

Speed-detachment tradeoff and its effect on track bound transport of single motor protein

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Abstract

The transportation of the cargoes in biological cells is primarily driven by the motor proteins on filamentous protein tracks. The stochastic nature of the motion of motor protein often leads to its spontaneous detachment from the track. Using the available experimental data, we demonstrate a tradeoff between the speed of the motor and its rate of spontaneous detachment from the track. Further, it is also shown that this speed-detachment relation follows a power law where its exponent dictates the nature of the motor protein processivity. We utilize this information to study the motion of motor protein on track using a random-walk model. We obtain the average distance travelled in fixed duration and average time required for covering a given distance

by the motor protein. These analyses reveal non-monotonic dependence of the motor protein speed on its transport and, therefore, optimal motor speeds can be identified for the time and distance controlled conditions.

Keywords: motor protein, processivity, detachment

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1 Introduction

Motor proteins are deployed for the directional intra-cellular transportation. These proteins move along the filamentous tracks, formed of actin and tubulin proteins, at the expense of the energy released from ATP hydrolysis [1, 2]. The prominent examples of these motor proteins include kinesin, dynein and myosin which move along the microtubules and actin filaments. Kinesin and dynein motors move in the opposite directions on microtubules, whereas myosins travel towards the positive end of the F-actin [1–3]. The dynamics of the motor protein transport along the tracks has been studied extensively, and the aspect of the spontaneous motor protein detachment, that is without application of any external force, from the tracks has also been under investigation [4–6] (and references therein). The transport of the track bound motor protein and their detachment from it has been experimentally investigated by tracking of single motors in physiological [7–14] and non-physiological conditions [15, 16] as well as of their engineered counterparts [17–19]. Similarly, modeling approaches have also studied the influence of the spontaneous motor detachment [20–23] and binding [24] with the track on its overall transport properties. In all of these works the distance covered by the motor proteins before its detachment from the track has been defined as ‘processivity’ and the influence of different motor intrinsic properties (amino-acid sequence [17, 18], motor heads [8, 19]) and external factors (temperature [15, 16], track structure [14]) on processivity has been quantitatively studied by the measurement of motor speed and force generation.

Despite the availability of extensive quantitative measurements, the rate of spontaneous motor protein detachment from the track has not been measured explicitly under diverse conditions where motor speed and force are known to be influenced. As a result, in different modelling studies the spontaneous detachment rate is considered to be independent of the motor speed [21, 22]. In the following, we demonstrate that the rate of spontaneous motor detachment from the track and its speed are corre-

lated for Kinesin and Dynein. Further, using a one dimensional random walk model the influence of the spontaneous motor detachment from the track has also been presented. The effect of the motor speed and detachment rate relationship is studied in two conditions- time controlled setup and distance controlled setup. In these two conditions we obtain the distance travelled by the motor protein in a given duration and the time taken by the motor protein to cover a pre-specified distance, respectively.

2 Materials and Methods

2.1 Experimental observations: motor speed and detachment probability

The distance based processivity, as defined previously, does not give any insight into the detachment probability, p_e , at any given time. To obtain the experimental estimates of the p_e , we looked into the literature where duration of the motor attachment to the protein tracks was measured along with its speed. In the study performed by Nara et al. [15], the kinesin was incubated with microtubules at different temperatures, whereas in the works by Cleary et al. [17] and Yildiz et al., [18], the speeds and the attachment durations for dynein (with different mutations) and kinesin (with variable neck linker length) were measured, respectively (See Tables S1, S2 and S3 for detailed experimental data). When plotted on log-log scale, the average duration of the motor attachment to the track T_{avg} , and its speed reveal a monotonic relationship which can be approximated as a power law relation, $T_{avg} \sim v^{-\alpha}$ with $\alpha > 0$ (Fig. 1a). This correlation between the motor speed and rate of detachment was not highlighted in the respective studies [15, 17, 18]. Furthermore, a compilation of T_{avg} and the speeds of different motors in diverse experimental conditions also demonstrated similar relation with $\alpha = 1.1$ (Fig. 1b, see Table S4 for experimental data). The positive values of α indicate a tradeoff between the motor speed and its duration of

attachment to the track as an increase in the speed leads to faster detachment. In the following we have utilized this speed-attachment duration relation to explore the transport of motor proteins.

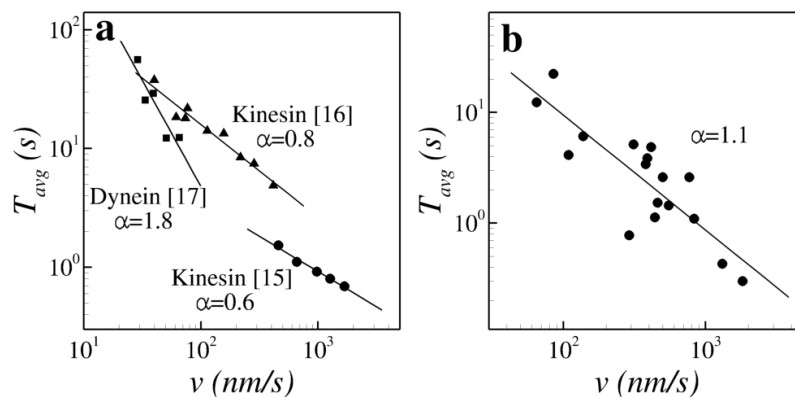


Fig 1. (a) Relationship between experimentally measured motor speed, v , and average duration of its attachment to the track, T_{avg} for Kinesin [15, 18] and Dynein [17] motors. (b) The speed and the average attachment duration for different motor proteins to their respective tracks as per the experimental data available in literature. The lines in (a) and (b) show the power law fit $T_{avg} \sim v^{-\alpha}$.

2.2 Mathematical model

2.2.1 Drift-diffusion with detachment

The detachment of motor protein from the track limits it from reaching its target destination, the end of the filament track within a finite time. Therefore, an estimate of the distance covered by the motor protein in given duration (time controlled setup) and the time required for covering a prespecified distance (distance controlled setup) are crucial aspects for complete understanding of the motor driven cellular transportation.

In general, the motion of the motor proteins on track is constituted of forward (and in some cases backward too) steps of different sizes where each step is driven by ATP hydrolysis [1]. Additionally, the motor protein can also spontaneously get detached from the track at any cycle with a detachment probability p_e . Considering the motion of the motor proteins on the tracks as a one-dimensional random walk,

its position on the track at any given time can be characterized by the probability density $P(x, t)$ which follows the Fokker-Planck equation [25]

$$\frac{\partial P(x, t)}{\partial t} = -v \frac{\partial P(x, t)}{\partial x} + D \frac{\partial^2 P(x, t)}{\partial x^2} - P(x, t) r_e \quad (1)$$

where v and D are the motor speed and its diffusion constant on the track, respectively, whereas r_e rate of motor detachment from the track and is related to the detachment probability p_e as [26]

$$r_e = -\log(1 - p_e)/\tau, \quad (2)$$

where τ is the time required for the hydrolysis of single ATP. It has to be noted that for small values of p_e , $r_e = p_e/\tau$. In order to understand the properties of the stochastic processes, the first passage time distribution is often used [25]. In the context of the motor protein motion the first passage time distribution, $f(L, t)$, is defined as the time distribution for the motor protein crossing a target distance L . In other words, the probability that the motor protein will cover a distance L between time t and $t + dt$ is given by $f(L, t)dt$. Using the approach described in [25] we can derive the first passage time distribution corresponding to the equation 1 as

$$f(L, t) = \frac{L}{\sqrt{4\pi Dt^3}} \exp \left(-r_e t - \frac{(L - vt)^2}{4Dt} \right) \quad (3)$$

In the scenario where the motor does not detach from the track ($r_e = 0$), the above expression reduces to the first passage time distribution for the Brownian particle with drift. In the following, we will use the first passage time distribution in the time and distance controlled setups.

2.2.2 Time controlled setup: Distance travelled in fixed time

A measure of a motor protein transport can be obtained in terms of the distance covered by it in a prespecified duration. The average distance covered in time T can

be written as

$$L_m(T) = \int_0^\infty \int_0^T L \left(\frac{\partial f}{\partial L} \right) dt dL. \quad (4)$$

In general, the analytical evaluation of the above integral is not straight forward but it can be calculated for some special cases. For the purely ballistic motion, that is $D = 0$, we can evaluate the above integral by substituting the first passage time distribution $f(L, t) = \delta(t - L/v)$ to obtain

$$L_m(T, D = 0) = \frac{v}{r_e} (1 - e^{-r_e T}). \quad (5)$$

On the other hand, for the purely diffusive motion ($v = 0$), we obtain

$$L_m(T, v = 0) = \sqrt{\frac{D}{r_e}} \operatorname{erf}(\sqrt{r_e T}) \quad (6)$$

where $\operatorname{erf}(x)$ is the error function. From the relations 5 and 6, it is apparent that L_m attains finite values $L_s = v/r_e$ and $L_s = \sqrt{D/r_e}$, respectively, for $T \rightarrow \infty$ and is defined as processivity.

2.2.3 Distance controlled setup: Motor transport to fixed distance

Similar to time controlled setup, the motor transport can also be analyzed in the distance controlled setup where the rate of motor travel to a fixed distance is calculated. In this scenario, due to its detachment from the track the motor protein is not necessary to reach the pre-specified distance. Therefore, first we need to calculate the probability that the motor protein can reach the given distance. This probability is given by

$$P_r(L) = \int_0^\infty f(L, t) dt. \quad (7)$$

In the case it can cover the distance ($P_r(L) > 0$), the average time taken to achieve it can be written as

$$T_m(L) = \frac{1}{P_r(L)} \int_0^\infty t f(L, t) dt. \quad (8)$$

It has to be noted that for $r_e = 0$, the above integral diverges but $r_e > 0$ results in finite T_m . Further, in this distance controlled setup the ratio $\phi(L) = P_r/T_m$ can be defined as the rate of motor transport to a fixed distance. The physical interpretation of $\phi(L)$ can be understood as the fraction of the motor proteins reaching a target distance per unit time. For instance, low transport rate ($P_r/T_m \rightarrow 0$) means that if a motor protein starts at some location of the track it does not reach the specified distance. This failure could either be due to the detachment of the motor protein from the track or due to its extremely slow motion along the track. On the other hand, P_r/T_m takes high values only if P_r is high and T_m is low.

Similar to the time controlled setup, we can evaluate the probability and average time taken for reaching the target distance in the limiting cases. For ballistic motion, we obtain

$$P_r(L, D = 0) = e^{-r_e L/v}, \quad (9)$$

$$\text{and } T_m(L, D = 0) = \frac{L}{v}. \quad (10)$$

For diffusive motion

$$P_r(L, v = 0) = \exp\left(-\sqrt{\frac{L^2 r_e}{D}}\right), \quad (11)$$

$$\text{and } T_m(L, v = 0) = \frac{L}{2\sqrt{D r_e}}. \quad (12)$$

Expectedly, for ballistic motion the average time T_m is not dependent on the detachment probability. On the other hand for diffusive transport ($v = 0$), we obtain $T_m \rightarrow 1/\sqrt{p_e}$ as $p_e \rightarrow 0$.

2.2.4 Incorporation of experimental observations

As observed in the experiments (Fig. 1), the motor speed and the rate of motor detachment from the track are not independent. For the power-law relations between the detachment probability (p_e , Fig. 1A-B) we have

$$\frac{1 - e^{-r_e(v)\tau}}{1 - e^{-r_e^0\tau}} = \left(\frac{v}{v_0}\right)^\alpha \quad (13)$$

where v_0 and r_e^0 are the reference motor speed and the rate of detachment, respectively. We substitute the expression for r_e from the above relation to obtain the average distance covered in finite time and the transport rate to a finite distance as a function of the exponent α .

3 Results and Discussion

3.1 Parameter values

In this paper we have taken the transport of kinesin motor on microtubule as an example to understand the effects of the speed dependent detachment rate. The values of the model parameters for kinesin motor are shown in Table 1. The similar

Parameter	Value	Reference
v_0	640 nm/s	[2]
p_e^0, r_e^0	0.01, 0.35/s	[15]
τ	1/80 s	[2]
D	2500 nm ² /s	[27]

Table 1. Values of the model parameters for kinesin motor used in the current study

analysis can also be performed for dynein and myosin motor proteins.

3.2 Influence of motor detachment from the track

The detachment of the motor protein from the track limits the distance it can cover in finite time and the rate of its transport to a specific distance. In order to study the effect of the change in velocity with the detachment probability we first calculated the processivity of the motor protein when its velocity does not change with p_e . Thus calculated processivity of a kinesin motor on microtubule track for fixed velocity and diffusivity is shown in Fig. 2a. If the motor velocity remains fixed, for small values of p_e its processivity decreases as $1/p_e$ and $1/\sqrt{p_e}$ for velocity and diffusivity dominant transports, respectively. This decrease in processivity, however, is contrary to the experimental observations where it shows an increase with p_e [15, 18]. This shows that the assumption of fixed rate of detachment [21, 22] independent of motor speed may not be correct.

In the distance controlled setup, for fixed velocity and diffusivity the probability of motor protein reaching a target distance decreases with p_e (Fig. 2b) in both of the diffusion and drift dominated modes of transport. The transport rate to the target distance $\phi(L)$, however, shows different behaviors in diffusion and drift dominated motions (Fig. 2c). For purely drift driven motor protein transport, the transport rate decreases with p_e . But in the diffusion driven transport, the transport rate follows a non-monotonic relationship with p_e . This is because for large p_e , the probability of reaching the target distance is negligible whereas for very small p_e the time taken for complete transport is very large (see relations 11 and 12). The disagreement between the experimental observations of increased processivity with the detachment rate and model predictions with constant motor speed suggests that the dependence of motor speed on the detachment rate has significant effect on its transport properties. In the following we will study the effect of motor speed-detachment rate relationships on its transport under time and distance controlled conditions.

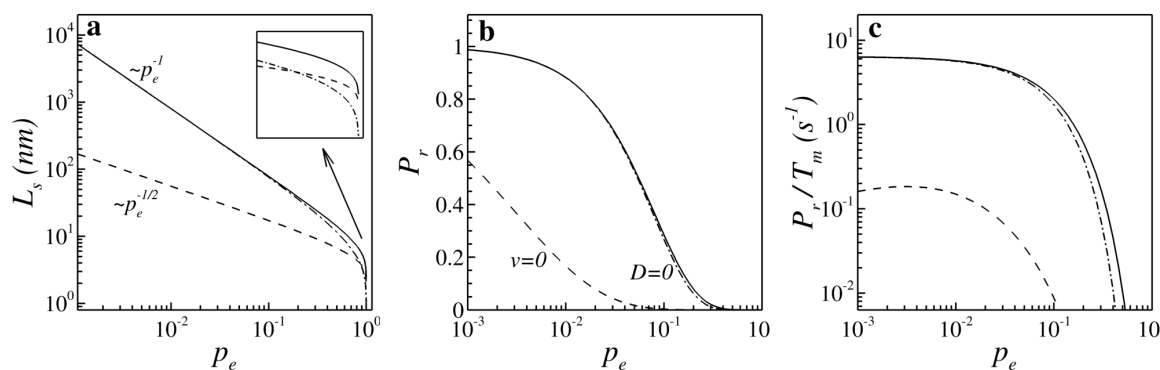


Fig 2. Effect of kinesin detachment from microtubule on its transport for fixed speed and diffusivity. (a) Dependence of kinesin processivity L_s under diffusive transport ($v = 0$ and $D = 2500 \text{ nm}^2/\text{s}$, dashed line), ballistic transport ($v = 640 \text{ nm/s}$ and $D = 0$, dash-dotted line), and mixed transport ($v = 640 \text{ nm/s}$, $D = 2500 \text{ nm}^2/\text{s}$, solid line) on detachment probability p_e . Inset shows the enlarged version of the same plot for large p_e . (b) Probability, P_r , of covering a distance of 100 nm by kinesin on a microtubule track before detachment under diffusive (dashed), ballistic (dash-dotted) and mixed (solid) modes of transport. (c) Rate of kinesin transport on microtubule to a distance of 100 nm for aforementioned three modes of transport.

3.3 Effect of speed dependent detachment rate

3.3.1 Motor transport in fixed time

The experimental data showed (Fig. 1) that the motor speed and its detachment rate can be characterized as power law with exponent α . With this power-law relationship, the distance covered by the motor protein in finite time (Fig. 3a) shows a non-monotonic dependence on p_e which is unlike monotonically decreasing dependence when the motor speed does not change (Fig. 2a). For very small values of p_e the motor speed goes to zero and the distance covered in finite time takes a constant value ($L_m(T) = 2\sqrt{DT/\pi}$) which is determined by the diffusivity of the motor protein alone. On the other hand, for drift dominated scenario ($D = 0$) the distance covered in finite time increases as $p_e^{1/\alpha}$ for small values of p_e . For large p_e , the motor protein get detached from the track very fast and does not traverse any distance. Fig. 3b shows the distance covered by the kinesin on microtubule in finite time for different α . Apart from the maximum value attained by L_m , the nature of the dependence of L_m on detachment probability does not change with the power law exponent α . As

$T \rightarrow \infty$ the distance covered by the motor on track converges to its processivity, L_s and it is shown in Fig. 3c. As opposed to the distance covered in finite time, the qualitative nature of processivity depends significantly on α . It can be seen that for the motor proteins with $\alpha < 1$, such as kinesin, the processivity increases with the detachment probability, whereas for motor proteins like dynein, for which $\alpha > 1$, it decreases. This dependence of processivity on α is evident from the substitution of relation 13 in 5 for drift dominated transport, which gives for small p_e

$$L_s = \frac{v_0 \tau}{(p_e^0)^{1/\alpha}} p_e^{(1-\alpha)/\alpha}. \quad (14)$$

This can be understood by comparing the relative changes in the velocity and detachment probability. For $\alpha < 1$, an increase in detachment probability leads to much larger increase in the motor velocity and hence increased processivity and vice a versa. Therefore, the power law exponent α describes the nature of the processivity of the motor proteins.

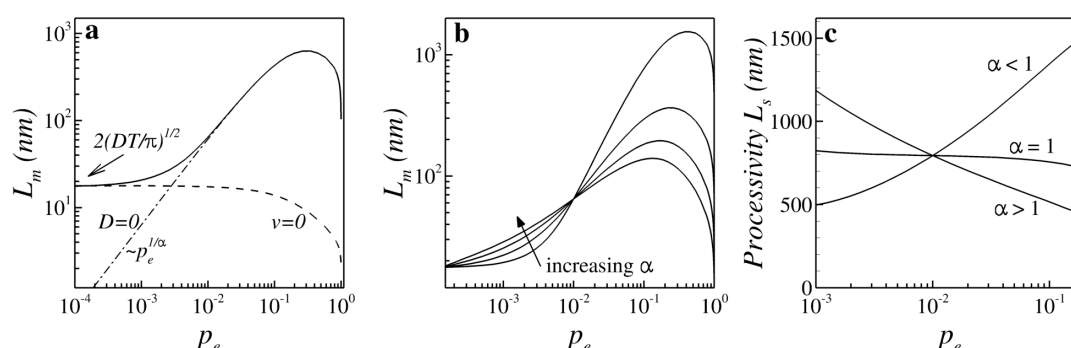


Fig 3. Distance travelled by kinesin on microtubule in $100\mu s$ with velocity dependent detachment rate. (a) Distance covered under diffusive (dashed), ballistic (dash-dotted) and mixed (solid line) modes of transport with $\alpha = 1$. (b) Distance covered by kinesin for $\alpha = 0.8, 1.2, 1.6, 2.0$. (c) Dependence of motor protein processivity on p_e for different α .

3.3.2 Motor transport to fixed distance

Similar to the track bound transport of motor protein in finite time we can also study the effect of the $v - p_e$ relations (Fig. 1 and equation 13) on its transport to a

fixed distance. The probability of reaching a target distance by the kinesin motor on microtubule is shown in Fig. 4a which shows that for drift dominated scenario ($D = 0$) the probability P_r attains a maxima. This is opposed to the scenario when the motor speed does not change with the detachment probability (Fig. 2b). On the other hand, for the rate of motor transport $\phi(L)$ both of the drift and diffusion dominated regimes attain local maxima (Fig. 4b). Further, for small values of p_e the rate of transport ϕ increases as $\sqrt{p_e}$ and $p_e^{1/\alpha}$ in the drift and diffusion dominated motions of the motor protein on the track, respectively. Figs. 4c,d show the dependence of P_r and ϕ on p_e for different values of α . It has to be noted that the maxima attained by the P_r vanishes for $\alpha > 1$. However, the rate of transport ϕ shows a maximal transport for all values of α . This demonstrates that for track bound transport of motor proteins to a fixed distance there exists an optimal velocity which maximizes its rate of transport to the target location.

3.3.3 Optimum motor velocity

As shown in Fig. 3b and Fig. 4d the track bound transport of the motor proteins has non-monotonic dependence on the motor speed (or detachment rate). Therefore, faster motor speed on a track does not necessarily mean its faster transport and it is possible to obtain the motor velocity corresponding to the farthest transport in fixed time and fastest transport to a pre-specified distance.

For kinesin, its velocity in physiological conditions $v = 640nm/s$ turns out to be optimal for its farthest transport in time $T \sim 10s$. For the cellular functions, this duration is too large. On the other hand, the same physiological velocity of kinesin is optimal for the fastest transport to a distance of $L > 5\mu m$. This distance is roughly of the same order of magnitude as that of the size of a single cell. This demonstrates that kinesin motor is more likely to move at speeds to maximize the transport rate to a given distance instead of maximizing the distance in given time. This observation is reasonable as in physiological conditions the transport of cellular cargo is to fixed

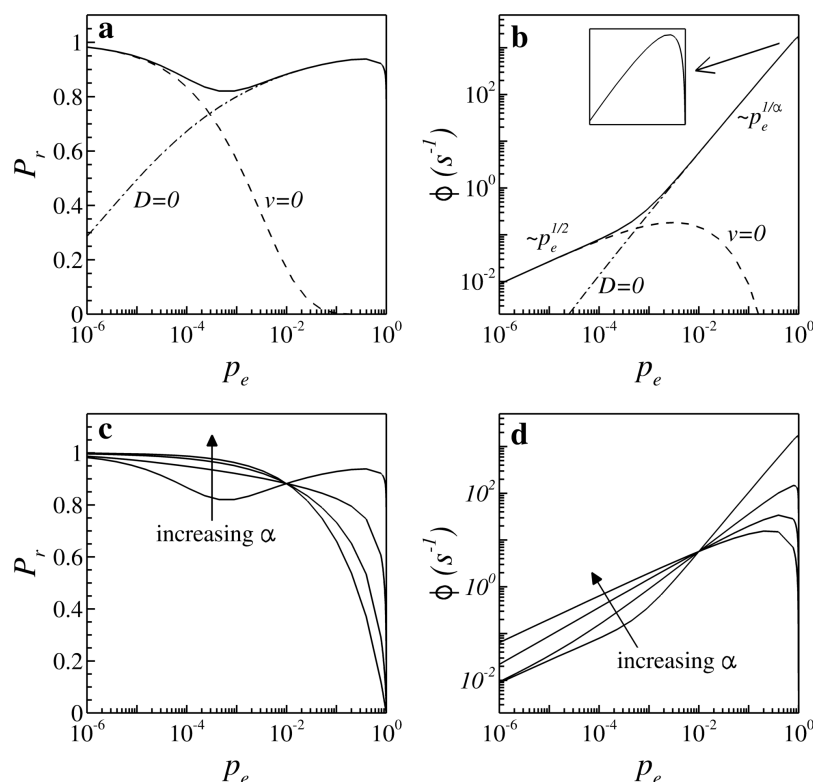


Fig 4. Transport of kinesin to a fixed distance with velocity dependent detachment rate. (a) Probability P_r of reaching and (b) rate of transport of kinesin motor to distance of $100\mu m$ before detachment under three modes of transport. (c) The probability P_r and (d) the transport rate to the target distance of $100\mu m$ for $\alpha = 0.8, 1.2, 1.6, 2.0$.

distances as the cell size remains more or less unchanged.

It has to be noted that in physiological conditions motor protein does not constantly move on a single track. For instance, in case of kinesin transport on microtubule tracks it keeps hopping among different microtubule filaments [28] and also undergoes diffusive motion in cytosol. Furthermore, consumption of ATP is another factor governing the motor transport in biological systems. From the economy viewpoint, the optimal motor velocity can also be determined by the one which requires minimal ATP consumption. Therefore the estimation of optimal speed of the motor protein has to take these factors into account which is not in the scope of present study.

3.4 Biological implications and future directions

In this paper, using existing experimental data, we have demonstrated a novel monotonic relationship between the speed of the motor protein and the duration of its attachment to the track as a tradeoff between the two. Although an insight into the exact nature of this relationship will require a detailed experimental and modelling endeavour, a physical understanding of its monotonic nature for bipedal motors can be obtained by the following argument. The kinesin and other bipedal motors move on the tracks by the sequential attachment and detachment of the two heads [3]. The speed and the detachment probability depends on the duration of attachment of each motor head in each cycle. In case of high (low) motor speed, its both heads undergo fast (slow) attachment-detachment transitions which also leads to high (low) detachment probability. For the range of the motor speeds presented here, a power-approximation leads to an easy prediction that increase in the speeds of the kinesin ($\alpha < 1$) and dynein ($\alpha > 1$) motors would result in higher and lower processivity, respectively. For kinesin, it has already been observed experimentally by varying motor speed by temperature changes [16]. However, the same is yet to be experimentally verified for dynein.

Further, the observation of the tradeoff is based on different experimental studies performed under diverse experimental conditions. Therefore, a systematic experimental study is warranted to test the conditions under which the speed-detachment tradeoff holds. To achieve this the model predictions presented in this paper can be utilized.

It has to be noted that although the exponent α is the characteristic of the motor protein, it also depends on its microenvironment. This can be seen from the experimental data shown in Figs. 1a where the average duration of attachment of the kinesin motor to the microtubule track is obtained by two groups ([17] and [15]) differs significantly if not by an order of magnitude. Similarly, in Fig. 1B also we observe multiple values of the attachment duration and the speed of the kinesin motors. The

reason for this discrepancy is the differing experimental conditions used in each setup and hence this aspect has to be kept in consideration during classification of motor proteins based on α . Similar speed-accuracy tradeoffs have also been observed in the context of DNA replication [29], road-safety [30], human movements [31, 32], decision making [33, 34] and perceptual learning[35]. Although, the underlying mechanisms of the speed-accuracy tradeoffs might be different in different systems, its influence on the overall system dynamics would still hold.

Furthermore, it is known that motor proteins often undergo collective motions on the tracks. Therefore, it would be interesting to see the effect of the speed-detachment tradeoff on the collective motion of the motor proteins. Additionally, the model can also be extended to study the effect of speed-detachment tradeoff on the motor transport in more realistic scenario where the motor protein can also reattach to the track.

4 Conclusion

This work utilizes the available experimental observation to propose a novel relationship between the speed of motor proteins and the rate of their detachment from the track. This tradeoff is further utilized to study the characteristics of the motor transport along the track in fixed time and to a fixed distance. It is shown that faster motor speed does not necessarily mean faster or farthest transport. Therefore, optimal speed can be estimated for the transport of motor proteins along the cytoskeletal filaments.

References

1. H. Lodish, A. Berk, S. L. Zipursky, P. Matsudaira, D. Baltimore, and J. Darnell. *Molecular Cell Biology*. W. H. Freeman, New York, 2000.

2. J.M. Berg, J.L. Tymoczko, and Stryer L. *Biochemistry*. W. H. Freeman, New York, 5th edition, 2002.
3. J. Howard. Molecular motors: structural adaptations to cellular functions. *Nature*, 389(6651):561–567, Oct 1997.
4. S. A. Endow and D. S. Barker. Processive and nonprocessive models of kinesin movement. *Annu. Rev. Physiol.*, 65:161–175, 2003.
5. R. D. Vale and R. A. Milligan. The way things move: looking under the hood of molecular motor proteins. *Science*, 288(5463):88–95, Apr 2000.
6. G. Muthukrishnan, Y. Zhang, S. Shastry, and W. O. Hancock. The processivity of kinesin-2 motors suggests diminished front-head gating. *Curr. Biol.*, 19(5):442–447, Mar 2009.
7. S. L. Reck-Peterson, A. Yildiz, A. P. Carter, A. Gennerich, N. Zhang, and R. D. Vale. Single-molecule analysis of dynein processivity and stepping behavior. *Cell*, 126(2):335–348, Jul 2006.
8. Y. Okada and N. Hirokawa. A processive single-headed motor: kinesin superfamily protein KIF1A. *Science*, 283(5405):1152–1157, Feb 1999.
9. P. Pierobon, S. Achouri, S. Courty, A. R. Dunn, J. A. Spudich, M. Dahan, and G. Cappello. Velocity, processivity, and individual steps of single myosin V molecules in live cells. *Biophys. J.*, 96(10):4268–4275, May 2009.
10. R. S. Rock, S. E. Rice, A. L. Wells, T. J. Purcell, J. A. Spudich, and H. L. Sweeney. Myosin VI is a processive motor with a large step size. *Proc. Natl. Acad. Sci. U.S.A.*, 98(24):13655–13659, Nov 2001.
11. E. Toprak, A. Yildiz, M. T. Hoffman, S. S. Rosenfeld, and P. R. Selvin. Why kinesin is so processive. *Proc. Natl. Acad. Sci. U.S.A.*, 106(31):12717–12722, Aug 2009.

12. W. O. Hancock and J. Howard. Kinesin's processivity results from mechanical and chemical coordination between the ATP hydrolysis cycles of the two motor domains. *Proc. Natl. Acad. Sci. U.S.A.*, 96(23):13147–13152, Nov 1999.
13. W. Qiu, N. D. Derr, B. S. Goodman, E. Villa, D. Wu, W. Shih, and S. L. Reck-Peterson. Dynein achieves processive motion using both stochastic and coordinated stepping. *Nat. Struct. Mol. Biol.*, 19(2):193–200, Feb 2012.
14. D. Cai, D. P. McEwen, J. R. Martens, E. Meyhofer, and K. J. Verhey. Single molecule imaging reveals differences in microtubule track selection between Kinesin motors. *PLoS Biol.*, 7(10), 2009.
15. I. Nara and S. Ishiwata. Processivity of kinesin motility is enhanced on increasing temperature. *Biophysics*, 2:13–21, 2006.
16. K. Kawaguchi and S. Ishiwata. Temperature dependence of force, velocity, and processivity of single kinesin molecules. *Biochem. Biophys. Res. Commun.*, 272(3):895–899, Jun 2000.
17. F. B. Cleary, M. A. Dewitt, T. Bilyard, Z. M. Htet, V. Belyy, D. D. Chan, A. Y. Chang, and A. Yildiz. Tension on the linker gates the ATP-dependent release of dynein from microtubules. *Nat Commun*, 5:4587, 2014.
18. A. Yildiz, M. Tomishige, A. Gennerich, and R. D. Vale. Intramolecular strain coordinates kinesin stepping behavior along microtubules. *Cell*, 134(6):1030–1041, Sep 2008.
19. K. S. Thorn, J. A. Ubersax, and R. D. Vale. Engineering the processive run length of the kinesin motor. *J. Cell Biol.*, 151(5):1093–1100, Nov 2000.
20. J. Hughes, S. Shastry, W. O. Hancock, and J. Fricks. Estimating Velocity for Processive Motor Proteins with Random Detachment. *J Agric Biol Environ Stat*, 18(2):204–217, Jun 2013.

21. S. Klumpp and R. Lipowsky. Active diffusion of motor particles. *Phys. Rev. Lett.*, 95(26):268102, Dec 2005.
22. M. J. Saxton. A biological interpretation of transient anomalous subdiffusion. I. Qualitative model. *Biophys. J.*, 92(4):1178–1191, Feb 2007.
23. S. Fedotov, H. Al-Shamsi, A. Ivanov, and A. Zubarev. Anomalous transport and nonlinear reactions in spiny dendrites. *Phys Rev E Stat Nonlin Soft Matter Phys*, 82(4 Pt 1):041103, Oct 2010.
24. M. J. Saxton. Anomalous diffusion due to binding: a Monte Carlo study. *Biophys. J.*, 70(3):1250–1262, Mar 1996.
25. M. Ding and G. Rangarajan. First passage time problem: A fokker-planck approach. In L. Wille, editor, *New Directions in Statistical Physics*, pages 31–46. Springer Berlin Heidelberg, 2004.
26. R. M. Feldman and C. Valdez-Flores. *Applied Probability and Stochastic Processes*. Springer Heidelberg Dordrecht London New York, 2010.
27. H. Lu, M. Y. Ali, C. S. Bookwalter, D. M. Warshaw, and K. M. Trybus. Diffusive movement of processive kinesin-1 on microtubules. *Traffic*, 10(10):1429–1438, Oct 2009.
28. J. L. Ross, H. Shuman, E. L. Holzbaur, and Y. E. Goldman. Kinesin and dynein-dynactin at intersecting microtubules: motor density affects dynein function. *Biophys. J.*, 94(8):3115–3125, Apr 2008.
29. C. Tomasetti and B. Vogelstein. Cancer etiology. Variation in cancer risk among tissues can be explained by the number of stem cell divisions. *Science*, 347(6217):78–81, Jan 2015.
30. G. Nilsson. *Traffic safety dimensions and the power model to describe the effect of speed on safety*. PhD thesis, Lund Institute of Technology, 2004.

31. R. Plamondon and A. M. Alimi. Speed/accuracy trade-offs in target-directed movements. *Behav Brain Sci*, 20(2):279–303, Jun 1997.
32. M. Dean, S. W. Wu, and L. T. Maloney. Trading off speed and accuracy in rapid, goal-directed movements. *J Vis*, 7(5):1–12, 2007.
33. W. A. Wickelgren. Speed-accuracy tradeoff and information processing dynamics. *Acta Psychologica*, 41:67–85, 1977.
34. R. P. Heitz. The speed-accuracy tradeoff: history, physiology, methodology, and behavior. *Front Neurosci*, 8:150, 2014.
35. C. C. Liu and T. Watanabe. Accounting for speed-accuracy tradeoff in perceptual learning. *Vision Res.*, 61:107–114, May 2012.