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Press Release

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Motor Transport in Bio-Nano Systems

Max Planck researchers determine optimal parameters for biomimetic transport systems based on molecular motors

Molecular motors are nanoscale engines which move along very thin rod-like filaments and, in this way, drive the heavy traffic of molecular cargo within biological cells. Both motors and filaments can be isolated from the cells and used to construct biomimetic transport systems. In order to increase the flux of the cargo transport, it would be necessary to increase the number of motors that contribute to this transport but, at the same time, avoid the build-up of traffic jams. Scientists from the Max Planck Institute of Colloids and Interfaces in Potsdam and from the University of Amsterdam have now modelled and simulated the motor traffic for different compartment geometries and filament arrangements, and have determined the optimal conditions for the transport of nanocargo in these systems (Biophysical Journal, 88, 3118-3132, May 2005).

Each cell of our body contains a huge number of small vesicles which exhibit complex patterns of intracellular traffic: some vesicles travel from the cell center to the periphery and vice versa, some shuttle between different organelles or cellular compartments. An extreme case is provided by the long-ranged transport of vesicles and organelles along the axons between our nerve cells, which can be as long as half a meter. All of these movements are based on two molecular components: very thin rod-like filaments, which form a complex network of rails, and molecular motors, which move along those filaments and carry vesicles and other nanocargo along. When bound to the filaments, the motors are able to transform the chemical energy of a single ATP molecule into mechanical work. In this way, they can utilize the smallest possible amount of fuel.

Both filaments and motors can be isolated from biological cells and used to construct biomimetic transport systems. A relatively simple example for such a system consists of filaments which are aligned on a substrate surface as shown in Figure 1. The filaments are polar and have two different ends, a ‘plus’ end and a ‘minus’ end. In Figure 1, the filaments are arranged in such a way that all ‘plus’ ends point into the same direction. Such an arrangement provides many parallel tracks for the molecular motors and, thus, represents a multi-lane highway in the nanoregime. Using such a biomimetic model system, scientists can study the transport properties in a quantitative manner, identify useful control parameters, and determine the functional dependence of the transport properties on these parameters. This is the only possible strategy to obtain the basic knowledge that is necessary to improve the system design and to optimize its performance.

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We now have a basic understanding of the behavior of single motors. These motors are dimeric proteins with two legs, which make discrete steps along the filament. Each step corresponds to a motor displacement of about 10 nanometers, comparable to the size of its legs. In one second, the motor makes about 100 steps which leads to a velocity of about one micrometer per second. The absolute value of this velocity is not very impressive, but relative to its size, the motor molecule moves very fast: indeed, on the macroscopic scale, its movement would correspond to an athlete who runs 200 meters in one second! This is even more surprising if one realizes that the motor moves in a very viscous environment since it steadily undergoes many collisions with a large number of water molecules. Because of these collisions, the molecular motor has a finite run length: After a few seconds, it unbinds from its track and performs random Brownian motion in the surrounding water until it rebinds to the same or another filament.

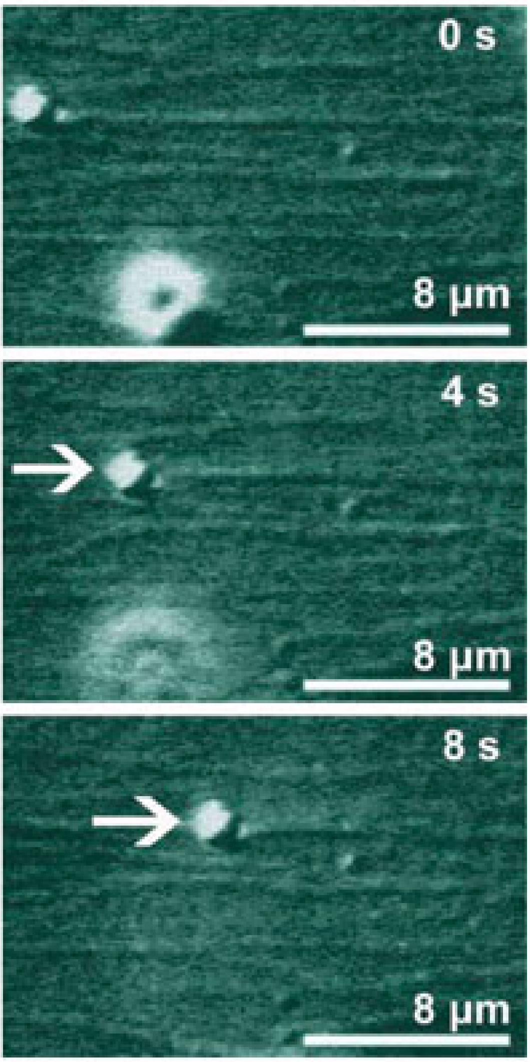

Fig. 1: *Three snapshots showing the transport of a micrometer bead (white arrow) at 0, 4, and 8 seconds. The bead is pulled by molecular motors, which are too small to be visible, along parallel filaments, which are immobilized on a substrate surface. All filaments are aligned in such a way that their 'plus' ends point to the right and form a multi-lane highway in the nanoregime. The bead moves about 8 micrometers in 8 seconds; during this time, each motor makes about 800 steps.*

Image: Max Planck Institute of Colloids and Interfaces

In order to understand the motor traffic in biological cells and in biomimetic systems, it is necessary to go beyond the single motor level and consider the cooperative behavior of many motors. To obtain a large flux of cargo transport, it is obviously useful to let many motors work in parallel. However, when several motors move along the same track, they start to bump into each other and to form molecular traffic jams. These jams are similar to the jams on our highways but there are also important differences. First, the molecular motors cannot `see' other motors and their cargo before they bump into them. Second, in contrast to our cars, which cannot leave the highway when they are caught in a jam, the molecular motors can unbind from the filament and, thus, escape into the third dimension.

In order to study these complex patterns of movements, the Max Planck researchers have developed new theoretical models which are based on the known properties of single motors and which enable them to study the cooperative behavior of many motors and their interactions. In the framework of these models, one can determine the functional dependence of the motor transport on the compartment geometry and on the arrangement of the filaments. Two particularly interesting architectures are uniaxial arrangements of filaments within tube-like compartments, which resemble axons of nerve cells, see Figure 2, and radial arrangements of filaments within disk-like compartments, which resemble large cells adhering to a substrate surface.

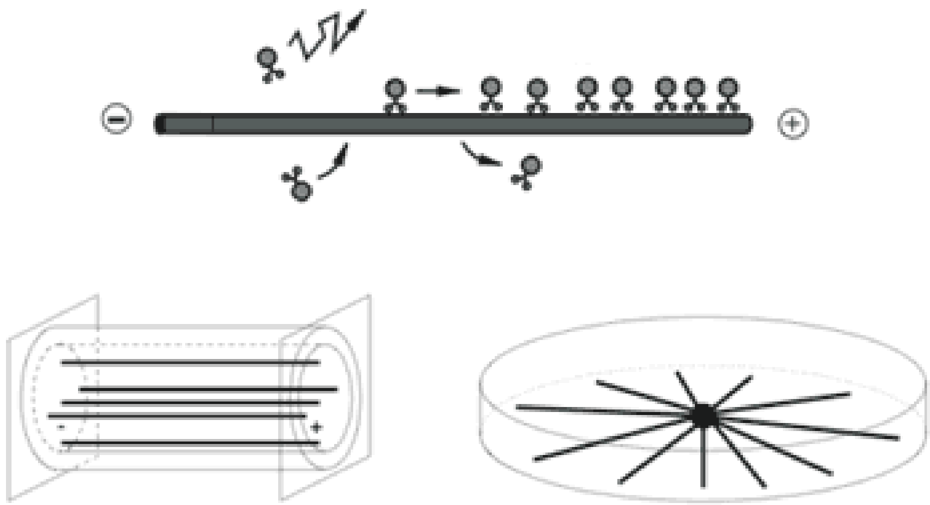

Fig. 2: *(Top) Schematic diagram of molecular motors that run along a single filament or diffuse in the surrounding water. The running motors form a traffic jam close to the 'plus' end of the filament. (Bottom) The jamming effect depends strongly on the compartment geometry and is much more pronounced in uniaxial systems (left) than in radial systems (right).*

Image: Max Planck Institute of Colloids and Interfaces

Surprisingly, the geometry of the system has a rather strong effect on the build-up of traffic jams. In uniaxial systems, traffic jams cannot be avoided as one increases the number of motors involved in the cargo transport. In radial systems, on the other hand, jams can be avoided, to a large extent, provided the motors leave the filament sufficiently fast after they have reached its 'plus' end. However, both types of systems exhibit a characteristic, intermediate motor concentration for which the cargo transport is optimal. With the models the researchers can predict how this optimal motor concentration depends on the single motor properties.

The theoretical results are in agreement with the available experimental data, both for biomimetic systems and for biological cells. The theory has been extended to more complex systems such as two-way traffic of two motor species that move along the same filament but in opposite directions. The latter system exhibits a genuine phase transition from a low flux to a high flux state. Likewise, regular patterns of filaments have been shown to lead to enhanced motor diffusion along the substrate surface. All of these results have been obtained from a combination of analytical calculations and computer simulations.

These theories can guide the design of new transport systems by exploring different system architectures in a systematic way before they are actually constructed in the lab. The enhanced diffusion of motors at regular patterns of filaments provides an instructive example: When integrated into existing microarrays for DNA and RNA hybridization, these transport systems would act to increase the hybridization rates.

In general, biomimetic systems based on molecular motors and filaments have many potential applications in bionanotechnology, pharmacology, and medicine. During the next couple of years, we may witness the development of sorting devices for biomolecules and biocolloids, drug delivery systems that utilize the motor transport within human cells, and motile components for nanoscale manufacturing. Long term, we should also be able to construct `smart' biomimetic systems which are able to respond to and `survive' in a changing environment.

Original work:

Stefan Klumpp, Theo M. Nieuwenhuizen, and Reinhard Lipowsky
Self-organized density patterns of molecular motors in arrays of cytoskeletal filaments
Biophysical Journal 88, 3118-3132 (2005)

Stefan Klumpp and Reinhard Lipowsky
Phase transitions in systems with two species of molecular motors
Europhysics Letters 66, 90-96 (2004)

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