BP 13: Multicellular Systems I

Time: Tuesday 9:00–11:00 Location: BPb

BP 13.1 Tue 9:00 BPb

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 13.2 Tue 9:20 BPb

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.

Invited Talk BP 13.3 Tue 9:40 BPb

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 are not only interacting with their substrate but also with their neighbors. The way forces from adhesion complexes are transmitted leads to various collective behaviors and plays a role in the active nature of cellular monolayers. 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. 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 the 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 13.4 Tue 10:10 BPb

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].

30 min. Meet the Speaker