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Distilling Muscle Actomyosin Interactions for Length Dependent Activation: Reducing a 15-State Model to 3 States TIMOTHY ALCID, WILLIAM HUNTER, Biomedical Engineering Dpt., New Jersey Inst of Tech — Muscle proteins myosin and actin interact to produce force. These proteins align along filaments bundled together into sarcomeres. Actin contains sites where myosin heads attach to form crossbridges. Our basis was an existing crossbridge model (Caremani, 2015): 12 attached and 3 detached states cycle through ATP binding, hydrolysis and subsequent release of ADP and phosphate. A reduced, regulated computational model was created to have 1 detached and 2 attached kinetic states. Such reduction is critical because this actomyosin model will be part of complex, higher order models that include other aspects of muscle regulation. One detached state exists in an equilibrium mixture of 3 rapidly interacting structures, including the recently discovered super-relaxed structure. In this, the myosin head is held back against the filament backbone. When force is applied along the filament by the protein titin, these myosin heads release for interaction. Titin's role alters at different sarcomere lengths. Agreeing with data (Dobesh, 2002), the model can predict the probability of crossbridge formation and force production as sarcomere length changes. We anticipate this model (coupled with more data) will improve understanding of this length-dependent effect in actomyosin interactions.

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