BP 22: Migration and Multicellular Systems

Time: Thursday 9:30–12:15 Location: H15

Invited Talk BP 22.1 Thu 9:30 H15

Cell and tissue mechano-plasticity in development — •Verena Ruprecht — Centre for Genomic Regulation (CRG), Barcelona, Spain

The development of a single fertilised cell into an embryo is a highly dynamic process that establishes the structural and functional architecture of the organism. The building of complex multicellular structures fundamentally emerges from the spatio-temporal coordination of dynamic behaviours at the single cell level. How this multi-scale process occurs with high fidelity and robustness is still a major open question. Here I will discuss how embryonic stem cells are able to sense and adapt to mechanical shape deformations in their 3D tissue environment. I will explore the function of the cell nucleus as an intracellular mechano-sensor and how it can act as a non-genetic controller of cell mechanics and migration plasticity. I will further discuss how cellular error correction is established in the earliest stages of embryo development by mechanical cell cooperation that promotes the efficient phagocytic clearance of aberrant apoptotic cells. Theoretical modelling of mechanical force fluctuations at the cell cortex and protrusive force generation in cell collectives will be presented to mechanistically describe the emergence of mechano-plasticity at the single cell and tissue level mediating robust embryo development.

BP 22.2 Thu 10:00 H15

Active T1 transitions in cellular networks — •Charlie Duclut[1,2], Joris Paijmans[1], Mandar M. Inamdar[3], Carl D. Modes[4,5,6], and Frank Jülicher[1,5,6] — [1]Max Planck Institute for the Physics of Complex Systems, Nöthnitzer Str. 8, 01187 Dresden, Germany — [2]Université Paris Cité, Laboratoire Matière et Systèmes Complexes, Paris, France — [3]Department of Civil Engineering, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India — [4]Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG), Dresden 01307, Germany — [5]enter for Systems Biology Dresden, Pfotenhauerstrasse 108, 01307 Dresden, Germany — [6]Cluster of Excellence, Physics of Life, TU Dresden, Dresden 01307, Germany

In amorphous solids as in tissues, neighbour exchanges can relax local stresses and allow the material to flow. In this talk, I will use an anisotropic vertex model to study T1 rearrangements in polygonal cellular networks. We consider two different physical realization of the active anisotropic stresses: (i) anisotropic bond tension and (ii) anisotropic cell stress. Interestingly, the two types of active stress lead to patterns of oriented T1 transitions that are different. I will describe and explain these observations through the lens of a continuum description of the tissue as an anisotropic active material. I will furthermore discuss the energetics of the tissue and express the energy balance in terms of internal elastic energy, mechanical work, chemical work and heat. This allows us to define active T1 transitions that can perform mechanical work while consuming chemical energy.

BP 22.3 Thu 10:15 H15

Bistability between sessile and motile solutions in a nonlinear active gel model for cell migration — •Oliver M. Drozdowski, Falko Ziebert, and Ulrich S. Schwarz — Institute for Theoretical Physics and BioQuant, Heidelberg University, 69120 Heidelberg, Germany

Cell motility is one of the hallmarks of life and often is based on flow in the actin cytoskeleton that is driven by myosin II motors. The standard model to describe such flows is active gel theory, in which myosin II contractility enters as active stress. Recently, we have shown how to include optogenetic control in a minimal active gel model [1]. Here we ask how active gel descriptions of motility need to be modified to explain the experimental observation that a cell's state can be switched between sessile and motile. We show that such bistability emerges in active gel theory if the myosin II motors are modeled as a supercritical van der Waals fluid, including volume exclusion and short-range attraction. We present phase diagrams in cell adhesion and contractility that include sessile, bistable and motile regimes in experimentally relevant parameter ranges. Including optogenetic perturbations of contraction, as done before for a simpler model [1], we find that such external activation can be used to control cell locomotion, in agreement with recent experiments [2].

[1] O. M. Drozdowski, F. Ziebert, and U. S. Schwarz, Phys. Rev. E 104, 024406 (2021),
[2] A. Hadjitheodorou, et al., Nat. Commun. 12, 6619 (2021).

BP 22.4 Thu 10:30 H15

Rotation of an aspherical organoid within its matrix - a continuum model — •Anne Materne[1], Charlie Duclut[1,2], and Frank Jülicher[1,3,4] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Université Paris Cité, Laboratoire Matière et Systèmes Complexes, Paris, France — [3]Center for Systems Biology Dresden, Dresden, Germany — [4]Cluster of Excellence Physics of Life, TU Dresden, Germany

Organoids and other 3D *in vitro* multicellular systems have frequently been observed to display rotational motion within their matrix. Collective rotational motion can also be witnessed *in vivo*, for example in the *Drosophila* egg chamber. We propose that this motion results from cell-matrix interactions. Cells are thought to move similarly to 2D migration - however, a (near-)spherical geometry of cell clusters can lead to the observed rotation in 3D. Here, we present a continuum mechanics descripion of an organoid rotating within its embedding matrix. We discuss the extreme cases of the matrix being either purely elastic or purely viscous. The organoid is considered to be a non-deformable solid with a surface polarity field, exerting traction forces on the matrix. Importantly, our study is not limited to perfectly spherical organoids but takes small shape deformations into account. This permits to distinguish between purely rotational and deformation-induced cell-matrix interactions. Our work clarifies how matrix material properties and cellular traction forces enable collective organoid rotation. Reciprocally, the rotating organoid can serve as an active rheology probe, revealing key information about the matrix properties.

15 min. break

BP 22.5 Thu 11:00 H15

Exploiting Onsager regression in passive measurements to reveal active mechanics of living systems — Till Münker, Gabriel Knotz, Matthias Krüger, and •Timo Betz — Faculty of Physics, Georg-August-University Göttingen

Understanding life is arguably among the most complex scientific problems faced in modern research. From a physics perspective, living systems are complex dynamic entities that operate far from thermodynamic equilibrium. This active, non-equilibrium behaviour, with its constant hunger for energy, allows life to overcome the dispersing forces of entropy, and hence drives cellular organisation and dynamics at the micrometer scale. Unfortunately, most analysis methods provided by the powerful toolbox of statistical mechanics cannot be used in such non-equilibrium situations, forcing researchers to use sophisticated and often invasive approaches to study the mechanistic processes inside living organisms. Inspired by Onsager's regression hypothesis, we introduce here a Mean Back Relaxation (MBR) observable, which detects active motion in purely passive measurements of particle fluctuations. The MBR, which is based on three point probabilities, is theoretically and experimentally shown to exhibit markers of non-equilibrium, i.e., of detailed balance breaking dynamics. We furthermore observe an astonishing relation between the MBR and the effective non-equilibrium energy in living cellular systems. This is used to successfully predict the viscoelastic response function and the complex shear modulus from a purely passive approach, hence opening the door for rapid and simple passive mechanics measurements even in active systems.

BP 22.6 Thu 11:15 H15

Redirecting early embryogenesis of the model organism *Caenorhabditis elegans* via altered mechanical cues — •Vincent Borne and Matthias Weiss — Experimental Physics I, University of Bayreuth, Universitätsstr. 30, D-95447 Bayreuth, Germany

During early development, somatic and germline precursor cells of the model organism *Caenorhabditis elegans* undergo an apparently predetermined and robust division scheme, suggesting early embryogenesis to run on autopilot. While the role of biochemical signaling in this process has long been recognized, the influence of mechanical forces for proper cell arrangement until gastrulation has only recently been revealed. Aiming to further explore, how mechanical cues contribute

to proper embryogenesis, we have challenged the natural development at early stages via laser microsurgery and physical compression. As a result, we were able to significantly perturb the embryonic division scheme with both approaches, leading to catastrophic failures of cell divisions. While defects introduced by laser ablation remained mostly restricted to cells that had been challenged, compression frequently resulted in a global perturbation: Cytokinesis was compromised, leading to multinucleated cells or even a syncytium state in which nuclei kept on dividing up to stages of 60 nuclei or more with similar timing characteristics as observed in unperturbed embryos. Our data therefore underline the crucial role of properly adjusted mechanical cues during the early embryogenesis of *C. elegans*.

BP 22.7 Thu 11:30 H15

Active cell mechanisms reveal rich tissue-wide structures and dynamics in simulations — •Maxime Hubert[1], Lovro Nuić[2], Kevin Höllring[1], and Ana-Sunčana Smith[1,2] — [1]PULS group, FAU Erlangen-Nürnberg, Erlangen, Germany — [2]Group for Computational Life Sciences, Ruđer Bošković Institute, Zagreb, Croatia

Dissipative Particle Dynamics simulations provide a robust numerical platform of investigation to understand the dynamics of epithelial tissues. The technique allows to implement various properties at the cell level that can be related to tissue-wide structures and dynamics on various time scales, from hours to days in experiments. In this talk, we present our recent progresses in the field of epithelium numerical simulations by implementing different active ingredients that relate to the immediate neighbourhood of the cell within a tissue monolayer. We show, through comparisons with experiments performed with MDCK-II cells, that we are able to capture the formation of macroscopic compartments of the tissue, the complex relation between average cell velocity and cell density, and the rate of expansion of the tissue. These results highlight the importance of "nuclei"-based approaches along with "membrane"-based approaches in order to provide a complete numerical and mechanical perspective of epithelial tissues across various time- and length-scales.

BP 22.8 Thu 11:45 H15

'Forcing' changes in health and disease: New access into bioengineered skeletal muscle mechanics — •Arne Hofmeier[1,2], Till Muenker[2], Fabian Herkenrath[1], and Timo Betz[1,2] — [1]University of Muenster, Muenster, Germany — [2]University of Goettingen, Goettingen, Germany

Mechanical properties of skeletal muscles are tightly related to proper functionality, which makes experimental access to the biomechanics of skeletal muscle tissue a key requirement to advance our understanding of muscle function, development and disease. Recently devised in vitro culture chambers allow for raising 3D skeletal muscle tissues under controlled conditions and to measure global tissue force generation. However, these PDMS-based systems are inherently incompatible with high resolution microscopy. Here, we present a new chamber design that allows real-time high resolution 3D microscopy and simultaneous non-invasive quantification of global contractile forces and local tension during muscle formation for the first time. With this in hand, we observed an early mechanical homeostasis within mouse myoblast derived skeletal muscle tissues after one week of development, despite progressing myotube maturation. Additionally, we raised human in vitro skeletal muscles derived from patients suffering from Duchenne muscular dystrophy caused by loss of a functional membrane linker protein, called dystrophin. Interestingly, bioengineered Duchenne skeletal muscles displayed a disturbed mechanical homeostasis that correlates with functional impairment, suggesting a novel function of dystrophin being a molecular tension sensor and regulator.

BP 22.9 Thu 12:00 H15

On multistability and constitutive relations of cell motion on Fibronectin lanes — Behnam Amiri[1], •Johannes Clemens Julius Heyn[2], Joachim Oskar Rädler[2], and Martin Falcke[1,3] — [1]Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Robert Rössle Str. 10, 13125 Berlin, Germany — [2]Ludwig-Maximilians-Universität München (LMU), Fakultät für Physik, Geschwister-Scholl-Platz 1, 80539 München, Germany — [3]Dept. of Physics, Humboldt University, Newtonstr. 15, 12489 Berlin, Germany

Migration of eukaryotic cells is a fundamental process for embryonic development, wound healing, immune responses, and tumour metastasis. Many cell types exhibit coexisting steady and oscillatory morphodynamics on flat substrates. There is, however, little quantitative understanding of how adhesion controls these dynamic states.

We study the motion of MDA-MB-231 cells on microlanes of a broad range of Fibronectin densities to address this topic and derive a biophysical model.

The experiments exhibit cells with steady or oscillatory morphodynamics and either spread or moving with spontaneous transitions between the dynamic states. Our biophysical model is based on the force balance at the protrusion edge, the noisy clutch of retrograde flow and a response function of friction and membrane drag to integrin signaling. The theory reproduces the experimentally observed cell states, characteristics of oscillations and state probabilities.