Model representation of the force response to step-like length changes in constantly activated cardiac muscle.

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The force response, $F(t)$, of constantly-activated cardiac muscle to step-like length changes, ΔL, is used experimentally to characterize the muscle's contractile condition. Frequently, only individual phases of the response are analyzed for a specific cardiac muscle study. Doing so, however, neglects fundamental nonlinear contractile processes that result in the response to quick stretch being qualitatively different from the response to quick release. We sought to reproduce the full $F(t)$ transient plus its nonlinear features with a simple mathematical model that would find routine use for evaluating contractile features of constantly-activated cardiac muscle. The model treats muscle force as the product of two variables: 1) stiffness, $\varepsilon(t)$, of all parallel, strongly-bound cross-bridges (XB) and 2) average elastic distortion, $x(t)$, of XBs within this population. A step increase in ML does two things: 1) it immediately increases $x(t)$ and this increase quickly dissipates to isometric levels as ΔL-distorted XBs are replaced with new XB and 2) it recruits more XBs into the force-bearing state to increase $\varepsilon(t)$ but this recruitment is slower than the dissipation of distortion. The addition of a one-parameter $\varepsilon(t)$-$x(t)$ interaction term in the differential equation for $\varepsilon(t)$ sufficed to reproduce virtually all of the observed nonlinear behavior. When fit to a family of $F(t)$s from graded amplitude, step-like ΔL (±2% ML in 0.5% increments) in constantly-activated rat ventricular muscle fibers, the model reproduced all the essential features of $F(t)$ (R^2 ~ 98%) with good certainty in the parameter estimates. The model clearly distinguished the contractile dynamics from force responses collected from two groups of cardiac muscle fibers (wild type vs. fibers with TnT mutations), showing significant difference in the parameters associated with $\varepsilon(t)$ and $x(t)$ dynamics and that associated with nonlinear $\varepsilon(t)$-$x(t)$ interaction.