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Unrevealed part of myosin's powerstroke accounts for high efficiency of muscle contraction

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Abstract

Background: Myosin II, the motor protein driving muscle contraction, uses energy of ATP hydrolysis to produce movement along actin. The key step of energy transduction is the powerstroke, involving rotation of myosin's lever while myosin is attached to actin. Macroscopic measurements indicated high thermodynamic efficiency for energy conversion. However, single-molecule experiments indicated lower efficiency, provoking a long-standing discrepancy.

Methods: Based on the Fluctuation-Dissipation Theorem, we built a sufficiently detailed but low degree-of-freedom model reconstructing the entire mechanoenzymatic cycle.

Results: We show that a high axial stiffness of the lever during an initial, experimentally yet unrevealed part of the powerstroke results in a short-time, ratchet-like Kramers effect, and is responsible for the missing efficiency. The second part of the powerstroke is an Eyring-like relaxation that dominantly contributes to lever rotation, but produces only a minor part of the work.

Conclusions: The model reveals the structural background of myosin's capability to function as a robust molecular engine and a very precise load sensor as well. Our model also suggests an explanation for the malfunction of myosins

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