BP 38: Active cell and tissue mechanics (focus session) II

Time: Thursday 15:00–17:30 Location: HÜL 386

Topical Talk BP 38.1 Thu 15:00 HÜL 386

Analyzing integrin's force transduction using novel biosensors — •Carsten Grashoff — Max-Planck-Institute of Biochemistry, Group of Molecular Mechanotransduction, Am Klopferpsitz 18, 82152 Planegg, Germany

Cell adhesion to the extracellular matrix is mediated by integrin receptors which connect to the cytoskeleton in complex structures called focal adhesions (FAs). The ability of these adhesions to bear and transduce mechanical forces is central to many developmental or homeostatic processes and plays an important role in a range of pathological situations; yet our understanding of how integrin forces are propagated in FAs remains fragmentary.

One reason for our limited understanding has been the lack of suitable methods to study force propagation on the sub-cellular level in the living cell. Therefore, we have previously developed a FRET-based method to visualize and quantify mechanical forces within cells.

Here, I will introduce a novel, calibrated biosensor and describe its application to the integrin activator talin-1.

BP 38.2 Thu 15:30 HÜL 386

Transduction channel's gating controls friction on vibrating hair-cell bundles in the ear — •Volker Bormuth[1], Jérémie Barral[1], Jean-François Joanny[1], Frank Jülicher[2], and Pascal Martin[1] — [1]Laboratoire Physico-Chimie Curie, CNRS, Institut Curie, UPMC; 75005 Paris, France — [2]2Max Planck Institute for the Physics of Complex Systems, 01187 Dresden, Germany

Hearing starts when sound-evoked mechanical vibrations of the hair-cell bundle activate mechanosensitive ion channels, giving birth to an electrical signal. As for any mechanical machine, friction impedes movements of the hair bundle and thus constrains the sensitivity and frequency selectivity of auditory transduction. Using dynamic force measurements on single hair-cell bundles, we demonstrate here that the opening and closing of the transduction channels produce internal friction forces that can dominate viscous drag on the micrometric hair-bundle structure. A theoretical analysis reveals that channel friction arises from coupling the dynamics of the conformational change associated with channel gating to tip-link tension. We propose that this intrinsic source of friction contributes to the process that sets the hair cell's characteristic frequency of responsiveness.

BP 38.3 Thu 15:45 HÜL 386

Mechanical properties of syncytial Drosophila embryos by high-speed video microrheology — •Alok D. Wessel and Christoph F. Schmidt — Drittes Physikalisches Institut, Georg-August-Universität Göttingen, Germany

In the early syncytial stage Drosophila melanogaster embryos nuclei are duplicating, but are not yet separated by membranes. They are interconnected by cytoskeletal polymer networks consisting of actin and microtubules. Between division stages 9 and 13, nuclei and the cytoskeletal networks form a well-ordered 2D cortical layer. To understand the underlying mechanical properties and dynamics of this self-organizing "pre-tissue", we have measured shear elastic moduli of the interior of the embryo and its cortical layer by high-speed video microrheology. We have recorded position fluctuations of injected micron-sized fluorescent beads with a high-speed camera at kHz sampling frequencies. In that manner we can analyze the local mechanics of the embryo in time and space. The interior of syncytial embryos shows a homogeneous, viscously dominated character with a viscosity approximately 300 times higher than water. In the actin-rich outer layers, near the nuclei, we measured a viscoelastic response. Furthermore we were able to resolve temporal variations of the shear modulus inside the layer.

BP 38.4 Thu 16:00 HÜL 386

Active mechanics and dynamics of epithelia during morphogenesis — •Amitabha Nandi[1], Marko Popovic[1], Matthias Merkel[1], Raphaël Etournay[2], Suzanne Eaton[2], Guillaume Salbreux[1], and Frank Jülicher[1] — [1]Max-Planck Institute for the Physics of Complex Systems, Nöthnitzer Str. 38, 01187 Dresden, Germany — [2]Max-Planck Institute of Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, 01307 Dresden, Germany

During development of an organism, epithelial tissues are dynamically remodeled due to forces generated in the cells, cellular rearrangements, and cell division and apoptosis. Such remodeling occurring over long time-scales leads to reorganization of the tissue allowing to establish the shape of the organism. In this work, we introduce a physical description of the slow timescale behavior of an epithelium. We obtain the hydrodynamic constitutive equations describing the continuum mechanics of an epithelium in two dimensions on spatial scales larger than a cell. Within this framework, topological rearrangements relax elastic stresses in the tissue and can be actively triggered by internal cell processes. We study simple limit cases of the flows and deformation predicted by the continuum theory. Using segmentation of the wing disc cell packing at pupal stage of the fly, we analyze experimental coarse-grained patterns of flow field and tissue shear. We show that our continuum theory can account for the key features of the cell flow and deformation fields. We find that a gradient of active contractile stress acting together with active cell rearrangement that are polarized in the tissue plane can explain the flow patterns observed in experiments.

15 min. break

BP 38.5 Thu 16:30 HÜL 386

Impact of heating on passive and active biomechanics of suspended cells — •Chii Jou Chan[1,2], Graeme Whyte[1,3], Lars Boyde[1], Guillaume Salbreux[4], and Jochen Guck[1,2] — [1]Cavendish Laboratory, Department of Physics, University of Cambridge, UK — [2]Biotechnology Center, TU Dresden, Dresden, Germany — [3]Department of Physics and Institute of Medical Biotechnology, University of Erlangen-Nuremberg, Germany — [4]MPI PKS, Dresden, Germany

Heating can have a dramatic effect on cell mechanical properties, similar to its impact on the dynamics of artificial polymer networks. We investigated such mechanical changes by the use of an optical stretcher which allowed us to probe single-cell mechanics at different heating conditions and time-scales. We find that HL60/S4 myeloid precursor cells become mechanically more compliant and fluid-like when subjected to either a sudden temperature increase or a prolonged exposure to higher ambient temperature. Above a critical temperature of 52°C, we observed active cell contraction which was strongly correlated with calcium influx through temperature-sensitive TRPV2 ion channels. The change from passive to active cellular response can be effectively described by a mechanical model incorporating cell viscoelastic components and an additional time-dependent active component. Our work highlights the role of TRPV2 in regulating the thermo-mechanical response of cells, and offers insights on how cortical tension and osmotic pressure can actively regulate cell shape changes in response to heat and mechanical stress.

BP 38.6 Thu 16:45 HÜL 386

The mechanics of cultured cell monolayers — •Guillaume Charras — University College London, London, UK

One-cell thick monolayers are the simplest tissues in multi-cellular organisms, yet they fulfil critical roles in development and normal physiology. In early development, embryonic morphogenesis results largely from monolayer rearrangement and deformation due to internally generated forces. Later, monolayers act as physical barriers separating the internal environment from the exterior and must withstand externally applied forces. Though resisting and generating mechanical forces is an essential part of monolayer function, simple experimental methods to characterise monolayer mechanical properties are lacking. Using a novel tensile testing system that enables examination of monolayer mechanics at subcellular, cellular and tissue-scales, we provide measurements of monolayer elasticity and show that this is two orders of magnitude larger than the elasticity of their isolated cellular components. Monolayers could withstand more than a doubling in length before failing through rupture of intercellular junctions. Measurement of stress at fracture enabled a first estimation of the average force needed to separate cells within truly mature monolayers, ˜9-fold larger than measured in pairs of isolated cells. As in single cells, monolayer mechanical properties were strongly dependent on the integrity of the actin cytoskeleton, myosin, and intercellular adhesions interfacing adjacent cells. This multiscale study of monolayer response to

deformation enabled by our novel device provides the first quantitative investigation of the link between monolayer biology and mechanics.

BP 38.7 Thu 17:00 HÜL 386

Individual cell phenotype determines growth modes of cell colonies — •Ben Fabry[1], Janina Lange[1], Pamela Strissel[2], Julian Steinwachs[1], and Claus Metzner[1] — [1]Department of Physics, University of Erlangen-Nuremberg, Erlangen, Germany — [2]Women's Hospital, University Clinics, Erlangen, Germany

Many tumor cells proliferate without anchorage to the matrix and often lack the cell-contact inhibition that normally prevents cells from proliferating beyond confluency. It is unclear, however, how individual cells contribute to the collective behavior and growth in a colony. Here we study colonies of different tumor and non-tumor cells lines on planar substrates. Despite the stochastic behavior of individual cells, deterministic features emerge at the colony level that are qualitatively independent of cell type, such as the linear increase of colony radius with time, a global radial streaming motion of cells away from the colony center, and a strong increase of streaming velocity and persistence at the colony border. Quantitatively, however, we find systematic differences between 6 differently adhesive and cohesive cell lines. All measured collective and single cell parameters showed a strong covariance, and no single parameter emerged as a principle component. Rather, all parameters correlated or anticorrelated strongly with the ranking order of these cell lines from a mesenchymal to an epithelial cell phenotype, suggesting that collective behavior is tightly linked with individual cell mechanical behavior.

BP 38.8 Thu 17:15 HÜL 386

Furrow constriction in animal cell cytokinesis — •Hervé Turlier[1,2], Basile Audoly[3], Jean-François Joanny[1,4], and Jacques Prost[1,4] — [1]Physico-chimie Curie, Institut Curie, Paris, France — [2]EMBL, Heidelberg, Germany — [3]Institut Jean-le-Rond d'Alembert, UPMC, Paris, France — [4]ESPCI, Paris, France

Cytokinesis is the process of physical cleavage at the end of cell division; it proceeds by ingression of an actomyosin furrow at the equator of the cell. Its failure leads to multinucleated cells and is a possible cause of tumorigenesis. We calculate the full dynamics of furrow ingression and predict cytokinesis completion above a well-defined threshold of equatorial contractility. The cortical acto-myosin is identified as the main source of mechanical dissipation and active forces. Thereupon, we propose a viscous active nonlinear membrane theory of the cortex that explicitly includes actin turnover and where the active RhoA signal leads to an equatorial band of myosin overactivity. The resulting cortex deformation is calculated numerically, and reproduces well the features of cytokinesis such as cell shape and cortical flows toward the equator. Our theory gives a physical explanation of the independence of cytokinesis duration on cell size in embryos. It also predicts a critical role of turnover on the rate and success of furrow constriction. Scaling arguments allow for a simple interpretation of the numerical results and unveil the key mechanism that generates the threshold for cytokinesis completion: cytoplasmic incompressibility results in a competition between the furrow line tension and the cell poles* surface tension.