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Supplemental information

FiberSim: A flexible open-source model of myofilament-level contraction

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FiberSim: a flexible open-source model of myofilament-level contraction

Supporting Material

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ISOMETRIC TWITCH

Fig. S1 shows an isometric twitch simulation similar to the one presented in https://campbell-muscle-lab.github.io/FiberSim/pages/demos/getting_started/isometric_twitch/isometric_twitch.html, except that the number of thick filaments is increased from 16 to 196. The simulation takes approximatively 30 minutes to run on a standard Windows laptop, using 3 of the 4 processors (meaning that other tasks still can be performed during the FiberSim simulations). As a comparison, an equivalent simulation performed with MUSICO (with 200 thick filaments) takes approximatively 10 hours on a system with 192 processors (2).

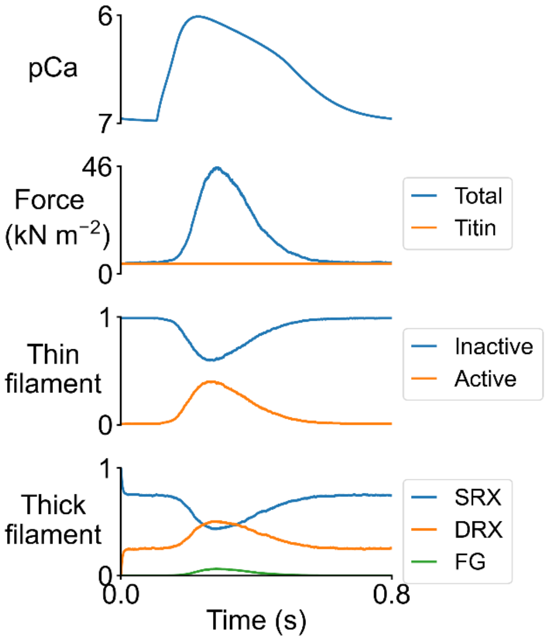

Fig. S1: Isometric twitch simulation. Calcium transient (first panel) is extracted from the ten Tusscher and Panfilov model of human ventricular cell (1).

TIME-STEP

Fig. S2 shows four isometric activations similar to the one presented in https://campbell-muscle-lab.github.io/FiberSim/pages/demos/getting_started/isometric_activation/isometric_activation.html. Each simulation is run with a different (constant) time-step.

Since the thin filament kinetics model is associated with the fastest rates, this will determine the maximal time-step we should use. The probability for a regulatory unit to activate is calculated using $k_{on} . [Ca^{2+}]$, where in the model files from the presented demos k_{on} is equal to 3.10^{7} M^{-1} s^{-1}. Thus, for an isometric activation such as the one presented in Fig. S2, the activation rate is given by $3.10^{7}.10^{-4} = 3000$ s^{-1}. The chosen time-step Δt should be small enough so that $\Delta t < \frac{1}{3000} \sim 3.10^{-4}$ s. We chose to work with $\Delta t = 10^{-4}$ s in all the simulations presented in this paper. According to Fig. S2, this step size is enough to accurately describe thin and thick filaments activation while keeping a reasonable computational time.

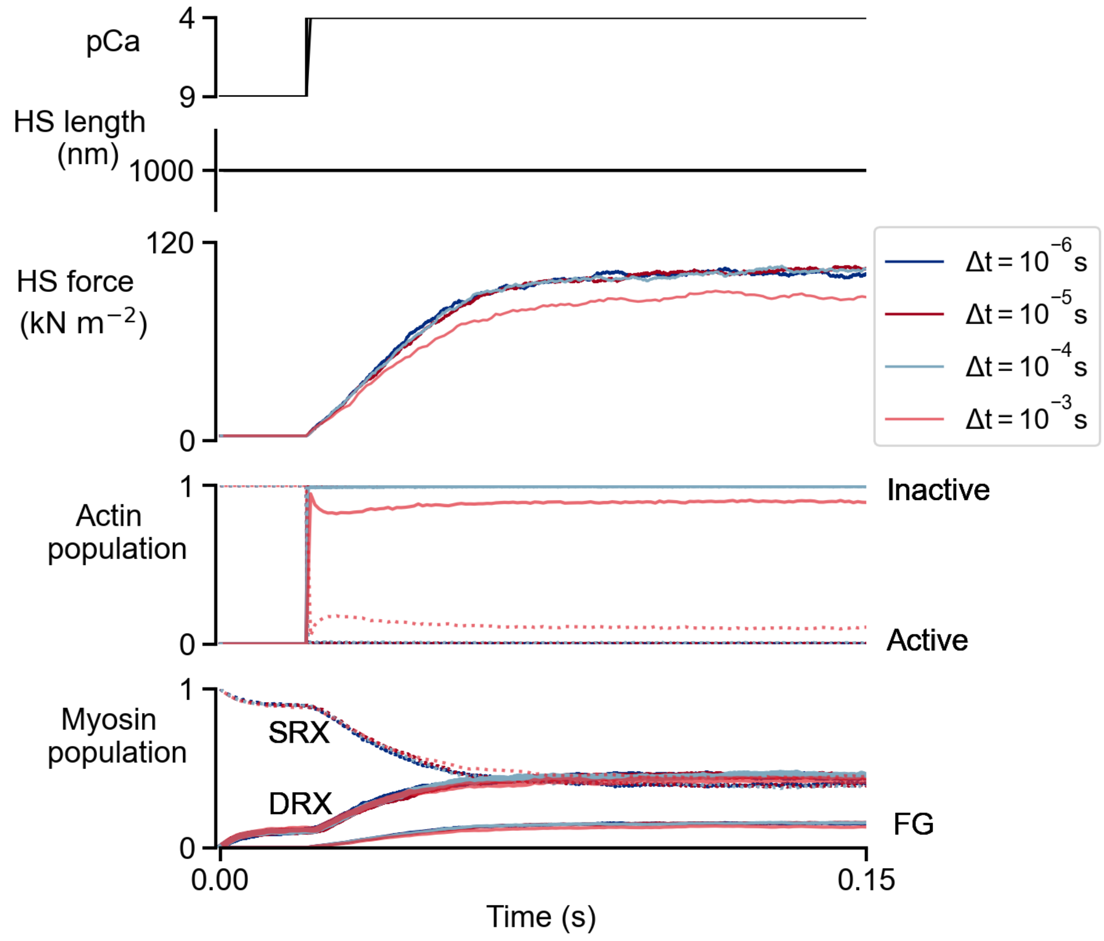

Fig. S2: Isometric activations run with different (constant) time-steps.

THIN FILAMENT ACTIVATION CURVES

Fig. S3 shows two thin filament activation curves. The active binding sites proportion is calculated at different calcium concentrations in the absence of cross-bridges. When cooperativity is turned off ($\gamma_{coop} = 0$), the Hill coefficient is close to 1. When cooperativity is turned on ($\gamma_{coop} = 10$), the Hill coefficient increases to ~4. This last curve is in good agreement with the experimental data from (3).

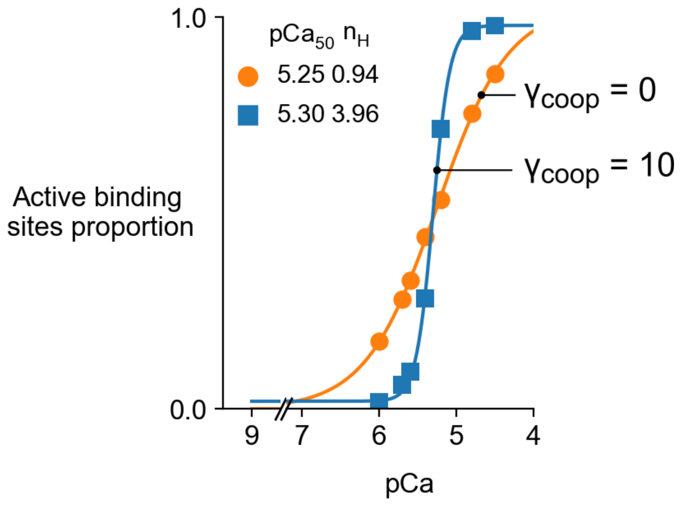

Fig. S3: Thin filament activation as a function of calcium concentration.

SUPPORTING REFERENCES

1. ten Tusscher, K. H., and A. V. Panfilov. 2006. Alternans and spiral breakup in a human ventricular tissue model. *Am J Physiol Heart Circ Physiol*. 291(3):H1088-1100, doi: 10.1152/ajpheart.00109.2006.
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3. Kampourakis, T., Y. B. Sun, and M. Irving. 2016. Myosin light chain phosphorylation enhances contraction of heart muscle via structural changes in both thick and thin filaments. *Proc Natl Acad Sci U S A*. 113:E3039-E3047, doi: 10.1073/pnas.1602776113.