Modeling Hand-Over-Hand and Inchworm Steps in Myosin VI

AMANDA JACK, Denison University, IAN LOWE, University of Pennsylvania, RIINA TEHVER, Denison University — Myosin VI is a molecular motor protein that moves along actin filaments to transport cargo within a cell. There is much experimental evidence that the myosin VI dimer moves “hand-over-hand” along actin; however, recent experiments suggest that the protein can also move via an “inchworm” mechanism. We created a mechanochemical kinetic model to predict myosin VI’s behavior under different ATP, ADP, and force conditions, taking these alternative mechanisms into account. Our model’s calculations agree well with experimental results and can also be used to predict myosin VI’s behavior outside experimentally tested regimes, such as under forward force. We also predict an optimized motor function for the protein around physiological (-2 pN) load and anchoring under -3 pN load. By using our model to predict myosin VI’s response to environmental change, we can gain insight into the behavior of a protein that can be difficult to observe experimentally.

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