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Motor-motor interactions in ensembles of muscle myosin: using theory to connect single molecule to ensemble measurements SAM WALCOTT, University of California, Davis

Interactions between the proteins actin and myosin drive muscle contraction. Properties of a single myosin interacting with an actin filament are largely known, but a trillion myosins work together in muscle. We are interested in how single-molecule properties relate to ensemble function. Myosin's reaction rates depend on force, so ensemble models keep track of both molecular state and force on each molecule. These models make subtle predictions, e.g. that myosin, when part of an ensemble, moves actin faster than when isolated. This acceleration arises because forces between molecules speed reaction kinetics. Experiments support this prediction and allow parameter estimates. A model based on this analysis describes experiments from single molecule to ensemble. In vivo, actin is regulated by proteins that, when present, cause the binding of one myosin to speed the binding of its neighbors; binding becomes cooperative. Although such interactions preclude the mean field approximation, a set of linear ODEs describes these ensembles under simplified experimental conditions. In these experiments cooperativity is strong, with the binding of one molecule affecting ten neighbors on either side. We progress toward a description of myosin ensembles under physiological conditions.