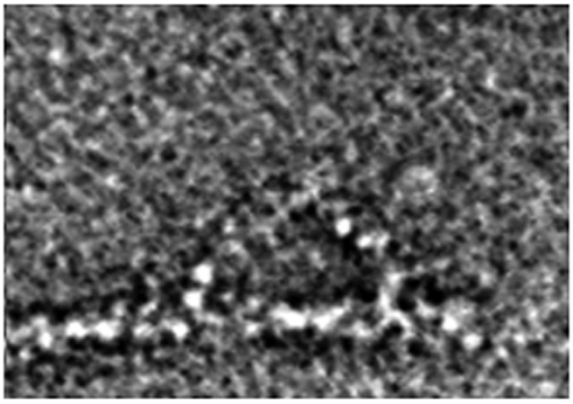
Steppin' out: processive myosin V movement on actin filaments

Myosins use the energy of ATP hydrolysis to fuel their movement along actin filaments. Because different myosins have distinct biochemical interactions with actin, it is thought that they also have different modes of movement. As the actin filament is a helical polymer, at least two modes of translocation can be envisaged for double-headed myosins. In one, the motor protein churns around the circumference of the actin filament, whereas in the other, it takes large steps that are equal in dimension to the actin helical repeat, so that motion is linear along one face of the filament.

Like muscle myosin, myosin V is a dimer with two globular heads, a long neck and a coiled-coil tail. Although two states of myosin V binding had been observed by electron microscopy — either one head bound or the two heads of a single myosin bound to different actin filaments — neither seems compatible with its proposed linear, 'processive' motion. However, in a recent issue of *Nature* (**405,** 804–807, 2000), Walker *et al.* report the use of electron microscopy to observe two-headed binding to a single actin filament, under conditions in which the rate of movement was limited by ATP binding.

Their micrographs have clearly settled the issue regarding the separation and orientation of the two myosin heads. Heads were found to be spaced roughly 13 actin molecules (36 nm) apart, a significant value because this is the length of the actin helical repeat. This myosin can therefore move linearly on actin. Both heads and the neck domain exhibit a specific orientation in binding and lean in the same direction (see picture). Furthermore, all of the myosin V molecules on a single filament are orientated in the same way. The more sharply angled leading head-neck domain (right in picture) is nearest to the barbed end of the filament and indicates the direction of movement.



What insight does this provide into the mechanism of translocation? The angle of the trailing neck domain (left in picture) is significantly less (40°) than that of the leading neck (which averages 115°). The trailing head is therefore thought to be in a rigor state. The leading head has a structure that has been proposed but never previously visualized, and which is likely to represent the start of the power stroke. When the trailing head binds to ATP it releases actin, and the power stroke in the leading head swings the free head forward. When the free head then hydrolyses the ATP molecule it rebinds to filament one helical repeat further along. In the meantime, ADP is released from the new trailing head, inducing rigor and completing the cycle. As a result of these conformational changes, myosin V strides along the filament in a straightforward motion. Although myosins with shorter necks may have shorter strides, the conformational changes observed in the attached heads of myosin V are proposed to occur in most myosins.

Movies showing myosin V translocating along actin filaments can be found at http://www.leeds.ac.uk/bms/research/muscle/muscle.htm.

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