Diffusion in discrete ratchets

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The phenomenon of noise-induced transport in ratchet devices offers an explanation for directed motion on the molecular scale observed in many biological systems. Net transport through a series of discrete states, occurring in cyclic processes or reactions, can be related to widely investigated continuous ratchet models in the context of thermally activated transitions. The transport process can be described effectively in terms of two characteristic coefficients: velocity and diffusion. Their relation to model parameters and limitations for the ratchet mechanism are discussed in this paper. As an application we consider a four-state model for uphill transmembrane transport and compare theoretical results with existing data from a related experiment. [S1063-651X(99)10207-1]

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I. INTRODUCTION

The phenomenon of noise-induced transport offers an explanation for directed motion observed on the molecular scale. It has been mainly discussed in the context of biological systems, e.g., actin/myosin [1], kinesin/microtubules [2] or transmembrane transport [3].

The two indispensable prerequisites for this molecular transport mechanism are (unbiased but) nonthermal fluctuations and a broken reflection symmetry. Whereas the first requirement becomes transparent in connection with the second law of thermodynamics [4] the second is needed to select a preferred direction of net transport. The broken symmetry is usually introduced by choice of a periodic but asymmetric potential, a so-called ratchet or washboard potential.

Depending on the system under consideration the coordinate may be a spatial axis or a reaction coordinate. As an example for the latter case we mention the transport of a substance (ion) through a membrane. The catalyzing macromolecule is apt to conformational changes and possesses different binding sites. This situation has led to the formulation of a four-state model [5] and underlines the practical relevance of discrete ratchet models.

Transport in spatially continuous systems can be described by means of a Fokker-Planck equation [6]. Within this framework the central quantity of interest, the stationary current, can be formulated rigorously. However, analytic results can be found for a few examples only. On the other hand, for a discrete-state model, and especially for chemical kinetics, a formulation in terms of rate equations is possible. In mathematical terms this involves simple linear algebra, hence, allowing for analytical expressions quite generally. Both descriptions are connected by Kramer's theory relating rates to the shape of potentials [7]. It should be noted that the kinetic description is only valid in some appropriate adiabatic limit.

So far, most investigations have concentrated on quantifying and comparing currents that can be achieved when using different mechanisms to drive the system out of equilibrium: rocking (e.g., [8–10]) or flashing (e.g., [11,12]) the ratchet, applying dichotomic (e.g., [11,12]), harmonic [13], or Ornstein-Uhlenbeck (e.g., [8,14,15]) noise, including (e.g., [10,16,17]) or ignoring inertia (the majority of publications), etc. Moreover, the phenomenon of current reversal has attracted much interest (e.g., [16–19]).

In contrast to these efforts, only a few authors [10,20,21] have payed attention to diffusion accompanying the transport process in a ratchet. In [10] the authors considered a periodically rocked, purely deterministic ratchet including inertia effects. Their system possessed regular or chaotic attractors depending on the system parameters. In the chaotic regime the asymptotic distribution tended to a dispersing Gaussian just as for ordinary diffusive systems. This motivated an effective description based on a cumulant expansion with dominant corrections accounted for by a universal scaling law.

The same observation of an effective Gaussian was also the basis for an envelope description applied to a dichotomically flashing overdamped ratchet [21]. Explicit expressions for the velocity and effective diffusion coefficient could be derived; however, they still required numerical evaluation of involved functions. In this paper we will apply the same approach adapted to a discrete three-state model first introduced and analyzed in the context of various flashing modes [22]. The discrete system has the advantage that velocity and diffusion coefficient can be explicitly related to system parameters. Thus we can study their analytic dependence on the system parameters. We should mention that the investigation of velocity and diffusion constant in a periodic one-dimensional hopping model was done earlier [23] in a different context.

Diffusion counteracts the desired transport. To illustrate this statement consider some molecular system that requires the cargo to be delivered at its destination reliably, i.e., within a small time interval. In this case large diffusion means large variance of the times of arrival, i.e., low reliability. As another example we might think of some separation device. Here, diffusion affects the efficacy of the separation

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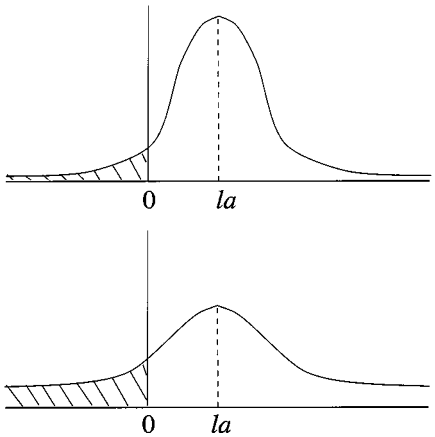

FIG. 1. After the time $\tau_l = la/v$ the peak of the distribution has shifted l units to the right. The probability that the particle still is left of the starting point, i.e., $P(x<0,\tau_l)$, corresponds to the shaded regions. The distributions are shown for a large (top) and a small (bottom) Péclet number.

mechanism. Recently the use of two-dimensional sieves was proposed for a continuous sorting of differently sized molecules (DNA fragments) [24,25]. Lateral diffusion, i.e., in a direction perpendicular to electrophoretic drift, effects the separation; however, it also limits the range of sufficient resolution.

The competition between drift v and diffusivity D in advection-diffusion problems is often expressed by a dimensionless number, the Péclet number,

$$\mathrm{Pe} = \frac{|v|a}{D}. \tag{1}$$

Here a is a typical length scale, in our case the length of a single ratchet element. The larger the Péclet number, the more net drift predominates over diffusion.

To discuss this point quantitatively we consider the situation sketched in Fig. 1 (cf. Fig. 4). Net transport moves particles to the right. After the time $\tau_l = la/v$ the peak has moved l units to the right. The probability to find the particle still at the starting point or even left of it is given by the expression

$$P(x<0,\tau_l) = \frac{1}{\sqrt{4\pi D\tau_l}} \int_{-\infty}^{0} \exp\left(-\frac{(x-v\tau_l)^2}{4D\tau_l}\right) dx, \tag{2}$$

$$= \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{-\frac{v\tau_l}{\sqrt{2D\tau_l}}} \exp\left(-\frac{y^2}{2}\right) dy, \tag{3}$$

$$= \Phi\left(-\sqrt{\frac{l}{2}\mathrm{Pe}}\right). \tag{4}$$

Referring to the statements above and to Sec. III we have made use of the fact that the distribution effectively becomes a dispersing Gaussian. For Pe approaching zero the particle will be found on the left side with probability 0.5 whereas

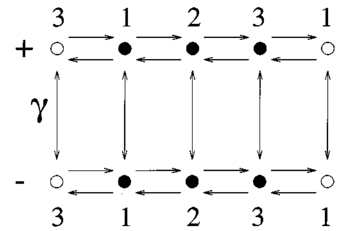

FIG. 2. The discrete three-state ratchet model.

for large Pe this probability will become vanishingly small (cf. Summary and Conclusion).

The break-even point beyond which drift wins over diffusion defines a critical length $L_c = 2D/v$. Demanding this length to be not larger than the length of a ratchet unit a requires Peclet numbers not smaller than 2.

II. A MINIMAL DISCRETE RATCHET MODEL

As a starting point for discrete ratchet models we consider Fig. 2. It comprises three states interconnected by transitions $w(n\rightarrow m,\sigma)$ (with $n,m=1,2,3$ and $\sigma=-1,+1$). It is minimal since the ratchet mechanism requires spatial asymmetry, which cannot be devised with less than three states. The linear ordering indicates the chainlike character with the connection between 1 and 3 accounting for its periodicity. Due to flashing there exist two disjoint transition sets represented by the upper $(+1)$ and lower (-1) ladder. The switching is modeled by a dichotomic process (random-telegraph process) with γ denoting the average switching rate. The probabilistic evolution of the system is described by a related master equation of the form

$$\partial_t P(n,\sigma,t) = [W+\Gamma] P(n,\sigma,t). \tag{5}$$

The master matrix $[W+\Gamma]$ has dimension 6×6 and is compound of lateral transition rates $w(n\rightarrow m,\sigma)$ (in W) and the switching rate γ (in Γ).

The dichotomic switching provides the basic mechanism to drive the system out of equilibrium. The second prerequisite for a nonvanishing net current, namely, the broken reflection symmetry, is induced by appropriate choice of transition rates. In the context of thermally activated transitions we have to endow a modified sawtooth potential with metastable states. This is done by deforming the potential giving rise to three local minima each separated from its neighbors by barriers, cf. Fig. 3. In the context of Kramer's theory [7] the parameters $\Delta U_0, U_1, U_2, U_3, \Delta U_{12}, \Delta U_{23}$, and ΔU_{31} can be chosen to yield

$$k = w(1\rightarrow 2,+1) = w(2\rightarrow 3,+1)$$
$$= \frac{1}{w(2\rightarrow 1,+1)} = \frac{1}{w(3\rightarrow 2,+1)}, \tag{6}$$

$$k^2 = w(1\rightarrow 3,+1) = \frac{1}{w(3\rightarrow 1,+1)}, \tag{7}$$

$$1 = w(n\rightarrow n\pm 1,-1) \tag{8}$$

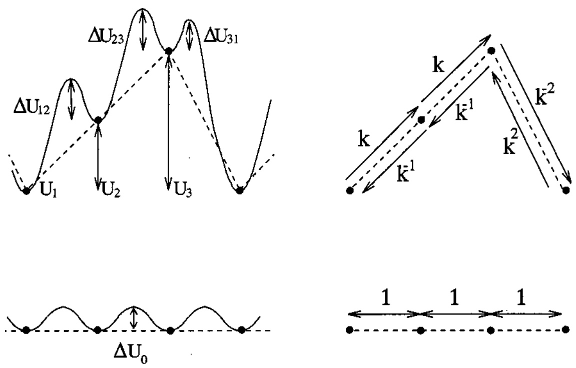

FIG. 3. The continuous linear on-off potentials (dashed) are endowed with a well structure (solid). By an appropriate choice of barrier heights it is possible to map the continuous system shown left to the rate system sketched schematically right.

(cf. Fig. 3). We specify rates in this way for the sake of computational convenience and in order to be compatible with existing literature [22].

III. EFFECTIVE DESCRIPTION OF NOISE-INDUCED TRANSPORT

Considering transport in a ratchet potential one wants to quantify the probability that the particle has moved some units to the left or to the right of the initial unit. This means that one is interested in a description on a coarser scale formulated through an envelope function. As already mentioned in the introduction it was observed [10,21] that the evolution of the probability envelope effectively becomes that of a dispersing Gaussian, see Fig. 4. Before approaching this notion in a systematic way (cf. [21]) let us introduce some notation. By $\mathcal{P}$ we denote the envelope function whereas the distribution defined on the refined scale will be denoted by P. The observation of a spreading Gaussian means that we have the following equation for the envelope:

$$\partial_t \mathcal{P}(x/\lambda,t) = \partial_x[(-v + D\partial_x)\mathcal{P}(x/\lambda,t)], \tag{9}$$

with λ denoting some length scale, which is large as compared to the length a of the asymmetric unit. Note that an expansion in powers of spatial derivatives thus corresponds to an expansion in powers of $1/\lambda$. Hence, we can understand Eq. (9) as a truncated series expansion. We have introduced two effective coefficients, namely, the velocity v and the diffusion coefficient D. We want to relate them to the parameters determining the ratchet system, i.e., to the flipping rate γ and to the parameter k coding the shape of the asymmetric unit. These parameters enter the description through the dynamics ruling the evolution of P, which is nothing but the master equation (5). Consequently, a connection between $\mathcal{P}$ and P will yield the desired relation. This connection is given by the following gradient expansion:

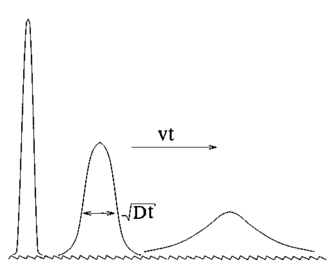

FIG. 4. The probabilistic evolution of an ensemble in a ratchet potential is reduced to a consideration of a time-dependent envelope. The latter can be effectively described by a dispersing Gaussian moving with constant drift.

$$P(x,\sigma,t) = \sum_{n=0}^{\infty} p^{(n)}(x,\sigma)\partial_x^n \mathcal{P}(x/\lambda,t). \tag{10}$$

It involves an infinite set of periodic functions $p^{(n)}$ of period a. Small n terms describe the smooth components and, hence, one would expect only the first functions $p^{(0)}$, $p^{(1)}$, and perhaps $p^{(2)}$ to be involved in the envelope description. Indeed, this is the case as can be seen when inserting the ansatz (10) in the master equation (5). Equating terms of order $1/\lambda^n$ yields

$$[W+\Gamma]p^{(0)} = 0, \tag{11}$$

$$[W+\Gamma]p^{(1)} = -(v-\hat{V})p^{(0)}, \tag{12}$$

$$[W+\Gamma]p^{(2)} = (D-\hat{T})p^{(0)} - (v-\hat{V})p^{(1)}, \tag{13}$$

with $\hat{V}$ and $\hat{T}$ being two operators (matrices) involving rates $w(n \to m,\sigma)$ (cf. the Appendix). Equation (11) reveals that $p^{(0)}$ is the stationary solution of Eq. (5). Taking traces and obeying correct normalization,

$$\mathrm{tr}\{p^{(n)}\} = \sum_{\sigma=-1}^{+1} \sum_{i=1}^{3} p^{(n)}(i,\sigma) = \delta_{n,0} \tag{14}$$

yields the desired relations for the effective coefficients:

$$v = \mathrm{tr}\{\hat{V}p^{(0)}\}, \tag{15}$$

$$D = \mathrm{tr}\{\hat{T}p^{(0)}\} - \mathrm{tr}\{\hat{V}p^{(1)}\}. \tag{16}$$

The fact that the function $p^{(2)}$ is not involved becomes transparent when taking the traces of Eqs. (11)–(13). Due to the norm-conserving property of the operator $[W+\Gamma]$ traces of the left sides vanish identically. The functions $p^{(0)}$ and $p^{(1)}$ are achieved solving Eqs. (11) and (12), respectively.

In [21] where a continuous ratchet model was investigated the traces required integration and scalar products with the continuous functions $p^{(0)}$ and $p^{(1)}$. A quantitative evaluation of these expressions, hence, required numerical computation. In contrast, in the discrete ratchet model all manipulations necessary to yield Eqs. (15) and (16) are done in the framework of linear algebra. They can be performed by an algebraic computer program like MAPLE. The resulting expressions are rather long and cannot be simplified. However, they still grant the benefit of being analytically exact and explicit. In particular, exact limits can be evaluated.

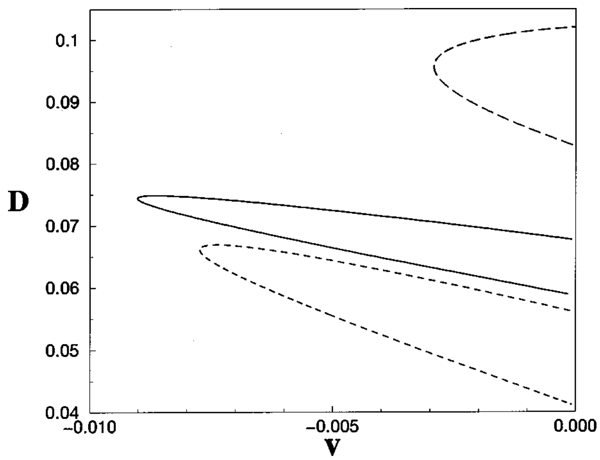

FIG. 5. The relation between velocity v and diffusion coefficient D for the flashing ratchet when varying the flashing rate γ for three different asymmetry parameters: $k=0.1$ (dashed), $k=0.2$ (solid), and $k=0.5$ (long dashed).

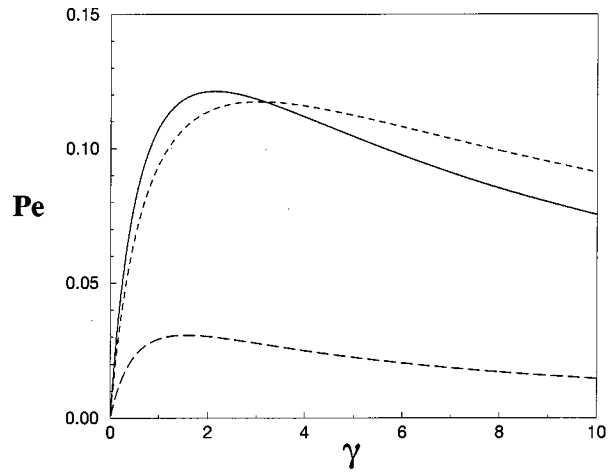

FIG. 6. The Péclet number Pe for the flashing ratchet when varying the flashing rate γ for three different asymmetry parameters: $k=0.1$ (dashed), $k=0.2$ (solid), and $k=0.5$ (long dashed).

In the remainder of the present paper we will visualize and discuss the dependence of v and D on the parameters γ and k of our discrete ratchet model. In the following we set the unit length $a=1$.

IV. DRIFT VS DIFFUSION FOR THE MINIMAL DISCRETE RATCHET

In this section we apply the method to the flashing three-state ratchet sketched in Fig. 3. The alternation between asymmetric concentration of probability in the (on state) and ''free diffusion,'' i.e., over the barriers ΔU_0 (in the off state), gives rise to a net transport directed to the left, i.e., the net velocity is negative. As a generic feature of the ratchet mechanism the net current becomes extremal for an optimally chosen γ; the flashing rate has to be tuned to maximally experience the asymmetry between motion to the left and to the right. The important question is now whether large net currents can be achieved simultaneously avoiding large diffusion. To this end we consider how the diffusion constant $D(\gamma,k)$ varies with the flashing rate γ and plot-related values of v and D in Fig. 5. The tendency to simultaneously attain extremal values clearly can be seen from the diagonal structure of the curves.

In Fig. 6 we depict the related Péclet numbers Pe. We see that Peclet numbers never reach values of the order of 1. This basic example clearly demonstrates that diffusion effects are far from being negligible (cf. the discussion in the Summary and Conclusion). In passing we mention that the same qualitative result was found in the analysis of a discrete rocking ratchet.

V. APPLICATION TO TRANSMEMBRANE TRANSPORT

In this section we want to show how this analysis applies to a realistic biochemical system. The active transport of substances (ions) through biomembranes has been described successfully in terms of a four-state model [5]. The four states are defined through combining some electroconformational polarity of a membrane macromolecule (pointing either inside or outside) with the bound or dissociated states of the substance. Applying an external varying field induces transitions between the conformational states of the macromolecule, thus creating and maintaining a nonequilibrium situation. The indispensable asymmetry comes in through different affinities on both sides of the membrane. In this way the uphill transport, i.e., against a concentration gradient, can be modeled by a discrete four-state ratchet. Besides experiments with oscillating fields [26,27] there was also an experiment with a randomly fluctuating electric signal (random telegraph noise) [28]. The influx, i.e., the number of particles (^{86}Rb) crossing the membrane (of human erythrocytes) against a concentration gradient, was measured as a function of the applied bias Φ (related to the electric signal amplitude) and mean switching rate γ. Nonmonotonic behavior with respect to both parameters was found [29]. The measurement data could be reproduced by simulations based on a four-state kinetic description (for a sketch of the model we refer to Fig. 3 of [28]).

With the rates given in [28] (specified there in the legend of Fig. 3) we can compute the net velocity together with the diffusion coefficient. The results are shown in Figs. 7 and 8 for varying bias Φ and γ, respectively. The unit for v was

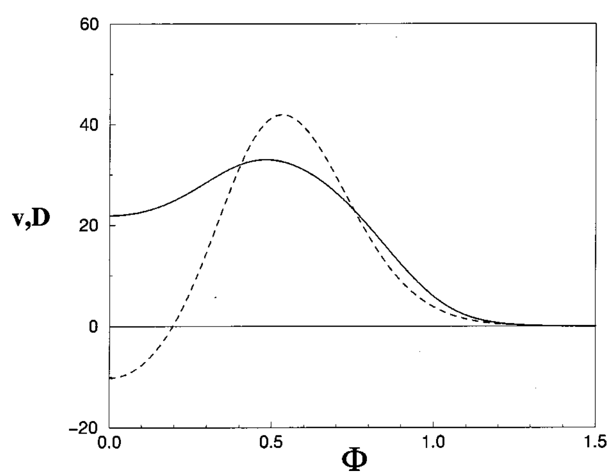

FIG. 7. The effective coefficients v (dashed) and D (solid) for the four-state electroconformational coupling model specified in [28] as a function of varying external bias Φ.

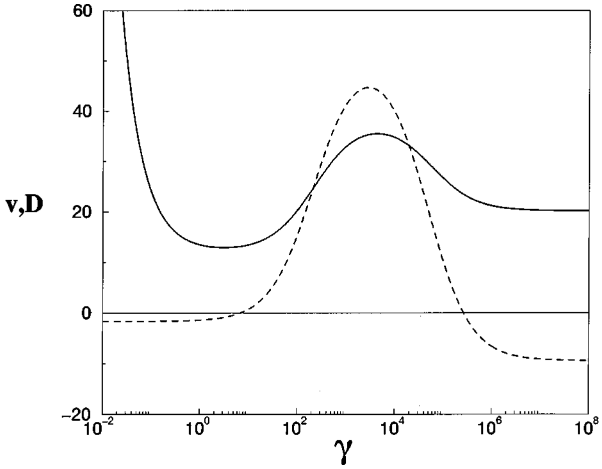

FIG. 8. The effective coefficients v (dashed) and D (solid) for the four-state electroconformational coupling model specified in [28] as a function of varying mean switching frequency γ.

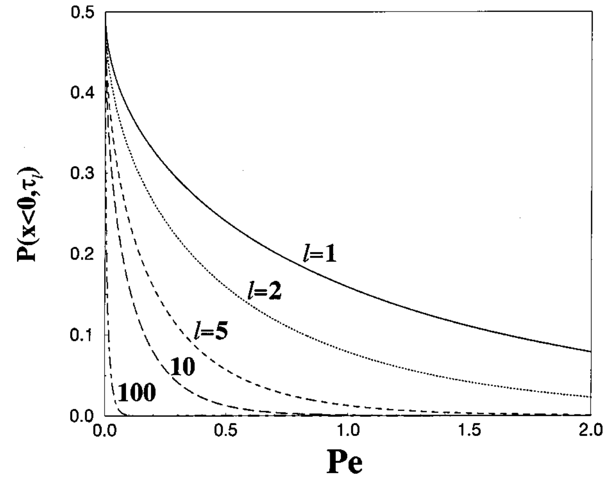

FIG. 9. The probability $P(x<0,\tau_l)$ that a particle, initially located at $x=0$, never crosses to the preferred side within the time $\tau_l = la/v$ strongly depends on the Péclet number Pe.

chosen as *attomol of ion substance per erythrocyte per hour* to allow for comparison with the cited literature [28]. The unit for D follows in accordance. As before, we find that diffusion and velocity are increasing simultaneously. The related Peclet numbers never reach the value 1.5.

VI. SUMMARY AND CONCLUSION

We have analyzed net transport in discrete ratchet models relevant for (biochemical) cyclic reactions moving ''uphill.'' Asymmetry was reflected by asymmetric rates whereas nonequilibrium was prepared by switching between (two) different sets of transition rates. A description in terms of a dispersing probability envelope yielded expressions for two effective coefficients, drift velocity v and diffusivity D, as a function of given rates. We applied the theoretical results to discrete versions of a flashing and a rocking ratchet. Finally, as a rather practical application, we considered diffusion accompanying active transport of substances across a biomembrane.

As a general feature we found that maximal drift is linked with rather high diffusion. The limitation diffusion imposed on the transport efficiency can be considered quantitatively in terms of the dimensionless Péclet number Pe. As explained in the Introduction, for net drift to overcome diffusion at a distance of one unit Peclet numbers should not be smaller than 2. In contrast to this demand we found Peclet numbers as small as 0.15 for the flashing ratchet, 0.6 for the rocking ratchet, and 1.5 for the transmembrane model.

A more sophisticated interpretation relates Péclet numbers to the probability $P(x<0,\tau_l)$ that particles, initially located at $x=0$, never move to positive valued locations (the preferred side) within the time $\tau_l = la/v$. Of course, with elapsing time τ_l this probability (cf. Fig. 9) will diminish. Nevertheless, small Péclet numbers stir the question whether ratchets really work. This criticism even holds true when considering a collection of N independent ratchets. However, synchronization effects induced by an external signal [30] or by a feedback mechanism [31] may generate coherent behavior and thus might yield an effective suppression of deteriorating diffusion.

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APPENDIX

Here we derive explicit expressions for the operators $\hat{V}$ and $\hat{T}$ involved in Eqs. (12)–(16). We start by inserting Eq. (10) in the left side of Eq. (5). Making use of Eq. (9) yields a power series

$$\sum_{n=1}^{\infty} c_n \frac{1}{(\lambda \Delta x)^n} \frac{\partial^n \mathcal{P}(y,t)}{\partial y^n}\Big|_{y=x/\lambda}, \tag{A1}$$

with $c_1 = -vp^{(0)}$ and $c_n = Dp^{(n-2)} - vp^{(n-1)}$ for $n \geqslant 2$ and $\Delta x = a/3$. The right side of Eq. (5) explicitly reads

$$\begin{aligned}[W+\Gamma]P(i,\sigma) := {} & w(i-1\rightarrow i,\sigma)P(i-1,\sigma,t) \\ & + w(i+1\rightarrow i,\sigma)P(i+1,\sigma,t) \\ & - [w(i\rightarrow i-1,\sigma) + w(i\rightarrow i+1,\sigma)] \\ & \times P(i,\sigma,t) - \gamma[P(i,\sigma,t) - P(i,-\sigma,t)].\end{aligned} \tag{A2}$$

Inserting the gradient expansion (9) here and expanding $\mathcal{P}(y \pm 1/\lambda)$ around $y = i/\lambda$ also leads to a power series

$$\sum_{n=0}^{\infty} \tilde{c}_n \frac{1}{(\lambda \Delta x)^n} \frac{\partial^n \mathcal{P}(y,t)}{\partial y^n}\Big|_{y=x/\lambda}, \tag{A3}$$

with

$$\tilde{c}_n=\sum_{l=1}^{n}[(-1)^l w(i-1\rightarrow i,\sigma)p^{(n-l)}(i-1,\sigma)+w(i+1\rightarrow i,\sigma)p^{(n-l)}(i+1,\sigma)]\times\frac{(\Delta x)^l}{l!}+[W+\Gamma]p^{(n)}(i,\sigma). \quad \text{(A4)}$$

From this we can readily write down Eqs. (11)–(13) and define the operators $\hat{V}$ and $\hat{T}$ through their action on the functions $p^{(n)}$ as

$$\hat{V}p^{(n)}(i,\sigma):=[w(i-1\rightarrow i,\sigma)p^{(n)}(i-1,\sigma)-w(i+1\rightarrow i,\sigma)p^{(n)}(i+1,\sigma)]\Delta x, \quad \text{(A5)}$$

$$\hat{T}p^{(n)}(i,\sigma):=[w(i-1\rightarrow i,\sigma)p^{(n)}(i-1,\sigma)+w(i+1\rightarrow i,\sigma)p^{(n)}(i+1,\sigma)]\frac{(\Delta x)^2}{2}. \quad \text{(A6)}$$

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