Nanofabricated Devices Based on Molecular Motors: Biosensing, Computation and Detection

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Naturally occurring machines are ubiquitous in nature. For example, plants, algae and cyanobacteria use sunlight (radiant energy) and water to create fuel (energy-rich chemical substances), in the process of photosynthesis. These and other chemical substances are also used as energy sources for other reactions in nature, such as the generation of motion by molecular motors. Due to their high energy-efficiency, speed, flexibility and ability to transport cargo, these molecular motors have been proposed as nano-sized machines for use in, for example, diagnostics and drug discovery. Using state-of-the-art technology, it is possible to control these molecular motors in an artificial environment, and harness their unique self-propelled motion in a range of other applications. Figure 1 shows actin filaments transported by myosin motors over a planar substrate. The actin filament is labeled with fluorescent molecules to allow for viewing in a fluorescent microscope. This thesis is focused on the use of myosin motors, which transport actin filaments, however, the kinesin-microtubule motor system is also commonly used for similar techniques.

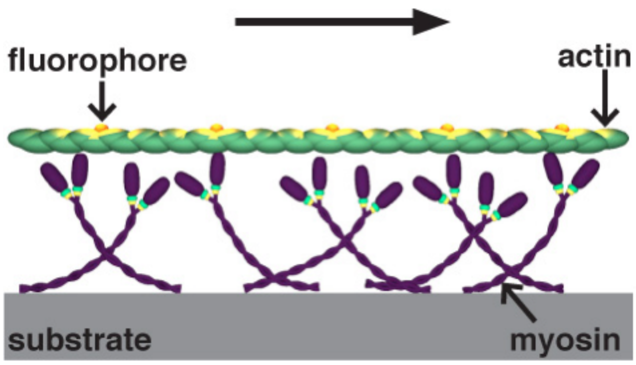

Figure 1. Schematic of actin filaments propelled by myosin motors. Myosin is immobilized on a substrate. Fluorescently labeled actin filaments glide along the surface as they are propelled by the myosin. The conformation of myosin is directly related to the surface properties of the substrate.

Nano-scale structures. The structural elements, used for controlling molecular motor motion, are typically a few hundred nanometers wide (1 nanometer is 1 billionth of a meter, e.g. 10,000 times smaller than the width of a human hair), and a few or few tens of micrometers long, having similar dimensions as the molecular motors (myosin; 5 by 70 nanometers and actin; 10 by several 1000 nanometers). In this size range, many individual devices can be patterned onto millimeter-sized samples (chips), where experiments are carried out. This type of work is known as a lab-on-a-chip technology. Within this thesis I describe the fabrication of nano-scale structures, such as nanochannels and nanowires, on millimeter sized chips for two particular applications i.e. biosensing and biocomputation with molecular motors. The continued advancement of these types of structures will likely provide more opportunities for molecular motor research to expand in other areas of science and medical diagnostics.

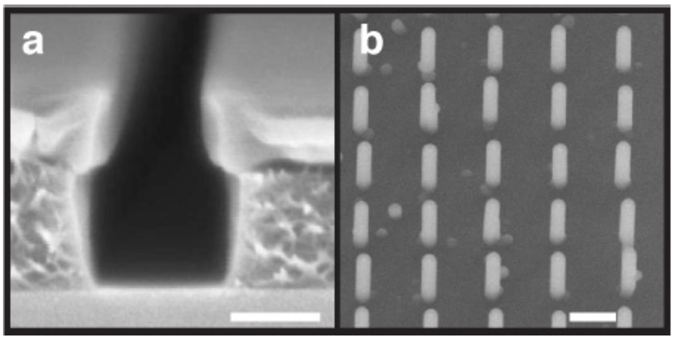

Figure 2. Scanning electron micrographs of nanostructures for molecular motor control. a) Cross-sectional view of nanochannel made from polymer resists on top of silicon oxide substrate. Guidance through these nanochannels is well controlled in one-dimension. Scale bar: 200 nm. b) Side view of nanowires for use in biosensing devices. These nanowires are coated with an aluminum oxide layer in order to achieve suitable adsorption of molecular motors for actin filament guidance. Nanowire diameter and length here is approximately 200 nm and 1 µm, respectively. Sample tilt: 30°. Scale bar: 500 nm.

Three-dimensional interactions. By harnessing the robustness of these molecular motors it has been shown previously, that a variety of devices can be made to control the molecular motors and cytoskeletal filaments outside of their natural environment. However, these studies use motors in two dimensions, which can be seen as a primary limitation in, for example, understanding how myosin interacts with the actin under physiological conditions. Therefore, I show here how hollow nano-sized tubes (hollow nanowires) can be used to achieve interactions, between actin and myosin in a three-dimensional environment, at physiological length scales. These hollow nanowires may also prove useful in other applications described below.

Biosensing and diagnostics. The primary aim of biosensing is to be able to identify the presence of a very small amount of a chemical substance, which is useful for example, it patient diagnostics. Through the use of molecular motors and engineered nano-structures there is a high potential to be able to sense foreign molecules and diagnose patients, while using a very low sample volume. Recent demonstrations reveal that it is possible to collect and concentrate very small amounts of molecules on a chip using kinesin molecular motors transporting microtubules. Here, I show how myosin molecular motors transporting actin filaments can be used to concentrate molecules attached to actin in two-dimensions on a surface or in one-dimension on nanowires. Here, the devices operate in a much shorter temporal and spatial scale than those previously demonstrated devices. These results are highly relevant for fast diagnostics and performance in lab-on-a-chip technology.

Biocomputation. Molecular motors can also be useful within the field of computational mathematics. It is known that problems exist for which there is no fast way to determine a solution. These problems arise in areas of, for example, cryptography (encryption and decoding) and in optimization (network routing). An example optimization problem is the traveling salesman problem, which asks for the optimal (shortest) path that a salesman (motile agent) can take to visit all cities (points) on a map (network) exactly once. Such problems quickly become difficult for modern computers when the number of cities becomes very large. Molecular motors, however, have been proposed as a possible substitution. By finding solutions in parallel, they can effectively decrease the computation time. Here, I show how myosin and actin filaments can be used to find all solutions to a given instance of a problem mapped out into a two-dimensional network of nano-sized channels, in a fast and energetically efficient way. I also discuss the challenges of scaling-up such a device for solving computationally more challenging problems.

Architectural elements. While the above mentioned biocomputation device has potential for solving highly complex mathematical problems, the scaling up of such a device requires the development of architectural elements to increase performance. In scaling up these biocomputation devices, the number of agents (actin filaments) and outputs (solutions) also increases quickly. Therefore, I show here how oxide coated metal detectors can be used to count and track these filaments. A secondary requirement for biocomputation is to provide error-free computations, which can be extremely detrimental when scaling up such a device. Here, I show how hollow nanowires can be used to transport actin filaments in a fully enclosed one-dimensional channel. By using these hollow nanowires, it is possible to remove error in the biocomputation network and essentially eliminate error.