

TOWARD THE ULTIMATE SKELETAL MUSCLE MODEL

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INTRODUCTION

Mathematical models of muscle are a useful tool for exploring theories of motor control as well as for guiding the clinical restoration of movement to paralyzed muscles through functional electrical stimulation. We have previously developed a model for these purposes that more accurately predicts muscle force over a wider range of operating conditions than any previous model (Brown et al., 1999; Brown and Loeb, 2000b; Cheng et al., 2000). However, our previous model had some limitations: most notably there was no obvious way to extract energy consumption nor was there any simple way to model other effects such as fatigue.

METHODS

The data upon which our model is based were collected primarily from the exclusively fast-twitch feline caudofemoralis muscle and published in Brown et al. (1999) and Brown and Loeb (2000b). Additional data for slow-twitch muscle and tendon properties were garnered from numerous previously published studies on feline soleus (cited in our prior papers). For each step in the modeling process, parameter estimation was accomplished using the Levenberg-Marquardt algorithm for non-linear least-squares curve-fitting.

THE MODEL

The basic form of the model (Figure 1) is the same as our previous version and that of many others. The tendon and aponeurosis are represented by a series elasticity (SE)

and the passive properties of fascicles are represented by a parallel elasticity (PE). There are then one or more parallel and independently controlled contractile elements (CE) that represent sub-populations of motor units. In its simplest form, a model might consist of just one CE, representing all motor units in a given muscle. More realistically, particularly for muscles composed of multiple fiber types, multiple CEs will be used, each representing the force production of a sub-population of real motor units firing at a particular frequency.

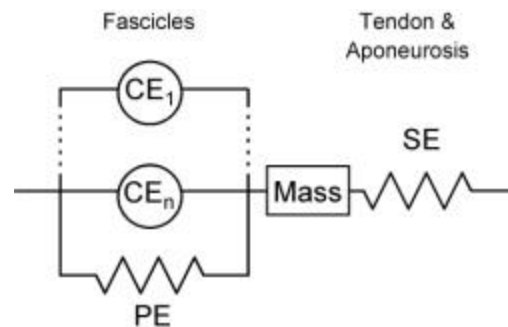


Figure 1: Schematic representation of the basic form of the model.

The SE and PE are represented simply as non-linear springs as described previously (Brown et al., 1999). In contrast, there has been a major re-working of the form of the CE as compared to our previous model. The summary equation for the CE is shown below, in which A represents the fraction of attached, force-producing cross-bridges relative to maximal activation when $A=1$; FL represents filament overlap that accounts for the isometric force-length relationship

and F_X represents the mean force per-cross-bridge (normalized so that $F_X=1$ under isometric conditions). Note that there is no force-velocity (FV) relationship explicitly stated here. The effects of velocity emerge through the effects of velocity on both A and F_X .

$$(1) F_{CE}=A*FL*F_X$$

The activation term A is calculated via two first order processes. The first process represents the calcium release/uptake dynamics. This process is presumed to be length and velocity independent. There is an indirect effect of activation in that the rate of calcium uptake is modeled to increase during a contraction for fast-twitch muscles (which is a proposed mechanism for sag during sustained contractions at subtetanic frequencies). The second process represents the rates of cross-bridge attachment and detachment. We assume that velocity affects these rates because length changes shift the cross-bridge angle. We assume that both attachment and detachment rates are also length dependent as a result of effects on filament lattice spacing in isovolumetric muscle fibers. We model the binding of calcium to troponin as if it were in a fast-equilibrium because it is a significantly faster process than either of the other two processes. We assume that calcium binding is cooperative. Similarly, we assume that there is cooperativity in cross-bridge attachment. These combined cooperative mechanisms are necessary to reproduce the steep force-frequency relationship that is known to exist and also to reproduce the prolonged duration of activation that occurs following high frequency stimulation.

The cross-bridge force term, F_X , is calculated by tracking mean cross-bridge distortion and assuming that F_X is linearly related to distortion. Cross-bridge distortion

is calculated by accounting for changes in distortion that occur as a result of (i) movement; (ii) cross-bridge detachment at one angle and reattachment at another angle; (iii) changes in the number of attached cross-bridges.

RESULTS & DISCUSSION

This version of our model is able to replicate all features of our previous model. This includes the tetanic FL and FV relationships; the effects of stimulus frequency on FL; the effects of stimulus frequency and length on each of FV, sag and rise and fall times; the effects of stimulus frequency, length and velocity on yielding.

New features that this model now accounts for include the effects of velocity on fall time and the transient forms of shortening-induced force depression and stretch-induced force enhancement (Brown and Loeb, 2000a). Furthermore energy consumption can be calculated directly from the rate of cross-bridge detachment.

The new model is actually simpler and easier to understand because its basic elements are tied more closely to underlying physiological processes. This should also make it easier to add elements to the model to account for features such as fatigue, which occurs through changes in one or more of those processes.

REFERENCES

- Brown, I.E., et al., G.E. (1999). *J. Muscle Res. Cell Motil.* **20**: 443-456.
- Brown, I.E. & Loeb, G.E. (2000a). *J. Muscle Res. Cell Motil.* **21**: 21-31.
- Brown, I.E. & Loeb, G.E. (2000b). *J. Muscle Res. Cell Motil.* **21**: 33-47.
- Cheng, E., Brown, I.E. & Loeb, G.E. (2000) *J. Neurosci. Meth.* **101**, 117-130