA

Animal tissue cells continuously probe the mechanical properties of their environment, with dramatic consequences for cell adhesion, migration, differentiation and fate. Cellular forces originate mainly from the actomyosin system and are transmitted to the extracellular space via focal adhesions. A method called traction force microscopy has been developed to quantify these forces from the deformation of soft elastic substrates and to correlate them with observable structures of the cytoskeleton. For strongly adherent cells, major force generators are actin stress fibers, which have further been classified into different subtypes. However, the reconstruction of traction fields in this context is an ill-posed problem, which requires the use of regularization techniques. We present a new type of traction force microscopy that abolishes the need for regularization and allows us to directly estimate internal cell forces using a biophysical model for cell contractility. We use this method to demonstrate that ventral stress fibers are typically under higher tension than transverse arcs or dorsal stress fibers.

BP 16.21 Mon 17:30 Poster A

Mechanically tunable biomimetic hyaluronic acid based hydrogels — •Frederike Derksen and Florian Rehfeldt — 3rd Institute of Physics - Biophysics, Georg-August-University, Friedrich-Hund-Platz 1, 37077 Göttingen, Germany

Mechanical properties of the microenvironment of cells, e.g. matrix elasticity, influence many aspects of cell behavior including morphology, motility and even more complex processes such as differentiation. Therefore, it is important to design and characterize hydrogels for cell culture that resemble the in vivo environment of cells. Cross-linked hyaluronic acid (HA) matrices offer an alternative to conventionally used polyacrylamide hydrogels as HA is biocompatible and therefore not toxic for cells. Using different thiol modifications of HA, we prepare hydrogels with a well-defined elasticity in the physiologically relevant range of E = 0.1 kPa to 100 kPa, which is much softer than glass or tissue culture plastic. Another advantage is the possibility of preparing 3D culture environments by embedding cells during hydrogel polymerization. Gelation kinetics of the hydrogels were investigated by rheology using oscillatory deformation tests. Both the storage modulus G' as well as the loss modulus G" were measured in order to analyze the viscoelastic properties of the cross-linked hydrogels.

BP 16.22 Mon 17:30 Poster A

Symmetry breaking motility of Flavobacterium johnsoniae — •HsuanYi Chen — Department of Physics, National Central University, Taoyuan, Taiwan

A Flavobacterium johnsoniae moves on a substrate by processive adhesive proteins which are distributed in a close-loop track. Even in a homogeneous medium, the bacterium nevertheless breaks the front-rear symmetry and shows directional movement. I will show that at sufficiently high adhesive protein speed, the distribution of closed bonds between the proteins and the substrate has a bifurcation that leads to a directional movement for the bacterium. Such mechanism has the advantage that the bacterium can tune the adhesive protein speed to detect small gradient of nutrient or toxin in the environment.

BP 16.23 Mon 17:30 Poster A

Alteration of rolling adhesion in aged monocytes. — •Samira Khalaji[1], Lisa Zondler[2], Jochen Weishaupt[2], Veselin Grozdanove[2], Karin Danzer[2], Ulla Nolte[1], and Kay-E Gottschalk[1] — [1]Institut für Experimentelle Physik, Universität Ulm, Ulm, Germany — [2]Klinik für Neurologie , Universitätsklinikum Ulm, Ulm, Germany

Aging is associated with a deterioration in immune function. Consequently susceptibility to inflammation and degenerative age-related diseases are increased. This complicated multi-level process is among other factors mediated by activated cells of the innate immune system, such as monocytes. For instance, adhesion of monocytes to the artery walls is an important early step in the development of atherosclerotic lesions. The adhesion of monocytes often takes place at positions with exposed collagen. To study the effect of age on monocyte rolling and adhesion, 'human aged monocyte' (isolated from 8 individuals >48 years old) were compared to 'human young monocytes' (Isolated from 8 individuals 25-36 year old). We measured the adhesion rate and rolling velocity of monocytes on collagen coated microfluidic flow chambers at a shear stress of 0.6 dynes/cm2. The function of cells were compared additionally by their ability to be activated by lipopolysaccharide. Our results shows a significantly higher number of firmly adhered aged monocyte compared to the young monocytes (P=0.022) in LPS stimulated monocytes. This study shows that aging is associated with alterations in monocytes function, which may have beneficial implications for the development of studies regarding age-related diseases.

BP 16.24 Mon 17:30 Poster A

Microtubule-based intracellular transport: a liquid crystal approach — •Marco Linke[1,2], Vytaute Starkuviene-Erfle[2], and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University — [2]BioQuant, Heidelberg University

Mammalian cells show great variability in cell shape and intracellular structure 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 cellular organization is missing. In order to investigate the consequences for microtubule-based transport, here we model the microtubule cytoskeleton as a nematic liquid crystal and minimize the free energy functional considering biologically plausible boundary conditions. The resulting nematic director configuration describes the preferred transport direction inside the cell and is used to simulate vesicle transport from the cell periphery towards the perinuclear region. We compare the simulation results to experimental measurements of internalized integrin and investigate changes in the distributions caused by RNAi mediated knockdown of genes that are responsible for the regulation of endocytosis and intracellular transport.

BP 16.25 Mon 17:30 Poster A

Viscoelastic mechanics of non-adhering cells — •Samaneh Rezvani Boroujeni, Abhinav Sharma, and Christoph F. Schmidt — 3rd Institute of Physics - Biophysics, Georg-August-Universität Göttingen, Germany

Cells sense their micro-environment through biochemical and mechanical interactions. They can respond to biochemical and mechanical stimuli by undergoing shape- and possibly volume-changes. To understand such responses, one needs a quantitative model for the mechanical properties of a cell. The key components in determining the mechanical response of a cell are the viscoelastic properties of the actomyosin cortex, effective surface tension, and the osmotic pressure. We probe suspended rounded-up cells by active and passive microrheology and construct a model to describe the roles of the various components.

BP 16.26 Mon 17:30 Poster A

Cell response to lateral constraints — •Andreas Müller and Tilo Pompe — Universität Leipzig, Institute of Biochemistry, Johannisallee 21-23, 04109 Leipzig, Germany

Living cells are subjected to a plethora of exogenous cues which encompass chemical agents as well as physical quantities. One external regulator of cell fate that is often overlooked is spatial constraint, which is omnipresent in multicellular arrangements.

We show that a bimodal behavior for human umbilical vein endothelial cells, elicited by lateral constraints and indicated by changes in actin stress fiber spacing [1], persists despite changes in mechanical and biochemical parameters. We use soft hydrogel matrices micropatterned with adhesion proteins as substrates for biochemical inhibition assays and as substrates for cell traction force measurements of laterally confined cells. We find that inhibition of myosin activity does not lead to a change in bimodal behavior. Furthermore, the bimodal stress fiber behavior is also present in human dermal fibroblasts, hinting at geometry as a general regulator for cell behavior.

[1] Müller, A., Meyer, J., Paumer, T., Pompe, T. Cytoskeletal Transition in Patterned Cells Correlates with Interfacial Energy Model.

Soft Matter, 2014, 10, 2444-2452.

BP 16.27 Mon 17:30 Poster A

Cellular mechanics at the onset of phagocytosis — •Konrad Berghoff, Steve Keller, and Holger Kress — Department of Physics, University of Bayreuth, Universitätsstr. 30, 95447 Bayreuth

The phagocytic internalization and digestion of external objects by macrophages belongs to the most fundamental processes of the mammalian immune system. Phagocytosis can be induced by antibody recognition mediated by Fc receptors. Fc receptors give rise to intracellular signaling cascades which finally lead to particle uptake. The onset of particle uptake can be explained by a zipper-like mechanism consistent of a successive increase of receptor-ligand bonds at adjacent binding sites and subsequent membrane protrusion around the target object. The mechanics of this zipper-like interaction are not yet fully understood. We are therefore studying these mechanics on living cells. We hypothesize that the increasing number of ligand-receptor bonds during uptake leads to a temporally increasing rupture force necessary to break the bond between bead and cell. We also hypothesize that increasing local actin accumulation during the uptake results in local stiffening of the cellular uptake region. Using optical trapping in combination with high-speed image acquisition we test these hypotheses by inducing targeted single cell-particle binding between immunoglobulin-G coupled microbeads and J774 macrophages and by monitoring the cellular response when put under mechanical load. Our findings will give new insights on the mechanics of phagocytic uptake and will help to understand the role of zipper-like cell-membrane interactions and actin accumulation at the onset of phagocytosis.

BP 16.28 Mon 17:30 Poster A

Modelling adhesion of malaria-infected red blood cells — •Anil K. Dasanna and Ulrich S. Schwarz — Heidelberg University

During the blood stage of the malaria lifecycle, merozoites released by the infected liver infect healthy Red Blood Cells (RBC) which then develop adhesive protrusions on their surfaces. The infected RBCs adhere to endothelial cells in the microvasculature, leading to capillary obstruction. Using Brownian dynamics simulations, we modeled infected RBC as a spherical shell covered with knobs having multiple receptors on each knob. First, we studied adhesive strength of infected RBC as a function of its knob structure by applying an external loading. The adhesive strength or lifetime of receptor-ligand bond cluster depends on the density of knobs, external loading, and the mean number of receptors per knob. We also simulated the capture efficiency of infected RBC in hydrodynamic shear flow. We will discuss different dynamic states such as rolling adhesion, firm adhesion and free motion, which depend on flow strength and bond kinetic rates. Finally we will briefly discuss the ongoing work on non-spherical cell shapes and explicit modeling of the shapes which corresponds to in vivo situation.

BP 16.29 Mon 17:30 Poster A

Characterization of intracellular phagosome transport — •Steve Keller, Konrad Berghoff, and Holger Kress — Department of Physics, University of Bayreuth, Bayreuth, Germany

As one of the key processes during the immune response, phagocytosis of bacteria plays a significant role in the mammalian immune system. During phagocytosis invaders larger than a few hundred nanometers are internalized by macrophages followed by lysosome fusion and digestion. A key part of this maturation process is the phagosomal transport from the cell membrane to the perinuclear region. While on average, phagosomes are transported to this region, individual phagosomes undergo complex motion which frequently consists of directed transport with interjacent phases of putative random motion. Up to now it is largely unknown what determines these high phagosome to phagosome variations of the individual transport paths. Natural differences between these phagosomes in vivo are their size and shape as well as the position, where the first contact to the cell membrane and the subsequent engulfment occurs. To investigate these naturally occurring phagosome variations systematically, we move IgG-coupled polystyrene beads with different diameters to well-defined positions at the cell membrane of J774 macrophages by using holographic optical tweezers. By tracking the bead motion during and after internalisation, we are able to characterize the transport of individual phagosomes. Preliminary results indicate that larger particles move faster and in a more persistent way towards the perinuclear region whereas smaller particles move slower with more interjacent phases of random motion.

BP 16.30 Mon 17:30 Poster A

Stochastic modeling of gliding motility — •Thorsten Erdmann[1,2] and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University, Heidelberg, Germany — [2]BioQuant, Heidelberg University, Heidelberg, Germany

Gliding motility is a form of movement observed in unicellular organisms such as bacteria or single-celled eukaryotes. In the sporozoites of malaria parasites, gliding is driven by the formation of adhesion bonds with the substrate which are displaced relative to the cell body by the activity of molecular motors. Experimental trajectories of sporozoites reveal strong fluctuations of gliding velocity: On a sub-second time scale, stick-slip-like movement is observed; on larger time scales, gliding is occasionally arrested by large, stationary adhesion patches. In order to investigate the stochastic dynamics of gliding motility, we derive a model for a propulsion mechanism based on the cooperation of multiple, actively displaced adhesion bonds. We study the dynamic regimes of gliding motility emerging from the binding characteristics of the adhesion bonds, which are described either as slip bonds or catch bonds, and from the effective processivity and force-velocity relation characterizing the displacement of the adhesion bonds. In order to assess the role of flexibility of the cell body, we study the motion of elastically coupled, stiff segments of the basic model.

BP 16.31 Mon 17:30 Poster A

Model analysis of P-Selectin-mediated leukocyte rolling — •Mats Moskopp[1], Andreas Deussen[1], Triantafyllos Chavakis[2], and Peter Dieterich[1] — [1]Institut für Physiologie, TU Dresden, Germany — [2]Klinische Pathobiochemie, TU Dresden, Germany

Invasion of leukocytes from the blood stream into tissue proceeds as coordinated sequence called leukocyte adhesion cascade and is indispensable for an efficient immune response. Numerous proteins realize interactions between leukocytes and vessel covering endothelial cells allowing rolling, adhesion, crawling and transmigration towards the tissue. In this study we observe P-Selectin-mediated rolling of THP1 myelomyonocytic cells in flow chambers where coating densities of P-Selectin are varied. Cell contours are extracted automatically by image-segmentation. The resulting positions of THP1 cells show a mean drift superimposed by intermittent fluctuations. Assuming that these fluctuations result from the properties of the bonds allows to assess their biomechanical properties. Therefore, we construct a simplified biomechanical model incorporating coupling to fluid shear stress, viscoelastic behavior of bonds, force-dependent rupture kinetics, and variations of receptor and ligand densities. Simulations of artificial position data are performed to extract the corresponding biomechanical parameters with Bayesian data analysis. This approach unveils the possibilities and limitations of parameter extraction from position curves and is further applied to experimental data. In summary, the combination of experiments and modeling allows the estimation of biomechanical properties at the nano-scale from observations of the whole cell.

BP 16.32 Mon 17:30 Poster A

Mechanical Coupling of the Cytoskeleton with the Nucleus — •Gabriele Straass and Florian Rehfeldt — Third Institute of Physics - Biophysics, Georg-August-University, Göttingen, Germany

It is nowadays widely acknowledged that mechanical cues are as important for cellular behaviour as traditional biochemical ones. Strikingly, adult stem cells can be guided to differentiate towards various cell types when cultured on elastic hydrogels with appropriate Young's modulus E . While the differentiation process takes several days, the actomyosin cytoskeleton organisation shows significant differences within the first 24 hours after plating. We investigate the mechanical properties of the nucleus by atomic force microscopy and fluorescence microscopy and demonstrate the impact of substrate elasticity E on nuclear morphology via acto-myosin stress fibres. Elucidating the mechanical coupling of the cytoskeleton and the nucleus might reveal a direct mechanical pathway that alters gene transcription and might impact adult stem cell differentiation.

BP 16.33 Mon 17:30 Poster A

Complex thermorheology of cells — •Enrico Warmt, Sebastian Schmidt, Tobias Kiessling, Anatol Fritsch, Roland Stange, and Josef Käs — Universität Leipzig Faculty of Physics and Earth Sciences, Leipzig, Germany

Temperature has a reliable and nearly instantaneous influence on mechanical responses of cells. We measured thermorheological behaviour

of eight common cell types within physiologically relevant temperatures and applied thermorheological time-temperature superposition to creep compliance curves. Our results showed that superposition is not a universal feature, and is only applicable in four of the eight cell types. Cells with more complex temperature responses transitioned around 36°C. Activation energies were calculated for all cell types, albeit cells with complex temperature responses do not fit the model. These results reveal broad insights into thermally sensitive stress-strain relations of various cell types.