BP 21: Cell Adhesion and Migration, Multicellular Systems I

Time: Wednesday 9:30–13:00 Location: HÜL 386

Invited Talk BP 21.1 Wed 9:30 HÜL 386

Cellular mechanosensing within synthetic 3D extracellular matrices — •Britta Trappmann — Max Planck Institute for Molecular Biomedicine, Münster, Germany

Cell fate decisions are influenced by many cues, which together constitute the cell microenvironment. One critical regulator is the extracellular matrix (ECM), which varies not only in composition, but also in physical properties such as stiffness. The impact of matrix stiffness on cell spreading and differentiation has been studied intensively on 2D surfaces using synthetic hydrogels, but very little is known about stiffness sensing within more complex 3D matrices.

Here, a major hurdle is to isolate the role of ECM stiffness from other matrix properties, in particular degradability. If cells are fully encapsulated, changes in bulk stiffness also influence the amount of matrix crosslinks that a cell has to cleave in order to spread and interact with its surroundings, impacting cell shape and function. Here, we have developed a sugar-based hydrogel system that offers independent control over mechanical properties, adhesive ligand density and matrix degradation rates. Using this system, we study the impact of matrix stiffness and degradability on cell spreading, mesenchymal stem cell differentiation and angiogenic sprouting. In particular, we demonstrate that matrix degradability, mechanics and adhesivity jointly control the multicellularity of 3D endothelial cell invasion.

BP 21.2 Wed 10:00 HÜL 386

Elongated Cells Fluidize Malignant Tissues — •Steffen Grosser, Jürgen Lippoldt, Linda Oswald, Frédéric Renner, and Josef A. Käs — Peter Debye Institute for Soft Matter Physics, Universität Leipzig

Tissue morphology changes during tumour progression. In 2D cell cultures, different tissue states, such as fluid, jammed and nematic, are linked to cell shapes. While it is not clear if these results hold true in three dimensions, they suggest to investigate cell shapes and tissue states of matter in 3D. To explain cell motility in tumors, we compare 3D cell spheroids composed of cells from a cancerous and a non-cancerous cell line. Through spheroid fusion experiments and live cell tracking, we show that the epithelial sample behaves solid-like and the malignant sample is fluidized by active cells moving through the tissue. Full 3D-segmentations of the samples show that the fluid-like tissue has elongated cell shapes. This links cell shapes to cell motility and bulk mechanical behaviour. We reveal two active states of matter in 3D tissues: an amorphous glass-like state with characteristics of 3D cell jamming, and a disordered fluid state.

BP 21.3 Wed 10:15 HÜL 386

Relation between tissue homeostasis and mechnosensitivity in model epithelium — •Maxime Hubert[1], Sara Kaliman[1], Carina Wollnik[2], Simone Gehrer[1], Damir Vurnek[1], Diana Dudziak[3], Florian Rehfeldt[2], and Ana-Suncana Smith[1,4] — [1]PULS Group, Friedrich Alexander University Erlangen-Nurnberg, Erlangen, Germany — [2]Cell & Matrix Mechanics Group, Georg-August-University Gottingen, Gottingen, Germany — [3]Group for the Biology of Dendritic Cells, University Clinic Erlangen-Nurnberg, Erlangen, Germany — [4]Group for Computational Life Sciences, Ruder Boskovic Institute, Zagreb, Croatia

Despite recent efforts to understand homeostasis in epithelial tissues, there are many unknowns surrounding this cooperative steady state. In the context of cell morphology, single cell studies set mechanosensitivity as an important regulatory process. However, mechanoresponse in tissues remains heavily debated. Here we show that changes in matrix stiffness induce a non-equilibrium transition from tubular to squamous tissues. Despite adopting different cell shapes and densities, all homeostatic states display equivalent topologies. This suggests that the latter property is actively targeted in homeostasis. On the contrary, we observe a dramatic change in the self-assembled organization of the colonies on the macroscopic scale. Such behavior is recovered in simulations by introducing stiffness-dependent activity. Our results unequivocally relate the mechanosensitive properties of individual cells to the evolving macroscopic structures, an effect that could be important for understanding the emergent pathology of living tissues.

BP 21.4 Wed 10:30 HÜL 386

Stress Fiber vs. Cortical Contractility and its Relevance for Tissue and Cancer Development — •Enrico Warmt, Steffen Grosser, Eliane Blauth, and Josef Käs — Uni Leipzig, Soft Matter Physics, Leipzig

It is the current perception that cell contractility is solely based on a force dipole like interaction requiring stress fibers that pull between cellular adhesion sites for migratory and invading purposes. However, our observations suggest a clear differentiation between stress fiber and cortical contractility. We investigate on one hand suspended cells, lacking stress fibers and adhesion points, regarding active cortical contractility and on the other hand adhered cells, in an ECM environment displacing biomechanical properties based on oriented actin stress fiber contractility. Epithelial cells assemble a strong actomyosin cortex providing cortical tension exhibiting mechanosensitive contractile behavior. In contrast mesenchymal cell cortices behave less contractile, while they express more prominent stress fibers generating stronger contractile forces in 3D collagen gels. We propose an actomyosin rearrangement from cortical to stress fiber structures during epithelial*mesenchymal transition. We investigate the formation of cell-cell contacts up to the formation of cell spheroids, which is accompanied, for epithelial cells, with rearrangement of their contractile actomyosin cortices building up a collective actomyosin cortex surrounding the aggregates. In contrast, mesenchymal cells, do not form stable cell-cell contacts neither collective actomyosin rims, due to lacking cortical contractile potential, suggesting low surface tension like behavior.

BP 21.5 Wed 10:45 HÜL 386

On moving nuclei and membranes - interkinetic nuclear migration on the cell level — •Anne Herrmann and Raymond E. Goldstein — Department of Applied Mathematics and Theoretical Physics, University of Cambridge, Cambridge, United Kingdom

In developing pseudostratified epithelia, nuclei move repeatedly between the apical and basal surfaces of cells. This process is termed interkinetic nuclear migration (IKNM) and has been studied extensively in the brain, retina and spinal cord of multiple organisms. But despite these efforts many questions about the precise mechanism of IKNM remain. Based on *in vivo* light sheet microscopy we previously developed a quantitative model for the phenomenological properties of IKNM on the tissue level [1]. In this talk, we now examine the properties of IKNM on the level of individual cells. First, we investigate the random walk behaviour of individual nuclei within the tightly packed tissue environment to make estimates of the forces involved in this process. Secondly, we aim to understand the role of the interaction between nucleus and cell membrane. This not only appears to influence IKNM but possibly even has implications for the overall cell architecture.

[1] Afnan Azizi, Anne Herrmann, Yinan Wan, Salvador J. R. P. Buse, Philipp J. Keller, Raymond E. Goldstein, William A. Harris. *sub judice* (2019), arXiv: 1903.05414

30 min. coffee break

BP 21.6 Wed 11:30 HÜL 386

cell competition in mouse embryo — •Gabriele Lubatti[1], Antonio Scialdone[1], Tristan Tristan[2], Ana Lima[2], and Shankar Srinivas[3] — [1]Institute of Epigenetics and Stem Cells, Helmholtz Zentrum Munich, Munich, Germany — [2]National Heart and Lung Institute, Imperial College London, Hammersmith Hospital Campus, London, UK — [3]Department of Physiology Anatomy & Genetics, University of Oxford, Oxford, UK

Cell competition is a biological process whereby cells eliminate their less fitted neighbours [1] [2]. It has myriad positive roles in the organism: it selects against mutant cells in developing tissues, prevents the propagation of oncogenic cells and eliminates damaged cells during ageing. While it was first characterized in drosophila [3], it is currently unclear what are the transcriptional features of cells eliminated through competition and what are the roles of cell competition during mammalian development. We analysed single-cell transcriptomic data from mouse embryos around the time gastrulation starts (stage E6.5) where apoptosis was inhibited. We show that in these embryos a new population of epiblast cells emerges, expressing markers of cell competition previously characterized [4]. Our analysis also identifies

additional features of eliminated cells, including disrupted mitochondrial activity that we validate in vivo. Moreover, by using physical modelling, we show that cell competition might play a role in the regulation of embryo size, which could be particularly important around gastrulation [5].

BP 21.7 Wed 11:45 HÜL 386

Encoding memory in biological network hierarchy — •Mirna Kramar[1] and Karen Alim[1,2] — [1]Max Planck Institute for Dynamics and Self-Organization, 37077 Göttingen, Germany — [2]Physik-Department, Technische Universität München, Garching, Germany

Remembering sources of food and threat is essential for survival. While higher animals rely on their nervous system, even very simple organisms are able to encode sensory information that aids them in tackling complex environments. The true slime mould *Physarum polycephalum* is a giant unicellular eukaryote whose body consists of a protoplasm-filled network of tubes which undergoes constant reorganization.The mechanism behind the reorganization of *P. polycephalum* body upon food encounter has not been explained previously. Here, we identify the imprint the food stimulus leaves on network morphology as memory and show that the network relies on tube growth and flows to encode stimulus information. We hypothesise an encoding mechanism introducing a local release of a chemical agent that affects the mechanical properties of the tubes and spreading through the network by protoplasmic flows. Using a theoretical model, we test our hypothesis and find the model yields a correct prediction of flow-dependent stimulus response. Finally, we investigate the role of network hierarchy in memory encoding and show that both hierarchy and the orientation of tubes are relevant in stimulus encoding. Our findings demonstrate *P. polycephalum*'s ability to encode memory and likely open doors to the use of the organism in bioinspired design.

BP 21.8 Wed 12:00 HÜL 386

Relation between long- and short-time wave dynamics in Physarum polycephalum — •Adrian Fessel and Hans-Günther Döbereiner — Universität Bremen, Bremen, Germany

In the recent past, the slime mold Physarum polycephalum has attracted considerable attention due to its behavioral complexity, which is unparalleled in unicellular systems. However, the interplay of mechanisms giving rise to the non-neural information processing observed in the slime mold still lacks detailed understanding. The physical processes believed to be at the basis include mechanochemical oscillations. These organize as peristaltic wave patterns propagating on, and simultaneously modifying, a time-variant network topology. Comparable stable patterns are observed in micrometer-sized fragments and on extended networks, and share some visual similarity with spatiotemporal modulation of neuron activity in the brain. Here, we present a quantitative computational approach for the analysis of travelling waves on centimeter-sized network topologies. Employing a clustering method, we characterize recurring patterns. This leads to the identification of a functional link between wave dynamics at very different time-scales, extending to the migratory behavior of the slime mold.

BP 21.9 Wed 12:15 HÜL 386

A lumped-parameter model illustrates information processing and migration in the slime mold *Physarum polycephalum* — •Christina Oettmeier and Hans-Günther Döbereiner — Institut für Biophysik, Universität Bremen

The slime mold *P. polycephalum* exhibits rich spatiotemporal oscillatory behavior. The organism's size spans orders of magnitude, from large meter-sized stationary transport networks down to micrometer-sized amoebae. All morphotypes show actomyosin-based contraction-relaxation cycles resulting in protoplasmic streaming. Furthermore, the giant amoeba shows a very high behavioral plasticity, leading to speculations about the origins of cellular minimal cognition. The underlying functions are not neuron-based, but are emergent phenomena, resulting from mechanochemical processes on the tubular network. In this context, we investigate how the slime mold processes information. At different parts of a migrating amoeba, oscillation frequencies vary. Oscillations in the back cause endoplasm flows through the internal vein system and expand the frontal membrane. We use the electronic-hydraulic analogy, implemented in a lumped-parameter model, to investigate this special case of information processing. A single vein segment can be described as a flexible tube, possessing a fluidic resistance (R) and fluidic capacitance (C) due to wall elasticity. The electronic equivalent is a passive RC low pass filter. Thus, the oscillation frequencies at the back are higher than those at the front due to filtering. The model can also explain the onset of locomotion.

BP 21.10 Wed 12:30 HÜL 386

Identifying the blue-light photoreceptor underlying light-switchable adhesion of *Chlamydomonas* to surfaces. — •Rodrigo Catalán[1], Antoine Girot[1], Theresa Büttner[1], Alexandros Fragkopoulos[1], Simon Kelterborn[2], Peter Hegemann[2], and Oliver Bäumchen[1] — [1]Max Planck Institute for Dynamics and Self-Organization (MPIDS), Am Fassberg 17, 37077 Göttingen, Germany. — [2]Humboldt University of Berlin, Institute of Biology, Invalidenstrasse 42, 10115 Berlin, Germany.

Photosynthetic microorganisms have developed several photoactive responses to spatial and temporal light variations. Interestingly, the unicellular, eukaryotic microalga *Chlamydomonas reinhardtii* swims freely in red light but exhibits flagella-mediated adhesion to surfaces when exposed to blue light (Kreis *et al.*, Nature Physics, 2018). We performed adsorption experiments to establish the spectral sensitivity of the adhesiveness of wild-type *Chlamydomonas* and found a maximum of the cell adsorption rate at 470 nm. These results provide evidence that a blue-light photoreceptor triggers light-switchable adhesiveness. There are 18 known photoreceptors in *Chlamydomonas*, most of which are blue-light sensitive. We use targeted gene editing tools to establish photoreceptor-deletion mutants and perform adsorption experiments and complementary micropipette force spectroscopy experiments on these strains. We find that channelrhodopsin 1 and 2 as well as phototropin are not the functional photoreceptors mediating light-switchable adhesion, which is interesting since they account for other important responses, namely phototaxis and the cell's life cycle.

BP 21.11 Wed 12:45 HÜL 386

Characterization of Spider Silk for Elucidating the Reasons Behind its Medical Success in Nerve Regeneration Applications — •Aida Naghilou[1], Lena Pöttschacher[2], Flavia Millesi[1], Anda Mann[1], Paul Supper[1], Ellen Backus2[2], and Christine Radtke[1] — [1]Research Laboratories of the Division of Plastic and Reconstructive Surgery, Medical University of Vienna, Vienna, Austria — [2]Department of Physical Chemistry, University of Vienna, Vienna, Austria

Spider silk has been established as a fascinating materials due to its unique strength, toughness, and elasticity [1]. One of the more remarkable applications of the spider silk is its use for nerve growth and nerve regeneration [2]. The Schwann cells, which are a crucial part of the nerve regeneration process, adhere well to spider silk and migrate along it [3]. However, the reasons behind the medical success of the silk is unclear.

In this work, we performed systematic studies for the material characterization and medical performance of various spider silks. The characterization experiments focus on the Raman spectroscopy, morphology, and wettability of the silk. The medical assessment of the silk in evaluated by in vitro experiments with Schwann cells, where the adhesion, motility, and the proliferation of the cells on the spider silk in monitored. [1] L. Römer, T. Scheibel, Prion, 2 (2008) 154. [2] C. Radtke, Int J Mol Sci, 17 (2016) 1754. [3] T. Kornfeld, P.M. Vogt, V. Bucan, C.-T. Peck, K. Reimers, C. Radtke, J Funct Biomater, 7 (2016) 30.