complex, in which LIS1 binds the dynein motor domain in an ADP-VO4 transition state-specific manner. LIS1 enhanced the affinity of dynein for microtubules, but only under transition state conditions. In single molecule bead assays, LIS1 dramatically prolonged the interaction of dynein with microtubules under load, providing the first evidence for a role in dynein force regulation. To measure the resistance of dynein to detachment from microtubules directly, we have now used ''superforce'' analysis, subjecting beads with associated single dyneins to sudden increases in laser trap strength above the dynein stall force. LIS1 alone or in combination with NudE decreased the detachment of dynein from microtubules by up to 5-fold. To test how LIS1 and NudE affect dynein force production under multi-motor conditions, we monitored beads coated with ~2-3 dynein molecules at a laser trap strength of 3.7 pN. LIS1 and NudE induced an increased frequency of multi-motor events and caused a dramatic increase in trap escape. In silico simulations confirm that the prolongation of individual dynein-microtubule interactions should result in enhanced force production by multiple motors. These results appear to explain the need for LIS1 and NudE in dynein-dependent, high-load intracellular movements, where multi-motor activity is critical. Support: GM47434, GM068952, HD40182, GM070676.

**3779-Pos**
**Dynamic Regulation of Bidirectional Vesicle Transport**
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The motor proteins dynein and kinesin function collectively to achieve long-range, bidirectional transport along microtubules. Transport in live cells, imaged using phase microscopy, exhibits distinct modes of motility, with fast, unidirectional movement in both anterograde and retrograde directions as well as saltatory, bidirectional movement. To examine transport in a simplified environment, we isolated axonal transport vesicles from transgenic mice expressing GFP-dynamitin. The fluorescent vesicles were imaged with high resolution using total internal reflection fluorescence microscopy. Using automated tracking software, we tracked all vesicles associated with polarity-marked microtubules. The purified vesicles move bidirectionally with 40% of motility in the anterograde direction and 60% in the retrograde direction, similar to the bidirectional population of vesicles observed in live cells. Inhibitory antibodies to dynein modulate the direction of transport. We compared the predictions of a simple tug-of-war model, proposed by Müller et al., [PNAS, 2008] to the observed motility in vitro, and found good agreement when 6-7 dynein motors and 1 kinesin motor are active. This prediction is in striking agreement to quantitation of motor numbers through photobleaching and quantitative western blotting, which estimate approximately 6 dynein motors per vesicle and a ratio of $6.3 \pm 0.7$ dynein motors to each kinesin-1 motor. Together, the analysis of vesicle transport in live cells, purified vesicles in vitro, and mathematical modeling indicate that vesicles move robustly with a small complement of motors. The results suggest an efficient regulatory scheme where small changes in the number of active motors manifest in large changes in the motility of the cargo.

**3780-Pos**
**Steady States of a tug-of-war Model for Organelle Transport**
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Constructing a reasonable model to describe the motion of organelles and vesicles moved by motor proteins in cells is not straightforward but may assist in understanding the mechanism. Recently, Muller, Klumpp and Lipowsky (PNAS 105, 4609-14, 2008) have developed a tug-of-war model to describe this motion. Their model exhibits several qualitatively different motility regimes that depend on the precise value of the single motor parameters. They suggested that parameter variation could be used by a cell to regulate its cargo traffic. We have carried out a detailed theoretical analysis of this tug-of-war model in the limit that the numbers of the two different motor species bound to the cargo becomes large [1]. All the stable, i.e., biophysically observable steady states and their stability domains can then be obtained. Depending on the parameter values, the tug-of-war model may exhibit either uni-, bi- or tristability. The steady state motion of the cargo, transported by two different motor protein species, is determined by the initial numbers of the motors bound to the track. Monte Carlo simulations confirm that our theoretical results are accurate when there are a large number of motors but also remain useful for only a few motors. Theoretical analysis of the small motor-number situation is planned.
[1] Y. Zhang, Phys. Rev. E. 79, 061918 (2009).

**3781-Pos**
**Non-Monotonic Force-Dissociation Rate Relation Improves Ensemble Performance of Multiple Molecular Motors**
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Molecular motor-based intracellular transport is important for cell function. There is mounting experimental evidence that multiple motors work together to transport cargos in a cell. However, how these motor assemblies perform collectively is poorly understood and in particular it is still unclear how different mechano-chemical parameters of single motors affect ensemble function. Here we investigate whether using monotonic force-dissociation relation above and below motor stall force is a correct approximation for single motor dynamics and whether it can reproduce experimentally observed in-vitro multiple motor behavior. This is a relevant and important question because recent models of multiple motor based transport use Kramers's theory formula for the force dependent dissociation rates of a single motor employing an assumption that the force-dissociation relation for single motors is monotonic. We find that a detailed analysis of our experimental observations is inconsistent with such an assumption. Instead, we propose a class of single motor models where force dissociation relations need not be monotonic above single motor stall force and which successfully explain the experimental observations.

**3782-Pos**
**The Birefringence and Molecular Fine- Structure of Axonemes**
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To shed light on the molecular arrangements and structural changes occurring inside microtubule based structures, we observed single axonemes using a liquid crystal polarized light microscope (LC-PolScope, Oldenbourg et al., Biophys J., 74, 645-54, 1998) to measure their birefringence, a sensitive indicator of structural parameters characterizing ''crystal-like'' biopolymers directly in living cells. The birefringence of rod-like particles such as axonemes is caused by their shape and by the arrangement of molecular bonds inside their structure. The latter is called intrinsic birefringence and can be used to monitor the molecular conformation during dynamic processes such as axoneme beating under physiological conditions. Similar to microtubules, we found that axonemes have an intrinsic birefringence that is about 10% of their total birefringence and that can be used to detect structural changes inside axonemes by measuring their retardance (=birefringence times thickness of sample) with polarized light microscopy. We analyzed individual axoneme retardance and found that the maximum retardance of a single demembranated axoneme was 1.7nm. After extracting the outer dynein arms the retardance decreased to ~1.3nm. Thus, dynein molecular motors contribute to the birefringence of axonemes. We also analyzed the retardance of static axonemes that were bent as a result of axonemal beating frozen due to ATP depletion. The axoneme retardance varied in a systematic manner that seemed to be related to the curvature of the bends. Our combined results lead us to propose that the structure of microtubules and dynein contribute to axoneme birefringence, in addition to its form birefringence. The intrinsic birefringence of bent axonemes is likely caused by structural changes inside axonemes and is affected by the mutual interactions between microtubules and dynein molecular motors.

## Cell & Bacterial Mechanics & Motility III

**3783-Pos**
**Physics of Phagocytosis in Self Recognition: Particle Size and Myosin Forces**
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Cells make a number of key decisions by actively applying forces to the objects that they 'touch'. How a macrophage decides to adhere to and 'eat'a foreign object (microbes to drug carriers) while leaving 'self'cells alone is a central decision in macrophage function. The molecularly specific adhesion systems that activate (or inhibit) will be shown to function from nanometer to micron length scales and to be made efficient by signaling (or not) to force-generating myosin motors in macrophages. Additional effects of particle shape - relevant to filamentous viruses perhaps - will be discussed. Collectively, the results suggest new means of achieving compatibility and the CD47 findings even appear relevant to engraftment of stem cells.