A PARRONDO'S PARADOX OF FREE ENERGY AND ITS APPLICATION ON MOLECULAR MOTORS

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Dedicated to Professor Henk Broer for his 60th Birthday

Abstract. We give a Parrondo's paradox of free energy in the classical flashing ratchet model, which is a different viewpoint from the existing examples. Further, we show that the Parrondo's paradox of free energy gives a different viewpoint of molecular motor, with which we may analysis its efficiency. Our example shows that the molecular motors can gain up to 20% in the free energy during the process. In addition, we report a noise induced stochastic resonance like phenomenon in the flashing ratchet model.

1. Introduction

In this article, we are to discover some connection among Parrondo's paradox, molecular motor and free energy functional.

Parrando's paradox is a well known concept in the game theory. Roughly speaking, the paradox states that it is possible to construct a winning strategy by playing two losing strategies alternately [6, 7, 4]. The classical example of Parrondo's paradox is a coin toss game. There also exists an extensive literature on the paradox. And it has been used for many different problems such as a flashing ratchet model for the molecular motors. We refer to [8] and references therein for more discussions on the subject. Here, we explain the paradox for the flashing ratchet model from the free energy point of view.

As it comes to Molecular motor, we are talking about a kind of proteins that conduct essential movements in living organisms. These tiny biological machines carry out most forms of movements in the living world. There are many different kinds of molecular motors, such as Myosin, Kinesin, Dynein, Actin, Microtubule, Dynamin, ATP synthase, RNA polymerase and many more. Although different kinds of molecular motors are for different biological tasks, they share similar basic working principle, which is to convert chemical energy into mechanical motions. There exist many different models and theory to explain the working mechanism of molecular motors[1, 15] . Some of them are drastically different. However, despite of the differences among different models, most of them use randomness, such as Brownian motions, to handle the uncertainties in molecular motors. This is why

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molecular motors are also called Brownian motors in some literature. A major reason that one needs to consider uncertainties is that molecular motors have small sizes, hence they are more sensitive to thermal noise.

Among different mathematical models for molecular motors, a flashing ratchet model, which is related to the well-known Parando's paradox discussed above, has been an interesting one that draws attention in recent years [1, 8, 10, 17]. The main idea behind the flashing ratchet model is that it describes molecular motors as Brownian particles moving in an asymmetric potential field that is turned on and off periodically. Then the oscillatory pattern of the potential field causes directional motions of the Brownian particles, just like how flashing ratchets allow movements in designed directions. More precisely, the flashing ratchet model describes the motion of a molecular motor $X \in \mathbb{R}^d$ by a stochastic differential equation,

$$\mathrm{d}X = -\nabla\Psi(X,t)\mathrm{d}t + \sqrt{2\tau}\mathrm{d}W_t, \tag{1.1}$$

where $\Psi(x,t)$ is a time dependent potential function taking non-negative values for different time intervals, W_t is the standard Brownian motion in $\mathbb{R}^d$, and τ is in proportion to the current temperature of the system.

The flashing ratchet has been intensively studied by several researchers [10, 8, 22, 16, 12, 21]. In this paper, we present a different viewpoint based on free energy, give a new example of Parrondo's paradox, and explain the flashing ratchet model and estimate the efficiency of molecular motors.

The concept of free energy plays an important role in this article. Roughly speaking, the free energy refers to the maximal amount of work that can be extracted from a system. By (1.1), the motion of a molecular motor is a random function, for which we denote its probability density function by P. Then the free energy is expressed as a functional in terms of P,

$$F(P) = U(P) - \tau S(P), \tag{1.2}$$

where $U(P)$ is the potential energy, $S(P)$ is the entropy, and τ is a constant that is in proportion to the current temperature. Here, we have the potential energy defined by

$$U(P) := \int_{\mathbb{R}^N} \Psi(x)P(x)dx.$$

And the entropy is given by

$$S(P) := -\int_{\mathbb{R}^N} P(x)\log P(x)dx,$$

which is also called Gibbs-Boltzmann entropy functional in some literature. Since in the flashing ratchet model the probability density function evolves with time, the corresponding free energy could be a valuable index of the current status of the system.

Obviously, to calculate the free energy, one needs to know the probability density function P. In fact, in the flashing ratchet model mentioned above, it can be computed by the well-known Fokker-Planck equation. The Fokker-Planck equation is a linear parabolic equation which describes the time evolution of probability density

function $P(x,t)$ of a stochastic process. For the flashing ratchet motions defined by (1.1), the corresponding Fokker-Planck equation is

$$\frac{\partial P(x,t)}{\partial t} = \nabla \cdot (\nabla \Psi(x,t) P(x,t)) + \tau \Delta P(x,t). \tag{1.3}$$

Using Fokker-Planck equations, we can calculate the probability density function $P(x,t)$ which is used to compute the free energy at any given time t. Then our system efficiency is defined by the relative gain (in percentile) of the free energy in the process.

In the rest of the paper, we describe in detail on how to use the free energy to give another Parrondo's paradox of the flashing ratchet model, explain the flashing ratchet model and estimate the system efficiency. Furthermore, we also show an interesting stochastic resonance like behavior of the flashing ratchet model. For the resonance like behavior, we mean the efficiency of molecular motors would reach its maximal at certain level of environmental noise. When we consider the molecular motor model, we generally assume the movement of particles are slow because small particle has higher Reynolds number. So we didn't count the kinetic energy in this article.

2. Parrondo's Paradox in Flashing Ratchet: Old and New

As mentioned in Section 1, the flashing ratchet model uses a randomly perturbed dynamical equation (1.1) to describe the motion of a molecular motor. Meanwhile, flashing ratchet model is also a classical example of Parrondo's paradox [8],[10]. In this section, we are to review the classical Parrondo's paradox of flashing ratchet, and demonstrate the new Parrondo's paradox with the viewpoint of free energy.

In both cases, the key component in the model is that the asymmetric potential field $\Psi(x,t)$ is time dependent and can be turned on and off periodically or randomly, i.e. we can assume that the potential function $\Psi(x,t)$ is a given asymmetric function $G(x)$ when it is turned on and 0 when turned off:

$$\Psi(x,t) = \begin{cases} G(x) & \text{if} \quad n \le t < n + 1/2 \\ 0 & \text{if} \quad n + 1/2 \le t < n + 1. \end{cases}$$

We remark that the integer time intervals $[n, n+1/2)$ and $[n+1/2, n+1)$ are taken for convenience. And they can be other time intervals with non-integer lengths.

To model molecular motors, it is important to select an asymmetric potential function $G(x)$, for example, a seesawed function as in Figure 2.

$$G(x) = \begin{cases} -1.5x - 1.2 & \text{if} \quad x \le -1 \\ 5x + 5.3 & \text{if} \quad -1 < x \le -0.5 \\ -1.5x + 2.05 & \text{if} \quad -0.5 < x \le 1 \\ 3x - 2.45 & \text{if} \quad x \ge 1 \end{cases}$$

The asymmetry of $G(x)$ is reflected around each minimal point, at which the slope from the left is different from the slop from the right. When Brownian particles are subjected to alternating forces from the asymmetric potential field and Brownian

motions, one may observe a directed motion, and that forms the flashing ratchet model.

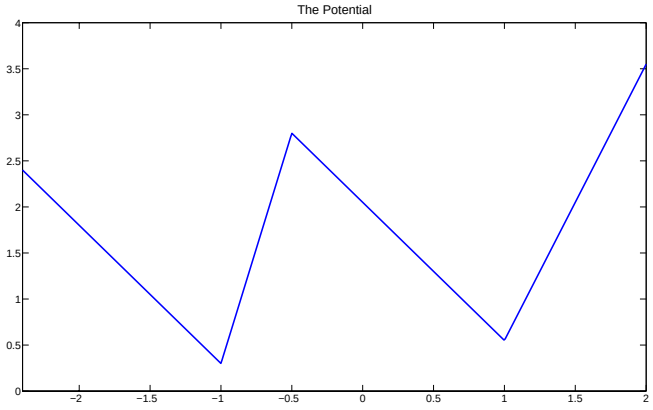

FIGURE 1. The asymmetric potential function.

The classical Fokker-Planck equation gives a probability explanation of this directed motion. Intuitively, the mechanism is easy to understand. When the potential is "turned off", the Brownian particle could getting out of its original potential wall. When the potential is "turned on" again, the particle will be driven to the vinicity of the local minimum. Because of the asymetry, in the next diffusion process when the potential if "turned off" again, it is harder to moving back than moving forward. That's why the probability distribution would concentrate at the local minimum on the right.

The probability distribution of the motions of molecular motors are governed by Fokker-Planck equation (1.3). Here we use the standard central difference scheme to compute a numerical simulation that demonstrates this directed motion. The environmental noise level is set as $\epsilon = \sqrt{0.4}$. We take the initial distribution given by the blue solid curve as shown in Figure 2, we also show the distribution of molecular motors at $T = 60$ by the red dashed curve in the same figure. Clearly, the mass of the distribution function is shifted from the left to the right. This implies that more molecular motors are moved from left to the right.

We note that the given potential function $G(x)$ has lower values on the left end and higher values on the right, and when the potential is turned off, it becomes a standard diffusion process. So we have two "losing" or "fair" strategy. However the molecules move from lower potential places to higher ones, which is certainly against the normal intuition. This is the classical explanation of Parrondo's paradox in the flashing ratchet model – losing game that wins. It has been well studied and a rigorous analysis is given in [10, 17].

Our new viewpoint is the Parrondo's paradox of free energy. Here we introduce the free energy to estimate the performance of molecular motors. The definition of the free energy functional is given in (1.2). As shown in [9, 11, 13] the free energy decreases along the solution of Fokker-Planck equation if the potential function

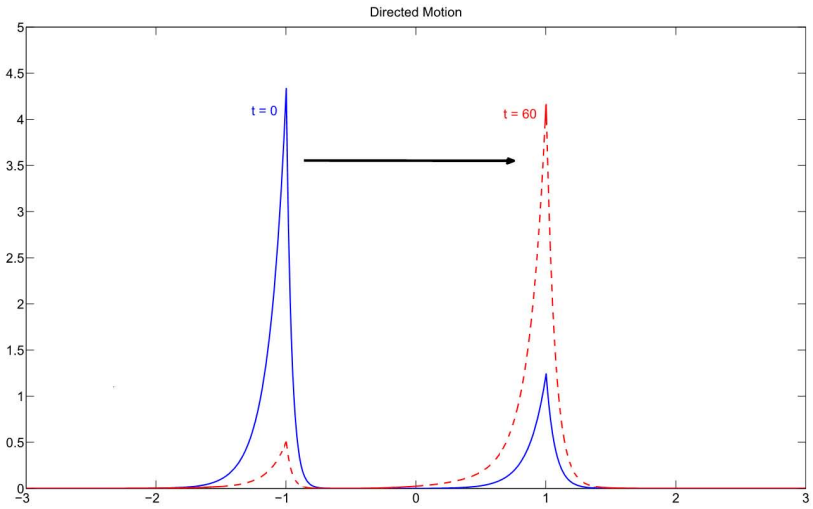

FIGURE 2. The blue curve is the probability density function at $t = 0$; the red curve is the probability density function at $t = 60$.

does not dependent on time. However, this is no longer true for the flashing ratchet model, due to the fluctuation of $\Psi(x,t)$. In fact, we have two different processes depending on whether the potential function is 0 or $G(x)$. For convenience, we call the stochastic process with $\Psi(x,t) = G(x)$ "Process A" and the pure diffusion process with $\Psi(x,t) = 0$ "Process B".

The time evolution of the probability density function in Process A is governed by

$$\frac{\partial P(x,t)}{\partial t} = \nabla \cdot (\nabla G(x) P(x,t)) + \frac{1}{2}\epsilon^2 \Delta P(x,t), \tag{2.1}$$

while the time evolution of the probability density function in Process B is given by

$$\frac{\partial P(x,t)}{\partial t} = \frac{1}{2}\epsilon^2 \Delta P(x,t). \tag{2.2}$$

Clearly both processes are energy dissipative, i.e. the free energy decreases with both processes (losing stragegy). However, when applying Process A and Process B alternatively, the free energy increases with time (winning game). This is another analogue of Parrondo's paradox which is famous for creating a winning strategy by (randomly) alternating two losing strategies in game theory [4, 5, 6, 7, 8].

To better illustrate Parrondo's paradox of free energy, we use the following numerical example. The asymmetric potential field $G(x)$ is given in Figure 3,

$$G(x) = \begin{cases} -4(x+7)+1 & \text{if} \quad x < -7 \\ -(x+4)/3 & \text{if} \quad -7 \le x < -4 \\ 3(x+4) & \text{if} \quad -4 \le x < -3.5 \\ -(x+0.5)/3 + 0.5 & \text{if} \quad -3.5 \le x < -0.5 \\ 3(x+0.5)+0.5 & \text{if} \quad -0.5 \le x < 0 \\ -(x-3)/3+1 & \text{if} \quad 0 \le x < 3 \\ 3(x-3)+1 & \text{if} \quad 3 \le x < 3.5 \\ -(x-6.5)/3+1.5 & \text{if} \quad 3.5 \le x < 6.5 \\ 4(x-6.5)+1.5 & \text{if} \quad x \ge 6.5 \end{cases}$$

There are five local minima and their heights increase from left to right. We pick the initial distribution as the Gibbs distribution, denoted by $\Phi(x)$, the global minimum of free energy functional, given by

$$\Phi(x) = \frac{1}{K} e^{-\Psi(x)/\beta}$$

where $\beta = 1/2\epsilon^2$, and $K = \int_{\mathbb{R}^N} e^{-\Psi(x)/\beta} dx$ is the normalizer. The Gibbs distribution as $\beta = 0.1$ concentrates at the left local minimum, as shown in Figure 4. At this initial state, the system has the free energy value 0.1091.

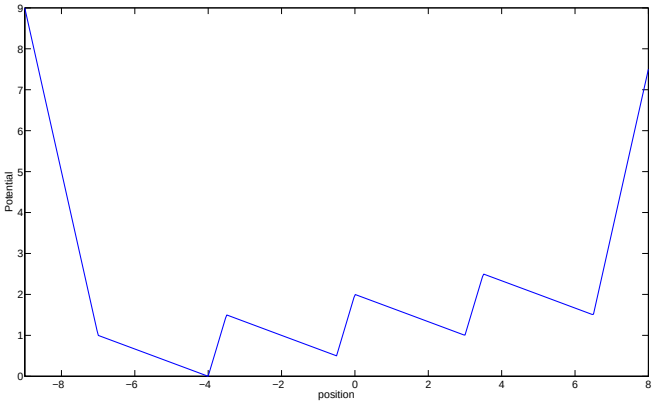

FIGURE 3. A seesawed potential function.

After turning on and off the potential function periodically with period $T = 1$ for 1200 times, we observe the directed motion from the left end to the right. And the probability distribution is concentrated at the right local minimum, which has higher potential energy and lower entropy. The overall free energy, which is increased to 1.5009, is higher at the final state.

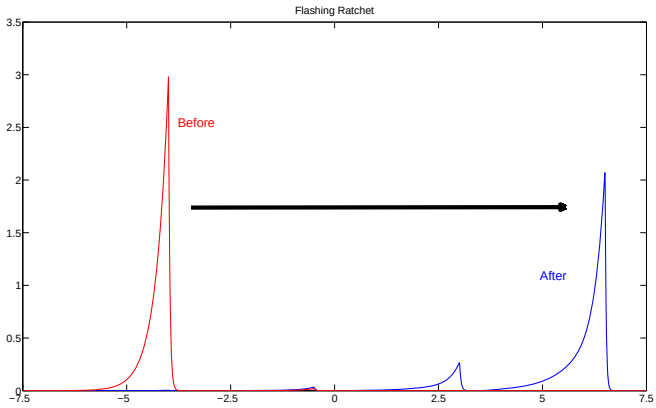

FIGURE 4. Probability density function shows a directed motion by molecular motors.

Figure 5 shows the free energy values at each time when the potential function is turned off. Clearly, the free energy is increased. Comparing the values at $t = 0$ with that at $t = 500$, the free energy increases from 0.1091 to 1.5009.

To see the detail of the free energy changes, we plot the free energy values in the first 10 periods in alternating Process A and B in another example. The time interval is still $T = 1$, while the noise level is set as $\beta = 0.4$. The upper branches correspond to Process A when the potential is turned on. The lower branches are for Process B when the potential field is turned off. Clearly, both processes cause decrease in the free energy (so they are all "losing game"), while jumps occurs when the potential is turned on and off. Overall, the free energy is increased as in Figure 6 – the losing game wins The free energy at five points A, B, C, D, E are $-0.2085, -1.9681, -2.1806, -0.1184, -0.2009$ respectively. Then after this period, the free energy is increased from -0.2085 to -0.2009.

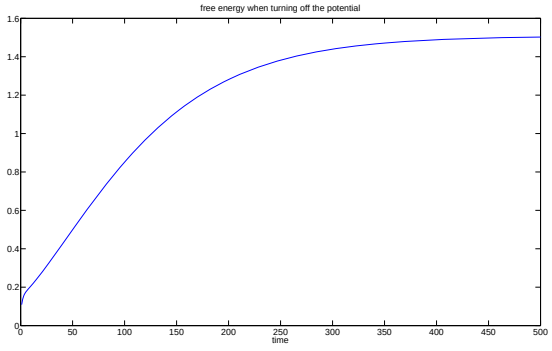

FIGURE 5. The free energy at each time when the potential is turned off.

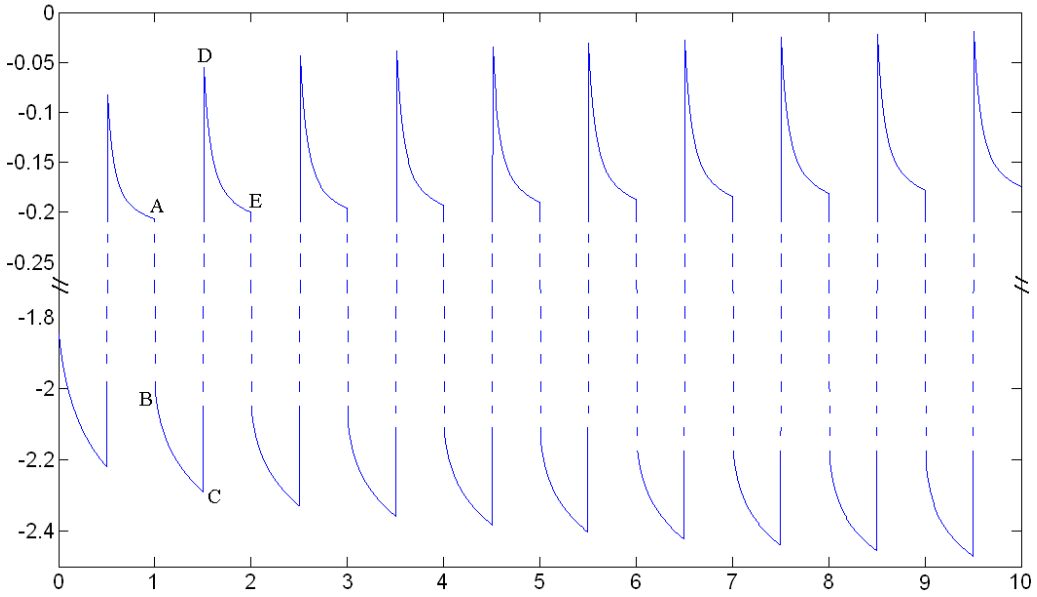

FIGURE 6. The free energy in the first 10 periods. The y-axis on the upper half is the free energy with potential turned on, on the lower half is the free energy with potential turned off.

3. Application in Molecular Motor

From the previous section, we see that alternating two energy dissipative processes actually causes the increase in the free energy, we call it Parrondo's paradox of free energy. Parrondo's paradox is more than a mathematical game, it could give new viewpoint of molecular motor.

To discuss this new viewpoint of molecular, on should answer a natural question – where the energy comes from? Furthermore, we can ask whether it is possible to use the free energy to compute the efficiency of molecular motors. Actually, the efficiency of molecular motors is discussed in existing articles such as by using different methods or models. The classical method is to compute the average kinetic energy of particles as the output of motor [3, 12, 16, 14, 18, 22, 23, 24]. Some researchers also count the entropy production into the dissipation of energy [22], but the basic viewpoint is still the kinetic energy. The classical method works well when the kinetic energy could be significant, for example in an open system with external forcing. However, in an isothermal system with high viscosity, the change of free energy may overcome the very small kinetic energy in case of no external force given. If we omit the change of free energy, sometimes we may miscalculate the efficiency.

Briefly, the free energy comes from the change of potential energy during the period when the potential is shut down. When the potential is turned off, the particles are only subject to the Brownian diffusion. After a period of Brownian motion, when the potential is turned on again, the potential energy has increased. In picture 6, when the potential is turned on again at D, we could see the increase

of free energy clearly. Intuitively, when the potential is "shut down", we may treat it as another object compounds with the original Brownian particle, and gives a certain force to eliminate the effect that comes from the potential field. Then the source of free energy is nothing but the work of this object.

To understand this mechanism better, we may recall the illustration of the working mechanism of a molecular motor given in [1]. Here we use the same symbols as used in [1] to represent the proteins and particles involved in the system. We consider a negatively charged protein E which is moving in an asymmetric potential field formed by the protein molecules with electrical polarity as shown in Figure 7. Moreover, we assume E is an enzyme that catalyzes a chemical reaction (Picture 1 and 2 in Figure 8), i.e.

$$SH \Longleftrightarrow S^- + H^+$$

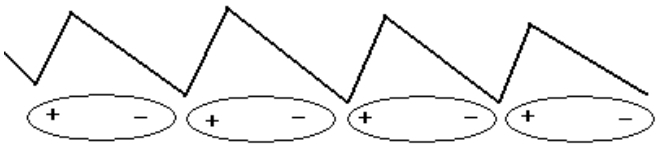

FIGURE 7. An asymmetric electric field.

The compound EHS is negatively charged initially. When S^- dissociates from EHS, EH becomes neutrally charged. So the protein E does not sense the existence of the potential field, and moves as a Brownian particle (Picture 3 in Figure 8). This is corresponding to Process B, in which the potential function is turned off. When H^+ dissociates from the protein, E becomes negatively charged again. Then the protein moves with the influence of the potential field (Picture 4 in Figure 8). This is Process A. Both processes are repeated periodically and the protein E moves from low potential area to high potential region with increased free energy.

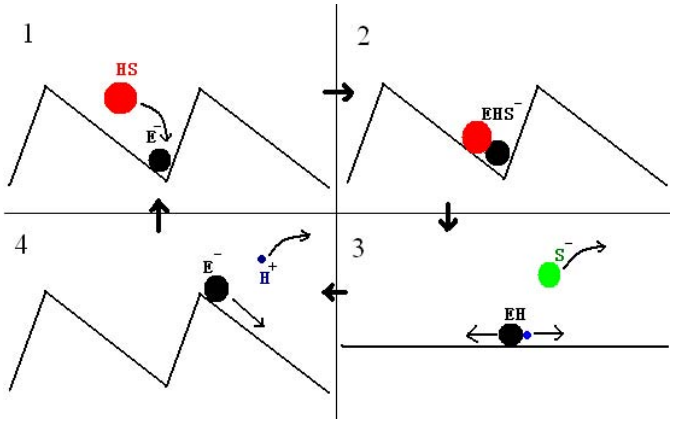

FIGURE 8. A the mechanism of a molecular motor.

When the potential field is "turned off", it does not really vanish. In fact, it is only neutralized by H^+. Therefore the potential energy of EH does not change before the dissociation of H^+. However, the potential energy of H^+ decreases. As a consequence, the potential energy of E must increase to maintain the overall potential energy by EH. Hence, when the potential field is "turned on" again, the free energy of E increases. In summary, the increased free energy comes from the decreased potential energy of H^+ when it dissociates from E. On the other hand, not all of the lost potential energy of H^+ can be converted into the free energy of E due to the environmental noise.

Moreover, we can compute the efficiency of the molecular motor. Again, we take figure 6 as an example. We consider the free energy at five points A, B, C, D and E, and the free energy at A, D, E are F_A, F_D, F_E respectively; the free energy with vanished potential (or the negative entropy) at B and C are S_B and S_C respectively.

At time $t = A = B$, the potential function is turned off. The free energy at this time is

$$F_A = U_A + S_A = U_A + S_B$$

where U is the potential energy.

At time $t = C = D$, the potential function is turned on again. At this time, the free energy with vanished potential is S_C, the free energy with regular potential is F_D. Then we have

$$F_D = U_D + S_D = U_C + S_C$$

So the total energy that comes from external environment is

$$U_C - U_B = F_D - F_A + S_B - S_C$$

And the gains of the free energy is $F_E - F_A$. So the efficiency of the molecular motor is

$$\gamma = \frac{F_E - F_A}{F_D - F_A + S_B - S_C}$$

From stochastic process (1.1), it is clear that the noise level $\epsilon = \sqrt{2\tau}$ and time interval T of switching the potential field on and off are two major factors to determine the free energy gain by molecular motors. We plot their relationships for this example in Figure 9. We vary the noise level ϵ from 0 to 5, and the time interval T from 0 to 0.5. From the plot, we see higher efficiency with faster switching. But please note that the rate of free energy gain does not increase with faster switching, so this is a trade-off – faster switching gives higher efficiency as well as less power. On the other hand, the efficiency are smaller for too low and too high level of noise. In fact, as shown in Figure 10, there exists a value for ϵ that the efficiency reaches it maximal. This corresponds to the maximal efficiency for molecular motors. In other words, the molecular motors attains its maximal efficiently if the noise level is set at the right place. Like in the classical bistable model of stochastic resonance, the noise does not disturb the model, but enhance the performance of the model. We call this a stochastic resonance like behavior. In fact, the mechanism of this phenomenon is different from that of the classical bistable model as well as that of the stochastic resonance in the quantum Brownian motors [19, 20].

We remark that evaluating the performance of molecular motors from the free energy point of view is different from the existing studies, such as the method used in [12], in which the output energy is calculated by the power of the stopping force. The efficiency of molecular motors measured in the free energy can reach near 20%. For example, with the potential function in our example, when the time interval is $T = 0.001$, and the noise level is $\epsilon = 3.5$, the maximal efficiency is as high as $\gamma = 18.74\%$. This is different from the observations reported in [12], which indicates a low efficiency (around 5%) of molecular motors. (In some open systems with external force, the efficiency could be higher [22], which is different form our case)

Finally, if the state space is not a Euclidean space but a finite set of points, then our new Parrondo's paradox of free energy and our viewpoint of molecular motor based on the free energy (and also applied by using Fokker-Planck equation(s)) is given in [2].

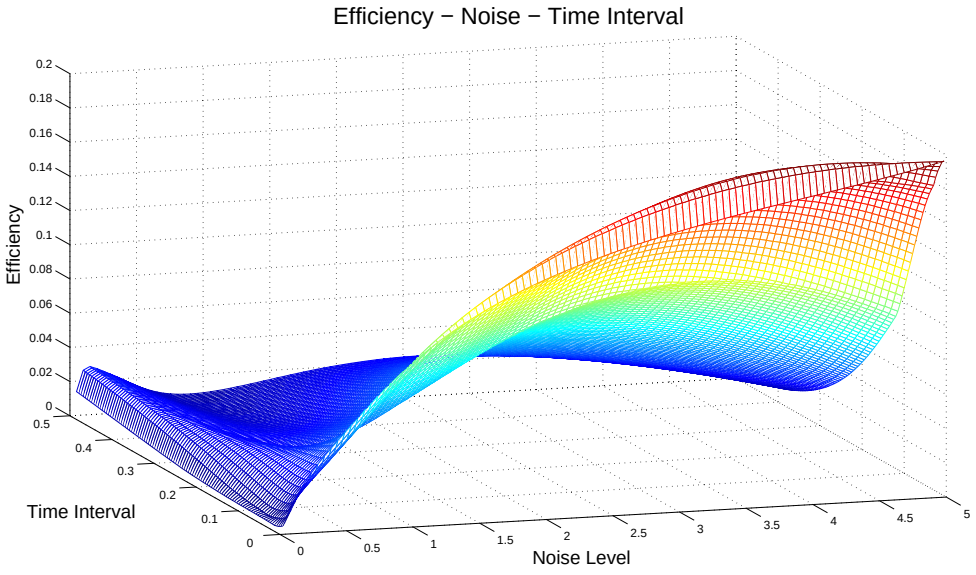

FIGURE 9. Free energy gain v.s. noise level and time interval of switching potential field.

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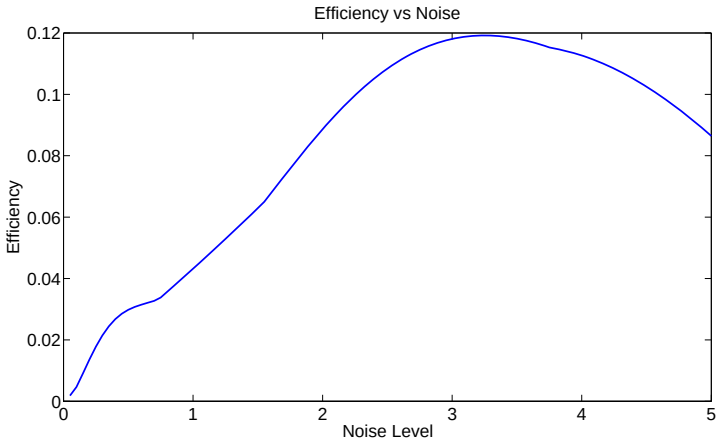

FIGURE 10. Stochastic resonance – noise vs. efficiency.

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