Extreme escape with killing for diffusing particles in one dimension

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January 19, 2022

Abstract

The extreme narrow escape theory describes the statistical properties of the fastest among many identical stochastic particles to escape from a narrow window. We study here the arrival of the fastest particle when a killing term is added inside a one dimensional interval. Killing represents a degradation that leads to removal of the moving particles with a given probability. Using the time dependent flux for the solution of the diffusion equation, we compute asymptotically the mean time for the fastest to escape alive. We also study the role of several killing distributions on the mean extreme time for the fastest and compare the results with Brownian simulations. Finally, we discuss some possible applications to cell biology.

1 Introduction

The extreme narrow escape theory describes the statistical properties for the fastest among equals stochastic particles to escape a bounded domain through a narrow window. Examples are Brownian motions, particles that can switch between different states or can alternate between motion along the boundary and inside of a domain, such as bacteria or spermatozoa. This extreme statistics theory has recently regain interest due to applications in cell biology. The time scale of the fastest defines the rate of molecular activation in cell biology. Indeed, when particles such as calcium ions or ligands are produced in a certain location of the cell, the first particles to arrive to a target channel or receptor, triggers a cellular response.

We study here the rate of arrival of the first particle among many to an absorbing boundary when in addition, a killing field is added, the role of which is

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to terminate at random time the particle trajectories. In this model, particle termination occurs inside the domain, as shown in the schematic Fig. 1A. Such killing could thus modify the rate of arrival of particles to the boundary, because the first one can be killed before escape. Such effect was previously studied in the context of modeling viral infection in cells [13] and spermatozoa in the uterus [14, 15].

We adopt here the simplified one-dimensional model of the diffusive motion (Fig. 1A) and we shall consider different type of killing such as δ-Dirac killing measure, in which the termination of diffusing particles occurs at a single point [16, 17]. The killing measure is the probability per unit time and unit length to terminate a trajectory. However, a moving particle can pass through a killing site many times without being terminated, in contrast to an absorbing boundary, where the trajectory is terminated with probability 1.

Using short term asymptotic expansion of the diffusion equation with a killing, we derive here asymptotic formula for a δ-Dirac killing measure. We also compute the mean time for the first among many trajectories to escape before being killed (Fig. 1B). The manuscript is organized as follows: in the second section, we present the theory for the mean first escape time under a killing field. In section 3, we focus on deriving formula for the escape in half-a-line, containing multiple δ-Dirac killing measures. In section 4, we consider the case of uniform killing rate occurring on various intervals. Several formula could be extended to the case of a partially absorbing target [18].

Figure 1: **Escape versus killing for the fastest particles.** A. 1D Brownian motion passing through the point $x_1$ where a Dirac killing field is positioned. The particle is absorbed when reaching the boundary on the left. B. Realization of 5 random walks, where 4 of them are terminated while the extreme survival trajectory (green) reaches the boundary.
2 Killing measure versus the survival probability

2.1 Stochastic framework

A stochastic process \( x(t) \) in the domain \( \Omega \) satisfies the equation

\[
 dx = b(x) \, dt + \sqrt{2B(x)} \, dw(t) \quad \text{for} \quad x \in \Omega,
\]

where \( b(x) \) is a smooth drift vector, \( B(x) \) is a diffusion tensor, and \( w(t) \) is a vector of independent standard Brownian motions. A killing measure \( k(x) \) is added in the domain \( \Omega \) with boundary \( \partial \Omega = \partial \Omega_a \cup \partial \Omega_r \), where \( \partial \Omega_a \) is a small absorbing part and \( \partial \Omega_r \) is reflecting. The transition probability density function (pdf) of the process \( x(t) \) with killing and absorption is the pdf of trajectories that have neither been killed nor absorbed in \( \partial \Omega_a \) by time \( t \),

\[
 p(x, t \mid y) \, dx = \Pr\{x(t) \in x + dx, \tau^k > t, \tau^e > t \mid y\},
\]

where \( \tau^k \) is the time for the particle to be killed and \( \tau^e \) is the time of absorption. This pdf is the solution of the Fokker-Planck equation (FPE) [19]

\[
 \frac{\partial p(x, t \mid y)}{\partial t} = \mathcal{L}_xp(x, t \mid y) - k(x)p(x, t \mid y) \quad \text{for} \quad x, y \in \Omega,
\]

where \( \mathcal{L}_x \) is the forward operator

\[
 \mathcal{L}_xp(x, t \mid y) = \sum_{i,j=1}^{d} \frac{\partial^2 \sigma^{i,j}(x)p(x, t \mid y)}{\partial x^i \partial x^j} - \sum_{i=1}^{d} \frac{\partial b^i(x)p(x, t \mid y)}{\partial x^i},
\]

and \( \sigma(x) = \frac{1}{2}B(x)B^T(x) \). The operator \( \mathcal{L}_x \) can be written in the divergence form \( \mathcal{L}_xp(x, t \mid y) = -\nabla \cdot J(x, t \mid y) \), where the components of the flux density vector \( J(x, t \mid y) \) are

\[
 J^i(x, t \mid y) = -\sum_{j=1}^{d} \frac{\partial \sigma^{i,j}(x)p(x, t \mid y)}{\partial x^j} + b^i(x)p(x, t \mid y), \quad (i = 1, 2, \ldots, d).
\]

The initial and boundary conditions for the FPE (3) are

\[
 p(x, 0 \mid y) = \delta(x - y) \quad \text{for} \quad x, y \in \Omega
\]

\[
 p(x, t \mid y) = 0 \quad \text{for} \quad t > 0, \quad x \in \partial \Omega_a, \quad y \in \Omega
\]

\[
 J(x, t \mid y) \cdot n(x) = 0 \quad \text{for} \quad t > 0, \quad x \in \partial \Omega - \partial \Omega_a, \quad y \in \Omega.
\]

The probability of trajectories that are killed before reaching \( \partial \Omega_a \) is given by [16],

\[
 \Pr\{\tau^k < \tau^e \mid y\} = \int_{0}^{\infty} \int_{\Omega} k(x)p(x, t \mid y) \, dx \, dt.
\]
The absorption probability flux on \( \partial \Omega_a \) is

\[
J(t \mid y) = \oint_{\partial \Omega} J(x, t \mid y) \cdot n(x) \, dS_x,
\]

(9)

and \( \int_0^\infty J(t \mid y) \, dt \) is the probability of trajectories that have been absorbed at \( \partial \Omega_a \). Thus the probability to escape before being killed is

\[
\Pr\{\tau^e < \tau^k \mid y\} = \int_0^\infty J(t \mid y) \, dt.
\]

(10)

The pdf of the killing time \( \tau^k \) is the conditional probability of killing before time \( t \) of trajectories that have not been absorbed in \( \partial \Omega_a \) by that time

\[
\Pr\{\tau^k < t \mid \tau^e > \tau^k, y\} = \frac{\Pr\{\tau^k < t, \tau^e > \tau^k \mid y\}}{\Pr\{\tau^e > \tau^k \mid y\}} = \frac{\int_0^t \int_\Omega k(x)p(x, s \mid y) \, dx \, ds}{\int_0^\infty \int_\Omega k(x)p(x, s \mid y) \, dx \, ds}.
\]

The probability distribution of the time to absorption at \( \partial \Omega_a \) is the conditional probability of absorption before time \( t \) of trajectories that have not been killed by that time

\[
\Pr\{\tau^e < t \mid \tau^k > \tau^e, y\} = \frac{\int_0^t J(s \mid y) \, ds}{1 - \int_0^\infty \int_\Omega k(x)p(x, s \mid y) \, dx \, ds}.
\]

Thus the narrow escape time (NET) is the conditional expectation of the absorption time of trajectories that are not killed in \( \Omega \), that is,

\[
\mathbb{E}[\tau^e \mid \tau^k > \tau^e, y] = \int_0^\infty \Pr\{\tau^e > t \mid \tau^k > \tau^e, y\} \, dt
\]

\[
= \frac{\int_0^\infty sJ(s \mid y) \, ds}{1 - \int_0^\infty \int_\Omega k(x)p(x, s \mid y) \, dx \, ds}.
\]

(11)
The survival probability of trajectories that have not been terminated by time \( t \) is given by

\[
S(t | y) = \int_\Omega p(x, t | y) \, dx. \tag{12}
\]

2.2 Extreme escape statistics with killing

For \( n \) independent identically distributed copies of the stochastic process (1), that can escape at time \( t_1, \ldots, t_n \), prior to get killed, we consider the arrival time of the fastest and we shall derive here a formula for the probability and mean arrival time of the fastest. The extreme mean first passage time (EMFPT) \( \tau_{EMFPT}(n) \) \cite{13, 16} is the first time for a particle to escape through one of a narrow window located on the surface of the domain \( \Omega \), that is

\[
\tau_{EMFPT}(n) = \min\{t_1, \ldots, t_n\},
\]

where \( n \) is the number of survival particles. The conditional mean first passage time (MFPT) \( \tau_j \) of the \( j \)th particle is used to compute the absorbing time \( \tau_{EMFPT}(n) \) of the first particle that has reached the absorbing boundary \( \partial\Omega_a \).

The pdf of the escape time of the first particle prior to time \( t \) with an initial density \( p_0 \) is given by

\[
P(t) = \Pr\{\tau_{EMFPT}(n) < t | \tau_{EMFPT}(n) < \tau_{EMFPT}(n), p_0\}.
\]

The conditional MFPT \( \bar{\tau}_{EMFPT}(n) \) is defined by

\[
\bar{\tau}_{EMFPT}(n) = \int_{0}^{\infty} t \frac{dP(t)}{dt} \, dt = \int_{0}^{\infty} [P(\infty) - P(t)] \, dt. \tag{13}
\]

Using Bayes’ law, we obtain the decomposition

\[
P(t) = \frac{\Pr\{\bar{\tau}_{EMFPT}(n) < t, \tau_{EMFPT}(n) < \tau_{EMFPT}(n), p_0\}}{\Pr\{\tau_{EMFPT}(n) < \tau_{EMFPT}(n), p_0\}} = \frac{N(t)}{P_\infty}, \tag{14}
\]

where \( P_\infty \) is the probability that the first one escape.

2.2.1 Probability that the first particle escapes

The probability that the first particles escapes alive the domain is computed as follows:

\[
P_\infty = \Pr\{\tau_{EMFPT}(n) < \tau_{EMFPT}(n), p_0\} = 1 - \Pr\{\tau_{EMFPT}(n) > \tau_{EMFPT}(n), p_0\}.
\]
Using that particles are independent, we get

\[ P_\infty = 1 - \prod_{j=1}^{n} \Pr\{ \tau^e_j > \tau^k_j, p_0 \}, \]

which can be written as

\[ P_\infty = 1 - \left( 1 - \Pr\{ \tau^e < \tau^k, p_0 \} \right)^n. \]

According to relation (10), because the probability that a single particle escapes before being killed is given by \( \Pr\{ \tau^e < \tau^k, p_0 \} = \int_0^\infty \int_{y\in\Omega} J(t|y)p_0(y)dy \, dt \) then,

\[ P_\infty = 1 - \left( 1 - \int_0^\infty \int_{y\in\Omega} J(t|y)p_0(y)dy \, dt \right)^n. \]

For a \( \delta \)-Dirac initial distribution at position \( y \), we get

\[ P_\infty = 1 - \left( 1 - \int_0^\infty J(t|y)dy \, dt \right)^n, \quad (15) \]

where the flux \( J \) is given by relation (9). Finally, the probability that \( n - k \) particles are killed and only \( k \) escape alive is given by the Binomial distribution:

\[ \Pr\{ \tau^k < \tau^e, \tau^q > \tau^e, q = k + 1, n \} = \binom{n}{k} \left( \int_0^\infty J(t|y)dy \, dt \right)^k \left( 1 - \int_0^\infty J(t|y)dy \, dt \right)^{n-k}. \]

### 2.2.2 Mean time for the fastest to escape without being killed

The conditional probability that the first one escapes alive before time \( t \) is given by

\[ N(t) = \Pr\{ \tau^e_{EMFPT}(n) < t, \tau^e_{EMFPT}(n) < \tau^k_{EMFPT}(n), p_0 \}, \]

that is,

\[ \Pr\{ \tau^e_{EMFPT}(n) < t, \tau^e_{EMFPT}(n) < \tau^k_{EMFPT}(n), p_0 \} = 1 - \Pr\{ \tau^e_{EMFPT}(n) > t \text{ or } \tau^e_{EMFPT}(n) > \tau^k_{EMFPT}(n), p_0 \}. \]

The event \( \{ \tau^e_{EMFPT}(n) > t \text{ or } \tau^e_{EMFPT}(n) > \tau^k_{EMFPT}(n) \} \) contains none of the \( n \) particles that have escaped alive by time \( t \). Because particles are independent, we obtain

\[ \Pr\{ \tau^e_{EMFPT}(n) > t \text{ or } \tau^e_{EMFPT}(n) > \tau^k_{EMFPT}(n), p_0 \} = \prod_{j=1}^{n} \left[ 1 - \Pr\{ \tau^e_j < t, \tau^e_j < \tau^k_j, p_0 \} \right]. \]
where \( \tau^e_j \) (reps. \( \tau^k_j \)) is the first time that the \( j^{th} \) particle is absorbed (resp. killed). Because the normal flux density at the boundary is the pdf of the exit point \([19]\), we get that for any of the particles

\[
Pr\{\tau^e_j < t, \tau^e_j < \tau^k_j, p_0\} = \int_0^t \oint_{\partial \Omega} J(x, t) \cdot n(x) \, dS_x = \int_0^t J(s) \, ds, \tag{16}
\]

where the flux \( J(s) \) is defined in relation \([9]\). Therefore the numerator in equation \((14)\) is

\[
N(t) = Pr\{\tau^{EMFPT}_n < t, \tau^{EMFPT}_n < \tau^{EMFPT}_n, p_0\} = 1 - \left(1 - \int_0^t J(s) \, ds\right)^n.
\]

To conclude, the conditional probability that the first particle, with an initial density \( p_0 \), escapes alive at the absorbing boundary prior to time \( t \) is given by

\[
P(t) = \frac{N(t)}{P_\infty} = \frac{1 - \left(1 - \int_0^t J(s) \, ds\right)^n}{1 - \left(1 - P^{(1)}_\infty\right)^n},
\]

where

\[
P^{(1)}_\infty = \int_0^\infty J(s) \, ds,
\]

and the conditional MFPT \( \bar{\tau}_{EMFPT}(n) \) (see equation \((13)\)) is

\[
\bar{\tau}_{EMFPT}(n) = \int_0^\infty \frac{\left(1 - \int_0^t J(s) \, ds\right)^n - \left(1 - \int_0^\infty J(s) \, ds\right)^n}{1 - \left(1 - \int_0^\infty J(s) \, ds\right)^n} \, dt. \tag{17}
\]

In first approximation, we shall neglect all other terms except the first one,

\[
\bar{\tau}_{EMFPT}(n) \sim \frac{1}{1 - \left(1 - P^{(1)}_\infty\right)^n} \int_0^\infty \int_0^t J(s) \, ds \left(1 - \int_0^t J(s) \, ds\right)^{n-1} \, dt. \tag{18}
\]
3 Extreme escape versus killing with a finite number of isolated points

3.1 General theory

We consider here killing at \( m \) points, with total weight \( V = \sum_{i=1}^{m} V_i \) distributed among them. Specifically, the killing measure is given by

\[
k(x) = \sum_{i=1}^{m} V_i \delta(x - x_i).
\]

Brownian particles with diffusion coefficient \( D \) can escape at the boundary \( x = 0 \) of the half-line \( \Omega = \mathbb{R}_+ \). To determine the formula for the fastest particle to escape alive, we solve the diffusion equation with \( m \) Dirac-killing terms by using the Green’s function [17]. This method allows us to obtain an integral representation for the survival probability. The FPE is given by

\[
\frac{\partial p(x, t \mid y)}{\partial t} = D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} - \sum_{i=1}^{m} V_i \delta(x - x_i)p(x, t \mid y) \tag{19}
\]

\[
p(x, 0 \mid y) = \delta(x - y)
\]

\[
p(0, t \mid y) = 0.
\]

This equation can be decomposed into:

\[
\frac{\partial p(x, t \mid y)}{\partial t} - D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} = F
\]

\[
p(x, 0 \mid y) = 0,
\]

with \( F = \sum_{i=1}^{m} V_i \delta(x - x_i)p(x, t \mid y) \), and

\[
\frac{\partial p(x, t \mid y)}{\partial t} - D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} = 0 \tag{21}
\]

\[
p(x, 0 \mid y) = \delta(x - y)
\]

\[
p(0, t \mid y) = 0.
\]

The fundamental solution of equation \( \text{(21)} \) is the heat kernel

\[
G(x, t \mid y) = \frac{1}{2\sqrt{\pi Dt}} \left( \exp \left\{ -\frac{(x - y)^2}{4Dt} \right\} - \exp \left\{ -\frac{(x + y)^2}{4Dt} \right\} \right),
\]

while the solution of equation \( \text{(20)} \) is given by Duhamel’s formula, in the form

\[
P(x, t \mid y) = \int_{0}^{t} \int_{\mathbb{R}} F(s, y) G(x, t - s \mid y) \, dy \, ds.
\]
The general solution of equation (19) is the sum of the solutions of equations (20) and (21). Thus, we obtain

\[ p(x, t \mid y) = G(x, t) \]
\[ - \sum_{i=1}^{m} \int_0^t \frac{V_i p(x_i, s \mid y)}{\sqrt{4\pi D(t-s)}} \left( \exp \left\{ -\frac{(x-x_i)^2}{4D(t-s)} \right\} - \exp \left\{ -\frac{(x+x_i)^2}{4D(t-s)} \right\} \right) ds. \]

The pdf \( p(x, t \mid y) \) is known once \( p(x_1, t \mid y), \ldots, p(x_m, t \mid y) \) are determined. Setting \( x = x_1, x = x_2, \ldots, x = x_m \) in equation (22) we obtain a system of integral equation in the single variable \( t \) for the unknown functions

\[ \phi_j(t) = p(x_j, t \mid y) \quad \text{for} \quad j = 1, m. \]

We obtain

\[ \phi_j(t) = G_j(t) - \sum_{i=1}^{m} \int_0^t \frac{V_i \phi_i(s)}{\sqrt{4\pi D(t-s)}} \left( \exp \left\{ -\frac{|x_j-x_i|}{\sqrt{D}} \right\} - \exp \left\{ -\frac{|x_j+x_i|}{\sqrt{D}} \right\} \right) ds, \]

where \( G_j(t) = G(x_j, t) \). The solution \( p(x, t \mid y) \) will be determined once all the function \( \phi_i(t) \) are known. To compute this, we use Laplace’s transform in time and we shall derive a system of linear equations

\[ \hat{\phi}_j(t) = \hat{G}_j(t) - \sum_{i=1}^{m} \frac{V_i \hat{\phi}_i(s)}{\sqrt{4\pi Dq}} \left( \exp \left\{ -\frac{|x_j-x_i|}{\sqrt{D}} \right\} - \exp \left\{ -\frac{|x_j+x_i|}{\sqrt{D}} \right\} \right) ds. \]

Using the parameters \( d_{ij} = \frac{|x_j-x_i|}{\sqrt{D}} \), \( m_{ij} = \frac{|x_j+x_i|}{\sqrt{D}} \), \( W_i = \frac{V_i}{\sqrt{4\pi D}} \), we rewrite the system (23) in the matrix form

\[ M \hat{\Phi} = \hat{G}, \]

where

\[ M(x_1, \ldots, x_m) = \begin{pmatrix}
1 + W_1 e^{-d_{11}\sqrt{q}} - e^{-m_{11}\sqrt{q}} & \cdots & W_m e^{-d_{1m}\sqrt{q}} - e^{-m_{1m}\sqrt{q}} \\
\vdots & \ddots & \vdots \\
W_1 e^{-d_{1m}\sqrt{q}} - e^{-m_{1m}\sqrt{q}} & \cdots & 1 + W_m e^{-d_{mm}\sqrt{q}} - e^{-m_{mm}\sqrt{q}}
\end{pmatrix} \]

and

\[ \hat{\Phi} = \begin{pmatrix}
\hat{\phi}_1 \\
\vdots \\
\hat{\phi}_m
\end{pmatrix}, \quad \hat{G} = \begin{pmatrix}
\hat{G}_1 \\
\vdots \\
\hat{G}_m
\end{pmatrix}. \]
To invert the matrix $M$, we shall use the form

$$M(x_1, \ldots, x_m) = I_m + \frac{N(x_1, \ldots, x_m)}{\sqrt{q}}$$

where

$$N(x_1, \ldots, x_m) = [W_j \left( e^{-d_{ij}\sqrt{q}} - e^{-m_{ij}\sqrt{q}} \right)]_{ij}$$

for $i, j = 1, m$ and the coefficients of $N(x_1, \ldots, x_m)$ are the algebraic functions $d_{ij}$ and $m_{ij}$ depending on $q$. Thus, for $q$ large, we have the formal expansion

$$M^{-1}(x_1, \ldots, x_m) = \left( I_m + \frac{N(x_1, \ldots, x_m)}{\sqrt{q}} \right)^{-1} = \sum_{k=0}^{\infty} \left( -\frac{N(x_1, \ldots, x_m)}{\sqrt{q}} \right)^k \approx I_m - \frac{N(x_1, \ldots, x_m)}{\sqrt{q}}. \quad (24)$$

The solution is then, $\hat{\Phi} = M^{-1} \hat{G}$. We will use below the first order approximation in power of $\frac{1}{\sqrt{q}}$ to estimate the leading order term of the mean extreme escape time.

We shall now compute the probability that the first particle escapes alive. Using relation (10), we have

$$\int_0^\infty J(s) ds = D \int_0^\infty \frac{\partial p}{\partial x}(x = 0, t|y) dt.$$

Differentiating relation (22) and evaluating the Laplace’s transform in $q = 0$,

$$D \int_0^\infty \frac{\partial p}{\partial x}(x = 0, t|y) dt = 1 - \sum_{i=1}^{m} V_i \hat{\phi}_i(0).$$

Finally, using relation (15), we get for the escape probability

$$P_\infty = 1 - \left( \sum_{i=1}^{m} V_i \hat{\phi}_i(0) \right)^n.$$

We shall now compute the EMFPT for the fastest. From formula (17), we expand in the short-time limit

$$s(t) = \left( 1 - \int_0^t J(s) ds \right)^n - \left( 1 - \int_0^\infty J(s) ds \right)^n.$$
We compute first

\[
\int_0^t J(s) \, ds = D \int_0^t \frac{\partial p}{\partial x} (x = 0, s \mid y) \, ds
\]

\[
= D \int_0^t \frac{\partial G}{\partial x} (x = 0, s \mid y) \, ds - D \sum_{i=1}^m V_i \int_0^t \phi_i(u) \frac{\partial G}{\partial x} (x = 0, s - u \mid x_i) \, du \, ds
\]

\[
= \text{erfc} \left( \frac{y}{\sqrt{4Dt}} \right) - D \sum_{i=1}^m V_i \int_0^t \phi_i(u) \text{erfc} \left( \frac{x_i}{\sqrt{4D(t-u)}} \right) \, du.
\]

For \( t \) small, the order of the integral

\[
F_i(t) = DV_i \int_0^t \phi_i(u) \text{erfc} \left( \frac{x_i}{\sqrt{4D(t-u)}} \right) \, du,
\]

depends on \( \phi_i(u) \) and \( \text{erfc} \left( \frac{x_i}{\sqrt{4D(t-u)}} \right) \) that are continuous and differentiable functions in \([0, t]\) and \((0, t)\) respectively. There is a function \( c(t) \in [0, t] \) such that

\[
F_i(t) = DV_i \phi_i(c_i(t)) \text{erfc} \left( \frac{x_i}{\sqrt{4D(t-c_i(t))}} \right) t,
\]

and, thus for \( t \) small, \( c_i(t) \) is small, and using the expansion for large argument of the \( \text{erfc}(x) \), we have the approximation,

\[
F_i(t) = O \left( \exp \left\{ -\frac{x_i^2}{4D(t-c_i(t))} \right\} \sqrt{(t-c_i(t))t^{1+k}} \right),
\]

where \( k \) is the order of \( \phi_i(c_i(t)) \). We have \( \phi_i(0) = 0 \) for \( x_i \neq y \). When \( x_i = y \), we have \( \phi_i(0) = 1 \), but in any case, we have that

\[
F_i(t) = O \left( \exp \left\{ -\frac{x_i^2}{4Dt} \right\} t^{3+k} \right) > O \left( \exp \left\{ -\frac{x_i^2}{4Dt} \right\} t^{\frac{3}{2}} \right).
\]

Then, for \( t \) small, the short-time asymptotic of \( s(t) \) is dominated by the short-time asymptotic of

\[
D \int_0^t \frac{\partial G}{\partial x} (x = 0, s \mid y) \sim \text{erfc} \left( \frac{y}{\sqrt{4Dt}} \right).
\]
Finally, we obtain from relation (17),

\[ \bar{\tau}_{EMFPT}(n) \sim \int_0^{\infty} \frac{\left(1 - \frac{\sqrt{4Dt}}{y\sqrt{\pi}} \right)^n - \left(\sum_{i=1}^{m} V_i \hat{\phi}_i(0)\right)^n}{1 - \left(\sum_{i=1}^{m} V_i \hat{\phi}_i(0)\right)^n} \, dt. \]

This integral is dominated for \( t \) small when \( n \) large, thus,

\[ \bar{\tau}_{EMFPT}(n) \sim \int_0^{\delta} \frac{\left(1 - n \frac{\sqrt{4Dt}}{y\sqrt{\pi}} \left(1 - \left(\sum_{i=1}^{m} V_i \hat{\phi}_i(0)\right)^n\right)\right)}{\exp \left\{ -\frac{y^2}{4Dt} \right\}} \, dt \]

\[ \approx \int_0^{\infty} \exp \left\{ -n \frac{\sqrt{4Dt}}{y\sqrt{\pi}} \left(1 - \left(\sum_{i=1}^{m} V_i \hat{\phi}_i(0)\right)^n\right)\right\} dt, \]

and proceeding as in [20], we get

\[ \bar{\tau}_{EMFPT}(n) \sim \frac{y^2}{4D \log \left(\frac{n}{\sqrt{\pi}(1 - \left(\sum_{i=1}^{m} V_i \hat{\phi}_i(0)\right)^n)}\right)}. \]

We shall now compute to leading order the term

\[ T(V_1, ..., V_n) = \sum_{i=1}^{m} V_i \hat{\phi}_i(0), \]

with respect with the initial parameter using the inverse matrix (24). In the first approximation,

\[ \hat{\phi}_i(0) = \sum_j \left( I_m - \frac{N(x_1, ..., x_m)}{\sqrt{q}} \right)_{ij} \hat{G}_j, \]

then,

\[ \sum_{i=1}^{m} V_i \hat{\phi}_i(q) = \sum_{i,j} \left( V_i \hat{G}_i(q) - V_i V_j \alpha_{ij}(q) \frac{\hat{G}_j(q)}{2\sqrt{Dq}} \right), \]

where \( \alpha_{ij}(q) = e^{-d_{ij}\sqrt{q/D}} - e^{-m_{ij}\sqrt{q/D}} \). Using the expression of the Laplace’s Green function below (25), we have

\[ \hat{G}(x_i, q \mid y) = \frac{1}{2\sqrt{Dq}} \left( \exp \left\{ -|y - x_i|/\sqrt{q/D} \right\} - \exp \left\{ -|y + x_i|/\sqrt{q/D} \right\} \right). \]
To conclude, at \( q = 0 \), we get

\[
T(V_1, \ldots, V_n) = \sum_{i=1}^{m} \frac{V_i}{2D} (|y - x_i| - |y + x_i|) - \sum_{i,j=1}^{m} \frac{V_i V_j}{2D^2} (|y - x_i| - |y + x_i|)(d_{ij} - m_{ij}).
\]

### 3.2 Survival probability with a \( \delta \)-Dirac killing measure

We compute here the extreme escape for first among \( n \) survival particles to escape alive in the presence of a Dirac killing measure at a single point \( x_1 \) located on the half-line \( x > 0 \). The survival probability is determined from equation (12). The FPE is given by

\[
\frac{\partial p(x, t \mid y)}{\partial t} = D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} - V_1 \delta(x - x_1)p(x, t \mid y) \tag{26}
\]

\[
p(x, 0 \mid y) = \delta(x - y)
\]

\[
p(0, t \mid y) = 0.
\]

The general solution of equation (26) is the integral equation

\[
p(x, t \mid y) = G(x, t \mid y) + V_1 \int_0^t \frac{p(x_1, s \mid y)}{2\sqrt{\pi D(t - s)}} \left( \exp \left\{ -\frac{(x - x_1)^2}{4D(t - s)} \right\} - \exp \left\{ -\frac{(x + x_1)^2}{4D(t - s)} \right\} \right) ds \tag{27}
\]

Setting \( x = x_1 \) in equation (27) reduces it to an integral equation in the single variable \( t \) for the unknown function \( \phi(t) = p(x_1, t \mid y) \). The solution \( p(x, t \mid y) \) is completely determined once \( \phi(t) \) is known. To compute this term, we use Laplace’s transform in time. The integral equation (27) becomes

\[
\hat{\phi}(q) = -V_1 \hat{\phi}(q) \left( 1 - \exp \left\{ -|x_1|\sqrt{\frac{2q}{D}} \right\} \right) + \hat{G}(x_1, q \mid y), \tag{28}
\]

where

\[
\hat{G}(x_1, q \mid y) = \frac{1}{2\sqrt{Dq}} \left( \exp \left\{ -|y - x_1|\sqrt{\frac{q}{D}} \right\} - \exp \left\{ -|y + x_1|\sqrt{\frac{q}{D}} \right\} \right).
\]

The solution is

\[
\hat{\phi}(q) = \frac{\hat{G}(x_1, q \mid y)}{1 + \frac{V_1}{2\sqrt{Dq}} \left( 1 - \exp \left\{ -|x_1|\sqrt{\frac{2q}{D}} \right\} \right)} = \frac{\exp \left\{ -|y - x_1|\sqrt{\frac{q}{D}} \right\} - \exp \left\{ -|y + x_1|\sqrt{\frac{q}{D}} \right\}}{V_1 \left( 1 - \exp \left\{ -x_1\sqrt{\frac{2q}{D}} \right\} \right) + 2\sqrt{Dq}}. \tag{29}
\]

13
We have
\[ \hat{\phi}(0) = \frac{|y + x_1| - |y - x_1|}{V_1^2 x_1 + 2D}. \] (30)

When \( \hat{\phi}(q) \) is known, we obtain the general solution of (27) as
\[ \hat{p}(x, q \mid y) = \hat{G}(x, q \mid y), \] (31)
\[ - V_1 \frac{\hat{\phi}(q)}{2\sqrt{D}q} \left( \exp \left\{ -|x - x_1|\sqrt{\frac{q}{D}} \right\} - \exp \left\{ -|x + x_1|\sqrt{\frac{q}{D}} \right\} \right) , \]
and thus,
\[ \hat{p}(x, q \mid y) = - \frac{V_1}{4Dq + V_1\sqrt{4Dq}} \left( 1 - \exp \left\{ -2|x_1|\sqrt{\frac{q}{D}} \right\} \right) e^{-|y-x_1|+|x-x_1|}\sqrt{\frac{q}{D}} \]
\[ - e^{-(|y+x_1|+|x-x_1|)\sqrt{\frac{q}{D}}} + e^{-(|y+x_1|+|x+x_1|)\sqrt{\frac{q}{D}}} - e^{-(|y-x_1|+|x+x_1|)\sqrt{\frac{q}{D}}} \]
\[ + \hat{G}(x, q \mid y). \] (32)

Dividing \( \hat{p}(x, q \mid y) = \hat{p}_1(x, q \mid y) + \hat{p}_2(x, q \mid y) + \hat{p}_3(x, q \mid y) + \hat{p}_4(x, q \mid y) \), we have
\[ \hat{p}_1(x, q \mid y) = - \frac{V_1}{4D} e^{-|y-x_1|+|x-x_1|}\sqrt{\frac{q}{D}} \]

Applying the inverse Laplace transform for each solution we get
\[ \mathcal{L}^{-1} \left( \frac{e^{-a\sqrt{q}}}{q + \sqrt{D}\frac{V_1}{2\sqrt{D}}} \right) = \exp \left\{ \frac{\alpha V_1}{2\sqrt{D}} + \frac{V_1^2}{4D} t \right\} \text{erfc} \left( \frac{\alpha}{2t^{1/2}} + \frac{V_1}{2\sqrt{D}t^{1/2}} \right) , \]
and then,
\[ \hat{p}_1(x, t \mid y) = - \frac{V_1}{4D} \exp \left\{ \frac{|y - x_1| + |x - x_1|V_1}{2D} \right\} \times \text{erfc} \left( \frac{|y - x_1| + |x - x_1|}{\sqrt{4Dt}} + \frac{V_1}{2\sqrt{D}t^{1/2}} \right) . \]

For \( t \) small, we have
\[ p_1(x, t \mid y) \approx - \frac{V_1}{4D} \exp \left\{ \frac{|y - x_1| + |x - x_1|V_1}{2D} \right\} \text{erfc} \left( \frac{|y - x_1| + |x - x_1|}{\sqrt{4Dt}} \right) \]
\[ p_2(x, t \mid y) \approx \frac{V_1}{4D} \exp \left( \frac{|y + x_1| + |x - x_1|V_1}{2D} \right) \text{erfc} \left( \frac{|y + x_1| + |x - x_1|}{\sqrt{4Dt}} \right) \]
\[ p_3(x, t, |y) \approx -\frac{V_1}{4D} \exp \left\{ \frac{(y + x_1 + |x + x_1|)V_1}{2D} \right\} \text{erfc} \left( \frac{(y + x_1 + |x + x_1|)}{\sqrt{4Dt}} \right) \]

\[ p_4(x, t, |y) \approx \frac{V_1}{4D} \exp \left\{ \frac{(y - x_1 + |x + x_1|)V_1}{2D} \right\} \text{erfc} \left( \frac{(y - x_1 + |x + x_1|)}{\sqrt{4Dt}} \right). \]

We shall now compute the probability that the first particle escape alive. Using relation (10), we have

\[
\int_0^\infty J(t) dt = D \int_0^\infty \frac{\partial p}{\partial x}(x = 0, t | y) dt.
\]

Differentiating relation (31) and evaluating in \(q = 0\), we get

\[
D \int_0^\infty \frac{\partial p}{\partial x}(x = 0, t | y) dt = 1 - V_1 \hat{\phi}(0).
\]

Finally, using relation (15) and (30), we get

\[
P_\infty = 1 - (V_1 \hat{\phi}(0))^n = 1 - \left( V_1 \frac{|y + x_1| - |y - x_1|}{V_1^2 |x_1| + 2D} \right)^n.
\]

We shall now compute the EMFPT for the fastest. From formula (17), we are looking for the short-time asymptotic of

\[
s(t) = \left( 1 - \int_0^t J(s) ds \right)^n - \left( 1 - \int_0^\infty J(s) ds \right)^n.
\]

As in the general case, using the expansion of the complementary error function for large argument, we get from relation (17)

\[
\bar{\tau}_{EMFPT}(n) \sim \int_0^\infty \left( 1 - \frac{\sqrt{4Dt} \exp \left\{ \frac{-y^2}{4Dt} \right\}}{y \sqrt{\pi} \left( 1 - (V_1 \hat{\phi}(0))^n \right)} \right) dt.
\]

This integral is dominated for \(t\) small when \(n\) large, thus,

\[
\bar{\tau}_{EMFPT}(n) \sim \int_0^\delta \left[ 1 - n \frac{\sqrt{4Dt} \exp \left\{ -\frac{y^2}{4Dt} \right\}}{y \sqrt{\pi} \left( 1 - (V_1 \hat{\phi}(0))^n \right)} \right] dt
\]

\[
\sim \int_0^\infty \exp \left\{ -n \frac{\sqrt{4Dt} \exp \left\{ -\frac{y^2}{4Dt} \right\}}{y \sqrt{\pi} \left( 1 - (V_1 \hat{\phi}(0))^n \right)} \right\} dt.
\]
and proceeding as in [20], we get

\[
\tilde{\tau}_\text{EMFPT}(n) \sim \frac{y^2}{4D \log \left( \frac{n}{\sqrt{\pi (1 - (V_1 \hat{\theta}(0))^n))} \right)}
\]

\[
\sim \frac{y^2}{4D \left[ \log \left( \frac{n}{\sqrt{\pi}} \right) - \log \left( 1 - \left( \frac{|y + x_1| - |y - x_1|}{V_1 2|x_1| + 2D} \right)^n \right) \right]}.
\]

We can also have the approximated escape time distribution from equation (33) as

\[
Pr \{ \tau^1 = t \} = -\frac{d}{dt} S(t) \sim -\frac{d}{dt} \left[ \exp \left\{ -n \sqrt{4D} t e^{-\frac{y^2}{4D(t)}} \right\} \right] \left( \frac{1}{y \sqrt{\pi}} \left( 1 - (V_1 \hat{\theta}(0))^n \right) \right) \left[ \frac{1}{2t} + \frac{y^2}{4D(t^2)} \right].
\]

Interestingly, there are two limit cases: when \( X = \left( \frac{|y + x_1| - |y - x_1|}{V_1 2|x_1| + 2D} \right) \ll 1, \)

\[-\log(1 - X^n) \approx X^n, \text{ thus}
\]

\[
\tilde{\tau}_\text{EMFPT}(n) \sim \frac{y^2}{4D \log \left( \frac{n}{\sqrt{\pi}} \right)}.
\]

(34)

If \( X = \left( \frac{|y + x_1| - |y - x_1|}{V_1 2|x_1| + 2D} \right) \approx 1, \)

we expand in \( Y = 1 - X, \) thus we get for the log term \(-\log(n(1 - X)^n - 1), \) finally,

\[
\tilde{\tau}_\text{EMFPT}(n) \sim \frac{y^2}{4Dn (\log(1 - X)^{-1})}
\]

and the arrival time for the fastest decay with \( 1/n, \) similar to a Poisson process.

### 3.3 Escape for the fastest with a uniform killing in half-line

We now consider the escape time for the fastest when the killing measure \( k(x, t) = V_0 \) is constant over the half line \( x > 0. \) The diffusion coefficient is \( D \) and the survival FPE for each individual particle is

\[
\frac{\partial p(x, t \mid y)}{\partial t} = D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} - V_0 p(x, t \mid y), \quad \text{for } x \in \mathbb{R}_+, \ t > 0
\]

\[
p(x, 0 \mid y) = \delta(y - x)
\]

\[
p(0, t \mid y) = 0.
\]

(36)
The solution is given by
\[ p(x, t | y) = \exp \{-V_0 t\} \frac{1}{2\sqrt{\pi Dt}} \left( \exp \left\{ -\frac{(x - y)^2}{4Dt} \right\} - \exp \left\{ -\frac{(x + y)^2}{4Dt} \right\} \right) \] (37)
and the flux is
\[ J(t | y) = D \frac{\partial p}{\partial x}(x = 0, t | y) = \exp \{-V_0 t\} \frac{y}{t\sqrt{4\pi Dt}} \left( \exp \left\{ -\frac{y^2}{4Dt} \right\} \right). \]

Thus using the inverse Laplace
\[ \int_0^\infty \frac{1}{\sqrt{\pi t^{3/2}}} e^{-at-b/t} dt = \frac{1}{2\sqrt{b}} \exp \{-2\sqrt{ab}\}, \]

we find the expression for the probability to escapes alive for one particle
\[ \int_0^\infty J(t | y) dt = \exp \left\{ -y\sqrt{\frac{V_0}{D}} \right\}, \]

Thus the probability that the first one escape alive in an ensemble of \( n \) is
\[ P_\infty = 1 - \left( 1 - \int_0^\infty J(t | y) dt \right)^n = 1 - \left( 1 - \exp \left\{ -y\sqrt{\frac{V_0}{D}} \right\} \right)^n. \]

Similarly, we obtain the expression for the total flux for a single particle
\[ \int_0^t J(s | y) ds = \int_0^t \frac{y \exp \{-V_0 s\} \exp \left\{ -\frac{y^2}{4Ds} \right\}}{\sqrt{4D\pi ss}} ds = \frac{1}{2} \left( \exp \left\{ -y\sqrt{\frac{V_0}{D}} \right\} \text{erfc} \left( \frac{y}{\sqrt{4Dt}} - \sqrt{V_0 t} \right) + \exp \left\{ y\sqrt{\frac{V_0}{D}} \right\} \text{erfc} \left( \frac{y}{\sqrt{4Dt}} + \sqrt{V_0 t} \right) \right). \]

For \( t \) small, using the expansion for the complementary error function we compute the numerator of the EMFPT (relation 25):
\[ s(t) \sim \left( 1 - \frac{e^{-\frac{y^2}{4Dt}}} {y\sqrt{\pi}} \left( \frac{e^{-y\sqrt{\frac{V_0}{D}}} + e^{y\sqrt{\frac{V_0}{D}}}}{2} \right) \right)^n - \left( 1 - e^{-y\sqrt{\frac{V_0}{D}}} \right)^n \]
\[ \sim 1 - \left( 1 - e^{-y\sqrt{\frac{V_0}{D}}} \right)^n + \sum_{k=1}^n \binom{n}{k} \left( \frac{e^{-\frac{y^2}{4Dt}} \sqrt{4Dt}} {y\sqrt{\pi}} \left( \frac{e^{-y\sqrt{\frac{V_0}{D}}} + e^{y\sqrt{\frac{V_0}{D}}}}{2} \right) \right)^k. \]
This, leads to the following integral dominated for $t$ small when $n$ large, thus,

$$
\tau_{EMFPT}(n) \sim \int_0^\delta \left[ 1 - n \frac{\sqrt{4Dt} \exp \left\{ -\frac{y^2}{4Dt} \right\} \left( e^{-y\sqrt{\frac{V_0}{D}}} + e^{y\sqrt{\frac{V_0}{D}}} \right) }{2y\sqrt{\pi} \left( 1 - \left( 1 - e^{-y\sqrt{\frac{V_0}{D}}} \right)^n \right)} \right] dt \quad (38)
$$

and proceeding as in [20], we get

$$
\tau_{EMFPT}(n) \sim \frac{y^2}{4D \log \left( \frac{n \left( e^{-y\sqrt{\frac{V_0}{D}}} + e^{y\sqrt{\frac{V_0}{D}}} \right)}{2\sqrt{\pi} \left( 1 - \left( 1 - e^{-y\sqrt{\frac{V_0}{D}}} \right)^n \right)} \right)} . \quad (39)
$$

Note that, when $V_0 = 0$, we recover the asymptotic formula for the case without killing and the Dirac-delta function as initial condition.

### 3.4 Killing in a finite interval in half a line with initial point outside the interval

We consider the diffusion of a particle that starts at a point $y$ outside the interval $[0, L]$. The pdf of that particle’s trajectory satisfies the equation

$$
\frac{\partial p(x, t \mid y)}{\partial t} = D \frac{\partial^2 p(x, t \mid y)}{\partial x^2} - V \chi_{[0,L]}(x)p(x, t \mid y) \quad \text{on } \mathbb{R}_+ \quad (40)
$$

$$
p(x, 0 \mid y) = \delta(x - y)
$$

$$
p(0, t \mid y) = 0.
$$

To compute the explicit solution, $p(x, t \mid y)$, we Laplace transform the equation with respect to $t$ and obtain the equation

$$
u''(x) - \left( \frac{q + V}{D} \right) u(x) = 0 \quad \text{for } x \in [0, L]
$$

$$
u''(x) - \left( \frac{q}{D} \right) u(x) = -\frac{1}{D} \delta(x - y) \quad \text{for } x \in (L, +\infty),
$$
where \( u(x, q) = \mathcal{L}(p(x, t \mid y)) \), and the bounded solutions in \( \mathbb{R}_+ \) are in the form
\[
\begin{align*}
u(x) &= A \exp \left\{ -\sqrt{\frac{q+V}{D}} x \right\} - A \exp \left\{ \sqrt{\frac{q+V}{D}} x \right\} \quad \text{for } x \in [0, L] \\
u(x) &= \frac{1}{\sqrt{4Dq}} \exp \left\{ -\sqrt{\frac{q}{D}} |x-y| \right\} + B \exp \left\{ -\sqrt{\frac{q}{D}} |x+y| \right\} \quad \text{for } x \in (L, +\infty).
\end{align*}
\]

We are looking for the solutions that are continuous at \( x = L \) and its first derivative is also continuous at \( x = L \), then solving the corresponding system we get
\[
\begin{align*}A &= - \frac{e^{\sqrt{D}(L-y)}}{D \left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) e^{-\sqrt{\frac{q+V}{D}} L} + \left( \sqrt{\frac{q+V}{D}} + \sqrt{\frac{q}{D}} \right) e^{\sqrt{\frac{q+V}{D}} L}} \left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) e^{-\sqrt{\frac{q+V}{D}} L} - \left( \sqrt{\frac{q+V}{D}} + \sqrt{\frac{q}{D}} \right) e^{\sqrt{\frac{q+V}{D}} L} \\
B &= \frac{\sqrt{4Dq} \left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) e^{\sqrt{\frac{q+V}{D}} L} + \left( \sqrt{\frac{q+V}{D}} + \sqrt{\frac{q}{D}} \right) e^{\sqrt{\frac{q+V}{D}} L}}{\sqrt{4Dq} \left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) e^{-\sqrt{\frac{q+V}{D}} L} + \left( \sqrt{\frac{q+V}{D}} + \sqrt{\frac{q}{D}} \right) e^{\sqrt{\frac{q+V}{D}} L}}.
\end{align*}
\]

Using relation (10), we have
\[
\begin{align*}
\int_0^\infty J(t) dt &= D \int_0^t \frac{\partial p}{\partial x}(x = 0, t \mid y) dt = D \frac{\partial u}{\partial x}(0, 0) = \frac{1}{\cosh \left( \sqrt{D} L \right)}.
\end{align*}
\]

For \( t \) small, we have
\[
\begin{align*}
\int_0^t J(s) ds &= D \int_0^t \frac{\partial p}{\partial x}(x = 0, s \mid y) ds \\
&\sim \int_0^t \left[ \mathcal{L}_s^{-1} \left( e^{-y\sqrt{D}} \right) - V L \mathcal{L}_s^{-1} \left( \frac{e^{-y\sqrt{D}}}{\sqrt{4Dq}} \right) \right] ds \\
&\sim \text{erfc} \left( \frac{y}{\sqrt{4Dt}} \right).
\end{align*}
\]

Then, we have
\[
P_\infty = 1 - \left( 1 - \int_0^\infty J(t \mid y) dt \right)^n = 1 - \left( 1 - \frac{1}{\cosh \left( \sqrt{D} L \right)} \right)^n.
\]
and

\[ s(t) \sim \left(1 - \frac{e^{-\frac{y^2}{4Dt} \sqrt{4Dt}}}{y\sqrt{\pi}}\right)^n - \left(1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)}\right)^n \]

\[ \sim 1 - \left(1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)}\right)^n + \sum_{k=1}^{n} \left(\begin{array}{c} n \\ k \end{array}\right) \left(\frac{e^{-\frac{y^2}{4Dt} \sqrt{4Dt}}}{y\sqrt{\pi}}\right)^k. \]

This, leads to the following integral dominated for \(t\) small when \(n\) large, thus,

\[ \tilde{\tau}_{EMFPT}(n) \sim \int_{0}^{\delta} \left[1 - n \frac{\sqrt{4Dt} \exp\left\{ -\frac{y^2}{4Dt}\right\}}{y\sqrt{\pi} \left(1 - \left(1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)}\right)^n\right)}\right] dt \]

\[ \sim \int_{0}^{\infty} \exp\left\{ -n \frac{\sqrt{4Dt} \exp\left\{ -\frac{y^2}{4Dt}\right\}}{y\sqrt{\pi} \left(1 - \left(1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)}\right)^n\right)}\right\} dt, \]

and proceeding as in [20], we get

\[ \tilde{\tau}_{EMFPT}(n) \sim \frac{y^2}{4D \log\left(\frac{n}{\sqrt{\pi} \left(1 - \left(1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)}\right)^n\right)}\right)}. \]

(41)

Note that, when \(V = 0\), we recover the asymptotic formula for the case without killing and the Dirac-delta function as initial condition. When \(V \gg 1\), then \(X = 1 - \frac{1}{\cosh\left(\sqrt{\frac{V}{D}}L\right)} \approx 1\), we expand in \(Y = 1 - X\), thus we get for the log term \(-\log(n(1 - X)^{n-1})\), finally,

\[ \tilde{\tau}_{EMFPT}(n) \sim \frac{y^2}{4Dn \left(\log\left(\cosh\left(\sqrt{\frac{V}{D}}L\right)\right)\right)} \]

(42)

and again, the arrival time for the fastest decay with \(1/n\), similar to a Poisson process.

### 3.5 Killing in a finite interval in half a line with initial point inside the interval

In this case, we consider the diffusion of a particle that starts at a point \(y\) inside the interval \([0, L]\), then the pdf of the particle’s trajectory satisfies the
But when we apply the Laplace Transform to this equation, we get

\[ u''(x) - \left( \frac{q + V}{D} \right) u(x) = -\frac{1}{D} \delta(x - y) \quad \text{for } x \in [0, L] \]

\[ u''(x) - \left( \frac{q}{D} \right) u(x) = 0 \quad \text{for } x \in (L, +\infty), \]

where \( u(x, q) = \mathcal{L}(p(x, t \mid y)) \). Here, the bounded solutions in \( \mathbb{R}_+ \) are in the form

\[
    u(x) = A \left( \exp \left\{ -\sqrt{\frac{q+V}{D}}|x-y| \right\} - \exp \left\{ -\sqrt{\frac{q+V}{D}}|x+y| \right\} \right) \\
    + \left( A - \frac{1}{\sqrt{4D(q+V)}} \right) \left( \exp \left\{ \sqrt{\frac{q+V}{D}}|x-y| \right\} - \exp \left\{ \sqrt{\frac{q+V}{D}}|x+y| \right\} \right) \quad \text{for } x \in [0, L] \\
    u(x) = B \exp \left\{ -\sqrt{\frac{q}{D}}x \right\} \quad \text{for } x \in (L, +\infty).
\]

Because we are looking for the continuous solutions at \( x = L \) with first derivative continuous at \( x = L \), we can solve the corresponding system and we get

\[
    A = \frac{-\left( \sqrt{\frac{q+V}{D}}+\sqrt{\frac{q}{D}} \right) \left( e^{\frac{q+V}{2D}(L-y)} - e^{\frac{q+V}{2D}(L+y)} \right)}{\left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) \left( e^{-\frac{q+V}{2D}(L-y)} - e^{-\frac{q+V}{2D}(L+y)} \right)} \\
    B = \frac{e^{-\sqrt{\frac{q}{D}}L}}{D \left( \sqrt{\frac{q+V}{D}} - \sqrt{\frac{q}{D}} \right) \left( e^{-\frac{q+V}{2D}(L-y)} - e^{-\frac{q+V}{2D}(L+y)} \right)}.
\]

Using relation (10), we have

\[
    \int_0^\infty J(t)dt = D \int_0^t \frac{\partial p}{\partial x}(x = 0, t \mid y) dt = D \frac{\partial u}{\partial x}(0, 0) = \exp \left\{ -y \sqrt{\frac{V}{D}} \right\}.
\]

For \( t \) small, we have

\[
    \int_0^t J(s)ds = D \int_0^t \frac{\partial p}{\partial x}(x = 0, s \mid y) ds = \int_0^t \mathcal{L}_s^{-1} \left( e^{-y \sqrt{s}} \right) ds = \text{erfc} \left( \frac{y}{\sqrt{4D}} \right).
\]

Then, as in the case for the uniform killing, we get the asymptotic

\[
    \bar{\tau}_{\text{EMFPT}}(n) \sim \frac{y^2}{4D \log \left( \frac{n \left( e^{-y \sqrt{\frac{V}{2}}} + e^y \sqrt{\frac{V}{2}} \right)}{2 \sqrt{\pi} \left( 1 - \left( 1 - e^{-y \sqrt{\frac{V}{2}}} \right)^n \right)} \right)}.
\]
If $V \gg 1$, then $X = 1 - e^{-y \sqrt{V}} \approx 1$, we expand in $Y = 1 - X$, thus we get for the log term $- \log(n(1-X)^{n-1})$, finally,

$$
\bar{\tau}_{EMFPT}(n) \sim \frac{y^2}{4Dn \left(y \sqrt{\frac{V}{D}}\right)}
$$

(43)

and again, the arrival time for the fastest decay with $1/n$, similar to a Poisson process.

### 4 Numerical Simulations

Finally, we have tested the accuracy of the asymptotic formulas found with stochastic simulations for the first escape time under the killing regime for the case of a Dirac-delta initial distribution $\delta(x-y)$ and different values of $n$ and the killing weight $V_1$. Due to the scheme for the states of particles (alive or dead)

$$
A \xrightarrow{V_1} D,
$$

(44)

where $V_1$ is the rate of being killed, the probability to be alive in the moment $t + \Delta t$ is $P_A(t + \Delta t) = P_A(t) - V_1 \cdot \Delta t \cdot P_A(t)$, and thus, the probability to kill each time the particle crosses the killing point is $V_1 \cdot \Delta t$. For the simulations the started point $y = 2$, the diffusion coefficient $D = 1$, the killing point $x_1 = 1$, and the time step $dt = 0.01$ were considered following the Euler’s scheme shown in Fig. 1A,

$$
x(t + \Delta t, i) = \begin{cases} 
x(t) + \sqrt{2D} \Delta w(t) & \text{w.p } 1 - V_1 \Delta t + o(\Delta t) \\
x(t) & \text{w.p } V_1 \Delta t + o(\Delta t)
\end{cases}
$$

(45)

The initial number of particles were not fixed, instead, an unknown number of particles were initiated until we reach $n$ survival particles with $n = [500 1000 2500 5000 10000]$. The mean escape time decays with the killing weight $V_1$ increase as predicted by formula eq. 33 and illustrated by numerical simulations (Fig 2A). In addition, the fastest particles crosses the killing point only a few times and this number decreases with an increasing killing weight (Fig 2B). Thus after the fastest particles has crossed the killing zone do not cross again, which would otherwise increases the killing probability. Finally, as $n$ increases, the fastest particle move directly in the direction of the absorbing point to exit. The EMFPT decreases with the number of survival particles (Fig 2C) as predicted by eq. 34. This figures shows a good agreement between the formula and stochastic simulations. When we now fix the initial number of particles $N_0 = [500 1000 2500 5000 10000]$, but not the number of survival particles, we
Figure 2: Influence of the killing rate on the escape time for the fastest particle. 

A. Stochastic simulations for the escape time distribution of the fastest \( \hat{\tau}^1 \) for particles distributed with respect to \( p_0(x) = \delta(x - y) \) with \( y = 2 \) and a killing point in \( x_1 = 1 \) for \( n = 10000 \) with 1000 runs. 

B. Decrease in the number of time the fastest particle crosses the killing point \( x_1 = 1 \) with the increasing of the killing weight for 1000 runs. 

C. EMFPT vs \( n \) obtained from stochastic simulations (colored disks) and the asymptotic formulas (continuous lines) with \( y = 2, x_1 = 1 \) and 1000 runs.
Figure 3: Influence of the killing rate on the escape time for a large number $N_0 \gg 1$ of initial particles. A. Stochastic simulations for the escape time $\bar{\tau}_1$ distribution of the fastest particles, when the initial distribution is $p_0(x) = \delta(x - y)$ with $y = 2$ and a killing measure at point $x_1 = 1$ for $N_0 = 10000$ with 1000 runs. B. EMFPT vs $N_0$ obtained from stochastic simulations (colored disks) and the asymptotic formulas (continuous lines) with $y = 2$, $x_1 = 1$ and 1000 runs. C. Influence of the killing weight $V_1$ in the number of survival particles. D. Decay of the number of time the fastest particle crosses the killing point $x_1 = 1$ when the killing weight increases (1000 runs).
obtain a very different statistics for the EMFPT: First, the mean escape time increases with the killing term (Fig.3A), and second the EMFPT increases with the killing probability (Fig.3B). Both effects are the consequences of decreasing the number of survival particles, leading to the correction term $\alpha$ in the asymptotic formula for the EMFPT, as shown in Fig.3B. When the killing weight $V_1$ increases, the number of arriving particles $n$ decreases, as shown in Fig.3C. In that regime, the fastest particles avoid crossing the killing point multiple times (Fig.3D).

5 Conclusions, applications, and perspective

We reported here various escape laws for the fastest particles to reach the boundary of an interval (dimension 1) when there are multiple killing processes. We derived explicitly formulas that revealed the mixed role of dynamics and killing that influences the fastest particle to escape.

This framework can be used to model generic biochemical processes, where signaling occurs through the fastest. This framework can also account for the time to activate an ensemble of chemical processes [21] or the time for a message to be transported when it is carried by few particles among many [10,22]. Finding a target is always key to activate subcellular process [1]. However, during that processes binding molecules can trap or destroy the path of the fastest. These binding molecules introduce delays, explained by formulas 33,38,39,41,42 and 43. However, these formula revealed that the distribution of killing sources has a small influence on the fastest arrival time.

There are ubiquitous examples where the present theory can be relevant: in the cell nucleus, transcription factors (TFs) are switching between different states before arriving to a small target site: the TFs are moving as a Brownian particles and can bind to various ligands to change state (acethylation or sumolysation [23]). Gene activation occurs in one appropriate state only. This example shows that the number of TFs can accelerate mARN production, but the time of arrival could be limited by killing processes: permanent binding of TFs. In a different context, calcium ions need to reach a target to activate neuronal or glial processes: all binding calcium molecules can interfere with the fastest ion to reach a small target. It would be interesting to extend the present study to higher dimensions.

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