Taking Giant, Irregular Leaps: The Surprising Mechanics of Myosin VI

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- Title: Myosin VI is a processive motor with a large step size
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The Cell's Internal Transportation System

Every cell in our body contains a complex network of protein "roads" called actin filaments [1]. These roads are essential for moving materials like nutrients and waste from one part of the cell to another. To navigate these roads, the cell uses molecular "motors" called myosins. Most of these motors move in one direction, that being towards the outer edges of the cell. However, myosin VI is unique: it is the only known motor that moves in reverse, traveling toward the cell's interior [1].

This so called, "backward" movement is critical for our most sensitive organs. myosin VI is found in high concentrations in sensory areas like the eyes and ears [1]. In the inner ear, it is responsible for maintaining the structure of the tiny hair cells that detect sound. When this motor doesn't work correctly, it leads to severe deafness and coordination problems, as seen in "Snell's waltzer" mice, as referenced in the introduction [1]. Because this motor is so vital for our senses, scientists have spent years trying to figure out exactly how it "walks" along its actin track (keep in mind this paper was from 2001 we now know how it walks).

A Marathon Runner, Not a Sprinter

To study myosin VI, researchers tagged the motor with Green Fluorescent Protein (GFP) so they could watch individual molecules under a high-powered microscope [1]. One of the first major questions was whether myosin VI was processive, meaning, can a single motor take multiple steps without falling off its track?

The researchers found that myosin VI is indeed a long-distance runner. On average, a single motor traveled approximately 226 nanometers before releasing [1]. This confirmed that myosin VI is a heavy-duty transporter capable of hauling cargo deep into the cell without the need for a team of other motors to keep it on track [1].

The so-called "Impossible" Giant Stride

The most shocking discovery came when the team measured the size of the motor's "stride." Most molecular motors have a rigid "neck" that acts like a leg, determining how far they can step. Based on the physical structure of myosin VI, which has a very short neck, scientists predicted it could only take tiny steps of about 5 nanometers [1].

However, using a "force-feedback" system with laser tweezers, the researchers measured a massive average step size of 30 nanometers [1]. This is nearly six times larger than what was thought physically possible! It's the equivalent of a toddler suddenly taking the stride of an Olympic hurdler, which, as one could imagine, was extremely surprising! This result proved that myosin VI isn't using a standard, rigid "leg" to walk, rather, it must have a much more flexible way of reaching forward than was initially expected.

Myosin VI A Messy, "Promiscuous" Walker

Unlike other motors that land precisely on the same spot every time, myosin VI is a "messy" walker. The researchers found a broad distribution of step sizes [1]. While most steps were around 30 nm, some were much larger or smaller, and the motor even took frequent "backsteps" of about 11 nm when it got stuck or faced high resistance [1].

This suggests that myosin VI is "promiscuous;" basically, it doesn't have one favorite landing spot on the actin road. Instead, it seems to have a highly flexible "insert" in its structure that acts like a stretchy tether, allowing the motor to reach out and grab whatever available spot on the track is nearby, making it incredibly efficient at moving materials [1].

Why These Results Matter

These results completely rewrote the rulebook for how we think about cellular movement! They proved that you don't need a long, stiff "leg" to take giant steps and that motors can move efficiently in both directions on the same track [1]. By understanding the mechanics of how myosin VI takes these giant, irregular leaps, scientists can better understand the root causes of sensory disorders. When this flexible motor fails to navigate the cell's interior, the delicate structures in our eyes and ears can break down, leading to the loss of our most vital senses [1].

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[1] R. S. Rock, S. E. Rice, A. L. Wells, T. J. Purcell, J. A. Spudich, and H. L. Sweeney, Myosin vi is a processive motor with a large step size, Proceedings of the National Academy of Sciences **98**, 13655 (2001).