BP 30: Cell Adhesion and Migration, Multicellular Systemadhesion and Migration, Multicellular Systems II

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

Invited Talk BP 30.1 Thu 9:30 HÜL 386

Active behaviors of cellular monolayers. — •Benoit Ladoux — Institut Jacques Monod, CNRS & Université de Paris, Paris, France

The actomyosin machinery endows cells with contractility at a single cell level. Within a tissue, cells can show either contractile or extensile stresses based on the direction of pushing or pulling forces exerted by their neighbours or on the substrate. In the first part, I will show how these active behaviours and stresses govern fundamental biological processes such as cell extrusion. By modelling the epithelium as an active nematic liquid crystal and measuring mechanical parameters such as strain rates and stresses measurements within cellular monolayers, we show that apoptotic cell extrusion is provoked by singularities in cell alignments in the form of comet-shaped topological defects. The results highlight the importance of active nematic nature of epithelia. However, cellular monolayers display various active behaviors as exemplified by the contractile nature of fibroblasts and the extensile nature of epithelial cells or neural crest cells. In a second part, I will discuss how these two contradictory modes of force generation can coexist. Through a combination of experiments and in silico modeling, we uncover the mechanism behind this switch in behaviour of cell monolayers from extensile to contractile as the weakening of intercellular contacts. We find that this switch in active behaviour also promotes the buildup of tension at the cell-substrate interface through an increase in actin stress fibers and higher traction forces. Such differences in extensility and contractility act to sort cells, thus determining a general mechanism for mechanobiological pattern formation.

BP 30.2 Thu 10:00 HÜL 386

Embryonic Inversion in *Volvox carteri*: The Flipping and Peeling of Elastic Lips — •Pierre A. Haas and Raymond E. Goldstein — Department of Applied Mathematics and Theoretical Physics, University of Cambridge, United Kingdom

The embryos of the green alga *Volvox carteri* are spherical sheets of cells that turn themselves inside out at the close of their development through a program of cell shape changes. This process of inversion is a simple model for the cell sheet deformations in the development of higher organisms. Inversion starts with four lips opening up at the anterior pole of the cell sheet; these lips then flip over, and peel back to invert the embryo. Experimental studies have revealed that inversion is arrested in mutants or if some of these cell shape changes are inhibited chemically, but the mechanical basis for these observations has remained unclear. We analyze the mechanics of this inversion by deriving an averaged elastic theory for the cell sheet and the lips in particular and we interpret the experimental observations in terms of the mechanics and evolution of inversion [1].

[1] P. A. Haas and R. E. Goldstein, Phys. Rev. E **98**, 052415 (2018)

BP 30.3 Thu 10:15 HÜL 386

Tissue-wide integration of mechanical cues promotes efficient auxin patterning — •João R. D. Ramos[1], Alexis Maizel[2], and Karen Alim[1,3] — [1]Max Planck Institute for Dynamics and Self-Organization, 37077 Göttingen, Germany — [2]Center for Organismal Studies, University of Heidelberg, Heidelberg, Germany — [3]Physik-Department, Technische Universität München, Garching, Germany

New plants organs form by local accumulation of auxin, which is transported by PIN proteins that localize following mechanical stresses. As auxin itself modifies tissue mechanics, a feedback loop between tissue mechanics and auxin patterning unfolds, yet the impact of tissue-wide mechanical coupling on auxin pattern emergence remains unclear. Here, we use a hybrid model composed of a vertex model for plant tissue mechanics, and a compartment model for auxin transport to explore the collective mechanical response of the tissue to auxin patterns and how it feeds back onto auxin transport. We compare a model accounting for a tissue-wide mechanical integration to a model where mechanical stresses are averaged out across the tissue. We show that only tissue-wide mechanical coupling leads to focused auxin spots, which we show to result from the formation of a circumferential stress field around these spots, self-reinforcing PIN polarity and auxin accumulation.

BP 30.4 Thu 10:30 HÜL 386

(In-)stability of growing tissue interfaces — •Tobias Büscher, Gerhard Gompper, and Jens Elgeti — Theoretical Soft Matter and Biophysics, Institute of Complex Systems and Institute for Advanced Simulations, Forschungszentrum Jülich, 52425 Jülich, Germany

Interfaces of tissues are ubiquitous, between tissue and environment as well as between populations of different cell types. The propagation of an interface can be driven mechanically, e.g. by a difference in the respective homeostatic stress of the different cell types [1,2]. Computer simulations of growing tissues are employed to study the competition of two tissues on a substrate. In particular, we focus on the stability of the interface between them [3]. Two identical tissues of course mix with time. Even a small difference in tissue properties results in competition and demixing. A stable interface emerges for competition driven by a difference in homeostatic stress. However, it becomes unstable above a critical difference for reduced apoptosis rates of the weaker tissue. A finger-like protrusion remains in the stronger, invading, tissue.

A difference in directed bulk motility also suffices to result in competition and a stable interface between them, even for otherwise identical tissues. Larger differences in motility force however result in a clear finite-wavelength instability of the interface. Interestingly, this instability seems to be bound by higher order terms, such that the amplitude of the undulation only grows to a finite value.

[1] Podewitz *et al.*, 2016, *New J. Physics* **18**, 083020
[2] Ranft *et al.*, 2014, *New J. Phys.* **16**, 035002
[3] Williamson *et al.*, 2018, *Phys. Rev. Lett.* **121**, 238102

BP 30.5 Thu 10:45 HÜL 386

Complex fluid flow, cell polarity and cilia beating patterns in the brain ventricles — •Christian Westendorf[1], Shoba Kapoor[2], Yong Wang[1], Gregor Eichele[2], and Eberhard Bodenschatz[1] — [1]Max Planck Institute for Dynamics and Self-Organization, Am Fassberg 17, 37077, Goettingen. — [2]Max Planck Institute for Biophysical Chemistry, Am Fassberg 11, 37077, Goettingen.

The brain ventricles are filled with cerebrospinal fluid (CSF) and are lined with a specialized cilia bundle carrying epithelium. The spatially organized beating of the cilia creates CSF flows along the epithelial surface. Particle tracking shows that these flows are very complex, forming a network of flows that varies little between individual mice (Faubel et al., Science, 2016). Using immunohistochemistry with suitable antibodies, we now show that the flow pattern is grounded on the translational and rotational polarity of the epithelial cells. For example whirl like flows are created above cells, whose cilia bundles are oriented accordingly. Additionally, these investigations revealed highly regular patterns in cell shape and cell size, and eccentricity and orientation of the cilia bundles. We further imaged the beating cilia with DIC microscopy with high spatial and temporal resolution over the expanse of the entire ventricular wall. This allowed us to determine the beating properties of cilia and the coordination of beating between the cilia bundles. Alltogether these data suggest that genetic factors make a major contribution to the organization of the flow patterns along the ventricular wall.

30 min. coffee break

BP 30.6 Thu 11:30 HÜL 386

Migration of immune cells in an obstacle park — •Doriane Vesperini[1], Zeinab Sadjadi[3], Heiko Rieger[3], and Franziska Lautenschläger[1,2] — [1]INM-Leibniz Institute for New Materials, 66123 Saarbrücken, Germany — [2]Experimental Physics, Saarland University, 66123 Saarbrücken, Germany — [3]Theoretical Physics, Saarland University, 66123 Saarbrücken, Germany

Several crucial processes in biological systems can be described as a search problem such as: finding food resources or pathogens. The presence of obstacles like non-targeted cells or extracellular matrix in biological environments induces a perturbation of the initial cell trajectory. For example, the presence of bystander cells has been shown to increase the velocity and the persistency of natural killer cells [1]. Besides obstacles density, their spatial disposition may also influence the search efficiency. It has been demonstrated that the density and

geometry of pillar lattices affect migration strategies of cells [2].

We investigate how search efficiency is influenced by spatial arrangement of obstacles. A microfluidic device is designed to track HL-60 cells differentiated into neutrophils in confined 2D environments. Our device consists of pillar forests of different diameters distributed in triangular or square arrangements. We calculate the mean first passage time and diffusion properties of the searcher in different densities and geometries of pillars and investigate which key parameters influence the search efficiency.

[1] Zhou X., et al. Scientific Reports (2017)
[2] Gorelashvili M., et al. New Journal of Physics (2014)

BP 30.7 Thu 11:45 HÜL 386

Cell-cell adhesion and 3D matrix confinement explain plasticity of breast cancer invasion — •Simon Syga[1], Peter Friedl[2], and Andreas Deutsch[1] — [1]Center for Information Services and High Performance Computing, Technische Universität Dresden, Dresden, Germany — [2]Department of Cell Biology, Radboud Institute for Molecular Life Sciences, Radboud University Medical Center, Nijmegen, The Netherlands

Plasticity of cancer invasion and metastasis depends on the ability of cancer cells to switch between collective invasion modes and single cell dissemination, under the control of cadherin-mediated cell-cell junctions. E-cadherin is considered a tumor suppressor, the downregulation of which causes single-cell scattering in 2D environments. In clinical samples, however, E-cadherin expressing and deficient tumors both invade collectively and metastasize equally, implicating additional mechanisms controlling cell-cell cooperation and dissemination.

Using a cellular automaton model we identify physical confinement by the extracellular matrix (ECM) as the dominant physical mechanism that supports collective invasion irrespective of the composition and stability of cell-cell junctions. In particular, we predict that downregulation of E-cadherin results in a transition from coordinated to uncoordinated collective movement along extracellular boundaries, whereas single-cell escape depends on locally free tissue space.

BP 30.8 Thu 12:00 HÜL 386

Confined cell migration: learning a dynamical systems theory from data — •David Brückner[1], Alexandra Fink[2], Matthew Schmitt[1], Nicolas Arlt[1], Joachim Rädler[2], and Chase Broedersz[1] — [1]Arnold Sommerfeld Center for Theoretical Physics and Center for NanoScience, Ludwig-Maximilians-Universität, München — [2]Faculty of Physics and Center for NanoScience, Ludwig-Maximilians-Universität, München

In many biological phenomena, cells migrate through confining environments. However, a quantitative conceptual framework for confined migration has remained elusive. To provide such a framework, we employ a data-driven approach to infer the dynamics of cell movement, morphology and interactions of cells confined in two-state micropatterns. In this confinement, cells stochastically migrate back and forth between two square adhesion sites connected by a thin bridge. By inferring a stochastic equation of motion directly from the experimentally determined short time-scale dynamics, we show that cells exhibit intricate non-linear deterministic dynamics that adapt to the geometry of confinement. This approach reveals that different cell lines exhibit distinct classes of dynamical systems, ranging from bistable to limit cycle behavior. To connect these findings to underlying migratory mechanisms, we track the evolution of cell shape and develop a framework for the dynamics of cell morphology in confinement. Our approach yields a conceptual framework for the motility and morphology of confined cells which we also generalize to more complex environments including multiple interacting confined cells.

BP 30.9 Thu 12:15 HÜL 386

Cell Motility Using Race Tracks on Elastic Substrates — Daniel Meyer[1], Christoph Schreiber[2], Joachim Rädler[2], Matthias Weiss[3], and •Florian Rehfeldt[1,3] — [1]3rd Institute of Physics - Biophysics, Georg-August University, Göttingen, Germany — [2]Faculty of Physics, Soft Condensed Matter Group, Ludwig-Maximilians-University, Munich, Germany — [3]Experimental Physics 1, University of Bayreuth, Bayreuth, Germany

Cell motility and migration processes are vital during biological development and homeostasis. They are essential in tissue regeneration, morphogenesis, but also in pathological mechanisms like tumor metastasis. While migration due to biochemical gradients (e.g. chemotaxis) is very well studied, the influence of other parameters of the microenvironment such as topography and stiffness are less understood.

Here, we use polyacrylamide (PA) hydrogels in combination with a novel microcontact printing (μCP) protocol to generate patterned substrates with well-controlled Young's modulus E . These collagen-coated tracks are used to analyze the migration behavior of human mesenchymal stem cells (hMSC) and NIH3T3 fibroblasts by parallelized life cell microscopy under physiological conditions.

We demonstrate that both, elasticity as well as the geometry of the tracks affect the migration velocity and that the two cell types show distinct motile behavior.

BP 30.10 Thu 12:30 HÜL 386

Morphological and Mechanical Dynamics of Migrating Platelets Investigated with Scanning Ion Conductance Microscopy — •Johannes Rheinlaender, Jan Seifert, and Tilman E. Schäffer — Institute of Applied Physics, Eberhard Karls University Tübingen, Germany

Platelets or thrombocytes are the central element of the hemostatic system as being the first cells adhering to the site of a vessel injury, orchestrating the blood clot formation, and thereby establishing the initial steps of sealing the wound. In addition, platelets have been quite recently identified to be very motile cells, which can actively migrate towards sites of inflammation or bacterial pathogens. However, many aspects of the underlying cellular machinery are still unknown. We therefore studied migrating platelets using scanning ion conductance microscopy (SICM), an imaging technique providing topography images together with quantitative mechanical sample properties at nanoscale resolution. Thereby, we found that migrating platelets exhibit a three-dimensional shape anisotropy, which is directionally correlated with the direction of migration. Furthermore, we used SICM to record time-lapsed maps of the elastic modulus of migrating platelets, which revealed a characteristic subcellular distribution. We show that this distribution is caused by a dynamics reorganization of the platelet's actin cytoskeleton and thereby give direct mechanical evidence that platelet migration is driven by active cytoskeletal reorganization.

BP 30.11 Thu 12:45 HÜL 386

Nanoprobing of osteoblasts adhered to micro-contact printed dendrimer and protein layers — •Christian Völkner[1], Issam Assi[1], Martina Grüning[2], Regina Lange[1], Barbara Nebe[2], Ingo Barke[1], and Sylvia Speller[1] — [1]Institute of Physics, Physics of Surfaces & Interfaces, University of Rostock, 18059 Rostock — [2]University Medical Center, Dept. of Cell Biology, University of Rostock, 18057 Rostock

Chemical and physical surface gradients to control local cell adhesion and migration may allow to find routes to improve osseointegration of implants. Therefore, the local as well as the mesoscopic responses of living osteoblast-like cells (MG-63) were studied by means of Scanning Ion Conductance Microscopy (SICM) [1] and Fluorescence Microscopy, respectively. To achieve molecular landscapes with a small topographic corrugation height, amine-terminated PAMAM dendrimers and albumin were deposited in a stripe pattern on glass cover slips by direct micro-contact printing [2]. A distinct spindle shape oriented parallel to the surface pattern as well as a preferential adhesion of the cells on the glass site is observed when the width of the stripes is in the regime of 20 microns. We discuss in how far the pre-treatment of the glass and small protruding heights of a few nm are involved in the preference of the cells.

[1] Korchev et al., Biophys. J. 73, 653 (1997)
[2] Whitesides et al., Chem. Rev. 105, 1171 (2005)