BP 18: Tissue Mechanics

Time: Wednesday 9:30–13:00 Location: H44

Invited Talk BP 18.1 Wed 9:30 H44

Mechanical Imprints of Cell Competition — •Benoit Ladoux — Institut Jacques Monod, Université Paris Cité & CNRS

Epithelial tissues are dynamic communities of cells characterized by close intercellular communication and highly coordinated motion. The mechanical properties of these tissues are crucial for understanding key biological processes, such as homeostasis, morphogenesis, and metastasis, and are tightly regulated through cell-cell interactions. In this presentation, I will explore the role of mechanical forces in cell competition - a process where the expansion of one cell population drives the elimination of another. I will demonstrate how intercellular force transmission governs this competitive interaction, shedding light on the interplay between mechanics and cellular mechanisms.

BP 18.2 Wed 10:00 H44

Regulation of Homeostatic Tissue Composition and Self-Organization via Pressure-mediated Cell Cycle Control in Stem Cell-Derived Epithelial Tissues — •Johannes Krämer[1], Edouard Hannezo[2], Gerhard Gompper[1], and Jens Elgeti[1] — [1]Forschungszentrum Jülich, Institute for Advanced Simulations — [2]Institute of Science and Technology Austria

Tissue homeostasis relies on a precise balance between cellular proliferation and differentiation, with spatial cell distribution playing a critical role in effective replenishment. The mechanisms governing self-renewing cell types, including their proliferation rates, mechanical interactions, and spatial organization, remain incompletely understood. Here, we present a study of epithelial tissue dynamics using a descendant lineage model derived from slow-cycling, self-renewing stem cells. Through mean-field analysis, we establish conditions for cell cycle parameters that maintain a well-defined tissue configuration and demonstrate the influence of mechanical regulation on division control. To further explore spatio-temporal properties, we implement the lineage model in an agent-based computational framework, incorporating cell-cell mechanical interactions. Our findings reveal a regime in which stem cells exhibit long-range order, forming small, localized niche-like clusters with slow diffusion. These insights offer a novel perspective on the interplay between proliferation, differentiation, and the role of mechanical interactions on the spatial organization of cells, advancing our understanding of tissue homeostasis.

BP 18.3 Wed 10:15 H44

Spatiotemporal Analysis of Active Deformation of Patient-derived Colon Cnacer — •Shogo Nagai[1], Ryo Suzuki[2], Go Yamakawa[3], Akihisa Fukuda[3], Hiroshi Seno[3], and Motomu Tanaka[1,4] — [1]Physical Chemistry of Biosystems, Heidelberg University, Heidelberg, Germany — [2]Department of Biosciences and Informatics, Keio University, Tokyo, Japan — [3]Department of Gastroenterology and Hepatology, Kyoto University Graduate School of Medicine, Kyoto, Japan — [4]Center for Integrative Medicine and Physics, Kyoto University, Kyoto, Japan

Biomedical cancer research has relied on the investigation of fixed cells and tissues, in which the non-equilibrium dynamics of cancer have been largely overlooked. Extending the recent studies shedding light on the dynamics of the isolated cells, spatiotemporal analysis of cancer on a multicellular level is expected to reveal the dynamic mechanisms of cancer progression.

In this study, the time evolution of active deformation of growing colorectal cancer organoids (miniaturized organ model) was quantitatively evaluated by the Fourier expansion. Thereby, the larger deformation of malignant genetic mutated organoids was extracted, which was attributed to the slow effective viscoelastic relaxation. The simulation of the double-cell stage indicated the characteristic dynamics of organoids could be related to cell-cell junctions. In addition, biomedical evaluations showed lower cell-cell junctions of malignant colorectal cancer on a protein and RNA level.

BP 18.4 Wed 10:30 H44

a novel 3D platform for investigating cancer cell migration and tissue organization under mechanical load — •Mattias Luber, Bruno Schmelz, Mahboubeh Farajian, and Timo Betz — Third Institute of Physics - University of Göttingen - Germany

Recent advances in tissue engineering and mechanobiology have highlighted the critical role of mechanical forces in guiding cellular organization and extracellular matrix (ECM) remodeling. Building on these findings, we introduce a novel platform for engineering connective tissues that facilitates high-resolution live imaging of self-organization and ECM remodeling under diverse experimental conditions. This platform employs controlled mechanical loading to induce fibroblast alignment, resulting in the formation of highly organized tissue structures. By enabling both global and localized measurements of tissue tension and providing precise control over mechanical load, it allows for the detailed investigation of ECM remodeling, cellular dynamics, and nuclear deformation. A key application of this platform is in uncovering how mechanical properties of the tissue environment influence cancer cell behavior. By integrating models of MDA-MB-231 breast cancer cells, we demonstrated how variations in tissue tension and ECM structure directly modulate cancer cell migration patterns. These findings highlight the critical interplay between mechanical forces and cellular invasiveness, providing insights into the biomechanical drivers of cancer progression.

BP 18.5 Wed 10:45 H44

Bridging the gap between single cell and tissue mechanics — •Mathilde G. Lettinga[1], Antje Garside[1], Vaibhav Mahajan[1], Franziska Baenke[2], Valeria Lozovanu[2], Daniel Stange[2], Ingolf Sack[3], and Anna V. Taubenberger[1] — [1]Center for Molecular and Cellular Bioengineering (CMCB), BIOTEC, Dresden University of Technology, Germany — [2]Department of Visceral, Thoracic and Vascular Surgery, University Hospital Dresden, Germany — [3]Department of Radiology, Charité - Universitätsmedizin Berlin, Germany

Tumours exhibit altered biophysical properties across spatial scales. Compared to healthy tissue, solid tumours are typically stiffer, while individual cancer cells are more compliant. The increased tissue stiffness can partly be attributed to the extracellular matrix. However, the contributions of single cell mechanics and collective cell behaviour to the emergent tissue properties remain unclear.

To bridge this gap between single cell and tissue mechanics, we have established a 3D in vitro tumour model, based on patient-derived colorectal liver metastasis organoids grown in hydrogels mimicking the extracellular matrix. Cells retrieved from dissociated organoids were mechanically characterised with real-time deformability cytometry and AFM. These data were benchmarked to the morphometric and mechanical properties of intact organoids, which were assessed in situ by confocal and Brillouin microscopy. The bulk mechanical properties of our model system were investigated using tabletop magnetic resonance elastography. Our data contribute to a better understanding of the mechanical coupling between single cells and tissues.

BP 18.6 Wed 11:00 H44

Exploring glassy dynamics in retina organoids through time-series imaging — •Alexander Johann Zangl[1], Achim Theo Brinkop[1,2], Elijah R. Shelton[1], Marie Lackmann[1,2], Teresa Rogler[1,2], and Friedhelm Serwane[1,2,3] — [1]Faculty of Physics & Center for NanoScience, LMU Munich, Germany — [2]Institute of Biophysics, Ulm University, Ulm, Germany — [3]Munich Cluster for Systems Neurology (SyNergy) & Graduate School of Systemic Neuroscience (GSN), Munich, Germany

Quantifying cell dynamics and the mechanical forces guiding such movements can provide crucial insights for understanding tissue development and disease progression. Stem cell derived neuronal organoids provide an accessible system for studying nervous tissue development in the laboratory. Recently, magnetic droplet based mechanical measurements in retina organoids revealed a weak power-law scaling in the mechanical properties, suggesting that the retinal tissue is a glassy material. While the mechanical observations are consistent with predictions of soft glassy rheology, whether the movements of the individual cells making up those tissues are also in agreement with a glassy material is still unknown. Using confocal fluorescent time-series imaging, we observe the movements of nuclei in the forming retina. By tracking cells, we can determine whether cellular movements also point to the retina as a solid-like material just above a glass transition. We characterize the cell dynamics of the tissue by analysing the scaling of the mean-square displacements of the nuclei. This will help us understand how mechanical cues guide retina formation.

15 min. break

BP 18.7 Wed 11:30 H44

Statistical Inference and Selection of a Mechanistic Model during Tissue Specification in Beetle Embryogenesis — •Zoë Lange[1,2], Franziska Krämer[3], Frederic Strobl[3], Ernst H.K. Stelzer[3], and Franziska Matthäus[1,4] — [1]Frankfurt Institute for Advanced Studies — [2]Fachbereich Physik, Universität Frankfurt am Main — [3]Buchmann Institute for Molecular Life Sciences — [4]Fachbereich Informatik und Mathematik, Universität Frankfurt am Main

During development of the beetle Tribolium castaneum, the blastoderm differentiates into embryo and extra-embryonic serosa tissues with distinct morphologies. Using statistical inference, we estimate effective cell tensions and pressures based on cell geometry and a force-balance assumption. Our analysis reveals an inverse relationship between tension and cell shape with characteristic slopes for serosa and embryo tissues. We identify and parametrize a mechanistic vertex model that captures the differing properties of serosa and embryo cells. This study demonstrates how statistical inference can guide the selection and refinement of mechanistic models to understand tissue dynamics during embryogenesis.

BP 18.8 Wed 11:45 H44

Dynamics and mechanics of germband extension in *Drosophila* — •Maryam Setoudeh[1,2,3], Giulia Serafini[3], Pavel Tomancak[3,4], and Pierre A. Haas[1,2,3] — [1]Max Planck Institute for the Physics of Complex Systems — [2]Center for Systems Biology Dresden — [3]Max Planck Institute of Molecular Cell Biology and Genetics — [4]Cluster of Excellence Physics of Life, TU Dresden

During *Drosophila* development, cell intercalations and cell divisions drive the extension of the germband on the dorsal side of the embryo towards its anterior. We and others [1] have recently observed that the shape of the germband is often curved, even in the wild-type, contrary to the textbook picture of a straight germband. Here, we develop a mechanical model in which the germband midline appears as an elastic line pushed by an effective force resulting from germband extension. Its motion is resisted by frictional forces from surrounding tissues and attachment at the tip mediated by the integrin scab. In this model, we discover an instability of the straight shape that explains the observed variability in the wild-type as well as the twisting phenotype observed in embryos in which scab is depleted. We also find that an alternative model of a growing rather than pushed elastic line cannot explain the observed instability. This highlights the mechanical role of these pushing forces in germband extension.

[1] Smits *et al.*, Curr. Biol. **33**, 3536 (2023)

BP 18.9 Wed 12:00 H44

A mechanical model of the symmetry breaking of the shape of the primordial hindgut — Daniel S. Alber[1,2], Shiheng Zhao[3,4,5], Eric F. Wieschaus[2,6], Stanislav Y. Shvartsman[2,6,7], and •Pierre A. Haas[3,4,5] — [1]Department of Chemical and Biological Engineering, Princeton University — [2]Lewis-Sigler Institute for Integrative Genomics, Princeton University — [3]Max Planck Institute for the Physics of Complex Systems — [4]Max Planck Institute of Molecular Cell Biology and Genetics — [5]Center for Systems Biology Dresden — [6]Department of Molecular Biology, Princeton University — [7]Center for Computational Biology, Flatiron Institute

During early *Drosophila* morphogenesis, as the germband extends and the midgut invaginates, the initially circular primordial hindgut moves from the posterior pole of the embryo to its dorsal side and folds into a characteristic keyhole shape. Here, we develop a minimal model of this symmetry breaking in which the hindgut appears as an inextensible elastic ring in the plane. We discover that, as the area enclosed by the ring decreases (midgut invagination) while a diameter is held fixed (germband extension), the circular shape bifurcates robustly into the observed keyhole shape. Moreover, we show how embryonic curvature breaks symmetry further to select the observed orientation of the keyhole shape. This demonstrates that morphogenesis of the primordial hindgut can be a passive mechanical consequence of active deformations of the tissues that surround it.

BP 18.10 Wed 12:15 H44

What mouse embryos can teach us about tissue spreading — •María-José Franco-Oñate[1], Ricard Alert[1], and Kate Cavanaugh[2] — [1]MPI for the Physics of Complex Systems, Dresden, Germany — [2]University of San Francisco in California, United States

Processes such as embryogenesis, tissue repair and cancer metastasis are dependent upon the migration of large groups of cells through changes in group morphogenesis or collective migration. These processes entail both molecular and mechanical interactions between cells and their surrounding environment. Several attempts have been made to create models of these interactions [1].

In this study, we focus our attention on mouse embryos during implantation. In this process, the embryo adheres to the substrate and extends along it. The results of ongoing experiments indicate that embryos derived from older mice are unable to implant, resulting in a lack of spreading of the tissue that adheres to the substrate. The objective of this study is to gain insight into the mechanisms underlying the spreading process and its dependence on the age of the embryo. To this end, we employ a coarse-grained approach, in which the tissue is conceptualised as an active polar fluid, to investigate the dynamics of a spreading tissue [2]. To validate our theoretical model, we utilise traction force microscopy, which enables us to quantify the forces exerted by the tissue.

[1] R. Alert and X. Trepat. Ann. Rev. 11: 77-LF1 (2020)
[2] C. Pérez-González, R. Alert, et al. Nat. Phys. 15: 79-88 (2019)

BP 18.11 Wed 12:30 H44

Growth control in development and regeneration in the zebrafish pectoral fin — •Maximilian Kotz[1,2], Lucas de Oliveira Petrocchi Ribas[1,3], Shivani G. Ramkumar[1,3], Rita Mateus[1,3], and Benjamin M. Friedrich[1,2] — [1]PoL, Dresden, Germany — [2]cfaed, Dresden, Germany — [3]MPI-CBG, Dresden, Germany

Although all multicellular organisms can develop from a single cell, only few organism can regenerate lost body parts in adulthood. If it as an open question whether the mechanisms controlling growth in regeneration are the same as those in development. We combine theory and experiment to address this question using the pectoral fin of zebrafish as a model system. As a novel paradigm, we compare unperturbed development and regeneration after partial amputation during development. To quantify growth, we developed machine learning-based image analysis pipelines and introduce a curvilinear coordinate system to describe the geometry of the tissue. Tissue samples from different individuals became comparable by defining diffeomorphisms that minimize an elastic pseudo-energy, which enables a rigorous statistical comparison of proliferation rates, shape changes and even morphogen gradients. This quantification revealed that volume growth is driven by distinct processes. In particular, growth along the different body axes is markedly different, with thickness growth apparently uncoupled from in-plane growth. To identify the underlying mechanisms of growth control, we probe predictions from different mathematical models by investigating different amputation scenarios, along with genetic or pharmacological perturbations.

BP 18.12 Wed 12:45 H44

Model of growth arrests and proportional growth inspired by axolotl limb regeneration — •Natalia Lyubaykina[1,2], Dunja Knapp[3], Pietro Tardivo[4], Tatiana Sandoval-Guzmán[3], Elly Tanaka[4], and Benjamin M Friedrich[1,2] — [1]Cluster of Excellence 'Physics of Life', Technical University Dresden, Dresden, Germany — [2]Center for Advancing Electronics, Technical University Dresden, Dresden, Germany — [3]CRTD/Center for Regenerative Therapies TU Dresden, Germany — [4]Research Institute of Molecular Pathology, Vienna Biocenter (VBC), Campus Vienna Biocenter, Vienna, Austria

Axolotl can regenerate lost limbs even as adults, posing the question of how the size of a regenerating limb is matched to a variable animal size. Two interacting morphogens, SHH and FGF8, regulate limb development and regeneration. Inspired by this biological example, we theoretically investigate general mechanisms of morphogen-controlled growth arrest and proportional growth. In the proposed model, tissue growth increases the spatial distance between both morphogen gradients, thus providing negative feedback that eventually arrests growth. We propose two distinct scaling scenarios of morphogen gradients: either dynamic scaling with regenerating blastema size, or static scaling with animal size. We show that only the latter ensures robust growth arrest and proportional growth. We compare theory predictions to experimental quantification of SHH and FGF8 dynamics at different time points of regeneration in different-sized animals, suggestive of scaling with animal size.