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Extended kinetic models with waiting-time distributions: Exact results

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Inspired by the need for effective stochastic models to describe the complex behavior of biological motor proteins that move on linear tracks, exact results are derived for the velocity and dispersion of simple linear sequential models (or one-dimensional random walks) with general *waiting-time distributions*. The concept of “mechanicity” is introduced to conveniently quantify departures from simple “chemical,” kinetic rate processes, and its significance is briefly indicated. The results are extended to more elaborate models that have finite side branches and include death processes (to represent the detachment of a motor from the track). © 2000 American Institute of Physics. [S0021-9606(00)50948-9]

I. INTRODUCTION AND SUMMARY

Motor proteins, such as kinesins, dyneins, myosins, and DNA and RNA polymerases, are important for the biological functioning of cells. Consuming energy obtained from the hydrolysis of ATP or related compounds, and moving along rigid linear tracks (microtubules, actin filaments, DNA molecules, etc.), they play a significant role in cell division, cellular transport, muscle contraction, and genetic transcription.^{1,2} Such molecular motors can move with velocities, V , up to 1000 nm/s,^{3–6} and may sustain an external load, F , of 5–8 pN for kinesins⁶ and up to 30–40 pN for DNA and RNA polymerases.^{7,8} Understanding the detailed mechanism of the functioning of motor proteins is a major challenge of modern biology.

In recent years, significant advances have been made in experimental techniques for studying motor proteins: one can now observe and investigate accurately the mechanical properties of single molecules over wide parameter ranges.^{3–8} However, our theoretical understanding of how these proteins work is still incomplete. Theoretical modeling of molecular motors has followed two main directions. One class of models is based on “thermal ratchets”^{9–12} in which the motor protein is viewed as a Brownian particle that diffuses in two or more periodic but asymmetric potentials between which it switches stochastically. Another, more traditional “chemical” approach is based on multistate kinetic descriptions of the motion with various rate processes determining the transitions between the states.^{13–23} In this paper we consider various extensions of the chemical kinetic schemes for which we derive exact, closed-form results in terms of the underlying transition rate parameters.

The simplest periodic sequential kinetic model assumes that a motor protein molecule moves along a periodic molecular track (a microtubule in the case of a kinesin) and binds at sites at $x = ld$ ($l = 0, \pm 1, \pm 2, \dots$). It is postulated that there are N discrete states, $j = 0, 1, \dots, N-1$, between consecutive binding sites and the motor protein in state j_l (“at”

site l) can move forward to state $(j+1)_l$ (normally pulling a load) at a rate u_j and can slip backward, to state $(j-1)_l$ at a rate w_j .^{18,19} This basic N -state model is, clearly, precisely isomorphic to a discrete but, in general, biased random walk on a periodic one-dimensional lattice. Such random walks are of broad interest for a variety of applications,^{24–29} in particular, for studying diffusion in random environments^{28–30} which may, for example, be approached by allowing the period N to become infinite.²⁸ Indeed, some time ago Derrida²⁸ presented a mathematical approach that provides formally exact and explicit formulas for the asymptotic drift velocity

$$V_0 = V_0(\{u_j, w_j\}) = \lim_{t \rightarrow \infty} \frac{d}{dt} \langle x(t) \rangle \quad (1)$$

and for the dispersion (or effective diffusion constant)

$$D_0 = D_0(\{u_j, w_j\}) = \frac{1}{2} \lim_{t \rightarrow \infty} \frac{d}{dt} [\langle x^2(t) \rangle - \langle x(t) \rangle^2], \quad (2)$$

where $x(t)$ is the spatial position of the motor protein molecule or, equally, of the random walker along the linear track at time t and, by periodicity $u_{j \pm N} = u_j$ and $w_{j \pm N} = w_j$. Derrida’s results have recently been exploited in developing theory for molecular motors.^{17–20,23} A valuable feature of the exact closed expressions is that it is quick and straightforward to explore the precise effects of a wide range of parameter values, revealing a variety of different characteristic types of behavior,^{18–20} in contrast to employing approximate numerical schemes or Monte Carlo simulations, or to studying oversimplified models.

The “purpose” of a motor protein in a biological setting is to move various biochemical entities, such as vesicles, etc., that exert load forces, F , which act on the protein molecule. The questions of what force can be exerted by a motor protein within the basic model and how the transition rates should be changed by the load, F , have been discussed critically.^{18,19} The resulting calculations for these models show qualitative and good semi-quantitative agreement with the experimentally observed behavior of normal two-headed kinesins.^{3–8,18,19,23}

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To describe motor proteins more realistically, however, and to understand the behavior of proteins other than two-headed kinesins,^{7,8,31,32} extensions of the basic N -state periodic sequential kinetic model were recently introduced.²⁰ These extended models take into consideration the complexity of real biochemical cycles (multiple kinetic paths and branched states) and allow for the irreversible stochastic detachment of molecular motors from the linear track which is always observed. Exact expressions for velocities and dispersions have been derived for these extended chemical kinetic models²⁰ in terms of the basic forward and backward rate constants, u_j and w_j , the corresponding rate constants for the side branches, and the death rates from any of the N intermediate states.

Now, the basic concept underlying chemical kinetic models is the idea that the motion of the motor protein is essentially “chemical,” i.e., the molecule undergoes a transition or “jump” from one chemical state to a nearest neighbor state (in the kinetic diagram) at a given rate, having “forgotten” how it arrived at the state. The time intervals between such jumps are thus distributed exponentially according to Poisson statistics. In other words, the time intervals are described by exponential *waiting-time distribution* functions in which the coefficient in the exponent represents the overall rate of transition from the state in question.

A conceptually possible alternative picture of the motion is that it is “purely mechanical” so that the motor works like a clock, jumping from state to state within narrowly distributed time intervals. Real molecular motors work with a surprisingly high mechanical efficiency (which may be estimated as 80%–90% for kinesins). This, in turn, suggests that some of the steps in the dynamical sequence of the motion might reasonably be described as rather more mechanical than purely random in nature. In that case, the waiting-time distribution functions for the time intervals marking transitions between different internal states might be modeled more effectively or more economically²³ as *non* exponential. To that end we present here a generalization of the basic periodic chemical kinetic models, and of their extensions, that explicitly considers *general* waiting-time distributions. By using the results of Montroll and co-workers^{24–27} we are, again, able to obtain explicit, exact results for V and D for the various models. We also briefly explore the quantitative significance of the “mechanical” factors that could represent departures from purely chemical kinetic processes in the motion of molecular motors.

To proceed, consider first the extension of the simple sequential kinetic model (with period N) shown schematically in Fig. 1. To characterize the dynamics of the motor protein (or random walkers) we introduce waiting-time distribution functions $\psi_j^\pm(t)$ and $\psi_j^0(t)$, where $\psi_j^+(t)dt$ is the probability of jumping one step forward from state j in the time interval t to $t+dt$ after arriving in state j , while $\psi_j^-(t)dt$ is the corresponding probability of jumping one step backward from state j , and $\psi_j^0(t)dt$ is the probability of attempting to move in the same time interval but failing to do so and hence restarting at the same site after the attempt. The allowance for $\psi_j^0(t)$ is potentially useful in modeling motor proteins since it can describe, say, the “futile” hydrolysis of

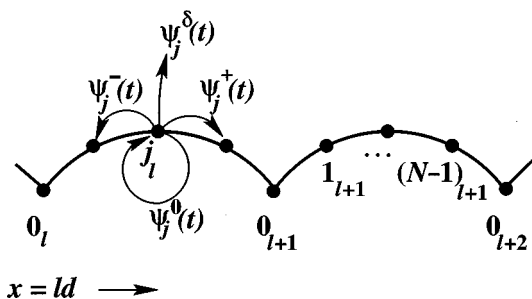


FIG. 1. A schematic general linear, periodic, stochastic process with forward and backward waiting-time distributions, $\psi_j^+(t)$ and $\psi_j^-(t)$, failing or futile attempt distributions $\psi_j^0(t)$, and irreversible death rates, $\psi_j^\delta(t)$, from states j_l , where the reference states, 0_l , are located at positions $x=ld$. [Note that the precise locations of the intermediate states $1_{l+1}, 2_{l+1}, \dots, (N-1)_{l+1}$, have no significance for the velocity, V , and dispersion, D , since these are defined asymptotically for large times, $t \rightarrow \infty$.]

an ATP molecule without achieving a forward step.

A more complicated model allows for the possibility of irreversible detachments or “deaths.” Deaths are described by a distribution $\psi_j^\delta(t)$ such that $\psi_j^\delta(t)dt$ is the probability of leaving from state j in the time interval t to $t+dt$ but not appearing in any other state.²⁰ Alternatively, the detachment or death process may carry the motor, or walker, to a reservoir (or graveyard) from which no returns are allowed.

Finally, another possible extension of the simple kinetic sequential scheme is to incorporate finite side-branch processes:²⁰ see Fig. 2. If state $(j,k)_l$ labels a state k on a branch emanating from the primary state j_l , the dynamics can be described by additional distributions $\psi_{j,k}^\beta(t)$ where $\psi_{j,k}^\beta(t)dt$ is the probability of jumping one step further out from the branch state $(j,k)_l$ in the time interval t to $t+dt$ ($k=0,1,\dots,L-1$), while $\psi_{j,k}^\gamma(t)dt$ is the corresponding probability of jumping one step back in toward the primary state $j_l \equiv (j,0)_l$ from the branch state $(j,k)_l$ ($k=1,2,\dots,L$). Note that without loss of generality we may assume that all side branches are of the same length L : see Ref. 20.

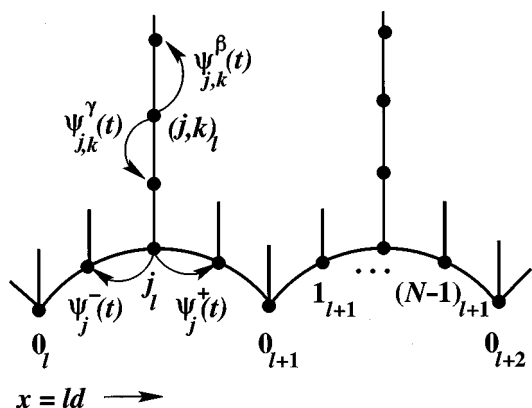


FIG. 2. A schematic periodic stochastic process with branches of finite length ($\leq L$) grown from each primary site $(j,0)_l \equiv j_l$; outward and inward waiting-time distributions, $\psi_{j,k}^\beta(t)$ with $k=0,1,\dots,(L-1)$, and $\psi_{j,k}^\gamma(t)$ with $k=1,2,\dots,L$, are specified at each branch site $(j,k)_l$. Failing or futile attempt distributions, $\psi_{j,k}^0(t)$, are not shown but may be considered as present.

The waiting-time distribution functions respect the basic N -state periodicity so that

$$\psi_{j,k}^{\zeta}(t) = \psi_{j \pm N, k}^{\zeta}(t), \quad (3)$$

where $\zeta = +, -, 0, \delta, \beta$, or γ . Furthermore, for any state (j, k) normalization requires

$$\sum_{\zeta} \int_0^{\infty} \psi_{j,k}^{\zeta}(t) dt = 1. \quad (4)$$

For all these extensions of the original chemical kinetic model we have derived explicit general expressions for the drift velocities and for the dispersions by generalizing Derrida's method.²⁸ When appropriate exponential waiting-time distribution functions are substituted, we recover Derrida's original formulas²⁸ for the simple linear model and, likewise, our previous results for the extended kinetic models.²⁰ For convenience, we present all of our concrete results, namely, the expressions for the mean velocities and for the dispersions, in this section. The detailed, and unavoidably somewhat involved, calculations and derivations are described in Secs. III–V.

To quantify the importance of ‘‘purely mechanical’’ factors in the motion of motor proteins the concept of *mechanicity* is introduced and discussed in Sec. II. The mechanicity varies from 0 for a ‘‘chemical’’ or Poisson process (with exponential waiting-time distribution functions) to 1 for a purely mechanical process (with clockwork or delta-function waiting-time distributions). It provides a convenient quantitative measure of deviations from a simple chemical picture of the dynamics of molecular motors which may well prove useful in applications.²³

To simplify the presentation of our results it is convenient to introduce the *overall waiting-time distribution*, $\psi_{j,k}(t)$, which is merely the sum of all the distinct distributions associated with the state (j, k) . [Recall that $k=0$ corresponds to primary states, $j_l \equiv (j, 0)_l$, on the linear sequence.] We will need the Laplace transform of the overall distribution defined by

$$\tilde{\psi}_{j,k}(s) = \int_0^{\infty} e^{-st} \psi_{j,k}(t) dt = 1 - s\mu_{1;j,k} + \frac{1}{2}s^2\mu_{2;j,k} - \dots, \quad (5)$$

where $\mu_{n;j,k}$ ($n=0, 1, \dots$) is the n th moment of $\psi_{j,k}(t)$ and we have used the normalization condition Eq. (4) to conclude $\mu_{0;j,k} \equiv 1$. The transforms, $\tilde{\psi}_{j,k}^{\zeta}(s)$, of the partial waiting-time distributions and their moments $\mu_{n;j,k}^{\zeta}$ are defined similarly. Of course, for the specific models that we consider some of $\tilde{\psi}_{j,k}^{\zeta}$ will be absent (and, so, can be set to zero).

Analysis reveals that a crucial role is played by the associated *waiting-time rate distributions*, $\varphi_{j,k}^{\zeta}(t)$, which are defined via their Laplace transforms

$$\tilde{\varphi}_{j,k}^{\zeta}(s) \equiv s\tilde{\psi}_{j,k}^{\zeta}(s)/[1 - \tilde{\psi}_{j,k}(s)], \quad (6)$$

where ζ , as before, can be $+, -, 0, \delta, \beta$ or γ . Note that it is the transform $\tilde{\psi}_{j,k}$ of the total or overall waiting-time distribution that appears here in the denominator.

TABLE I. Expressions for the rate moments in terms of waiting-time moments. See Eqs. (5)–(7) and note that $v_n^{\zeta} \equiv 0$ for $n \geq 1$ when $\psi^{\zeta}(t) \propto \psi(t) \propto e^{-ct}$ for any $c(>0)$.

$v_0^{\zeta} = \frac{\mu_0^{\zeta}}{\mu_1}$	$v_1^{\zeta} = \frac{\mu_1^{\zeta}}{\mu_1} - \frac{\mu_0^{\zeta}\mu_2}{2(\mu_1)^2}$
$v_2^{\zeta} = \frac{\mu_2^{\zeta}}{\mu_1} - \frac{\mu_1^{\zeta}\mu_2}{(\mu_1)^2} - \frac{\mu_0^{\zeta}\mu_3}{3(\mu_1)^2} + \frac{\mu_0^{\zeta}(\mu_2)^2}{2(\mu_1)^2}$	

It then transpires, as seen below and proved in Secs. III–V, that in terms of the $\tilde{\varphi}_{j,k}^{\zeta}(s)$ one can readily define *effective kinetic transition rates*: i.e., u_j and w_j , for the forward and backward rates along the primary linear sequence; δ_j for the death processes from states $j \equiv (j, 0)$; and side-branch rates, $\beta_{j,k}$ and $\gamma_{j,k}$, outward and inward from the states (j, k) . In the main, especially for the velocity $V[\{\psi_{j,k}^{\zeta}(t)\}]$, these effective kinetic rates play the same role in our results as do the simple (Poissonian) rates, denoted by the same symbols,^{18–20} in the analysis of the original kinetic models with exponential waiting-time distributions. Furthermore, for the velocity and dispersion (in the absence of death processes), only low order moments of $\varphi_{j,k}^{\zeta}(t)$ enter explicitly. These, in turn, can be expressed in terms of low order waiting-time moments, $\mu_{n;j,k}$ and $\mu_{n;j,k}^{\zeta}$. To be explicit, dropping the state labels (j, k) , we can write

$$\tilde{\varphi}^{\zeta}(s) = v_0^{\zeta} - s v_1^{\zeta} + \frac{1}{2} s^2 v_2^{\zeta} - \dots, \quad (7)$$

where the rate moments v_n^{ζ} are expressed in terms of μ_n and μ_n^{ζ} in Table I. We will assume that all the moments displayed in the table are finite.

As previously found in analyzing the various simple kinetic models, our expressions for V and D in the extended models with waiting-time distributions depend on certain linear sequential products of rate ratios. Following Ref. 20, we thus define two types of product for the sequential model with waiting times, namely,

$$\Pi_j^k \equiv \prod_{i=j}^k \frac{w_i}{u_i} \quad \text{and} \quad \tilde{\Pi}_j^{\dagger k} \equiv \prod_{i=j}^k \frac{w_{i+1}}{u_i} = \frac{w_{k+1}}{w_j} \Pi_j^k, \quad (8)$$

where we recall the periodicity $u_{j \pm N} = u_j$ and $w_{j \pm N} = w_j$. The model with branches requires one more type, namely, the branch products

$$\Pi_j^{\beta, k} \equiv \prod_{i=1}^k \frac{\beta_{j, i-1}}{\gamma_{j, i}}. \quad (9)$$

For the model with deaths or irreversible detachments we introduce modified analogs of Eq. (8), namely, $\tilde{\Pi}_j^k$ and $\tilde{\Pi}_j^{\dagger k}$, that are obtained simply by substituting u_j and w_j by the ‘‘renormalized’’ values

$$\tilde{u}_j = u_j \epsilon_{j+1} / \epsilon_j \quad \text{and} \quad \tilde{w}_j = u_j \epsilon_{j-1} / \epsilon_j, \quad (10)$$

where the periodic renormalization coefficients, $\epsilon_j \equiv \epsilon_{j \pm N}$ ($j=0, 1, \dots, N-1$), are conveniently normalized by the condition

$$\epsilon_0 \equiv 1. \quad (11)$$

The remaining coefficients ϵ_j then form the components of the right eigenvector, $\epsilon = [\epsilon_j]$, corresponding to the smallest eigenvalue, $\lambda = \lambda(\{u_j, w_j\})$, of the $N \times N$ transition rate matrix $\mathbf{M}[\{u_j, w_j; \delta_j\}]$ which is defined by the nonzero elements

$$M_{j,j-1} = -w_j, \quad M_{j,j} = u_j + w_j + \delta_j, \quad M_{j,j+1} = -u_j, \quad (12)$$

and, because of periodicity,

$$M_{0,-1} \equiv M_{0,N-1} = -w_0 \quad \text{and} \quad M_{N-1,N} \equiv M_{N-1,0} = -u_{N-1}. \quad (13)$$

With these preliminaries established we can now present our explicit results in fairly compact form.

A. Results for the simple sequential model with waiting times

The formal expression for the velocity in this case is precisely the same as derived by Derrida²⁸ for the sequential chemical kinetic model, that is,

$$V = d(1 - \Pi_1^N)/R_N, \quad (14)$$

where, using the definitions given above,

$$R_N = \sum_{j=0}^{N-1} r_j, \quad r_j = u_j^{-1} \left[1 + \sum_{k=1}^{N-1} \Pi_{j+1}^{j+k} \right], \quad (15)$$

and d is a distance between neighboring binding sites on the linear track. However, the effective transition rates u_j and w_j are now given by

$$u_j, \quad w_j = \varphi_j^\pm(s=0) = v_{0;j}^\pm = \frac{\int_0^\infty \psi_j^\pm(t) dt}{\int_0^\infty t \psi_j(t) dt}, \quad (16)$$

where we have used Eq. (7) and Table I and may recall that $\psi_j = \psi_j^+ + \psi_j^- + \psi_j^0$.

The dispersion takes a new, more complex form which can be written as

$$D = D_0 + D_1, \quad (17)$$

where the first term is given by

$$D_0 = (d/N) \{ [VS_N + dU_N]/(R_N)^2 - \frac{1}{2}(N+2)V\beta \}, \quad (18)$$

$$S_N = \sum_{j=0}^{N-1} s_j \sum_{k=0}^{N-1} (k+1)r_{k+j+1}, \quad U_N = \sum_{j=0}^{N-1} u_j r_j s_j, \quad (19)$$

in which new coefficients s_j are determined by

$$s_j = u_j^{-1} \left[1 + \sum_{k=1}^{N-1} \Pi_{j-1}^{j-k} \right]. \quad (20)$$

The second contribution to the dispersion is found to be

$$D_1 = (d/N) [NV/(R_N)^2] \sum_{j=0}^{N-1} s_j (g_j^+ r_j - g_{j+1}^- r_{j+1}), \quad (21)$$

where new, ‘‘nonexponential parameters,’’ g_j^\pm , are defined by

$$g_j^\pm = \frac{d\tilde{\varphi}_j^\pm}{ds} \Big|_{s=0} = - \int_0^\infty t \varphi_j^\pm(t) dt = -v_{1;j}^\pm. \quad (22)$$

For the relation of these parameters to the waiting-time moments, see Table I. When the waiting times are exponentially distributed with, in particular, $\psi_j^+(t)$, $\psi_j^-(t)$, and $\psi_j^0(t)$, each proportional to $\exp(-ct)$, the parameters g_j^\pm vanish identically. When this occurs for all j , the dispersion D is given by D_0 alone and, as mentioned, Derrida’s original formula is recovered.^{18,19,28} We remark that the g_j^\pm are typically negative but may, in fact, also be positive: Their character is discussed in more concrete terms in Sec. II.

B. Sequential model with branches and waiting times

For models with branches of finite length (see Fig. 2) the velocity is given by

$$V_\beta(\beta, \gamma) = d(1 - \Pi_1^N)/R_N^\beta, \quad (23)$$

which is identical to the expression Eq. (14) for the unbranched models except for the modified functions

$$R_N^\beta = \sum_{j=0}^{N-1} r_j^\beta, \quad r_j^\beta = r_j \left[1 + \sum_{k=1}^L \Pi_j^{\beta,k} \right], \quad (24)$$

in which the effective transition rates in and out of the branch states are defined in parallel to Eq. (16) by

$$\beta_{j,k} = \tilde{\varphi}_{j,k}^\beta(s=0), \quad \gamma_{j,k} = \tilde{\varphi}_{j,k}^\gamma(s=0). \quad (25)$$

It is appropriate to recall, however, that the rates $\beta_{j,0}$, u_j , and w_j involve $\psi_{j,0}(t)$, which now entails the *three* distributions ψ_j^+ , ψ_j^- , and $\psi_{j,0}^\beta$.

The dispersion can be expressed as

$$D_\beta = D_{0,\beta} + D_{1,\beta} + D_{2,\beta}, \quad (26)$$

where the first two terms are very similar to D_0 and D_1 for the unbranched models: explicitly we find

$$D_{0,\beta} = (d/N) \{ [V_\beta S_N^\beta + dU_N^\beta]/(R_N^\beta)^2 - \frac{1}{2}(N+2)V\beta \}, \quad (27)$$

$$D_{1,\beta} = (d/N) [NV_\beta/(R_N^\beta)^2] \sum_{j=0}^{N-1} s_j^\beta (g_j^+ r_j - g_{j+1}^- r_{j+1}), \quad (28)$$

where the modified functions, analogous to S_N and U_N in Eq. (19), are

$$S_N^\beta = \sum_{j=0}^{N-1} s_j^\beta \sum_{k=0}^{N-1} (k+1)r_{k+j+1}^\beta, \quad U_N^\beta = \sum_{j=0}^{N-1} u_j r_j s_j^\beta, \quad (29)$$

in which, in parallel to Eq. (20), we require

$$s_j^\beta = u_j^{-1} \left[1 + \sum_{l=1}^L \Pi_j^{\beta,l} + \sum_{k=1}^{N-1} \left(1 + \sum_{l=1}^L \Pi_{j-k}^{\beta,l} \right) \Pi_{j-k}^{\beta,j-1} \right]. \quad (30)$$

The third term in Eq. (26), which is a contribution due to the presence of branches, is given by

$$D_{2,\beta} = V_\beta^2 \sum_{j=0}^{N-1} \sum_{k=1}^L W_{j,k}^\beta, \quad (31)$$

where, for the coefficients, we have

$$W_{j,k}^\beta = \frac{r_j}{R_N^\beta \gamma_{j,k}} \left[\sum_{l=k}^L \Pi_j^{\beta,l} - g_{j,k-1}^\beta \Pi_j^{\beta,k-1} + g_{j,k}^\gamma \Pi_j^{\beta,k} + \sum_{i=1}^{k-1} \frac{\beta_{j,i}}{\beta_{j,0}} \Pi_j^{\beta,i} \left(\sum_{l=k-i}^L \Pi_j^{\beta,l} - g_{j,k-i-1}^\beta \Pi_j^{\beta,k-i-1} + g_{j,k-i}^\gamma \Pi_j^{\beta,k-i} \right) \right]. \quad (32)$$

The nonexponential parameters, $g_{j,k}^\beta$ and $g_{j,k}^\gamma$, are defined in precise analogy to Eq. (22) by

$$g_{j,k}^\beta = (d\tilde{\varphi}_{j,k}^\beta/ds)|_{s=0} = -v_{1;j,k}^\beta, \quad (33)$$

$$g_{j,k}^\gamma = (d\tilde{\varphi}_{j,k}^\gamma/ds)|_{s=0} = -v_{1;j,k}^\gamma$$

where, again, the relation to the waiting-time moments follows from Table I. Similarly, if $\psi_{j,k}^\zeta(t) = Q_{j,k}^\zeta \exp(-c_{j,k}t)$ holds for all (j,k) , the results of Ref. 20 are once more obtained. Section II discusses expressions for $g_{j,k}^\zeta$ in terms of associated ‘‘mechanicities’’ $M_{j,k}^\zeta$.

C. Sequential model with deaths and waiting times

The mean velocity is now given by

$$V_\delta = d(1 - \tilde{\Pi}_1^N)/R_N^\delta, \quad (34)$$

where $\tilde{\Pi}_1^N$ and the \tilde{r}_j (appearing below) are defined, using \tilde{u}_j and \tilde{w}_j [see Eq. (10)], in exact analogy to Eqs. (8) and (15). However, in contrast to Eq. (16), the effective transition rates u_j and w_j and the death rate δ_j , which enter the expression for R_N^δ , require new definitions. Specifically, we find

$$u_j, w_j \equiv \tilde{\varphi}_j^\pm(s = -\lambda) = \frac{\lambda \int_0^\infty e^{+\lambda t} \psi_j^\pm(t) dt}{\int_0^\infty (e^{+\lambda t} - 1) \psi_j(t) dt}, \quad (35)$$

and $\delta_j = \tilde{\varphi}_j^\delta(s = -\lambda)$ which can, likewise, be expressed in the integral form exhibited in Eq. (35), where it may be recalled that $\psi_j = \psi_j^+ + \psi_j^- + \psi_j^0 + \psi_j^\delta$. In these expressions λ is, as stated above, the smallest eigenvalue of the transition rate matrix $\mathbf{M}[\{u_j, w_j; \delta_j\}]$ [see Eqs. (12) and (13)]. The function R_N^δ is then given by

$$R_N^\delta = \sum_{j=0}^{N-1} r_j^\delta, \quad r_j^\delta = [1 + (1 - \alpha_j) g_j^\delta] \tilde{r}_j, \quad (36)$$

where the modified death and nonexponential parameters g_j^δ and \tilde{r}_j are embodied in

$$\alpha_j \equiv [g_j^+(\epsilon_{j+1} - \epsilon_j) + g_j^-(\epsilon_{j-1} - \epsilon_j)] / (\epsilon_j h_j^\delta), \quad (37)$$

while the parameters themselves are now given by

$$g_j^\delta \equiv (d\tilde{\varphi}_j^\delta/ds)|_{s=-\lambda}, \quad \tilde{r}_j \equiv (d\tilde{\varphi}_j^\pm/ds)|_{s=-\lambda}, \quad (38)$$

where the integral expressions corresponding to that in Eq. (35) are somewhat more elaborate but may be found straightforwardly from Eq. (6) and will mirror the form of v_1^ζ in Table I. Recall from Eqs. (10)–(13) that the coefficients ϵ_j form the right eigenvector of \mathbf{M} for λ , the smallest eigenvalue.

Finally, the dispersion can be written as

$$D_\delta = D_{0,\delta} + D_{1,\delta} + D_{2,\delta}, \quad (39)$$

where the first term is given by

$$D_{0,\delta} = (d/N) \{ [V_\delta S_N^\delta + dU_N^\delta] / (R_N^\delta)^2 - \frac{1}{2}(N+2)V_\delta \}, \quad (40)$$

in which S_N^δ and U_N^δ are defined in precise analogy to Eq. (19), that is,

$$S_N^\delta = \sum_{j=0}^{N-1} s_j^\delta \sum_{k=0}^{N-1} (k+1) r_{k+j+1}^\delta, \quad U_N^\delta = \sum_{j=0}^{N-1} \tilde{u}_j \tilde{r}_j s_j^\delta, \quad (41)$$

\tilde{r}_j being defined just after Eq. (34), while the analog of Eq. (20) is

$$s_j^\delta = \tilde{u}_j^{-1} \times \left[1 + (1 - \alpha_j) g_j^\delta + \sum_{k=1}^{N-1} [1 + (1 - \alpha_{j-k}) g_{j-k}^\delta] \Pi_{j-1}^{\delta,j-k} \right]. \quad (42)$$

The second term in Eq. (39) is then given by

$$D_{1,\delta} = (d/N) [NV_\delta / (R_N^\delta)^2] \sum_{j=0}^{N-1} s_j^\delta (\tilde{g}_j^+ \tilde{r}_j - \tilde{g}_{j+1}^- \tilde{r}_{j+1}), \quad (43)$$

where we have introduced the renormalized modified nonexponential parameters

$$\tilde{g}_j^\pm = g_j^\pm \epsilon_{j\pm 1} / \epsilon_j. \quad (44)$$

Finally, the last term in the dispersion, which arises solely because of the possibility of death or detachment, is given by

$$D_{2,\delta} = \frac{1}{2} (V_\delta^2 / R_N^\delta) \sum_{j=0}^{N-1} (1 - \beta_j) h_j^\delta \tilde{r}_j, \quad (45)$$

where the new functions

$$\beta_j = [h_j^+(\epsilon_{j+1} - \epsilon_j) + h_j^-(\epsilon_{j-1} - \epsilon_j)] / (\epsilon_j h_j^\delta), \quad (46)$$

incorporate the second-order nonexponential parameters

$$h_j^\pm = (d^2 \tilde{\varphi}_j^\pm / ds^2)|_{s=-\lambda} = \int_0^\infty t^2 e^{\lambda t} \varphi_j^\pm(t) dt, \quad (47)$$

$$h_j^\delta = (d^2 \tilde{\varphi}_j^\delta / ds^2)|_{s=-\lambda} = \int_0^\infty t^2 e^{\lambda t} \varphi_j^\delta(t) dt. \quad (48)$$

It is interesting that these higher moments of the waiting-time rates, $\varphi_j^\pm(t)$ and $\varphi_j^\delta(t)$, arise only when death processes come into play. They can be written as integrals of the corresponding $\psi_j^\zeta(t)$, as in Eq. (35), but will then exhibit the structure of v_2^ζ in Table I and entail, in particular, the modified third moments $\int_0^\infty t^3 e^{\lambda t} \psi_j^\zeta(t) dt$, etc. Note that when the probability of death or detachment vanishes, one has $\lambda = 0$ and the coefficients α_j , β_j , h_j^\pm , h_j^δ , and g_j^δ all vanish; then we recapture the results stated above for simple sequential model with waiting times.

II. DEGREES OF MECHANICITY

Our analysis of the velocity and dispersion for the stochastic models with waiting-time distributions has revealed that, in terms of the effective rates u_j , w_j , etc. [as defined in Eqs. (16), (25), and (35)], deviations from Poisson processes

with nonexponential waiting times do *not* change the formal expressions for the velocities: Compare, e.g., Eqs. (14), (23), and (34) with the corresponding results presented in Ref. 20. On the other hand, the expressions for the dispersions change dramatically and, in particular, involve new “nonexponential parameters” like g_j^\pm [see Eqs. (22), (33), (39), etc.] that evidently provide a measure of some sort for the departures from simple “chemical,” kinetic processes. To gain a more concrete and intuitive picture of what these departures involve, we introduce a quantitative concept which we call the *mechanicity*, M_j^ζ , of the specific transition process described by the waiting-time distribution $\psi_j^\zeta(t)$ (where, as previously, $\zeta = +, -, 0, \dots$).

The basic idea is to discriminate, in an explicit way, a standard exponential distribution from distributions that depart from it in varying degrees, and from a sharp, “clockwork” distribution of zero width. Now, if \bar{t} is the mean waiting time for a particular process, the mean square deviation $\overline{(\Delta t)^2} = \bar{t}^2 - \bar{t}^2$ provides a natural measure of the width of the distribution. Then the dimensionless ratio $\Theta = \overline{(\Delta t)^2} / \bar{t}^2$ represents a scale-free index of the relative width. In the purely mechanical or clockwork limit $\Delta t = t - \bar{t}$ must vanish identically and so $\Theta = 0$; conversely, if the distribution $\psi(t)$ yielding \bar{t} and $\overline{(\Delta t)^2}$ is a simple exponential, one has $\Theta = 1$. Thus the mechanicity parameter $M \equiv 1 - \Theta$ vanishes for a Poisson or “chemical” process but attains the value unity for a purely mechanical process.

More illustratively,¹⁸ suppose the waiting-time distribution has the familiar general form

$$\psi(t) = Q t^{\nu-1} e^{-\sigma t} \quad (\nu > 0). \quad (49)$$

An elementary calculation then yields

$$M \equiv 1 - \Theta = 1 - \nu^{-1}. \quad (50)$$

By construction, the chemical limit is described by $\nu = 1$; conversely, the mechanical limit is realized when $\nu \rightarrow \infty$. This example also shows that M may be *negative* (and, then, indefinitely large). Evidently, this arises when $\psi(t)$ is sharply peaked at the origin exhibiting a power law behavior $\sim 1/t^\chi$ with $\chi = |M|/(1 + |M|)$ (for $M < 0$).

In applying these considerations to a general waiting-time distribution, $\psi_j^\zeta(t)$, with moments

$$\langle t_\zeta^n \rangle_j \equiv \mu_{h,j}^\zeta = \int_0^\infty t^n \psi_j^\zeta(t) dt, \quad (51)$$

a little care is needed since the zeroth moment, $\mu_{0,j}^\zeta \equiv \langle t_\zeta^0 \rangle_j$, represents the total probability that the transition of type ζ occurs which, in general, is less than unity. The appropriate definition of the mechanicity for the process ζ from a state j is thus

$$M_j^\zeta \equiv 1 - \Theta_j^\zeta = 2 - \langle t_\zeta^0 \rangle_j \langle t_\zeta^2 \rangle_j / \langle t_\zeta \rangle_j^2, \quad (52)$$

Now, in applying the various expressions displayed in Sec. I for the dispersions, D , it would be convenient if the nonexponential parameters, g_j^\pm (or g_j^β and g_j^γ), could be expressed directly in terms of the associated mechanicities, M_j^\pm (and/or M_j^β and M_j^γ) and the effective rates

$$u_j = \langle t_+^0 \rangle_j / \tau_j \quad \text{and} \quad w_j = \langle t_-^0 \rangle_j / \tau_j \quad (53)$$

(and/or $\beta_{j,k}$ and $\gamma_{j,k}$), where if, for simplicity, we suppose only forward and backward processes act from state j , the mean dwell time is just

$$\tau_j = \langle t_+ \rangle_j + \langle t_- \rangle_j = (u_j + w_j)^{-1}. \quad (54)$$

However, because $g_{j,k}^\zeta$ are defined via the rate distributions $\phi_{j,k}^\zeta(t)$, which, in turn, as seen in Eq. (6), require the total waiting-time distributions, $\psi_{j,k}(t)$, matters are not entirely straightforward. If one stays with the simplest case ($\psi_j^0 = \psi_j^\beta = \psi_j^\gamma = 0$) a single *extra* parameter proves essential: this might, for example, be taken as the dimensionless ratio:

$$\theta_j^+ = \langle t_+ \rangle_j / \tau_j \leq 1. \quad (55)$$

But the resulting formula, derived from

$$g_j^+ = \frac{u_j}{2\tau_j} [\langle t_+^2 \rangle_j + \langle t_-^2 \rangle_j - 2\langle t_+ \rangle_j / u_j], \quad (56)$$

which in turn follows with the aid of Table I, has a paradoxical feature (for which reason we do not quote it). Namely, even if the separate mechanicities, M_j^+ and M_j^- , vanish, parameters g_j^+ and g_j^- do *not*, in general, vanish! The reason is that in a pure kinetic scheme with forward and backward rates u_j and w_j describing departures from the same state j , the resulting waiting-time distributions, $\psi_j^+(t)$ and $\psi_j^-(t)$, share a *common* exponential factor, namely, $\exp[-(u_j + w_j)t] = e^{-t/\tau_j}$. Thus even if $\psi_j^+(t)$ and $\psi_j^-(t)$ are both simple exponentials, the overall process will *not* have a simple chemical description unless the + and - decay rates match. More generally, however, if $M_j^+ = M_j^- = 0$ and the (single) additional condition

$$\langle t_\pm^0 \rangle_j = \langle t_\pm \rangle_j \tau_j / (\langle t_+ \rangle_j^2 + \langle t_- \rangle_j^2) \quad (57)$$

is met, then, indeed, g_j^+ and g_j^- vanish. (Similar considerations apply, of course, to the behavior on branches; but the extra process available at a primary state, where a branch starts, must not be forgotten.)

Despite these conceptual complications, one can devise instructive examples with simpler dependence on the mechanicities. One useful case when only forward and backward transitions from a state j occur is described by

$$\psi_j^\pm(t) = Q_j^\pm t^{\nu_\pm-1} e^{-\nu_\pm t / \tau_j}, \quad (58)$$

where, with Eq. (53), the relations

$$Q_j^\pm = (u_j, w_j) \tau_j^{1-\nu_\pm} \nu_\pm^{\nu_\pm} / \Gamma(\nu_\pm) \quad (59)$$

ensure that the normalization condition $\int_0^\infty (\psi_j^+ + \psi_j^-) dt = 1$ is satisfied. The mechanicities are clearly

$$M_j^+ = 1 - \nu_+^{-1} \quad \text{and} \quad M_j^- = 1 - \nu_-^{-1}, \quad (60)$$

where, of course, ν_+ and ν_- could also depend on the state j ; the nonexponential parameters are then given by

$$g_j^\pm = -\frac{1}{2}(u_j, w_j) \tau_j^2 (u_j M_j^+ + w_j M_j^-). \quad (61)$$

This result *does* depend only on the effective rates and the associated mechanicities and the g_j^\pm do vanish when $M_j^\pm \rightarrow 0$ in accord with the naive expectations.

Similar examples can be devised when branching and death processes occur from a state j . For modeling purposes²³ we believe the associated loss of full generality is likely to be insignificant. But note that, by Eq. (61), g_j^\pm are always negative for the special cases considered; if, however, $\nu_+ = \nu_- = 1$ so that $M_j^+ = M_j^- = 0$ but there are *distinct* time constants, $\tau_j^+ \neq \tau_j^-$, then g_j^+ and g_j^- will have *opposite* signs. We stress, nonetheless, that the results presented in Sec. I apply for quite general waiting-time distributions: The mechanistic may be regarded as an auxiliary concept of intuitive and descriptive value.

III. PERIODIC SEQUENTIAL MODEL WITH GENERAL WAITING TIMES

To derive the results presented in Sec. I, consider first the general periodic sequential model with waiting-time distributions as specified in Fig. 1. This model can be regarded as a one-dimensional *continuous-time random walk* with N internal states ($j=0,1,\dots,N-1$), a class of walks considered some decades ago by Montroll and co-workers.^{24-27,29} The crucial result, demonstrated by Landman, Montroll, and Shlesinger in 1977,²⁷ is that the probability $P_j(l,t)$ of finding the walker at site l in state j at time t satisfies the *generalized master equation*

$$\begin{aligned} \frac{d}{dt} P_j(l,t) = & \int_0^t \{ \varphi_{j-1}^+(\tau) P_{j-1}(l,t-\tau) \\ & + \varphi_{j+1}^-(\tau) P_{j+1}(l,t-\tau) \\ & - [\varphi_j^+(\tau) + \varphi_j^-(\tau)] P_j(l,t-\tau) \} d\tau, \end{aligned} \quad (62)$$

where the relaxation or memory functions, $\varphi_j^\pm(t)$, are directly related to the waiting-time distribution functions, $\psi_j^\pm(t)$, precisely as specified in Eq. (6). This master equation replaces the simple kinetic rate equations which were the starting points of the previous analyses.^{17-20,28}

For our purposes, we may, without loss of generality, assume that the initial condition is $P_j(l,0) = P_j^0 \delta_{l,0}$: i.e., the walker starts at the origin $x=l=0$. Conservation of probability then dictates

$$\sum_{l=-\infty}^{+\infty} \sum_{j=0}^{N-1} P_j(l,t) = 1 \quad (\text{all } t). \quad (63)$$

On the other hand, in any arbitrary state j_l in the kinetic picture the normalization requirement Eq. (4) yields

$$\int_0^\infty [\psi_j^+(t) + \psi_j^-(t) + \psi_j^0(t)] dt = 1, \quad (64)$$

or, in terms of Laplace transforms,

$$\tilde{\psi}_j^+(s=0) + \tilde{\psi}_j^-(s=0) + \tilde{\psi}_j^0(s=0) = 1. \quad (65)$$

To find the drift velocity V and dispersion D we now generalize Derrida's method²⁸ by defining two auxiliary functions for each state j , namely,

$$B_j(t) \equiv \sum_{l=-\infty}^{+\infty} P_j(l,t), \quad C_j(t) \equiv \sum_{l=-\infty}^{+\infty} (j+nl) P_j(l,t). \quad (66)$$

The generalized master equation (62) then yields

$$\begin{aligned} \frac{d}{dt} B_j(t) = & \int_0^t \{ \varphi_{j-1}^+(\tau) B_{j-1}(t-\tau) + \varphi_{j+1}^-(\tau) B_{j+1}(t-\tau) \\ & - [\varphi_j^+(\tau) + \varphi_j^-(\tau)] B_j(t-\tau) \} d\tau. \end{aligned} \quad (67)$$

Similarly, we obtain

$$\begin{aligned} \frac{d}{dt} C_j(t) = & \int_0^t \{ \varphi_{j-1}^+(\tau) C_{j-1}(t-\tau) + \varphi_{j+1}^-(\tau) C_{j+1}(t-\tau) \\ & - [\varphi_j^+(\tau) + \varphi_j^-(\tau)] C_j(t-\tau) - \varphi_{j+1}^-(\tau) \\ & \times B_{j+1}(t-\tau) + \varphi_{j-1}^+(\tau) B_{j-1}(t-\tau) \} d\tau. \end{aligned} \quad (68)$$

Again, following Derrida²⁸ we introduce the ansatz

$$B_j(t) \rightarrow b_j, \quad C_j(t) - a_j t \rightarrow T_j, \quad (69)$$

which should be valid when $t \rightarrow \infty$. Because of the periodicity in j we have

$$b_{j+N} = b_j, \quad a_{j+N} = a_j, \quad \text{and} \quad T_{j+N} = T_j. \quad (70)$$

After long times a steady state, $dB_j/dt=0$, will be achieved. Then, recalling in Eq. (35) that $\int_0^\infty \varphi_j^\pm(t) dt = \tilde{\varphi}_j^\pm(s=0)$, we introduce the effective transition rates u_j and w_j defined, in anticipation, in Eq. (16). Thus Eq. (67) yields

$$0 = u_{j-1} b_{j-1} + w_{j+1} b_{j+1} - (u_j + w_j) b_j. \quad (71)$$

Following precisely the arguments given in Ref. 20 [see Eqs. (45)-(47)] we can then conclude

$$b_j = \frac{r_j}{R_N}, \quad \text{with} \quad r_j = \frac{1}{u_j} \left[1 + \sum_{k=1}^{N-1} \Pi_{j+1}^{j+k} \right], \quad (72)$$

where the compact notation introduced in Eqs. (8) and (15) has been used.

To determine the coefficients a_j and T_j that control the behavior of $C_j(t)$ in Eq. (69), we substitute this ansatz into Eq. (68) concluding, for $t \rightarrow \infty$,

$$\begin{aligned} a_j = & \int_0^\infty \{ \varphi_{j-1}^+(\tau) [a_{j-1}(t-\tau) + T_{j-1}] \\ & + \varphi_{j+1}^-(\tau) [a_{j+1}(t-\tau) + T_{j+1}] - [\varphi_j^+(\tau) + \varphi_j^-(\tau)] \\ & \times [a_j(t-\tau) + T_j] - \varphi_{j+1}^-(\tau) b_{j+1} \\ & + \varphi_{j-1}^+(\tau) b_{j-1} \} d\tau. \end{aligned} \quad (73)$$

Now we may introduce the first moments of the relaxation functions via

$$- \int_0^\infty \tau \varphi_j^\pm(\tau) d\tau = (d\tilde{\varphi}_j^\pm/ds)|_{s=0} = g_j^\pm, \quad (74)$$

[see also Eq. (22)] which leads to

$$\begin{aligned} a_j = & t [u_{j-1} a_{j-1} + w_{j+1} a_{j+1} - (u_j + w_j) a_j] \\ & + [g_{j-1}^+ a_{j-1} + g_{j+1}^- a_{j+1} - (g_j^+ + g_j^-) a_j] \\ & + [u_{j-1} T_{j-1} + w_{j+1} T_{j+1} - (u_j + w_j) T_j] \\ & + [u_{j-1} b_{j-1} - w_{j+1} b_{j+1}]. \end{aligned} \quad (75)$$

The secular term proportional to t should vanish here, which condition requires

$$0 = u_{j-1}a_{j-1} + w_{j+1}a_{j+1} - (u_j + w_j)a_j, \quad (76)$$

while the coefficients T_j then satisfy

$$\begin{aligned} a_j = & [g_{j-1}^+ a_{j-1} + g_{j+1}^- a_{j+1} - (g_j^+ + g_j^-) a_j] \\ & + [u_{j-1} T_{j-1} + w_{j+1} T_{j+1} - (u_j + w_j) T_j] \\ & + [u_{j-1} b_{j-1} - w_{j+1} b_{j+1}]. \end{aligned} \quad (77)$$

Comparing Eq. (76) with Eq. (71) one can conclude that

$$a_j = A b_j, \quad (78)$$

where, using the normalization $\sum_{j=0}^{N-1} b_j = 1$ following from Eqs. (66) and (63), the constant A can be calculated by summing Eqs. (77) on j : the T_j identically, cancel which leads to

$$A = \sum_{j=0}^{N-1} a_j = \sum_{j=0}^{N-1} (u_j - w_j) b_j. \quad (79)$$

Then, on using the result Eq. (72) for b_j , we find

$$A = N[1 - \Pi_1^N]/R_N. \quad (80)$$

To obtain the coefficients T_j we introduce, following Ref. 20 [see Eqs. (54)–(57)],

$$y_j \equiv w_{j+1} T_{j+1} - u_j T_j, \quad (81)$$

and rewrite Eq. (75) as

$$\begin{aligned} y_j - y_{j-1} = & a_j - [g_{j-1}^+ a_{j-1} + g_{j+1}^- a_{j+1} - (g_j^+ + g_j^-) a_j] \\ & - u_{j-1} b_{j-1} + w_{j+1} b_{j+1}. \end{aligned} \quad (82)$$

The solution of this equation, which is achieved using the strategy described in Ref. 20, yields

$$\begin{aligned} y_j = & u_j b_j + (A/N) \sum_{i=0}^{N-1} (i+1) b_{j+i+1} \\ & + (a_j g_j^+ - a_{j+1} g_{j+1}^-) + c, \end{aligned} \quad (83)$$

where c is an arbitrary constant which will cancel in the final formula for the dispersion, D (see Refs. 20 and 28). The fact that this expression solves Eq. (82) can be checked with the help of the relation

$$u_j b_j - w_{j+1} b_{j+1} = A/N, \quad (84)$$

which follows from Eqs. (72) and (79). Then, iterating Eq. (81) and invoking the periodicity Eq. (70) yields the relation

$$T_j = -\frac{1}{u_j} \left[y_j + \sum_{k=1}^{N-1} y_{j+k} \Pi_{j+1}^{j+k} \right] / (1 - \Pi_1^N), \quad (85)$$

which, via Eqs. (83), (78), (79), and (72), represents an explicit result in terms of the effective rates defined in Eq. (16).

Now we can calculate the drift velocity, V , and the diffusion constant, D , using the long-time definitions Eqs. (1) and (2). The mean position of a particle is given by

$$\langle x(t) \rangle = \frac{d}{N} \sum_{l=-\infty}^{+\infty} \sum_{j=0}^{N-1} (j + Nl) P_j(l, t) = \frac{d}{N} \sum_{j=0}^{N-1} C_j(t). \quad (86)$$

With the aid of the generalized master equation (62) the derivative can be taken which, when $t \rightarrow \infty$, leads to

$$\lim_{t \rightarrow \infty} \frac{d}{dt} \langle x(t) \rangle = \frac{d}{N} \sum_{j=0}^{N-1} (u_j - w_j) b_j = \frac{d}{N} A. \quad (87)$$

Using the result Eq. (80) yields our final formula for the drift velocity, namely,

$$V_\alpha = d[1 - \Pi_1^N]/R_N, \quad (88)$$

where we recall that R_N is defined in Eq. (15). This expression corresponds exactly to Derrida's original result for the simple sequential kinetic model.

A similar approach suffices to determine the dispersion. We start from

$$\langle x^2(t) \rangle = \frac{d^2}{N^2} \sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} (j + Nl)^2 P_j(l, t), \quad (89)$$

and again appeal to the master equation (62) in the long-time limit. This leads to

$$\begin{aligned} \lim_{t \rightarrow \infty} \frac{d}{dt} \langle x^2(t) \rangle = & 2 \frac{d^2}{N^2} \left[\sum_{j=0}^{N-1} (u_j - w_j) (a_j t + T_j) \right. \\ & \left. + \frac{1}{2} \sum_{j=0}^{N-1} (u_j + w_j) b_j + a_j (g_j^+ - g_j^-) \right]. \end{aligned} \quad (90)$$

Then, using Eqs. (86), (87), and the definition Eq. (2), we obtain

$$\begin{aligned} D = & \frac{d^2}{N^2} \left[\sum_{j=0}^{N-1} (u_j - w_j) T_j + \frac{1}{2} \sum_{j=0}^{N-1} (u_j + w_j) b_j \right. \\ & \left. + \sum_{j=0}^{N-1} a_j (g_j^+ - g_j^-) - A \sum_{j=0}^{N-1} T_j \right]. \end{aligned} \quad (91)$$

Coefficients T_j can be re-expressed using Eqs. (85) and (83) from which the constant c then cancels.^{20,28} Finally, the definitions Eqs. (19) and (20) allow us to write the dispersion in the form presented in Eqs. (17)–(21), while the nonexponential parameters first introduced in Eq. (22) are confirmed by Eq. (74). Note that the dispersion consists of two terms, D_0 and D_1 , the second arising purely from the deviations of the waiting-time distribution functions from the ‘‘chemical,’’ Poissonian forms.

IV. PERIODIC MODEL WITH BRANCHES AND WAITING TIMES

Now consider the one-dimensional periodic model with branches and waiting-time distributions as presented in Fig. 2. Let $P_{j,k}(l, t)$ be the probability of finding the walker at site l in state j of the main sequence (labeled $k=0$) or in state $k=1, \dots, L$, on the associated side branch, at time t . Appealing again to Landman *et al.*²⁷ this probability is governed by the generalized master equation

$$\begin{aligned} \frac{d}{dt}P_{j,0}(l,t) &= \int_0^t \{ \varphi_{j-1}^+(\tau)P_{j-1,0}(l,t-\tau) \\ &+ \varphi_{j+1}^-(\tau)P_{j+1,0}(l,t-\tau) \\ &+ \varphi_{j,i}^\gamma(\tau)P_{j,i}(l,t-\tau) - [\varphi_j^+(\tau) + \varphi_j^-(\tau) \\ &+ \varphi_{j,0}^\beta(\tau)]P_{j,0}(l,t-\tau) \} d\tau, \end{aligned} \quad (92)$$

for $k=0$, by

$$\begin{aligned} \frac{d}{dt}P_{j,k}(l,t) &= \int_0^t \{ \varphi_{j,k-1}^\beta(\tau)P_{j,k-1}(l,t-\tau) \\ &+ \varphi_{j,k+1}^\gamma(\tau)P_{j,k+1}(l,t-\tau) - [\varphi_{j,k}^\beta(\tau) \\ &+ \varphi_{j,k}^\gamma(\tau)]P_{j,k}(l,t-\tau) \} d\tau, \end{aligned} \quad (93)$$

for $1 \leq k < L$, while for $k=L$ we have

$$\begin{aligned} \frac{d}{dt}P_{j,L}(l,t) &= \int_0^t [\varphi_{j,L-1}^\beta(\tau)P_{j,L-1}(l,t-\tau) \\ &- \varphi_{j,L}^\gamma(\tau)P_{j,L}(l,t-\tau)] d\tau. \end{aligned} \quad (94)$$

The relaxation functions $\varphi_j^+(t)$, $\varphi_j^\beta(t)$, and $\varphi_j^\gamma(t)$, are defined, as before, via their Laplace transforms as specified in Eq. (6). At $t=0$ we may assume that $P_{j,k}(l;0) = P_{j,k}^0 \delta_{l,0}$ and normalization requires

$$\sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} \sum_{k=0}^L P_{j,k}(l,t) = 1 \quad (\text{all } t). \quad (95)$$

Again following the strategy of Derrida's method as described in the previous section, we introduce the auxiliary functions

$$\begin{aligned} B_{j,k}(t) &\equiv \sum_{l=-\infty}^{\infty} P_{j,k}(l,t), \\ C_{j,k}(t) &\equiv \sum_{l=-\infty}^{\infty} (j+nl)P_{j,k}(l,t). \end{aligned} \quad (96)$$

The time evolution of $B_{j,k}(t)$ is then described by the set of $L+1$ equations

$$\begin{aligned} \frac{d}{dt}B_{j,0}(t) &= \int_0^t \{ \varphi_{j-1}^+(\tau)B_{j-1,0}(t-\tau) \\ &+ \varphi_{j+1}^-(\tau)B_{j+1,0}(t-\tau) + \varphi_{j,1}^\gamma(\tau)B_{j,1}(l,t-\tau) \\ &- [\varphi_j^+(\tau) + \varphi_j^-(\tau) + \varphi_{j,0}^\beta(\tau)]B_{j,0}(t-\tau) \} d\tau, \end{aligned} \quad (97)$$

$$\begin{aligned} \frac{d}{dt}B_{j,1}(t) &= \int_0^t \{ \varphi_{j,k-1}^\beta(\tau)B_{j,0}(t-\tau) + \varphi_{j,k+1}^\gamma(\tau)B_{j,2}(t-\tau) \\ &- [\varphi_{j,k}^\beta(\tau) + \varphi_{j,k}^\gamma(\tau)]B_{j,0}(t-\tau) \} d\tau, \end{aligned} \quad (98)$$

⋮

$$\begin{aligned} \frac{d}{dt}B_{j,L}(t) &= \int_0^t [\varphi_{j,L-1}^\beta(\tau)B_{j,L-1}(t-\tau) \\ &- \varphi_{j,L}^\gamma(\tau)B_{j,L}(t-\tau)] d\tau. \end{aligned} \quad (99)$$

Similarly, the time evolution of $C_{j,k}(t)$ obeys the equations

$$\begin{aligned} \frac{d}{dt}C_{j,0}(t) &= \int_0^t \{ \varphi_{j-1}^+(\tau)C_{j-1,0}(t-\tau) \\ &+ \varphi_{j+1}^-(\tau)C_{j+1,0}(t-\tau) + \varphi_{j,1}^\gamma(\tau)C_{j,1}(l,t-\tau) \\ &- [\varphi_j^+(\tau) + \varphi_j^-(\tau) + \varphi_{j,0}^\beta(\tau)]C_{j,0}(t-\tau) \\ &+ \varphi_{j-1}^+(\tau)B_{j-1,0}(t-\tau) \\ &- \varphi_{j+1}^-(\tau)B_{j+1,0}(t-\tau) \} d\tau, \end{aligned} \quad (100)$$

$$\begin{aligned} \frac{d}{dt}C_{j,1}(t) &= \int_0^t \{ \varphi_{j,k-1}^\beta(\tau)C_{j,0}(t-\tau) + \varphi_{j,k+1}^\gamma(\tau)C_{j,2}(t-\tau) \\ &- [\varphi_{j,k}^\beta(\tau) + \varphi_{j,k}^\gamma(\tau)]C_{j,0}(t-\tau) \} d\tau, \end{aligned} \quad (101)$$

⋮

$$\begin{aligned} \frac{d}{dt}C_{j,L}(t) &= \int_0^t [\varphi_{j,L-1}^\beta(\tau)C_{j,L-1}(t-\tau) \\ &- \varphi_{j,L}^\gamma(\tau)C_{j,L}(t-\tau)] d\tau. \end{aligned} \quad (102)$$

The previous arguments^{20,28} lead to the expectation

$$B_{j,k}(t) \rightarrow b_{j,k}, \quad C_{j,k}(t) - a_{j,k}t \rightarrow T_{j,k}, \quad (103)$$

for $t \rightarrow \infty$. At large times the equations of motion (97)–(99) then yield the relations

$$\begin{aligned} w_{j+1}b_{j+1,0} - u_j b_{j,0} &= w_j b_{j,0} - u_{j-1} b_{j-1,0} \\ &+ (\beta_{j,0} b_{j,0} - \gamma_{j,1} b_{j,1}), \end{aligned} \quad (104)$$

$$\begin{aligned} \beta_{j,0} b_{j,0} - \gamma_{j,1} b_{j,1} &= \beta_{j,1} b_{j,1} - \gamma_{j,2} b_{j,2} \\ &= \dots = \beta_{j,L-1} b_{j,L-1} - \gamma_{j,L} b_{j,L} = 0, \end{aligned} \quad (105)$$

where we have invoked the definitions Eqs. (16) and (25) for rates u_j , w_j , $\beta_{j,k}$ and $\gamma_{j,k}$. Recalling, likewise, the definitions Eqs. (22) and (33), the coefficients $a_{j,k}$ and $T_{j,k}$ must satisfy, first,

$$\begin{aligned} a_{j,0} &= [g_{j-1}^+ a_{j-1,0} + g_{j+1}^- a_{j+1,0} - (g_j^+ + g_j^-) a_{j,0}] \\ &+ [u_{j-1} T_{j-1,0} + w_{j+1} T_{j+1,0} - (u_j + w_j) T_{j,0}] \\ &+ [u_{j-1} b_{j-1,0} - w_{j+1} b_{j+1,0}] \\ &+ [g_{j,1}^\gamma a_{j,1} - g_{j,0}^\beta a_{j,0} + \gamma_{j,1} T_{j,1} - \beta_{j,0} T_{j,0}], \end{aligned} \quad (106)$$

$$\begin{aligned} a_{j,1} &= [g_{j,0}^\beta a_{j,0} + g_{j,2}^\gamma a_{j,2} - (g_{j,1}^\beta + g_{j,1}^\gamma) a_{j,1}] \\ &+ [\beta_{j,0} T_{j,0} + \gamma_{j,2} T_{j,2} - (\beta_{j,1} + \gamma_{j,1}) T_{j,1}], \end{aligned} \quad (107)$$

⋮

$$\begin{aligned} a_{j,L} &= [g_{j,L-1}^\beta a_{j,L-1} - g_{j,L}^\gamma a_{j,L} \\ &+ \beta_{j,L-1} T_{j,L-1} - \gamma_{j,L} T_{j,L}], \end{aligned} \quad (108)$$

while the vanishing of the secular terms yields, also,

$$\begin{aligned} w_{j+1} a_{j+1,0} - u_j a_{j,0} \\ = w_j a_{j,0} - u_{j-1} a_{j-1,0} + (\beta_{j,0} a_{j,0} - \gamma_{j,1} a_{j,1}), \end{aligned} \quad (109)$$

$$\begin{aligned} \beta_{j,0}a_{j,0} - \gamma_{j,1}a_{j,1} &= \beta_{j,1}a_{j,1} - \gamma_{j,2}a_{j,2} \\ &= \cdots = \beta_{j,L-1}a_{j,L-1} - \gamma_{j,L}a_{j,L} = 0. \end{aligned} \quad (110)$$

The side-branch functions $b_{j,k}$ are found easily by solving Eqs. (105) recursively, which gives

$$b_{j,k} = \prod_j^{\beta,k} b_{j,0} \quad (k=1, \dots, L), \quad (111)$$

where we have used the product notation Eq. (9). To obtain an expression for $b_{j,0}$ we follow exactly the method used to derive Eq. (72) in Sec. III, thereby finding

$$b_{j,0} = r_j / R_N^\beta, \quad (112)$$

where r_j is defined in Eq. (15) while R_N^β was introduced in Eq. (24). Comparing Eqs. (104) and (105) with (109) and (110) leads to

$$a_{j,k} = A b_{j,k} \quad \text{with} \quad A = N(1 - \Pi_1^N) / R_N^\beta. \quad (113)$$

The final derivation of the expressions for the drift velocity and the dispersion now follows along the lines developed in the previous section for models without branches. The results have been presented in full in Sec. IB. As regards the velocity, the branches generate no changes beyond the replacement of r_j by r_j^β and R_N by R_N^β . However, an additional term, $D_{2,\beta}$, appears in the dispersion: see Eqs. (31)–(33).

V. PERIODIC MODEL WITH DEATHS AND WAITING TIMES

Consider, finally, the periodic sequential model with waiting-time distributions and the possibility of an irreversible detachment or death from each state that is described by a waiting-time distribution function $\psi_j^\delta(t) = \psi_{j \pm N}^\delta(t)$: see Fig. 1. The generalized master equation for the probability $P_j(l, t)$ now reads²⁷

$$\begin{aligned} \frac{d}{dt} P_j(l, t) &= \int_0^t \{ \varphi_{j-1}^+(\tau) P_{j-1}(l, t - \tau) \\ &+ \varphi_{j+1}^-(\tau) P_{j+1}(l, t - \tau) \\ &- [\varphi_j^+(\tau) + \varphi_j^-(\tau) + \varphi_j^\delta(\tau)] P_j(l, t - \tau) \} d\tau, \end{aligned} \quad (114)$$

where, as before, the relaxation functions $\varphi_j^\pm(t)$ and $\varphi_j^\delta(t)$ are related to waiting-time distribution functions via Eqs. (5) and (6). We may again assume that the initial condition is

$$P_j(l, 0) = P_j^0 \delta_{l,0} \quad \text{with} \quad \sum_{j=0}^{N-1} P_j^0 = 1. \quad (115)$$

However, as discussed in Ref. 20, because the total probability is no longer conserved [so that $\sum_{l=-\infty}^{+\infty} \sum_{j=0}^{N-1} P_j(l, t > 0) < 1$], we look for long-time solutions of the generalized master equation (114) that are of the form

$$P_j(l, t) \approx e^{-\lambda t - \tau_j} \tilde{P}_j(l, t), \quad (116)$$

where, as before,²⁰ the decrement and the periodic state coefficients, $\tau_j \equiv \tau_{j \pm N}$, are to be found from the requirement that $\tilde{P}_j(l, t)$ satisfies a suitably ‘‘renormalized,’’ probability conserving master equation

$$\begin{aligned} \frac{d}{dt} \tilde{P}_j(l, t) &= \tilde{u}_{j-1} \tilde{P}_{j-1}(l, t) + \tilde{w}_{j+1} \tilde{P}_{j+1}(l, t) \\ &- (\tilde{u}_j + \tilde{w}_j) \tilde{P}_j(l, t). \end{aligned} \quad (117)$$

By substituting the ansatz Eq. (116) into the full generalized master equation (114), we obtain, for large times, the equation

$$\begin{aligned} \frac{d}{dt} \tilde{P}_j(l, t) &= u_{j-1} e^{\tau_j - \tau_{j-1}} \tilde{P}_{j-1} + w_{j+1} e^{\tau_j - \tau_{j+1}} \tilde{P}_{j+1} \\ &- (u_j + w_j + \delta_j - \lambda) \tilde{P}_j, \end{aligned} \quad (118)$$

in which the modified rate definitions Eq. (35) *et seq.*, which depend explicitly on λ , have been used. Matching terms with those in Eqs. (117) generates the identifications

$$\tilde{u}_j = u_j \epsilon_{j+1} / \epsilon_j \quad \text{and} \quad \tilde{w}_j = u_j \epsilon_{j-1} / \epsilon_j \quad \text{with} \quad \epsilon_j = e^{\tau_j}. \quad (119)$$

It also yields a condition which the ϵ_j must satisfy for consistency, namely,

$$-w_j \epsilon_{j-1} + (u_j + w_j + \delta_j) \epsilon_j - u_j \epsilon_{j+1} = \lambda \epsilon_j. \quad (120)$$

But, recognizing the periodicity in j , this is precisely equivalent to the eigenvalue equation $\mathbf{M}\boldsymbol{\epsilon} = \lambda \boldsymbol{\epsilon}$, where \mathbf{M} is the $N \times N$ matrix specified in Eqs. (12) and (13). Since the asymptotic decay is required in Eq. (116), λ must be the smallest eigenvalue which, clearly, should be real and positive.

To find expressions for the drift velocity and the dispersion we now require three auxiliary functions, namely,

$$B_j(t) \equiv \sum_{l=-\infty}^{\infty} P_j(l, t), \quad C_j(t) \equiv \sum_{l=-\infty}^{\infty} (j + Nl) P_j(l, t), \quad (121)$$

and also

$$E_j(t) \equiv \sum_{l=-\infty}^{\infty} (j + Nl)^2 P_j(l, t). \quad (122)$$

For large t we may expect the asymptotic behavior

$$B_j(t) \approx e^{-\lambda t - \tau_j} \tilde{B}_j(t), \quad C_j(t) \approx e^{-\lambda t - \tau_j} \tilde{C}_j(t), \quad \text{and} \quad (123)$$

$$E_j(t) \approx e^{-\lambda t - \tau_j} \tilde{E}_j(t),$$

with, extending Derrida’s ansatz,

$$\tilde{B}_j(t) \rightarrow b_j, \quad \tilde{C}_j(t) - a_j t \rightarrow T_j, \quad \text{and} \quad (124)$$

$$\tilde{E}_j(t) - e_j t^2 - f_j t \rightarrow X_j.$$

The explicit formulas for the coefficients b_j , a_j , T_j , e_j , f_j , and X_j can now be found straightforwardly by extending the procedures outlined in Secs. III and IV. However, the detailed calculations are fairly tedious and, because of the presence of the functions $E_j(t)$, give rise to the higher order nonexponential parameters, h_j^\pm and h_j^δ , defined in Eqs. (47) and (48).

The mean displacement at time t must now be suitably normalized so as to include only surviving walkers. Thus we have

$$\begin{aligned} \langle x(t) \rangle &= \frac{d}{N} \sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} (j+Nl) P_j(l,t) \bigg/ \sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} P_j(l,t) \\ &= \frac{d}{N} \sum_{j=0}^{N-1} C_j(t) \bigg/ \sum_{j=0}^{N-1} B_j(t), \end{aligned} \quad (125)$$

while the desired mean-square displacement is similarly given by

$$\begin{aligned} \langle x^2(t) \rangle &= \frac{d^2}{N^2} \sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} (j+Nl)^2 P_j(l,t) \bigg/ \\ &\quad \sum_{l=-\infty}^{\infty} \sum_{j=0}^{N-1} P_j(l,t) \\ &= \frac{d^2}{N^2} \sum_{j=0}^{N-1} E_j(t) \bigg/ \sum_{j=0}^{N-1} B_j(t). \end{aligned} \quad (126)$$

On taking the derivatives required by Eqs. (1) and (2) and the steady-state limit, these expressions yield the results for the velocity and the dispersion given in Eqs. (34) and (39)–(48). Naturally, when there is no possibility of detachments [$\psi_j^\delta(t) \equiv 0$, $\lambda = 0$] one recovers all the results for the periodic sequential models with waiting times as reported in the Introduction and Summary and in Sec. III.

This completes the description of our mathematical analysis. In brief summary, we have introduced linear, periodic sequential stochastic models with general waiting-time distributions and have found explicit expressions for the corresponding mean velocities and dispersions that have been reported in Sec. I. The simplest sequential models have been extended by including finite branches and by allowing for the possibility of death or detachment processes. Deviations from the exponential waiting-time distribution functions that characterize standard kinetic models embodying Poisson processes do not change the form of the velocity expressions; however, the dispersions entail nonexponential parameters that enter in a more complicated manner. The concept of ‘‘mechanicity,’’ introduced in Sec. II, is useful to quantify and visualize the departures from the usual ‘‘chemical’’ kinetic descriptions.

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