BP 12: Cytoskeleton I

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

Invited Talk BP 12.1 Tue 9:30 BAR/0205

Tuning the Tracks: Functional Diversity Encoded in Microtubule Lattice States — •Lukas Kapitein — Utrecht University

Microtubules are active polymers that power intracellular transport and signaling. In cells, functionally distinct microtubule subsets are known to coexist, but the underlying mechanisms that specify these subsets have remained unclear. I will show that microtubule lattice conformation, specifically expanded and compacted states, acts as a tunable structural parameter that regulates both motor-driven transport and cytoskeletal signaling. Whereas expanded lattice states define tracks for Kinesin-1 driven transport, compacted states sequester specific signaling factors, both independently of tubulin chemical modification. These findings identify microtubule lattice plasticity as a fundamental mechanism by which active cytoskeletal matter encodes functional diversity.

BP 12.2 Tue 10:00 BAR/0205

Mechanical tension extends the microtubule lattice and modulates kinesin-1 binding in an isoform-dependent manner — Yannic Lurz[1], Benedikt Fischer[1], Laura Muras[2], Antoine Rittaud[3], Hevré Morhbach[4], Igor Kulic[3], E. Michael Ostap[5], Erik Schaffer[1], and •Serapion Pyrpassopoulos[1] — [1]University of Tübingen — [2]University of Uppsala — [3]ICS, Strassburg — [4]ICPM, Metz — [5]University of Pennsylvania

Recent work has shown that the microtubule lattice possesses remarkable structural plasticity, with its conformation modulated by MAPs and motor binding. However, how this plasticity responds to mechanical forces remains poorly understood. We developed assays to measure the effect of tensile forces on single microtubules using optical tweezers and fluorescence microscopy. Decorating microtubules with quantum dots enabled us to measure, with nm-precision, mechanical distortions of ~0.4% under changes in average tensile force $<\Delta F> = 10.4$ pN, within the rage of Fmin = 1.29 pN to Fmax = 20.4 pN, forces comparable to those generated by one to three kinesin-1 motors. Under forces in this range, the average binding rate of KIF5B decreased by ~20%, while its dissociation rate increased by ~10%, reducing its average run length. In extreme cases, run length dropped by up to 46% under tension. By contrast, no statistically significant effects were observed for KIF5C at the same forces. Together, these experiments provide new insights into how microtubules can act as sensors and transducers of mechanical and biochemical cues across the cell.

BP 12.3 Tue 10:15 BAR/0205

Beyond the tip: lattice dynamics, seams, and the mechanism of microtubule fracture — •Amir Zablotsky[1], Subham Biswas[2], Laura Schaedel[2,3], and Karin John[1] — [1]Université Grenoble-Alpes, CNRS, Laboratoire Interdisciplinaire de Physique 38000 Grenoble, France — [2]Experimental Physics and Center for Biophysics, Saarland University, 66123 Saarbrücken, Germany — [3]PharmaScienceHub (PSH), 66123 Saarbrücken, Germany

The structural integrity of microtubules is paramount for cellular function. While tip behavior has been extensively studied, the dynamics of the microtubule lattice remain less explored. We present a theoretical analysis of lattice fracture mechanisms, focusing on the influence of multi-seam structures arising from monomer defects and aiming to provide a more accurate estimation of GDP lattice parameters.

Our findings reveal that seams function as pre-existing pathways that accelerate damage propagation. Consequently, monomer vacancies destabilize the lattice due to the inherent structural loss of tubulin-tubulin contacts and the additive acceleration of fracture through multiple seams. Furthermore, comparison of our simulations with experiments on lattice fracture suggests that the intrinsic ratio of longitudinal to lateral binding energies is bounded at approximately 1.5, challenging previous predictions of lattice anisotropy from tip-growth models.

These results emphasize the urgent need to revise current microtubule growth models to incorporate parameters obtained from lattice dynamics and reassess their implications for overall microtubule stability and tip dynamics.

BP 12.4 Tue 10:30 BAR/0205

Microtubule mechanics in actin network — •Komal Bhattacharyya, Sarah Köster, and Stefan Klumpp — University of Göttingen, Göttingen, Germany

The cytoskeleton provides structural support while enabling dynamic cellular processes such as growth and migration. Actin filaments and microtubules are key cytoskeletal components: actin is semiflexible, whereas microtubules are comparatively stiff and rod-like. The interplay between these two filament systems underlies many biological behaviors. For example, microtubules exhibit increased resistance to compressive forces when embedded within an actin network. In our work, we use the simulation package Cytosim to investigate composite actin-microtubule networks. In particular, we examine the buckling behavior of microtubules subjected to compressive loads and thermal fluctuations, and how these responses are altered by mechanical coupling to actin. Our results show that the mechanical response of a probe filament such as a microtubule is governed primarily by its immediate local interactions rather than by the bulk properties of the surrounding network. Indicating the actin network can not influence the microtubule dynamics as an uniform elastic medium but only through direct interactions through crosslinkers or molecular motors.

BP 12.5 Tue 10:45 BAR/0205

Polydispersity-Induced Traveling Waves in Microtubule-Motor Mixtures — •Katrina Wharam[1], Ivan Maryshev[1], Filippo De Luca[2], and Erwin Frey[1] — [1]Ludwig-Maximilians Universität München, Germany — [2]University of Cambridge, United Kingdom

Microtubule-motor mixtures are exemplary active systems that self-organize into a variety of non-equilibrium phases, including asters, bilayers, and active foams. While previous theoretical work has largely assumed monodisperse filament lengths, we investigate a mixture with two microtubule populations of distinct lengths and derive a continuum field theory using a Boltzmann-Ginzburg-Landau approach. Analytical and numerical analysis shows that, despite reciprocal microscopic interactions, the system develops emergent asymmetric behaviour at the macroscopic scale. We identify the filament length ratio as a key control parameter: small length ratios yield stationary nematic bands, whereas increasing the disparity leads to traveling waves - a pattern absent in monodisperse models. Our results reveal a generic, collective route to traveling states in non-self-propelling active matter and connect ad-hoc asymmetric-alignment theories with biologically realistic microtubule systems.

15 min. break

BP 12.6 Tue 11:15 BAR/0205

Hold on tight no matter what! How cholesterol and cytoskeletal fibers affect microtentacles formation. — •Enrique Colina Araujo[1,2], Lucina Kainka[1,2], and Franziska Lautenschläger[1,2,3] — [1]Department of Experimental Physics, Saarland University, Saarbrücken, 66123, Germany — [2]Center for Biophysics, Saarland University, Saarbrücken, 66123, Germany — [3]Max Planck School, Matter to Life, Heidelberg, 69120, Germany

Following the formation of a primary tumor, cancer cells in the outer areas may detach and undergo an epithelial-to-mesenchymal (EMT) transition, enabling them to migrate and colonize new tissues, ultimately leading to metastasis. Circulating tumor cells (CTCs) play a key role during this invasion. Invasion can only occur after CTCs have attached to the blood vessel wall and extravasated from the bloodstream. Recent work suggests that such adhesion is mediated by microtubule (MT)-based membrane protrusions, known as microtentacles (McTNs). However, it remains unclear how McTNs protrude from the CTC and how they facilitate cell adhesion. In this work, we analyzed McTN formation in MDA-MB-231 cells. Using the actin depolymerizing drug latrunculin A and the cholesterol-depleting drug methyl-β-cyclodextrin (MβCD), we show that McTNs growth results from a reorganization of the actin cortex into areas of high actin concentration as well as from variations in cholesterol distribution in the plasma membrane of CTCs. Furthermore, McTNs' adhesion is integrin-based. Integrin-β-2 is evenly distributed across the surface of McTN, enabling adhesion at every potential contact with the blood vessel walls.

BP 12.7 Tue 11:30 BAR/0205

Coexistence and selection of branched actin networks

— •Valentin Wössner[1,2], Falko Ziebert[1,2], and Ulrich S. Schwarz[1,2] — [1]Institute for Theoretical Physics, Heidelberg University, Philosophenweg 19, 69120 Heidelberg, Germany — [2]BioQuant, Heidelberg University, Im Neuenheimer Feld 267, 69120 Heidelberg, Germany

The actin cytoskeleton is crucial for essential cellular processes such as division, migration, and shape regulation. Most cellular actin structures are continuously turned over while keeping similar sizes. However, they are coupled through a shared and finite pool of actin monomers, which begs the question of how they can control their sizes. For branched actin networks, we suggest that local depletion of actin monomers at the leading edge constitutes a generic negative feedback mechanism between the current state of a structure (filament density) and its growth rate (creation of new branches). We derive a single equation capturing this local feedback and the global competition between different networks. Our theory leads to well-defined steady states even in the case of multiple networks sharing the same pool of monomers, without any need for specific molecular processes, in agreement with recent experiments on reconstituted systems. We also present the phase diagram for the transition from coexistence to selection under increased competition.

BP 12.8 Tue 11:45 BAR/0205

Phase Separation Strength Controls Actin Filament Treadmilling — •Beatrice Nettuno[1], Davide Toffenetti[1], Timon Nast-Kolb[2], Moritz Striebel[1], Erwin Frey[1], and Andreas Bausch[2] — [1]Arnold Sommerfeld Center for Theoretical Physics (ASC), Department of Physics, Ludwig-Maximilians-Universität München, Theresienstrasse 37, München, D-80333, Germany — [2]Heinz Nixdorf Chair in Biophysical Engineering of Living Matter, Technical University of Munich, Ernst-Otto-Fischer Str.8, Garching bei München, D-85748, Germany

Actin treadmilling underlies diverse forms of cellular motility, yet the physical principles enabling stable, persistent turnover remain unclear. In our work, we reconstitute a minimal system in which phase-separated condensates of zyxin and VASP balance cofilin-driven severing to produce robust treadmilling and higher-order actin organization. To uncover the mechanistic basis of this emergent behavior, we develop agent-based simulations that quantitatively recapitulate the experimental dynamics. Our modeling reveals that persistent treadmilling requires an optimal condensate cohesion: phase separation must be strong enough to locally concentrate and crosslink filaments, yet sufficiently fluid to permit barbed-end growth and internal rearrangements. Too weak a cohesion fails to stabilize bundles, whereas overly cohesive condensates suppress filament dynamics and prevent sustained turnover. Together, experiments and theory identify a physical mechanism by which the material properties of multivalent protein condensates regulate cytoskeletal turnover.

BP 12.9 Tue 12:00 BAR/0205

Anisotropic stretch biases the self-organization of actin fibers in multicellular Hydra aggregates — •Anais Bailles, Giulia Serafini, Heino Andreas, Christoph Zechner, Carl Modes, and Pavel Tomancak — Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

Hydra displays a striking planar pattern of actin fibers at the organism scale, and mechanics influence the morphogenesis of biological structures during its prepatterned regeneration. However, how mechanics participate in the formation of an ordered pattern from a totally disordered state remains unknown. To study this, we used cellular aggregates formed from dissociated Hydra cells, which initially lose all actin polarity yet regenerate a long-range actin pattern. We showed quantitatively that the actin meshwork evolves from a disordered symmetric state to an ordered state in which rotational symmetry is broken, and translation symmetry is partially broken, with the nematic and smectic order parameters increasing over days. During the first hours, the actin meshwork displayed spatial heterogeneity in the nematic order parameter, and ordered domains separated by line defects progressively grew and fused. This suggests that local cell-cell interactions drive the transition from disorder to order. To understand the mechanism of ordering, we perturbed the tissue's physical constraints. We showed that while topology and geometry do not have a direct effect, anisotropic stretch biases the emerging orientation of the actin meshwork within hours. This demonstrates the role of tissue mechanics in the alignment of the actin fibers during the disorder-to-order transition.

BP 12.10 Tue 12:15 BAR/0205

Bridging Scales in the Cytoskeleton: Towards a nonperturbative renormalization group framework — •Patrick Jentsch, Thomas Quail, Niccolò Banterle, and Anna Erzberger — European Molecular Biology Laboratory, Heidelberg, Germany

Microtubules (MTs) and their interactions are microscopically well characterized, yet the connection between these interactions and the emergent, functionally relevant collective behavior of the cytoskeleton remains incomplete. To develop an analytic framework that links these scales, we aim to explore the use of nonperturbative renormalization group (NPRG) methods to derive large-scale effective theories of MT networks from a microscopic model of interacting MTs. Using *Xenopus laevis* egg extract as a model system, we have begun inferring a phenomenological theory of interacting MTs at the micrometer scale based on TIRF microscopy data. In the next stage, this model will be coarse-grained using NPRG methods to obtain an effective description at the millimeter scale, enabling us to track the scale dependence of interaction couplings and the emergence of new dynamical processes. Ultimately, the resulting effective theory will be evaluated by comparing predicted correlation functions with experimental measurements of spontaneously formed MT asters which we are currently imaging using millimeter-scale widefield and confocal techniques.

BP 12.11 Tue 12:30 BAR/0205

Bayesian inference of bond parameters from interactions between single filaments — •Kristian Angeli Pajanonot[1,2], Sascha Lambert[1,2], Pallavi Kumari[1], Stefan Klumpp[2], and Sarah Köster[1] — [1]Institute for X-Ray Physics, University of Göttingen, Germany — [2]Institute for the Dynamics of Complex Systems, University of Göttingen, Germany

Interactions among cytoskeletal filaments-actin, microtubules, and intermediate filaments-regulate cell structure, movement, and transport. Single-filament direct interactions can be measured using a quadruple optical tweezers setup. In this approach, filaments are attached to two separate bead pairs held in optical traps and positioned in a cross configuration. As the vertical filament is pulled across the other one, the bond that forms between these filaments experiences increasing mechanical load until it breaks. Previous analysis using Kolmogorov-Smirnov (KS) tests allows for the estimation of bond parameters but lacks a probabilistic interpretation. Here, we present a Bayesian inference framework to estimate bond parameters from the interaction data. Using published data on the interaction between two vimentin filaments, we show that Bayesian inference provides consistent results with the KS test and with narrower parameter estimates. We then investigate how the pulling velocity influences the bond parameters and find that probing different pulling velocities improves inference compared to using a single velocity. Finally, we apply the method to other cytoskeletal filament interactions demonstrating broader applicability and offering guidance for future experimental optimization