BP 3: Tissue Mechanics I

Time: Monday 9:30–12:45 Location: BAR/0205

Invited Talk BP 3.1 Mon 9:30 BAR/0205

The unreasonable effectiveness of computational models in biological patterning and morphogenesis — •Michel Milinkovitch — Dept. of Genetics & Evolution, University of Geneva, Geneva, Switzerland

I will discuss how vertebrate skin colours and skin appendages (scales, feathers, hairs) are spatially patterned through Turing and mechanical instabilities. First, I will show that Reaction-diffusion (RD) models are particularly effective for understanding skin colour patterning at the macroscopic scale, without the need to parametrise the profusion of variables at the microscopic scales. I suggest that the efficiency of RD is due to its intrinsic ability to exploit continuous colour states and the relations among growth, skin-scale geometries, and the (Turing) pattern intrinsic length scale. Second, I will show how drug treatments can permanently trigger transitions between scale appendage types or even between chemical and mechanical self-organisation. Third, I will show that a three-dimensional mechanical model, integrating growth and material properties of embryonic skin layers, captures most of the dynamics and steady-state pattern of head scales in crocodiles and tortoises. Fourth, I will show that the spectacular morphogenesis of the strongly overlapping snake scales can be recapitulated with a mechanical model integrating tissue plasticity and active material properties. These studies indicate that Biology, despite its 'messy' nature (with its unmanageable profusion of cellular and molecular variables) can be efficiently and quantitatively investigated mathematically, including with simple phenomenological models.

BP 3.2 Mon 10:00 BAR/0205

Mechano-chemical stabilisation of topological defects in an elasto-nematic sheet — •Suganthan Senthilkumar[1], Kinneret Keren[2], and Marko Popović[1,3] — [1]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [2]Technion-Israel Institute of Technology, Haifa, Israel — [3]Ruder Bošković Institute, Zagreb, Croatia

Self-organisation of patterns during animal development involves a complex interplay of various biophysical and biochemical mechanisms. A striking example is *Hydra*, where ordered arrays of nematic actin fibers give rise to orientational order on animal-scale with +1 topological defects at the head and foot of an adult animal. To study the nematic patterns observed during *Hydra* regeneration we recently proposed a mechano-chemical feedback loop that involves orientational order, tissue strain and morphogen gradients[1]. Here we develop a continuum formulation of the same feedback loop in 2d and show that it can stabilise aster shaped +1 topological defects in a self organised manner. We obtain a phase diagram for +1 defect stability using analytical calculations and compare it with vertex model simulations that employ the feedback loop. Finally, we calculate the correction to the mobility coefficient of the +1 defect due to the morphogen field associated with it.

References:

1. Maroudas-Sacks *et al* Development, (February 2025) 152; doi: https://doi.org/10.1242/dev.204514

BP 3.3 Mon 10:15 BAR/0205

What jellyfish teach us about tissue mechanics and shape programming — •Anne Materne[1,2], Zhiqi Shen[1,2,3], Daniel Font-Martín[4], Vladislav Koren[5], Ulyana Shimanovich[5], Chiara Sinigaglia[4], and Carl D. Modes[1,2] — [1]MPI of Molecular Cell Biology and Genetics, Dresden, Germany — [2]Center for Systems Biology Dresden, Germany — [3]Southern University of Science and Technilogy, Shenzhen, China — [4]CNRS Languedoc-Roussillon, France — [5]Weizmann Institute of Science, Israel

Jellyfish are little-studied marine organisms with astounding regenerative capacities. Their rapid wound closure has been implicated to rely, at least partially, on the mechanical properties of the individual tissues in the jellyfish umbrella. In particular, this includes the mesoglea, a thick extracellular matrix structure essential for jellyfish shape and body function. Here, we model the mesoglea's role in wound closure using a coarse-grained spring lattice approach. In this way, we can capture essential material processes without knowledge of all molecular- and cellular-scale underpinnings. Our work shows that simple mesoglea pre-strain is sufficient to initiate closure in a broad spectrum of wound shapes. This finding is in line with previous experimental work in the hydrozoan jellyfish *Clytia hemisphaerica* and confirms the essential role of tissue mechanics in the life history of marine invertebrates. It will be interesting to explore this role more systematically in the future. Furthermore, our results presented here also provide unexpected insights for the field of 3D shape-programmable materials.

BP 3.4 Mon 10:30 BAR/0205

Apical extracellular matrix regulates fold morphogenesis in the Drosophila wing disc — •Vincenzo Maria Schimmenti[1], Jana F. Fuhrmann[2], Natalie A. Dye[3,4], and Marko Popovic[1] — [1]Max Planck Institute for Physics of Complex Systems, Dresden, Germany — [2]Aix Marseille Univ, CNRS, IBDM, Marseille, France — [3]Mechanobiology Institute, National University of Singapore, Singapore — [4]Biomedical Engineering Department, National University of Singapore, Singapore

Tissue folding is a fundamental process in animal organ development. We investigate how fold shape and mechanics change during Drosophila wing disc morphogenesis, from larval stages (when folds deepen and grow) to early pupa, when the tissue unfolds into a bilayer. Using 3D apical surface segmentation, we introduce quantitative metrics for fold depth and width on a curved surface. We also identify a fibrous apical extracellular matrix (aECM) that physically links the two sides of each fold. A lateral vertex model with an adhesive aECM layer predicts that unfolding requires aECM removal. Genetic perturbations confirm that aECM adhesion stabilizes folds: its loss distorts fold shape and dynamics, while failure to remove it prevents unfolding. These perturbations produce adult wing defects, demonstrating that larval fold morphology influences adult wing shape. Together, our work highlights a central mechanical role for aECM in stabilizing epithelial folds during animal development.

BP 3.5 Mon 10:45 BAR/0205

Elastic coupling between nucleus and cell shape drives a mechanical transition in epithelial architecture — •Ian D. Estabrook[1], Anne Rosfelter[2], Yu-Chiun Wang[2], and Anna Erzberger[1] — [1]European Molecular Biology Laboratory (EMBL), Heidelberg, Germany — [2]RIKEN Center for Biosystems Dynamics Research, Kobe, Japan

As the largest organelle, the cell nucleus can affect the shape, spatial organisation and mechanics of cells in a variety of tissue contexts. Despite extensive studies on the molecular mechanisms underlying nuclear positioning and mechanics, it remains unclear whether the nucleus actively controls tissue architecture.

Here, we combine elasticity theory and the Drosophila blastoderm stage embryo as a generic experimental model to investigate the mechanical role of nuclei on epithelial organisation.

By developing a general method that integrates mechanical and geometrical properties extracted from imaging data, we show that from elastic coupling between nuclei and the cell surface, a mechanically driven phase transition emerges between simple columnar and pseudostratified tissue architectures. Genetic and optogenetic experimental perturbations provide evidence supporting such coupling and confirm the predicted transitions following changes in mechanical and geometric parameters.

Our work identifies a novel mechanical role of nuclear elasticity, independent of specialised machineries and may represent a general, generic mechanism controlling emergence of tissue level structures.

15 min. break

BP 3.6 Mon 11:15 BAR/0205

Mechanical regulation of neuroepithelial development — •Niklas Gampl[1,2], Alex Kingston[3], Caren Norden[4], and Kristian Franze[1,2,5] — [1]Max-Planck-Zentrum für Physik und Medizin, Erlangen, DE — [2]Medical Institute of Biophysics, FAU Erlangen-Nürnberg, DE — [3]Cambridge Stem Cell Institute, University of Cambridge, UK — [4]Gulbenkian Institute for Molecular Medicine, Oeiras, PT — [5]Department of PDN, University of Cambridge, UK

During embryonic development, initially flat neuroepithelial tissues remodel themselves into complex 3D structures such as the brain or

retina. This process is driven by intrinsically generated forces that depend on the cells' mechanical environment. However, how accumulated tension in the tissue feeds back on individual cells to influence their fate or migration patterns is not well understood. To address this, we downregulated the cellular force sensor Piezo1 in zebrafish and *Xenopus laevis* embryos, thereby reducing local mechanosensing capabilities. Piezo1 downregulation led to impaired retinal lamination, deformed retinae and nuclear rounding. Additionally, live imaging of Piezo1-deficient zebrafish eye primordia revealed defects in retinal progenitor migration during optic cup morphogenesis. These finding suggest that Piezo1 activity contributes to coordinating force generation and tissue level tension in the developing neuroepithelium, thus leading to nuclear and tissue shape changes. Combining laser ablation to locally perturb force propagation with direct measurement of tissue tension will clarify how Piezo1-dependent mechanical feedback links nuclear shape, cell fate decisions and tissue morphogenesis.

BP 3.7 Mon 11:30 BAR/0205

Emergence of hyperuniform tiling in the developing retina — •Mehmet Can Ucar[1] and Sandra Siegert[2] — [1]University of Sheffield, Sheffield, UK — [2]Institute of Science and Technology Austria, Klosterneuburg, Austria

Efficient tiling and space-filling are fundamental design principles of living systems: from neurons and immune cells to vascular networks, these structures must optimize spatial coverage for proper function. Yet how cells collectively achieve non-redundant coverage during growth remains largely unexplored. Here, we combine a theoretical model of growing, branched cells with tunable local interactions and experimental analysis of developing retinal microglia. Our model shows that simple neighbor repulsion during growth is sufficient to drive non-redundant tiling, yielding a substantial increase in coverage with minimal territory overlap. Strikingly, this mechanism also leads to the emergence of a hyperuniform organization, where density fluctuations are progressively suppressed. Consistent with these predictions, microglia in the developing retina exhibit both efficient tiling and suppressed fluctuations, supporting the proposed mechanism for retinal patterning. Together, these findings reveal how local interactions can generate both efficient tiling and hyperuniform order, suggesting a general principle for tissue-wide optimization.

BP 3.8 Mon 11:45 BAR/0205

Reshaping morphogen gradients through porous tissue architecture — •Diana Khoromskaia[1,2], Mohit Dalwadi[4], and Zena Hadjivasiliou[2,3] — [1]Universität Münster, Germany — [2]Francis Crick Institute, London, UK — [3]University College London, UK — [4]University of Oxford, UK

The morphogenesis of tissues during embryonic development is controlled by concentration gradients of morphogens – signalling molecules whose readout determines cell fate decisions. How the spread of morphogens is affected in tissues with complex geometry and spatially heterogeneous architecture is not well understood. To address this question, we introduce a porous vertex model, by explicitly considering the network of extracellular spaces between the cells. Morphogens produced by source cells disperse through the tissue via three modes of transport: extracellular diffusion, membrane-bound diffusion, and cell-based transport through recycling. With this model we investigate how cell-scale geometry, such as cell size, cell shape anisotropy, and cell distance, influences effective diffusion and degradation of morphogens at tissue-scale, employing numerical and semi-analytical upscaling methods. A non-linear coupling between cell packing and morphogen concentration renders the morphogen gradient robust to perturbations by locally buffering fluctuations in the production. Our characterisation of tissues as active porous materials provides new insights into how morphogenesis and cell fate determination may interact during embryonic development.

BP 3.9 Mon 12:00 BAR/0205

Mechanics and hydraulics of the *C. elegans* germ line — •Chandraniva Guha Ray[1,2,3], Jonathan Jackson[2], Jonas Neipel[1,2,3], Julia Pfanzelter[2], Stephan W. Grill[2,3,4], and Pierre A. Haas[1,2,3] — [1]Max Planck Institute for the Physics of Complex Systems — [2]Max Planck Institute of Molecular Cell Biology and Genetics — [3]Center for Systems Biology Dresden — [4]Cluster of Excellence Physics of Life, TU Dresden

In the cylindrical germ line of the nematode *Caenorhabditis elegans*, germ cells surround a tube called the rachis, to which all germ cells are connected via openings in the cells called rachis bridges. These rachis bridges allow exchange of cytoplasm between the rachis and the germ cells, which mature as they move towards the proximal end of the germ line where a hydraulic instability decides germ cell fate [1]. However, cortical contractility would collapse static germ cells by releasing their cytoplasm into the rachis through the rachis bridges. Here, we explain how the hydraulic flows in the germ line prevent this collapse and thus stabilise the germ line mechanically: We present a coarse-grained vertex model of a steady-state germ line that couples these hydraulic effects to cell mechanics. We compare the model to experimental observations and thus show how the interplay of fluid pumping and cell contractility can build a dynamically stable germ line.

[1] N. T. Chartier *et al.*, Nat. Phys. **17**, 920 (2021)

BP 3.10 Mon 12:15 BAR/0205

Hydrodynamic theory of two-dimensional human gastruloid development — •Oliver M. Drozdowski[1], Chloé Roffay[2], Sarah Jay[2], Diana Pinheiro[2], and Edouard Hannezo[1] — [1]Institute of Science and Technology Austria, Klosterneuburg, Austria — [2]Research Institute of Molecular Pathology, Vienna, Austria

Gastrulation is a crucial stage of embryonic development, as it entails the formation of the three germ layers. Two-dimensional in-vitro systems derived from human embryonic stem cells, so-called gastruloid discs, recapitulate the underlying patterning mechanisms, resulting in the formation of concentric rings of extraembryonic amnion-like cells at the edge and the three germ layers. Starting from experimental data of flattening amnion-like cells at the gastruloid edge, we developed a cross-sectional bubbly vertex model to describe the observed columnar to squamous transition. In agreement with experimentally measured morphometrics and mechanical properties, cell flattening is shown to be driven by local active wetting. Since gastruloids display fluid-like tissue properties, we developed a hydrodynamic description of the tissue-scale dynamics derived from the vertex model. This model predicts a gastruloid morphology consistent with experimental observations, suggesting that local cellular mechanics contribute to human gastruloid shape dynamics.

BP 3.11 Mon 12:30 BAR/0205

A mechanical origin for implantation defects in embryos from aged females — Kate E. Cavanaugh[1,2], •Maria-Jose Franco-Oñate[3,4], Diana J. Laird[5], Patrick W. Oakes[6], Ricard Alert[3,4,7], and Orion D. Weiner[1,2] — [1]Cardiovascular Research Institute, University of California, San Francisco, USA — [2]Department of Biochemistry and Biophysics, University of California, San Francisco, USA — [3]Max Planck Institute for the Physics of Complex Systems, Dresden, Germany — [4]Center for Systems Biology Dresden, Germany — [5]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, USA — [6]Department of Cell and Molecular Physiology, Loyola University Chicago Stritch School of Medicine, IL USA — [7]Cluster of Excellence Physics of Life, TU Dresden, Germany

Women over 35 experience reduced fertility, linked to impaired embryo implantation. In mouse embryos from aged mothers, we observe defective spreading of the extra-embryonic tissue. To uncover the mechanism, we use a continuum model that treats the tissue as a droplet of active polar fluid. Fitting the model to experimental data shows that increased tissue surface tension and viscosity in aged embryos account for the impaired spreading. Experimental measurements of forces and spreading dynamics confirm that these mechanical changes are sufficient to explain the implantation defect. This work shows how physical modeling of embryo mechanics can quantitatively predict implantation success and guide embryo selection in Assisted Reproductive Technologies.