Cooperative Transport by Molecular Motors

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Molecular motors are proteins that transform chemical energy into work and directed movement. Our group is particularly interested in cytoskeletal motors which transport cargoes along the tracks provided by the filaments of the cytoskeleton. Our current understanding of these motors is to a large extent based on biomimetic model systems which consist of only a small number of different components such as motors, filaments, and ATP, the chemical fuel used by these motors. These systems allow us to study molecular motors systematically within a controlled environment.

Important quantities that characterize molecular motors are their velocity and their run length. The latter quantity describes the distance over which the motor moves along the filament before it falls off the track. This run length is typically 1 µm for a single motor molecule. Such unbinding events are unavoidable for molecular motors since they constantly undergo thermal collisions with other molecules.

Cooperative Cargo Transport by Several Motors

In cells, cargo particles such as vesicles and organelles are usually transported by teams of several molecular motors. Because each motor unbinds from and rebinds to the filament, the actual number of motors is not fixed but varies with time. We have developed a model for this type of transport process based on the known properties of single motor molecules **[1]**. This model describes the movement of a cargo particle to which a number N of motors are immobilized. These motors bind to and unbind from a filament in a stochastic manner, so that the number of motors that actually pull the cargo changes stochastically between 1 and N, as shown in **Fig. 1**. The theoretical predictions derived from our model are accessible to in vitro experiments using the same techniques that have been used to study single motors.

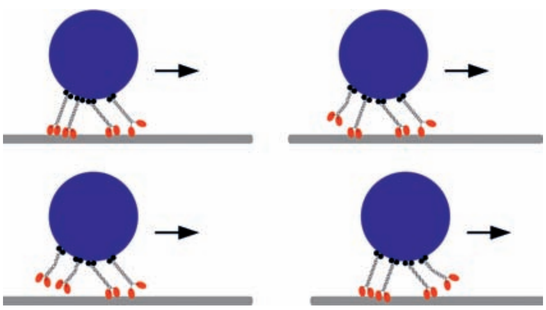

Fig. 1: A cargo particles (blue) is pulled along a filament (grey rod) by four molecular motors. These motors bind to the filament and unbind from it in a stochastic manner, so that the number of actually pulling motors changes between 1 and 4.

The main effect of motor cooperation is an enormous increase in run length, which depends exponentially on the number of motors. We have estimated that 7-8 motors are sufficient for transport over centimetres and that the cooperation of 10 motors leads to run lengths of over a meter **[1]**. Transport over such long distances occurs in the axons of nerve cells, which represents the biggest challenge for long-range transport in cells. The increase in run length has recently been confirmed in experiments done in the group of R. Dimova using latex beads pulled by varying numbers of kinesin motors.

If the cargo is pulled against an opposing force, its movement is slowed down. In addition, the force increases the motors' tendency to unbind from the filament. Since unbinding of motors increases the force that the remaining bound motors have to sustain, this increases their unbinding probability even further and leads to a cascade of unbinding events. As a result of these unbinding cascades, the force-velocity relationship for a cargo pulled by several motors is markedly non-linear, in contrast to the approximately linear force-velocity relations observed for single motors (see **Fig. 2**).

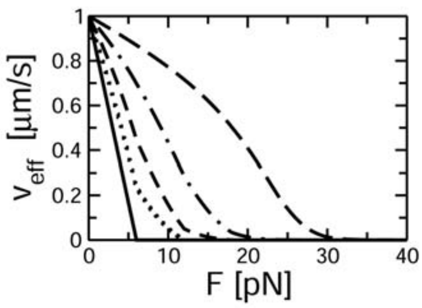

Fig. 2: The force-velocity relation for cargoes transported cooperatively by N motors against an opposing force F. The graph shows curves for N=1,2,3,5, and 10 (from left to right). While the velocity exhibits a linear decrease for a single motor, the curves are non-linear for transport by more than one motor due to the forced decrease of the number of bound motors.

Unbinding cascades also play an important role in systems where cargoes are pulled by two types of motors which move into opposite directions. In that case, the unbinding cascades lead to a tug-of-war-like instability. As a consequence of that instability, the cargo is not stalled by being pulled into opposite directions, but rather switches stochastically between quick runs back and forth **[2]**.

Active Diffusion

Passive diffusion or Brownian motion is too slow to transport larger objects such as vesicles and organelles within cells. This fact is usually taken as an argument for the necessity of active transport. Active transport, however, is not necessarily directed, but can also be used to generate effectively diffusive movements, e.g. if the direction of motion of a motor-driven cargo particles changes from time to time in a random fashion. We call the resulting diffusive, but energy-consuming movements *active diffusion*. There are examples for active diffusion within cells, but active diffusion can also be used in artificial systems as a method to speed up diffusive processes such as the search for an immobile binding partner. Such artificial systems can be expected to have many applications in bionanotechnology. We have studied active diffusion for several systems with regular arrangements of filaments on structured surfaces (see **Fig. 3**) which can be prepared using a number of techniques established during recent years. Our theoretical results indicate that active diffusion is most useful for the transport of large objects – for micron-sized particles in water active diffusion can be 100 times faster than passive Brownian motion – and/or for transport in very viscous environments. Again the cooperation of several motors is helpful, since the maximal active diffusion coefficient that can be generated is proportional to the product of run length and motor velocity.

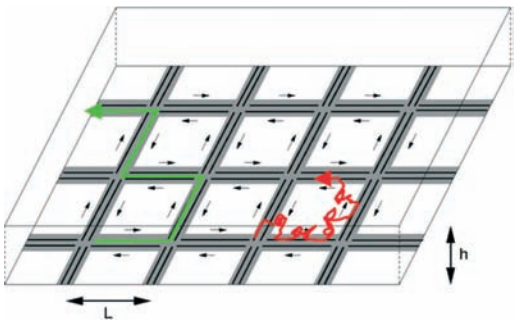

Fig. 3: An array of filaments (black lines) specifically adsorbed on a structured surface. The molecular motor-driven movements along such filament systems exhibit active diffusion, energy-consuming, but effectively diffusive movements as indicated by the green and red trajectories. The characteristic diffusion coefficient of these movements can be much larger than the usual diffusion coefficient which arises from Brownian motion.

Traffic Phenomena

If many molecular motors (or cargo particles pulled by molecular motors) move along the same filament, the traffic may become congested. In contrast to the familiar vehicular traffic jams, however, molecular motors can escape from a congested filament by unbinding from it. We have studied traffic jams of molecular motors that arise from different types of bottlenecks and in different types of compartments **[4]**. In particular, we have recently studied the effect of defects on the filaments and the influence of the compartment geometry on the length of traffic jams. In the latter project, we found that in several types of tube-like compartments, traffic jams are strongly enhanced by the compartment geometry.

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