Conformational flexibility of loops of myosin enhances global bias in the actin-myosin interaction landscape†

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Received Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
First published on the web Xth XXXXXXXXXX 200X
DOI: 10.1039/b000000x

Electronic Supporting Information (ESI) for the functional form of potentials

Functional form of potentials

Peptide chains in the simulated system are represented in a coarse-grained manner by chains connecting beads of C_α atoms. Hereafter, the superscript 0 is used to represent the value of the variables in the reference structures. Bond length $r_{i,i+1}$ between the neighboring residues along the polypeptide chain is restrained to $r^0_{i,i+1}$ by the RATTLE algorithm [1].

The total potential energy of the actomyosin system, $E_{\rm total}$, represents the interactions among C_α atoms;

$$E_{\rm total} = E_{\rm intra} + E_{\rm inter} + E_{\rm restr}. \quad (1)$$

Here, $E_{\rm intra}$ consists of the Gō-like potentials [2,3] acting within myosin and those acting within actin filament. The reference structures for myosin and actin filament defined in the main text minimize $E_{\rm intra}$ with

$$E_{\rm intra} = E_{\rm angle} + E_{\rm dihedral} + E_{\rm contact}. \quad (2)$$

Here, $E_{\rm angle}$ is the bending potential of model peptide chains,

$$E_{\rm angle} = \sum_{\text{all bond angles}} k_\theta(\theta_i - \theta_i^0)^2, \quad (3)$$

and θ_i is the bond angle defined by C_α atoms of three successive residues i, $i+1$, and $i+2$. $E_{\rm dihedral}$ is the torsion potential of model peptide chains,

$$E_{\rm dihedral} = \sum_{\text{all dihedral angles}} \left[k^1_\phi[1+\cos(\phi_i-\phi_i^0)] + k^3_\phi[1+\cos(3(\phi_i-\phi_i^0))]\right], \quad (4)$$

where ϕ_i is the dihedral angle defined by four successive residues i, $i+1$, $i+2$, and $i+3$.

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The residue pair i and j within the same chain is referred to as native pair when at least one pair of nonhydrogen atoms are within 4.5 Å from each other in the reference structure with $|i-j| \geq 4$. As there are multiple subunits within myosin or within actin filament, the residue pair between different subunits is also regarded as native pair when at least one pair of nonhydrogen atoms are within 4.5 Å from each other in the reference structure of myosin or in the reference structure of actin filament. All other pairs are called nonnative pairs. $E_{\rm contact}$ is the contact potential of the residue pairs,

$$E_{\rm contact} = E_{\rm native} + E_{\rm nonnative}. \quad (5)$$

and $E_{\rm native}$ is defined by

$$E_{\rm native} = \sum_{\text{all native pairs}} E^{\rm native}_{i,j}, \quad (6)$$

where $E^{\rm native}_{i,j}$ is the potential for the native pairs consisting of the short-range attractive and repulsive potentials,

$$E^{\rm native}_{i,j} = \begin{cases} k_{\rm native}\left[5\left(\frac{r^0_{i,j}}{r_{i,j}}\right)^{12} - 6\left(\frac{r^0_{i,j}}{r_{i,j}}\right)^{10}\right] & (r_{i,j} \geq r^0_{i,j}) \\ k_{\rm core}(r_{i,j}-r^0_{i,j})^2 - k_{\rm native} & (r_{i,j} < r^0_{i,j}), \end{cases} \quad (7)$$

and $E_{\rm nonnative}$ is the potential for the nonnative pairs, which lacks the attractive part as

$$E_{\rm nonnative} = \sum_{\text{all nonnative pairs}} E^{\rm nonnative}_{i,j}, \quad (8)$$

with

$$E^{\rm nonnative}_{i,j} = \begin{cases} 0 & (r_{i,j} \geq r^0_{\rm nonnative}) \\ k_{\rm core}(r_{i,j}-r_{\rm nonnative})^2 & (r_{i,j} < r_{\rm nonnative}), \end{cases} \quad (9)$$

where the cutoff distance is set to be $r_{\rm nonnative} = 4.0$ Å. We use $k_\theta = 6.67$ kcal/mol/rad^2, $k^1_\phi = -1.67\times10^{-2}$ kcal/mol, $k^3_\phi = -8.33\times10^{-3}$ kcal/mol, $k_{\rm native} = 3.33\times10^{-1}$ kcal/mol and $k_{\rm core} = 1.33$kcal/mol/Å^2.

Interactions between myosin and actin are represented by $E_{\rm inter}$, which are composed of the electrostatic interactions and van der Waals interactions as

$$E_{\rm inter} = E_{\rm ele} + E_{\rm vdW}. \quad (10)$$

$E_{\rm ele}$ is the Debye-Hückel potential,

$$E_{\rm ele} = \sum_{r_{i,j} \le r_{\rm ele}} k_{\rm ele} \frac{q_i q_j}{r_{i,j}} \exp\left(-\frac{r_{i,j}}{l_{\rm D}}\right), \quad (11)$$

with $l_{\rm D} = 19$ Å, $k_{\rm ele} = 4.48$ kcal $\cdot$ Å/mol, and $r_{\rm ele}$=59.3Å. Electric charges are defined as $q_i = -1$ for Asp and Glu, $+1$ for Lys and Arg, and $+0.5$ for His. The 12-6 type Lennard-Jones potential is used for the van der Waals interaction by replacing the short-ranged repulsive part with the spring-like potential,

$$E_{\rm vdW} = \sum_{i,j} E_{i,j}^{\rm vdW}, \quad (12)$$

where

$$E_{i,j}^{\rm vdW} = \begin{cases} k_{\rm vdW}\left[\left(\frac{r_{\rm vdW}}{r_{i,j}}\right)^{12} - 2\left(\frac{r_{\rm vdW}}{r_{i,j}}\right)^{6}\right] & (r_{i,j} \ge r_{\rm vdW}) \\ k_{\rm core}(r_{i,j} - r_{\rm vdW})^2 - k_{\rm vdW} & (r_{i,j} < r_{\rm vdW}) \end{cases}. \quad (13)$$

Here, $k_{\rm vdW}$=0.015 kcal/mol, $r_{\rm vdW}$=8.0 Å, and $k_{\rm core}$=1.33 kcal/mol/Å^2.

The spatial restraints to myosin and the actin filament are applied by the potential

$$E_{\rm restr} = E_{\rm restr}^{\rm myosin} + E_{\rm restr}^{\rm actin}. \quad (14)$$

The tip of the myosin lever-arm (sequence number 830-843 in heavy chain and sequence number 1-83 in regulatory light chain) is restrained by the curtain-rail potential

$$E_{\rm restr}^{\rm myosin} = \sum_i k_{\rm restr}^{\rm myosin}\left[(x_i - x_i^{\rm helical})^2 + (y_i - y_i^{\rm helical})^2\right], \quad (15)$$

where $k_{\rm restr}^{\rm myosin} = 0.2$ kcal/mol/Å^2. The z-axis runs parallel to the center line of the reference structure of actin filament, and x and y are coordinates perpendicular to the z-axis. We assume that the curtain-rail runs helically around the actin filament so that the whole system has the same helical symmetry as the reference structure of actin filament [4], 3.2° rotation per 35.867 nm, as

$$\begin{aligned} x_i^{\rm helical} &= x_i^0 \cos\theta_{\rm helical} + y_i^0 \sin\theta_{\rm helical}, \\ y_i^{\rm helical} &= -x_i^0 \sin\theta_{\rm helical} + y_i^0 \cos\theta_{\rm helical}, \end{aligned} \quad (16)$$

with $\theta_{\rm helical}(z_i) = -3.2^\circ \times (z_i - z_i^0)/35.867$ nm. In Eq.16, x_i^0 and y_i^0 are determined by consulting the corresponding coordinates in the EM structure of actin-myosin complex [5]. The results are insensitive to the variation of the height of the curtain-rail due to the small shift in x_i^0 and y_i^0. In accord with the single molecular measurement [6], no force is applied with respect to the movement of the tip of the lever-arm of myosin along the curtain-rail. All residues in actin filament are restrained by the potential

$$E_{\rm restr}^{\rm actin} = \sum_i k_{\rm restr}^{\rm actin}\left[(x_i - x_i^0)^2 + (y_i - y_i^0)^2 + (z_i - z_i^0)^2\right], \quad (17)$$

where we use $k_{\rm restr}^{\rm actin} = 3.33 \times 10^{-3}$ kcal/mol/Å^2.

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