Passive viscoelastic response of striated muscles

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S-1. DETAILED MICROSCOPIC MODEL AND ADIABATIC ELIMINATION OF FAST VARIABLES

We derive in this section a detailed microscopic expression for the energy of the half-sarcomere, based on the schematic in Fig. S-1. It will then be simplified by an adiabatic elimination of some fast variables to justify the model (1), which we use for our calculations.

Suppose that the size of the half-sarcomere is $l(t)$, which is defined as the distance between the Z-disc and the M-lines. The variable $s(t)$ is the distance between the Z disc and the fist actin monomer forming a cross-bridge, while $u(t)$ is the distance between the M line and the position of the closest cross-bridge (which is the furthest from the Z disc). The index i labels the cross-bridges from the closer to the Z disc to the furthest, and Δ is the distance between cross-bridges which we assume constant. Finally the variable x_i, defined in the main text, is the configuration of the cross-bridge.

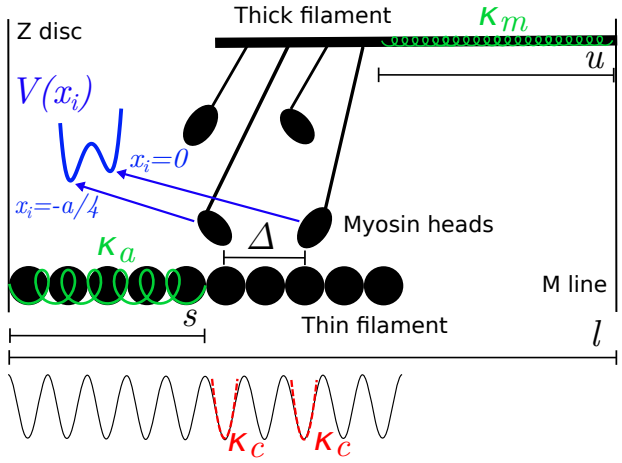

FIG. S-1: Schematic representation of a single thick filament and a single thin filament interacting though several cross-bridges. The myosin heads close to the thin filament are those which, forming cross-bridges, play a role in the phases 1 and 2 of the transient response.

Considering thin and thick filaments as elastic, and the myosin heads as fixed to their actin binding site (we are modeling the system at timescales at which the binding and unbinding are negligible), we can write the energy of interacting thin and thick filaments as:

$$E = \frac{\kappa_a}{2}\left(s - s_0\right)^2 + \frac{\kappa_m}{2}\left(u - u_0\right)^2 + \sum_{i=1}^{N}\left[V(x_i) + \frac{\kappa_c}{2}\left(s + u + \Delta\left(N-1\right) - l + x_i\right)^2\right], \tag{S-1}$$

where N is the number of cross-bridges, s_0 and u_0 are the rest values of s and u (when there are no forces stretching them), and the stiffnesses of the thin and thick filaments are respectively κ_a and κ_m. Then the first two terms are the elastic potential of thin and thick filaments, while the last term represents the cross-bridges. It includes the potential $V(x_i)$, described in the main text, and an elastic coupling between myosin heads and the corresponding actin binding sites whose locations, for the i-th cross-bridge are, respectively, $l - u - \Delta\left(N - i\right) - x_i$ and $s + \Delta\left(i - 1\right)$. The potential

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describing this interaction is periodic (see Fig. S-1), since myosin heads can bind to each actin site, but since in our description we neglect detachment of the myosin heads, we can consider each myosin fixed to an actin monomer, and approximate the periodic potential with a quadratic one with stiffness κ_c.

Since the variables $s(t)$ and $u(t)$ describe the deformation of the macroscopic filaments, we can assume that they relax instantaneously [1, 2] and therefore eliminate them adiabatically. This procedure implies neglecting the dynamics of their relaxation and presumes that they are always relaxed at the energy minimum. That means that their values at each time are obtained from the relations $\frac{\partial E}{\partial s} = 0$ and $\frac{\partial E}{\partial u} = 0$, which give the values:

$$s = s_0 + \frac{N\,\kappa_c\,\kappa_m\,(l - s_0 - u_0 - \Delta\,(N-1) - \langle x\rangle)}{N\,\kappa_m\,\kappa_c + \kappa_a\,\kappa_m + N\,\kappa_c\,\kappa_a} \tag{S-2}$$

and

$$u = u_0 + \frac{N\,\kappa_c\,\kappa_a\,(l - s_0 - u_0 - \Delta\,(N-1) - \langle x\rangle)}{N\,\kappa_m\,\kappa_c + \kappa_a\,\kappa_m + N\,\kappa_c\,\kappa_a}\,, \tag{S-3}$$

to be substituted back in (S-1). After that, defining $\kappa_f = \frac{\kappa_a\,\kappa_m}{\kappa_a + \kappa_m}$ as the combined elasticity of thin and thick filaments, we obtain (1) which also implies substituting the value of y given in (2). In that relation $z = l - s_0 - u_0 - \Delta\,(N-1)$ is the difference between the actual half-sarcomere length and its value when all cross-bridges are in the pre-power stroke state and the sarcomere does not generate force.

We notice that although this energy has been derived for a single pair of thin and thick filaments, it can also be used for a half-sarcomere, which can be seen as a collection of thin and thick filaments joined together at the Z disc and M line respectively. Since the values of l, s and u is the same for each thick-thin filament pair, this is achieved simply by rescaling N by the number of thick or thin filaments, in such a way that it becomes the number of cross-bridges in a half-sarcomere.

S-2. DERIVATION OF THE FOKKER-PLANCK EQUATION

We start from the Langevin equations for the x_i:

$$\dot{x}_i = -\frac{\partial\,E(\{x_i\},z,t)}{\partial\,x_i} + \xi_i = -\frac{\partial\,H(\{x_i\},z,t)}{\partial\,x_i} + \xi_i\,, \tag{S-4}$$

where ξ_i is a Gaussian noise with $\langle\xi_i\rangle = 0$ and $\langle\xi_i(t)\,\xi_j(t')\rangle = (2/\beta)\,\delta(t-t')\,\delta_{ij}$. If $p_N(\{x_i\};z,t)$ is the N-body distribution function, which is also a function of time and of the value z, the Fokker-Planck equation that describes its evolution is

$$\frac{\partial p_N(\{x_i\};z,t)}{\partial t} = \sum_{i=1}^{N}\frac{\partial}{\partial x_i}\left[\frac{\partial H}{\partial x_i} + \frac{1}{\beta}\frac{\partial}{\partial x_i}\right]\,p_N(\{x_i\};z,t)\,, \tag{S-5}$$

where, since z is a macroscopic variable, we considered it deterministic and neglected its fluctuations. The correlations between x_i are of order of $1/N$ for systems with mean-field coupling [6, 7], so for large N the N-body distribution function can be approximated as:

$$p_N(\{x_i\};z,t) \simeq \Pi_{i=1}^{N}\,p(x_i;z,t)\,, \tag{S-6}$$

where $p(x_i;z,t)$ is the one-body distribution function. Integrating (S-5) in all the variables x_i except one gives (8).

S-3. FLUCTUATION-DISSIPATION RELATION

We derive in this section the relation between $\chi_{xx}(t)$, defined in (14), and the single element correlation function $S_{xx}(t)$. Since p_s is a stationary solution of (8), we have:

$$\frac{\partial}{\partial x}p_s = \beta\,\left(\frac{\partial V}{\partial x} + x - \frac{\langle x\rangle + \lambda_f z}{1+\lambda_f}\right)p_s\,. \tag{S-7}$$

Furthermore using the definition of L given in (12) and (S-7), we can show:

$$L\,x\,p_s = \frac{1}{\beta}\frac{\partial p_s}{\partial x}\,, \tag{S-8}$$

so that using this relation in the definition of χ_{xx}, we obtain:

$$\chi_{xx}(t) = -\beta\,\Theta(t)\,\frac{\mathrm{d}}{\mathrm{d}t}\int \mathrm{d}x\,x\,e^{L\,t}\,x\,p_s(x) = -\beta\,\Theta(t)\,\frac{\mathrm{d}}{\mathrm{d}t}\int \mathrm{d}x\,\mathrm{d}x'\,x\,e^{L\,t}\,\delta(x-x')\,x'\,p_s(x') = -\beta\,\Theta(t)\,\frac{\mathrm{d}S_{xx}}{\mathrm{d}t}\,, \tag{S-9}$$

where the last equality is justified by the fact that $e^{L\,t}\,\delta(x-x')$ is the probability of being at the state x at time t, provided that at time 0 the system was at the state x', for a system whose evolution is described by L.

S-4. AUTOCORRELATION OF A SINGLE CROSS-BRIDGE

The quantity $S_{xx}(t)$ is the autocorrelation function of a single cross-bridge in the stationary bistable potential $U(x,z)$ defined in (10). To calculate it we use the approximation of high barrier, considering that x_0 and x_1 are the minima of the wells of the potential U, and x_M the local maximum between them, and define the probability of being in each of the two wells as a function of time as:

$$p_0(t) = \frac{1}{Z}\int_{-\infty}^{x_M}\mathrm{d}x\,p_x(x,t) \qquad \text{and} \qquad p_1(t) = \frac{1}{Z}\int_{x_M}^{\infty}\mathrm{d}x\,p_x(x,t)\,, \tag{S-10}$$

where $p_x(x,t) = p_x(x,t;\langle x\rangle_s,z)$ is the probability density for the stochastic motion of a single element in the potential U at fixed $\langle x\rangle_s$ and z. The dynamics for the evolution of $p_{0,1}$ is given by:

$$\frac{\mathrm{d}p_0(t)}{\mathrm{d}t} = -\frac{\mathrm{d}p_1(t)}{\mathrm{d}t} = -r_{01}\,p_0(t) + r_{10}\,p_1(t) \tag{S-11}$$

with r_{10} and r_{01} that are the rates of transition between wells [3]:

$$r_{01} = \left[\beta\,p_0^s\int_{x_0}^{x_1}\mathrm{d}x\,p_s^{-1}(x)\right]^{-1} \qquad \text{and} \qquad r_{10} = \left[\beta\,p_1^s\int_{x_0}^{x_1}\mathrm{d}x\,p_s^{-1}(x)\right]^{-1}\,, \tag{S-12}$$

where $p_{0,1}^s$ are the equilibrium values of $p_{0,1}(t)$ obtained substituting p_s to $p_x(x,t)$ in (S-10).

In the high barrier approximation the integrals including p_s, over a region of the system, can be performed over the whole space if we choose between the approximations:

$$U(x) \simeq \begin{cases} U(x_0) + U''(x_0)\,(x-x_0)^2 & \text{if} \quad x\sim x_0 \\ U(x_1) + U''(x_1)\,(x-x_1)^2 & \text{if} \quad x\sim x_1 \\ U(x_M) - |U''(x_M)|\,(x-x_M)^2 & \text{if} \quad x\sim x_M \end{cases}\,, \tag{S-13}$$

the one for which the value of the integrand has its maximum in the region of integration.

In this approximation S_{xx} can be written as [4, 5]:

$$S_{xx}(t) \simeq \langle x(t)\,x(0)\rangle_{wells} + \sum_{i=0,1} p_i^S\,\langle x(t)\,x(0)\rangle_i\,, \tag{S-14}$$

where the first term is the autocorrelation function of the dynamics of the probabilities (S-11):

$$\langle x(t)\,x(0)\rangle_{wells} \simeq l_U^2\,e^{-\frac{t}{\tau_x}}\,, \tag{S-15}$$

where l_U is the variance of the system characterized by the two states x_0 and x_1 with probabilities p_0 and p_1, and:

$$\tau_x = \frac{1}{r_{ab}+r_{ba}}\,. \tag{S-16}$$

The second term is a sum of the autocorrelations within each single well, whose timescales are $1/U''(x_{0,1}) \ll \tau_x$. So we can define $\tau_0 \simeq 1/U''(x_{0,1})$ and write this term as $d^2\,\exp -t/\tau_0$, where d is the amplitude of fluctuations in each single well, weighted by the probability of being in such well. The values of these quantities for physiological parameters, in dimensionless units, are: $l_U \simeq 0.0516$, $d \simeq 0.0123$, $\tau_x \simeq 7753$ and $\tau_0 \simeq 0.017$, and their analytical forms are given in sec. 3.

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[1] H. Huxley, A. Stewart, H. Sosa and T. Irving, *Biophys. J.*, 1994, **67**, 2411–2421.

[2] K. Wakabayashi, Y. Sugimoto, H. Tanaka, Y. Ueno, Y. Takezawa and Y. Amemiya, *Biophys. J.*, 1994, **67**, 2422–2435
[3] C. W. Gardiner, *Handbook of stochastic methods*, Springer, Berlin Heidelberg New York, 1985
[4] J. L. Skinner and P. G. Wolynes, *J. Chem. Phys.*, 1978, **69**, 2143–2150.
[5] R. Pratolongo, A. Perico, K. F. Freed and A. Szabo, *J. Chem. Phys.*, 1995, **102**, 4683–4690
[6] T. S. Lundgren and Y. B. Pointin, *J. Stat. Phys.*, 1977, **17**, 323–355.
[7] P.-H. Chavanis, *Phys. A*, 2006, **361**, 55–80.