BP 13: Cell Mechanics I

Time: Tuesday 9:30–12:45 Location: SCH A251

Invited Talk BP 13.1 Tue 9:30 SCH A251

On another plane: curling and buckling in epithelia — •Guillaume Charras[1], Jonathan Fouchard[1], Tom Wyatt[1], Ana Lisica[1], Nargess Khalilgharibi[1], Pierre Recho[2], Amsha Proag[3], Magali Suzanne[3], Buzz Baum[1], and Alexandre Kabla[4] — [1]University College London, London, UK — [2]Universite Grenoble Alpes, Grenoble, France — [3]Universite Paul Sabatier, Toulouse, France — [4]Cambridge University, Cambridge, UK

During embryonic development and adult life, epithelia are constantly subjected to external forces. The resulting deformations can have a profound impact on tissue development and function. In particular, compressive deformations are central to tissue morphogenesis as they can trigger cell extrusion or differentiation via mechanosensory mechanisms. These processes are all controlled by the relationship between compression and the mechanical state of the tissue, however, this remains poorly understood. Using suspended epithelia, we uncover the response of epithelial tissues to the application of large in-plane compressive strains.

While most epithelia must withstand mechanical stresses without rupture, some developmental epithelia need to rupture allow emergence of mature organs. In Drosophila leg imaginal disks, the peripodial membrane breaks to release the leg. As it breaks, the peripodial membrane curls basally, indicating the presence of spontaneous curvature. Similar curling is observed suspended epithelia. We investigate the biology and physics of monolayer curling to estimate the contribution of active torques to out-of-plane deformation in epithelia.

BP 13.2 Tue 10:00 SCH A251

Bridging microtubules promote centering of kinetochores by length-dependent pulling forces — Agneza Bosilj[1], Iva Tolic[2], and •Nenad Pavin[1] — [1]Department of Physics, Faculty of Science, University of Zagreb — [2]Ruder Bošković Institute, Zagreb

The mitotic spindle, by exerting forces, segregates chromosomes into two daughter cells during cell division. During metaphase, chromosome are positioned in the equatorial plane of the mitotic spindle, which is necessary to prevent lagging chromosomes and abnormal nuclear envelope reformation. It has been proposed that two centering mechanisms play a key role here, microtubule catastrophe promoted by kinesin-8 motors and pushing forces exerted by chromokinesins. Here we show, by combining a theoretical model and quantitative experiments, that kinetochore microtubules cross-linked by bridging microtubules exert length-dependent centering pulling forces. Our model also shows that length-dependent catastrophe and rescue regulated by motor proteins and passive cross-linkers are necessary for well defined length of microtubules and their antiparallel overlap, respectively. We predict that stable antiparallel overlaps exert length-dependent forces on kinetochores to navigate their positioning in the center of the metaphase plate.

BP 13.3 Tue 10:15 SCH A251

Intracellular activity and mechanics in dividing epithelial cells — •Sebastian Hurst, Bart E. Vos, Matthias Brandt, Till Münker, and Timo Betz — Institute of Cell Biology, ZMBE, Münster, Germany

While there is a good understanding of cortical mechanics during cell division, surprisingly little is known about the intracellular mechanics and activity during this fundamental process. Nevertheless, intracellular mechanics have a tremendous impact on both chromosome and organelle distribution. Furthermore, an increase in intracellular activity would help to distribute organelles before cytokinesis. This so-called active diffusion is achieved by random, undirected fluctuations, e.g. generated through motor protein activity.

To quantify the intracellular mechanics, we perform active and passive microrheology measurements using optical tweezers on phagocytosed exogenous particles inside dividing MDCK cells. We obtain the frequency-dependent complex shear modulus and the effective energy, which quantifies the activity in units of thermal energy. We observe global differences between interphase and mitosis. Focusing on mitosis, current results suggest that the cells become more fluid-like in pro- and metaphase, while they become more solid-like towards the end of mitosis. Compared to interphase, the effective energy drops in mitosis, whereas it does not change drastically during cell division. Moreover, experiments with cells in mitotic arrest show that the activity is mostly myosin driven. This data supports a published model connecting mechanics to intracellular activity.

BP 13.4 Tue 10:30 SCH A251

Pulling, failing and adaptation of macrophage filopodia — •Alexander Rohrbach and Rebecca Michiels — Bio- und Nano-Photonik, Universität Freiburg

Macrophages are cells of the immune system, which use filopodia to connect to pathogens and withdraw them towards the cell body for phagocytosis. The withdrawal of living targets requires to overcome counteracting forces, which the cell generates after a mechanical stimulus is transmitted to the filopodium. Adaptation to mechanical cues is an essential biological function of cells, but it is unclear whether optimization strategies are essential for filopodia pulling. We use optically trapped beads as artificial targets and interferometric particle tracking to investigate factors contributing to filopodia performance. We find that bead retractions are interrupted by sudden failure events caused by mechanical rupture of the actin-membrane connection. Filopodia resume pulling only milliseconds after ruptures by reconnecting to the actin backbone. Remarkably, we see a gradual increase of filopodia force after failures, which points towards a previously unknown adaptation mechanism. Fluorescence microscopy reveals that particles are transported in a stop-and-go behavior with the actin retrograde flow via a force-dependent linker at the filopodium tip. Additionally, we see that the strength of the attachment between bead and filopodium increases under load, a characteristic of catch bond adhesion proteins. Our findings show how mechanical adaptation enable macrophage cells to optimize their performance under load.

BP 13.5 Tue 10:45 SCH A251

Rayleigh-Plateau instability of anisotropic biological interfaces — •Katharina Gräßel, Christian Bächer, and Stephan Gekle — Biofluid Simulation and Modeling, Theoretische Physik VI, Universität Bayreuth

Tubular vesicles under tension are known to undergo a pearling instability similar to the Rayleigh-Plateau instability of a liquid jet. We extend the classical model for this Rayleigh-Plateau instability to treat complex interfaces with anisotropic surface tension, as found in cells. We do so both in the limit of high and low Reynolds number and accordingly cover both liquid jet and vesicle behaviour. Combining theory and simulations we show that the dominant instability wavelength is determined by the anisotropy of the surface tension. We further show that including bending elasticity of vesicle membranes has negligible influence for isotropic tension, but strongly affects or even completely suppresses the instability if the tension is anisotropic. Our results can be highly relevant for vesicles or tissues with anisotropic interfacial properties.

30 min. coffee break

BP 13.6 Tue 11:30 SCH A251

Measuring Viscoelasticity of Cells by Atomic Force Microscopy — Sandra Perez Dominguez, Shruti Kulkarnie, Carmela Rianna, Prem Kumar Viji Babu, and •Manfred Radmacher — Universität Bremen

Mechanical properties of cells are important for understanding many cellular processes like cell division, cell migration or wound healing. From a mechanical point of view, the most important component of a (mammalian) cell is the actin cytoskeleton, which is an active polymeric network able to generate internal stresses and external forces. If a local deformation is applied to a cell, e.g. by an AFM tip, the response will be viscoelastic, where the elastic forces are mainly generated by the cytoskeleton, and the viscous forces may stem from the interaction of the cytoskeleton with the highly viscous cytoplasm. There are various experimental methods to determine this viscoelastic response by AFM: the simplest are applying a jump in force or a modulating force. The former measures the creep of the sample, the latter is conceptually related to polymer rheology. We will discuss and compare both methods in AFM to determine the viscoelastic response of different cell types.

We have investigated several cell types, including cancer and nor-

mal cells, but also various types of fibroblasts, which are related to wound healing or Dupuytren's disease. In all cases we could quantify differences in the mechanical properties: in the elastic and the loss modulus, and in the power law exponents of these quantities as a function of frequency.

BP 13.7 Tue 11:45 SCH A251

The dynamics of burst-like collective migration in 3D cancer spheroids — •Swetha Raghuraman[1], Fatemeh Abbasi[1], Raphael Wittkowski[2], and Timo Betz[1] — [1]Institute of Cell Biology, ZMBE, Münster, Germany — [2]Center for Soft Nanoscience

Collective migration of cells is a striking behavior observed during morphogenesis, wound healing and cancer cell invasion. Spherical aggregates of cells are known to migrate in 3D matrices like collagen, matrigel or fibronectin *in-vitro*. Although biochemical signaling is the main research focus, the biophysical properties of the spheroid leading to an invasion is less explored. We observe a striking phenotypical difference when HeLa cervical cancer spheroids were embedded in different concentrations of collagen I matrices. HeLa spheroids in lower collagen concentration (LCC) 0.5 mg/ml, displayed an explosion invasion-like behavior within 6 hours, while those in higher collagen concentration (HCC) 2.5 mg/ml were consistently growing over 48 hours, without any invasion like behavior. The migration dynamics of cells in HCC were more fluid-like with lower velocity as compared to the burst-like phenotype in LCC, which showed higher velocity and super diffusive characteristics. We hypothesize that in LCC, spheroids generate an increased surface tension due to a force imbalance. Exceeding a critical tension, the spheroid ruptures, which leads to a pushing of cells into the matrix. We believe that such mechanical interplay can pave the way to understand migration behavior of cancer cells with respect to their biophysical properties.

BP 13.8 Tue 12:00 SCH A251

EMT-induced cell mechanical changes enhance mitotic rounding strength — •Kamran Hosseini[1], Anna Taubenberger[1], Carsten Werner[2], and Elisabeth Fischer-Friedrich[1] — [1]Biotechnology Center, TU Dresden, Germany — [2]Leibniz Institute of Polymer Research Dresden, Max Bergmann Center, Dresden, Germany

To undergo mitosis successfully, animal cells need to acquire a round shape to provide space for the mitotic spindle. This mitotic rounding relies on mechanical deformation of surrounding tissue and is driven by forces emanating from actomyosin contractility. Cancer cells are able to maintain successful mitosis in mechanically challenging environments such as the increasingly crowded environment of a growing tumor, thus, suggesting an enhanced ability of mitotic rounding in cancer. Here, we show that epithelial mesenchymal transition (EMT), a hallmark of cancer progression and metastasis, gives rise to a cell-cycle dependent cell-mechanical switch and enhanced mitotic rounding strength in breast epithelial cells. Furthermore, we show that this cell-mechanical change correlates with a strong EMT-induced change in the activity of Rho GTPases RhoA and Rac1. Accordingly, we identify Rac1 as a cell-cycle dependent regulator of actin cortex mechanics. Our findings hint at a new role of EMT in successful mitotic rounding and division in mechanically confined environments such as a growing tumor.

BP 13.9 Tue 12:15 SCH A251

Estimating biomechanical properties of Head and Neck Squamous Carcinoma Cells (HNSCC) with single-molecular force microscopy — •Hsiao-Ching Tsai[1], Julia Kristin[2], Jörg Schipper[2], and Mathias Getzlaff[1] — [1]Institue of Applied Physics, Heinrich-Heine-Universität Düsseldorf — [2]Hals-Nasen-Ohren-Klinikum Düsseldorf

AFM is one of the most common approach to access the loading deformation behavior of different soft materials such as tissue or cells. With AFM, a complete data base of biomechanical properties like displacement or deformation could be easily established. The progress of the fundamental biomechanical discovery engages further investigation of living matters. To our knowledge, cancer is one of the most lethal diseases lacking effective treatment. Thus, the development of supplementary or improvement of therapeutic methods lead to an urgent requirement of biomechanics in detail. By means of AFM, cytoskeleton network changing due to the disease progression which is closely associated to the biomechanics is confirmed. In this study, we cultured different head and neck squamous cells from the same area (tongue) at different cancer stages (healthy, benign, cancerous and metastatic) and examined them using a nanoindentation technique. The Hertz model of contact mechanics is adopted to extract the elastic modulus by analyzing the force-indentation curves. Our results present a quantitative model to distinguish the disease conditions of head and neck squamous cells. Three dimensional images of living cells in liquid environment can be visualized simultaneously.

BP 13.10 Tue 12:30 SCH A251

Elucidating cell mechanics regulators from mechano-transcriptomics data using unsupervised machine learning — •Marta Urbanska[1,2], Yan Ge[1], Maria Winzi[1], Konstantinos Anastasiadis[1], Jochen Guck[1,2], and Carlo V. Cannistraci[1] — [1]Biotechnology Center, CMCB, TU Dresden, Dresden, Germany — [2]Max Planck Institute for the Science of Light, Erlangen, Germany

Mechanical properties of cells determine their capability to perform many physiological functions, such as migration, cell-fate specification or circulation through vasculature. Identifying the molecular factors that govern the mechanical phenotype is therefore a subject of great interest. Here we present an approach that enables establishing links between mechanophenotype changes and the genes responsible for driving them. In particular, we employ an unbiased machine learning method termed PC-corr to correlate cell mechanical states, measured by real-time deformability cytometry (RT-DC), with large-scale transcriptome datasets across different biological systems. We validate the obtained functional gene module in silico on four further datasets and show that the five identified genes have the capacity to discriminate between stiffer and softer cell states of 70 to 93%. Finally, we validate experimentally the influence of the top scoring gene on cell mechanics by its down- and up-regulation. The data-driven approach presented here has the power of de novo identification of genes involved in the regulation of cell mechanics and will extend the toolbox for tuning the mechanical properties of cells on demand to enable biological function or prevent pathologies.