A simplified tether model for molecular motor transporting cargo*

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Molecular motors are proteins or protein complexes which function as transporting engines in biological cells. This paper models the tether between motor and its cargo as a symmetric linear potential. Different from Elston and Peskin's work for which performance of the system was discussed only in some limiting cases, this study produces analytic solutions of the problem for general cases by simplifying the transport system into two physical states, which makes it possible to discuss the dynamics of the motor–cargo system in detail. It turns out that the tether strength between motor and cargo should be greater than a threshold or the motor will fail to transport the cargo, which was not discussed by former researchers yet. Value of the threshold depends on the diffusion coefficients of cargo and motor and also on the strength of the Brownian ratchets dragging the system. The threshold approaches a finite constant when the strength of the ratchet tends to infinity.

Keywords: molecular motor, Brownian ratchet, symmetric linear potential, motor–cargo system
PACC: 0540, 0250, 8715

1. Introduction

Molecular motors are a protein or protein complex which functions as a transporter in biological cells. They move along rotatory or translatory track against an external force by converting the biochemical energy source, adenosine triphosphate (ATP), to mechanic work.[1] Filaments (actin filaments, microtubules), tracks that motor proteins in eukaryotic cells move along, are composed of periodic and relatively rigid protein structures with a periodicity of order 10 nanometers.[2,3] Molecular motors play essential roles in cell division and cellular material transport. Alongside their importance in cellular processes, their small size and high efficiency inspire wide interests, both in basic research and engineering fields.

While the performance mechanism of molecular motors has not been answered definitively, many valuable models for motor protein function have been proposed. The Brownian ratchet model is one of the well-known models.[4−12] In such a model, both the diffusion coefficient of a motor and the diffusion coefficient of its cargo impose fundamental effects on the performance of a motor.

It should be noted that within cells, cargo often consists of larger vesicles instead of single molecules.[13] Thus, generally the cargo, which the motor transports, is considerably larger than the motor itself in size. For example, newly synthesized synaptic vesicles with a diameter of 20–50 nm from the soma of a neuron are transported to the synapses at the end of the axons up to one meter away, by a much smaller kinesin's motor with size of only 7×4.5×4.5 nm.

According to the Einstein relation $D = k_{\mathrm{B}}T/\gamma = k_{\mathrm{B}}T/6\pi\eta r$, where γ is the drag coefficient, diffusion constants decrease sharply as particle size increases. Therefore, for the Brownian ratchet models the molecular motor would hardly work with a cargo of large size and relatively small diffusion coefficient. Researchers proposed ways to overcome this problem. Berg and Kahn,[5] and Meister *et al.*[6] as well, suggested an elastic linkage between the motor and its cargo. This spring potential allows a small motor to diffuse rapidly without missing its cargo by stretching the linkage.

Elston and Peskin *et al.*[14] reported a model which introduced a linear spring with zero rest length between the cargo and motor and put the system into the Brownian ratchet model. The elastic tether between the cargo and motor overcame the problem caused by the relatively small diffusion coefficient of the cargo. However, there is a serious pitfall for this model: when the distance between the cargo and motor becomes very large, the stretching force between

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the cargo and motor as well becomes extremely large. This is impossible in a real situation, since a large distance will obviously make them disassociated. Another description of the pitfall is as follows: in this model, a very weak linkage between the cargo and motor also works well, which is obviously impossible too.

In our previous work,[15] we proposed a linear symmetric potential as the tether between the cargo and motor. In this study, we propose an assumption that the cargo–motor system is categorized into two states with regard to the relative position of the motor and the cargo in the movement. Based on this simplification, analytic solutions are achieved with the performance of the motor–cargo system being discussed in detail.

The following part of the paper is arranged as follows. In Section 2, we briefly describe our linear symmetric potential model, and then discuss the simplification of the problem and general solution for the model. In Section 3, the impact of the diffusion coefficient of the cargo and motor on the transport of the system is presented. In Section 4, we discuss the impact of the strength of the ratchet dragging the motor on the transport system. Some discussions are given in Section 5. We finish up with some conclusions in Section 6.

2. Formulation and general solution of our model

Although the cargo is free to move in any direction, its mean velocity perpendicular to the track is zero apparently. Thus we can just take the motion of the cargo parallel to the track into consideration in our problem. The potential energy of the system satisfies the following equation:

$$U(x_1, x_2) = \phi(x_1) + S(|x_1 - x_2|), \tag{1}$$

where x_1 stands for the position of the motor and x_2 stands for the position of the cargo. The potential $\phi(x_1)$ describes the interaction between the motor and track, whereas $S(|x_1 - x_2|)$ describes the tether which connects the cargo to the motor.

For the potential $\phi(x_1)$ between the motor and track, we adopt the imperfect Brownian ratchet model proposed by Elston and Peskin.[14] In their model the motor–cargo system moves in a 'staircase' potential $\phi(x_1)$ (Fig. 1), which is a special case of the 'titled' periodic potential.

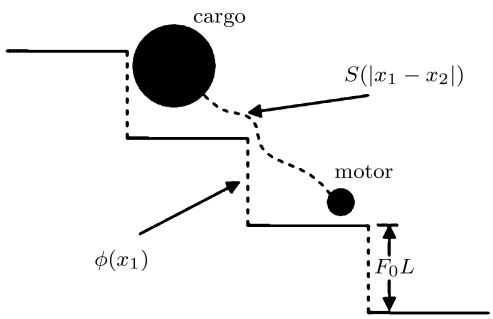

Fig. 1. The motor–cargo system moving in the imperfect ratchet potential plus an applied load force F_l. The ratchet is characterized by the barrier potential F_0L.

We propose that the tether between the cargo and motor is a linear symmetric potential. So the potential between cargo and motor takes the form:[15]

$$S(r) = \kappa r, \tag{2}$$

where κ is a measure of the intensity of the potential and $r = |x_1 - x_2|$ is the distance between the cargo and motor.

In principle, this problem can be solved by combining with diffusion equations. However, it is quite hard to obtain an analytical solution for the general case. Analytical solutions have been achieved in some limiting cases.[14]

When the system is examined by considering the relative physical position of the cargo and motor in the transport, the system falls into two states since the motor and cargo are under an overdamped situation where acceleration of the system can be omitted. One is the state that the cargo is moving behind the motor and the other is the state that the cargo is moving ahead of the motor. In the transport system, the average velocity of motor and cargo is equal. For the sake of simplicity, intermediate states were not taken into consideration in our model. Under this two-state assumption we can formulate the system's average velocity as

$$v = v_{1\mathrm{c}}p + v_{2\mathrm{c}}(1-p) = v_{1\mathrm{m}}p + v_{2\mathrm{m}}(1-p), \tag{3}$$

where $v_{1\mathrm{c}}$, $v_{1\mathrm{m}}$ are the velocities of cargo and motor when the cargo lags behind the motor (state 1), respectively, and $v_{2\mathrm{c}}$, $v_{2\mathrm{m}}$ are the velocities of cargo and motor when the cargo goes in front of the motor (state 2), respectively, p is the probability of state 1 in which cargo lags behind the motor. Advantages of this model lie in the simplicity of its description. It is easy to obtain an analytical solution for it.

In our simplified model, the cargo is always within constraint of the symmetric linear potential. In state

1 for which the cargo lags behind the motor, since the cargo feels a constant force κ, its mean velocity is simple:

$$v_{1\mathrm{c}} = \frac{\kappa D_2}{k_\mathrm{B} T} = \frac{D_2}{L}\omega_l, \tag{4}$$

where D_2 is the diffusion coefficient of the cargo and $\omega_l = \kappa L/k_\mathrm{B}T$.

When the cargo jumps into state 2, that is, when the cargo moves in front of the motor it still feels a constant, but with opposite direction to state 1, force κ, so its speed gets into

$$v_{2\mathrm{c}} = \frac{-\kappa D_2}{k_\mathrm{B} T} = \frac{-D_2}{L}\omega_l. \tag{5}$$

The load-speed curve of an imperfect Brownian ratchet gives the speed of the motor which is followed by the constant load force κ. Following the results obtained by Elston and Peskin[14] we can directly get the speed of the motor in state 1 and state 2, respectively:

$$v_{1\mathrm{m}} = \frac{D_1}{L}\frac{\omega_l^2}{\dfrac{(\exp(\omega_0)-1)(\exp(\omega_l)-1)}{\exp(\omega_0)-\exp(\omega_l)} - \omega_l}\ , \tag{6}$$

$$v_{2\mathrm{m}} = \frac{D_1}{L}\frac{\omega_l^2}{\dfrac{(\exp(\omega_0)-1)(\exp(-\omega_l)-1)}{\exp(\omega_0)-\exp(-\omega_l)} - (-\omega_l)}\ , \tag{7}$$

where $\omega_l = \kappa L/k_\mathrm{B}T$, $\omega_0 = (F_0/k_\mathrm{B}T)L$ and D_1 is the diffusion coefficient of the motor.

Substituting Eqs. (4)–(7) into Eq. (3) we can calculate the values of p and v as follows:

$$\begin{aligned} p &= \frac{v_{2\mathrm{m}} - v_{2\mathrm{c}}}{v_{1\mathrm{c}} - v_{2\mathrm{c}} - v_{1\mathrm{m}} + v_{2\mathrm{m}}} \\ &= \frac{\dfrac{D_1\omega_l}{\dfrac{(\exp(\omega_0)-1)(\exp(-\omega_l)-1)}{\exp(\omega_0)-\exp(-\omega_l)} + \omega_l} + D_2}{2D_2 - \dfrac{D_1\omega_l}{\dfrac{(\exp(\omega_0)-1)(\exp(\omega_l)-1)}{\exp(\omega_0)-\exp(\omega_l)} - \omega_l} + \dfrac{D_1\omega_l}{\dfrac{(\exp(\omega_0)-1)(\exp(-\omega_l)-1)}{\exp(\omega_0)-\exp(-\omega_l)} + \omega_l}}\ , \end{aligned} \tag{8}$$

$$\begin{aligned} v &= v_{1\mathrm{c}}p + v_{2\mathrm{c}}(1-p) \\ &= \frac{D_2}{L}\frac{D_1\omega_l\left(\dfrac{1}{\dfrac{(\exp(\omega_0)-1)(\exp(-\omega_l)-1)}{\exp(\omega_0)-\exp(-\omega_l)} + \omega_l} + \dfrac{1}{\dfrac{(\exp(\omega_0)-1)(\exp(\omega_l)-1)}{\exp(\omega_0)-\exp(\omega_l)} - \omega_l}\right)}{2D_2\omega_l + D_1\left(\dfrac{1}{\dfrac{(\exp(\omega_0)-1)(\exp(-\omega_l)-1)}{\exp(\omega_0)-\exp(-\omega_l)} + \omega_l} - \dfrac{1}{\dfrac{(\exp(\omega_0)-1)(\exp(\omega_l)-1)}{\exp(\omega_0)-\exp(\omega_l)} - \omega_l}\right)}\ . \end{aligned} \tag{9}$$

We first consider how p, which denotes the probability that cargo lags behind the motor, changes with κ. The κ–p curve was given in Fig. 2. It turns out that p decreases with increasing κ. And there is a lower limit for p when $\kappa \to \infty$. Making $\kappa \to \infty$ in Eq. (8) we get this lower limit of p which is 1/2.

It could be explained that, when the force between the cargo and motor is so strong that they could hardly separate from each other, chances for the two states are equal and p trends towards 1/2.

Note that in the left region of Fig. 2 the value of p is above unit. Since equation (8) is derived from Eq. (3) we can find that the appearance of p greater than 1 stems from the hypothesis for which the motor and cargo always hold a common mean velocity. It is self-obvious that we should not get a p greater than 1 in a real situation and this constraint hints a threshold for κ which we name as κ_0, i.e., the value of κ that makes p equal to 1. This point means that the cargo always trails behind the motor and when $\kappa < \kappa_0$, p is greater than 1. Substituting p with 1 into Eq. (3) and combining it with Eqs. (4) and (6) we get

$$\frac{D_2}{D_1} = \frac{\omega_l}{\dfrac{(\exp(\omega_0)-1)(\exp(\omega_l)-1)}{\exp(\omega_0)-\exp(\omega_l)} - \omega_l}\ . \tag{10}$$

This equation implicitly determines ω_l, or equally κ_0. Substituting κ_0 into Eq. (4) or Eq. (6) determines the common speed of the motor and cargo with the corresponding unit p, which is denoted by v_0.

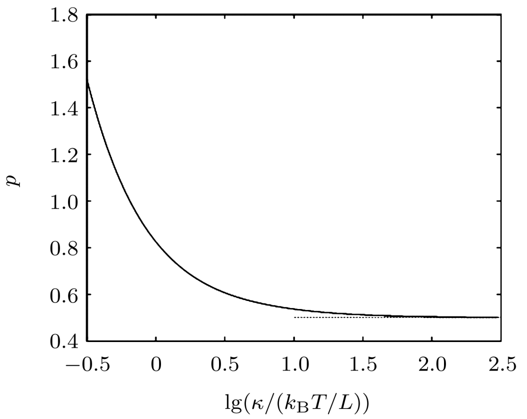

Fig. 2. The probability of cargo lagging behind the motor in transport versus the logarithm of the potential strength κ in units of $k_{\rm B}T/L$. There is a lower limit 0.5 for the probability. F_0 is set to 1 $k_{\rm B}T/L$.

Now we have understood the behaviour of the system for the case of $\kappa \geq \kappa_0$. That is, the motor and cargo as a whole move ahead together and the cargo moves around the motor as well, and the mean system speed can be obtained by solving Eq. (9). But what about the system behaviour when $\kappa < \kappa_0$? As noted before, p is greater than 1 when $\kappa < \kappa_0$ (Fig. 2). Since the hypothesis that the motor and cargo have a common mean velocity results in the unrealistic p, it does not hold anymore in this region of κ. Note that $v_{\rm 1m}$ decreases as κ increases (according to Eq. (6)) while $v_{\rm 1c}$ increases as κ increases (according to Eq. (4)) and they are identical at the point $\kappa = \kappa_0$. Thus we can deduce that in the region of $\kappa < \kappa_0$ the speed of the cargo induced by the linear tether is lower than that of the motor, so the cargo will always lag behind the motor and the distance between them becomes larger and larger until eventually the cargo goes out of the linear potential and is disassociated from the motor, then diffused freely in the cell.

Figure 3 shows the dependence of the mean velocity of transport on the value of κ. Because the cargo will depart from the motor when $\kappa < \kappa_0$, only the curve of region $\kappa \geq \kappa_0$ is given. We can see from the figure that the curve is increasing as κ increases and will get its upper limit as $\kappa \to \infty$. This upper limiting velocity can be obtained by solving Eq. (9), i.e.

$$\lim_{\kappa\to\infty} v = \frac{1}{2L}\frac{D_1 D_2}{D_1 + D_2}[\exp(\omega_0) - \exp(-\omega_0)]. \quad (11)$$

And the lower limit of the average velocity as $\kappa \to \kappa_0$ can be calculated by Eq. (4) or Eq.(6).

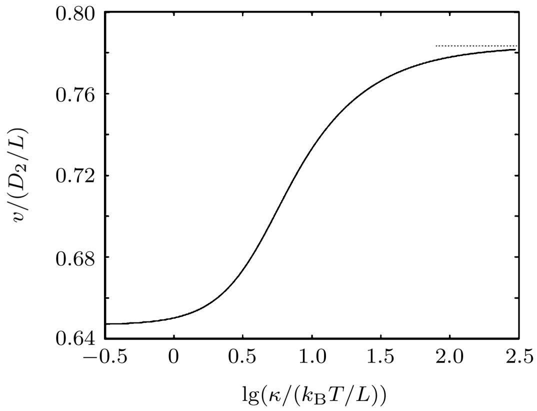

Fig. 3. The mean velocity of the transport in units of D_2/L versus the logarithm of the potential strength κ in units of $k_{\rm B}T/L$ for an imperfect ratchet with the barrier potential $k_{\rm B}T$ when $\kappa > \kappa_0$. F_0 is set to 1 $k_{\rm B}T/L$. The upper horizontal line stands for the value of velocity with the limit $\kappa \to \infty$.

3. Impact of diffusion coefficients on the system's transport

Performance of the molecular motor system highly depends on the diffusion coefficients of the system's components. Firstly we consider dynamics of the threshold κ_0 with regard to the diffusion coefficients of the cargo and motor. The value of κ_0 depends not only on the strength of the ratchet F_0 but also on the ratio of diffusion coefficient of the cargo to that of the motor. Define this ratio as $\varepsilon = D_2/D_1$. From Eq. (10) we can deduce that κ_0 is the increasing function with respect to F_0 but decreasing function with respect to ε. Figure 4 shows how κ_0 changes with ε. The height of the ratchet barrier is taken as 1 $k_{\rm B}T$. It shows that κ_0 is within the range $0 < \kappa_0 < F_0$.

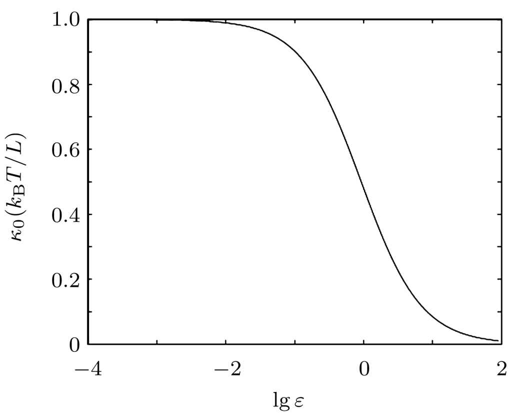

Fig. 4. The threshold of the tether strength κ in units of $k_{\rm B}T/L$ versus the logarithm of ε. F_0 is set to 1 $k_{\rm B}T/L$.

Equation (10) can also give the limiting values of κ_0 for the cases $\varepsilon \to 0$ and $\varepsilon \to \infty$ respectively. Letting $D_1 \to \infty$ with all other parameters fixed we get

$$\lim_{\varepsilon\to 0} \kappa_0 = F_0. \tag{12}$$

And letting $D_2 \to \infty$ with all other parameters fixed, we get

$$\lim_{\varepsilon\to\infty} \kappa_0 = 0. \tag{13}$$

Equation (12) means that, for large value of 1, the minimum force κ_0 required for the cargo to move together with the motor approaches the strength F_0 of the ratchet dragging the motor, and equation (13) indicates that the diffusion coefficient of the cargo helps to enhance the transport of system.

Then we discuss how the average velocity of the transport system changes with the diffusion coefficients of the cargo and motor. It can be easily seen from Eq. (9) that the average velocity of the system increases with both D_1 and D_2. Also, we can easily deduce the upper limits of the average velocity as $D_1 \to \infty$ or $D_2 \to \infty$. The computation of these limiting values is left for the reader.

Reversely, the transport of the system will terminate as long as one of the two diffusion coefficients trends towards zero. This phenomenon shows that the diffusion coefficients of cargo and motor both play key roles in the transport of system

4. Impact of F_0 on the system's transport

Now we test the dynamics of the system with varying strength F_0 of the ratchet dragging the system. Intuitively, the velocity of transport increases as F_0 gets larger. Since the threshold κ_0 is the increasing function of F_0 then when F_0 gets large enough κ_0 will go above κ and the cargo and motor will become disassociated. So we first discuss how κ_0 depends on F_0. Equation (10) implicitly determines the relationship between κ_0 and F_0. Figure 5 is a plot of κ_0 as a function of F_0. As is shown, κ_0 increases as F_0 increases and there is an upper-limit for κ_0. By setting $F_0 \to \infty$ in Eq. (10) we can implicitly express this upper limit of κ_0 as the following equality:

$$\varepsilon = \frac{\omega_l}{\exp(\omega_l) - 1 - \omega_l}\ , \tag{14}$$

where $\omega_l = \kappa_0 L/k_{\rm B}T$.

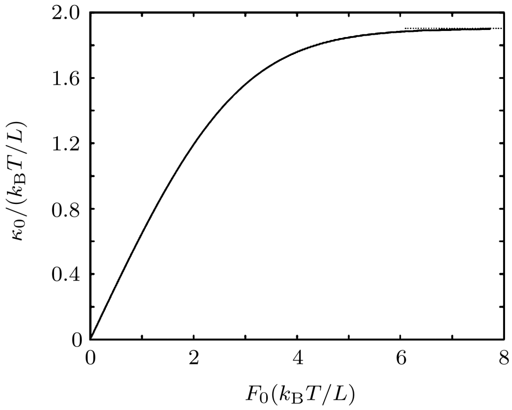

Fig. 5. The threshold κ_0 of the tether potential in units of $k_{\rm B}T/L$ versus F_0: the strength of the ratchet dragging the motor in units of $k_{\rm B}T/L$. The upper horizontal line denotes the value of κ_0 while $F_0 \to \infty$. D_1 is taken as 2 and D_2 is taken as 1.

This result indicates that if the linkage strength between cargo and motor exceeds this upper-limit of threshold it becomes impossible for the cargo to depart from motor, no matter how large the ratchet strength is. With parameters as $D_1 = 2$ and $D_2 = 1$ the upper-limit of κ_0 is $1.90k_{\rm B}T/L$.

Impact of F_0 on the average velocity of the motor–cargo system is determined by Eq. (9). For the sake of simplicity, we just consider the situation where κ is above the upper-limit of κ_0, which is determined by Eq. (14). The average velocity of the motor–cargo system increases with F_0 while there is an upper-limit for it. We can derive from Eq. (9) the upper limit value of transport speed:

$$\lim_{F_0\to\infty} v = \frac{D_2}{L}\frac{D_1\omega_l[\exp(\omega_l)+\exp(-\omega_l)-2]}{2D_2\omega_l[\exp(-\omega_l)-1+\omega_l][\exp(\omega_l)-1-\omega_l]+D_1[\exp(\omega_l)-\exp(-\omega_l)-2\omega_l]}\ . \tag{15}$$

This equation shows that too large ratchet strength cannot enhance the efficiency of the system significantly any more and so is not necessary for the system's transport.

5. Discussions

In the previous sections the performance of the motor–cargo transport system was checked in detail. It was shown in our study that the diffusion coefficients of cargo and motor both play key roles in the transport of the system. The threshold for the linkage strength between cargo and motor depends not only on the strength of the ratchet F_0 but also on the ratio of the diffusion coefficient of the cargo to that of the motor. As the diffusion coefficient of the motor tends to be large enough in comparison with the diffusion coefficient of the cargo, the threshold tends to be identical to the strength of the ratchet dragging the motor. The average velocity of the motor–cargo system increases with the increasing diffusion coefficient of the motor or that of the cargo. The transport of the system will terminate as long as one of the two diffusion coefficients trends towards zero. These results show that the diffusion coefficients of cargo and motor both help to accelerate their common motion in cell.

The impact of the strength of the ratchet dragging the motor on the transport system was also studied in this article. The threshold for the linkage strength between cargo and motor increases as the strength of the ratchet dragging the motor increases, and an upper-limit for it was revealed. This result makes sense in that if the linkage strength between cargo and motor exceeds this upper-limit of threshold the cargo–motor system will never collapse, no matter how large the ratchet strength is. The average velocity of the motor–cargo system increases as the strength of the ratchet dragging the motor becomes larger. However, in the situation that the linkage strength between cargo and motor is lower than the maximum (as the ratchet strength tends to infinity) of the threshold the common speed of the system may not exist, since the cargo will depart from the motor and the system collapses when the ratchet strength gets large enough. On the other hand, for the linkage strength greater than the maximum threshold there is also an upper-limit for the average velocity as the ratchet strength tends to infinity.

6. Conclusions

With a proposal that the tether between the cargo and motor acts as a linear symmetric potential, and together with a simplification of the problem, an analytical solution for the molecular transport system was easily obtained. By contrast, for Elston and Peskin's model[14] they only got analytical solutions for three limiting cases, i.e. large motor diffusion coefficient limit, stiff-spring limit and soft-spring limit. It turns out that the average velocity of transport increases as the intensity of linear symmetric potential between the cargo and motor increases and there is an upper limit of the velocity. A threshold for the linkage strength between cargo and motor was revealed in our model, which makes our model physically more reasonable in comparison with the spring model reported by Elston and Peskin *et al.*[14] Only when the linkage stiffness exceeds the threshold can the cargo keep up with the movement of the motor. Otherwise, the cargo will be dissociated from the motor and diffuse freely in the cell. Generally, the threshold is smaller than the strength of the ratchet dragging the motor but when the diffusion coefficient tends to be infinite, the threshold is identical with the strength of the ratchet dragging the motor. However, in Elston and Peskin's model, there is no threshold for the stiffness of the spring linking the cargo and motor and the cargo always keeps up with the motor. Obviously, it is not physically reasonable in reality, in which a too soft linkage should not be capable of dragging the cargo. Introducing the above threshold in our model erased this pitfall.

The explanation of such a difference between our model and the spring model is as follows. For a spring connecting the motor and the cargo, the minimum force required for the cargo to keep up with the motor can always be achieved by stretching their distance. However, in our model such a mechanism does not exist, since the force produced by the symmetric linear potential is constant, independent of the distance between the motor and the cargo.

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