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Duality between relaxation and first passage in reversible Markov dynamics: rugged energy landscapes disentangled

David Hartich¹ and Aljaž Godec

Mathematical Biophysics Group, Max-Planck-Institute for Biophysical Chemistry, Göttingen D-37077, Germany

¹ Author to whom any correspondence should be addressed.

E-mail: david.hartich@mpibpc.mpg.de and agodec@mpibpc.mpg.de

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Abstract

Relaxation and first passage processes are the pillars of kinetics in condensed matter, polymeric and single-molecule systems. Yet, an explicit connection between relaxation and first passage time-scales so far remained elusive. Here we prove a duality between them in the form of an interlacing of spectra. In the basic form the duality holds for reversible Markov processes to effectively one-dimensional targets. The exploration of a triple-well potential is analyzed to demonstrate how the duality allows for an intuitive understanding of first passage trajectories in terms of relaxational eigenmodes. More generally, we provide a comprehensive explanation of the full statistics of reactive trajectories in rugged potentials, incl. the so-called ‘few-encounter limit’. Our results are required for explaining quantitatively the occurrence of diseases triggered by protein misfolding.

1. Introduction

Relaxation dynamics are a paradigm for describing complex dynamical phenomena spanning condensed matter [1], polymeric [2], granular [3] and single-molecule systems [4, 5], and even cellular regulatory networks [6]. Relaxation concepts underlie most spectroscopic methods [1]. Moreover, our understanding of metastability is built entirely on the properties of relaxation spectra [7–11]. Complementary to relaxation processes are the statistics of the first passage time, the time a random process reaches a prescribed threshold value for the first time. First passage time statistics in turn are central to the kinetics of chemical reactions [12–22], signaling in biological cells [20–31], transport in disordered media [32], the foraging behavior of bacteria and animals [33–35], up to the spreading of diseases [36, 37] or stock market dynamics [38]. Further important applications of first passage concepts include the persistence properties in non-equilibrium systems [39–41] and stochastic thermodynamics [42–47].

Both relaxation and first passage processes are essential for theories building on a diffusive exploration of (free) energy landscapes $U(x)$ [48], which have proven to be particularly invaluable in explaining the kinetics of chemical reactions [49, 50], protein dynamics [51, 52] incl. recent single protein folding experiments [53], and the dynamics of supercooled liquids and glasses [9–11, 54]. Whereas relaxation processes can be understood intuitively in terms of the eigenmodes and eigenvalues of the underlying Fokker–Planck or Kramers operators [9–11, 55], general, and in particular intuitive results about the full first passage time statistics are much sparser, and currently do not reach beyond a crude division between so-called direct and indirect first-passage trajectories for the simplest smooth potential landscapes [17, 20, 24, 26, 27]. Our general understanding of first passage phenomena would therefore substantially benefit from a deeper connection to the corresponding relaxation process.

Indeed, in the limit of high energy barriers a well-known link relates $\chi_1^{-1}$, the longest relaxation time, and the mean first passage time to surmount the highest barrier in the landscape [7–11, 56]. However, in spite of the
immense success and universal applicability of this approximate relationship, an explicit bridge between first passage and relaxation time-scales has not been explored further.

Here we establish such a link rigorously for microscopically reversible Markovian dynamics. We prove that the first-passage process to an effectively one-dimensional target is in fact the dual to the corresponding relaxation process. The duality takes the form of a spectral interlacing of characteristic time-scales, in which each pair of successive relaxation time-scales encloses a first-passage time-scale. We establish an explicit relationship between relaxation and first-passage spectra, and express the full statistics of first passage time exactly in terms of the relaxation eigensystem. As a case study we consider a diffusive exploration of a triple-well potential. Moreover, exploiting the duality we disentangle first passage time statistics in general rugged energy landscapes. We argue why our results are important for a quantitative understanding of the occurrence of diseases related to protein misfolding.

The paper is organized as follows. In section 2 we expose the duality between first passage and relaxation processes. In section 3 we determine the first passage time statistics in a simple triple-well potential and demonstrate that knowing the full probability density is mandatory in studies of many-particle first passage problems in the few encounter limit. In section 4 we determine the first passage time density for a truly rugged energy landscape generated by a truncated Karhunen–Loève expansion of a Wiener process. The large deviation limit of the first passage time distribution, which is relevant for single-molecule first passage problems, is presented in section 5. We conclude in section 6. A proof of the duality between first passage and relaxation is relegated to the appendix.

2. First passage time density from the relaxation spectrum

We consider reversible Markovian dynamics in continuous time governed by a Fokker–Planck operator

\[ L = \partial_x D(x) [\beta U'(x) + \partial_x], \]

where \( x \) is the position, \( U(x) \) a potential with \( U'(x) \equiv \partial_x U(x) \), and \( D(x) \) the diffusion landscape. We assume \( \beta \) to be the inverse temperature, such that according to the fluctuation–dissipation theorem \( \beta D(x) \) is the inverse friction coefficient. For any initial condition \( x_0 \) the dynamics governed by the Fokker–Planck operator \( L \) relaxes to the Boltzmann distribution \( P_0(x) = e^{-\beta U(x)} / \int e^{-\beta U(x')} dx' \).

Adopting the bra-ket notation we expand \( P_0 \) in a complete bi-orthogonal set of left and right eigenstates,

\[ L = -\sum \lambda_k |\psi_k^R\rangle \langle \psi_k^L|, \]

\( \lambda_k \) denoting the eigenvalues and \( \langle \psi_k^L| \psi_k^R \rangle = \delta_k \) with \( |\psi_k^R\rangle \equiv e^{\beta U(x)} |\psi_k^L\rangle \). The propagator encoding the probability to be at \( x \) at a time \( t \) after starting from \( x_0 \) at \( t_0 = 0 \), is defined as

\[ P(x, t|x_0) \equiv \langle x|e^{tL}|x_0 \rangle = \sum_k \langle x|\psi_k^L\rangle \langle \psi_k^R|x_0 \rangle e^{-\lambda_k t}. \]

Since we assumed temporally homogeneous dynamics, we can define the first passage time probability density from some \( x_0 \) to a target at \( a \), \( \varphi_{a|x_0}(t) \), by the renewal theorem [57]

\[ P(x, t|x_0) = \int_0^t \varphi_a(\tau|x_0) P(x, t - \tau|\tau) d\tau, \]

(2)

where either \( x_0 < a \leqslant x \), or symmetrically \( x_0 > a \geqslant x \). Equation (2) follows from a direct enumeration of paths between \( x_0 \) and \( x \), by which construction must pass through \( a \). Laplace transforming equation (2) we obtain \( \tilde{\varphi}_{a}(s|x_0) = \tilde{P}(x, s|x_0)/\tilde{P}(x, s|a) \), which is the starting point of our analysis. Using equation (1), which after Laplace transform reads \( \tilde{P}(x, s|x_0) = \sum_k (s + \lambda_k)^{-1} \langle x|\psi_k^R\rangle \langle \psi_k^L|x_0 \rangle \), yields

\[ \tilde{\varphi}_{a}(s|x_0) = \sum_k (s + \lambda_k)^{-1} \langle x|\psi_k^R\rangle \langle \psi_k^L|x_0 \rangle \]

\[ \sum_k (s + \lambda_k)^{-1} \langle x|\psi_k^R\rangle \langle \psi_k^L|a \rangle. \]

The Laplace transform of the first passage time density \( \tilde{\varphi}_{a}(s|x_0) \) is a meromorphic function having simple poles \( -\lambda_k \) on the negative real axis [58]. Moreover, the poles have no accumulation point in the left half plane (Re(\( s \)) < 0). Similarly, \( \tilde{P}(y, s|x) \) is meromorphic with simple poles \( -\lambda_k \) arranged along the non-positive real axis. In particular, \( \lambda_0 = 0 \) and \( \langle x|\psi_0^R\rangle \langle \psi_0^L|x_0 \rangle \equiv P_0(x) \).

The Laplace transforms of the propagators \( \tilde{P}(x, s|x_0) \) and \( \tilde{P}(x, s|a) \) have coinciding poles, while the poles of \( \tilde{\varphi}_{a}(s|x_0) \) are those zeroes of \( \tilde{P}(x, s|a) \), which are different from the zeroes of \( \tilde{P}(x, s|x_0) \). Generally, \( \tilde{P}(x, s|x_0) \) and \( \tilde{P}(x, s|a) \) have infinitely many coinciding zeroes alongside the distinct ones (see proof in [59]), because the region beyond \( a \) cannot affect the first passage time from \( x_0 \), whereas it must affect the relaxation. However, all common zeroes result in a vanishing residue.

One can prove that setting \( x = a \) in equations (2) and (3) guarantees that all relevant eigenvalues (i.e. those satisfying \( \langle a|\psi_k^R\rangle = 0 \)) of the relaxation and first passage processes interlace

\[ \lambda_{k-1} < \mu_k < \lambda_k, \forall k \geqslant 1, \]

(4)

which is due to the fact that \( \langle a|\psi_k^R\rangle \langle \psi_k^L|a \rangle > 0 \) (see also [59]). Based on the interlacing in equation (4) we are now in the position to determine the entire first passage time statistics from the relaxation eigenspectrum,
We computed the first 40 left and right relaxation eigenvectors, $\langle x | \psi_k^n \rangle$ and $\langle \psi_k^n | a \rangle$, and eigenvalues $\lambda_k$ numerically using a reflecting boundary condition at the target $a$. The four lowest $\langle x | \psi_k^n \rangle$ of the relaxation process are depicted in figure 1(b). From $\{ \lambda_k, | \psi_k^n \rangle, \langle \psi_k^n | \} \}$. We calculate the first 30 $\mu_k$ and $w_k(x_0)$ using the duality, i.e. equations (5) and (9). The spectrum of first passage eigenvalues is depicted in figure 1(c), with the corresponding first passage time probability densities shown in figure 1(d) (lines) and compared to the result of Brownian dynamics simulations (symbols). We find an excellent agreement between theory and simulations. Note that the deviations of the theoretical results from simulations observed on extremely short timescales are a
direct consequence of truncating the sums in equations (1) and (8) (i.e. we considered 40 eigenvalues in the relaxation spectrum and 30 first passage eigenvalues).

We now link metastability to the first passage time behavior. A potential \( U(x) \) has metastable states if the minima are separated by high barriers \( > k_B T \). The probability mass in the ground state \( P_a(x) \) is concentrated around these minima. The barriers give rise to a separation of time-scales between inter-well (see, e.g. \( \psi_1^R, \psi_2^R \) in figure 1(b)) and intra-well dynamics (see \( \psi_{1,2}^L \)) and thus create gaps in the relaxation spectrum [8–11]. As a result we observe in figure 1(c) (see filled gray circles) two gaps \( 0 = \lambda_0 \ll \lambda_1 \ll \lambda_2 < \lambda_3 \) when the reflecting boundary is at \( a_1 \), corresponding to the crossing of a single barrier. Conversely, three gaps, \( 0 \ll \lambda_1 \ll \lambda_2 < \lambda_3 < \lambda_4 \), appear when the reflecting boundary is at \( a_3 \), corresponding to the global relaxation to \( P_{gs}(x) \), to direct transitions between the leftmost and right-most wells, and to the transition to the central well from both sides, respectively (see figure 1(b)). These gaps are independent of \( x_0 \).

Due to the interlacing (equation (4)), and because \( \lambda_1 \gg 0 \), the \( N \)-gaps in the relaxation spectrum reflecting all the metastable basins translate to \( N-1 \) gaps in the first passage spectrum due to the \( N-1 \) barriers. The first passage spectrum is shifted to shorter times, since contrary to relaxation, all trajectories must surmount the barriers. The spectral weights \( w_k \) depend on the initial position, gauging the contribution of each relaxation mode with respect to the given first passage time-scale \( \mu_k^{-1} \) (see equation (9)). The four lowest \( w_k \) for the first passage process \( x_0 \to a_3 \) are shown in figure 2(a).

In view of [26, 27] (see also [20]) we now separate all first passage trajectories into two classes—the so-called ‘globally indirect’ and the rest. The class of ‘globally indirect’ trajectories includes those exploring the entire accessible phase space prior to absorption. These trajectories therefore arrive on the slowest time-scale \( \mu_1^{-1} \) and their associated weight \( w_1 \) is approximately the fraction of all first passage trajectories that reach quasi-equilibrium before hitting the target. Correspondingly, \( w_1 \)—the weight of globally indirect trajectories decreases as the starting position \( x_0 \) approaches the target at \( a \) (see, e.g. blue solid line in figure 2(a) for \( a = 1.7 \)). In other words, the closer \( x_0 \) is to the target the more unlikely are globally indirect trajectories.

Pushing this picture even further we can also identify in figure 1(d) \( (x_0 \to a_3) \) a second pronounced time-scale \( \mu_2^{-1} \) with weight \( w_2 \), reflecting what we may call ‘locally indirect’ trajectories—those that first equilibrate locally within the central well but cross the second barrier without returning to the left, deepest well. Comparing the second weight \( w_2 \) from figure 2(a) (see dashed—dotted red line) and the potential landscape figure 1(a) we find that ‘locally indirect’ trajectories are most pronounced in the sense of the largest value of \( w_2 \) if the starting position is within the central well. The locally indirect trajectories account for local equilibration prior to absorption and become relevant as soon as the potential landscapes has more than one deep free energy basin, such as for example the one depicted in figure 1. Our work therefore extends the present understanding of first
passage processes [20, 26, 27] by explicitly identifying locally indirect trajectories—those equilibrating only locally prior to absorption.

For $x_0$ within the central well the fraction of globally indirect trajectories decreases, and locally indirect trajectories become likelier, i.e. $w_2$ increases. Concurrently, higher spectral weights also grow, rendering direct trajectories more likely. As a result, an additional time-scale appears, giving rise to a second ‘bump’ in $\varphi_0(t)$ (see figure 1(d), blue lines). This reasoning extends to arbitrary landscapes; $w_k, \mu_k$ reflect a hierarchy of time-scales, on which trajectories equilibrate locally in the sequence of all intervals between consecutive basins and $a_i$ before hitting $a_i$. The highest modes encode direct trajectories.

### 3.2. Few encounter kinetics require the full first passage time distribution

The full first passage time statistics are crucial for kinetics in the few-encounter limit, when only the first of many particles needs to find the target [26, 27]. We highlight this on hand of first passage time statistics in a non-interacting $N$-particle system. The $N$-particle survival probability—the probability that none of the $N$ particles starting from $x_0$ has reached the target until time $t$—is simply given by

$$P_a(t|x_0)^N \equiv \left[ \int_0^\infty \varphi_a(t|x_0)dt \right]^N = \left[ \sum_{k>0} w_k(x_0)e^{-\mu_k t} \right]^N,$$

(12)

where we have inserted equation (8). We note that if the initial conditions where not identical with $x_i = x_0$ for all $i = 1, \ldots, N$ one would replace the survival probability $P_a(t|x_0)^N$ by the product $[1 - P_a(t|x_0)]^N$. For convenience, we will restrict our discussion to the scenario in which all particles start from the same position. Using the survival probability (12) the $N$-particle first passage time density follows directly from the single particle case

$$\psi_a^{(N)}(t|x_0) \equiv -\frac{\partial}{\partial t} P_a(t|x_0)^N = N \varphi_a(t|x_0) P_a(t|x_0)^{N-1},$$

(13)

which is the probability density that one of $N$ particles reaches the target $a_i$ at time $t$ under the condition that none of the remaining $N - 1$ particles has arrived before. Obviously, $N$-particles will find the target on average in a shorter time than a single particle. More precisely, the mean first passage time in the many particle setting reads

$$\langle t_a(x_0) \rangle_N \equiv \int_0^\infty \psi_a^{(N)}(t|x_0)dt = \int_0^\infty P_a(t|x_0)^Ndt,$$

(14)

where we have inserted equation (13) and performed an integration by parts in the last step.

Let us now focus on the mean first passage time and start with a single particle exploration ($N = 1$) in which case the mean according to equation (10) is simply given by $\langle t_a(x_0) \rangle_1 = \sum_{k>0} w_k(x_0)/\mu_k$. If there are free energy barriers between the initial position of the particle and the target, which lead the emergence of a local
Table of content:

1. Introduction
2. Methods
3. Results
4. Discussion
5. Conclusion

Figure 3. Narrowing of the first passage time density in the few-encounter limit. (a) $N$-particle density for $x_0 \to a_1$. The thick solid line corresponds to the solid blue line in figure 1(d). The diamonds depict the respective mean first passage times $\langle t_\phi(x_0) \rangle_N$. The survival probability $P_\phi(t|x_0)^N$ that none of the remaining $N-1$ particles has reached the target. According to equation (12) each colored curve in (a) is the product of the thick curve $N=1$ and the corresponding survival probability in (b).

The text continues with detailed analysis and equations related to the first passage time density, survival probability, and their dependencies on the number of particles and other factors. The content delves into the dynamics of particles reaching a target, with a focus on the effects of particle number and target location on the first passage time statistics.
of the details of the underlying dynamics. Further studies specifically targeting the short time limit of first passage time distributions can be found in [65, 66].

In general, the \( N \)-particle first passage problem is essential for describing nucleation kinetics, since the occurrence of the first stable nucleus triggers the spontaneous growth of the new phase (see e.g. [65, 66]). A particular form thereof is the occurrence of misfolding-triggered protein aggregation resulting in many diseases [61–64]. Namely, in many-protein systems the free energy minimum does not correspond to a folded state, but rather to an aggregate of misfolded proteins [63, 64]. Misfolding of a single protein, which indeed occurs by slow diffusion in a rough energy landscape [61, 62], seeds aggregation similar to a nucleation phenomenon. To predict the onset of aggregation and hence disease from the protein’s energy landscape, an understanding of the full first passage time statistics is required, and our work provides the foundations to do so. In the following section we briefly show that our exact theory from section 2 can also be applied to systems with truly rugged energy landscapes.

4. Rugged energy landscapes

In the previous section we have demonstrated that our theory from section 2 can readily be used to obtain first passage time densities for multi-well barrier crossing problems with barrier heights \( > k_B T \). Moreover, we have discussed the few-encounter limit, for which it is imperative to have access to the full first passage time distribution, since any attempt to explain many-particle first passage kinetics by single-particle moments are prone to fail.

To model a rugged energy landscape containing, in addition to high barriers, also barriers which are \( \lesssim k_B T \), we use a parabolic potential plus a Karhunen–Loève expansion of a realization of a Brownian motion

\[
U(x) = x^2/4 + \sum_{k=1}^{K} z_k \sin((2k - 1)\pi x)/(2k - 1),
\]

where we have truncated the potential after \( K \) terms and where \( z_k \) are Gaussian random numbers. Once \( z_k \) are generated we keep them constant. In figure 4(a) we depict the potential generated from equation (16) with \( K = 16 \). As before, we determine the eigenvalues \( \{\lambda_k\} \) and eigenfunctions \( \{\psi_k(x)\} \) of the relaxation process with \( \psi_k^E \) being the equilibrium Boltzmann density (see left panel of figure 4). Exploiting the theory from section 2 we obtain the first passage time density \( \gamma_\mathrm{f}(t|x_0) \) in figure 4(c) (see solid black line), which is corroborated by extensive Brownian dynamics simulations (see blue open circles). The inset of figure 4(c) depicts the first passage density on a linear scale. In order to indicate the short-time cutoff, which is dominated by diffusive transport, we

![Figure 4](https://via.placeholder.com/150)
also plot the short time asymptotic for free diffusion ($U(x) = 0$). In figure 4(d) we depict the corresponding $N$-particle first passage time densities for the few-encounter limit, which clearly reveal the drastic narrowing of the first passage time distribution arising from the aforementioned interplay between the diffusive short-time cutoff and the suppression of the long-time asymptotics for increasing $N$. This example illustrates that our theory can readily be applied to arbitrarily rough potential landscapes.

### 5. Large deviation limit

For single-particle problems the mean first passage time as well as higher moments are typically dominated by the long-time asymptotics of the first passage time distribution, which we have also demonstrated in figure 2(b) for the triple-well potential. The long-time limit is encoded in the principal first passage eigenvalue $\mu_1$. As we demonstrate in the appendix, the principal eigenvalue $\mu_1$ can be obtained in a simplified manner by formally setting $\tilde{\mu}_0 = 0$ and $k^2 = 0$ in equation (7). Moreover, a powerful approximation can be obtained by truncating in equation (7) all coefficients with $n > 2$ (for a formal justification see last paragraph of the appendix),

$$\mu_1 \approx \tilde{\mu}_1 = \frac{\sigma_2(a)}{2\sigma(a)} \left[ 1 + 4 \frac{P_{eq}(a)\sigma_2(a)}{\sigma(a)^2} - 1 \right],$$

(17)

where we introduced $\sigma_n(a) = \sum_{i=2}^n \langle \psi_i^a \rangle^2 \langle \psi_i^a \rangle / \lambda^n$. Since equation (17) is derived from a Taylor expansion around $s = 0$ (see equation (A,7)) it is expected to be quite accurate as soon as the formal condition $\mu_1 \ll \lambda_1$ is met, which in turn translates self-consistently into $\tilde{\mu}_1 \ll \lambda_1$. The relative error $\epsilon = |\mu_1 - \tilde{\mu}_1|/\mu_1$ is expected to scale as $\epsilon \propto (\tilde{\mu}_1/\lambda_1)^2$. For example, in the presence of at least one high barrier and as long as $a$ is not the deepest point of $U(x)$ the condition $\lambda_1 \gg \mu_1$ is indeed satisfied (see, e.g. figures 1(a) and (c)). Thus, rescaling $\phi_\mu(t)$ according to equation (17), all curves must collapse for long times onto a unit exponential $\phi_{\mu}(t = 0/\tilde{\mu}_1)/(w(x_0)\tilde{\mu}_1) = e^{-\theta}$, which is indeed fully confirmed in figure 5. The relative errors for the triple-well potential (see open colored symbols) are strictly bounded, $|\mu_1 - \tilde{\mu}_1|/\mu_1 < 0.02$ for any $a$.

Moreover, equation (17) holds for relaxation spectra obtained under a reflecting boundary at $a$, as well as for natural boundary conditions if there is no deeper minimum beyond $a$. If furthermore $P_{eq}(a) \rightarrow 0$ in equation (17) (i.e. the case of ‘rare-event’ absorption), then $\tilde{\mu}_1 \approx P_{eq}(a)/\sigma_1(a)$, where particularly

$$\sigma_1(a) = \int_0^\infty [P(a, t; a) - P_{eq}(a)] \, dt.$$

(18)

Equation (17) generalizes the ‘Poissonization’ phenomenon observed in [26, 27]. We note that equation (17) can also accurately describe the long-time first passage asymptotics in rugged energy landscapes with an arbitrary number of lower barriers (i.e. $< k_B T$; see closed magenta rectangles in figure 5). Further technical remarks including an extension to discrete state systems can be found in [59].

### 6. Conclusion

This paper establishes rigorously the duality between relaxation and first-passage processes for ergodic reversible Markovian dynamics. Based on the duality, an intuitive explanation of first passage time statistics in general
rugged energy landscapes is provided. The full first passage time statistics are shown to be required for explaining correctly the kinetics in the few-encounter limit—particularly relevant cases thereof are the triggering of diseases by protein misfolding and related nucleation-limited phenomena. In addition, we obtained accurate large deviation asymptotics dominating the mean first passage time, which emerge from a time-scale separation in the relaxation process. We show in [59] that all concepts presented here can readily be extended to discrete state-space network dynamics, which, inter alia extends the duality between first passage and relaxation to higher dimensional networks. Notably, they allowed us to determine, for the first time, analytically the full first passage time statistics of the Ornstein–Uhlenbeck process (see [59]). Our work provides an exact unified framework for studying the full statistics of first passage time under detailed balance conditions. Generalizations to irreversible dynamics will be pursued in our future studies.

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Appendix. Proof of the duality

In this appendix we sketch the proof of the duality, which allows us to determine analytically the first passage time distribution from the corresponding relaxation spectrum, i.e. the weights \( \{ w_k \} \) (not necessarily positive) and first passage rates \( \{ \mu_k \} \) that satisfy

\[
\tilde{\varphi}_k(s|x_0) = \sum_{k>0} w_k(x_0) \frac{\mu_k}{\mu_k + s} \tag{A.1}
\]

directly from the relaxation spectrum \( \{ \lambda_k, \psi_k^s \} \). A detailed technical derivation including an extension to discrete state dynamics can also be found in [59]. Since the first passage eigenvalues \( \mu_k \) correspond to the poles of \( \tilde{\varphi}_k(s|x_0) \) and the renewal theorem states \( \tilde{\varphi}_k(s|x_0) = \tilde{P}(a, s|x_0)/\tilde{P}(a, s|a) \), our goal will be to find the zeros of

\[
\tilde{P}(a, s|a) = \sum_{\ell \geq 0} \frac{\langle \psi_{\ell}^R \rangle \langle \psi_{\ell}^I | a \rangle}{s + \lambda_{\ell}}, \tag{A.2}
\]

where the reversibility of the Fokker–Planck operator imposes \( \langle \psi_{\ell}^R \rangle \langle \psi_{\ell}^I | a \rangle > 0 \) for all relevant relaxation modes \( \langle \psi_{\ell}^R \rangle \neq 0 \).

For the \( k \)th first passage rate \( \mu_k \) we introduce the auxiliary functions

\[
F(k', s) \equiv (s + \lambda_{k'}) \tilde{P}(a, s|a), \tag{A.3}
\]

which for any \( k' = k, k - 1 \) by design are strictly concave \( \partial^2 F_{k'} < 0 \) within the interval \( -\lambda_k < s < -\lambda_{k-1} \). We choose \( k^* = k \) or \( k^* = k - 1 \) such that \( F(k^*(k), s) \) is restricted to be negative at \( s = -\bar{\mu}_k = -(\lambda_k + \lambda_{k-1})/2 \), i.e.

\[
k^*(k) = \begin{cases} 
  k & \text{if } F_k(-\bar{\mu}_k) < 0, \\
  k - 1 & \text{otherwise.}
\end{cases} \tag{A.4}
\]

Consequently, \( F(k^*(k), s) \) is both negative and concave between \( s = -\bar{\mu}_k \) and \( s = -\mu_k \), with \( F(k^*(k), -\mu_k) = 0 \), which implies that any Newton iteration starting from \( \bar{\mu}_k \) will strictly converge towards \( \mu_k \).

The final step is to use an infinite Newton series—an analytical version of Newton's iteration—in form of a series of almost triangular matrices [26]. First, we take the Taylor expansion of

\[
F(k^*(k), s) = \sum_{n=0}^{\infty} \frac{f_n(k)}{n!} (s + \bar{\mu}_k)^n, \tag{A.5}
\]

where \( f_n(k) = \partial^n F(k^*(k), s)|_{s=-\bar{\mu}_k} \), which are explicitly given in equation (7). Note that equation (A.4) implies \( f_0(k) < 0 \). According to the interlacing theorem in equation (4) the Taylor series in equation (A.5) converges on full interval \( -\lambda_k < s < -\lambda_{k-1} \) including the \( s = -\mu_k \). Furthermore, the auxiliary function from equations (A.3) and (A.4) guarantee the Newton series to converge to the true root \( s = -\mu_k \) at which \( F(k^*(k), -\mu_k) = 0 \). Hence, the \( k \)th first passage rate \( \mu_k \) is exactly and explicitly given by the converging sum in equation (5).

Having determined the first passage eigenvalue \( \mu_k \) the corresponding weight can simply be determined from \( \tilde{\varphi}_k(s|x_0) = \tilde{P}(a, s|x_0)/\tilde{P}(a, s|a) \) and equation (A.1) by using the residue theorem that finally yields
\[ w_k(x_0) = \frac{P(a_s - \mu_k | x_0)}{\mu_k \delta P(a_s | x_0)|_{a_s = \mu_k}}. \tag{A.6} \]

Equation (A.6) is equivalent to equation (9) and completes the proof since all first passage weights \( w_k(x_0) \) and eigenvalues \( \mu_k \) fully characterize the first passage time density \( \varphi_0(t|x_0) = \sum_{k \geq 0} w_k(x_0) \mu_k e^{-\mu_k t} \).

We finally provide some remarks on the principal eigenvalue \( \mu_1 \). If only the principal eigenvalue is of interest the aforementioned discussion can be simplified in the following way. First, we realize that there exist no relaxation eigenvalue, which is smaller than \( \lambda_0 \). Therefore, the simple choice \( k^* = 0 \) allows for a Taylor expansion of \( F(k^* = 0, s) \) around \( \mu_1 = 0 \) in equation (A.5) that converges on the full interval \(-\lambda \leq s \leq +\lambda\), which includes the lowest first passage eigenvalue \( s = -\mu_1 \). Inserting \( k^* = 0 \) and \( \mu_1 = 0 \) in equation (A.5) and using equation (7) finally yields

\[ F(0, s) = P_{eq}(a) + \sum_{n=1}^{\infty} (-1)^{n+1} c_n(a) s^n, \tag{A.7} \]

where \( c_n(a) \equiv \sum_{\ell \geq 0} \langle a | \psi_R^{\ell} | \psi_I^{\ell} | a \rangle / \lambda_0^n \), with \( \mu_1 \) being the negative zero of \( F(0, s) \), i.e. \( F(0, -\mu_1) = 0 \). If we truncate the series (A.7) after \( n = 2 \) we obtain a simple parabolic equation with the solution \( \mu_1 \) given in equation (17). Note that equation (17) finally follows from equation (5) if one formally sets therein \( f_n(1) = 0 \) for all \( n > 2 \) (see also [39]).

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