Multidimensional Crossbridges: Not a rope of sand

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Abstract

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Keywords: myosin; spatially-explicit model; crossbridge kinetics

Author Summary: Models of muscle contraction have long treated the molecular motor myosin as a simple spring oriented parallel to its direction of movement. This does not allow for the investigation of phenomena such as the perpendicular force observed during shortening, or the dependence of the maximum force produced on spacing between the contractile filaments that comprise muscle. We demonstrate an alternative model, computationally simple enough to use in large networked models, that incorporate both linear and torsional or angular springs. These models capture much of the behavior missing from pervious efforts.

1 Introduction

Sarcomere-scale modeling of muscle contraction has largely changed since the introduction of the sliding crossbridge model in the 1950s, but the geometry of the individual crossbridges used has remained largely unaltered. While thermodynamic account had been introduced to the crossbridge kinetics, compliance has been introduced to the filaments, and multiple filaments have been arranged to mimic the lattice, the one dimensional single spring nature of the crossbridge has continued to be used as a model of the mechanism of force generation.

History of Models

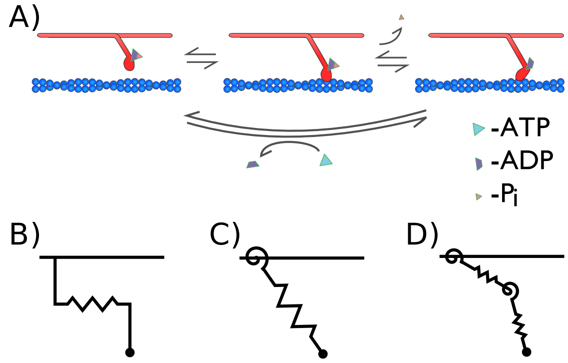

Figure 1: Kinetic scheme and crossbridge types under investigation. A) Three state kinetics used in most models and extended here. B) Single spring crossbridge model used in models since (**?**). C) Two spring system, consisting of a torsional/angular spring and a linear spring. D) Four spring system using two torsional and two linear springs.

Increasing knowledge of myosin

Materials and Methods

Historical 1-D Crossbridge

Geometry and Force/Displacement Equations

$$\begin{aligned} U_1(r) &= 0 \\ U_2(r) &= \frac{1}{2}k_r(r-r_0)^2 \\ U_3(r) &= \frac{1}{2}k_r(r)^2 \qquad (1) \\ & \qquad (2) \end{aligned}$$

$$r_{12}(r) = Dependentondiffusion$$

$$
\begin{aligned}
r_{23}(r) &= 0.001 + 0.5 * (1 + \tanh(\\
&\quad 0.6(U_1(r,\theta) - U_2(r,\theta)))) \qquad (3) \\
r_{31}(r) &= e^{-1/U_2(r,\theta)} \qquad (4)
\end{aligned}
$$

Kinetics: Equations and Figures

A 2-D 2-Spring Crossbridge

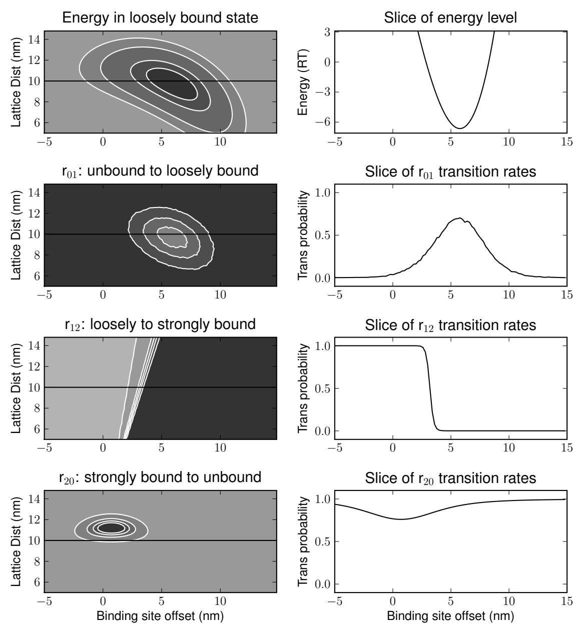

Figure 2: Energy and kinetics of the two-spring crossbridge at varying horizontal offsets from a resting location and varying lattice spacings.

Geometry and Force/Displacement Equations

$$
\begin{aligned}
U_1(r,\theta) &= 0 \\
U_2(r,\theta) &= \frac{1}{2}k_r(r - r_0)^2 + \frac{1}{2}k_\theta(\theta - \theta_0)^2 \\
U_3(r,\theta) &= \frac{1}{2}k_r(r - r_1)^2 + \frac{1}{2}k_\theta(\theta - \theta_1)^2 \qquad (5) \\
& \qquad (6)
\end{aligned}
$$

$$
\begin{aligned}
r_{12}(r,\theta) &= Dependentondiffusion \\
r_{23}(r,\theta) &= 0.001 + 0.5 * (1 + \tanh(\\
&\quad 0.6(U_1(r,\theta) - U_2(r,\theta)))) \qquad (7) \\
r_{31}(r,\theta) &= e^{-1/U_2(r,\theta)} \qquad (8)
\end{aligned}
$$

Kinetics: Equations and Figures

Cutting out cross-sections

A 2-D 4-Spring Crossbridge

Geometry and Force/Displacement Equations

$$
\begin{aligned}
&U(\phi, \ell, r, \theta) = \\
&\quad \frac{1}{2}k_\phi(\phi - \phi_0)^2 + \frac{1}{2}k_\ell(\ell - \ell_0)^2 + \\
&\quad \frac{1}{2}k_r(r - r_0)^2 + \frac{1}{2}k_\theta(\theta - \theta_0)^2 \qquad (9)
\end{aligned}
$$

Kinetics: Equations and Figures

Cutting out cross-sections

Results

Discussion

Lattice Spacing Dependence of Binding Rates

Forward Biased Binding