BP 25: Cell Mechanics II

Time: Thursday 15:00–17:30 Location: BAR Schö

BP 25.1 Thu 15:00 BAR Schö

Nuclear mechanics probed by optical tweezers-based active microrheology — •Bart Vos[1], Till Müncker[1], Ivan Avilov[2], 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. Consequently, the mechanical properties of the cytoskeleton, providing shape, motility and mechanical stability to the cell, have been extensively studied. However, remarkably little is known about the mechanical environment within the nucleus of a cell, and fundamental questions remain unanswered, such as the role of nuclear actin or the sudden "freezing" of the cell during cellular division that prevents diffusion or active mixing of the nucleus and the cytoplasm.

To address these questions, we perform optical tweezers-based microrheology in the cellular nucleus. Microrheology has proven to be a suitable tool for intracellular mechanical measurements, as it enables local, non-invasive measurements. However, although the cytoskeleton has been extensively studied this way, the cell nucleus has not been investigated, mainly due to difficulties with inserting appropriate probe particles. By using starfish oocytes that have larger dimensions than most other cell types, we are able to perform microinjection of micrometer-sized particles. We observe viscoelastic behavior of the nucleoplasm that is profoundly different from the cytoskeleton. In addition, we mechanically follow the oocyte during meiotic cell division.

BP 25.2 Thu 15:15 BAR Schö

Mechanosensitive binding of filamins in the actin cytoskeleton of live cells — •Valentin Ruffine and Elisabeth Fischer-Friedrich — DFG Cluster of Excellence Physics of Life, Technische Universität Dresden, Dresden, Germany

Filamins A and B are cross-linkers of the actin cytoskeleton expressed in a wide range of human cell types. In particular, filamins are crucial in actin cytoskeleton interactions with the extracellular matrix and therefore are major molecular players in cartilage and bone development. Filamins form dimers which can bind and cross-link two actin filaments and thus contribute to the mechanical integrity of cytoskeletal structures such as the actin cortex. Myosin-generated contractile tension in the actin cortex is likely translated into a tensile force on the filamin-actin bonds in cross-linking filamins. Filamin binding to actin is transient with unbinding events after a characteristic bond lifetime. This enables large reorganizations of the cytoskeleton at longer timescales. However, tensile force in filamin-actin bonds may affect their unbinding kinetics. Here, we study the binding dynamics of filamins A and B to actin, in the cortex of mitotic HeLa cells. With a set-up combining a confocal and an atomic force microscope, we measure how changes in contractile tension in the actin cortex change filamin binding dynamics. Our results suggest a substantial increase of the lifetime of filamin-actin bonds under increased tensile force. This behavior is termed "catch-binding" and may act as a fast rescue mechanism that prevents rupture of filamin-containing actin cytoskeletal structures upon sudden tension increase.

BP 25.3 Thu 15:30 BAR Schö

T-cell migration: Improving searching efficiency by targeting Microtubules — •Galia Montalvo[1,2,3], Bin Qu[3,4], and Franziska Lautenschläger[1,2,3] — [1]University of Saarland, Department of Experimental Physics — [2]University of Saarland, Center for Biophysics — [3]Biophysics, Center for Integrative Physiology and Molecular Medicine (CIPMM), School of Medicine — [4]Leibniz Institute for New Materials

Cytotoxic T lymphocytes (CTLs) are the key players in the adaptive immune system to eliminate tumor cells. Proper mobility in three-dimensional environments is a prerequisite for CTLs to execute their killing function and the cytoskeleton plays a central role in CTL migration in 3D. In dense matrices, migration and the consequent killing efficiency of CTLs is greatly impaired. Interestingly, we observed that in 3D matrices, CTLs go through narrow quasi-1D channels. Manufactured micro-channels are a recently emerged promising tool with well-defined parameters to investigate cell migration in 1D. In this project, we characterize MTs as a major cytoskeletal component regulating the migration of CTLs in micro-fabricated environments and in dense collagen matrices. To this end, we expose CTLs to MTs disturbing drugs. We studied the mechanics of treated cells and described the role of actin in the observed stiffness increase after MT depolymerization. Our main conclusion is that searching efficiency and killing capacity of CTLs is enhanced after MT depolymerization through stiffness increase.

BP 25.4 Thu 15:45 BAR Schö

Global membrane tension is independent of polyacrylamide substrate stiffness — •Eva Kreysing[1], Jeffrey McHugh[1,2], Sarah Foster[1,3], Kurt Andresen[4], Ryan Greenhalgh[1], Eva Pillai[1,5], Andrea Dimitrcopoulus[1], Ulrich Keyser[1], and Kristian Franze[1,6] — [1]University of Cambridge, UK — [2]Collège de France, Paris — [3]University of Tübingen; Germany — [4]Gettysburg College, USA — [5]EMBL Heidelberg, Germany — [6]University Erlangen/Nürnberg, Germany

Cellular processes such as cell migration or axonal pathfinding have been shown to depend strongly on mechanical properties of the cell*s environment such as stiffness. It has been shown that Piezo1 is one of the mechanosensitive ion channels that contributes to such behaviour. It is hypothesised that Piezo1 is activated by changes in membrane tension. This raises the question whether membrane tension is influenced by stiffness of the cell*s environment. We measured membrane tension as a function of substrate stiffness in different cell types with optical tweezers. To our surprise, we found that global membrane tension is independent of substrate stiffness in the physiological range. However, we found strong differences between membrane tension on compliant substrates and glass substrates. To explain these observations, this work introduces a toy model for substrate, membrane and cortex interaction.

BP 25.5 Thu 16:00 BAR Schö

Self-stabilization of cell adhesions under load — •Benedikt Sabass — LMU München

Mechanical loading generally weakens adhesive structures and eventually leads to their rupture. However, biological systems can adapt to loads by strengthening adhesions, which is essential for maintaining the integrity of tissue and whole organisms. Inspired by cellular focal adhesions, we discuss generic, molecular mechanisms that enable adhesions to harness applied loads for self-stabilization through adhesion growth. The mechanisms are based on conformation changes of adhesion molecules that are dynamically exchanged with a reservoir. Tangential loading drives the occupation of some states out of equilibrium, which, for thermodynamic reasons, leads to association of further molecules with the cluster. The self-stabilization principle can be realized in many ways in complex adhesion-state networks and we show how it naturally occurs in cellular adhesions involving the adaptor proteins talin and vinculin.

Braeutigam, A., Simsek, A.N., Gompper, G., and Sabass, B., Nature Communications 13(1):1-9, 2022

15 min. break

BP 25.6 Thu 16:30 BAR Schö

Unraveling the light activation of flagellar adhesiveness in *Chlamydomonas* — •Rodrigo Catalan[1,2], Antoine Girot[1,2], Alexandros Fragkopoulos[1,2], Simon Kelterborn[3], Darius Rauch[3], Olga Baidukova[3], Peter Hegemann[3], and Oliver Bäumchen[1,2] — [1]Max Planck Institute for Dynamics and Self-Organization (MPIDS), 37077 Göttingen, Germany — [2]University of Bayreuth, Experimental Physics V, 95447 Bayreuth, Germany — [3]Humboldt University Berlin, Institute of Biology, 10115 Berlin, Germany

Photoreceptors are essential constituents of photoactive microbes and control several biological processes, such as circadian life cycle, sexual reproduction and phototaxis. *Chlamydomonas reinhardtii*, a unicellular model organism to study light-activated microbial functionalities, exhibits light-switchable flagellar adhesion to surfaces upon blue-light exposure [Kreis *et al.*, Nature Physics 2018]. Using single-cell micropipette force spectroscopy, we compare the adhesion forces of wild-type (WT) cells and several blue-light photoreceptor-deletion mutants.

We find that the wavelength response of flagellar adhesion forces in WT cells resembles the absorption spectrum of plant cryptochrome (pCRY) and animal cryptochrome (aCRY) photoreceptors. We further assess the involvement of pCRY and aCRY photoreceptors in the light-switchable adhesion of *C. reinhardtii* by means of adsorption experiments [Catalan *et al.*, arXiv:2208.01338] at the population level using photoreceptor-deletion mutants lacking either one or both CRYs.

BP 25.7 Thu 16:45 BAR Schö

Chromatin and Nucleocytoplasmic Transport Control the Nuclear Biophysical Properties during Assembly in Egg Extracts — •Omar Muñoz[1,2], Abin Biswas[1,4], Kyoohyun Kim[1,3], Simone Reber[4], Jochen Guck[1,3], and Vasily Zaburdaev[1,2] — [1]Max-Planck-Zentrum für Physik und Medizin — [2]Department of Biology, Friedrich-Alexander-Universität Erlangen-Nürnberg — [3]Max Planck Institute for the Science of Light — [4]IRI Life Sciences, Humboldt-Universität zu Berlin

Biophysical properties of the cell nucleus are important for various cellular processes from migration to stress responses, but largely are still not well understood. One fundamental example is the mass density: we observed that the nuclear mass density consistently displays a lower value than its cytoplasmic counterpart for a wide range of species, which is surprising given that it contains the highly compacted genetic material. To understand the mechanisms behind this, we measured volume and mass density of growing nuclei reconstituted in Xenopus egg extracts. Our results identified nucleocytoplasmic transport and chromatin as the main determinants for the dry mass and volume of then nucleus, and suggest a coupling of chromatin with nucleocytoplasmic transport. We propose a theoretical model informed by experiments, which incorporates active transport of proteins and balance of colloid osmotic pressure and an entropic polymer pressure exerted by chromatin. With only a few adjustable parameters, our model can fully describe the nuclear volume and mass dynamics as observed in the experiments.

BP 25.8 Thu 17:00 BAR Schö

Dyneins, unite! How a weak motor protein can drive efficient transport of large cargoes — •Simon Wieland[1,2], Christina Steininger[1], David E. Gitschier[1], Marius M. Kaiser[1], Wolfgang Gross[1], Abdullah R. Chaudhary[3], Jana Ritschar[4], Christian Laforsch[2], Adam G. Hendricks[3], and Holger Kress[1] — [1]Biological Physics, University of Bayreuth, Germany — [2]Animal Ecology I, University of Bayreuth, Germany — [3]Department of Bioengineering, McGill University, Montreal, Canada — [4]Laboratory of Molecular Parasitology, University of Bayreuth, Germany

To promote robust transport of organelles, dyneins need to work together to overcome intracellular drag forces and opposing forces of kinesins. However, current models of dynein cooperativity cannot explain how dyneins produce very high forces to power transport of large organelles with diameters of several microns. Here, we show that many dynein teams interact with multiple microtubules to drive efficient transport of large organelles. We measured retrograde transport forces of phagosomes with diameters of 1-5 μm. These forces were adapted to the cytoplasmic viscosity, enabling equally fast transport of all phagosomes. Furthermore, we labeled and quantified dyneins on isolated phagosomes. By modeling the distribution of microtubules around the phagosomes we linked the observed transport forces to the corresponding dynein numbers. We show that both dynein's cooperativity and size-dependent interactions of organelles with microtubules contribute to the production of high collective transport forces.

BP 25.9 Thu 17:15 BAR Schö

The formation of microtentacles — •Lucina Kainka[1], Reza Shaebani[2,3], Kathi Kaiser[1], Ludger Santen[2,3], and Franziska Lautenschläger[1,3] — [1]Department of Experimental Physics, Saarland University, Saarbrücken, Germany — [2]Department of Theoretical Physics, Saarland University, Saarbrücken, Germany — [3]Center for Biophysics, Saarland University, Saarbrücken, Germany

It is widely assumed that cellular stiffness decreases during cancer progression, and this is mainly attributed to changes in their actin cortex properties. It has recently been proposed that a weakened actin cortex enables the formation of so called microtentacles. Microtentacles are microtubule-based membrane protrusions that are formed by circulating tumor cells. It is assumed that microtentacles promote reattachment of circulating tumor cells to the tissue and the escape from the blood stream.In this study, we aim to understand how the actin cortex structure changes during cancer progression to enable microtentacle formation. We further ask how microtubules generate forces to protrude the cell membrane.In our experiments, we use noncancer RPE-1 cells as a model system. By treating these cells with actin affecting compounds while they are in suspension, they form microtentacles. We further can control the number and length of microtentacles by varying the concentration of compounds applied. We analyze the actin cortex and microtubule network in these cells with fluorescence and scanning electron microscopy. We further study the microtubule dynamics inside microtentacles by fluorescence recovery after photobleaching (FRAP).