

Notes on Weak Noise Escape Problems

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1. Preliminaries

1.1. Introduction

This document summarizes the broad strokes of a calculation for the mean first passage time of switching between metastable states in a higher dimensional stochastic system. Consider the Fokker-Planck equation

$$\frac{\partial p}{\partial t} = -\nabla \cdot \{b(x)p(x, t)\} + \frac{\varepsilon}{2} \nabla^2 p(x, t), \quad x \in \mathbb{R}^n, \quad (1)$$

which is equivalent to the Itô Langevin stochastic differential equation

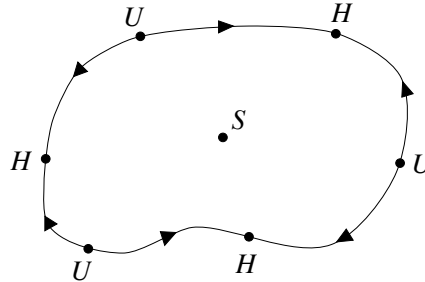
$$dx(t) = b(x) dt + \sqrt{\varepsilon} dW(t), \quad (2)$$

where $W(t)$ is a vector of n independent Weiner processes with $\langle W_i(t)W_j(\tau) \rangle = \delta_{ij}(t - \tau)$.

We interpret (2) as some stochastic process in n variables where $x_i(t)$ evolves according to some deterministic function $b_i(x)$ and also with noise with magnitude proportional to ε . The Fokker-Planck equation, (1) roughly describes the probability of this system being in configuration x at time t .

A technical note is that we could also have included a diffusion tensor $\bar{D}(x)$, however we will only discuss the case that the magnitude of the noise is *independent* of x . [MS97] derives all of this theory for the more general case.

Of particular interest is when the drift, or deterministic part of our stochastic process, $b(x)$ has multiple stable attractors. We then observe that the system will, due to noise, switch between these two *metastable* states. We then consider Ω to be the basin of attraction of one of these stable attractors, where the separatrix could contain some hyperbolic or unstable attractors.



Let S denote the stable attractor. The overall goal of these notes is to calculate the mean time for the process to exit this basin of attraction, given that $x(0) = S$. In one dimension, this problem has a very straightforward analysis, see [Gar09], however in higher dimensions, the geometry of the process complicates matters significantly.

It's also worth noting that the problem simplifies greatly when the drift is of a special form, said to be *gradient* or *conservative* if:

$$b(x) = -\nabla\Phi(x) \quad \Leftrightarrow \quad \nabla \times b(x) = 0.$$

for some scalar potential Φ . In general, this is *not* the case. In any situation that detailed balance fails to hold, no Φ can be found. However, if b is of this form, then the calculation reduces to being very similar to the one dimensional problem.

1.2. Eigenfunction Expansion

Consider rewriting the Fokker-Planck equation (1)

$$\frac{\partial p}{\partial t} = -\nabla \cdot \{b(x)p\} + \frac{\varepsilon}{2}\nabla^2 p := -\nabla J(x, t) \tag{3}$$

where $J(x, t)$ is what we'll refer to as the flux.

Let τ denote the random variable describing the time for a trajectory to escape the aforementioned basin of attraction. We can then define the survival probability $S(t)$ that the trajectory has not escaped from Ω yet by time t . In other words,

$$S(t) := \mathbb{P}[t > \tau] = \int_{\Omega} p(x, t) dx,$$

from which we can compute the probability density $f(t)$ using (1) and the divergence theorem to yield

$$f(t) = -\frac{dS}{dt} = -\int_{\Omega} \frac{\partial p}{\partial t} dx \tag{4}$$

Define the operator

$$\mathbb{L}_\varepsilon p := -\frac{\varepsilon}{2} \nabla^2 p - b \nabla p,$$

which has adjoint

$$\mathbb{L}_\varepsilon^* p = -\frac{\varepsilon}{2} \nabla^2 p - \nabla \cdot \{bp\},$$

which, we note, is exactly the right hand side of the Fokker-Planck equation, meaning we can rewrite (1) as

$$\frac{\partial p}{\partial t} = -\mathbb{L}_\varepsilon^* p(x, t), \quad (5)$$

where $J(x, t)$ is the flux. We now consider the problem (5) with *absorbing* (Dirichlet) boundary conditions on $\partial\Omega$, that is

$$p(x, t)|_{x \in \partial\Omega} = 0.$$

It can be proved that the eigenvalues of both \mathbb{L}_ε and its adjoint have a principle (smallest) eigenvalue that is real and exponentially small (that is, $\lambda_\varepsilon^0 \sim e^{-c/\varepsilon}$) and also that the other eigenvalues satisfy $0 < \lambda_\varepsilon^0 < \text{Re}\{\lambda_\varepsilon^1\} < \text{Re}\{\lambda_\varepsilon^2\} < \dots$ with corresponding eigenvectors ϕ_ε^j . Consider the eigenfunction expansion

$$p_\varepsilon(x, t) = \sum_j c_j e^{-\lambda_\varepsilon^j t} \phi_\varepsilon^j(x).$$

For large t , the principle eigenvalue dominates, meaning that

$$p_\varepsilon(x, t) \sim c_0 e^{-\lambda_0 t} \phi_0(x). \quad (6)$$

Thus, if we compute the mean first passage time, we see, using (4) and (6)

$$\mathbb{E}[\tau] := \int_0^\infty t f(t) dt \sim \frac{1}{\lambda_\varepsilon^0} \int_\Omega \phi_\varepsilon^0(x) dx.$$

However, we can also consider integrating (3) over the region with (6) to see that

$$\lambda_\varepsilon^0 \int_\Omega \phi_\varepsilon^0(x) dx = \int_\Omega \nabla J_\varepsilon^0(x, t) dx,$$

which after using the divergence theorem, we get

$$\lambda_0 = \frac{\int_{\partial\Omega} J_\varepsilon^0(x, t) \cdot n dx}{\int_\Omega \phi_\varepsilon^0(x) dx}.$$

In other words, the rate of escape is effectively the flux across the boundary and determined exclusively by the principle eigenfunction ϕ_ε^0 . However, we recall that $\lambda_\varepsilon^0 \sim e^{-c/\varepsilon}$ for some c . Thus, in the weak noise limit $\varepsilon \rightarrow 0$, $\lambda_\varepsilon^0 \rightarrow 0$. Thus, rather than solve the principle eigenfunction equation $\mathbb{L}_\varepsilon^* \phi_\varepsilon^0 = \lambda_\varepsilon^0 \phi_\varepsilon^0$, we can actually solve

$$\mathbb{L}_\varepsilon^* \phi_\varepsilon^0 = 0, \quad (7)$$

that is, we need to find the *quasistationary distribution* of the Fokker-Planck equation and make corrections to the boundary since solving for the eigenfunction using this technique will not produce the appropriate absorbing boundary condition.

1.3. Wentzell-Friedlin Hamiltonian Structure

In this section, we're trying to solve for the quasistationary distribution of the Fokker-Planck equation on the body of Ω . Through probabilistic large deviation approaches, it can be shown that the appropriate ansatz for this solution is of the WKB form

$$\phi_\varepsilon^0 \sim K(x)e^{-W(x)/\varepsilon}, \quad (8)$$

where we take the normalization of these functions to be such that $W(S) = 0$ and $K(S) = 1$. For reasons discussed later, $W(x)$ is referred to as the *quasipotential* and $K(x)$ is the *prefactor*.

We then collect powers of ε by plugging (8) into (7) and to leading order, we find the leading order equation is a *Hamilton-Jacobi* system described by

$$H(x, \nabla W) = 0 \quad \text{where} \quad H(x, p) := b(x) \cdot p + \frac{1}{2} (p \cdot p). \quad (9)$$

The structure (9) is referred to as the *Wentzell-Friedlin Hamiltonian* [FW12] and is also referred to as the *eikonal* equation of the asymptotic analysis.

This particular structure is convenient because it has a very closely related analog in classical physics. We can interpret the Hamiltonian as the “energy” of the system and consider a particle evolving with position described by $x(t)$ and momentum $p(t)$. Associated with every Hamiltonian is a *Lagrangian*, which is defined to be

$$L(x, \dot{x}) = \{\dot{x} - b(x)\} \cdot \{\dot{x} - b(x)\}, \quad (10)$$

then we can introduce the notion of the classical action, defined to be

$$S_T[x] := \int_0^T L(x, \dot{x}) dt,$$

which provides us an alternative definition of the quasipotential:

$$W(x) = \inf_{\substack{T>0 \\ y:[0,T] \rightarrow \Omega \\ y(0)=S, y(T)=x}} S_T[y] \quad (11)$$

In other words, the quasipotential $W(x)$ is a measure of how “difficult” it is for the particle to move from S to some point x . The interpretation of this is now: there is a “least difficult path” or the path of “least action” in space with zero energy and the quasipotential is sharply peaked around this path as $\varepsilon \rightarrow 0$, meaning we really only care about behavior along this path, which again, from large deviation theory can be proved to be the “most probable” in some sense.

2. Numerical Techniques

2.1. Shooting/Ray Method

If we now consider a trajectory approach to studying this Hamilton-Jacobi system, that is, we parameterize $x(t)$ and $p(t)$, which is effectively studying the characteristics of the system. The equivalent statement to

the Euler-Lagrange equation minimizing (10) are Hamilton's equations, which describe how the position and momentum evolve with time:

$$\dot{x}_k = \frac{\partial H}{\partial p_k} = \delta_{jk} p_j + b_k(x), \quad \dot{p}_k = -\frac{\partial H}{\partial x_k} = -\frac{\partial b_i(x)}{\partial x_k} p_i. \quad (12)$$

Here, we've switched to the component-wise (Einstein notation) description of x, p . From now on, we'll abbreviate derivatives as $b_{i,j} := \frac{\partial b_i}{\partial x_j}$. It should also be noted that the momentum and velocity are interchangeable, using the above to see that

$$p_i = \delta_{ij} \{ \dot{x}_j - b_j(x) \}. \quad (13)$$

Recalling that $p_i = \partial_{x_i} W$ along the most probable path, we find

$$\dot{W} = \frac{\partial W}{\partial x_i} \dot{x}_i = p_i \dot{x}_i = p_i \{ \delta_{ij} p_j + b_i(x) \}. \quad (14)$$

One issue is that if we are considering trajectories from one stable fixed point to another attractor (which effectively is a heteroclinic orbit), then this trajectory will take $T \rightarrow \infty$. Thus, we consider taking our starting point $t_0 \rightarrow -\infty$ in the definition of (10). From (13), at the starting point $x = S$ at $t = -\infty$, we have that $p = 0$. In terms of dynamical systems, we want to find the *unstable* manifold through $(x, p) = (S, 0)$.

One technical issue is: how do we know that $W(x)$ is single valued? As in, how do we know paths do not cross each other? They in fact, *can* cross each other and form what are called *caustics*, but this will not be discussed further.

We now have evolutions for x, p, W , but the last piece of information we require is knowledge of the prefactor K . We note that using the fact that

$$\dot{K} := \dot{x}_i \frac{\partial K}{\partial x_i} = \frac{\partial H}{\partial p_i} \frac{\partial K}{\partial x_i},$$

we go to the next power in ε using (8) in (7), we get, along trajectories

$$\dot{K} = - \left\{ \frac{\partial^2 H}{\partial x_i \partial p_i} + \frac{1}{2} \frac{\partial^2 W}{\partial x_i \partial x_j} \frac{\partial H}{\partial p_i} p_j \right\} K. \quad (15)$$

We now have a nice transport equation for K , however, integration of this equation requires knowledge of the Hessian matrix $W_{,ij} := \partial_{x_i} \partial_{x_j} W$. If we differentiate the Hamilton-Jacobi equation (9) twice with respect to a position on the trajectory, we see

$$\left\{ \frac{\partial}{\partial x_i} + \frac{\partial p_k}{\partial x_i} \frac{\partial}{\partial p_k} \right\} \left\{ \frac{\partial}{\partial x_j} + \frac{\partial p_\ell}{\partial x_j} \frac{\partial}{\partial p_\ell} \right\} H = 0,$$

and rearranging, using that, by definition $\partial_{x_i} p_j := W_{,ij}$, we get the (Riccati) transport equation

$$\dot{W}_{,ij} = -\frac{\partial^2 H}{\partial p_k \partial p_\ell} W_{,ik} W_{,j\ell} - \frac{\partial^2 H}{\partial x_j \partial p_k} W_{,ik} - \frac{\partial^2 H}{\partial x_i \partial p_k} W_{,jk} - \frac{\partial^2 H}{\partial x_i \partial x_j}. \quad (16)$$

From this, we now have differential equations describing all of the quantities we need, described by (12), (14), (15), (16).

It can be assumed that W attains a minimum on $\partial\Omega$ at H , thus we're effectively looking for the intersection of the stable manifold through $(H, 0)$ and the unstable manifold through $(S, 0)$ of Hamilton's equations.

We have not, however, specified the initial conditions for this integration. Starting the integrating at $(S, 0)$ exactly would not produce the rays we hope for, thus we must perturb slightly away. If $t \rightarrow -\infty$, $\dot{W} = 0$ in (16) and we know $p = 0$, so if we define

$$\mathbf{Z} := [W_{,ij}(S, 0)], \quad \mathbf{B} := [b_{i,j}(S)],$$

then (16) becomes an algebraic Riccati equation

$$\mathbf{Z}\mathbf{Z} + \mathbf{Z}\mathbf{B} + \mathbf{B}^T\mathbf{Z} = 0.$$

This is also more readily solvable by defining $\mathbf{C} = \mathbf{Z}^{-1}$ yielding the Riccati equation

$$\mathbf{I} + \mathbf{B}\mathbf{C} + \mathbf{C}\mathbf{B}^T = 0.$$

MATLAB is able to solve algebraic Riccati equations with the `care` command. Thus, if we recall that \mathbf{Z} is the Hessian of W and that the Jacobian vanishes since $p = 0$ at the starting location, we can make the quadratic approximation

$$W \approx \frac{1}{2}(\Delta x)^T\mathbf{Z}(\Delta x),$$

and therefore for some small (but non-zero) ω serving as our perturbation, we take

$$\frac{1}{2}(\Delta x)^T\mathbf{Z}(\Delta x) = \omega.$$

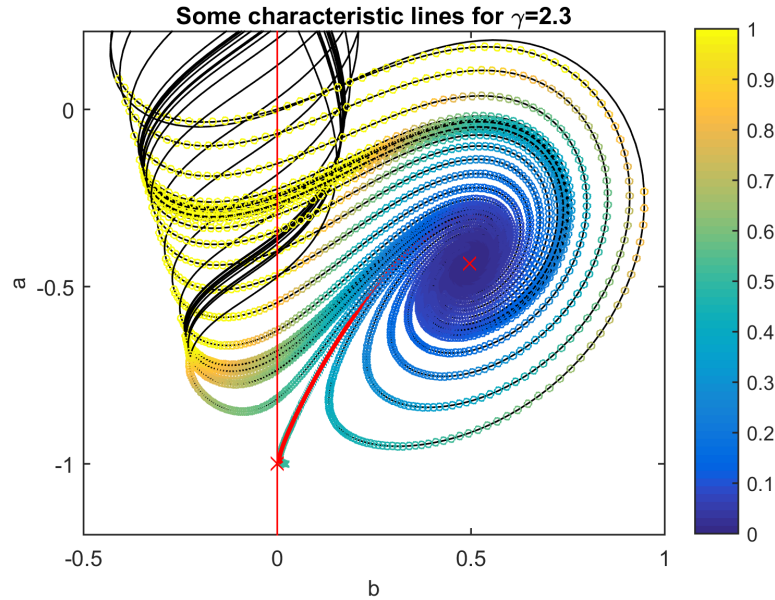
Recalling that also $W_{,ij} = \partial_{x_i}p_j$, we recover the appropriate momentum values

$$\Delta p = \mathbf{Z}(\Delta x),$$

where $\Delta x := x - S$. In other words, we take points close to our stable attractor and use the \mathbf{Z} matrix to recover the appropriate momentum for this starting position.

We now have a set of differential equations and a set of initial conditions to shoot from. We then take these points around the ellipse and shoot until the point closest to H is attained. In practice, a bisection method is recommended. Also, using a symplectic integrator (one that conserves energy, which we desire since $H \equiv 0$ on all paths) is another recommendation. One can be found here:

<http://www.mathworks.com/matlabcentral/fileexchange/7686-symplectic-integrators>



The above figure is an example of performing the shooting method taken from [GPJ11]. In this case, we see that the path that goes from the stable fixed point to the hyperbolic point is the accepted path of least action, in essence, the heteroclinic orbit of the Hamilton-Jacobi system we desire.

2.2. Geometric Minimum Action Method (gMAM)

Although the shooting method is suitable for many applications, the heteroclinic orbit may be difficult to obtain (due to stiffness of the problem) even using a bisection method. From a PDEs perspective, we're able to solve the eikonal equation with a variational approach rather than a characteristic approach. In the context of this problem, we have a more reliable technique for computing the most probable exit path: the *geometric minimum action method* (gMAM).

The motivation for this method comes from the integral (action) interpretation of the quasipotential described in (11). Specifically, we know that the quasistationary density is proportional to $e^{-W(x)/\varepsilon}$, where, using (11), we want to consider the minimization of the action

$$S_T[x] := \frac{1}{2} \int_0^T \|\dot{x}(t) - b(x)\|^2 dt. \quad (17)$$

Again, the quasistationary distribution is sharply peaked (as $\varepsilon \rightarrow 0$) around the path x^* that minimizes (17). Note that this is an infinite dimensional minimization, as it's also the minimum over all T and x .

We first use the inequality

$$\|\dot{x}\|^2 + \|b(x)\|^2 \geq 2\|\dot{x}\| \|b\| \quad (18)$$

which implies that

$$\min_{x,T} S_T[x] \geq \min_{x,T} \hat{S}_T[x],$$

where

$$\hat{S}_T[x] := \int_0^T \|\dot{x}\| \|b\| - \dot{x} \cdot b(x) dt.$$

[HVE08] made two insightful observations about the above quantity: t can be reparameterized such that the inequality (18) becomes an equality without changing the actual path but ensuring that $\|\dot{x}\| = \|b(x)\|$ along the path. The other observation to make is that T can be parameterized out of the line integral, as this will only change the value of \hat{S}_T , not whether it is minimized. Thus, we can just set $T = 1$ to find the actual path. One convenient way to parameterize is $\|\dot{x}\| = \text{constant}$, which is equivalent to thinking of t as a normalized arclength through our path. With these reductions, we now have the following problem:

$$\min_{\substack{x(s) \\ x(0)=S, x(1)=H}} \hat{S}_1[x] \quad \text{subject to } \|\dot{x}(s)\| = \text{constant}. \quad (19)$$

The minimizer of (19) must satisfy the Euler-Lagrange equation $\frac{\partial \hat{S}_1}{\partial x} = 0$. Computing this functional derivative, we find

$$\lambda \frac{\partial \hat{S}_1}{\partial x} = -\lambda^2 \ddot{x} + \lambda (\nabla b - \nabla b^T) \dot{x} + (\nabla b)^T b - \lambda \dot{\lambda} \dot{x},$$

where $\lambda := \|b\|/\|\dot{x}\|$ and ∇b is the Jacobian tensor of the system. Thus, to find when this functional derivative is zero, a preconditioned steepest-descent method in the direction of $-\lambda \partial \hat{S}_1 / \partial x$ is proposed.

Roughly, an initial path of grid points is formed, evolved via the steepest descent step, and then reparameterized such that the grid points are equal arclength to ensure the constraint is satisfied. In other words, take a path $x^0(0) = S$, $x^0(1) = H$ and discretize into $N + 1$ equidistant points between the two, denoted $x_i^0 = x^0(i/N)$.

Until convergence, we then repeat the process: given some discretized curve $\{x_i^k\}_{i=0, \dots, N}$ set $\lambda_0^k = \lambda_N^k = 0$ and compute $\dot{x}_i := (x_{i+1}^k - x_{i-1}^k)/(2/N)$, and then $\lambda_i^k = \|b(x_i^k)\|/\|\dot{x}_i^k\|$ as well as $\dot{\lambda}_i^k = (\lambda_{i+1}^k - \lambda_{i-1}^k)/(2/N)$ for $i = 1, \dots, N - 1$. Then, solve the tridiagonal system for \tilde{x}_i (using the Thomas algorithm)

$$\frac{\tilde{x} - x_i^k}{\tau} = (\lambda_i^k)^2 \frac{\tilde{x}_{i+1} - 2\tilde{x}_i + \tilde{x}_{i-1}}{1/N^2} - \lambda_i^k [\nabla b(x_i^k) - \nabla b^T(x_i^k)] \dot{x}_i^k - \nabla b^T(x_i^k) b(x_i^k) + \lambda_i^k \dot{\lambda}_i^k \dot{x}_i^k$$

with the boundary conditions fixing the endpoints $\tilde{x}_0 = S$, $\tilde{x}_N = H$. Next, interpolate a set of equidistant $N + 1$ points across the interpolation of \tilde{x} and repeat.

Along this path, the momentum p can be recovered using, coming from (13)

$$p_i = \lambda_i \dot{x}_i - b(x_i),$$

the true time can be recovered from the choice of parameterization, by setting $t_0 = 0$ and

$$t_i = \frac{1}{2\lambda_0^k} + \frac{1}{\lambda_1^k} + \dots + \frac{1}{\lambda_{i-1}^k} + \frac{1}{2\lambda_i^k}.$$

The action can be evaluated independent of the parameterization of time by observing (11)

$$\hat{S} = \frac{1}{N} \left(\frac{3}{2} \dot{x}_1 \cdot p_1 + \sum_{i=2}^{N-2} \dot{x}_i \cdot p_i + \frac{3}{2} \dot{x}_{N-1} \cdot p_{N-1} \right).$$

If other quantities, such as the prefactor are required, the shooting transport equations can be used along this geometric minimum path by the appropriate parameterization of t .

3. Evaluation of Escape Time

3.1. Matching at the Hyperbolic Point

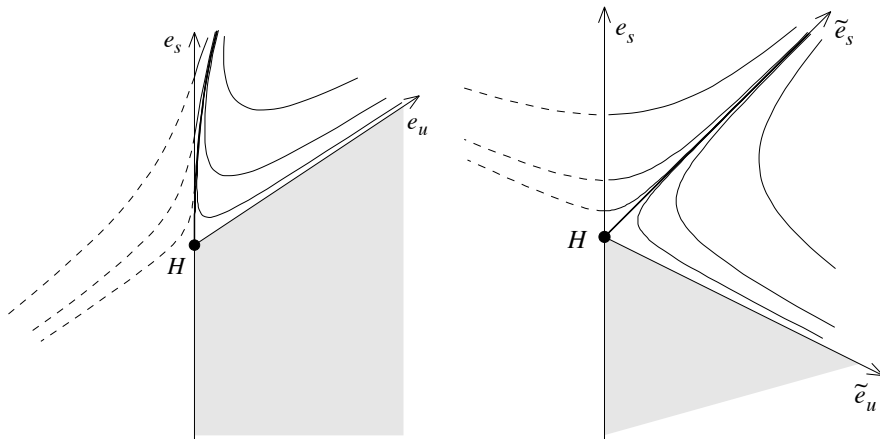
Regardless of what numerical technique is used to find the most probable exit path and associated quantities, matching at the hyperbolic point, H still needs to be done, as the quasistationary distribution was only valid for the interior of the domain and the exit time must have an absorbing boundary at the separatrix.

Ultimately, the behavior near H falls into two distinct categories depending on the very important parameter:

$$\mu := \frac{|\lambda_s|}{\lambda_u}$$

, where λ_u and λ_s are the unstable (and stable) eigenvalues of the deterministic flow field $b(x)$ at the hyperbolic point H .

If $\mu < 1$ or equivalently, $b_{i,i}(H) > 0$, then the approach of the most probable exit path is tangent to the separatrix. If $\mu > 1$ or $b_{i,i}(H) < 0$, then this is not the case. The difference can be seen in the figure below, in each case, the most probable exit path (MPEP) is the bold line.



The details of this matching are omitted but can be found in great detail in [MS97] and deal with subtle geometric arguments depending on the different scenarios of μ .

3.2. Final Expressions

Ultimately, from the previous section we have seen that there are effectively two different scenarios depending on the value of μ . In the case that $\mu > 1$, where the approach to the hyperbolic point H is *not* tangent to the separatrix, the result follows a classical Eyring-like law:

$$2\langle t \rangle^{-1} \sim \lambda_\varepsilon^0 \sim \frac{K(H)}{2\mu} \sqrt{\det \mathbf{Z}(s)} e^{-W(H)/\varepsilon} \text{ as } \varepsilon \rightarrow 0.$$

The case where $\mu < 1$ is a little less straightforward for a variety of reasons. Here, the most probable exit path is tangent to the separatrix and the prefactor $K(H) \rightarrow 0$, meaning the above formula would not produce the result we desire. For this reason, the limiting value (along the most probable exit path) must be taken and produces an Arrhenius-like law:

$$2\langle \tau \rangle^{-1} \sim \lambda_\varepsilon^0 \sim \frac{\mu A^{1/\mu} L}{4\pi} \sqrt{\det \mathbf{Z}(S)} e^{-W(H)/\varepsilon} \quad \text{as } \varepsilon \rightarrow 0, \quad (20)$$

where here we have normalized such that $\lambda_u(H) = 1$ and we define the quantities

$$L := \lim_{x \rightarrow H} \frac{K(x)}{(\Delta x_2)^{(1/\mu)-1}}, \quad A := \lim_{x \rightarrow H} \frac{\Delta x_2}{(\Delta x_1)^\mu},$$

where $\Delta x_1 := x_1 - H_1$ and $\Delta x_2 := x_2 - H_2$, that is, the first and second components of the difference between x and H . Thus, (20) simplifies to

$$2\langle \tau \rangle^{-1} \sim \lambda_\varepsilon^0 \sim \lim_{\substack{x \rightarrow H \\ \text{along MPEP}}} \frac{\mu K(x)(x_2 - H_2)}{4\pi(x_1 - H_1)} \sqrt{\det \mathbf{Z}(S)} e^{-W(H)/\varepsilon} \quad \text{as } \varepsilon \rightarrow 0,$$

4. Other Resources

The best resource for exploring this topic further is (in my opinion) the original papers by Maier and Stein. [MS97] is the most complete summary of their work and includes a mathematically rich geometric analysis of the weak noise escape problem. In [MS93], [MS96] they study the phenomenon of caustics in the quasipotential.

Examples from mathematical biology of this calculation being used can be found in [GPJ11], a paper on motor-mediated transport, and [WBK14] a paper on rod formation in bacteria.

A more rigorous analysis of the geometric minimum action method can be found in [HVE08] and [VEH08]. Other numerical techniques have been used to study these problems. Of particular note, [Cam12] details an ordered upwind method and proves a variety of useful facts about non-gradient quasipotentials. [Moo+15] provides an R package called QPot for computing the quasipotential using the ordered upwind method.

This analysis can also be modified to other types of stochastic differential equations, notably stochastic hybrid systems, which is summarized in [Bre14] and an example of performing this calculation can be found in [New14] which provides an analysis on the stochastic Morris-Lecar equation.

References

- [Bre14] P. C. Bressloff. “Stochastic Processes in Cell Biology.” Vol. 41. Interdisciplinary Applied Mathematics. Springer International Publishing, 2014.
- [Cam12] M. K. Cameron. “Finding the quasipotential for nongradient SDEs.” *Phys. D Nonlinear Phenom.* 241.18 (2012).
- [FW12] M. I. Freidlin and A. D. Wentzell. “Random Perturbations of Dynamical Systems.” 3rd ed. Vol. 260. A Series of Comprehensive Studies in Mathematics. Springer Berlin Heidelberg, 2012.
- [Gar09] C. Gardiner. “Stochastic Methods: A Handbook for the Natural and Social Sciences.” 4th. Vol. 13. Springer Series in Synergetics. Springer Berlin Heidelberg, 2009.
- [GPJ11] T. Guérin, J. Prost, and J.-F. Joanny. “Bidirectional motion of motor assemblies and the weak-noise escape problem.” *Phys. Rev. E* 84.4 (2011).
- [HVE08] M. Heymann and E. Vanden-Eijnden. “The geometric minimum action method: A least action principle on the space of curves.” *Commun. Pure Appl. Math.* 61.8 (2008).
- [MS93] R. S. Maier and D. L. Stein. “Effect of focusing and caustics on exit phenomena in systems lacking detailed balance.” *Phys. Rev. Lett.* 71.12 (1993).
- [MS96] R. S. Maier and D. L. Stein. “A scaling theory of bifurcations in the symmetric weak-noise escape problem.” *J. Stat. Phys.* 83.3-4 (1996).
- [MS97] R. S. Maier and D. L. Stein. “Limiting Exit Location Distributions in the Stochastic Exit Problem.” *SIAM J. Appl. Math.* 57.3 (1997).
- [Moo+15] C. M. Moore et al. “QPot: An R Package for Stochastic Differential Equation Quasi-Potential Analysis.” *R J.* (2015).
- [New14] J. M. Newby. “Spontaneous Excitability in the Morris–Lecar Model with Ion Channel Noise.” *SIAM J. Appl. Dyn. Syst.* 13.4 (2014).
- [VEH08] E. Vanden-Eijnden and M. Heymann. “The geometric minimum action method for computing minimum energy paths.” *J. Chem. Phys.* 128.6 (2008).
- [WBK14] L. Wettmann, M. Bonny, and K. Kruse. “Effects of molecular noise on bistable protein distributions in rod-shaped bacteria.” *Interface Focus* 4.6 (2014).