Protein harnesses power of 'silly walks'

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The 'stiff-legged' walk of a motor protein along a tightrope-like filament has been captured for the first time.

Because cells are divided in many parts that serve different functions some cellular goodies need to be transported from one part of the cell to another for it to function smoothly. There is an entire class of proteins called 'molecular motors', such as myosin 5, that specialise in transporting cargo using chemical energy as fuel.

Remarkably, these proteins not only function like nano-scale lorries, they also look like a two-legged creature that takes very small steps. But exactly how Myosin 5 did this was unclear.

The motion of myosin 5 has now been recorded by a team led by Oxford University scientists using a new microscopy technique that can 'see' tiny steps of tens of nanometres captured at up to 1000 frames per second. The findings are of interest for anyone trying to understand the basis of cellular function but could also help efforts aimed at designing efficient nanomachines.

'Until now, we believed that the sort of movements or steps these proteins made were random and free-flowing because none of the experiments suggested otherwise,' said Philipp Kukura of Oxford University's Department of Chemistry who led the research recently reported in the journal *eLife*. 'However, what we have shown is that the movements only appeared random; if you have the capability to watch the motion with sufficient speed and precision, a rigid walking pattern emerges.'

One of the key problems for those trying to capture proteins on a walkabout is that not only are these molecules small – with steps much smaller than the wavelength of light and therefore the resolution of most optical microscopes – but they are also move very quickly.

Philipp describes how the team had to move from the microscope equivalent of an iPhone camera to something more like the high speed cameras used to snap speeding bullets. Even with such precise equipment the team had to tag the 'feet' of the protein in order to precisely image its gait: one foot was tagged with a quantum dot, the other with a gold particle just 20 nanometres across. (Confusingly, technically speaking, these 'feet' are termed the 'heads' of the protein because they bind to the actin filament).

So how does myosin stride from A to B?

The researchers have created a short animation [see above] to show what their imaging revealed: that Myosin 5a takes regular 'stiff-legged' steps 74 nanometres in length. The movement resembles the twirling of a dividing compass used to measure distances on a map. With each step the heads of Myosin 5a bind to the actin filament before releasing to take another step. In the animation flying sweets represent ATP, which provides the energy to power the motor protein.

'I describe the motion as a bit like the walks in the Monty Python sketch about the Ministry of Silly Walks,' said Philipp. He adds that we have to imagine that this movement is taking place in a hostile and chaotic nanoscale environment: 'Think of it being rather like trying to walk a tightrope in a hurricane whilst being pelted with tennis balls.'

'We've uncovered a very efficient way that a protein has found to do what it needs to do, that is move around and ferry cargos from A to B,' explains Philipp. 'Before our discovery people might have thought that artificial nanomachines could rely on random motion to get around but our work suggests this would be inefficient. This study shows that if we want to build machines as efficient as those seen in nature then we may need to consider a different approach.'

It seems that if you're designing tiny machines 'silly' walks may not be so silly after all.

More information: "Structural dynamics of myosin 5 during processive motion revealed by interferometric scattering microscopy." DOI: dx.doi.org/10.7554/eLife.05413

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