AKB 25 Cell Mechanics I

Time: Thursday 15:00–18:00 Room: ZEU 260

AKB 25.1 Thu 15:00 ZEU 260

F-actin bundle mechanical properties — •Mark Bathe[1], Mireille Claessens[2], Claus Heussinger[1], Andreas Bausch[2], and Erwin Frey[1] — [1]Ludwig-Maximilians-Universitaet Muenchen — [2]Technische Universitaet Muenchen

Animal cells express a myriad of actin-binding proteins (ABPs) that associate with Filamentous actin (F-actin) to form stiff bundles in vivo. The physiological function of F-actin bundles varies from passive mechanical structures such as microvilli present on the surface of epithelial cells in the intestinal lining to active structures such as filopodia formed at the leading edge of cells during migration.

A biomimetic emulsion technique, recently introduced by our lab, has been used to measure directly the bending stiffness of isolated F-actin bundles associated with biologically-relevant ABPs. Results demonstrate that bundle stiffness depends sensitively on the number of actin filaments constituting the bundle, bundle length, and ABP type and concentration. Here, we use a combination of molecular simulation and analytical theory to elucidate the origin of the observed bundle mechanical properties. We also determine for the first time the molecular stiffnesses of the various ABPs examined.

AKB 25.2 Thu 15:15 ZEU 260

Phase behaviour and micro-mechanical properties of crosslinked actin-networks — •Oliver Lieleg and Andreas R. Bausch — Lehrstuhl für Biophysik E22, Physik-Department, Technische Universität München, D-85747 Garching, Deutschland

Cell shape, mechanics and motility are mainly determined by crosslinked actin-networks. Despite their importance, the mechanical function of crosslinking molecules is not well understood. As in living cells many different actin crosslinking molecules are used simultaneously, it is necessary to study their effect in in vitro systems. Here two structural related crosslinking molecules are compared: α-actinin and I-plastin. Their effect on the structure and mechanics of in vitro actin networks is investigated. Actin networks crosslinked by α-actinin or I-plastin show pronounced differences in their elastic properties as a function of the crosslinker-to-actin-ratio. Interestingly, these differences are observed although both crosslinking molecules use the same calmodulin-homologous domain for actin binding. For both systems at least three distinct phases of actin-networks with different viscoelastic properties are observed. By rheological and optical methods these are related to the microscopic structure of the networks. The occurrence of mixed networks containing bundles embedded in an isotropic network indicates that a sharp distinction between crosslinking and bundling proteins might be artificial and multiple phases could also be possible for other actin-crosslinking proteins.

AKB 25.3 Thu 15:30 ZEU 260

Nonlinear mechanical properties of entangled and cross linked actin networks — •Christine Semmrich, Rainer Tharmann, Bernd Wagner, and Andreas R. Bausch — Lehrstuhl für Biophysik E22, Physik-Department, Technische Universität München,D-85747 Garching, Deutschland

The mechanical response of cells is predominantly determined by the actin cytoskeleton. The nonlinear behaviour of crosslinked network show a pronounced dependence on the applied stresses spanning orders of magnitude in their elastic response. This can be related to the nonlinear mechanical behaviour of single filaments of this semiflexible polymer. In contrast, for purely entangled networks a tube model describes the mechanical response and thus no strain hardening is expected. By means of different rheological approaches we are able to investigate the nonlinear response of purely entangled actin networks. Interestingly, under standard conditions a strain hardening at temperatures below 23°C is observed. Highering the temperature, a strain softening occurs. The temperature dependence of the nonlinear behaviour is also highly dependent on the buffer salt concentration. This suggests that the interaction potential between filaments plays an important role for the observed behaviour. We discuss these results within theoretical predictions of entangled and crosslinked networks.

AKB 25.4 Thu 15:45 ZEU 260

Non-Affine Deformations: "elementary excitations" for the elasticity of random fiber networks — •Claus Heussinger and Erwin Frey — LMU Munich, Arnold-Sommerfeld-Zentrum, Theresienstr. 37, 80333 München

We numerically study the elasticity of random fibrous networks in two dimensions. Highly non-affine deformations on the scale of the single fiber are found to lead to anomalous elastic properties even on the macroscopic scale. This has to be contrasted with classical elasticity theory where material elements deform in an affine way and microstructure is not accounted for.

We identify the characteristic features of the microscopic deformation field and provide a scaling argument that allows the calculation of macroscopic quantities like the shear modulus.

Our work highlights the importance of architecture to the elastic response of fibrous structures and applies to diverse physical systems ranging from paper sheets to biological networks of semiflexible polymers like the cytoskeleton.

AKB 25.5 Thu 16:00 ZEU 260

Active and passive one- and two-particle microrheology in cytosksletal networks — •Daisuke Mizuno, Frederick C. MacKintosh, and Christoph F. Schmidt — Dept. Physics, Vrije Universiteit, Amsterdam, NL

We have developed a microrheology (MR) technique that uses micron sized particles to probe the viscoelastic properties of soft samples on small length scales and with high bandwidth. This can be done passively, by observing the Brownian fluctuations of particles embedded in the medium to be tested, or actively by moving the particle with a known force. One can measure the frequency dependent response of one particle on a force on it, or the response of a second particle to a force on the first. The latter (2-particle MR) makes it possible to get around surface artefacts. One can also measure response by actively moving a particle (n our case with an aousto-optic modulator) and observing the corresponding response. Comparison of active and passive experiments provides a test of the fluctuation-disspation theorem. We demonstrate agreement between the techniques in various samples including actin gels as long as samples are in equilibrium.

AKB 25.6 Thu 16:15 ZEU 260

High-frequency stress relaxation in semiflexible polymer solutions and networks — •Gijsberta H. Koenderink[1], Maryam Atakhorrami[2], Frederick C. MacKintosh[2], and Christoph F. Schmidt[2] — [1]Division of Engineering and Applied Sciences, Harvard University, Cambridge, USA — [2]Dept. Physics, Vrije Universiteit, Amsterdam, NL

We measure the linear viscoelasticity of sterically entangled as well as chemically crosslinked networks of actin filaments over more than five decades of frequency. The high-frequency response reveals rich dynamics unique to semiflexible polymers, in particular a previously unobserved relaxation due to rapid axial tension propagation. For high molecular weight, and for crosslinked gels, we obtain quantitative agreement with theoretical predictions of the shear modulus in both amplitude and frequency dependence.

AKB 25.7 Thu 16:30 ZEU 260

Cytoskeletal mechanics and dynamics in living cells — •Carina Raupach, Philip Kollmannsberger, Johannes Pauli, Claudia Mierke, and Ben Fabry — Zentrum für Medizinische Physik und Technik, Henkestr. 91, 91054 Erlangen

Cytoskeletal (CSK) mechanics and dynamics are important for essential processes in living cells including crawling, division, and mechanochemical signal transduction. Here we measured the creep-response (passive mechanics) of subconfluent human vascular endothelial cells (HUVEC) and different human cancer cell lines. Step forces of ∼1 nN were generated with magnetic tweezers acting on superparamagnetic, fibronectin-coated beads bound to the cytoskeleton via cell adhesion receptors (integrins). We also measured the spontaneous motion of these beads (dynamics) and computed their autocorrelation function (AC). The AC displayed diffusive behaviour at short time scales (< 1 s) and superdiffusive behaviour at longer time scales that was well described by

a power law: $AC(t) = \alpha \cdot (\frac{t}{t_0})^{\beta}$. The creep response γ also followed a power law: $\gamma(t) = a \cdot (\frac{t}{t_0})^{b}$. We found a significant ($p < 0.01$) correlation between α and a, but not between the power-law exponents β and b. These data suggest that different mechanisms give rise to power-law rheology and power-law superdiffusivity.

AKB 25.8 Thu 16:45 ZEU 260

Osmotically Driven Shape Instability in Axons — •Pramod Pullarkat[1], Paul Dommersnes[2], Pablo Fernandez[1], Jean-François Joanny[2], and Albrecht Ott[1] — [1]Experimentalphysik I, University of Bayreuth,*D-95440, Bayreuth, Germany — [2]Institut Curie, UMR 168, 26 rue d'Ulm, F-75248, Paris Cedex 05, France

We report a cylindrical–peristaltic shape transformation occurring in axons exposed to a controlled osmotic perturbation. The peristaltic shape relaxes and the axon recovers its original geometry within minutes. Using a flow chamber technique, we show that the shape instability depends critically on swelling rate and that volume and membrane area regulation are responsible for the shape relaxation. We propose that volume regulation occurs via leakage of ions driven by elastic pressure, and present an analysis for the peristaltic shape dynamics taking into account the internal structure of the axon. The results obtained provide a framework for understanding peristaltic shape dynamics in nerve fibers occurring *in vivo*.

AKB 25.9 Thu 17:00 ZEU 260

Quantitative force measurements during cystogenesis — •Jens Ulmer[1], Aldo Ferrari[2], Ruth Kroschewski[2], and Joachim Spatz[1] — [1]Max-Planck-Institute for Metals Research, Heisenbergstr. 3, 70569 Stuttgart, Germany — [2]Institut f. Biochemie, Schafmattstr. 18, ETH-Hoenggerberg, CH-8093 Zuerich

Adhesion of cells to the extracellular matrix (ECM) is a crucial event in developing multi-cellular organism. It can modulate cellular processes such as cell growth, differentiation, apoptosis and is mediating epithelial morphogenesis through mechanical interactions between cells and the ECM network. We studied cyst formation of Madin-Darby Canine Kidney (MDCK) cells in a three-dimensional (3D) culture connected to a force sensitive surface. Microfabricated PDMS posts, which have a post height dependent spring constant between 0.2-0.04N/m were developed in order to obtained cell exerted forces during cystogenesis. Further on it was shown that anisotropic vicinity can alter cyst morphology from spherical to tubular like structures. With the biomimetic capabilities of the microfabricated arrays it should be possible to provide a more natural environment for epithelial cells, combined with the ability to measure quantitative forces from multicellular structures during development.

AKB 25.10 Thu 17:15 ZEU 260

Micromechanics of the pericellular matrix — •Jennifer Curtis[1,2], Heike Boehm[1,2], Christian Schmitz[1,2], Ralf Richter[1,2], and Joachim Spatz[1,2] — [1]University of Heidelberg, Department of Biophysical Chemistry, INF 253, D-69120 Heidelberg — [2]Max-Planck-Institute for Metals Research, Department New Materials & Biosystems, Heisenbergstr. 3, D-70569 Stuttgart

In recent years, much attention has been directed towards the properties and activities of the cell surface. In particular, the coupling of the membrane to the underlying protein polymer network called the actin cortex, plays an important role in many events. The other side of the cell surface is less studied, although it too often has a bound polymer network comprised of gigantic cross-linked polysaccharides (sugars). Called the pericellular matrix (PCM), it is associated with many cells including fibroblasts, chondrocytes, endothelial and smooth muscle cells. Its thickness can vary from 10's of nanometers to 10 microns and it is associated with adhesion dependent events like migration and mitosis. Biologists often hypothesize that its viscoelastic properties are responsible for modulating adhesion activities. To investigate this idea, we measure the PCM's viscoelasticity using microrheology and probe the sharpness of its edge and its mesh size. The elastic modulus of the PCM under different condition is determined, and we characterize the long, elastic cables that can be pulled from the PCM. These results are compared with an externally reconstituted model PCM on the cell surface.

AKB 25.11 Thu 17:30 ZEU 260

Force Generation during Tumor Cell Invasion in Three-Dimensional Collagen Gels — •Thorsten Koch, Johannes Pauli, Claudia Mierke, and Ben Fabry — Friedrich-Alexander-Universität Erlangen-Nürnberg - Zentrum für Medizinische Physik und Technik - Lehrstuhl für Physikalisch-Medizinische Technik - Henkestraße 91 - D-91052 Erlangen

Tumor cells exert forces on surrounding tissue during invasion, but the magnitudes of these forces are unknown. We measured forces during invasion by extending methods for 2-D traction microscopy to 3-D. We used collagen gels ($E = 300$ Pa) to provide an *in vitro* environment for tumor cell invasion. MDA-MB-231 breast cancer cells were plated on the gel surface and allowed to invade for two days. Cells assumed a spindle-shaped morphology and contracted the gel mainly along their primary axis. To quantify gel contraction, fluorescent beads serving as fiducial markers were embedded in the gels. The 3-D bead positions were determined with a center-of-mass algorithm applied to images taken at various focal depths. To obtain the undeformed state of the gels, we disrupted the actin cytoskeleton and hence force transmission by treatment with cytochalasin-D (4 μM). We then calculated the dipole moment of the cells from the bead displacements between the initial and cytochalasin-D treated states. The magnitudes of dipole moments were on the order of 10^{-12} Nm, comparable to those generated by maximally contracted smooth muscle cells in 2-D culture (Butler JP et al., Am J Physiol Cell Physiol 282:C595, 2002). Our results show that MDA-MB-231 tumor cells exert substantial forces on surrounding tissue during invasion.

AKB 25.12 Thu 17:45 ZEU 260

Cell Characterization by Optical Deformability — •Stefan Schinkinger, Falk Wottawah, Bryan Lincoln, Franziska Lautenschlaeger, and Jochen Guck — Universitaet Leipzig; Institut fuer Experimentelle Physik I, Abt. PWM; Linnestrasse 5, 04103 Leipzig

In an optical stretcher, infrared laser light is used to exert surface stress on biological cells, causing an elongation of the trapped cell body along the laser beam axis. These optically induced deformations allow rheological measurements of individual cells and characterization by their optical deformability. Analyzing the deformation behavior of various cancer cell lines and primary stem cells, significant differences in axial elongation to control populations, even for small sample sizes, are measurable. It is shown that differentiation of stem cells and functional de-differentiation in different states of cancer progression allows to be classified with the optical stretcher, as functional and mechanical properties are strongly connected. When integrated within a microfluidic chamber delivering cells into the trap high throughput rates are possible. That way this technique allows measurement of statistically significant numbers of cells within short time. This enables for diagnosis of diseases, on a cellular level, that are associated with cytoskeletal processes. Additionally, the characterization of differentiation states during cell maturation ultimately allows sorting of cells with high accuracy in a non-contact manner.