MOLECULAR MOTORS

Shifting gears with light

The speed and direction of myosin and kinesin motors can be optically controlled by adding a protein domain that changes conformation in response to blue light.

Samara L. Reck-Peterson

The transport of intracellular cargoes, which is required for the movement, division and homeostasis of cells, as well as communication between cells, is powered by molecular motors that travel along the cytoskeleton. These motors — myosins, kinesins and dyneins — move either along actin (myosins) or microtubule (kinesins and dyneins) tracks, which are polar polymers with distinct ends termed 'plus' and 'minus'. The polarity of the tracks governs the directionality of the motors, and myosins and kinesins are part of large gene families where members have evolved to be either plus- or minus-end-directed motors.

Decades of experiments on these motors has led to a detailed understanding of how they move unidirectionally along their respective filaments[1]. More recently, myosin and kinesin have also drawn attention as potential tools for nanotechnology. However, exploiting our knowledge of these natural motors to engineer variants that can be controlled by external signals is a significant challenge. Writing in *Nature Nanotechnology*, Zev Bryant and colleagues at Stanford University now report engineered myosin and kinesin motors whose speed and directionality can be controlled by light with the help of a genetically encoded photosensor[2].

Myosins and kinesins are distantly related to each other and their motility mechanisms share similarities[3]. Structural changes that occur during the adenosine triphosphate hydrolysis cycle in myosins drive rotation of a 'converter' domain. This rotation is amplified by a 'lever arm' to generate force, in a process termed the 'power stroke'. The length of the lever arm and its position within the structure determines the directionality of the motor. For example, a type of myosin known as class VI myosins walk towards the minus end of actin filaments due to a unique insert at the base of their lever arm (Fig. 1a)[4]. Other classes

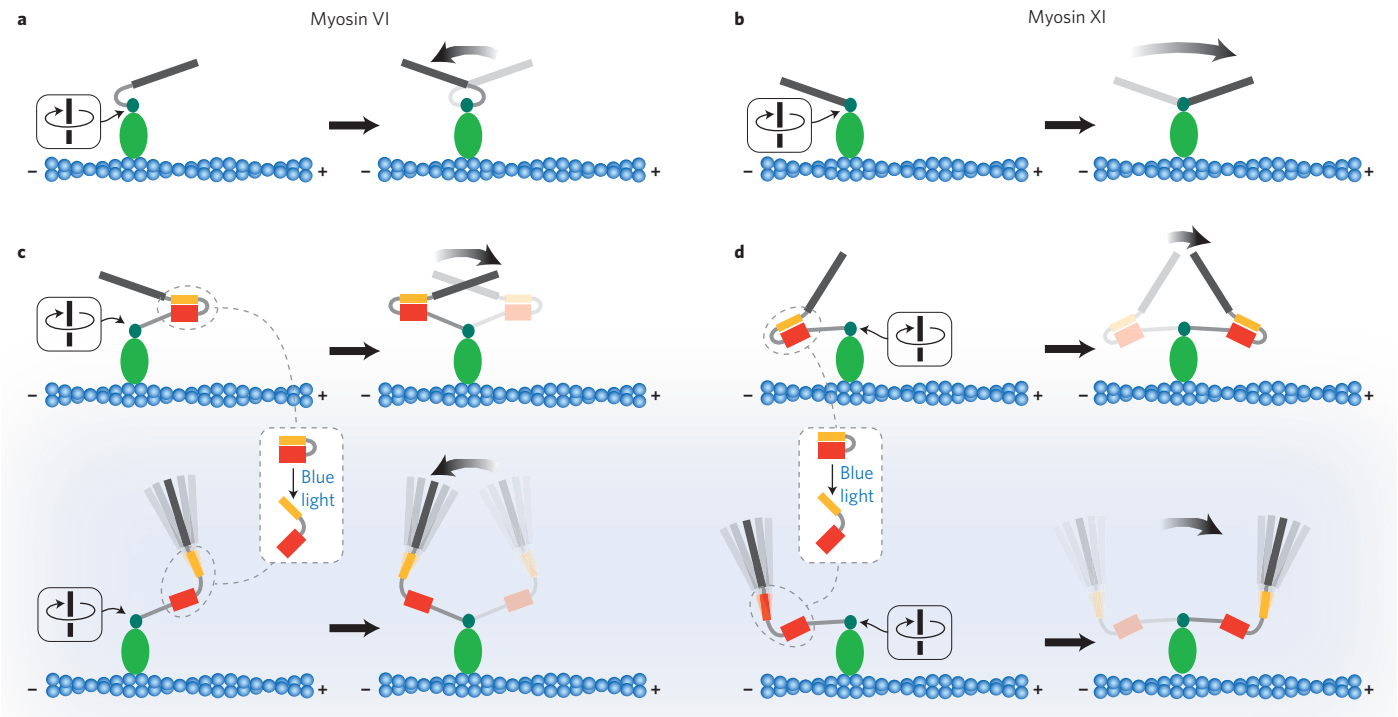

Figure 1 | Controlling the direction of myosin motors with light. **a**, Myosin VI normally moves towards the minus end of an actin filament (blue). **b**, Myosin XI normally moves towards the plus end. In myosin XI, a rotation of the converter (green circle) causes a plus-end-directed movement of the lever arm (grey). In myosin VI, a unique insert repositions the lever arm leading to minus-end-directed motility. **c**, A myosin VI chimera containing a LOV2 (light, oxygen or voltage) domain (red and orange) within a lever arm engineered to lead to plus-end-directed motility. In the dark (top panel), the alpha helix (orange) of the LOV2 domain is in a closed conformation and plus-end-directed motility is observed. In response to blue light (bottom panel), the alpha helix of the LOV2 domain adopts an open conformation leading to minus-end-directed movement. **d**, In a variation of this approach, myosin XI was engineered to contain a LOV2 domain within an engineered lever arm[2]. The engineered myosin XI moved slowly in the plus-end direction in the dark (top panel), but in the presence of blue light (bottom panel) moved faster in the same direction.

of myosin, such as myosin V and the closely related myosin XI, are plus-end directed because they lack the insert found in myosin VI (Fig. 1b)[5]. Like myosins, class 14 kinesins (minus-end-directed microtubule-based motors) also use a lever arm to amplify structural changes occurring in the motor domain to drive motility[6].

Bryant and colleagues have previously engineered myosin VI to move backwards by changing the length of the lever arm[7]. To do this, they inserted a domain between the motor domain and the lever arm that could switch between a rigid and a flexible conformation in response to calcium concentration[7]. This proof-of-principle experiment showed that motor directionality could be controlled by an external stimulus. However, varying calcium concentrations in a localized manner, or over short timescales, is difficult. Optical signals would instead provide the ideal level of control[8].

Bryant and colleagues now achieve optical control of myosin and kinesin motors by adding a protein domain called LOV (light, oxygen or voltage) that changes conformation in response to blue light[9]. The LOV2 domain, in particular, undergoes a conformational change in the blue light that causes the undocking of an alpha helix from the photosensitive domain[10] (Fig. 1c). Based on this principle, the researchers designed a series of chimeras in which the LOV2 domain is inserted between the motor and the lever arm of myosin VI, myosin XI or kinesin-14. All of their designs are based on the principle that the LOV2 domain adopts a rigid hairpin conformation in the dark and an open and more flexible conformation in the light. This switch allows them to control the position of the lever arm relative to the motor cores.

For myosin VI, which is normally a minus-end-directed motor (Fig. 1a), the researchers first engineered it to be plus-end directed using an approach they previously developed[7] (Fig. 1c, top panel). This myosin VI also contains the LOV2 domain and can switch its directionality from plus- to minus-end-directed in response to light (Fig. 1c, bottom panel). Furthermore, a variation of this myosin VI construct was engineered to switch, when irradiated with blue light, from faster to slower plus-end-directed motility. Likewise, myosin XI, normally a fast, plus-end-directed motor (Fig. 1b) could be converted, in response to light, from a slow to fast plus-end-directed motor (Fig. 1d). As a final proof of the versatility of their approach, Bryant and colleagues used a similar strategy to generate kinesin-14 motors that changed direction when illuminated.

To determine the speed and directionality of different engineered motor chimeras, Bryant and colleagues performed gliding filament assays, in which myosin or kinesin motors labelled with a fluorescent tag are tethered to glass by the non-motor end of the protein. Fluorescent actin filaments or microtubules, with one end of the filament marked to determine polarity, are then observed as the motors push them along the glass. These light-induced speed changes occur on the order of seconds and can be repeated more than 50 times.

These studies show that motor activity can be controlled reversibly with high spatial and fast temporal resolution. Although the motors used in these studies are much slower than the natural motors they were derived from, the experiments are an exciting starting point to further design myosins and kinesins. For example, the motors used by Bryant and colleagues are monomeric, but both myosin VI and XI can travel for long distances without dissociating from their tracks when dimeric[5,11]. One of the most exciting potential applications of this technology will be to express light-tunable motors in cells, allowing optical control of motor behaviour in living cells and organisms. ❐

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SPINTRONICS

Electrons act constructively

Interference effects in semiconductor quantum structures provide an elegant way to electrically map the strength and direction of spin–orbit fields.

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Electrons in solid-state systems can behave like waves, and, in both metals and semiconductors, quantum-relativistic effects can influence the motion of the charge carriers. One of these effects is the spin–orbit interaction, which describes the coupling of the orbital and spin degrees of freedom of the electrons, and manifests itself as an effective momentum-dependent magnetic field seen by the carriers. The interference of relativistic, spin–orbit-coupled electrons has in the past been considered primarily in terms of destructive interference[1]. Furthermore, previous measurements of the strength of the spin–orbit coupling by phase coherent transport could only return approximate values. Writing in *Nature Nanotechnology*, Junsaku Nitta and colleagues at Tohoku University and the University of Regensburg now report observing constructive interference effects in relativistic electrons in semiconductor quantum structures, and use these effects to precisely map the relativistic field, including its momentum-dependent direction[2].

When electrons in a conductor scatter off intentionally introduced dopants, alloy disorder or unintentional impurities the constructive interference of backscattered electron waves ψ_+ and ψ_- (corresponding to time-reversed paths) leads to a phenomenon known as weak localization (Fig. 1a). The backscattering probability given by $|\psi_+ + \psi_-|^2$ has the incoherent contribution $|\psi_+|^2 + |\psi_-|^2$ and an interference contribution $\psi_+^*\psi_- + \psi_-^*\psi_+$. In the absence of a magnetic field, which breaks time-reversal symmetry, the phase shift acquired by the two