BP 10: Poster III

Cell Mechanics (BP 10.1 – BP 10.25); Systems Biology, Evolution & Neural Networks (BP 10.26 – 10.32)

Time: Monday 17:30–19:30 Location: P2/3OG

BP 10.1 Mon 17:30 P2/3OG

A time resolved study of blood platelet spreading — •Anna Zelena[1], Magdalena Haaf[1], Sebastian Isbaner[2], Daja Ruhlandt[2], Anna Chizhik[2], Alexey Chizhik[2], Jörg Enderlein[2], Ulrich S. Schwarz[3], and Sarah Köster[1] — [1]Institute for X-Ray Physics, University of Göttingen, Germany — [2]Third Institute of Physics - Biophysics, University of Göttingen, Germany — [3]Institute for Theoretical Physics, Heidelberg University, Germany

Human blood platelets are non-nucleated fragments of larger cells (*megacaryocytes*) and of high importance for blood clotting. The hemostatic function of platelets is directly linked to their mechanics and cytoskeletal morphology. However, the exact mechanism of spreading and contraction remains elusive. In our study we focus on the investigation of single blood platelets *in vitro* employing Traction Force Microscopy (TFM) and Metal-Induced Energy Transfer (MIET) imaging. By combined TFM and microscopy, we are able to correlate the force generation with the emerging actin structures in a time resolved manner. Our force maps show a hot spot distribution, typically in spindle-like, triangular or circular shape. Additionally, from fast scanning and static MIET experiments, we reconstruct the temporal evolution of the membrane-to-surface distance during adhesion and spreading with nanometer resolution. We observe in MIET three-dimensional height profiles, analogous to the TFM, hot spot distribution shapes of areas with lower membrane-to-surface distances.

BP 10.2 Mon 17:30 P2/3OG

Probing the real-time mechanical properties of cardiac fibroblasts using optical trap-based rheometry — •Heidi Somsel[1], Anna Blob[1], Wolfram-Hubertus Zimmermann[2], and Sarah Köster[1] — [1]Institute for X-Ray Physics, University of Göttingen, Göttingen — [2]Institute of Pharmacology and Toxicology, University Medical Center Göttingen, Göttingen

In order to further develop treatments and cures for cardiovascular diseases (CVDs), the workings of individual components of the heart must be better understood. Cardiac fibroblasts (CFs), a primary constituent of the heart, contribute to the mechanical properties, normal homeostasis, and cell-cell communication within the heart. However, CFs were widely ignored in the past, thus creating a barrier in the development of future CVD treatments. Here, we focus on the mechanical properties of primary and stem-cell derived CFs, and how they respond to commonly used cardiac drugs. Single CFs are probed via active rheometry in a dual optical trap where a cell in suspension is caught between two beads via focal adhesions. This allows us to determine an effective cell stiffness by approximating the cell as a linear-elastic element. The optical trap is combined with a microfluidic chip permitting for a real-time readout of the response and recovery of individual cells to an applied drug. Integrating optical tweezers and microfluidics allows us to probe, for the first time, the mechanical properties of a cell in a quasi-3D environment in response to drugs in real-time.

BP 10.3 Mon 17:30 P2/3OG

Effect of channel geometry on RBC shape in microfluidic devices — •Mohammed Nouaman[1], Alexander Kihm[1], Steffen Recktenwald[1], Lars Kaestner[1,2], and Christian Wagner[1] — [1]Saarland University, Experimental Physics, Dynamic of Fluids, Campus E2 6, Saarbrücken, Germany. — [2]Saarland University, Theoretical Medicine & Biosciences, Campus University Hospital, Homburg, Germany

Red blood cells (RBCs) exhibit a broad range of different shapes in capillary flows depending on various parameters, such as flow velocity, applied pressure drop, and lateral position. In microfluidic flows in small rectangular channels (e.g. 10x12 microns), two main stable RBC shapes exist. For low-pressure drops, RBCs preferentially show a croissant-like shape, a transition toward slipper-like RBCs can be observed with the increase of pressure drop. However, the effect of the channel dimensions on this transition remains vaguely unknown. Therefore, we perform detailed statistical analysis of the RBC shapes, covering a range of microfluidic channel height and width (e.g. 10-30 microns). In order to enable an unbiased analysis of RBC shape, we further use a convolutional neuronal network CNN, which provides fast data processing and determination of the transition point between the two main stable RBC shapes.

BP 10.4 Mon 17:30 P2/3OG

Spherical harmonics analysis of *in-vivo* force probes for tissue stress quantification — •Alejandro Jurado, Bernhard Wallmeyer, Christoph Engwer, and Timo Betz — Institute of Cell Biology, ZMBE, University of Münster

The mechanical analysis of tissue motion offers a new insight in key biological processes such as embryogenesis, cancer cell invasion and wound healing. Force quantification at this scale has been drastically improved with the emergence of *in-vivo* sensors such as oil droplets or hydrogel beads which open up the possibility of non-invasive studies. Many approaches in recent literature rely on numerical processes to iteratively reconstruct the surface of measured beads, which can be computationally expensive and rendering results that are difficult to interpret. In this work we present the analysis of arbitrarily deformed beads based on the expansion in Spherical Harmonics in a Python custom software. We exploit the fast converging algorithms offered by SHTools [1] to reduce the great complexity of three-dimensional radial deformations to an affordable harmonic coefficient table which is directly fed into an analytical solution of the Navier-Cauchy equation. As a first proof-of-concept we show the performance of the software with polyacrylamide beads injected into zebrafish embryo at early developmental stages, in which the stress field could help understanding the processes of epiboly and shield formation.

[1] Wieczorek M.A., Meschede M., 2018. SHTools: Tools for working with spherical harmonics, Geochem. Geophys. Geosyst. 19(8), 2574-2592

BP 10.5 Mon 17:30 P2/3OG

Characterization of an ultrasonic transmitter for mechanical manipulation of cancer cells in vitro — •Simon Sommerhage[1], Hsiao-Ching Tsai[1], Monika Illenseer[1], Paul Dunst[2], Tobias Hemsel[2], and Mathias Getzlaff[1] — [1]Institute of Applied Physics, Heinrich Heine University Düsseldorf — [2]Dynamics and Mechatronics, Paderborn University

Ultrasound is a well-established medical application for diagnostic and therapeutic purposes (e.g. HIFU). In this study the effect of unfocused ultrasound with lower intensities compared to HIFU on human oral squamous cancer cells (UD-SSC-1) was investigated. Recent studies have shown that cancer cells exhibit a significantly lower Young's modulus than their healthy counterparts. This should cause a different response to external mechanical stimuli by ultrasound. According to recent study's theoretical analysis the frequency-response of a cell should show a resonance-like characteristic with a peak frequency lying within the range 10^4-10^6 Hz. To be able to test this hypothesis, the electrodynamical properties of an ultrasonic transmitter must be characterized. Therefore, the vibration velocity depending on the adjusted electrical current was measured using a laser Doppler vibrometer (Polytec LSV 60). This was done for different resonance frequencies yielding two suitable resonance modes at about 24 and 67 kHz. The UD-SCC-1 cells were irradiated and observed with an inverted light-microscope in vitro. At constant distance and vibration velocity the qualitative effect was higher for the 67 kHz than for the 24 kHz mode. These results may be a proof of principle for the cell-resonance hypothesis.

BP 10.6 Mon 17:30 P2/3OG

Endothelial cell mechanics in inflammation under shear stress inflicted by flow — •Matthias Brandt[1], Volker Gerke[2], and Timo Betz[1] — [1]Institut für Zellbiologie, ZMBE, Universität Münster — [2]Institut für Medizinische Biochemie, ZMBE, Universität Münster

Localized and tightly controlled leukocyte extravasation is a hallmark of the early inflammatory response. Whereas many cell and protein interactions regulating this process are well described, here we focus on the mechanical role of the endothelium in inflammation prior to leukocyte transmigration. Mimicking inflammation in a human umbilical vein endothelial cell (HUVEC) monolayer via chemical stimulants such as TNF-alpha, traction force and intramonolayer stress microscopy re-

veal a rapid (30 min) response in traction stress and even more in cell-cell stresses. The majority of cells is found to transfer increasing amounts of internal stress to their neighbors. Intuitively, the quickly altered mechanical state of the endothelium may help in guiding arriving leukocytes. As differences in mechanics for cells under flow as opposed to static conditions have been reported for HUVEC layers in a non-inflammatory state, using a microfluidic setup allowing for the preparation of micropatterned gels inside a flow chamber, we expose the endothelial cells to different levels of shear stress induced by flow. Potential contributions of altered forces among the endothelium to the transmigration process itself will be studied in future experiments via transmigration assays of human neutrophils and a controlled activation of contractility by pharmacologic and optogenetic tools.

BP 10.7 Mon 17:30 P2/3OG

Neutrophil mechanotransduction during durotaxis — •Fatemeh Abbasi, Matthias Brandt, and Timo Betz — Institute of Cell Biology, ZMBE Institute, Münster, Germany

Cell migration based on the environment stiffness gradient towards the stiffer substrate is called durotaxis. Durotaxis might be important for immune cells, since they migrate from bone marrow to the cite of infection. We hypothesized that durotaxis might be a leading factor of immune cells migration from the blood circulation to the infected tissue, since inflammation leads to swelling and stiffness increase. To investigate this hypothesis, we developed a biomimetic system to reconstitute both, the mechanical and the chemical environment of neutrophils. Cells are confined between two elastic polyacrylamide (PAA) hydrogels with controlled elastic moduli and functionalized surface chemistry. By controlling the distance between the PAA hydrogel surfaces, we vary the compression forces exerted by the substrates on the cells. We engineered a sandwich-like configuration of two elastic PAA layer with stiffness between 1 and 10 kPa and confined neutrophils in between these layers, giving them the chance of attaching to both layers simultaneously. Consistent with durotaxis, we find a striking tendency of neutrophils to detach from soft and attach to stiffer layers. We are able to track cell behavior and the cytoskeletal reorganization during the shifting from soft to stiff substrates while measuring the forces.

BP 10.8 Mon 17:30 P2/3OG

Calcium as a key regulator in Physarum polycephalum — •Björn Kscheschinski[1], Mirna Kramar[1], and Karen Alim[1,2] — [1]Max Planck Institute for Dynamics and Self-Organization, Göttingen — [2]Technical University of Munich

The tubular network-forming slime mold *Physarum polycephalum* is able to maintain long-scale contraction patterns driven by an actomyosin cortex forming the tube walls. The resulting flow transports mass effectively in the organism. Recent models suggest feedback mechanisms for self-oragnized contractions by coupling the actomyosin activity to a regulating chemical, which is in turn advected by the flow. These models predict system sized contraction patterns. However, the exact effect of the regulating chemical is not yet fully understood. Here, we present ratiometric measurements of free intracellular calcium in single *Physarum* tubes suggesting an inhibitory effect of calcium on the acto-myosin activity. The spatio-temporal patterns of the free calcium concentration reveal an anti-correlated relation to the tube diameter, while the main patterns of the contractions are preserved. By controlling the morphology of *Physarum* we can relate our experimental data directly to numerical simulations with simple geometries. Our results suggest that calcium is a key regulator of the acto-myosin activity enabling the organized flow patterns emerging in *Physarum* networks. Thus, our findings might allow further insights into processes in *Physarum* related to the flows.

BP 10.9 Mon 17:30 P2/3OG

Elastic beads as tension sensors to measure the spatial force distribution in reconstructed muscle — •Tamara Limón, Arne Hofemeier, Alejandro Jurado, Bernhard Wallmeyer, and Timo Betz — University of Münster, ZMBE, Institute for Cell Biology

The quantification of forces within the niche of skeletal muscles has gained an increasing importance in the field of regenerative medicine especially in terms of satellite cell (SC) activation. Recent studies have shown that force sensors based on known material properties are a useful tool to analyze cell mechanics. Here, we present a technique using characterized elastic beads as tension sensors to measure forces in reconstructed muscle. The elastic beads are seeded together with the myoblast cell line C2C12 into a fibrin-geltrex scaffold on a silicon substrate to generate a three-dimensional *in vitro* muscle. Due to the deformation of incorporated beads we calculated the tension present in 7-day old muscles by a custom-made bead analysis software. First results indicate differences in force axes and in magnitude of bead deformation giving rise to a spatial force distribution ranging between 1.6 - 4.1 kPa tension in the muscle. A possible explanation might be related to dissimilar stress fiber formation with thicker stress fibers at the lateral sides. Understanding the aspects of a spatial force distribution in muscles could enlighten mechanisms involved in SC activation and improve handling with SC for gene therapy.

BP 10.10 Mon 17:30 P2/3OG

Active and passive microrheology for measurement of intracellular mechanics — •Till Münker, Sebastian Hurst, and Timo Betz — Institute of Cell Biology, University of Muenster, Muenster, Germany

Active mechanics that arises from ATP consuming processes like molecular motors or cytoskeletal polymerization have been shown to play an important role for fundamental cellular processes such as proliferation, migration or morphology. However, studies on understanding the more general principles that dictate force generation in this complex structure are missing. Using an optical tweezers based active-passive microrheology approach we determine the viscoelastic shear modulus and the free fluctuations of phagocytosed particles in different cell types. These measurements give access to an effective energy that is indicative for the cellular activity. By comparing the results from different cell types such as epithelial, carcinoma, muscle and immune cells we observe that all cell types follow a similar energy-frequency dependency. We then compared the outcome of these experiments to a simplified model that describes the cytoskeleton as a viscoelastic cage. In our model, we assumed the cytoskeleton to be a soft glassy material which is displaced by a single random force on a distinct timescale. In this approach the functional dependence of the effective energy is determined by the viscoelastic material properties. First experiments confirm this model where a small set of parameters can describe the overall mechanical activity within the cytosol across various cell types.

BP 10.11 Mon 17:30 P2/3OG

Determining the viscoelastic shear modulus of zebrafish embryos during embryogenesis on the tissue scale — •Julian Vondereck, Sebastian Hurst, Bart Vos, and Timo Betz — University of Münster, ZMBE, Institut of Cell Biology

Understanding the physical principles of collective cell movements is key to acquiring deeper knowledge about fundamental biological processes ranging from wound healing over metastatic cancer invasion to development. A distinguished model to study these processes is collective cell migration in embryogenesis. The first coordinated tissue motion in a zebrafish embryo is called epiboly, where the blastocyte cells spreads over the yolk cell. To understand the mechanical properties during this process, we use in vivo, optical tweezer based microrheology. Epiboly can be described by the behavior of the three embryonic regions: the epithelial monolayer or enveloping layer (EVL), the yolk syncytial layer (YSL) and the deep cells (DEL) of the blastoderm. EVL, YSL and DEL all undergo epiboly. 10 micrometer sized particles are microinjected in these regions as tissue-based probes. Microrheology in vivo allows to determine the viscoelastic shear modulus on the tissue scale, while resolving spatial and temporal changes during development. Illuminating cell and tissue differentiation on the different regions in general and at certain key points is to be expected. This provides new insights into the biomechanical processes controlling collective cell movements, of which a detailed understanding yet remains elusive.

BP 10.12 Mon 17:30 P2/3OG

Microrheology of human umbilical vein endothelial cells using Acoustic Force Spectroscopy — •Alfred Nguyen and Timo Betz — Institute of Cell Biology, University of Münster, Münster, Germany

We present a novel method for microrheology using acoustic forces in the range of pN-nN to oscillate particles inside a microfluidic chip. For this method we used the Acoustic Force Spectroscope (AFS) which was introduced as a single-molecule technique to measure mechanochemical properties of biomolecules in parallel. Our new application for the AFS enables the measurement of the dynamics of the viscoelastic properties of cells exposed to different conditions, such as flow shear stresses or drug injections. To validate our new method for microrheology on living cells in vitro, we cultured a monolayer of human umbilical vein

endothelial cells (HUVEC) inside the measurement chip and exerted oscillatory forces on particles attached on top of the cells. By determining the force and measuring the position of the particle, the complex shear modulus G*(ω) could be measured. We confirm a decrease in shear modulus after perturbing actin polymerization by cytochalasin B. This effect was reversible after washing the drug out. Although these measurements are possible, we provide a critical discussion of the AFS showing its advantages as well as its drawbacks and how to process the obtained data.

BP 10.13 Mon 17:30 P2/3OG

Elastic beads as cellular tension sensors within muscle tissue — •Arne Hofemeier[1,2], Tamara Limon[1], Till Münker[1], Alejandro Jurado[1], Bernhard Wallmeyer[1], Penney Gilbert[2], and Timo Betz[1] — [1]Institute of Cell Biology, University of Münster, Germany — [2]Donnelly Centre, University of Toronto, Canada

Mechanical tension has recently been recognized as a key element to understand many biological processes such as cell fate determination or collective cell migration. For instance, muscle stem cells are known to strongly react to changes of physical properties of their microenvironment in vitro. However, direct experimental access to determine mechanical tension in cellular niches remains a major challenge. Here, we present a novel experimental approach that allows direct measurement of mechanical stress inside in vitro and in vivo muscle tissue. By injecting fluorescent polyacrylamide (PAA) beads of known size and elasticity into muscle tissues, we are able to measure the deformation of their surface and obtain the resulting force exerted on the bead. With this in hand, we show three applications of this novel technique. Firstly, PAA beads were incorporated into biomimetic muscle tissue in order to trace cellular tension during development and diseased tissues. Secondly, elastic beads were injected into zebrafish embryos to investigate tissue stress on muscle cells during late embryogenesis in vivo. Lastly, we transplanted PAA beads into injured EDL muscles of mice to evaluate local forces after 3 weeks of muscle regeneration for the first time.

BP 10.14 Mon 17:30 P2/3OG

Three-dimensional modeling of a viscous active cell cortex — •Christian Bächer[1], Diana Khoromskaia[2], Guillaume Salbreux[2], and Stephan Gekle[1] — [1]Biofluid Simulation and Modeling, Theoretische Physik VI, Universität Bayreuth, Germany — [2]The Francis Crick Institute, London, UK

In a biological cell active mechanical stresses in the cortex can lead to flows resulting in strong deformations. We use a thin shell formulation of an active gel in the viscous limit [1] to build a numerical model of a fully three dimensional viscous, active cell cortex. For given active stress distribution, we numerically determine the flow field in the cortex, which directly gives the triggered deformation. Our algorithm consists of two parts: first, a minimization ansatz solves the force balance in presence of viscous and active stresses on the triangulated, three-dimensional cortex. Second, the viscous stresses at a node are expressed in terms of the velocity vectors of the neighboring nodes using an analytically inverted parabolic fitting procedure. Together, this leads to a system of equations which we solve numerically for the flow field on the discretized cortex. Our algorithm provides a versatile and flexible tool, which can easily be extended, e.g., to an active stress coupled to a concentration field, and furthermore allows for a dynamic coupling of the cell cortex to an inner and surrounding fluid.

[1] G. Salbreux, F. Jülicher, Phys. Rev. E 96(3), 2017

BP 10.15 Mon 17:30 P2/3OG

Cryo Scanning Electron Microscopy investigations on penetration of Titanium dioxide particles in human skin — •Hanna-Friederike Poggemann[1], René Gustus[1], and Wolfgang Maus-Friedrichs[1,2] — [1]Clausthal Centre of Material Science, Agricolastraße 2, 38678 Clausthal-Zellerfeld, Germany — [2]Institute of Energy Research and Physical Technology, Leibnizstraße 4, 38678 Clausthal-Zellerfeld, Germany

Titanium dioxide nanoparticles can be found in a lot of cosmetically products as for example sunscreen. Titanium dioxide (TiO2) is not toxic for humans in micrometer size but the Nano sized particles have different material properties. TiO2 nanoparticles are for example photocatalytic active and so able to damage human cells if they get in to the living dermal layers. Previous studies have pointed out that most particles cannot penetrate the topmost dermal layer, the stratum corneum. Accordingly only a small amount of the TiO2 gets into the living cell area. But several studies also underlined the necessity of further research especially in the case of previously damaged skin. (According to actual statistics 14 % of all children und up to 3 % of the adults in Germany suffer from neurodermatitis and particularly for those persons it is inevitable to use sunscreen on their skin) In this regard we analyzed the TiO2 nanoparticles of commercially available sunscreens in our FE-SEM by SEM and EDX. Furthermore we examined samples of human skin with and without sunscreen treatment by Cryo-SEM and Focused Ion Beam to prove that out method is appropriate for continuing research on this subject.

BP 10.16 Mon 17:30 P2/3OG

Measuring intracellular stiffness in epithelial cells — •Bart E. Vos[1], Sebastian Hurst[1], Ying Zhang[2], Paul H.J. Kouwer[2], and Timo Betz[1] — [1]Institute of cell biology, ZMBE, Münster, Germany — [2]Spectroscopy and Catalysis, Radboud University, Nijmegen, the Netherlands

Epithelial cells form the boundary between an organ (or an entire organism) and its environment. Hence, epithelial cells experience a strong asymmetry in their environment: "out" versus "in". It is therefore not surprising that epithelial cells are strongly polarized; for example, the actin meshwork is denser at the apical, or "outward facing"-side of the cell, while the nucleus is always located at the basal, or "inward facing"-side of the cell. However, to date it remains unclear if and how polarity is established and maintained by a gradient in intracellular stiffness and/or motor activity. Furthermore, since the extracellular matrix (ECM) is of crucial importance to cells, we hypothesize that variations in the extracellular matrix also have an influence on intracellular mechanics.

Here I will present a project that focuses on measurement of intracellular stiffness and activity in MDCK-cells. Using both active and passive microrheology, we obtain cellular stiffness and activity as a function of position within the MDCK-cell. Using a synthetic, biomimicking ECM, we systematically vary the mechanical environment of the epithelial cells, where we observe a strong response in the shape and growth rate of the cells.

BP 10.17 Mon 17:30 P2/3OG

Target size dependency of cellular resolution limits during phagocytosis — •Manuel Eisentraut, Adal Sabri, and Holger Kress — Biological Physics Group, Department of Physics, University of Bayreuth, Germany

Antibodies can interact with phagocytic receptors on macrophages and trigger signalling cascades which initiate phagocytosis. A large number of the molecular components of these signalling networks are well known, but it remains unclear how fast and how far the corresponding signals propagate in the cell.

To address this issues, we investigated the spatial spreading of phagocytic signalling by measuring how well cells can resolve whether one or two particles are attached to the cell membrane. In our experiments, we attach pairs of equally-sized polystyrene beads opsonized with antibodies to single macrophages. We were able to precisely control the distance of the beads during the attachment by utilizing holographic optical tweezers. The subsequent uptake into two separate or one joint phagosome was distinguished by analysing the intracellular particle trajectories after the uptake. We found that the probability for separate uptake is very high for large distances and very low for small distances, with a transition between these regimes at surface-to-surface distances of several hundreds of nanometers. A comparison between measurements with different bead sizes suggests that the separate uptake probability not only depends on the bead distance, but also on the total size of the target bead pair. Our results provide quantitative insights into the spatial spreading of signalling during phagocytosis.

BP 10.18 Mon 17:30 P2/3OG

Characterization of cell deformability in patients with major depressive disorder — •Lisa Kwapich[1], Tobias Neckernuss[1,2], Daniel Geiger[1,2], Jonas Pfeil[1,2], Patricia Schwilling[1], Alexander Karabatsiakis[3], Iris-Tatjana Kolassa[3], and Othmar Marti[1] — [1]Institute of Experimental Physics, Ulm University — [2]Sensific GmbH — [3]Institute of Psychology and Education, Ulm University

Major depressive disorder is a debilitating disease that affects more than 300 million people worldwide. Despite advances in the understanding of the etiology of major depression, no established mechanism can explain all aspects of the disease. A promising approach in this context is the analysis of mechanical cell properties by deformability cytometry. The method 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. The advantage of this method is that cells are purely deformed by hydrodynamic interactions and without contact with channel walls. The deformability of cells is indicative of underlying membrane, cytoskeletal, or nuclear changes associated with changes in cell state and various disease processes. We investigated differences in deformability of peripheral blood mononuclear cells between patients with major depressive disorder and non-depressed control subjects. A custom-built algorithm (ODIN technology) was used for image analysis, data collection, and postprocessing analysis. The algorithm detects the presence of a cell, determines its contour, and quantifies several parameters.

BP 10.19 Mon 17:30 P2/3OG

What thermal fluctuations of an optically trapped bead can tell us about the properties of an interface — •Tetiana Udod, Felix Jünger, and Alexander Rohrbach — Lab for Bio- and Nano-Photonics, IMTEK, University of Freiburg, Georges-Koehler-Allee 102, 79110 Freiburg, Germany

Thermal position fluctuations of optically trapped beads can be measured in 3D with nanometer precision at MHz rates with back focal plane interferometry. The bead fluctuations change in amplitude and time upon interaction with interfaces, which can be characterized by different surface potentials or viscosities. Bead position fluctuations encode the hydrodynamic momentum transfer and repulsion at plane glass coverslips, giant unilamellar vesicles or even living cells, with complex and dynamic surface structures. However, defining and determining the contact between the fluctuating bead and an interface is far from trivial. When studying particle binding and induction of the phagocytic uptake pathway, the following question is of particular interest: When does a cell start to feel an approaching particle? To better understand such processes taking place on very small length and time scales, we first analyze the position fluctuation at simplified interface systems. Therefore, we use combination of experiments with Photonic Force Microscopy, Brownian Dynamic simulation and analytical theory to model and explain the impact of surface potentials and viscosities on the 3D bead position fluctuations. This allows us to identify the contact point and thereby to measure distance -dependent interactions even of living cells.

BP 10.20 Mon 17:30 P2/3OG

Adherent Cell Optical Stretcher: Quantifying Laser Induced Heating — •Alexander Janik[1], Tobias Neckernuss[1], Cornelius Maurer[1], Seiichi Uchiyama[2], and Othmar Marti[1] — [1]Institute of Experimental Physics, Ulm University — [2]Graduate School of Pharmaceutical Sciences, The University of Tokyo

Cell stiffness is a valuable indicator for cell functionality, especially in cell types that naturally undergo strong mechanical deformation, such as alveolar epithelial cells. We therefore recently developed a method to stretch adherent cells with a parallel laser beam to determine their viscoelastic properties.

The impact on cells is kept low, for they are stretched uniformly, and the procedure does not require fluorescent labeling. However, heating induced by the 800 nm stretching laser is a side effect. Our contribution focuses on quantification and real-time monitoring of intracellular temperature change during the stretching process. A ratiometric temperature dependent fluorescent dye is used whose two emission bands are detected simultaneously on two cameras. Improvements of the setup for cell height detection, which currently employs beads as markers, are also discussed.

BP 10.21 Mon 17:30 P2/3OG

Why do rigid tumors contain soft cancer cells? — •Thomas Fuhs[1], Franziska Wetzel[1], Anatol W. Fritsch[1], Dapeng Bi[2], Roland Stange[1], Steve Pawlizak[1], Tobias R. Kiesling[1], Erik Morawetz[1], Steffen Grosser[1], Frank Sauer[1], Jürgen Lippoldt[1], Fred Renner[1], Sabrina Friebe[1], Mareike Zink[1], Bahriye Aktas[3], Lars-Christian Horn[3], Klaus Bendrat[4], Axel Niendorf[4], Michael Höckel[3], and Josef A. Käs[1] — [1]Leipzig University, Germany — [2]Northeastern University, Boston, USA — [3]University Hospital Leipzig, Germany — [4]Pathology Hamburg-West, Germany

Palpatation used since acient times, utilizes that solid tumors are stiffer than surrounding tissue. However, cancer cell lines are softer, which facilitates invasion. This paradox raises several questions: Does softness emerge from adaptation to mechanical and chemical cues in the external microenvironment? Or are soft cells already present inside a rigid primary tumor? We investigate primary samples from patients with mammary and cervical carcinomas on multiple length scales from tissue level down to single cells. We show that primary tumors a highly heterogeneous in their mechanical properties on the tissue level as well as cells do exhibit a broad distribution of rigidities, with a higher fraction of softer and more elongated cells compared to normal tissue. Mechanical modelling based on patient data reveals that tumors remain solid containing a significant fraction of very soft cells. Moreover, it predicts that in such tissues, softer cells spontaneously self-organize into multicellular streams, which we observe experimentally.

BP 10.22 Mon 17:30 P2/3OG

Using real-time fluorescence and deformability cytometry and deep learning to transfer molecular specificity to label-free sorting — •Ahmad Ahsan Nawaz[1], Marta Urbanska[1,2], Maik Herbig[1], Martin Kraeter[1], Marketa Kubankova[1], Salvatore Girardo[1], Angela Jacobi[1], and Jochen Guck[1] — [1]Max Planck Institute for the Science of Light, Erlangen — [2]Biotec, Technische Universität Dresden

The identification and separation of specific cells from heterogeneous populations is an essential prerequisite for further analysis or use. Conventional passive and active separation approaches rely on fluorescent or magnetic tags introduced to the cells of interest through molecular markers. Such labeling is time- and cost-intensive, can alter cellular properties, and might be incompatible with subsequent use, for example, in transplantation. Alternative label-free approaches utilizing morphological or mechanical features are attractive, but lack molecular specificity. Here we combine image-based real-time fluorescence and deformability cytometry (RT-FDC) with downstream cell sorting using standing surface acoustic waves (SSAW). We demonstrate basic sorting capabilities of the device by separating cell mimics and blood cell types based on fluorescence as well as deformability and other image parameters. In addition, the classification of blood cells using established fluorescence-based markers provides hundreds of thousands of labeled cell images used to train a deep neural network. The trained algorithm is then used to identify and sort unlabeled blood cells. This approach transfers molecular specificity into label-free sorting.

BP 10.23 Mon 17:30 P2/3OG

A Machine Learning Approach to Computing the Traction Field of Adherent Cells — •Martin Kolaczek, Timo Betz, and Christoph Engwer — Institute for Cell Biology, University of Münster

Adherent cells exert tractions on their surrounding in the course of a variety of cell functions including contraction, spreading, crawling and invasion. Using Traction force microscopy, these forces can be measured by observing the displacements of beads embedded on a flexible hydrogel gel substrate. Computing the traction field algorithmically is computationally intensive, hence making a real time evaluation of traction forces impossible. To overcome this challenge, we pursue a different data-intensive approach to solve this task by harnessing the power of machine learning. Our first and utmost objective is to speed up the computation of the traction field to get a near-instantaneous computation of the traction field during measurement accepting a trade-off for accuracy. Since observing the displacement of beads is time-consuming, an assessment of the measurement right at the beginning is desirable. First attempts with artificially generated data was a success. Using ensembles of white pixels on a black background and generating single pixel and more complex displacements and to a field allowed training a deep neuronal network. This neural network was able to compute displacements with high accuracy with high speed. The next step will be to extend the given model to process real data. Noise and vanishing particles are some of the obstacles to cross.

BP 10.24 Mon 17:30 P2/3OG

Visualisation of cytoplasmic flows in epithelial cells by single particle tracking — •Christoph Engwer, Mariam Ristau, and Timo Betz — Institute of Cell Biology, Center for Molecular Biology of Inflammation, Münster, Germany

Correct polarization of epithelial cells is highly important for tissues to perform their respective function. Failure during polarity formation is connected to different diseases such as polycystic kidney disease and malignant cancers. Whereas biochemical signalling, responsible for establishing cellular polarity is well understood, only little is known about the mechanical processes that play a role during polarity formation. In this project, we investigate how cytoplasmic flows may

influence cellular polarity or vice versa. As model system, we use spherical cysts made from kidney epithelial cells from domestic dog (MDCK). These cysts form within three to four days when grown in a pseudo-3D environment of extra cellular matrix components. Prior to cyst formation, far-red labelled nanoparticles that serve as tracers for intracellular flows, are ballistically injected into the cells. For the analysis of intracellular flows, we develop a Python based single particle tracking software based using Trackpy. Cysts are imaged over time and particle tracks are obtained from maximum intensity projections around the equatorial plane. To gain average values, cells are registered using labelled nuclei and F-actin. After rotating and projecting each cell into a unit cell, we obtained activity maps of intracellular particle movement.

BP 10.25 Mon 17:30 P2/3OG

stress stiffening of suspended cells — •elham mirzahossein[1], sebastian muller[2], stephan geckle[2], and ben fabry[1] — [1]University of Erlangen-Nuremberg — [2]Department of Physics, university of Bayreuth

The stiffness of adherent cells has been shown to increase linearly with contractile (pre-) stress of the cytoskeleton and externally applied stress. Previous studies of suspended cells that are forced through small microfluidic constrictions reported the same stress stiffening behavior as in adherent cells, however, the mechanical loading of cells in a microfluidic constriction is complex. to overcome these limitations, here we measure the deformations of adherent suspended cells in response to simple shear stress. nih-3t3 fibroblasts are mixed in shear-thinning 2% alginate solution and are pressed at 1-3 bar through a $200 \times 200\ \mu m$ and 5 cm long microfluidic channel. the shear stress is zero in the channel center and increases linearly towards the walls. as a consequence, cells appear round in the channel center and become elongated towards the walls, with aspect ratios of up to 3. the Taylor strain,ϵ , of the cells versus fluid shear stress, σ, shows a non-linear relationship. This relationship is well described by a differential cell stiffness of the form $E = \frac{\partial \sigma}{\partial \epsilon} = E_0 + \alpha \cdot \sigma$. Cell stiffness is$E_0 = 100Pa$ at low shear stress and linearly increases with shear stress with a factor $\alpha = 8$. at the highest shear stress value of 300 Pa that we apply in our study, differential cells stiffness increases to 1700 pa on average. thus, our measurements of suspended cells show a pronounced stress stiffening that is similar to the behavior found in adherent cells.

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A dynamic model for proteome partitioning — •Anne-Lena Moor, Kalok Kam, and Stefan Klumpp — Institut für Dynamik komplexer Systeme Georg-August-Universität Göttingen

To reproduce as efficiently as possible, bacteria adapt their proteome and metabolism to different environments with different nutrient availability. A key ingredient of this adaptation is the regulation of the fraction of ribosomes in the proteome, which is subject to simple growth laws. In this work, the growth laws are used to analyze the dynamics of cell growth and proteome adaptation, specifically how the ratio of ribosomes to metabolic proteins is modulated to achieve the maximal growth rate. A model is presented that describes the dynamics of this regulation.

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Coupling of growth, replication and division in E. coli — Mareike Berger and •Pieter Rein ten Wolde — AMOLF, Amsterdam, the Netherlands

Growth, DNA replication and division are key features of every living organism. The precise temporal control of these processes is essential for survival. We investigate how the model organism E. coli couples its replication to its division cycle under different growth conditions. According to the phenomenological general growth law, E. coli initiates replication at a constant volume per origin of replication and divides a constant time later. This simple mechanism allows E. coli to divide faster than it takes to replicate its DNA while maintaining cell size homeostasis. It is a longstanding open question how the general growth law is realized on a molecular level. We present a theoretical model that is based on experimentally observed molecular mechanisms and that can reproduce the phenomenological general growth law. This novel model allows us to make quantitative predictions on the regulation of replication in E. coli.

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Robust ligand discrimination by dimeric membrane receptors — •Patrick Binder[1,2,3], Nikolas Schnellbächer[1,2], Nils Becker[2,3], Thomas Höfer[2,3], and Ulrich Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University, Heidelberg, Germany — [2]BioQuant, Heidelberg University, Heidelberg, Germany — [3]Division of Theoretical Systems Biology, German Cancer Research Center, Heidelberg, Germany

Many cytokine pathways transduce signals across the cell membrane via ligand-induced receptor dimerization. As differences in cellular response show, the dimeric Interferon-I receptor system can not only sense ligand concentration, but also discriminate between different types of ligand that all bind to the same receptor type. Here we investigate, using information-theoretic methods, which architectural features optimize the ligand discrimination performance of receptor systems. By defining a basic ligand discrimination task and comparing monomeric, homodimeric and heterodimeric receptors, we find that each step in complexity improves the sensory mutual information. We first observe that monomeric receptors are insufficient to sense the ligand presence and type simultaneously. Second, due to the bell-shaped activation curve, the affinity of dimeric receptors is encoded in the maximal activation. Third, asymmetric binding of ligand to heterodimeric receptors broadens the maximum into a plateau, which buffers concentration fluctuations in the physiological range of the type-I interferon system. Fourth, additional turnover of receptors further steepen the response and broaden the plateau.

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Exploring theoretical limits for the lifespan of C. elegans dauer larvae under periodic feeding — xingyu zhang[1,2] and •vasily zaburdaev[1,2] — [1]Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany — [2]Max Planck Zentrum für Physik und Medizin, Erlangen, Germany

Extending lifespan of organisms has long been an appealing topic of biological sciences. Recent experimental work demonstrated that the lifespan of C. elegans dauer larvae could be extended by providing them with external ethanol solution as a carbon source. A mathematical model for the simplified metabolic network of the dauer allowed us to explain the lifespan prolongation and two possible mechanisms leading to the death of the worm. The model relates the well-being of the worm to its mitochondria, which can be irreversibly damaged either by starvation or toxic compounds accumulated during metabolism. However, by incorporating two omitted but important mechanism into the model, namely degradation of toxic compounds and regeneration of mitochondria, we can extend the survival of dauers even further by choosing an optimal feeding protocol. Thus, modified model reproduces the experimental observation when the feeding ethanol concentration stays constant in time. However, when the feeding ethanol concentration varies as a sinusoidal function, the model gives rise to solutions where the worm lives forever. Detailed analysis of the model suggests that large amplitude and moderate frequency of the periodic feeding give better chances for the worm to have an infinite lifespan, which we now plan to test experimentally.

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Embryonic lateral inhibition as optical modes — •Jose Negrete Jr and Andrew C Oates — École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Spatial gene expression patterns define regions where specialised cells emerge within an embryo. Lateral inhibition is a common mechanism that creates fine grained patterns with a characteristic wavelength of the size of 2 cells. Here we developed a generic model for patterning with lateral inhibition, and study its characteristics by making an analogy with crystal phonons from solid state physics. The tissue is redefined in terms of a Bravais lattice where the basis of the crystal contains two to three cells. The steady states are analogous to the optical modes of phonons. The model predicts that there are two different lateral inhibition states that can coexist in a certain parameter regime. Finally, our work suggests that gene expression patterns can be thought as crystal phonons, where long wavelength (Turing like) patterns corresponds to accosting modes and lateral inhibition patterns to optical modes.

Reference: Negrete Jr J and Oates AC, Phys Rev E 99, 042417 (2019)

BP 10.31 Mon 17:30 P2/3OG

Nonlinear response of noisy neurons with spike-triggered adaptation — •Christoph H. Egerland[1] and Benjamin Lindner[1,2] — [1]Humboldt-Universität zu Berlin, Berlin, Germany — [2]Bernstein Center for Computational Neuroscience, Berlin, Germany

A basic question in neuroscience is how a noisy neuron responds to an external stimulus signal. For weak stimuli, typically only the linear response in the firing rate has been considered. More recently, the weakly nonlinear response to periodic stimulu has been in the focus, demonstrating pronounced effects in particular for stimuli consisting of two harmonic signals [1]. Here we extend this analysis to neurons with adaptation currents because it is unclear how these slow currents that are present in many cells will affect the weakly nonlinear response. We show results obtained from simulations and compare them to analytically obtained expressions in the appropriate limits.

[1] Voronenko & Lindner New J. Phys. 19, 033038 (2017)

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Influence of the mechanical environment on neuronal maturation — •Eva M. Kreysing, Hélène O. B. Gautier, Ragnhildur T. Káradóttir, and Kristian Franze — University of Cambridge

During the development of the nervous system, neurons extend long axons as well as shorter and highly branched dendrites to connect to other cells. Once integrated in the neuronal network, neurons mature and the conductivity of their cell membrane changes for certain ion types, resulting in their electrical activity. While mechanical interactions between neurons and their environment are crucial for axon growth and pathfinding, the influence of mechanical signals on neuronal maturation is currently poorly understood. Here, we cultured primary hippocampal neurons on polyacrylamide gels of different stiffness and studied how substrate mechanics impacts the electrical maturation of the cells using Patch-Clamp measurements. Currents through voltage-gated sodium channels, potassium channels, as well as spontaneous activity all started several days earlier in neurons cultured on soft substrates if compared to stiff substrates. These differences in the onset of electrical activity were accompanied by increased synaptic densities on soft substrates as assessed by immunocytochemistry. Our results suggest that mechanical signals play an important role in neuronal maturation, and that local brain tissue stiffness may thus be a key parameter for proper brain development.