BP 27: Cell Mechanics II

Time: Thursday 9:30–12:45 Location: H 1028

Invited Talk BP 27.1 Thu 9:30 H 1028

Size and Mechanical Scaling of Blood Platelets — Aastha Mathur, Sandra Correia, Serge Dmitrieff, Romain Gibeaux, Iana Kalinina, Tooba Quidwai, Jonas Ries, and •Francois Nedelec — EMBL Heidelberg

Blood platelets play a major role in hemostasis, the process of stopping blood loss from injured vessels. Platelets have a discoid shape while floating free in the blood in the so-called resting state but come in various sizes, ranging from 1.6 to 5 micrometers. I will argue that their size, in this case, can be understood from the competition between the elasticity of a circular bundle of microtubules, and surface tension at the cell edge. Such a mechanical equilibrium predicts a scaling law that is verified by imaging a large number of individual platelets live, from Mouse and Human blood samples. I will then discuss the dynamics that is observed at the onset of platelet activation, on the path towards platelet adhesion and aggregation. The microtubule ring maintaining the shape of platelets initially coils but is later able to recover within 30 minutes. This can be understood as the ring is made of multiple microtubules that are dynamically connected, and can respond both elastically or viscously. Importantly, given the mechanical properties of these components, we can explain why the overall mechanical response of platelets is dependent on their size, a fact that is known to be important for the physiology of platelets in vivo.

BP 27.2 Thu 10:00 H 1028

Active prestress leads to an apparent linear stiffening of the cytoskeleton through geometrical coupling and shear-induced nematic alignment — •Elisabeth Fischer-Friedrich — Biotec, TU Dresden, Tatzberg 47-49, 01307 Dresden, Germany

Tuning of active prestress e.g. through activity of molecular motors constitutes a powerful cellular tool to adjust cellular stiffness through nonlinear material properties. Understanding this tool is an important prerequisite for our comprehension of cellular force response, cell shape dynamics and tissue organization. Experimental data obtained from cell-mechanical measurements often show a simple linear dependence between mechanical prestress and measured differential elastic moduli corresponding to a power law with exponent one. While these experimental findings could point to the theoretically predicted "pull-out" of soft bending modes, we propose here a surprisingly simple alternative explanation. In a theoretical study, we show how active prestress in the cytoskeleton gives rise to a linear increase of measured cellular force response and resulting apparent stress-stiffening through geometrical-coupling and shear-induced nematic alignment. We argue that a new experimental paradigm is required to separate this apparent stress-stiffening from actual nonlinearities in prestressed biological materials.

BP 27.3 Thu 10:15 H 1028

Mechanical strain sensing in rod-shaped Escherichia coli — •Lars Renner[1], Felix Wong[2], Gizem Özbaykal[3], Sven van Teeffelen[3], and Ariel Amir[2] — [1]Leibniz Institute of Polymer Research Dresden — [2]Harvard University, Cambridge, USA — [3]Institut Pasteur, Paris, France

Why bacteria have evolved and maintained their specific shapes is a central question in bacterial cell biology. Bacteria are remarkably successful in achieving a precise shape and tightly coordinating cellular processes such as DNA replication, protein production and cell division, yet the underlying biophysical cues and the evolutionary advantage for one shape over another are largely unknown. We are setting out to understand how rod-shaped bacteria maintain their shape when subjected to mechanical deformation. In particular, we explore how mechanical force changes the bacteria morphology and consequently affects the bacterial shape after the mechanical force is released. We combine microfabrication tools and mathematical models to analyse cell shape recovery of E. coli with intentionally modified cell morphology under mechanical stress. When confined, cells are readily adapting to the new morphology. When released, bacterial cells recover their straight, rod-shaped morphologies. We find a straightening rate that is approximately twice the growth rate. By developing a theory of residual stresses, we identify mechanical stress-based nucleation of new growth sites to explain the enhanced straightening rate. Our results indicate a stress-based mechanism for shape regulation in rod-shape bacteria.

BP 27.4 Thu 10:30 H 1028

Poroelastic two-phase model for moving droplets of Physarum polycephalum with free boundaries — •Dirk Alexander Kulawiak[1], Jakob Löber[3], Markus Bär[2], and Harald Engel[1] — [1]Institut für Theoretische Physik, TU Berlin, Berlin, Germany — [2]Physikalisch-Technische Bundesanstalt, Berlin, Germany — [3]Max-Planck-Institut für Physik komplexer Systeme, Dresden Germany

Motivated by recent experiments, we model the flow-driven amoeboid motility that is exhibited by protoplasmic droplets of Physarum. Here, a feedback loop between a chemical regulator, active mechanical deformations, and induced flows give rise to spatio-temporal contraction patterns that result in directed motion. Our model describes the droplet's cytoskeleton as an active viscoelastic solid phase that is permeated by a passive viscous fluid representing the cytosol. The active tension in the solid phase depends on the concentration of a regulating agent that is advected by the fluid phase. Previously, it was shown that under rigid boundary conditions that impose a fixed shape, this model reproduces a large variety of mechano-chemical patterns such as antiphase oscillations and rotating spirals. This in line with experimental observations of contraction patterns in these droplets. Here, we present an approach that includes free boundary conditions, nonlinear friction between droplet and substrate and a nonlinear reaction kinetic for the regulator to model the movement of these droplets. We find deformations of the droplet boundary as well as oscillatory changes in the droplets position with a net motion in each cycle.

BP 27.5 Thu 10:45 H 1028

The Mechanics of Vesicle Blebbing — •Sebastian Hillringhaus, Gerhard Gompper, and Dmitry A. Fedosov — Institute of Complex Systems, Forschungszentrum Jülich, Jülich, Germany

A broad range of *in silico* models, including liquid and viscoelastic drop models, has been introduced for simulating the complex mechanical properties of different cell types. These models are used to understand and quantify experimental measurements. In this work, we employ a coarse-grained cell model in two and three dimensions which incorporates the membrane properties similar to the RBC-model and an elastic inner mesh to include the cytoskeletal properties. The model is formulated in the framework of the dissipative particle dynamics simulation method. It is used to investigate cell-blebbing, which is observed in synthetic vesicles. Cell-blebbing describes the dissociation of the membrane from the inner network, in this case as result of inner stress. We analyze the influence of different parameters on the blebbing process and show that the occurrence of blebbing is a result of the instability of the connection between membrane and actin-network.

30 min. break

BP 27.6 Thu 11:30 H 1028

Simulations of stem cells in microjets — •Carina Bezold, Christian Bächer, and Stephan Gekle — Biofluid Simulation and Modeling, Bayreuth, Germany

3D bioprinting offers the opportunity to create tissues and organs which could be used for transplantation. The tissue is built up layer for layer by a continuous jet containing stem cells.We develop a model for stem cells as elastic spheroids, using tools of the finite element method. We validate our model using the Hertzian theory for small deformations. To simulate the fluid, we use 3D Lattice-Boltzmann simulations including the transition from the printer nozzle into the free liquid jet. This region is of particular interest since high extensional forces are present. Due to the different flow profiles at the transition we observe a change in the cell shape.

BP 27.7 Thu 11:45 H 1028

Induction of cytoplasmic flows reveals: asymmetric cell division is a digital decision based on gradually varying PAR polarization states — M. Mittasch[1], M. Nestler[2], P. Gross[3], A. Fritsch[1], M. Kar[1], S. Grill[3], A. Voigt[2], and •M. Kreysing[1] — [1]MPI-CBG — [2]Dept. of Mathematics, TUD — [3]Biotec, TUD (all Dresden)

Throughout the last decades, access to genetic perturbations boosted our molecular-level understanding of cell biological processes. However, it was suggested that the spatio-temporal organization of cells and developing embryos also depends on physical transport processes, which remains an experimental challenge to confirm.

Here we present *Focused light induced cytoplasmic streaming* (FLUCS) which enables the dynamic control of cytoplasmic flows in cells and developing embryos via thermoviscous expansion phenomena (Weinert & Braun, J Appl Phys 2008). FLUCS allows to systematically dissect the role of flows during PAR polarization. We find that i) cytoplasmic flows towards the membrane drive PAR loading locally, ii) cytoplasmic flows parallel to the membrane induce cortical flows. iii) Control over cortical flows enables to move pre-established PAR domains. iv) We find that small displacements of PAR domains are self-corrected and cells divide normally. v) For rotations beyond 90 degrees, however, we observe a flip of the PAR defined body axis, followed by inverted asymmetric cell divisions. Our results suggest that asymmetric cell division is a digital decision based on a gradually varying PAR polarization states. Ref: Mittasch et al (accepted).

BP 27.8 Thu 12:00 H 1028

Entropic swelling of chromatin drives neutrophil extracellular trap release — •Daniel Meyer[2,3], Elsa Neubert[1,2], Luise Erpenbeck[1], and Sebastian Kruss[2,3] — [1]Department of Dermatology, Venereology and Allergology, University Medical Center, Goettingen University, Germany — [2]Institute of Physical Chemistry, Göttingen University, Germany — [3]Center for Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), Göttingen, Germany

Neutrophilic granulocytes are the most abundant immune cells in humans and essential to defeat pathogens. They can release their own DNA as neutrophil extracellular traps (NETs) to capture and eliminate bacteria, fungi and viruses. DNA expulsion (NETosis) has also been documented for other immune cells but also for amoebas and plant cells, and has been implicated in many diseases, including cancer, vascular and chronic inflammatory disorders.

During NETosis, neutrophils undergo dynamic and dramatic alterations of their cellular as well as sub-cellular morphology whose biophysical basis is poorly understood. We investigated NETosis in real-time on the single-cell level using high-resolution fluorescence and atomic force microscopy. Our results show that NETosis is highly organized into distinct phases with a clearly defined point of no return. Entropic chromatin swelling is the major driving force and the reason for cell morphology changes, mechanical changes and the rupture of both nuclear envelope and plasma membrane. Through its material properties, chromatin thus directly and actively orchestrates this biological process.

BP 27.9 Thu 12:15 H 1028

Effect of Arp2/3 on 3D migration and cellular mechanical properties — •Stefanie Puder, Tom Kunschmann, and Claudia Tanja Mierke — Biological Physics Division, Peter Debye Institute for Soft Matter Physics, University of Leipzig, Germany

Cellular motility is essential in many physiological processes such as tissue repair during wound healing. The migration of cells in 3D extracellular matrices (ECM) is regulated by the actin cytoskeleton. The actin related protein complex Arp2/3 facilitates nucleation and polymerization of new actin branches, which is supposed to impact cellular mechanical properties. However, whether Arp2/3 affects cellular mechanical properties and subsequently migration of cells is not well understood. We suggested that the Arp2/3 complex facilitates 3D motility into ECM by regulating cellular mechanical properties. Our study focuses on Arp3 conditional knock-down fibroblast cells induced by 4-OH-tamoxifen. Cells are analyzed for their ability to migrate in dense 3D ECM. The knock-down of Arp3 accompanies with a significant reduced invasiveness. Cellular mechanical properties are quantified by an optical cell stretcher and AFM resulting in comparable characteristics of cellular deformability and Young's modulus. We found that Arp3 knock-down cells are less deformable (stiffer) compared to control treated cells in both presented techniques. In conclusion, Arp2/3 complex and its subunit Arp3 are essential for providing mechanical cellular stiffness regulating motility into 3D ECM. We demonstrated that Arp2/3 regulates cellular deformability, stiffness and transmission promoting Arp2/3-dependent cell invasion.

BP 27.10 Thu 12:30 H 1028

Influence of matrix and cellular properties on human cancer cell migration in 3D biomimetic matrices — •Tony Fischer and Claudia Tanja Mierke — Universität Leipzig, Peter-Debye-Institut

3D cellular motility in connective tissue is a fundamental process during tissue development and cancer progression, mostly studied in biomimetic in vitro models. Crucial factors for cancer metastasis are cellular motility and mechanical properties of the migrating cell and topology and elasticity of the surrounding matrix. ECM and cell properties are altered in many tumors as stiffness of the matrix and cells is linked to malignancy and metastasis. Different ECM models and quantifying algorithms exist to measure matrix topology, cell elasticity, motility and cell-matrix interactions. We used a collagen I ECM model comprised of rat tail collagen building elongated fibrils and bovine dermal collagen building node-shaped scaffolds to adapt to local inhomogeneities. Pore-size and topology was analyzed using a euclidean distance map approach to bubble analysis and a gel reconstruction algorithm using fuzzy-connectedness. Elastic properties of both cells and gels were determined using AFM. Cellular motility was analyzed using an invasion assay. Cell-mediated fiber displacement was determined using optical flow measurements. Our findings show that stiffer matrices indeed enhanced cellular motility. Malignant MDA-MB-231 cancer cells were softer, more motile and deformed their surrounding ECM more than less invasive MCF-7 cells. We are able to study cancer cell migration and mechanotransduction in our ECM model with tunable topology and mechanics and measure topological influences.