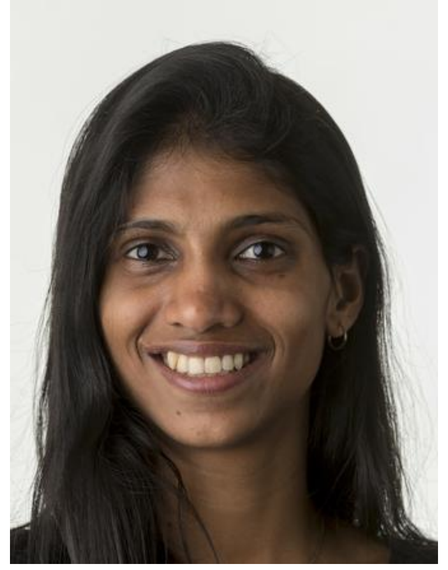
ISB 2025 Tutorial

Musculoskeletal simulations with biophysical muscle models

Lena Ting, Surabhi Simha, Hansol Ryu,
Tim van der Zee, Friedl De Groote

Funded by NIH HD HD90642 + NIH software supplement

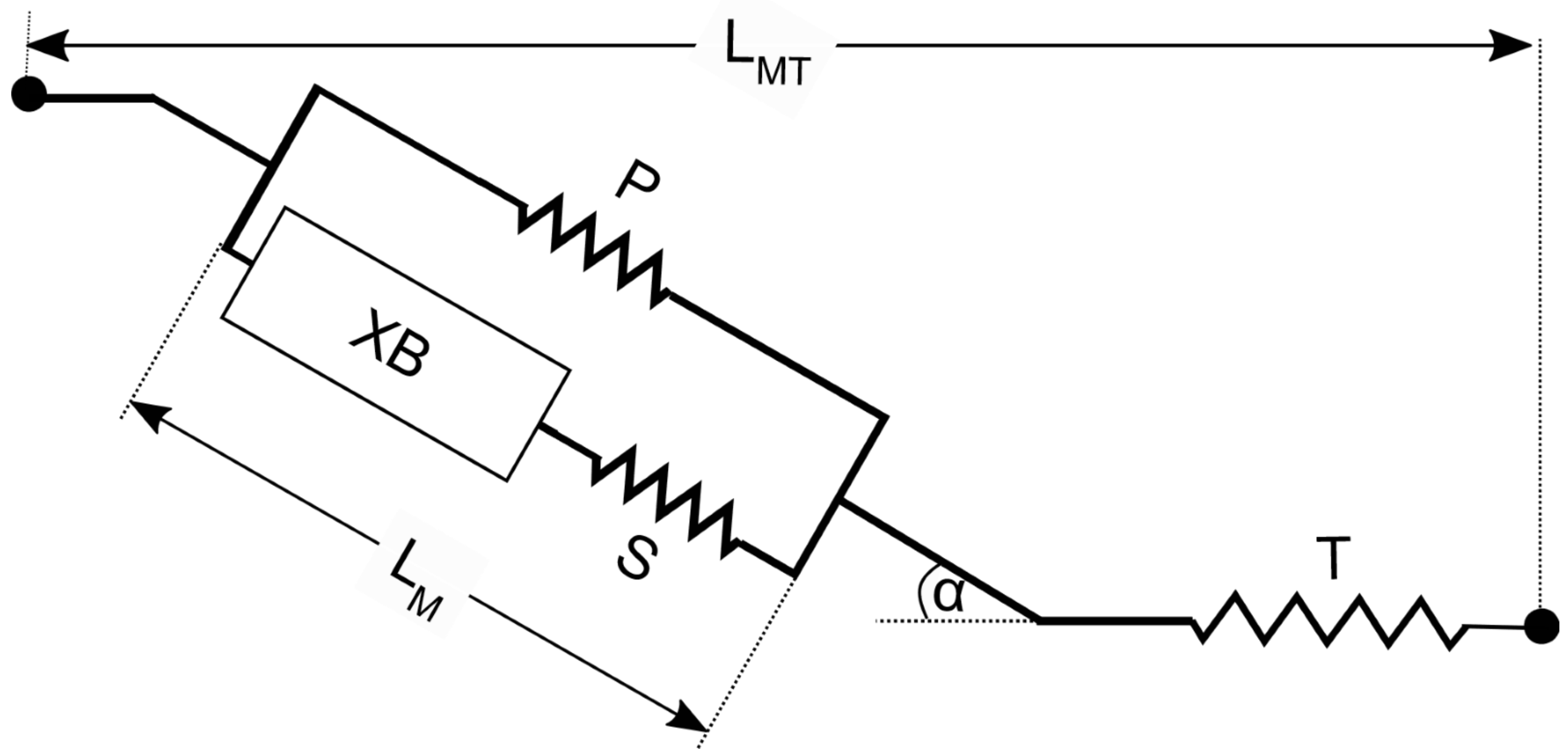


Surabhi Simha
ISB talk (T 10am)
Tuning muscle spindle signals for locomotion

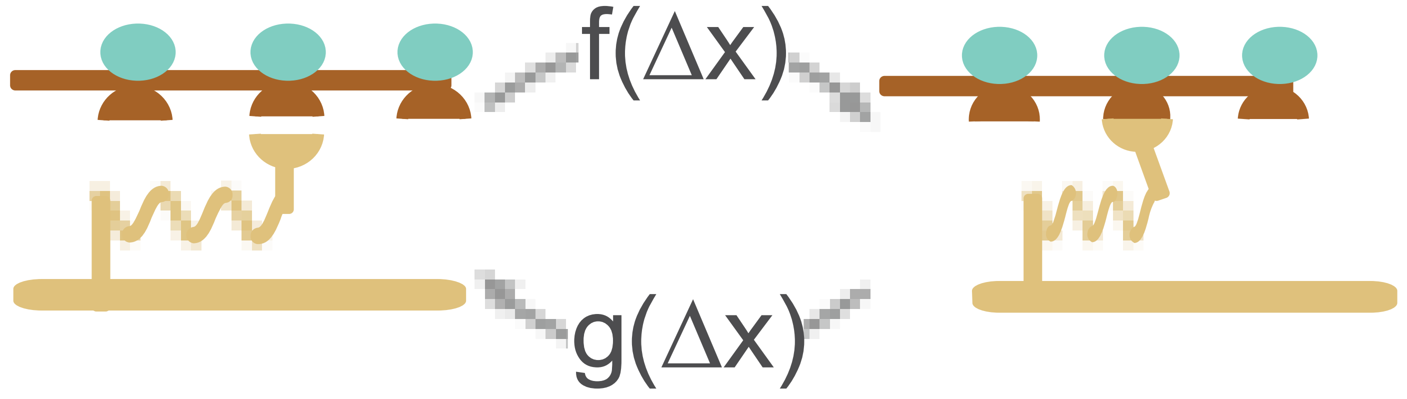
Tim van der Zee
ISB talk (M 2:50), poster (W 5pm)
Biophysical muscle models for musculoskeletal simulation

Hansol Ryu
ISB talk (M 3:20pm)
Biophysical model for postural control

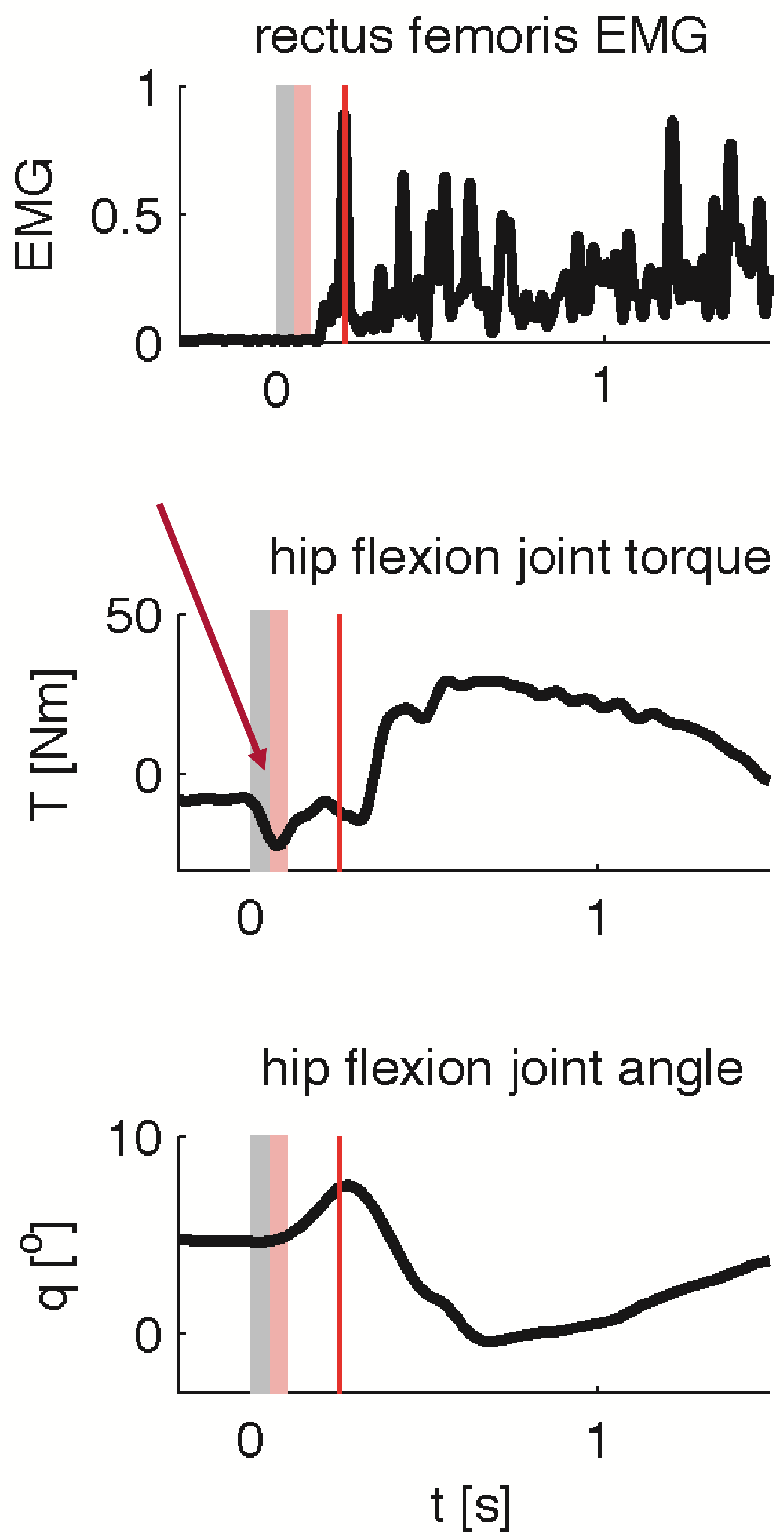
Transient force properties of muscle are needed to use musculoskeletal modeling to understand unsteady movement



Zajac 1989



Initial ‘stiff’ response to perturbations of standing balance cannot be captured by Hill muscle model



De Groote et al., *J Biomech*, 2017; Jakubowsi et al 2025

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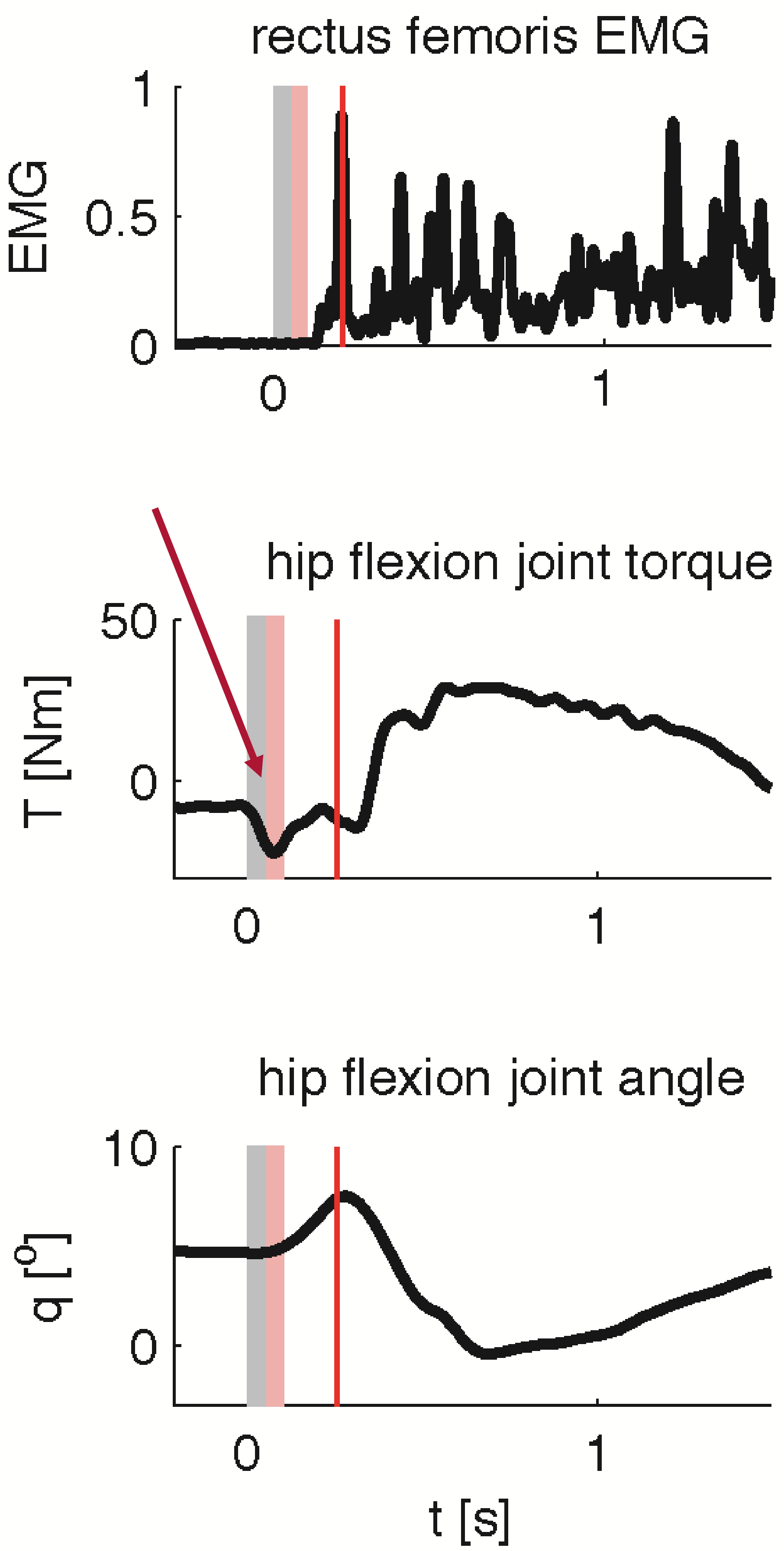
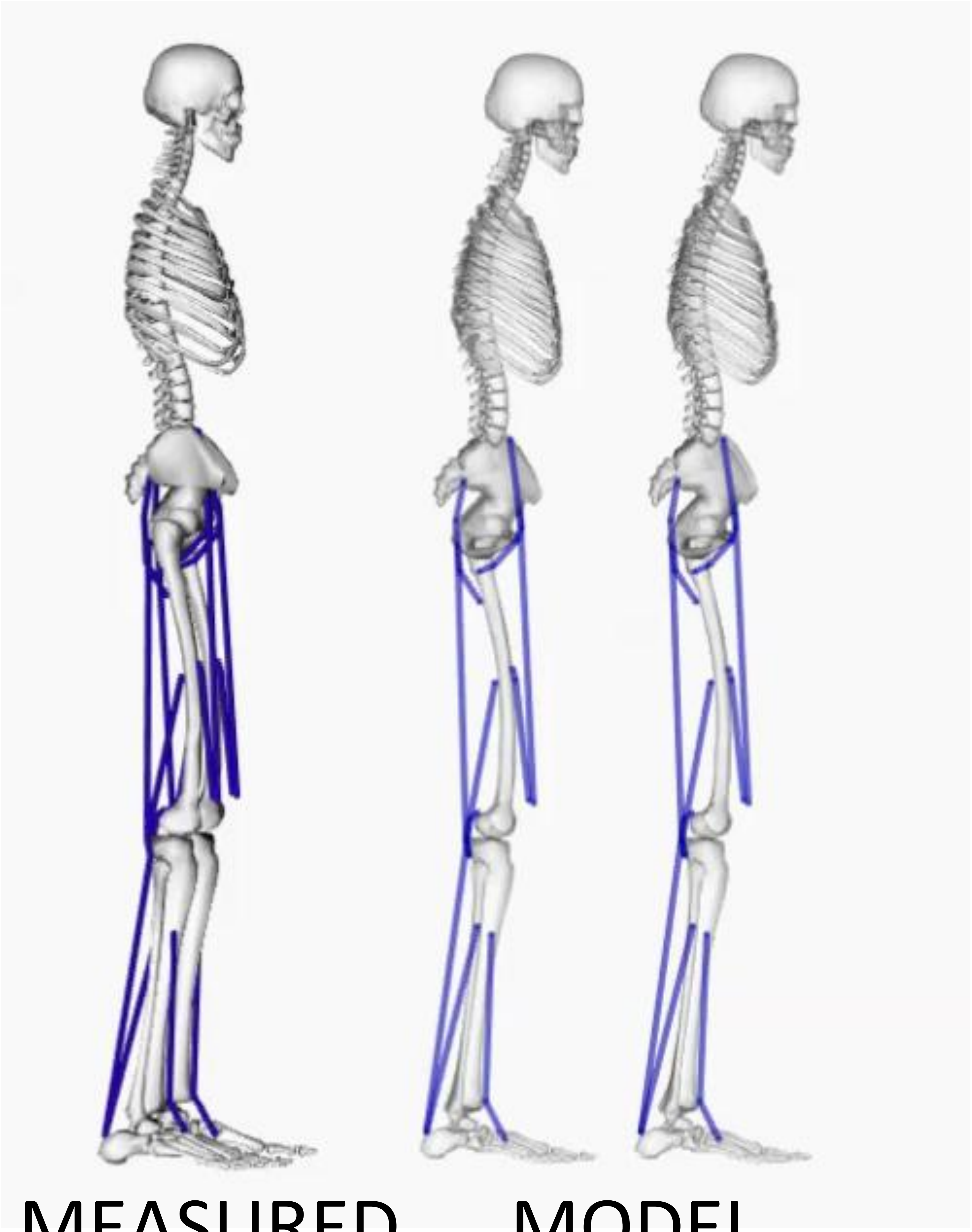




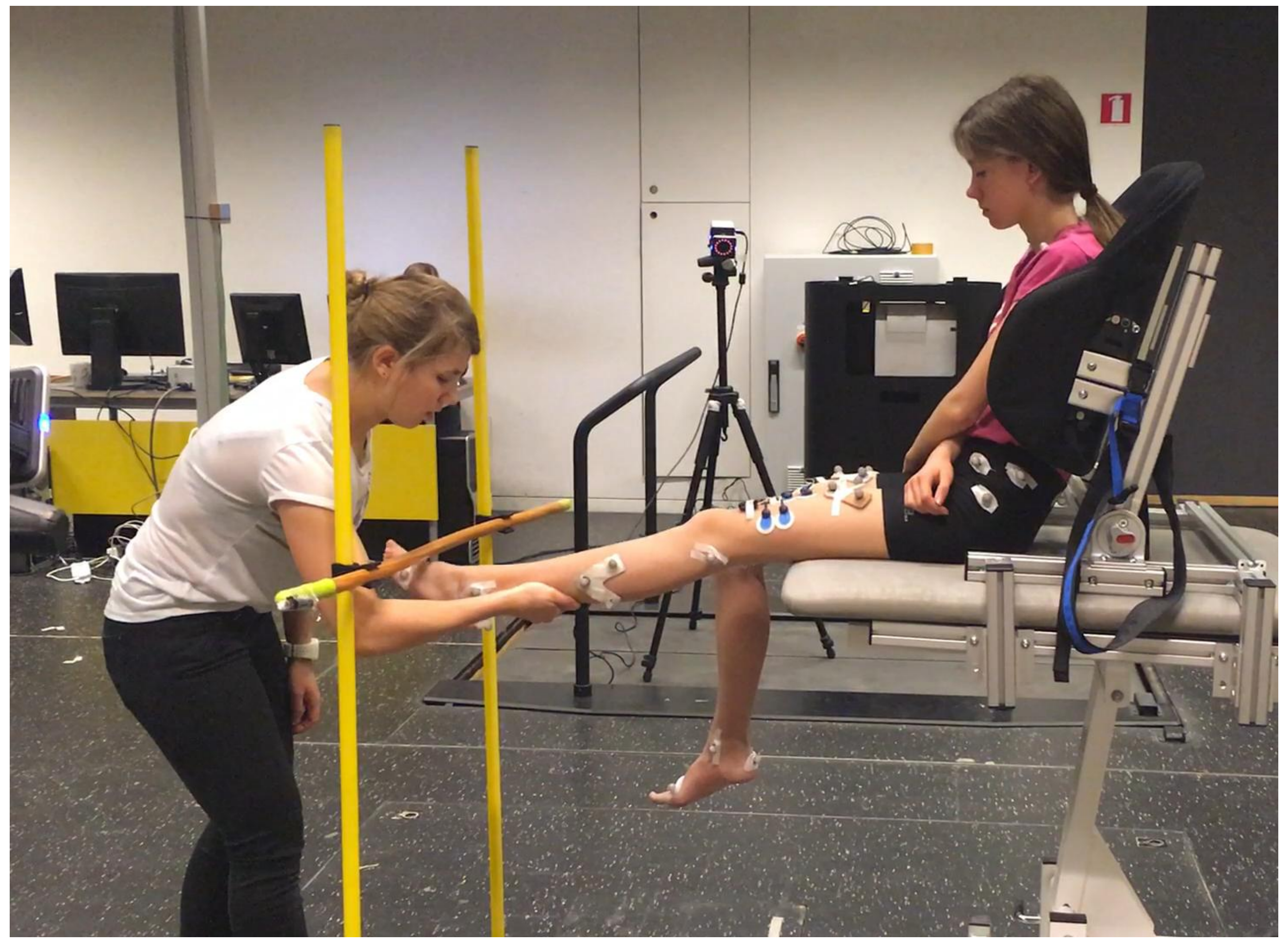
MEASURED MODEL

Hill Hill + SRS

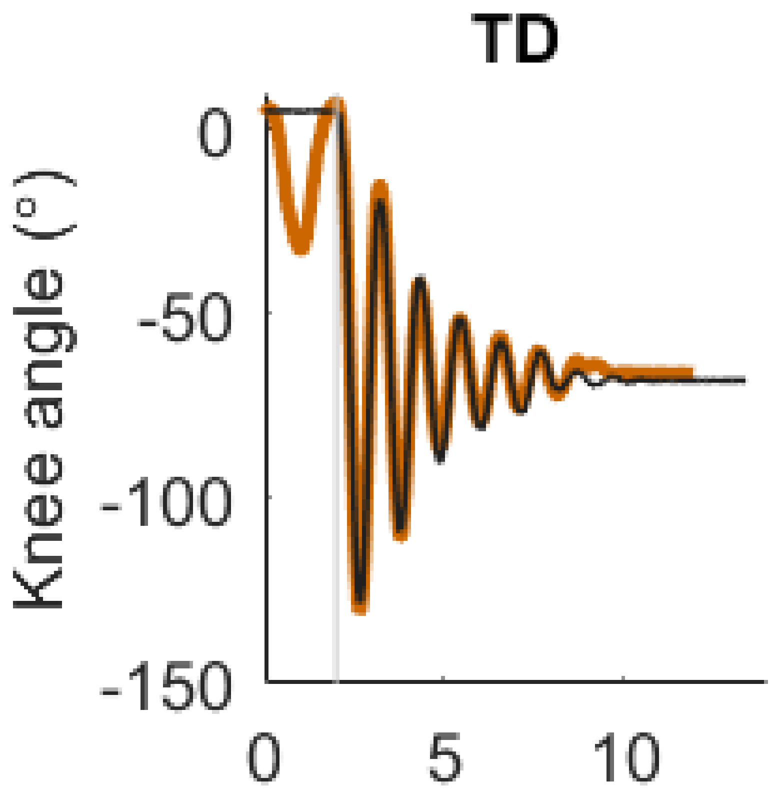
De Groote et al., *J* Biomech, 2017

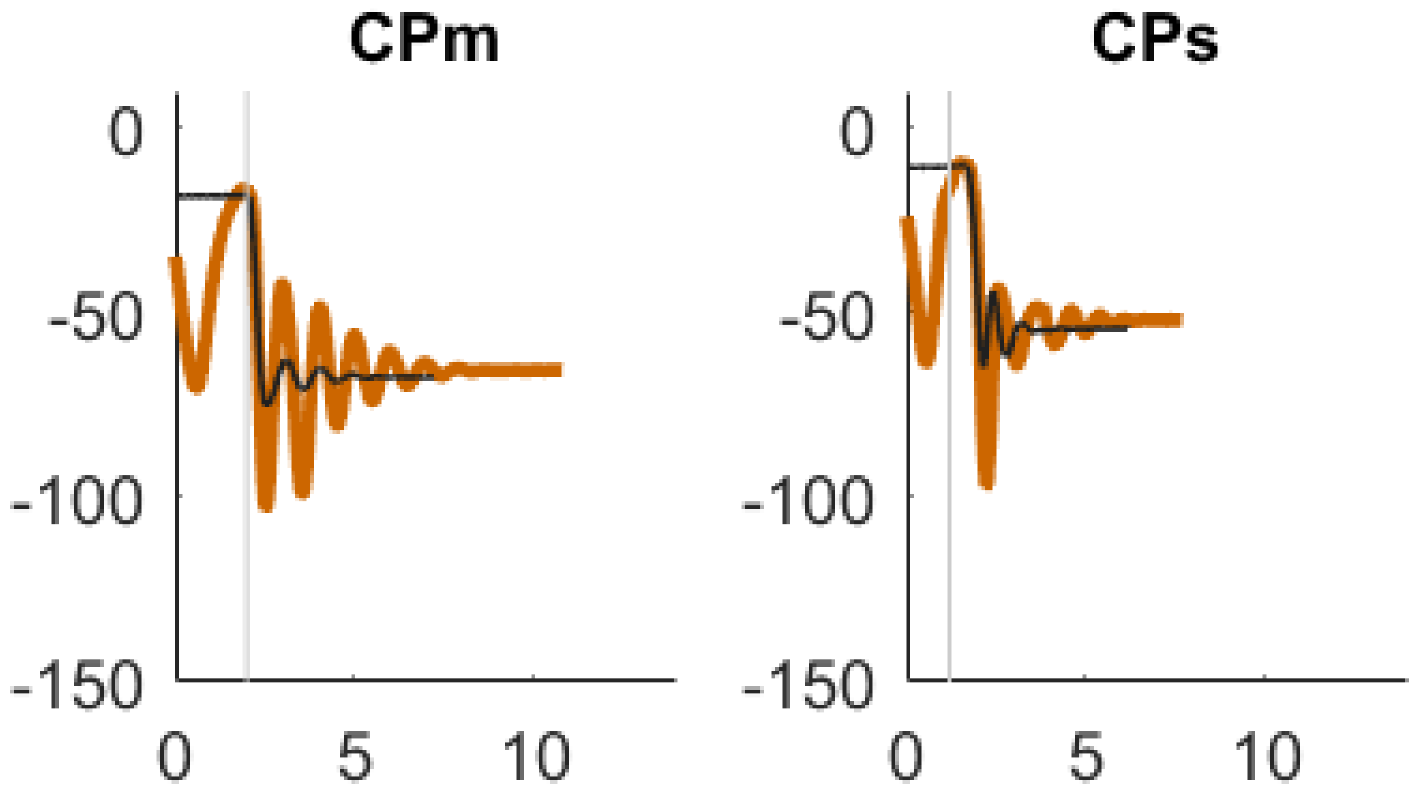
Pendulum test of spasticity is movement history dependent

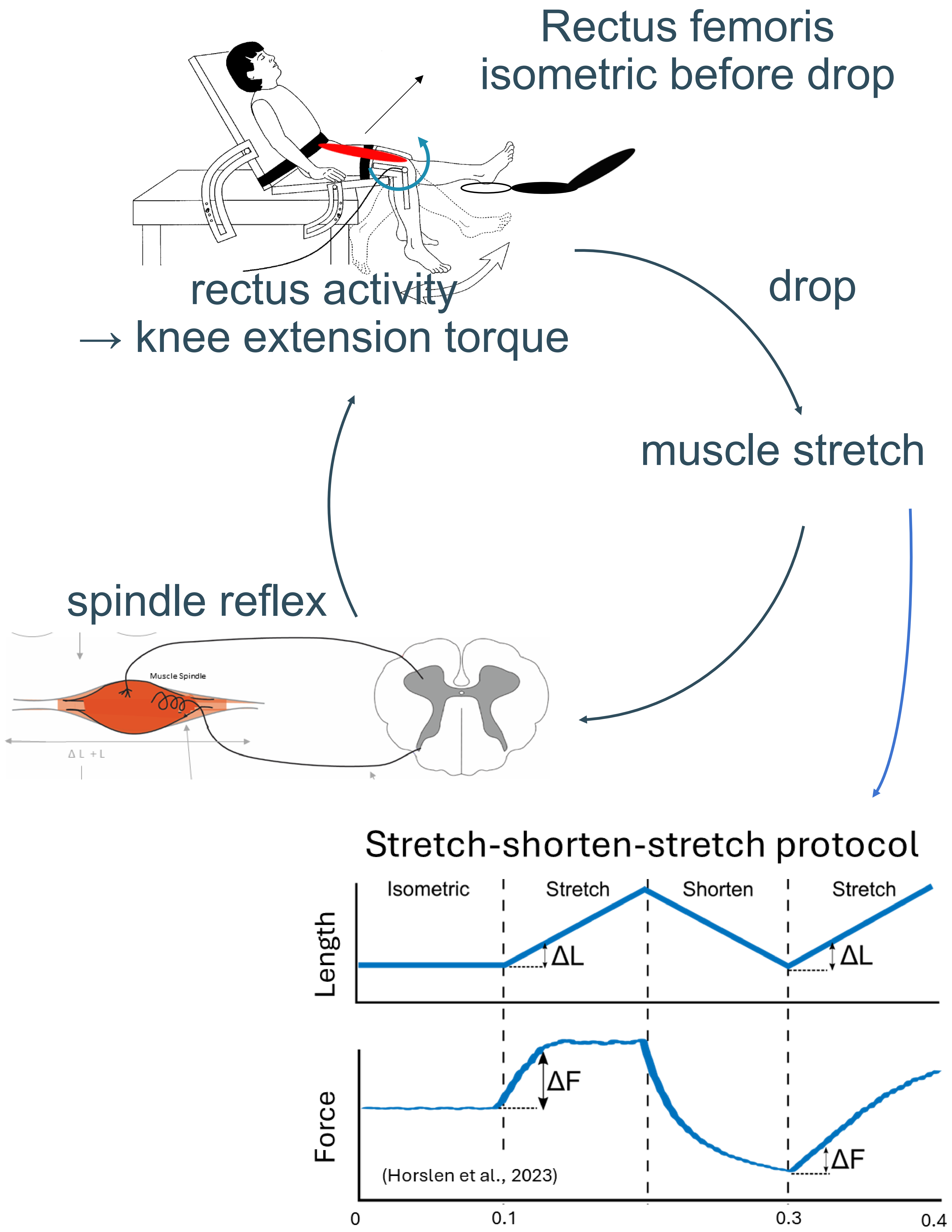
Typically developing child



Child with cerebral palsy (CP)







Willaert et al 2020, 2024; De Groote et al., *J Biomech*, 2018

Georgia Tech | Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University | EMORY UNIVERSITY

Simulating muscle force using a biophysical model

Lena Ting, <u>Surabhi Simha</u>, Hansol Ryu, Tim van der Zee, Friedl De Groote

July 27th 2025

Neuromechanics Lab

Physiology: muscle active force comes from crossbridge binding

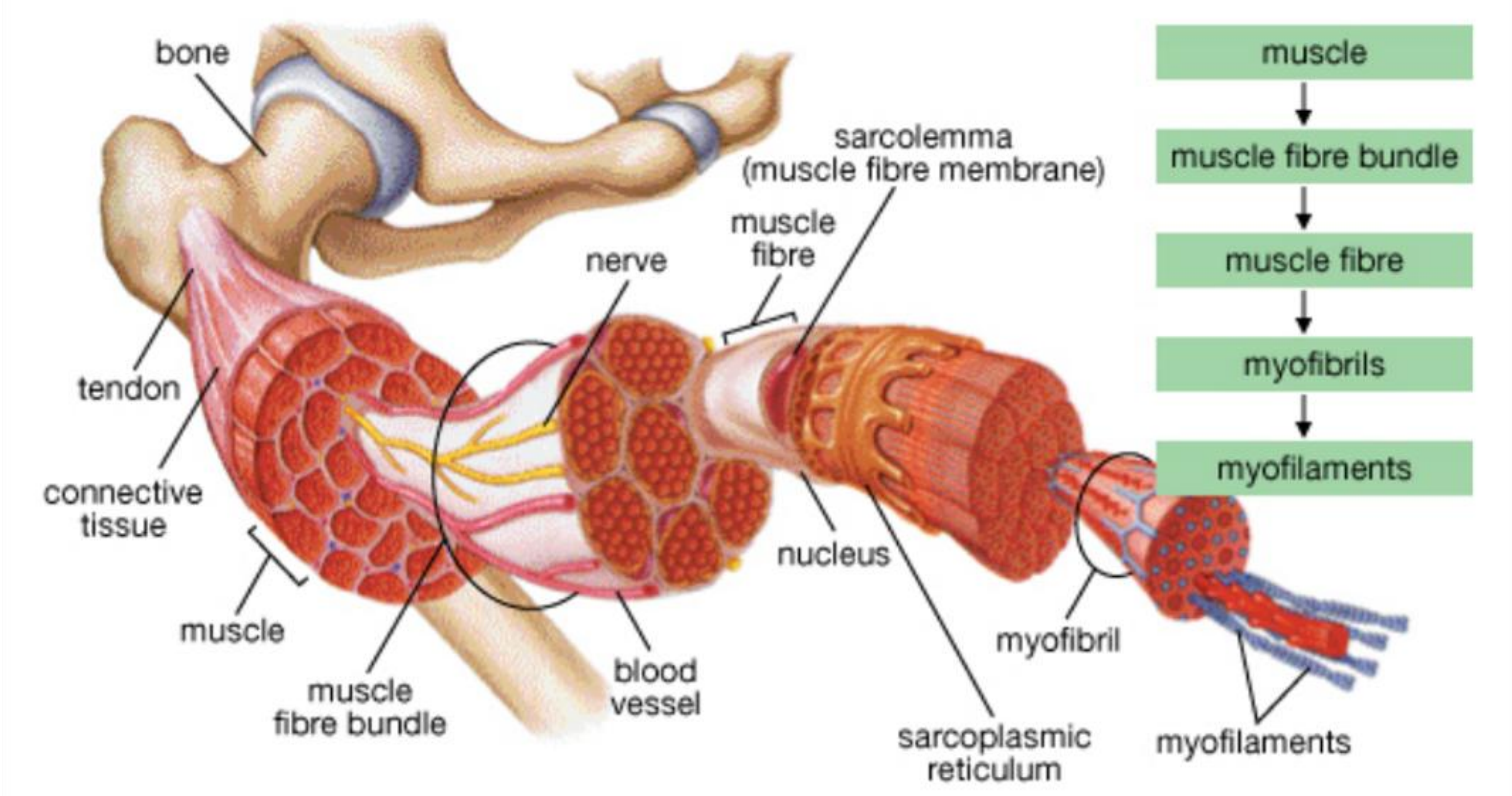
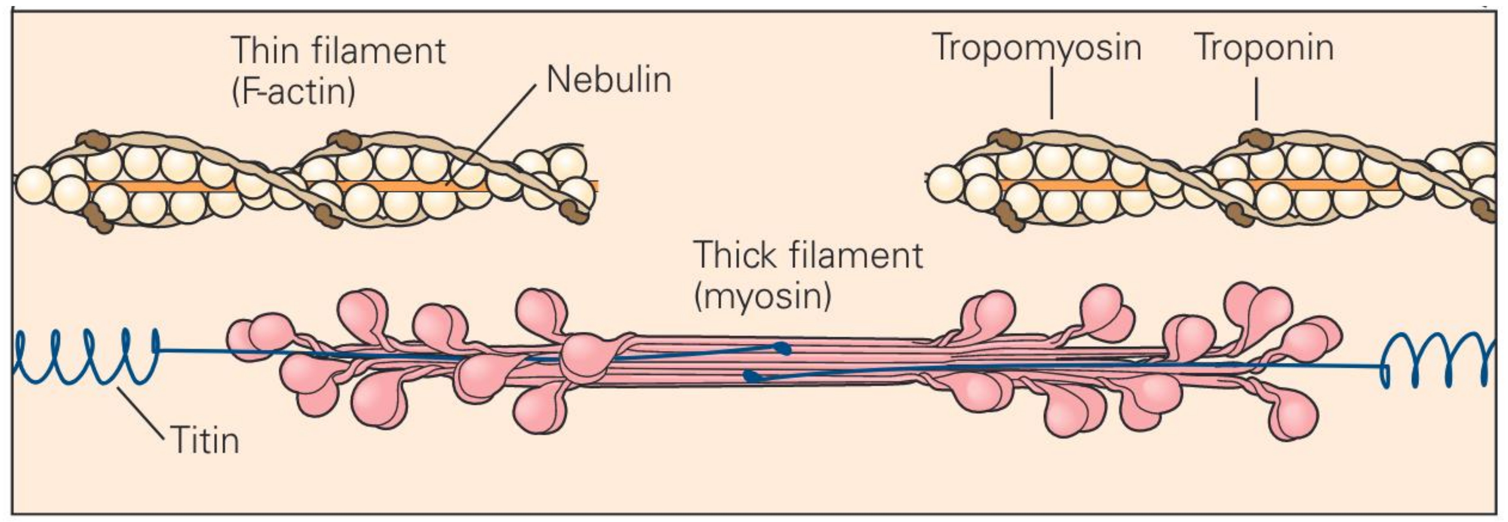
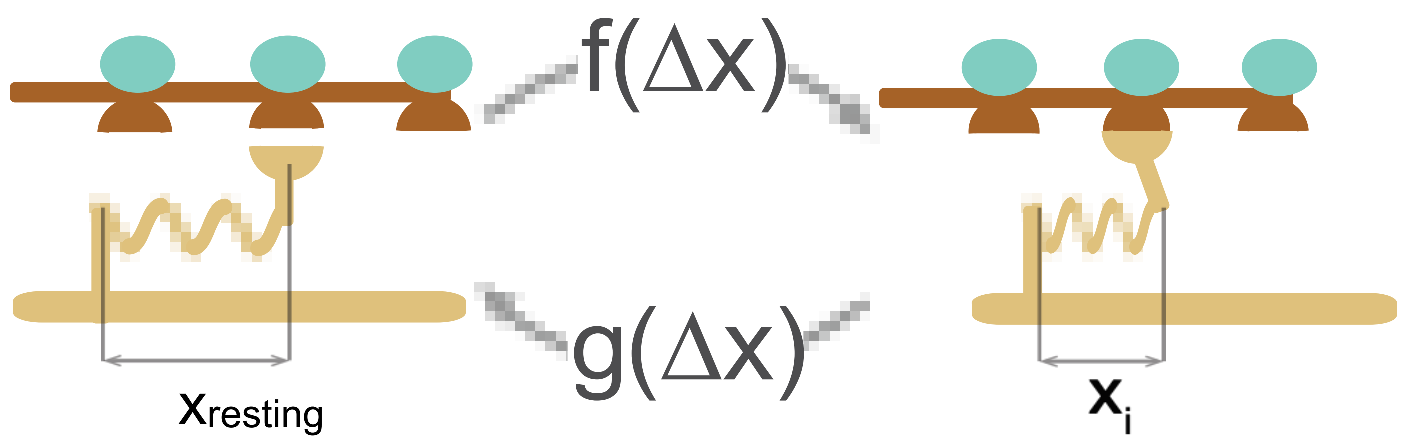


Image credit: Sarah Kosta



Kandell, Schwartz, Jessell 2013

Crossbridge model: spring that continuously transitions b/w attached and detached



$\Delta x = x_i - x_{resting}$

Simplify the crossbridge

1 dimensional spring

2 states (detached or attached)

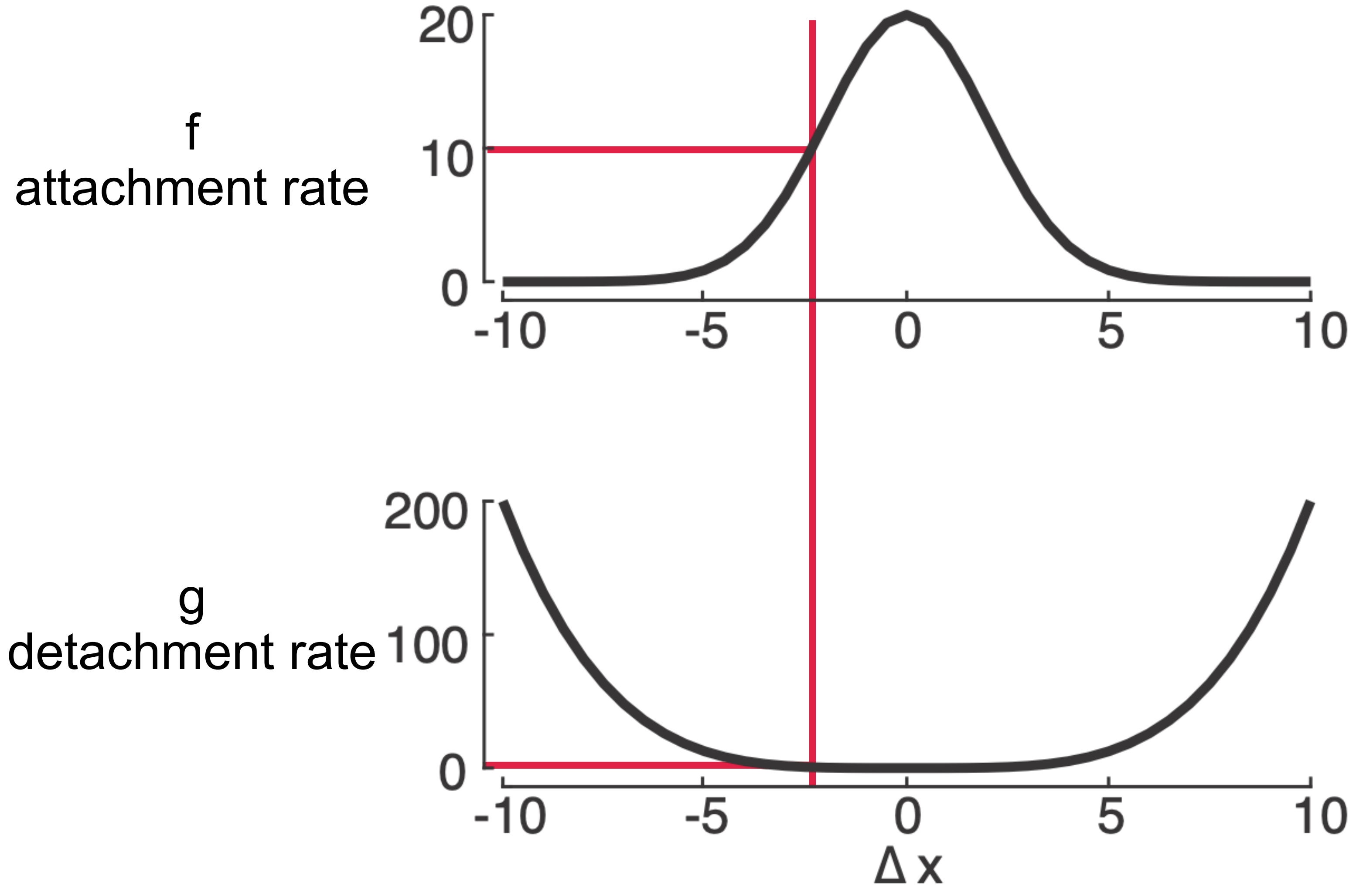
Count number of attached crossbridges

states continuously transition

90 10 1000 2 10 5

$$\frac{dn_{attached}}{dt} = f(x) \cdot n_{detached} - g(x) \cdot n_{attached}$$

attachment rate   detachment rate



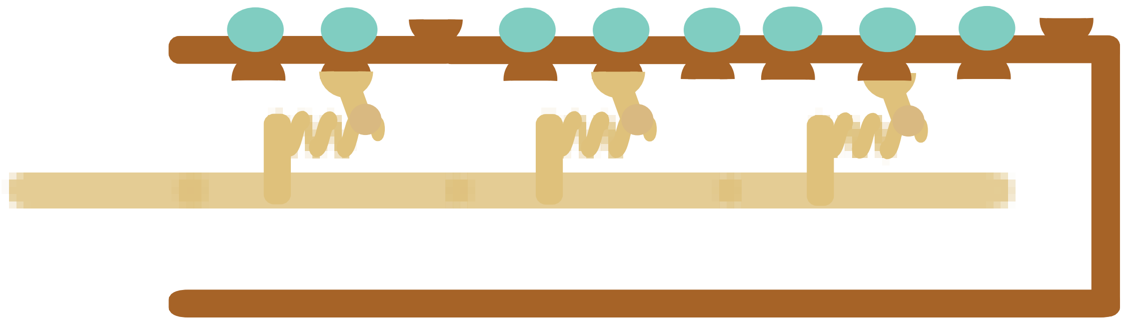
count attached crossbridges at single time point (numerical integrator)

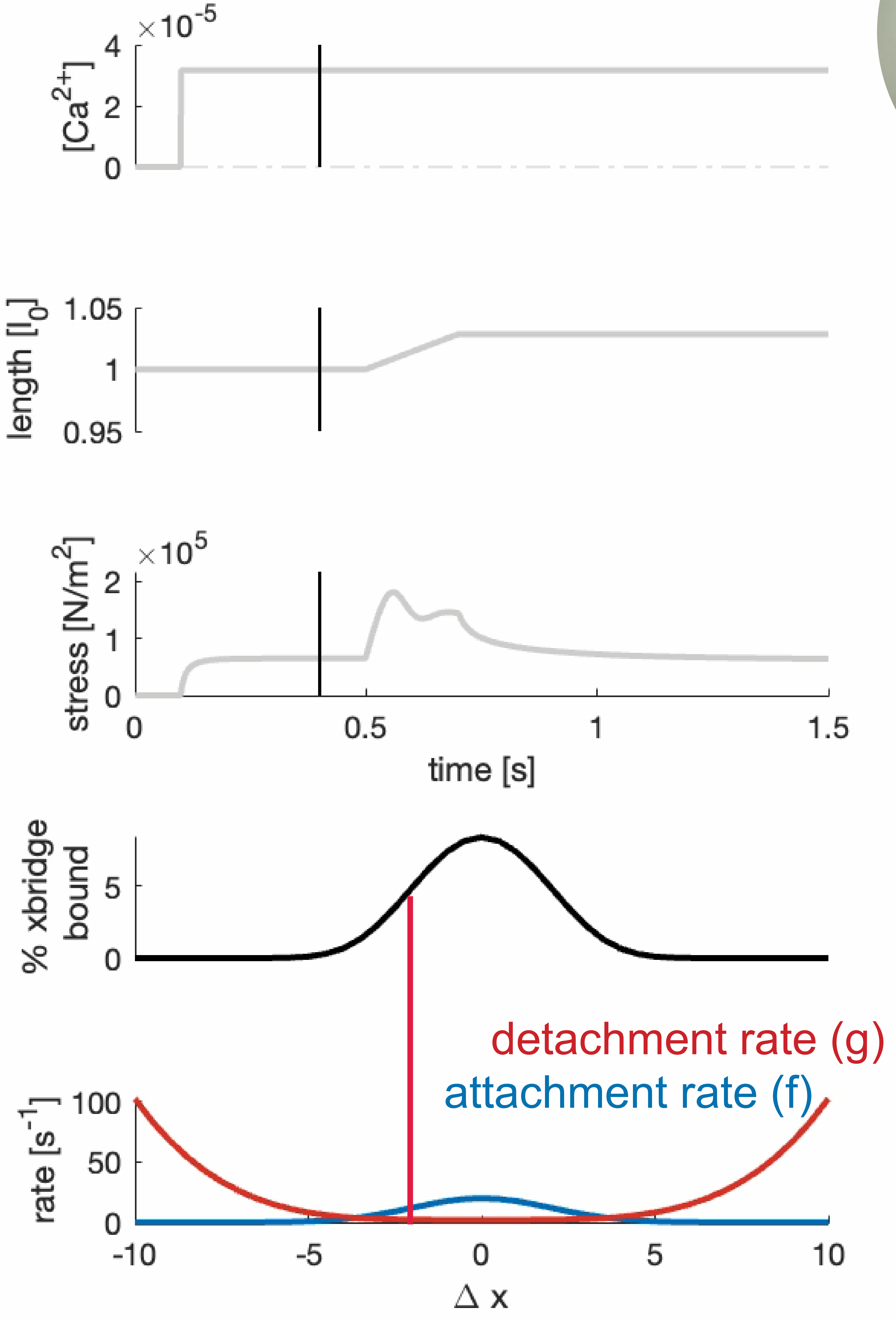
MyoSim

A.F. Huxley, 1954

van der Zee et. al. 2025; *in prep*

Muscle model: distribution of “cross-bridge springs”





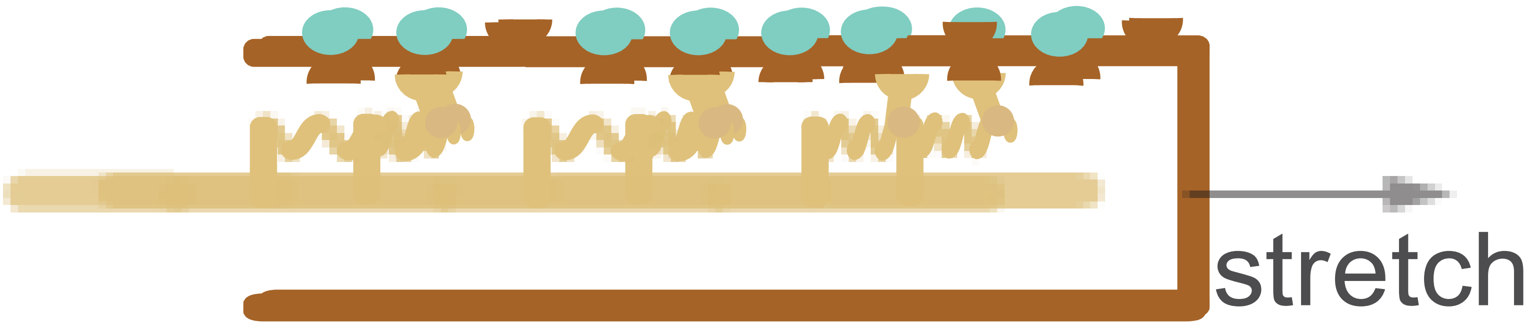
Calculate force from one attached crossbridge

spring force $F = k_{cb} \cdot \Delta x$

Add forces from all attached crossbridges

$$F_{total} = \sum_{i=0}^{i=n_{bound}} F_i$$

Muscle model: distribution of “cross-bridge springs”



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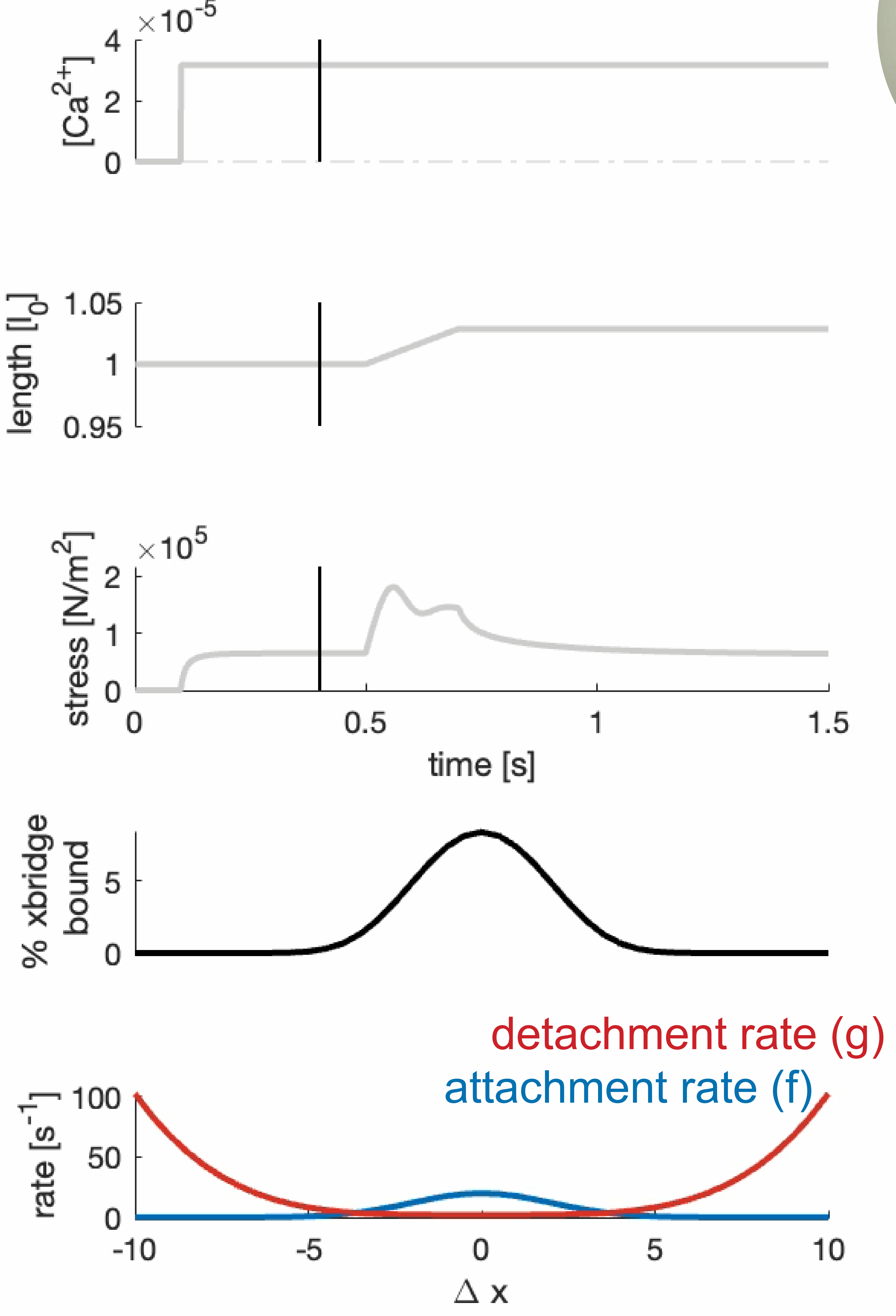
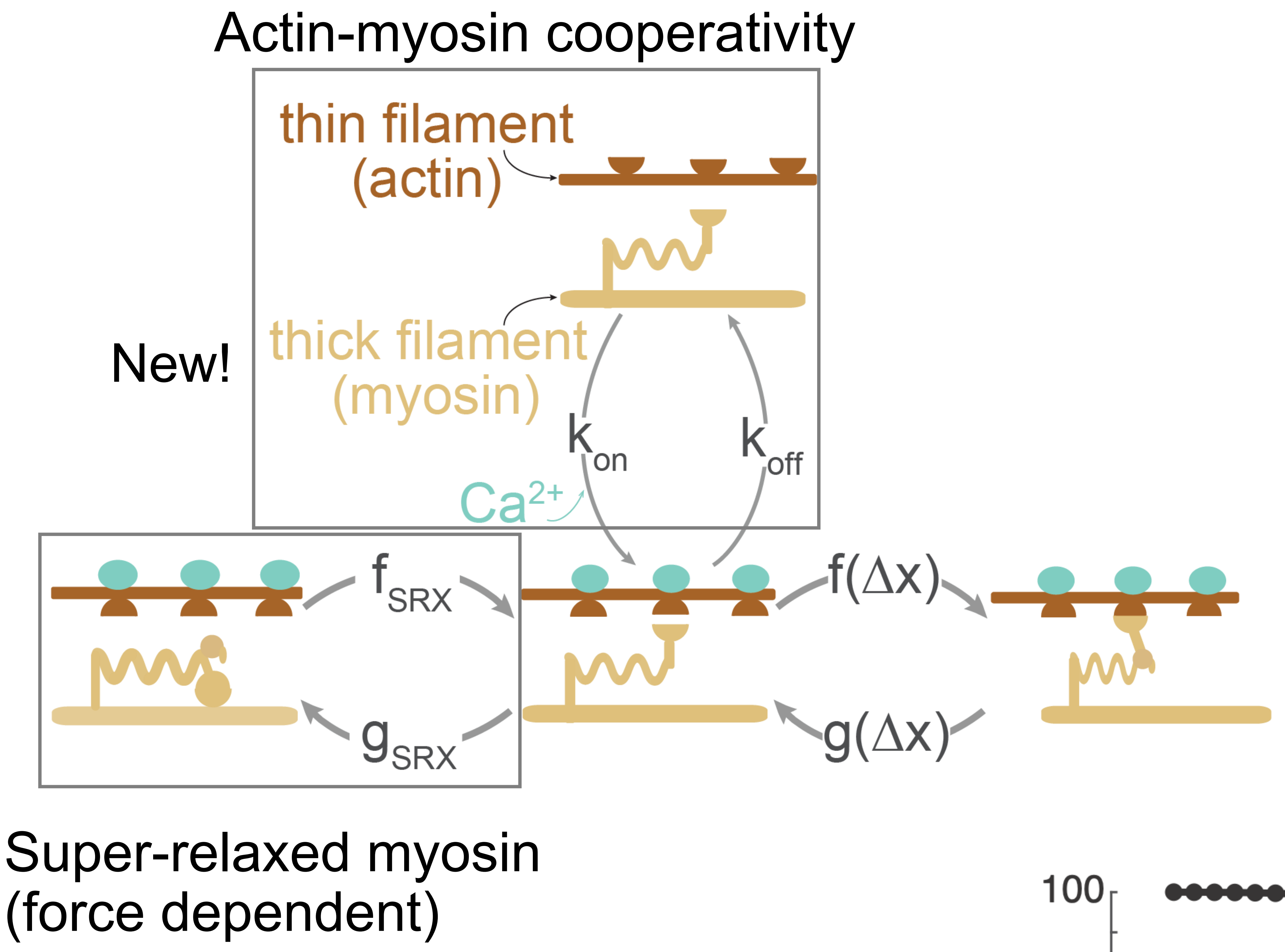
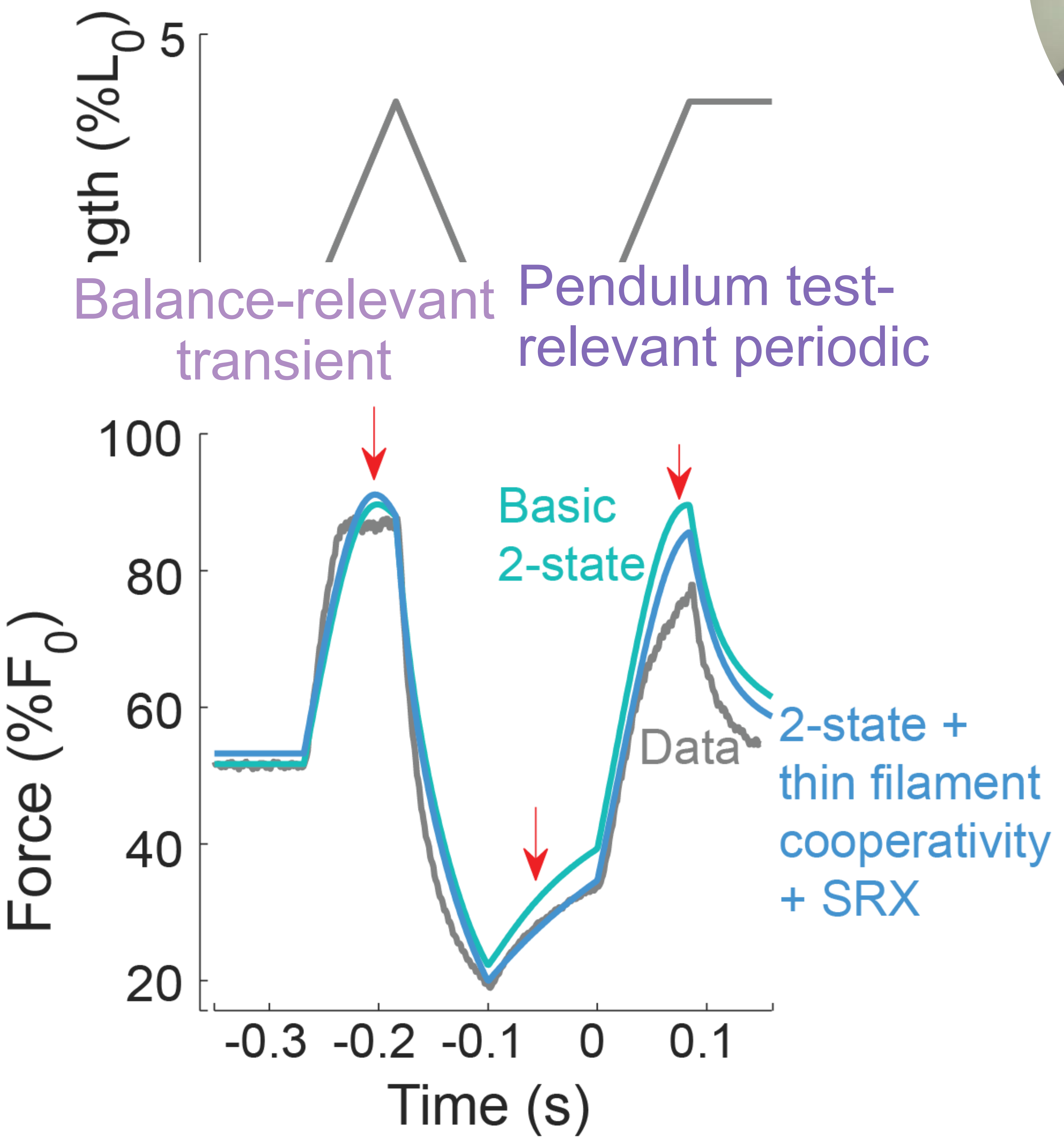
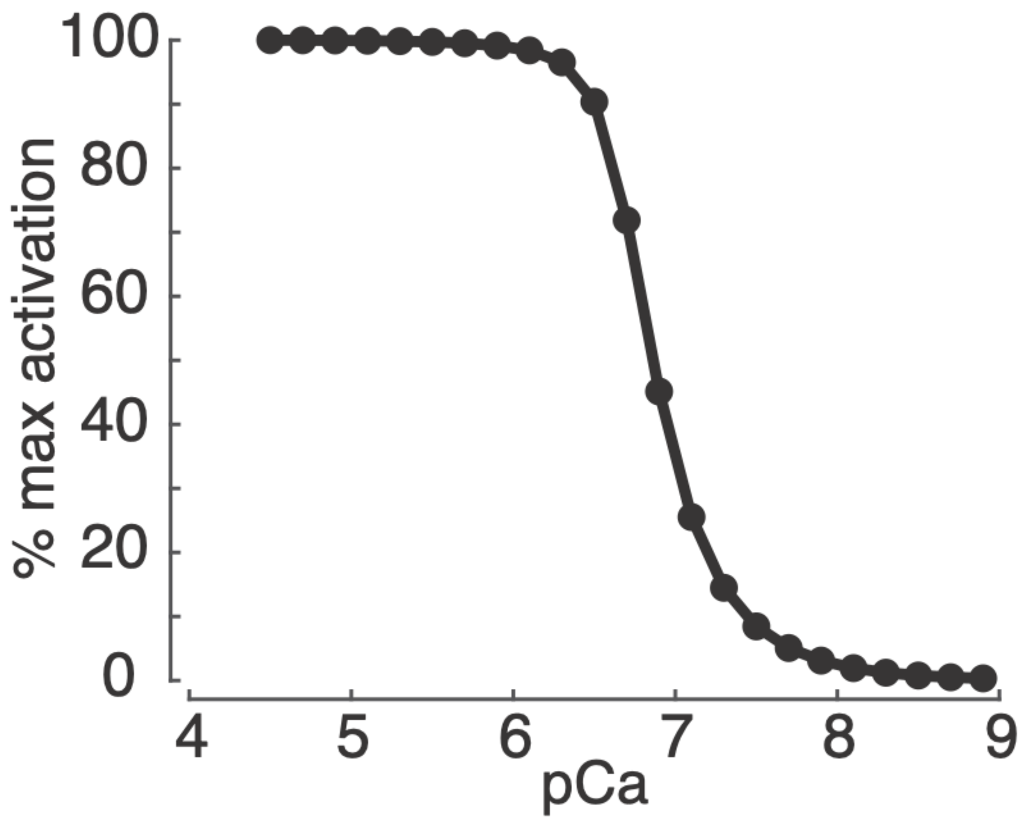


Add 2 more states for good force response to cyclic stretches





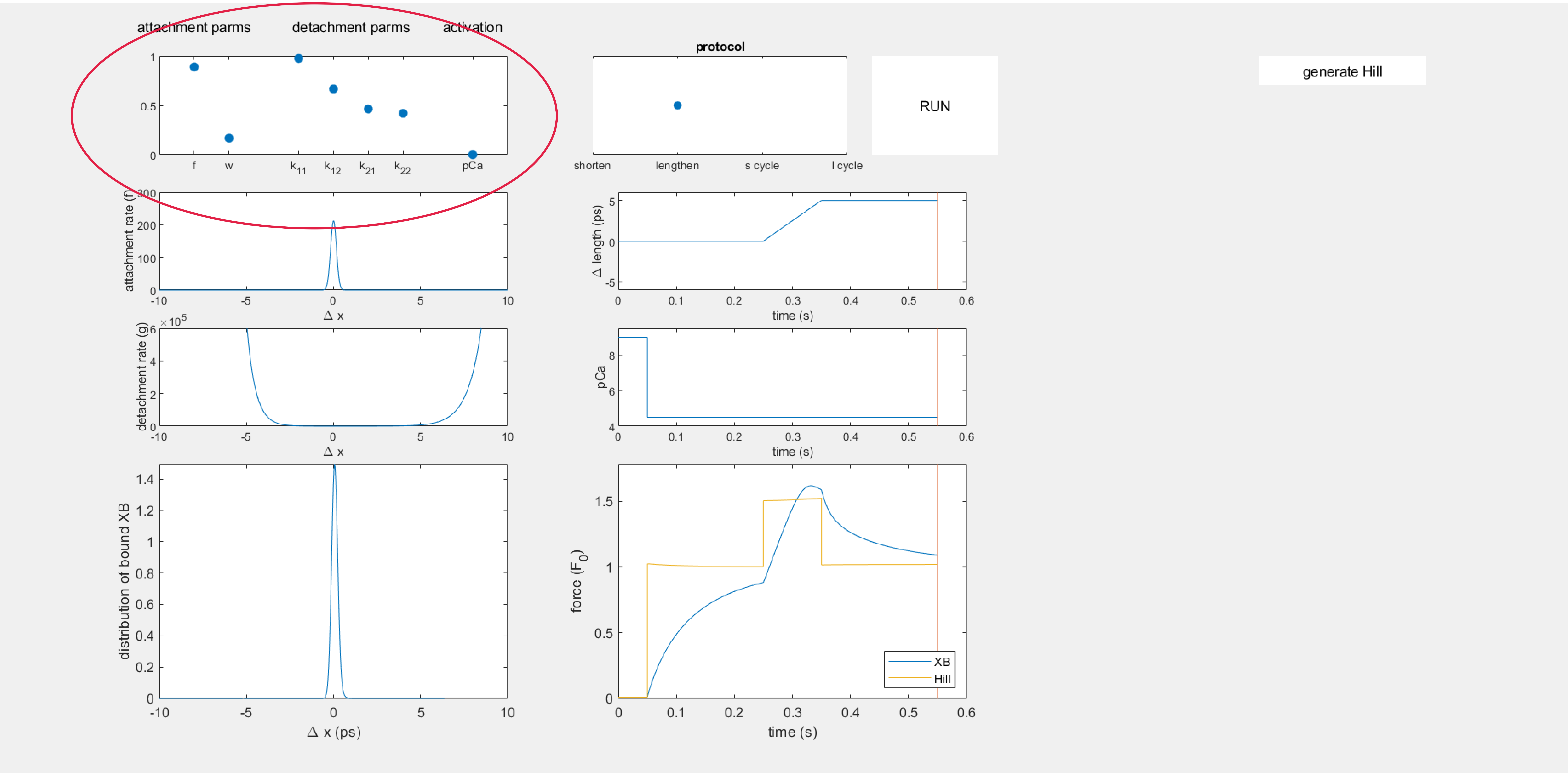
pCa activation curve



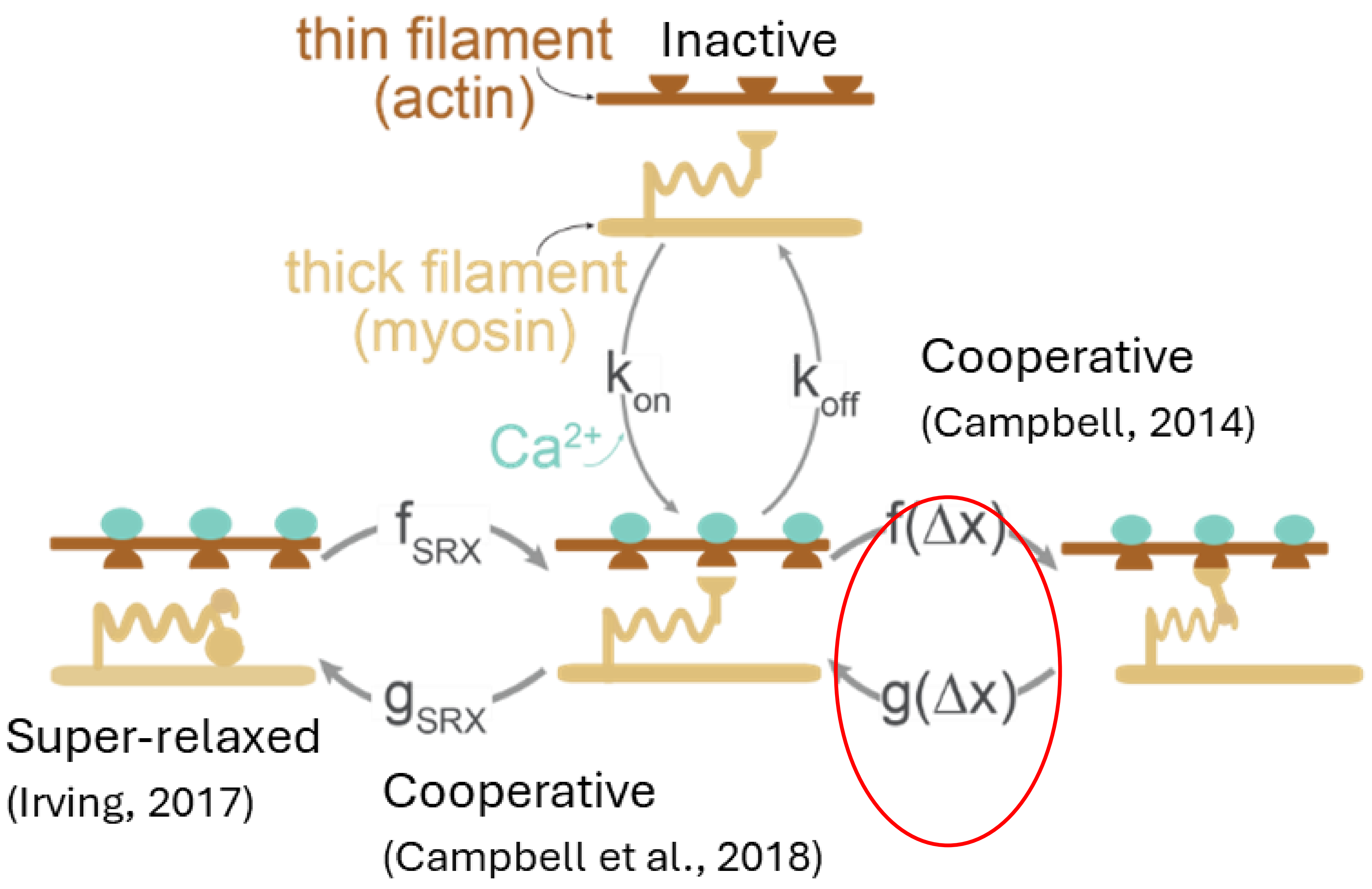
van der Zee et. al. 2025, *in prep*

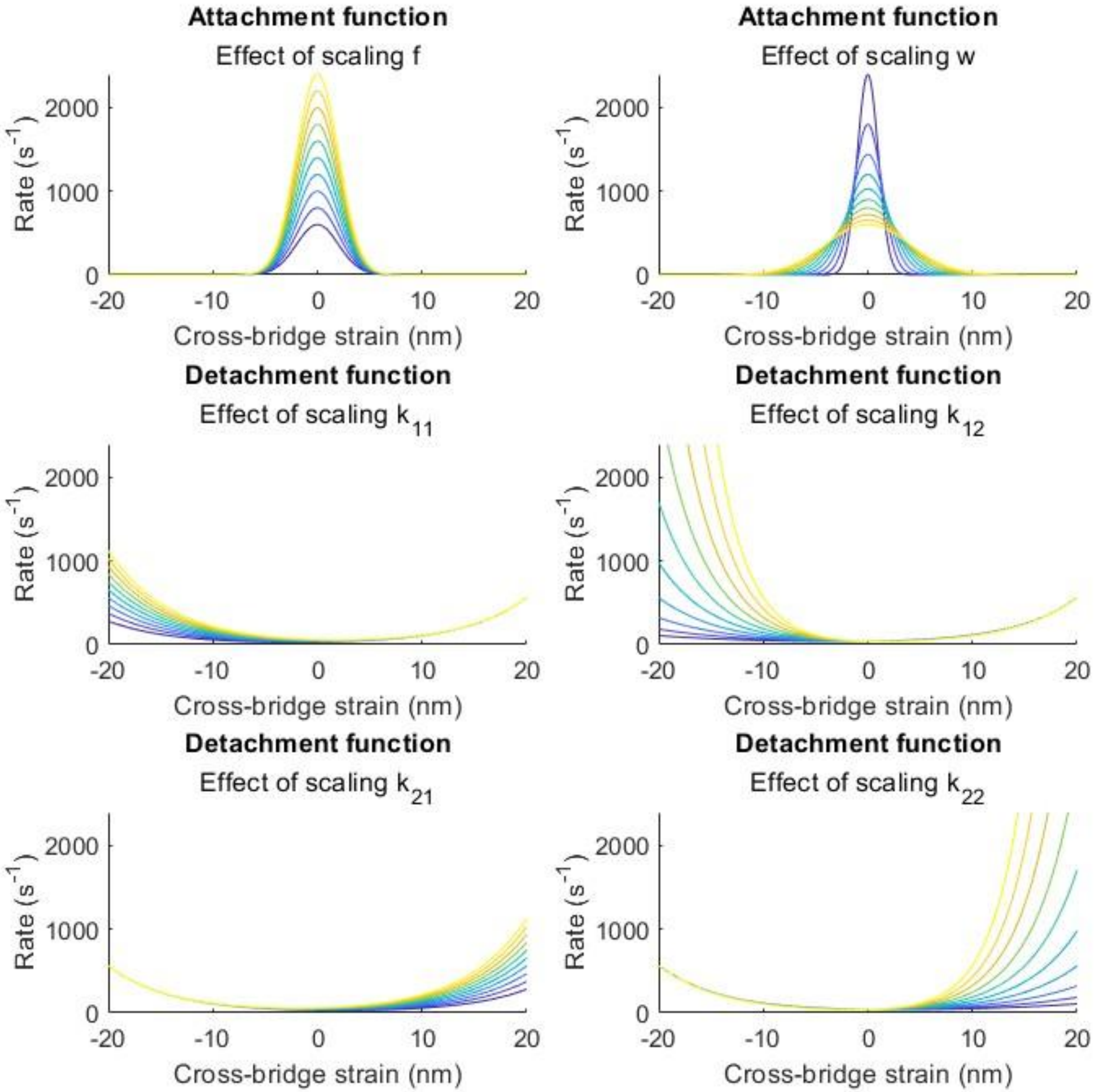
Simha & Ting, *J. Expt. Phys., 2023*

Tutorial Part 1: simulating a biophysical muscle model



Attachment and detachment rate functions





- Attachment rate f(Δx) = f(f,w)
- Detachment
  k21, k22)

The cross-bridge attachment functions $f(x)$ and $\phi(x)$ are gaussians:

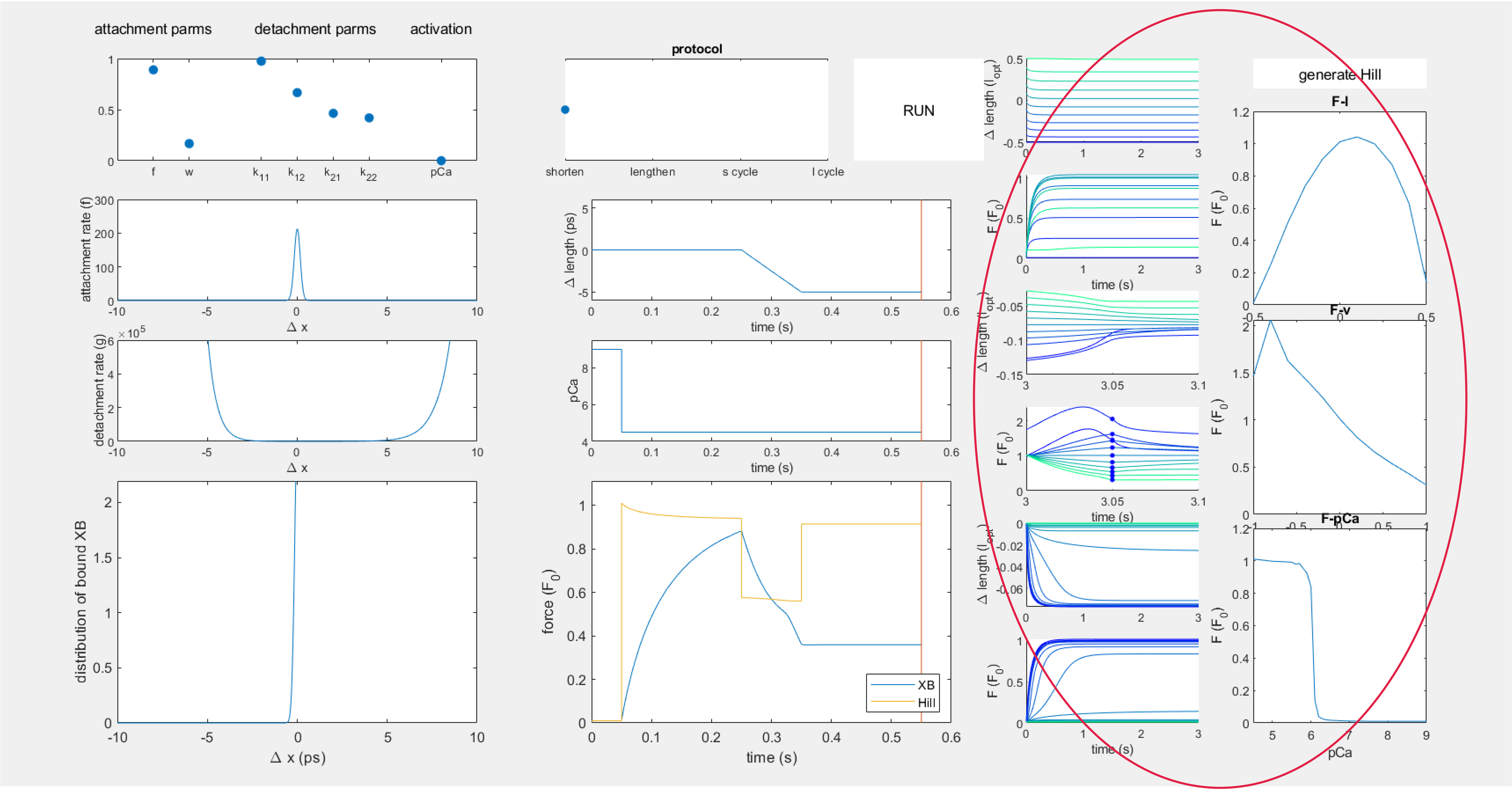
$$f(x) = \frac{f_1}{\sqrt{2\pi \cdot w^2}} \cdot e^{-\frac{x^2}{2 \cdot w^2}}$$

$$\phi(x) = \frac{\phi_1}{\sqrt{2\pi \cdot w^2}} \cdot e^{-\frac{x^2}{2 \cdot w^2}}$$

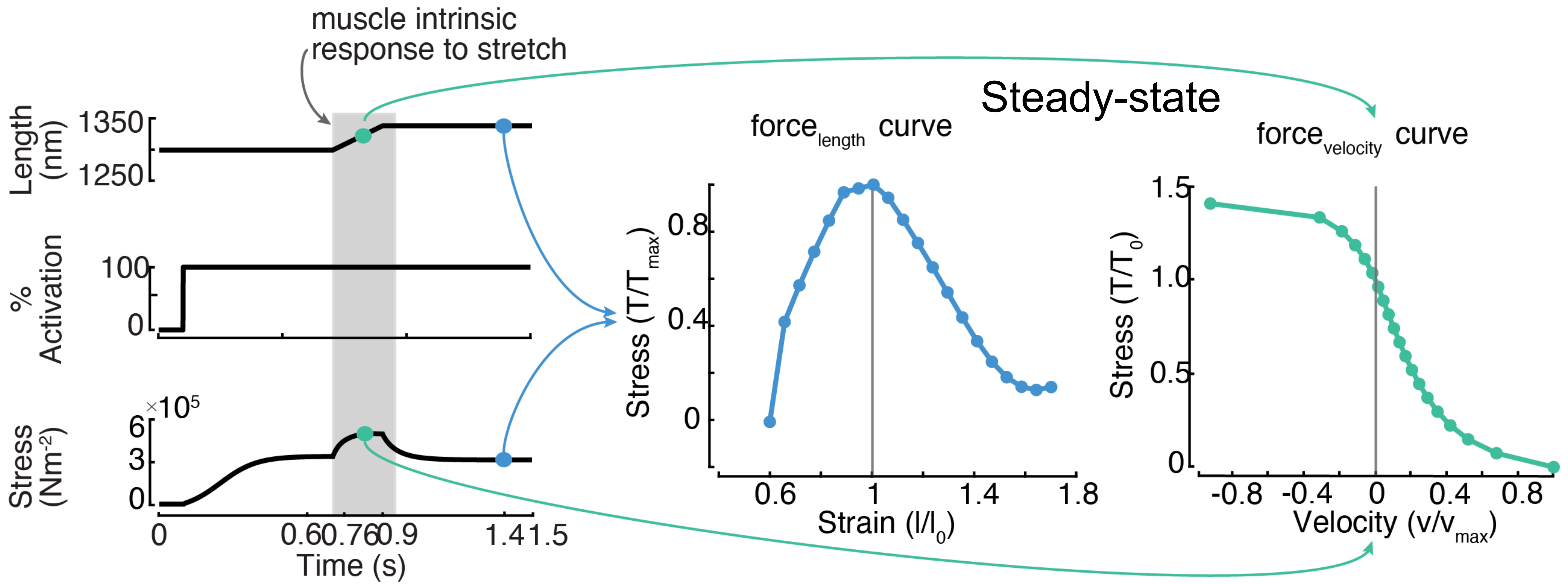
The cross-bridge detachment function $g(x)$ is the sum of two exponentials:

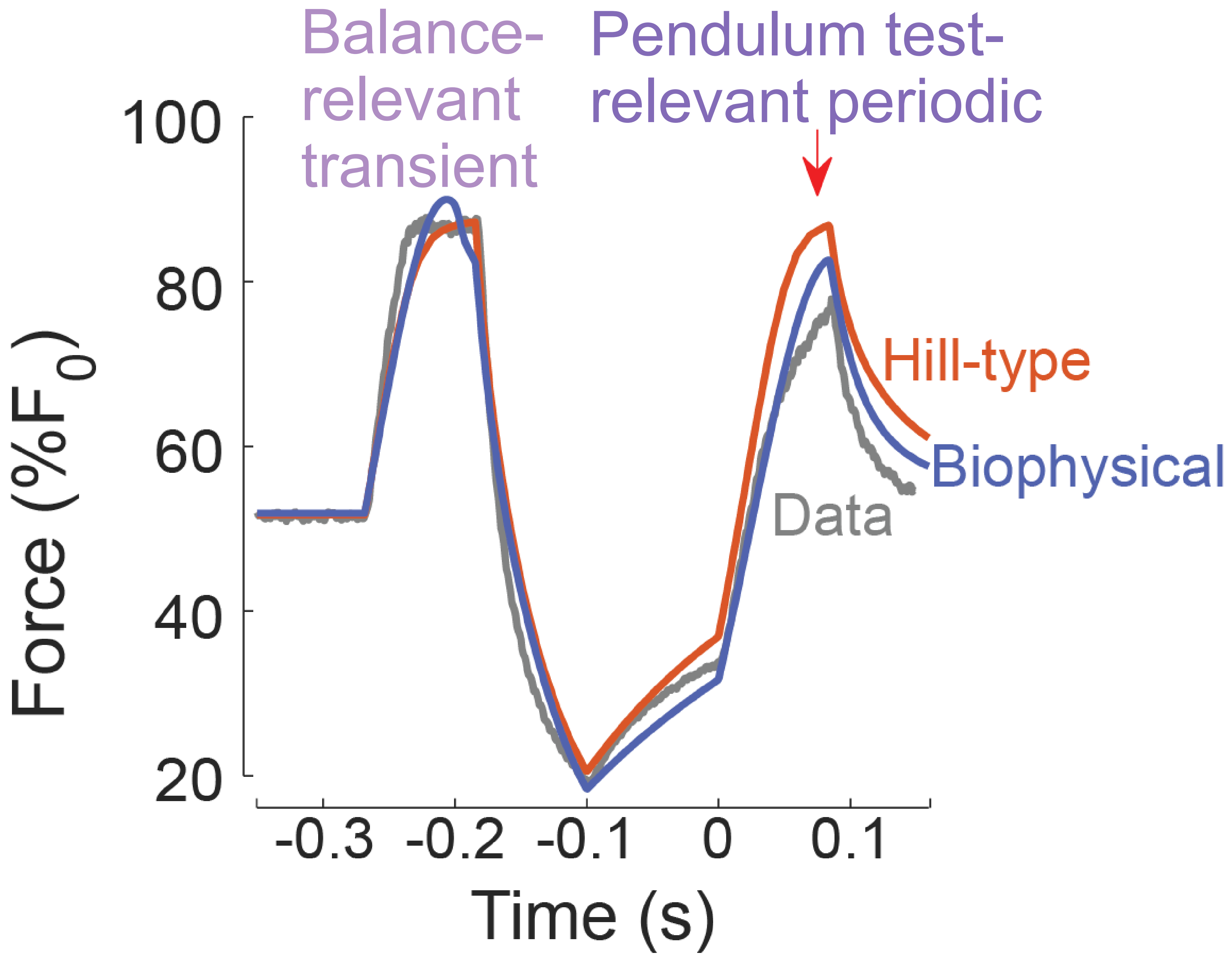
$$g(x) = \sum^{2} g_i \cdot e^{x \cdot E_i}$$

Tutorial Part 1: generating an equivalent Hill model



Hill-type force-velocity emerges from biophysical model





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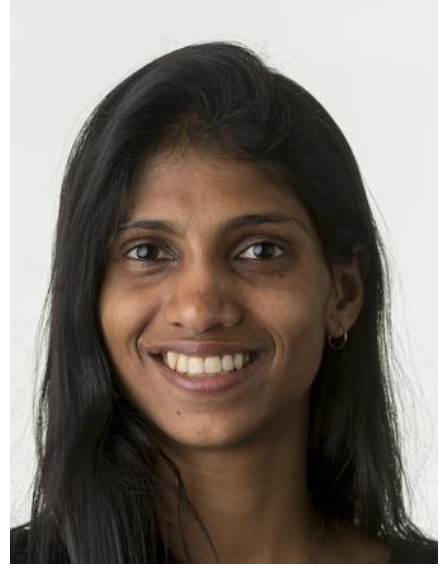

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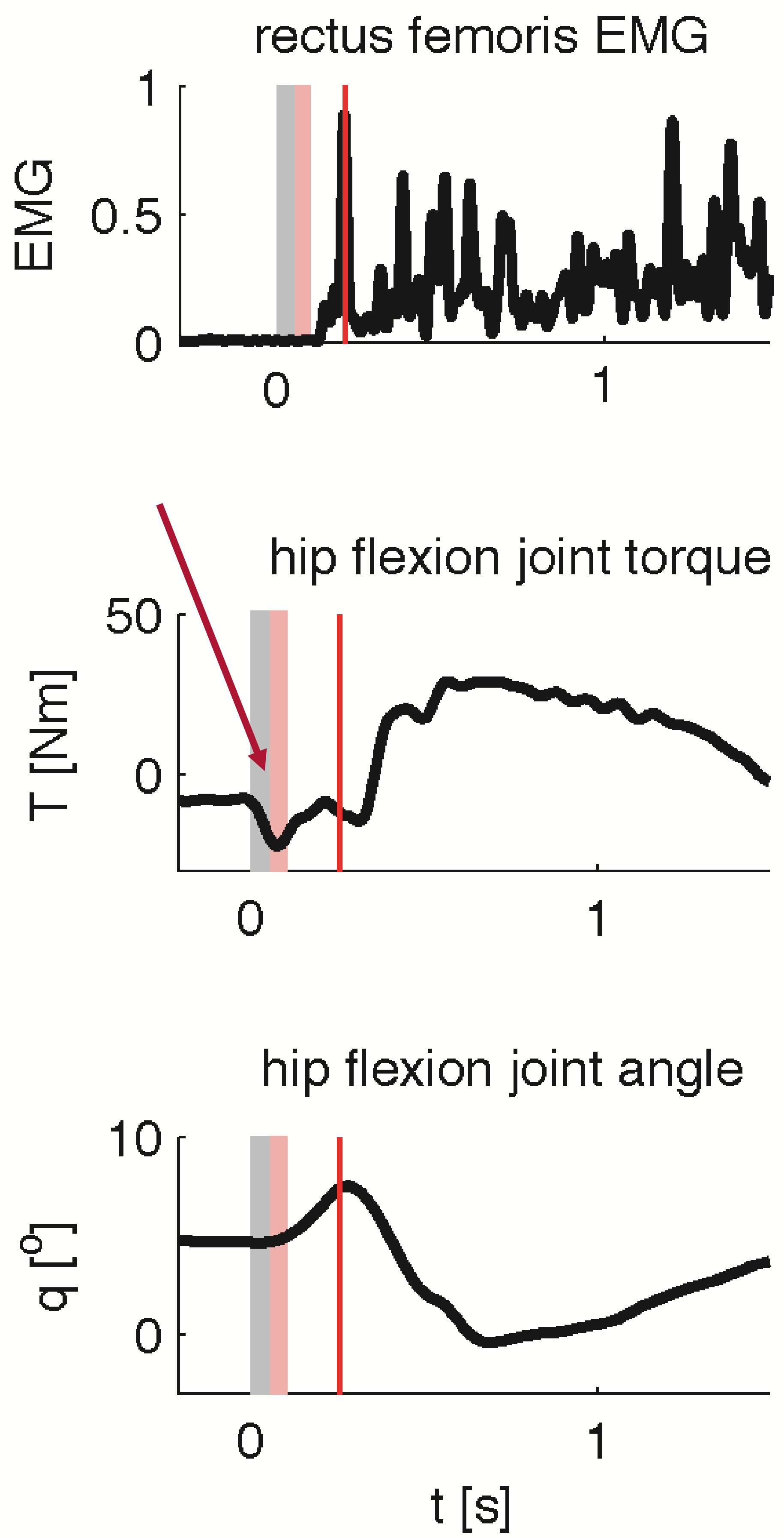

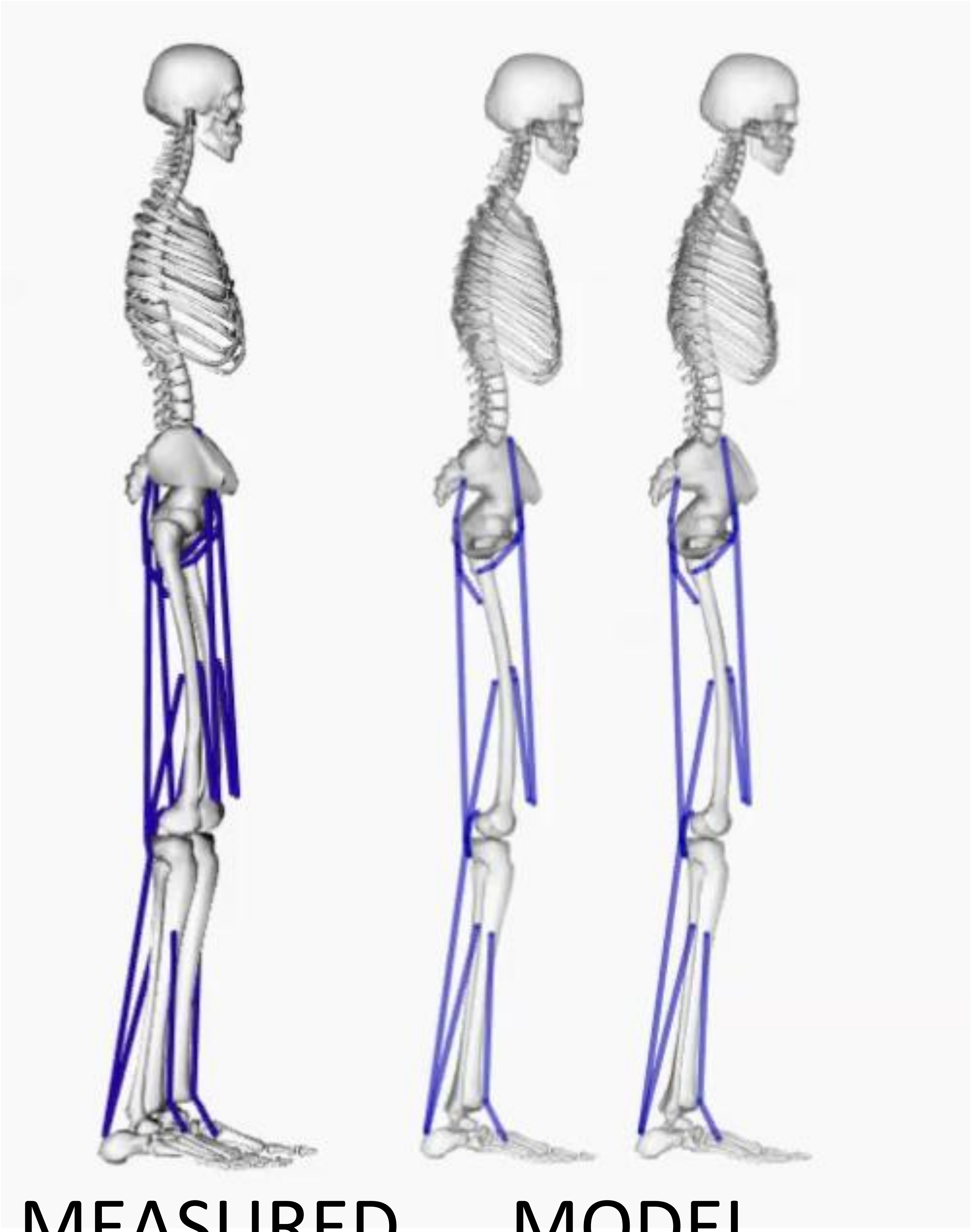

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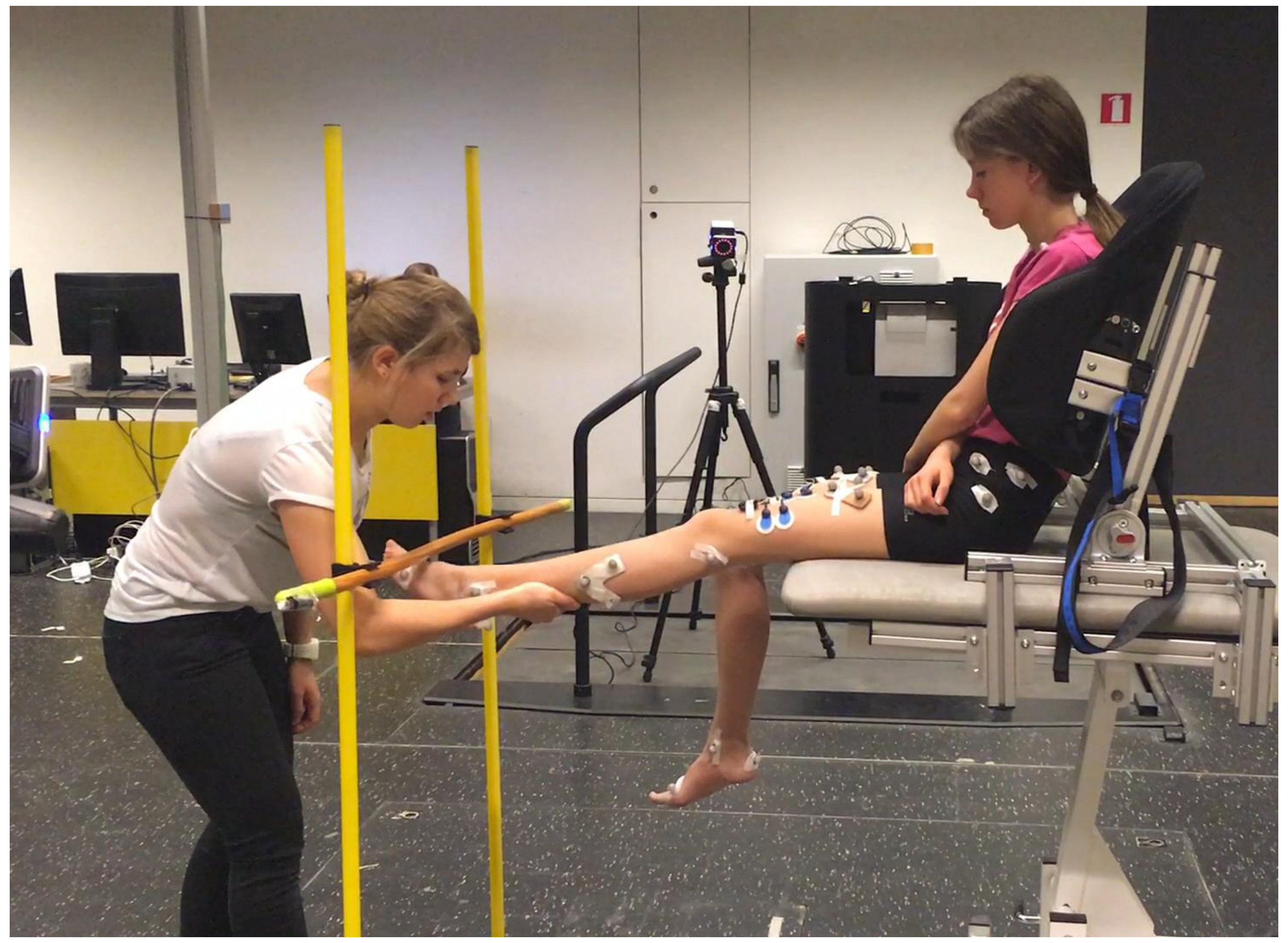

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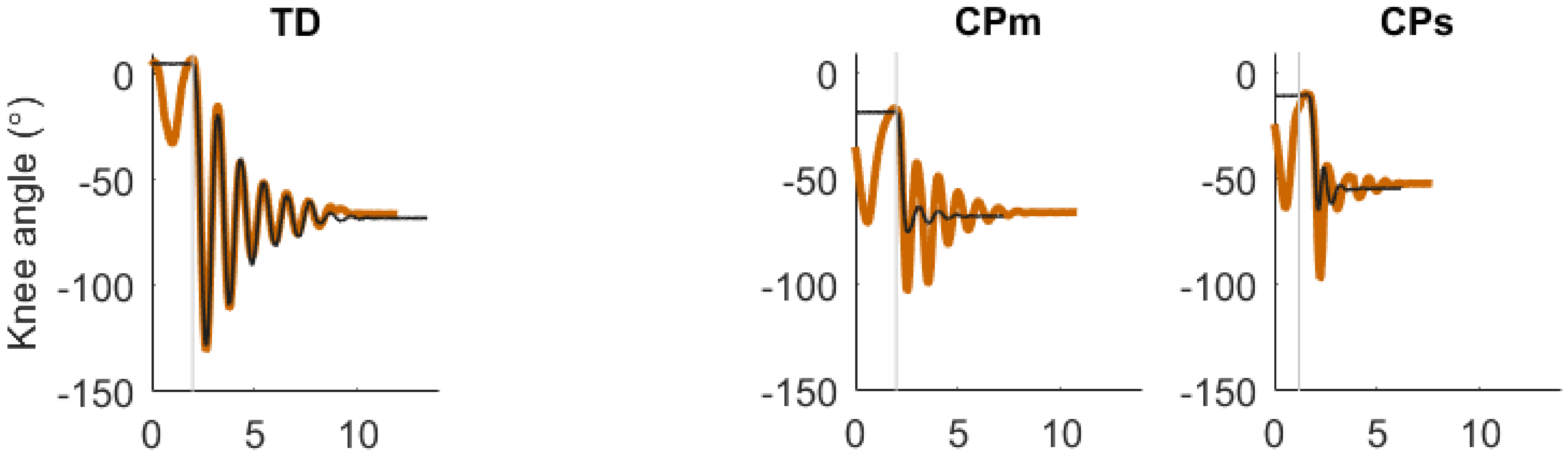
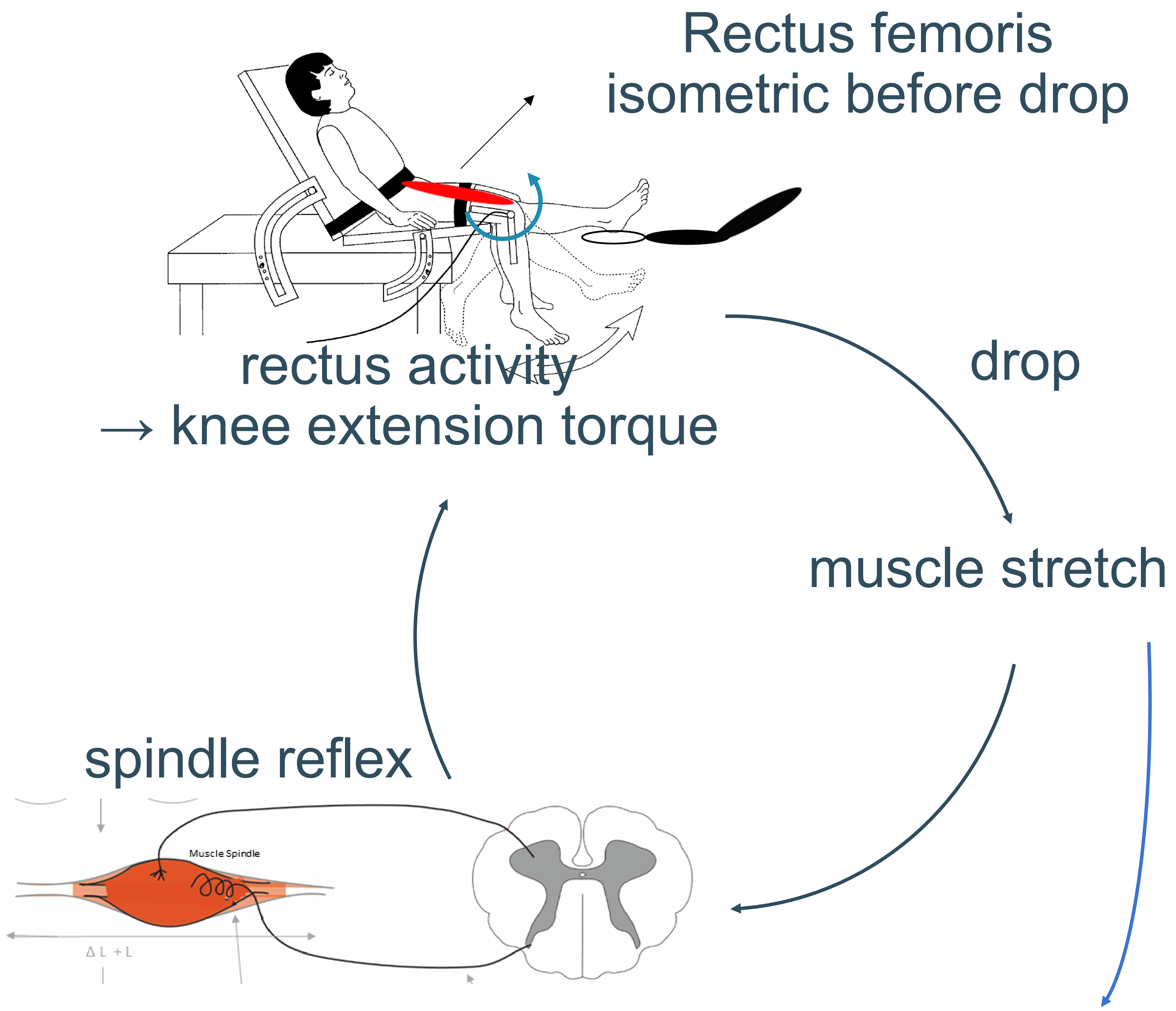
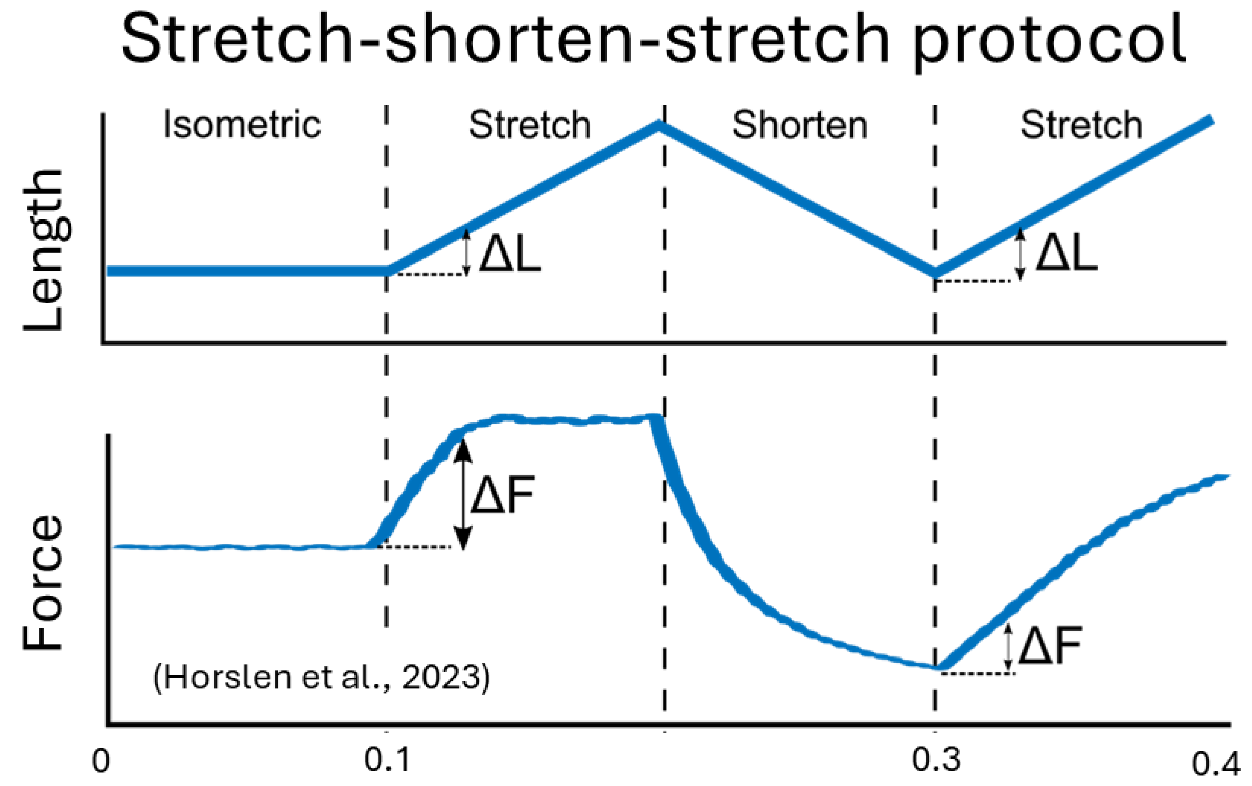
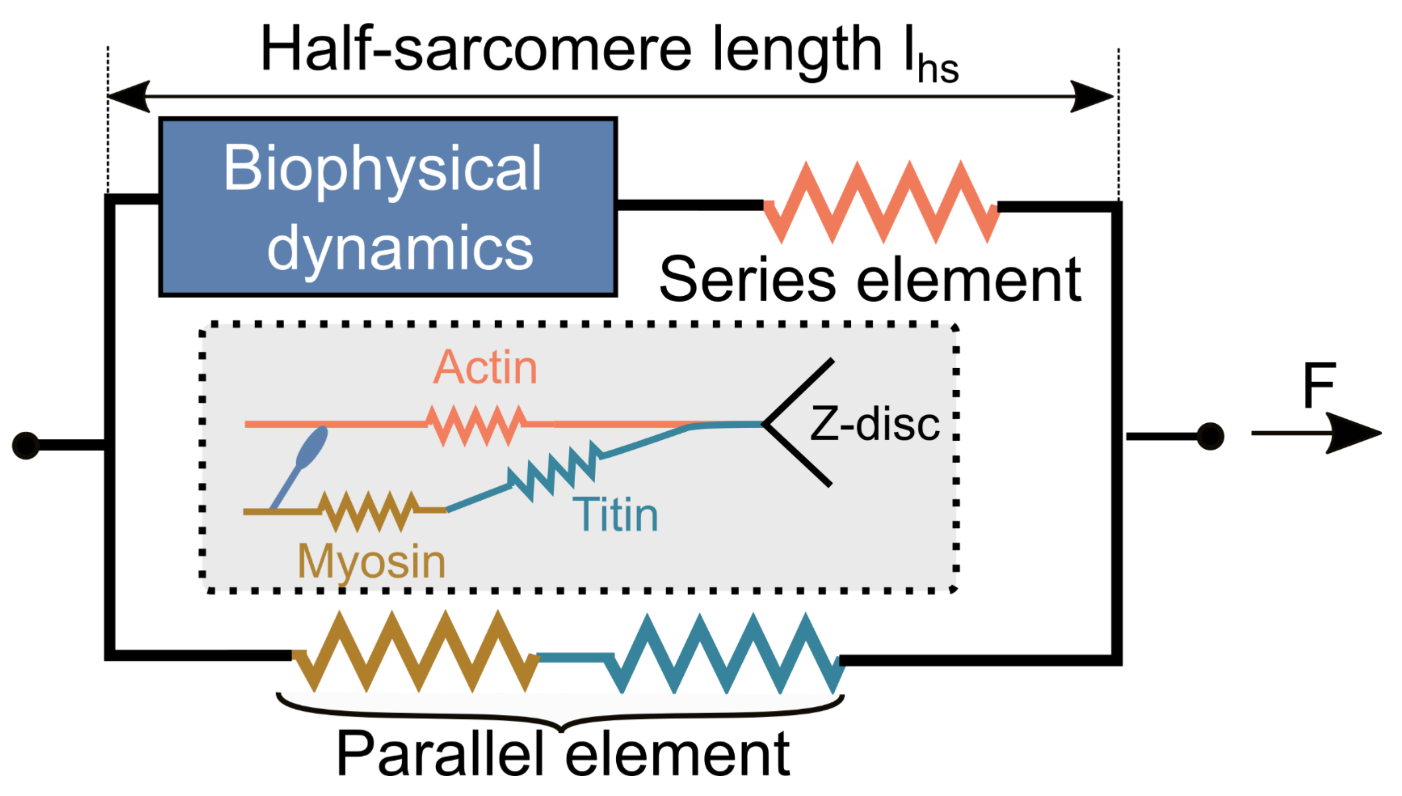


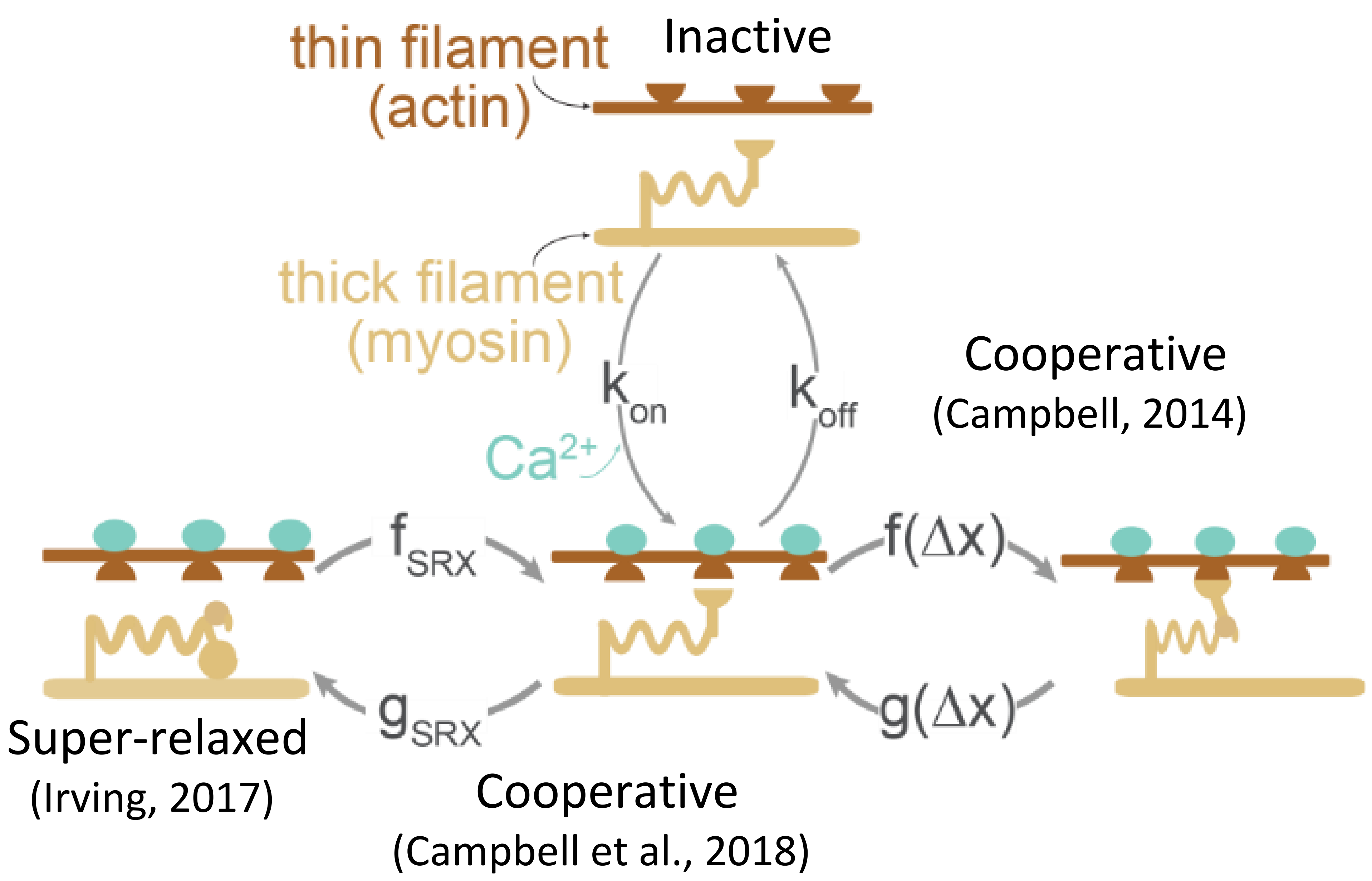


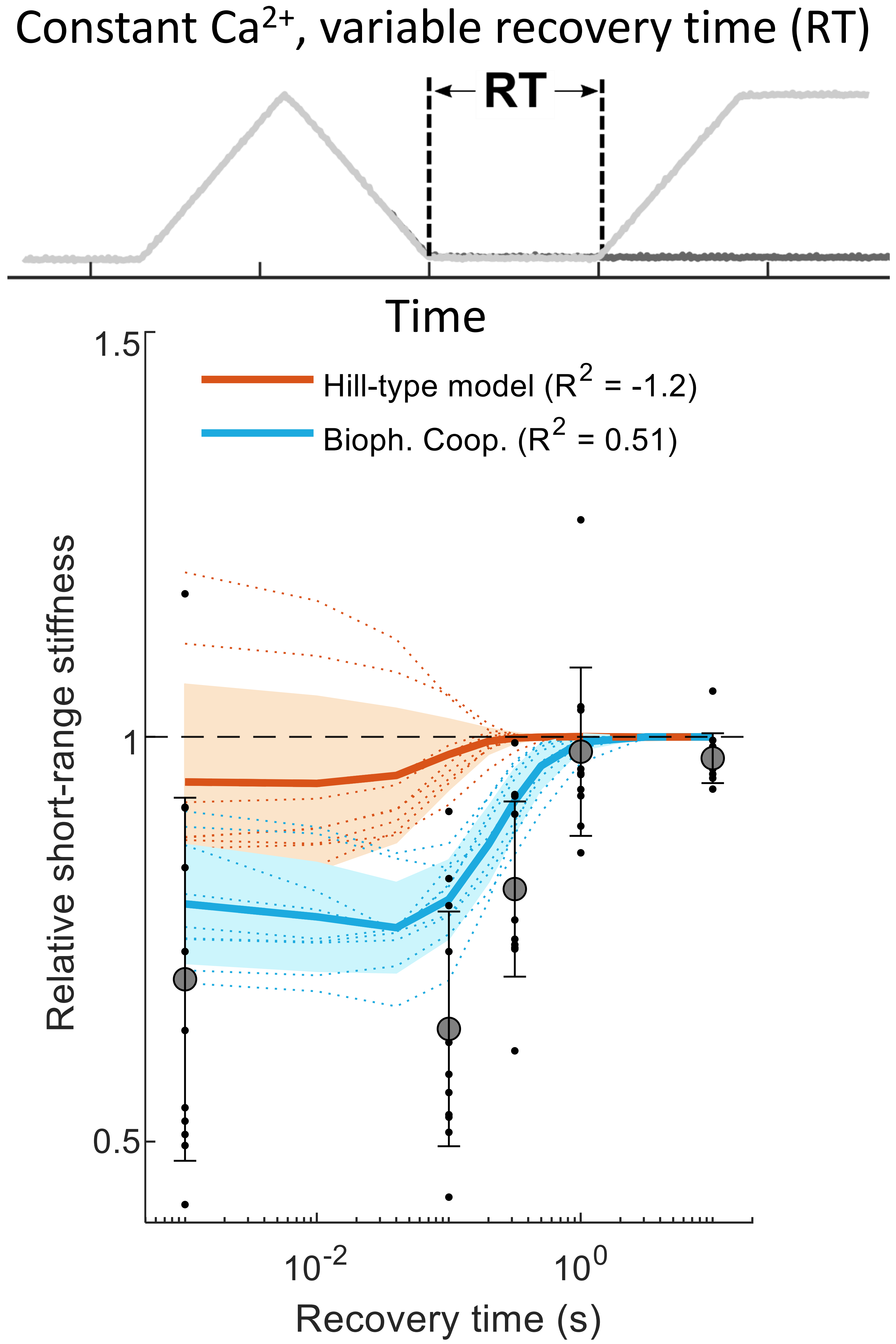


Willaert et al 2020, 2024; De Groote et al., *J Biomech*, 2018

Four-state cross-bridge model – but not Hill model – captures movement history-dependent short-range stiffness

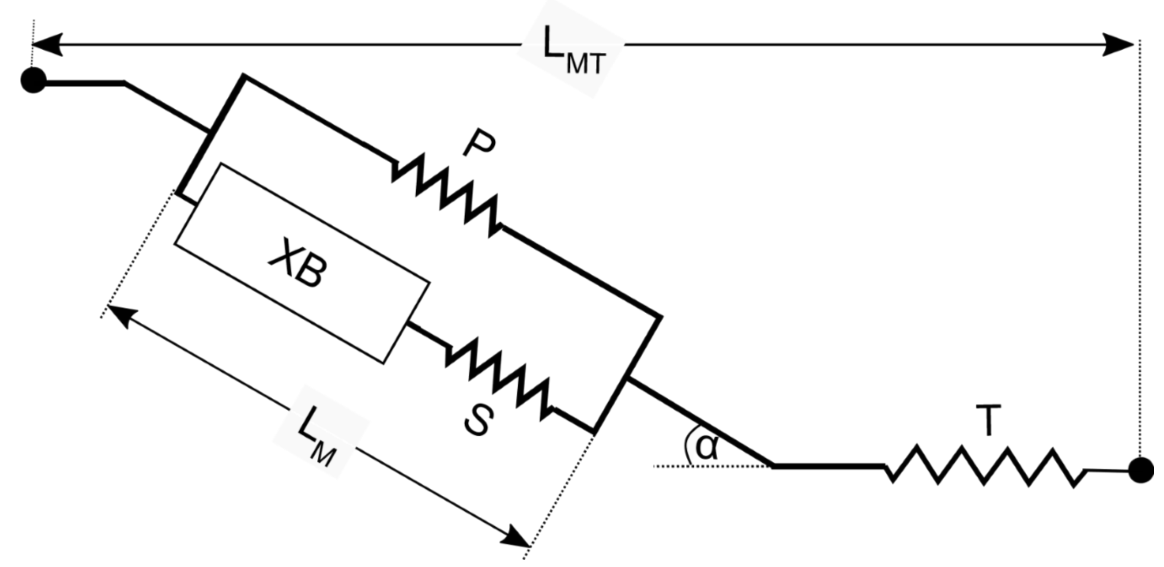




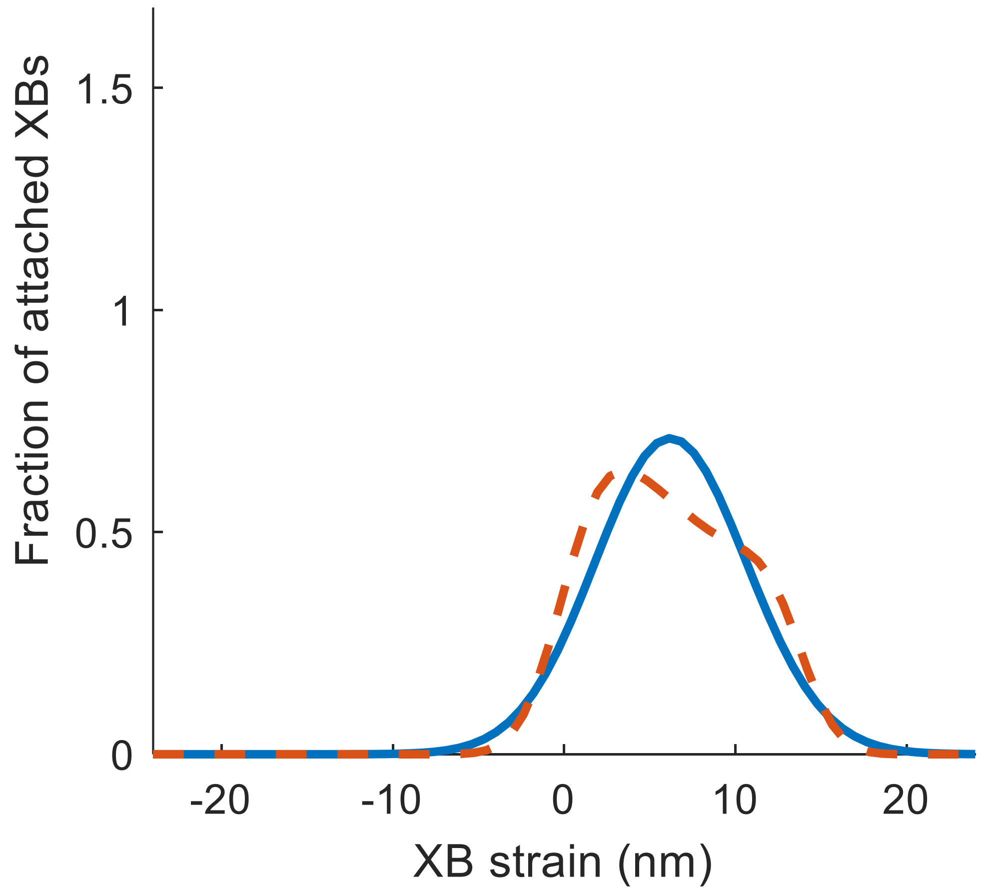


Using the biophysical muscle model in musculoskeletal simulations

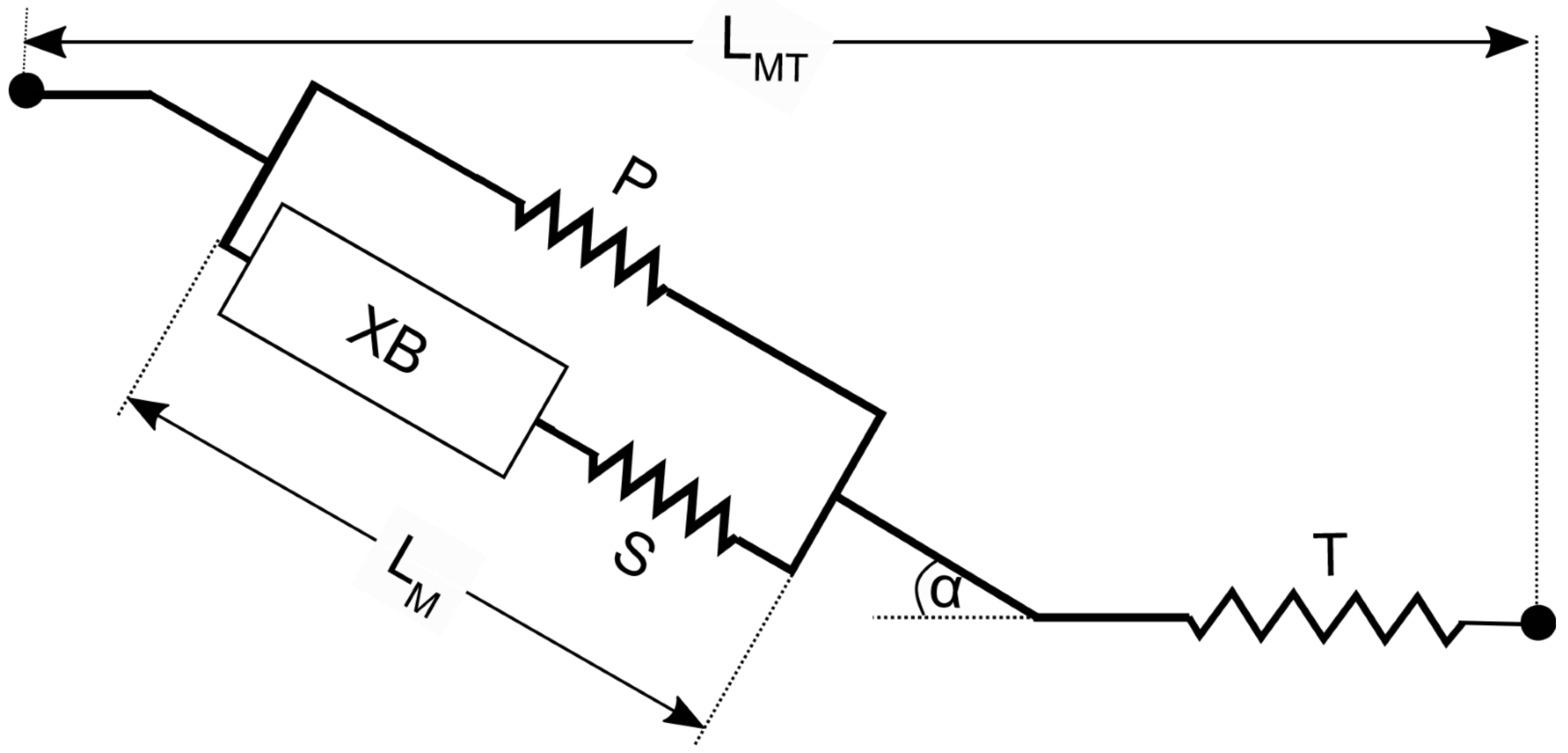
- **Scale half-sarcomere up to whole muscle**



- Distribution moment approximation to improve numerical efficiency



Scaling up a half sarcomere to a muscle



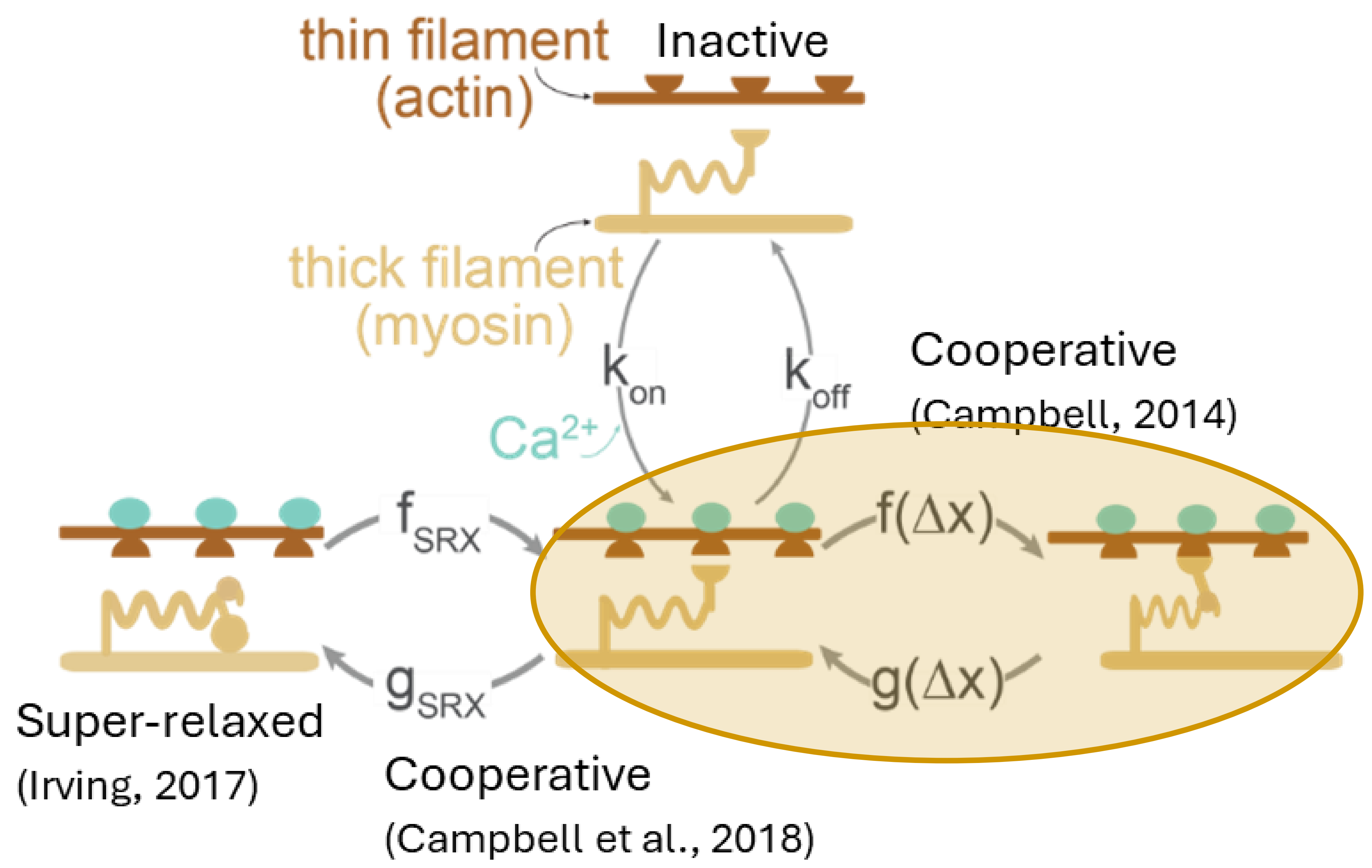
- Scale contractile force based on F_{max}
- Scale resting length based on optimal fiber length from Hill-type muscle model
- Add tendon (T) with stiffness based on Hill model
- Passive stiffness (P) and pennation angle (α) based on Hill-model
- Rate constants estimated from experimental data collected
  in rat soleus muscle fibers at low temperature not representative for in vivo human muscle
  → Estimate rate parameters

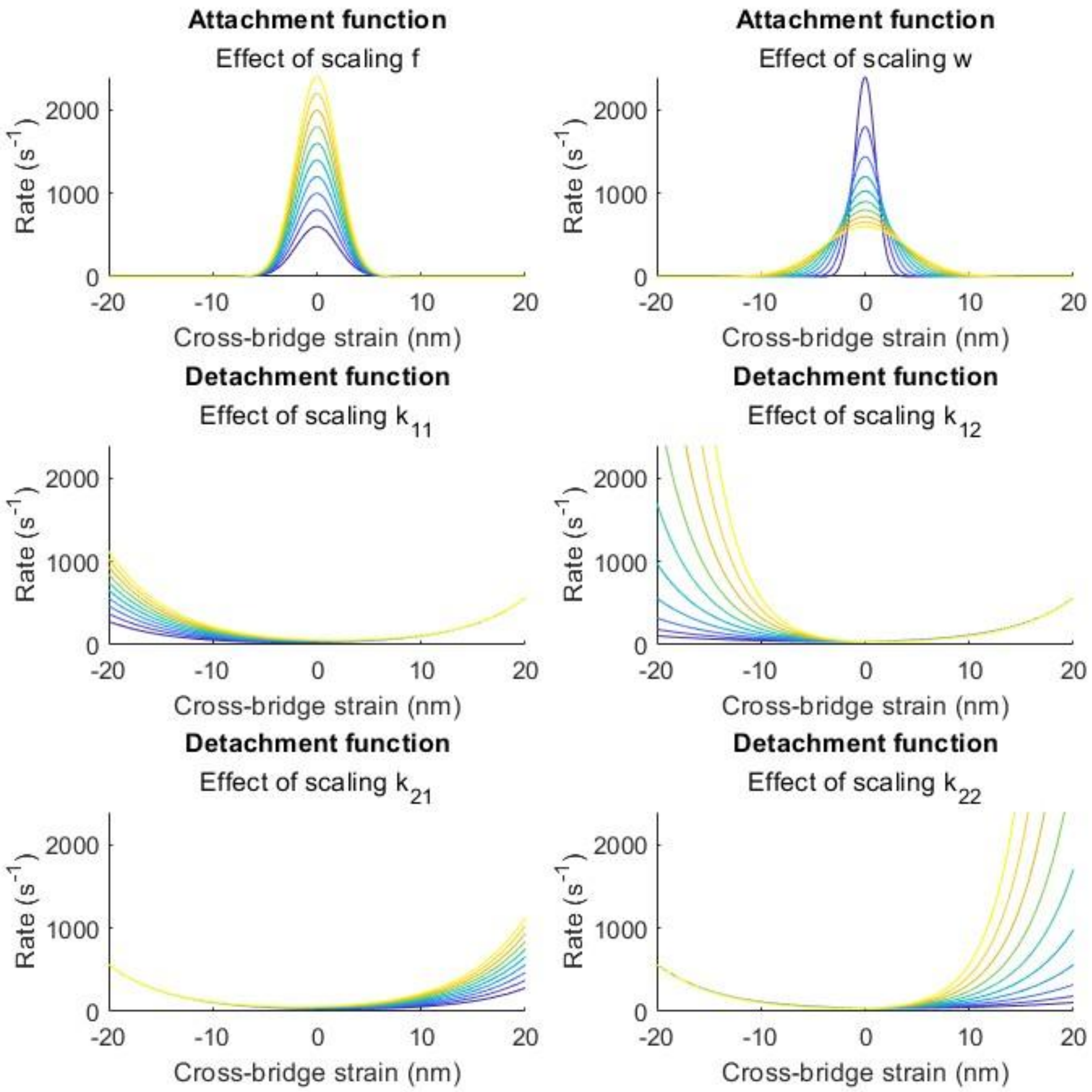
Estimate rate constants

6 parameters to specify the attachment and detachment rates

n(x) is distribution of attached XB

$$\frac{dn}{dt} - \frac{\partial x}{\partial t}\cdot\frac{\partial n}{\partial x} = f(x)\cdot DRX\cdot \underbrace{\left\{N_{on} - \int n(x)\,dx\right\}}_{\text{open binding sites}} - g(x)\cdot n(x)$$



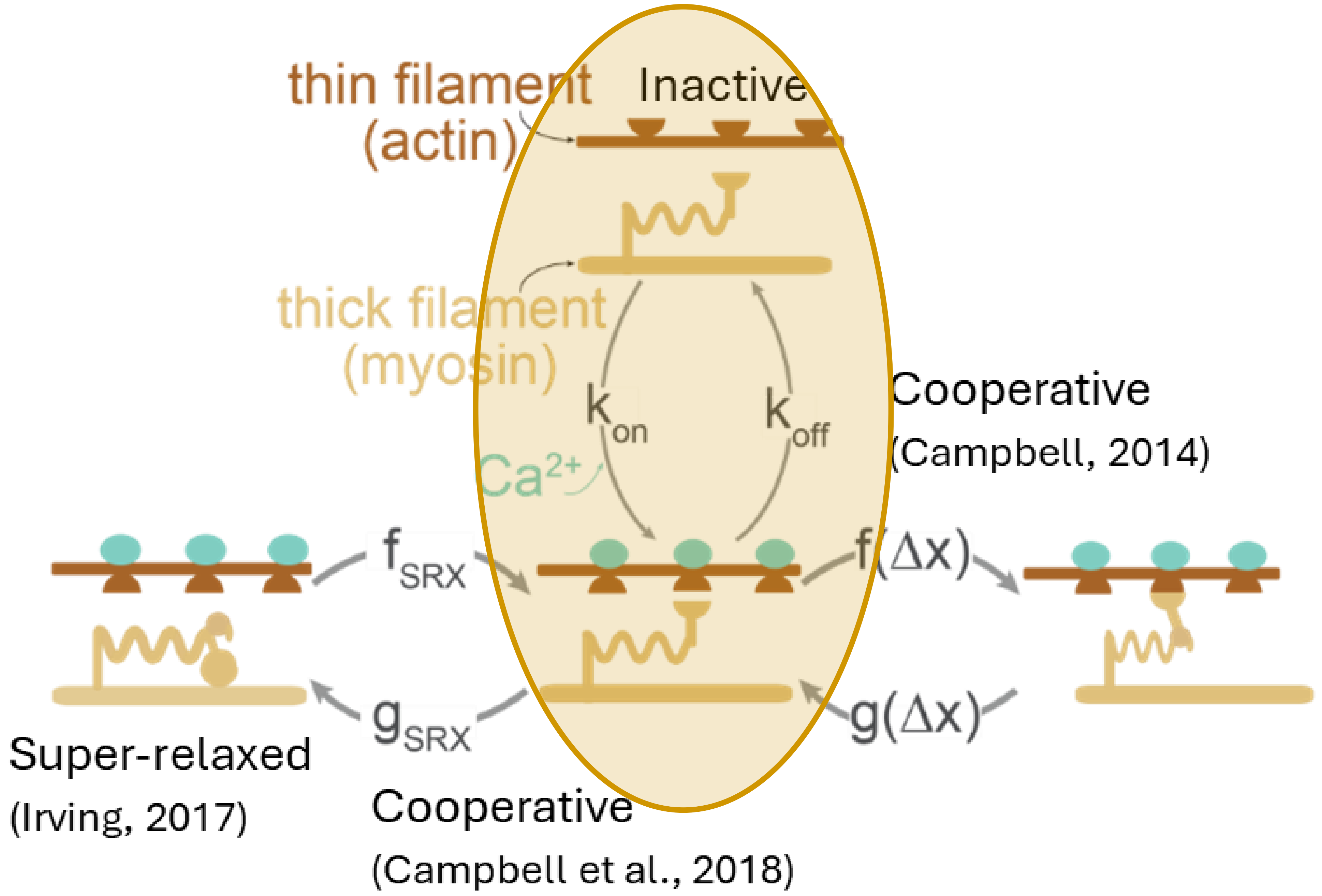


Estimate rate constants

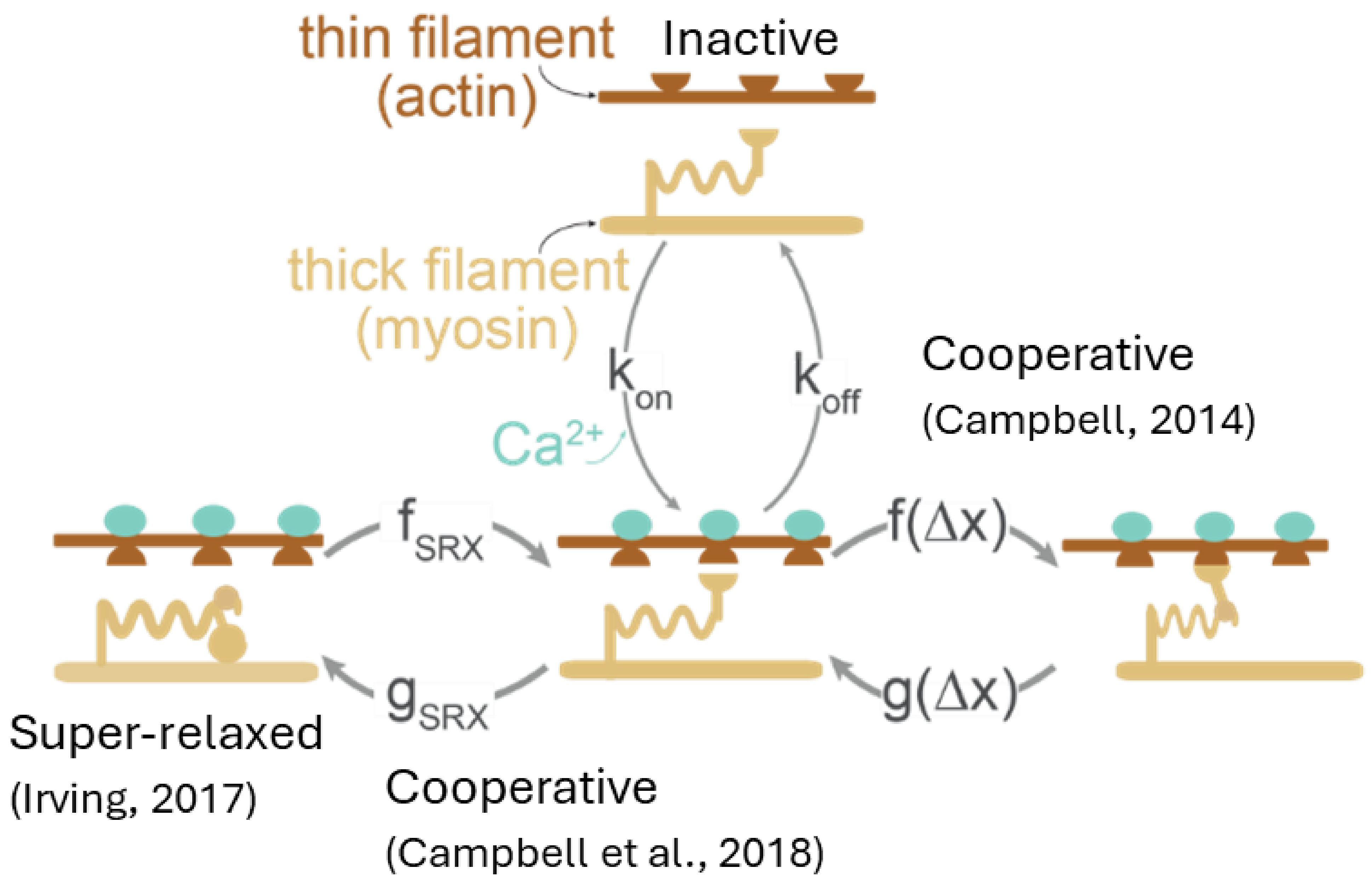
3 parameters to specify thin filament dynamics rates

N_{on} is number of available binding sites on active

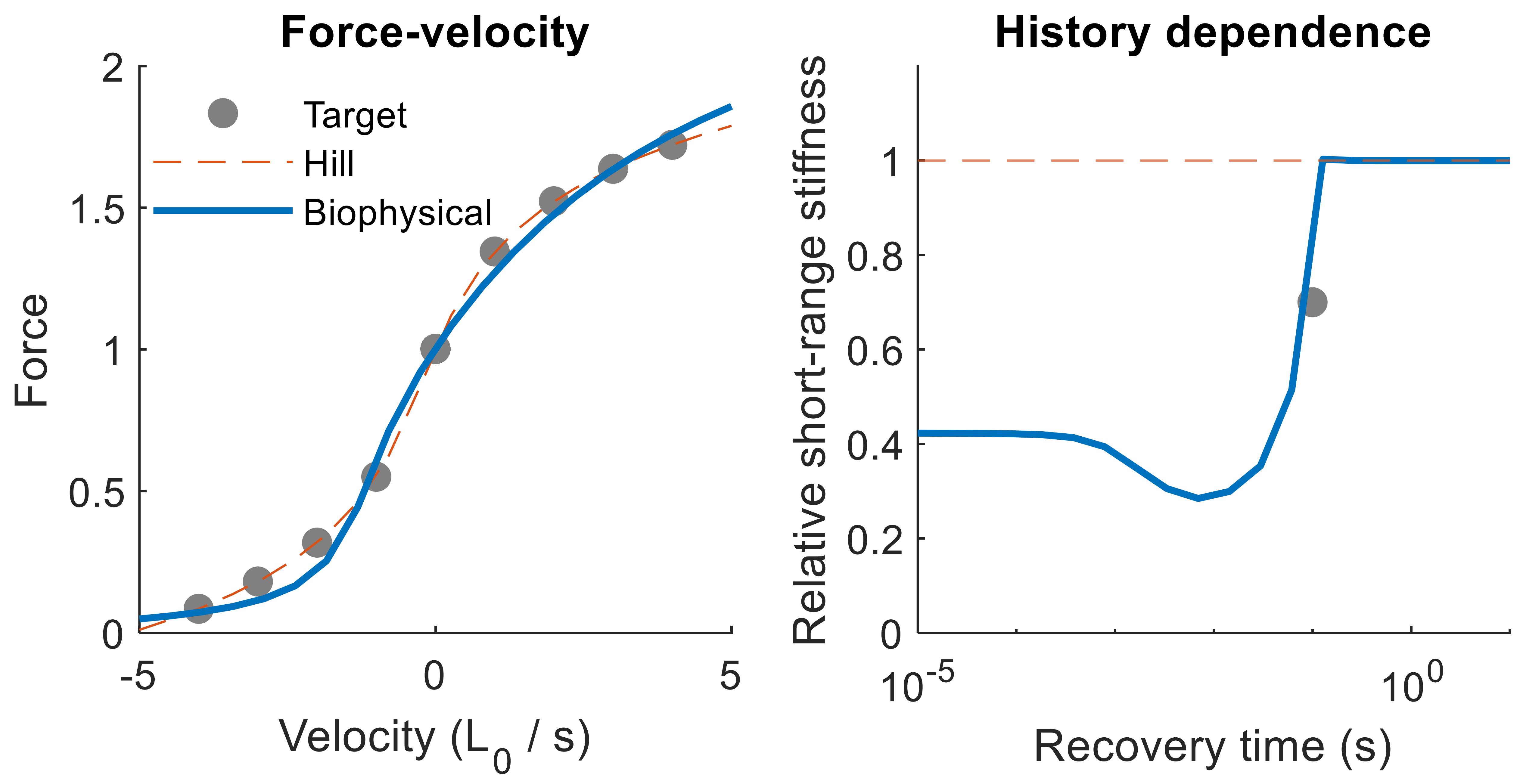
$$\frac{dN_{on}}{dt} = k_{on} \cdot Ca \cdot (F_{overlap} - N_{on}) \cdot \left(1 + k_c \cdot \frac{N_{on}}{F_{overlap}}\right) - k_{off} \cdot \left(N_{on} - \int n(x)\, dx\right) \cdot (1 + koop \cdot \frac{f_L - N_{on}}{f_L})$$



Estimate rate constants

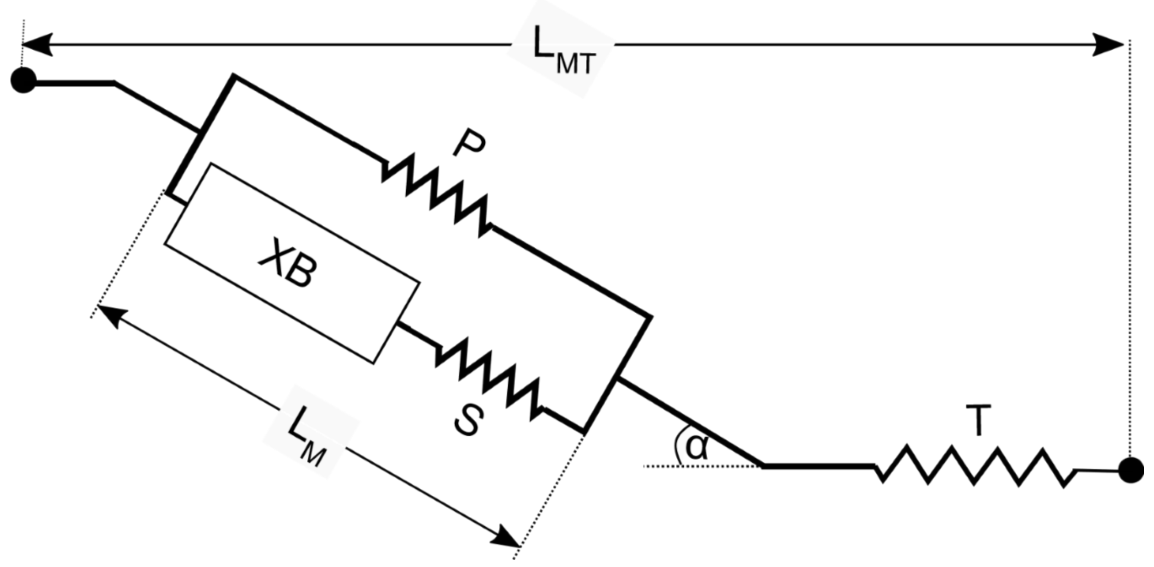


Find rate functions by maximizing the fit between target and modelled force-velocity and history dependence

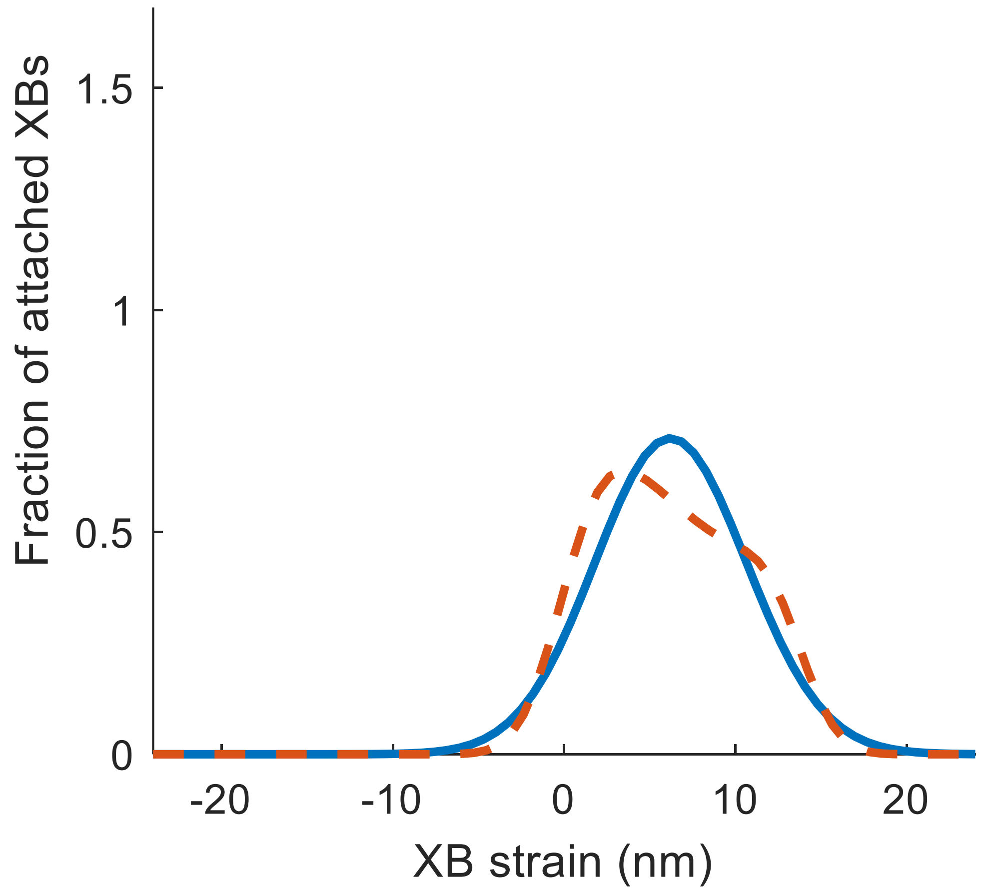


Using the biophysical muscle model in musculoskeletal simulations

- Scale half-sarcomere up to whole muscle



- **Distribution moment approximation to improve numerical efficiency**

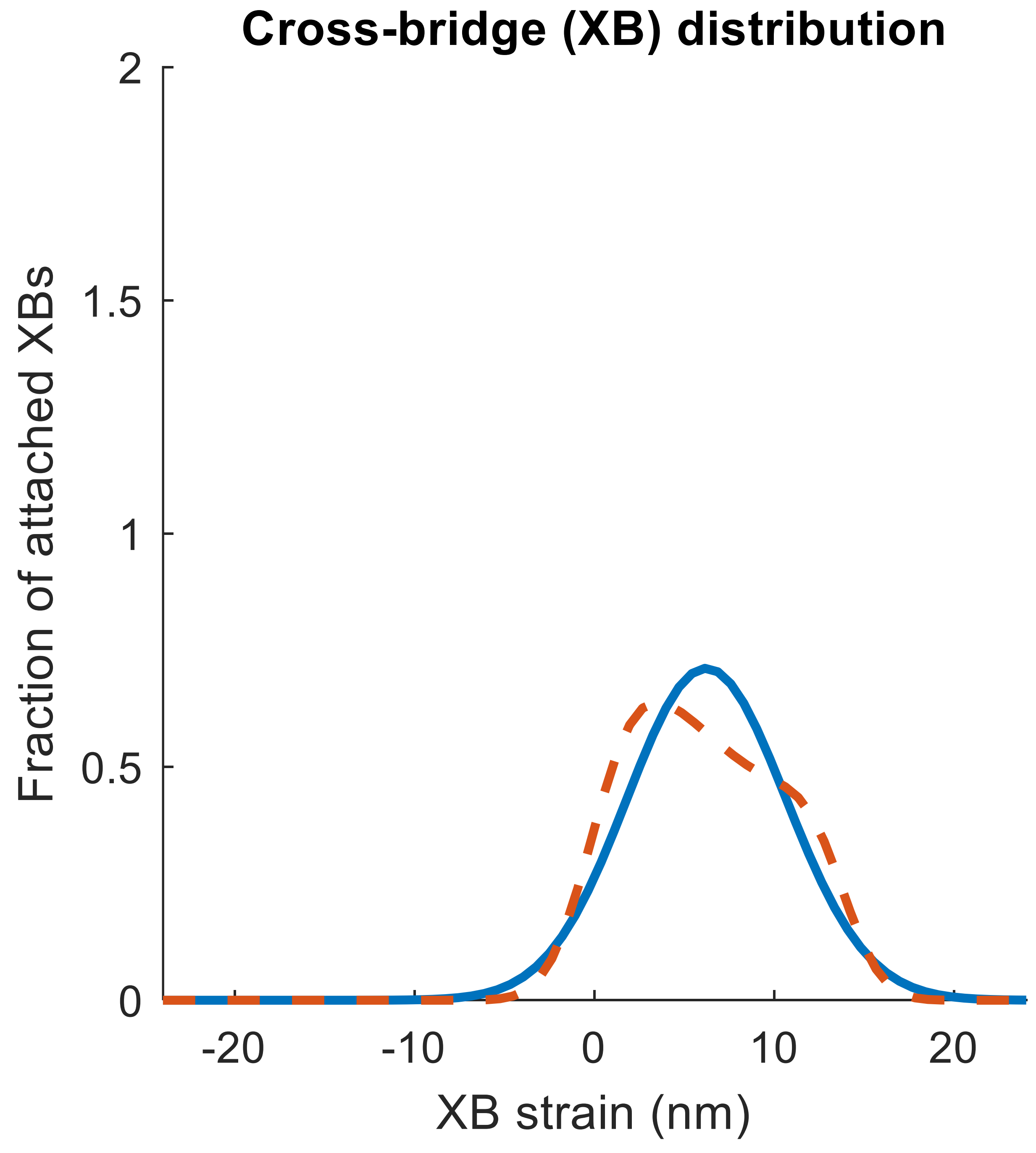


Distribution moment approximation to improve computational efficiency

- Need to discretize cross-bridge distribution to perform forward simulations
  → many states → long computational times

- Only lower-order moments of distribution needed to describe macroscopic muscle behavior.

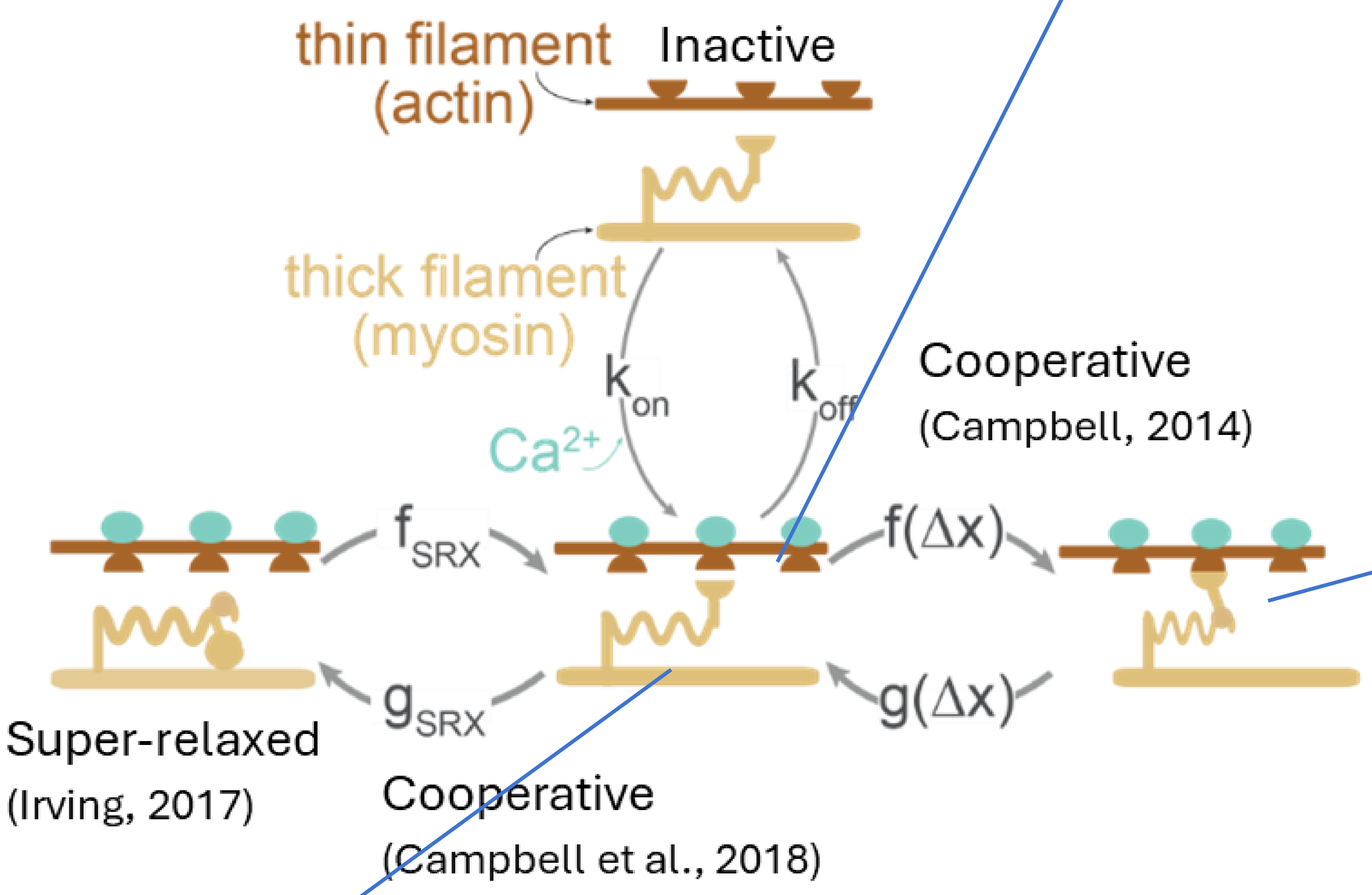
- Approximate distribution by a Gaussian (Zahalak, 1981)
  Moments of Gaussian distribution have physical meaning:
  - Q_0 is number of attached XB/muscle stiffness
  - Q_1 is proportional to force given constant XB stiffness
  - Q_2 is proportional to elastic energy stored in XB

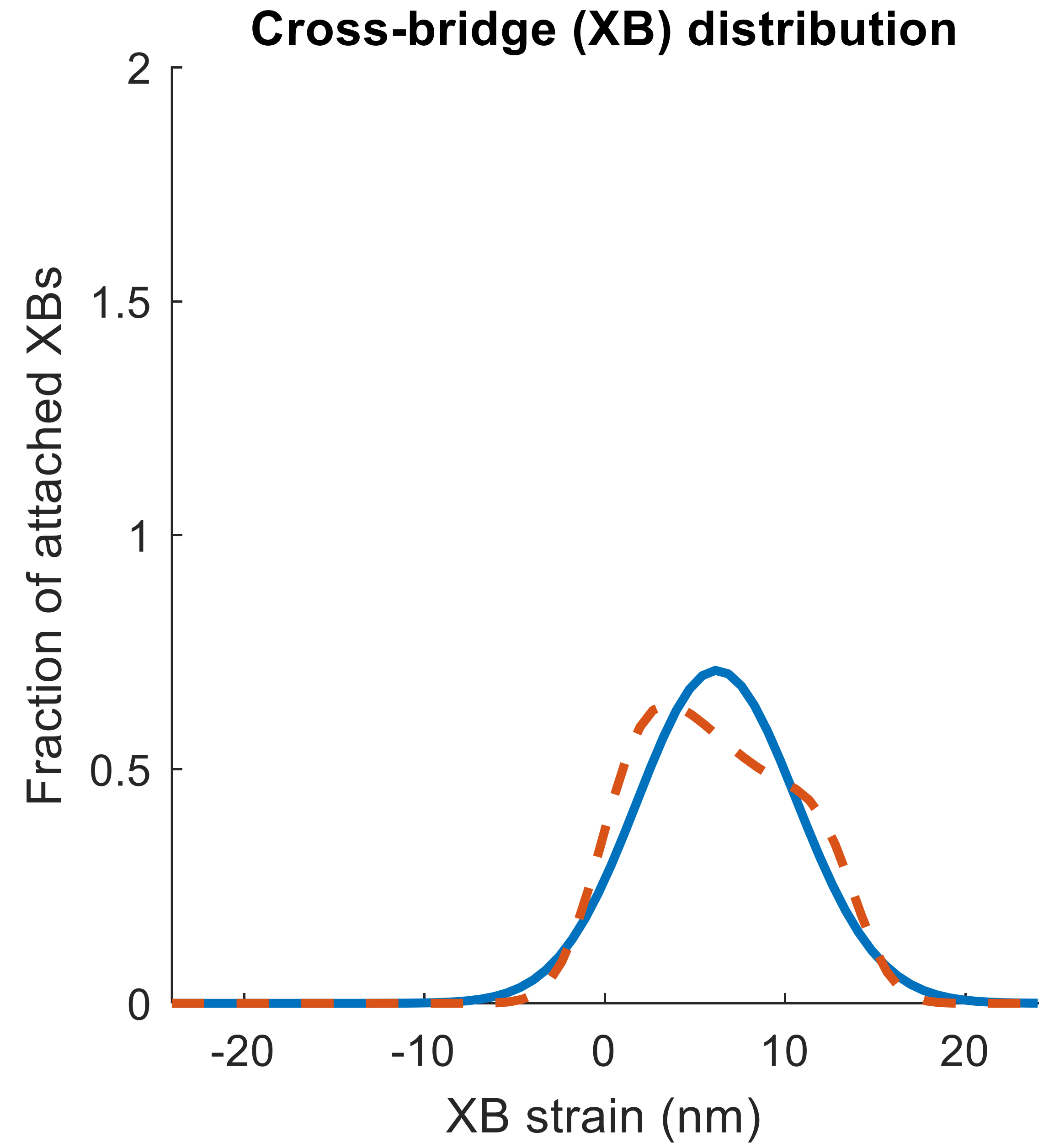


Distribution moment approximation to improve computational efficiency

5 states

N_{on} is number of available binding sides





DRX is number of active myosin heads

$\boldsymbol{Q_0}$ is number of attached XB/muscle stiffness

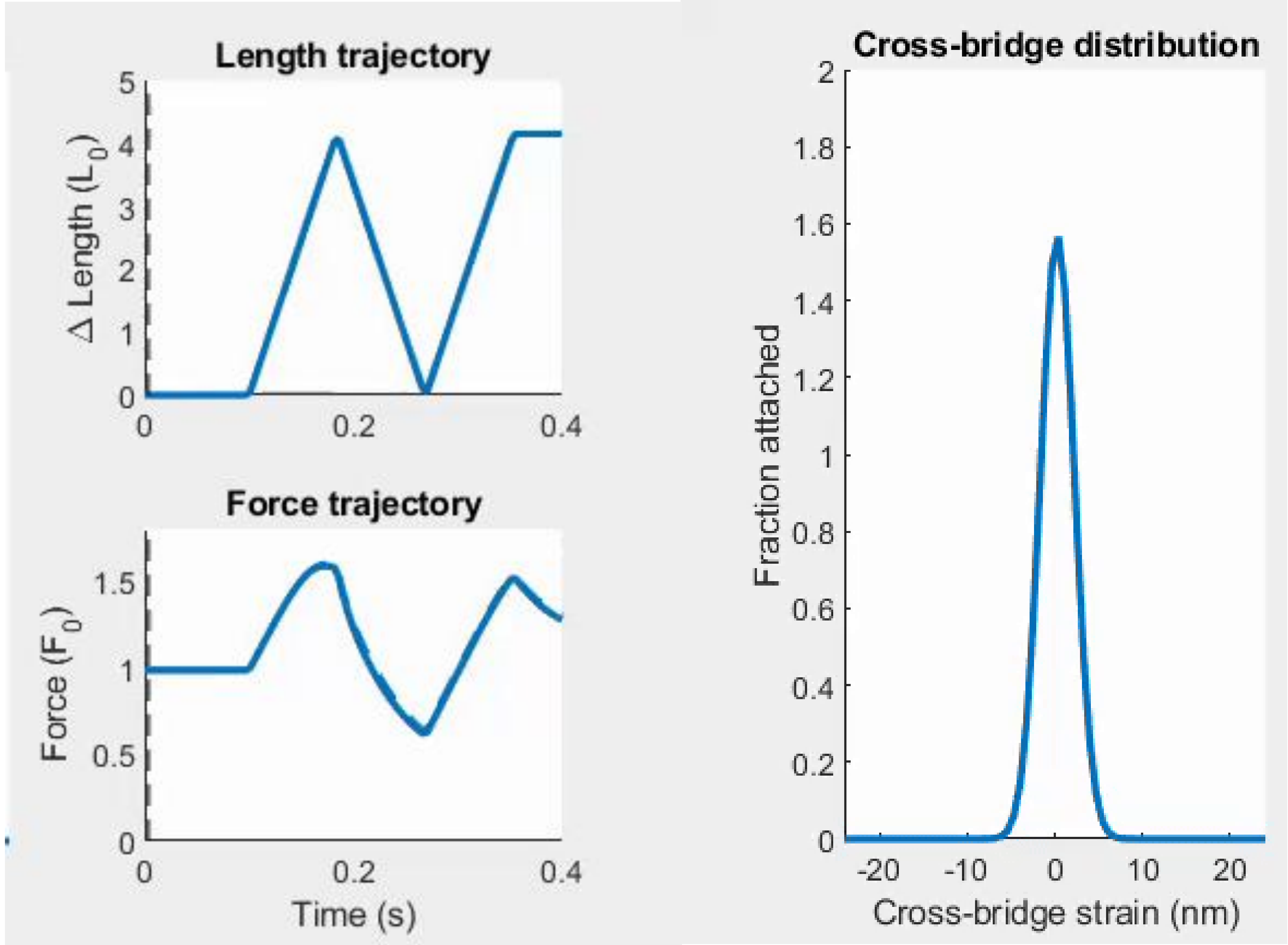
Q_1 is proportional to force given constant XB stiffness

→ normalized tendon force **fse**

$\boldsymbol{Q_2}$ is proportional to elastic energy stored in XB

The equations

The DM approximation accurately captures fiber force in response to stretch



$$\mathrm{F} \propto \int n(x) \cdot x \, dx$$

Force

Distribution

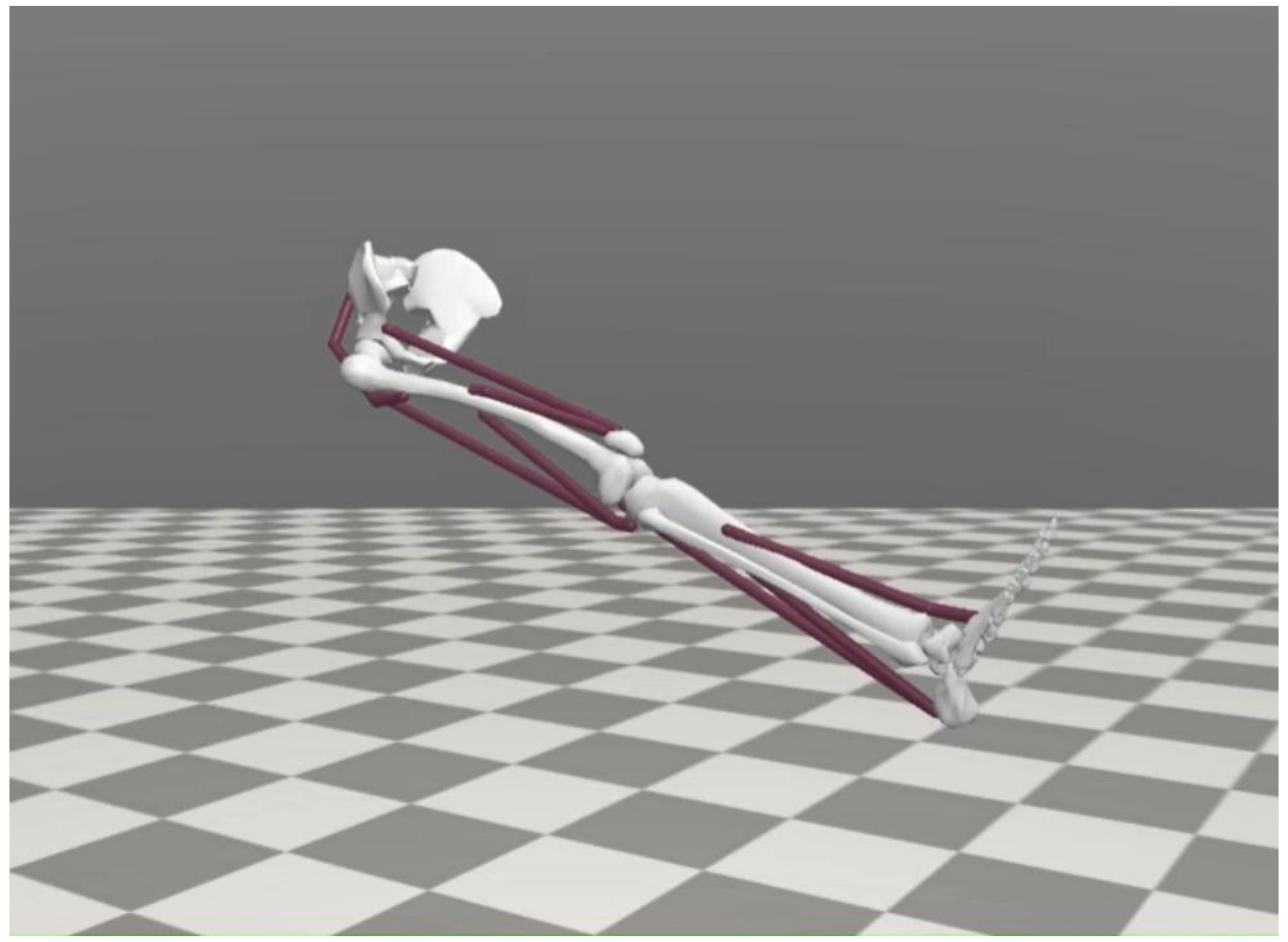
Strain

Extra: (refer to comparison of both as extra for tutorial)

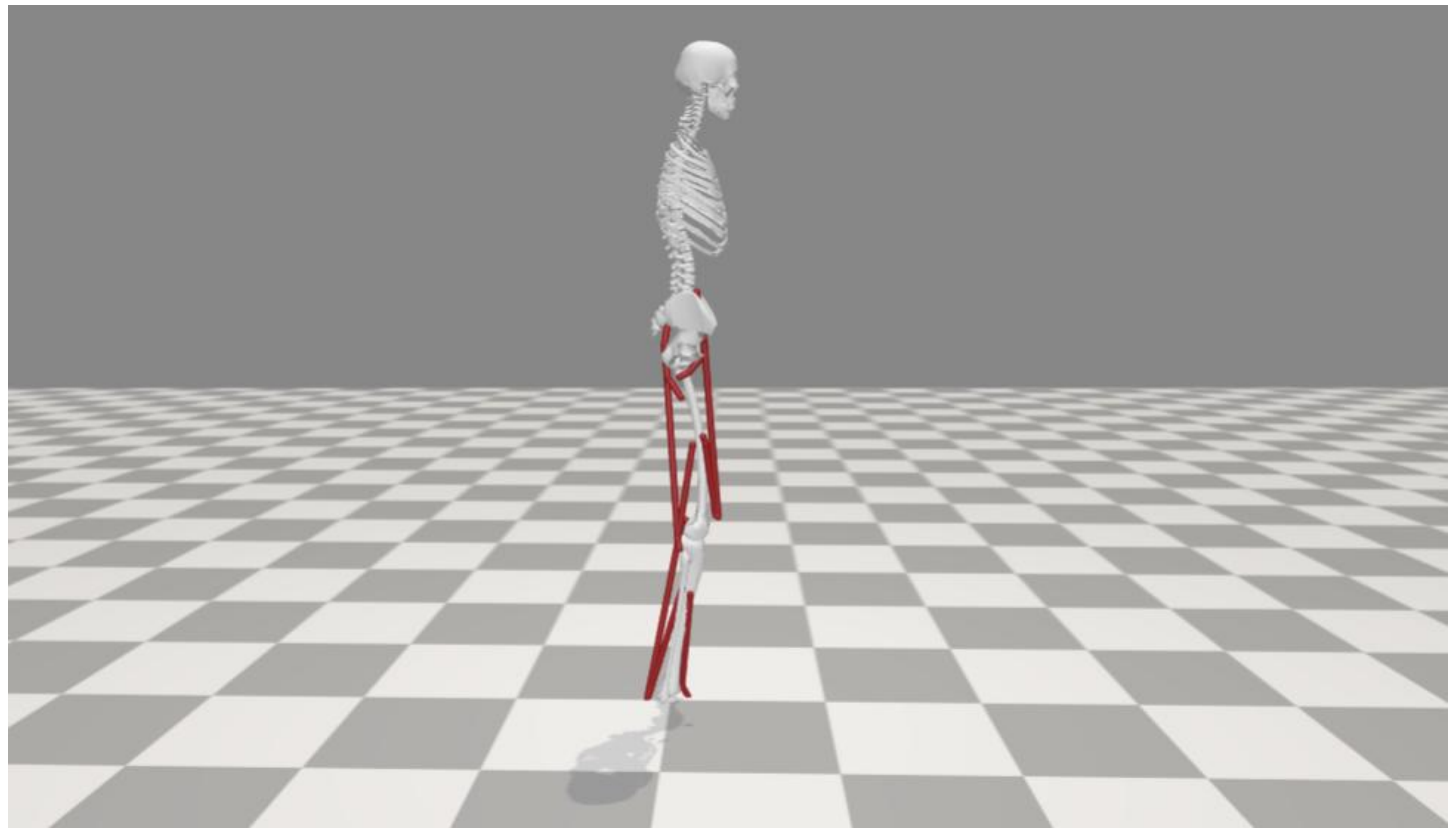
Tutorial - option 1
Musculoskeletal simulations through matlab-OpenSim interface

https://github.com/timvanderzee/ISB2025 Part 2 - OpenSim

Example 1: “pendulum test” leg swing



Example 2: perturbed standing balance



Tutorial - option 2

Musculoskeletal simulations based on simple models in Matlab

https://github.com/timvanderzee/ISB2025 Part 2 - Custom