BP 9: Physics of Cells I

Time: Tuesday 9:30–12:45 Location: H43

Invited Talk BP 9.1 Tue 9:30 H43

Mechanics of Cellular Aggregates — •Françoise Brochard-Wyart[1], Christophe Clanet[2], Damien Cuvelier[1], Sylvie Dufour[1], David Gonzalez-Rodriguez[1], and Karine Guevorkian[1] — [1]Physical Chemistry Curie, Institut Curie, Paris, France — [2]Laboratoire d'Hydrodynamique, Ecole Polytechnique, Palaiseau, France

Embryonic morphogenesis, wound healing, cancer growth, and metastasis are all examples where the mechanical properties play an important role in the functioning of a tissue. It has been suggested that certain embryonic tissues mimic the behavior of viscous fluids. However, due to the immense variety of tissues ranging from very soft (brain) to very hard (bone), such an analogy between tissues and fluids remains not well understood. We shall describe aspiration and compression experiments performed on cell aggregates, which provide a convenient laboratory model to characterize the mechanical properties of tissue. Using this characterization, we study the spreading of cell aggregates on a coated substrate, as well as their deformation and detachment under flow. In addition, we perform analogous experiments on viscous pastes, which provide a comparison with an inert system. Our results should yield insights in the understanding of pathologies related to artery obstruction, such as atherosclerosis or thrombosis.

BP 9.2 Tue 10:00 H43

Centering of dynamic microtubule asters by cortical pulling forces — Liedewij Laan[1], •Nenad Pavin[2,3], Guillaume Romet-Lemonne[1], Frank Julicher[2], and Marileen Dogterom[1] — [1]FOM Institute for Atomic and Molecular Physics (AMOLF), Amsterdam, The Netherlands — [2]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [3]Department of Physics, Faculty of Science, Zagreb, Croatia

Dynamic microtubules (MTs) interact with the cortex to generate pushing and/or pulling forces that position organelles correctly with respect to the confining geometry of living cells. In particular, pulling forces mediated by dynein linked to the cortex, provide a versatile mechanism to properly position MT organizing centers in systems ranging from small yeast cells to large embryonic cells. Nevertheless, the respective roles of pushing and pulling forces, and especially the mechanism by which pulling forces may contribute to centering processes, remain poorly understood. We address this question in an in vitro experiment, where MT asters are grown in microfabricated chambers. Pushing forces arise from MT polymerization and buckling forces, and pulling forces arise from interactions between MT ends and dynein motor proteins attached to the chamber walls. Surprisingly, we find that MT asters center more reliably by a combination of pulling and pushing forces than by pushing forces alone. Our theoretical results obtained for various geometries, imply distinct positioning strategies employed in different cell types.

BP 9.3 Tue 10:15 H43

Structure formation of the bacterial cytoskeletal protein FtsZ - a theoretical study — •Elisabeth Fischer-Friedrich, Roie Shlomovitz, and Nir Gov — Department of Chemical Physics, The Weizmann Institute of Science, P.O.B. 26, Rehovot 76100, Israel

The bacterial protein FtsZ polymerizes and attaches to the inner site of the bacterial membrane in a ring-shaped struture. This FtsZ ring marks the future site of the septum of bacterial cell division. Membrane located FtsZ structures have also been reported to occur in a helical shape, neighboring the Ftsz ring in a normally dividing cell, or during the process of sporulation in *Bacillus subtilis*. The mechanism behind FtsZ assembly and structure formation as well as switching between ring and helix structures remains obscure. Here, we examine the process of structure formation theoretically using a coarse-grained model to describe FtsZ densities on the membrane and taking into account a spontaneous curvature of FtsZ polymers.

BP 9.4 Tue 10:30 H43

Photonic force based investigations of intracellular molecular motor dynamics during phagocytic filopodia retraction — •Felix Kohler and Alexander Rohrbach — Albert-Ludwigs-Universität , Freiburg, Germany

Phagocytes use intelligent mechanisms to efficiently uptake bacteria and other particles. A fascinating method of the cell is to extract and retract lamellopodia or thin filopodia to withdraw and uptake the particles. Besides actin polymerization and depolymerization, coordinated transport of molecular motors seems to control filopodia mechanics. We use photonic force microscopy to investigate different mechanical concepts of the cell to take up $1\mu m$ beads, which serve as synthetic bacteria. The motion of an optically trapped bead is tracked interferometrically in 3D with nanometer precision at microsecond timescale. The measurement of e.g. the beads mean displacement allows determining the retraction forces of filopodia at various retraction speeds. We have measured F-actin dependent 36-nanometer steps inside living cells during filopodia retraction likely belonging to actin-based molecular motors [1]. Steps remaine clearly visible even at force regimes clearly beyond the stall force of a single myosin motor. This indicates a kind of inter-motor coupling, a phenomenon which will be presented in this talk and which we try to explain by a stochastic multi-state model.

[1] Kress, Stelzer, Holzer, Buss, Griffiths, and Rohrbach: "Filopodia act as phagocytic tentacles and pull with discrete steps and a load-dependent velocity", PNAS, Vol.104, 2007, 11633-11638

BP 9.5 Tue 10:45 H43

Structural transitions in growing actin networks — •Julian Weichsel and Ulrich Schwarz — University of Heidelberg, Institute for Theoretical Physics

The directed polymerization of a branched actin network is a universal propulsion system used in many different contexts of biological relevance, including the migration of animal cells and the motility of intracellular pathogens like *Listeria*. It also can be reconstituted in cell-free assays, for example to propel plastic beads or vesicles. Despite the universal nature of the underlying mechanisms of filament growth, branching and capping, conflicting results have been reported for the force-velocity relation of growing actin networks. Using a relatively simple theoretical model, we show that the interplay between filament and network growth leads to structural transitions in the network which can explain the experimental observations. Using a rate equation approach, we analytically calculate a phase diagram which is in excellent agreement with stochastic simulations of network growth.

15 min. break

BP 9.6 Tue 11:15 H43

Shell-String Model of Global Cell Motions, Intracellular Trafficking and Phagocytosis — •Erich Sackmann[1], Felix Keber[2], and Doris Heinrich[2] — [1]Biophysik E22, Physik Department, TU München, Germany — [2]Fakultät für Physik und CeNS, LMU München, Germany

The survival of cells depends on the ongoing intracellular motions and the rapid reorganisation of intracellular macromolecular scaffolds. Thus, the cytoplasmic space is explored by superpositions of directed transport along and by random walks between microtubules. Further, cell locomotion and phagocytosis are driven by actin gelation waves. This requires cells to combine a high degree of plasticity of the intracellular space with mechanical robustness. We first provide evidence that this astonishing mechanical robustness can be explained in terms of dynamic coupling of the microtubule aster to the actin cortex. Large forces in the nN range are balanced by coupling of the microtubules to actin gelation waves rather than cellular micromuscles. Second, we show that rapid global shape changes, associated with locomotion and phagocytosis, are driven by solitary actin gelation waves acting as travelling force fields. We finally present a model explaining the travelling force field in terms of the synchronous motion of signalling lipids with adhesion domains spreading on surfaces.

BP 9.7 Tue 11:30 H43

Probing mechanical characteristics of differentiating pluripotent mouse stem cells — •Lena A. Lautscham[1], Thomas Schulz[2], Ahmed Mansouri[2], Christoph F. Schmidt[1], and Florian Rehfeldt[1] — [1]Drittes Physikalisches Institut, Georg-August-Universität, Göttingen, Germany — [2]Molecular Cell Differentiation Group, Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

In the last decade it has become increasingly evident that local microenvironments of living cells differ significantly, not only in biochemical composition, but also in their mechanical properties. The physical characteristics of different tissue and cell types (e.g. muscle, neurons, osteoblasts) correlate with the function of the various differentiated phenotypes.

It remains a challenge to accurately determine mechanical properties of cells such as their viscoelasticity, and to quantify their own active mechanical output, e.g. contractile forces generated by the cells. Our approach uses a dual optical trap by which cells are suspended between two trapped micron-sized beads. Using a combination of active and passive microrheology allows us to precisely determine physical parameters at high resolution and bandwidth and to simultaneously quantify the fluctuating forces that the cells produce.

We here present data showing distinct changes of the mechanical properties of differentiating pluripotent mouse stem cells after well-defined biochemical stimulation was applied to differentiate the cells to either muscle cells or neuronal cells.

BP 9.8 Tue 11:45 H43

The mechanical characteristics of embryonic stem cells influence their first fate decisions — •Kevin Chalut[1], Penelope Hayward[2], Franziska Lautenschlaeger[1], Chea Lim[2], Alfonso Martinez-Arias[2], and Jochen Guck[1] — [1]Cavendish Laboratory, Department of Physics, University of Cambridge, Cambridge, UK — [2]Department of Genetics, University of Cambridge, Cambridge, UK

The level of expression of the gene Nanog in embryonic stem (ES) cells defines their pluripotency: ES cells with a high expression of Nanog (HN) remain pluripotent while ES cells with a low expression of Nanog (LN) tend to differentiate. We used optical stretching and atomic force microscopy to explore the differences in mechanical phenotype between HN and LN embryonic stem cells. We found that LN cells are softer and more elastic than HN cells, while HN cells are highly plastic and maintain a high level of active response to forces in the environment. We will show that the highly active response of the HN cells is very robust, and has significant implications for sorting of ES cells in the embryo. Moreover, the high level of compliance of the LN cells compared to HN cells implies a susceptibility to physical cues in the environment that can steer the fate decisions of the ES cells. Finally, we present evidence that the actomyosin cytoskeleton network, which mediates the cells' active responses to their environment, fulfils an extremely important role in the fate decisions of ES cells, and in fact may define whether they maintain their pluripotent state or shift to lineage commitment.

BP 9.9 Tue 12:00 H43

Measuring cell mechanics and cell membrane properties by vertical pulling — •Schanila Nawaz[1], Sai Li[2], Mikael Simons[1], and Iwan A.T. Schaap[2] — [1]Max Planck Institute for Experimental Medicine, 37077 Göttingen, Germany — [2]III. Physkalisches Institut, Georg-August-Universität, 37077 Göttingen, Germany

Based on optical tweezers we have developed a portable (and affordable) trapping instrument that is able to work at the surface vicinity up to 50 μm away from the surface and can exert and measure vertical forces up to 0.1 nN. We have used our method to investigate the mechanical forces driving morphological changes during the development of myelin-forming cells. Such measurements heavily rely on the vertical pulling geometry because of the flatness of myelin cells (as thin as 50 nm). A trapped bead was automatically brought down to the cell and bead-cell contact was detected via a force feedback loop. The trapped bead was then pulled in vertical direction, away from the contact point. From the force-extension curves we can detect cell deformation, from which we can calculate the elastic response. At higher forces we pulled membrane tubes (tethers) out of the cell membrane. From the measured forces required to form these tethers we estimated the membrane tension in different stages of cell development.

BP 9.10 Tue 12:15 H43

Force transduction in blood platelets — •Sarah Schwarz G. Henriques[1], Hansjörg Schwertz[2], Alexander Strate[3], and Sarah Köster[1] — [1]Courant Research Centre Nano-Spectroscopy and X-Ray Imaging, Universität Göttingen, Germany — [2]Division of Vascular Surgery, University of Utah, Salt Lake City, United States of America — [3]Transfusion Department, University Clinic, Universität Göttingen, Germany

Blood platelets (thrombocytes) are essential for the repair of damaged blood vessels. When they become activated to form a blood clot they change their shape within minutes by dramatically rebuilding their cytoskeleton. This highly dynamic non-equilibrium process is known to be triggered by external cues and driven by cellular forces, but the basic mechanical principles are not yet understood. In our experiments we investigate the physics underlying platelet activation by measuring the forces, which platelets impose on their environment. To this end, we use traction force microscopy, a well-established technique, in which the cells are placed on thin PAA (polyacrylamide) gels of a known elastic modulus. Fluorescent tracer beads are embedded into the PAA to visualize gel deformations, which are then translated into traction force fields. In addition to measuring traction force fields, we take fluorescence microscopy images of the platelets at different activation stages. Both vinculin as well as actin are previously stained in order to map focal adhesion sites and conclude upon cytoskeletal reorganization steps. Our experimental findings are finally gathered into a mechanical model for the early stages of platelet activation.

BP 9.11 Tue 12:30 H43

Strain Energy and its Density Distribution around Invasive and Non-Invasive Carcinoma Cells in 3D Collagen Gels — •Thorsten Koch[1], Stefan Münster[1], Claudia Mierke[1], James Butler[2], and Ben Fabry[1] — [1]Department of Physics, University of Erlangen-Nuremberg, Germany — [2]Physiology Program, Harvard School of Public Health, Boston, MA, USA

Cell invasion through a 3D matrix is believed to depend on the ability of cells to generate traction forces. To quantify the role of cell tractions during invasion in a collagen gel (shear modulus 118 Pa, 500 μm thickness, mesh size 1.6 μm), we measured the strain energy of invasive MDA-MB-231 breast and A-125 lung carcinoma cells, as well as non-invasive MCF-7 breast and A-431 lung carcinoma cells for comparison. In all cases, cells locally contracted the gel, quantified by tracking 3D positions of embedded fluorescent beads. These positions served as nodes in a finite element mesh used to compute the strain energy. The strain energy of invasive breast carcinoma cells (1.4 $\pm$ 0.2 pJ, n=31) was significantly higher than that of non-invasive breast carcinoma cells (0.8 $\pm$ 0.1 pJ, n=28). Surprisingly, the strain energy of non-invasive lung carcinoma cells (4.2 $\pm$ 0.7 pJ, n=31) was similar to that of invasive lung carcinoma cells (3.5 $\pm$ 0.4 pJ, n=34). Invasive cells assumed an elongated morphology as opposed to the round shape of non-invasive cells. Accordingly, the distribution of strain energy density around invasive cells followed patterns of increased anisotropy. These results suggest that magnitude and directionality of traction generation are important for cell invasion in 3D collagen gels.