PHYSICAL REVIEW E **94**, 012117 (2016)

Optimal search strategies of run-and-tumble walks

Jean-François Rupprecht,[1,2,*] Olivier Bénichou,[1] and Raphael Voituriez[1,3]

[1]*Sorbonne Universités, UPMC Université Paris 06, UMR 7600, Laboratoire de Physique Théorique de la Matière Condensée, 4 Place Jussieu, Paris, France*

[2]*Mechanobiology Institute, National University of Singapore, 5A Engineering Drive 1, 117411, Singapore*

[3]*Sorbonne Universités, UPMC Université Paris 06, Laboratoire Jean Perrin, UMR 8237 CNRS/UPMC, 4 Place Jussieu, Paris, France*

(Received 11 March 2016; revised manuscript received 1 June 2016; published 14 July 2016)

The run-and-tumble walk, consisting of randomly reoriented ballistic excursions, models phenomena ranging from gas kinetics to bacteria motility. We evaluate the mean time required for this walk to find a fixed target within a two- or three-dimensional spherical confinement. We find that the mean search time admits a minimum as a function of the mean run duration for various types of boundary conditions and run duration distributions (exponential, power-law, deterministic). Our result stands in sharp contrast to the pure ballistic motion, which is predicted to be the optimal search strategy in the case of Poisson-distributed targets.

DOI: 10.1103/PhysRevE.94.012117

I. INTRODUCTION

Run-and-tumble walks (RTWs) are usually defined as randomly reoriented ballistic excursions, or runs, of constant speed in $\mathbb{R}^d$. Historically, such processes were introduced to model the dynamics of particles in scattering environments, such as the motion of atoms in a gas [1,2] or electrons in a metal [3–5], as well as the scattering of light or neutrons [6,7]. RTWs raised a renewed interest more recently as it was realized that they provide a minimal model of self-propelled particle dynamics [8], notoriously exemplified by swimming bacteria [9]. Their range of applications has since then been extended from the microscopic scale, as is the case of molecular motors [10], to the cellular scale [11] or the macroscopic scale in the case of animal behavior [12,13].

In the context of living agents, it is usually hypothesized that motion is aimed at fulfilling a biological function. A prototypical example of such function is the search for targets—as is the case for immune system cells looking for pathogens, sperm cells searching for an ovocyte, or bacteria or larger organisms foraging for food [12–15]. In these examples, the optimization of the search efficiency, which appears as essential, amounts to minimizing the search time for targets. In this context, Lévy walks—RTWs with power-law distributed run lengths—have been repeatedly invoked as optimal foraging strategies [16]. This optimality, however, holds only in the particular case where the targets are distributed in space according to a Poisson law, and are in addition assumed to regenerate at the same location after a finite time. In the opposite case of destructive search, where each target can be found only once, the search is optimized by the trivial ballistic excursion. These restrictive conditions have weakened the robustness of Lévy strategies and made their applicability to field data rather disputed over the years [17–20]. In this context, assessing the search efficiency of general RTWs, and in particular Lévy walks, in the basic setting of a single target in a finite domain appears as a very important issue that has remained unsettled so far: this is the goal of this paper.

From a technical point of view, a natural observable to quantify the search efficiency is the mean first-passage time (MFPT) to a target. In the case of a single target in the interior of a bounded domain, or equivalently regularly spaced targets in infinite space, the full FPT statistics, and in particular its mean, have been derived asymptotically for Markovian scale-invariant random walks [21–23] (see also Ref. [24] for an extension to non-Markovian processes). These results have been be extended to the narrow-escape case, in which the target is embedded in the boundary of the confining domain [25–29].

While these results apply in particular to Brownian particles that are subject to thermal fluctuations, most models of self-propelled particles, and in particular RTWs, are not scale invariant. These walks exhibit a crossover from a short-time ballistic scaling to a long-time diffusive scaling. Despite their extensive analysis in infinite space [30], the study of the FPT statistics of RTWs in confinement requires new approaches. First steps in this direction were made in Refs. [31–34]. More recently, the MFPT for lattice persistent random walks has been studied in Ref. [35]. This, however, does not solve the case of RTWs, which cannot be defined as a continuous limit of lattice walks, a striking difference being that the MFPT for lattice walks can be controlled by infinitely long periodic orbits [35], which do not exist for general domain shapes or boundary conditions in continuous space. Some previous work addressed the search optimization of RTWs in terms of their mean run time. First, Ref. [36] considers the optimal search problem by mortal RTWs, which may die at any time according to an exponential decay law. There, the optimal reorientation time maximizes the probability that the target is found before the death of the searcher. We also mention that Ref. [37] considers a directed RTW search where, on average, tumbles reorient the searcher in the direction of the target. Due to this bias in the directions of reorientation, the mean search time remains finite even in the absence of a confining domain. An optimal reorientation time appears when a waiting time is associated to each tumbling events. However, the origin of such optimum cannot apply to the problem considered here (see the concluding discussion of Sec. II).

In this paper, we first consider the case of a RTW with exponentially distributed run lengths that is confined within a spherical domain of radius b. We derive an accurate analytical approximate of the MFPT to a centered target of size a. Beyond

*mbijr@nus.edu.sg

the single-target problem, this setting efficiently approximates the destructive search of infinitely many regularly spaced targets with concentration $\rho = 1/(\pi b^2)$ [two-dimensional (2D)] or $\rho = 3/(4\pi b^3)$ (3D). We show that the MFPT is minimized for a mean run duration $\tau = \tau_{\rm opt} \sim \gamma b/\log(b/a)$, where γ is a constant that depends both on the spatial dimension and the choice of boundary conditions. However, the existence of the minimum is independent of the specific nature of the boundary condition, which pleads for its robustness. In addition, we show that similar optima exist for deterministic run durations (with respect to the run duration τ) and for power-law-distributed run durations (with respect to the scale parameter τ of the power law), i.e., Lévy walks. In sharp contrast with the case of Poisson-distributed targets, our results highlight the crucial role of the spatial distribution of targets in search problems, and put forward the robustness of optimal RTWs for single-target search problems.

II. EXPONENTIALLY DISTRIBUTED RUNS

We first assume that the duration of each run is exponentially distributed with mean τ, which we call persistence time. We denote by θ the angle between the position vector $\mathbf{r}$ of the searcher and its velocity vector $\mathbf{v}$, the origin being the target center (see Fig. 1). At each tumble, a new direction θ is set according to a uniform distribution $\mu(\theta) = 1/\pi$ in two dimensions and $\mu(\theta) = \sin(\theta)/2$ in three dimensions. In three dimensions, the angle θ refers to the elevation angle of $\mathbf{v}$ with respect to $\mathbf{r}$. For symmetry reasons the azimuthal angle ϕ can be reset to 0 after each tumble event; hence the 3D search problem with isotropic reorientations corresponds to a 2D search problem with nonisotropic reorientations characterized by $\mu(\theta) = \sin(\theta)/2$.

The MFPT for a searcher starting at a distance r from the target center with a velocity angle θ is denoted $t(r,\theta)$. We define the averaged MFPT over all possible starting angles as $\langle t \rangle = \int_0^\pi d\mu(\theta)\, t(r,\theta)$; we will be mainly interested in the global MFPT (GMFPT), defined as the spatial average: $\langle \bar{t} \rangle = \int_a^b d\nu(r)\, \langle t(r) \rangle$, where $\nu(r)$ is the uniform spatial measure, which reads $\nu(r) = dr^{d-1}/(b^d - a^d)$ in terms of the spatial dimension d. The MFPT can be shown to satisfy the following

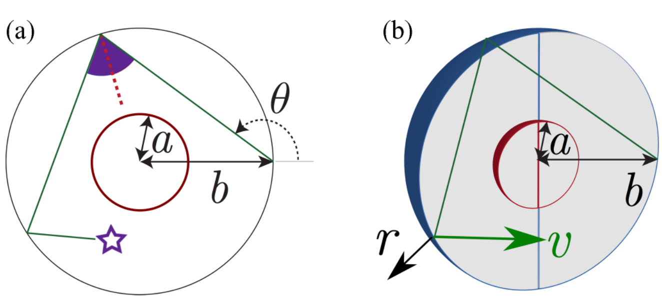

FIG. 1. Scheme of a run-and-tumble walk. (a) In two dimensions, with specular confinement at the radius b, and a single tumble (star). Mind that a ballistic run, which is not initially directed towards the target, will not cross it at any ulterior time. (b) In three dimensions, due to the spherical symmetry, the search time does not depend on the azimuthal angle ϕ between the velocity vector v and the position vector r.

integrodifferential backward equation [39]:

$$v \cos\theta\, \partial_r t(r,\theta) + \frac{1}{\tau} \int_0^\pi d\phi\, \{t(r,\phi) - t(r,\theta)\} = -1, \qquad (1)$$

which admits a unique solution when completed by boundary conditions. First, $t(r = a,\theta) = 0$ for $\theta \in [\pi/2,\pi]$ as the process is stopped as soon as the searcher crosses the target. Second, we will consider three types of confining boundary at $r = b$: (i) the specular boundary, which reflects the incoming searcher according to Descartes law, as a mirror would reflect a ray of light; (ii) the scattering boundary, which scatters the searcher in a random direction, with reinitialization of the run duration; (iii) the stubborn boundary, for which the searcher waits for the next favorable reorientation to leave the boundary. In the diffusive limit $\tau \ll a/v$, we expect to have effectively $\partial_r \langle t(r) \rangle = 0$ at $r = b$ for any choice of boundary condition. However, for arbitrary values of τ, defining the appropriate boundary condition at $r = b$ of the MFPT is a challenging problem.

Analytical solutions of Eq. (1) are only available in 1D geometries, for which the orientation angle is either $\theta = 0$ or $\theta = \pi$. Following Refs. [39,40], we find that the mean search time in the presence of a specular boundary condition reads $\langle \bar{t} \rangle = \{(a-b)^2[3D - (a-b)v]\}/(3bDv)$, where $D = v^2\tau$. Mind that the latter expression predicts that the GMFPT is a monotonically decreasing function of τ, in sharp contrast with the main results of this paper concerning the 2D and 3D geometries. As no such exact solutions are available in these higher dimensions, we resort below to an approximate scheme that interpolates the exact asymptotics obtained in both limits $\tau \ll a/v$ and $b/v \ll \tau$.

A. Diffusive limit

In the diffusive limit $\tau \ll a/v$, the MFPT is independent both of the direction of the initial velocity θ and of the nature of the confining boundary (e.g., specular, scattering, or stubborn). Following Ref. [12], it can be shown that in this limit the MFPT satisfies the equation: $D\Delta\langle t(r) \rangle = -1$ where $D = v^2\tau/d$. In the large volume limit $a \ll b$, it is straightforward to obtain that [41]

$$\langle \bar{t} \rangle \underset{\tau \ll a/v}{\sim} \bar{t}^{(1)} = \frac{b^2}{v^2\tau} \ln\left(\frac{b}{a}\right), \qquad (2)$$

in two dimensions, and $\langle \bar{t} \rangle \sim \bar{t}^{(1)} = \pi b^3/(3av^2\tau)$ in three dimensions. We emphasize that in the diffusive limit, the search time is a decreasing function of the persistence time, for any type of confining boundary (specular, scattering, or stubborn).

B. Ballistic limit and uniform approximation

In the limit $\tau \gg b/v$, the behavior of the search time crucially depends on the boundary condition at $r = b$. We derive the expression of the optimal reorientation time for three particular types of boundary condition.

1. Specular boundary condition

We first consider the case of a specular boundary that reflects incoming searchers according to Descartes law. To evaluate the search time in this regime, we follow an approach introduced in Ref. [37], which we call uniform approximation. This approach also shares similarity with the method presented in Ref. [29]. We first write the probability of hitting the target within a single run after a tumble event as

$$p_h = \int_a^b dr\ p_r(r) p_{\rm dir}(r) p_{\rm reach}(r), \tag{3}$$

where: (i) $p_r(r)$ is the probability distribution of the position at the previous reorientation event. For $r \gg a$, it can be assumed that p_r is uniform over the domain. (ii) $p_{\rm dir}(r)$ is the probability of choosing a direction that crosses the target (either directly or after a single reflection at $r = b$). In the case of a specular confining boundary, $p_{\rm dir}(r) = 2 \cdot a/(\pi r)$ (2D) and $p_{\rm dir}(r) = 2 \cdot a^2/(4r^2)$ (3D) at first order in $a/r \ll 1$. The factor 2 in the latter two expressions is due to trajectories that cross the target after a single reflection on the boundary $r = b$. (iii) $p_{\rm reach}(r)$ is the probability of performing a sufficiently long run to reach the target, which for exponentially distributed runs reads:

$$p_{\rm reach}(r) = (e^{-r/(v\tau)} + e^{-(2b-r)/(v\tau)})/2. \tag{4}$$

Partitioning over the first run, one writes $\langle \bar{t} \rangle = p_h \tau_f + (1 - p_h)(\langle \bar{t} \rangle + \tau)$, where τ_f is the mean duration of a successful run. In the joint ballistic and small target limit ($a/b \ll 1$), we find that $p_h \ll 1$, hence that $\langle \bar{t} \rangle \sim \tau/p_h$ and

$$\langle \bar{t} \rangle \underset{b/v \ll \tau}{\sim} \bar{t}^{(2)} \equiv \frac{\pi b^2}{2va} \frac{1}{\left(1 - e^{-\frac{2b}{\tau v}}\right)} \underset{b/v \ll \tau}{\sim} \tau \frac{\pi}{4} \frac{b}{a}, \tag{5}$$

in two dimensions, while in three dimensions,

$$\langle \bar{t} \rangle \underset{b/v \ll \tau}{\sim} \bar{t}^{(2)} \equiv \frac{4b^3}{3a^2 v} \frac{1}{\left(1 - e^{-\frac{2b}{\tau v}}\right)} \underset{b/v \ll \tau}{\sim} \tau \frac{2}{3} \frac{b^2}{a^2}. \tag{6}$$

The GMFPT is therefore an increasing function of τ in the limit $\tau \gg b/v$ that diverges in the limit $\tau = \infty$. Indeed, a ballistic particle that is not initiated in the direction of the target will never cross the target. Together with the above analysis of the diffusive regime, this shows that the GMFPT can be minimized as a function of τ.

We now verify that an accurate uniform approximate of the GMFPT is given by

$$\langle \bar{t} \rangle^{\rm ua} = \bar{t}^{(1)} + \bar{t}^{(2)}. \tag{7}$$

The fact that $\bar{t}^{(2)} \to 0$ in the diffusive limit and $\bar{t}^{(1)} \to 0$ in the ballistic limit shows that this approximation is accurate in both limit regimes; it was further checked numerically that the agreement is good for all values of τ [see Figs. 2(a), 2(b)]. Importantly, this approximate solution makes it possible to analyze analytically the minimization of the GMFPT. The condition of minimization of expression (7) leads to:

$$\frac{\pi b^3 X}{a(1-X)^2} - b^2 \log\left(\frac{b}{a}\right) = 0, \tag{8}$$

in terms of $X = \exp[-2b/(v\tau)]$. In the large volume limit $a \ll b$, the condition defined in Eq. (8) leads to the following expression for the optimal reorientation time:

$$\tau_{\rm opt}^{\rm ua} \underset{a \ll b}{\sim} 2 \frac{b}{v \ln(b/a)}, \tag{9}$$

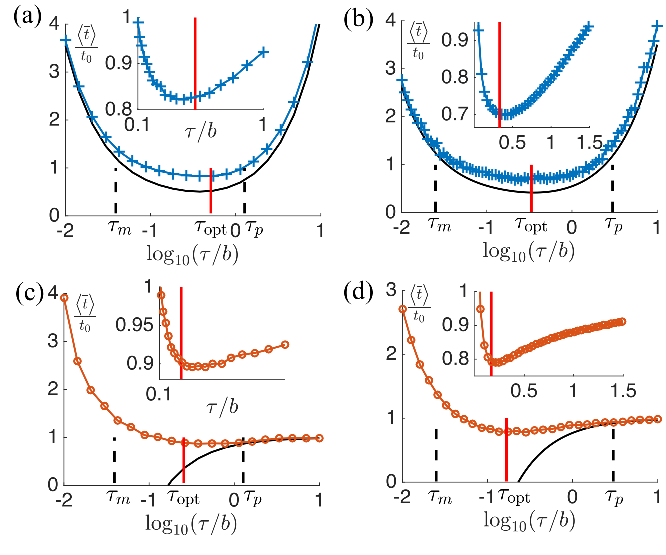

FIG. 2. Search time (GMFPT) to a disk (2D) or a sphere (3D) of radius a as a function of the persistence time τ: (a), (c) in two dimensions, with a confinement radius $b = 50\,a$; (b), (d) in three dimensions, with $b/a = 20$, obtained by simulations with a confining boundary that is [(a), (b), blue crosses] specular or [(c), (d), orange circles] scattering; [(a), (b), solid black line] analytical prediction expression from Eq. (7); [(c), (d), black dashed circles] asymptotic relations from Eqs. (15) and (16). The search time is close to 1 over the predicted plateau range $[\tau_m/b, \tau_p/b]$ (τ_m and τ_p (black vertical dashed lines). (Insets) Search time at optimality: (red solid vertical lines) optimal persistence time from (a), (b) Eq. (10) and (c), (d) Eq. (17). The search time is scaled by $t_0 = 2(b/v)(b/a)^{d-1}$.

in both two and three dimensions. Analysis of the simulations confirm the scaling of Eq. (9), as we find that:

$$\tau_{\rm opt} \underset{a \ll b}{\sim} \gamma_d^{\rm spec} \frac{b}{v \ln(b/a)}, \tag{10}$$

where $\gamma_d^{\rm spec}$ is a constant that only depend on the space dimension d: $\gamma_2^{\rm spec} = 1.95 \pm 0.02$ in two dimensions and $\gamma_3^{\rm spec} = 1.5 \pm 0.02$ in three dimensions (see Fig. 3). Hence, the uniform approximate provides the $b/\log(b/a)$ scaling of the optimal reorientation time, but it estimates only approximately the prefactor $\gamma_d^{\rm spec}$.

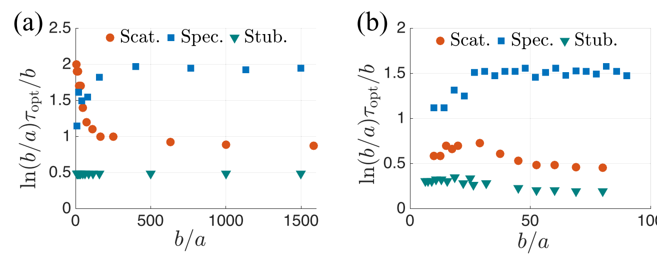

FIG. 3. Scaling of the optimal reorientation time: convergence of the ratio $\gamma = \log(b/a)v\tau_{\rm opt}/b$ as a function of the domain size b (a) in two dimensions and (b) in three dimensions. The corresponding boundary condition is (orange circle) scattering; (blue square) specular; (green triangle) stubborn.

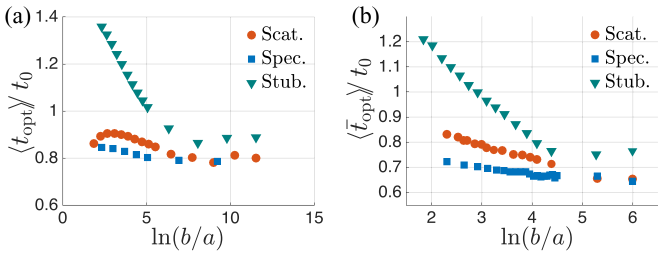

FIG. 4. Scaling of the optimal search time: convergence of the ratio $\langle \bar{t}\rangle_{\rm opt}/t_0$, with $t_0 = 2(b/v)(b/a)^{d-1}$, as a function of the domain size b (a) in two dimensions and (b) in three dimensions. The corresponding boundary condition is (orange circle) scattering; (blue square) specular; (green triangle) stubborn. For large values of the confining domain [$\ln(b/a) > 6$ in (a); $\ln(b/a) > 4$ in (b)] we estimate the search time at the value of the reorientation time indicated by Eqs. (10), (17), (22).

At the optimal reorientation time, the minimal mean search time scales as

$$\langle \bar{t}\rangle_{\rm opt} \underset{a\ll b}{\sim} 2\xi_d^{\rm spec}(b/v)(b/a)^{d-1}, \tag{11}$$

where $\xi_d^{\rm spec}$ are constants that read $\xi_2^{\rm spec} = 0.825 \pm 0.01$ in two dimensions and $\xi_3^{\rm spec} = 0.64 \pm 0.02$ in three dimensions. The convergence of the ratio $\langle \bar{t}\rangle_{\rm opt}/(b/a)^{d-1}$ is represented in Fig. 4.

We find that the mean search time exhibits a large plateau in τ around $\tau_{\rm opt}$ in which it does not significantly differ from $\langle \bar{t}\rangle_{\rm opt}$ (see Fig. 2). We estimate the lower bound of the plateau τ_m as the crossover reorientation time from the diffusive limit to the optimal regime, i.e., as the solution of the equation: $\bar{t}^{(1)}(\tau_m) = \bar{t}_{\rm opt}$. We obtain $\tau_m = a/(2v)\ln(b/a)$ in two dimensions, and $\tau_m = \pi a/(6v)$ in three dimensions. Similarly, for the upper bound of the plateau τ_p, the condition $\bar{t}^{(2)}(\tau_m) = \bar{t}_{\rm opt}$ leads to $\tau_p = (8b)/(\pi v)$ (2D) and $\tau_p = (3b)/(v)$ (3D). Mind that the length of the interval $\tau_p - \tau_m$ is an increasing function of b: the search time is all the more flat around its optimum as the size of the confinement b is increased. Therefore, the statistical uncertainty on the value of the optimal reorientation time increases significantly with the size of the confinement radius. In Fig. 3, the search time—which is computed for each value of b and τ—is averaged over a larger number of trajectories: 10^7 in two dimensions and 10^5 in three dimensions.

2. *Scattering boundary*

We now consider the case of a scattering boundary, at which the searcher is scattered in a random direction. This condition corresponds to a widely used assumption about gas scattering on weakly adsorbing surfaces, known as the Knudsen cosine law [42]. It can also be used to model the behavior of bacteria at the encounter of a boundary [43]. We mention that Ref. [14] considered a similar problem: the narrow escape of a ballistic particle confined by an otherwise scattering boundary.

We introduce the quantity p_s as the probability that the target is found between two successive scattering events at the boundary. We introduce its large τ expansion by writing $p_s = p_s^{(0)} + p_s^{(1)}/\tau + O(1/\tau^2)$ at second order. The quantities $p_s^{(n)}/\tau^n$ correspond to the probability for the searcher to perform n tumble events before hitting the target and before visiting the boundary. At first order in $a \gg b$, the probability $p_s^{(0)}$ to reach the target within a single run from the boundary reads in two dimensions:

$$p_s^{(0)} = \frac{2}{\pi}\arcsin\left(\frac{a}{b}\right) \underset{a\ll b}{\sim} \frac{2a}{b\pi}, \tag{12}$$

while $p_s^{(0)} = a^2/(2b^2)$ in three dimensions.

The next order probability $p_s^{(1)}/\tau$ can be calculated as a sum of two terms: $p_s^{(1)}/\tau = p_+^{(1)}/\tau - p_s^{(0)}/\tau$. The negative contribution $(-p_s^{(0)}/\tau)$ corresponds to the probability that a tumble occurs on a run that is initiated towards the target at the boundary. The positive contribution $(p_+^{(1)})$ corresponds to the probability that a tumble provides the direction to the target. The latter quantity can be expressed by the following integral:

$$p_+^{(1)} = 2\int_{\pi/2}^{\pi-\theta_c} d\mu(\theta)\int_0^{-2b\cos(\theta)} dt\; p_{\rm dir}[r(t)]p_{\rm reach}, \tag{13}$$

where (i) $p_{\rm reach} = 1$ at first order in τ; (ii) $\theta_c = \arcsin(a/b)$ is the angular aperture of the target as seen from the boundary; (iii) $r(t) = \sqrt{v^2t^2 + 2vbt\cos\theta + b^2}$ is the position along the cord at the time t after departure from the boundary; (iv) $p_{\rm dir}(r)$ is the probability of choosing a direction that crosses the target after a reorientation event at the radius r. At first order in $a/r \ll 1$, one finds $p_{\rm dir}(r) = a/(\pi r)$ (2D) or $p_{\rm dir}(r) = a^2/(4r^2)$ (3D). We perform the change of variable $u = bt/v$ in Eq. (13) to obtain the scaling relation $p_s^{(1)} = (a/v)(a/b)^{d-2}\chi_d$ where χ_d equals:

$$2\int_{\pi/2}^{\pi} d\mu(\theta)\int_0^{-2\cos(\theta)} du\; p_{\rm dir}(\sqrt{u^2 + 2u\cos\theta + 1}). \tag{14}$$

Numerical integration leads to the values $\chi_2 \approx 0.74$ in two dimensions and $\chi_3 \approx 0.61$ in three dimensions.

We next introduce the time τ_c corresponding to the mean length of cords between two points on the boundary $r = b$, which reads $\tau_c = (4/\pi)b$ in two dimensions and $\tau_c = b$ in three dimensions. In the limit $b \gg a$, the GMFPT is then given by $\langle \bar{t}\rangle \sim \tau_c/p_s$. Using the above expression for p_s, we obtain:

$$\langle \bar{t}\rangle = \frac{2b^2}{va} - (\pi\chi_2 - 2)\frac{b^3}{v^2a}\cdot\tau^{-1} + o(\tau^{-1}), \tag{15}$$

in two dimensions, while in three dimensions

$$\langle \bar{t}\rangle = \frac{2b^3}{va^2} - (2\chi_3 - 1)\frac{2b^4}{v^3a^2}\cdot\tau^{-1} + o(\tau^{-1}). \tag{16}$$

Mind that $\pi\chi_2 - 2 \approx 0.17 > 0$ and similarly $2\chi_3 - 1 \approx 0.23 > 0$. We verify the predictions of Eqs. (15)–(16) in Figs. 2(c), 2(d).

We conclude that, in the ballistic limit, increasing the rate of tumble $1/\tau$ necessarily decreases the search time as compared to the pure ballistic motion. Our intuitive interpretation for this behavior is that tumbles may occur close to the target, where the probability for a reorientation in the direction of the target is high. The asymptotic relations Eqs. (15) and (16) thus prove the existence of an optimum when the confining boundary is scattering in two and three dimensions, respectively.

For this case of scattering boundary conditions, the uniform approximation cannot be used to determine the minimum of the MFPT, as the MFPT converges to a finite value in the limit

$\tau \to \infty$. However, analysis of numerical simulations confirm a similar scaling to Eq. (7) for the optimal reorientation time:

$$\tau_{\text{opt}} \underset{a \ll b}{\sim} \gamma_d^{\text{scat}} \frac{b}{v \ln(b/a)}, \tag{17}$$

where $\gamma_2^{\text{scat}} = 0.87 \pm 0.2$ and $\gamma_3^{\text{scat}} = 0.45 \pm 0.02$ (see Fig. 3). At the optimal reorientation time, the minimal mean search time scales as

$$\langle \bar{t} \rangle_{\text{opt}} \underset{a \ll b}{\sim} 2\xi_d^{\text{scat}}(b/v)(b/a)^{d-1}, \tag{18}$$

where $\xi_2^{\text{scat}} = 0.88 \pm 0.01$ in two dimensions and $\xi_3^{\text{scat}} = 0.65 \pm 0.02$ in three dimensions. The convergence of the ratio $\langle \bar{t} \rangle_{\text{opt}}/(b/a)^{d-1}$ is represented in Fig. 4.

We point out that $\xi_d^{\text{scat}} = \langle \bar{t} \rangle_{\text{opt}}/t_0$ corresponds to a measure of the search efficiency at optimality, where we recall that $t_0 = 2(b/v)(b/a)^{d-1}$ corresponds to the GMFPT in the ballistic limit. As $\xi_d^{\text{spec}} < \xi_d^{\text{scat}}$, we conclude that the optimal search process is faster for a specular boundary than for a scattering one. This can be interpreted by a geometrical factor: in the ballistic limit, the probability to select a direction that leads to the target $p_{\text{dir}}(r)$ is two times higher for a specular boundary than for a scattering boundary.

3. Stubborn boundary

We call stubborn condition the case in which the searcher sticks upon arrival at the external boundary, and remains at the boundary for the remaining time before the next reorientation towards the interior of the domain. This situation corresponds to the case of fully inelastic collision, which is often used to describe overdamped self-propelled particles in confinement [44]. Indeed, a fully inelastic collision between the searcher and the boundary results in the sliding motion of the searcher along the boundary; due to the complete spherical symmetry of the problem, this sliding motion condition is equivalent to the particle being stuck in place.

Under this choice of boundary condition, we expect the search time to diverge in the ballistic limit $b/v \ll \tau$. More precisely, we expect that $\langle \bar{t} \rangle \sim \tau/p_s^{(0)}$ where $p_s^{(0)}$ is the probability $p_s^{(0)}$ to reach the target in a single run from the boundary, following the definition of Eq. (12). In the large volume limit $a/b \ll 1$, the latter expression for the GMFPT reads

$$\langle \bar{t} \rangle \underset{b/v \ll \tau}{\sim} \bar{t}^{(2)} \equiv 2\tau b^2/a^2, \tag{19}$$

while $\langle \bar{t} \rangle \sim \bar{t}^{(2)} \equiv 4b^2\tau/(3a^2)$ in three dimensions.

Therefore, the GMFPT is an increasing function of τ in the ballistic limit. On the other hand, we justified in Sec. II A that the search time is a decreasing function of τ in the diffusive limit. Therefore, we expect the GMFPT to be an optimizable function of the reorientation time τ.

We now seek an analytical expression for the optimal reorientation time τ_{opt}; similarly to the specular case, we define an uniform approximate of the GMFPT $\langle \bar{t} \rangle^{\text{ua}}$. The minimization of the uniform approximate of the GMFPT leads to the condition

$$\frac{\pi b X}{a(1-X)^2} - 2\log\left(\frac{b}{a}\right) = 0, \tag{20}$$

in terms of $X = \exp(-b/\tau)$, in both the 2D and 3D cases. We then expand the solution of Eq. (20) in the large volume limit $a \ll b$ and we find the following expression for the optimal mean run duration (in both two dimensions and three dimensions)

$$\tau_{\text{opt}}^{\text{ua}} \underset{a \ll b}{\sim} \frac{b}{v \ln(b/a)}. \tag{21}$$

Analysis of simulations confirm the scaling of Eq. (21) and we find that:

$$\tau_{\text{opt}} \underset{a \ll b}{\sim} \gamma_d^{\text{stub}} \frac{b}{v \ln(b/a)}, \tag{22}$$

where $\gamma_2^{\text{stub}} = 0.49 \pm 0.01$ in two dimensions and $\gamma_3^{\text{stub}} = 0.19 \pm 0.02$ in three dimensions. We conclude that the uniform approximation provides the appropriate scaling of the optimal reorientation time, but not the exact value of the proportionality factor γ_{stub}. At the optimal reorientation time, the minimal mean search time scales as

$$\langle \bar{t} \rangle_{\text{opt}} \underset{a \ll b}{\sim} 2\xi_d^{\text{stub}}(b/v)(b/a)^{d-1}, \tag{23}$$

where $\xi_2^{\text{stub}} = 0.88 \pm 0.05$ in two dimensions and $\xi_3^{\text{stub}} = 0.76 \pm 0.05$ in three dimensions. Equation (23) corresponds to the same scaling as in Eq. (18) and Eq. (11) The convergence of the ratio $\langle \bar{t} \rangle_{\text{opt}}/(b/a)^{d-1}$ appears to be relatively slow compared to the specular and scattering cases, hence the larger confidence intervals on the value of ξ_d^{stub} (see Fig. 4).

4. Discussion

For the three choices of boundary conditions discussed above, we found similar scaling expressions for the optimal reorientation time τ_{opt} and for the optimal search time $\langle \bar{t} \rangle_{\text{opt}}$. The existence of an optimal reorientation time appears to be an intrinsic property of RTWs in confinement, independently of the nature of the boundary condition. We emphasize that, compared to pure ballistic motion, tumbles allow for reorientations close to the target. However, frequent tumble results in a redundant exploration of regions distant to the target. Therefore, our intuitive interpretation is that the existence of an optimal reorientation time results from a tradeoff between an enhanced ability to explore the region near the target and an increased risk to return to regions that have already been explored. We emphasize that the predicted scaling for the optimal search time (i.e., $\langle \bar{t} \rangle_{\text{opt}} \propto (b/v)(b/a)^{d-1}$) is characteristic of a noncompact process [21,23]; hence the optimal search is significantly more efficient than a diffusive search, which scales according to Eq. (2).

We now compare our results to previous studies on RTWs in confinement. First, Ref. [35] analyzed a discrete version of the problem considered in the present work, where the target was a single site of a regular lattice. Reference [35] suggested a linear scaling of the optimal reorientation time in terms of the confinement radius b: $\tau_{\text{opt}} = \xi b/v$, with a relatively small proportionality coefficient $\xi \approx 0.10$. However, we suggest that the observed low value for ξ could result from a contribution of a $1/\log(b/a)$ correction.

Second, we point out that Ref. [33] considers a geometry, which is identical to the one considered in the present paper. However, the choice for the detection criteria was very different in this earlier reference, since the target could be detected only during tumbling events, and not during runs. This leads to very different criteria for minimizing the search time.

Third, we emphasize that in Ref. [37], the RTW is biased towards the target. The optimal reorientation time is found when a finite waiting time is associated to each tumble event. The existence of an optimal reorientation time requires that a finite waiting time is associated to each tumble event. Therefore, we expect that the prediction for the optimal reorientation time in Ref. [37] (i.e., $\tau_{\mathrm{opt}} \propto a^{1/3}$) to be different from the one presented in our paper. Nevertheless, it is worth noticing that the existence of an optimal reorientation time in Ref. [37] results from a cost-risk tradeoff between short runs, which reduces the risk of picking a wrong direction but at the cost of frequent stopping, and long runs, which are efficient to explore space but at the risk of missing the target.

Finally, the very recent numerical study [38] considers the first-passage properties of self-propelled particles, which change their orientation through rotational diffusion (instead of tumbles here). In contrast to our result, Ref. [38] concludes on an expression for the optimal reorientation time that is proportional to the size of the confining domain, yet with a relatively low value for the proportionality coefficient. However, the existence of an optimal search strategy appears to be a generic property of persistent random walks.

III. LÉVY WALKS

We next study numerically the case of Lévy walks, whose run durations are distributed according to a symmetric Lévy law that is restricted to the positive axis, with an index $\alpha > 1$ and a scale parameter τ. In particular, the distribution of run duration is heavy tailed $P(t) \sim t^{-\alpha-1}$ for $t \to \infty$. Here, we focus on a 2D geometry with specular boundary conditions. For $0 < \alpha < 1$, the persistence length is infinite, hence, with specular boundary, the search time is infinite. For all $\alpha > 1$, the search time can be minimized as a function of τ. The optimal value τ_{opt} decreases when α is increased [see Fig. 5(a)]. In particular, the search time for the Lévy strategy is minimized when $\alpha = 2$, i.e., when the length of the ballistic excursions has a finite second moment and the central limit applies. We point out that the choice of a Lévy walk, even with exponents close to $\alpha = 2$, does not provide any quantitative advantage to find the target over exponential RTW [see Fig. 5(a)].

IV. REGULAR WALKS

In this section we focus on the 2D geometry and we find that the regular-step walk, i.e., with reorientations at deterministic time intervals τ, can outperform both Lévy and exponential RTWs, both in the presence of a specular or a scattering confinement.

With a specular confining boundary, we find numerically that the mean search time is minimized for $\tau_{\mathrm{opt}} = \gamma_2^{\mathrm{r|spec}} b/v$, where $\gamma_2^{\mathrm{r|spec}} = 1.4 \pm 0.1$. The optimal search time also follows a scaling of $\langle \bar{t} \rangle_{\mathrm{opt}} \underset{a \ll b}{\sim} 2\xi_d^{\mathrm{r|spec}} (b/v)(b/a)^{d-1}$, where $\xi_2^{\mathrm{r|spec}} = 0.78 \pm 0.01$.

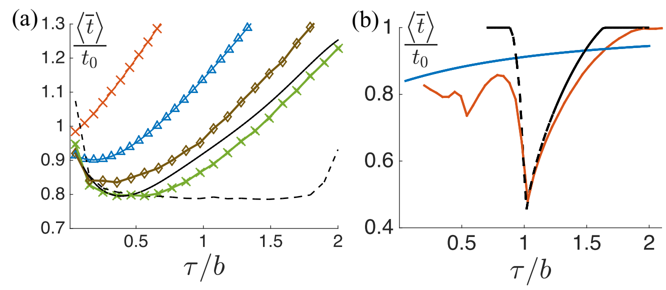

FIG. 5. (a) Search time of a 2D disk with confinement at $b/a = 200$ with specular confinement, for (solid colored lines with symbols) Lévy walks with the following values of α: 1.4, 1.6, 1.8, and 2 (from top to bottom); (solid black line) exponentially distributed step walk; (dashed black line) regular step walk. (b) Search time of a 2D disk with confinement at $b/a = 200$ for a regular-step walk with scattering confinement: simulations (solid orange line) indicate a sharp minimum at $\tau = b$, as predicted by our approximate expression (dashed black lines), which outperforms the exponential walk (solid upper blue line).

With a scattering confining boundary, simulations indicate that the GMFPT displays a sharp minimum at $\tau_{\mathrm{opt}} = \gamma_2^{\mathrm{r|scat}} b/v$ with $\gamma_2^{\mathrm{r|scat}} = 1.01 \pm 0.01$ [see Fig. 5(b)]. The GMFPT also displays local minima at $\tau = b/(2v)$ and $\tau = b/(3v)$. Indeed, the values $\tau = b/(nv)$ maximize the probability to reach the target after nth reorientation events before a new scattering event at the boundary. We present an analytical description of the minimum at $\tau = b/v$ in Appendix A. At optimality, the search time scales as $2(b/v)(b/a)$, with a relatively small proportionality constant $\xi_2^{\mathrm{r|scat}} = 0.28 \pm 0.02$. As $\xi_2^{\mathrm{r|spec}} < \xi_2^{\mathrm{spec}}$ and $\xi_2^{\mathrm{r|scat}} < \xi_2^{\mathrm{scat}}$, we conclude that the regular RTW with constant step durations can outperform any exponential RTWs.

Similar scalings hold in the stubborn case, both for the optimal reorientation time and for the optimal search time, and we find that the proportionality constants read $\gamma_2^{\mathrm{r|scat}} = 1.01 \pm 0.01$ (similarly to the scattering case) and $\xi_2^{\mathrm{r|stub}} = 0.78 \pm 0.01$ (similarly to the specular case).

V. CURVED GEOMETRY

We now show that these results can be extended to other geometries. We consider a RTW with exponentially distributed runs on a sphere, which is represented in Fig. 6(a). The coordinate r here refers to the latitude on the sphere, with $r \in [0,\pi]$; the target consists in the north pole region with maximal latitude a. The implementation of simulation is detailed in Appendix B. We now proceed to the analysis of the optimal reorientation time using the uniform approximate scheme developed above.

In the diffusive limit, the search time reads $\langle \bar{t} \rangle \sim [8/(v\tau)] \ln(\pi/a)$ when $a \ll 1$ [25]. To study the ballistic limit, we define the probability p_h according to Eq. (3). In the limit $a \ll 1$, we expect the probability distribution of the position at reorientation events to follow the uniform distribution on the sphere, hence that $p_r(r) \sim \sin(r)/2$. The probability of choosing a direction that crosses the target, either directly or after a passing over the south pole, reads $p_{\mathrm{dir}}(r) = (2/\pi)\theta_a$,

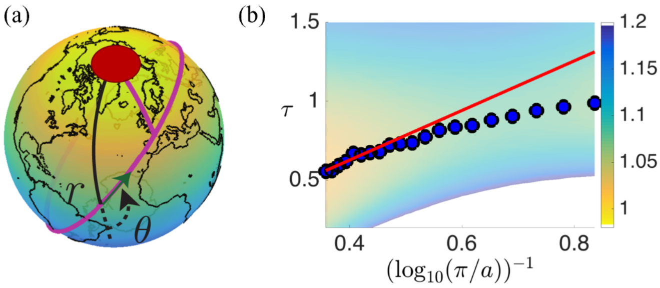

FIG. 6. Search of a cap on a sphere. (a) The coordinate $r \in [0,\pi]$ represents the latitude on the sphere. The target is a spherical cap of latitude a (red circle). (b) Search time normalized by $t_0 = v/(\pi a)$, in terms of the persistence time τ and of the size of the target a [measured as $\log_{10}(\pi/a)^{-1}$], and optimal reorientation time $\tau_{\rm opt}$ obtained by (blue circles) simulations and (red line) curve $\tau_{\rm opt}$ from Eq. (24).

where θ_a is defined in Eq. (B3). Last, the probability of performing a sufficiently long run to reach the target reads: $p_{\rm reach}(r) = (e^{-r/\tau} + e^{-(2\pi - r)/\tau})/2$.

We notice that $p_r(r) \times p_{\rm dir}(r) \sim a/\pi$ in the limit $a/r \ll 1$. Hence we obtain that $\langle \bar{t} \rangle \sim 2\pi/\{1 - \exp(-2\pi/\tau)\}$ in this limit. Using the uniform approximation method presented in Sec. II B, we find that the optimal search time reads $\tau_{\rm opt} \sim 2\pi/\log(\pi/a)$ at leading order in $a \ll 1$. Analysis of simulations indicate a noncompact scaling for the optimal search time $\langle \bar{t} \rangle_{\rm opt} \underset{a \ll 1}{\sim} \pi \xi^{\rm sph}/(av)$,, where $\xi^{\rm sph} = 1.0 \pm 0.1$ (see Fig. 6). We also find that the optimal reorientation time scales as

$$\tau_{\rm opt} \underset{a \ll \pi}{\sim} \gamma_{\rm sph} \frac{\pi}{v \log(\pi/a)}, \tag{24}$$

where $\gamma_{\rm sph} = 0.5 \pm 0.1$. The uniform approximation provides the appropriate scaling of the optimal reorientation time, however it does not predict the exact value of the proportionality factor $\gamma_{\rm sph}$.

We point out that Eq. (24) yields the same scaling as Eq. (10), with, however, a smaller numerical prefactor. We suggest that the origin of this discrepancy is related to the following specificity of the spherical geometry: at the south pole ($r \in [\pi - a, \pi + a]$), all ballistic trajectories eventually cross the target at the north pole (see Appendix B). The optimal reorientation time is shifted to lower values, since shorter reorientation times enhance the probability of tumbles within the south pole region whereby the probability to reach the north pole during the next run is high.

VI. EXTENSIONS AND CONCLUSION

To conclude, we have shown that the search time for a target in a bounded domain for a run-and-tumble searcher can be minimized by tuning the persistence time. This result is robust and holds for different boundary conditions in two and three dimensions; it was also obtained for deterministic walks and Lévy walks with finite first moment. This optimal search strategy, which applies to single targets or equivalently regularly spaced targets, therefore notably differs from the case of Poisson-distributed targets [16], in which case the straightforward ballistic motion minimizes the search time. These results therefore highlight the crucial role of the spatial distribution of targets in search problems, and put forward the robustness of optimal RTWs for single-target search problems.

We suggest that our result could also apply to a many-body billiard problem, in which the short-range interactions between freely ballistic particles result in trajectories that can be described as RTWs. The Knudsen regime, in which the mean-free path is comparable to the dimension of the confinement [45,46], is the analog of the ballistic limit. In this context, as the mean-free path is controlled by the density of particles, our main result suggests that an optimal density could enhance the reaction kinetics of a tracer particle with a fixed target.

APPENDIX A: ANALYTICAL RESULTS FOR A REGULAR RUN-AND-TUMBLE WALK

Here, we consider that reorientations occur at regular time intervals τ, i.e., the distribution of reorientation times reads $\pi(t) = \delta(t - \tau)$, where δ is the Dirac function. We recall that in the presence of a scattering boundary condition at $r = b$, the search time exhibits a sharp minimum at $\tau = b/v$. We obtain an analytical description for the minima at $\tau = b/v$ in two dimensions.

We start by considering that the searcher is started at the scattering boundary $r = b$. After a time τ, the position of the particle is either $\tilde{r}(\theta) = \sqrt{b^2 + v^2\tau^2 + 2bv\tau\cos(\theta)} \in]a,b[$, $\tilde{r}(\theta) = a$ or $\tilde{r}(\theta) = b$. These three situations may occur, depending on the value of the ratio $(v\tau)/b$.

First case: $b < v\tau < 2b$. Here, we distinguish three subsituations, according to the value of the initial direction $\theta \in [0,\pi/2]$ (see Fig. 7).

If $\pi - \theta_a < \theta < \pi$, where $\theta_a = \arcsin(a/b)$, the searcher hits the target in a time b/v (up to a minor term that scales as a/v).

If $\pi - \theta_b < \theta < \pi - \theta_a$, where $\theta_b = \arccos[\tau/(2b)]$, the searcher is reoriented at the position $\tilde{r}(\theta) \in]a,b[$. The final radius of a searcher whose initial direction is $\theta = \theta_a$ is denoted $r_b \equiv \tilde{r}(\theta_a)$ and reads:

$$r_b = \sqrt{b^2 - 2\sqrt{b^2 - a^2}v\tau + v^2\tau^2}. \tag{A1}$$

The distribution of final position $\tilde{r}$ after a single run is a nonuniformly distributed random variable, with a density

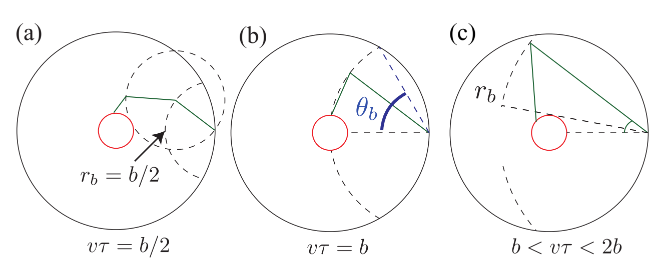

FIG. 7. Sketches of the search process. The choice $\tau = b/(nv)$ maximizes the probability to reach the target after the nth reorientation event: (a) $n = 2$, (b) $n = 1$, (c) the search time increases when $\tau > b/v$.

probability equal to the Jacobian:

$$\left|\frac{\partial\theta}{\partial\tilde{r}}\right| = \frac{2\tau\,\tilde{r}}{b\tau\sqrt{4b^2\tau^2-(b^2-\tilde{r}^2+\tau^2)^2}}. \tag{A2}$$

Notice that the Jacobian defined in Eq. (A2) diverges for $b-\tau$ (i.e., $\theta=0$), which is expected since a small variation of $\tilde{r}$ around $b-\tau$ corresponds to an abrupt change in the value of θ.

Finally, if $\pi/2<\theta<\pi-\theta_b$, the searcher takes a time $t_b(\theta)=-2b\cos(\theta)/v$ to reach its final position at $\tilde{r}=b$. In two dimensions, the mean return time to the boundary $r=b$, averaged over the angles $\theta\in[\theta_b,\pi/2]$, reads:

$$\int_{\pi/2}^{\pi-\theta_b}\frac{2d\theta}{\pi}\,t_b(\theta) = \frac{2b\left(2-\sqrt{4-\frac{v^2\tau^2}{b^2}}\right)}{\pi v}. \tag{A3}$$

Second case: $v\tau<(b-a)$. Here, the final position of the particle $\tilde{r}(\theta)$ takes all values between b and its minimal value $r_b\equiv b-v\tau$.

Third case: $2b<v\tau$. The search time is a constant of τ and is strictly equal to the expression of Eq. (2). Within a single run from the boundary, the target is either hit or is missed and the final position is $\tilde{r}=b$. We set $\theta_b=\theta_a$ if $2b<v\tau$.

Let us detail the situation in the case $b<v\tau<2b$. The renewal equation method (as presented in Ref. [41]) leads to the following integral equation on the search time:

$$\langle t(b)\rangle = \frac{2a}{\pi b}\frac{b}{v} + \int_{r_b}^{b}\frac{2d\tilde{r}}{\pi}\left|\frac{\partial\theta}{\partial\tilde{r}}\right|\{\tau+\langle t(\tilde{r})\rangle\} + \left[1-\frac{2\theta_b}{\pi}\right]\left[\frac{2b}{\pi v}\left(2-\sqrt{4-\frac{v^2\tau^2}{b^2}}\right)+\langle t(b)\rangle\right], \tag{A4}$$

where (i) the first term in the right-hand side of Eq. (A4) corresponds to the product of the probability to reach the target in a single run by the characteristic time of the run; (ii) the second term corresponds to the reorientation events at a random position $\tilde{r}\in[r_b,b]$; and (iii) the last term corresponds to the product of the probability to reach the boundary at $\tilde{r}=b$ in a single run by the sum of (a) the average time Eq. (A3) to reach the boundary at $\tilde{r}=b$ and (b) of the averaged search time from $\tilde{r}=b$.

To simplify the expression of Eq. (A4), we make the assumption that

$$\langle t(\tilde{r})\rangle = \frac{1}{\pi}\frac{a}{\tilde{r}}\frac{\tilde{r}}{v} + \{\tau+\langle t(b)\rangle\}\left[1-\frac{a}{\pi\tilde{r}}\right], \tag{A5}$$

which is justified as (i) the first term on the right-hand side of Eq. (A5) corresponds to a success to encounter the target after the reorientation event, and (ii) the second term corresponds to a failure to encounter the target after the reorientation event. With the approximation of Eq. (A5), Eq. (A4) becomes:

$$\langle t(b)\rangle = \frac{\frac{2a}{b\pi}\frac{b}{v} + \int_{r_b}^{b}\frac{2d\tilde{r}}{\pi}\left|\frac{\partial\theta}{\partial\tilde{r}}\right|(2\tau+a/v) + \left[1-\frac{2\theta_b}{\pi}\right]t_d}{1-\int_{r_b}^{b}d\tilde{r}\left|\frac{\partial\theta}{\partial\tilde{r}}\right|\left[1-\frac{a}{\pi\tilde{r}}\right]-\left[1-\frac{2\theta_b}{\pi}\right]}, \tag{A6}$$

where

$$t_d = \left[\frac{2b}{\pi v}\left(2-\sqrt{4-\frac{v^2\tau^2}{b^2}}\right)\right].$$

The expression Eq. (A6) provides a satisfactory description of the minimum at $\tau=b/v$ [see Fig. 7(b)]. The arguments presented here can be extended to the 3D geometry.

APPENDIX B: SPHERE GEOMETRY

We consider a ballistic particle starts moving from its initial position at the zenith angle r_0 (on the surface of a sphere of radius 1), where θ_0 refers to the angle between the velocity vector and the position vector (see Fig. 6). The equation of motion of this ballistic particle reads [47]

$$\cos r(t) = \cos r_0\cos t + \sin r_0\sin t\cos\theta_0, \tag{B1}$$

where we have set $v=1$. To determine whether the particle will cross the target, we solve Eq. (B1) in terms of t_a with the final condition $r(t_a)=a$ and we find:

$$t_a = \frac{\cos(r)\cos(r_0)-\sqrt{\sin^2(r_0)\cos^2(\theta_0)\Delta}}{\sin^2(r_0)\cos^2(\theta_0)+\cos^2(r_0)}, \tag{B2}$$

where

$$\Delta = \cos^2(r_0)-\cos^2(r)+\sin^2(r_0)\cos^2(\theta_0).$$

The condition $\Delta>0$ defines the critical angle

$$\theta_a = \arccos\left(\frac{\sqrt{\cos^2 a-\cos^2 r_0}}{\sin r_0}\right). \tag{B3}$$

Hence, the trajectory crosses the target if the initial angle θ_0 lies either in the interval $[0,\theta_a]$ or in $[\pi-\theta_a,\pi]$. Notice that for tumbles occurring in the south pole region $r\in[\pi-a,\pi+a]$, we have $\theta_a=\pi$, as expected. Indeed, in this region, all ballistic trajectories will eventually cross the target at the north pole.

Along a trajectory between r and r' of length vt, the change in longitude $\delta\phi$ can be computed through the relation:

$$\cos(vt) = \sin r_0\sin r + \cos r_0\cos r'\cos(\delta\phi). \tag{B4}$$

The set of kinematic equations (B2) and (B4) are used to achieve a RTW on the surface of the sphere.

[1] T. Einwohner, J. Chem. Phys. **49**, 1458 (1968).

[2] M. Knudsen, *The Kinetic Theory of Gases: Some Modern Aspects* (Methuen, London, 1950), p. 64.

[3] K. Martens, L. Angelani, R. Di Leonardo, and L. Bocquet, Eur. Phys. J. E **35**, 1 (2012).

[4] P. J. W. Moll, P. Kushwaha, N. Nandi, B. Schmidt, and A. P. Mackenzie, Science **351**, 1061 (2016).

[5] J. Zaanen, Science (New York, N.Y.) **351**, 1026 (2016).

[6] A. Zoia, E. Dumonteil, and A. Mazzolo, Phys. Rev. Lett. **106**, 220602 (2011).

[7] A. Zoia, E. Dumonteil, and A. Mazzolo, Phys. Rev. E **83**, 041137 (2011).
[8] P. Romanczuk, M. Bar, W. Ebeling, B. Lindner, and L. Schimansky-Geier, Eur. Phys. J. E **202**, 1 (2012).
[9] H. C. Berg, ed., *PloS one*, Biological and Medical Physics, Biomedical Engineering, Vol. 7 (Springer, New York, 2004), p. 133.
[10] F. Jülicher, A. Ajdari, J. Prost, and F. Julicher, Rev. Mod. Phys. **69**, 1269 (1997).
[11] M. L. Heuzé, P. Vargas, M. Chabaud, M. Le Berre, Y.-J. Liu, O. Collin, P. Solanes, R. Voituriez, M. Piel, and A.-M. Lennon-Duménil, Immunol. Rev. **256**, 240 (2013).
[12] O. Bénichou, C. Loverdo, M. Moreau, and R. Voituriez, Rev. Mod. Phys. **83**, 81 (2011).
[13] M. F. Shlesinger, J. Phys. Math. Theor. **42**, 434001 (2009).
[14] J. Yang, I. Kupka, Z. Schuss, and D. Holcman, J. Math. Biol. **73**, 423 (2016).
[15] B. Meerson and S. Redner, Phys. Rev. Lett. **114**, 198101 (2015).
[16] G. M. Viswanathan, S. V. Buldyrev, S. Havlin, M. G. E. da Luz, E. P. Raposo, and H. E. Stanley, Nature (London) **401**, 911 (1999).
[17] A. M. Edwards, R. A. Phillips, N. W. Watkins, M. P. Freeman, E. J. Murphy, V. Afanasyev, S. V. Buldyrev, M. G. E. da Luz, E. P. Raposo, H. E. Stanley, and G. M. Viswanathan, Nature (London) **449**, 1044 (2007).
[18] S. Benhamou, Ecology **88**, 1962 (2007).
[19] A. James, M. J. Plank, and A. M. Edwards, J. R. Soc. Interface **8**, 1233 (2011).
[20] V. V. Palyulin, A. V. Chechkin, and R. Metzler, Proc. Natl. Acad. Sci. USA **111**, 2931 (2014).
[21] S. Condamin, O. Bénichou, V. Tejedor, R. Voituriez, and J. Klafter, Nature (London) **450**, 77 (2007).
[22] O. Bénichou, C. Chevalier, J. Klafter, B. Meyer, and R. Voituriez, Nature Chem. **2**, 472 (2010).
[23] O. Bénichou and R. Voituriez, Phys. Rep. **539**, 225 (2014).
[24] T. Guérin, O. Bénichou, and R. Voituriez, Nature Chem. **4**, 568 (2012).
[25] A. Singer, Z. Schuss, D. Holcman, and R. Eisenberg, J. Stat. Phys. **122**, 437 (2006).
[26] A. Singer, Z. Schuss, and D. Holcman, J. Stat. Phys. **122**, 465 (2006).
[27] Z. Schuss, A. Singer, and D. Holcman, Proc. Nat. Acad. Sci. USA **104**, 16098 (2007).
[28] J.-F. Rupprecht, O. Bénichou, D. S. Grebenkov, and R. Voituriez, J. Stat. Phys. **158**, 192 (2014).
[29] S. A. Isaacson and J. Newby, Phys. Rev. E **88**, 012820 (2013).
[30] T. Gilbert, H. C. Nguyen, and D. P. Sanders, J. Phys. Math. Theor. **44**, 065001 (2011).
[31] S. Blanco and R. Fournier, Europhys. Lett. **61**, 168 (2003).
[32] O. Bénichou, M. Coppey, M. Moreau, P. H. Suet, and R. Voituriez, Europhys. Lett. **70**, 42 (2005).
[33] O. Bénichou, C. Loverdo, M. Moreau, and R. Voituriez, Phys. Rev. E **74**, 020102 (2006).
[34] O. Benichou, C. Loverdo, M. Moreau, and R. Voituriez, J. Phys.: Condens. Matter **19**, 065141 (2007).
[35] V. Tejedor, R. Voituriez, and O. Bénichou, Phys. Rev. Lett. **108**, 088103 (2012).
[36] D. Campos, E. Abad, V. Mendez, S. B. Yuste, and K. Lindenberg, Phys. Rev. E **91**, 052115 (2015).
[37] P. Romanczuk and G. Salbreux, Phys. Rev. E **91**, 042720 (2015).
[38] J. Wang, Y. Chen, W. Yu, and K. Luo, J. Chem. Phys. **144**, 204702 (2016).
[39] C. Gardiner, *Stochastic Methods: A Handbook for the Natural and Social Sciences* (Springer, Berlin, 2009), p. 447.
[40] G. H. Weiss, J. Stat. Phys. **37**, 325 (1984).
[41] S. Redner, *A guide to First- Passage Processes* (Cambridge University Press, Cambridge, 2001).
[42] R. Feres and G. Yablonsky, Chemical Engineering Science **59**, 1541 (2004).
[43] J. Tailleur and M. E. Cates, Phys. Rev. Lett. **100**, 218103 (2008).
[44] P. K. Ghosh, V. R. Misko, F. Marchesoni, and F. Nori, Phys. Rev. Lett. **110**, 268301 (2013).
[45] K. Malek and M. O. Coppens, Phys. Rev. Lett. **87**, 125505 (2001).
[46] S. Blanco and R. Fournier, Phys. Rev. Lett. **97**, 230604 (2006).
[47] J. W. Harris and H. Stocker, Comput. Math. Appl. **37**, 133 (1999).