BP 11: Cell Mechanics I

Time: Tuesday 9:30–12:45 Location: H 2032

Invited Talk BP 11.1 Tue 9:30 H 2032

Mechanochemical regulation of epithelial barrier formation and function — •Carien Niessen — Department Cell Biology of the Skin and CECAD, University of Cologne

How cell shape and mechanics controls epithelial barrier morphogenesis and regeneration is still poorly understood. In the squamous stratifying epithelium of the skin, the epidermis, stereotypic changes in cell shape guide the differentiation and upward migration of cells to form a barrier that is robustly renewed in the face of multiple challenges including mechanical stress. Combining cell and mechanobiology, genetics and in collaboration with the Manning lab (Syracuse University) in silico modelling, my laboratory asks how cell shape, fate and position are coordinated to control the formation and renewal of spatially defined functional compartments within the epidermis. I will discuss how adhesive junctions and associated cytoskeletons control tissue mechanics and how dynamic changes in junctions and signalling locally alter cell mechanics to coordinate cell fate, shape and position in the epidermis that enable renewal while maintaining epithelial barrier function. I furthermore will touch how changes in these mechanochemical networks disturb tissue homeostasis and promote disease.

BP 11.2 Tue 10:00 H 2032

Passive viscoelastic response of striated muscles — •Fabio Staniscia[1] and Lev Truskinovsky[2] — [1]Department of Theoretical Physics, Jožef Stefan Institute, Ljubljana SI-1000, Slovenia — [2]PMMH, CNRS UMR 7636, ESPCI, PSL, 75005, Paris, France

Muscle cells with sarcomeric structure exhibit highly non trivial mechanical response. The difficulty of its continuum modeling is due to the presence of long-range interactions transmitted by extended protein skeleton. To build a rheological model for muscle passive behaviour, relevant at time-scales of the order of the millisecond after a perturbation, we use a stochastic micromodel, and derive a linear response theory for a half-sarcomere, which can be extended to the whole fibre. Instead of the first order rheological equation, anticipated by Hill on the phenomenological grounds, we obtain a novel second order equation which shows that tension depends not only on its current length and the velocity of stretching, but also on its acceleration. Expressing the model in terms of elementary rheological elements, we show that one contribution to the visco-elastic properties of the fibre originates in cross-bridges, while the other can be linked to inert elements which move in the the sarcoplasm. We apply this model to explain the striking qualitative difference between the relaxation in experiments involving perturbation of length vs. those involving perturbation of force, and we use the values of the microscopic parameters for frog muscles to show that the model is in excellent quantitative agreement with physiological experiments.

BP 11.3 Tue 10:15 H 2032

Mechanical complexity of living cells can be mapped onto simple homogeneous equivalents — •Sebastian Wohlrab, Sebastian Johannes Müller, and Stephan Gekle — Biofluid Simulation and Modeling, Universität Bayreuth, Deutschland

Despite the complex composition of a biological cell with its constituents varying in both size and stiffness, experimental data analysis and numerical simulations often assume a strongly simplified homogeneous cell model. Accordingly, a single elastic modulus is assigned to the entire cell. This ad-hoc simplification has so far mostly been used without proper justification.

With our research we methodically demonstrate that indeed a mechanically heterogeneous cell can effectively be replaced by a homogeneous equivalent cell with a volume averaged elastic modulus. Using computer simulations we investigate a hyperelastic cell with a heterogeneous interior under compression and in shear/channel flow mimicking atomic force and microfluidic measurements, respectively.

We find that the homogeneous equivalent cell reproduces quantitatively the behavior of its heterogeneous counterpart, and that this equality is largely independent of the stiffness or spatial distribution of the heterogeneity. Our results thus validate in hindsight the simplifying approaches taken in many previous experimental and computational works, but also provide a solid basis on which future experimental data can be analyzed and physically reliable computer simulations can be constructed.

BP 11.4 Tue 10:30 H 2032

Shaping the embyo: a mechanical analysis of embryonal symmetry breaking — •Alejandro Jurado Jiménez[1], Leon Lettermann[1], Bernhard Wallmeyer[2], Lea Krüger[3], and Timo Betz[1] — [1]Third Institute of Physics - Biophysics, Friedrich-Hund-Platz 1, University of Göttingen — [2]Institute of Cell Biology, ZMBE, Von-Esmarch-Str. 56, University of Münster — [3]Institut für Theoretische Physik, Wilhelm-Klemm-Straße 9, University of Münster

In this work we present a hydrodynamical analysis of early Zebrafish development which aims to understand the mechanical state of the tissue leading to its first symmetry breaking during epiboly: the shield formation. A full mechanical characterization of the blastoderm is achieved using a combination of Light-Sheet microscopy, state-of-the-art cell tracking of the cells nuclei and force measurements using polyacrylamide beads as in-vivo sensors. The analysis of our huge datasets required ad-hoc tools for embryo alignment, image segmentation, beads/nuclei detection and derivation of the forces from elastic deformations. All of them have proven to be very powerful when tacking similar experiments in living tissue, and we share them publicly in an online repository. Our experimental analysis is being supported and expanded by a NeuronalODE model, able to retrieve a full dynamical description of the blastoderm only using the velocity field of the embryo. Alltogether we expose a stress asymmetry prior and during the shield formation, form which we can learn more about the mechanical origin of embryonal symmetry breaking.

15 min. break

BP 11.5 Tue 11:00 H 2032

In-situ high-throughput analysis of mitochondrial membrane tension under pathophysiological conditions — •Eric Sündermann, Bob Fregin, Jan Maurice Wilder, Doreen Biedenweg, Stefanie Spiegler, and Oliver Otto — Institute of Physics, University of Greifswald, Greifswald, Germany

The development of high-throughput methods for cell mechanical research is becoming increasingly important in biology, medicine and physics as the analysis of large samples increases the statistical robustness to identify rare cell populations and to transfer results from basic science into clinical applications. While most studies focus on 2D/3D cellular systems, little is known about how chemical and physical stress propagates inside the cell and impacts the mechanical properties of organelles.

Here, we applied membrane tension cytometry (MTC), a technology recently developed in our lab, to study the intracellular response of mitochondrial mechanics to hydrodynamic and oxidative stress. As a model system, HL60 cells have been chosen that were incubated with hydrogen peroxide to generate mitochondrial superoxide as reactive oxygen species. After staining cells with Mito Flipper-TR we took advantage of the fact that its fluorescence lifetime is proportional to the membrane tension of mitochondria. Preliminary experiments using MTC show that hydrodynamic stress propagates linearly to mitochondria inside the cytosol and that oxidative stress leads to their softening - in agreement with earlier results studying isolated mitochondria using real-time deformability cytometry.

BP 11.6 Tue 11:15 H 2032

Cellular Contraction of Fibroblast-Populated Collagen Gels Reveals Potential Cooperative Cell Behaviors — •Lydia Rebehn[1], Christin Heinrichs[1], Hans Kestler[2], Karin Scharffetter-Kochanek[3], Paul Walther[4], and Kay-E Gottschalk[1] — [1]Institute for Experimental Physics, Ulm University, Ulm, Germany — [2]Institute for Medical Systems Biology, Ulm University, Ulm, Germany — [3]Department of Dermatology and Allergology, Ulm University, Ulm, Germany — [4]Central Facility for Electron Microscopy, Ulm University, Ulm, Germany

Tissue homeostasis is maintained by a delicate balance of mechanical and chemical cues exchanged between the extracellular matrix and the incorporated cells. The mechanical properties of the matrix and the cells themselves cooperate to give tissues their structure and function. To understand the mechanical implications of these cell-matrix interactions we investigate fibroblast contraction in collagen matrices via a 3D printed microscale device [1]. We explore the contraction of

fibroblast-populated collagen gels with different cell densities for revealing potential cooperative effects. Furthermore, we use SEM and TEM imaging to expose the impact of cell density on contraction and matrix customization with by the embedded cells. The results highlight the necessity of further investigation into potential collective cell behaviors and the need to explore possible fibroblast transdifferentiation during the experiment. [1] Zhang, Tianzi, et al. "Investigating fibroblast-induced collagen gel contraction using a dynamic Microscale platform". Frontiers in Bioengineering and Biotechnology, vol. 7, 2019

BP 11.7 Tue 11:30 H 2032

Trade-offs in physiology and cellular stress determine lipid productivity in motile phytoplankton — •Narges Kakavand[1] and Anupam Sengupta[1,2] — [1]Physics of Living Matter Group, Department of Physics and Materials Science, University of Luxembourg — [2]Institute for Advanced Studies, University of Luxembourg

One of the long-standing challenges in our quest to produce biofuel sustainably is the negative correlation between lipid productivity and cell growth. Following our recent study on the role of nutrients in lipid generation [1], here we demonstrate how biomechanical cues could be used as an additional parameter to control lipid production without compromising biomass. By imposing hydrodynamic cues to stress motile phytoplankton at specific time points along the growth stages (indicating different nutritional states), we quantified the resulting cell growth, photo-physiological traits, and motility, in relation to the volume of lipid produced. Late induction of hydrodynamic stresses suppressed growth and photo-physiological traits, however, when applied at a relatively earlier time point after inoculation, flow-induced stresses allowed to significantly increase lipid content without observable changes in cell growth. Our findings indicate that hydrodynamic stress, coupled with physiology and motility may offer a controlling mechanism to tune lipid generation in diverse algal species. [Ref. 1] A. Sengupta,..., N. Kakavand, Science Advances 8, eabn6005, 2022.

15 min. break

BP 11.8 Tue 12:00 H 2032

Investigating single heart cell communication through TNTs using multi-mode ROCS microscopy — •arash felekary and alexander rohrbach — Lab for Bio- and Nano-Photonics, IMTEK, Freiburg, Germany

Cell-cell communication performs various biological functions, particularly in the heart. Among other communication pathways, tunneling nanotubes (TNTs) are of high interest due to their distinctive characteristics and functions. TNTs are dynamic, thin protrusions, up to 100μm long, and are not in contact with the substrate. To understand TNT functions in cardiac cell communication, we used Rotating Coherent Scattering (ROCS) microscopy, a label-free super-resolution imaging in different imaging modes. Using ROCS microscopy in total internal reflection (TIR), and dark-field (DF) modes, we quantified the growth of TNTs in Fibroblasts (FB) in the absence and presence of cardio-myocytes (CM), and we studied the influence of the Transforming Growth Factor beta (TGF-β) on TNT growth speed. After TNT establishment, we recorded and analyzed the dynamics of lamellipodia motion along TNTs using ROCS in Non-TIR and Bright field (BF) mode. Our findings revealed a linear relationship between TNT density and lamellipodia motion velocity. This suggests that TNTs facilitate cell-cell communication. Our findings also suggest that the interaction between FB cells undergoes distinct phases or steps, characterized by the spatial and temporal evolution of protrusions. We have developed a mathematical model to describe lamellipodia motion along TNTs and compare the results with those from experiments.

BP 11.9 Tue 12:15 H 2032

the role of the cytoskeleton for spatial and temporal control of cell mechanics studied using an average cell — •mohammad amin eskandari, bart vos, and till münker — Third institute of physics - Biophysics, Göttingen, Germany

Mechanical properties of cells have been shown to play a vital role in many biological functions such as migration, differentiation and division. While the cell mechanics has been largely studied at the cortex, hence the cellular interface to the environment, the intracellular mechanical properties are only recently within experimental reach. By doing active-passive microrheology using optical tweezers, we are able to directly measure the viscoelastic properties of the cytoplasm. The importance of intracellular mechanics for transport, organization, and even reaction kinetics is obvious, which suggests tight regulation by the cells. In contrast to this, we find that the viscoelastic shear modulus, which characterizes the intracellular mechanics varies over many orders of magnitude within a single cell type. To explain this discrepancy between expectations and measurement, we hypothesize that such heterogeneity arises from both, local and temporal variation cell compositions to test this we use micropatterns to create polarized cells in a well-defined way to achieve spatially registered microrheology experiments. Here I report on the challenge and present our solution for obtaining sufficient statistics, given that the probe particles used in the optical tweezers experiment are randomly distributed in the cytoplasm.

BP 11.10 Tue 12:30 H 2032

Multimodal quantum sensors for probing non-equilibrium thermodynamics at the nanoscale — •Sophia Belser[1], Louise Shanahan[1], Jack Hart[1], Qiushi Gu[1], David Jordan[2], Eric Miska[2], Mete Atatüre[1], and Helena Knowles[1] — [1]Cavendish Laboratory, University of Cambridge, JJ Thompson Avenue, Cambridge, CB3 0HE, United Kingdom — [2]Department of Biochemistry, University of Cambridge, 80 Tennis Ct Rd, Cambridge CB2 1GA, United Kingdom

Probing transient effects at the nanoscale enables us to understand living systems. However, challenges arise from small length scales, small signal amplitudes, and the risk of perturbing processes during observation. Thus, the isolation of a signal of interest in dynamic systems remains challenging. Due to their low cytotoxicity, amenability to surface functionalisation, and magneto-optical properties, nanodiamonds (NDs) have emerged as promising bio quantum sensors [1]. NDs enable real time *in vitro* and *in vivo* sub-degree thermometry and nanoscale rheometry [2]. We have developed a microfluidics compatible chip that allows for simultaneous local heating, on-chip and ND temperature readout. We have shown reliable quantum thermometry and rheometry in abiotic media and live cells with a temperature sensitivity of 2.3 °C/$\sqrt{\text{Hz}}$ and a 3.7-nm spatial resolution with 9.6-ms update rate in living cells [2]. We demonstrate biocompatibility in cells and non-anaesthetized roundworms. Next steps include targeting organelles in biological organisms to gain insights into local metabolic activity. [1] Belser *et al.* APL (2023), [2] Gu *et al.* ACS Nano (2023)