

Mechano-kinetic characterisation of a small ensemble of myosin motors: a stochastic fitting approach to actin-myosin interaction dynamics

Myosin II is the muscle molecular motor responsible for the generation of force by cyclical ATP-driven interactions with the actin filaments. Different isoforms of the myosin motor in skeletal muscles account for the different functional requirements of slow muscles (primarily responsible for the posture) and fast muscles (responsible for voluntary movements). In a recent paper (Buonfiglio et al., Commun Biol 2024) we investigated the isoform-dependent mechano-kinetic parameters underpinning the different performances of slow and fast skeletal muscles, with a sarcomere-like synthetic machine powered by a small ensemble of myosin motors purified from mammalian skeletal muscle. The ensemble displays the steady force typical of isometric contraction, in solution with physiological ATP concentration. To characterise the out-of-equilibrium force of the ensemble, as well as the probability distribution of the force fluctuations around the steady state, we developed a stochastic model for the dynamics of a one-dimensional system constituted by a single actin filament interacting with N myosin motors. Experimental data fitting provides a self-consistent estimate of the mechano-kinetic properties of the motor ensemble, including the motor force, the fraction of actin-attached motors, and the rate of transition through the attachment-detachment cycle. The analysis was limited to experimental data obtained in a high-temperature regime, and for this reason could not resolve the kinetic details of the actin-myosin interaction cycle. We recently took a step forward by exploring a non-trivial extension of the mentioned fitting strategy, which allows for multiple temperatures datasets to be simultaneously examined.

Role

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