BP 49: Molecular motors

Time: Thursday 16:45–18:45 Location: H 1028

Invited Talk BP 49.1 Thu 16:45 H 1028

Directional bias in the kinesin superfamily of molecular motors — •Robert Cross — Warwick Medical School, Coventry CV4 7AL, UK

The molecular stepping mechanisms of various members of the kinesin family are being dissected by a number of labs using experimental protein engineering and single molecule mechanics. The mechanisms of directional bias are of major interest. Kinesin-1 walks towards microtubule plus ends, holding on with one motor head and biasing the attachment direction of the other. Some of this bias may originate in electrostatic steering. The stability of microtubule binding is strain-dependent, and this gives rise to biased detachment, in which the probability of detachment of each motor head depends on the magnitude and direction of the strain it experiences. Docking and undocking of the C-terminal neck linker domain will be strain dependent and can influence both microtubule binding and binding of the ATP fuel and the ADP product of ATP hydrolysis. Altering the tethering point of the motor domains can influence direction, but does not always do so. Other contributors to directional bias are also emerging. Recently, it has emerged that kinesin-5, the architect of bipolarity in the mitotic spindle, slows down and ultimately reverses direction as the number of motors engaged with the microtubule is progressively increased. Our own most recent work addresses the influence of the ATP:ADP ratio in the bathing solution on the directionality of kinesin-1.

BP 49.2 Thu 17:15 H 1028

Microfluidic setup for highly-parallel force-velocity measurements on single motor proteins — •Marta Urbanska[1], Karl Duderstadt[2], Annemarie Lüdecke[1], Wim Walter[3], Antoine van Oijen[2], and Stefan Diez[1] — [1]B CUBE, TU Dresden, Germany — [2]Zernike Institute for Advanced Materials, University of Groningen, Netherlands — [3]Biozentrum Klein Flottbek, Uni Hamburg, Germany

Cytoskeletal motor proteins are essential for long-range, directed transport within cells. In vitro, it has been shown that external loads alter the velocity with which these ATP-driven molecules step along their filamentous tracks. So far, such force-velocity studies have been performed almost exclusively using optical traps. While optical trapping provides the highest force and spatio-temporal accuracy, it allows for one measurement at a time only. Here, we describe an alternative method to simultaneously measure multiple force-velocity relations based on the application of calibrated hydrodynamic forces to stepping motors via DNA-tethered beads. In particular, 1-um beads were attached to the SNAP-tag-labelled tails of kinesin-1 motors via λ-DNA linker. Such motor-DNA-bead complexes were applied to surface-immobilized microtubules and controlled flow was used to exert forces onto the motors. By observing the bead positions over time we were able to simultaneously track stepping of hundreds of individual motors with nanometer precision. The highly parallel nature of the measurements enables efficient collection of statistically significant quantities of data. Moreover, our approach is readily applicable to other motors and constitutes a new methodology for single-molecule force studies.

BP 49.3 Thu 17:30 H 1028

Control of cytoplasmic dynein force production and processivity by its C-terminal domain — Matthew Nicholas[1], Peter Höök[2], Sibylle Brenner[1], Caitlin Lazar[3], Richard Vallee[3], and •Arne Gennerich[1] — [1]Albert Einstein College of Medicine, Bronx, NY 10128 — [2]University of Notre Dame, Notre Dame, IN 46556 — [3]Columbia Uuniversity, New York, NY 10032

Cytoplasmic dynein is a microtubule motor involved in cargo transport, nuclear migration and cell division. Despite structural conservation of the dynein motor domain from yeast to higher eukaryotes, the extensively studied S. cerevisiae dynein behaves distinctly from mammalian dyneins, which produce far less force and travel over shorter distances. However, isolated reports of yeast-like force production by mammalian dynein have called interspecies differences into question. We report that functional differences between yeast and mammalian dynein are real and attributable to a C-terminal motor element absent in yeast, which resembles a "cap" over the central pore of the mammalian dynein motor domain. Removal of this cap increases the force generation of rat dynein from 1 pN to a yeast-like 6 pN and greatly increases its travel distance. Our findings identify the CT-cap as a novel regulator of dynein function.

BP 49.4 Thu 17:45 H 1028

Segregation of diffusible and directionally moving particles on a polar filament — •Denis Johann, Debajit Goswami, and Karsten Kruse — Saarland University, Saarbrücken, Germany

Directed transport in living cells relies on the action of motor proteins. These enzymes can transform chemical energy into mechanical work and move directionally along filamentous tracks. At the same time, these filaments serve as a substrate for the binding of proteins performing other functions, but that also obstruct the motors' motion. Motivated by the mobile cross-linker Ase1, we theoretically study a system of molecular motors in the presence of diffusible particles. Both the motors and the obstacles shuttle between the filament and its surrounding. Numerical simulations of this system show a segregation between motors and obstacles if the filament ends act as diffusion barriers for the obstacles. A phenomenological mean-field theory captures the essential effects observed in the simulations [1].

[1] Johann, Goswami, and Kruse, Phys. Rev. E **89**, 042713 (2014)

BP 49.5 Thu 18:00 H 1028

Time scales explain different transport behavior of elastically coupled molecular motors — •Florian Berger[1], Corina Keller[2], Stefan Klumpp[2], and Reinhard Lipowsky[2] — [1]Howard Hughes Medical Institute and Laboratory of Sensory Neuroscience, The Rockefeller University, 10065 New York, USA — [2]Max Planck Institute of Colloids and Interfaces, 14424 Potsdam, Germany

Cellular transport is achieved by the cooperative action of molecular motors which are elastically linked to a common cargo. When the motors pull on the cargo at the same time, they experience fluctuating elastic strain forces induced by the stepping of the other motors. These elastic coupling forces can influence the motors' stepping and unbinding behavior. To develop an intuitive understanding of cargo transport by two elastically coupled motors exposed to an external load force, we introduced four different time scales for four different processes: (i) spontaneous unbinding, (ii) force induced unbinding, (iii) force induced stalling and (iv) load sharing. In particular the time scale for load sharing allows us to predict how the regulation of single motor parameters influence the cooperativity.

BP 49.6 Thu 18:15 H 1028

Filamin Inhibition of Myosin Groups Potentiates with Group Size — Zsombor Balassy[1], •Lennart Hilbert[1,2], Nedjma B Zitouni[1], and Anne-Marie Lauzon[1] — [1]McGill University, Montréal, Canada — [2]Center for Systems Biology, Dresden, Germany

Filamin is an actin-actin crosslinker found in smooth muscle and non-muscle cells and inhibitis actin filament sliding in *in vitro* motility assays. Here, we investigate how inhibition by filamin scales with myosin group size. In our *in vitro* motility assay (smooth muscle myosin), filamin did not disrupt the bistable stop-and-go motion of actin [1], did not affect the velocity of sliding actin, but decreased the fraction of actin in the sliding state (f_{mot}). Full arrest occurred for [Filamin]=15 nM ([Actin] = 30 nM). For [Filamin]=5 nM, f_{mot} had a maximum ($f_{mot} = 0.6$) at intermediate actin length ($L = 1.0\,\mu$m). For shorter actin, f_{mot} displayed the typical reduction to lower f_{mot}. For longer actin, however, an atypical decrease of f_{mot} with L was observed ($f_{mot} = 0.45$ for $L = 1.7\,\mu$m). We extended our mathematical model of actin propulsion by myosin groups [1] and reproduced these results. The model now explicitly treats the location of myosin and filamin binding sites on actin (spacing 35.5 nm), mechanical coupling strength decays exponentially along actin (characteristic length 175 nm). In the model, filamin binding is established and resolved in locally confined domains, each of which can lead to global arrest of actin sliding. On longer actin there are more localized domains, each of which can independently arrest the whole filament, leading to a greater likelihood of arrest. [1] Hilbert et al., Biophys J, 2013

BP 49.7 Thu 18:30 H 1028

Thermodynamically consistent coarse-graining of molecular motor models — •Eva Zimmermann and Udo Seifert — II. Institut für Theoretische Physik, Universität Stuttgart

Many single molecule experiments for molecular motors comprise not

only the motor but also large probe particles coupled to it. The theoretical analysis of these assays, however, often takes into account only the degrees of freedom representing the motor. We present a coarse-graining method that maps a model comprising two coupled degrees of freedom which represent motor and probe particle to such an effective one-particle model by eliminating the dynamics of the probe particle in a thermodynamically and dynamically consistent way. The coarse-grained rates obey a local detailed balance condition and reproduce the net currents. Moreover, the average entropy production as well as the thermodynamic efficiency is invariant under this coarse-graining procedure. Our analysis reveals that only by assuming unrealistically fast probe particles, the coarse-grained transition rates coincide with the transition rates of the traditionally used one-particle motor models. Additionally, we find that for multicyclic motors the stall force can depend on the probe size. We apply this coarse-graining method to specific case studies of the F_1-ATPase and the kinesin motor.