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Efficiency of collective myosin II motors studied with an elastic coupling power-stroke ratchet model*

Zi-Qing Wang(汪自庆)[1], Jin-Fang Li(李金芳)[1], Ying-Ge Xie(解迎革)[1], Guo-Dong Wang(王国栋)[1], and Yao-Gen Shu(舒咬根)[2,†]

[1] College of Science, Northwest A & F University, Yangling 712100, China
[2] CAS Key Laboratory of Theoretical Physics, Institute of Theoretical Physics, Chinese Academy of Sciences (CAS), Beijing 100190, China

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We proposed a modified ratchet model including power-stroke and elastic coupling to study the efficiency of collective non-processive motors such as myosin II in muscle. Our theoretical results are in good agreement with the experimental data. Our study not only reveals that the maximum efficiency depends on elasticity and is independent of transition rates but also indicates that the parameters fitted to fast muscle are different from those fitted to a slow one. The latter may imply that the structure of the fast muscle is different from that of the slow one. The main reason that our model succeeds is that velocity in this model is an independent variable.

Keywords: efficiency of collective non-processive motors, ratchet model, power-stroke, elasticity

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1. Introduction

The efficiencies of processive motors such as F_oF_1-ATPase and kinesin have been investigated.[1–6] The efficiency of F_oF_1-ATPase approaches nearly 100% due to the elastic rotor γ subunit,[2] while that of kinesin-1 also reaches at 70% because neck-linker will extent elastically during docking.[5] However, it is very difficult for non-processive motors such as myosin II to be studied to determine their efficiency at single molecule level due to low duty ratio. Fortunately, most non-processive motors work collectively; for example, the contraction of muscle results from the cooperation of large amount of myosin II motors.[7–14] The elementary unit of muscle is sarcomere, which is composed of regular arrays of thick filament and thin filament.[8,15–17] Each thick filament is self-assembled with a large number of myosin II motors. These motors "walk along" the thin filaments, which leads to relative sliding between thick filament and thin one. The contraction of muscle results from this sliding.

Some researchers have theoretically studied the efficiency of muscle based on kinetic models,[12,18–20] and their results are consistent with experiments.[21–25] Jülicher *et al.* also studied the efficiency of collective motors based on a simplest ratchet model.[26] In the ratchet model, the motors are simplified as Brownian particles which diffuse among periodic potentials and transit between the potentials.[26–31] In the kinetic models, the motors transit directly between different states with different rates and the detailed diffusion is not considered. The ratchet model, however, involved more physical information.

In this paper, motivated by experimental results,[21] we add an elastic element, which corresponds the long coiled coil stalk[32,33] with stiffness about 1.5 pN/nm$\sim$ 3 pN/nm,[11,33–35] and a power-stroke, which corresponds the cross-bridge so that localized the transition of particle between states, into the ratchet model to study the efficiency of collective myosin II motors.

2. Models

2.1. Model I: The simplest ratchet model with elastic coupling

We first recall the ratchet model under consideration of motor elasticity.[36] In this model, motors are elastically coupled to a backbone with periodical spacing s by a springs (with a stiffness of k_m) as shown as Fig. 1. The motor heads can transit between state 1 and state 2. Here, the periodic potentials W_1 with period $l = a + b$ corresponds the situation that the head is attaching at the thin filament, while the flat W_2 does the situation that the head is detaching and can diffuse freely along z. We denote x as the position of the coupled point of motor on the backbone at time t, and z as the position of the motor head in state 1 or state 2. The transition rate ω_{on} (corresponding to binding rate) is a constant over the period l, and the transition rate $\omega_{off}(z) = \omega^0_{off}\Phi(z)$ (corresponding to unbinding rate, or equivalently as the ATP excitation) is a piecewise constant.[26]

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†Corresponding author. E-mail: shuyg@itp.ac.cn

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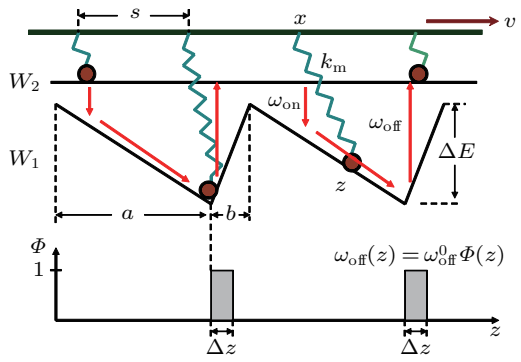


Fig. 1. (color online) Schematic diagram of a two-state ratchet model with elastic coupling (Model I). Motors are periodically (with spacing s) coupled to a backbone (which corresponds the thick filament) by springs (which corresponds the stalk of myosin II, its stiffness is k_m). The motor heads can transit between state 1 and state 2. The sawtooth periodic potential W_1 with period $l = a+b$ corresponds the situation that the head is attaching at the thin filament, while the flat W_2 does the situation that the head is detaching and can diffuse freely along z. The rate of ATP excitation is $\omega_{off}(z) = \omega^0_{off}\Phi(z)$, which means that ATP excitation only occurs within an interval of Δz.

2.2. Model II: Model I adds a power stroke

At the molecular level, muscle contraction is the sliding between a thick filament and a thin one, which is cyclically driven by myosin cross-bridges (which consists mainly of myosin head, lever arm and elastic stalk) between the two filaments. The energy outputted by a single cross-bridge during a cycle of attachment is coupled to the hydrolysis of one molecule of ATP. The 'mechanical' power-stroke of the attached cross-bridge can reach 5 nm$\sim$ 10 nm in each cycle, as shown in Fig. 2(a). First, myosin attaches to the actin filament in a specific conformation "A", which corresponds to weak bound pre-power-stroke state (actin · myosin · ADP · Pi). It then transits into the conformation "B" accompanying with a power-stroke, which corresponds to strong post-power-stroke state (actin · myosin). Finally, the myosin detaches from the actin filament due to ATP excitation, and the lever arm reprimes to the conformation "C" (unbound state: myosin · ADP · Pi). A chemical cycle, which is coupling to a mechanical cycle, completed and the next cycle begins.[11,32,33,37,38]

According to Fig. , we propose a modified model (Model II) as shown in Fig. 2(b). Here, the joint point in coordinate z (marked by red star in panel (a)) of motor stalk (spring) and lever arm equivalents to the position of motor head domain in Model I. The binding with the rate of ω_{on} only occurs in a narrow region (A) at the right side of the reflection boundary because myosin attaches initially to the actin filament with a pre-power-stroke state "A", which is denoted by a local potential maximum of W_1 due to weak binding. ATP excitation with a rate of ω_{off}, however, occurs after a power-stroke; *i.e.*, after the motor arrives at the state "B", and is localized at the left side (B) of reflection boundary. Both ω_{on} and ω_{off} are reversible, and the rates of their reversible processes are denoted by ω^-_{on} and ω^-_{off} respectively. The directed transition from one potential well of W_1 to another is forbidden due to the reflection boundary.

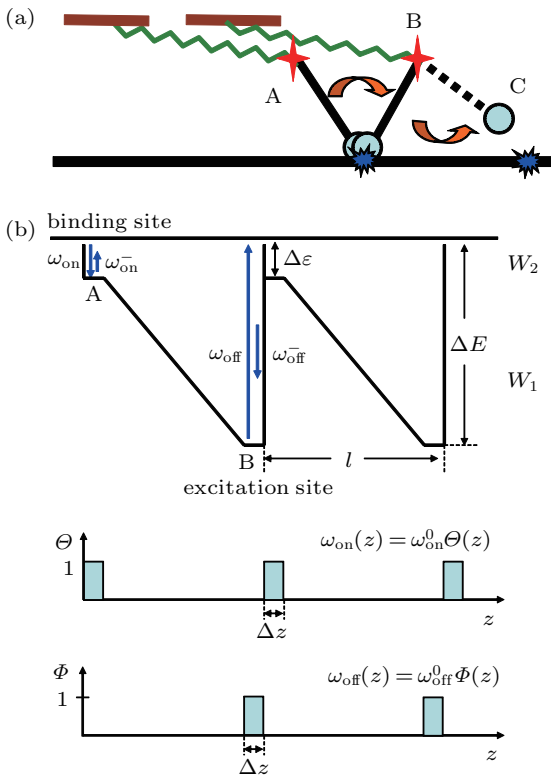


Fig. 2. (color online) Schematic model of Model I under consideration of power stroke (Model II). (a) The process from A to B represents the power-stroke, while the process from B to C does the recovery process of power-stroke. in recovery process motor head detaches from the thin filament due to ATP excitation and the lever arm reprimes. (b) In modified W_1, there is a reflection boundary that forbids motor to transit directly from one W_1 well to another one. At the same time, both transitions between W_1 and W_2, *i.e.*, ω_{on} and ω_{off}, are localized at right side (A) and left side (B) of the reflection boundary by $\Theta(z)$ and $\Phi(z)$ respectively. The joint point in coordinate z (marked by red star in panel (a)) of motor stalk (spring) and lever arm equivalents to the position of motor head domain in Model I.

Furthermore, we simplify the potential W_1 into a piecewise one. There is a platform and a bottom in each period of W_1, the platform corresponds to the weak bound pre-power-stroke state of myosin and is denoted by "A", while the bottom corresponds to post-power-stroke state and is denoted by "B". Therefore, the transition from "A" to "B" is the power-stroke process. After a power-stroke, the motor can detach from the actin filament and lever arm reprimes by a recovery power-stroke, the next cycle then begins. This idea is consistent with the cross-bridge model of muscle.[7,9]

3. Results

We define the probability density $p_i(x,z,t)$ for a motor with its tail at x and head at z in the state i ($i = 1,2$), which obey the following coupled Fokker–Planck equations[36]

$$\begin{aligned}\partial_t p_1 &= D\partial_z[p_1(\partial_z W_1 - F_s)/k_B T + \partial_z p_1] \\ &\quad - v\partial_x p_1 - \omega_{off}(z)p_1 + \omega_{on}(z)p_2, \qquad (1)\\ \partial_t p_2 &= D\partial_z[-p_2 F_s/k_B T + \partial_z p_2] \\ &\quad - v\partial_x p_2 + \omega_{off}(z)p_1 - \omega_{on}(z)p_2, \qquad (2)\end{aligned}$$

where D is the diffusion constant, v is the velocity of the backbone, and $F_s = k_m(x-z)$ is the elastic force acting on the head. The probability density p_i can be calculated numerically from Eqs. (1) and (2) (see Ref. [36]). Here, we only focus on the situation of steady state. The unbinding at A is dependent on force and can be simplified into[39]

$$\frac{\omega_{on}^{-}(F_s)}{\omega_{on}^{-}(0)} \approx \exp\left(\frac{|F_s|}{F_d}\right) \tag{3}$$

due to the unbinding is localized in Δz, where F_d is the detached force of a single motor,[39] and

$$\frac{\omega_{on}^{-}(0)}{\omega_{on}} = \exp\left(-\frac{\Delta\varepsilon}{k_B T}\right), \tag{4}$$

$$\frac{\omega_{off}^{-}}{\omega_{off}} = \exp\left(\frac{\Delta E - \Delta G_{ATP}}{k_B T}\right) \tag{5}$$

because of detailed balance in the chemical reactions.[40]

The average external force applied on one motor is given by[36]

$$F_{ext} = \lambda_0 v - F_{motor}, \tag{6}$$

where $-\lambda_0 v$ is the average damping force of single motor due to the drag of backbone, λ_0 is the damping coefficient, and F_{motor} is the average force exerted by a single motor on the backbone, where

$$F_{motor} = \int_0^l \mathrm{d}x \int_{-\infty}^{\infty} k_m(z-x) p_1(x,z)\mathrm{d}z. \tag{7}$$

Because the friction force is usually a few orders of magnitude lower than F_{motor},[42] the first term in Eq. (6) can be ignored, thus $F_{ext} \approx -F_{motor}$.

3.1. Efficiency of collective motors

The efficiency of collective motors that are elastically coupled is an important property at steady state. For comparison with experimental results,[21] it can be defined as

$$\eta = \frac{-F_{ext} v}{\Delta H_{ATP} \int_0^l \mathrm{d}x \int_{-\infty}^{\infty} (p_1 \omega_{off} - p_2 \omega_{off}^{-})\mathrm{d}z}, \tag{8}$$

i.e., the ratio of the rate of mechanical power output to that of enthalpy output, where ΔH_{ATP} is the enthalpy change per molecule of ATP split.

The numerical results of Eq. (8) are shown in Fig. 3 at different velocities or different unbinding rates. η_{max} increases with increasing of k_m at fixed ω_{off}^0, however, it rarely depend on ω_{off}^0 at fixed k_m. Thus, η_{max} depends on elasticity and is independent of transition rates. Comparison with experimental data[21] in Fig. 3(a), our results show that it seems reasonable for fast muscle that $k_m \approx 1.5$ pN/nm at $\omega_{off}^0 = 2000\ s^{-1}$. For slow muscle, however, it seems reasonable that $k_m \approx 3.0$ pN/nm at $\omega_{off}^0 = 1000\ s^{-1}$. The value of η that is calculated by Model I (at left-down) is much lower than that is calculated by Model II.

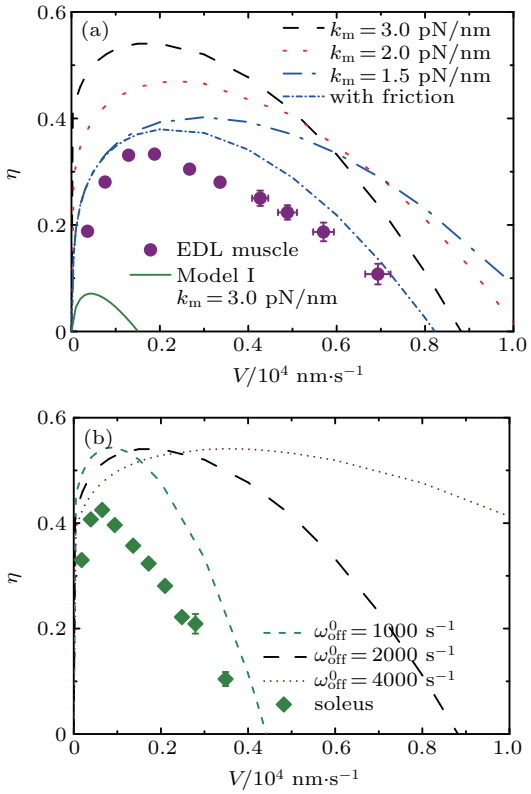


Fig. 3. (color online) (a) The efficiency of collective motor vs velocity for different motor stiffness at $\omega_{off}^0 = 2000\ s^{-1}$.[11,41] The symbols are experimental data of EDL muscle (fast muscle).[21] The short dashed-dotted line is the efficiency of Model II under consideration of friction ($\lambda_0 = 0.005$ pN·s/μm), while the long dashed-dotted line is that without friction. The solid line at the lower left corner is calculated by Model I with $b/l = 0.1$, which is much more smaller than that is calculated by Model II. (b) The efficiency of collective motor vs velocity for different ω_{off}^0 at $k_m = 3$ pN/nm. The symbols are experimental data of Soleus (slow muscle).[21] Here, $\Delta E = 60$ pN·nm[42] $< \Delta G_{ATP} \approx 80$ pN·nm, $\Delta H_{ATP} \approx 80$ pN·nm,[43,44] $\Delta\varepsilon = 5$ pN·nm,[32] $F_d = 3$ pN,[39] $\Delta z = l/10$, and $l = 10$ nm, $\omega_{on} = 20\ s^{-1}$ in Model I,[12] while $\omega_{on}^0 = 200\ s^{-1}$ in Model II due to $l/\Delta z = 10$, and $D \approx 10^6$ nm^2/s.[42]

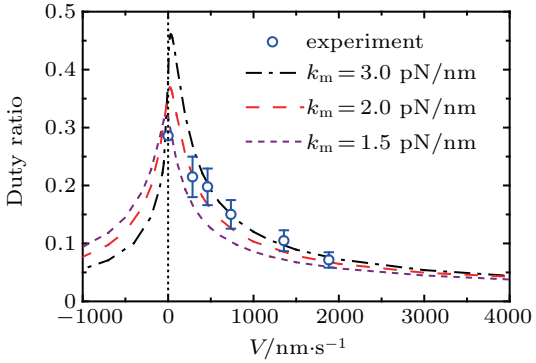


Fig. 4. (color online) Duty ratio of collective motors versus velocity for different motor stiffness at $\omega_{off}^0 = 2000\ s^{-1}$. The parameters of Model II are the same with those of Fig. 3. The experimental data (cycles) come from Ref. [11].

3.2. Duty ratio of collective motors

Duty ratio of collective motors can be defined as

$$\text{duty ratio} = \int_0^l \mathrm{d}x \int_{-\infty}^{\infty} p_1(x,z)\mathrm{d}z. \tag{9}$$

Figure 4 shows the relation between duty ratio and velocity for different stiffness at fixed ω_{off}^0. Duty ratio decreases with

increasing of velocity. According to the experimental data,[11] our results show that $k_{\rm m} \in (1.5, 3.0)$ pN/nm seems reasonable at $\omega_{\rm off}^0 = 2000\ {\rm s}^{-1}$.

4. Discussion and conclusion

We have lumped the ratchet model, power-stroke and elastic coupling together into Model II. The relation between efficiency and velocity, as well as the relation between duty ratio and velocity has been investigated. The experimental data has been successfully explained. The reasonable parameters such as $k_{\rm m}$ and $\omega_{\rm off}^0$ have also been sorted out. However, the parameters that are fitted to fast muscle are different from those are fitted to the slow one, which may imply that the structure of the fast muscle is different from that of the slow one.

The mean velocity is the main variable that has to be calculated in study of collective motors. For example, the mean field method can be engaged to study efficiency of the rigid coupling collective motors if the number of motors (N) is large enough and s is incommensurate with l,[27,31] otherwise, N-coupling-equations have to be numerically simulated if N is limited.[45,46] However, the mean velocity here is independent variable. In Model II, the cooperation among motors has been involved in $F_{\rm ext}$. This may be a convenient method to estimate the efficiency. Theoretical results revealed that it is the elasticity, local transition and reflection boundary that improve the efficiency of collective elastic coupling motors. It must be pointed that the final results does not depend on the value of l; *i.e.*, it is flexible (for example, $l = 8$ nm for microtubule and $l = 36$ nm for actin filament) because of $\int_0^l {\rm d}x \int_{-\infty}^{\infty} (p_1 + p_2) {\rm d}z = 1$.

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