Sampling rare trajectories using stochastic bridges

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The numerical quantification of the statistics of rare events in stochastic processes is a challenging computational problem. We present a sampling method that constructs an ensemble of stochastic trajectories that are constrained to have fixed start and end points (so-called stochastic bridges). We then show that by carefully choosing a set of such bridges and assigning an appropriate statistical weight to each bridge, one can focus more processing power on the rare events of a target stochastic process while faithfully preserving the statistics of these rare trajectories. Further, we also compare the stochastic bridges we produce to the Wentzel-Kramers-Brillouin (WKB) optimal paths of the target process, derived in the limit of low noise. We see that the generated paths, encoding the full statistics of the process, collapse onto the WKB optimal path as the level of noise is reduced. We propose that the method can also be used to judge the accuracy of the WKB approximation at finite levels of noise.

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I. INTRODUCTION

The most uncommonly occurring events in stochastic systems are often the most consequential. Instances where this unlikely-yet-important combination occurs include fade-outs of epidemics [1,2], the extinction of species in ecology [3,4], the dynamics of biological switches [5–10], the escape of a Brownian particle from a double-well potential [11,12], large fluctuations in chemical reactions [13], and the detection or prediction of rare natural disasters such as earthquakes, storms, or heavy rains [14,15]. The broad range of these applications justifies the considerable recent effort expended on developing sampling algorithms for rare events in models of stochastic phenomena [16–20].

Rare events can often be conceived of as paths in phase space connecting long-lived states. A number of different approaches exist to generate these transition paths for a given system. The celebrated Wentzel-Kramers-Brillouin (WKB) method, for example, is not only used to compute quasistationary distributions and nonequilibrium landscapes [7,10,21–24], but it also delivers paths describing rare events. This approach relies on a saddle-point approximation in the limit of weak noise. As a consequence, little can be learned from the WKB approach about the statistics of transition paths in stochastic systems with finite noise. Instead, the WKB instanton only provides information about the most likely path by which a system transits from one long-lived state to another [1,4,25–29].

Transition path sampling algorithms [30–32] and forward flux techniques [31,33,34] to sample rare events account for stochasticity with finite amplitude. Transition path sampling starts from an initial trajectory connecting two long-lived states and then uses a Metropolis scheme to systematically update this path. Forward flux techniques divide phase space (or a reduced reaction coordinate space) into patches. Transition paths are then constructed as a sequence of small segments connecting these patches. Other techniques such as so-called weighted ensemble methods [35,36] also rely on a segmentation of phase space. Methods that introduce artificial temperatures and sample rare trajectories associated to rare values of a target macroscopic quantity are also of extended use [37–39].

While these powerful tools are widely used to sample rare events, each of these approaches also has limitations. Transition path sampling methods require detailed balance [32], and forward flux algorithms are known to draw statistically biased trajectories [40]. Recent work has focused on combining the strengths of these two strategies [41].

In this paper we use so-called "stochastic bridges" [42], which pass through specified start and end points by construction, to quantify the statistics of rare trajectories. Stochastic bridges are used in physics [43–47], finance [48,49], and information processing [50]. Further, Langevin bridges have also been applied to generate trajectories connecting long-lived states of stochastic differential equations (SDEs) [51,52].

The method we present here can be summarized as follows: For a given target stochastic process, we define a bespoke stochastic bridge process. We show that the statistics of the target process can be recovered by associating a statistical weight with each stochastic bridge. This allows us to dedicate more computational effort to rare trajectories without introducing bias or interdependence. The method is flexible; the target process is fully general, detailed balance is not required, no small-noise approximation is made, and it is not limited to the sampling of trajectories associated to a target macroscopic quantity, nor does it require the introduction of artificial parameters such as temperatures.

We show further that the stochastic bridges produced provide the full statistics of the ensemble of transition paths between long-lived states of the target process. This allows one to sample fluctuations around the WKB instanton, and thus to judge if the WKB approximation scheme is accurate at various levels of noise.

II. MOTIVATION AND SIMPLE EXAMPLE

We first consider a Markov process in discrete time, $t = 0, 1, 2, \dots, T$, with a discrete set of states which we label x_t. The process is defined by the transition probabilities $W^t_{x\to y} = P(x_{t+1} = y|x_t = x)$ and a probability distribution $P_0(x_0)$ for the initial state x_0. As indicated by the superscript t we allow for an explicit time dependence of the transition probabilities. We will refer to the ordered sequence of states visited in a realization of the process as a *path*. We write this as $\mathcal{T} = (x_0, x_1, x_2, \dots, x_T)$, noting that the same state can be visited multiple times along a path. The probability to observe a particular path $\mathcal{T}$ is

$$\mathcal{P}(\mathcal{T}) = P_0(x_0)W^0_{x_0\to x_1}W^1_{x_1\to x_2}\cdots W^{T-1}_{x_{T-1}\to x_T}. \quad (1)$$

These probabilities fully characterize the process. For example, the probability of finding the system in state x at time t is the marginal $P(x,t) = \sum_{\mathcal{T}} \mathcal{P}(\mathcal{T})\delta_{x,x_t}$, where $\delta_{x,y}$ is the Kronecker delta.

A random walk on the set of non-negative integers is a simple example of such a process. We assume that the walker departs from a fixed state x_0. The transition rates are $W_{x\to x+1} = p$ and $W_{x\to x-1} = 1 - p$ $(0 \leqslant p \leqslant 1)$. Typical paths of this process are illustrated in Fig. 1(a). In the figure the random walk is biased towards lower integers. The probability that a realization terminates at a state $x_T > x_0$ is then low, in particular when x_T is much larger than x_0, or when p is much smaller than 1/2. It is then difficult to sample paths ending at values $x_T > x_0$ in direct simulations of the biased walk.

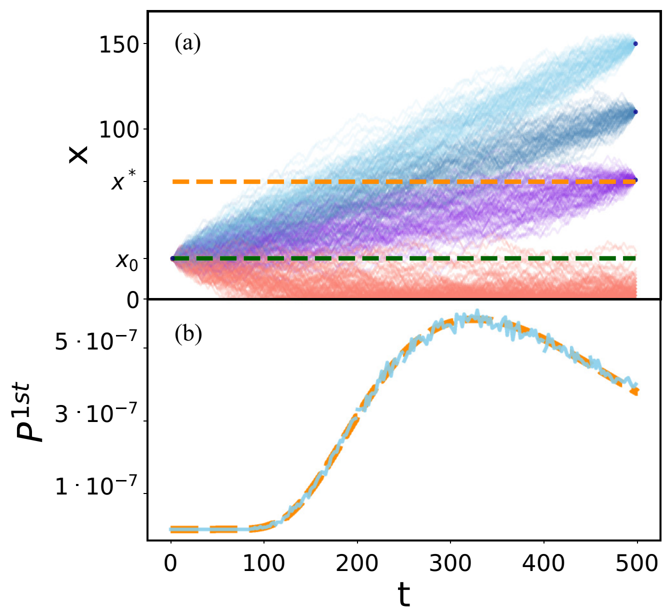

FIG. 1. (a) Red (bottom) lines show trajectories generated from simulations of the biased random walk described in the text (for $p = 0.45$), departing from $x_0 = 25$. We use reflecting boundary conditions ($W_{0\to1} = 1$). None of these trajectories were found to cross $x^* = 70$ before time $t = 500$. Lines in the upper part of (a) show stochastic bridges with fixed initial state $x_0 = 24$ and final states $x_T = 150$, $x_T = 130$, and $x_T = 70$, respectively (top to bottom). (b) Distribution of first-passage times at $x = x^*$ computed from our approach (see Sec. S2 of SM [53] for details). Also shown (dashed line) is the analytical result from Ref. [54].

III. METHOD

Our strategy for sampling paths of a given target dynamics connecting specific start and end points, x_0 and x_T, respectively, is based on what we will call an "associated bridge process." This process operates backwards in time, that is, paths of this bridge process are generated from x_T to x_0. We first describe this for the case of discrete time and discrete states (generalizations are discussed below).

We define the associated bridge process via transition probabilities $\tilde{W}^t_{x\leftarrow y} = P(x_t = x|x_{t+1} = y)$. That is to say, $\tilde{W}^t_{x\leftarrow y}$ is the probability that the target process was at x at time t, given that state y is visited at time $t+1$. To define the associated bridge process we also need to specify a probability distribution $\tilde{P}_T(x)$ for the state x_T, which must satisfy $\tilde{P}_T(x) = 0$ if $P(x,T) = 0$.

By virtue of Bayes' theorem we have

$$\tilde{W}^t_{x\leftarrow y} = W^t_{x\to y}\frac{P(x,t)}{P(y,t+1)}. \quad (2)$$

As a consequence, the probabilities $\tilde{W}^t_{x\leftarrow y}$ will in general be time dependent, even if the transition probabilities of the original model do not depend on time.

The rates $\tilde{W}^t_{x\leftarrow y}$ defined in Eq. (2) might seem reminiscent of a Doob transform of the target process [51,55–57]. However, it is important to note that there are significant differences between the two. In particular, the probabilities $P(x,t)$ and $P(y,t+1)$ on the right-hand side of Eq. (2) are not conditioned on any final state x_T, so improving the overall efficacy of the sampling method [see Sec. S1 of the Supplemental Material (SM) [53] for further details].

We now focus on a fixed path $\mathcal{T} = (x_0, \dots, x_T)$ of the target process. The path can also occur in the associated bridge process where it is traversed starting at x_T and ending at x_0. The probability to observe path $\mathcal{T}$ in the associated bridge process is

$$\tilde{\mathcal{P}}(\mathcal{T}) = \tilde{P}_T(x_T)\tilde{W}^T_{x_{T-1}\leftarrow x_T}\cdots\tilde{W}^1_{x_0\leftarrow x_1}. \quad (3)$$

Combining Eqs. (1)–(3) we obtain a relation between the probabilities of finding path $\mathcal{T}$ in the target and associated processes respectively,

$$\mathcal{P}(\mathcal{T}) = \tilde{\mathcal{P}}(\mathcal{T})\frac{P(x_T,T)}{\tilde{P}_T(x_T)}. \quad (4)$$

Equations (2) and (4) are the key components of our approach. We use the process defined by Eq. (2) to generate paths $\mathcal{T}$, i.e., we sample from $\tilde{P}(\mathcal{T})$. Using Eq. (4) we then read off the probability with which each sample path occurs in the target process.

If we choose $\tilde{P}_T(x) = P(x,T)$ then $\mathcal{P}(\mathcal{T}) = \tilde{\mathcal{P}}(\mathcal{T})$ and paths that are rare in the target process will also be rare in the associated bridge process. Equations (2) and (4) then do not constitute an efficient sampling method for rare paths. If, on the other hand, we choose $P_0(x) = \delta_{x,x_0}$ and $\tilde{P}_T(x) = \delta_{x,x_T}$, the trajectories generated from the process in Eq. (2) will constitute stochastic bridges connecting x_T and x_0. For such paths Eq. (4) then reduces to

$$\mathcal{P}(\mathcal{T}) = \tilde{\mathcal{P}}(\mathcal{T})P(x_T, T). \tag{5}$$

While the most demanding part of the procedure in terms of computing time is the calculation of $P(x,t)$ for $t = 0, 1, \dots, T$, this can usually be obtained efficiently. Depending on the nature of the stochastic process (continuous/discrete states and time), $P(x,t)$ can be found with a number of established numerical methods (e.g., Refs. [58–61]).

We note that the knowledge of $P(x,t)$ does not disclose the whole statistical characterization of the enquired stochastic processes. For example, the maximum span of a trajectory or the description of transition paths is not accessible with the only knowledge of $P(x,t)$. Instead, any quantity of interest can be obtained from a representative set of paths. There is, therefore, a genuine value in estimating $P(\mathcal{T})$ using $P(x,t)$ as an input.

The complexity can be reduced further for escape paths from long-lived states. The distribution P in Eq. (2) can then be replaced by the time-independent quasistationary distribution P^{QS} describing the metastable state, which can often be approximated analytically (see, e.g., Refs. [3,25,58,62,63]). Analytical expressions for P^{QS} will make available a general expression for the rates of one-dimensional and one-step stochastic bridge process (see Sec. S4 of SM [53]). This is of particular interest since the explicit form of the generator for stochastic bridges is only known for a few systems (see, e.g., Refs. [45,51,64]). If the transition probabilities of the target process are time independent, so are then the probabilities of the associated process $\tilde{W}_{x\leftarrow y} = W_{x\to y}P^{\mathrm{QS}}(x)/P^{\mathrm{QS}}(y)$.

We now return to the example of a biased random walk. Figure 1(a) shows three ensembles of bridges, all starting at a fixed value of x_0 at $t = 0$ and each ensemble ending at a different choice of x_T at time $t = T$. These paths were generated from the associated process in Eq. (2), where we have chosen $\tilde{P}(x_T)$ as delta functions at the desired end points.

For a fixed final time T and choice of x_T we can determine whether the generated trajectories have crossed a fixed x^* ($x_0 < x^* < x_T$) by time T. For each trajectory we record the first crossing time. Repeating the process for different values of x_T and weighting trajectories according to Eq. (4) we then obtain the distribution of first-passage times through x^* (see Sec. S2 of the SM [53] for details). A comparison of our simulations with the analytical predictions in Ref. [54] is shown in Fig. 1(b), confirming the validity of our sampling method.

IV. CONTINUOUS-TIME PROCESSES

The method can also be used when time or the state space of the target process are continuous. The only modification is an adjustment of the expression in Eq. (2),

$$\tilde{\omega}^t_{x\leftarrow y} = \omega^t_{x\to y}\frac{P(x,t)}{P(y,t+dt)} = \omega^t_{x\to y}\frac{P(x,t)}{P(y,t)} + O(dt), \tag{6}$$

where $\omega^t_{x\to y}$ are the transition rates of the target dynamics, and $\tilde{\omega}^t_{x\leftarrow y}$ those of the associated process. For discrete states a process with time-dependent rates can be simulated for example using Lewis' thinning algorithm [65,66].

We note that $\tilde{\omega}^t_{x\leftarrow y}$ is a Gaussian bridge process [42,44,50] when the original process is Gaussian (for details see Sec. S3 of the SM [53]).

V. APPLICATIONS: MODELS OF AN EPIDEMIC AND OF A SIMPLE GENETIC SWITCH

In the context of two examples, we now compare the WKB trajectories of the target process to the associated bridge trajectories. The WKB optimal path of the target process is the most likely path that the system will take (in the limit of small noise) given the end points x_0 and x_T. At finite noise levels our method captures stochastic fluctuations about the WKB instanton. As the level of noise is reduced, we find that the realizations of the associated bridge process approach the WKB trajectory.

We first focus on the extinction of an epidemic (or "fade-out") in the individual-based susceptible-infected-susceptible (SIS) model. Conceptually this is similar to extinctions of species in ecology [67]. The model describes N individuals, of which n are infected. The population evolves in continuous time via infection and recovery processes, with rates

$$\omega_{n\to n+1} = \beta\frac{n(N-n)}{N}, \quad \omega_{n\to n-1} = \gamma n. \tag{7}$$

The parameters β and γ characterize speed of infection and recovery, respectively.

When $\beta > \gamma$, the model is known to evolve to a quasistationary "endemic" state in which the number of infected individuals fluctuates around $N(1-\gamma/\beta)$ [68]. The population will remain in this metastable state until a large fluctuation drives the epidemic to extinction. The mean time to reach this absorbing state grows exponentially with the population size N [69]. For large populations it is therefore difficult to observe extinction in direct simulations of the SIS dynamics. Such paths can however be generated straightforwardly using the associated bridge process with rates given by Eq. (6). To evaluate these rates we use the analytical solution for the quasistationary distribution in $P^{\mathrm{QS}}(n)$ [69] (see also Sec. S4 of the SM [53]).

An ensemble of extinction paths is shown in Fig. 2(a), along with the WKB instanton to extinction [25,63]. As illustrated in Fig. 2(a), the extinction paths at finite N fluctuate around the WKB instanton. We also show the distribution of transition times (τ) towards the infection-free state in Fig. 2(b). This timescale characterizes the duration of the transition towards extinction once the system has left the endemic state, and is not to be confused with the lifetime of the metastable state itself [3,21,25,62,63], nor with the fixed total duration of the stochastic bridges (T) (see Sec. S4 of the SM [53]). This distribution is relatively broad for small populations, but becomes more and more concentrated on the WKB estimate for larger N.

As a second example, we focus on a model of cell differentiation discussed in Ref. [7]. The two real variables $x_1 \geqslant 0$ and $x_2 \geqslant 0$ in the model describe protein concentrations, governed

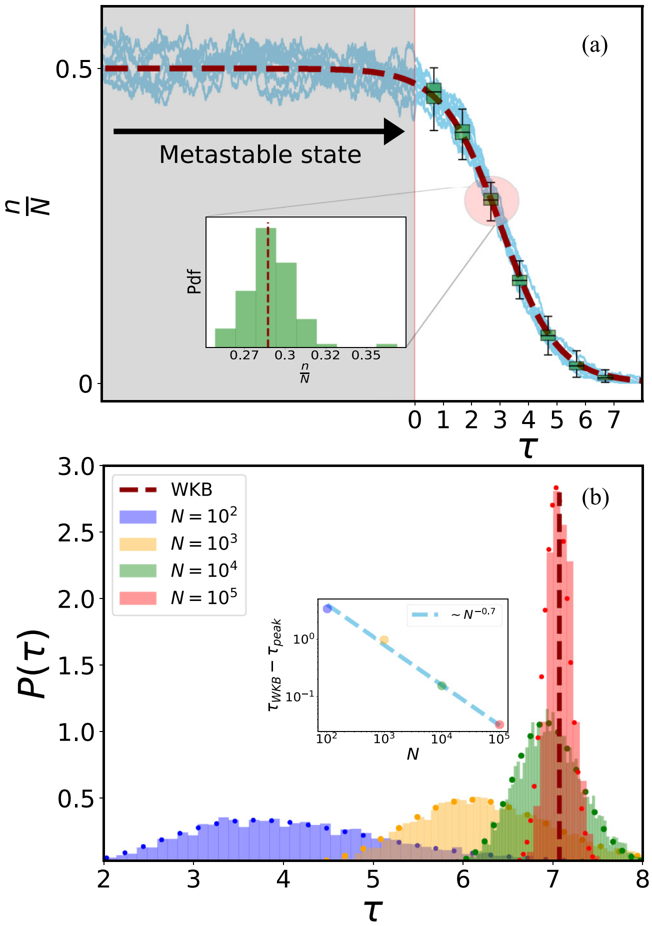

FIG. 2. Extinction paths for the SIS model ($\beta = 2, \gamma = 1$). (a) Paths leading to extinction from a common starting point $x_0 = \frac{n}{N} = 1 - \frac{\gamma}{\beta} = 0.5$ to $x_T = 0$ for $N = 10^3$, which have been shifted in time to match the WKB instanton, shown as a dashed line (see Sec. S4 of the SM [53] for additional information about this procedure). The time $\tau = 0$ corresponds to the point where the WKB instanton crosses $n/N = 0.48$. Boxes indicate the median and first quartiles, and error bars the observed range of the ensemble of stochastic paths. The inset shows the distribution of n/N at time $\tau = 2.8$. (b) Distribution of transition times for extinction trajectories from the quasistationary state towards the absorbing state (see Sec. S4 of the SM [53] for details). Dots show fits to log-normal distributions. The inset shows that the modes τ_{peak} of these fits approach the value predicted from the WKB instanton, with $|\tau_{\text{WKB}} - \tau_{\text{peak}}| \sim N^{-0.7}$.

by the SDEs

$$\dot{x}_1 = \frac{x_1^n}{S^n + x_1^n} + \frac{S^n}{S^n + x_2^n} - x_1 + \sqrt{2D}\xi_1(t),$$
$$\dot{x}_2 = \frac{x_2^n}{S^n + x_2^n} + \frac{S^n}{S^n + x_1^n} - x_2 + \sqrt{2D}\xi_2(t), \qquad (8)$$

where $\xi_1(t)$ and $\xi_2(t)$ are Gaussian noise variables with mean zero and $\langle \xi_i(t)\xi_j(t')\rangle = \delta_{ij}\delta(t - t')$. The noise describes effects external to the gene circuit and its strength is governed by the model parameter $D \geqslant 0$. The deterministic terms on the right-hand side of Eqs. (8) represent self-activation, mutual inhibition, and degradation, respectively [23].

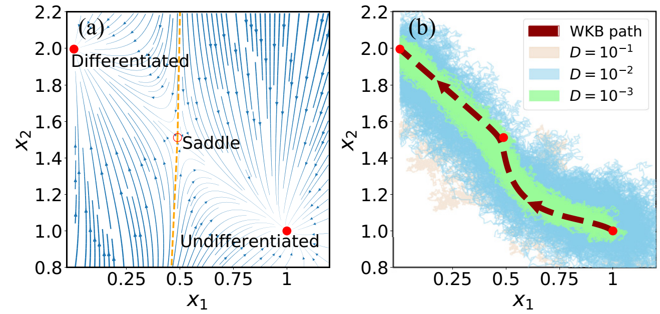

FIG. 3. (a) Phase portrait of the system in Eqs. (8) for $D = 0$. Arrows indicate the deterministic flow. Due to the $x_1 \leftrightarrow x_2$ symmetry we only show one of the two fixed points describing differentiated states, and one saddle point. The corresponding separatrix is indicated as a dashed line. (b) Stochastic transition paths from the undifferentiated to one the differentiated states obtained with our sampling method. The dashed line is the WKB instanton. In both panels, $n = 4$ and $S = 0.5$.

In the deterministic limit ($D = 0$) Eqs. (8) have three stable fixed points: (i) one with $x_1 = x_2 = 1$, (ii) one with $x_1 > x_2$, and (iii) a third one obtained from the second by exchanging x_1 and x_2. The first fixed point describes an undifferentiated cell state, and the other two differentiated states [7]. The deterministic model also has two saddle points on the separatrices between the basins of attraction of the fixed points. The resulting phase portrait is shown in Fig. 3(a).

For $D > 0$, noise-driven transitions from the undifferentiated to either one of the differentiated states become possible. Similar to the SIS model the typical escape time grows exponentially with the inverse noise strength [70]. For small noise amplitudes, numerical integration of Eqs. (8) is therefore unlikely to generate transition paths within realistic computing times.

To sample these rare paths we first discretize time using an Euler-Maruyama scheme [61,71]. The resulting process is described by Gaussian transition rates. These are then used in Eq. (6) together with the quasistationary distribution describing the undifferentiated state (see Sec. S5 of the SM [53] for details). As a result of this procedure we obtain an ensemble of trajectories starting from the undifferentiated state and ending in the differentiated state $x_2 > x_1$ (see also Sec. S6 in the SM [53]). In Fig. 3(b) we show ensembles of transition paths for different noise amplitudes. As demonstrated in the figure the stochastic trajectories approach the WKB instanton as $D \to 0$.

The level of noise at which the WKB approximation is useful very much depends on the application. The above examples illustrate that the comparison between the generated stochastic bridges and the WKB instantons allows us to appraise the accuracy of WKB results.

VI. CONCLUSIONS

In this paper, we have presented a method to sample rare trajectories. The core component of the approach is a process in reverse time that generates stochastic bridges connecting desired start and end points. Using Eq. (4) we can then calculate the probability with which these paths occur in the target process under consideration. This allows us to quantify the statistics of rare events such as first passage times. Our approach does not require the noise in the model to be weak, and it generates uncorrelated and unbiased transition paths.

Our approach goes beyond the WKB method, and delivers an ensemble of transition paths along with their statistical weights. This enables us to obtain entire distributions of first-passage times or other characteristics in simulations.

We envisage that the method that we have developed will have applications in myriad systems where sampling rare events is important. We imagine that it can also be used as a numerical aid to intuit when the WKB method will be accurate and useful. The approach presented here can also be extended to sample stochastic trajectories constrained to pass through more than two desired points.

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