Modeling muscle cross-bridge dynamics for movement simulations

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Summary
Muscles have transient and history-dependent properties that may be important in dynamic movements and unpredictable interactions with the environment, such as running on uneven terrain. Hill-type muscle models do not model a variety of phenomena emergent from acto-myosin interactions, such as short-range stiffness that transiently increases the resistance of the muscle to externally imposed stretch. Here we developed a Matlab-based 2-state model of muscle cross-bridge kinetics within a half sarcomere. As a first step, we verified that the steady state properties (i.e. force-length and force-velocity relationships) generated by the model are similar to those measured experimentally. Our simulated half-sarcomere can be integrated into existing musculoskeletal simulations, using the same inputs as the contractile element of a Hill-type model. Simulating cross-bridge dynamics within muscle-tendon units may be critical to understanding the role of intrinsic muscle properties in highly dynamic and robust movements.

Introduction
Hill-type muscle models have historically been poor at modeling the forces generated in-vivo during locomotion as they do not simulate transient and history dependent properties of muscle [1]. Transient forces that emerge from acto-myosin interactions could significantly influence energy storage and transfer within muscle-tendon units, particularly when locomoting over complex and uneven terrains.

Our objective was to generate a half-sarcomere model of cross-bridge kinematics appropriate for musculoskeletal simulations for movement. We performed in silico simulations of the half-sarcomere to replicate classic constant length and constant velocity experiments. We characterized the force-length and force-velocity properties emergent from the model.

Methods
Our contractile element model consists of a single half sarcomere with 6.9 x 10^16 cycling cross-bridges. The simulation takes as inputs the fraction of activated actin binding sites and the length change of the half-sarcomere. The active force is calculated by summing the forces of all the attached myosin heads at each point in time. The total force is the sum of the active and passive components [2].

Simulations to generate the force-length relationship were conducted by fixing the muscle model at lengths between 500 and 2000 nm and applying an activation level of 100% to the actin binding sites. The active force was taken at the end of each 10-second simulation after the simulation reached steady state.

Simulations to generate the force-velocity relationship were conducted by contracting and stretching the muscle at constant velocities from -0.02 µm/s to 0.04 µm/s for a 4-second duration. Initial lengths were specified such that all simulations reached optimal fiber length at the midpoint of the stretch period, where the active force was evaluated.

Results and Discussion

![Figure 1](image1.png)

Figure 1: (A) Normalized cross-bridge forces plotted against muscle length as a fraction of the optimal length; (B) Normalized cross-bridge plotted against stretch velocity.

Our simulations produced characteristic force-length and force-velocity curves (Figure 1). Maximum isometric force occurs at the half-sarcomere’s optimal length (Figure 1a). Due to the 80nm bare zone on the thick filament, where there are no myosin heads, optimal length occurs when actin-myosin overlap reaches 100% between 1120 nm and 1200 nm. The ascending limb of the active force-length curve is 47% steeper than the descending limb. Maximum muscle force during imposed velocities occurred during the lengthening simulations, and exhibited a characteristic sharp decline as the muscle shortening velocity increased (Figure 1b).

Conclusions
We validated that characteristic force-length and force-velocity relationships in muscle were emergent from the cross-bridge kinetics in our half-sarcomere model. The model can be used in existing simulations of movement in order to compare the performance afforded by Hill-type versus acto-myosin based muscle models. Our goal is to simulate hopping on uneven terrain to understand the effects of transient and history dependent muscle properties on stability of unsteady locomotion [3].

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References