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A new derivation of the randomness parameter

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For a stochastic stepper that can only step forward, there are two randomnesses: (1) the randomness in the cycle time and (2) the randomness in the number of steps (cycles) over long time. The equivalence between these two randomnesses was previously established using the approach of Laplace transform [M. J. Schnitzer and S. M. Block, "Statistical kinetics of processive enzymes," Cold Spring Harbor Symp. Quant. Biol. **60**, 793 (1995)]. In this study, we first discuss the problems of this approach when the cycle time distribution has a discrete component, and then present a new derivation based on the framework of semi-Markov processes with age structure. We also show that the equivalence between the two randomnesses depends on the existence of the first moment of the waiting time for completing the first cycle, which is strongly affected by the initial age distribution. Therefore, any derivation that concludes the equivalence categorically regardless of the initial age distribution is mathematically questionable. *© 2007 American Institute of Physics.* [DOI: 10.1063/1.2795215]

I. INTRODUCTION

Many molecular motors move in steps. For example, a kinesin dimer walks on a microtubule filament in 8 nm steps.[1–4] For a kinesin dimer, each motor step is coupled to one adenosine triphosphate (ATP) hydrolysis cycle.[1,5] Assuming at the end of each reaction cycle, the kinesin dimer returns to the same statistical configuration as the one at the beginning of the cycle with the roles of two heads switched; in other words, each reaction cycle starts with the same statistical configuration, then each reaction cycle is independent of any other reaction cycle. This allows us to model the kinesin dimer as a stochastic stepper, a special case of semi-Markov processes,[6] in which the cycle time of each motor step has the same distribution and is statistically independent of that of any other step.[7] The distribution of the cycle time, however, can be arbitrary and is not necessarily exponential. The framework of stochastic steppers is a very general one. It can accommodate backward motor steps and variable motor step sizes.[8] In this study, we focus on the simple case where the stochastic stepper can only move forward and the step size is uniform.

As a first step in peeking into the chemical reaction inside the motor and deciphering the motor mechanism, one would like to obtain the statistics of the cycle time. A key statistical quantity of the motor that one would like to know is the randomness in the cycle time, which is defined as the variance of cycle time divided by the square of the average cycle time.[9,7] Unfortunately, with the current single molecule experimental technologies, it is still not possible to observe/record the position of motor directly and accurately. If the motor position could be measured directly and accurately, then it would be straightforward to collect a large number of samples of the cycle time. As shown in Fig. 1, in many single molecule motor experiments, the position of motor is inferred by following the position of a large cargo (a latex bead) that is elastically linked to the motor.[1,10,2,11] Although certain behaviors of the motor can still be observed by following the cargo position, it is difficult to extract accurate sample values of cycle time from the time series of

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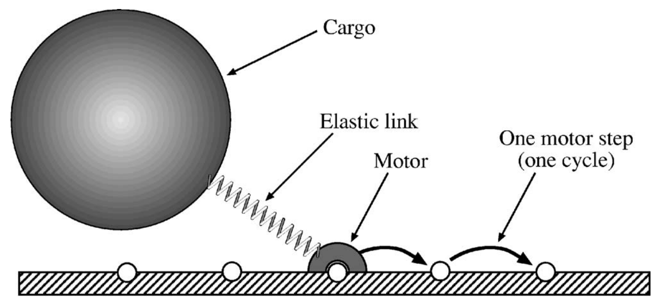

FIG. 1. Schematic diagram of a motor-cargo system in single molecule experiments.[1,10,2,11] The motor moves on a polymer track in steps. Each motor step corresponds to one reaction cycle and is statistically independent of any other steps. Mathematically, the motor is modeled as a stochastic stepper. The motor is elastically linked to a cargo that is much larger than the motor, and can be controlled and monitored by a laser trap. The motor behaviors are inferred from the measurements of the cargo.

cargo positions. On the positive side, the motor and the cargo are linked. Consequently, over long time, they must have asymptotically the same average displacement and the same variance in displacement. Thus, the average velocity and the effective diffusion coefficient of the motor can be calculated from the measured time series of cargo positions.

Since the statistics of motor displacement over long time can be measured reliably, we can consider the randomness in the number of motor steps over long time, which is defined as the variance of number of motor steps divided by the average number of steps. In Ref. 7, it was established that the randomness in the number of motor steps is the same as the randomness in the cycle time. This result is very significant in that it relates what we can measure externally from the time series of cargo positions to what we want to know about the internal motor operation. The equivalence between the two randomnesses was derived using the approach of Laplace transform.[7] As we will show below, when the cycle time distribution has a discrete component the approach of Laplace transform breaks down but amazingly the equivalence between the two randomnesses still holds. In this study, we present a new derivation for the equivalence between the two randomnesses. The new derivation is based on the framework of semi-Markov processes with age structure.[12,13] More precisely, we prove the equivalence between these two randomnesses for the general case where the cycle time of regular cycles has the first two moments and the waiting time for completing the first cycle has the first moment. We also give an example to show that the two randomnesses are different if the first moment of the waiting time for completing the first cycle is not finite. The waiting time for completing the first cycle is strongly affected by the initial age distribution. Therefore, any serious attempt on proving the equivalence between these two randomnesses must take into consideration the initial age distribution. In other words, any derivation that concludes the equivalence categorically regardless of the initial age distribution is doomed mathematically not rigorous, and consequently, such a derivation should not be viewed as a rigorous substitution for the derivation presented here.

The rest of the paper is organized as follows. In Sec. II, we first describe the renewal model for molecular motors and review the equivalence proof using the approach of Laplace transform. Then we present a counter example to show how the approach of Laplace transform breaks down. In Sec. III, we present a new derivation for the equivalence between the two randomnesses. To facilitate the new proof, the renewal model introduced in Sec. II is described again in the framework of semi-Markov processes with age structure. The new proof is based on this framework. In Sec. IV, we give a special example to demonstrate that the initial age distribution does affect the validity of the equivalence.

II. RANDOMNESS PARAMETER

As shown in Fig. 1, we consider a motor-cargo system in which (a) the motor goes forward stochastically in steps of uniform size, (b) each motor step corresponds to one reaction cycle and is independent of any other steps, (c) the cycle time of every step has the same probability density function $p(t)$, and (d) the motor and the cargo are elastically linked whereas only the cargo behaviors are measurable in experiments. Let L be the motor step size, and T be the random cycle time of a motor step, i.e., the time it takes to complete a motor step. Let $p(t)$ denote the probability density of the random cycle time T. Mathematically, that is,

$$p(t) = \lim_{\Delta t\to 0} \frac{\Pr[t \leqslant T < t+\Delta t]}{\Delta t}. \tag{1}$$

The randomness in the cycle time is defined as

$$R_T \equiv \frac{\mathrm{var}(T)}{\langle T\rangle^2}, \tag{2}$$

where $\langle T\rangle$ denotes the mean and $\mathrm{var}(T)=\langle T^2\rangle-\langle T\rangle^2$ denotes the variance of random cycle time T. As we pointed out above, R_T informs us about the internal motor operation but R_T is not directly measurable in experiments. A quantity that can be measured in experiments is the randomness in the number of steps over long time. Let $N(t)$ be the stochastic number of steps the motor has finished by time t, and $Y(t)$ be the stochastic position of the cargo at time t. The stochastic position of the motor at time t is $X(t)=N(t)L$. Since the motor and the cargo are linked, over long time, $X(t)$ and $Y(t)$ must have asymptotically the same mean and the same variance. The randomness in the number of steps is defined below and can be calculated from $Y(t)$:[9,14]

$$R_N \equiv \lim_{t\to\infty} \frac{\mathrm{var}(N(t))}{\langle N(t)\rangle} = \lim_{t\to\infty} \frac{\mathrm{var}(X(t))}{\langle X(t)\rangle L} = \lim_{t\to\infty} \frac{\mathrm{var}(Y(t))}{\langle Y(t)\rangle L}. \tag{3}$$

If each reaction cycle is simply a Markov step with transition rate r, then the cycle time has the exponential distribution, $p(t)=re^{-rt}$, and the number of steps finished by time t has the Poisson distribution, $\Pr[N(t)=n]=\lambda^n e^{-\lambda}/n!$, where $\lambda=rt$. It follows that $\langle T\rangle^2=\mathrm{var}(T)=1/r^2$, and $\langle N(t)\rangle=\mathrm{var}(N(t))=\lambda$. Thus, we have $R_T=R_N$ for this special case. In Ref. 7, $R_T=R_N$ was established for the general case using the approach of Laplace transform. Below we first review the derivation of $R_T=R_N$ in Ref. 7. Then we discuss the problems of this approach. In the next section, we present a new derivation of $R_T=R_N$.

Suppose the motor has just arrived at step 0 at time 0. This specification is necessary because the advance from step 0 to step 1 may not be a Markov step and the motor system does remember how long it has been waiting at step 0. Let $P(n,t)\equiv\Pr[N(t)=n]$. For $n\geqslant 0$, $P(n,t)$ satisfies

$$P(0,t) = \int_t^\infty p(\tau)d\tau,$$

$$P(n+1,t) = \int_0^t P(n,t-\tau)p(\tau)d\tau. \tag{4}$$

Let $\tilde{f}(s)$ denote the Laplace transform of $f(t)$: $\tilde{f}(s)\equiv L[f(t)]\equiv\int_0^\infty e^{-st}f(t)dt$. Taking the Laplace transform of Eq. (4) gives us

$$\tilde{P}(0,s) = \frac{1-\tilde{p}(s)}{s},$$

$$\tilde{P}(n+1,s) = \tilde{P}(n,s)\tilde{p}(s). \tag{5}$$

Applying Eq. (5) recursively, we obtain an explicit expression for $\tilde{P}(n,s)$:

$$\tilde{P}(n,s) = \frac{1-\tilde{p}(s)}{s}\tilde{p}^n(s). \tag{6}$$

Expressing $\langle N(t)\rangle$ and $\langle N^2(t)\rangle$ in terms of $P(n,t)$, we have

$$\langle N(t)\rangle = \sum_{n=0}^{\infty} nP(n,t),$$

$$\langle N^2(t)\rangle = \sum_{n=0}^{\infty} n^2 P(n,t). \tag{7}$$

Taking the Laplace transform of $\langle N(t)\rangle$ and $\langle N^2(t)\rangle$ yields

$$L[\langle N(t)\rangle](s) = \sum_{n=0}^{\infty} n\tilde{P}(n,s) = \frac{1-\tilde{p}(s)}{s}\sum_{n=0}^{\infty} n\tilde{p}^n(s) = \frac{\tilde{p}(s)}{s(1-\tilde{p}(s))}, \tag{8}$$

$$L[\langle N^2(t)\rangle](s) = \sum_{n=0}^{\infty} n^2\tilde{P}(n,s) = \frac{1-\tilde{p}(s)}{s}\sum_{n=0}^{\infty} n^2\tilde{p}^n(s) = \frac{\tilde{p}(s)+\tilde{p}^2(s)}{s(1-\tilde{p}(s))^2}. \tag{9}$$

In deriving Eqs. (8) and (9) we have used the summation formulas listed below:

$$\sum_{n=0}^{\infty} x^n = \frac{1}{1-x},$$

$$\sum_{n=0}^{\infty} nx^n = x\frac{d}{dx}\left(\sum_{n=0}^{\infty} x^n\right) = \frac{x}{(1-x)^2},$$

$$\sum_{n=0}^{\infty} n^2x^n = x\frac{d}{dx}\left(\sum_{n=0}^{\infty} nx^n\right) = \frac{x+x^2}{(1-x)^3}.$$

To find the behaviors of $L[\langle N(t)\rangle](s)$ and $L[\langle N^2(t)\rangle](s)$ for small s, we expand $\tilde{p}(s)$:

$$\left.\frac{d^k\tilde{p}(s)}{ds^k}\right|_{s=0} = \left.\int_0^{\infty}(-t)^k e^{-st}p(t)dt\right|_{s=0} = (-1)^k\langle T^k\rangle,$$

$$\tilde{p}(s) = 1 - \langle T\rangle s + \frac{\langle T^2\rangle}{2}s^2 + O(s^3).$$

Substituting the expansion into $L[\langle N(t)\rangle](s)$ and $L[\langle N^2(t)\rangle](s)$ yields

$$L[\langle N(t)\rangle] = \frac{1}{\langle T\rangle}\frac{1}{s^2} - \left(\frac{2\langle T\rangle^2 - \langle T^2\rangle}{2\langle T\rangle^2}\right)\frac{1}{s} + O(1), \tag{10}$$

$$L[\langle N(t)^2\rangle] = \frac{2}{\langle T\rangle^2}\frac{1}{s^3} - \left(\frac{3\langle T\rangle^2 - 2\langle T^2\rangle}{\langle T\rangle^3}\right)\frac{1}{s^2} + O\left(\frac{1}{s}\right). \tag{11}$$

In Ref. 7, it was assumed that $\langle N(t)\rangle$ and $\langle N^2(t)\rangle$ have Laurent expansions as $t\to\infty$:

$$\text{Assumption:}\langle N(t)\rangle = \sum_{k=-\infty}^{\infty} c_k^{(1)} t^k, \quad \langle N^2(t)\rangle = \sum_{k=-\infty}^{\infty} c_k^{(2)} t^k. \tag{12}$$

Under this assumption, the coefficients in the Laurent expansions as $t \to \infty$ are calculated from the Laurent expansions as $s \to 0$ of their Laplace transforms (10) and (11).

$$\langle N(t)\rangle = \frac{1}{\langle T\rangle} t - \left(\frac{2\langle T\rangle^2 - \langle T^2\rangle}{2\langle T\rangle^2}\right) + O\left(\frac{1}{t}\right), \tag{13}$$

$$\langle N(t)^2\rangle = \frac{1}{\langle T\rangle^2} t^2 - \left(\frac{3\langle T\rangle^2 - 2\langle T^2\rangle}{\langle T\rangle^3}\right) t + O(1), \tag{14}$$

which leads to

$$\lim_{t\to\infty} \frac{\langle N^2(t)\rangle - \langle N(t)\rangle^2}{\langle N(t)\rangle} = \frac{\langle T^2\rangle - \langle T\rangle^2}{\langle T\rangle^2}. \tag{15}$$

In other words, the two randomnesses are the same: $R_N = R_T$. Assumption (12) is the key in the derivation in Ref. 7. Note, in particular, that the existence of Laurent expansion as $s \to 0$ for the Laplace transform does not imply the existence of Laurent expansion as $t \to \infty$ for the original function. For example, $f(t) = t + \sin t$ does not have a Laurent expansion as $t \to \infty$ while its Laplace transform $\tilde{f}(s) = (1/s^2) + [1/(s^2+1)]$ has a Laurent expansion as $s \to 0$: $\tilde{f}(s) = (1/s^2) + 0(1/s) + O(1)$. When the cycle time has a discrete distribution, assumption (12) breaks down but the conclusion $R_N = R_T$ still holds. To illustrate this, we consider the cycle time distribution given below:

$$\Pr[T = t] = \begin{cases} 0.5, & t = 1 \\ 0.5, & t = 2 \\ 0 & \text{otherwise}. \end{cases} \tag{16}$$

The first two moments of T and the randomness in T are given by

$$\langle T\rangle = \tfrac{3}{2}, \quad \langle T^2\rangle = \tfrac{5}{2}, \quad \operatorname{var}(T) = \tfrac{1}{4}, \quad R_T = \tfrac{1}{9}. \tag{17}$$

For time t in $[k, k+1)$ where k is an integer, the first two moments of $N(t)$ have the expressions (see Appendix for the derivation)

$$\langle N(t)\rangle = \frac{2}{3}k - \frac{1}{9}\left[1 - \left(\frac{-1}{2}\right)^k\right], \quad k \le t < k+1, \tag{18}$$

$$\langle N^2(t)\rangle = \frac{4}{9}k^2 - \frac{2}{27}k\left[1 - \left(\frac{-1}{2}\right)^k\right] + \frac{1}{9}\left[1 - \left(\frac{-1}{2}\right)^k\right], \quad k \le t < k+1. \tag{19}$$

It is clear that Laurent expansions (13) and (14), predicted from the Laplace transform, are invalid for this discrete cycle time distribution. The equivalence between R_N and R_T, however, still holds. The randomness in $N(t)$ as $t \to \infty$ is $R_N = 1/9$, the same as R_T.

III. A NEW DERIVATION

The motor is modeled as a stochastic stepper, a special case of semi-Markov processes.[15] In a semi-Markov process, the system does not remember how it got to the current state but it does remember its age. The age of the system is defined as the time elapsed since the latest arrival at the current state. At the moment when the system jumps to another state, the age is reset to zero. After that, the age increases with the time until the next jump. Let $A(t)$ be the age of the system at time

t. Let $\rho(n,\tau,t)$ be the probability density that the system has age τ in state n at time t. Here n refers to the number of motor steps completed. Mathematically, $\rho(n,\tau,t)$ is defined as

$$\rho(n,\tau,t) \equiv \lim_{\delta\tau\to 0} \frac{\Pr[N(t)=n,\ \tau \leqslant A(t) < \tau+\delta\tau]}{\delta\tau}. \tag{20}$$

For our motor system, $\rho(n,\tau,t)$ is governed by the conservation of probability:

$$\frac{\partial\rho(n,\tau,t)}{\partial t} = -\frac{\partial\rho(n,\tau,t)}{\partial\tau} - \rho(n,\tau,t)\beta(\tau),$$

$$\beta(\tau) \equiv \frac{p(\tau)}{\displaystyle\int_\tau^\infty p(s)ds}, \tag{21}$$

where $\beta(\tau)$ is called the hazard function and is the conditional rate of completing the current cycle at age τ given that the cycle is not completed in age $[0,\tau)$. In Eq. (21), the first term on the right hand side corresponds to the fact that if no transition occurs then the age of the system increases with the time. The second term on the right hand side of Eq. (21) reflects that a transition out of a state reduces the probability of that state. From its definition, it follows that the hazard function $\beta(\tau)$ satisfies

$$-\int_0^\tau \beta(s)ds = \log\left(\int_\tau^\infty p(s)ds\right). \tag{22}$$

This relation between $\beta(s)$ and $p(s)$ will be very useful in the analysis below. Since all new arrivals have age 0, the boundary condition for $\rho(n,\tau,t)$ is

$$\rho(0,0,t) = 0, \quad t > 0,$$

$$\rho(n,0,t) = \int_0^\infty \rho(n-1,\tau,t)\beta(\tau)d\tau, \quad t>0, \quad n>0. \tag{23}$$

Here $\rho(0,0,t)=0$ reflects the fact that the motor system starts in state 0 at time 0. Because we assume that the motor goes only forward there is no transition into state 0. To determine the evolution of $\rho(n,\tau,t)$, an initial state-age distribution needs to be specified. A straightforward initial state-age distribution is

$$\text{initial distribution 0:} \quad \rho(0,\tau,0) = \delta(\tau),$$

$$\rho(n,\tau,0) = 0, \quad n > 0, \tag{24}$$

which corresponds to that all motors in the ensemble start with age 0 in state 0 at time 0. It turns out that this seemingly simple initial condition is neither experimentally easy to implement nor mathematically convenient. In experiments, to implement the initial condition $\rho(0,\tau,0)=\delta(\tau)$, we need to start a new cycle with age 0 at the beginning of the experiment, or equivalently we need to detect accurately the time at which a cycle is completed and the next cycle is started. In experiments, a more realistic situation is that the system has a random age at time 0. This is especially true if in the statistical calculation the ensemble is created by cutting one or a few long time series into many time series.[9,1,14] Thus, it is more consistent with the experiments if we use the stationary age distribution as the initial condition. Mathematically, the age distribution (regardless of the state) at time t is

$$\rho(\tau,t) \equiv \sum_{n=0}^{\infty} \rho(n,\tau,t). \tag{25}$$

The governing equation and the boundary condition for the age distribution are obtained by summing Eqs. (21) and (23) over all states:

$$\frac{\partial \rho(\tau,t)}{\partial t} = -\frac{\partial \rho(\tau,t)}{\partial \tau} - \rho(\tau,t)\beta(\tau),$$

$$\rho(0,t) = \int_0^{\infty} \rho(\tau,t)\beta(\tau)d\tau. \tag{26}$$

Let $\rho^{(S)}(\tau)$ be the stationary age distribution. Setting the left side of Eq. (26) to zero, solving for $\rho^{(S)}(\tau)$, and using the relation (22) yield

$$\rho^{(S)}(\tau) = \frac{\exp\left(-\int_0^{\tau}\beta(s)ds\right)}{\int_0^{\infty}\exp\left(-\int_0^{\tau}\beta(s)ds\right)d\tau} = \frac{\int_{\tau}^{\infty}p(s)ds}{\int_0^{\infty}\int_{\tau}^{\infty}p(s)dsd\tau} = \frac{\int_{\tau}^{\infty}p(s)ds}{\int_0^{\infty}\tau p(\tau)d\tau} = \frac{\int_{\tau}^{\infty}p(s)ds}{\langle T\rangle}. \tag{27}$$

A more reasonable (more consistent with experiments) initial state-age distribution is to start the ensemble of motors at state 0 with the stationary age distribution $\rho^{(S)}(\tau)$:

$$\text{initial distribution 1:} \quad \rho(0,\tau,0) = \rho^{(S)}(\tau),$$

$$\rho(n,\tau,0) = 0, \quad n > 0. \tag{28}$$

In the rest of this section, we will first prove $R_N = R_T$ for initial state-age distribution (28). Then we will extend the conclusion $R_N = R_T$ to initial state-age distribution (24). Finally, we will extend the conclusion $R_N = R_T$ to the general case where the first moment of the waiting time for completing the first cycle is finite. To demonstrate the importance of the first moment of the waiting time for completing the first cycle, in the next section, we will present an example to show $R_N \neq R_T$ if the first moment of the waiting time for completing the first cycle is not finite.

A. The derivation in the case of initial condition (28)

With the initial condition (28), the age distribution will remain stationary: $\Sigma_{n=0}^{\infty}\rho(n,\tau,t) = \rho^{(S)}(\tau)$. To calculate $\langle N(t)\rangle$, we first express $\langle N(t)\rangle$ in terms of $\rho(n,\tau,t)$:

$$\langle N(t)\rangle = \sum_{n=0}^{\infty} n \int_0^{\infty} \rho(n,\tau,t)d\tau. \tag{29}$$

Differentiating with respect to t, using differential equation (21) and boundary condition (23), we obtain

$$\begin{aligned}\frac{d\langle N(t)\rangle}{dt} &= -\sum_{n=0}^{\infty} n \int_0^{\infty}\left(\frac{\partial \rho(n,\tau,t)}{\partial \tau} + \rho(n,\tau,t)\beta(\tau)\right)d\tau = \sum_{n=0}^{\infty} n(\rho(n,0,t) - \rho(n+1,0,t)) \\ &= \sum_{n=0}^{\infty}\rho(n,0,t) = \rho^{(S)}(0) = \frac{1}{\langle T\rangle}.\end{aligned} \tag{30}$$

Similarly, for the second moment, we have

$$\langle N^2(t)\rangle = \sum_{n=0}^{\infty} n^2 \int_0^{\infty} \rho(n,\tau,t)d\tau. \tag{31}$$

Differentiating with respect to t, using differential equation (21) and boundary condition (23), yields

$$\frac{d\langle N^2(t)\rangle}{dt} = -\sum_{n=0}^{\infty} n^2 \int_0^{\infty}\left(\frac{\partial\rho(n,\tau,t)}{\partial\tau} + \rho(n,\tau,t)\beta(\tau)\right)d\tau = \sum_{n=0}^{\infty} n^2(\rho(n,0,t)-\rho(n+1,0,t))$$
$$= \sum_{n=0}^{\infty}(2n-1)\rho(n,0,t) \equiv \frac{2}{\langle T\rangle}q(0,t) + \frac{2t}{\langle T\rangle^2} - \frac{1}{\langle T\rangle}, \tag{32}$$

where function $q(\tau,t)$ is defined as

$$q(\tau,t) \equiv \langle T\rangle\sum_{n=0}^{\infty} n\rho(n,\tau,t) + (\tau-t)\rho^{(S)}(\tau). \tag{33}$$

The initial condition (28) implies $\langle N(0)\rangle=0$ and $\langle N^2(0)\rangle=0$. Integrating Eqs. (30) and (32) with respect to t yields

$$\langle N(t)\rangle = \frac{t}{\langle T\rangle}, \tag{34}$$

$$\langle N^2(t)\rangle = \frac{2}{\langle T\rangle}\int_0^t q(0,s)ds + \frac{t^2}{\langle T\rangle^2} - \frac{t}{\langle T\rangle}. \tag{35}$$

Here we should point out that result (34) corresponds to the renewal theorem in Ref. 16. Using these results to calculate R_N, we obtain

$$R_N \equiv \lim_{t\to\infty}\frac{\langle N^2(t)\rangle - \langle N(t)\rangle^2}{\langle N(t)\rangle} = \lim_{t\to\infty}\frac{2}{t}\int_0^t q(0,s)ds - 1 = 2\left(\lim_{t\to\infty}\frac{1}{t}\int_0^t q(0,s)ds - \frac{\langle T^2\rangle}{2\langle T\rangle^2}\right) + R_T. \tag{36}$$

For the limit enclosed in the parentheses in Eq. (36), we have the theorem below.

Theorem 1: Function $q(\tau,t)$ defined in Eq. (33) has the property

$$\lim_{t\to\infty}\frac{1}{t}\int_0^t q(0,s)ds = \frac{\langle T^2\rangle}{2\langle T\rangle^2}. \tag{37}$$

Remark: Combining the result of Theorem 1 and Eq. (36) leads immediately to the desired conclusion $R_N = R_T$.

To facilitate the proof of Theorem 1, we introduce a lemma.

Lemma 1: Consider a function $q(\tau,t)$ [not necessarily the one defined in Eq. (33)]. Suppose $q(\tau,t)$ satisfies the differential equation

$$\frac{\partial q(\tau,t)}{\partial t} = -\frac{\partial q(\tau,t)}{\partial\tau} - q(\tau,t)\beta(\tau). \tag{38}$$

Then we have

$$q(\tau,t) = q(\tau-c,t-c)\frac{\rho^{(S)}(\tau)}{\rho^{(S)}(\tau-c)}. \tag{39}$$

Proof of Lemma 1: We rewrite differential equation (38) as

$$\frac{d}{ds}q(\tau+s,t+s) = -q(\tau+s,t+s)\beta(\tau+s).$$

It follows that

$$q(\tau,t) = q(\tau-c,t-c)\exp\left(-\int_{\tau-c}^{\tau}\beta(s)ds\right).$$

Using property (22) of $\beta(\tau)$ and the expression of $\rho^{(S)}(\tau)$ given in Eq. (27), we obtain

$$\exp\left(-\int_{\tau-c}^{\tau}\beta(s)ds\right) = \frac{\rho^{(S)}(\tau)}{\rho^{(S)}(\tau-c)},$$

which leads directly to Eq. (39).

Proof of Theorem 1: Using Eqs. (21), (23), and (27), it is straightforward to verify that $q(\tau,t)$ defined in Eq. (33) satisfies differential equation (38) and boundary condition

$$q(0,t) = \int_0^{\infty} q(\tau,t)\beta(\tau)d\tau. \tag{40}$$

Setting $t=0$ in Eq. (33), we see that $q(\tau,t)$ satisfies the initial condition $q(\tau,0)=\tau\rho^{(S)}(\tau)$. Using differential equation (38), boundary condition (40), and Lemma 1, one can show the following.

(i) $q(\tau,t)$ is non-negative.
(ii) $\int_0^\infty \tau\rho^{(S)}(\tau)d\tau=\int_0^\infty\tau\int_\tau^\infty p(s)dsd\tau/\langle T\rangle=\int_0^\infty\tau^2p(\tau)d\tau/2\langle T\rangle=\langle T^2\rangle/2\langle T\rangle\equiv\alpha$.
(iii) $\int_0^\infty q(\tau,t)d\tau=\int_0^\infty q(\tau,0)d\tau=\alpha$.
(iv) It follows from (iii) that $\int_0^t\int_0^\infty q(\tau,s)d\tau ds=\alpha t$.
(v) It follows from Lemma 1 that $q(\tau,t)=(\tau-t)\rho^{(S)}(\tau)$ for $\tau>t$.
(vi) It follows from Lemma 1 that $q(\tau,t)=q(0,t-\tau)\rho^{(S)}(\tau)\langle T\rangle$ for $\tau<t$.

For the convenience of discussion below, let us introduce

$$h(t) \equiv \int_0^t q(0,s)ds. \tag{41}$$

We divide the integration region in (iv) into two parts: the region of $\tau>t$ and the region of $\tau<t$. For the region of $\tau>t$, using result (v) listed above and then applying integration by parts, we have

$$\int_0^t\int_s^\infty q(\tau,s)d\tau ds = \int_0^t\int_0^\infty \tau\rho^{(S)}(\tau+s)d\tau ds = \frac{1}{2\langle T\rangle}\int_0^t\int_0^\infty \tau^2p(\tau+s)d\tau ds. \tag{42}$$

The inner layer integral on the right hand side of Eq. (42) satisfies

$$0<\int_0^\infty \tau^2p(\tau+t)d\tau<\int_0^\infty(\tau+t)^2p(\tau+t)d\tau=\int_t^\infty\tau^2p(\tau)d\tau. \tag{43}$$

Since the second moment of T exists, we have $\lim_{t\to\infty}\int_t^\infty\tau^2p(\tau)d\tau=0$. Combining this result with inequality (43) yields $\lim_{t\to\infty}\int_0^\infty\tau^2p(\tau+t)d\tau=0$. Dividing Eq. (42) by t, taking the limit as $t\to\infty$, and applying L'Hospital's rule, we obtain

$$\lim_{t\to\infty}\frac{1}{t}\int_0^t\int_s^\infty q(\tau,s)d\tau ds = \lim_{t\to\infty}\frac{1}{2\langle T\rangle}\int_0^\infty\tau^2p(\tau+t)d\tau=0. \tag{44}$$

Thus, using result (iv) listed above and result (44), we arrive at

$$\lim_{t\to\infty}\frac{1}{t}\int_0^t\int_0^s q(\tau,s)d\tau ds=\lim_{t\to\infty}\frac{1}{t}\left(\alpha t-\int_0^t\int_s^\infty q(\tau,s)d\tau ds\right)=\alpha. \tag{45}$$

On the other hand, for the region of $\tau<t$, using result (vi) listed above, we have

$$\begin{aligned}\int_0^t\int_0^s q(\tau,s)d\tau ds&=\int_0^t\int_\tau^t q(\tau,s)dsd\tau=\langle T\rangle\int_0^t\int_\tau^t q(0,s-\tau)\rho^{(S)}(\tau)dsd\tau\\&=\langle T\rangle\int_0^t\left(\int_0^{t-\tau}q(0,s)ds\right)\rho^{(S)}(\tau)d\tau=\langle T\rangle\int_0^t h(t-\tau)\rho^{(S)}(\tau)d\tau.\end{aligned} \tag{46}$$

Combining results (45) and (46) for the region of $\tau<t$ yields

$$\lim_{t\to\infty}\frac{g(t)}{t}=\frac{\alpha}{\langle T\rangle}, \tag{47}$$

where $g(t)\equiv\int_0^t h(t-s)\rho^{(S)}(s)ds$. Since $\rho^{(S)}(s)$ is a probability density, for any $\epsilon>0$ there exists M such that $\int_0^M\rho^{(S)}(s)ds\geqslant(1-\epsilon)$. Recall that $h(t)$ is non-negative and nondecreasing. It follows that

$$g(t)=\int_0^t h(t-s)\rho^{(S)}(s)ds\leqslant h(t)\int_0^t\rho^{(S)}(s)ds\leqslant h(t),$$

$$\begin{aligned}g(t+M)&=\int_0^{t+M}h(t+M-s)\rho^{(S)}(s)ds\geqslant\int_0^M h(t+M-s)\rho^{(S)}(s)ds\geqslant h(t)\int_0^M\rho^{(S)}(s)ds\\&\geqslant h(t)(1-\epsilon).\end{aligned}$$

Combining these two inequalities, we obtain

$$\frac{g(t)}{t}\leqslant\frac{h(t)}{t}\leqslant\frac{1}{1-\epsilon}\frac{t+M}{t}\frac{g(t+M)}{t+M}.$$

Taking the limit as $t\to\infty$, using Eq. (47), and then taking the limit as $\epsilon\to0$, we arrive at

$$\lim_{t\to\infty}\frac{h(t)}{t}=\frac{\alpha}{\langle T\rangle}=\frac{\langle T^2\rangle}{2\langle T\rangle^2},$$

which is equivalent to property (37). This completes the proof of Theorem 1.

B. Extending the conclusion to the general case

In the previous subsection, we proved the equivalence of the two randomnesses $R_N=R_T$ for initial condition (28). In single molecule motor experiments, initial condition (28) is the only realistic and relevant initial condition. Thus, in studies of single molecule motors, we need $R_N=R_T$ only for initial condition (28). For mathematical completeness, in this subsection, we first extend the conclusion $R_N=R_T$ to the case of initial condition (24). The case of initial condition (24) can be regarded as the canonical case where all motors start with age 0 at state 0 at time 0. Finally, based on the results for the canonical case, we extend the conclusion $R_N=R_T$ to the general case where the first moment of the waiting time for completing the first cycle is finite.

In the discussion below, we need to refer to both of these two cases. To clearly distinguish them, for the canonical initial condition (24) we shall use $\rho_0(n,\tau,t)$ and $N_0(t)$ to denote the probability density and the number of motor steps; for initial condition (28) we shall use the notations $\rho_1(n,\tau,t)$ and $N_1(t)$. In the previous subsection, we have proved

$$\langle N_1(t)\rangle = \frac{t}{\langle T\rangle}, \quad \lim_{t\to\infty}\frac{\mathrm{var}(N_1(t))}{t} = \frac{R_T}{\langle T\rangle}. \tag{48}$$

Below we will first extend the conclusion to the canonical case (Theorem 2)

$$\lim_{t\to\infty}\frac{\langle N_0(t)\rangle}{t} = \frac{1}{\langle T\rangle}, \quad \lim_{t\to\infty}\frac{\mathrm{var}(N_0(t))}{t} = \frac{R_T}{\langle T\rangle}. \tag{49}$$

Then we will extend the conclusion to the general case (Theorem 3)

$$\lim_{t\to\infty}\frac{\langle N_{1*}(t)\rangle}{t} = \frac{1}{\langle T\rangle}, \quad \lim_{t\to\infty}\frac{\mathrm{var}(N_{1*}(t))}{t} = \frac{R_T}{\langle T\rangle}. \tag{50}$$

We shall proceed step by step and present the derivation as a sequence of lemmas leading to the main theorems.

Lemma 2:

(i) $\langle N_0(t)\rangle$ is non-negative, is a nondecreasing function of t, and satisfies

$$0 \leqslant \langle N_0(t_1+t_2)\rangle - \langle N_0(t_1)\rangle \leqslant c_0 + c_0 t_2 \quad \text{for } t_1 \geqslant 0, \quad t_2 \geqslant 0. \tag{51}$$

(ii) $\langle N_0^2(t)\rangle$ is non-negative, is a nondecreasing function of t, and satisfies

$$0 \leqslant \langle N_0^2(t_1+t_2)\rangle^{1/2} - \langle N_0^2(t_1)\rangle^{1/2} \leqslant c_1 + c_1 t_2 \quad \text{for } t_1 \geqslant 0, \quad t_2 \geqslant 0, \tag{52}$$

where constants $c_0 > 1$ and $c_1 > 1$ are independent of t_1 and t_2.

Remark: Note that $\langle N_0(t)\rangle$ and $\langle N_0^2(t)\rangle$ may be discontinuous. Result (i) of Lemma 2 corresponds to a modified form of the renewal theorem in Ref. 16.

Proof of Lemma 2: Since each realization $N_0(t)$ is non-negative and is a nondecreasing function of t, it follows that both $\langle N_0(t)\rangle$ and $\langle N_0^2(t)\rangle$ are non-negative and are nondecreasing functions of t. Each realization of $N_0(t_1+t_2)$ can be written as

$$N_0(t_1+t_2) = \begin{cases} N_0(t_1) + 1 + N_0(t_2 - t_c), & 0 < t_c \leqslant t_2 \\ N_0(t_1), & t_c > t_2, \end{cases} \tag{53}$$

where t_1+t_c is the time at which the first motor step after time t_1 is completed. Taking average on both sides of Eq. (53) yields

$$\langle N_0(t_1+t_2)\rangle \leqslant \langle N_0(t_1)\rangle + 1 + \langle N_0(t_2)\rangle. \tag{54}$$

Setting $t_2=1$ in Eq. (54) and applying Eq. (54) repeatedly, we obtain that for positive integer k,

$$\langle N_0(t_1+k)\rangle \leqslant \langle N_0(t_1)\rangle + c_0 k, \quad c_0 = 1 + \langle N_0(1)\rangle. \tag{55}$$

For $k-1 < t_2 \leqslant k$, we have

$$\langle N_0(t_1+t_2)\rangle \leqslant \langle N_0(t_1)\rangle + c_0 + c_0 t_2. \tag{56}$$

To derive (ii), we set $t_2=1$ in Eq. (53), square both sides, and then take average

$$\langle N_0^2(t_1+1)\rangle \leqslant \langle (N_0(t_1) + 1 + N_0(1))^2\rangle.$$

Expanding the average on the right hand side, using the Cauchy-Schwarz inequality, and then taking square root of both sides, we obtain

$$\begin{aligned}\langle N_0^2(t_1+1)\rangle^{1/2} &\leq (\langle N_0^2(t_1)\rangle + 2\langle N_0(t_1)(1+N_0(1))\rangle + \langle (1+N_0(1))^2\rangle)^{1/2} \\ &\leq (\langle N_0^2(t_1)\rangle + 2\langle N_0^2(t_1)\rangle^{1/2}\langle (1+N_0(1))^2\rangle^{1/2} + \langle (1+N_0(1))^2\rangle)^{1/2} \\ &= \langle N_0^2(t_1)\rangle^{1/2} + \langle (1+N_0(1))^2\rangle^{1/2}. \end{aligned} \tag{57}$$

Applying Eq. (57) repeatedly, we obtain that for positive integer k,

$$\langle N_0^2(t_1+k)\rangle^{1/2} \leq \langle N_0^2(t_1)\rangle^{1/2} + c_1 k, \quad c_1 = \langle (1+N_0(1))^2\rangle^{1/2}. \tag{58}$$

For $k-1 < t_2 \leq k$, we have

$$\langle N_0^2(t_1+t_2)\rangle^{1/2} \leq \langle N_0^2(t_1)\rangle^{1/2} + c_1 + c_1 t_2. \tag{59}$$

This completes the proof of Lemma 2.

Let us consider $\rho_1(0,\tau,t)$, the probability density of age τ at state 0 at time t for initial condition (28). $\rho_1(0,\tau,t)$ satisfies differential equation (38). Lemma 1 tells us that

$$\rho_1(0,\tau,t) = \begin{cases} \rho_1(0,\tau-t,0)\dfrac{\rho^{(S)}(\tau)}{\rho^{(S)}(\tau-t)} = \rho^{(S)}(\tau) & \text{for } \tau \geq t \\ 0 & \text{for } \tau < t. \end{cases} \tag{60}$$

$\int_0^\infty \rho_1(0,\tau,t)d\tau$ is the probability of having not completed the first cycle by time t. The probability density of the waiting time for completing the first cycle is

$$p_1^{(1)}(t) = -\frac{d}{dt}\int_0^\infty \rho_1(0,\tau,t)d\tau = \rho^{(S)}(t). \tag{61}$$

Here the superscript (1) refers to the first cycle. Below we shall use the notation $p_1^{(1)}(t)$ instead of $\rho^{(S)}(t)$ although they are the same. Furthermore, we shall use only the property that $\int_0^\infty t p_1^{(1)}(t)dt$ is finite. The benefit of doing so is that all lemmas developed below will still be valid in the general case where the first moment of the waiting time for completing the first cycle is finite.

At the moment the first cycle is completed, the system is renewed and continues with the canonical initial condition (24).[17] Thus, $\langle N_1(t)\rangle$ and $\langle N_0(s)\rangle$ are related by the convolution

$$\langle N_1(t)\rangle = \int_0^t \langle 1 + N_0(t-\tau)\rangle p_1^{(1)}(\tau)d\tau. \tag{62}$$

It should be pointed out that this convolution relation was used in Ref. 16 to relate a delayed renewal process to an ordinary renewal process.

Lemma 3: $\langle N_0(t)\rangle$ is bounded in terms of $\langle N_1(t)\rangle$ by

$$\langle N_1(t)\rangle - 1 \leq \langle N_0(t)\rangle \leq \langle N_1(t)\rangle + c_2, \tag{63}$$

where constant $c_2 > 1$ is independent of t.

Proof of Lemma 3: Combining $\langle N_0(t-\tau)\rangle \leq \langle N_0(t)\rangle$ with Eq. (62), we have

$$\langle N_1(t)\rangle \leq 1 + \langle N_0(t)\rangle,$$

which leads to the first half of Eq. (63). Subtracting $\langle N_0(t)\rangle$ from both sides of Eq. (62) and then using the result of Lemma 2 yields

$$\langle N_0(t)\rangle - \langle N_1(t)\rangle \leq \int_0^t (\langle N_0(t)\rangle - \langle N_0(t-\tau)\rangle) p_1^{(1)}(\tau) d\tau + \int_t^\infty \langle N_0(t)\rangle p_1^{(1)}(\tau) d\tau$$
$$\leq \int_0^\infty (c_0 + c_0\tau) p_1^{(1)}(\tau) d\tau = c_0 + c_0 \int_0^\infty \tau p_1^{(1)}(\tau) d\tau,$$

which leads to the second half of Eq. (63). Here we have used that $\int_0^\infty \tau p_1^{(1)}(\tau) d\tau$ is finite. This completes the proof of Lemma 3.

The significance of Lemma 3 is that Eq. (63) leads to

$$0 \leq \langle (N_1(t) - \langle N_0(t)\rangle)^2\rangle - \mathrm{var}(N_1(t)) = \langle (N_1(t) - \langle N_1(t)\rangle + \langle N_1(t)\rangle - \langle N_0(t)\rangle)^2\rangle - \mathrm{var}(N_1(t))$$
$$= (\langle N_1(t)\rangle - \langle N_0(t)\rangle)^2 \leq c_2^2. \tag{64}$$

Thus, we can replace $\mathrm{var}(N_1(t))$ in the limit of Eq. (48) with $\langle (N_1(t) - \langle N_0(t)\rangle)^2\rangle$. Furthermore $\langle (N_1(t) - \langle N_0(t)\rangle)^2\rangle$ is expressed in a convolution form similar to Eq. (62):

$$\langle (N_1(t) - \langle N_0(t)\rangle)^2\rangle = \int_0^t \langle (1 + N_0(t-\tau) - \langle N_0(t)\rangle)^2\rangle p_1^{(1)}(\tau) d\tau. \tag{65}$$

The two lemmas below relate $\mathrm{var}(N_1(t))$ to $\mathrm{var}(N_0(t))$ through Eq. (65).

Lemma 4: Let $P_1(t) \equiv \int_0^t p_1^{(1)}(\tau) d\tau$ and let

$$Q(t) \equiv |\mathrm{var}(N_1(t)) - \mathrm{var}(N_0(t)) P_1(t)|. \tag{66}$$

We have

$$Q(t) \leq c_3 + c_1^2 \sigma(t) + 2c_4 \sqrt{\mathrm{var}(N_0(t))}, \tag{67}$$

where all constants are independent of t and $\sigma(t)$ satisfies $\lim_{t\to\infty} \sigma(t)/t = 0$.

Proof of Lemma 4: We first relate the right hand side of Eq. (65) to $\mathrm{var}(N_0(t))$. Let

$$I(t,\tau) \equiv |\langle (1 + N_0(t-\tau) - \langle N_0(t)\rangle)^2\rangle - \mathrm{var}(N_0(t))|. \tag{68}$$

Step 1: We show that for $0 \leq \tau \leq t$, $I(t,\tau)$ is bounded by

$$I(t,\tau) \leq (c_1 + c_1\tau)^2 + 2(c_1 + c_1\tau)\sqrt{\mathrm{var}(N_0(t))}. \tag{69}$$

Each realization of $N_0(t)$ can be written as

$$N_0(t) = N_0(t-\tau) + 1 + V(t-\tau,\tau), \tag{70}$$

where random variable $V(t-\tau,\tau)$ is given by

$$V(t-\tau,\tau) = \begin{cases} N_0(\tau - t_c), & 0 < t_c \leq \tau \\ -1, & t_c > \tau, \end{cases} \tag{71}$$

and $t-\tau+t_c$ is the time at which the first motor step after time $t-\tau$ is completed. Let $p_c \equiv \Pr[t_c > \tau]$. Using Eq. (71) directly to calculate $\langle V^2(t-\tau,\tau)\rangle$, using the result of Lemma 2, and using the fact that $c_1 > 0$, we obtain

$$\langle V^2(t-\tau,\tau)\rangle \leq \langle N_0^2(\tau)\rangle (1-p_c) + p_c \leq (c_1 + c_1\tau)^2. \tag{72}$$

Using Eq. (70) to expand Eq. (68) yields

$$I(t,\tau) = |\langle (N_0(t) - \langle N_0(t)\rangle - V(t-\tau,\tau))^2\rangle - \mathrm{var}(N_0(t))|$$
$$\leq \langle V^2(t-\tau,\tau)\rangle + 2|\langle V(t-\tau,\tau)(N_0(t) - \langle N_0(t)\rangle)\rangle|. \tag{73}$$

Applying the Cauchy-Schwarz inequality and using inequality (72) lead directly to Eq. (69).

Step 2: We show that $Q(t)$ is bounded by inequality (67). Combining inequality (64), Eq. (65), notation (68), and inequality (69) yields

$$Q(t) \leqslant c_2^2 + \int_0^t I(t,\tau) p_1^{(1)}(\tau) d\tau \leqslant c_2^2 + c_1^2 \int_0^t (1+\tau)^2 p_1^{(1)}(\tau) d\tau + 2c_1 \int_0^t (1+\tau) p_1^{(1)}(\tau) d\tau \sqrt{\mathrm{var}(N_0(t))}$$
$$\leqslant c_3 + c_1^2 \sigma(t) + 2c_4 \sqrt{\mathrm{var}(N_0(t))}, \tag{74}$$

where $\sigma(t) \equiv \int_0^t \tau^2 p_1^{(1)}(\tau) d\tau$, and constants c_3 and c_4 are given by

$$c_3 = c_2^2 + c_1^2 \left(1 + 2\int_0^\infty \tau p_1^{(1)}(\tau) d\tau\right),$$

$$c_4 = c_1 \left(1 + \int_0^\infty \tau p_1^{(1)}(\tau) d\tau\right). \tag{75}$$

We now show $\lim_{t\to\infty} \sigma(t)/t = 0$. Using integration by parts, we write $\sigma(t)/t$ as

$$\frac{\sigma(t)}{t} = \frac{\int_0^t \tau^2 p_1^{(1)}(\tau) d\tau}{t} = \frac{\int_0^t \tau d\left(-\int_\tau^\infty s p_1^{(1)}(s) ds\right)}{t} = -\int_t^\infty s p_1^{(1)}(s) ds + \frac{\int_0^t \left(\int_\tau^\infty s p_1^{(1)}(s) ds\right) d\tau}{t}. \tag{76}$$

Since $\int_0^\infty s p_1^{(1)}(s) ds$ is finite, we have $\lim_{t\to\infty} \int_t^\infty s p_1^{(1)}(s) ds = 0$. Applying L'Hospital's rule yields $\lim_{t\to\infty} \sigma(t)/t = 0$. This completes the proof of Lemma 4.

Lemma 5: $\mathrm{var}(N_0(t))$ is bounded in terms of $\mathrm{var}(N_1(t))$ by

$$\sqrt{\frac{\mathrm{var}(N_1(t)) - c_3 - c_1^2\sigma(t)}{P_1(t)} + \left(\frac{c_4}{P_1(t)}\right)^2} - \frac{c_4}{P_1(t)} \leqslant \sqrt{\mathrm{var}(N_0(t))}$$
$$\leqslant \sqrt{\frac{\mathrm{var}(N_1(t)) + c_3 + c_1^2\sigma(t)}{P_1(t)} + \left(\frac{c_4}{P_1(t)}\right)^2} + \frac{c_4}{P_1(t)}. \tag{77}$$

Proof of Lemma 5: Dividing both sides of Eq. (67) by $P_1(t)$ yields

$$\frac{\mathrm{var}(N_1(t))}{P_1(t)} - \mathrm{var}(N_0(t)) \leqslant \frac{c_3 + c_1^2\sigma(t)}{P_1(t)} + \frac{2c_4}{P_1(t)} \sqrt{\mathrm{var}(N_0(t))}.$$

Moving $\mathrm{var}(N_0(t))$ to the right side and completing the square, we have

$$\frac{\mathrm{var}(N_1(t)) - c_3 - c_1^2\sigma(t)}{P_1(t)} + \left(\frac{c_4}{P_1(t)}\right)^2 \leqslant \left(\sqrt{\mathrm{var}(N_0(t))} + \frac{c_4}{P_1(t)}\right)^2.$$

Taking the square root leads to the first half of Eq. (77). The second half of Eq. (77) is proved in a similar way. This completes the proof of Lemma 5.

Now we extend the conclusion to the canonical case.

Theorem 2: $N_0(t)$ satisfies

$$\lim_{t\to\infty} \frac{\langle N_0(t)\rangle}{t} = \frac{1}{\langle T\rangle}, \quad \lim_{t\to\infty} \frac{\mathrm{var}(N_0(t))}{t} = \frac{R_T}{\langle T\rangle}. \tag{78}$$

Proof of Theorem 2: Dividing inequality (77) by $\sqrt{t}$, taking the limit as $t\to\infty$, and using $\lim_{t\to\infty} P_1(t) = 1$, $\lim_{t\to\infty} \sigma(t)/t = 0$, and Eq. (48), we obtain

$$\lim_{t\to\infty}\sqrt{\frac{\operatorname{var}(N_0(t))}{t}} = \sqrt{\frac{R_T}{\langle T\rangle}}. \tag{79}$$

Using the result of Lemma 3 and Eq. (48), we arrive at

$$\lim_{t\to\infty}\frac{\langle N_0(t)\rangle}{t} = \frac{1}{\langle T\rangle}. \tag{80}$$

This completes the proof of Theorem 2.

Finally, we extend the conclusion to the general case.

Theorem 3: Consider the general case where the first moment of the waiting time for completing the first cycle is finite. (Of course, by using $\langle T\rangle$ and $\langle T^2\rangle$, we have assumed that the first two moments of the cycle time of regular cycles are finite.) Let $N_{1*}(t)$ denote the number of steps completed by time t. Then $N_{1*}(t)$ satisfies

$$\lim_{t\to\infty}\frac{\operatorname{var}(N_{1*}(t))}{\langle N_{1*}(t)\rangle} = R_T. \tag{81}$$

Proof of Theorem 3: In deriving Lemmas 2–5, we only used that $\int_0^\infty \tau p_1^{(1)}(\tau)d\tau$ is finite. As a result, Lemmas 2–5 are also valid for $N_{1*}(t)$. Using Lemma 3 and Theorem 2, we have

$$\lim_{t\to\infty}\frac{\langle N_{1*}(t)\rangle}{t} = \lim_{t\to\infty}\frac{\langle N_{1*}(t)\rangle}{\langle N_0(t)\rangle}\frac{\langle N_0(t)\rangle}{t} = \frac{1}{\langle T\rangle}. \tag{82}$$

Using the result of Lemma 4, we obtain

$$\begin{aligned}&\operatorname{var}(N_0(t))P_1(t) - c_3 - c_1^2\sigma(t) - 2c_4\sqrt{\operatorname{var}(N_0(t))}\\ &\quad\leqslant \operatorname{var}(N_{1*}(t)) \leqslant \operatorname{var}(N_0(t))P_1(t) + c_3 + c_1^2\sigma(t) + 2c_4\sqrt{\operatorname{var}(N_0(t))}.\end{aligned} \tag{83}$$

Dividing inequality (83) by t, taking the limit as $t\to\infty$, and using $\lim_{t\to\infty}P_1(t)=1$, $\lim_{t\to\infty}\sigma(t)/t=0$, and Theorem 2, we arrive at

$$\lim_{t\to\infty}\frac{\operatorname{var}(N_{1*}(t))}{t} = \frac{R_T}{\langle T\rangle}. \tag{84}$$

Combining Eqs. (82) and (84) leads immediately to the desired conclusion.

IV. AN EXAMPLE OF $R_N \neq R_T$ AND DISCUSSION

In this section, we present an example to demonstrate that the initial age distribution does affect the validity of $R_N=R_T$. This example indicates that any serious attempt on proving $R_N=R_T$ must take into consideration the initial age distribution. In other words, all proofs that conclude $R_N=R_T$ categorically without considering the initial age distribution are, at least, mathematically questionable.

We consider a stochastic stepper with cycle time probability density

$$p(t) = (2+a)(1+t)^{-(3+a)}, \quad t\geqslant 0, \quad 0<a<1. \tag{85}$$

The first two moments of the cycle time and the randomness in the cycle time are

$$\langle T\rangle = \frac{1}{1+a}, \quad \langle T^2\rangle = \frac{2}{a(1+a)}, \quad \operatorname{var}(T) = \frac{2+a}{a(1+a)^2}, \quad R_T = \frac{2+a}{a}. \tag{86}$$

The stationary age distribution is

$$\rho^{(S)}(\tau) = \frac{\int_\tau^\infty p(s)ds}{\langle T\rangle} = (1+a)(1+\tau)^{-(2+a)}. \tag{87}$$

Let us start with the initial age distribution,

$$\text{initial distribution 2:} \quad \rho_2(0,\tau,0) = a(1+\tau)^{-(1+a)},$$

$$\rho_2(n,\tau,0) = 0, \quad n > 0. \tag{88}$$

We shall use subscript 2 to denote quantities corresponding to initial condition (88). $\rho_2(0,\tau,t)$ satisfies differential equation (38). Using the result of Lemma 1, we have

$$\rho_2(0,\tau,t) = \begin{cases} \rho_2(0,\tau-t,0)\dfrac{\rho^{(S)}(\tau)}{\rho^{(S)}(\tau-t)} = a(1+\tau-t)(1+\tau)^{-(2+a)} & \text{for } \tau \geqslant t \\ 0 & \text{for } \tau < t. \end{cases} \tag{89}$$

$\int_0^\infty \rho_2(0,\tau,t)d\tau$ is the probability of having not completed the first cycle by time t. The probability density of the waiting time for completing the first cycle is

$$p_2^{(1)}(t) = -\frac{d}{dt}\int_0^\infty \rho_2(0,\tau,t)d\tau = a(1+t)^{-(2+a)} + \frac{a}{1+a}(1+t)^{-(1+a)}, \tag{90}$$

where the superscript (1) refers to the first cycle. It is important to notice that the first moment of $p_2^{(1)}(t)$ diverges. As we will see below, the nonexistence of the first moment is the cause of $R_N \neq R_T$.

Let $N_2(t)$ denote the number of steps completed by time t for initial condition (88). At the moment the first cycle is completed, the system is renewed and continues with the canonical initial condition (24). Thus, we have

$$\langle N_2(t)\rangle = \int_0^t \langle 1 + N_0(t-\tau)\rangle p_2^{(1)}(\tau)d\tau,$$

$$\langle N_2^2(t)\rangle = \int_0^t \langle (1 + N_0(t-\tau))^2\rangle p_2^{(1)}(\tau)d\tau. \tag{91}$$

The variance of $N_2(t)$ satisfies

$$\begin{aligned} \operatorname{var}(N_2(t)) = \langle N_2^2(t)\rangle - \langle N_2(t)\rangle^2 &= \int_0^t \operatorname{var}(N_0(t-\tau))p_2^{(1)}(\tau)d\tau + \int_0^t \langle 1 + N_0(t-\tau)\rangle^2 p_2^{(1)}(\tau)d\tau - \langle N_2(t)\rangle^2 \\ &\geqslant \int_0^t \langle 1 + N_0(t-\tau)\rangle^2 p_2^{(1)}(\tau)d\tau - \langle N_2(t)\rangle^2 \equiv I_2 - \langle N_2(t)\rangle^2. \end{aligned} \tag{92}$$

Now we use the result of Lemma 3 and $\langle N_1(t)\rangle = t/\langle T\rangle = (1+a)t$ to estimate I_2 and $\langle N_2(t)\rangle$.

$$\begin{aligned} I_2 &= \int_0^t \langle 1 + N_0(t-\tau)\rangle^2 p_2^{(1)}(\tau)d\tau \geqslant \int_0^t \langle N_1(t-\tau)\rangle^2 p_2^{(1)}(\tau)d\tau \\ &= (1+a)^2\int_0^t (t-\tau)^2\left[a(1+\tau)^{-(2+a)} + \frac{a}{1+a}(1+\tau)^{-(1+a)}\right]d\tau \\ &= (1+a)^2\left[(1+t)^2 - \frac{2}{(1-a^2)(2-a)}(1+t)^{(2-a)} + O(t) + \cdots\right], \end{aligned} \tag{93}$$

$$\langle N_2(t)\rangle = \int_0^t \langle 1+N_0(t-\tau)\rangle p_2^{(1)}(\tau)d\tau \leq \int_0^t \langle N_1(t-\tau)\rangle^2 p_2^{(1)}(\tau)d\tau + (1+c_2)$$
$$= (1+a)\int_0^t (t-\tau)\left[a(1+\tau)^{-(2+a)} + \frac{a}{1+a}(1+\tau)^{-(1+a)}\right]d\tau + O(1)$$
$$= (1+a)\left[(1+t) - \frac{1}{(1-a^2)}(1+t)^{(1-a)} + O(1) + \cdots\right]. \quad (94)$$

Combining Eqs. (92)–(94) yields

$$\mathrm{var}(N_2(t)) \geq I_2 - \langle N_2(t)\rangle^2 \geq (1+a)^2\left[\frac{2}{(1+a)(2-a)}(1+t)^{(2-a)} + O(t) + \cdots\right], \quad (95)$$

which leads to

$$R_N = \lim_{t\to\infty} \frac{\mathrm{var}(N_2(t))}{\langle N_2(t)\rangle} \geq \lim_{t\to\infty} \frac{\frac{2}{(2-a)}(1+t)^{(1-a)} + O(1) + \cdots}{1 + O(t^{-a}) + \cdots} = \infty. \quad (96)$$

Therefore, for initial condition (88), we have $R_N \neq R_T$.

This example demonstrates that besides the existence of $\langle T\rangle$ and $\langle T^2\rangle$, the validity of $R_N = R_T$ also depends on the existence of the first moment of $p^{(1)}(t)$, the waiting time distribution for completing the first cycle. If the first moment of $p^{(1)}(t)$ diverges, then we have $R_N=\infty$. If the first moment of $p^{(1)}(t)$ is finite, then we have $R_N=R_T$ (Theorem 3 in the previous section).

In conclusion, we discussed the randomness in the cycle time and the randomness in the number of cycles over long time. We showed the equivalence between these two randomnesses for the general case where the cycle time of regular cycles has the first two moments and the waiting time for completing the first cycle has the first moment. In general, if the tails of the density of the waiting time for completing the first cycle are no worse than those of subsequent cycles, then the two randomnesses are equivalent. The waiting time for completing the first cycle is strongly affected by the initial age distribution. Therefore, any serious attempt on proving the equivalence between these two randomnesses must take into consideration the initial age distribution. In other words, any derivation that concludes the equivalence categorically regardless of the initial age distribution is mathematically not rigorous, and consequently, such a derivation should not be viewed as a rigorous substitution for the derivation presented here.

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APPENDIX: DERIVATION OF EQUATIONS (18) and (19)

The cycle time is either 1 or 2 with equal probabilities. It follows that $\langle N(t)\rangle$ can change only at an integer time. For $k<2$, we have $\langle N(0)\rangle=0$ and $\langle N(1)\rangle=0.5$. For $k\geq 2$, we have the recursive relation

$$\langle N(k)\rangle = \tfrac{1}{2}[1+\langle N(k-1)\rangle] + \tfrac{1}{2}[1+\langle N(k-2)\rangle]. \quad (A1)$$

To solve this recursive equation, we write $\langle N(k)\rangle=(2/3)k+a_k$. The term $(2/3)k$ is chosen such that $\{a_k\}$ satisfies a homogeneous recursive equation, which is

$$a_k = \frac{1}{2}a_{k-1} + \frac{1}{2}a_{k-2}, \quad a_0 = 0, \quad a_1 = \frac{-1}{6}. \tag{A2}$$

Substituting $a_k=\lambda^k$ into Eq. (A2) to get a quadratic equation for λ, calculating the two roots of the quadratic equation, and using linear combination $a_k=c_1\lambda_1^k+c_2\lambda_2^k$ to satisfy the two initial conditions, we arrive at $a_k=(-1/9)[1-(-1/2)^k]$, which leads immediately to Eq. (18). For $\langle N^2(t)\rangle$, we have $\langle N^2(0)\rangle=0$, $\langle N^2(1)\rangle=0.5$, and the recursive relation

$$\begin{aligned}\langle N^2(k)\rangle &= \tfrac{1}{2}\langle(1+N(k-1))^2\rangle + \tfrac{1}{2}\langle(1+N(k-2))^2\rangle \\ &= 1 + \langle N(k-1)\rangle + \langle N(k-2)\rangle + \tfrac{1}{2}\langle N^2(k-1)\rangle + \tfrac{1}{2}\langle N^2(k-2)\rangle.\end{aligned} \tag{A3}$$

To solve this recursive equation, we write $\langle N^2(k)\rangle=(2/3)k\langle N(k)\rangle+b_k$. The term $(2/3)k\langle N(k)\rangle$ is chosen such that $\{b_k\}$ satisfies a homogeneous recursive equation, which is

$$b_k = \tfrac{1}{2}b_{k-1} + \tfrac{1}{2}b_{k-2}, \quad b_0 = 0, \quad b_1 = \tfrac{1}{6}. \tag{A4}$$

Using the method described above for solving Eq. (A2), we obtain $b_k=(1/9)[1-(-1/2)^k]$, which leads directly to Eq. (19).

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