

BP 59: Multi-Cellular-Systems

Time: Friday 9:30–11:00

Location: HÜL 386

Invited Talk

BP 59.1 Fri 9:30 HÜL 386
Spatially-resolved transcriptomics and single-cell lineage tracing — ●JAN PHILIPP JUNKER — Berlin Institute for Medical Systems Biology, MDC Berlin, Germany

Tissues and organs are complex mixtures of many different cell types, each of which is defined by a characteristic set of expressed genes. Systematic analysis of tissue architecture hence requires approaches that analyze gene expression on the single cell level. Recent progress in single-cell RNA sequencing now enables gene expression analysis of single cells on the level of the whole transcriptome, an important advance over microscopy-based methods that are typically limited to studying just one or a few genes at a time. However, information about the spatial position and lineage history of cells, which can be obtained by microscopy, is lost in sequencing experiments. Here, we present tomo-seq, a method that combines traditional histological techniques with low-input RNA sequencing and mathematical image reconstruction to generate a high-resolution genome-wide 3D atlas of gene expression in the zebrafish embryo at three developmental stages. Importantly, our technique allows searching for genes that are expressed in specific spatial patterns without manual image annotation. Furthermore, we introduce scartrace, a strategy for massively parallel clonal analysis in the zebrafish based on CRISPR/Cas9 technology. We exploit the fact that Cas9-induced generation of double-strand breaks leads to formation of short insertions or deletions (genetic scars), which are variable in their length and position. We demonstrate that these genetic scars are ideal cellular barcodes for lineage analysis.

BP 59.2 Fri 10:00 HÜL 386
How cell division timing leads to robust development in *Caenorhabditis elegans* — ●ROLF FICKENTSCHER, PHILIPP STRUNTZ, and MATTHIAS WEISS — Experimental Physics 1, University of Bayreuth, Universitätsstr. 30, 95444 Bayreuth

Embryogenesis of the small nematode *Caenorhabditis elegans* is a remarkably robust and reproducible, but still poorly understood self-organization phenomenon. Here, we show that the coupling of cellular volumes and cell cycle times in combination with a mechanically guided arrangement process is key for a fail-safe embryogenesis of *C. elegans*.

In particular, we have monitored cell trajectories and cellular volumes in *C. elegans* embryos over several hours at different ambient temperatures by means of a custom-made lightsheet microscope. Embryonic cell trajectories are accurately described by a simple mechanical framework, i.e. cells migrate to and adopt positions of least mechanical constraints within the confining eggshell [1]. Our experimental data also revealed an anticorrelation of cell volumes and cell cycle durations, with significant differences between somatic and germline cells. This observation can be rationalized via a simple model that invokes a limiting molecular component supporting cell division, e.g. nuclear pore complexes. Integrating this aspect into the aforementioned mechanical framework, we observed that the different scaling of the germline precursor lineage is crucial for a robust cellular arrangement process during early embryogenesis [2].

- [1] R. Fickentscher, P. Struntz & M. Weiss, *Biophys. J.* **105** (2013)
 [2] R. Fickentscher, P. Struntz & M. Weiss, *PRL* **117** (2016)

BP 59.3 Fri 10:15 HÜL 386
Dynamic pattern scaling as a critical point of self-organized growth control — ●STEFFEN WERNER^{1,2}, DANIEL AGUILAR-HIDALGO¹, ORTRUD WARTLICK³, MARCOS GONZÁLEZ-GAITÁN⁴, FRANK JÜLICHER¹, and BENJAMIN M. FRIEDRICH² — ¹MPI for the Physics of Complex Systems, Dresden, Germany — ²cfaed, TU Dresden, Dresden, Germany — ³MRC Laboratory for Molecular Cell Biology, University College London, UK — ⁴Department of Biochemistry, University of Geneva, Geneva, Switzerland

We present a theoretical framework of self-organized growth control, inspired by the mutual interplay of pattern formation and growth in developing organisms. There, signaling molecules instruct tissue growth,

while in turn growth changes the spatial concentration profiles of the molecules, e.g. by convection and dilution. By studying this feedback loop between chemical pattern formation and growth dynamics, we identify a critical point that corresponds to perfect proportionate pattern scaling and homogeneously growing domains.

We apply our theory to two biological model systems, the wing and the eye of the fruit fly *Drosophila melanogaster*. Despite their different developmental dynamics, our theoretical framework can quantitatively explain patterning and growth in both systems, including proportionate scaling of chemical patterns with tissue size. This observation suggests that the biological system is tuned close to criticality, in order to generate pattern scaling and homogeneous growth.

BP 59.4 Fri 10:30 HÜL 386
Active T1 transitions in the developing wing imaginal disc — ●MARKO POPOVIC¹, NATALIE DYE², GUILLAUME SALBREUX³, SUZANNE EATON², and FRANK JÜLICHER¹ — ¹Max Planck Institute for Physics of Complex Systems — ²Max Planck Institute of Molecular Cell Biology and Genetics — ³Francis Crick Institute

The adult wing of the fruit fly develops from a precursor tissue called imaginal disk. We study the wing pouch region of the wing imaginal disk, a single layer epithelium from which the adult wing blade forms. Observing the two-dimensional network of cells in the wing pouch projected on a plane reveals a radially symmetric pattern of elongated cell shapes. Peripheral cells have larger apical area and are more elongated tangentially than central ones. How does this cell shape pattern emerge and how is it related to mechanical forces in the tissue?

We study this process in third instar larval wing disks growing in culture over 13 hours. We track individual cells in time and space and identify different cellular processes: divisions, extrusions and neighbor exchanges. We calculate contributions of these cellular processes to the tissue shape changes. We use a hydrodynamic theory to relate tissue stresses to tissue deformations and cell shape changes [Etournay et al. eLife e07090; Etournay et al. eLife e14334; Merkel et al., arXiv:1607.00357; Popovic et al., arXiv:1607.03304].

We find that the tangential elongation of cell shapes increases over time in the cultured discs. We further find that active radially oriented T1 transitions contribute to tissue shape change. We solve the hydrodynamic equations for a radially symmetric tissue to investigate how active T1 transitions can influence mechanical stresses in the tissue.

BP 59.5 Fri 10:45 HÜL 386
How demixing and crowding behavior influence the invasive potential of composite tumor-like systems — ●PAUL HEINE, JÜRGEN LIPPOLDT, STEFFEN GROSSER, and LINDA OSWALD — Soft Matter Physics, University of Leipzig, Germany

The progression of cancer invasion is regulated through microenvironmental properties and their transformation for example in compartment penetration but critically also by the tumor composition itself. The heterogeneity of this system gives rise to an interesting phenomenon termed the jamming transition, a switch from a fluid-like unjammed cell layer to an almost solid-like state.

While not entirely understood, recent studies have revealed that single-cell properties like contractility, cortical tension, adhesion and motility influence this transition and have an profound impact on the cell layer behavior in a crowded environment. During the epithelial-mesenchymal transition a plethora of mechanical and biochemical changes lead to a drastic shift in cell polarity, shape, cell-cell adhesion, migratory and invasive properties.

Our investigation of mixed systems of metastatic and benign cells exposed a demixing process of the two cell types and vastly different crowding performance. While epithelial cells form a dense sheet of caged cells, the mesenchymal-like cells compose seemingly uncaged pools within the layer. This makes this a particularly fascinating system to study due to its bifurcational nature, which could allow for a transition between fluid and solid cell layer and vice versa.