BP 17: Poster V

Biomaterials and Biopolymers (BP 15.1 – BP 15.10); Focus: Biological Cells in Microfluidics (BP 15.11 – BP 15.31)

Time: Tuesday 14:00–16:00 Location: P2/1OG

BP 17.1 Tue 14:00 P2/1OG

Surface Analysis of (Bioactive) Glasses and pH-dependent Protein Adsorption observed by X-ray Reflectometry — •Annemarie Prihoda, Michail Goldes, and Tobias Unruh — Institute of Crystallography and Structural Physics (ICSP), Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Staudtstr. 3, 91058 Erlangen, Germany

Since 1977 bioactive glass has been used in medicine and dentistry as a bone implant or toothpaste ingredient. In contact with liquids a hydroxyapatite layer forms on the glass surface by releasing alkali metal ions from the glass surface. Osteoblasts adhere to this layer and thus form new bone structure (1). A basic understanding of the medical compatibility on a molecular level has, however, not been achieved yet.

We have tried to simulate the first steps of glass interaction after implantation by studying protein adsorption on glasses. We present X-Ray Reflectivity (XRR) data showing the adsorption of BSA on glasses (soda lime and borosilicate glass). We were able to identify protein layers whose thickness and roughness we determined on angstrom scale. Furthermore, we show the dependence of the degree of coverage on the pH-value of the protein solution. In addition, we are sensitive to aging effects of the glass surface, e.g. glass corrosion, which occurs when the glasses are immersed in liquids. For the first time we were able to characterize the surface of Bioglass 45S5 with XRR and compared the results to non-bioactive glasses.

(1) Baino F. et al. Journal of functional biomaterials 2018, 9 (1)

BP 17.2 Tue 14:00 P2/1OG

Tailoring Network Structure of Collagen Type 1 by High-Energy Electron Irradiation — •Catharina Krömmelbein[1], Stefanie Riedel[1], Tom Kunschmann[2], and Stefan Mayr[1,2] — [1]Leibniz-Institut für Oberflächenmodifizierung e. V., Leipzig, Germany — [2]Fakultät für Physik und Geowissenschaften, Universität Leipzig, Leipzig, Germany

Imitating mammalian's extracellular matrix is essential to investigate cell behavior like adhesion and migration *in vitro* and is of great importance for biomedical applications as well. Collagen as main component of the mammalian's extracellular matrix is well suited as biomimetic material due to its excellent biocompatibility and biodegradability. Mostly, the fabrication of collagen type 1 matrices with defined network pore size involves the usage of cytotoxic chemicals. Herein, we adjust the pore size by covalent crosslinking, using high-energy electron irradiation of 0 kGy, 50 kGy and 100 kGy. Thereby, electron beam treatment is an effective and noninvasive method to ensure biocompatibility without the need for further chemicals. In addition, the pore size dependence of collagen type 1 networks on protein concentration is examined, using 1 mg/ml, 2 mg/ml and 3 mg/ml. In this contribution, we present a method to tailor the hydrogel's pore size by adjusting the gel concentration and the irradiation dose.

BP 17.3 Tue 14:00 P2/1OG

Observing polymer conformations at the 2D theta point — •Julian M. Philipp[1], Joachim O. Rädler[1], and Eugene P. Petrov[2] — [1]LMU, Munich, Germany — [2]PTB, Berlin, Germany

Important biological processes at cellular membranes involve interaction of biopolymers with the elastic deformable lipid bilayer. It has been found previously that conformations of DNA macromolecules adsorbed to freestanding cationic lipid membranes are controlled by the DNA-membrane attraction: whereas at low membrane charge densities membrane-bound DNA molecules behave as 2D swollen chains, an increase in the DNA-membrane attraction leads to membrane-driven coil-globule transition [1, 2]. These two regimes should be separated by the theta point, at which electrostatic and steric repulsion and membrane-mediated attraction of polymer segments compensate each other. Although theoretical predictions for the scaling of the macromolecule dimensions at the 2D theta-point are known [3]: $R_g \sim L^{4/7}$, the 2D theta-point behavior has never been observed directly in experiments. Using fluorescence microscopy we study conformations of single DNA molecules on freestanding cationic lipid bilayers at the membrane compositions close to those inducing the coil-globule transition and find that the dependence of R_g on L follows the scaling predicted for polymers at the theta-point in 2D. This represents the first direct experimental observation of polymer conformations at the 2D theta point. [1] C. Herold, P. Schwille, E.P. Petrov, Phys.Rev.Lett. 104(2010)148102; [2] A.G. Cherstvy, E.P. Petrov, Phys.Chem.Chem.Phys. 16(2014)2020; [3] B. Duplantier, H. Saleur, Phys.Rev.Lett. 59(1987)539.

BP 17.4 Tue 14:00 P2/1OG

Interaction of Neuronal Cells with Electrode Materials — •Alice Abend, Chelsie Steele, and Mareike Zink — Universität Leipzig, Peter Debye Institut für Physik der weichen Materie, Leipzig, Deutschland

Deep brain stimulation of neuronal cells with neuroelectrodes is already employed for medical treatment of different diseases such as epilepsy and Parkinson's. Additionally, coupling of neuronal cells to multielectrode and lab-on-a-chip materials offers new perspectives in in-vitro assessments ranging from neuronal network formation to drug testing. However, many biomaterials lack the ability to promote adhesion of neurons important for biomaterial performance. Employing the human glioblastoma cell line U87-MG as well as the human neuroblastoma cell line SH-SY5Y, we investigate the neuronal cells' adhesion dynamics, bioactivity as well as network formation on custom-made electrode materials composed of gold, indium tin oxide, titanium nitride with and without nanocolumnar surface patterning.

BP 17.5 Tue 14:00 P2/1OG

The Inhomogeneous Chain Ensemble Model for Semiflexible Polymer Networks — •Constantin Huster and Klaus Kroy — Universität Leipzig, Institut für theoretische Physik

When considering the theoretical descriptions of the mechanical properties of semiflexible polymer networks one might conclude that they suffer from a severe case of multi personality disorder: They can appear viscoelastic, plastic or inelastic, have been called time-fractals, can be self-heal and may soften or harden. Here we introduce a new perspective on semiflexible polymer networks called the inhomogeneous chain ensemble model which combines the bottom-up approach for biomechanics with ideas from super-statistics and core principles underlying the theory of soft glassy materials as well as the theory of floppy modes and non-affine deformation to show that the multi personality disorder of semiflexible polymer networks might not be as severe as it seams.

BP 17.6 Tue 14:00 P2/1OG

Analysis of protein secondary structure in silkworm and spider silk fibroins using Raman spectroscopy — •Emilia Pozarowska[1], Tomasz Runka[2], and Jan Ingo Flege[1] — [1]BTU Cottbus - Senftenberg, Germany — [2]Poznan University of Technology, Poland

Spider silks carry outstanding mechanical properties, such as the combination of high strength and large extensibility. The aim of this work is to investigate the protein secondary structure, in particular β - sheets, occurring in silkworm and spider silk fibers from different species, by Raman spectroscopy. The analysis of the Raman spectra provides information about characteristic conformations, such as amide I, III and protein secondary structure. A Steatoda grossa spider silk was compared with a silk of the Bombyx mori silkworm. The former shows smaller amount of β - sheets and more random coil and/or α - helix, suggesting better elastic properties. Furthermore, the analysis of dragline silks of 16 different spider species was performed resulting in specific Raman fingerprints corresponding to the silk structure and the sequence of amino acids within. Dragline silks of P. alticeps and S. grossa exhibit a larger contribution of proline and carbonyl (C=O) groups compared to other species. Data of polarized Raman spectroscopy confirmed the parallel alignment of the molecular chains to the fiber axis for all spider silks. Stress-strain curve measurements of one selected spider silk, tubiliform silk of S. grossa, revealed very good mechanical properties, i.e. a maximal strain of approximately 12.2% and final tensile stress at break of 1575 MPa.

BP 17.7 Tue 14:00 P2/1OG

Mechanoradicals in tensed tendon collagen as a new source of oxidative stress — •Christopher Zapp[1,2], Agnieszka Obarska-Kosinska[1,3], Reinhard Kappl[4], and Frauke Gräter[1,5] — [1]Heidelberg Institute for Theoretical Studies, Heidelberg — [2]Institute for Theoretical Physics, Heidelberg University — [3]Unit c/o DESY, European Molecular Biology Laboratory, Hamburg — [4]Institute for Biophysics, Saarland University Medical Center, Homburg — [5]Interdisciplinary Center for Scientific Computing, Heidelberg University

Mechanoradicals originate from homolytic bond scission in polymers. The existence, nature and biological relevance of mechanoradicals in proteins, instead, are unknown. We show that mechanical stress on collagen, a biopolymer, produces radicals and subsequently reactive oxygen species, essential biological signaling molecules. Electron-paramagnetic resonance (EPR) spectroscopy of stretched rat tail tendon, atomistic Molecular Dynamics simulations and quantum calculations show that radicals form by covalent bond scission in collagen due to mechanical stress. Radicals migrate to adjacent clusters of oxidized aromatic residues radicals, giving rise to a distinct and stable EPR spectrum consistent with a stable dihydroxyphenylalanine (DOPA) radical. The protein mechanoradicals, as a yet undiscovered source of oxidative stress, finally convert into hydrogen peroxide. Our study suggests collagen I to have evolved as a radical sponge against mechano-oxidative damage and proposes a new mechanism for exercise-induced oxidative stress and redox-mediated pathophysiological processes.

BP 17.8 Tue 14:00 P2/1OG

High Coverage Inductive Interface for Implants in Small Animals — •Ana Domingues[1], Christian Bentler[2], and Thomas Stieglitz[3] — [1]anadomingues53@gmail.com — [2]christian.bentler@imtek.de — [3]thomas.stieglitz@imtek.uni-freiburg.de

In Biomedical Engineering inductive wireless power transfer (IWPT) has been investigated by many researchers to charge active implantable medical devices (AIMDs) since IWPT is safe and avoids the implementation of cables, preventing infections through the skin and movement limitations.

This research develops a high coverage inductive interface to build a cage that works as a tool to acquire and study the neuronal activity in small animals. The coverage is constituted by big transmitter coils in order to charge homogeneously implants in free-moving small animals, where the receiver coil is fully implanted. Different approaches as the implementation of bigger coils, segmentation technique, multicoil array were combined to maximize the covered area and optimize the power distribution homogeneity as well as the power transfer efficiency.

It was found that segmentation technique significantly mitigated the power losses. Another important finding was that larger distances between transmitter and receiver coils decreased the misalignment sensitivity. Finally, after testing three different arrangements of multicoil arrays, it was concluded that overlapped coils provided the most homogeneous magnetic flux over the inductive surface compared with separated and adjacent coils.

BP 17.9 Tue 14:00 P2/1OG

Structural Dynamics Correlation of Peptides derived from Nucleoporins: Time-resolved X-ray Scattering and Computational Modelling — •Naireeta Biswas[1] and Simone Techert[1,2] — [1]FS-SCS, Deutsches Elektronen-Synchrotron (DESY), Notkestraβe 85, 22607 Hamburg, Germany — [2]University of Göttingen, Institute for X-ray Physics, Friedrich-Hund-Platz 1, 37077 Göttingen, Germany

Nuclear pore complexes (NPCs) form aqueous conduits along the nuclear membrane, controlling exchange of macromolecules between the cytoplasm and the cell nucleus is built up of ~ 30 different types of proteins called as nucleoporins(Nups) which contain phenylalanine-glycine (FG) repeating motifs know as FG repeat domains. FG repeat domains are intrinsically disordered. The FG domains facilitate a highly selective, bidirectional passage of macromolecules through the NPCs thus forming the permeability barrier. Several models for the highly selective nature of the permeability barrier of the NPCs have been proposed. According to the selective phase model, the NPC permeability barrier is constructed through cohesive meshwork of the FG domains by weak hydrophobic interactions between the phenylalanine residues forming a sieve like 3D hydrogel within the central channel of the NPCs.

To get an insight in the structural dynamics of these FG Nups, we are investigating the molecular dynamics of the FG repeat domains and their interactions during the gelation process using time-resolved small/wide-angel X-ray scattering (TR-SAXS/WAXS) techniques and molecular dynamics simulation.

BP 17.10 Tue 14:00 P2/1OG

First passage method to thermal fragmentation of amyloid fibrils — •Mohammadhosein Razbin[1], Panayotis Benetatos[2], and Ali Akbar Moosavi-Movahedi[3] — [1]Department of Energy Engineering and Physics, Amirkabir University of Technology, 14588 Tehran, Iran — [2]Department of Physics, Kyungpook National University, 80 Daehakro, Bukgu, Daegu 41566, Republic of Korea — [3]Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran

Using the mean first passage method, we calculated the fragmentation rate in a given position along an amyloid fibril. We consider the fibril as one dimensional Rouse chain. The thermal fluctuations define the first passage time (FPT) associated to the fragmentation of the chain. The fragmentation rate is the inverse of the average of the FPT. Our expression for the rate is a function of the number of monomers, the position of the fragmentation along the filament, the ratio of the bond energy to the thermal energy, and the Rouse relaxation time. Our model predicts the fragmentation rate of insulin fibrils under optimal growth conditions which is consistent with the experimental data.

BP 17.11 Tue 14:00 P2/1OG

X-ray measurements of bovine red blood cells in continuous flow — •Jan-Philipp Burchert[1], Gerrit Brehm[1], Rita Graceffa[1], Manfred Burghammer[2], and Sarah Köster[1] — [1]Institut für Röntgenphysik, Georg-August-Universität Göttingen, Germany — [2]European Synchrotron Radiation Facility, Grenoble, France

Due to their high penetration depth and resolution, X-rays are ideally suited to study structures and structural changes within biological samples. For this reason, X-ray-based techniques have been used by various authors to investigate adhesive cells on solid supports. However, these techniques cannot conveniently study suspended cells in flow. We developed an X-ray compatible microfluidic device that serves as a sample delivery system and measurement environment. In our experiments, this device is applied to measure fixed bovine red blood cells by small-angle X-ray scattering (SAXS). We find a good agreement between in-flow and static SAXS data. Thus, we demonstrate that suspended cells can be measured with SAXS in continuous flow.

BP 17.12 Tue 14:00 P2/1OG

Deformability-based cell sorting by a microfluidic ratchet effect — •Sebastian W. Krauss, Pierre-Yves Gires, Winfried Schmidt, Walter Zimmermann, and Matthias Weiss — University Bayreuth, Bayreuth, Germany

Various physiological states impact on the rigidity of cells, e.g. aging, infection, or cancer. Cellular rigidity can be quantified with a high throughput by monitoring cell deformations during passage through a narrow constriction in a microfluidic device [1]. In contrast to this mere feed-forward approach, we use an asymmetric periodic flow protocol to exploit flow-induced deformations for sorting cells according to their stiffness. In particular, we apply an asymmetrically oscillating flow in a microfluidic channel that leads to a zero net drift of solid polystyrene particles, whereas deformable cells (e.g. HeLa or red blood cells) experience a nonzero deformation-dependent displacement in each cycle. Preliminary results suggest this approach to be a versatile tool for screening the physiological state of cells.

[1] Otto, O., et al. (2015) Nature Methods 12.3, 199

BP 17.13 Tue 14:00 P2/1OG

DNA origami encoded shaping of synthetic cells — •Julius Fichtler[1,2], Kevin Jahnke[1,2], Dimitris Missirlis[3], and Kerstin Göpfrich[1,2] — [1]Biophysical Engineering Group, Max Planck Institute for Medical Research, Jahnstraße 29, 69120 Heidelberg, Germany — [2]Department of Physics and Astronomy, Heidelberg University, 69120 Heidelberg, Germany. — [3]Department of Cellular Biophysics, Max Planck Institute for Medical Research, Jahnstraße 29, 69120 Heidelberg, Germany

Over the past decades, DNA nanotechnology, especially DNA origami, has developed a ever-increasing opportunities to create arbitrary two- or three-dimensional nanoscale objects out of DNA. Here, we report a strategy in bottom-up synthetic biology to qualitatively as well as

quantitatively establish a link between information and compartment shape of synthetic cells. This is achieved via the deformation of giant unilamellar vesicles (GUVs) with information-encoding DNA origami. Variants of a squared-shaped two-layer DNA origami plate, displaying different degrees of polymerisation, were attached onto the surface of GUVs resulting in quantitatively clearly distinguishable membrane deformations that were evaluated by statistical analysis of the GUV's circularity. The strength of deformation correlates with the respective degree of polymerisation of DNA origami, induced by blunt end stacking, ranging from 100% nonspherical GUVs for the highest to 45% nonspherical GUVs for the lowest degree of polymerisation.

BP 17.14 Tue 14:00 P2/1OG

Flow-accelerated platelet biogenesis is due to an elasto-hydrodynamic instability — •Christian Bächer[1], Markus Bender[2], and Stephan Gekle[1] — [1]Biofluid Simulation and Modeling, Theoretische Physik VI, Universität Bayreuth, Germany — [2]Institute of Experimental Biomedicine I, University Hospital and Rudolf Virchow Center, Würzburg, Germany

Blood platelets form out of long protrusions, which are extended by stem cells into blood vessels of the bone marrow. After extension, these protrusions form swellings which eventually mature into blood platelets. Interestingly, experiments show a strong acceleration of platelet genesis in presence of blood flow. We use a newly developed 3D Lattice-Boltzmann/Immersed-Boundary method for active elastic cell membranes in presence of fluid flow [1] to provide a biophysical understanding of the swelling formation and its connection to blood flow. Our simulations show that actomyosin contractility triggers a pearling instability, which is similar to the Rayleigh-Plateau instability of a liquid jet and leads to the platelet-like swellings along the protrusion. Instability dynamics strongly accelerate as function of the blood flow velocity. Rather than to a biochemical regulation of platelet size, this points to a pure physical regulation, namely by the dominant wavelength of the instability.

[1] C. Bächer, S.Gekle, Phys. Rev. E 99, 062418, 2019

BP 17.15 Tue 14:00 P2/1OG

Dynamics of light-sensing microbial populations in microfluidic model habitats — •Sebastian Raum, Alexandros Fragkopoulos, and Oliver Bäumchen — Max Planck Institute for Dynamics and Self-Organization (MPI-DS), D-37077 Göttingen, Germany

The natural habitats of many microorganisms are complex porous environments, where surface interactions of the cells play an important role, e.g., for navigation and survival of cell populations. By performing phototaxis, photosynthetic microbes are able to migrate towards optimal light conditions, where they can eventually adhere to surfaces. The goal of our work is to study the competition between surface interactions, light-regulated motility and surface adhesion. We designed an experimental setup that mimics the natural environment of the microorganisms and simultaneously allows for precisely tailoring the light conditions. A suspension of the light sensing *Chlamydomonas reinhardtii* cells is confined in a quasi-two-dimensional microfluidic compartment consisting of randomly distributed circular pillars. We account for natural light gradients by using an optical density filter for the illumination of the model habitat. Measurements of the spatial cell distributions are conducted in blue and red light, in order to switch the cellular light responses on and off. We test the hypothesis that the interplay of phototaxis and light-regulated adhesiveness represents an evolutionary adaptation to optimize the cell's photosynthetic efficiency in their natural habitat.

BP 17.16 Tue 14:00 P2/1OG

Label-free, High Throughput, Optical Characterization and Sorting of Particles and Cells in Microfluidic Channels — •Daniel Geiger, Tobias Neckernuss, Jonas Pfeil, Lisa Kwapich, Patricia Schwilling, and Othmar Marti — Ulm University, Institute of Experimental Physics

We present ODIN, a high performance, label-free optical sensing system for real-time detection, analysis and sorting of biological and synthetic particles and complex structures in a continuous flow. It combines a fast and sensitive CMOS camera sensor and a field programmable gate array, a high-performance data processing unit, with smart evaluation algorithms in a single device. Our algorithms reduce the dimensionality of the data from the camera, which condenses the amount of data tremendously but maintains all important information and in addition decreases noise. This enables ODIN to perform advanced image analysis in real-time at very high frame rates without buffering so that it can run continuously. Hence, we can analyze a large number of objects at very high throughput rates of several thousand objects per second. ODIN analyzes properties like size, shape and morphology of different kinds of particles like microplastic, cells, droplets, algae or complex structures like encapsulated objects. Since our modular analysis toolkit runs in real-time, we can control a microfluidic sorting device to sort objects and cells based on predefined conditions. We show the base technology as well as selected applications from the fields of Lab-on-a-Chip testing, drug delivery and cell mechanics.

BP 17.17 Tue 14:00 P2/1OG

Mechanical phenotyping beyond geometrical constraints using virtual channels — •Muzaffar H. Panhwar, Venkata A.S. Dabbirru, Yesaswini Komaragiri, Ricardo H. Pires, and Oliver Otto — ZIK HIKE, University of Greifswald, Greifswald, Germany

Microfluidic techniques have proven to be of key importance for achieving high-throughput cell mechanical measurements. However, their design modifications require sophisticated cleanroom equipment. Here, we introduce virtual fluidic channels as a flexible and robust alternative to Poly-dimethylsiloxane chips. Virtual channels are liquid-bound fluidic systems that can be created in almost arbitrary fluidic systems, e.g. standard flow cytometer cuvettes, and tailored in three dimensions within seconds for rheological studies on a wide size range of biological samples. We show that cell deformation in narrow virtual channels inside micrometer-sized systems is mainly driven by shear stress. By contrast, cells inside virtual channels of a large cuvette or capillary are deformed by an interfacial normal stress originating from the liquid-liquid interface. We demonstrate that this liquid-liquid interface acts as a high-frequency liquid cantilever for probing cell rheology on a millisecond timescale. As a proof-of-principle, cells are treated with the actin depolymerizing drug cytochalasin D. A significant reduction in elastic modulus is found compared to untreated cells. In summary, we show that virtual channels might offer the ability for high-throughput mechanical cell characterization in almost arbitrary geometries.

BP 17.18 Tue 14:00 P2/1OG

The effect of oxygen deprivation on mechanical properties of HEK293 cells — •Giulio Bianchi[1,2], Doreen Biedenweg[3], Ricardo H. Pires[2], and Oliver Otto[2] — [1]Physiolab, University of Florence, Florence, Italy — [2]ZIK HIKE, University of Greifswald, Greifswald, Germany — [3]University of medicine of Greifswald, Greifswald, Germany

Hypoxia plays an important role in triggering a variety of diseases and is also an important stimulus during embryogenesis. Despite our detailed understanding of the molecular events associated with oxygen starvation, its consequences to the mechanical stability of the cell remain to be fully scrutinized. Using recombinant expression of fluorescently labeled Hypoxia Inducible Factor-1 (HIF-1) in HEK293 cells, we have monitored inducement of cellular response to a 1% oxygen atmosphere by epifluorescence microscopy to study modifications in the cytoskeleton. We link this molecular state of the cells to changes in the mechanical phenotype as a label-free functional parameter. Performing real-time deformability cytometry on HEK293 cells at different times after inducing hypoxia, our results demonstrate a significant increase in the elastic modulus after 12h, an effect that becomes reversed after 48h. Using fluorescence-based methods we have correlated our findings to an increased number of apoptotic cells 24h after induction of hypoxia.

BP 17.19 Tue 14:00 P2/1OG

The role of substrate contacts in 2D and 3D microenvironments for cell mechanical properties — •Venkata Dabbiru[1], Emmanual Manu[1], Huy Tung Dau[1], Nora Bödecker[1], Doreen Biedenweg[2], Ricardo Pires[1], and Oliver Otto[1] — [1]University of Greifswald, Germany — [2]University Medicine Greifswald, Germany

Cells form with their microenvironment a network of biological and physicochemical signals that stem from cell-cell and cell-matrix contacts. Several pathologies including oncological disorders are associated with changes in such contacts but a comparative investigation by different approaches substantiating their relevance towards cell mechanics has, to our knowledge, never been conducted.

Here, we examine the role played by the substrate for the mechanical properties of HEK293T cells grown in 2D monolayers and spheroids as a 3D cell culture model. Experiments are performed using atomic force microscopy (AFM) and real-time deformability cytometry (RT-

DC) in comparative assays. Our AFM results show that cells cultured in 2D have a Young's modulus that is significantly higher than that of spheroids. Interestingly, when cells are detached from the 2D substrate or the 3D matrix and captured in suspension, they become considerably stiffer. Comparing our AFM data to RT-DC results, which probes cells in suspension, we observe the same increase in elastic modulus independent of cell culture geometry. Our findings suggest, that the mechanical phenotype of adherent cells is to a large extent dominated by the presence of a substrate and less by the dimensionality of the cell environment.

BP 17.20 Tue 14:00 P2/1OG

Physical properties of cells required for efficient microcirculation — •Martin Krater[1,2], Stefanie Tietze[2], Angela Jacobi[1,2,3], Anna Taubenberger[2], Martin Bornhauser[3], and Jochen Guck[1,2] — [1]MPI for the Science of Light Erlangen — [2]Biotechnology Center TU Dresden — [3]Medical Clinic I, University Hospital TU Dresden

Biological cells in blood encounter successive constrictions smaller than their own diameter when circulating through microcapillaries such as the pulmonary networks. This is relevant for blood cells, circulating tumor cells or cells transplanted for therapeutic purposes such as mesenchymal stromal cells (MSC). While the cell size has been shown to be a relevant parameter to overcome capillary entrapment, the cells mechanical properties have so far not been considered. Here we investigated the microcirculation of MSCs as a function of their physical phenotype quantified using real-time deformability cytometry and atomic force microscopy. When MSCs were expanded in organ-like 3D mesenspheres, as opposed to MSCs classically cultured on 2D surfaces, we found them to be smaller and more compliant. Resulting in a more effective circulation in vitro, using a microfluidic microcirculation mimetic and improved in vivo circulation after intravenous transplantation to NOD/SCID mice. The initially large and stiff MSCs cultured in 2D could be reprogrammed into a physical phenotype suitable for circulation by subsequent culture in 3D systems. Thus, the physical properties of cells are essential to overcome capillary entrapment and are a promising therapeutic target to improve effective circulation.

BP 17.21 Tue 14:00 P2/1OG

High-throughput characterization of the time-dependent mechanical properties of hydrogel beads, liquid droplets and biological cells — •Felix Reichel[1,2], Lucas Wittwer[1,3], Marta Urbanska[1,2], Shada Abuhattum[1], Sebastian Aland[3], and Jochen Guck[1] — [1]Max Planck Institute for the Science of Light and Max-Planck-Zentrum für Physik und Medizin, Erlangen — [2]Biotechnology Center, Center for Molecular and Cellular Bioengineering, Technische Universität Dresden, Dresden — [3]Hochschule für Technik und Wirtschaft Dresden, Dresden

In recent years, microfluidic tools have emerged that are capable of characterizing the mechanical properties of hundreds of thousands of cells individually within minutes. These tools, termed deformability cytometry, often focus on the deformation of the cell at a single time point once it has reached steady-state. Because of this, the strain information can only be linked to the elastic response of the deformed object. Here, we extend this approach and analyze the time-dependent deformation of spherical objects over a stress profile to determine their viscoelastic response when flowing through a microfluidic channel. Experiments on standardized hydrogel beads, phase-separated liquid droplets, and biological cells are compared to FEM-simulation data to derive both Young's Modulus and bulk viscosity. The simulations are also used to identify suitable mechanical models to describe the stress-strain relation of these different objects. With our approach we are broadening the mechanical information gained from deformation studies of spherical objects in high-throughput microfluidic assays.

BP 17.22 Tue 14:00 P2/1OG

Mechanical dissociation of tissue for real-time deformability cytometry — •Markéta Kubánková[1], •Despina Soteriou[1], Oana-Maria Thoma[2], Andrea-Hermina Györfi[3], Alexandru-Emil Matei[3], Stefan Scheuermann[4], Felix Dirla[5], Maximilian Waldner[2], Jörg Distler[3], Jens Langejürgen[4], and Jochen Guck[1] — [1]Max Planck Institute for the Science of Light, Erlangen, DE — [2]Dept. of Medicine 1, FAU Erlangen-Nürnberg, DE — [3]Dept. of Medicine 3, FAU Erlangen-Nürnberg, DE — [4]Fraunhofer IPA, Mannheim, DE — [5]BioITix, Frankfurt/Main, DE

Real-time deformability cytometry (RT-DC) is a high-throughput method used for characterizing single cells in suspension. Here we apply RT-DC for analyzing cells obtained from solid tissues. We used an enzyme-free approach based on mechanical dissociation of tissue, TissueGrinder (TG), to obtain heterogeneous single cell suspensions from various mouse tissues. The dissociation procedure resulted in high cell yield and viability and was significantly faster (~ 20 min) compared to conventional enzymatic methods (hours). RT-DC analysis allowed us to distinguish subpopulations of cells in label-free manner and to extract further information from single cell images, such as deformability. A key advantage of this method is that it is non-destructive and cells may be further reused. Moreover, a cell population of interest can be sorted according to image-based parameters. The combination of TG with RT-DC has potential as a fast and high-throughput diagnostic pipeline to detect pathological changes in tissue biopsies and to reveal cell populations invisible to marker-based approaches.

BP 17.23 Tue 14:00 P2/1OG

Droplet-Based Multiplexed Screening of Single NK Cells' Interferon-γ Release and Cytotoxicity — •Tobias Abele[1,2], Silvia Antona[1,2], Kevin Jahnke[1,2], Yannik Dreher[1,2], Ilia Platzman[1,2], and Joachim P. Spatz[1,2] — [1]Max Planck Institute for Medical Research, Heidelberg, Germany — [2]Department of Biophysical Chemistry, University of Heidelberg, Germany

Interferon-gamma (IFN-γ) is a fundamental cytokine secreted by natural killer (NK) cells and activated T cells. The amount of IFN-γ released by cytotoxic cells strongly immunomodulates several antitumor mechanisms. Therefore, single-cell analysis of IFN-γ release can help disentangle the heterogeneity of immune cells, leading to breakthrough findings. Towards this end, we exploited droplet-based microfluidics to investigate IFN-γ secretion from single NK cells in correlation with their cytolytic activity. Our method relies on co-encapsulation of activated NK-92 cells, polystyrene beads conjugated with specific IFN–γ capture antibodies and fluorescently labeled detection antibodies within surfactant stabilized water-in-oil compartments. The secreted cytokines are captured and detected via localized fluorescence at the periphery of the beads. Using this method, we thoroughly correlated the IFN-γ released from activated NK-92 cells with their ability to kill a specific target. We believe that the developed method represents a straight-forward approach to unravel the complex heterogeneity of NK cells. Furthermore, we envision our droplet-based assay to deepen the understanding of further immunological challenges such as aberrant IFN-γ expression related to autoimmune diseases.

BP 17.24 Tue 14:00 P2/1OG

MPI-based multi-GPU extension of the Lattice Boltzmann Method — •Fabian Häusl, Moritz Lehmann, and Stephan Gekle — Biofluid Simulation and Modeling, University of Bayreuth, Germany

The lattice Boltzmann method (LBM) is a highly versatile flow solver which benefits greatly from graphics processing unit (GPU) computing. However, the LBM is very memory-intensive while at the same time the on-board memory of GPUs is quite limited, which directly restricts simulation domain size. This poster presents a muli-GPU implementation based on the framework OpenCL and the Message Passing Interface (MPI) which is able to widen this limitation as well as to gain additional speedup. By using spezialized buffer types and memory layouts as well as applying the concept of templates to OpenCL-kernels in order to reduce memory access, it is precisely tailored to the requirements of GPUs and MPI. It differs from comparable implementations especially in that the domain can be subdivided along all three spatial directions. The communication scheme remains independent of the velocity set selected, can easily be adapted to the various extensions of the LBM and guarantees optimal buffer bandwidth. Communication time consumption can be hidden for the most part by overlapping it with computation, so the algorithm can reach 95% of its theoretical optimum in the weak-scaling and 13000 MLUPs using 4 Radeon VII GPUs for a cubic benchmark setup can be observed.

BP 17.25 Tue 14:00 P2/1OG

Analysis of red blood cells behaviour in a microfluidic device — •Amirreza Gholivand[1,2], Knut Dahlhoff[3], Timo Dickscheid[4], and Minne Paul Lettinga[1,2] — [1]Laboratory of Soft Matter and Biophysics, KU Leuven, Leuven, Belgium — [2]ICS-3 Soft Condensed Matter, Forschungszentrum Jülich, Jülich, Germany — [3]ZEA-1 Engineering, Electronics and Analytics, Forschungszentrum Jülich, Jülich, Germany — [4]INM-1 Neuroscience and Medicine, Forschungszentrum Jülich, Jülich, Germany

The blood flow dynamics through the micro-vascular system, which

is the end of our vascular system, depend on many factors, such as the exact shape of the vessels, the aggregation and disaggregation and deformation of the red blood cells (RBCs). The effects of these parameters have been systematically studied in microfluidics, mainly using 2D channels with rectangular cross section, which are very different from the physiological vessels.

Here we present first data the flow of concentrated dispersions of (attractive) red blood cells in model 3-D microfluidic channels as well as physiologically relevant shaped channels. We used a novel technique, Selective Laser-induced Etching (SLE), to produce 3D structures in glass that allows the design of bifurcations into different planes with any desirable shape. To study the shape memory of the vessels the second generation of the bifurcation has been implemented with a parallel and perpendicular orientation relative to the first bifurcation,

BP 17.26 Tue 14:00 P2/1OG

Rectification of Bacterial Diffusion in Microfluidic Labyrinths — •Ariane Weber[1,2], Marco Bahrs[3], Zahra Alirezaeizanjani[3], Xingyu Zhang[1,4], Carsten Beta[3], and Vasily Zaburdaev[1,4] — [1]Friedrich-Alexander-Universität Erlangen-Nürnberg, Deutschland — [2]Max-Planck-Institut für Menschheitsgeschichte, Jena, Deutschland — [3]Universität Potsdam, Deutschland — [4]Max-Planck-Zentrum für Physik und Medizin, Erlangen, Deutschland

Bacteria are able to explore large areas and move through complex environments. Both are of importance in various fields ranging from medicine over ecological sciences to industrial processes. In complex environments, bacteria interact with their surroundings and are strongly guided by confinement. To investigate how the dispersal of bacteria can be augmented by confinement, we study the long-term dispersal of bacteria which exhibit the run-and-tumble motility pattern in microfluidic labyrinths. Here we focus on two labyrinths made of obstacles regularly arranged in a square and a hexagonal lattice. We present an analytical description of the bacterial dispersal and numerical simulations of the underlying random walk for both geometries. To validate our theoretical predictions, we compare our results to experimental data of *E. coli* bacteria swimming through microfluidic labyrinths. Both in theory and experiments we observe enhanced dispersal of bacteria in labyrinths as compared to freely swimming cells for realistic motility and labyrinth parameters. For an extended initial period, the dispersal exhibits non-Gaussian diffusion, where the geometry of the labyrinth is imprinted in the bacterial density profiles.

BP 17.27 Tue 14:00 P2/1OG

Better, faster, stronger: a new era of measuring cell mechanics and why we should care about strain rates — •Marta Urbanska[1,2], Hector E. Muñoz[3], Josephine Shaw Bagnall[4], Oliver Otto[1,5], Scott R. Manalis[4], Dino Di Carlo[3], and Jochen Guck[1,2] — [1]TU Dresden, Dresden, Germany — [2]MPL, Erlangen, Germany — [3]UCLA, Los Angeles, CA, USA — [4]MIT, Cambridge, MA, USA — [5]University of Greifswald, Greifswald, Germany

The mechanical phenotype of a cell is an inherent biophysical marker of its state and function, with potential value in clinical diagnostics. Several microfluidic-based methods developed in recent years have enabled single-cell mechanophenotyping at throughputs comparable to flow cytometery, thereby opening a new era of cell mechanical characterization. Here we present a highly standardized cross-laboratory study comparing three leading microfluidic-based approaches to measure cell mechanical phenotype: constriction-based deformability cytometry (cDC), shear flow deformability cytometry (sDC), and extensional flow deformability cytometry (xDC). We show that all three methods detect cell deformability changes induced by exposure to altered osmolarity. However, a dose-dependent deformability increase upon latrunculin B-induced actin disassembly was detected only with cDC and sDC, which suggests that when exposing cells to the high strain rates imposed by xDC, other cell components dominate the response. The direct comparison presented here serves to unify deformability cytometry methods and provides context for the interpretation of deformability measurements performed using different platforms.

BP 17.28 Tue 14:00 P2/1OG

Dynamic RT-DC: red blood cell viscoelasticity as a label-free biomarker — •Bob Fregin[1,3], Fabian Czerwinski[1], Konstanze Aurich[2], Doreen Biedenweg[2], Stefan Gross[3], Gerlad Kerth[4], and Oliver Otto[1,3] — [1]ZIK HIKE, Universität Greifswald, Germany — [2]Universitätsklinikum Greifswald, Germany — [3]DZHK, Universität Greifswald, Germany — [4]Angewandte Zoologie und Naturschutz, Universität Greifswald, Germany

Real-Time Deformability Cytometry (RT-DC) is a label-free technique for single cell mechanical analysis with high-throughput of up to 1,000 cells/second. Initially, RT-DC was limited to steady-state deformation captured at the end of the channel enabling the calculation of time-independent information as the Young's modulus.

We introduce an extension of RT-DC towards dynamic single cell measurements with the possibility to capture full viscoelastic properties at up to 100 cells/s. Cellular shape-changes along the entire length of the microfluidic channel are tracked in real-time and are subsequently analyzed by a Fourier decomposition discriminating cell responses to interfering stress distributions. We demonstrate that dRT-DC allows for cell mechanical assays at the millisecond time scale independent of cell shape. We use this approach for a comparison of peripheral blood cells based on their Young's modulus and viscosity.

In proof-of-principle experiments we use dRT-DC to approach the question of temperature control in hibernating animals. Initial experiments on bats and humans suggest a role of red blood cell viscoelasticity to maintain blood flow at low temperatures.

BP 17.29 Tue 14:00 P2/1OG

Stimulation Dynamics of Circular Dorsal Ruffles in Fibroblast Cells — •Malte Ohmstede and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen, Bremen

Circular Dorsal Ruffles (CDRs) are ring shaped, propagating protrusions on the dorsal cell surface in - among others - fibroblast cells. These dense actin structures play a major role in macropincytosis and are orchestrated using a complex molecular pathway. The upstream stimulation of CDRs is done by activation of Receptor Tyrosine Kinases using various types of growth factors. In this work, Platelet Derived Growth Factor (PDGF) in conjunction with a microfluidic perfusion chamber is used to perform precise stimulation and re-stimulation of adherent fibroblast cells. Combined with fibronectin micro-contact printing, this method reproducibly yields large amounts of data from equally shaped cells. Through usage of circular kymographs and further image processing, the dynamics of cellular responses to PDGF stimuli are measured. For different PDGF concentrations, various characteristics of CDRs are evaluated. CDRs only form on the lamellipodium of adherent cells and are reflected by the nucleus and the cell edge. Incorporating deep learning based image segmentation, the influence of lammelipodial shape as boundary condition on CDR dynamics is evaluated.

BP 17.30 Tue 14:00 P2/1OG

Impact of cell culture age and structural modifications on the mechanical properties of hiPSCs derived cardiomyocytes. — •Emmanuel Manu[1], Nithya Shree[1], Ricardo Pires[1], Stefan Gross[2], and Oliver Otto[1] — [1]Biomechanics, ZIK HIKE, University of Greifswald, Germany — [2]DZHK, University of Greifswald, Greifswald, Germany

Cardiomyocytes derived from human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) are important biological models in drug screening and in understanding the pathophysiology of many cardiac diseases. Here, using atomic force microscopy, we focus on understanding the mechanical properties of cardiomyocytes as a function of culture age, using Cytochalasin D (CytoD) to promote actin-network depolymerisation. We observed that between the second to the fifteenth day of culture, the Young*s modulus (mean * SEM) of hiPSC-CM increased from 657 * 93 Pa to 1967 * 159 Pa. Exposing hiPSC-CMs to CytoD of varying concentrations, we determined an EC50 of 3.892 *M. Interestingly, the effect of actin depolymerization on the mechanical properties of cells decreases with cell culture age. This indicates that maturation of hiPSC-CMs involves remodelling of the actin network towards increased stability, possibly through the predominant incorporation of actin filaments into sarcomeres. Finally, we compared the elastic modulus of hiPSC-CMs when the cells are characterized in suspension as well as in adherent state. Interestingly, both methods yield elastic modulus values in good agreement.

BP 17.31 Tue 14:00 P2/1OG

Impact of cell culture age and structural modifications on the mechanical properties of hiPSCs derived cardiomyocytes — •Emmanuel Manu[1], Nithya Shree[1], Ricardo Pires[1], Stefan Gross[2], and Oliver Otto[1] — [1]ZIK HIKE, University of Greifswald, Greifswald, Germany — [2]DZHK, University Medicine Greifswald, Greifswald, Germany

Cardiomyocytes derived from human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM) are important biological models

in drug screening and in understanding the pathophysiology of many cardiac diseases.

Here, using atomic force microscopy, we focus on analysing the mechanical properties of cardiomyocytes as a function of culture age and cytoskeletal modifications, using Cytochalasin D (CytoD) to promote actin-network depolymerisation. We observed that between the second to the fifteenth day of culture, the Young's modulus (mean +/- SEM) of hiPSC-CM increased from 657 +/- 93 Pa to 1967 +/- 159 Pa. Exposing hiPSC-CMs to CytoD of varying concentrations, we determined an EC50 of 3.892 uM. Interestingly, the effect of actin depolymerization on the mechanical properties of cells decreases with cell culture age. This indicates that maturation of hiPSC-CMs involves remodelling of the actin network towards increased stability, possibly through the predominant incorporation of actin filaments into sarcomeres. Finally, we compared the elastic modulus of hiPSC-CMs when the cells are characterized in suspension as well as in adherent state. Interestingly, both methods yield elastic modulus values in good agreement.