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The Use of an 'Effective Potential' to Describe the Directed Motion of a Two-State Molecular Motor

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Abstract—Force generation and directed motion of molecular motors using a simple two-state model are studied in the paper. Here we consider the asymmetric and periodic potential in the model. The symmetric and periodic potential is adopted to describe the interactions between motor proteins and filaments that are periodic and polar. The flux and the slope of the effective potential as functions of the temperature and transition rates are calculated in the two-state model. The ratio of the slope of the effective potential to the flux is also calculated. It is concluded that the directed motion of motor proteins is relevant to the effective potential. The slope of the effective potential corresponds to an average force. The non-vanishing force therefore implies that detailed balance is broken in the process of transition between different states. Moreover, we compare the theoretical relationship of load force and velocity with the experimental data. It is shown that they are consistent.

I. INTRODUCTION

Motor proteins are molecular machines that convert the chemical energy derived from the hydrolysis of Adenosine triphosphate(ATP) into mechanical work used power cellular motility. Both rotatory and translationary motors are known to exist. One essential feature of molecular motors in living cells that intrigues much interest of scientists is their ability to generate directed motion and force in the process such as material transport and the movement of organelles. The energy source of the movement comes from the chemical reactions while the Adenosine triphosphate (ATP) is hydrolyzed. Molecular motors play a key role not only in muscular contraction but also in cell division, cellular traffic, flagellar motion, material transport along the axons of the nerve cells, etc. molecular motors, such as kinesins, myosins, dyneins, all move along the periodical and asymmetric tracks. fluctuation in ratchet systems has been an active research field [1], which has attracted much interest of researchers over the last decades. In these systems, directed motion can be induced in the presence of asymmetric potential and external nonthermal fluctuation. Various ratchet models have been proposed over the last decades, such as rocked ratchet [2,3,4], correlation ratchet [5], diffusion ratchet [6] and flashing ratchet [7,8].The recent experimental results on molecular motors have inspired a lot of theoretical work on such motors. In all these studies the potential is taken to be asymmetric and periodic to describe the interaction between motors and filaments. By suitably changing the system parameters such as temperature, friction coefficient, mass, transition rate, etc, one can calculate the flux and the efficiency [9,10,11,12]. In this paper a flashing ratchet model is discussed, in which detailed balance is broken, and the asymmetric potential steps from one state to another.

In the model the flux and the slope of the effective potential are analyzed primarily. It is shown that the directed motion [13] of the motor proteins is relevant to the effective potential. Here the effective potential is a statistical physical concept. In general, in correlation ratchet and flashing ratchet, the directed motion of the particles corresponds to a certain slope of the effective potential. So the effective potential can be discussed in many homologous problems that can improve our understanding of the mechanism for the corresponding process.

II. MODEL AND THEORY

To discuss force generation and motion of linear molecular motors, a simple two-state model is studied. We concentrate our analysis on this model to find out the mechanism on the physical and chemical coupling of molecular motors. The interaction between motors and filaments change significantly which means that the coupling between them change from tight binding to loose binding. Therefore the potential will switch between different states and conformation change is brought between motors and filaments as well. At a molecular scale motor proteins can convert chemical energy into mechanical work and lead to directed motion [14,15,16].

To construct this model, several important features, such as the polarity and the asymmetry of the filament, have been considered .Then the interaction between the motors and the filaments can be described by an asymmetric potential. For different states the potentials have different forms too. In this paper, we adopt a kind of more simplified saw-tooth potential fluctuating between two states (see Fig.1.)

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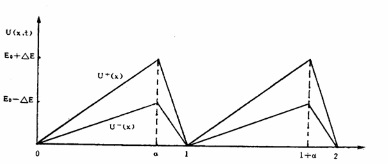

Fig.1 Sketch map of the piecewise linear potential in two states. $U^+(x)$ and $U^-(x)$ describe the energy profile of the two states, transitions from one to the other take place at rates γ_1 and γ_2, respectively. Here the period L takes the value 1 and α is the asymmetric coefficient.

The potential fluctuates between high barrier($E_0 + \Delta E$) and low barrier ($E_0 - \Delta E$). The parameters $\gamma_{i,j}$ (i,j=1,2, for convenience let $\gamma_{1,2} = \gamma_1$, $\gamma_{2,1} = \gamma_2$) represent the flipping rate of the barrier fluctuation between $E_0 + \Delta E$ and $E_0 - \Delta E$. The symmetry of the filament is reflected in the symmetry of the potential. In order to develop a stochastic description of the dynamics, we introduce the probability density for the motor to be at position x at time t for different states. The sketch map of the potential in two states is displayed in Fig.1. The evolution of the system can be described by Fokker-Planck equations with source terms.

$$\frac{\partial}{\partial t}P_1(x,t) = -\frac{\partial}{\partial x}J_1(x,t) - \gamma_1 P_1(x,t) + \gamma_2 P_2(x,t) \tag{1}$$

$$\frac{\partial}{\partial t}P_2(x,t) = -\frac{\partial}{\partial x}J_2(x,t) + \gamma_1 P_1(x,t) - \gamma_2 P_2(x,t) \tag{2}$$

Here the fluxs result from diffusion, the interaction with the filament, and the action of a possible load force F_0 ($V_1 = U^+(x)$ and $V_2 = U^-(x)$).

$$J_i = \mu_i\left[-k_B T\partial_x P_i - P_i\partial V_i - P_i F_0\right] \tag{3}$$

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III. CALCULATIONS AND ANALYSIS

We can evaluate the steady-state particle flux $J = J_1 + J_2$ for l-periodic of $P(x)$. With $P=P_1+P_2$ and $\lambda(x) = P_1(x)/P(x)$, effective mobility given by $\mu_{eff} = \mu_1\lambda(x) + \mu_2(1-\lambda(x))$, so the flux J has the following form

$$J = \mu_{eff}\left[-K_B T\partial_x P - \left[\frac{\mu_1\lambda\partial V_1 + \mu_2(1-\lambda)\partial V_2}{\mu_{eff}} + \frac{K_B T}{\mu_{eff}}(\mu_1 - \mu_2)\partial_x\lambda\right]P - PF_0\right] \tag{4}$$

So, $$\partial V_{eff} = \frac{\mu_1\lambda\partial V_1 + \mu_2(1-\lambda)\partial V_2}{\mu_{eff}} + \frac{K_B T}{\mu_{eff}}(\mu_1 - \mu_2)\partial_x\lambda \tag{5}$$

J takes the form

$$J = \mu_{eff}\left[-k_B T\partial_x P - P\partial V_{eff} - PF_0\right] \tag{6}$$

the effective potential reads

$$V_{eff}(x') - V_{eff}(0) = \int_0^{x'} dx\frac{\mu_1\lambda\partial_x V_1 + \mu_2(1-\lambda)\partial_x V_2}{\mu_1\lambda + \mu_2(1-\lambda)} + k_B T\left[\ln(\mu_{eff})\right]_0^{x'} \tag{7}$$

Eq. (7) is the definition of the effective potential, it’s a statistical result and it is the affected by the barrier of each state and surrounding environments.The slope of the effective potential is defined as follow:

$$E_p = \left[V_{eff}(nL) - V_{eff}(0)\right]/nL \tag{8}$$

For asymmetric potentials, the effective potential generally has a nonzero slope $\left[V_{eff}(nL) - V_{eff}(0)\right]/nL$ on large scale, although V_1 and V_2 are flat on large scale. This average slope corresponds to an average force that pushes the motor to move directly and can even generate motion against weaker external load forces F_0. If the potential is symmetric, the effective potential is periodic: $V_{eff}(nL) = V_{eff}(0)$ for integer n that is thus flat on large scales and no directed motion can be generated.

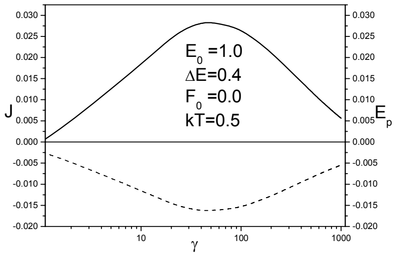

Fig.2 Relationship of the slope of the effective potential *Ep* (solid line) and flux *J* (dashed line) as a function of the transition rate

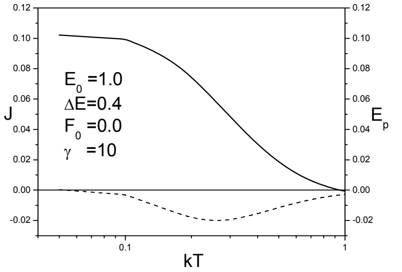

Fig.3 Relationship of the slope of the effective potential *Ep* (solid line) and the flux *J* (dashed line) as a function of the temperature

We choose the parameters of the potential $\alpha = 10/11$ with the same value of the two transition rates ($\gamma_1 = \gamma_2$) and without any load force first.

It is shown from Fig.2 that the flux and the slope of the effective potential can both attain maximum at almost the same value when the transition rates are nearly 40. It is also seen that the flux and the slope of the effective potential can increase or decrease simultaneously. So the directed motion of motor protein is relevant to the effective potential when the temperature is given.

It can also be seen from Fig.3 that the flux and the slope of the effective potential do not change simultaneously when the temperature is smaller. Only when the temperature takes a proper value, the flux and the slope of the effective potential can change simultaneously. This shows that the flux and the slope of effective potential are relevant only when the temperature takes a proper value.

To understand the concept of the effective potential clearly, we study the simple system that is equivalent to the one we have just discussed. In the overdamped limit, the distribution function of x obeys the following Smoluchowski equation.

$$\frac{\partial P}{\partial t}=\frac{\partial}{\partial x}\left(U^{'}(x)-F+k_BT\frac{\partial}{\partial x}\right)P=-\frac{\partial J}{\partial x} \tag{9}$$

Here $U(x)=V(x)+Fx$, $V(x)$ is the total potential. In stationary, the probability flux J is constant.

$$J=\frac{k_BT\left(1-e^{-FL/k_BT}\right)}{\int_0^L e^{V(x)/k_BT}dx\int_0^L e^{-V(x)/k_BT}dx-\left(1-e^{-FL/k_BT}\right)\int_0^L e^{-V(x)/k_BT}\int_0^x e^{V(x^{'})/k_BT}dx^{'}dx} \tag{10}$$

Here F is the average force, the period of potential, L=1.

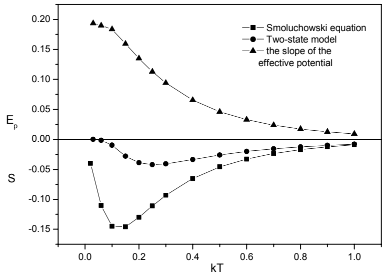

Fig.4 The flux under the two different theoretical frames and under the same the effective potential

From Fig.4 we can see that the trend of the two curves is identical. But strictly speaking, when the temperature is very small, the flux of the Smoluchowski equation does not near zero, it is larger than the flux of the two-state model. In the low temperature range, the reason why the flux differ in two cases, may attribute to the fact that the average force is estimated too larger. When the temperature is larger, one flux is nearly consistent with the other. In summery, the trend of the flux is identical in two different theoretical frames and the concept of the effective potential is successful especially in the high temperature range.

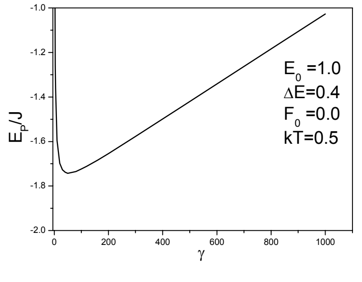

Fig.5 Ratio of the slope of the effective potential to the flux as a function of the transition rate

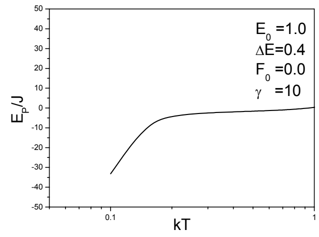

Fig.6 Ratio of the slope of the effective potential to flux as a function of the temperature

From Fig.5 it is seen that the ratio reduces with the increment of the transition rates when the transition rate is smaller. However, the ratio attains minimum when the transition rate takes proper value, then the ratio increases with the increment of the transition rates. It is shown that the slope of the effective potential increases or decreases faster than the flux. All of these facts indicate that the flux and the slope are not simply linear relevant.

From Fig.6 we can see that the ratio does not always change simultaneously when the transition rate is given. The ratio increases with the increment of the temperature when the temperature is less than 0.2, this shows that the slope of the effective potential increases faster than the flux. It increases very slower when the temperature is between 0.2 and 1.0, this shows that the flux and the slope of the effective potential near linear relevant. The results show that the flux and the slope of the effective potential change simultaneously when the temperature is in a certain range.

The slope of the effective potential corresponds to an average force. Because of the existence of the average force, motor proteins can have directed motion against the load force. If the load force is zero, the directed motion is vanished. When the temperature is smaller, even if there is the slope of the effective potential, most Brownian particles (motor proteins) can not span the potential. Therefore the flux is small, the ratio of the slope of the effective potential to the flux is not linear relevant simply. When the temperature is larger, the particles can span the potential at the effect of the average force, so the ratio of them is near linear relevant. Besides, the interaction between particles is not considered. This interaction also has an effect on the flux.

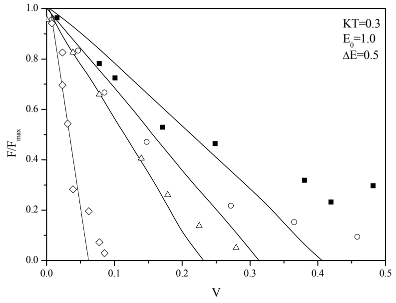

Fig.7. The relationship of the force-flux. The solid lines are fits of the model and the scattered symbols are experimental data. From left to right, ATP concentration is 10, 50, 100, 500μM

Fig.7 is the relationship of load force and velocity, different curves correspond to different concentrations. The dots is experimental data. From the Fig.7, with the increment of the load force, the velocity is reduced. Because the load force is increased the combination ability between motor and ATP is weaken. With the increment of the ATP concentration, the velocity of molecular motor is increased, the stop force of the molecular motor is more and more increasable. It's because the association probability between molecular motor and ATP molecule become bigger. So the force for directed motion is also bigger, then the external force for stopping is bigger too. From the above, the motion of the motor and ATP concentration is correlated closely.

However, the average force exists only if the system consumes chemical energy. If no energy is provided to the system, detailed balance has to be satisfied:

$$\gamma_1(x) = \gamma_2(x)\exp\left[\frac{V_1(x) - V_2(x)}{k_B T}\right] \qquad (11)$$

In general, when any process and the corresponding inverse process counteract each other, it is called detailed balance. If the system does not satisfy the detailed balance, energy is exchanged with environment. This is not only the root of producing the effective potential but also the origin of the nonzero flux. Generally in biological systems detailed balance is broken by the hydrolysis of ATP. So only ATP is present, the directed motion appears. That is to say, ATP is necessary for the generation of the directed motion.

IV. CONCLUSIONS

In the paper, we have discussed the directed motion of the Brownian motors, and learned more about the mechanism of the force generation and motion of linear molecular motors. The motor proteins move along filaments which are polar and periodic. The motors' conformation change generates their directed motion. In this paper, first a simplified physical model has been proposed to study this process in the view of two-state stochastic fluctuation. Second, we calculated the flux and the slope of the effective potential with the changes of some parameters and the ratio of the flux to the slope of the effective potential. It is shown that the flux and the slope of the effective potential change simultaneously with the change of the transition rates, but the potential changes faster than the flux; the flux and the slope of the effective potential change simultaneously when the temperature is larger. That is to say, the flux and the slope of the effective potential are not always relevant. Third, we have calculated the flux under two different theoretical frames at the same potential, the trend of the flux is identical under two different theoretical frames and the concept of the effective potential is successful especially in the high temperature range. Fourth, we calculated the relationship of load force and velocity, with the increment of the ATP concentration, the velocity of molecular motor is increased, the stop force of the molecular motor is more and more increasable.

The directed motion of the motor can be attributed to the nonzero slope of the effective potential. This corresponds to an average force that can make the motor move against an external load force as it carries some cargos along the track. The average force exists only if the system consumes chemical energy, that is to say the detailed balance is broken, which make the motor move. In the end, the directed motion of the motor is relevant to the effective potential. So the proposing of the effective potential is helpful for the understanding of the directed motion greatly. We expect to use the effective potential to understand the analogical mechanism better.

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