BP 4: Cell Mechanics

Time: Monday 14:30–17:00 Location: HÜL 186

BP 4.1 Mon 14:30 HÜL 186

Stem Cell Cytoskeleton Polarization Dictated by Matrix Elasticity - Modelling Cellular Biomechanics with Force Dipoles — •Florian Rehfeldt[1,2], Assaf Zemel[3], Andre E.X. Brown[1], Allison L. Zajac[1], Samuel A. Safran[4], and Dennis E. Discher[1] — [1]University of Pennsylvania, Philadelphia, USA — [2]III. Physikalisches Institut, Georg-August-Universität, Göttingen, Germany — [3]Hebrew University, Jerusalem, Israel — [4]Weizmann Institute of Science, Rehovot, Israel

Biological cells are as responsive to their mechanical environment as they are to biochemical stimuli. As reported recently, human mesenchymal stem cells (hMSCs) plated on collagen-coated gels, differentiated towards the neurogenic, myogenic, and osteogenic lineage, depending on the Young's elastic modulus *E*. We present experimental data and a physical model to explain the non-monotonic dependence of stress-fibre polarization on matrix elasticity. Cytoskeletal organization is analyzed with immunofluorescence images of NMM IIa and actin using an automated segmentation algorithm. The theory generalizes Eshelby's treatment of elastic inclusions in solids to living inclusions (cells) that are capable of building up contractility. Their active polarizability, analogous to the electrical polarizability of non-living matter, results in the feedback of cellular forces that develop in response to matrix stresses. We demonstrate experimentally that matrix rigidity dictates cytoskeletal organization in two and three dimensional environments - a bio-mechanical process yielding different cell shapes that finally leads to lineage specific differentiation.

BP 4.2 Mon 14:45 HÜL 186

Force-induced movement of focal adhesions — •Benedikt Sabass[1,2], Sergey V. Plotnikov[3], Clare Waterman[3], and Ulrich S. Schwarz[1,2] — [1]University of Heidelberg, Bioquant 0013, Im Neuenheimer Feld 267, 69120 Heidelberg, Germany — [2]University of Karlsruhe, Theoretical Biophysics Group, Kaiserstrasse 12, 76131 Karlsruhe, Germany — [3]National Institutes of Health, Bethesda, Maryland 20892-8019NIH, USA

Adhesion and migration of tissue cells in the extracellular matrix is based on the localization of integrin adhesion receptors into so-called *focal adhesions*, where biochemical and mechanical signals are integrated to determine the cellular response. We have performed high resolution traction force microscopy measurements on fibroblasts to compare the magnitude of transmitted traction with the intensity of the fluorescently labeled cytoplasmic adhesion protein paxillin. We find that the ratio between traction and paxillin fluorescence is highest at the distal side of focal adhesions. The force at focal adhesions can also induce their movement. Analysis of the dynamical behavior of sliding adhesions revealed three characteristic regimes: stationary adhesion, creeping with force transmission and slipping without force transmission. We evoke simple physical models to qualitatively explain these three regimes.

BP 4.3 Mon 15:00 HÜL 186

The compaction of gels by cells: a case of collective mechanical activity — •Pablo Fernandez and Andreas R. Bausch — E27 Zellbiophysik, Technische Universität München, D-85748 Garching, Germany

With our growing understanding of force generation and transduction in biological systems, mechanics is acquiring the status of an organising principle connecting tissue architecture to single cell shape and phenotype. To understand mechanotransduction, purely mechanical phenomena resulting from the crosstalk between contractile cells and their elastic surroundings must be distinguished from adaptive responses to mechanical cues. Here, we revisit the compaction of freely suspended collagen gels by embedded cells (osteoblasts and fibroblasts), an amazing process where a small volume fraction of cells compacts the surrounding matrix by two orders of magnitude. We find it to be crucially determined by mechanical aspects. Gel compaction results from an anisotropic deformation following the mechanical anisotropy at the gel boundaries. The existence of a critical cell density shows the effect to be cooperative, revealing a mechanical interaction between cells. As a consequence of the nonlinear properties of biopolymer gels, the large deformations imposed by the cells irreversibly compact the matrix and render it anisotropic. This intricate interplay between contractility and matrix mechanics provides a robust structure-follows-shape principle with implications for the formation of tissues, and raises questions as to the nature of adaptive cytomechanical responses.

BP 4.4 Mon 15:15 HÜL 186

ATP dependent nonequilibrium mechanics of red blood cells — •Timo Betz, Martin Lenz, Jean-François Joanny, and Cécile Sykes — Institut Curie, UMR CNRS 168, 11 rue Pierre et Marie Curie, 75248 Paris, France

Red blood cells are extremely elastic objects, able to recover their shape even after large deformation as when passing through tight capillaries. The reason for this exceptional properties is found in the composition of the RBC membrane and its interaction with the spectrin cytoskeleton. We investigate the mechanics of the RBC membrane by a novel noninvasive technique that allows for the measurement of the fluctuation amplitudes with μs time and sub nm spatial resolution. This technique was used to determine the internal viscosity and the membrane bending modulus of normal red blood cells. We show that the mechanics do highly depend on the interaction between the membrane and the spectrin cytoskeleton which was altered by inhibition and activation of the 4.1 R proteins that connects the spectrin cytoskeleton with the membrane. Our results show that on short timescales (faster 100ms) the fluctuation are excited exclusively by thermal energy, whereas at timescales longer than 100ms an active energy that we contribute to the ATP consuming phosphorylation of the 4.1R protein can be measured. Hence at high frequencies, RBC membrane fluctuation can be described by thermodynamic equilibrium, whereas at longer timescales an active energy should be considered.

BP 4.5 Mon 15:30 HÜL 186

A Biomechanical Perspective on Cancer: From cell line to primary cells — •Kenechukwu David Nnetu, Franziska Wetzel, and Josef Käs — University of Leipzig, Institute of Experimental Physics I, Leipzig

Cancer being a fatal illness in the case of metastasis has been the subject of considerable scientific research. A vivid understanding of the microscopic changes within a cell leading to the initiation, development and spread of this disease is vital to the diagnosis and treatment of the disease. The cytoskeleton of living cells behaves non-linearly by amplifying microscopic changes within the cells. These cytoskeletal changes affect cellular structures and as a result cellular functions. The cytoskeleton being the main contributor to cell mechanics allows for the probing of cell elasticity with a suitable device such the Microfluidic optical stretcher as in this case.

We therefore, report on the mechanical properties of non-tumorigenic, tumorigenic, metastatic cell lines and primary cells. It was found out that metastatic cell lines were softest while malignant but non-metastatic cell lines were softer compared to non-tumorigenic cell lines. Additionally, cell lines were found to be softer than primary cells. Furthermore, metastatic cell lines were found to be the fastest proliferating cell lines while the malignant but non-metastatic cell lines were faster compared to the non-tumorigenic cell lines. Finally, by using cytochalasin D and jasplakinolide which disrupts and stabilizes actin respectively, the cell lines were found to be softer. The cell lines were also treated with the chemotherapeutic drug taxol.

15 min. break

BP 4.6 Mon 16:00 HÜL 186

Integrin expression increased contractile force generation that regulate cell invasion and tumor outgrowth — •Claudia Mierke[1], Martina Fellner[1], Benjamin Frey[2], and Martin Herrmann[2] — [1]Universität Erlangen, Department für Physik, LS für Physikalisch-Medizinische Technik — [2]Universitätsklinikum Erlangen, Innere Medizin 3, Erlangen, Germany

The process of metastasis formation includes cell invasion that causes malignant progression of tumors. The role of cell mechanics on the malignancy of tumor cells has not been investigated systematically. Highly-invasive tumor cells expressed significantly higher amounts of the a5b1 integrin compared to weakly-invasive. We hypothezise that high-a5b1 expressing cells increase contractile force generation that

increased cell invasion into a collagen matrix. Our results show that high a5b1 integrin expression increased cell invasiveness and increased the contractile force generation. Whether the increased contractile force generation is a prerequiste for enhanced cell invasiveness, we inhibited the invasiveness through blocking of the myosin light chain kinase by ML-7 or ROCK kinase by Y27632. Indeed, the reduction of contractile force decreased the cell invasiveness. Furthermore, we analyzed whether high-a5b1 and low-a5b1 cells formed tumor in nude mice. The tumor formation/ growth is impared in high-a5b1 compared to low-a5b1 cells. The integrin a5b1 acts as enhancer of cell invasiveness where contractile forces are necessary to overcome the viscous drag, but as suppressor of primary tumor formation/ growth where increased motility is rather a hindrance for cell clustering to form solid tumors.

BP 4.7 Mon 16:15 HÜL 186

High-Resolution Measurements of Cellular Contractile Forces — •Florian Schlosser[1], Florian Rehfeldt[1], Daisuke Mizuno[2], and Christoph Schmidt[1] — [1]3. Physikalisches Institut, Fakultät für Physik, Georg-August-Universität, 37077 Göttingen — [2]Organization for the Promotion of Advanced Research, Kyushu Univ., 812-0054, Fukuoka, Japan

Biological cells constantly communicate with their surroundings. Besides their well-characterized biochemical interactions, cells also use physical interactions. Cells sense external forces, and they actively probe the mechanical properties of their environment with contractile forces generated by their actin/myosin cytoskeleton. Using a dual optical trap, we have performed high-resolution measurements of the forces a cell generates between two fibronectin-coated beads. We have monitored the fluctuations of the beads at high spatial and temporal resolution and have analyzed the correlated motions. This approach allows us to measure simultaneously the total force cells generate between the two beads and the fraction of force transmitted to the environment. We present data of different cells attached to beads trapped with different stiffness, demonstrating that the generated forces depend on the elasticity of their environment.

BP 4.8 Mon 16:30 HÜL 186

Contribution of cytoskeletal components to the nonlinear rheology of cells — •Navid Bonakdar[1], Philip Kollmannsberger[1], Karen Kasza[2], and Ben Fabry[1] — [1]Center for Medical Physics and Technology, Biophysics Group, Dept. of Physics, University of Erlangen-Nuremberg, Erlangen, Germany — [2]School of Engineering and Applied Sciences, Harvard University, Cambridge, Mass., USA

The rheology of cells is governed by a creep or stress relaxation response that follows a weak power law over several decades in time, and a highly nonlinear stress-strain relationship, in particular a pronounced stress stiffening. In model cytoskeletal networks, stress stiffening is strongly increased in the presence of filamin A (FLNa), an F-actin crosslinker with the ability to unfold under force. The role of FLNa for the nonlinear rheology of living cells has so far not been characterized. We compared the stiffening response of a FLNa-deficient melanoma cell line (M2) and a variant stably transfected with FLNa (A7). Cell deformations in response to stepwise increasing forces applied to membrane-bound magnetic beads were analyzed using a non-linear superposition model to dissect stress relaxation from stress-stiffening responses. While stiffness and bead binding was reduced in FLNa-deficient cells, there was no difference in the degree of stress stiffening, indicating that contributions from other cytoskeletal components mask the effect of FLNa. The role of actin filaments, microtubules, intermediate filaments and myosin-generated cellular prestress in FLNa expressing and deficient cells was examined by pharmacological interventions.

BP 4.9 Mon 16:45 HÜL 186

Optical Cell Stretching and Cell Squeezing — •Tobias Kiessling, Franziska Wetzel, Karla Müller, Anatol Fritsch, K. David Nnetu, and Josef Käs — University of Leipzig

Rheological measurements on single cells are in general considered to be important for the understanding of living organisms. Determined by the cytoskeleton, the mechanical response provides an insight to the molecular structure and reflects the healthiness of each single cell. For biomechanical measurements, the Optical Cell Stretcher, a tool generating optical surface forces on single cells is of great importance since it provides a noninvasive access to the viscoelastic behavior of about 100 single cells per hour. The induced surface forces tend to stretch the cell and by applying optically induced step-stress experiments on single cells, an intimately relation between deformability and malignancy is revealed. With a slight change of setup paramters optical surface forces can be redistributed leading to a squeezed-like deformation instead of a stretch, and enabling various applications such as frequency dependent single cell rheology.