Cooperative Cargo Transport by Several Molecular Motors

– Supporting Information –

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A Technical aspects of the calculations

A.1 Mean First Passage Times

The effective unbinding rate as given by Eq. (8) has been derived by a simple equilibrium argument. The same equation can also be obtained by calculating the mean first passage time. Let us denote by $T_{m,N}$ the mean first passage time to the state $|0\rangle$ with no bound motor if we start from state $|m\rangle$ with m bound motors at time $t = 0$ (the second index N indicates the total number of motors). The effective unbinding rate is then given by $1/T_{1,N}$, since the cargo particle first binds to the filament through a single motor.

The first passage times fulfill the recursion relations

$$T_{m,N} = \frac{1}{\epsilon_m + \pi_m} + \frac{\pi_m}{\epsilon_m + \pi_m} T_{m+1,N} + \frac{\epsilon_m}{\epsilon_m + \pi_m} T_{m-1,N} \tag{S.1}$$

for $m \neq 0, N,$, see, e.g., [1], with the boundary recursions

$$T_{N,N} = \frac{1}{\epsilon_N} + T_{N-1,N} \quad \text{and} \tag{S.2}$$

$$T_{0,N} = 0. \tag{S.3}$$

Because of the boundary condition $T_{0,N} = 0$, the recursion relation (S.1) with $m = 1$ can be used to express $T_{2,N}$ in terms of $T_{1,N}$. Next, starting from (S.1) with $m = 2$ and using the relation between $T_{2,N}$ and $T_{1,N}$, we can also express $T_{3,N}$ in terms of $T_{1,N}$. Iteration of this procedure leads to explicit expressions for $T_{m,N}$ in terms of $T_{1,N}$. Finally, when these expressions are used in (S.2), we obtain an implicit equation for $T_{1,N}$ which is solved by

$$T_{1,N} = \frac{1}{\epsilon_1}\left(1 + \sum_{i=1}^{N-1}\prod_{n=1}^{i}\frac{\pi_n}{\epsilon_{n+1}}\right), \tag{S.4}$$

which is exactly the inverse of Eq. (8).

A.2 Distribution of Unbinding Times

To calculate the distribution of unbinding times, we consider the probability distribution for the passage from state $|m\rangle$ with m bound motors at time $t = 0$ to the unbound state $|0\rangle$ at time t which we denote by $\tilde{\psi}_{m,N}(t)$. The distribution of unbinding times is then given by $\tilde{\psi}_N(\Delta t_\mathrm{b}) \equiv \tilde{\psi}_{1,N}(t = \Delta t_\mathrm{b})$ since the initial bound state of the cargo particle is provided by state $|1\rangle$ with $m = 1$ for which the particle is bound to the filament by a single motor.

The probability distributions $\tilde{\psi}_{m,N}(t)$ fulfill the recursion relations

$$\tilde{\psi}_{m,N}(t) = \int_0^t e^{-(\epsilon_m+\pi_m)\tau}\left[\pi_m\,\tilde{\psi}_{m+1,N}(t-\tau) + \epsilon_m\,\tilde{\psi}_{m-1,N}(t-\tau)\right]\mathrm{d}\tau \tag{S.5}$$

for $m \neq 0, N$,

$$\tilde{\psi}_{N,N}(t) = \int_0^t e^{-\epsilon_N\tau}\epsilon_N\,\tilde{\psi}_{N-1,N}(t-\tau)\mathrm{d}\tau, \qquad \text{and} \tag{S.6}$$

$$\tilde{\psi}_{0,N}(t) = \delta(t). \tag{S.7}$$

These recursion relations are obtained by considering the first binding/unbinding event explicitly, summing over the two possibilities for this step (to $m \pm 1$), and integrating over all possible times τ at which this first event occurs. The exponential terms express the probability that no binding/unbinding event occurred until the time τ.

Using Laplace transforms, we can transform the convolution integrals into algebraic equations and iteratively obtain all the Laplace transformed distributions $\tilde{\psi}_{m,N}(s)$. The solution is given by a finite continued fraction of depth N, which has the form

$$\tilde{\psi}_{1,N}(s) = \cfrac{\epsilon_1}{\epsilon_1 + s + \pi_1\left(1 - \cfrac{\epsilon_2}{\epsilon_2+s+\pi_2\left(1-\cfrac{\cdots}{\cdots+\pi_{N-1}\left(1-\frac{\epsilon_N}{\epsilon_N+s}\right)\cdots}\right)}\right)}, \tag{S.8}$$

see chapter 9 of Ref. [2].

In general, the inverse Laplace transform of (S.8) can be expressed as

$$\tilde{\psi}_{1,N}(t) = \sum_{i=1}^{N} e^{-z_i t} \, \mathrm{Res}(-z_i), \tag{S.9}$$

where the parameters $-z_i$ are the poles of $\tilde{\psi}_{1,N}(s)$ and $\mathrm{Res}(-z_i)$ are the corresponding residues, see [3]. All poles $-z_i$ are real and negative. Using the definition $\tilde{\psi}_N(\Delta t_\mathrm{b}) \equiv \tilde{\psi}_{1,N}(t = \Delta t_\mathrm{b})$ in the relation (S.9), we obtain the binding time distribution as given by Eq. (9).

In general, the poles and the residues have to be calculated numerically, but in the two simplest cases, $N = 1$ and $N = 2$, the inverse Laplace transform can be obtained in closed form. For $N = 1$, we can check that we recover the single exponential $\tilde{\psi}_{1,1}(t) = \epsilon_1 e^{-\epsilon_1 t}$, and for $N = 2$ the first passage time distribution is given by

$$\begin{aligned} \tilde{\psi}_{1,2}(t) \quad &= \quad \frac{\epsilon}{2}\Big[\Big(1 - \frac{\epsilon_1 + \pi_1 - \epsilon_2}{R}\Big) e^{-\frac{1}{2}(\epsilon_1+\epsilon_2+\pi_1-R)t} \\ &\qquad + \Big(1 + \frac{\epsilon_1 + \pi_1 - \epsilon_2}{R}\Big) e^{-\frac{1}{2}(\epsilon_1+\epsilon_2+\pi_1+R)t}\Big] \end{aligned} \tag{S.10}$$

with $R \equiv \sqrt{(\epsilon_1 + \epsilon_2 + \pi_1)^2 - 4\epsilon_1\epsilon_2}$.

B Mutual Exclusion of Motors

In general, several motor molecules, which are bound to a certain cargo particle, may compete for the same binding site of the filament. Such a competition may arise, for example, because the motor molecules are densely packed on the cargo particle or because they move along a single protofilament of the microtubule. In such a situation, mutual exclusion or hard core repulsion between the motors should to be taken into account. Exclusion reduces the binding of motors to the filament and the velocity of the bound motors [4, 5]. Within a mean-field approximation, these two effects can be incorporated into our model by using modified binding rates π_n and modified bound state velocities v_n as given by

$$\pi_n = (N - n)\pi_\mathrm{ad}\left[1 - \frac{n}{N_s}\right] \qquad \text{and} \qquad v_n = v\left[1 - \frac{n-1}{N_s - 1}\right] \tag{S.11}$$

for $n \leq N_s$ where N_s is the number of accessible binding sites that the motors can reach for a given position of the cargo particle. The terms $[1 - n/N_s]$ and

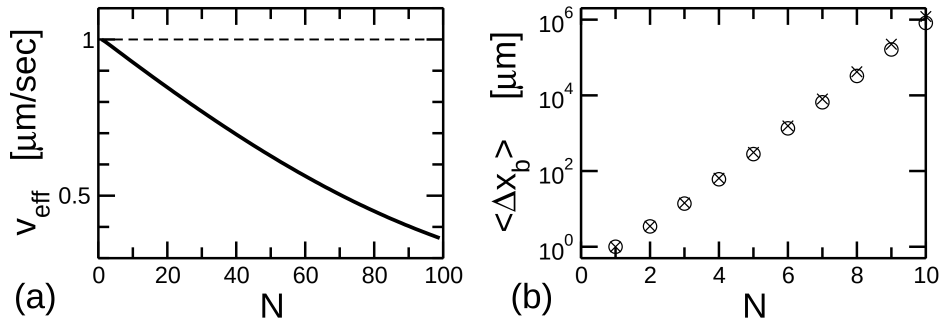

Figure 6: Exclusion effects: (a) Average velocity $v_{\rm eff}$ and (b) average walking distance $\langle \Delta x_{\rm b} \rangle$ as functions of the number N of motors attached to the cargo. The chosen parameter values are those of kinesin as described in the text. The number of binding sites which are accessible to the motors for a given position of the cargo particle is $N_s = 100$ as appropriate for a cargo with radius $\sim 1\mu$m [solid line in (a) and circles in (b)]. The values indicated by the dashed line in (a) and the crosses in (b) are obtained if exclusion effects are not taken into account. For typical motor numbers $N \lesssim 10$, direct comparison shows that exclusion effects are small.

$[1-(n-1)/(N_s-1)]$ describe the probability that the site to which a motor attempts to bind or to move is not occupied by another motor.[1] For $n \geq N_s$, all binding sites, that could be reached by the motors, are occupied, so that $\pi_n = 0$ for $n \geq N_s$. The unbinding rates ϵ_n are unaffected by exclusion and are again given by $\epsilon_n = n\,\epsilon$. If the number of accessible binding sites N_s is much larger than the number of motors attached to the cargo particle, the motors are effectively non-interacting, and Eq. (S.11) can be approximated by Eq. (12).

For typical cargoes such as beads or vesicles with diameters between 100 nm and 1 μm, we can estimate the number of binding sites within the contact zone of the cargo particle to be of the order of 50–150, while the number of motors is typically 1–10. For these motor numbers and for the parameter values corresponding to kinesin, exclusion effects are rather small. Inspection of Fig. 6(a). shows that the average velocity is reduced by a few percent as compared to non-interacting motors. The average walking dis-

[1] The difference between these two expressions arises from a finite-size effect. When an unbound motor attempts to bind to the state $|n\rangle$, it encounters n out of N_s binding sites that are already occupied. In contrast, a bound motor in state $|n\rangle$ 'feels' only $n-1$ motors which are bound to $n-1$ out of the remaining $N_s - 1$ binding sites.

tance is more sensitive to exclusion, but still of the same order of magnitude as for non-interacting motors. For example, for $N = 5$, the walking distance which is $\simeq 310$ nm without exclusion is reduced to 280 nm, see Fig. 6(b).

If motors are closely packed on the cargo particle, i.e. for $N \simeq N_s$, a reduction of the velocity to about 35 percent of the value without exclusion is obtained as shown in Fig. 6(a). For very high motor densities, a reduction of the velocity of the order of 50 percent has indeed been observed both in microtubule gliding assays [6] and bead assays (J. Beeg, private communication) for kinesin.

In principle, exclusion implies that the walking distance exhibits a maximum as a function of the number of motors, since at very large motor numbers, the velocity approaches zero. Using the rates (S.11) in Eq. (11), we find, however, that this maximum occurs at walking distances which are far too large to be experimentally accessible.

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