# BP 37: Cell Mechanics and Migration

Time: Wednesday 9:30–12:45 Location: H44

**Invited Talk** BP 37.1 Wed 9:30 H44

**Reconstituting basic mitotic spindles in artificial confinement** — •Marileen Dogterom — Department of Bionanoscience, Kavli Institute of Nanoscience, Delft University of Technology, The Netherlands

Microtubules are stiff dynamic polymers that can generate pushing and pulling forces by growing and shrinking. To fulfill their function, microtubules adopt specific spatial patterns, like the mitotic spindle during cell division. To understand the basic principles of mitotic spindle organization, we reconstitute a dynamic microtubule cytoskeleton inside three-dimensional water-in-oil emulsion droplets, using lipids that can be functionalized with dynein molecular motors. We then study the positioning of centrosomes, from which microtubules are nucleated that exert pushing and/or dynein-mediated pulling forces when reaching the boundary. We find that two centrosomes adopt an equilibrium position balancing a dynein-mediated centering effect with a repulsion force between the two centrosomes, thereby already reproducing a basic mitotic spindle like organization. We are now using this system as a platform to study how other essential spindle components affect the force balance of basic mitotic spindles.

BP 37.2 Wed 10:00 H44

**Microglia mechanics: From traction forces to durotaxis** — •David Koser[1,2], Lars Bollmann[1], and Kristian Franze[1] — [1]University of Cambridge, Cambridge, United Kingdom — [2]German Cancer Research Center, Heidelberg, Germany

Microglial cells are key players in the primary immune response of the central nervous system. Their functionality in healthy and pathological conditions highly depends on their chemical as well as their mechanical environment. While the impact of chemical signaling on microglial behavior has been studied thoroughly, the current understanding of mechanical signaling in controlling the cells' behavior is very limited. Here we investigated the dependency of microglial traction forces on substrate stiffness and the cells' migratory behavior on substrates incorporating stiffness gradients. Primary microglia adapted their actin cytoskeleton and morphology to the stiffness of the culturing substrate. Traction force microscopy revealed that stresses exerted by the cells initially increase with substrate stiffness until reaching a plateau. On substrates incorporating a stiffness gradient microglial cells preferentially migrated towards stiff in a process termed durotaxis. Immune-activation of microglia through lipopolysaccharide led to a modulation of traction forces, increased migration velocities, and an enhancement of durotaxis. Finally, the experimental findings can be reproduced by combining a phenomenological stress fluctuation and a biased random walk model. Our results clearly demonstrate that microglia are mechanosensitive, which might be essential in central nervous system development and pathologies.

BP 37.3 Wed 10:15 H44

**Gating mechanosensitive channels in bacteria with an atomic force microscope** — •Renata Garces[1], Samantha Miller[2], and Christoph F. Schmidt[1] — [1]Third Institute of Physics-Biophysics, Georg August University, Göttingen, Germany — [2]School of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom

The regulation of growth and integrity of bacteria is critically linked to mechanical stress. Bacteria typically maintain a high difference of osmotic pressure (turgor pressure) with respect to the environment. This pressure difference (on the order of 1 atm) is supported by the cell envelope, a composite of lipid membranes and a rigid cell wall.

Turgor pressure is controlled by the ratio of osmolytes inside and outside bacteria and thus, can abruptly increase upon osmotic downshock. For structural integrity bacteria rely on the mechanical stability of the cell wall and on the action of mechanosensitive (MS) channels: membrane proteins that release solutes in response to stress in the cell envelope.

We here present experimental data on MS channels gating. We activate channels by indenting living bacteria with the cantilever of an atomic force microscope (AFM). We compare responses of wild-type and mutant bacteria in which some or all MS channels have been eliminated.

BP 37.4 Wed 10:30 H44

**Using photonic force microscopy to investigate filopodia mediated phagocytosis** — •Rebecca Michiels and Alexander Rohrbach — Lab for Bio- and Nano-Photonics, University of Freiburg, Georges-Koehler-Allee 102, 79110 Freiburg, Germany

Macrophage cells are immune cells which internalize and digest foreign matter, cell debris and bacteria in the body. This process is called phagocytosis and is often initiated by filopodia which pull particles to the cell body where they are taken up by reorganization of the membrane. Filopodia contain tight bundles of filamentous actin that protrude from the actin cortex and are connected with the cell membrane via linker molecules. Retraction towards the cell body is driven by molecular motors which work in ensembles. The underlying physical principles that allow macrophages to tune their actions during phagocytosis are only little understood. We use a Photonic Force Microscope in which we combine DIC microscopy with optical tweezers and interferometric particle tracking. Polystyrene beads are held in an optical trap to enable controlled placement in the vicinity of the cells. The motion of the bead in the trap can be tracked in 3D with nanometer precision at a microsecond timescale using back focal plane interferometry. By changing the optical forces spatially or temporally, we investigate how the cell reacts to external forces and which mechanisms determine success or failure when attempting to bind and digest particles. We present novel experiments, which reveal binding, pulling and unbinding events of macrophage filopodia on a molecular scale.

BP 37.5 Wed 10:45 H44

**Elastic Resonator Stress Microscopy (ERISM) – A Novel Tool for Cell-Mechanical Investigations** — •Philipp Liehm, Nils M. Kronenberg, Anja Steude, Andrew Morton, and Malte C. Gather — School of Physics & Astronomy, University of St Andrews, St Andrews, Scotland, UK

We present a novel cell force sensing technique based on an elastic optical micro-cavity. By measuring the spatially resolved interference pattern of a deformed micro-cavity, we are able to accurately detect vertical displacements with resolution in the nm range. Integrated into a conventional inverted fluorescence microscope, our technique can easily be combined with phase contrast and fluorescence imaging. The low light intensity required for readout, enables long-term measurements — over periods as long as several days — without any photo-toxic effects on the cells. ERISM does not require detaching the cells after a measurement, thus allowing continuous data acquisition for hundreds of cells at different positions on one sensor (substrate). The wide-field character of the measurement permits high frame rates ($< 2\,s$ per frame) and thus enables tracking fast cell movement. The local deformations are evaluated with a Finite Element Method (FEM) to obtain local stress information.

In this presentation we will give an introduction to this new micro-cavity based sensor concept. Furthermore, we show data on the mechanical characterization of the elastic micro-cavity with an Atomic Force Microscope (AFM). Finally, we apply our technique to a wide range of different cell types including neuroglia.

**30 min break**

BP 37.6 Wed 11:30 H44

**Fibroblast mechanics: a story of history** — •Mathias Sander and Albrecht Ott — Universität des Saarlandes, Saarbrücken, Germany

Cell mechanics is a key player in development, disease and many other biological processes. Living cells exhibit a complex nonlinear response to mechanical cues, which is not understood yet. A stiffening as well as softening is observed, depending on the stimulus and the experimental technique. Here, we apply large amplitude oscillatory shear (LAOS) to a monolayer of fibroblast cells using the cell monolayer rheology technique. We find that the nonlinear cell response not only depends on the amplitude and the frequency of oscillations. Moreover, it is highly susceptible to a mechanical preconditioning. Cell response can exhibit hallmarks of nonlinear viscoelasticity, elastoplastic kinematic hardening or inelastic fluidization for the same steady state oscillations. Experimental results indicate that a preconditioning changes cytoskeletal network structure in a rate dependent way. Network alterations can be driven by passive filament reorganisations, filament

rupture and the binding/unbinding of crosslinking proteins. We speculate that the pronounced strain path dependence of nonlinear cell response might obscure the underlying universality of nonlinear cell mechanics on a microscopic scale. Our results highlight the interplay between viscoelastic and inelastic contributions to the cell mechanical response.

BP 37.7 Wed 11:45 H44

**Transfer of mechanical stimuli along single microtubules and small networks** — •Alexander Rohrbach and Matthias Koch — Universität Freiburg, IMTEK, Georges-Köhler-Allee 102, 79100 Freiburg

Mechanic stimulation allows integrating different parts of a cell nearly instantaneously and is relevant for the response to pressure, gravity, osmotic changes, but also to organize different regions of a dynamic cell into one entity. To explain how a stimulus can propagate across a few tens of micrometers within milliseconds inside a crowded cell is far from trivial. Using time multiplexed optical tweezers and 3D interferometric tracking, we investigate how mechanical stimuli travel along single filaments or through small networks of deforming microtubules. We find that the transduction of signals depends on frequency with faster oscillations being transmitted more efficiently due to microtubule stiffening. Surprisingly, the observed elastic behavior can also be transferred to small networks, which are mechanically different. The dependency on both the frequency and the network geometry, i.e. direction-dependent signal transport are important for biological self-organization based on tensegrity.

BP 37.8 Wed 12:00 H44

**The mechano-response of flagellar oscillators** — •Gary Klindt[1], Benjamin Friedrich[1], Christian Ruloff[2], and Christian Wagner[2] — [1]MPI PKS, Dresden — [2]Universität des Saarlandes, Saarbrücken

Motile cilia and flagella are slender cell appendages that beat rhythmically, powered by the collective dynamics of thousands of molecular motors inside. The beat of flagella transports fluids in airways and the brain of mammals.

Cellular microswimmers use beating flagella for self-propulsion, such as the green alga 'Chlamydomonas' that swims like a breast-swimmer with two flagella.

We characterize the load characteristic and dynamic force-velocity relationship of beating flagella using controlled microfluidic flows. We obtain a description in terms of a limit-cycle oscillator [1] with force-dependent phase and amplitude dynamics.

We incorporate this flagellar mechano-response into hydrodynamic simulations of flagellar swimming based on a fast boundary element method [2]. With this we computationally assess the role of the active waveform compliance of flagellar beating on swimming and synchronization.

[1] 1. Ma, R., Klindt, G. S., Riedel-Kruse, I. H., Jülicher, F. & Friedrich, B. M. Active Phase and Amplitude Fluctuations of Flagellar Beating. Phys. Rev. Lett. 113, 048101 (2014). [2] Klindt, G. S., Friedrich, B. M., Flagellar swimmers oscillate between Pusher- and Puller-type swimming, Phys. Rev. E, submitted and accepted.

BP 37.9 Wed 12:15 H44

**Actin structural dynamics under geometrical and biomechanical control** — •Julia Strübig, Erik Bernitt, and Hans-Günther Döbereiner — Institut für Biophysik, Uni Bremen, Deutschland

The morphology of cells is a crucial effector for the overall spatiotemporal dynamics of protein densities. The complexity and randomness of morphologies of adherent cells comprise a considerable challenge for the comparability of data obtained on individual cells. Further, the comparison of experimental data to theoretical studies is severely compromised. This is especially true for the dynamics of actin, as this protein has the outstanding capability to deform the spatial domain in which it resides.

Here we introduce an experimental system with which we overcome the aforementioned issues. We utilize micro-contact printing to force cells into disc-like morphologies for the study of two different actin-based structures, namely (i) waves of polymerizing actin at the dorsal cell side (CDRs) and (ii) lamellipodia-embedded moving filopodia. Due to the simplified cell edge geometry and periodic boundary conditions in lateral direction, both structures exhibit remarkably regular dynamics facilitating quantitative analysis.

On that basis we test the response of the actin machinery to biochemical interference with drugs targeting actin and myosin systems, which reveals fundamental insight into the mechanisms underlying the dynamics of actin waves and filopodia motion. We demonstrate that our data is explained very well by theoretical models for both systems.

BP 37.10 Wed 12:30 H44

**Membrane tension feedback on shape and motility in a phase field model for crawling cells** — •Benjamin Winkler[1], Igor Aranson[2,3], and Falko Ziebert[1] — [1]Albert-Ludwigs-Universität, 79104 Freiburg, Germany — [2]Materials Science Division, Argonne National Laboratory, 9700 S. Cass Avenue, Argonne, IL 60439, USA — [3]Engineering Sciences and Applied Mathematics, Northwestern University, 2145 Sheridan Road, Evanston, IL 60202, USA

In the framework of a 2D phase field model of a single cell crawling on a substrate, we investigate how specific properties of the cell membrane affect the shape and motility of the cell. The membrane influences the cell dynamics on multiple levels and we take into account: (i) the reduction of the actin polymerization rate by membrane tension; (ii) area conservation of the cell's two-dimensional cross-section vs. conservation of the circumference (related to membrane inextensibility); and (iii) the contribution from the membrane's bending energy to the shape and integrity of the cell. We find that the most important effect for freely moving cells is the feedback of membrane tension on the actin polymerization. Bending rigidity induces only minor effects, which can be made visible in dynamic reshaping events, as exemplified by modeling cells encountering obstacles and squeezing through channels.