Isometric and Work-loop contractions:



**o--** ES curve for WL contractions with dynamic Ca2+

**\*--** ES curve for Isometric contraction with dynamic Cai2+

Cai2+ from Work-Loop Contractions at Varying Afterloads:



Cai2+ from Isometric Contractions at Varying Sarcomere Lengths:



The result of inserting isometric Cai2+ of varying ‘widths’ into work-loop contractions. The effect of Cai2+ width on ES curve location:



o-- WL with dynamic Ca2+

\*-- Isometric contraction with dynamic Cai2+

\_\_ WL with fixed Cai2+

-At a glance, there does look like there is convergence with the fixed ES curves… As in, wider Cai2+ transients do result in a leftward shift of the ES curve, but this effect lessens as the width gets larger (there appears to be a cap on the



Comparing Isometric (gray) and work-loop (black) calcium



The mechanisms that underlie ES curve placement, whether it is for an isometric or WL contraction, are not fully understood (references?).

so what:

This is a problem because the ES curve is often used to characterize muscle contractility.

so what:

It is known that isometric and work-loop contractions produce different ES curves (contractility metrics). The mechanism(s) responsible for this difference are not fully understood. Having a metric that is not fully understood limits the usefulness of the metric and causes confusion among the metric-users (academics).

so what:

what does understanding the ES curve solve? What phenomenon does this manuscript reveal?

We want to understand what factors are involved in determining:

1. How much force an isometric contraction can generate at a given SL
2. How much shortening a WL can produce at a given force (afterload)
3. Why these two intercepts are not the same??

The existence of two different ES force-length curves along with a lack of a sufficient explanatory mechanism suggests there is room to better understand the events and contributors to force generation, and sarcomere shortening in cardiac muscle. This could lead to more accurate model scaling in the future (cell-tissue-whole organ) .

Things to consider:

1. Perhaps do not plot isometric contractions past 0.85 normalised ?

The logic of my story