Campbell, http://www.jgp.org/cgi/content/full/jgp.201311078/DC1

This supplement provides additional information about the simulations that were described in the main text. Data files and tutorials explaining how to reproduce the modeling results are available at http://www.myosim.org.

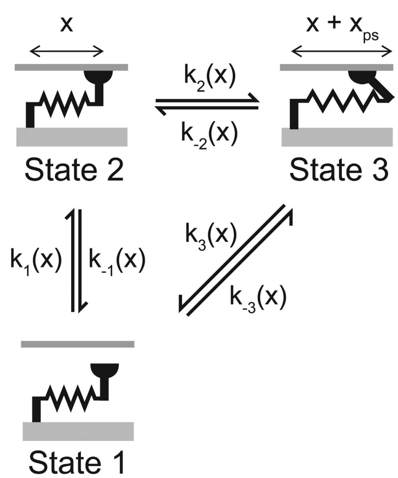

Figure S1. Three-state myosin scheme.

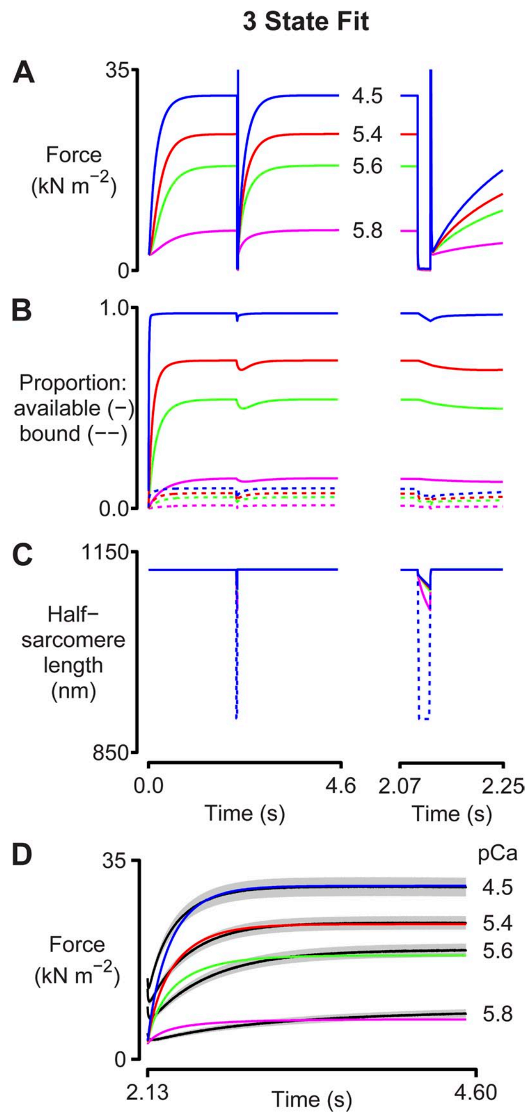

Figure S2. Three-state fit. Simulations fitted to tension-recovery records measured with chemically permeabilized myocardial samples. The calculations used the three-state myosin scheme shown in Fig. S1 with the model parameters listed in Table S5. Panels show (A) predicted force records, (B) the proportion of binding sites that are available (solid lines) and that are bound (dotted lines), and (C) the half-sarcomere lengths. The imposed length change is shown by the dotted line. The left-hand axes show the entire simulation. The right-hand axes show the response to the length perturbation on an expanded time scale. (D) The simulated force records overlaid on the experimental force records (black lines). The gray regions around each line show the standard error of the experimental data.

Table S1

Model parameters for simulations in Figs. 1 and 2

Parameter	Value	Units
N_0[a]	6.9×10^{16}	m^{-2}
a_{on}	10^7	$s^{-1}\ M^{-1}$
a_{off}	50	s^{-1}
$k_1(x)$, fast[b]	$10\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$
$k_{-1}(x)$, fast	100	s^{-1}
$k_1(x)$, slow	$0.5\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$
$k_{-1}(x)$, slow	5	s^{-1}
x_{ps}	5	nm
k_{cb}	2	$pN\ nm^{-1}$

x is as defined in Fig. 1 A in nanometers.

[a]N_0 is the number of myosin heads in a hypothetical cardiac half-sarcomere with a cross-sectional area of 1 m^2. This estimate was obtained by assuming that thick filaments contain 283 myosin heads and have a spatial density of $0.407 \times 10^{15}\ m^{-2}$ within myofibrils (Linari et al. 2007. *Biophys. J.* 92:2476–2490), and that myofibrils occupy 60% of the cross-section of myocardium (the remainder being mitochondria).

[b]k_B is Boltzmann's constant (1.381×10^{-23} J K^{-1}). T is the experimental temperature (assumed to be 288 K).

Table S2

Model parameters for simulations in Fig. 3 (two-state fit)

Parameter	Value	Units	Source[a]
N_0	6.9×10^{16}	m^{-2}	Predefined
a_{on}	$10^{6.52}$	$s^{-1}\ M^{-1}$	Calculated
a_{off}	9.33	s^{-1}	Calculated
$k_1(x)$	$0.318\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$	Calculated
$k_{-1}(x)$	$5.65 + 0.845\ x^4$ for $x > 0$ $5.65 + 3.48\ x^4$ for $x < 0$	s^{-1}	Calculated
k_{plus}	47.5	s^{-1}	Calculated
k_{minus}	4.69	s^{-1}	Calculated
x_{ps}	1.61	nm	Calculated
k_{cb}	2	$pN\ nm^{-1}$	Predefined
$F_{passive}$[b]	$3.21 \times 10^{-8}\left(e^{\frac{HSL}{44.6}} - 1\right)$	$N\ m^{-2}$	Predefined

HSL is the half-sarcomere length in nanometers.

[a]Predefined parameters were set at the beginning of the calculations based on values from the literature and prior experience. Calculated parameter values were obtained by fitting the simulations to the experimental data.

[b]$F_{passive}$ is the passive elastic force generated by titin and/or collagen filaments and was determined from separate experiments in which the muscle preparations were stretched in solutions with a pCa value of 9.0 (minimal activation).

Table S3
Model parameters for simulations in Fig. 5 (six-state fit)

Parameter	Value	Units	Source
N_0	6.9×10^{16}	m^{-2}	Predefined
a_{on}	$10^{6.72}$	$s^{-1}\ M^{-1}$	Calculated
a_{off}	13.1	s^{-1}	Calculated
$k_1(x)$	$9.34\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$	Calculated
$k_{-1}(x)$	$499 + 9.38\ x^{4.02}$	s^{-1}	Calculated
$k_2(x)$	2.68	s^{-1}	Calculated
$k_{-2}(x)$	0	s^{-1}	Predefined
$k_3(x)$	3.85	s^{-1}	Calculated
$k_{-3}(x)$	0	s^{-1}	Predefined
$k_4(x)$	17.3 for $x > 0$ $17.3 + 0.0507\ x^{4.02}$ for $x < 0$	s^{-1}	Calculated
$k_{-4}(x)$	0	s^{-1}	Predefined
$k_5(x)$	1,000	s^{-1}	Predefined
$k_{-5}(x)$	0	s^{-1}	Predefined
$k_6(x)$	$828\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$	Calculated
$k_{-6}(x)$	$0.130 + 0.153\ x^{4.01}$	s^{-1}	Calculated
k_{plus}	73.7	s^{-1}	Calculated
k_{minus}	7.44	s^{-1}	Calculated
$x_{ps,1}$	4.38	nm	Calculated
$x_{ps,2}$	1.16	nm	Calculated
k_{cb}	2	$pN\ nm^{-1}$	Predefined
$F_{passive}$	$3.21\times10^{-8}\left(e^{\frac{HSL}{44.6}}-1\right)$	$N\ m^{-2}$	Predefined

Table S4
Model parameters for simulations in Fig. 6 (unloaded twitch contraction)

Parameter	Value	Units	Source
N_0	6.9×10^{16}	m^{-2}	Predefined
a_{on}	$10^{7.71}$	$s^{-1}\ M^{-1}$	Calculated
a_{off}	977	s^{-1}	Calculated
$k_1(x)$	$1{,}320\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$	Calculated
$k_{-1}(x)$	$512 + 4.87\ x^4$ for $x > 0$ $512 + 12.1\ x^4$ for $x < 0$	s^{-1}	Calculated
k_{plus}	55.6	s^{-1}	Calculated
x_{ps}	5.87	nm	Calculated
k_{cb}	2	$pN\ nm^{-1}$	Predefined
$F_{passive}$[a]	$1{,}000 \times (HSL - 950)$	$N\ m^{-2}$	Predefined

HSL is measured in nanometers.
[a]$F_{passive}$ is an estimate of the passive elastic force generated by titin filaments.

Table S5
Model parameters for simulations in Fig. S2 (three-state fit)

Parameter	Value	Units	Source
N_0	6.9×10^{16}	m^{-2}	Predefined
a_{on}	$10^{6.46}$	$s^{-1}\ M^{-1}$	Calculated
a_{off}	6.33	s^{-1}	Calculated
$k_1(x)$	$32.7\ e^{-\frac{k_{cb}x^2}{2k_BT}}$	$s^{-1}\ nm^{-1}$	Calculated
$k_{-1}(x)$	$1584 + 0.721\ x^4$	s^{-1}	Calculated
$k_2(x)$	5.00	s^{-1}	Calculated
$k_{-2}(x)$	0	s^{-1}	Predefined
$k_3(x)$	$4.50 + 5.33\ x^4$	s^{-1}	Calculated
$k_{-3}(x)$	0	s^{-1}	Predefined
k_{plus}	29.5	s^{-1}	Calculated
k_{minus}	4.10	s^{-1}	Calculated
x_{ps}	5.49	nm	Calculated
k_{cb}	2	$pN\ nm^{-1}$	Predefined
$F_{passive}$	$3.21\times10^{-8}\left(e^{\frac{HSL}{44.6}}-1\right)$	$N\ m^{-2}$	Predefined