**Introduction**

* Myotropes are a new kind of calcium-independent therapeutic drugs that bind to sarcomeric proteins
* Their clinical development has reinforced the need for new quantitative understanding of sarcomere-level function
* Mathematical models can be used to produce in silico predictions regarding the impact of myotropes on contractility

**Methods**

* FiberSim ([1](#_ENREF_1)) is a spatially explicit computer model of half-sarcomere contraction
* FiberSim can be used to evaluate sarcomere contractility as a function of a myotrope dose, specifically mavacamten in this study
* It was hypothesized that mavacamten stabilizes the SRX (super-relaxed state) of myosin ([2](#_ENREF_2))
* KD of mavacamten and myosin was determined from previously published ATPase data ([3](#_ENREF_3)) and used to calculate the proportion of SRX myosin associated with mavacamten
* Isometric force was then calculated for different mavacamten concentrations

**Key results**

* Isometric force decreases with increasing mavacamten concentrations, consistent with experimental data showing a decrease in ATPase activity of isolated actomyosin assays

* IC50 (mavacamten dose for 50% isometric force) is ~40% lower than KD.
* This implies that contractile force is more sensitive to mavacamten than the ATPase of isolated myosins.
* Simulations suggest that mavacamten inhibiting a myosin head’s force-generating ability also reduces recruitment of additional myosin heads due to the force-dependency of the SRX to DRX transition
* FiberSim can be used to investigate the effects of other myotropes and help accelerate the development of myotrope-based therapies for muscle disease

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