Solutions of burnt-bridge models for molecular motor transport

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Transport of molecular motors, stimulated by interactions with specific links between consecutive binding sites (called "bridges"), is investigated theoretically by analyzing discrete-state stochastic "burnt-bridge" models. When an unbiased diffusing particle crosses the bridge, the link can be destroyed ("burned") with a probability p, creating a biased directed motion for the particle. It is shown that for probability of burning $p=1$ the system can be mapped into a one-dimensional single-particle hopping model along the periodic infinite lattice that allows one to calculate exactly all dynamic properties. For the general case of $p<1$ a theoretical method is developed and dynamic properties are computed explicitly. Discrete-time and continuous-time dynamics for periodic distribution of bridges and different burning dynamics are analyzed and compared. Analytical predictions are supported by extensive Monte Carlo computer simulations. Theoretical results are applied for analysis of the experiments on collagenase motor proteins.

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I. INTRODUCTION

Molecular motors, or motor proteins, play an important role in the functioning of biological systems [1–3]. They transform a chemical energy into mechanical work with a high efficiency and move along linear molecular tracks. Conventional molecular motors fuel their motion by hydrolyzing adenosine triphosphate (ATP) or related compounds, and the chemical energy influx creates a biased directed motion along one-dimensional protein filaments. During the translocation of motor proteins the chemical state of linear protein tracks remains unchanged.

Recently, another type of molecular motor, independent of ATP hydrolysis, has been discovered [4,5]. A special protein called collagenase moves along collagen fibrils, which are the main component of extracellular matrix [1], and it cleaves the filament at special sites. Collagen proteolysis provides a chemical energy that produces a directed motion of the motor protein molecule. It was found that the random motion of an enzyme molecule can be transformed into the biased diffusion along the linear track if, after the cleavage of collagen, the motor protein could only move on one side of the broken link [5].

It was suggested that the dynamics of collagenases can be explained by a so-called "burnt-bridge" model (BBM) [4–7]. According to this approach, the motor protein is viewed as a random walker hopping along the one-dimensional lattice that consists of two types of links: Strong and weak. Strong links are not affected when the particle passes them, however crossing the weak links might destroy them with a probability $0<p\leqslant 1$, and the random walker is not allowed to move again over the "burnt" links. Using a spatial continuum approximation that neglects the underlying lattice, the burnt-bridge model has been discussed in the limiting cases of very low p and $p\to 1$ [6]. This approximation is only valid in the limit of very low concentrations of the special links, although in biological systems the density of bridges might be significant [4,5]. Antal and Krapivsky [7] have investigated BBM by using a discrete-time random walk approach that allowed one to calculate exactly velocities and dispersions for some sets of parameters for several versions of the model. However, discrete-time dynamics is unrealistic for motor proteins since their dynamics is tightly coupled to a set of chemical transitions [8], and time intervals between these transitions are distributed exponentially according to Poisson statistics. A discrete-time statistics implicitly assumes a delta-function waiting time distribution between consecutive steps. In addition, the approach presented in Ref. [7] is mathematically very involved, and not all relevant dynamic properties have been computed. The goal of this paper is to investigate more realistic continuous-time discrete-state stochastic burnt-bridge models using simple analytical approaches and extensive Monte Carlo computer simulations.

II. MODEL

Let us consider a single random walker that moves along an infinite one-dimensional lattice as shown in Fig. 1. The particle can hop in both directions with the same rate $v_0=1$, i.e., initially there is no bias in the motion of the random walker. We set the size of the lattice spacing to be equal to one. There are two types of links between consecutive binding sites on the lattice. The random walker does not interact with the strong links, while crossing the weak link leads to burning of the bridge with the probability p. We assume that after the burning of the bridge the particle is always on the

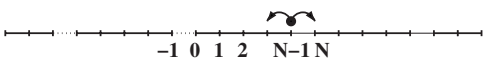

FIG. 1. A schematic view of the motion of the particle in the system with burnt bridges. Thick solid lines are strong links, while thin solid lines are weak links, or "bridges" that can be burnt. Dotted lines are already burnt bridges. The particle can jump with equal rates to the right or to the left unless the link is broken.

right side from it, and there are no burnt bridges at the initial time. Thus the particle is never trapped between broken links, and it moves continuously forward.

We distinguish two different possibilities of burning the bridge. In the first option, the bridge is burned only when the particle crosses it from left to right, but nothing happens when the walker moves from right to left. This model is called a forward BBM. In the second option, the particle burns the bridge on any forward and backward motion across the weak link, describing a forward-backward BBM. It is important to note that both cases are identical for $p=1$, while for $p<1$ dynamics differs significantly for different burning scenarios. Dynamic properties of the system also depend on the details of the particle behavior near the already burned bridge [7]. In the standard version of BBM the particle sitting next to the broken link can only move forward in the right direction. In the modified version of BBM the walker tries to cross the burnt bridge, but the attempt fails and the particle does not change its position.

The dynamics of the motor protein molecule in different BBMs is directly determined by two parameters: The probability of burning p and the concentration of weak links c. The distribution of bridges strongly influences the dynamic properties [7], and two different cases can be discussed: Periodic and random distributions. The case when the bridges are found at equal distance $N=1/c$ lattice spacings apart from each other describes the periodic distribution. In this paper we will analyze in detail this situation, although our methods can be also applied to random distribution of bridges.

III. BURNT-BRIDGE MODELS WITH $p=1$

First, we consider a special case of BBM with $p=1$ when any crossing of the bridge leads to its burning. In addition, it is assumed that the first burnt bridge was crossed from the left. Thus the particle drifts in the right (forward) direction. For the periodic distribution of bridges the dynamic properties of the system can be evaluated explicitly by mapping the model into the motion of the random walker on infinite one-dimensional periodic lattice, for which exact solutions have been derived by Derrida in 1983 [8–10]. The particle at site j $(j=0,1,\ldots,N-1)$ moves forward (backward) with the rate u_j (w_j), and the periodicity requires that $u_j \equiv u_{j+N}$ and $w_j \equiv w_{j+N}$, where N is the size of the period. For this model the explicit expression for the mean velocity V is given by [9]

$$V = \frac{N}{\sum_{j=0}^{N-1} r_j}\left[1 - \prod_{i=1}^{N}\left(\frac{w_i}{u_i}\right)\right], \tag{1}$$

while the dispersion, or diffusion coefficient, can be found from

$$D = \frac{1}{\left(\sum_{j=0}^{N-1} r_j\right)^2}\left\{V\sum_{j=0}^{N-1} s_j \sum_{i=0}^{N-1}(i+1)r_{j+i+1} + N\sum_{j=0}^{N-1} u_j s_j r_j\right\} - \frac{V(N+2)}{2}, \tag{2}$$

with auxiliary functions

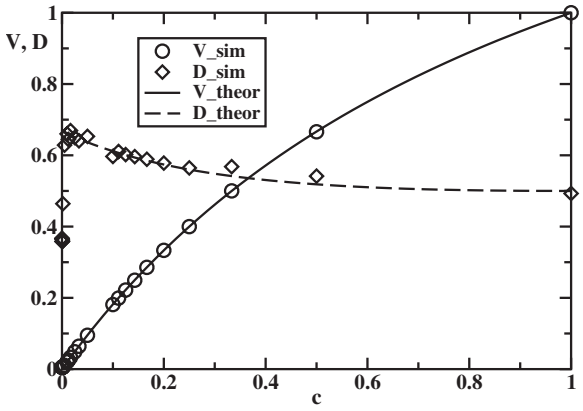

FIG. 2. Dynamic properties of a continuous-time burnt-bridge model with periodic distribution of bridges for $p=1$. Lines are from analytic calculations, while symbols are obtained from Monte Carlo computer simulations—see text for details.

$$r_j = \frac{1}{u_j}\left[1 + \sum_{k=1}^{N-1}\prod_{i=j+1}^{j+k}\left(\frac{w_i}{u_i}\right)\right] \tag{3}$$

and

$$s_j = \frac{1}{u_j}\left[1 + \sum_{k=1}^{N-1}\prod_{i=j-1}^{j-k}\left(\frac{w_{i+1}}{u_i}\right)\right]. \tag{4}$$

The BBM with $p=1$ corresponds to the particle hopping model with $u_j=w_j=1$ for all j with the exception of $w_0=0$, which reflects the complete burning of the bridge. Then from Eq. (1) the explicit formula for the velocity is given by

$$V = \frac{2}{N+1} = \frac{2c}{c+1}. \tag{5}$$

The dispersion can be obtained from Eq. (2), yielding

$$D = \frac{2(c^2+c+1)}{3(c+1)^2}. \tag{6}$$

The dynamic properties of BBM with $p=1$ are shown in Fig. 2 as functions of the concentration of bridges. The velocity is a monotonically growing function of c, while the dispersion is always decreasing. It is interesting to consider their behavior in limiting cases. When every link on the lattice is a bridge $(c=1)$ we obtain $V=1$ and $D=1/2$, as expected. More interesting is the limit of $c\to 0$. The velocity goes to zero, $V\simeq 2c$, as expected, and this reproduces the result of the continuum theory of Mai *et al.* [6]. But, surprisingly, it is found that $D_{\mathrm{BBM}}(c=0)=2/3$ and it is not equal to the dispersion of a free particle on the lattice without bridges, $D_{\mathrm{free}}=1$. This jump in the dispersion might correspond to a dynamic transition, indicating qualitatively different behavior of the particle moving in the system without weak links and particle diffusing in BBM. Similar behavior has been observed in the discrete-time BBM [7]. However, this interesting phenomenon requires a more careful and detailed investigation.

The mapping of BBM to the particle hopping model on the periodic lattice can also be used to investigate discrete-

time burnt-bridge models. It was found [9] that in this case the explicit expression for the velocity is the same as in the continuous case, while for the diffusion coefficient it can be shown that $D_{\text{discr}}=D_{\text{cont}}-V^2/2$, and D_{cont} and V can be obtained from Eqs. (1) and (2). However, the rate constants u_j and w_j have to be reinterpreted as jumping probabilities, leading to

$$u_j = w_j = \frac{1}{2} \quad \text{for } j = 1,2,\ldots,N-1. \tag{7}$$

At the same time, for the particle near the burned bridge the rates are $u_0=1$ and $w_0=0$ for the standard BBM, while $u_0=1/2$ and $w_0=0$ for the modified BBM. Then the dynamic properties of the standard discrete-time BBM are

$$V = c, \quad D = \frac{1}{3}(1-c^2), \tag{8}$$

and for the modified BBM we obtain

$$V = \frac{c}{c+1}, \quad D = \frac{1}{3(c+1)} - \frac{c^2}{6(c+1)^2}. \tag{9}$$

These results fully agree with those obtained in Ref. [7] for periodic bridge distribution. Note, however, that our approach based on Derrida's analysis is much more straightforward.

IV. BURNT-BRIDGE MODELS WITH $p<1$

Derrida's method cannot be easily extended to include the general case of bridge burning with the probability $p<1$ since it is not clear how the hopping rates u_j and w_j depend on p. To calculate dynamic properties of BBM we introduce another method that is very general and applicable for many different systems. Below we analyze in detail several BBMs to illustrate our approach.

A. Continuous-time forward BBM for the periodic distribution of bridges

Now we consider a continuous-time BBM with the particle destroying the link with the probability p only when the bridge is crossed from left to right. The distribution of weak links is periodic, i.e., they are positioned $N=1/c$ sites apart from each other. Let us define $R_j(t)$ as the probability to find the random walker j sites apart from the last burnt bridge at time t. The probabilities $R_j(t)$ are associated with the moving system of coordinates with the last burned bridge always at the origin. The corresponding kinetic scheme is shown in Fig. 3(a). The dynamics of the system can be described by a set of master equations. For the lattice sites not connected to weak links or connected only from the left side we have

$$\frac{dR_{kN+i}(t)}{dt} = R_{kN+i-1}(t) + R_{kN+i+1}(t) - 2R_{kN+i}(t), \tag{10}$$

for $k=0,1,2,\ldots$ and $i=1,2,\ldots,N-1$. For all other lattice sites (except the origin) one can show that

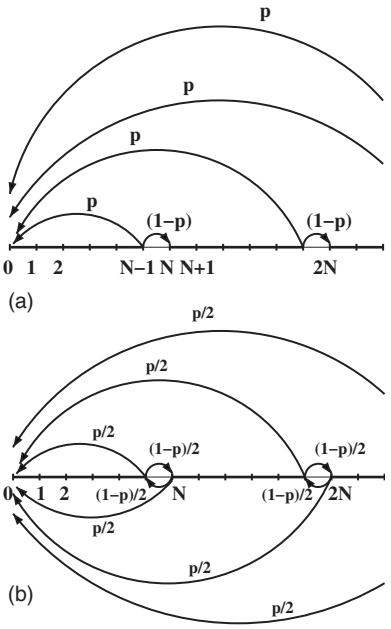

FIG. 3. Reduced kinetic schemes for systems with periodic distribution of bridges: (a) Continuous-time forward BBM (only transition rates not equal to unity are shown); (b) discrete-time forward-backward BBM (only transition rates not equal to 1/2 are shown). The origin corresponds to the right end of the last burnt bridge.

$$\frac{dR_{kN}(t)}{dt} = (1-p)R_{kN-1}(t) + R_{kN+1}(t) - 2R_{kN}(t) \quad \text{for} \quad k = 1,2,\ldots. \tag{11}$$

The dynamics are different at the origin [see Figs. 1 and 3(a)] where

$$\frac{dR_0(t)}{dt} = p\sum_{k=1}^{\infty}[R_{kN-1}(t)] + R_1(t) - R_0(t). \tag{12}$$

In addition, there is a normalization condition,

$$\sum_{k=0}^{\infty}\sum_{i=0}^{N-1} R_{kN+i}(t) = 1, \tag{13}$$

which is valid at all times.

In the stationary-state limit ($t\to\infty$) we have $(d/dt)R_j(t)=0$, and Eqs. (10)–(12) simplify significantly,

$$R_i = R_0 - ipS, \quad S = \sum_{k=1}^{\infty} R_{kN-1} \quad \text{for } i = 0,1,\ldots,N \tag{14}$$

and

$$R_{kN+i} = (i+1)R_{kN} - i(1-p)R_{kN-1} \quad \text{for } i = 0,1,\ldots,N, \quad k = 1,2,\ldots. \tag{15}$$

To find the solutions of Eqs. (14) and (15) we assume that it has the following form:

$$R_{kN+i} = R_0 e^{ak} - iB(k), \tag{16}$$

where a and $B(k)$ are unknown parameters. This expression assumes a linear dependence between the weak links and an exponential decrease for consecutive periods. To eliminate $B(k)$, we observe that Eqs. (14) and (15) simultaneously hold for $i=N$, giving us

$$R_{(k+1)N} = R_0 e^{a(k+1)} = R_{kN+N} = R_0 e^{ak} - NB(k), \tag{17}$$

which leads to

$$B(k) = \frac{R_0}{N} e^{ak}(1 - e^a). \tag{18}$$

To obtain the expression for a, we substitute R_{kN+i} from Eq. (16) in the recurrent formula (15),

$$R_0 e^{ak} - iB(k) = (i+1)R_0 e^{ak} - i(1-p) \times [R_0 e^{a(k-1)} - (N-1)B(k-1)]. \tag{19}$$

Then using the expression (18) for $B(k)$ and defining $x \equiv e^a$, Eq. (19) eventually reduces to

$$x^2 - [2 + p(N-1)]x + (1-p) = 0. \tag{20}$$

Since R_{kN+i} is a decreasing function, the parameter a is always less than 1, and we choose a physically reasonable solution of Eq. (20),

$$x = 1 + \frac{1}{2}p(N-1) - \frac{1}{2}\sqrt{p^2(N-1)^2 + 4pN}. \tag{21}$$

Note that generally $0 \leqslant x \leqslant 1$ and $x=0$ for $p=1$, while $x=1$ for $p=0$. The probability to find the particle next to the burnt bridge, R_0, can be found from the normalization condition (13) and Eq. (21), yielding

$$R_0 = \frac{2(1-x)}{N+1+x(N-1)} = \frac{2p}{\sqrt{p^2(N-1)^2 + 4pN}} = \frac{2pc}{\sqrt{p^2(1-c)^2 + 4pc}}, \tag{22}$$

and the solution for R_{kN+i} in terms of x and R_0 is finally given as

$$R_{kN+i} = R_0 x^k \left[1 - \frac{i}{N}(1-x)\right]. \tag{23}$$

Exact solutions for the probabilities R_j to find the particle at given distance from the last burnt bridge allow us to calculate many dynamic properties of the system. Specifically, the mean velocity of the particle is given by

$$V = \sum_{j=0}^{\infty} (u_j - w_j) R_j. \tag{24}$$

However, since the rates to go forward and backward are the same at all sites except the origin, all contributions to the velocity cancel out and only the $j=0$ term survives,

$$V(c,p) = R_0 = \frac{2pc}{\sqrt{p^2(1-c)^2 + 4pc}}. \tag{25}$$

For $p=1$ this equation reduces to $V(c,p=1)=2c/(c+1)$, which agrees exactly with the result (5) derived using the mapping to Derrida's random hopping model. In the limit of $p \to 0$ and $c \to 0$ $(p \ll c)$ Eq. (25) becomes $V \approx \sqrt{pc}$ as compared to $V \approx \sqrt{2pc}$ in [6]. The discrepancy is due to the fact that in our model only forward burning is considered, while in Ref. [6] the bridge can be burned on both forward and backward motions of the motor protein molecule. The expression for the velocity (25) also simplifies in the case of $N=c=1$, giving $V=\sqrt{p}$.

Another useful dynamic property that can be obtained from our analysis is average and average-squared distances between the particle and the last burnt bridge, namely

$$\langle j \rangle = \sum_{j=0}^{\infty} j R_j, \quad \langle j^2 \rangle = \sum_{j=0}^{\infty} j^2 R_j. \tag{26}$$

Substituting Eq. (23) into the expressions (26) we obtain

$$\langle j \rangle = R_0 \left\{ \frac{N^2 x}{(1-x)^2} + \frac{N^2 - 1}{6} \right\} \tag{27}$$

and

$$\langle j^2 \rangle = R_0 \left\{ \frac{N^3 x(x+1)}{(1-x)^3} + \frac{1}{12} N(N^2-1) \frac{x+1}{1-x} \right\}, \tag{28}$$

where x and R_0 are given by Eqs. (21) and (22). For $p=1$ one can show that

$$\langle j \rangle = (N-1)/3, \quad \langle j^2 \rangle = N(N-1)/6. \tag{29}$$

In the limit of $p \ll c$ we have

$$\langle j \rangle \simeq \sqrt{N/p}, \quad \langle j^2 \rangle \simeq 2N/p, \tag{30}$$

while in the opposite limit of $c \ll p$ the results are

$$\langle j \rangle \simeq N/3, \quad \langle j^2 \rangle \simeq N^2/6. \tag{31}$$

For the special case of $N=c=1$ we obtain

$$\langle j \rangle = \frac{1}{\sqrt{p}} - 1, \quad \langle j^2 \rangle = \left(\frac{1}{\sqrt{p}} - 1\right)\left(\frac{2}{\sqrt{p}} - 1\right). \tag{32}$$

We can also calculate the average and average-squared distances between the consecutive burnt bridges. Because the burning is a stochastic process, i.e., $p<1$, this distance generally deviates from N. In order to compute these properties we introduce P_{kN} as a probability that the next bridge that will be destroyed is kN sites away from the given burnt bridge. Then

$$P_{kN} = \frac{pR_{kN-1}}{\sum_{k=1}^{\infty} (pR_{kN-1})}, \quad k = 1,2,\ldots. \tag{33}$$

The average and average-squared distances between the consecutive burnt bridges can be found from the following expressions:

$$\langle l\rangle = \sum_{k=1}^{\infty} kNP_{kN}, \quad \langle l^2\rangle = \sum_{k=1}^{\infty} (kN)^2 P_{kN}. \tag{34}$$

By substituting Eqs. (23) and (33) into (34) and using Eq. (21) we found that

$$\langle l\rangle = \frac{N}{1-x}, \quad \langle l^2\rangle = \frac{N^2(1+x)}{(1-x)^2}. \tag{35}$$

The average distance $\langle l\rangle$ is related to the fraction of unburnt bridges q via the following expression:

$$q = \frac{(\langle l\rangle/N - 1)}{\langle l\rangle/N} = 1 - N/\langle l\rangle = x, \tag{36}$$

which gives the physical meaning of the variable x used in our analysis. In the limiting cases we obtain the following results:

$$\langle l\rangle = N, \quad \langle l^2\rangle = N^2, \quad \text{for } p = 1,$$

$$\langle l\rangle = 1/\sqrt{p}, \quad \langle l^2\rangle = 2/p - 1/\sqrt{p}, \quad \text{for } N = c = 1,$$

$$\langle l\rangle = \sqrt{N/p}, \quad \langle l^2\rangle = 2N/p, \quad \text{for } p \ll c,$$

$$\langle l\rangle = N, \quad \langle l^2\rangle = N^2, \quad \text{for } p \gg c. \tag{37}$$

B. Discrete-time forward-backward BBM for the periodic distribution of bridges

Our theoretical method is very general and it can be applied to any version of BBM. As another example, we analyze a motion of the particle in discrete-time framework with periodically located bridges that can burn with the probability p during the forward and backward transitions. We again introduce a modified kinetic scheme by putting the last burnt bridge at the origin, as shown in Fig. 3(b). The important difference between continuous-time and discrete-time models is the fact that instead of transition rates in the continuous-time case transition probabilities are used in the discrete-time dynamics. As a result, the sum of transition probabilities at each site is equal to unity. We assume that at the sites that do not support the weak links the transition probabilities are equal, i.e., $u_{kN+i}=w_{kN+i}=1/2$ and $w_{kN-1}=u_{kN}=1/2$ for any k and for $i=1,2,\ldots,N-2$. The transition probabilities are also equal at the sites that surround the weak links, giving $u_{kN-1}=w_{kN}=(1-p)/2$ for $k=1,2,\ldots$ [see Fig. 3(b)]. In addition, at the origin it is assumed that $u_0=1$ and $w_0=0$.

As before, we define $R_j(t)$ as the probability to find the random walker at the position j at time t. The dynamics of the system is governed by a set of discrete-time Master equations that are different from the continuous-time version [7,9]. For the lattice sites that do not support the weak links the corresponding master equations are

$$R_{kN+i}(t+1) = \frac{1}{2}R_{kN+i-1}(t) + \frac{1}{2}R_{kN+i+1}(t), \tag{38}$$

for any k and with $i=1,2,\ldots,N-2$ (with the exception of R_0 and R_1—see below). For the lattice sites around the bridges we have

$$R_{kN-1}(t+1) = \frac{1}{2}R_{kN-2}(t) + \frac{1-p}{2}R_{kN}(t),$$

$$R_{kN}(t+1) = \frac{1-p}{2}R_{kN-1}(t) + \frac{1}{2}R_{kN+1}(t), \tag{39}$$

for $k=1,2,\ldots$. The dynamics is different near the origin,

$$R_0(t+1) = \frac{p}{2}S' + \frac{1}{2}R_1(t),$$

$$R_1(t+1) = R_0(t) + \frac{1}{2}R_2(t), \tag{40}$$

where $S' = \Sigma_{k=1}^{\infty}[R_{kN-1}(t) + R_{kN}(t)]$. At large times the system reaches a stationary state with $R_{kN+i}(t+1) = R_{kN+i}(t)$, and Eqs. (38)–(40) simplify to yield for the first period ($k=0$),

$$R_i = 2R_0 - ipS' \quad \text{for } i = 1,2,\ldots,N-1,$$

$$R_N = \frac{1}{1-p}(2R_0 - NpS'), \tag{41}$$

while for all other periods ($k \geqslant 1$) one can obtain

$$R_{kN+i} = (i+1)R_{kN} - i(1-p)R_{kN-1}, \quad \text{for } i = 0,1,\ldots,N-1,$$

$$R_{kN+N} = \frac{1}{1-p}[(N+1)R_{kN} - N(1-p)R_{kN-1}]. \tag{42}$$

In order to solve Eqs. (41) and (42) it is natural to look for a solution in the form

$$R_{kN+i} = 2R_0 e^{ak} - iB(k), \tag{43}$$

for all k and i except the origin ($k=i=0$). Note that the factor of 2 in front of R_0 in Eq. (43) is necessary to ensure the consistency between the solutions for $k=0$ from Eq. (41) and for $k \geqslant 1$ [see Eq. (42)]. The solutions can be obtained using the same approach as was discussed in the previous section for the continuous-time forward BBM. The final expressions are

$$R_0 = \frac{1-x}{N + [N - p(N-1)]x},$$

$$R_{kN+i} = 2R_0 x^k \left[1 - \frac{i}{N}(1 - (1-p)x)\right], \tag{44}$$

where we again define $x \equiv e^a$, and it can be shown that

$$x = \frac{1}{2}(\alpha - \sqrt{\alpha^2 - 4}), \quad \alpha = \frac{N+1}{1-p} - (1-p)(N-1). \tag{45}$$

The dynamic properties of the particle in this model can be calculated as presented above for the continuous-time for-

ward BBM. For the velocity we obtain the following formal expression:

$$v = R_0 + \frac{p}{2}\sum_{k=1}^{\infty} R_{kN}. \tag{46}$$

The validity of this equation can be seen from the fact that the forward and backward hopping rates cancel each other on all sites except at the origin and the sites labeled kN ($k=1,2,\ldots$). From Eq. (44) it follows that $R_{kN}=2R_0x^k$. Substituting this result into Eq. (46) yields

$$v = R_0\frac{1+(p-1)x}{1-x}, \tag{47}$$

that can be transformed with the help of Eq. (44) into

$$v = \frac{1-(1-p)x}{N+[N-p(N-1)]x}. \tag{48}$$

Finally, replacing x according to Eq. (45) and using $N=1/c$ we obtain

$$v(c,p) = \frac{c(1-p)(2c+Z)}{2c(1-p)-[1-p(1-c)]Z}, \tag{49}$$

where

$$Z = [2c+p(2-p)(1-c)]\left\{-1 + \sqrt{1-\frac{4c^2(1-p)^2}{[2c+p(2-p)(1-c)]^2}}\right\}. \tag{50}$$

After some rearrangement, it can be shown that this formula is identical to the expression for the velocity obtained by Antal and Krapivsky [7]. But note again that our derivation is much simpler.

V. DISCUSSIONS

To check the validity of our theoretical approach we performed extensive Monte Carlo computer simulations for several BBMs. A general algorithm for continuous-time and discrete-time random walks, discussed in detail in Ref. [11], has been utilized. Velocities have been calculated from the single simulations, consisting of 10^6–10^7 steps, via the basic formula $V=\langle x\rangle/t$. Diffusion constants have been determined using the expression $D=(\langle x^2\rangle-\langle x\rangle^2)/2t$, and typically more than 10^5 simulation runs have been averaged over to reduce the stochastic noise in the data. The results of simulations, as shown in Figs. 2, 4, and 6, in all cases are in excellent agreement with available analytical calculations, supporting our analytical predictions.

Theoretical calculations show that the velocity of the particle in BBM is a monotonically increasing function of the concentration of weak links and burning probability: see Figs. 2, 4, and 5. However, the behavior of the dispersion is more complex, as can be judged from Figs. 2 and 6. For fixed values of p it decreases as a function of c, although note large fluctuations when $c\to 0$. Increase in the burning probability first lowers significantly the dispersion, and then it starts to increase slowly. Our computer simulations indicate [see Fig. 6(a)] that when every link in the system is a potential bridge ($c=1$) the dispersion is always equal to $1/2$ for any $p\neq 0$.

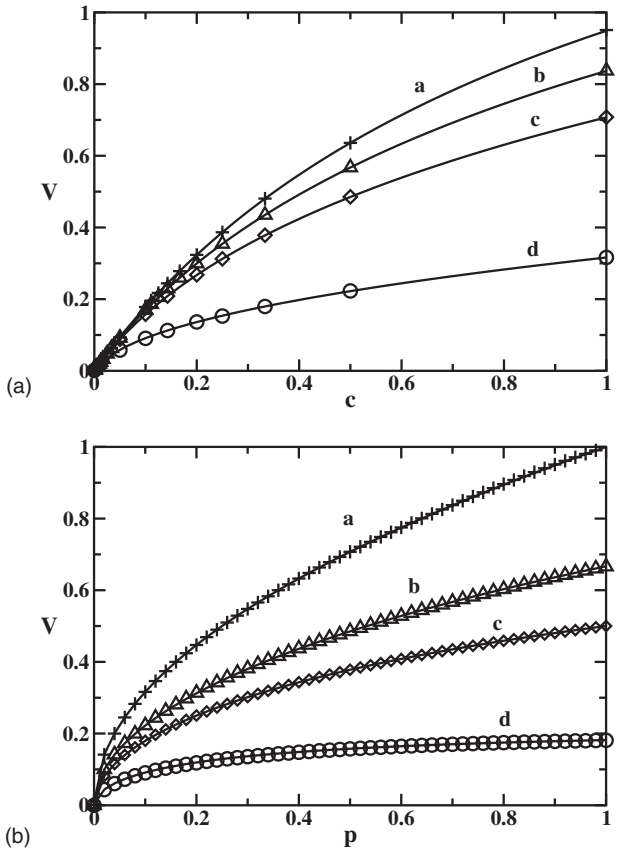

FIG. 4. (a) Velocity as a function of concentration of bridges for different burning probabilities for the periodic forward continuous-time BBM. Solid lines are results of analytical calculations, and symbols are from Monte Carlo simulations. Curve a corresponds to $p=0.9$, curve b corresponds to $p=0.7$, curve c corresponds to $p=0.5$, and curve d corresponds to $p=0.1$. (b) Velocity as a function of burning probability for different concentrations of weak links for the periodic forward continuous-time BBM. Solid lines are results of analytical calculations and symbols are from Monte Carlo simulations. Curve a corresponds to $c=1$, curve b corresponds to $c=1/2$, curve c corresponds to $c=1/3$, and curve d corresponds to $c=1/10$.

Our theoretical computations also indicate that details of burning process (forward versus forward-backward) are affecting the dynamics of the particle. Under the same conditions, the random walker moves faster in the forward-backward BBM, and this effect is significant for large p and c: see Fig. 5. These results are expected since the burning of the bridge fuels the forward motion of the particle. The possibility of burning in the forward and backward motion accelerates the motion of the random walker.

Developed theoretical method allows us to analyze experimental data on the motion of collagenases motor proteins [4]. Using fluorescence correlation spectroscopy it was determined that the diffusion coefficient is $D=8\pm1.5$

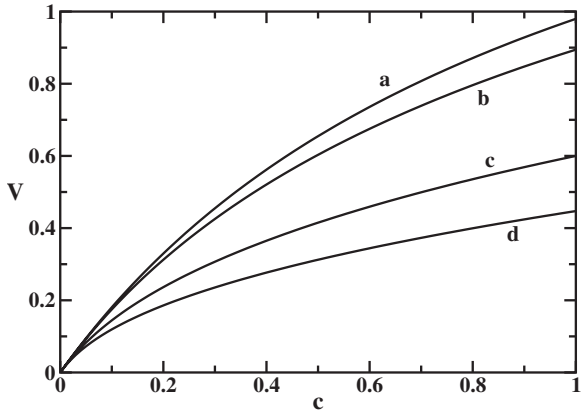

FIG. 5. Velocity as a function of concentration for different burning realizations for the continuous-time periodic BBM. Solid lines are results of analytical calculations. Curve a corresponds to forward-backward BBM with $p=0.8$, curve b corresponds to forward BBM with $p=0.8$, curve c corresponds to forward-backward BBM with $p=0.2$, and curve d corresponds to forward BBM with $p=0.2$.

$\times 10^{-13}$ m^2 s^{-1} and the mean drift velocity is $V=4.5\pm0.36 \times 10^{-6}$ m s^{-1} [4]. Our theoretical results are obtained assuming that the lattice spacing and transition rates are equal to unity. To restore the correct units we assume that the motor protein moves in discrete steps of size a. Although the exact value of a is unknown we can reasonably take $a \simeq 10$ nm, which is of the same order as step sizes of other molecular motors [2]. From the structure of the collagen it is known that cleavage sites, that correspond to the bridges, are separated by the distance $\Delta=300$ nm [1,4]. It suggests that BBM with periodic distribution of bridges and $c=a/\Delta=1/30$ is appropriate to describe the dynamics of the system. Since at low concentrations the predictions for the dynamic properties in the forward and forward-backward BBM are very similar (see Fig. 5), for the velocity we use Eq. (25) multiplied by av_0,

$$V(c,p) = av_0 \frac{2pc}{\sqrt{p^2(1-c)^2+4pc}}, \tag{51}$$

where v_0 is the transition rate. For the diffusion coefficient analytical results are not known, but for $c \ll 1$ the limiting result of $c=0$ can be used, yielding

$$D = a^2 v_0. \tag{52}$$

Equations (51) and (52) with two unknowns, p and v_0, can be easily solved, and we obtain

$$p \simeq 0.28, \quad v_0 \simeq 8 \times 10^3 \text{ s}^{-1}. \tag{53}$$

Our estimate of the burning probability $p \simeq 28\%$ is larger than the result $p=10\%$ obtained in Monte Carlo simulations [4]. However, the difference can be attributed to different versions of BBM used in our theoretical analysis and in computer simulations [4], and to the uncertainty in the determination of the step size a.

It is also interesting to analyze the efficiency of the motor protein driven by burning of bridges. Our theoretical analysis indicates that the motion of the particle in the system with burnt bridges can be viewed as a biased random walk. We assume that the dynamic properties of the random walker in BBM can be effectively written as

$$V = a(u_{\text{eff}} - w_{\text{eff}}), \quad D = \frac{1}{2}a^2(u_{\text{eff}} + w_{\text{eff}}), \tag{54}$$

where u_{eff} and w_{eff} are effective transition rates of the biased random walk. Then the force exerted by the molecular motor can be found from [10,12]

$$F = \frac{k_B T}{a} \ln \frac{u_{\text{eff}}}{w_{\text{eff}}}. \tag{55}$$

Substituting experimental values for V and D into Eqs. (54) to obtain the effective rates u_{eff} and w_{eff}, the exerted force can be calculated, yielding $F \simeq 0.023$ pN, which is two orders of magnitude weaker than the forces produced by other motor proteins [2]. However, this force is exerted over the distance of $\Delta=300$ nm, which is 10–100 times larger than for conventional molecular motors, producing $W=F\times\Delta \simeq 6.9$ pN$\times$nm of work. The cleavage of three peptide bonds simultaneously, that fuels the motion of collagenase, liberates $E \simeq 62.7$ kJ/mole or 104.4 pN$\times$nm of energy [4]. The calculated efficiency of the collagenase motor protein, $\nu = W/E \simeq 6.3\%$, is only slightly lower than the efficiency of 15% obtained from the experimental estimates [4]. Thus single collagenase protein is a weak molecular motor and its

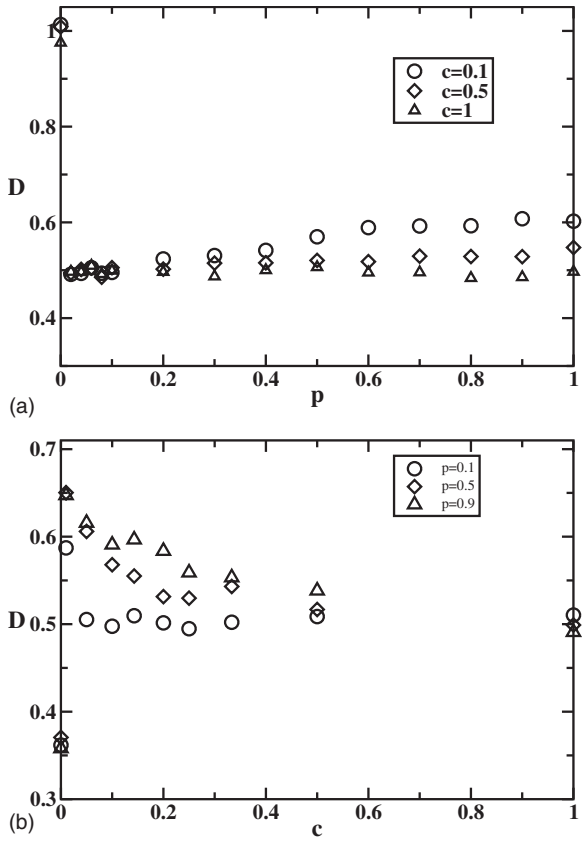

FIG. 6. Dispersion in the forward continuous-time periodic BBM from Monte Carlo simulations (a) as a function of burning probability and (b) as a function of concentration of bridges.

efficiency is not very high in comparison with other motor proteins. However, it was suggested recently [5] that coupling of several enzymes might produce a very efficient motor protein.

VI. SUMMARY AND CONCLUSIONS

A general theoretical analysis of particle dynamics in different one-dimensional burnt-bridge models is presented. It is shown that, when the probability of burning is equal to unity, the system can be mapped into the model of the single particle hopping along the periodic infinite lattice. This allows us to obtain all dynamic properties in exact and explicit form. For the general case of $p<1$ we developed a method of analyzing the dynamics by considering a reduced kinetic scheme with respect to the last burnt bridge. It is found that distribution of weak links and the details of the burning mechanism strongly influence the particle dynamics in BBM. Theoretical calculations are fully supported by Monte Carlo computer simulations. Application of this theoretical method to experiments on collagenase motor proteins provides the estimates of the burning probability and the exerted force, leading to the conclusion that this molecular motor is rather weak and not very efficient, in contrast to conventional motor proteins.

Although the presented theoretical approach investigates explicitly the dynamic properties of many BBMs and it is successfully applied for analysis of experimental data, there are several problems that should be addressed in the future studies. We have not been able to obtain expressions for the diffusion coefficient in the general case of $p<1$, and our analysis is given only for the periodic distribution of weak links. It is also not clear what is the origin of jump in the dispersion in the limit of $c\to 0$. It will be interesting to investigate the motion of the motor protein on lattices with periodic rates [10] and with bridge burning, and it is reasonable to suggest that the approach developed in this paper can be generalized for this case too. In addition, a more realistic approach will be to allow the molecular motor to jump between parallel tracks [4]. Future experiments on single motor proteins that utilize bridge burning mechanisms will be important to test the validity of the presented theoretical approach.

ACKNOWLEDGMENTS

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