

MATHEMATICAL ANALYSIS OF TEMPERATURE ACCELERATED DYNAMICS*

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Abstract. We give a mathematical framework for temperature accelerated dynamics (TAD), an algorithm proposed by Sørensen and Voter in [*J. Chem. Phys.*, 112 (2000), pp. 9599–9606] to efficiently generate metastable stochastic dynamics. Using the notion of *quasi-stationary distributions*, we propose some modifications to TAD. Then considering the modified algorithm in an idealized setting, we show how TAD can be made mathematically rigorous.

Key words. accelerated molecular dynamics, temperature accelerated dynamics, Langevin dynamics, stochastic dynamics, metastability, quasi-stationary distributions, kinetic Monte Carlo

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1. Introduction. Consider the stochastic dynamics X_t on \mathbb{R}^d satisfying

$$(1.1) \quad dX_t = -\nabla V(X_t) dt + \sqrt{2\beta^{-1}} dW_t,$$

called *Brownian dynamics* or *overdamped Langevin dynamics*. Here, $V : \mathbb{R}^d \rightarrow \mathbb{R}$ is a smooth function, $\beta = (k_B T)^{-1}$ is a positive constant, and W_t is a standard d -dimensional Brownian motion [23]. The dynamics (1.1) is used to model the evolution of the position vector X_t of N particles (in which case $d = 3N$) in an energy landscape defined by the potential energy V . This is the so-called molecular dynamics. Typically, this energy landscape has many metastable states, and in applications it is of interest to understand how X_t moves between them. Temperature accelerated dynamics (TAD) is an algorithm for computing this *metastable dynamics* efficiently. (See [27] for the original algorithm, [19] for some modifications, and [25] for an overview of TAD and other similar methods for accelerating dynamics.)

In TAD, each metastable state is associated to a basin of attraction D for the gradient dynamics $dx/dt = -\nabla V(x)$ of a local minimum of the potential V . Temperature is raised to force X_t to leave each basin more quickly. What would have happened at the original low temperature is then extrapolated. To generate metastable dynamics of $(X_t)_{t \geq 0}$ at low temperature, this procedure is repeated in each basin. This requires the following assumptions:

- (H1) X_t immediately reaches local equilibrium upon entering a given basin D .
- (H2) An Arrhenius law may be used to extrapolate the exit event at low temperature.

The Arrhenius (or Eyring–Kramers) law states that, in the small temperature regime, the time it takes to transition between neighboring basins D and D' is

$$(1.2) \quad \nu^{-1} \exp \left[\frac{|\delta V|}{k_B T} \right],$$

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where δV is the difference in potential energy between the local minimum in D and the lowest saddle point along a path joining D to D' . Here, ν is a constant (called a *prefactor*) depending on the eigenvalues of the Hessian of V at the local minimum and at the saddle point, but not on the temperature. In practice, the Arrhenius law is used when $k_B T \ll |\delta V|$. We refer to [2, 4, 11, 17] for details.

TAD is a very popular technique, in particular for applications in material sciences; see, for example, [1, 3, 5, 12, 18, 24, 28, 29, 30, 31, 32]. In this article we provide a mathematical framework for TAD and, in particular, a mathematical formalism for (H1)–(H2). Our analysis will actually concern a slightly modified version of TAD. In this modified version, which we call *modified TAD*, the dynamics is allowed to reach local equilibrium after entering a basin, thus circumventing assumption (H1). The assumption (H1) is closely related to the no recrossings assumption in transition state theory; in particular, one can see the local equilibration steps (modifications (M1) and (M2) below) in modified TAD as a way to account for recrossings. We note that modified TAD can be used in practice and, since it does not require the assumption (H1), may reduce some of the numerical error in (the original) TAD.

To analyze modified TAD, we first make the notion of local equilibration precise by using *quasi-stationary distributions* (QSDs), in the spirit of [15], and then we circumvent (H2) by introducing an idealized extrapolation procedure which is *exact*. The result, which we call *idealized TAD*, yields exact metastable dynamics; see Theorem 3.6 below. Idealized TAD is not a practical algorithm because it depends on quantities related to QSDs which cannot be efficiently computed. However, we show that idealized TAD agrees with modified TAD at low temperature. In particular, we justify (H2) in modified TAD by showing that at low temperature, the extrapolation procedure of idealized TAD agrees with that of modified TAD (and of TAD), which is based on the Arrhenius law (1.2); see Theorem 4.1 below.

In this article, we focus on the overdamped Langevin dynamics (1.1) for simplicity. The algorithm is more commonly used in practice with the Langevin dynamics

$$(1.3) \quad \begin{cases} dq_t = M^{-1} p_t dt, \\ dp_t = -\nabla V(q_t) dt - \gamma M^{-1} p_t dt + \sqrt{2\gamma\beta^{-1}} dW_t. \end{cases}$$

The notion of QSDs still makes sense for the Langevin dynamics [22], so an extension of our analysis to that dynamics is in principle possible, though the mathematics there are much more difficult due to the degeneracy of the infinitesimal generator of (1.3). In particular, some results on the low temperature asymptotics of the principal eigenvalue and eigenvector for hypoelliptic diffusions are still missing.

The paper is organized as follows. In section 2, we recall TAD and present modified TAD. In section 3, we introduce idealized TAD and prove that it is exact in terms of metastable dynamics. Finally, in section 4, we show that idealized TAD and modified TAD are essentially equivalent in the low temperature regime. Our analysis in section 4 is restricted to a one-dimensional setting. The extension of this to higher dimensions will be the purpose of another work.

Throughout the paper it will be convenient to refer to various objects related to the dynamics (1.1) at a high and low temperature, β^{hi} and β^{lo} , as well as at a generic temperature, β . To do so, we use superscripts hi and lo to indicate that we are looking at the relevant object at $\beta = \beta^{hi}$ or $\beta = \beta^{lo}$, respectively. We drop the superscripts to consider objects at a generic temperature β .

2. TAD and modified TAD. Let X_t^{lo} be a stochastic dynamics obeying (1.1) at a low temperature $\beta = \beta^{lo}$, and let $S : \mathbb{R}^d \rightarrow \mathbb{N}$ be a function which labels the basins of V . (So each basin D has the form $S^{-1}(i)$, where $i \in \mathbb{N}$.) The goal of TAD is to efficiently estimate the metastable dynamics at low temperature, in other words,

- efficiently generate a trajectory $\hat{S}(t)_{t \geq 0}$ which has approximately the same distribution as $S(X_t^{lo})_{t \geq 0}$.

The aim then is to get approximations of *trajectories*, including distributions of hitting times, time correlations, etc., and thus not only the evolution of the averages of some observables or averages of observables with respect to the invariant distribution.

At the heart of TAD is the problem of efficiently simulating an exit of X_t^{lo} from a generic basin D , since the metastable dynamics are generated by essentially repeating this. To efficiently simulate an exit of X_t^{lo} from D , the temperature is raised so that $\beta^{hi} < \beta^{lo}$ and a corresponding high temperature dynamics X_t^{hi} is evolved. The process X_t^{hi} is allowed to search for various exit paths out of D until a stopping time T_{stop} ; each time X_t^{hi} reaches ∂D , it is reflected back into D , the place and time of the attempted exit is recorded, and the Arrhenius law (1.2) is used to extrapolate a low temperature exit. After time T_{stop} , the fastest extrapolated low temperature exit is selected. This exit is considered an approximation of the first exit of X_t^{lo} from D . The original algorithm is described in section 2.1 below; a modified version is proposed in section 2.2 below.

2.1. TAD. In the following, we let D denote a generic basin. We let x_0 be the minimum of V inside D , and we assume there are finitely many saddle points, x_i ($i \geq 1$), of V on ∂D . The original TAD algorithm [27] for generating the approximate metastable dynamics $\hat{S}(t)$ is as follows.

ALGORITHM 2.1 (TAD). *Let X_0^{hi} be in the basin D and start a low temperature simulation clock T_{tad} at zero: $T_{tad} = 0$. Then iterate on the visited basins the following:*

1. Let $T_{sim} = 0$ and $T_{stop} = \infty$. These are the simulation and stopping times for the high temperature exit search.
2. Evolve X_t^{hi} at $\beta = \beta^{hi}$ starting at $t = T_{sim}$ until the first time after T_{sim} at which it exits D . (Exits are detected by checking if the dynamics lands into another basin via gradient descent, i.e., the deterministic dynamics $dx/dt = -\nabla V(x)$.) Call this time $T_{sim} + \tau$.
3. Associate a nearby saddle point, x_i , of V on ∂D to the place where X_t^{hi} exited D . (This can be done by using, for example, the nudged elastic band method [14]; see below.)
4. Advance the high temperature simulation clock by τ : $T_{sim} = T_{sim} + \tau$.
5. If an exit at x_i has already been observed, go to step 8. If an exit at x_i has not yet been observed, set $T_i^{hi} = T_{sim}$ and extrapolate the high temperature exit time to low temperature using the formula

$$(2.1) \quad T_i^{lo} = T_i^{hi} e^{-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))}.$$

This equation comes from the Arrhenius law (1.2) for exit rates in the low temperature regime; see the remarks below.

6. Update the smallest extrapolated exit time

$$T_{\min}^{lo} = \min\{T_{\min}^{lo}, T_i^{lo}\}$$

and the (index of) the corresponding exit point

$$I_{\min}^{lo} = i \quad \text{if} \quad T_{\min}^{lo} = T_i^{lo}.$$

7. Update T_{stop} . The stopping time is chosen so that with confidence $1 - \delta$, an extrapolated low temperature exit time smaller than T_{min}^{lo} will not be observed. See (2.8) below for how this is done.
8. If $T_{sim} \leq T_{stop}$, reflect X_t^{hi} back into D and go back to step 2. Otherwise, proceed to step 9.
9. Set

$$\hat{S}(t) = S(D) \quad \text{for } t \in [T_{tad}, T_{tad} + T_{min}^{lo}],$$

and advance the low temperature simulation clock by T_{min}^{lo} :

$$T_{tad} = T_{tad} + T_{min}^{lo}.$$

10. Send X_t^{hi} to the new basin, namely, the neighboring basin of D which is attained through the saddle point $x_{I_{min}^{lo}}$. Then, go back to step 1, the domain D now being the neighboring basin.

The nudged elastic band method [14] consists, starting from a trajectory leaving D , of computing by a gradient descent method the closest minimum energy path leaving D , with the end points of the trajectory being fixed. This minimum energy path necessarily leaves D through a saddle point.

Remark 2.2. When the overdamped Langevin dynamics leaves a basin near a saddle point, its first reentrance into that basin is immediate. Thus, Algorithm 2.1 does not really make sense for overdamped Langevin dynamics. (With the Langevin dynamics (1.3), however, this difficulty does not arise.) In modified TAD, defined below, we will allow the dynamics to evolve away from the boundary of a basin after an exit event, thus circumventing this problem.

Below we comment on (2.1), from which low temperature exit times are extrapolated, as well as the stopping time T_{stop} .

• **Low temperature extrapolation.**

The original TAD uses the following kinetic Monte Carlo (KMC) framework [33]. For a given basin D , it is assumed that the time \tilde{T}_i to exit through the saddle point x_i of V on ∂D is exponentially distributed with rate κ_i given by the Arrhenius law (1.2):

$$(2.2) \quad \kappa_i \equiv \nu_i e^{-\beta(V(x_i) - V(x_0))},$$

where we recall that ν_i is a temperature independent prefactor and x_0 is the minimum of V in D . An exit event from D at temperature β is obtained by sampling independently the times \tilde{T}_i for all the saddle points x_i on ∂D and then selecting the smallest time and the corresponding saddle point.

In TAD, this KMC framework is used for both temperatures β^{lo} and β^{hi} . That is, it is assumed that the high and low temperature exit times \tilde{T}_i^{hi} and \tilde{T}_i^{lo} through each saddle point x_i satisfy

$$(2.3) \quad \begin{aligned} \mathbb{P}(\tilde{T}_i^{hi} > t) &= e^{-\kappa_i^{hi} t}, \\ \mathbb{P}(\tilde{T}_i^{lo} > t) &= e^{-\kappa_i^{lo} t}, \end{aligned}$$

where

$$(2.4) \quad \begin{aligned} \kappa_i^{hi} &= \nu_i e^{-\beta^{hi}(V(x_i) - V(x_0))}, \\ \kappa_i^{lo} &= \nu_i e^{-\beta^{lo}(V(x_i) - V(x_0))}. \end{aligned}$$

Observe that then

$$\tilde{T}_i^{hi} \frac{\kappa_i^{hi}}{\kappa_i^{lo}} = \tilde{T}_i^{hi} e^{-(\beta^{hi}-\beta^{lo})(V(x_i)-V(x_0))}$$

has the same probability law as \tilde{T}_i^{lo} . This leads to the extrapolation formula (2.1).

The assumption of exponentially distributed exit times T_i^{hi} and T_i^{lo} is valid only if the dynamics at both temperatures immediately reach local equilibrium upon entering a basin; see (H1) and Theorem 3.1 below. In modified TAD, described below, we circumvent this immediate equilibration assumption by allowing the dynamics at both temperatures to reach local equilibrium. In particular, in modified TAD the low temperature assumption is no longer needed to get exponential exit distributions as in (2.3). On the other hand, to get the *rate constants* in (2.4)—and by extension the extrapolation rule (2.1); see (H2)—a low temperature assumption is required. We will justify both (2.3) and (2.4) in the context of modified TAD. More precisely, we show that (2.3) will be valid at any temperature, while a low temperature assumption is needed to justify (2.4). Note that, inspecting (2.4), the low temperature assumption will be required for *both* temperatures used in TAD—so $1/\beta^{hi}$ will be small in an absolute sense but large compared to $1/\beta^{lo}$.

- **Stopping time.**

The stopping time T_{stop} is chosen so that if the high temperature exit search is stopped at time T_{stop} , then with probability $1 - \delta$, the smallest extrapolated low temperature exit time will be correct. Here, δ is a user-specified parameter.

To obtain a formula for the stopping time T_{stop} , it is assumed that, in addition to (H1)–(H2), the following holds:

(H3) There is a minimum, ν_{\min} , to all the prefactors in (2.4):

$$\forall i \in \{1, \dots, k\}, \nu_i \geq \nu_{\min},$$

where k denotes the number of saddle points on ∂D .

Let us now explain how this assumption is used to determine T_{stop} . Let T be a deterministic time. If a high temperature first exit time through x_i , $T_i^{hi} > T$, extrapolates to a low temperature time less than T_{\min}^{lo} , then from (2.1),

$$V(x_i) - V(x_0) \leq \frac{\log(T_{\min}^{lo}/T)}{\beta^{lo} - \beta^{hi}}$$

and so

$$(2.5) \quad \kappa_i^{hi} = \nu_i e^{-\beta^{hi}(V(x_i)-V(x_0))} \geq \nu_{\min} \exp\left(\frac{\beta^{hi} \log(T_{\min}^{lo}/T)}{\beta^{hi} - \beta^{lo}}\right).$$

In TAD, it is required that this event has a low probability δ of occurring, that is,

$$(2.6) \quad \mathbb{P}(T_i^{hi} > T) = e^{-\kappa_i^{hi} T} < \delta.$$

Using (2.5) in (2.6), one sees that it suffices that

$$\exp\left[-\nu_{\min} \exp\left(\frac{\beta^{hi} \log(T_{\min}^{lo}/T)}{\beta^{hi} - \beta^{lo}}\right) T\right] < \delta.$$

Solving this inequality for T , one obtains

$$(2.7) \quad T > \frac{\log(1/\delta)}{\nu_{\min}} \left(\frac{\nu_{\min} T_{\min}^{lo}}{\log(1/\delta)} \right)^{\beta^{hi}/\beta^{lo}}.$$

The stopping time T_{stop} is then chosen to be the right-hand side of the above:

$$(2.8) \quad T_{stop} \equiv \frac{\log(1/\delta)}{\nu_{\min}} \left(\frac{\nu_{\min} T_{\min}^{lo}}{\log(1/\delta)} \right)^{\beta^{hi}/\beta^{lo}}.$$

(It is calculated using the current value of T_{\min}^{lo} .) The above calculation shows that at simulation time T_{stop} , with probability at least $1 - \delta$, T_{\min}^{lo} is the same as the smallest extrapolated low temperature exit time which would have been observed with no stopping criterion.

For TAD to be practical, the stopping time T_{stop} must be (on average) smaller than the exit times at low temperature. The stopping time of course depends on the choice of ν_{\min} and δ . In practice, a reasonable value for ν_{\min} may be known a priori [27] or obtained by a crude approximation [25]. For a given δ , if too large a value of ν_{\min} is used, the low temperature extrapolated times may be incorrect with probability greater than δ . On the other hand, if the value of ν_{\min} is too small, then the extrapolated times will be correct with probability $1 - \delta$, but computational efficiency will be compromised. The usefulness of TAD comes from the fact that, in practice, ν_{\min} and δ can often be chosen such that the correct low temperature exit event is found by time T_{stop} with large probability $1 - \delta$, and T_{stop} is on average much smaller than the exit times which would be expected at low temperature. In practical applications, TAD has provided simulation timescale boosts of up to 10^9 [28].

Remark 2.3. One alternative to TAD is a brute force saddle point search method, in which one evolves the system at a high temperature β^{hi} to locate saddle points of V on ∂D . (There are other popular techniques in the literature to locate saddle points, many of which do not use high temperature or dynamics; see, for example, [21].) Once one is confident that all the physically relevant saddle points are found, the times \tilde{T}_i^{lo} to exit through each x_i at low temperature can be directly sampled from exponential distributions with parameters κ_i as in (2.2), using $\beta \equiv \beta^{lo}$. (Estimates are available for the ν_i at low temperature; they depend on the values of V and the Hessian matrix of V at x_i and x_0 . See, for example, [4].)

The advantage of TAD over a brute force saddle point search method is that in TAD, there is a well-defined stopping criterion for the saddle point search at temperature β^{hi} , in the sense that the saddle point corresponding to the correct exit event at temperature β^{lo} will be obtained with a user-specified probability. In particular, TAD does not require all the saddle points to be found. Moreover, TAD does not require the prefactors ν_1 to be estimated (only a lower bound is required).

2.2. Modified TAD. Below we consider some modifications, (M1)–(M3), to TAD, calling the result modified TAD. The main modifications, (M1)–(M2) below, will ensure that the exponential rates assumed in TAD are justified. We also introduce a different stopping time, (M3). (See the discussion that is below Algorithm 2.5.) We note that some of these features are currently being used by practitioners of TAD [35]. Here are the three modifications:

- (M1) We include a decorrelation step in which an underlying low temperature dynamics $(X_t^{lo})_{t \geq 0}$ finds local equilibrium in some basin D before we start searching for exit pathways at high temperature.

(M2) Before searching for exit pathways out of D , we sample local equilibrium at high temperature in the current basin D without advancing any clock time.

(M3) We replace the stopping time (2.8) with

$$(2.9) \quad T_{stop} = T_{\min}^{lo}/C,$$

where C is a lower bound of the minimum of $e^{-(\beta^{hi}-\beta^{lo})(V(x_i)-V(x_0))}$ over all the saddle points, x_i , of V on ∂D .

Remark 2.4. In (M3) above we are assuming some a priori knowledge of the system, in particular a lower bound of the energy barriers $V(x_i) - V(x_0)$, $i \in \{1, \dots, k\}$. Such a lower bound will not be known in every situation, but in some cases, practitioners can obtain such a bound; see, for example, [19]. See also the discussion “Stopping time” below.

The modified algorithm is as follows; for the reader’s convenience we have boxed off the steps of modified TAD which are different from TAD.

ALGORITHM 2.5 (Modified TAD). *Let X_0^{lo} be in the basin D , set a low temperature simulation clock T_{tad} to zero: $T_{tad} = 0$, and choose a (basin-dependent) decorrelation time $T_{corr} > 0$. Then iterate on the visited basins the following.*

Decorrelation step:

1. Starting at time $t = T_{tad}$, evolve X_t^{lo} at temperature $\beta = \beta^{lo}$ according to (1.1) in the current basin D .
2. If X_t^{lo} exits D at a time $T_{tad} + \tau < T_{tad} + T_{corr}$, then set

$$\hat{S}(t) = S(D), \quad t \in [T_{tad}, T_{tad} + \tau],$$

advance the low temperature clock by τ : $T_{tad} = T_{tad} + \tau$, and then go back to step 1, where D is now the new basin. Otherwise, set

$$\hat{S}(t) = S(D), \quad t \in [T_{tad}, T_{tad} + T_{corr}],$$

advance the low temperature clock by T_{corr} : $T_{tad} = T_{tad} + T_{corr}$, and initialize the exit step by setting $T_{sim} = 0$ and $T_{stop} = \infty$. Then proceed to the exit step.

Exit step:

1. Let $X_{T_{sim}}^{hi}$ be a sample of the dynamics (1.1) in local equilibrium in D at temperature $\beta = \beta^{hi}$. See the remarks below for how this sampling is done. None of the clocks are advanced in this step.
2. Evolve X_t^{hi} at $\beta = \beta^{hi}$ starting at $t = T_{sim}$ until the first time after T_{sim} at which it exits D . Call this time $T_{sim} + \tau$.
3. Using the nudged elastic band method, associate a nearby saddle point, x_i , of V on ∂D to the place where X_t^{hi} exited D .
4. Advance the simulation clock by τ : $T_{sim} = T_{sim} + \tau$.
5. If an exit at x_i has already been observed, go to step 8. If an exit at x_i has not yet been observed, set $T_i^{hi} = T_{sim}$ and

$$(2.10) \quad T_i^{lo} = T_i^{hi} e^{-(\beta^{hi}-\beta^{lo})(V(x_i)-V(x_0))}.$$

6. Update the lowest extrapolated exit time

$$T_{\min}^{lo} = \min\{T_{\min}^{lo}, T_i^{lo}\},$$

and the (index of) the corresponding exit point

$$I_{\min}^{lo} = i \quad \text{if} \quad T_{\min}^{lo} = T_i^{lo}.$$

7. Update T_{stop} :

$$(2.11) \quad T_{stop} = T_{\min}^{lo}/C,$$

where C is a lower bound of the minimum of $e^{-(\beta^{hi}-\beta^{lo})(V(x_i)-V(x_0))}$ over all the saddle points, x_i , of V on ∂D .

8. If $T_{sim} \leq T_{stop}$, go back to step 1 of the exit step; otherwise, proceed to step 9.

9. Set

$$\hat{S}(t) = S(D) \quad \text{for} \quad t \in [T_{tad}, T_{tad} + T_{\min}^{lo}]$$

and advance the low temperature simulation clock by T_{\min}^{lo} :

$$T_{tad} = T_{tad} + T_{\min}^{lo}.$$

10. Set $X_{T_{tad}}^{lo} = X_{T_I^{hi}}^{hi}$, where $I \equiv I_{\min}^{lo}$. Then go back to the decorrelation step, the domain D now being the neighboring basin, namely, the one obtained by exiting through $X_{T_I^{hi}}^{hi}$.

Below we comment in more detail on modified TAD.

• **Local equilibrium in D : (M1) and (M2).**

We introduce the decorrelation step—see (M1)—in order to ensure that the low temperature dynamics reaches local equilibrium in D . Indeed, for sufficiently large T_{corr} , the low temperature dynamics reaches local equilibrium in some basin. The convergence to local equilibrium will be made precise in section 3 using the notion of the QSD. See also [26, 15], in particular for a discussion of the choice of T_{corr} . Local equilibrium will in general be reached at different times in different basins, so we allow T_{corr} to be basin dependent. We note that a similar decorrelation step is used in another accelerated dynamics proposed by Voter, the parallel replica dynamics [34]. The decorrelation step accounts for barrier recrossing events: the dynamics is allowed to evolve exactly at low temperature after the exit step, capturing any possible barrier recrossings, until local equilibrium is reached in one of the basins.

The counterpart of the addition of this decorrelation step is that, from (M2), in the exit step we also start the high temperature dynamics from local equilibrium in the current basin D . A similar step is actually being used by current practitioners of TAD [35], though this step is not mentioned in the original algorithm [27]. To sample local equilibrium in D , one can, for example, take the end position of a sufficiently long trajectory of (1.1) which does not exit D . See [15, 26] for some algorithms to efficiently sample local equilibrium.

To extrapolate the exit event at low temperature from the exit events at high temperature, we need the dynamics at both temperatures to be in local equilibrium. We note that the changes (M1)–(M2) in modified TAD are actually a practical way to get rid of the error associated with the assumption (H1) in TAD.

- **Stopping time: (M3).**

In (M3) we introduce a stopping T_{stop} such that, with probability 1, the shortest extrapolated low temperature exit time is found by time T_{stop} . (Recall that with the stopping time of TAD, we have only a confidence level $1 - \delta$.) Note that for the stopping time T_{stop} to be implemented in (2.11), we need some a priori knowledge about energy barriers, in particular a lower bound $E_{min} > 0$ for all the differences $V(x_i) - V(x_0)$, where x_i ranges over the saddle points on the boundary of a given basin:

(H3') There is a minimum, E_{min} , to all the energy barriers:

$$\forall i \in \{1, \dots, k\}, V(x_i) - V(x_0) \geq E_{min}.$$

If a lower bound E_{min} is known, then we can choose C accordingly so that in (2.11) we obtain

$$(2.12) \quad T_{stop} = T_{min}^{lo} e^{(\beta^{hi} - \beta^{lo}) E_{min}}.$$

A simple computation then shows that under assumption (H3'), any high temperature exit time occurring after T_{stop} cannot extrapolate to a low temperature exit time smaller than T_{min}^{lo} . To see that (2.12) leads to an efficient algorithm, recall that TAD is expected to be correct only in the regime where $\beta^{hi} \gg E_{min}$, which, since $\beta^{hi} \ll \beta^{lo}$, means the exponential in (2.12) should be very small.

As the computational savings of TAD comes from the fact that the simulation time of the exit step, namely, T_{stop} , is much smaller than the exit time that would have been observed at low temperature, the choice of stopping time in TAD is of critical importance. Both of the stopping times (2.8) and (2.9) are used in practice; see [19] for a presentation of TAD with the stopping formula (2.9), and [20] for an application. The original stopping time (2.8) requires a lower bound for the prefactors in the Arrhenius law (2.4). (See assumption (H3) above, in the remarks following Algorithm 2.1.) The stopping time (2.9) requires an assumption on the minimum energy barriers; see assumption (H3') above. The formula (2.9) may be preferable in the case that minimum energy barriers are known, since it is known to scale better with system size than (2.8). The formula (2.8) is advantageous if minimum energy barriers are unknown but a reasonable lower bound for the minimum prefactor ν_{min} is available.

We have chosen the stopping time (2.9) instead of (2.8) mostly for mathematical convenience—in particular so that in our section 3 analysis we do not have the error δ associated with (2.8). A similar analysis can be done under assumption (H3) with the stopping time (2.8), modulo the error δ .

We comment that modified TAD is an algorithm which can be implemented in practice and which circumvents the error in the original TAD arising from the assumption (H1).

3. Idealized TAD and mathematical analysis. In this section, we show that under certain idealizing assumptions, namely, (I1)–(I3) and (A1) below, modified TAD is *exact* in the sense that the simulated metastable dynamics $\hat{S}(t)_{t \geq 0}$ has the same law as the true low temperature metastable dynamics $S(X_t^{lo})_{t \geq 0}$. We call this idealization of modified TAD *idealized TAD*. Our analysis will show that idealized TAD and modified TAD agree in the limit $\beta^{hi}, \beta^{lo} \rightarrow \infty$ and $T_{corr} \rightarrow \infty$. Since

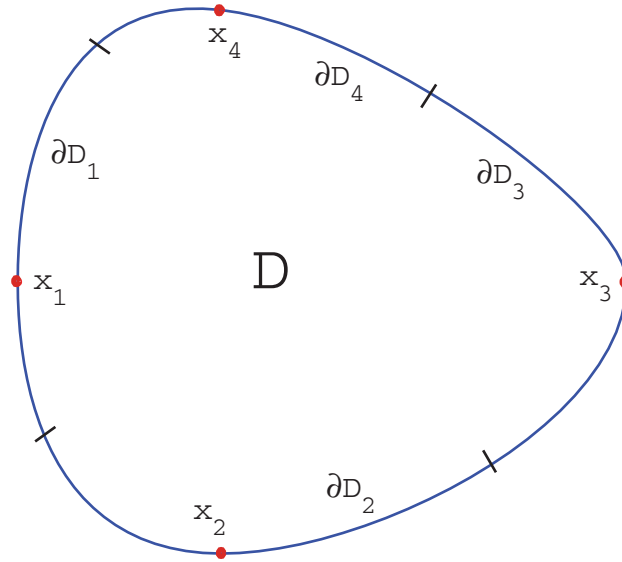


FIG. 1. The domain D with boundary partitioned into $\partial D_1, \dots, \partial D_4$ (here $k = 4$) by the black line segments. V has exactly one saddle point in each ∂D_i , located at x_i .

idealized TAD is exact, it follows that modified TAD is exact in the limit $\beta^{hi}, \beta^{lo} \rightarrow \infty$ and $T_{corr} \rightarrow \infty$.

In idealized TAD, we assume that at the end of the decorrelation step and at the start of the exit step of modified TAD, we are in *exact* local equilibrium; see (A1) and (I1). We formalize this using the notion of QSDs, defined below. We also assume that the way in which we exit near a given saddle point x_i in the exit step does not affect the metastable dynamics in the decorrelation step; see (I2). The remaining idealization, whose relation to modified TAD is maybe not so clear at first sight, is to replace the exponential $\exp[-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))]$ of (2.1) with a certain quantity Θ_i depending on the flux of the QSD across ∂D ; see (I3). In section 4, we justify this by showing that the two agree asymptotically as $\beta^{hi}, \beta^{lo} \rightarrow \infty$ in a one-dimensional setting.

3.1. Notation and QSD. Here and throughout, D is an (open) domain with C^2 boundary ∂D and X_t^x is a stochastic process evolving according to (1.1) starting at $X_0^x = x$. (We suppress the superscript where it is not needed.) We write $\mathbb{P}(\cdot)$ and $\mathbb{E}[\cdot]$ for various probabilities and expectations, the meaning of which will be clear from context. We write $Y \sim \mu$ for a random variable sampled from the probability measure μ and $Y \sim \mathcal{E}(\alpha)$ for an exponentially distributed random variable with parameter α .

Recalling the notation of section 2, we assume that ∂D is partitioned into k (Lebesgue measurable) subsets ∂D_i containing the saddle points x_i of V , $i = 1, \dots, k$ (see Figure 1):

$$\partial D = \cup_{i=1}^k \partial D_i \quad \text{and} \quad \partial D_i \cap \partial D_j = \emptyset \text{ if } i \neq j.$$

We assume that any exit through ∂D_i is associated to the saddle point x_i in step 3 of TAD. In other words, ∂D_i corresponds to the basin of attraction of the saddle point x_i for the nudged elastic band method.

Essential to the analysis below will be the notion of QSD, which we define below, recalling some facts which will be needed in our analysis. Consider the infinitesimal generator of (1.1),

$$L = -\nabla V \cdot \nabla + \beta^{-1} \Delta,$$

and let $(u, -\lambda)$ be the principal eigenvector/eigenvalue pair for L with homogeneous Dirichlet (absorbing) boundary conditions on ∂D :

$$(3.1) \quad \begin{cases} Lu = -\lambda u \text{ in } D, \\ u = 0 \text{ on } \partial D. \end{cases}$$

It is known (see [15]) that u is signed and $\lambda > 0$; we choose $u > 0$ and for the moment do not specify a normalization. Define a probability measure ν on D by

$$(3.2) \quad d\nu = \frac{u(x)e^{-\beta V(x)} dx}{\int_D u(x)e^{-\beta V(x)} dx}.$$

The measure ν is called the QSD on D ; the name comes from the fact that ν has the following property: for $(X_t)_{t \geq 0}$ a solution to (1.1), starting from any distribution with support in D ,

$$(3.3) \quad \nu(A) = \lim_{t \rightarrow \infty} \mathbb{P}(X_t \in A \mid X_s \in D, 0 \leq s \leq t) \quad \text{for any measurable set } A \subset D.$$

The following is proved in [15] and will be essential for our results.

THEOREM 3.1. *Let X_t be a solution to (1.1) with $X_0 \sim \nu$, and let*

$$\tau = \inf\{t > 0 : X_t \notin D\}.$$

Then (i) $\tau \sim \mathcal{E}(\lambda)$ and (ii) τ and X_τ are independent.

We will also need the following formula from [15] for the exit point distribution.

THEOREM 3.2. *Let X_t and τ be as in Theorem 3.1, and let $\sigma_{\partial D}$ be Lebesgue measure on ∂D . The measure ρ on ∂D defined by*

$$(3.4) \quad d\rho = -\frac{\partial_n (u(x)e^{-\beta V(x)}) d\sigma_{\partial D}}{\beta \lambda \int_D u(x)e^{-\beta V(x)} dx}$$

is a probability measure, and for any measurable $A \subset \partial D$,

$$\mathbb{P}(X_\tau \in A) = \rho(A).$$

As a corollary of these two results we have the following, which will be central to our analysis.

COROLLARY 3.3. *Let X_t , τ , and ρ be as in Theorems 3.1–3.2, and define*

$$(3.5) \quad p_i = \rho(\partial D_i)$$

to be the exit probability through ∂D_i . Let I be the discrete random variable defined by the following: for $i = 1, \dots, k$,

$$I = i \text{ if and only if } X_\tau \in \partial D_i.$$

Then (i) $\tau \sim \mathcal{E}(\lambda)$, (ii) $\mathbb{P}(I = i) = p_i$, and (iii) τ and I are independent.

Throughout we omit the dependence of λ , ν , and ρ on the basin D ; it should be understood from context.

Remark 3.4. We assume that D has C^2 boundary so that standard elliptic regularity results and trace theorems give a meaning to the formula (3.4) used to define ρ in Theorem 3.2. For basins of attraction this assumption will not be satisfied, as the basins will have “corners.” This is actually a minor technical point. The probability measure ρ can be defined for any Lipschitz domain D using the following two steps. First, ρ can be defined in $H^{-1/2}(\partial\Omega)$ using the following definition (equivalent to (3.4)): for any $v \in H^{1/2}(\partial D)$

$$\langle v, d\rho \rangle = \frac{\int_D (-\beta^{-1} \nabla w \cdot \nabla u + \lambda w u) \exp(-\beta V)}{\lambda \int_D u \exp(-\beta V)},$$

where $w \in H^1(D)$ is any lifting of v ($w|_{\partial D} = v$). Second, it is easy to check that ρ actually defines a *nonnegative* distribution on ∂D , for example, by using as a lifting the solution to

$$\begin{cases} Lw = 0 \text{ in } D, \\ w = v \text{ on } \partial D, \end{cases}$$

since, by the maximum principle, $w \geq 0$, and then, $\langle v, d\rho \rangle = \frac{\int_D \lambda w u \exp(-\beta V)}{\lambda \int_D u \exp(-\beta V)}$. One finally concludes using a Riesz representation theorem due to Schwartz: any nonnegative distribution with total mass one defines a probability measure.

3.2. Idealized TAD. In this section we consider an idealized version of modified TAD, which we call idealized TAD. The idealizations, (I1)–(I3) below, are introduced so that the algorithm can be rigorously analyzed using the mathematical formalisms in section 3.1.

- (I1) At the start of the exit step, the high temperature dynamics is initially distributed according to the QSD in D : $X_{T_{sim}}^{hi} \sim \nu^{hi}$.
- (I2) At the end of the exit step, the extrapolated low temperature exit point $X_{T_{tad}}^{lo}$ is sampled exactly from the conditional exit point distribution in $\partial D_{I_{min}^{lo}}$ at low temperature:

$$(3.6) \quad X_{T_{tad}}^{lo} \sim \left[\rho^{lo} \left(\partial D_{I_{min}^{lo}} \right) \right]^{-1} \rho^{lo}|_{\partial D_{I_{min}^{lo}}}.$$

- (I3) In the exit step, the quantity

$$e^{-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))}$$

is everywhere replaced by

$$(3.7) \quad \Theta_i \equiv \frac{\lambda^{hi} p_i^{hi}}{\lambda^{lo} p_i^{lo}},$$

where, as in (3.5), $p_i^{lo} = \rho^{lo}(\partial D_i)$ and $p_i^{hi} = \rho^{hi}(\partial D_i)$. Thus, the extrapolation equation (2.1) is replaced by

$$(3.8) \quad T_i^{lo} = T_i^{hi} \Theta_i,$$

and the formula for updating T_{stop} is

$$(3.9) \quad T_{stop} = T_{min}^{lo} / C,$$

where C is chosen so that $C \leq \min_{1 \leq i \leq k} \Theta_i$.

We state idealized TAD below as an “algorithm,” even though it is not practical: in general we cannot exactly sample ν^{hi} or the exit distributions $[\rho^{lo}(\partial D_i^{lo})]^{-1}\rho^{lo}|_{\partial D_i^{lo}}$, and the quantities Θ_i are not known in practice. (See the discussion below Algorithm 3.5.)

For the reader’s convenience, we put in boxes those steps of idealized TAD which are different from modified TAD.

ALGORITHM 3.5 (Idealized TAD). *Let X_0^{lo} be in the basin D , and set the low temperature clock time to zero: $T_{tad} = 0$, let $T_{corr} > 0$ be a (basin-dependent) decorrelation time, and iterate the following on the visited basins.*

Decorrelation step:

1. *Starting at time $t = T_{tad}$, evolve X_t^{lo} at temperature $\beta = \beta^{lo}$ according to (1.1) in the current basin D .*
2. *If X_t^{lo} exits D at a time $T_{tad} + \tau < T_{tad} + T_{corr}$, then set*

$$\hat{S}(t) = S(D), \quad t \in [T_{tad}, T_{tad} + \tau],$$

advance the low temperature clock by τ : $T_{tad} = T_{tad} + \tau$, and then go back to step 1, where D is now the new basin. Otherwise, set

$$\hat{S}(t) = S(D), \quad t \in [T_{tad}, T_{tad} + T_{corr}],$$

advance the low temperature clock by T_{corr} : $T_{tad} = T_{tad} + T_{corr}$, and initialize the exit step by setting $T_{sim} = 0$ and $T_{stop} = \infty$. Then proceed to the exit step.

Exit step:

- | |
|---|
| <ol style="list-style-type: none"> 1. <i>Sample $X_{T_{sim}}^{hi}$ from the QSD at high temperature in D: $X_{T_{sim}}^{hi} \sim \nu^{hi}$.</i> 2. <i>Evolve X_t^{hi} at $\beta = \beta^{hi}$ starting at $t = T_{sim}$ until the first time after T_{sim} at which it exits D. Call this time $T_{sim} + \tau$.</i> 3. <i>Record the set ∂D_i through which X_t^{hi} exited D.</i> 4. <i>Advance the simulation clock by τ: $T_{sim} = T_{sim} + \tau$.</i> |
|---|

- | |
|---|
| <ol style="list-style-type: none"> 5. <i>If an exit through ∂D_i has already been observed, go to step 8. If an exit through ∂D_i has not yet been observed, set $T_i^{hi} = T_{sim}$ and</i> |
|---|

$$(3.10) \quad T_i^{lo} = T_i^{hi} \Theta_i, \quad \Theta_i \equiv \frac{\lambda^{hi} p_i^{hi}}{\lambda^{lo} p_i^{lo}}.$$

6. *Update the lowest extrapolated exit time and corresponding exit spot:*

$$T_{\min}^{lo} = \min\{T_{\min}^{lo}, T_i^{lo}\},$$

$$I_{\min}^{lo} = i \quad \text{if} \quad T_{\min}^{lo} = T_i^{lo}.$$

- | |
|---|
| <ol style="list-style-type: none"> 7. <i>Update T_{stop}:</i> |
|---|

$$(3.11) \quad T_{stop} = T_{\min}^{lo}/C, \quad C \leq \min_{1 \leq i \leq k} \Theta_i.$$

8. *If $T_{sim} \leq T_{stop}$, go back to step 1 of the exit step; otherwise, proceed to step 9.*

9. Set

$$\hat{S}(t) = S(D) \quad \text{for } t \in [T_{tad}, T_{tad} + T_{\min}^{lo}],$$

and advance the low temperature simulation clock by T_{\min}^{lo} :

$$T_{tad} = T_{tad} + T_{\min}^{lo}.$$

10. Let

$$X_{T_{tad}}^{lo} \sim \left[\rho^{lo} \left(\partial D_{I_{\min}^{lo}} \right) \right]^{-1} \rho^{lo} |_{\partial D_{I_{\min}^{lo}}}.$$

Then go back to the decorrelation step, the basin D now being the one obtained by exiting through $X_{T_{tad}}^{lo}$.

Below we comment in more detail on idealized TAD.

• **The QSD in D : (I1) and (A1).**

In idealized TAD, the convergence to local equilibrium (see (M1) and (M2) above) is assumed to be reached, and this is made precise using the QSD ν . In particular, we start the high temperature exit search exactly at the QSD ν^{hi} ; see (I1). We will also assume that the low temperature dynamics reaches ν^{lo} at the end of the decorrelation step:

(A1) After the decorrelation step of idealized TAD, the low temperature dynamics is distributed according to the QSD in D : $X_{T_{tad}}^{lo} \sim \nu^{lo}$.

This will be crucial for extrapolating the exit event at low temperature. Assumption (A1) is justified by the fact that the law of X_t^{lo} in the decorrelation step approaches ν^{lo} exponentially fast in T_{corr} ; see [15, 26] for details. We also refer to [15, 26] for a presentation of algorithms which can be used to sample the QSD.

• **The exit position: (I2).**

To get exact metastable dynamics, we have to assume that the way the dynamics leaves D near a given saddle point x_i does not affect the metastable dynamics in the decorrelation step; see (I2). This can be justified in the small temperature regime by using Theorem 3.2 and some exponential decay results on the normal derivative of the QSD away from saddle points. Indeed, the conditional probability that, given that the dynamics leaves through ∂D_i , it leaves outside a neighborhood of x_i is of order $e^{-c\beta}$ as $\beta \rightarrow \infty$ (for a constant $c > 0$); see [13, 16].

• **Replacing the Arrhenius law extrapolation rule: (I3).**

In idealized TAD, we replace the extrapolation formula (2.1) based on the Arrhenius law by the idealized formulas (3.7)–(3.8); see (I3). This is a severe modification, since it makes the algorithm impractical. In particular the quantities λ^{lo} and p_i^{lo} are not known: if they were, it would be very easy to simulate the exit event from D ; see Corollary 3.3 above.

It is the aim of section 4 below to explain how the small temperature assumption is used to get practical estimates of the ratios Θ_i . For simplicity, we perform this small temperature analysis in one dimension. We will show that Θ_i is indeed close to the formula $\exp[-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))]$ used in the original and modified TAD; compare (3.10) with (2.1) and (2.10). We expect the same relation to be true in higher dimensions under appropriate conditions; this will be the subject of another paper.

In the analysis below, we need idealizations (I1) and (I3) to exactly replicate the law of the low temperature exit time and exit region in the exit step; see Theorem 3.7 below. With (I1) and (I3), the inferred low temperature exit events are statistically exact. This is based in particular on (A1), namely, the fact that the low temperature process is distributed according to ν^{lo} at the end of the decorrelation step. In addition, after an exit event, the dynamics in the next decorrelation step depends on the exact exit *point* in ∂D_i : this is why we also need (I2) to get exact metastable dynamics; see Theorem 3.6 below.

3.3. Idealized TAD is exact. The aim of this section is to prove the following result.

THEOREM 3.6. *Let X_t^{lo} evolve according to (1.1) at $\beta = \beta^{lo}$. Let $\hat{S}(t)$ be the metastable dynamics produced by Algorithm 3.5 (idealized TAD), assuming (A1), and let idealized TAD have the same initial condition as X_t^{lo} . Then*

$$\hat{S}(t)_{t \geq 0} \sim S(X_t^{lo})_{t \geq 0},$$

that is, the metastable dynamics produced by idealized TAD has the same law as the (exact) low temperature metastable dynamics.

Due to Corollary 3.3, (A1), (I2), and the fact that the low temperature dynamics is simulated exactly during the decorrelation step, it suffices to prove that the exit step of idealized TAD is exact in the following sense.

THEOREM 3.7. *Let X_t^{lo} evolve according to (1.1) at $\beta = \beta^{lo}$ with X_t^{lo} initially distributed according to the QSD in D : $X_0^{lo} \sim \nu^{lo}$. Let $\tau = \inf\{t > 0 : X_t^{lo} \notin D\}$ and I be the discrete random variable defined by the following: for $i = 1, \dots, k$,*

$$I = i \text{ if and only if } X_\tau^{lo} \in \partial D_i.$$

Let T_{\min}^{lo} and I_{\min}^{lo} be the random variables produced by the exit step of idealized TAD. Then, $(T_{\min}^{lo}, I_{\min}^{lo})$ has the same probability law as (τ, I) :

$$(T_{\min}^{lo}, I_{\min}^{lo}) \sim (\tau, I).$$

The proof of Theorem 3.7 will use (I1) and (I3) in particular. The theorem shows that the exit event from D produced by idealized TAD is exact in law compared to the exit event that would have occurred at low temperature: the random variable $(T_{\min}^{lo}, I_{\min}^{lo})$ associated with idealized TAD has the same law as the first exit time and location (from D) of a dynamics $(X_t^{lo})_{t \geq 0}$ obeying (1.1) with $\beta = \beta^{lo}$ and $X_0^{lo} \sim \nu^{lo}$.

To begin, we provide a simple lemma which shows that we can assume $T_{stop} \equiv \infty$ without loss of generality. We need this result in order to properly define all the random variables T_i^{hi} for $i = 1, \dots, k$, where we recall that k denotes the number of saddle points of V on ∂D .

LEMMA 3.8. *Consider the exit step of the idealized TAD and modify step 8 as follows:*

8. Go back to step 1 of the exit step.

This we loop between step 1 and step 8 of the exit step for infinite time, regardless of the values of T_{sim} and T_{stop} . Then $(T_{\min}^{lo}, I_{\min}^{lo})$ remains constant for all times $T_{sim} > T_{stop}$.

Proof. We want to show that without ever advancing to step 10, the exit step of idealized TAD produces the same random variable $(T_{\min}^{lo}, I_{\min}^{lo})$ as soon as $T_{sim} > T_{stop}$. To see this, note that if $T_i^{lo} < T_{\min}^{lo}$, then from (3.10),

$$T_i^{lo} = T_i^{hi} \frac{\lambda^{hi} p_i^{hi}}{\lambda^{lo} p_i^{lo}} < T_{\min}^{lo},$$

and so, comparing with (3.11),

$$T_i^{hi} < T_{\min}^{lo} \frac{\lambda^{lo} p_i^{lo}}{\lambda^{hi} p_i^{hi}} \leq \frac{T_{\min}^{lo}}{C} = T_{stop}.$$

Thus, if $T_{sim} > T_{stop}$, any escape event will lead to an extrapolated time T_i^{lo} which will be larger than T_{\min}^{lo} , and thus will not change the value of T_{\min}^{lo} anymore. \square

Let us now identify the laws of the random variables $(T_i^{hi})_{1 \leq i \leq l}$ produced by idealized TAD.

PROPOSITION 3.9. *Consider idealized TAD in the setting of Lemma 3.8, so that all the T_i^{hi} are defined, $i = 1, 2, \dots, k$.*

Let $(\tau^{(j)}, I^{(j)})_{j \geq 1}$ be independent and identically distributed random variables such that $\tau^{(j)}$ is independent from $I^{(j)}$, $\tau^{(j)} \sim \mathcal{E}(\lambda^{hi})$ and for $i = 1, \dots, k$, $I^{(j)}$ is a discrete random variable with law

$$\mathbb{P}(I^{(j)} = i) = p_i^{hi}.$$

For $i = 1, \dots, k$, define

$$(3.12) \quad N_i^{hi} = \min\{j : I^{(j)} = i\}.$$

Then we have the following equality in law:

$$(3.13) \quad (T_1^{hi}, \dots, T_k^{hi}) \sim \left(\sum_{j=1}^{N_1^{hi}} \tau^{(j)}, \dots, \sum_{j=1}^{N_k^{hi}} \tau^{(j)} \right).$$

Moreover, (i) $T_i^{hi} \sim \mathcal{E}(\lambda^{hi} p_i^{hi})$ and (ii) $T_1^{hi}, T_2^{hi}, \dots, T_k^{hi}$ are independent.

Proof. The equality (3.13) follows from Corollary 3.3, since in the exit step of idealized TAD, the dynamics restarts from the QSD ν^{hi} after each escape event.

Let us now consider the statement (i). Observe that the moment generating function of an exponential random variable τ with parameter λ is the following: for $s < \lambda$,

$$\mathbb{E}[\exp(s\tau)] = \int_0^\infty e^{st} \lambda e^{-\lambda t} dt = \frac{\lambda}{\lambda - s}.$$

So, dropping the superscript hi for ease of notation, we have the following: for $i \in \{1, \dots, k\}$ and for $s < \lambda p_i$,

$$\begin{aligned} \mathbb{E}[\exp(sT_i)] &= \sum_{m=1}^\infty \mathbb{E}[\exp(sT_i) \mid N_i = m] \mathbb{P}(N_i = m) \\ &= \sum_{m=1}^\infty \mathbb{E} \left[\exp \left(s \sum_{j=1}^m \tau^{(j)} \right) \right] (1 - p_i)^{m-1} p_i \\ &= \sum_{m=1}^\infty \mathbb{E} \left[\exp \left(s\tau^{(1)} \right) \right]^m (1 - p_i)^{m-1} p_i \\ &= \frac{\lambda p_i}{\lambda - s} \sum_{m=1}^\infty \left(\frac{\lambda(1 - p_i)}{\lambda - s} \right)^{m-1} \\ &= \frac{\lambda p_i}{\lambda p_i - s}. \end{aligned}$$

This shows $T_i^{hi} \sim \mathcal{E}(\lambda^{hi} p_i^{hi})$. \square

Before turning to the proof of the statement (ii) in Proposition 3.9, we need the following technical lemma.

LEMMA 3.10. *Let a_1, a_2, \dots, a_n be positive real numbers, and let S_n be the symmetric group on $\{1, 2, \dots, n\}$. Then*

$$(3.14) \quad \sum_{\sigma \in S_n} \prod_{i=1}^n \left(\sum_{j=i}^n a_{\sigma(j)} \right)^{-1} = \prod_{i=1}^n a_i^{-1}.$$

Proof. Note that (3.14) is of course true for $n = 1$. Assume it is true for $n - 1$, and let

$$S_n^{(k)} = \{\sigma \in S_n : \sigma(1) = k\}.$$

Then

$$\begin{aligned} \sum_{\sigma \in S_n} \prod_{i=1}^n \left(\sum_{j=i}^n a_{\sigma(j)} \right)^{-1} &= \left(\sum_{i=1}^n a_i \right)^{-1} \sum_{\sigma \in S_n} \prod_{i=2}^n \left(\sum_{j=i}^n a_{\sigma(j)} \right)^{-1} \\ &= \left(\sum_{i=1}^n a_i \right)^{-1} \sum_{k=1}^n \sum_{\sigma \in S_n^{(k)}} \prod_{i=2}^n \left(\sum_{j=i}^n a_{\sigma(j)} \right)^{-1} \\ &= \left(\sum_{i=1}^n a_i \right)^{-1} \sum_{k=1}^n \prod_{\substack{j=1 \\ j \neq k}}^n a_j^{-1} \\ &= \prod_{i=1}^n a_i^{-1}. \end{aligned}$$

By induction, (3.14) is valid for all n . \square

We are now in position to prove statement (ii) of Proposition 3.9.

Proof of Proposition 3.9 part (ii). In this proof, we drop the superscript hi for ease of notation. To show that the T_i 's are independent, it suffices to show that for s_1, \dots, s_k in a neighborhood of zero we have

$$(3.15) \quad \mathbb{E} \left[\exp \left(\sum_{i=1}^k s_i T_i \right) \right] = \prod_{i=1}^k \mathbb{E} [\exp (s_i T_i)].$$

We saw in the proof of part (i) that, for $s_i < \lambda p_i$,

$$(3.16) \quad \mathbb{E} [\exp (s_i T_i)] = \frac{\lambda p_i}{\lambda p_i - s_i}.$$

Consider then the left-hand side of (3.15). We start by a preliminary computation. Let $m_0 = 0$, $m_1 = 1$, and $s_i < \lambda p_i$ for $i = 1, \dots, k$. Then

$$\begin{aligned} &\sum_{1 < m_2 < m_3 \dots < m_k} \mathbb{E} \left[\exp \left(\sum_{i=1}^k s_i T_i \right) \mid \cap_{i=1}^k \{N_i = m_i\} \right] \mathbb{P} (\cap_{i=1}^k \{N_i = m_i\}) \\ &= \sum_{1 < m_2 < m_3 \dots < m_k} \mathbb{E} \left[\exp \left(\sum_{i=1}^k \left(s_i \sum_{j=1}^{m_i} \tau^{(j)} \right) \right) \right] p_1 \prod_{i=2}^k p_i \left(1 - \sum_{j=i}^k p_j \right)^{m_i - m_{i-1} - 1} \end{aligned}$$

$$\begin{aligned}
 &= p_1 \sum_{1 < m_2 < m_3 \dots < m_k} \prod_{i=1}^k \mathbb{E} \left[\exp \left(\left(\sum_{j=i}^k s_j \right) \sum_{j=m_{i-1}+1}^{m_i} \tau^{(j)} \right) \right] \\
 &\quad \times \prod_{i=2}^k p_i \left(1 - \sum_{j=i}^k p_j \right)^{m_i - m_{i-1} - 1} \\
 &= p_1 \sum_{1 < m_2 < m_3 \dots < m_k} \prod_{i=1}^k \mathbb{E} \left[\exp \left(\tau^{(1)} \sum_{j=i}^k s_j \right) \right]^{m_i - m_{i-1}} \\
 &\quad \times \prod_{i=2}^k p_i \left(1 - \sum_{j=i}^k p_j \right)^{m_i - m_{i-1} - 1} \\
 &= \left(\frac{\lambda p_1}{\lambda - \sum_{j=1}^k s_j} \right) \sum_{1 < m_2 < m_3 \dots < m_k} \prod_{i=2}^k p_i \left(\frac{\lambda}{\lambda - \sum_{j=i}^k s_j} \right) \\
 &\quad \times \left(\frac{\lambda \left(1 - \sum_{j=i}^k p_j \right)}{\lambda - \sum_{j=i}^k s_j} \right)^{m_i - m_{i-1} - 1} \\
 &= \left(\frac{\lambda p_1}{\lambda - \sum_{j=1}^k s_j} \right) \prod_{i=2}^k p_i \left(\frac{\lambda}{\lambda - \sum_{j=i}^k s_j} \right) \left(1 - \frac{\lambda \left(1 - \sum_{j=i}^k p_j \right)}{\lambda - \sum_{j=i}^k s_j} \right)^{-1} \\
 &= \left(\frac{\lambda p_1}{\lambda - \sum_{j=1}^k s_j} \right) \prod_{i=2}^k \lambda p_i \left(\sum_{j=i}^k \lambda p_j - s_j \right)^{-1} \\
 &= \prod_{i=1}^k \lambda p_i \left(\sum_{j=i}^k \lambda p_j - s_j \right)^{-1}.
 \end{aligned}
 \tag{3.17}$$

From (3.17) observe that

$$\begin{aligned}
 \mathbb{E} \left[\exp \left(\sum_{i=1}^k s_i T_i \right) \right] &= \sum_{\sigma \in S_k} \prod_{i=1}^k \lambda p_{\sigma(i)} \left(\sum_{j=i}^k \lambda p_{\sigma(j)} - s_{\sigma(j)} \right)^{-1} \\
 &= \left(\prod_{i=1}^k \lambda p_i \right) \sum_{\sigma \in S_k} \prod_{i=1}^k \left(\sum_{j=i}^k \lambda p_{\sigma(j)} - s_{\sigma(j)} \right)^{-1} \\
 &= \prod_{i=1}^k \frac{\lambda p_i}{\lambda p_i - s_i},
 \end{aligned}
 \tag{3.18}$$

where in the last step we have used Lemma 3.10. Comparing (3.15) with (3.16) and (3.18), we are done. \square

To complete the proof of Theorem 3.7, we finally need the following Lemma.

LEMMA 3.11. *Let T_1, \dots, T_k be independent random variables such that $T_i \sim \mathcal{E}(\lambda p_i)$ with $\lambda > 0$, $p_i > 0$, and $\sum_{j=1}^k p_j = 1$. Set*

$$T = \min_i T_i \quad \text{and} \quad I = \arg \min_i T_i.$$

Then (i) $T \sim \mathcal{E}(\lambda)$, (ii) $\mathbb{P}(I = i) = p_i$, and (iii) T and I are independent.

Proof. Since the T_i 's are assumed to be independent, it is well known that $T = T_I = \min_i T_i$ is an exponential random variable with parameter $\sum_i \lambda p_i = \lambda$. This proves (i). Turning to (ii) and (iii), note that $\min_{j \neq i} T_j$ is an exponential random variable independent of T_i with parameter

$$\sum_{j \neq i} \lambda p_j = \lambda(1 - p_i).$$

Thus,

$$\begin{aligned} \mathbb{P}(I = i, T_I \geq t) &= \mathbb{P}(t \leq T_i \leq \min_{j \neq i} T_j) \\ (3.19) \quad &= \int_t^\infty \int_s^\infty \lambda p_i e^{-\lambda p_i s} \lambda(1 - p_i) e^{-\lambda(1-p_i)r} dr ds \\ &= \int_t^\infty \lambda p_i e^{-\lambda s} ds \\ &= p_i \mathbb{P}(T_I \geq t). \end{aligned}$$

Setting $t = 0$ we obtain $\mathbb{P}(I = i) = p_i$, which proves (ii). Now (iii) follows from (3.19). \square

We are now in position to prove Theorem 3.7.

Proof of Theorem 3.7. First, by Lemma 3.8, we can assume that $T_{stop} = \infty$ so that all the T_i^{hi} 's are well defined for $i = 1, \dots, k$. Then Proposition 3.9 implies that the T_i^{hi} 's are independent exponential random variables with parameters $\lambda^i p_i^{hi}$. So by (3.10), the T_i^{lo} 's are independent exponential random variables with parameters $\lambda^{lo} p_i^{lo}$. Now by applying Lemma 3.11 to the T_i^{lo} 's, we get $T_{\min}^{lo} \sim \mathcal{E}(\lambda^{lo})$, $\mathbb{P}(I_{\min}^{lo} = i) = p_i^{lo}$, and T_{\min}^{lo} is independent of I_{\min}^{lo} . Referring to Corollary 3.3, we are done. \square

Remark 3.12. Observe that the proof of Theorem 3.7 does not use (I2), which is needed only to obtain correct metastable dynamics by iterating the exit step. Also, notice that we did not use the fact that D is the basin of attraction of a local minimum of V or that each set ∂D_i in the partition of ∂D is associated to a saddle point x_i for the moment. The latter assumption is crucial in the next section, in which we obtain computable estimates of the ratios Θ_i , $i = 1, \dots, k$; this will also require an assumption of large β which was not needed for Theorem 3.7.

4. Estimates for the Θ_i 's at low temperature in one dimension. In the last section we showed that modified TAD (Algorithm 2.5) is *exact* with the idealizations (II)–(I3) and the assumption (A1); see idealized TAD (Algorithm 3.5). In this section we justify (I3). In particular, we show in Theorem 4.1 below how the ratios Θ_i (see (3.7)) can be approximated by explicit practical formulas in one dimension. Compared to Theorem 3.7, the proof of Theorem 4.1 will require the additional assumption that temperature is sufficiently small.

4.1. Statement of the main result. We recall that the ratios Θ_i , $i = 1, \dots, k$ are unknown in practice. In TAD these ratios are approximated using the Arrhenius

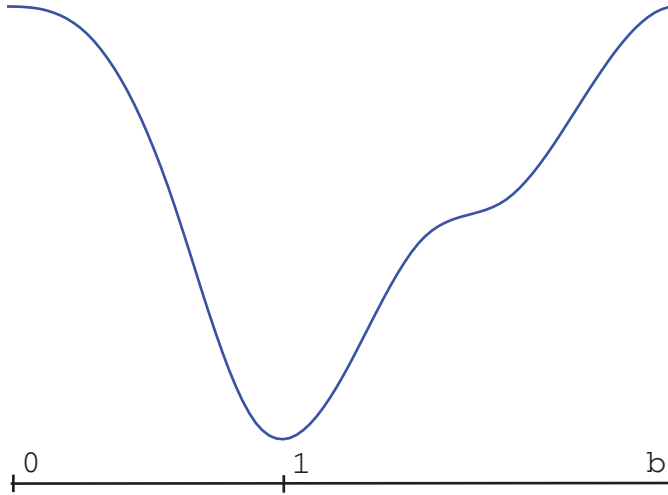


FIG. 2. A function $V : D \rightarrow \mathbb{R}$ satisfying (B1)–(B3).

law. The main result of this section, Theorem 4.1, gives precise asymptotics for Θ_i as $\beta^{hi}, \beta^{lo} \rightarrow \infty$. In particular, we show that Θ_i converges to $\exp[-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))]$.

Throughout this section we assume that we are *in a one-dimensional setting*. Moreover, we assume that D is the basin of attraction of the gradient dynamics $dy/dt = -V'(y)$ associated to a local minimum of V . (This is what is done in practice by Voter and co-workers.) Finally, the potential V is assumed to be a Morse function, which means that the critical points of V are nondegenerate. Under these assumptions, we may assume without additional loss of generality that (see Figure 2)

- (B1) $D = (0, b)$ with $b > 1$, $V(0) = 0$, and $V'(x) \neq 0$ for $x \notin \{0, 1, b\}$,
- (B2) $V'(0) = 0 = V'(b)$ and $V''(0) < 0$, $V''(b) < 0$,
- (B3) $V'(1) = 0$ and $V''(1) > 0$.

We also normalize u (see (3.1)) so that

- (B4) $u(1) = 1$.

In particular, the location of the minimum of V and the value of V at 0 are chosen for notational convenience and without loss of generality. In the following, we write $\{0\} = \partial D_1$ and $\{b\} = \partial D_2$.

We will prove the following.

THEOREM 4.1. *Under the assumptions stated above, we have the following formula: for $i = 1, 2$,*

$$(4.1) \quad \Theta_i = \frac{\lambda^{hi} p_i^{hi}}{\lambda^{lo} p_i^{lo}} = e^{-(\beta^{hi} - \beta^{lo})(V(x_i) - V(x_0))} \left(1 + O\left(\frac{1}{\beta^{hi}} - \frac{1}{\beta^{lo}}\right) \right)$$

as $\beta^{hi}, \beta^{lo} \rightarrow \infty$, $\beta^{lo}/\beta^{hi} = r$, where $x_1 = 0$, $x_2 = b$, and $x_0 = 1$, and $r > 0$ is constant.

The ratios $\frac{\lambda^{hi} p_i^{hi}}{\lambda^{lo} p_i^{lo}}$ involve integrals of the form $\int_D e^{-\beta V(x)} u(x) dx$ at high and low temperature. We will use Laplace expansions to analyze the integrals, but since u depends on β , extra care must be taken in the analysis.

4.2. Proof of Theorem 4.1. In all of what follows, $(u, -\lambda)$ denotes the principal eigenvector/eigenvalue pair of L with homogeneous Dirichlet boundary conditions;

see (3.1). We are interested in how the pair $(u, -\lambda)$ varies in the small temperature regime $\beta \rightarrow \infty$.

Throughout this section, we write c to denote a *positive* constant, the value of which may change without being explicitly noted. To begin, we will need some asymptotics for λ and u ; see Lemmas 4.2 and 4.3 below. The contents of both lemmas are found in or implied by [6], [9], and [10] (see also [8] and [7]) in the case where $V' \cdot n > 0$ on ∂D with n the normal to ∂D . (In our setting $n = 1$ on ∂D_2 and $n = -1$ on ∂D_1 .) Here, we consider the case of *characteristic boundary*, where from (B2) $V' \cdot n = 0$ on ∂D , so we adapt the classical results to this case.

LEMMA 4.2. *There exists $c > 0$ such that*

$$(4.2) \quad \lambda = O(e^{-c\beta}) \quad \text{as } \beta \rightarrow \infty.$$

Proof. Let $D' \subset D$ be a domain containing 1 such that $\overline{D'} \subset D$, and let $(u', -\lambda')$ be the principal eigenvector/eigenvalue pair for L on D' with homogeneous Dirichlet boundary conditions on $\partial D'$. Recall that λ is given by the Rayleigh formula

$$\lambda = \inf_{f \in H_V^1(D)} \frac{\beta^{-1} \int_D |\nabla f(x)|^2 e^{-\beta V(x)} dx}{\int_D f(x)^2 e^{-\beta V(x)} dx},$$

where $H_V^1(D)$ is the space of functions vanishing on $\mathbb{R} \setminus D$ such that

$$\int_D (|\nabla f(x)|^2 + f(x)^2) e^{-\beta V(x)} dx < \infty,$$

and similarly for λ' . Since every function vanishing on $\mathbb{R} \setminus D'$ also vanishes on $\mathbb{R} \setminus D$, we have

$$(4.3) \quad \lambda \leq \lambda'.$$

Now let X_t^1 obey (1.1) with $X_0^1 = 1$, and define $\tau' = \inf\{t > 0 : X_t^1 \notin D'\}$. Since D' is a subbasin of attraction such that V' points outward on $\partial D'$, we can use the following classical results (see, e.g., Lemmas 3–4 of [6]):

$$(4.4) \quad \lim_{\beta \rightarrow \infty} \beta^{-1} \log \mathbb{E}[1/\lambda'] = \lim_{\beta \rightarrow \infty} \beta^{-1} \log \mathbb{E}[\tau'] = \inf_{z \in \partial D'} \inf_{t > 0} I_{z,t},$$

where, by definition,

$$I_{z,t} = \inf_{f \in H_1^z[0,t]} \frac{1}{4} \int_0^t |\dot{f}(s) + V'(f(s))|^2 ds,$$

$$H_1^z[0,t] = \left\{ f : \exists \dot{f} \in L^2[0,t] \text{ s.t. } f(t) = z, \text{ and } \forall s \in [0,t], f(s) = 1 + \int_0^s \dot{f}(r) dr \right\}.$$

Observe that for any $t > 0$ and $f \in H_1^z[0,t]$, we have

$$\begin{aligned} & \frac{1}{4} \int_0^t \left| \dot{f}(s) + V'(f(s)) \right|^2 ds \\ &= \frac{1}{4} \int_0^t \left| \dot{f}(s) - V'(f(s)) \right|^2 ds + \int_0^t \dot{f}(s) V'(f(s)) ds \\ &\geq V(z) - V(1). \end{aligned}$$

Since $\partial D'$ is disjoint from 1, we can conclude that for $z \in \partial D'$, $I_{z,t} \geq c > 0$ uniformly in $t > 0$ for a positive constant c . Thus,

$$\lim_{\beta \rightarrow \infty} \beta^{-1} \log \mathbb{E}[\tau'] \geq c > 0,$$

which, combined with (4.3) and (4.4), implies the result. \square

Next we need the following regularity result for u .

LEMMA 4.3. *The function u is uniformly bounded in β , that is,*

$$(4.5) \quad \|u\|_\infty = O(1) \quad \text{as } \beta \rightarrow \infty,$$

where $\|\cdot\|_\infty$ is the L^∞ norm on $C[0, b]$.

Proof. Define $f(t, x) = u(x)e^{\lambda t}$ and set

$$\tau^x = \inf\{t > 0 : X_t^x \notin (0, 1)\},$$

where X_t^x obeys (1.1) with $X_0^x = x$. Fix $T > 0$. By Itô's lemma, for $t \in [0, T \wedge \tau^x]$ we have

$$\begin{aligned} f(t, X_t^x) &= u(x) + \lambda \int_0^t u(X_s^x) e^{\lambda s} ds + \int_0^t Lu(X_s^x) e^{\lambda s} ds + \sqrt{2\beta^{-1}} \int_0^t u'(X_s^x) dW_s \\ &= u(x) + \sqrt{2\beta^{-1}} \int_0^t u'(X_s^x) dW_s. \end{aligned}$$

Setting $t = T \wedge \tau^x$ and taking expectations gives

$$(4.6) \quad u(x) = \mathbb{E}[f(T \wedge \tau^x, X_{T \wedge \tau^x}^x)] = \mathbb{E}\left[e^{\lambda T \wedge \tau^x} u(X_{T \wedge \tau^x}^x)\right].$$

Recall that u is bounded for fixed β . We show in (4.11) below that $\mathbb{E}[e^{\lambda \tau^x}]$ is finite, so we may let $T \rightarrow \infty$ in (4.6) and use the dominated convergence theorem to obtain

$$(4.7) \quad u(x) = \mathbb{E}\left[e^{\lambda \tau^x} u(X_{\tau^x}^x)\right] \leq \mathbb{E}\left[e^{\lambda \tau^x}\right],$$

where we have recalled $u(0) = 0$ and, from (B4), $u(1) = 1$. The idea is then to compare τ^x to the first hitting time of 1 of a Brownian motion reflected at zero. Define

$$\sigma^x = \inf\{t > 0 : B_t^x \notin (-1, 1)\},$$

where

$$B_t^x = x + \sqrt{2\beta^{-1}}W_t$$

with W_t^x as in (1.1). Let \bar{B}_t^x and \bar{X}_t^x be given by reflecting B_t^x and X_t^x at zero. Since $V' < 0$ on $(0, 1)$, it is clear that $\bar{X}_t^x \geq \bar{B}_t^x$ for each $x \in (0, 1)$ and $t \geq 0$. Thus,

$$(4.8) \quad \begin{aligned} \mathbb{P}(\tau^x \geq t) &\leq \mathbb{P}(\inf\{s > 0 : \bar{X}_s^x = 1\} \geq t) \\ &\leq \mathbb{P}(\inf\{s > 0 : \bar{B}_s^x = 1\} \geq t) \\ &\leq \mathbb{P}(\inf\{s > 0 : \bar{B}_s^0 = 1\} \geq t) \\ &= \mathbb{P}(\sigma^0 \geq t). \end{aligned}$$

We will bound from above the last line of (4.8). Let $v(t, x)$ solve the heat equation $v_t = \beta^{-1}v_{xx}$ with $v(0, x) = 1$ for $x \in (-1, 1)$ and $v(t, \pm 1) = 0$. An elementary analysis shows that

$$(4.9) \quad v(t, 0) \leq \frac{4}{\pi} \exp(-\beta^{-1}\pi^2 t/4).$$

(The Fourier sine series for $v(t, x - 1)$ on $[0, 2]$ at $x = 1$ is an alternating series, and its first term gives the upper bound above.) We claim that for fixed t and $x \in [0, t]$,

$$(4.10) \quad v(t, 0) = \mathbb{P}(\sigma^0 \geq t).$$

To see this, let $w(s, x) = v(t - s, x)$ and observe that $w_s = -\beta^{-1}w_{xx}$, so by Itô's lemma, for $s \in [0, t \wedge \sigma^x]$

$$\begin{aligned} w(s, B_s^x) &= w(0, x) + \int_0^s (w_s + \beta^{-1}w_{xx})(r, B_r^x) dr + \sqrt{2\beta^{-1}} \int_0^s w_x(r, B_r^x) dW_r \\ &= w(0, x) + \sqrt{2\beta^{-1}} \int_0^s w_x(r, B_r^x) dW_r. \end{aligned}$$

By taking expectations and setting $s = t \wedge \sigma^x$, we obtain

$$\begin{aligned} v(t, x) = w(0, x) &= \mathbb{E}[w(t \wedge \sigma^x, B_{t \wedge \sigma^x}^x)] \\ &= \mathbb{E}[w(t, B_t^x) \mathbf{1}_{\{t \leq \sigma^x\}}] + \mathbb{E}[w(\sigma^x, B_{\sigma^x}^x) \mathbf{1}_{\{t > \sigma^x\}}] \\ &= \mathbb{E}[v(0, B_t^x) \mathbf{1}_{\{t \leq \sigma^x\}}] \\ &= \mathbb{P}(\sigma^x \geq t). \end{aligned}$$

From (4.8), (4.9), and (4.10), for $x \in [0, 1]$

$$\mathbb{P}(\tau^x \geq t) \leq \frac{4}{\pi} \exp(-\beta^{-1}\pi^2 t/4).$$

By Lemma 4.2, $\lambda\beta \rightarrow 0$ as $\beta \rightarrow \infty$. So for all sufficiently large β ,

$$\begin{aligned} \mathbb{E}[e^{\lambda\tau^x}] &= 1 + \int_1^\infty \mathbb{P}(e^{\lambda\tau^x} \geq t) dt \\ (4.11) \quad &\leq 1 + \frac{4}{\pi} \int_1^\infty t^{-\pi^2/(4\lambda\beta)} dt \\ &= 1 + \frac{4}{\pi} \frac{4\lambda\beta}{\pi^2 - 4\lambda\beta}. \end{aligned}$$

Now recalling (4.7),

$$(4.12) \quad u(x) \leq \mathbb{E}[e^{\lambda\tau^x}] \leq 1 + \frac{4}{\pi} \frac{4\lambda\beta}{\pi^2 - 4\lambda\beta}.$$

Using Lemma 4.2 we see that the right-hand side of (4.12) approaches 1 as $\beta \rightarrow \infty$. An analogous argument can be made for $x \in (1, b]$, showing that u is uniformly bounded in β as desired. \square

Next we define a function which will be useful in the analysis of (3.7). For $x \in [0, 1]$, let

$$(4.13) \quad f(x) = \frac{\int_0^x e^{\beta V(t)} dt}{\int_0^1 e^{\beta V(t)} dt}.$$

We compare u and f in the following lemma.

LEMMA 4.4. Let $\|\cdot\|_\infty$ the L^∞ norm on $C[0, 1]$. With f defined by (4.13), we have, in the limit $\beta \rightarrow \infty$,

$$\begin{aligned} \|f - u\|_\infty &= O(e^{-c\beta}), \\ \|f' - u'\|_\infty &= O(e^{-c\beta}). \end{aligned}$$

Proof. Observe that $g = f - u$, defined on $[0, 1]$, satisfies

$$(4.14) \quad \begin{aligned} -V'(x)g'(x) + \beta^{-1}g''(x) &= \lambda u(x), \\ g(0) = 0, \quad g(1) &= 0. \end{aligned}$$

Multiplying by $\beta e^{-\beta V(x)}$ in (4.14) leads to

$$\frac{d}{dx} \left(e^{-\beta V(x)} g'(x) \right) = \beta e^{-\beta V(x)} \lambda u(x)$$

so that

$$(4.15) \quad g'(x) = e^{\beta V(x)} \left(\lambda \beta \int_0^x e^{-\beta V(t)} u(t) dt + C_\beta \right).$$

Integrating (4.15) and using $g(0) = 0$,

$$(4.16) \quad g(x) = \lambda \beta \int_0^x \left(e^{\beta V(t)} \int_0^t e^{-\beta V(s)} u(s) ds \right) dt + C_\beta \int_0^x e^{\beta V(t)} dt.$$

Using Lemma 4.3 we have $\|u\|_\infty \leq K < \infty$. From (B1) and (B3) we see that V is decreasing on $[0, 1]$. So putting $g(1) = 0$ in (4.16), we obtain, for all sufficiently large β ,

$$(4.17) \quad \begin{aligned} |C_\beta| &= \lambda \beta \left(\int_0^1 e^{\beta V(t)} dt \right)^{-1} \int_0^1 \left(e^{\beta V(t)} \int_0^t e^{-\beta V(s)} u(s) ds \right) dt \\ &\leq \lambda \beta \left(\int_0^1 e^{\beta V(t)} dt \right)^{-1} \int_0^1 \left(\int_0^t u(s) ds \right) dt \\ &\leq \lambda \beta K \left(\int_0^1 e^{\beta V(t)} dt \right)^{-1} \\ &\leq 2\lambda \beta^{3/2} K \left(\frac{-2V''(0)}{\pi} \right)^{1/2}, \end{aligned}$$

where in the last line Laplace's method is used. Using Lemma 4.2, for all sufficiently large β ,

$$(4.18) \quad |C_\beta| \leq e^{-c\beta}.$$

From (B1) and (B3) we see that V is nonpositive on $[0, 1]$, so from (4.15),

$$(4.19) \quad \begin{aligned} |g'(x)| &\leq \lambda \beta \int_0^x e^{\beta(V(x)-V(t))} u(t) dt + |C_\beta| e^{\beta V(x)} \\ &\leq \lambda \beta K + e^{-c\beta}. \end{aligned}$$

Using Lemma 4.2 again, we get $\|g'\|_\infty = O(e^{-c\beta})$. As $g(0) = 0$, this implies $\|g\|_\infty = O(e^{-c\beta})$. This completes the proof. \square

Remark 4.5. A result analogous to Lemma 4.3 holds, with

$$f(x) = \frac{\int_x^b e^{\beta V(t)} dt}{\int_1^b e^{\beta V(t)} dt},$$

for $x \in [1, b]$.

We are now in position to prove Theorem 4.1.

Proof of Theorem 4.1. It suffices to prove the case $i = 1$, so we will look at the endpoint $\partial D_1 = \{0\}$. From Theorem 3.2 we have

$$\rho(\{0\}) = \frac{\frac{d}{dx} (u(x)e^{-\beta V(x)})|_{x=0}}{\beta \lambda \int_D u(x)e^{-\beta V(x)} dx}$$

so that

$$\lambda p_1 = \frac{e^{-\beta V(0)} u'(0)}{\beta \int_D u(x)e^{-\beta V(x)} dx}.$$

Introducing again the superscripts hi and lo ,

$$(4.20) \quad \frac{\lambda^{hi} p_1^{hi}}{\lambda^{lo} p_1^{lo}} = e^{-(\beta^{hi} - \beta^{lo})V(0)} \cdot \frac{\beta^{lo}}{\beta^{hi}} \cdot \frac{u^{hi'}(0)}{u^{lo'}(0)} \cdot \frac{\int_D u^{lo}(x)e^{-\beta^{lo}V(x)} dx}{\int_D u^{hi}(x)e^{-\beta^{hi}V(x)} dx}.$$

Dropping the superscripts, recalling the function f from (4.13), and using Lemma 4.4, we see that

$$u'(0) = f'(0) + O(e^{-c\beta}).$$

Since

$$f'(0) = \left(\int_0^1 e^{\beta V(t)} dt \right)^{-1} = (1 + k_1 \beta^{-1} + O(\beta^{-2})) \sqrt{\beta} \left(\frac{-2V''(0)}{\pi} \right)^{1/2},$$

where k_1 is a β -independent constant coming from the second term in the Laplace expansion, we have

$$(4.21) \quad \begin{aligned} u'(0) &= O(e^{-c\beta}) + (1 + k_1 \beta^{-1} + O(\beta^{-2})) \sqrt{\beta} \left(\frac{-2V''(0)}{\pi} \right)^{1/2} \\ &= (1 + k_1 \beta^{-1} + O(\beta^{-2})) \sqrt{\beta} \left(\frac{-2V''(0)}{\pi} \right)^{1/2}. \end{aligned}$$

This takes care of the third term of the product in (4.20). We now turn to the fourth term. Let $y \in (0, 1]$ and note that for $t \in (y, 1]$,

$$f'(t) = e^{\beta V(t)} \left(\int_0^1 e^{\beta V(x)} dx \right)^{-1} = O(e^{-c\beta}),$$

where here c depends on y . Since $f(1) = 1$, for all sufficiently large β ,

$$(4.22) \quad |f(t) - 1| \leq e^{-c\beta}$$

for $t \in [y, 1]$ and a different c . Also,

$$\int_y^1 e^{-\beta V(x)} dx = (1 + k_2\beta^{-1} + O(\beta^{-2})) \sqrt{\beta^{-1}} \left(\frac{\pi}{2V''(1)}\right)^{1/2} e^{-\beta V(1)},$$

where k_2 is a β -independent constant coming from the second term in the Laplace expansion. Thus

$$\begin{aligned} \int_0^1 f(x)e^{-\beta V(x)} dx &= O\left(e^{-\beta V(y)}\right) + \int_y^1 f(x)e^{-\beta V(x)} dx \\ &= O\left(e^{-\beta V(y)}\right) + (1 + O(e^{-c\beta})) \int_y^1 e^{-\beta V(x)} dx \\ (4.23) \quad &= O\left(e^{-\beta V(y)}\right) + (1 + k_2\beta^{-1} + O(\beta^{-2})) \\ &\quad \times \sqrt{\beta^{-1}} \left(\frac{\pi}{2V''(1)}\right)^{1/2} e^{-\beta V(1)} \\ &= (1 + k_2\beta^{-1} + O(\beta^{-2})) \sqrt{\beta^{-1}} \left(\frac{\pi}{2V''(1)}\right)^{1/2} e^{-\beta V(1)}. \end{aligned}$$

Using (4.23) and Lemma 4.4 again,

$$\int_0^1 u(x)e^{-\beta V(x)} dx = (1 + k_2\beta^{-1} + O(\beta^{-2})) \sqrt{\beta^{-1}} \left(\frac{\pi}{2V''(1)}\right)^{1/2} e^{-\beta V(1)}.$$

From Remark 4.5, we can make an identical argument on $[1, b)$ to get

$$(4.24) \quad \int_D u(x)e^{-\beta V(x)} dx = (1 + k_2\beta^{-1} + O(\beta^{-2})) \sqrt{\beta^{-1}} \left(\frac{2\pi}{V''(1)}\right)^{1/2} e^{-\beta V(1)}$$

with a different but still β -independent k_2 . This takes care of the fourth term in the product in (4.20). Observe that in the limit $\beta^{hi}, \beta^{lo} \rightarrow \infty$, $\beta^{lo}/\beta^{hi} = r$, we have

$$\begin{aligned} \frac{1 + k_1(\beta^{hi})^{-1} + O((\beta^{hi})^{-2})}{1 + k_1(\beta^{lo})^{-1} + O((\beta^{lo})^{-2})} &= 1 + O\left(\frac{1}{\beta^{hi}} - \frac{1}{\beta^{lo}}\right), \\ \frac{1 + k_2(\beta^{lo})^{-1} + O((\beta^{lo})^{-2})}{1 + k_2(\beta^{hi})^{-1} + O((\beta^{hi})^{-2})} &= 1 + O\left(\frac{1}{\beta^{hi}} - \frac{1}{\beta^{lo}}\right). \end{aligned}$$

Reintroducing the superscripts hi and lo and using (4.21) and (4.24) in (4.20) now gives

$$(4.25) \quad \frac{\lambda^{hi} p_1^{hi}}{\lambda^{lo} p_1^{lo}} = \left(1 + O\left(\frac{1}{\beta^{hi}} - \frac{1}{\beta^{lo}}\right)\right) e^{-(\beta^{hi} - \beta^{lo})(V(0) - V(1))}$$

as desired. \square

5. Conclusion. We have presented a mathematical framework for TAD which is valid in any dimension, along with a complete analysis of TAD in one dimension under this framework. This framework uses the notion of QSD and is useful in particular to clarify the immediate equilibration assumption (or no-recrossing assumption) which is underlying the original TAD algorithm and to understand the extrapolation rule using the Arrhenius law. We hope to extend this justification of the extrapolation

rule to high dimensions, using techniques from [16]; the analysis seems likely to be technically detailed.

We hope that our framework for TAD will be useful in cases where the original method is not valid. Indeed, we have shown that TAD can be implemented wherever accurate estimates for the ratios in (3.7) are available. This fact is important for transitions which pass through degenerate saddle points, in which case a preexponential factor is needed on the right-hand side of (4.1). For example, in one dimension, a simple modification of our analysis shows that if we consider degenerate critical points on ∂D , then a factor of the form $(\beta^{hi}/\beta^{lo})^\alpha$ must be multiplied with the right-hand side of (4.1).

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