Intermittent search process and teleportation

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The authors study an intermittent search process combining diffusion and “teleportation” phases in a d-dimensional spherical continuous system and in a regular lattice. The searcher alternates diffusive phases, during which targets can be discovered, and fast phases (teleportation) which randomly relocate the searcher, but do not allow for target detection. The authors show that this alternation can be favorable for minimizing the time of first discovery, and that this time can be optimized by a convenient choice of the mean waiting times of each motion phase. The optimal search strategy is explicitly derived in the continuous case and in the lattice case. Arguments are given to show that much more general intermittent motions do provide optimal search strategies in d dimensions. These results can be useful in the context of heterogeneous catalysis or in various biological examples of transport through membrane pores. © 2007 American Institute of Physics.

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I. INTRODUCTION

Chemical kinetics in a dense medium is often controlled by diffusion. In fact, the elementary reactive process should be described on the microscopic level, by quantum mechanics, but a classical, mesoscopic description is possible in the simple case of diffusion-limited reactions: the reaction is completed as soon as reactants meet (or with a given probability when they meet). In his pioneering work in 1917, von Smoluchowski used diffusion theory to calculate the rate of the diffusion-limited annihilation or capture reaction P+A → A for one spherical, immobile particle A, surrounded by particles P. He found that the reaction rate k(t) is time dependent and critically depends on the space dimension d: for d = 3, it tends at large times to the finite rate constant k = 4πRD, whereas for d = 1 and d = 2 its limit value is 0. These well known results have been extended in various directions, in particular, in the case of N mobile P particles (catalysts or predators, in the language of ecology) and one immobile A particle (target or prey) with a fluctuating reactivity. These studies confirm that the usual kinetic laws in general only hold in three dimensions (or more), and that even then they can break down, in particular, in asymptotic regimes.

A striking example where low-dimensional reaction paths drastically modify usual reaction kinetics is given to show that much more general intermittent motions do provide optimal search strategies in d dimensions. These results can be useful in the context of heterogeneous catalysis or in various biological examples of transport through membrane pores.

have the same mean duration (see also Refs. 15–19), which significantly accelerates the reaction. Such intermittent reaction paths combining two regimes, a “slow” reactive motion, during which the target can be discovered, and a “fast” but nonreactive motion, during which the searcher is unable to detect the target, have proved to play a crucial role in numerous search problems. In practice, the effect of low dimension on reaction kinetics is important if the targets A are located on the boundary ∂V of a domain V. The dynamics of a reactant P can then be described in a very general way as intermittent, similar to the above mentioned case of a protein reacting on a specific site on DNA:P will alternate adsorbed phases on the interface ∂V, where diffusional transport and reaction can occur, interrupted by bulk phases of free motion in the interior of V where targets A are absent. The case of a bidimensional boundary ∂V is widely realized in chemistry in the case of heterogeneous catalysis (see Fig. 1), or in the physics of porous media.

Another example comes from physiology: mammalian respiration can be described as O₂ molecules (reactants P) diffusing in the gas exchange units of lungs, called acini, toward their alveolar membrane, until they are adsorbed through a membrane pore (a target A). At a smaller scale, cell biology provides further examples of such P+A → A trapping reactions. Indeed, molecular (and, in particular, ionic) transport across channels of the cell membrane or even viral infection through the cell membrane involve a searcher P (molecule or virus) alternating bulk diffusion in the intracellular medium and adsorbed phases on the cell membrane before entering the cell through a “gate” A (channel or membrane receptor, see Fig. 1).

In this article, we present a model of intermittent search process which generalizes our one-dimensional model of protein search on DNA, later generalized by Eliazar et al. This model applies, in particular, in studying the above mentioned reactions of type P+A → A or the catalytic reaction.
P+A → C+A, where A are immobile targets located on a d-dimensional space Ω = ∂V. A mobile molecule P diffuses in Ω and interacts with an A as soon as it reaches it. However, at stochastic times, P is desorbed from Ω and performs a bulk excursion inside V (where no A is present) before readsoing on Ω and diffusion again. The main hypothesis of our model is to treat these bulk excursions as “teleportation” phases: we assume that P is randomly relocated in Ω after an exponentially distributed time or, more generally, after a stochastic time with a finite average, independent of this displacement (see Ref. 34 for related models). Keeping in mind the example of heterogeneous catalysis where Ω is a two-dimensional plane, a teleportation is an approximate of a three-dimensional diffusive excursion in the bulk in the following limit (Fig. 1): the volume V must be finite to ensure a finite mean return time (as opposed to power law distributions obtained for infinite V), and the typical distance covered during such a bulk phase must be larger than the typical intertarget distance to ensure that return locations are effectively uncorrelated. Note that a finite accessible volume V can be realized by a confining attractive potential (electrostatic for instance) toward the interface Ω. The net gain of such intermittent behavior is not clear, since teleportation is time consuming but, in principle, unproductive since no reaction can occur during such phases. We shall, however, treat this problem explicitly and show that intermittence permits one to minimize the time of first arrival of P at A (or search time) and thus, to hasten the reaction and increase the reaction rate. First, we present our d-dimensional continuous model, solve the corresponding equations, and compute the average search time of A. We treat the optimization problem and show that the search can be made much shorter, thanks to intermittence. Then, we consider a similar lattice model and prove that the optimization is also possible, but that the conditions for obtaining it can be significantly different. Eventually, we show that the conclusions can be extended to much more general stochastic search processes in an arbitrary d-dimensional space.

II. CONTINUOUS DIFFUSION IN A SYSTEM WITH SPHERICAL SYMMETRY

A. Model

We consider a point P searching for a given, immobile target. P moves in a finite region of a d-dimensional space, represented by a d-dimensional sphere B of radius b with a reflecting internal surface. The target is a concentric sphere A of radius a < b (Fig. 2). However, the searcher can only recognize the target when his sensors are activated. In fact, the searcher undergoes an intermittent movement, alternating between two dynamical regimes i = 1, 2.

1. During regime 1 (diffusion), he performs an isotropic diffusion, and its sensors are activated: he finds the target as soon as he reaches it in this regime.

2. During regime 2 (teleportation), the searcher is relocated with uniform probability at any point of sphere B. During the teleportation, however, his sensors are inactivated and the target cannot be found.

The duration $T_i$ of each regime $i$ is a stochastic variable independent of other events, with an exponential law:

$$P(T_i > t) = \exp(-\lambda_i t),$$

with $i=1,2$, the frequencies $\lambda_i$ being constant parameters.

The question is to find the optimal strategy—if any—to reach the target as rapidly as possible.

FIG. 1. Heterogeneous catalysis (left) and transport through a cell membrane (right) as an intermittent search process. The reactant (searcher P) freely diffuses in a three-dimensional confined volume (gray path) until it reaches the two-dimensional planar or spherical interface, where it remains adsorbed and diffuses during a random waiting time (black path), before desorbing back to the bulk. The process is continued until P reaches a target A (dark circles).

FIG. 2. Intermittent search with teleportation. Searcher, point P; target, sphere A with radius a; search domain, sphere B with radius b.
### B. Mean search time

In this problem, a basic variable is the search time $T_r$, i.e., the first arrival time $T_r$ of $P$ at the target $A$ in regime 1, starting from the initial position $x$. Let $F(t|x)$ be its probability density, and $F(t)=\langle F(t|x) \rangle_P$ its average over the uniform initial distribution of $P$ in volume $B$. It can be shown (see Sec. IV and Ref. 4) that the Laplace transform of $F(t)$, $\hat{F}(s)=\int_0^\infty e^{-st}F(t)$, is given by

$$
\hat{F}(s) = \frac{\langle \tilde{j}_1(\lambda_1+s|x) \rangle_B + v(A)/v(B)}{1 - (1 - v(A)/v(D) - \langle \tilde{j}_1(\lambda_1+s|x) \rangle_B)/(1 + s/\lambda_1)(1 + s/\lambda_2)},
$$

where $A$ is the space occupied by the target, $B$ the total available space, and $v(A)$ and $v(B)$ are the respective volumes of these regions.

Here $\tilde{j}$ is the Laplace transform of the first arrival density which is given \(^{35}\) by

$$
\tilde{j}_1(\lambda_1+s|x) = \left( \frac{d}{a} \right) \frac{D_{\nu,-}(r(\lambda_1+s)/D,b(\lambda_1+s)/D)}{D_{\nu,-}(a(\lambda_1+s)/D,b(\lambda_1+s)/D)},
$$

where $r=|x|$ and $D_{\nu,-}(x,y)=I_\nu(x)K_{\nu-1}(y)+K_\nu(x)I_{\nu-1}(y)$. $I_\nu(x)$ and $K_\nu(x)$ are modified Bessel functions \(^{36}\) with

$$
\nu = 1 - \frac{d}{2},
$$

After lengthy calculations (see Appendix A), we obtain

$$
\hat{F}(s) = \frac{-k(Y_1/X_1) + a^d/b^d}{1 - (1 - a^d/b^d + k(Y_1/X_1))/(1 + s/\lambda_1)(1 + s/\lambda_2)},
$$

with

$$
k = \frac{d}{b^d} \left( \frac{D}{\lambda_1+s} \right)^{1/2} a^{d-1},
$$

and

$$
X_\nu = K_{\nu-1} \left( b \sqrt{\frac{\lambda_1}{D}} \right) I_\nu \left( a \sqrt{\frac{\lambda_1}{D}} \right)
+ K_\nu \left( a \sqrt{\frac{\lambda_1}{D}} \right) I_{\nu-1} \left( b \sqrt{\frac{\lambda_1}{D}} \right),
$$

$$
Y_\nu = K_{\nu-1} \left( b \sqrt{\frac{\lambda_1}{D}} \right) I_\nu \left( a \sqrt{\frac{\lambda_1}{D}} \right)
- K_\nu \left( a \sqrt{\frac{\lambda_1}{D}} \right) I_{\nu-1} \left( b \sqrt{\frac{\lambda_1}{D}} \right).
$$

The mean time $\langle T \rangle$ is a relevant quantity to characterize the efficiency of the searcher. It is obtained from the derivative of the first passage density:

$$
\langle T \rangle = \left( \frac{\partial \hat{F}(s)}{\partial s} \right)_{s=0},
$$

which yields

$$
\langle T \rangle = \frac{\lambda_1 + \lambda_2 [(b/a)^d - 1]X_\nu + (d/a) \sqrt{D/\lambda_1} Y_\nu}{\lambda_1 \lambda_2}
- X_\nu - (d/a) \sqrt{D/\lambda_1} Y_\nu.
$$

This exact, explicit formula (10) is most useful for minimizing the mean search time as a function of the parameters, which is an important point in most practical cases. Since $a$, $b$, and $D$ are determined by the geometrical and physical properties of the medium, the relaxation frequencies $\lambda_1$ and $\lambda_2$, or the mean durations $\tau_1=1/\lambda_1$ and $\tau_2=1/\lambda_2$ of phases 1 and 2, are the main adjustable parameters.

### C. Optimization of the mean search time

The optimization with respect to $\lambda_2$ is obvious: the time lost in teleportation should be as short as possible, since the result is independent of it, so that $\lambda_2$ should be as high as possible. We now consider the minimization of $\langle T \rangle$ with respect to $\lambda_1$. From expression (10), the mean search time can be written as

$$
\langle T \rangle = \frac{\lambda_1 + \lambda_2 [(b/a)^d - 1] + 2(Z(x)/x)}{\lambda_1 \lambda_2}
- \frac{1 - 2(Z(x)/x)}{1 - 2(Z(x)/x)},
$$

with $Z(x)=-K_{\nu-1}(x)/K_\nu(x)$ and $x=a \sqrt{\lambda_1/D}$.

The analysis of the exact expression (11) has been treated numerically in the important cases of two and three dimensions (Figs. 3 and 4).

It is seen that two cases can occur: for small values of $\lambda_2$, $\langle T \rangle$ increases with $\lambda_1$, and the minimal value is obtained by choosing $\lambda_1=0$, or $\tau_1=\infty$, thus having an uninterrupted diffusive regime. Then, intermittence is not favorable to the search and should be avoided. On the other hand, for large values of $\lambda_2$, $\langle T \rangle$ decreases with $\lambda_1$ for small $\lambda_1$, it has a minimum for a finite value $\lambda_1$ of $\lambda_1$, and it increases for $\lambda_1 > \lambda_1$. Then, intermittence is favorable to the search and it allows reducing the search time substantially.

The critical value $\lambda_{c2}$ separating these regimes can be obtained explicitly, depending on the dimension $d$. It is given by simple expressions in the usual case $b/a \gg 1$. In two dimensions,
In three dimensions, \( \lambda_2^c \) is much larger than the volume of the search region \( B \). We now assume that the volume of the search region \( B \) is much larger than the volume of the search region \( B \).

\[
\lambda_2^c \sim \frac{96D \ln(b/a)}{7b^2} \quad \text{when } b \gg a.
\] (12)

If \( \lambda_2 > \lambda_2^c \), the optimal value \( \lambda_1 \) can be computed numerically. It is also possible to obtain simple approximations in specific situations. Such a situation occurs in the important case of the small density limit, which is currently observed.

**Small density limit.** We now assume that the volume of the search region \( B \) is much larger than the volume of the search region \( B \).
target $A : b^d \gg a^d$. Furthermore, we suppose that $b^2 \gg D / \lambda_1$, which implies that the average fraction of $B$ explored during a single diffusive phase is very small. Then,

$$Z(x) \sim -\frac{K_{p-1}(x)}{K_p(x)}. \quad (14)$$

On the other hand, we may assume that $b$ is large enough to satisfy

$$\left( \frac{b}{a} \right)^b \gg d \left| \frac{Z(x)}{x} \right|. \quad (15)$$

Then, formula (10) simplifies very much and allows for a simple analytical optimization of $\langle T \rangle$ in the cases of short and long waiting times. As we proceed to show, condition (12) or (13) is compatible with both cases, leading to a non-trivial optimization of the search time for $\lambda_2$ fixed.

Short waiting times. Let us first consider the case $x = a \sqrt{\lambda_1 / D} \gg 1$, or $\tau_1 \gg \tau = a^2 / D$. Then, $Z(x) \sim -1$, inequality (15) clearly holds, and the exact formula (10) can be approximated by

$$\langle T \rangle \sim \frac{1}{2} \left( \frac{b}{a} \right)^b \frac{\lambda_1 + \lambda_2}{\lambda_1 \lambda_2} \frac{x}{x + d}. \quad (16)$$

It is easily found that this expression reaches its minimal value if

$$\lambda_1 = \lambda_2 \left[ 1 + \frac{2}{d} \sqrt{\frac{\lambda_1 a^2}{D}} \right]. \quad (17)$$

Then, the assumption $x = a \sqrt{\lambda_1 / D} \gg 1$ implies that $a \sqrt{\lambda_2 / D} \gg 1$ and the optimal value $\bar{\lambda}_1$ of $\lambda_1$ is

$$\bar{\lambda}_1 \sim \frac{2}{d} \frac{a^2}{D} \lambda_2^2. \quad (18)$$

In other words, this case applies when the waiting times $\tau_1$ and $\tau_2$ are both much smaller than the characteristic time $\tau = a^2 / D$: when the optimal value of $\tau_1$ scales as $\tau_2^2$, we have $\tau_1 \ll \tau_2 \ll \tau$ and

$$\frac{\tau_1}{\tau} \sim \left( \frac{d}{2} \right) \left( \frac{\tau_2^2}{\tau} \right). \quad (19)$$

It should be remarked that in this case, the searcher spends more time in teleportation, although he cannot find the target in this regime, than in diffusion. This counterintuitive result had also been noticed in the case of alternating diffusion with ballistic motion. Then, the minimum search time is simply

$$\langle T \rangle_{\text{min}} = \frac{1}{2} \left( \frac{b}{a} \right)^d \tau_2. \quad (20)$$

These results hold in any dimension $d$. Thus, $\langle T \rangle_{\text{min}}$ has its effective smallest value when $\tau_2$ has its minimum possible value $\tau_{2\text{min}}$, as it has been already pointed out.

The efficiency of intermittence can be characterized by the ratio $E = \langle T \rangle_{\text{diff}} / \langle T \rangle_{\text{min}}$, $\langle T \rangle_{\text{diff}}$ being the search time in a purely diffusive regime (Appendix C). It is found that if $b \gg a$, in one, two, and three dimensions, $E$ has the respective values

$$E = \begin{cases} (2/3)(ab / D \tau_2) = (2/3)(b/a)(\pi / \tau_2) & \text{if } d = 1 \\ (a^2 / D \tau_2) \ln(b/a) = (\ln(b/a) / \pi \tau_2) & \text{if } d = 2 \\ (2/d(d-2)) / (\pi \tau_2) & \text{if } d \geq 3. \end{cases} \quad (21)$$

Thus, $E$ is much larger than 1 if $\tau_2 \ll \tau$ and, in one and two dimensions, $b/a \gg 1$. The latter enhancement factor disappears in three or higher dimensions. As a conclusion, in the limit of short waiting times $\tau_2$, or high frequencies $\lambda_2$, the efficiency is proportional to $\lambda_2$ in any dimension, as confirmed by numerical analysis (Fig. 5). It is clear that the efficiency of intermittence depends on the minimum possible value $\tau_{2\text{min}}$, and that it decreases as dimension $d$ increases. Nevertheless, intermittence can always be a favorable search.
strategy if $\tau_2$ can be made sufficiently small, and if the minimum realizable value of $\tau_1(\tau_{\text{min}})$ allows one to reach the optimal value $\tau_1$.

**Long waiting times.** The opposite limit of long waiting times, when both $\tau_1$ and $\tau_2$ are much larger than $\tau$, is in principle less favorable, and conditions (12) and (13) impose upper bounds on $\tau_2$ for intermittence to be favorable. Nevertheless, these conditions can be satisfied even with $\tau_2 \gg \tau$, and the case of long waiting times may allow one to minimize the search time for a finite value of $\tau_1$. This case is observed in practice if the characteristic time $\tau$, which is imposed by physical conditions, is much shorter than $\tau_{\text{min}}$ and $\tau_{\text{min}}$. It is shown in Appendix C that in this situation intermittence again allows one to reduce the search time significantly in one and two dimensions, but this strategy loses its interest in higher dimensions. More precisely, in one dimension, the optimal value of $\lambda_1$ is

$$\lambda_1 \sim \lambda_2$$

so that $\tau_1 \sim \tau_2 \ll \tau$; both waiting times should be equal, which was indeed the result found in Ref. 20 concerning the search of specific DNA site by a protein.

Furthermore,

$$\langle T \rangle_{\text{min}} \sim \frac{2b}{\sqrt{D} \tau_2}$$

and the efficiency is

$$E = \frac{2b}{3} \sqrt{\frac{\tau}{\tau_2}}$$

Here $(\tau/\tau_2)^{1/2} \ll 1$, but the large factor $b/a$ can allow the efficiency to be much larger than 1. In Two dimensions, the optimal value of $\lambda_1$ is

$$\lambda_1 = \frac{\lambda_2}{\ln(\gamma)} \left[ 1 - \frac{\ln(\gamma)}{\gamma} \right],$$

with $\gamma = \ln(a^2 \lambda_2/D)$, corresponding to the minimum search time

$$\langle T \rangle_{\text{min}} \sim \frac{b^4}{4D} \left[ \gamma + \ln(\gamma) \right].$$

and the efficiency of intermittence is

$$E \sim \frac{\ln(b^2/a^2)}{\ln(\tau_2/\tau)}.$$  

It can still be large for large values of $b/a$.

However, in three or more dimensions, it is shown that the efficiency cannot be significantly larger than 1 if $\tau_2 > \tau$, then, intermittence is only an interesting search strategy if $\tau_2 \ll \tau$.

Part of the conclusion of this section is extended qualitatively to more general situations in Sec. IV.

### III. DISCRETE SYSTEMS

We now assume that the searcher $P$ moves on a regular lattice.

#### A. One-dimensional lattice

Consider $N=2L+1$ equally spaced lattice points on an axis 0x. (Fig. 6) Between coordinates $-L$ and $L$ a target is located at coordinate 0. The searcher $P$ now switches between two dynamic regimes.

(i) During regime 1, $P$ performs a continuous time random walk between points $-L$ and $L$ which are reflecting points, whereas $A$ is absorbing. The transition rate from one lattice point $x$ to any of its next neighbours is $p/2$.

(ii) During regime 2, or teleportation, $P$ is randomly relocated on any lattice points in $(-L,L)$.

(iii) The duration $T_i$ of regime $i$ ($i=1,2$) is an exponential, independent, variable.

Mean search time. Formula (2) still applies and gives the Laplace transform of the search time density:
\[ \hat{F}(s) = \frac{\langle j_1(s|x) \rangle + 1/(2L + 1)}{1 - (1 - 1/(2L + 1)) - \langle j_1(s|x) \rangle/(1 + s/\lambda_1)(1 + s/\lambda_2)}, \]

(28)

where \( \langle j_1(s|x) \rangle \) is the Laplace transform of the search time density in regime 1, average on the initial position \( x \). Using Montroll’s paper\textsuperscript{37} and Hughes’ book\textsuperscript{38} in continuous time, it is found that

\[ \langle j_1(s|x) \rangle = \frac{1}{N} \left[ \frac{1}{(1 - p/(p + s))P(0,p/(p + s))} - 1 \right], \]

(29)

where \( P(0,z) \) is the generating function for all walks which start and end at the origin.

\[ \langle T \rangle = \frac{\lambda_1 + \lambda_2}{\lambda_1 \lambda_2} \frac{2L(\lambda_1 + p) - \alpha(2^{2L+1} + p^{2L+1}) - p(p + \alpha)(p^{2L} - \alpha^{2L})}{(2p + \lambda_1)(p^{2L+1} - \alpha^{2L+1})}, \]

with \( \alpha = \lambda_1 + p - \sqrt{\lambda_1 \lambda_2 + 2p} \).

**Optimization of the mean search time.** It can be seen that \( \langle T \rangle \) can have three possible behaviors as a function of \( \lambda_1 \) (Fig. 7).

(i) If \( p/\lambda_2 < 2L/(2L+1) \), \( \langle T \rangle \) increases continuously with \( \lambda_1 \), and \( \langle T \rangle \) is minimum if \( \lambda_1 = 0 \).

(ii) If \( 2L/(2L+1) < p/\lambda_2 < (2/15)(3L+L^2) \), \( \langle T \rangle \) is minimum for a finite value \( \lambda_1 \) of \( \lambda_1 \).

(iii) If \( p/\lambda_2 > (2/15)(3L+L^2) \), \( \langle T \rangle \) decreases with \( \lambda_1 \) and the minimization of the search time requires choosing \( \lambda_1 \) as large as possible.

It may be noticed that with condition (iii), \( \langle T \rangle \) decreases with \( \lambda_1 \) to a lower bound. Then, intermittence is always favorable. This is the main difference with the continuous model where this situation cannot occur. We will see in Sec. V that this behavior can be observed in more general intermittent systems with teleportation, but not if the search regime 1 is diffusive.

**Small density limit.** For \( L \to \infty \), \( \langle T \rangle \) can be approximated by

\[ \langle T \rangle = \frac{2\lambda_1 + \lambda_2}{\lambda_1 \lambda_2} \frac{1}{\sqrt{1 + 2(p/\lambda_1)}} \]

(33)

In this limit, condition (iii) cannot be satisfied, but one can obtain a minimum search time for a finite value of \( \lambda_1 \), if \( p > \lambda_2 \). Then, the optimal value of \( \lambda_1 \) is given by

\[ \lambda_1 = \frac{p}{p - \lambda_2} \lambda_2. \]

If \( p > \lambda_2 \), the random walk is approximately a diffusion and one finds that \( \lambda_1 \sim \lambda_2 \), as in the one-dimensional continuous case.

\[ P(0,z) = \frac{1}{N} \sum_{k=0}^{N-1} \frac{1}{1 - z \cos(2\pi k/N)} = \frac{1 + x^N}{1 - x^2 \sqrt{1 - z^2}}, \]

(30)

with

\[ x = \frac{1}{\sqrt{1 - z^2}}. \]

(31)

Eventually, after straightforward but lengthy calculations, \( \langle T \rangle \) writes

\[ \langle T \rangle = \frac{\lambda_1 + \lambda_2}{\lambda_1 \lambda_2} \frac{2L(\lambda_1 + p) - \alpha(2^{2L+1} + p^{2L+1}) - p(p + \alpha)(p^{2L} - \alpha^{2L})}{(2p + \lambda_1)(p^{2L+1} - \alpha^{2L+1})}, \]

(32)

**B. Two-dimensional lattice**

For a simple random walk on a square lattice of \( m \times m \) points, we have\textsuperscript{37,39}

\[ P(0,z) = \frac{1}{m^2} \sum_{k_1=0}^{m-1} \sum_{k_2=0}^{m-1} \frac{1}{1 - (1/2)(c_{k_1} + c_{k_2})}, \]

(35)

with \( c_k = \cos(2\pi k/m)0 \leq z \leq 1 \),

or

\[ P(0,z) = \frac{1}{m} \sum_{k=0}^{m-1} \frac{1}{1 - (1/2)c_k - \rho_k^2} - \frac{1}{1 - \rho_k^{-2}}. \]

(36)

where \( \rho_k = z(2 - c_k) \) and \( c_k = (1 - (1 - \rho_k^2)^{1/2})\rho_k^{-1} \).

It is found numerically that the three situations described in Sec. III A can occur (Fig. 8).

(i) For very small values of \( \lambda_2 \) (with respect to \( p \)), \( \langle T \rangle \) continuously increases with \( \lambda_1 \), and it is minimum for \( \lambda_1 = 0 \): intermittence is not favorable.

(ii) For intermediary values of \( \lambda_2 \), \( \langle T \rangle \) is minimum for a finite value \( \lambda_1 \) of \( \lambda_1 \).

(iii) For large values of \( \lambda_2 \), \( \langle T \rangle \) decreases with \( \lambda_1 \) and the search is optimized by taking \( \lambda_1 \) as large as possible. Because of the complexity of analytical formulas, it is difficult to give precise conditions for observing these situations.

In case (ii), numerical calculations of the optimal value \( \lambda_1 \) show that it can be approximately estimated by formula (25) of the two-dimension case when \( p \to \infty \).

**IV. MEAN SEARCH TIME: GENERAL RESULTS**

The intermittent motion of a point searcher alternating a slow motion (regime 1), which allows for the detection of an immobile target, and a fast motion (regime 2) without detec-
tion can be formulated more generally when the search region is any d-dimensional finite volume B and the target is a subvolume A included into B. General conclusions can be obtained although specific models are necessary to get explicit formulas. We now describe this general formalism.

Search regime 1. During this regime, the target is found as soon as P is in B. \( q_1(t|x) \) is the survival probability of the target at time \( t \) under regime 1, starting from \( x \).

The duration \( T_1 \) of regime 1 is an exponential stochastic variable, independent of other events,

\[
P(T_1 > t) = e^{-\lambda_1 t}.
\]

Thus, the probability density that regime 1 finishes at time \( t \) without discovering the target is

\[
\bar{p}_1(t|x) = \lambda_1 e^{-\lambda_1 t} q_1(t|x).
\]

Move regime 2. During this regime, P is redistributed in volume B with a given stationary density \( p_0(y) \), independent of its initial position \( x \) and of the duration of this regime. Teleportation corresponds to the special case of a uniform stationary density. The duration \( T_2 \) of regime 2 is a stochastic variable, independent of other events, not necessarily exponential in a general case. We denote its probability density \( q_2(t) = -d\psi_2(t)/dt, \psi_2(t) \) being the survival probability of regime 2 after a time \( t \).

Overall survival probability. The overall survival probability of P at time \( t \), starting at time 0 from position \( x \in B \), and knowing that P has previously experimented \( 2n \) regime changes at times \( 0 < t_1 < t_2 < \ldots < t_{2n} < t \), is clearly given by

\[
S_{2n}(t|t_1 \cdots t_{2n}) = \prod_{1 \leq k \leq n} \bar{p}_1(\tau_{2k-1}) \int_{x \in B-A} dx_2 \cdots dx_{2n},
\]

where \( \bar{p}_1(\tau) = \int_{x \in B-A} dx \bar{p}_1(\tau|x)p_0(x) \) and \( q_1(\tau) = \int_{x \in B-A} dx q_1(\tau|x)p_0(x) \).

Thus, the average probability that P survives at time \( t \) after \( 2n \) regime changes is

\[
S_{2n}(t) = \prod_{1 \leq k \leq n} \left[ d\tau \int_{\tau_{2k-1}}^{\tau_{2k}} e^{-\lambda_1 \tau} \right] \prod_{1 \leq k \leq n} [d\tau_{2k} e^{-\lambda_2 \tau}] S_{2n}(t|t_1 \cdots t_{2n}),
\]

and its Laplace transform is

\[
\tilde{S}_{2n}(s) = \left[ \lambda_1 \tilde{q}_1(s + \lambda_1) \right]^n \tilde{q}_1(s + \lambda_1) \tilde{\varphi}_2(s)^n,
\]

where \( \tilde{q}_1(s) \) and \( \tilde{\varphi}_2(s) \) are the Laplace transforms of \( q_1(t) \) and \( \varphi_2(t) \). Similarly, it is found that the Laplace transform of the survival probability after \( 2n + 1 \) regime changes is

\[
\tilde{S}_{2n+1}(s) = \left[ \lambda_1 \tilde{q}_1(s + \lambda_1) \right]^{n+1} \tilde{\varphi}_1(s),
\]

with \( \tilde{\varphi}_1(s) = (1 - \varphi_2(s))/s \) being the Laplace transform of \( \varphi_2(t) \); the survival probability of regime 2.

Summing Eqs. (42) and (43) over \( n \) yields the Laplace transform of the overall survival probability of particle P:

\[
\tilde{S}(s) = \frac{\tilde{q}_1(s + \lambda_1) [\lambda_1 \tilde{\varphi}_2(s) + 1]}{1 - \lambda_1 \tilde{q}_1(s + \lambda_1) \tilde{\varphi}_2(s)}.
\]

In the case of a uniform stationary probability density (teleportation), we have

\[
\tilde{q}_1(s) = \frac{1}{v(B)} \int_{x \in B-A} dx \left[ 1 - \tilde{J}_1(s|x) \right] = \frac{1}{s} \left[ \beta - \langle \tilde{J}_1(s) \rangle_B \right],
\]

where \( \tilde{J}_1(s|x) \) is the Laplace transform of the search time density during regime 1, and \( \langle \tilde{J}_1(s) \rangle_B \) is its average on region B. Furthermore, \( v(A) \) and \( v(B) \) are the volumes of A and B, and \( \beta = 1 - \alpha = (v(A) - v(B))/v(B) \).
As a result, if the initial density is uniform and if $T_2$ is exponential, the Laplace transform $\tilde{F}(s)$ of the mean search time density $-\partial S(t)/\partial t$ is given by

$$\tilde{F}(s) = \frac{\langle j_1(s|x) \rangle_B + \alpha}{1 - (1 - \langle j_1(s|x) \rangle_B) / (1 + s/\lambda_1)(1 + s/\lambda_2)}. \quad (46)$$

**Mean search time.** The mean search time $\langle T \rangle$ is obtained by taking $s=0$ in formula (44):

$$\langle T \rangle = \frac{\tilde{q}_1(\lambda_1)}{1 - \lambda_1 \tilde{q}_1(\lambda_1)} \left( 1 + \frac{\lambda_1}{\lambda_2} \right). \quad (47)$$

where we have noticed that $\varphi_2(0)=1$ if waiting time $T_2$ is finite with probability 1 and that $\tilde{\varphi}_2(0)=r_2=1/\lambda_2$ is the mean duration of regime 2. If $r_2$ is infinite, the mean search time is also infinite. Similar, more precise results are given in Ref. 33 but are not used here.

Let us assume that the mean duration of regime 2 is finite. $\langle T \rangle$ is obviously a decreasing function of $\lambda_2$, or an increasing function of $r_2$, so that $r_2$ should be as small as possible. It is clear that in practice the duration of regime 2 has some minimum realizable value $r_{2\text{min}}$ due to finite times necessary for all actual operations. Thus, we henceforth assume that the mean duration of regime 2 is $r_{2\text{min}}$ and we now consider $\langle T \rangle$ as a function of $r_1$.

**Asymptotic behavior of $\langle T \rangle$ when $\lambda_1 \to +\infty$.** It is easily seen that

$$\lambda_1 \tilde{q}_1(\lambda_1) = \beta \left[ 1 - \langle j_1(\lambda_1|x) \rangle_{B-A} \right], \quad (48)$$

where $\beta = \int_{x \in B-A} d\rho_0(x)$ is the stationary probability that $P \in B-A$ and $\langle j_1(\lambda_1|x) \rangle_{B-A} = \beta \int_{x \in B-A} d\rho_0(x)$ is the stationary average of $\tilde{j}_1(\lambda_1|x)$ normalized over $B-A$.

The behavior of $\tilde{j}_1(\lambda_1|x)$ when $\lambda_1 \to +\infty$ depends on the behavior of $j_1(t|x)$ when $t \to 0$, and it is found that if the search time density in regime 1 is finite for $t=0$, $j_1(0|x) = a_1(x)$, then $\lambda_1 \tilde{q}_1(\lambda_1) - \beta \left[ 1 - \langle a_1 \rangle_{B-A}/\lambda_1 \right]$ when $\lambda_1 \to +\infty$ and

$$\langle T \rangle \sim \frac{1}{\lambda_2} \left[ 1 + \frac{\langle a_1 \rangle_{B-A}}{\lambda_1} \right] \left[ 1 - \frac{1}{\lambda_1} \left( \frac{2}{1 - \beta} - 1 \right) \right]. \quad (49)$$

Thus, when $\lambda_1 \to +\infty$ the mean search time $\langle T \rangle$ tends to the finite limit $\beta/(1-\beta) r_2$. Furthermore, unless $a_1(x)=0$ for any $x \in B-A$, $\langle T \rangle$ tends to this limit by lower values provided that $1-\beta < \langle a_1 \rangle_{B-A} r_2$ (which is more easily satisfied as the stationary probability $1-\beta$ of the target is very small).

**Case of diffusive regime 1.** Formula (49) does not apply if the search time density is not analytic at $t=0$, which is the case for a diffusive regime 1. If, for instance, during regime 1 $P$ performs a one-dimensional diffusion between an absorbing point $a$ (the target) and a reflecting point $b$, we have $\langle \tilde{j}_1(\lambda_1) \rangle_{B-A} \sim C \lambda_1^{1/2}$, where $C$ can be a positive constant. Then, when $\lambda_1 \to +\infty$

$$\langle T \rangle \sim \frac{1}{\lambda_1} \frac{\beta}{1 - \beta} \left[ 1 + \frac{C}{\lambda_1} \right] \quad (50)$$

and $\langle T \rangle$ always tends to its limit by lower values. This can be generalized to $d$-dimensional diffusion (see Appendix C).

**Behavior of $\langle T \rangle$ when $\lambda_1 \to 0$.** Expression (47) of $\langle T \rangle$ can be written as

$$\langle T \rangle = \beta \tilde{r}_1(\lambda_1) \left( 1 + \frac{1}{\lambda_1} \right), \quad (51)$$

where $\tilde{r}_1(\lambda_1)$ is the Laplace transform of $\langle q_1(t) \rangle_{B-A}$, the average of the $q_1(t)$ over $B-A$. When $\lambda_1 \to 0$, we have

$$\langle T \rangle = \beta t_1 \left[ 1 - \lambda_1 \left( \frac{1}{2} \frac{\sigma_1}{t_1} \right)^2 + \frac{1}{2} - \beta - \frac{\sigma_2}{t_1} \right], \quad (52)$$

where $t_1 = \langle t_1(x) \rangle_{B-A}$ is the mean search time of the target $A$ in regime 1, averaged over $B-A$. Similarly, $\sigma_1^2 = \langle \dot{r}_1^2(x) \rangle_{B-A}$ is the corresponding variance.

When $\lambda_1 = 0$, $\langle T \rangle$ is just the mean search time $\beta t_1$ if regime 1 is maintained permanently. Thus, intermittence is surely favorable either if $\beta t_1 > \sigma_2/(1 - \beta)$ or if $\langle T \rangle / \lambda_1 \to 0$.

The first condition is verified if

$$\frac{\sigma_2}{t_1} < 1 - \beta, \quad (53)$$

which is always possible if the minimum possible value $r_{2\text{min}}$ is small enough. Condition $\langle T \rangle / \lambda_1 \to 0$ implies

$$\frac{\sigma_2}{t_1} < \frac{\frac{1}{2} \frac{\sigma_1}{t_1}^2}{2} - \beta. \quad (54)$$

Since $\sigma_1 / t_1 \geq 1$, condition (54) can surely be realized for small $r_2$ if $\beta < \sigma_2^2$, but in general, if the target is small, $\beta \sim 1$. Then, this condition implies that the fluctuations of the search time in regime 1 should be large enough for the right hand side of Eq. (54) to be positive. If this is the case, intermittence is surely favorable is $r_{2\text{min}}$ is sufficiently small.

If regime 1 is a three-dimensional diffusion, it can be shown that $\langle T \rangle / \lambda_1 \to 0$, so that conditions (53) and (54) are identical. Assuming that Eq. (50) holds (Appendix C), we conclude that if the minimum value $r_{2\text{min}}$ is small enough to satisfy Eq. (54), the search time is minimized for a finite value of $r_1$. If $r_2$ exceeds the critical value $r_{2\text{crit}} = (1 - \beta) t_1$, intermittence is no longer generically favorable, and the search time increases with $\lambda_1$ (unless some atypical minimum exists far from $\lambda_1=0$).

If the search time of regime 1 is regular at $t=0$, formula (49) allows one to anticipate other behaviors, with, for instance, $\langle T \rangle$ continuously decreasing with $\lambda_1$, as it is found possible in the lattice model of Sec. III. These conclusions show that the results of the previous sections can be qualitatively extended to much more general cases.

**V. CONCLUSION**

We have shown that a searcher, an animal or a molecule, searching for a target which does not allow for remote detection can have a reason to alternate regimes of slow, careful scanning, with periods of random relocation, when it is able to perform them. As in other intermittent behaviors, alternating slow scanning periods with fast, nonreactive displacements, the interest of such a strategy is not obvious and it depends on the situation. We have obtained exact results...
and explicit conclusions in the special case when the slow motion is a $d$-dimensional diffusion in a spherical system. Then, it has been proved that intermittence can allow one to reduce the search time considerably if the physical nature of the searcher and of its environment makes possible the realization of a very fast alternation of the two regimes, each one with a very short mean duration, compared to a characteristic time of the system. If this is the case, and if the mean durations of both regimes satisfy certain scaling laws, the search time of the system. If this is the case, and if the mean durations of both regimes satisfy certain scaling laws, the search time can be much shorter than in a purely diffusive regime, although the efficiency of intermittence decreases when the dimension increases. If the mean durations of the phases cannot be shorter than the characteristic time of the system, the situation is less favorable. Nevertheless, intermittence can still be an efficient strategy in one and two dimensions, but this is not always the case in higher dimensions. These explicit results can be partly generalized for much more general intermittent systems including teleportation, and it can still be concluded that intermittence can allow one to increase the efficiency of the search considerably, although obviously not in all cases. Thus, such a behavior can play an important role in chemical kinetics, especially in low-dimension systems, when the reagent can perform temporary excursions to a higher-dimension phase, which allow a fast relocation, as it has been shown in the special case of protein search of specific target on DNA.\textsuperscript{14,33}

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APPENDIX A: CALCULATION OF $\langle \tilde{j}(\lambda_1 + s|x) \rangle_B$

We proceed here to the calculation of $\langle \tilde{j}(\lambda_1 + s|x) \rangle_B$ from formulas (2) and (3).

$$\langle \tilde{j}(\lambda_1 + s|x) \rangle_B = \int_{v(B)} \tilde{j}(\lambda_1 + s|x) \frac{dr}{v(B)} = \frac{2(1 - \nu)}{b^{2(1-\nu)} a^{\nu} I_{\nu}(\tilde{b}) + K_{\nu}(\tilde{a})I_{\nu-1}(\tilde{b})} \left[ K_{\nu-1}(\tilde{b}) \int_a^b d\beta r^{1-\nu} I_{\nu}(\tilde{\beta}) + I_{\nu-1}(\tilde{b}) \int_a^b d\beta r^{1-\nu} K_{\nu}(\tilde{\beta}) \right].$$

The latter integrals can be evaluated explicitly,

$$\int_a^b d\beta r^{1-\nu} I_{\nu}(\tilde{\beta}) = \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \int_a^b du u^{1-\nu} I_{\nu}(u) = \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \left[ \tilde{b}^{1-\nu} I_{\nu-1}(\tilde{b}) - \tilde{a}^{1-\nu} I_{\nu-1}(\tilde{a}) \right],$$

$$\int_a^b d\beta r^{1-\nu} K_{\nu}(\tilde{\beta}) = \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \int_a^b du u^{1-\nu} K_{\nu}(u) = \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \left[ \tilde{a}^{1-\nu} K_{\nu-1}(\tilde{b}) - \tilde{b}^{1-\nu} K_{\nu-1}(\til{a}) \right].$$

Eventually, this allows us to compute analytically

$$\langle \tilde{j}(\lambda_1 + s|x) \rangle_B = \int_{v(B)} \tilde{j}(\lambda_1 + s|x) \frac{dr}{v(B)} = \frac{2(1 - \nu)}{b^{2(1-\nu)} a^{\nu} I_{\nu}(\til{b}) + K_{\nu}(\til{a})I_{\nu-1}(\til{b})} \left[ K_{\nu-1}(\til{b}) \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \left[ \tilde{a}^{1-\nu} K_{\nu-1}(\til{b}) - \til{b}^{1-\nu} K_{\nu-1}(\til{a}) \right] \right]$$

$$\times \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} \left[ \til{a} K_{\nu-1}(\til{a}) - \til{b} K_{\nu-1}(\til{b}) \right]$$

$$= \frac{2(1 - \nu)}{b^{2(1-\nu)} a^{\nu} I_{\nu}(\til{b}) + K_{\nu}(\til{a})I_{\nu-1}(\til{b})} \left[ K_{\nu-1}(\til{b}) I_{\nu-1}(\til{a}) - I_{\nu-1}(\til{a}) K_{\nu-1}(\til{b}) \right] \left( \frac{D}{\lambda_1 + s} \right)^{1-\nu/2} = -\frac{Y}{X},$$
with \( k = (da^{d-1}/b^d)(D/\lambda_1 + s)^{1/2} \).

**APPENDIX B: OPTIMIZATION IN LONG WAITING TIME LIMIT**

In this limit \( \tau_1 \gg \tau = a^2/D \), or \( x = a\sqrt{\lambda_1}/D \ll 1 \), we have, with notations of Sec. II,

\[
Z(x) = -\frac{K_{d-1}(x)}{K_d(x)} \begin{cases} 
-1 & \text{in } d = 1 \\
\sim 1/x \ln(x) & \text{in } d = 2 \\
\sim -(a-2)/x & \text{in } d = 3.
\end{cases}
\]  

(B1)

Thus, in order that Eq. (15) is satisfied, \( x \) should not be less than a lower bound \( x \) depending on \( b/a \), which we assume. On the other hand, we have when \( \lambda_1 \to 0 \)

\[
\langle T \rangle_{\text{diff}} = \begin{cases} 
\frac{b^2}{3D} = \frac{1}{3}(b/a)^2 \tau & \text{in } d = 1 \\
\frac{b^2}{2D} \ln(b/a) = \frac{1}{2}(b/a)^2 \ln(b/a) \tau & \text{in } d = 2 \\
\frac{b^2}{d}(d-2)Da^{d-2} = l/d(d-2)(b/a)^d \tau & \text{in } d \geq 3
\end{cases}
\]

(B2)

In *one dimension*, calculations are the same as in the short time limit and the optimal value of \( \lambda_1 \) satisfies Eq. (17), but now \( x \ll 1 \), so that

\[
\overline{\lambda_1} \sim \lambda_2
\]

and \( \tau_1 \sim \tau_2 \ll \tau \).

The minimum value of \( \langle T \rangle \) is given by

\[
\langle T \rangle_{\text{min}} = \frac{2b}{\sqrt{D}} \sqrt{\tau_2}.
\]

(B4)

and the efficiency is

\[
E = \frac{\langle T \rangle_{\text{diff}}}{\langle T \rangle_{\text{min}}} = \frac{2b}{\sqrt{3D}\tau_2} = \frac{2b}{3a} \sqrt{\frac{\tau}{\tau_2}}.
\]

(B5)

In *two dimensions*, we know that intermittence can only be favorable if condition (12) holds. In this case,

\[
\langle T \rangle \sim \frac{\lambda_1 + \lambda_2}{2a} \int \left[ x^2 \ln(x) \right] dx = \frac{b^2}{2D} \left[ 1 + \frac{\lambda_1}{\lambda_2} \right] \ln \left( a \sqrt{\frac{\lambda_1}{D}} \right).
\]

(B6)

If \( \lambda_2 > \lambda_2 \), the optimal value \( \lambda_1 \) of \( \lambda_1 \) satisfies

\[
\frac{\partial \langle T \rangle}{\partial \lambda_1} = \frac{\lambda_1}{\lambda_1 + \lambda_2} + \frac{1}{2} \ln(x) = 0,
\]

which implies

\[
x^2 \ln(x^2) = 2\lambda_2^2 D = c^2
\]

and \( c \ll 1 \). Eventually, one obtains

\[
\lambda_1 \sim \frac{\lambda_2}{\log(a^2(\lambda_2^2/D))} \left[ 1 - \frac{\log \log(a^2(\lambda_2^2/D))}{\log(a^2(\lambda_2^2/D))} \right]
\]

(B9)

so that \( \lambda_1 \ll \lambda_2 \) and \( \tau_1 \gg \tau_2 \gg \tau \).

Numerical analysis of the exact formulas shows that these approximations are very accurate in these situations, the relative error being of order \( 10^{-3} \).

Inserting this value into Eq. (B6) and taking Eq. (B8) into account, we find the minimum search time

\[
\langle T \rangle_{\text{min}} \sim \frac{b^2}{4D} \left[ \gamma + \ln(\gamma) + 1 + \cdots \right],
\]

(B10)

with \( \gamma = \ln(c^2)/[\ln(a^2\lambda_2/D)] \).

From Eqs. (B1) and (B2) it is seen that the efficiency of intermittence is now

\[
E \sim 2 \ln(b/a) \left[ \ln(b^2/a^2) \right] = \ln(\tau_2/\tau).
\]

(B11)

It is much larger than 1 if condition (15) is satisfied, since we have

\[
\frac{D\tau_2}{a^2} < \frac{7}{96} \frac{b^2}{a^2} \ll \frac{b^2}{a^2}.
\]

(B12)

Eventually, in *three dimensions*, we have

\[
Z(x) \sim \frac{K_3(x)}{K_1(x)} = \frac{x+1}{x},
\]

which holds for any \( x = a\sqrt{\lambda_1}/D \), and

\[
\langle T \rangle \sim \frac{b^3}{3Da^2} \left[ 1 + \frac{\lambda_1}{\lambda_2} \right] \frac{1}{1 + a\sqrt{\lambda_1}/D}.
\]

(B14)

The optimal value of \( \lambda_1 \) in three dimensions is then

\[
\lambda_1 = \frac{D}{a^2} \left[ 1 + \sqrt{1 + \frac{a^2\lambda_2}{D}} \right]^2.
\]

(B15)

It yields the minimal search time for any \( \lambda_2 \) or \( \tau_2 \).

\[
\langle T \rangle_{\text{min}} = \frac{b^3}{3Da^2} \left[ 1 + \sqrt{1 + \frac{a^2\lambda_2}{D}} \right]^2.
\]

(B16)

The condition \( x = a\sqrt{\lambda_1}/D \ll 1 \) implies \( a\sqrt{\lambda_2}/D \ll 1 \) and

\[
\lambda_1 \sim \frac{1}{4D} \lambda_2^2 \text{ or } \frac{\tau_1}{\tau} \sim \frac{1}{4} \frac{\tau_2}{\tau}.
\]

(B17)

Then, \( \tau \ll \tau_2 \ll \tau_1 \), and \( \tau_1 \) scales as \( \tau_2 \), as found in Eq. (18), and we have

\[
\langle T \rangle_{\text{min}} \sim \frac{b^3}{3Da^2} = \frac{b^3}{3a^3} \tau.
\]

(B18)

The efficiency is now

\[
E = \frac{1}{2} \left( 1 + \sqrt{1 + \frac{\tau}{\tau_2}} \right) > 1.
\]

(B19)

Once more, it increases if \( \tau_2 \) decreases, but if \( \tau_2 \gg \tau \), it is approximately 1.

In any case, the efficiency is not significantly higher than 1 if \( \tau_2 \gg \tau \), and intermittence is hardly useful in such a situation. It can be seen similarly that if \( \tau_2 \gg \tau \), intermittence is not a favorable search strategy in dimensions \( d > 3 \).

**APPENDIX C: MEAN SEARCH TIME OF THE TARGET IN A DIFFUSIVE REGIME**

Assume point \( P \) performs an ordinary diffusion along axis \( 0x \), between the absorbing point \( x=0 \) (target) and the
reflecting point \( x=L \). The probability density \( p_1(t|x) \) of the first absorption time \( T(x) \) of \( P \), starting from \( x \) at time 0, satisfies the diffusion equation

\[
\frac{\partial}{\partial t} j_1(t|x) = D \frac{\partial^2}{\partial x^2} j_1(t|x),
\]

(C1)

with the initial value \( j_1(0|x)=0 \) if \( x \neq 0 \) and the boundary condition \( j_1(t|0)=\delta(t), \left((\partial/\partial x)j_1(t|x)\right)_{x=L}=0 \).

The Laplace transform \( j_1(s|x) \) of \( j_1(t|x) \), satisfying the corresponding boundary condition, is given by

\[
\tilde{j}_1(s|x) = \frac{\cosh[\sqrt{s/D}(x-L)]}{\cosh[\sqrt{s/D}L]}.
\]

(C2)

Averaging with the uniform density on \((0,L)\), one obtains

\[
L(\tilde{j}_1)(s) = \sqrt{\frac{D}{s}} \tanh\left(\sqrt{\frac{s}{D}L}\right) \sim \left(\frac{s}{D}\right)^{-1/2}
\]

if \( L \sqrt{s/D} \gg 1 \).

(C3)

The last result can be obtained by computing the density of the first arrival time at 0 as computed for the infinite semiaxis \( 0x \).

Relation (C3) can be extended to a point \( P \) performing a \( d \)-dimensional diffusion inside a closed volume \( B \) containing an absorbing subvolume \( A \), representing a target. \( P \) starts from any position \( x \in B-A \). It is absorbed as soon as it touches the boundary \( \Sigma_A \) of \( A \), whereas it is reflected when it touches the boundary \( \Sigma_B \) of \( B \). The Laplace transform of the first absorption time density of \( P \) satisfies the equation

\[
s j_1(s|x) = D \frac{\partial^2}{\partial x^2} j_1(s|x)
\]

(C4)

where \( \partial/\partial x \) and \( \partial^2/\partial x^2 \) represent the gradient and the Laplacian, respectively) with the boundary conditions

\[
\tilde{j}_1(s|x) = 1 \quad \text{if} \quad x \in \Sigma_A,
\]

(C5)

\[
d\Sigma_B \cdot \frac{\partial}{\partial x} j_1(s|x) = 0,
\]

(C6)

If \( x \in \Sigma_B \) and if \( d\Sigma_B \) is the normal to \( \Sigma_B \).

Assuming that the stationary probability distribution is uniform, we consider the average

\[
\langle j_1(s|x) \rangle_{B-A} \approx \int_{x \in B-A} dx j_1(s|x) = I(s).
\]

(C7)

From Eqs. (C4)--(C6) it is seen that \( I(s) \) satisfies

\[
sI(s) = D \left[ \int_{\Sigma_B} d\Sigma_B \cdot \frac{\partial}{\partial x} \tilde{j}_1(s|x) - \int_{\Sigma_A} d\Sigma_A \cdot \frac{\partial}{\partial x} \tilde{j}_1(s|x) \right]
\]

\[
= -D \int_{\Sigma_A} d\Sigma_A \cdot \frac{\partial}{\partial x} \tilde{j}_1(s|x),
\]

(C8)

where \( d\Sigma_S \) is the vector surface element of \( \Sigma_S \), with \( S=A \) or \( B \). Let \( x_A \) be a point of \( \Sigma_A \) and \( x \) be a point of \( B-A \) in the neighborhood of \( x_A \). We define the new function

\[
q(y) = \tilde{j}_1(s|x_A + \left(\frac{s}{D}\right)^{-1/2} y),
\]

(C9)

with \( y = (s/D)^{1/2}(x-x_A) \).

It satisfies

\[
q(y) = -\frac{\partial^2}{\partial y^2} q(y),
\]

(C10)

with the boundary conditions

\[
q(y) = 1 \quad \text{if} \quad y \in \Sigma_A',
\]

(C11)

\[
d\Sigma_B' \cdot \frac{\partial}{\partial y} q(y) = 0,
\]

(C12)

if \( y \in \Sigma_B' \) and \( d\Sigma_B' \) is the normal to \( \Sigma_B', \Sigma_A' \) and \( \Sigma_B \) being the surfaces corresponding to \( \Sigma_A \) and \( \Sigma_B \), respectively.

When \( s \to \infty \), \( \Sigma_A' \) tends to the plane tangent to \( \Sigma_A \) at \( x_A \), whereas \( \Sigma_B' \) is sent to infinity. In this limit, \( q(y) \sim e^{-y} \), where \( y \) is the component along the normal to \( \Sigma_A \) at \( x_A \). Then,

\[
\frac{\partial}{\partial x} \left[ \int_{\Sigma_A} d\Sigma_A \cdot \frac{\partial}{\partial y} q(y) \right]_{y=0} \sim \int_{\Sigma_A} \frac{\partial}{\partial x} q(y)
\]

(C13)

and it results from Eq. (C8) that \( I(s) \sim (s/D)^{-1/2} \), which generalizes Eq. (C3). Thus, the asymptotic value (50) of the mean search time \( \langle T \rangle \) when \( \lambda_1 \to \infty \) should apply to \( d \)-dimensional diffusion and to any volumes \( A \) and \( B \), at least in the generic case (perhaps excluding also particular geometries which could give specific results).

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