Abstract Submitted
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A coarse-grained model to study calcium activation of the cardiac thin filament JING ZHANG, STEVEN SCHWARTZ, University of Arizona — Familial hypertrophic cardiomyopathy (FHC) is one of the most common heart disease caused by genetic mutations. Cardiac muscle contraction and relaxation involve regulation of crossbridge binding to the cardiac thin filament, which regulates actomyosin interactions through calcium-dependent alterations in the dynamics of cardiac troponin (cTn) and tropomyosin (Tm). An atomistic model of cTn complex interacting with Tm has been studied by our group. A more realistic model requires the inclusion of the dynamics of actin filament, which is almost 6 times larger than cTn and Tm in terms of atom numbers, and extensive sampling of the model becomes very resource-demanding. By using physics-based protein united-residue force field, we introduce a coarse-grained model to study the calcium activation of the thin filament resulting from cTn's allosteric regulation of Tm dynamics on actin. The time scale is much longer than that of all-atom molecular dynamics simulation because of the reduction of the degrees of freedom. The coarse-grained model is a good template for studying cardiac thin filament mutations that cause FHC, and reduces the cost of computational resources.

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