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On random search: Collection kinetics of *Paramecia* into a trap embedded in a closed domain

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We study the kinetics of a large number of organisms initially spread uniformly in a circular two-dimensional medium, at the center of which a smaller circular trap has been introduced. We take advantage of the acidophily of *Paramecium caudatum*, which, coming from a neutral medium, penetrates a region of moderate acidity but moves back in the opposite situation when it meets a sharp negative acidity gradient to quantify its rate of irreversible aggregation into a spot of acidified medium in water. Two regimes are distinguished: A ballistic regime characteristic of "fresh" paramecia where the organisms swim in a straight path with a well defined velocity and a Brownian regime characteristic of older paramecia where the mean free path of the organisms is smaller than the system size. Both regimes are characterized by distinct aggregation laws. They both result from a pure random trapping process that appears to have no adaptive strategy.

I. INTRODUCTION

The motion of most living animals in their natural environment is altered by various stimuli such as a physical obstacle, exposure to body forces (for example, gravitational, electric, and magnetic[1,2]), and the modification of the medium temperature or of its nature by a change in chemical composition. The net displacement in a given direction of a living organism that would otherwise wander around the same point caused by a gradient of nutrient is called *chemotaxis*.[3] A modification of its motility parameters (velocity and mean free path) by the medium composition, which may also give rise to a net displacement, is referred to as *chemokinesis*.[4,5] The detailed biochemical processes leading to a change in behavior induced by the medium are specific to each species and have begun to be understood for simple organisms such as bacteria.[6,7] The causes for the animals to move in the quest for more nutriments are not discussed in this paper.[8] Our goal is to document the motion itself and understand how the time the animal spends to find a favorable spot in a given domain depends on the motion and on the boundary conditions of the search process. For this purpose, we consider a simple organism and a simple geometry.

Paramecia are unicellular eukaryotes that swim in fresh water.[9] They propel themselves by beating thousands of cilia on their membrane in a synchronized fashion, conferring a helical motion around a rectilinear path. Several species, among them *Paramecium caudatum*, are known to collect in slightly acidified regions, the optimal *p*H range being 5.4–6.4.[9,10] We take advantage of this *acidophily* of *P. caudatum* to study the collection kinetics or aggregation of a large number of organisms initially spread uniformly in a nearly two-dimensional layer of neutral medium, into which an acidified region has been introduced (see Figs. 1 and 2). The acidified region has a circular geometry and is placed at the center of the embedding medium, which is also circular. The acidic spot is initially empty of paramecia, which progressively aggregate in it. Once a paramecium has entered the spot, it does not leave it. The entire paramecium population ultimately collects in the central acidic spot. With N_{tot} the number of paramecia present in the medium and $N(t)$ the current number of paramecia in the spot at time t, we determine experimentally how the ratio $N(t)/N_{\mathrm{tot}}$ goes from 0 to 1 with time and study the dependence of the time scale on the medium diameter L, acid spot diameter d, and features of the paramecia motion. In particular, we will distinguish between two regimes depending on the paramecia's motility: A ballistic regime characteristic of "fresh" paramecia where the organisms swim in a linear path with a well defined velocity u and a Brownian regime characteristic of "old" paramecia where the mean free path of the organisms is smaller than the system size L. Each regime gives rise to different behavior of $N(t)$.

This system is sufficiently simple to be used in the classroom to illustrate the behavior of random walkers. Paramecia can be obtained from biology departments or biology supply houses. Their large size allows for a simple visualization (a camera with a macrolens is sufficient), and the experimental setup is simple. It also shows that results from kinetic theory can be applied to simple living organisms.

II. MATERIALS AND METHODS

The medium consists of 50 ml of wheat grass powder infused for 20 min in 900 ml of water and then filtered and sterilized and supplemented by 50 ml of buffer solution (15 g of tris, 15 g of $Na_2HPO_42H_2O$, and 4 g of $NaH_2PO_4H_2O$ for 1 l of solution with fuming HCl added to adjust the *p*H value to 7) in 1 l of water. The medium is bacterized with *Klebsiella pneumoniae*[11] 1 day before use; then 0.8 mg/l of β-sitosterol is added. The cells are grown at room temperature for 3–7 days. Older paramecia, up to 20 days old, are also used in the experiment.

When the cell density has reached about 200 cells/ml, 1 g/l of disodium fluorescein is added. An acid solution is prepared at the same concentration of disodium fluorescein in distilled water, and the *p*H is adjusted to 6 by the addition of

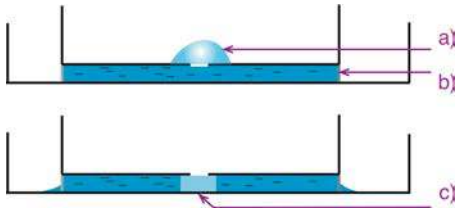

Fig. 1. Experimental setup and method for injecting a drop of concentrated acid (pH in the range of 4.5–6.5) at the center of the cell. (a) A drop of the acid solution is placed on a 1 mm diameter hole above the center of the (b) medium containing *P. caudatum* and flows by capillarity action to form a (c) circular spot of acid.

HCl. The disodium fluorescein is used to reveal the size of the acid spot (see the following) and also to enhance contrast and make the cells more visible.

Approximately 1 ml of the solution containing the paramecia fills the gap between two transparent circular plates (plastic Petri dishes), as seen in Fig. 1. The top plate is $L=50$ mm in diameter, and the gap width $h=0.4$ mm is imposed by three small spacers. A 1 mm diameter hole is drilled at its center. A drop of the acid solution of volume $V=50-300$ μl is placed on the hole and flows by capillarity to form a circular spot of acid at the center of the medium between the plates. Its diameter $d=(4V/\pi h)^{1/2}$ can be varied easily. The temperature is not controlled, and experiments are performed at room temperature (25 °C). We did not observe convective motion in the setup.

Two linear lights, each made of 24 white LEDs at an incidence of about 10° to the horizontal direction, are placed in parallel at 40 mm from the center of the setup and 10 mm below the bottom plate and provide uniform lighting of the setup placed above a dark background. The light makes the paramecia visible and excites the fluorescein. Images are acquired with a 1024×1024 CCD camera mounted above the setup at a right angle with a rate of 1 or 7 frames/s. A typical experiment lasts 15 min. The image resolution lets us view the whole field and locate with precision each paramecium (which is ≈100 μm long) at the same time.

The resulting movies are postprocessed using free MATLAB code[12] adapted for our purposes to track each paramecium, reconstruct trajectories, and measure velocities and rebound angles. The fluorescence level of disodium fluorescein decays strongly in an acid phase so that the diameter of the acid region d can be directly measured from the images.

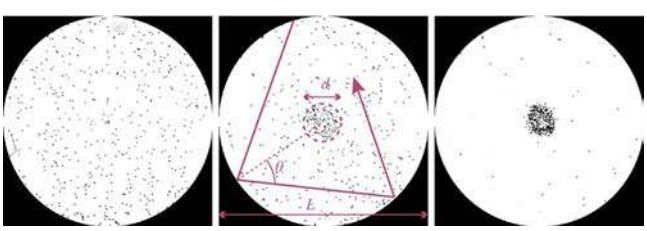

Fig. 2. The aggregation kinetics of a population of fresh *P. caudatum* into an acidic spot (pH=6). The paramecia are initially spread uniformly in the medium and progressively collect in the spot of diameter d. They do so by successive rebounds at the domain boundary (diameter $L=50$ mm), following straight paths between each rebound, sketched as gray lines. The reflection angle θ of the next path direction is random at each rebound, as seen in Fig. 4. The total duration of the process is of the order of 1000 s.

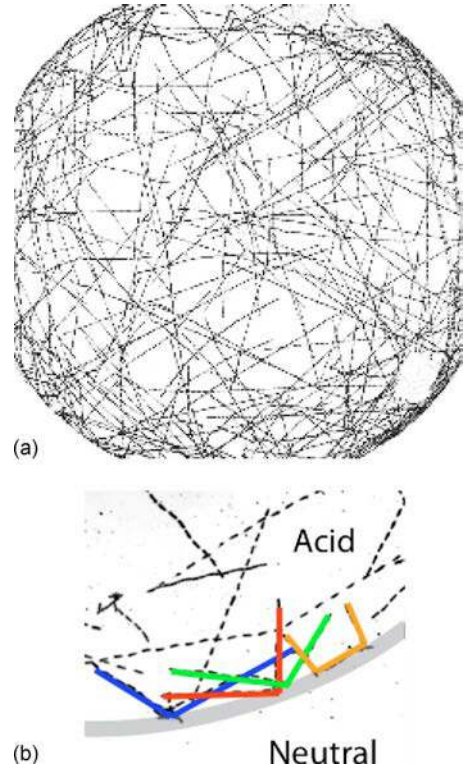

Fig. 3. (a) Traces of fresh paramecia recorded at 7 frames/s while swimming in a neutral medium before the introduction of the acid region. The motion is ballistic in this case, and the mean free path of the organisms is larger than the size L of the domain. The density of paramecia is sufficiently dilute so that their trajectories rarely interfere and can be considered as independent. (b) Typical trajectories of paramecia trapped into the acid region (pH=6) and meeting its boundary (thick gray line). Paramecia rebound at a random angle and sometimes follow the border before redirecting toward the acidic phase.

III. RESULTS

P. caudatum swims at a well defined velocity of the order of 1 mm/s for organisms having 3–7 days of incubation in the medium, and the motion is approximately linear. Their concentration is sufficiently diluted in our experiments, and their trajectories rarely interfere (they can overlap because the medium thickness $h=0.4$ mm is larger than the size of a paramecium and can thus be considered to be independent). Their velocity does not depend on the absolute acid concentration provided it is uniform in the medium. However, we have noticed a slight increase in the velocity up to 1.2 mm/s in a pH=5 medium.[13–15]

The motion of paramecia is strongly influenced by pH gradients in the medium and more precisely by the sign of the gradient: A paramecium swimming from a uniform neutral region at pH=7 into a moderately acid region (say, at pH=6) has an unperturbed trajectory even if the pH front separating the two regions is sharp. The motion of the paramecium is insensitive to the change of acidity. In contrast, a paramecium coming from an acid region and reaching a region of increase of pH stops suddenly, rotates on itself possibly several times, and swims back into the acidic region with the same speed but with a direction chosen at random, as seen in Fig. 3. The overall rebound lasts for a fraction of a second. This "avoiding reaction" has been known for a

long time[10] and can probably be traced back to the sensitivity to the pH of calcium ion channels in the paramecium membrane.[16,17]

In its normal state the paramecium moves forward with its cilia all beating in the forward mode. The ratio of intracellular to extracellular calcium ions Ca^{2+} concentration is fixed at its equilibrium value. An increase of Ca^{2+} influx through the membrane into the cell causes an increase of intracellular Ca^{2+} ions, inducing, in turn, a reversal of the ciliary beat.[18] The paramecium stops and then swims backward momentarily before the cilia recover their normal beating activity by normal regulation. The paramecium then swims forward again, in a new direction approximately chosen at random.[9] However, calcium ion currents through the membrane are known to be affected by intracellular pH: The intracellular increase of pH enhances inward the Ca^{2+} current, while a decrease of pH depresses the current.[17] Thus, if motion reversal is associated with an increase of Ca^{2+} current, it is likely to occur when paramecia attempt to cross a front of increasing pH and likely not to occur in the opposite situation, conferring to paramecia an apparent acidophily. This interpretation has its limitations because we have also observed that the same rebound phenomenon occurs for paramecia attempting to cross a neutral/acid front when the acidity is strong (that is, $p\mathrm{H}<3$), indicating that the calcium ions transfer at the membrane may also be altered in this limit.

For moderate acidity, for pH in the range of 4.5–6.5 in the central spot, paramecia penetrate the spot and remain trapped. For an unknown reason, the efficiency of the trap is enhanced by the addition of disodium fluorescein (which we use for visualization purposes) in the incubation solution. Without it, some paramecia escape the spot at longer times.

Our observations of the reaction of *P. caudatum* to acidity gradients hold for both fresh and older organisms. The motion of the organisms in a uniform area depends on their age, as discussed in the following.

A. Ballistic motion

In a freshly prepared solution (see Sec. II), *P. caudatum* swims in straight paths and typically explores the whole domain, rebounding at its border, as shown in Fig. 3. This behavior, which we call ballistic because the mean free path ℓ of the organisms is larger than the domain size L (a limit called the Knudsen regime for dilute gases), is characteristic of fresh paramecia that have spent less than 7 days in the medium. The velocity is also well characterized by ensemble averages. Figure 4 shows that the velocity u among the paramecium population is less widely distributed than a Maxwellian distribution in two dimensions, which would occur for a random walk (see Refs. 19 and 20 for measurements with *Chlamydomonas nivalis* and *Peridinium gatunense*). Also shown in Fig. 3 is the distribution of the rebound angle θ at the domain border, which is close to a uniform distribution with a maximum angle much smaller than $\pi/2$.

The overall motion of an individual paramecium in the population is thus made of straight lines across the domain and rebounds at the boundary with a new direction chosen at random at each rebound until the direction points sufficiently close to the domain center where the trapping spot is located. Once the path has crossed the spot border, the paramecium is trapped in the spot and joins those whose path had crossed the spot location earlier.

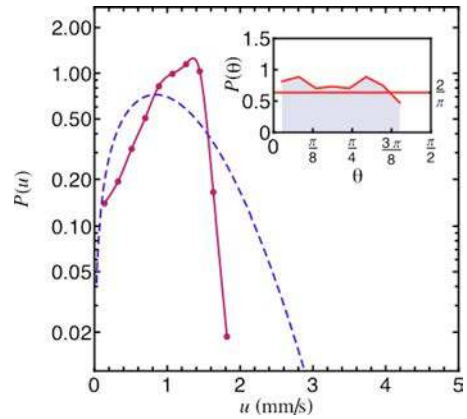

Fig. 4. Features of the individual's motion in the ballistic regime (strong paramecia). The velocity distribution $P(u)$ is superimposed with a Maxwellian distribution with the same mean. Insert: The distribution of rebound angle θ at the domain boundary as defined in Fig. 2 compared with the uniform distribution $P(\theta)=2/\pi$ used in the model.

The time-dependence of the number of paramecia $N(t)$ trapped in the acid spot normalized by the total number of paramecia in the medium N_{tot} is shown on Fig. 5. A good representation for $N(t)$ is

$$\frac{N(t)}{N_{\mathrm{tot}}} = 1 - e^{-t/\tau}, \tag{1}$$

where τ is a relaxation time, which decreases with the spot size d. Due to random exploration, it takes less time to find the spot when it is larger. The aggregation law, Eq. (1), is characteristic of Poisson processes and can be understood from elementary considerations. The rebound angle θ is chosen randomly in the interval $[-\pi/2,\pi/2]$ at each rebound. The probability p that a paramecium will be trapped is the probability that θ lies in the interval $[-\theta_t,+\theta_t]$ with $\theta_t = \arcsin(d/L)$ so that

$$p = \frac{2}{\pi}\arcsin\left(\frac{d}{L}\right). \tag{2}$$

The probability of capture after n independent rebounds is

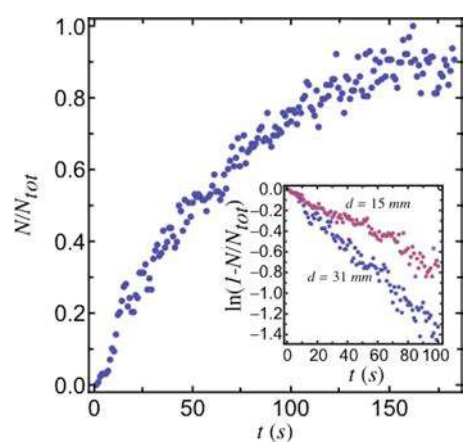

Fig. 5. Number of fresh paramecia that have aggregated in the central spot for a spot size $d=31$ mm as a function of time in the ballistic regime. Insert: Same relaxation process illustrated for two spot sizes $d=15$ and 31 mm. N_{tot} is the total number of paramecia in the medium.

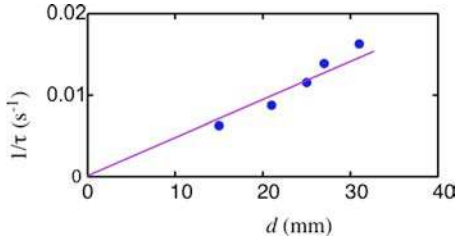

Fig. 6. The inverse of the time scale τ measured experimentally from $N(t)$ as in Fig. 5 for different spot diameters d. The line is the dependence expected from Eq. (7) with $L=5$ cm and $u=1$ mm/s.

$$P(n) = p(1-p)^{n-1}. \tag{3}$$

Assuming that all paramecia swim at the same velocity u (or that the dispersion of velocity around the mean can be disregarded; see Fig. 4), the duration of a crossing between two rebounds is $t(\theta)=(L/u)\cos\theta$. If θ is uniformly distributed in the ranges $[-\pi/2,-\theta_t]$ and $[\theta_t,\pi/2]$, the probability that the duration of crossing lies between t and $t+dt$ is

$$Q(t)dt = \int_{\theta\in\Theta} \frac{1}{\pi - 2\theta_t} d\theta, \tag{4}$$

where Θ is the range of values of θ such that $t(\theta)$ is in the range $[t,t+dt]$. We use the expression for $t(\theta)$ and obtain

$$Q(t) = \frac{u}{L}\frac{1}{\pi/2 - \arcsin(d/L)}\frac{1}{\sqrt{1-(ut/L)^2}}. \tag{5}$$

The distribution $T(t)$ of times t spent in the domain crossing and rebounding before being trapped in the acid spot is thus

$$T(t) = \sum_{n\geq 1} P(n) Q^{\otimes n}(t), \tag{6}$$

where $Q^{\otimes n}$ is the n-fold convolution of Q with itself.[21] This model cannot be solved exactly, but an approximate solution can be obtained as follows. The probability that a paramecium has made n rebounds before being trapped is $P(n) \propto e^{-pn}$ from Eq. (3) for $n \gg 1$ and $p \approx d/L \ll 1$, as seen from Eq. (2). The average number of rebounds before trapping is, from Eq. (3), given by $\langle n\rangle = 1/p$. Because the time spent rebounding before being trapped is proportional to the number of rebounds n and to the typical crossing time L/u, that is, $t \approx n(L/u)$, we have $T(t) \sim e^{-t/\tau}$ with

$$\tau \approx \frac{L^2}{ud}, \tag{7}$$

from which $N(t)/N_{\text{tot}}$ given in Eq. (1) follows. This model accounts for the experimentally observed $N(t)$, and the time scale τ has the order of magnitude and dependence on the spot size d expected from Eq. (7), as seen in Fig. 6.

B. Brownian motion

After 1 week of incubation in the same medium, the behavior of *P. caudatum* was observed to be qualitatively different and characterized by a "decline of vigor"[9] possibly due to aging or by the depletion of nutrients. The swimming speed is more broadly distributed and typically decreased by a factor of two ($u \approx 0.5$ mm/s). The overall trajectory of a paramecium exhibits a meandering path, with a mean free path ℓ much smaller than the domain size L (see Fig. 7). The paramecia were reinvigorated when entering the pH=6 acid spot, recovering their usual speed and correlated motion. We have no explanation for these possible physiological changes, but their consequences on the collection process are dramatic.

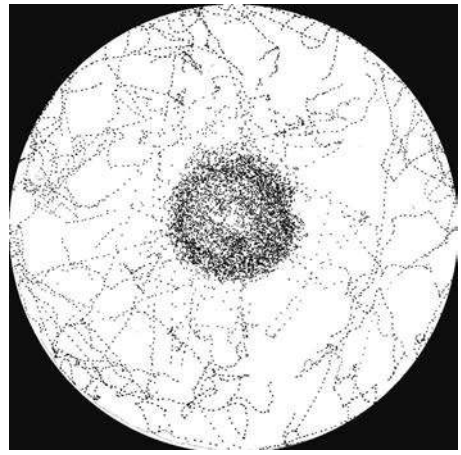

Fig. 7. Traces of older paramecia having incubated for 1 week in the same medium recorded at 1 frame/s while collecting in the central acid spot (pH=6). The path of paramecia in the neutral domain is characteristic of Brownian motion.

A way to study the motion's nature is to compute the correlation function $C(\Delta t)$ of the velocity vector defined as[22]

$$C(\Delta t) = \langle \mathbf{u}(t)\mathbf{u}(t+\Delta t)\rangle / \langle \mathbf{u}^2(t)\rangle, \tag{8}$$

where the brackets denote an average over the entire paramecium population. The function $C(\Delta t)$ was found to be independent of time t and to decay exponentially with Δt as $C(\Delta t) \sim e^{-\Delta t/t_c}$, with a correlation time t_c of the order of $t_c \approx 3.2$ s (see Fig. 8). The root mean square velocity $u_{\text{rms}} = \sqrt{\langle \mathbf{u}^2(t)\rangle}$ of the motion is observed to be constant for $12 < r < 25$ mm and of the order of $u_{\text{rms}} \approx 0.5$ mm/s (see Fig. 8). These features are typical of Brownian motion,[22] with a diffusion coefficient given by $D = u_{\text{rms}}^2 t_c = 0.8$ mm^2/s. The time increase of the mean square displacement $R^2(t) = \langle(\mathbf{r}(t)$

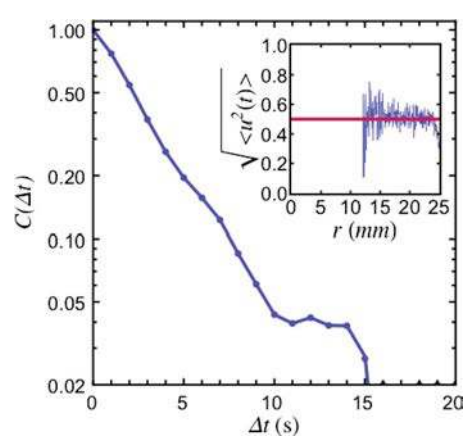

Fig. 8. The correlation function of the paramecia velocity vector defined in Eq. (8) decays exponentially, characteristic of Brownian motion, with a correlation time t_c of the order of 3.2 s. Insert: The root mean square velocity is approximately constant across the domain between the spot boundary at $r=d/2=12$ mm and the domain boundary at $r=L/2=25$ mm.

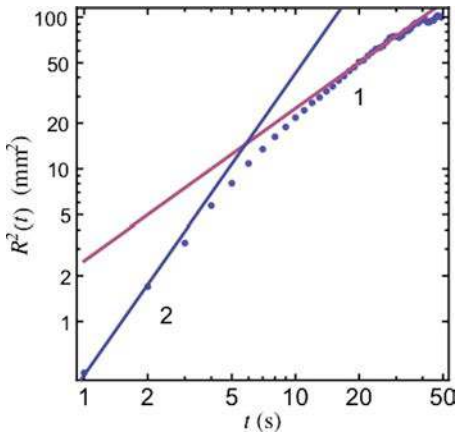

Fig. 9. The dispersion law $R^2(t)$ of the old paramecia from their initial location. The motion is ballistic for $t<t_c$, that is, $R^2(t)=(u_{\rm rms}t)^2$, and pure diffusion, that is, $R^2(t)=4Dt$ at larger times with the diffusion coefficient $D=0.8$ mm^2/s.

$-\mathbf{r}(0))^2\rangle$ of individual paramecium from their initial location $\mathbf{r}(0)$ is observed to be ballistic for short times for $t<t_c$, that is, $R^2(t)=(u_{\rm rms}t)^2$, and characteristic of pure diffusion in two dimensions at larger times, that is,

$$R^2(t) = 4Dt, \tag{9}$$

with a diffusion coefficient $D=0.8$ mm^2/s. This diffusion coefficient is several hundred times larger than that of HCl in water so that the concentration field of HCl does not change significantly over the entire aggregation period. The corresponding mean free path of the motion is $\ell=u_{\rm rms}t_c \approx 1.6$ mm, which is smaller than L (Fig. 9).

As in the ballistic regime, paramecia become trapped in the acid spot, which now behaves as a sink for the diffusion process occurring in the neutral medium surrounding the spot. Let $c(r,t)$ be the number of paramecia per unit area, depending on the radial location $d/2<r<L/2$ in the neutral medium and time t. The initial surface concentration $c(r,0)$ of paramecia is uniform, independent of r and thus $N_{\rm tot}=(\pi/4)(L^2-d^2)c(r,0)$. The solution for $c(r,t)$ at later times is analogous to that for the radial flow of heat in an infinite hollow cylinder with a fixed temperature in a smaller coaxial annular region. The full solution is complicated,[23] but the number of paramecia $N(t)$ trapped in the spot (equivalently the heat transferred at time t) is easily found. The concentration of paramecia varies appreciably within $r=d/2$, the location of the spot boundary, and $r=d/2+\delta(t)$ at time t where $\delta(t)$ is a diffusion length given by

$$\delta(t) \sim \sqrt{Dt}. \tag{10}$$

The flux $J(t)$ of paramecia absorbed in the sink (which behaves as if $c(d/2,t)=0$) is, for $\sqrt{Dt}<d$, given by

$$J(t) = D \left.\frac{\partial c}{\partial r}\right|_{r=d/2} \approx D\frac{c(r,0)}{\delta(t)}. \tag{11}$$

The number of paramecia that have crossed the spot perimeter πd irreversibly is thus

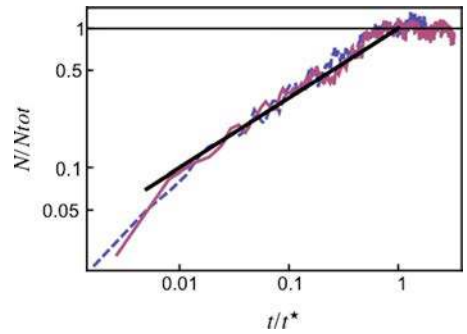

Fig. 10. The number of old paramecia collected in the central spot for two spot sizes $d=1.3$ cm and $d=1.8$ cm as a function of the rescaled time t/t^* in the Brownian regime. The black line is $N/N_{\rm tot}=\sqrt{t/t^*}$.

$$N(t) = \pi d \int_0^t J(t')dt' = 2\pi d c(r,0)\sqrt{Dt}, \tag{12}$$

or $N(t)/N_{\rm tot}=\sqrt{t/t^\star}$ with $\alpha=d/L$, and

$$t^\star = \frac{L^2}{D}\left(\frac{1-\alpha^2}{8\alpha}\right)^2. \tag{13}$$

As seen in Fig. 10, the collection process follows the square root dependence expected from Eq. (12) and is completed at $t=t^\star$, a further indication that the diffusion time scale $t^\star$ is relevant.

IV. DISCUSSION

The experiments and their analysis we have reported demonstrate that at least in the very simple geometrical configuration we have used, the fate of a population of *P. caudatum* swimming in a bounded domain can be understood from elementary random processes once the existence of the nonsymmetrical behavior of the individual paramecium at an acid front in the medium is recognized. If a circular acid spot is placed in the circular domain because of the nonsymmetrical way in which paramecia respond to the sign of acidity gradients, a trapping phenomenon occurs.

Depending on their strength, which is determined by their age in the medium, paramecia swim either like balls rebounding at the wall of their enclosing domain (fresh paramecia) or like Brownian walkers (old paramecia). In both cases, the nature of the motion and its parameters can be measured precisely, allowing us to infer the corresponding laws for the number $N(t)$ of paramecia trapped at time t. The laws are different in the two cases, but both result from an *a priori* knowledge of an individual paramecium's motion in the neutral medium, which is independent of the presence of the trap.

The localized spot configuration we have chosen eliminates any possibility for the paramecia to be aware of the presence of the trap before reaching the spot. It illustrates a pure random search process in the living world for which there is no possibility of self-adaptation in the paramecium behavior[24,25] nor any optimization of possible search parameters before becoming trapped.[26] Population aggregation occurs anyway, even if it is not driven by learning, nor is it the result of any adaptation (although we have not repeated the same experiment with paramecia having been trapped before and reintroduced in a clear medium to see if their motion is

altered by their previous experience). We have also made similar observations of trapping behavior when the acid spot has diffuse boundaries or when the spot is slowly moving in the domain (at a speed much lower than the speed of the paramecia). The trapping boundary corresponds in these cases to iso-*p*H equal to 5.5. Our study also demonstrates that there is no long-range hypothetical communication mechanism between the trap and the individuals, such as the odor waves proposed by Fabre in 1900 (Ref. 8) to explain the acute sense of smell of some animals.

A natural extension, probably more relevant to practical situations,[27] would be to consider more complex landscapes of acid barriers and/or time varying environments as in odor plumes.[28] There, it would be interesting to watch what kind of *taxis* an assembly of paramecia adopts in response to complex spatial and temporal distributions of acid barriers and if paramecia account for their previous experience of the medium to choose their way.[29]

ACKNOWLEDGMENTS

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