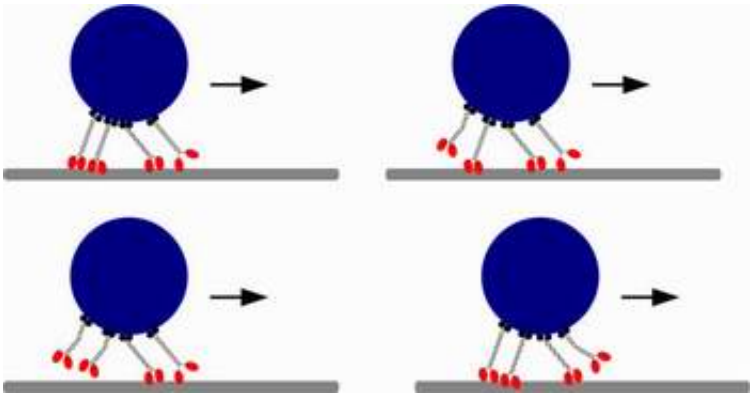
Marathon of Nano-Sprinters

November 16 2005



Processive bio-molecular motors, which move actively along cytoskeletal filaments, drive the cargo traffic in cells and in biomimetic systems. A single motor molecule is sufficient for continuous transport of cargoes such as vesicles or latex beads over a few micrometers. To achieve transport over larger distances, several motor mole-cules have to cooperate. Scientists from the Max Planck Institute of Colloids and In-terfaces in Potsdam have now developed a new theory that only seven or eight mo-tor molecules are sufficient for directed transport over centimeters or even meters.

Image above: Different bound states of a cargo particle, with several molecular motors which move along a filament. Each motor can unbind from and rebind to the filament, which implies that the number of motors that actually pull the cargo varies with time. (Max Planck Institute of

Colloids and Interfaces)

They also show that an applied load force, which is shared by the pulling motors, strongly reduces the cargo velocity and leads to a highly nonlinear force-velocity relationship (PNAS, Advanced Online Publication, November 14-18, 2005).

Molecular motors are nano-tractors for all kinds of cargo within the cells of living beings. They move in a stepwise manner along filaments of the cytoskeleton, consuming energy provided by the hydrolysis of ATP, which can be considered the fuel of the cell. Kinesin and dynein motors move along microtubules and myosins move along actin filaments. The step sizes of these motors are of the order of 10 nm. By stepping in a directed fash-ion along filaments, the motors pull cargo particles which are much larger than the mo-tors themselves. In addition to their importance for the functioning of cells, molecular motors have many possible applications as biomimetic transport systems and are likely to become a key component in the emerging bio-nanotechnology.

Active transport driven by molecular motors is particularly important for nerve cells, or neurons. These cells have extended compartments, axons, which connect the cell body with the synapse, where the nerve signals are transmitted from one neuron to another. The length of axons is in the centimeter or even meter range; examples of relatively long axons are those that connect our spinal cord with the tips of our fingers and toes. Within such an axon, microtubules provide the tracks along which molecular motors transport their cargo, such as vesicles filled with neurotransmitters.

During the last decade, our knowledge about molecular motors has increased rapidly. This was mainly due to the development of powerful single molecule experiments and biomimetic model systems which permit the study of molecular motors outside cells in a systematic

fashion. One example is the bead assay, where filaments are immobilized on a surface. Molecular motors pull latex beads along these filaments, and the movement of the beads is observed under the microscope.

One important result of these experiments is that molecular motors, unlike railways or cars, have a strong tendency to fall off their track and diffuse away into the surrounding aqueous solution. This is a direct consequence of their nanoscale size which makes them rather susceptible to thermal noise. Thus, a single molecular motor can only 'grab' onto the filament for a relatively short time, on the order of one second. During this time, a single motor covers about one micrometer, which represents only a tiny fraction, about 1/10000, of the long transport distances for cargo particles in axons. In other words, a single motor behaves much like a sprinter, whereas the whole cargo performs a mara-thon.

Scientists of the Max Planck Institute of Colloids and Interfaces in Potsdam have now provided a simple solution to this puzzle. If the cargo is pulled by several motors as shown in Fig.1, any motor that unbinds from the filament will stay close to that filament as long as the cargo and filament are still cross-linked by at least one bound motor. In such a situation, the unbound motor can rebind to the filament and then continue to pull the cargo - in contrast to human sprinters, molecular motors don't get tired.

This mechanism has been derived from a new theoretical model, which distinguishes the different bound states of the cargo particle and describes the transitions between these states. Using this model, the Max Planck scientists have been able to calculate several transport properties, such as the average velocity and the average walking distance of the cargo particle as a function of the maximum number of motors that can pull this par-ticle. For kinesin motors, for example, calculations show that only seven or eight motors are sufficient for the transport over

centimeter distances and that a cargo particle pulled by 10 motors has an average walking distance of about 1 meter.

If molecular motors move against an external load force, this force is shared among the pulling motors. One obvious consequence is that the movement of the cargo is slowed down. In addition, the force felt by each pulling motor strongly increases the unbinding probability for such a motor. Furthermore, as more motors unbind, each of the remaining pulling motors has to sustain a larger force, which would mean that their unbinding probability increases even further. This leads to a cascade of unbinding processes and to a strongly nonlinear dependence of the cargo velocity on the external load force. Simi-lar cascade processes are expected in more complex situations, in which the cargo transport is performed by different types of molecular motors.

All transport properties predicted by the new theory can be investigated in experiments using techniques which have been developed for single motors. In fact, preliminary ex-periments at the Max Planck Institute in Potsdam agree with the theoretical predictions. Likewise, the quantitative theory should also be useful in order to design biomimetic transport systems for lab-on-a-chip applications -- in which, for example, molecular mo-tors transport certain molecules to specific reaction sites. Depending on the arrange-ment of the filaments in these systems, varying the travel distance provides a strategy to control either the localization of the reagents to their target sites or, alternatively, their diffusion, which is enhanced by motor-driven active transport.

Source: Max Planck Institute of Colloids and Interfaces