BP 25: Cell Mechanics II

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

Invited Talk BP 25.1 Thu 9:30 H44

Oncogenic signaling and stiffness sensing — •Johanna Ivaska — University of Turku

Tissue homeostasis is dependent on the spatially controlled localization of specific cell types and the correct composition of the extracellular stroma. Integrin-mediated adhesions, in conjunction with the actin cytoskeleton and signaling by receptor tyrosine kinases, regulate cell fate and identity and allow cells to migrate and invade the surrounding extra-cellular matrix (ECM). We have previously uncovered key differences between normal and cancer-associated stroma, whereby the mechanical and architectural features of normal stroma inhibit tumour growth and may epigenetically reprogram aggressive breast cancer cells towards a more benign phenotype. Recently, we turned our attention to other putative crosstalk mechanisms between cancer cells and the tumor microenvironment as well as tumor cell interactions with distinct tissue borders during systemic dissemination in the body. I will describe different control mechanisms guiding cancer cell invasion across physiological borders and their relevance to cancer progression and metastasis.

BP 25.2 Thu 10:00 H44

Perfect stabilization of biomolecular adhesions under load — •Anton Francis Burnet[1,2] and Benedikt Sabass[1,2] — [1]Department of Veterinary Sciences, Ludwig-Maximilians-Universität München, 80752 Munich, Germany — [2]Faculty of Physics and Center for NanoScience, Ludwig-Maximilians-Universität München, 80752 Munich, Germany

Cell focal adhesions are complex molecular assemblies that demonstrate the remarkable capability to adapt to mechanical load by changing their size. Drawing from the molecular mechanisms believed to drive this behavior, we present a minimal adhesion model for mechanically induced aggregation of adhesion molecules. If the internal states of adhesion molecules are coupled to their aggregation dynamics sufficiently strongly, the system becomes instable and unbounded growth ensues. Unexpectedly, the very same type of instability can lead to perfect stability under mechanical load, where adhesions adapt their size to withstand arbitrarily large load without rupturing-a phenomenon we term perfect stabilization. We derive state diagrams characterizing adhesion stability under stationary load and show that perfect stabilization also occurs for dynamic loads on physiologically relevant timescales. Finally, we show that perfect stabilization is a generic phenomenon that can be realized in many different ways by coupling aggregation rates with internal molecular states and argue that the phenomenon has broad implications for understanding cellular mechanics.

BP 25.3 Thu 10:15 H44

Environmental stiffness regulates neuronal maturation via Piezo1-mediated TTR activity — •Eva Kreysing[1,2,3], Hélène Gautier[1], Leila Muresan[1], Sudipta Mukherjee[1,2,3], Alexander Winkel[1], Xiaohui Zhao[1], Ragnhildur Thóra Káradóttir[1], and Kristian Franze[1,2,3] — [1]University of Cambridge, UK — [2]FAU Erlangen — [3]MPZ Erlangen

During the development of the nervous system, neurons grow axons and dendrites to connect with other cells. As neurons become integrated into the neural network, they mature and develop electrical activity. While mechanical interactions between neurons and their environment are critical for axon growth and pathfinding, the role of mechanical cues in the electrical maturation of neurons, and thus the formation of circuits in the developing brain, remain unexplored. Here, we cultured rat hippocampal neurons on substrates with different mechanical properties and found that electrical activity developed earlier on soft hydrogels compared to stiff hydrogels. This stiffness-dependent neuronal maturation was mediated by the mechanosensitive ion channel Piezo1. Using RNA sequencing, pathway analysis and Western blots, we identified a downstream signalling cascade responsible for the differential expression of neurotransmitter receptors. Finally, we found that stiffening of the developing Xenopus brain leads to impaired synapse formation in vivo. Our findings highlight the critical role of mechanical signals in neuronal maturation and suggest that local brain tissue stiffness is a critical parameter for circuit formation in the developing brain.

BP 25.4 Thu 10:30 H44

The positioning of stress fibers in contractile cells minimizes internal mechanical stress — •Valentin Wössner[1,2], Lukas Riedel[3,4], Dominic Kempf[3], Falko Ziebert[1,2], Peter Bastian[3], and Ulrich S. Schwarz[1,2,3] — [1]Institute for Theoretical Physics, Heidelberg University, Heidelberg, Germany — [2]BioQuant, Heidelberg University, Heidelberg, Germany — [3]Interdisciplinary Center for Scientific Computing, Heidelberg University, Heidelberg, Germany — [4]Institute for Environmental Decisions, ETH Zürich, Zürich, Switzerland

Stress fibers are contractile bundles of actin filaments found in the cytoskeleton of animal cells. They play crucial roles in force generation, mechanical adaptation, shape control and mechanosensing. While the physical description of single stress fibers is well-developed, much less is known about their spatial distribution on the level of whole cells. Here, we combine a finite element method for one-dimensional fibers embedded in a two-dimensional elastic bulk medium with dynamical rules for stress fiber formation based on genetic algorithms [1]. We postulate that their main goal is to achieve minimal mechanical stress in the bulk material with as few fibers as possible. We find that stress fibers typically run through the cell in a diagonal fashion and that they cross each other under biaxial stretch. In the future, our approach can be extended to three dimensions and to stress fibers with viscoelasticity.

[1] Riedel et al., J. Mech. Phys. Solids 195 (2025) 105950

BP 25.5 Thu 10:45 H44

Towards a better understanding of the cytokinetic contractile ring — •Francine Kolley-Köchel[1] and Sebastian Aland[1,2] — [1]Faculty of Mathematics and Informatics, TU Freiberg, 09599 Freiberg, Germany — [2]Faculty of Informatics/Mathematics, HTW Dresden, 01069 Dresden, Germany

The dynamics of viscoelastic surfaces plays an important role in biological systems. One prominent example is the actin cortex, with elastic properties on short time scales and viscous on long time scale. Numerical simulations of such a system can provide a better understanding of the real biological system. Here we present a novel monolithic model of viscoelastic surfaces within a dominant surface rheology, capturing both, shear and dilational dynamics. We demonstrate that these full three dimensional simulations are numerically stable for low and high surface viscosities and show spontaneous pattern formation, induced by active stress regulation. We discuss how this model can guide future work towards a betters understanding of complex viscoelastic surface dynamics and the formation of the cytokinetic contractile ring.

BP 25.6 Thu 11:00 H44

Using microfluidics for measuring microplastic particle-cell interactions — •Matteo A. Kumar[1], Simon Wieland[1,2], Anja F.R.M. Ramsperger[1,2], Christian Laforsch[1,2], and Holger Kress[1] — [1]Biological Physics, University of Bayreuth, Germany — [2]Animal Ecology I and BayCEER, University of Bayreuth, Germany

The growing presence of microplastic particles (MPs) in the environment increases human exposure to these contaminants, which can accumulate in tissues and spread throughout the body. Various MP properties, such as shape, size, charge and surface morphology, influence their interactions with cells. We have recently shown that the zeta-potential of MPs significantly affects their adhesion to and internalization into cells*. However, the question, whether the zeta-potential directly or another underlying parameter influencing it (e.g. the number of functional surface groups) plays the decisive role, remains unsolved.

To address this, we use a microfluidic platform and combine it with a convolutional neural network to allow the measurement of hundreds of interactions in parallel. By allowing MPs with different surface functionalizations to sediment onto the cells, we determine their binding kinetics. We subsequently exert a well-defined flow force on the MPs to quantify their adhesion to the cells. Our work contributes to understanding which properties of MPs are determining particle-cell interaction and therefore identifying potential drivers for their biological impact.

*Wieland, S., Ramsperger, A.F.R.M., Gross, W. et al. Nat Commun 15, 922 (2024).

15. min. break

BP 25.7 Thu 11:30 H44

Direct mechanical communication of cellular to nuclear shape in oocytes — •Bart Vos[1], Yamini Vadapalli[2], Till Muenker[1], Peter Lenart[2], and Timo Betz[1] — [1]Third Institute of Physics, University of Göttingen, Göttingen, Germany — [2]Max Planck Institute for Biophysical Chemistry, Göttingen, Germany

Mechanics play a crucial role in a wide range of cellular processes, from differentiation to division and metastatic invasion. Additionally, mechanical signaling can regulate protein expression. Although the mechanical properties of the cytoskeleton, providing shape, motility and mechanical stability to the cell, have been extensively studied, remarkably little is known about the mechanical environment within the nucleus of a cell and the exact mechanisms of force transduction between the cytoplasm to the nucleus.

To address these questions, we apply external deformations to oocytes of different species to observe how cellular deformations can be transmitted to the nucleus, leading to nuclear deformations. We combine this with optical tweezers-based microrheology in the cellular nucleus, allowing a direct comparison between intracellular and intranuclear mechanics. The observed viscoelastic behavior of the nucleoplasm on various time scales is profoundly different from the cytoskeleton. In addition, we probe the role of activity in the mechanics of the nucleus. Depending on the mechanical properties of the cytoplasm and nucleoplasm, nuclei can be highly susceptible to external strain or be largely shielded, suggesting a mechanical communication that might be relevant for proper oocyte function.

BP 25.8 Thu 11:45 H44

Robust mitotic events in C. elegans embryos with and without mechanical perturbations — Vincent Borne and •Matthias Weiss — Experimental Physics I, University of Bayreuth, Germany

Early embryogenesis of the nematode Caenorhabditis elegans proceeds in an autonomous fashion within a protective chitin eggshell. Cell-division timing and the subsequent mechanically guided positioning of cells is virtually invariant between individuals, especially before gastrulation. By mechanically perturbing the embryo without breaking its eggshell, we have probed the limits of this stereotypical and robust developmental program. Compressing embryos to half of their native diameter frequently resulted in a loss of cytokinesis, yielding a non-natural syncytium that still allowed for multiple divisions of nuclei. The orientation of mitotic axes was strongly altered in the syncytium, but key features of division timing and spatial arrangement of nuclei remained surprisingly similar to those of unperturbed embryos in the first few division cycles. Our data suggest that few very robust mechanisms govern the progress of early embryogenesis of C. elegans.

BP 25.9 Thu 12:00 H44

Density and viscosity Measurements of the cytosol of human red blood cells — •Thomas John and Christian Wagner — Experimental Physics, Saarland University

We present a method to determine the viscosity of the intracellular liquid - the cytosol - of human red blood cells (RBCs). Our method combines the measurement of the mass density distribution of RBCs and the viscosity of the cytosol as a function of the water content. The density distribution is measured through buoyant density centrifugation combined with cell counting. By correlating this Gaussian distribution of cell population densities with the viscosity-density relation of the cytosol, we obtain a log-normal distribution of the cytosol viscosity of healthy RBCs. The viscosity contrast λ, defined as the ratio of viscosities between the RBC cytosol and the blood plasma under physiological conditions, is determined to have a mean value of $\bar{\lambda} = 10$. This value is significantly larger than those used in the literature for numerical simulations.

BP 25.10 Thu 12:15 H44

Aggregation and disaggregation of red blood cells — •Kirill Korneev[1], Nicolas Moreno[2], Thomas John[1], Christian Wagner[1], and Dmitry Fedosov[3] — [1]Experimental Physics, Saarland University — [2]Basque Center for Applied Mathematics, Bilbao Spain — [3]Theoretical Physics of Living Matter, Forschungszentrum Jülich

Laser tweezers (LT) are devices for manipulating, trapping and force measurement on particles into optical traps. Red blood cells (RBCs) are the majority of blood cells. Those cells are very deformable and show spontaneously forming complex structures at rest state, due to aggregation. The mechanisms of RBCs aggregation are not fully understood, however there are currently two main hypotheses that can explain it: the bridging model based on mobile and immobile bonds, and the depletion layer model. In this work, experimental values of the RBCs disaggregation force were obtained by stretching RBC aggregates. We will show, that the mechanism of RBCs disaggregation involves these two hypotheses. We will also show that the bridging model with mobile bonds reproduces well the corresponding experimental data, offering insights into the interplay between bridging and depletion interactions and providing a framework for studying similar interactions between other biological cells.

N. Moreno, et al., Aggregation and disaggregation of red blood cells: depletion versus bridging, bioRxiv 2024.11.20.624311 (2024)

BP 25.11 Thu 12:30 H44

Dynamic states of P. falciparum infected erythrocytes adhering in shear flow - a qualitative study of rolling and flipping motions — •Katharina Scholz[1], Leon Lettermann[2], Jessica Kehrer[3], Michael Lanzer[3], Ulrich Schwarz[2], and Motomu Tanaka[1] — [1]Institute for Physical Chemistry, University of Heidelberg, Germany — [2]Institute for Theoretical Physics, University of Heidelberg, Germany — [3]Center of Infectious Diseases, Heidelberg University Medical School, Germany

As surviving strategy, the malaria parasite remodels the red blood cell by causing the expression of adhesive proteins on its surface. The modification allows the infected cell to adhere to the endothelial cells in the blood stream, thereby avoiding clearance by the spleen.

This transformation also alters cell shape and movement behaviour during development. We used Reflection Interference Contrast Microscopy (RICM) in quantitative flow chamber experiments and employed a high-speed camera to gain more information about the contact footprint of cells. With this setup, we tracked parasitised erythrocytes individually, label-free and non-invasively. Early-stage trophozoites exhibited flipping behaviour, while late-stage schizonts showed a steady rolling motion. Our results provide a quantitative understanding of how parasite development affects dynamic cytoadhesion behaviour and shed light on understanding endothelial cell activation.

BP 25.12 Thu 12:45 H44

Deformability cytometry for large-scale mechano-genomic screening in interphase and mitosis — •Laura Strampe[1], Katarzyna Plak[2,3], Christine Schweitzer[1], Cornelia Liebers[1,2], Buzz Baum[3], Jona Kayser[1], and Jochen Guck[1,2] — [1]Max-Planck-Zentrum für Physik und Medizin, Erlangen, Germany — [2]Biotechnology Center of TU Dresden, Dresden, Germany — [3]MRC Laboratory of Molecular Biology, Cambridge, United Kingdom

We demonstrate the scalability of real-time fluorescence and deformability cytometry (RT-FDC) for large-scale cell cycle-resolved mechano-genomic screening. Using RNA interference, we screened 215 kinase and phosphatase genes on their effects on cell mechanics in interphase and mitosis. RT-FDC combines high throughput (up to 100 cells per second) with fluorescence-based cell cycle classification, enabling single-cell mechanical phenotyping of entire populations. We show that cell cycle resolution is essential for identifying genetic regulators of cell mechanics, as stiffness differences between interphase and mitotic cells can obscure genuine knockdown effects or generate false-positive hits. Genes regulating mitotic mechanics or softening cells upon knockdown are particularly likely to be masked. Of the 81 genes identified as affecting cell stiffness, 22 were detected only through cell cycle resolution. These include *PRL-1*, a cancer metastasis marker with opposing effects across the cell cycle: stiffening interphase cells and softening mitotic cells. This suggests that *PRL-1* overexpression in metastatic cells expands the range of mechanical phenotypes during cell cycle progression, facilitating tumor adaptability.