BP 1: Cell Mechanics I

Time: Monday 9:00–11:00 Location: BPa

BP 1.1 Mon 9:00 BPa

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 1.2 Mon 9:20 BPa

The dynamics of burst-like collective migration in 3D cancer spheroids — •Swetha Raghuraman[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 a 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 pressure due to a volume increase when they fail to engage rigid ECM contacts because of the soft environment. The volume increase then pushed the cells into the soft regions of the ECM, which tends to be inhomogeneous at the LCC. We believe that such mechanical interplay can pave the way to understand migration behavior of cancer cells with respect to their biophysical properties.

Invited Talk BP 1.3 Mon 9:40 BPa

Cyclic Strain Steers Animal Cells — •Rudolf Merkel — Forschungszentrum Jülich, IBI-2 Mechanobiology, 52428 Jülich, Germany

Throughout the organism, all tissue cells experience mechanical strain, e.g. due to the pulsating blood flow. Cells recognize, process, and act upon this signal. To study this mechanoresponse we applied well-defined mechanical strain cyclically to cultivated cells [1]. Cellular mechanoresponses were quantified via reorientation of cytoskeletal fibers. In cultivated endothelial cells we compared responses of actin, microtubules, and vimentin using a correlation-based algorithm and observed distinctly different ordering dynamics and amplitudes [2].

Even though the rigid skull protects the brain, it experiences intense mechanical deformations. Therefore we studied mechanoresponses of primary neurons from cortices of rat embryos. We observed a pronounced reorientation of neuronal dendrites upon cyclic strain and found a surprising mechanical resilience of these cells that survived even several days of uniaxial, cyclic stretching at an amplitude of 28% and a frequency of 300 mHz [3]. Moreover, results on neuronal activity and on the mechanobiology of further cell types of the brain will be shown.

[1] U. Faust et al., PLOS ONE 6, e28963 (2011).
[2] R. Springer et al., PLOS ONE 14, e0210570 (2019)
[3] J.-A. Abraham et al., Langmuir 35, 7423 (2019)

BP 1.4 Mon 10:10 BPa

Elucidating cell mechanics regulators from mechano-transcriptomic data using discriminative network analysis — •Marta Urbanska[1,2], Yan Ge[1], Maria Winzi[1], Shada Abuhattum[1,2], Maik Herbig[1,2], Martin Kräter[1,2], Nicole Töpfner[1], Anna Taubenberger[1], Carlo V. Cannistraci[1], and Jochen Guck[1,2] — [1]BIOTEC, 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, differentiation or circulation through vasculature. Identifying molecular factors that govern the mechanical phenotype is therefore a subject of great interest. Here we present an approach that enables establishing links between mechanical phenotype changes and the genes responsible for driving them. In particular, we employ a discriminative network analysis method termed PC-corr to associate cell mechanical states, measured by real-time deformability cytometry, with large-scale transcriptomic datasets across different biological systems. We obtain a conserved module of five target genes and validate their capacity to discriminate between soft and stiff cell states in silico, obtaining AUC-ROC values of 72-94%. We then show experimentally that the top scoring gene, CAV1, changes the mechanical phenotype of cells when silenced or overexpressed. The data-driven approach presented here has the power of de novo identification of genes involved in cell mechanics, thereby extending the toolbox for tuning the mechanical properties of cells on demand to enable biological function or prevent pathologies.

30 min. Meet the Speaker & coffee break