BP 16: Molecular Motors

Time: Wednesday 15:00–17:30 Location: H 1028

Invited Talk BP 16.1 Wed 15:00 H 1028

Molecular Crowding Creates Traffic Jams of Kinesin Motors On Microtubules — •Cecile Leduc[1,2], Kathrin Padberg-Gehle[3], Vladimír Varga[2], Dirk Helbing[4], Stefan Diez[2,5], and Jonathon Howard[2] — [1]LP2N-CNRS-U-Bordeaux 1 — [2]MPI-CBG, Dresden — [3]TU-Dresden — [4]ETH Zürich — [5]Technische Universität Dresden, B CUBE

Despite the crowdedness of the interior of cells, microtubule-based motor proteins are able to deliver cargoes rapidly and reliably throughout the cytoplasm. We hypothesize that motor proteins may be adapted to operate in crowded environments by having molecular properties that prevent them from forming traffic jams. To test this hypothesis, we reconstitute high-density traffic of purified kinesin-8 motor proteins along microtubules in a total-internal-reflection microscopy assay. We find that traffic jams, characterized by an abrupt increase in the density of motors with an associated abrupt decrease in motor speed, can even form in the absence of other obstructing proteins. To determine the molecular properties that lead to jamming, we altered the concentration of motors, their processivity and their rate of dissociation from microtubule ends. We find that traffic jams form when the motor density exceeds a critical value (density-induced jams) or when motor-dissociation from the microtubule ends is so slow that it results in a pile-up (bottleneck-induced jams). Through comparison of our experimental results with theoretical models and stochastic simulations, we characterize in detail under which conditions density- and bottleneck-induced traffic jams form or do not form.

Invited Talk BP 16.2 Wed 15:30 H 1028

Collective properties of molecular motors — •Jean-François Joanny — Institut Curie centre de recherche 26 rue d'Ulm 75248 Paris cedex 05

In many instances, in cells molecular motors such as myosins act in groups and show spectacular collective properties such as dynamic phase transitions, oscillations or bidirectional motion. We propose a "soft motor model" where the tail of the motors has a finite stiffness and is rigidly connected to the moving motor filament. The head of the motors is described by a classical two level system. The important parameter which governs the behavior of the motors is the pinning parameter which compares the maximum stiffness of the interaction potential to the stiffness of the motors.

At high enough activities, motor clusters can have two spontaneous velocities in opposite directions. If the number of motors in the cluster is not infinite, the motion reverses between the states corresponding to the two velocities over a finite reversal time. When the motors are rigidly bound to the motor filament, we calculate the reversal time as a first passage time between two non equilibrium states and show that it increases exponentially with the number of motors as found in simulations of Badoual et al.

Finally we discuss the case of molecular motors coupled via hydrodynamic interactions.

BP 16.3 Wed 16:00 H 1028

Forces and Fast Dynamics of Gliding Motors in Myxococcus Xanthus — •Fabian Czerwinski[1], Mingzhai Sun[1], Tam Mignot[2], and Joshua Shaevitz[1] — [1]Institute for Integrative Genomics, Princeton University, USA — [2]CNRS, Marseille, France

The gram-negative bacterium Myxococcus xanthus is an important model organism for studies of multicellular grouping as well as biofilm formation. Individual cells use a combination of twitching and gliding motility to form large, multicellular structures. We identified a new class of molecular motors that power gliding motility [1]. These motors, made of the AglQRS proteins, assemble within focal adhesion sites that link the bacterial cytoskeleton to the extracellular surroundings [2].

Our goal is to understand control and cooperativity of these motor complexes within single cells. For this purpose, we combined optical tweezers, fluorescence microscopy, and real-time tracking of attached marker beads. This allows us to assess the step-like activity of motors embedded in the adhesion complexes at high temporal and spacial resolution. We found motor function correlated to the helical pitch of the bacterial cytoskeleton. We further measured motor stalling forces and the time delay between single motor responses to various cell-motility regulators. Measurements of the gliding force of whole cells will complement our results. Our experiments quantitatively explain how the AglRQS motors drive cell gliding and the formation of multicellular structures.

[1] Sun et al., PNAS(108)7559, 2011. [2] Mignot et al., Science(315)853, 2007.

BP 16.4 Wed 16:15 H 1028

Altering the Native Neck-Linker Length Changes Processivity of Kinesin-5 Motor Proteins — •André Düselder[1], Christina Thiede[1], Stefanie Kramer[1], Stefan Lakämper[2], and Christoph F. Schmidt[1] — [1]Drittes Physikalisches Institut, Georg-August-Universität Göttingen, Germany — [2]current address: Institute for Mechanical Systems, D-MAVT, ETH Zurich, Switzerland

Processivity for kinesins relies on communication between the two heads of a dimeric molecule, such that binding strictly alternates. The main communicating elements are believed to be the neck linkers (NL). One proposed mechanism for the coordination is the transmission of intra-molecular stress through the NL, a mechanism dubbed front- or rear-head gating. It is believed that the efficiency of gating should dependent on the length of the NL. Recent studies have presented support for a simple model in which the length of the NL directly controls the degree of processivity. Here, we have analyzed the motility of a set of six motor constructs, based on a previously published Kinesin-1/Kinesin-5 chimera, Eg5Kin, in which we have now varied the length of the NL, starting from 13 amino acids up to the native 18 amino acids of Eg5. We found, surprisingly, that neither velocity nor force generation depended on the NL length. We also found that even the construct with the shortest NL was highly processive, and that the longest NL (17 and 18 amino acids) allowed run lengths twice those of the other constructs. This finding challenges the simple model equating a short NL with tight communication, but suggests that different kinesins might be optimized for different NL lengths.

BP 16.5 Wed 16:30 H 1028

Distinct Transport Regimes for Two Elastically Coupled Molecular Motors — •Florian Berger, Corina Keller, Stefan Klumpp, and Reinhard Lipowsky — Theory & Bio-Systems, Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany

Intracellular transport of cargos is mainly achieved by the cooperative action of molecular motors, which pull the cargos along cytoskeletal filaments. These motors are elastically coupled, which influences the motors' velocity and/or enhances their unbinding from the filament. We show theoretically that interference between two elastically coupled motors leads, in general, to four distinct transport regimes characterized by different effects on the mean velocity and/or the binding time. To gain an intuitive insight in the emergence of these transport regimes, we compare characteristic time scales for the strain force generation. These time scale arguments allow us to predict the transport regimes for different pairs of identical motors. In addition to a weak coupling regime, pairs of kinesin motors and pairs of dynein motors are found to exhibit a strong coupling and an enhanced unbinding regime, whereas pairs of myosin motors are predicted to attain a reduced velocity regime. All of the predicted regimes can be explored experimentally by varying the elastic coupling strength.

BP 16.6 Wed 16:45 H 1028

Direct observation of single dyneins diffusing and interacting with microtubules in vivo — •Nenad Pavin[1,2], Vaishnavi Ananthanarayanan[1], Martin Schattat[1], Sven Vogel[1], Alexander Krull[1], and Iva Tolic-Norrelykke[1] — [1]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany — [2]Department of Physics, Faculty of Science, University of Zagreb, Zagreb, Croatia

Cytoplasmic dynein is a motor protein that exerts force on microtubules and in doing so, drives a myriad of intracellular activities from mitotic spindle positioning to chromosome movements in meiotic prophase. These forces require dynein to be anchored, where the anchoring sites are typically found at the cell cortex. The key question is which mechanism single dyneins use to accumulate at sites where they can generate large collective forces. Here we directly observe single dyneins in fission yeast, which allowed us to identify key steps of

the dynein binding process: (i) from the cytoplasm to the microtubule, and (ii) from the microtubule to the cortical anchors. We uncovered that dyneins on the microtubule move, surprisingly, either in a diffusive or a directed manner, where the switch from diffusion to directed movement occurs upon binding of dynein to the cortex. This dual behavior of dynein on the microtubule, together with the two steps of binding, constitute the mechanism how dynein finds cortical anchors in order to generate large-scale movements in the cell.

BP 16.7 Wed 17:00 H 1028

Transcriptional proofreading in dense RNA Polymerase traffic — •Mamata Sahoo and Stefan Klumpp — Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany

The correction of errors during transcription involves the diffusive backward translocation (backtracking) of RNA polymerases (RNAPs) on the DNA. A trailing RNAP on the same template can interfere with backtracking as it progressively restricts the space that is available for backward translocation and thereby ratchets the backtracked RNAP forward. We analyze the resulting negative impact on proofreading theoretically using a lattice model of transcription introduced earlier [1]. Our detail analysis indicates that the efficiency of error correction is essentially determined by the rate for the initial backtracking step, while a high transcript cleavage rate ensures that the correction mechanism remains efficient at high transcription rates [2]. Our analysis can also be applied to cases with transcription-translation coupling where the leading ribosome on the transcript assumes the role of the trailing RNAP.

[1] S. Klumpp and T. Hwa, PNAS 105, 18159 (2008).

[2] M. Sahoo and S. Klumpp, Euro. Phys. Lett. (in press) (2011).

BP 16.8 Wed 17:15 H 1028

Microtubules search for lost kinetochores by pivoting around the spindle pole — •Damien Ramunno-Johnson[1], Iana Kalinina[1], Amitabha Nandi[2], Alexander Krull[1], Benjamin Lindner[2], Nenad Pavin[1,3], and Iva Tolic-Norrelykke[1] — [1]MPI-CBG, Dresden, Germany — [2]MPI-PKS, Dresden, Germany — [3]University of Zagreb, Zagreb, Croatia

For a mother cell to divide its genetic material equally between the two daughter cells, the chromosomes have to attach to microtubules, which will pull them apart. The linkers between chromosomes and microtubules are kinetochores, protein complexes on the chromosome. The pioneering idea explaining how microtubules find kinetochores, termed "search-and-capture," states that microtubules grow radially from a centrosome in all directions and shrink back, thereby exploring the intracellular space and by chance hitting and capturing the kinetochores. In fission yeast, kinetochore capture by microtubules can be observed when kinetochores are lost in the nucleoplasm, which can be induced by spindle disassembly during metaphase. It is, however, unknown how microtubules find lost kinetochores. We observed that lost kinetochores are captured by microtubules pivoting around the spindle pole body, instead of extending towards the kinetochores. By introducing a theoretical model, we show that the observed random movement of microtubules is sufficient to explain the process of kinetochore capture. We thus reveal a mechanism where microtubules explore space by pivoting, as they search for intracellular targets.