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ABSTRACT

A fundamental way to analyze complex multidimensional stochastic dynamics is to describe it as diffusion on a free energy landscape—free energy as a function of reaction coordinates (RCs). For such a description to be quantitatively accurate, the RC should be chosen in an optimal way. The committor function is a primary example of an optimal RC for the description of equilibrium reaction dynamics between two states. Here, additive eigenvectors (addevs) are considered as optimal RCs to address the limitations of the committor. An addev master equation for a Markov chain is derived. A stationary solution of the equation describes a sub-ensemble of trajectories conditioned on having the same optimal RC for the forward and time-reversed dynamics in the sub-ensemble. A collection of such sub-ensembles of trajectories, called stochastic eigenmodes, can be used to describe/approximate the stochastic dynamics. A non-stationary solution describes the evolution of the probability distribution. However, in contrast to the standard master equation, it provides a time-reversible description of stochastic dynamics. It can be integrated forward and backward in time. The developed framework is illustrated on two model systems—unidirectional random walk and diffusion.

I. INTRODUCTION AND MOTIVATION

A fundamental way to analyze complex multidimensional stochastic dynamics is to describe it as diffusion on a free energy landscape—free energy as a function of one or a few reaction coordinates (RCs).[1–8] For such a description to be qualitatively accurate, the RCs should be chosen in an optimal way, e.g., in order to minimize non-Markovian effects due to the projection.[9,10]

An important practical case is equilibrium reaction dynamics between two end states A and B. The optimal RC in this case is the committor function $q_B(x)$—the probability to reach state B before reaching state A starting from configuration x.[1,11] The free energy and the diffusion coefficient as functions of the committor define a diffusive model of the projected dynamics. This diffusive model can be used to compute exactly the following important properties of the dynamics—the equilibrium flux, the mean first passage times, and the mean transition path times between any two points on the committor.[12–15] This is true for free energy landscapes of any complexity and does not require separation of timescales. The diffusive model can be used to determine accurately and in a direct manner the free energy barrier and the pre-exponential factor—the two major determinants of the reaction dynamics.[15] For non-equilibrium dynamics (dynamics without the detailed balance), it is, however, necessary to consider the second committor function for time-reversed dynamics $q_A^-(x)$. The two committors are generally different functions, and it is not clear how to construct a diffusive model of such a dynamics analogous to the equilibrium case since it is not clear how to construct a single optimal RC from the two committors.

A practically important case of non-equilibrium dynamics is stochastic dynamics in the phase space. Many approaches for the RC analysis of MD simulations assume that dynamics is Markovian

in the configuration space. It introduces a lower bound on the time interval (lag time) that can be used for the analysis. In atomistic MD simulations, the dynamics is Newtonian at the integration time step. Hence, the lag time should be long enough for the system to forget its momenta. Consideration of non-equilibrium Markovian dynamics in the phase space and RCs as functions of phase space should significantly decrease the lower bound on lag times. This, in turn, should allow significantly shorter trajectories and higher efficiency in parallel approaches for exascale computing, which use a very large ensemble of short trajectories instead of a single long one.[16–23]

Another weak point of the committor function is that it requires two boundary states. While, for some simple cases, boundary states can be defined in an obvious way, a proper definition in a general case of a complex system is difficult.[24] One approach, which may work well for states associated with deep free energy minima, is to use eigenvectors of the transfer operator.[25,26] However, it will likely to fail for systems with many shallow minima, like intrinsically disordered proteins. For some systems, introduction of boundary states makes no sense at all, e.g., diffusion in a harmonic well.

In order to address the limitation of the committor function, here we extend the framework of optimal RCs to recently introduced additive eigenvectors (addevs).[27] They do not require boundary states and can be used to describe non-equilibrium dynamics without the detailed balance. The framework, however, assumes a single optimal RC for the forward and time-reversed dynamics. As a general solution, we suggest to consider all sub-ensembles of trajectories satisfying this condition. An addev master equation describing such sub-ensembles in a Markov chain is derived. The equations have a spectrum of stationary solutions analogous to the standard eigenvectors. Each solution describes a sub-ensemble of trajectories together with the corresponding optimal RC. The sub-ensemble describes a stationary current along an optimal RC with trajectories performing periodic stochastic motion along it. We suggest to call such sub-ensembles of trajectories performing periodic stochastic motion stochastic eigenmodes. A long trajectory may visit many such sub-ensembles, with each visit representing a rare event or a fluctuation, with probability exponentially decreasing with the time spent in a particular addev sub-ensemble. Thus, one can decompose the stochastic dynamics onto a collection of such stochastic eigenmodes. The derived equation can also be interpreted as an evolution equation for probability distribution. However, in contrast to the standard master equation for a Markov chain, it is symmetric with respect to time-reversal and can be integrated forward and backward in time. We emphasize that this notion of time-reversibility is different from the standard notion of time-reversible Markov chains, which just implies the validity of the detailed balance.

This paper is organized as follows: we start by introducing addevs for a Markov chain and showing how they can be incorporated into the framework of optimal RCs. We then derive the master equation for an addev and the corresponding sub-ensemble of trajectories. The properties of the equation and its solutions are illustrated on two model systems: unidirectional random walk and diffusion. The first one is relatively simple to obtain exact analytical results. The second is of larger practical interest; however, it is much more complex to be solved exactly. Hence, this manuscript contains only a very brief exposure to the results, and the detailed analysis is presented in the follow-up manuscript. We conclude with a discussion.

II. THEORY

A. Additive eigenvectors as optimal RCs

In this section, we define additive eigenvectors and show how they can be used as optimal RCs.

Consider a finite discrete-time Markov chain with transition probability matrix $P_\tau(j|i)$, which equals the probability of transition from state i to state j after time interval τ, and stationary probability $\pi(j)$. We assume that the detailed balance is not satisfied, and when stationary dynamics is projected on RC $W(j)$, there is a constant non-zero flux. The simplest example is a circular three state system $1 \to 2 \to 3 \to 1$ shown in Fig. 1(a), with the flux in the counterclockwise direction. Correspondingly, we assume that W has a circular topology: one can imagine $W(j)$ as the value of the angle of point j in polar coordinates or, equivalently, the position of point j when projected on a circle. Figure 1(b) shows a bit more generic, complex example of such a system. Rays from the center of the coordinate system, shown by dashed lines, denote different values of the angle or W RC. Figure 1(c) shows a model system with transitions in one direction (counterclockwise) whose RC points $W(j)$ are laying/projected on a circle.

To remove the flux, one considers an RC that moves with the flux, i.e., a moving frame of reference $S(j,t) = W(j) - vt$, which, in this case, corresponds to a uniformly rotating frame of reference. Since we consider stationary dynamics, the flux across any cutting surface, e.g., those shown by dashed lines in Fig. 1(b), is the same. To specify an RC that moves with the flux, we require that the average change of $S(j,t)$, computed along the stationary trajectories, is zero,[27]

$$\sum_j P_\tau(j|i)[S(j,t+\tau) - S(i,t)] = 0. \tag{1}$$

It is understood that indices, e.g., i and j, run over all the states of the Markov chain $1,\ldots,N$, where N is their total number. It is easy to see that (since $P_\tau(j|i) > 0$) for every state i, there are states with $S(j,t) > S(i,t)$ and with $S(j,t) < S(i,t)$. In other words, $S(i,t)$ has neither maximum nor minimum. In a finite Markov chain, it is possible if $S(i,t)$ is a multi-valued function.

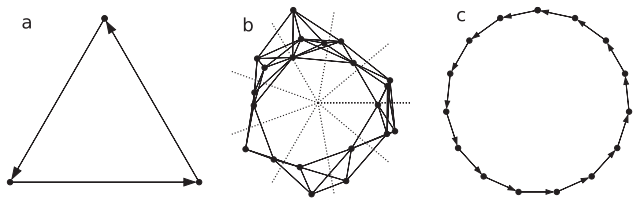

FIG. 1. Model systems with non-zero flux, where the detailed balance is not satisfied: (a) the simplest, three state system, (b) generic system, and (c) system on the circle with transitions in the counterclockwise direction only. Arrows indicate unidirectional transitions.

Substituting $S(j,t) = W(j) - vt$ in Eq. (1), one obtains

$$\sum_j P_\tau(j|i)W(j) = W(i) + v\tau, \tag{2}$$

where $W(j)$ is an additive eigenvector (or addev for brevity) and v is the additive eigenvalue.[27] The term addev is due to the following: the transition matrix transforms the vectors in a simple way—it just adds a constant to every component of the vector. If one recalls that W can be interpreted as the angle or be projected on a circle, the action of the matrix can be interpreted as a rotation of the RC by an angle.

Taking the limit $\tau \to 0$ and using $P_\tau(j|i) = e^{\tau K(j|i)} \approx \delta_{ji} + \tau K(j|i)$, where $K(j|i)$ is the rate matrix, one obtains from Eq. (1)

$$\sum_j K(j|i)[W(j) - W(i)] = v. \tag{3}$$

Generally, $W(j)$ is a multi-valued function, analogous to the angle. For example, consider the model system shown in Fig. 1(c), where the system jumps to the nearest state in the counterclockwise direction with rate r. Then, Eq. (3) gives $W(j+1) - W(j) = v/r$, i.e., the value of the RC W for the next state in the counterclockwise direction is incremented by a constant v/r. W constantly grows if one moves in the counterclockwise direction and the value of $W(j)$ for particular state j increments by Nv/r when one makes a full turn and returns to the same state (see Fig. 2); here, N is the total number of states in the system. It is analogous to the increment of the angle by $\pm 2\pi$ after the full turn. Note that Eqs. (1)–(3) define S, W, and v up to an overall factor. One can fix the factor by setting the increment of the RC after a full turn, which we denote by $\Delta_\odot W$, to some convenient value. For example, by setting $\Delta_\odot W = 2\pi$, the analogy with the angle variable can be made more complete.

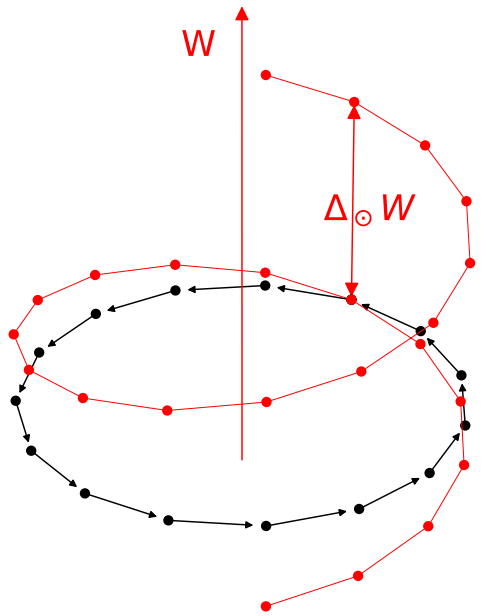

FIG. 2. Multi-valued RC W for the model system shown in Fig. 1(c). The model system is shown in black. A fragment of W, consisting of two overlapping branches, is shown in red. The entire multi-valued RC W consists of the infinite number of branches going from $-\infty$ to ∞. It is analogous to the angle variable. The distance between the branches, or the increment of W after a full turn, is indicated by $\Delta_\odot W$, which, for the angle, equals 2π.

It is easy to see that v has the meaning of the stationary flux. Consider a very long trajectory of length T, where the system completed many revolutions N_W. Then, the change in W will be dominated by $\Delta_\odot W N_W$ that equals vT; hence, $v = N_W/T\Delta_\odot W$ has the meaning of the stationary flux—the number of revolutions per second, multiplied by $\Delta_\odot W$. It also follows that if W is single valued, i.e., $\Delta_\odot W = 0$, then $v = 0$.

Note that, strictly speaking, addev equations for finite τ [e.g., Eqs. (1) and (2) and equations below] are valid only when contributions due to the multi-valued nature of S or W can be neglected, which introduces an upper bound on τ. For example, the change in W for a finite trajectory, starting in state i and ending in state j, equals $W(j) - W(i) + N_W\Delta_\odot W$, where N_W is the number of full revolutions around W completed by the trajectory. While $P_\tau(j|i)$ correctly accounts for the weight of trajectories from i to j, the $N_W\Delta_\odot W$ contribution is missing in the equations. One solution is to consider only such small τ that $N_W \approx 0$. Another is to explicitly consider different branches of W in the transition matrix.

Consider now time-reversed stationary dynamics. It can be obtained by time-reversing trajectories of the original process $X'_t = X_{T-t}$; we use primes to denote time-reversed quantities. The time-reversed stationary dynamics is described by a finite Markov chain with the transition probability matrix $P'_\tau(i|j) = P_\tau(j|i)\pi(i)/\pi(j)$. The addev for the time-reversed dynamics is defined via

$$\sum_j P'_\tau(j|i)[S'(j,t) - S'(i,t+\tau)] = 0. \tag{4}$$

Since P' is generally different from P, the addevs for forward and time-reversed dynamics generally differ.

Next, we extend the framework of optimal RCs[9,12,15,24,28] to addevs. During the derivation of the equations, we assume that the system dynamics is described by a finite Markov chain with transition probability matrix $P_\tau(i|j)$. However, final equations require only the knowledge of the RC time-series $r(i\tau)$, meaning that, in practice, one does not need to construct a Markov chain.

Validation criteria for addevs. Consider quantity $Z^{out}(x,\tau)$ whose derivative is defined as

$$\frac{dZ^{out}(x,\tau)}{dx} = \sum_{i,j}\delta[x - x(i)][x(j) - x(i) - v\tau]n_\tau(j|i), \tag{5}$$

where $n_\tau(j|i) = P_\tau(j|i)\pi(i)$ is the stationary number of transition from state i to j after time interval τ, δ is the Dirac delta function, and $x(i)$ is the position of state i of the Markov chain on the circular RC. If the putative RC closely approximates addev W, i.e., $x(i) \approx W(i)$ and then summing first over j, one finds that $\frac{dZ^{out}(x,\tau)}{dx} = 0$, i.e., Z^{out} along W is constant.

Analogously, quantity $Z^{in}(x,\tau)$ whose derivative is defined as

$$\frac{dZ^{in}(x,\tau)}{dx} = \sum_{i,j}\delta[x(j)-x][x(j)-x(i)-v\tau]n_\tau(j|i) \quad (6)$$

is constant when x closely approximates time-reversed addev W'.

These quantities can be computed from a long stationary RC time-series $r(i\tau)$ of length T as follows:

$$\frac{dZ^{out}(x,\tau)}{dx} = \sum_{i=1}^{T/\tau}\delta[x-r(i\tau)][r(i\tau+\tau)-r(i\tau)-v\tau], \quad (7a)$$

$$\frac{dZ^{in}(x,\tau)}{dx} = \sum_{i=1}^{T/\tau}\delta[r(i\tau+\tau)-x][r(i\tau+\tau)-r(i\tau)-v\tau]. \quad (7b)$$

Note that Z^{out} equals Z^{in} computed with time-reversed trajectory $r'(t)$ and vice versa.

Thus, if $Z^{out}(x,\tau)$ profiles computed for all time intervals τ are constant, up to statistical errors, then the putative RC closely approximates a forward addev and analogously for the time-reversed addevs. One way to see whether deviations from a constant are on the order of statistical uncertainty is to divide the trajectory into several parts, compute the profiles for each part separately, and compare them.

Diffusive model: estimation of $F(W)$ and $D(W)$. Assume now that the stochastic process/dynamics is such that the forward and time-reversed addevs are identical, $W = W'$. Define $Z_{C,1} = (Z^{in} + Z^{out})/2$, which can be considered as a generalization of $Z_{C,1}$ for $v \neq 0$.[12] $Z_{C,1}(x,\tau) = const$ for all x along W. Integrating $Z_{C,1}(x,\tau)$ over x, one obtains $2\int Z_{C,1}(x,\tau)dx = \sum_i[r(i\tau+\tau) - r(i\tau)][r(i\tau+\tau) - r(i\tau) - v\tau] = T/\tau\langle[r(t+\tau)-r(t)-v\tau]^2\rangle$, which is easy to show to be constant for all lag times $\tau(\tau \ll T)$;[12] we denote the constant as $2TD$. Hence, one obtains that $Z_{C,1}(x,\tau)\Delta_\odot W = TD$. From $\langle[r(t+\tau)-r(t)-v\tau]^2\rangle = 2D\tau$, one sees that the mean-squared displacement computed from the stationary addev time-series grows linear with time, like for simple diffusion.[12]

Consider very small τ when jumps from $r(t)$ to $r(t+\tau)$ are relatively short so that $Z_H^{st}(x)$, the conventional partition function or stationary probability, is approximately constant on the scale of jumps. Then, one obtains $Z_{C,1}(x,\tau) = \tau Z_H^{st}(x)D(x)$, where $D(x) = \langle[r(t+\tau)-r(t)-v\tau]^2\rangle/(2\tau)$ is the estimation of the position dependent diffusion coefficient computed from short trajectories in the region around x.[12] $Z_H^{st}(x)$ can be estimated using conventional histograms, which allows one to determine $D(x)$. However, note that Z_H^{st} measures a non-equilibrium or stationary partition function of dynamics with a non-zero flux. It is related to the true/equilibrium free energy of the diffusive model as $\beta F(x) = -\ln P^{st}(x) - \int^x \frac{Jdx}{D(x)P^{st}(x)}$, where β is an inverse temperature, J is the flux, and $P^{st}(x) = Z_H^{st}(x)/Z$, with $Z = T/\tau$.[29] For an addev RC W, one obtains

$$\beta F(W) = -\ln Z_H^{st}(W) - \alpha W, \quad (8)$$

where $\alpha = v/(Z_{C,1}/T)$ is constant. Note that while $Z_H^{st}(W)$ is single-valued, $\beta F(W)$ is multi-valued with the increment of $\alpha\Delta_\odot W$ for one complete revolution. For the model system in Fig. 2, $F(W)$ steadily decreases in the counterclockwise direction, i.e., the system steadily moves by decreasing F and increasing W. One may consider instead force $f(W) = -dF/dW$, which is single-valued. Since $Z_{C,1}$ and Z_H^{st} are single valued functions, periodic in W, in order to increase statistics during the calculation of these quantities from a finite RC time-series, it is useful to collect all the statistics in a single period of W.

Once $F(W)$ and $D(W)$ are computed, one may want to rescale W to the natural coordinate $\tilde{W}$ so that $D(\tilde{W}) = 1$ and the dynamics is described by the free energy profile $F(\tilde{W})$ only.[15]

Determination of j_+ and j_-. Constancy of $Z_{C,1}(x,\tau)$ for different lag times τ allows one to compute some large scale properties of the dynamics using the diffusive model. Consider, for example, the fluxes/rates to make a complete revolution in the positive (j_+) and negative (j_-) directions. To define them, consider a coarse-grained model of the dynamics, where the system performs random walk along W with steps of size $\pm\Delta_\odot W$ with rates $j_\pm$. For very large lag times, when the system jumps contain many revolutions, one can round them up to the nearest integer number of revolutions and neglect the difference. At this timescale, one obtains $D = \Delta_\odot W^2[j_+ + j_-]$ and $v = \Delta_\odot W[j_+ - j_-]$. The diffusive model allows the determination of D and v and thus $j\pm$.

In summary, given an addev time-series, one may construct a diffusive model that accurately approximates the dynamics. Given the free energy profile, one can locate the transition state or the rate limiting step and study its properties. One can determine the free energy barrier and the corresponding pre-exponential factor.[15] The dynamics projected on W has a constant drift v, meaning that the average position of the system moves with constant velocity v along periodic coordinate W; it performs stochastic periodic motion.

Generally, $W \neq W'$ and $Z_{C,1}(x,\tau)$ is not constant. However, close to equilibrium, when the flux is relatively small and W and W' are not very different, one may select such a coordinate that has $Z_{C,1}(x,\tau) = const$ for the smallest τ value. Since $Z_{C,1}(x,\tau)$ tends to a constant for large τ, it is likely that $Z_{C,1}(x,\tau)$ is approximately constant for all values of τ. Such a coordinate, denoted as W^{eq}, is obtained as an addev for the rate matrix, which is the sum of forward and time-reversed rate matrices $K + K'$. We believe that this approximation should work for such non-equilibrium biophysical systems of practical interest as, e.g., enzymatic reactions, molecular motors, and biochemical networks. Appendix A in the supplementary material contains detailed illustration of the developed framework on a model system close to equilibrium.

For the general, far-from-equilibrium case, e.g., stochastic dynamics in the phase space, we suggest a different strategy. In the analysis of stochastic dynamics, a process of interest often represents a rare event. To analyze the properties and likelihood of such rare events, one may study the stochastic dynamics of atypical trajectories conditioned on this event. For example, in the analysis of protein folding, one studies the transition paths (TPs) between folded and unfolded states. Analogously, we suggest to study all sub-ensembles of trajectories, for which $W' = W$ or in a general case $S' = S$, which can be described by the developed formalism. Such sub-ensembles with the smallest v eigenvalues, in particular, describe rare events representing the slowest periodic processes with the smallest fluxes.

B. Addev master equations and time-reversible description of stochastic dynamics

A usual way to specify a sub-ensemble of conditioned trajectories is to consider first the entire ensemble of all possible trajectories, say, length T, and select from it a sub-ensemble of trajectories satisfying the condition(s). For example, the TP sub-ensemble consists of all the trajectories connecting directly the boundary states.[30] Another example is to consider only those trajectories that avoid the so-called trap states.[31] Schrödinger first suggested considering an ensemble of stochastic trajectories that match not only the initial probability distribution but also the final one.[32–34] Such conditioned ensembles are now known as Schrödinger bridges.[35,36] One can condition trajectories to have some value of a rather general path functional, e.g., $A = 1/T \int f(X_t)dt$.[37–40] A more general conditioning is possible.[41] Dynamics in such a conditioned sub-ensemble is again described by a conservative Markov chain, however, with a different, biased, Doob's h-transformed, transition matrix.[37,39,40,42]

One way to find the law of such conditioned trajectories, e.g., their transition matrix, is to minimize the deviation from the typical/original dynamics, namely, the Kullback–Leibler divergence,[41,43,44] under constraint, which, for addev sub-ensembles, is $S' = S$. This approach, however, leads to a complex system of non-linear equations, which we were not able to solve in a general case. Numerical minimization for a one-dimensional model system produced just two obvious solutions: equilibrium dynamics without flux $J = 0$ or flux without the barrier $U = 0$. Below, we present another approach, where we describe a large family of conditioned trajectories with $S' = S$ whose equations can be obtained analytically. We start directly with the dynamics in the sub-ensemble, which we assume to be Doob's h-transformed. One may assume that a specific conditioning has been imposed to have the desired Doob's h-transform, which results in $S' = S$. We show later (Section IVC) how to select a conditioning to obtain a desired addev sub-ensemble.

We consider a finite discrete-time (and later continuous-time) Markov chain with the transition probability matrix $P_\tau(j|i)$. We assume that dynamics in the addev sub-ensemble is described by a Markov chain with a biased, generalized Doob's h-transformed,[39,40] conservative transition probability matrix $\tilde{P}$,

$$\tilde{P}(j,t+\tau|i,t) = P_\tau(j|i)\frac{u(j,t+\tau)}{u(i,t)} \quad \text{for } i \neq j, \tag{9a}$$

$$\sum_j \tilde{P}(j,t+\tau|i,t) = 1, \tag{9b}$$

i.e., the biased $\tilde{P}(i,t+\tau|i,t)$ is found from Eq. (9b); here, $\tilde{P}(j,t+\tau|i,t)$ is the probability to be found in state j at time $t+\tau$ if the system was in state i at time t and $u(i,t) > 0$ is a biasing factor, to be determined later. Note that while we assume initially that the dynamics is stationary, i.e., $\tilde{P}(j,t+\tau|i,t)$ does not depend on t, the equations are derived for the general case of non-stationary dynamics.

For forward addev $S(j,t)$, one has [cf. Eq. (1)]

$$\sum_j \tilde{P}(j,t+\tau|i,t)[S(j,t+\tau) - S(i,t)] = 0. \tag{10}$$

To define the time-reversed dynamics in the sub-ensemble, we assume that the (stationary) probability distribution of the sub-ensemble is expressed as $P(i,t) = u(i,t)v(i,t)$, which can always be done, since one can define $v(i,t) = P(i,t)/u(i,t)$. It means that

$$\sum_i \tilde{P}(j,t+\tau|i,t)P(i,t) = P(j,t+\tau). \tag{11}$$

Then, the transition probability for time-reversed dynamics (denoted as $\tilde{P}'$) is

$$\tilde{P}'(i,t|j,t+\tau) = \tilde{P}(j,t+\tau|i,t)P(i,t)/P(j,t+\tau). \tag{12}$$

We check that the total transition probability $\tilde{P}'$ sums to 1,

$$\sum_i \tilde{P}'(i,t|j,t+\tau) = 1, \tag{13}$$

where we used Eq. (11). $P(i,t)$ is the stationary probability for time-reversed dynamics too,

$$\sum_j \tilde{P}'(i,t|j,t+\tau)P(j,t+\tau) = P(i,t), \tag{14}$$

where we used Eq. (9b). From Eqs. (12) and (13), consequently, the transition probability for the time-reversed dynamics is biased analogous to that for the forward dynamics,

$$\tilde{P}'(i,t|j,t+\tau) = P_\tau(j|i)\frac{v(i,t)}{v(j,t+\tau)} \quad \text{for } i \neq j, \tag{15a}$$

$$\sum_i \tilde{P}'(i,t|j,t+\tau) = 1, \tag{15b}$$

i.e., the description is symmetric with respect to time-reversal. Finally, we require that the addev for the time-reversed dynamics is the same, i.e., forward and time-reversed dynamics are described by the same addev as follows:

$$\sum_j \tilde{P}'(j,t|i,t+\tau)[S(j,t) - S(i,t+\tau)] = 0. \tag{16}$$

To summarize, the final system of equations [Eqs. (10), (11), and (16)] can be written as

$$\sum_j P_\tau(j|i)\frac{u(j,t)}{u(i,t-\tau)}[S(j,t) - S(i,t)] = S(i,t-\tau) - S(i,t), \tag{17a}$$

$$\sum_j P_\tau(i|j)\frac{v(j,t)}{v(i,t+\tau)}[S(i,t) - S(j,t)] = S(i,t) - S(i,t+\tau), \tag{17b}$$

$$\sum_j P_\tau(i|j)\frac{u(i,t+\tau)}{u(j,t)}P(j,t) - \sum_j P_\tau(j|i)\frac{u(j,t+\tau)}{u(i,t)}P(i,t) = P(i,t+\tau) - P(i,t). \tag{17c}$$

Written in such a way, equations do not depend on the diagonal terms of the transition matrices that are biased in a complicated way, as they cancel out.

The equation for a continuous time Markov chain can be obtained by taking limit $\tau \to 0$ and using $P_\tau(j|i) = e^{\tau K(j|i)} \approx \delta_{ji} + \tau K(j|i)$, where $K(j|i)$ is the rate matrix,

$$\sum_j K(j|i)\frac{u(j,t)}{u(i,t)}[S(j,t) - S(i,t)] = -\frac{dS(i,t)}{dt}, \tag{18a}$$

$$\sum_j K(i|j)\frac{v(j,t)}{v(i,t)}[S(i,t) - S(j,t)] = -\frac{dS(i,t)}{dt}, \tag{18b}$$

$$\sum_j K(i|j)\frac{u(i,t)}{u(j,t)}P(j,t) - \sum_j K(j|i)\frac{u(j,t)}{u(i,t)}P(i,t) = \frac{dP(i,t)}{dt}, \tag{18c}$$

where $P(i,t) = u(i,t)v(i,t)$. It is a system of equations with three vectors of unknowns $S(i,t)$, $u(i,t)$, and $v(i,t)$. By summing Eq. (18c) over i, one finds that the total probability during temporal evolution is conserved as $d/dt \sum_i P(i,t) = 0$.

This equation, which we refer to as the addev master equation (AME), is the main result of this paper. It describes stochastic dynamics differently compared to the standard master equation (SME) for Markov processes. The rest of the paper is devoted to illustrating their properties on two model stochastic dynamics: unidirectional random walk and diffusion. We first provide a few general remarks about some of the AME properties.

The AME generally has a large set of stationary solutions. A stationary solution, $S(i,t) = W(i) - \nu t$, $u(i,t) = u(i)$, and $v(i,t) = v(i)$, describes an addev sub-ensemble of trajectories. We call the triple (S,u,v) an addev with S or W being the phase of the addev, u and v being the forward and time-reversed biasing factors, respectively, and ν the addev eigenvalue. The biasing factors u and v define the rate matrix of the biased process via Eq. (9) and the stationary probability as $P(i) = u(i)v(i)$. For this sub-ensemble of trajectories, W is the addev for forward and time-reversed dynamics, i.e., $W = W'$, and the framework of optimal RCs can be applied. The overall dynamics of trajectories projected on W is rather simple; they move (on average) with constant velocity ν along the periodic coordinate W. We call such a solution, representing a sub-ensemble of trajectories performing stochastic periodic motion, a stochastic eigenmode. Each stationary solution describes a different sub-ensemble of trajectories with a different pattern of global stationary current along a different RC and is of interest to understand the global properties of dynamics. Solutions with the smallest ν eigenvalues describe the slowest processes and are of particular interest. Thus, in contrast to the SME, which has a unique stationary probability distribution, to which every solution exponentially relaxes, the AME addev master equation has a spectrum of stationary solutions with different stationary probability distributions and a non-stationary solution does no relax to any of them.

An addev sub-ensemble describes a small sub-set of all possible trajectories, and a long equilibrium trajectory jumps from one such sub-ensemble to another. An example of how such a jump occurs, i.e., how a long equilibrium trajectory fluctuates to an addev sub-ensemble, stays there for some time, and then relaxes back, is illustrated in Sec. IV C. Each such fluctuation represents a rare event, with probability exponentially decreasing with the time spent in the addev sub-ensemble.[39,40] After visiting one addev, the trajectory may visit another and so on. One can approximate the entire ensemble of trajectories by all possible sequences of addevs, which leads to a path integral or sum over such sequences. An example is provided in Sec. IV C.

Consider non-stationary addev solutions. The AME does not define derivatives for $du(i)/dt$ and $dv(i)/dt$ separately; only derivative of their product $dP(i)/dt$ is defined. To integrate the AME in time, one can proceed as follows: introduce $u(i,t) = R(i,t)\alpha(i,t)$ and $v(i,t) = R(i,t)/\alpha(i,t)$ and then express α via R and S using Eqs. (18a) and (18b), thus eliminating α from the equations. Thus, one obtains a system of differential equations on just $R = \sqrt{P}$ and S, which we call the module and the phase of an addev. A non-stationary solution describes the evolution of the probability distribution (together with the auxiliary phase function). In contrast to the SME, this evolution is time-reversible. One can integrate the AME forward and backward in time. The SME can be formally integrated back in time; however, eventually, the probability distribution becomes negative. The reason is simple. The probability distribution can be represented as a superposition of eigenvectors. Eigenvectors other than the stationary one have negative components and negative eigenvalues. During integration back in time, their contribution becomes much larger than that of the stationary eigenvector.

III. ILLUSTRATIVE EXAMPLES: UNIDIRECTIONAL RANDOM WALK

Consider a model system shown in Fig. 1(c): a Markov chain with N states on a circle with transitions to the nearest neighbor in the counterclockwise direction only. The system is relatively simple so that exact analytical results can be obtained and equations can be simplified to allow numerical investigation of non-stationary solutions. It illustrates many peculiarities of the addev description of stochastic dynamics, such as time-reversibility, multi-valuedness of S, oscillatory dynamics of the probability distribution, and constructive interference.

A. Addev master equation

The rate matrix is $K(k+1|k) = r$ for $1 \le k < N$ and $K(1|N) = r$. The SME for the evolution of the probability distribution is

$$\frac{dP(k)}{dt} = -rP(k) + rP(k-1). \tag{19}$$

In this section, equations for the boundary values of $k = 1$ or $k = N$ are not given explicitly, and if they differ from the given equations for generic values of k, one has to modify the indices accordingly.

Qualitatively, the equation describes a dissipating wave moving in the counterclockwise direction. The initial probability distribution exponentially relaxes with time to the equilibrium one $\pi(j) = 1/N$. In the proper limit of many states $N \to \infty$, where the distance between states $\Delta x = 1/N$ and $c = r\Delta x = const$, the SME reduces to the equation describing the deterministic dynamics of the wave moving in the counterclockwise direction $\partial P/\partial t = -c\partial P/\partial x$, where x is measured along the perimeter of the circle.

Equation (18) for this system reads (the dependence on the time variable is omitted for brevity)

$$ru(k+1)/u(k)[S(k+1)-S(k)] = -\frac{dS(k)}{dt}, \tag{20a}$$

$$rv(k)/v(k+1)[S(k+1)-S(k)] = -\frac{dS(k+1)}{dt}, \tag{20b}$$

$$ru(k)v(k-1) - ru(k+1)v(k) = \frac{d[u(k)v(k)]}{dt}. \tag{20c}$$

We first consider a stationary solution, where $u(k,t) = u$ and $v(k,t) = v$, due to translational symmetry. Taking $S(k,t) = W(k) - vt$, we obtain the following equations: $r[W(k+1) - W(k)] = v$ for $1 \le k < N$, i.e., at each step from k to $k+1 W(k)$, it is incremented by a constant value of v/r, with general solution $W(k) = (k-1)v/r$. The stationary solution is rather simple. The multi-valued optimal RC W coincides with that discussed in detail at the beginning of Sec. II A and is shown in Fig. 2.

Consider now non-stationary, time-dependent solutions. From Eqs. (20a) and 20(b), one finds that $-P(k)\frac{dS(k)}{dt} = -P(k+1)\frac{dS(k+1)}{dt}$, meaning that $-P(k)\frac{dS(k)}{dt} = C$, where C is some positive constant, which leads to the following system of differential equations:

$$dS(k)/dt = -C/P(k), \tag{21a}$$

$$dP(k)/dt = \frac{C}{S(k)-S(k-1)} - \frac{C}{S(k+1)-S(k)}. \tag{21b}$$

Again, it is understood that Eq. (21) for $k = 1$ and $k = N$ is modified accordingly.

Introducing $Y(k) = S(k+1) - S(k)$ for $1 \le k < N$ and $Y(N) = S(1) - S(N)$, where the values of $S(1)$ and $S(N)$ are taken in the same branch, one obtains the following system of equations:

$$dY(k)/dt = C/P(k) - C/P(k+1), \tag{22a}$$

$$dP(k)/dt = C/Y(k-1) - C/Y(k). \tag{22b}$$

By taking the product of $ru(k+1)/u(k)P(k)Y(k) = C$ over all k values, one finds $C = r\sqrt[N]{\prod_k Y(k)P(k)}$. Taking the time derivative of $\ln C$, it is easy to see that C stays constant during evolution, which, in particular, means that neither $P(k)$ nor $Y(k)$ can become equal to 0. It is also evident that both $\sum P(k) = 1$ and $\sum Y(k) = \Delta_\odot S$ stay constant.

Taking $H = -NC$ as Hamiltonian, Eq. (21) can be given the following Hamiltonian form:

$$H(S,P) = -Nr\sqrt[N]{\prod_k [S(k+1)-S(k)]P(k)}, \tag{23a}$$

$$dP(k)/dt = -\partial H/\partial S(k), \tag{23b}$$

$$dS(k)/dt = \partial H/\partial P(k). \tag{23c}$$

The equilibrium stationary state, where $P(k) = 1/N$ and $Y(k) = \Delta_\odot S/N$, has the lowest value of H. For any other state, H is higher, and since H is constant during evolution, any such state does not relax to the equilibrium one. In the vicinity of the equilibrium state, where the quadratic expansion of H is quite accurate, the dynamics should be well approximated by a superposition of harmonic oscillations of normal modes.

If one selects the initial conditions as $Y(k) = 1/P(k)$, then on a timescale where this relation holds, Eq. (22) can be approximated by (C = r)

$$dY(k)/dt = rY(k) - rY(k+1), \tag{24a}$$

$$dP(k)/dt = rP(k-1) - rP(k), \tag{24b}$$

where Eq. (24b) is the SME [Eq. (19)]. Both equations describe waves running to the right with the average speed of $c = r\Delta x$ so that the relation $Y(k) = 1/P(k)$ is approximately valid for some time. Thus, starting with such initial conditions, the solution of Eq. (22) should approximate the standard solution for the Markov chain. In the continuum limit of $\Delta x \to 0$ and $r = c/\Delta x$, the deterministic equation of the wave running to the right is recovered $\partial P/\partial t = -c\partial P/\partial x$.

Let us illustrate numerical solutions of Eq. (22); the details of the analysis are provided in Appendix B in the supplementary material. We consider how a δ-like distribution in a 100 state system evolves with time (Fig. 3). Initial P was selected as $P(50) = 1$ and $P(k \ne 50) = 0.001$ followed by the normalization of total probability to one. Initial values of Y were taken as $Y(k) = 1/P(k)$ and then rescaled to have $\Delta_\odot S = 1$. The forward solution of Eq. (20) describes a wave moving to the right, which slowly dissipates [Fig. 3(a)]. In comparison, the same initial δ-like distribution, when evolved using the SME [Eq. (19)], dissipates much faster [Fig. 3(c)]. Both waves propagate with similar speed. One can evolve the probability distribution backward in time by integrating the corresponding equations

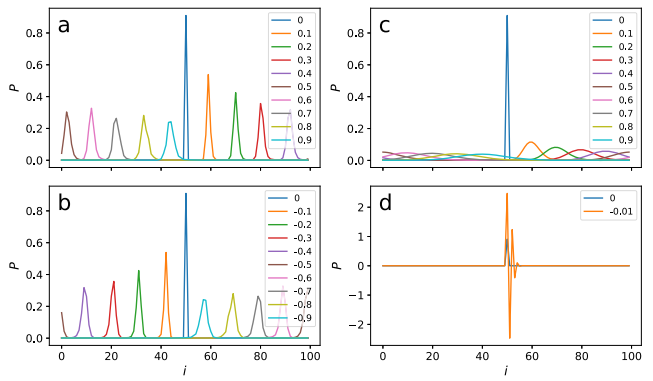

FIG. 3. Forward (a and c) and backward (b and d) time evolution of initial δ-like probability distribution obtained by integrating Eqs. 22(a) and 22(b) and Eqs. 19(c) and 19(d); legends show integration time. Coordinate i is periodic; the wave that disappeared at the right border reappears at the left border. Equation (22) can be integrated forward and backward in time. Integration of Eq. (19) backward in time results in negative probabilities (d). For details, see the text.

backward in time. For Eq. (22), the backward in time evolution of the initial δ-like distribution is very similar to the forward evolution, which describes a dissipating wave moving to the left [Fig. 3(b)]. The SME quickly leads to unphysical, negative values for the probability distribution [Fig. 3(d)].

Note that, for this particular initial condition, both forward and backward temporal evolutions obtained by integrating Eq. (22) describe a dissipating, spreading wave. However, if one starts with S and P vectors obtained for $t = -0.9$ [light blue curve in Fig. 3(b)] as initial vectors and integrates Eq. (22) forward in time, then the wave, in contrast, will initially focus by becoming higher and narrower [e.g., dark blue $t = 0$ curve in Fig. 3(b), or see Appendix B in the supplementary material]. Such a focusing can be interpreted as a constructive wave interference. If one computes the relative entropy $-\sum_j P(j,t)\log[P(j,t)/\pi(j)]$ as a function of time, it will decrease (see Appendix B in the supplementary material). For SME, the relative entropy monotonously increases.[45]

B. Two-state system

Decreasing the number of states, N, we arrive at the smallest system of just two states. Unlike systems with $N > 2$, this system satisfies the detailed balance since the two states are connected by backward and forward transitions. The SME describes an exponential decrease of an initial probability distribution to the equilibrium state $\pi(1) = \pi(2) = 1/2$. The dynamics described by the time-reversible equations is very different.

The dynamics is analyzed using Eq. (22). The following normalization is employed: $Y(1) + Y(2) = \Delta_\odot S = 1$. Denoting $Y(1) = Y$ and $P(1) = P$, one has

$$dY/dt = C/P - C/(1-P), \tag{25a}$$

$$dP/dt = C/(1-Y) - C/Y, \tag{25b}$$

where $C = r\sqrt{P(1-P)Y(1-Y)}$ and $r = 2$.

Figure 4(a) shows the phase portrait of the two-state system [Eq. (25)]. For the initial values of P close to the equilibrium value of $1/2$, the trajectories on the phase plane are circles, i.e., the system performs harmonic oscillations around the minimum of $H = -2C$ with the frequency of $2r = 4$. Figure 4(b) shows trajectories $P \sim 1/2 + a\sin(4t)$ and $Y \sim 1/2 - a\cos(4t)$. As amplitude increases, the oscillations become more non-linear. For the initial values of P significantly different from the equilibrium value, the phase curves start to deviate from circles, and for $P \approx 1$, they became square-like. The system exhibits non-linear oscillatory dynamics. The corresponding trajectories [Fig. 4(c)], which have a square-wave-like form, show that significant changes in one coordinate happen, while the other stay close to either 0 or 1. The period of these oscillations is shorter compared to the harmonic ones.

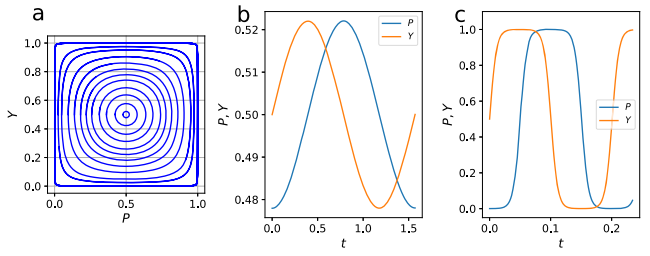

FIG. 4. Oscillating dynamics of the two-state system: (a) phase plane and (b) and (c) $P(t)$ and $Y(t)$ trajectories of the smallest curve (circle) and the largest curve (square) on the phase plane, respectively.

Let us discuss in more detail the multi-valued nature of the $S(k,t)$ functions. For large N, the multi-valuedness does not cause confusion since all the neighboring states (k), which appear in the same equation, can be considered to be at the same branch. However, for the system with just two states, the situation becomes confusing. For example, we used normalization $Y(1) + Y(2) = 1$. However, using $Y(1) = S(2) - S(1)$ and $Y(2) = S(1) - S(2)$, one obtains $0 = 1$. To recover the correct one, recall that the distance is measured on the circle rather than on the line and $S(1)$ in $Y(2)$ takes a different value from $S(1)$ in $Y(1)$. However, how this should be formalized in, e.g., Eq. (21b) or Eq. (25b), which contains both $Y(1)$ and $Y(2)$? One approach is to represent the multi-valued function as $S_{\rm mv}(k,t) = d_{\rm mv}(k) + S(k,t)$, where $d_{\rm mv}(k)$ is a fixed multi-valued function with the same multi-valued character as $S_{\rm mv}(k,t)$ and $S(k,t)$ is single valued. As $d_{\rm mv}(k)$, one can take, for example, a particular multi-valued solution $W(k)$. For example, for the N-state system considered here, as $d_{\rm mv}(k)$, one can take $d_{\rm mv}(k) = k/N\Delta_\odot S$, with $d_{\rm mv}(k+1) - d_{\rm mv}(k) = \Delta_\odot S/N$ appearing in the equations. For the two-state system with normalization $\Delta_\odot S = 2$, one obtains $S_{\rm mv}(2,t) - S_{\rm mv}(1,t) = 1 + S(2,t) - S(1,t)$ and $S_{\rm mv}(1,t) - S_{\rm mv}(2,t) = 1 + S(1,t) - S(2,t)$. Such a representation will be used in Sec. IV A, where one-dimensional random walk is considered. If the dependence on the spatial degree of freedom is neglected, the random walk is reduced to random changes in the direction—the two-state system considered here.

IV. ILLUSTRATIVE EXAMPLES: DIFFUSION

Next, we consider a more interesting and practically more important case of diffusion. The addev equations for diffusion are much more complex, and to keep the paper relatively short, we deferred most of the results to the follow-up paper. Here, we derive the addev equations for diffusion, obtain simple plane wave solutions, and show how the corresponding sub-ensembles can be obtained by conditioning.

A. Addev master equation for diffusion

Consider the Markov chain approximating diffusion on the line. The rate matrix $K(i+1|i) = K(i-1|i) = r$ describes transitions to the left and right nearest-neighbor states with constant rate r. If Δx denotes the distance between states, then the diffusion constant is $D = r\Delta x^2$.

From the physical point of view, if the spatial dependence is neglected, the dynamics can be roughly considered as two-state dynamics, where the system moves right or left and switches between the two such states with rate r. Thus, it should allow the two-state solutions considered in Sec. III B. To describe such solutions, the direction the system currently moves in needs to be distinguished. For this purpose, an internal degree of freedom is introduced; it

equals 1 or 2 when the systems moves right or left, respectively. The reaction rate matrix in the extended configuration space is $K(i+1,1|i,1) = K(i-1,2|i,2) = K(i+1,1|i,2) = K(i-1,2|i,1) = r$.

Equation (18) for the rate matrix in the extended configuration space reads (the internal degree of freedom is represented by a subscript, while the dependence on the time variable is omitted for brevity)

$$r\frac{u_1(i+1)}{u_1(i)}[S_1(i+1) - S_1(i)] + r\frac{u_2(i-1)}{u_1(i)}[1 + S_2(i-1) - S_1(i)] = -\frac{dS_1(i)}{dt}, \tag{26a}$$

$$r\frac{u_2(i-1)}{u_2(i)}[S_2(i-1) - S_2(i)] + r\frac{u_1(i+1)}{u_2(i)}[1 + S_1(i+1) - S_2(i)] = -\frac{dS_2(i)}{dt}, \tag{26b}$$

$$r\frac{v_1(i-1)}{v_1(i)}[S_1(i) - S_1(i-1)] + r\frac{v_2(i-1)}{v_1(i)}[1 + S_1(i) - S_2(i-1)] = -\frac{dS_1(i)}{dt}, \tag{26c}$$

$$r\frac{v_2(i+1)}{v_2(i)}[S_2(i) - S_2(i+1)] + r\frac{v_1(i+1)}{v_2(i)}[1 + S_2(i) - S_1(i+1)] = -\frac{dS_2(i)}{dt}, \tag{26d}$$

$$ru_1(i)v_1(i-1) + ru_1(i)v_2(i-1) - ru_1(i+1)v_1(i) - ru_2(i-1)v_1(i) = \frac{d[u_1(i)v_1(i)]}{dt}, \tag{26e}$$

$$ru_2(i)v_2(i+1) + ru_2(i)v_1(i+1) - ru_1(i+1)v_2(i) - ru_2(i-1)v_2(i) = \frac{d[u_2(i)v_2(i)]}{dt}. \tag{26f}$$

Here, the multi-valued function S is represented as $d_j + S_j(i,t)$, where $S_j(i,t)$ is single valued, while d_j is a multi-valued particular solution of the two-state system, meaning $d_1 - d_2 = d_2 - d_1 = 1$, where we used convenient normalization $\Delta_\odot S = 2$ (see the end of Sec. III B). It is straightforward to check that the following solution satisfies the equation $u_1(i,t) = u_2(i,t) = v_1(i,t) = v_2(i,t) = 1$ and $S_j(i,t) = -vt$, where $v = r$. It can be considered as a solution in the rest frame of reference. It just describes the internal dynamics of the internal degree of freedom; it is the solution of the two-state system.

B. Plane wave solutions

Some properties of Eq. (26) can be elucidated by considering a simple family of plane wave solutions. Let $u_1(i,t) = u_1$, $u_2(i,t) = u_2$, $v_1(i,t) = v_1$, $v_2(i,t) = v_2$, $S_1(i,t) = S_1' + i\Delta x k - vt$, and $S_2(i-1,t) = S_2' + i\Delta x k - vt$, where k is the wavenumber and S_1' and S_2' are some constants, and without loss of generality, S_1' can be set to 0. Eq. (26) simplifies to ($c = r\Delta x$)

$$ck + ru_2/u_1(1 + S_2') = v, \tag{27a}$$

$$-ck + ru_1/u_2(1 - S_2') = v, \tag{27b}$$

$$ck + rv_2/v_1(1 - S_2') = v, \tag{27c}$$

$$-ck + rv_1/v_2(1 + S_2') = v, \tag{27d}$$

$$u_1v_2 - u_2v_1 = 0. \tag{27e}$$

From Eq. (27e), one obtains that $u_2/u_1 = v_2/v_1$, which, together with Eqs. (27a) and (27c), means that $S_2' = 0$. From Eqs. (27a) and 27(b), one obtains the dispersion relation $v^2 = r^2 + k^2c^2$.

Interpretation of this stationary addev solution is as follows: it describes a sub-ensemble of trajectories with biased rate matrix $\tilde{K}(i+1,1|i,2) = ru_1/u_2$, $\tilde{K}(i-1,2|i,1) = ru_2/u_1$, and $\tilde{K}(i+1,1|i,1) = \tilde{K}(i-1,2|i,2) = r$, where $u_1/u_2 = \sqrt{v+ck}/\sqrt{v-ck}$ and stationary probabilities $P_1/P_2 = (v+ck)/(v-ck)$. A stochastic trajectory from this sub-ensemble performs a biased random walk, with a non-zero mean drift velocity of $v = r\Delta x(P_1 - P_2)/(P_1 + P_2) = c^2k/v$. Expressing v as a function of easily observable v leads to familiar relativistic expression $v = r/\sqrt{1 - v^2/c^2}$. c can be interpreted as an upper bound on drift velocity v, attained when the system moves only in one direction. Note that $c = r\Delta x$ is an average velocity for a trajectory of the Markov chain moving in one direction. A trajectory can move faster, however, with an exponentially decreasing likelihood.

C. Obtaining an addev sub-ensemble by conditioning

Here, we show that for every stationary addev solution, one can find such a function of a state of the Markov chain $f(i)$ and a value A that the sub-ensemble of trajectories conditioned on,

$$A = 1/T\int_0^T f(X_t)dt, \tag{28}$$

and the corresponding addev sub-ensemble are equivalent, i.e., they both are described by the same biased rate matrix $\tilde{K}(i|j)$; here, X_t is the trajectory. For simplicity, we consider a stationary case. Note that the conditioned trajectories are considered in the quasi-stationary regime at long T, i.e., for such t, that both t and $T - t$ are large.

Consider a finite continuous time Markov chain with rate matrix $K(i|j)$ from Sec. II B. We follow Ref. 40. Let λ and $L(j)$ be the largest eigenvalue and the corresponding left eigenvector of matrix $K(i|j) - \delta_{ij}f(i)$,

$$\sum_i L(i)K(i|j) - L(j)f(j) = \lambda L(j). \tag{29}$$

The sub-ensemble of trajectories satisfying condition Eq. (28), in the quasi-stationary regime, is described by the conservative Markov chain with rate matrix $M(i|j) = K(i|j)L(i)/L(j) - \delta_{ij}(f(j) + \lambda)$. Or equivalently, $M(i|j) = K(i|j)L(i)/L(j)$ for $i \neq j$ and $M(i|i)$ is found from $\sum_i M(i|j) = 0$. If one can find such $f(i)$ that $L(i) = u(i)$, then $M(i|j) = \tilde{K}(i|j)$. Using Eq. (29) as the equation on f and taking $L(i) = u(i)$ and $\lambda = 0$, one finds

$$f(j) = \sum_i K(i|j)u(i)/u(j). \tag{30}$$

For A, one finds by computing the average of Eq. (28)

$$A = \sum_j f(j)P(j) = \sum_j f(j)u(j)v(j)/\sum_j u(j)v(j). \tag{31}$$

To illustrate such a conditioning, we consider addev solutions describing plane waves from Sec. IV B. For f and A, one obtains $f(i,1) = r(u_2/u_1 - 1)$, $f(i,2) = r(u_1/u_2 - 1)$, and $A = r(r/v - 1)$. Details of simulation are provided in Appendix C in the supplementary material. Figure 5 shows that the addev sub-ensemble of trajectories agrees with that obtained from the conditioning. Figure 5(b) shows that in the conditioned trajectories, one can identify three regions: (1) small t, (2) large t and T–t, and (3) small T–t; here, $T = 30$ is the total length of the trajectories. Region 2 describes the quasi-stationary regime of the conditioned ensemble. Regions 1 and 3 describe non-stationary dynamics, leading to/from the quasi-stationary regime. Figure 5(c) shows that the rates $\tilde{K}$ are correct already in region 1.[40] Adding the equilibrium ensemble of trajectories for $t < 0$ and $t > T$, one obtains a possible picture of how an equilibrium trajectory fluctuates to an addev sub-ensemble and then relaxes back.

The probability to observe a trajectory in such an addev sub-ensemble for (sufficiently long) time Δt can be estimated as $\sim e^{A\Delta t}$ by using the large deviation principle[39,40] or the Kullback–Leibler divergence.[41] A can be expressed as $A = r(r/v - 1) = r(\sqrt{1 - v^2/c^2} - 1) = -L(v)$, where $v = \Delta x/\Delta t$ is the drift velocity and $c = r\Delta x$ is the maximal drift velocity (see Sec. IV B). The probability to observe a sequence of addevs, where each addev is independent, can be estimated as $\sim \exp(-\sum_i L(\Delta x_i/\Delta t_i)\Delta t_i)$. For small v, where $L(v) \approx rv^2/(2c^2)$, the obtained probability takes a familiar form of that for the path integral for Brownian motion, however, with the diffusion coefficient $D = c^2/(2r) = r\Delta x^2/2$ half of that for the underlying Markov chain. For large v, $L(v)$ allows propagation only with speed $|v| < c$, while the standard treatment of diffusion[46] and in particular this Markov chain allow propagation with infinite speed. Note that similar properties of the finite propagation speed and the diffusion coefficient of $c^2/(2r)$ or $\Delta x^2/(2\tau)$ have the stochastic telegraph process[47] and the discrete-time random walk,[46] respectively; here, c and r are the speed and rate of changing the direction of the telegraph process and Δx are τ the spatial and temporal steps of the random walk, respectively.

The suggested conditioning, which provides an addev sub-ensemble, is not unique. For example, one may assume that all states of the Markov chain are connected with rate $f(i)$ to a new "trap" state and consider trajectories conditioned on never visiting this state. This sub-ensemble of trajectories is described by the formalism of quasi-stationary distributions with the same equations as above.[31] One may interpret the trap state as representing the equilibrium ensemble of trajectories. Then, $f(i)$ describes the leakage of trajectories from the addev sub-ensemble to the equilibrium ensemble, and the conditioning can be interpreted as the requirement for the trajectory to stay forever in the addev sub-ensemble. Note that for $\lambda = 0$, some of $f(i)$ values are negative and serve as the source of trajectories rather than sink. Such $f(i)$ values are more appropriately interpreted as cloning rates.

The fact that conditioning that provides an addev sub-ensemble is not unique suggests that the addev equation is more fundamental. The derivation of the equation shows that there is not much flexibility. If one stays within the framework of the generalized Doob's h-transform[39,40] and assumes that forward and time-reversed dynamics are described by the same addev, the equation uniquely follows.

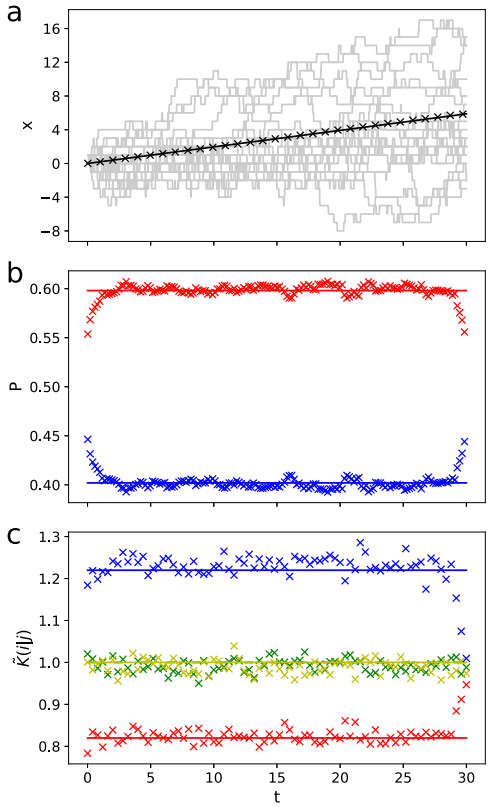

FIG. 5. Sub-ensemble of trajectories obtained by conditioning [Eq. (28)], corresponding to the addev solution describing plane waves with $k = 0.2$ (Sec. IV B). (a) A sample of trajectories (gray lines); the average displacement $\langle X_t \rangle$ computed from equations (black line) and estimated from the trajectories (black crosses). (b) Probabilities $P_1(t)$ and $P_2(t)$ are shown by red and blue colors, respectively. Lines show values computed from equations, while crosses show those estimated from trajectories. (c) Rates: $\tilde{K}(i+1,1|i,1)$ (yellow), $\tilde{K}(i-1,2|i,2)$ (green), $\tilde{K}(i+1,1|i,2)$ (blue), and $\tilde{K}(i-1,2|i,1)$ (red) as functions of time along the trajectory.

V. CONCLUDING DISCUSSION

In this manuscript, the framework of optimal reaction coordinates has been extended to include additive eigenvectors (addev). In particular, the addev validation criteria have been developed, and it was described how to determine the parameters of the diffusive model, which can be used to compute exactly some properties of the dynamics. The framework assumes that addevs for forward and time-reversed dynamics are equal. For systems not far from equilibrium, which include such practically important cases as enzymatic reactions, molecular motors, and chemical networks, the addevs for forward and time-reversed are not very different. In such cases, one can introduce an intermediate optimal RC, W^{eq}, so that the diffusive model provides a rather good approximation of the dynamics.

For systems far from equilibrium, in particular stochastic dynamics in phase space, which is a main motivation for the development, we suggested considering all sub-ensembles of trajectories conditioned on the forward and time-reversed addevs being the same. We have derived the addev master equation that describes such sub-ensembles for a Markov chain. A stationary solution of the equation is an addev. It describes a stochastic eigenmode, a stationary stochastic periodic process, which phase (on average) linearly grows with time. The biasing factor of the addev determines the biased rate matrix and specifies the sub-ensemble of trajectories. A non-stationary solution describes the evolution of the probability distribution (together with the auxiliary phase function). In contrast to the standard master equation for Markov chains, this evolution is time-reversible. One can integrate equations forward and backward in time.

The developed framework has been illustrated on two model dynamics—unidirectional random walk and diffusion. The first system demonstrates the following properties of the addev equation: (i) time-reversible description of stochastic dynamics; (ii) evolution of the probability distribution toward a more focused distribution, which can be interpreted as a constructive wave interference; and (iii) that the probability distribution has oscillatory dynamics and does not relax to an equilibrium distribution. A brief analysis of diffusion shows that the addev equation has a spectrum of stationary solutions. In particular, the plane-wave solutions were used to illustrate how an addev sub-ensemble can be obtained by conditioning and how such sub-ensembles approximate equilibrium dynamics.

In order to avoid overburdening of this manuscript, we have deferred the detailed analysis of diffusion to the follow-up manuscript, where we show, in particular, how to find exact numerical solutions of the derived equations in more complex cases of bound states. We also show that in some regimes, the solutions of the addev equation can be closely approximated by one-dimensional relativistic Dirac and Schrödinger equations, which support the notion that addevs describe stochastic periodic processes or stochastic eigenmodes. These developments are an essential step toward practical applications of the framework to the analysis of MD simulations.

The addev master equation provides a new time-reversible description of the evolution of probability distributions. While more complex, such a description can provide a better approximation to the stochastic dynamics in the phase space. First, at small timescales, the dynamics is close to the time-reversible classical Newton dynamics. Second, coherent state solutions of the Schrödinger equation approximate classical trajectories.[48,49] This suggests that an addev coherent state solution for diffusion in configuration space can describe/approximate classical Newtonian dynamics in phase space. Such a time-reversible description also solves the following fundamental problem: given current probability distribution $P(i,t_1)$, find $P(i,t_0)$ for any $t_0 < t_1$. One can formally introduce the time-reversed Markov process with transition probability $P'(i,t|j,t+\tau) = P_\tau(j|i)P(i,t)/P'(i,t|j,t+\tau)$ so that the time-reversed evolution satisfies $P(i,t) = \sum_j P'(i,t|j,t+\tau)P(j,t+\tau)$. However, first, P' is non-stationary and second, P' is different for different $P(i,t_0)$ values. So, it is not clear how find $P(i,t_0)$ from just knowing $P(i,t_1)$ or the state of the process at t_1. The addev master equation shows that just knowing $P(i,t_1)$ and $S(i,t_1)$, one can find $P(i,t_0)$ and $S(i,t_0)$ for any $t_0 < t_1$. If one is uncomfortable with including the auxiliary function S, one can modify the statement as follows: knowing $P(i,t_1)$ and $P(i,t_2)$, one can compute $P(i,t_0)$ for any t_0; $P(i,t_2)$ is used to determine $S(i,t_1)$.

SUPPLEMENTARY MATERIAL

See the supplementary material for Appendixes A–C as Jupyter Notebooks in a single zip archive file.

AUTHOR DECLARATIONS

Conflict of Interest

The author has no conflicts to disclose.

Author Contributions

Sergei V. Krivov: Conceptualization (equal); Investigation (equal); Methodology (equal); Writing – original draft (equal); Writing – review & editing (equal).

DATA AVAILABILITY

The data that support the findings of this study are available within the article and its supplementary material.

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