# Force-velocity relations for multiple-molecular-motor transport

Ziqing Wang[1,2] and Ming Li[3]
[1]*College of Science, Northwest A&F University, Yangling, Shaanxi 712100, China*
[2]*Institute of Theoretical Physics, Chinese Academy of Sciences, Beijing 100190, China*
[3]*College of Physical Science, Graduate University of Chinese Academy of Sciences, Beijing 100190, China*
(Received 21 June 2009; revised manuscript received 14 August 2009; published 22 October 2009)

A transition rate model of cargo transport by $N$ molecular motors is proposed. Under the assumption of steady state, the force-velocity curve of multimotor system can be derived from the force-velocity curve of a single motor. Our work shows, in the case of low load, that the velocity of multimotor system can decrease or increase with increasing motor number, which is dependent on the single motor force-velocity curve; and most commonly, the velocity decreases. This gives a possible explanation to some recent experimental observations.

DOI: 10.1103/PhysRevE.80.041923 PACS number(s): 87.16.Nn

## I. INTRODUCTION

The cargo transport by a single cytoplasmic molecular motor has been widely studied both experimentally [1–5] and theoretically [6–8]. Cargoes *in vivo*, however, are typically transported by several motors [9] and sometimes even by different kinds motors [10,11]. By far little has been known about the cooperativity of multiple motors during cargo transport and it is still an important and open research subject. Especially, cargo transport by multiple processive motors attracts much attention, since these motors can transport cargoes over long distances without unbinding from the track, which is convenient for experimental studies. Actually, experimental and theoretical studies on such systems have been carried out in the last decade. These works investigated systems of fluidlike cargoes [12–14], or rigid or elastic cargoes [15–20], in the existence of external load force. In the cases of rigid or elastic cargo, the cargo can induce strong coupling between motors, which is the focus of this paper.

Recently, Klumpp and Lipowsky proposed a transition rate model to study the cooperative cargo transport by processive motors [21]. In their model, motors are supposed to share the load force equally and have no other mutual interactions. By this treatment, the authors concluded that the velocity of the cargo increases with the increasing motor number. Theoretical analyses based on ratchet models also give the same results [18–20]. Nevertheless, experiments have shown that the cargo velocity is approximately independent of the number of motors pulling the cargo [16,17,22]. Very recently, Shubeita *et al.*'s experiment showed that increase in kinesin number leads to slightly reduced cargo velocity [23]. This result is out of expectation and contradicts some theoretical results [18–20] but is supported by the simulation results [24].

Most of the theoretical studies mentioned above fall into special cases since they are dependent on the modeling of single motor stepping. In this paper we want to generally investigate the dependence of the velocity of multimotor system on the number of motors pulling the cargo. For convenience, we suppose the motors cannot detach from the track. We proposed a steady-state transition model of transporting cargo by $N$ motors. Our calculation shows that the velocity of $N$ motors transport depends on the single motor's force-velocity ($F$-$V$) relation, and especially in the case of low load, the velocity of multimotor system may decrease with increasing motor number. This result provides an explanation to Ref. [23] and our work predicts a general behavior of multimotor transport.

## II. MODEL AND RESULTS

### A. Two-motor case

We first consider the situation of two motors (A and B in Fig. 1) transporting a cargo. The equilibrium distance between A and B is denoted as $l_0$. If motor A takes a forward step, the distance between A and B increases to produce a traction interaction between them [25,26] and the cargo is assumed to step forward with a distance $d/2$, where $d$ is the step size of the motor. This assumption is quite reasonable; e.g., it has been shown experimentally that in the case of two kinesins transporting a microtube, the step size of cargo is 4 nm which is half of a single motor's step size [17]. When motor B takes a forward step, resulting in a repulsion interaction between the two motors, the cargo also takes a forward step of $d/2$. Here we focus mainly on the cases where the single motor performs unidirected stepping, since it is a good enough description of processive motors such as kinesin.

States of the two-motor system can be specified by the "effective distances" $S_{\mathrm{eff}}=S_{AB}-l_0$, where $S_{AB}$ is the real distance between the two motors. So each state of the system can be denoted by $|i\rangle$, where $i=S_{\mathrm{eff}}/d$ are integers. When motor A takes a forward step, the system transits from state

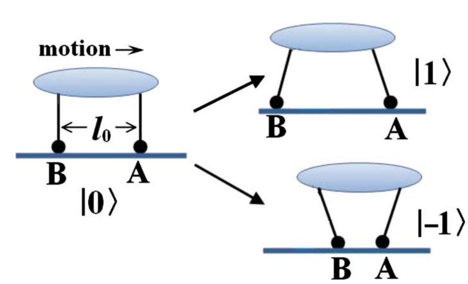


FIG. 1. (Color online) A cargo is transported by two motors A and B.

 

$|i\rangle$ to state $|i+1\rangle$. While motor B takes a forward step, the system transits from state $|i\rangle$ to state $|i-1\rangle$. Since the time for either motor performing the stepping motions is much shorter than the dwell time (e.g., The 8 nm stepping motion of kinesin occurs on the microsecond time scale while the dwell time is always larger than millisecond [2]. The 36 nm stepping motion of myosin-V occurs within a few milliseconds, far less than the dwell time scale of a second [27].), the two motors can never step forward simultaneously. Therefore, the transitions between states can be expressed as

$$|-n\rangle \underset{\omega_{-n+1}^-}{\overset{\omega_{-n}^+}{\rightleftarrows}} \cdots \underset{\omega_{-1}^-}{\overset{\omega_{-2}^+}{\rightleftarrows}} |-1\rangle \underset{\omega_{0}^-}{\overset{\omega_{-1}^+}{\rightleftarrows}} |0\rangle \underset{\omega_{1}^-}{\overset{\omega_{0}^+}{\rightleftarrows}} |1\rangle \underset{\omega_{2}^-}{\overset{\omega_{1}^+}{\rightleftarrows}} \cdots \underset{\omega_{n}^-}{\overset{\omega_{n-1}^+}{\rightleftarrows}} |n\rangle. \tag{1}$$

The minus represents the distance between the two motors smaller than $l_0$. The transition rates $\omega_i^{\pm}$ between states depend on the external load force and the cargo-mediated force between the two motors which will be discussed below. When stall force is reached on either motor, the system gets into the extremity states, $|n\rangle$ or $|-n\rangle$.

The cargo-mediated force exerted on either motor is quite intuitive; i.e., when $i>0$, motor B exerts a resistance force $f$ on motor A through the cargo, while motor A exerts an assistance force $-f$ on motor B; and it is contrary when $i<0$. The magnitude of $f$ is determined by the distance of the two motors and the stiffness of motor linkage which connects the motor heads to the cargo as shown in Fig. 1. For different kinds of motor and cargo, the stiffnesses of linkage are different. Here we take kinesin as an example and the methods can be extended to myosin-V directly, but it does not apply to dynein because of their complexity and unclear stepping behaviors [3,28]. The linkage of kinesin exhibited an adequately linear behavior [4,5]. In such cases, the internal force between the two motors can be easily expressed as $f=idk/2$, where $k$ is the linkage stiffness, and $i$ times $d$ is the effective distance between the two motors and each motor shares one half of the distance. When an external load $F$ is taken into account, the total force borne by each motor should be $(F/2+f)$ or $(F/2-f)$. Since the force-velocity relation $V_1(F)$ for single motor transport has been widely studied both experimentally and theoretically, one can easily know the step rates $R_1(F)=V_1(F)/d$ for either motor of the system. Then we can get the transition rates $\omega_i^{\pm}$ in Eq. (1),

$$\omega_i^{\pm} = R_1(F/2 \pm idk/2). \tag{2}$$

Now we turn to the mean velocity of the two-motor system denoting by $P_i$ the probability that the system is in state $|i\rangle$. Here we are concerned with the steady-state velocity of the system. The steady-state solution of the process described by Eq. (1) can be expressed as

$$P_i = P_0 \prod_{j=0}^{i-1} \frac{\omega_j^+}{\omega_{j+1}^-} \quad \text{for} \quad (i>0), \quad \text{and} \quad P_{-i} = P_i. \tag{3}$$

Considering the normalization $\sum_{i=-n}^{n} P_i = 1$, $P_0$ satisfies

$$P_0 = \left[ 1 + 2 \sum_{i=1}^{n} \prod_{j=0}^{i-1} \frac{\omega_j^+}{\omega_{j+1}^-} \right]^{-1}. \tag{4}$$

In the case of linear spring linkage, when either of the two motors takes a forward step, the cargo goes forward $d/2$. So the average velocity of the cargo is then given by

$$V_2(F) = \frac{d}{2} \sum_{i=-n}^{n} P_i(\omega_i^+ + \omega_i^-) = \sum_{i=-n}^{n} P_i \frac{[V_1(F/2+idk/2) + V_1(F/2-idk/2)]}{2}. \tag{5}$$

Defining $\widetilde{V}_2(F) \equiv V_2(2F)$. It is obvious that $\widetilde{V}_2(F) < V_1(F)$ rigorously holds if the single motor $F$-$V$ curve is purely concave, which is followed by two facts: (1) $V_2(F) < V_1(F)$ when the load $F$ is near zero; i.e., two-motor transport is slower than single motor transport at low load. (2) $V_2(F) > V_1(F)$ when $F$ is large; i.e., the two-motor transport is generally faster. While single motor $F$-$V$ curve is purely convex, then $\widetilde{V}_2(F) > V_1(F)$ rigorously holds, and two-motor transport is faster than single motor transport in the whole range of $F$.

Most real single motor $F$-$V$ curves, however, are usually a mixture of concave and convex regions, so one cannot intuitively know the characteristics of the two-motor $F$-$V$ curve from the single motor $F$-$V$ curve, but can still get some insight of $V_2(F)$ when $F$ is near zero. Roughly speaking, we have two typical categories of single motor $F$-$V$ curve as follows. Category A: the single motor velocity is more sensitive to resisting load than to assisting load [i.e., the $F$-$V$ region of assisting load is concave and much flatter than the region of mediate resisting load as illustrated by Fig. 2(a)]; $V_2(0) < V_1(0)$ may usually hold. Category B: the single motor velocity is more sensitive to assisting load than to resisting load [as illustrated by Fig. 2(b)]; $V_2(0) > V_1(0)$ holds. Therefore, for real single motor $F$-$V$ curves, we can obtain similar results as for purely concave and convex curves.

For the nonlinear-spring motor linkage case, the step spacing of the cargo varies. Equation (5) seems not able to be used in this case. But noticing that the average velocity of the cargo is equal to the average velocity of either motor in the long-time limit, the cargo velocity can be expressed as

$$V_2(F) = d \sum_i P_i \omega_i^+ = d \sum_i P_i \omega_i^- = \frac{d}{2} \sum_i P_i(\omega_i^+ + \omega_i^-), \tag{6}$$

where the transition rates are $\omega_i^{\pm} = V_1(F/2 \pm f_i)/d$ and $f_i$ is the internal force between motors for state $|i\rangle$. The last term of Eq. (6) is similar to Eq. (5).

Considering backward steps, we set the forward step rate and backward step rate for a single motor as $R_1^f(F)$ and $R_1^b(F)$, respectively, with $V_1(F) = [R_1^f(F) - R_1^b(F)]d$, and their ratio is $\varepsilon(F) = R_1^b(F)/R_1^f(F)$ which has been studied in Ref. [2]. If $V_1(F)$ and $\varepsilon(F)$ are given, $R_1^f(F)$ and $R_1^b(F)$ can be known. The transition rates $\omega_i^{\pm}$ in Eq. (1) are then

$$\omega_i^{\pm} = R_1^f(F/2 \pm f_i) + R_1^b(F/2 \mp f_i). \tag{7}$$

One gets the probabilities $P_i$ of state $|i\rangle$ by Eq. (3) and the average velocity of the two-motor system,

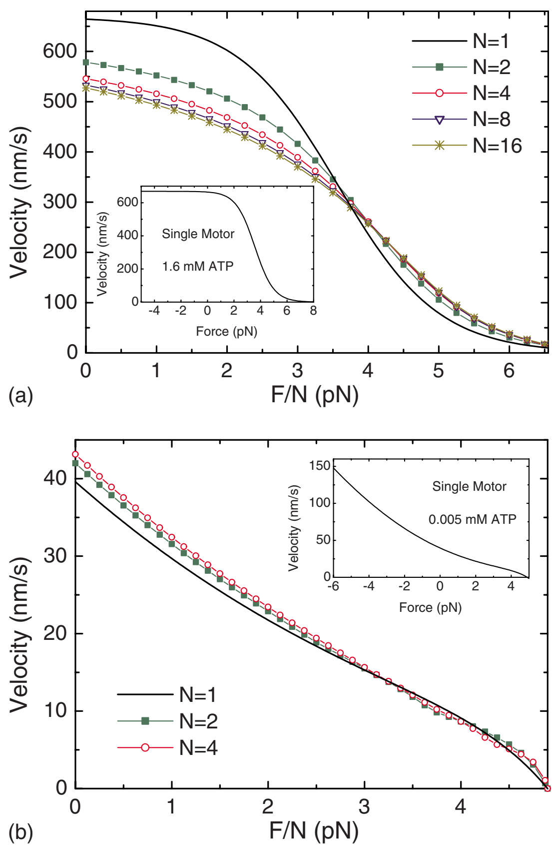


FIG. 2. (Color online) The $\tilde{V}_N(F/N)$ curves of $N$-motor system derived from two typical single motor $F$-$V$ curves as shown in insets. The linkage stiffness is taken as $k=0.3$ pN/nm just for illustration. The value is adopted from the experimental result of Ref. [5]. The curve in inset of (a) is fitted from the experimental data of Ref. [1] with [ATP]=1.6 mM. The inset of (b) is adapted from theoretical results of Ref. [7] with [ATP]=5 $\mu$M.

$$V_2(F) = \sum_{i=-n}^{n} P_i \frac{[V_1(F/2+f_i) + V_1(F/2-f_i)]}{2}, \tag{8}$$

which is the same form of Eq. (5).

### B. Multimotor case

For a general $N$-motor system, we can regard this system as the combination of a single motor and a $(N-1)$-motor subsystem. In order to conveniently describe the model, we call this very single motor as motor A and the $(N-1)$-motor subsystem as "motor" B. In the case of linear-spring motor linkage, if one of the $N$ motors takes a forward step, the $N$-motor system will progress $d/N$. So the step size of motor A is $d$, while the step size of motor B is $d/(N-1)$. Similar to the two-motor system, we can express the states of the $N$-motor system by the effective distance between motor A and motor B. Each state is denoted as $|i\rangle$, where $i$ is the value of the effective distance between motor A and motor B divided by $d/(N-1)$, i.e., $i=(N-1)S/d$, where $S$ is the effective distance between motor A and motor B. When motor A takes a forward step, the $N$-motor system will transit from state $|i\rangle$ to $|i+N-1\rangle$; while when motor B takes a forward step, the system will convert from state $|i\rangle$ to $|i-1\rangle$. Transitions between the states are shown in Fig. 3. The minus states represent that the effective distance between A and B is smaller than the equilibrium distance. If the effective distance between A and B is $S$, then this distance shared by motor A is $S(N-1)/N$ and shared by motor B is $S/N$, so the internal force between A and B is $f=idk/N$. Then the transition rates between the states can be given as

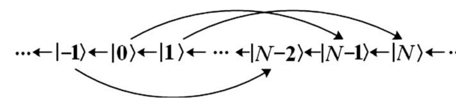


FIG. 3. Transitions between states for $N$-motor system.

$$\omega_i^+ = V_1(F/N + idk/N)/d,$$

$$\omega_i^- = (N-1)V_{N-1}[(N-1)F/N - idk/N]/d$$
$$\equiv (N-1)\tilde{V}_{N-1}[F/N - idk/(N^2-N)]/d, \tag{9}$$

where the definition $\tilde{V}_{N-1}[F/(N-1)] \equiv V_{N-1}(F)$ is used. The steady-state solution of the transition model shown in Fig. 3 can be obtained if $V_1(F)$ is given and $V_{N-1}(F)$ is known by the recursion of Eqs. (9)–(11) given below. Any one of the motors taking a forward step will make the system step forward $d/N$. The average velocity of the $N$-motor system is then given by

$$V_N(F) \equiv \tilde{V}_N(F/N) = \frac{d}{N}\sum_i P_i(\omega_i^+ + \omega_i^-). \tag{10}$$

According to the network structure of Fig. 3, we can get $\Sigma_i P_i \omega_i^- = (N-1)\Sigma_i P_i \omega_i^+$, the Eq. (10) can also be expressed as

$$V_N(F) \equiv \tilde{V}_N(F/N) = d\sum_i P_i\omega_i^+ = \frac{d}{N-1}\sum_i P_i\omega_i^-. \tag{11}$$

If the number of motors $N$ is even, the above description can be greatly simplified. Dividing these motors into two groups, each group contains the same number of motors, $N/2$. Then this $N$-motor system can be regarded as a two-big-motor system. If the $F$-$V$ curve of the $(N/2)$-motor system has already been known, we can easily obtain the $F$-$V$ curve for the $N$-motor system by the same method of the two-motor system. For convenience, we calculate the $F$-$V$ curves for this situation and show the results in Fig. 2.

Figure 2(a) displays the $F$-$V$ curves of multimotor transport, as well as the single motor $F$-$V$ curve of category A which is the most common case in many previous experimental and theoretical studies. The calculation shows that the velocity of multimotor system decreases with increasing motor number in the case of low load. This offers a possible explanation to a recent experimental observation [23]. We also notice that some experiments conclude that the increase in motor number does not affect the transport velocity of cargoes [16,17,22]. This may be a consequence of the fact that some $F$-$V$ curves of single motor are not far from linear, so all $V_N(0)(N=1,2,\ldots)$ are almost equal; i.e., multimotor transport is not significantly slower than single motor transport at low load.

One can also consider the consequence of motor detachment. Suppose $M$ motors adhering on a cargo. The number $N$ of binding motors is no longer constant but varies with time between zero and $M$. Therefore, the mean effective velocity of cargo transported by these $M$ motors can be expressed as weighted average of $V_N$ (e.g., Eq. (6) in [21]),

$$V_{\mathrm{eff}}^{M}(F) = \sum_{N=1}^{M} V_N P_N^M(F), \tag{12}$$

where $P_N^M(F)$ is the force-dependent equilibrium binding probability of $N$ motors. One can easily show that $V_{\mathrm{eff}}^{M_1}(F) > V_{\mathrm{eff}}^{M_2}(F)$ holds at low load if $M_1 < M_2$, by noticing that $V_N(F)$ decreases with $N$ at low load as shown in Fig. 2(a).

## III. DISCUSSIONS

In this paper the $F$-$V$ curve for cargo transport by multiple motors has been discussed. We focused on the linear-spring motor linkage case without considering the motor's backward steps. The results show that the $F$-$V$ curves of multimotor system depend on the $F$-$V$ curve of single motor. Insights are gained through our calculation; i.e., at low load, the velocity of the multimotor transport decreases with the increasing motor number if the single motor $F$-$V$ curve belongs to category A, and increases if the single motor $F$-$V$ curve belongs to category B. Our linear-spring motor linkage model can be extended to the nonlinear-spring motor linkage case and also the case of existence of backward steps. Results of both the latter models are qualitatively consistent with the result of the former model.

Our results contradict earlier results which predict multimotor transport is faster than single motor transport [18–20]. But the very recent experiment supports our results, which shows that increasing of motor number causes slight decrease in cargo velocity [23]. Reference [24] attributes the decreasing of cargo velocity to the detachment of motors from filament. From our results, even without motor detachment, the cargo velocity can still decrease with increasing motor number. In fact, Fig. 2 of Ref. [16] also shows a slight decrease in cargo velocity with the increasing of motor numbers. There is another difference between our results and the results of Ref. [24]. In Ref. [24], the simulation results show that the multimotor transport is slower than single motor transport in low load case, but if the motor number is larger than 2, the cargo velocity will increase with the increasing of motor number. Therefore, further experimental tests are needed, for example, hopefully by the method of Ref. [17].

## ACKNOWLEDGMENTS

This project was supported by the National Basic Research Program of China (973 Program) Grant No. 2007CB935903 and the Research Foundation for Talents of Northwest A&F University.

[1] S. M. Block, C. L. Asbury, J. W. Shaevitz, and M. J. Lang, Proc. Natl. Acad. Sci. U.S.A. **100**, 2351 (2003).
[2] N. J. Carter and R. A. Cross, Nature (London) **435**, 308 (2005).
[3] R. Mallik, B. C. Carter, S. A. Lex, S. J. King, and S. P. Gross, Nature (London) **427**, 649 (2004).
[4] C. M. Coppin, D. W. Pierce, L. Hsu, and R. D. Vale, Proc. Natl. Acad. Sci. U.S.A. **94**, 8539 (1997).
[5] C. M. Coppin, J. T. Finer, J. A. Spudich, and R. D. Vale, Proc. Natl. Acad. Sci. U.S.A. **93**, 1913 (1996).
[6] A. B. Kolomeisky and M. E. Fisher, Annu. Rev. Phys. Chem. **58**, 675 (2007).
[7] M. E. Fisher and A. B. Kolomeisky, Proc. Natl. Acad. Sci. U.S.A. **98**, 7748 (2001).
[8] S. Liepelt and R. Lipowsky, Phys. Rev. Lett. **98**, 258102 (2007).
[9] S. P. Gross, M. Vershinin, and G. T. Shubeita, Curr. Biol. **17**, R478 (2007).
[10] C. Kural, H. Kim, S. Syed, G. Goshima, V. I. Gelfand, and P. R. Selvin, Science **308**, 1469 (2005).
[11] M. J. I. Müller, S. Klumpp, and R. Lipowsky, Proc. Natl. Acad. Sci. U.S.A. **105**, 4609 (2008).
[12] O. Campàs, Y. Kafri, K. B. Zeldovich, J. Casademunt, and J.-F. Joanny, Phys. Rev. Lett. **97**, 038101 (2006).
[13] J. Brugués and J. Casademunt, Phys. Rev. Lett. **102**, 118104 (2009).
[14] C. Leduc, O. Campàs, K. B. Zeldovich, A. Roux, P. Jolimaitre, L. Bourel-Bonnet, B. Goud, J.-F. Joanny, P. Bassereau, and J. Prost, Proc. Natl. Acad. Sci. U.S.A. **101**, 17096 (2004).
[15] F. Jülicher and J. Prost, Phys. Rev. Lett. **75**, 2618 (1995).
[16] J. Beeg, S. Klumpp, R. Dimova, R. S. Graciä, E. Unger, and R. Lipowsky, Biophys. J. **94**, 532 (2008).
[17] C. Leduc, F. Ruhnow, J. Howard, and S. Diez, Proc. Natl. Acad. Sci. U.S.A. **104**, 10847 (2007).
[18] K. Mouri and T. Shimokawa, Physica A **387**, 5169 (2008).
[19] H. Y. Wang and J. D. Bao, Physica A **357**, 373 (2005).
[20] A. Igarashi, S. Tsukamoto, and H. Goko, Phys. Rev. E **64**, 051908 (2001).
[21] S. Klumpp and R. Lipowsky, Proc. Natl. Acad. Sci. U.S.A. **102**, 17284 (2005).
[22] J. Howard, A. J. Hudspeth, and R. D. Vale, Nature (London) **342**, 154 (1989).
[23] G. T. Shubeita, S. L. Tran, J. Xu, M. Vershinin, S. Cermelli, S. L. Cotton, M. A. Welte, and S. P. Gross, Cell **135**, 1098 (2008).
[24] A. Kunwar, M. Vershinin, J. Xu, and S. P. Gross, Curr. Biol. **18**, 1173 (2008).
[25] S. Leibler and D. A. Huse, J. Cell Biol. **121**, 1357 (1993).
[26] A. Vilfan, E. Frey, and F. Schwabl, Eur. Phys. J. B **3**, 535 (1998).
[27] G. Cappello, P. Pierobon, C. Symonds, L. Busoni, J. M. Gebhardt, M. Rief, and J. Prost, Proc. Natl. Acad. Sci. U.S.A. **104**, 15328 (2007).
[28] A. Gennerich, A. P. Carter, S. L. Reck-Peterson, and R. D. Vale, Cell **131**, 952 (2007).