# GENERAL RELATION BETWEEN DRIFT VELOCITY AND DISPERSION OF A MOLECULAR MOTOR*

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We model a processive linear molecular motor as a particle diffusing in a one-dimensional periodic lattice with arbitrary transition rates between its sites. We present a relatively simple proof of a theorem which states that the ratio of the drift velocity $V$ to the diffusion coefficient $D$ has the upper bound $2N/d$, where $N$ is the number of nodes in an elementary cell and $d$ denotes its length. This relation can be used to estimate the minimal value of internal states of the motor and the maximal value of the so called Einstein force, which approximately equals the maximal force exerted by a molecular motor.

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## 1. Introduction

Molecular motors are enzymes mediating intracellular transport and cellular motion in living cells. The most important examples are kinesins (responsible for transport of organelles), myosins (which drive muscle contraction) and dyneins (involved in cellular locomotion) [1].

Based on their function and structure, molecular motors can be divided into several families. Here we will focus on *processive linear* motors. A motor is linear if it moves along a complementary protein fiber (other types of motors include protein pumps, involved in transport across membranes, and rotary motors). A motor is processive if it can travel a long distance before it detaches from the filament.

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A typical example of a processive linear motor is kinesin. It is a mechanoenzyme which transduces the chemical energy of hydrolysis of ATP molecules into mechanical work, which is then used to move vesicles and organelles along microtubules. Each step is powered by hydrolysis of one ATP molecule. The main theoretical challenge is to explain how the chemical energy of ATP is transformed into practically unidirectional motion of protein motors.

Theoretical modeling of the motion of motor proteins has been mainly based on two approaches. The first one, called a thermal ratchet model, regards a motor protein as a Brownian particle diffusing in several periodic, asymmetric potentials which are alternatively switched on and off in stochastic time intervals [2]. In the following we employ the second approach, which is based on an assumption that the motion of a motor can be modeled as a sequence of transitions between discrete mechano-chemical states of the motor, which are represented as nodes of a linear lattice [3–5]. A segment of a microtubule corresponds to an elementary cell of the lattice, and the number of sites in an elementary cell, $N$, is equal to the number of different internal states in a full mechano-chemical cycle of a motor. For kinesin the lattice constant $d = 8$ nm [1,6,7] and $N \geq 4$ [5].

Any theoretical model must account for experimental results. Here we will be interested in an approach which attempts to determine internal properties of molecular motors based on the statistical analysis of their motion as observed in experiments. The fundamental quantities employed in this method are the mean velocity $V = \langle x(t) \rangle / t$ and the dispersion $D = \langle (x(t) - \langle x(t) \rangle)^2 \rangle / 2t$. Having determined these two parameters (in the limit of large $t$), one can find the so called *randomness* $r$ defined simply as [5,8]

$$r \equiv 2D/Vd\,. \tag{1}$$

This quantity can be used to estimate the number of internal states of a molecular motor. The idea is simple: if transitions constitute a Poisson unidirectional process with exactly the same transition rates $k$, then $r = 1/N$ [8]. This idea was extended by Fisher and Kolomeisky [3, 5], who made a conjecture that in a general case of a linear chain with bidirectional Poissonian transitions there is

$$N \geq 1/r\,, \tag{2}$$

which enables one to determine the minimal number of internal states in a full mechano-chemical cycle of a motor.

Another important quantity which can be directly related to $V$ and $D$ is the so called Einstein force

$$F_{\mathrm{E}} \equiv k_{\mathrm{B}} T \frac{V}{D}\,, \tag{3}$$

where $T$ is temperature and $k_{\mathrm{B}}$ denotes the Boltzmann constant. This quantity is a linear-response estimation of the force exerted by a molecular motor [3,5]. Conjecture (2) can be now written as

$$F_{\mathrm{E}} \leq 2k_{\mathrm{B}}T\frac{N}{d}\,. \tag{4}$$

The maximal value of the Einstein force is thus a simple function of three parameters: temperature $T$, a step length $d$ and the number $N$ of different internal states of a motor.

In a recent paper [9] we have given a rigorous proof of relation (2) for linear chains with arbitrary Poisson transitions between nearest-neighbor sites. However, that proof is rather lengthy and complicated. Here we present a different argument justifying (2) and (4). Not only is it much simpler, but it is also more general, as it can be used for systems with transitions between arbitrary lattice sites (provided the lattice is periodic).

The paper is organized as follows. In Section 2 we present a mathematical definition of the model. Section 3 contains the proof of equation (2), and Section 4 is devoted to the discussion of our results.

## 2. Model

We consider a one-dimensional lattice with its sites located at $x_n$, $n \in \mathcal{Z}$. At time $t = 0$ we put a particle at site $x_0 = 0$ and let it jump between the nearest-neighbor lattice sites. Transitions are assumed to represent a Poisson process governed by the master equation

$$\frac{\partial P(n,t)}{\partial t} = k^+_{n-1}P(n-1,t) + k^-_{n+1}P(n+1,t) - (k^+_n + k^-_n)P(n,t)\,, \tag{5}$$

where $P(n,t)$ denotes the probability of finding the particle at site $x_n$ at time $t$ and $k^{\pm}_n \geq 0$ are the (constant in time) transition rates from a site $x_n$ to $x_{n\pm1}$. We assume that the system is periodic in space with a period $N \geq 1$ and a lattice constant $d > 0$. We do not demand that the distances between consecutive lattice sites, $x_{n+1} - x_n$, should be all equal to each other. Our goal is to prove (2) for any choice of $N$, $k^+_n$ and $k^-_n$.

## 3. Proof of relation (2)

Relation (2) is equivalent to

$$D \geq \frac{Vd}{2N}\,. \tag{6}$$

We will prove this inequality by fixing the values of $V$, $d$ and $N$ and finding the minimal value of $D$ as a function of transition rates $k^{\pm}_n$,

$n = 1, \ldots, N$. Since $V/d$ and $D/d^2$ depend only on transition rates $k_n^{\pm}$ [10], the problem of proving (6) reduces to the one of minimizing a rather complicated function of $2N$ nonnegative variables $k_n^{\pm}$.

Probably the simplest proof of inequality (6) is based on a very general and nontrivial property of diffusive lattice systems [10]. Suppose we have a diffusion process on a periodic lattice with Poissonian transitions between its sites and let $k_{mn} \geq 0$ denote the transition rate from site $n$ to $m$. There exists a time interval $\tau$ such $k_{mn}\tau \leq 1$ for all $n$ and $m$. We can thus define another stochastic process on this lattice, in which transitions can occur only at regular intervals $\tau$ and are characterized by *probabilities* $k_{mn}\tau$ ($k_{mn}\tau$ is the probability of jumping from $n$ to $m$). It has been rigorously shown [10] that the drift velocity $V$ and dispersion $D$ calculated in the original, continuous-time system are related to the drift velocity $V^{\mathrm{D}}$ and dispersion $D^{\mathrm{D}}$ of its discrete-time counterpart through general formulae

$$V = V^{\mathrm{D}}, \quad D = D^{\mathrm{D}} + \frac{\tau}{2} V^2 . \tag{7}$$

The problem of finding the combination of transition rates $k_n^{\pm}$ which minimize the value of dispersion $D$ for some fixed values of $V$ and $d$ in the continuous-time process is therefore equivalent to the same problem posed for the corresponding discrete-time system. However, the latter problem is *much* simpler. By definition dispersion $D^{\mathrm{D}}$ cannot be negative. Moreover, $D^{\mathrm{D}} = 0$ for two particular choices of transition probabilities $k_n^{\pm}\tau$: either when $k_n^-\tau = 0$ and $k_n^+\tau = 1$ or when $k_n^-\tau = 1$ and $k_n^+\tau = 0$. In these two cases the motion of a diffusing particle is actually unidirectional and *deterministic* — hence the value of dispersion $D^{\mathrm{D}} = 0$. Clearly, $D^{\mathrm{D}}$ assumes the minimal possible value *only* in these two particular "degenerated" cases where the stochastic, bidirectional process turns into a unidirectional, deterministic one. Non-vanishing transition rates in the corresponding continuous-time process are equal $1/\tau$, and in this case $V = d/N\tau$ and $D = (d/N)^2/2\tau = Vd/2N$ [10]. The minimal value of dispersion $D$ is thus equal to $Vd/2N$, which completes the proof of (6).

It is worth noting that not only have we just proved inequality (6), but we also showed that $V/D$ assumes its maximal value, $2N/d$, if and only if all transitions are unidirectional and of the same magnitude, *i.e.* when for any $1 \leq n, m \leq N$ there is

$$k_n^+ = k_m^+ > 0,\ k_n^- = 0 \quad \text{or} \quad k_n^- = k_m^- > 0,\ k_n^+ = 0 .$$

It is also interesting to note that in our present approach we almost did not employ the assumption that only transitions between nearest-neighbor lattice sites are allowed. The same line of reasoning could be applied for more general systems. The only difference would be that in a general case

there would be several choices of transition rates for which the auxiliary discrete-time process is deterministic. Some of them could be characterized by different values of $N$ and we would have to plug the smallest of them in Eq. (6). However, in the case of molecular motors such complicated models do not seem to be appropriate, as we expect that their behavior is governed by the most probable reaction path [1].

## 4. Conclusions

We have rigorously proved that in diffusive processes on periodic lattices with Poissonian transitions between its nodes the value of diffusion coefficient $D$ is bounded from above by $Vd/2N$, where $V$ is the mean drift velocity, $d$ is the length of the elementary cell, and $N$ denotes the number of sites in the elementary cells. The present approach is much simpler than our previous method employed in Ref. [9]. It is also more general, as it can be applied to arbitrary lattice systems, while our previous approach was applicable only to linear lattices with transitions restricted to the nearest-neighbor sites.

Our result has interesting applications in the theory of molecular motors. First of all it implies that by measuring experimentally the randomness $r \equiv 2D/Vd$ one can determine the minimal number $N$ of internal states of a motor in its full mechano-chemical cycle. As a matter of fact, this approach was already employed in Ref. [5], where it was found that for kinesin $N \geq 4$. Our result gives firmer basis for this kind of argumentation.

Our result implies also that the maximal value of the Einstein force, $F_{\mathrm{E}}$, is $2k_{\mathrm{B}}TN/d$, where $T$ is the temperature and $k_{\mathrm{B}}$ — the Boltzmann constant. We showed that this maximal value is attained if and only if all transitions are unidirectional and of the same magnitude.

Although our approach is valid for any value of $N$ and an arbitrary choice of transition rates, in the context of molecular motors it still refers to a simplified situation. First, we assumed that the motion of a motor protein can be reduced to diffusion of a Brownian particle on a linear chain of lattice nodes, and other topologies deserve at least equal attention [2, 4, 11, 12]. Second, we assumed that transitions constitute a Poisson process. Although this hypothesis is confirmed by recent experiments on myosin [13], it is well known that transition rates with other probability density functions may lead to completely different upper bounds for dispersion $D$ (and hence the upper bound for $F_{\mathrm{E}}$ and the lower bound for $r$ may also change) [3–5]. Nevertheless, the force calculated using all these approximations (4.3 pN) agrees quite well with the experimental value of the stalling force $F_{\mathrm{s}}$ for kinesin (different experimental techniques yielded $F_{\mathrm{s}} \sim 4{-}8$ pN [1]). Further work is, of course, required to clarify the relevance of the above-mentioned problems.

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