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Manipulating a single microtubule by light

A cell is basically a miniature factory, which contains a large number of dedicated protein machines to perform various mechanical functions. For example kinesin is a linear motor protein which transport cargos such as organelles, chromosomes and vesicles along cytoskeletal tracks using chemical energy from ATP. In terms of energetic efficiency, biological machines can be superior to currently available man-made machines. Inspired by these natural wonders, it is worth developing molecular machines that exhibit controlled mechanical motion and perform sophisticated tasks in an artificial environment. In future, molecular machines can be utilized for the applications ranging from the controlled delivery of a therapeutic cargo in our body to the active separation (sorting) of molecules for the analysis with a high sensitivity. To actualize this, the system should ideally act in a reversible manner, with the capacity to complete repeated mechanical operations. Spatial and temporal controlling over this motion are further hallmarks of successful machines. One possible approach for building such molecular machines is to combine natural molecules such as proteins or DNAs in our body with synthetic molecules in order to control the functions of natural molecules.

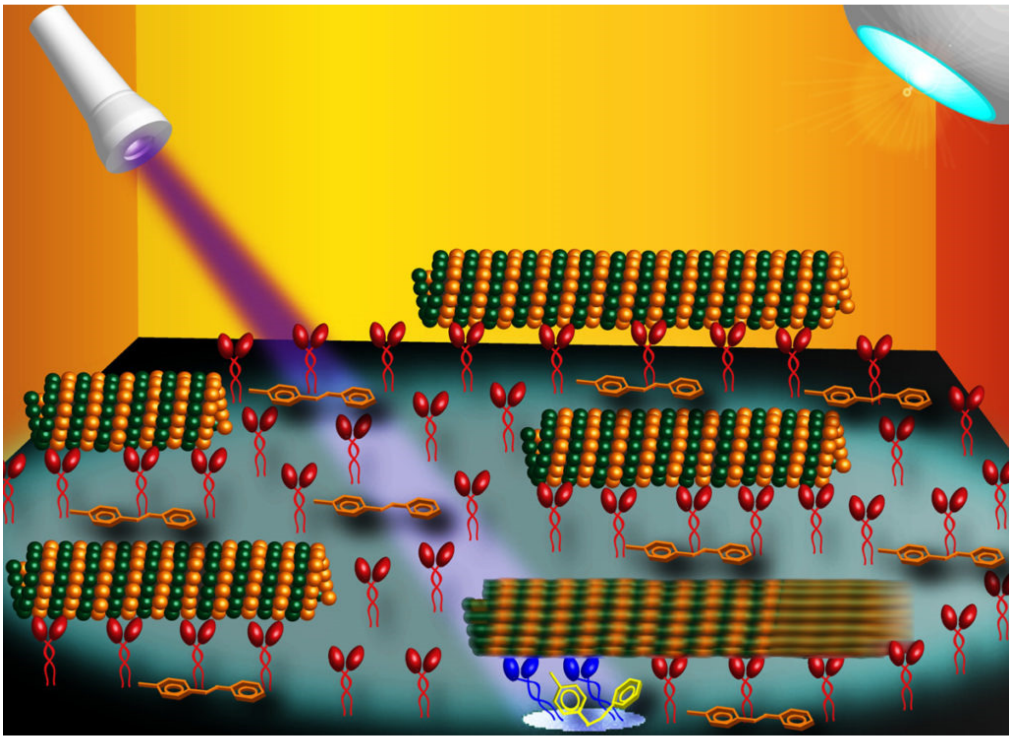

Fig. 1. Schematic drawing showing selective driving a single microtubule by light. We can see a gliding microtubule under the illumination by a spot of near ultra violet light deactivating the inhibitor and other microtubules under blue light completely arrested by the function of active inhibitor for the kinesin.

Building on our previous work realizing the complete ON/OFF photo-switching of the motility of a nano-biomolecular machine, we developed a molecular system which allows free regulation of the motion of single microtubules on kinesin. The microtubules, tube-like well-defined structures of tubulin proteins with

25 nm in diameter, could potentially serve as carriers of various molecular cargos in future nano-transportation systems. In our recent article (*Lab chip*. 2016, 16, 4702), we successfully demonstrated the local concentration and dispersion of the microtubules at any desired position and time on plain glass substrate without any surface patterning. We have also performed several selective and specific regulations of single microtubules, for example transporting, bending, and cutting, all under the influence of light (a movie: https://www.youtube.com/watch?v=d2Ul_RhooV4).

The key to this success was the synthesis of a photo-switchable inhibitor for the motor protein kinesin, which propels the microtubules by using the energy from ATP. In addition a new optical set up – illuminating areas of the sample at two different wavelengths of light – which deactivates the inhibitor precisely at the location of a target single microtubule and activates the inhibitor in the surrounding area to arrest all other microtubules.

Our strategy was to use a reversibly photo-switchable agent-azobenzene to solve the diffusion problem. We introduced the azobenzene structure to the inhibitor molecules via a covalent bond, to reversibly switch the inhibition property upon photo-isomerization of azobenzene through the illumination of light at an appropriate wavelength selected from blue or near ultra violet. The diffusing deactivated inhibitor molecules from the target microtubule's site are photochemically activated again by the blue light immediately after reaching the surroundings.

Although we could selectively transport single microtubules at any desired moment by photo-irradiation, it was still difficult for us to change the direction of the movement by light. At the moment, in order to change the direction of a microtubule we are interested to prepare light pathways in advance. Therefore our next goal is to develop a method to change the direction of the movement of microtubules by photo-irradiation.

In the present work we used kinesin-1. However, among the kinesin family there are other proteins such as EG5 and CENPE, that are target molecules for anti-cancer drugs. We believe that our concept of photo-responsive inhibitors can be applied to the targeted drug delivery for cancer treatment. In future nano-medical application we could envisage that the inhibitor function is switched on at the cancer cell sites by the irradiation at the suitable wavelength while at healthy cells' site the inhibitory activity can be ceased by light at the other wavelength.

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Publication

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