A Model Based Analysis of Steady-State versus Dynamic Aspects of the Relationship between Calcium and Force

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Although the calcium-force relationship is dynamic (i.e., calcium-induced force generation is not instantaneous) during physiological contractions of cardiac muscle, this relationship is often studied only under steady-state conditions. We used a mathematical model that links intracellular free calcium and force to investigate how dynamic and steady-state aspects are affected by perturbations of three cellular processes: calcium binding kinetics, crossbridge kinetics, and cooperativity. Model parameters corresponding to the three processes were systematically varied. Indices describing steady-state and dynamic aspects were quantified using the model-based solutions. Results indicate that changes in all three processes affected both steady-state and dynamic aspects; however, the relative sensitivity of changes in the dynamic aspects were significantly greater (2.3-21.4 fold increase, $P = 0.011$). Thus, the dynamic aspects of calcium-force relationship are physiologically important in cardiac contraction and the model-based analysis may help guide future experimental work in this area.