Optimal search in \textit{E.coli} chemotaxis

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We study chemotaxis of a single \textit{E.coli} bacterium in a medium where the nutrient chemical is also undergoing diffusion and its concentration has the form of a Gaussian whose width increases with time. We measure the average first passage time of the bacterium at a region of high nutrient concentration. In the limit of very slow nutrient diffusion, the bacterium effectively experiences a Gaussian concentration profile with a fixed width. In this case we find that there exists an optimum width of the Gaussian when the average first passage time is minimum, \textit{i.e.}, the search process is most efficient. We verify the existence of the optimum width for the deterministic initial position of the bacterium and also for the stochastic initial position, drawn from uniform and steady state distributions. Our numerical simulation in a model of a non-Markovian random walker agrees well with our analytical calculations in a related coarse-grained model. We also present our simulation results for the case when the nutrient diffusion and bacterial motion occur over comparable time-scales and the bacterium senses a time-varying concentration field.

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\section{I. INTRODUCTION}

In a wide variety of physical systems, search process plays an important role \cite{1}. Examples can be found in systems such as animals searching for food \cite{2}, proteins searching for the binding site on DNA \cite{3}, or, diffusion-limited reactions \cite{4}. A search process is often characterized by the first passage time, which is defined as the time taken to reach the target for the first time (or complete the search process). An efficient search process corresponds to a short first passage time. Therefore it is crucial to determine how the first passage time depends on the system parameters.

The most efficient search strategy is often determined by looking into the minimum of the first passage time in this parameter space \cite{5,6}.

We consider the search process in one of the most well studied biological systems, \textit{viz.}, \textit{E.coli} chemotaxis, which describes the motion of \textit{E.coli} bacteria in response to a chemical concentration gradient \cite{7}. When such bacteria are placed in an inhomogeneous concentration of a nutrient, they show a tendency to migrate towards the nutrient-rich region \cite{8,9}. We ask the questions: How long does it take for the bacteria to find the most favorable region, and under what conditions is this search process most efficient?

The motion of \textit{E.coli} takes place in two different modes: run and tumble. During a run the bacteria move along a given direction with a fixed velocity $v \sim 20 \mu\text{m/s}$, and during a tumble they do not undergo appreciable displacement but change their orientation randomly. In a homogeneous medium, the average run duration is about 1s, and at the end of one run the bacteria go into the tumbling mode, which lasts for about 0.1s before another run in a new direction starts \cite{10,11}. In the presence of an inhomogeneous nutrient concentration in the medium, the small size ($\sim 2 \mu\text{m}$) of an \textit{E.coli} cell prevents it from directly sensing the spatial gradient of the concentration field. Therefore, to navigate to the nutrient-rich region, the bacteria rely on temporal integration and modulate their run durations in different directions in the medium via a memory kernel, shown in Fig. 1 \cite{12}. The kernel effectively compares the concentration experienced in the recent past to that in distant past, and if the difference is positive (negative) the run duration in the current direction is extended (shortened). Following the above description, the motion of a single bacterium in a spatially varying chemical environment is modeled as a non-Markovian random walker with run and tumble modes, and the switching rates between these modes depend on the nutrient concentration along its recent trajectory \cite{12,10}.

In many physical situations, the chemotaxis motion may take place in a medium where the nutrient is also undergoing diffusion. Imagine a situation where a puff of nutrient is injected into the medium such that immediately after injection, all the chemical is concentrated in a narrow region. As time goes on, this chemical spreads over the medium via diffusion and at any given time its concentration profile has the form of a Gaussian. At a certain stage of this nutrient diffusion, when the nutrient has already spread through some distance in the medium, a bacterium is released somewhere in the medium which would perform chemotaxis. If the time scale of nutrient diffusion is much longer than that of bacterial motion, the bacterium would effectively experience a Gaussian concentration profile of fixed width. When the nutrient diffusion and bacterial motion occur over comparable time scales, then the concentration sensed by the bacterium will be time dependent and can be described as a Gaussian whose width keeps increasing (and peak height keeps decreasing) with time. The region around the peak of the Gaussian profile, where the nutrient concentration is highest, is therefore the most favorable region for the bacterium.
FIG. 1: (Color online) Bilobe response function of wild-type *E. coli* used in our simulations. For computational simplicity, we have used a discrete sampling of the experimental data presented in [21] instead of working with the complete data set. This did not affect our conclusions.

In this paper, we study chemotaxis motion of a single bacterium in the presence of a Gaussian concentration field of the nutrient, using the model of a non-Markovian random walker described above. As considered in the experiments involving bacteria in a micro-fluidic channel or capillary assay [17–19], we consider the motion of the bacterium in one dimension. We measure the average first passage time of the bacterium at the neighborhood of the Gaussian peak using Monte Carlo simulation. In the limit of slow nutrient diffusion, if the chemotaxis starts at a stage when the width of the Gaussian profile is $\sigma$, then this width does not change appreciably during the search process. The average first passage time in this case shows a minimum as a function of $\sigma$. In other words, there is an optimum value of $\sigma$ for which the search process is most efficient. This finding is interesting since $\sigma$ is a parameter that can be easily tuned in an experiment, and our study shows that when $\sigma$ is set at a special value, the bacterium becomes the most efficient searcher and is able to find its favorable region in the shortest possible time. We also perform analytical calculations of mean first passage time within a coarse-grained model which allows an approximate Markovian description of the bacterial motion [15, 16]. We find reasonably good agreement between our analytics and numerics. We consider a deterministic initial condition as well as a stochastic initial condition, drawn from uniform and steady state distribution. In all the cases our numerical simulation and analytical calculations show the existence of an optimum width of the nutrient concentration profile when the search process is most efficient.

In the case when the time scale of nutrient diffusion is comparable to that of bacterial motion, the bacterium experiences a time-varying concentration profile, a Gaussian whose width increases with time. The search process now crucially depends on the nutrient diffusivity, as well as the extent of spread of the nutrient in the medium at the onset of chemotaxis. Our simulations show that if the chemotaxis starts at an early stage of nutrient diffusion, when the width of the Gaussian is still small, then the mean first passage time shows a minimum as a function of the nutrient diffusivity. But if the chemotaxis starts at a late stage, when the nutrient has already spread considerably in the medium and the width of the Gaussian profile is large, the mean first passage time increases monotonically with nutrient diffusivity.

In the next section, we present our model and summarize earlier results. Sections 3 and 4 contain our analytical and numerical results, respectively, for a Gaussian nutrient concentration. In section 5 we present our results for a time-varying concentration field. The conclusion is presented in section 6.

II. DESCRIPTION OF THE MODEL AND EARLIER RESULTS

A. Simulation in a model of a non-Markovian random walker

Following [15, 16, 20], we model the motion of a single bacterium in one dimension as a non-Markovian random walker whose dynamics is governed by runs and tumbles. During a run the bacterium moves along one particular direction with a fixed velocity. The duration of a run is a stochastic variable and follows a Poissonian distribution with a mean of 1s in a homogeneous medium. At the end of a run, the bacterium goes into a tumbling mode, in which it rotates about itself in a random fashion, without much net displacement, before it starts running again in a new direction. Because the average tumble duration is much smaller than that of runs, tumbles are modeled as instantaneous events which allow the bacterium to change its direction between two successive runs. In our present one-dimensional model, the probability that the run direction is changed (reversed) is denoted as $q$. In the presence of a nutrient concentration gradient in the medium, the tumbling rate depends on the recent history. The probability
that a running bacterium tumbles during a time interval \([t, t + dt]\) is then given by

\[
\frac{dt}{\tau} \left( 1 - \int_{-\infty}^{t} dt' R(t - t')c(t') \right),
\]

where \(\tau\) is the mean run duration in a homogeneous environment, \(c(t')\) is the concentration experienced at a past instant \(t' < t\), and \(R(t)\) is the response kernel. \(R(t)\) contains information about the signaling pathway present inside the bacterial cell, and it was measured experimentally for wild-type bacteria in \([12, 21]\). \(R(t)\) was shown to have a bilobe shape, with a relatively sharp positive lobe at smaller \(t\) and a shallow negative lobe at larger \(t\) that vanishes for \(t > 4s\) (see Fig. 1). The area under the positive lobe is roughly equal to the area under the negative lobe, and this ensures that the response kernel merely measures the concentration gradient and is insensitive to any overall change in the background concentration level. Because of this property, it is called an adaptive response kernel.

We are interested in the linear response regime, where the integral in Eq. \([1]\) is much less than unity. Within this linear theory, we can decompose the above bilobe response kernel into \(\delta\)-function response kernels of suitably chosen amplitudes, and from a superposition of the solutions for these \(\delta\)-function kernels, we can obtain the solution for the full bilobe response. Hence we first consider \(R(t) = \alpha\delta(t - \Delta)\) and analyze this case in detail, where we keep terms only up to first order in \(\alpha\). Later, we generalize our results for the full response kernel.

**B. Analytical calculation in a coarse-grained Markovian description**

In an earlier study \([13]\) a simple coarse-grained model was proposed for describing a single bacterium in a concentration gradient in one dimension. The bacterium was assumed to be confined in a one-dimensional box of length \(L\) with reflecting boundary walls. Although the dependence of the tumbling rate on the past trajectory makes the cell trajectory was included in the description by introducing additional ‘internal variables’, and the resulting process, characterized by a larger number of degrees of freedom, now becomes Markovian. Starting from this Markovian description, using the homogenization method \([22, 23]\) the same coarse-grained equation as above was obtained \([16]\).

The chemotactic drift velocity \(V(x)\) and the diffusivity \(D(x)\) in Eq. \([2]\) depend on the nutrient concentration profile \(c(x)\), and the dependence can be derived from the microscopic dynamics. In an earlier calculation by de Gennes an approximate expression for the drift velocity was obtained within the simplifying assumption that whenever a running bacterium tumbles, its past memory is lost. Considering the response function \(R(t) = \alpha\delta(t - \Delta)\), the resulting expression

\[
V(x) = \alpha \frac{\nu^2 \tau}{2q} e^{-\frac{2q\Delta}{\tau}} \partial_x c(x)
\]

was found to show good agreement with the simulation results \([14]\). To calculate the diffusivity \(D(x)\), the effective tumbling frequency was calculated within the coarse-grained model by averaging over a population of non-interacting bacteria within the coarse-graining length scale. Although the tumbling frequency of a single bacterium depends on the details of its past trajectory, this dependence is lost when averaged over a large number of bacteria with all possible run directions. The average tumbling frequency at a position \(x\) can be shown to be \([1 - \alpha c(x)]/\tau\), from which the diffusivity turns out to be \([15]\)

\[
D(x) = \frac{\nu^2 \tau}{2q}[1 + \alpha c(x)].
\]

Using Eqs. \([3]\) and \([4]\) it can be easily shown from Eq. \([2]\) that in the steady state the bacterial density \(P(x)\) has the form

\[
P(x) = P_0 + \alpha P_0(e^{-\frac{2q\Delta}{\tau}} - 1) \left( c(x) - P_0 \int_0^L c(x) dx \right),
\]

\([5]\)
The solution of this equation has the form

\[ G(x,t) = V(x)\partial_x G(x,t) + D(x)\partial_x^2 G(x,t), \]

with the initial condition \( G(x,0) = 1 \). The reflecting and absorbing boundary conditions are implemented as \( \partial_t G(0, t) = 0 \) and \( G(x_0, t) = 0 \), respectively.

By definition, \( G(x,t) \) is the probability that the first passage time is larger than \( t \), and hence the first passage time distribution is given by \( -\partial_t G(x,t) \). Mean first passage time \( T(x) = -\int_0^\infty dt \partial_t G(x,t) = \int_0^\infty dt G(x,t) \), which follows the equation

\[ V(x)\partial_x T(x) + D(x)\partial_x^2 T(x) = -1. \]

The solution of this equation has the form

\[ T(x) = \int_x^{x_0} \frac{dy}{\psi(y)} \int_y^\infty \frac{\psi(z)}{D(z)}. \]

where \( \psi(x) = \exp \left[ \int_0^x dx' V(x')/D(x') \right] \). Now, using Eqs. 3 and 11 and keeping terms only up to first order in \( \alpha \), one can write \( \psi(x) = \exp [\alpha e^{-2q\Delta/\tau} \{ c(x) - c(0) \}] = 1 + \alpha e^{-2q\Delta/\tau} [c(x) - c(0)] \). After a few steps of simple algebra we finally have

\[ T(x) = \frac{2q}{v\tau} \left( \frac{x-x_0}{2} \right)^2 - \alpha(1 - e^{-2q\Delta/\tau}) \int_x^{x_0} dy \int_y^\infty dz c(z) \frac{\psi(y)}{D(z)}, \]

which can be written in the form \( T(x) = T_0(x) + \alpha T_1(x) \), where \( T_0(x) \) stands for the mean first passage time for an ordinary Brownian motion in the absence of any concentration gradient and \( T_1(x) \) gives the first order correction term when position-dependent drift and diffusion are present due to a spatially varying concentration field \( c(x) \) [24]. In the rest of this work we focus on \( T_1(x) \).

For a Gaussian concentration profile \( c(x) = \exp[-(x-\bar{x})^2/2\sigma^2] \) the drift velocity \( V(x) \) and diffusivity \( D(x) \) show rapid variation close to the peak at \( \bar{x} \). In our coarse-grained description, which allows for analytical treatment, we deal with length scales much larger than the mean free path of the bacteria, and any spatial variation that occurs over a smaller length scale must be neglected in our coarse-grained model. When \( \sigma \) is not too large, the variation of \( V(x) \) and \( D(x) \) around the peak is too fast to be considered in our coarse-grained formalism. Because of this, we choose the target position \( x_0 \) slightly away from the peak such that both the initial position \( x \) and the target lie on
the same side of the peak. For our choice of \( x < x_0 < \bar{\tau} \) we use the Gaussian \( c(x) \) in Eq. (10) and get

\[
T_1(x) = \frac{2q}{v^2 \tau} \left[ \frac{1}{2} \text{Erf} \left( \frac{\bar{\tau} - x_0}{\sqrt{2}\sigma} \right) \left( e^{-\frac{2q\Delta}{\tau}}(2\tau - x_0) - (\tau - x_0) \right) \\
+ \frac{1}{2} \text{Erf} \left( \frac{x - \bar{x}}{\sqrt{2}\sigma} \right) \left( e^{-\frac{2q\Delta}{\tau}}(x - \bar{x}) - (x - \bar{x}) \right) \\
+ \frac{1}{2} \text{Erf} \left( \frac{\bar{x} - x}{\sqrt{2}\sigma} \right) \left( (e^{-\frac{2q\Delta}{\tau}} - 1)(x_0 - x) \right) \\
+ \left( e^{-\frac{(x-x_0)^2}{2\sigma^2}} - e^{-\frac{(\bar{x}-x_0)^2}{2\sigma^2}} \right) \left( 2e^{-\frac{2q\Delta}{\tau}} - 1 \right) \frac{\sigma}{\sqrt{2}\pi} \right].
\]

(11)

So far we have considered the first passage time with a deterministic initial condition, where the bacterium always starts from a fixed initial position \( x \). Now we consider the case of stochastic initial position when \( x \) can take any value within the interval \( 0 < x < x_0 \); that is, the initial position can lie anywhere between the left boundary and the target, with certain distribution function. We consider two specific cases: (i) when \( x \) follows a uniform distribution \( P_0 \) and (ii) when \( x \) is drawn from the steady state distribution \( P(x) \) in Eq. (5). In the first case, the \( \alpha \) order correction in the first passage time can be obtained by simply integrating Eq. (11) over \( x \):

\[
T_1^{(u)} = P_0 \int_0^{x_0} dxT_1(x)
\]

\[
= \frac{2qP_0}{v^2 \tau} \left[ \frac{1}{4} \left\{ \text{Erf} \left( \frac{\bar{\tau} - x_0}{\sqrt{2}\sigma} \right) - \text{Erf} \left( \frac{\bar{x} - x_0}{\sqrt{2}\sigma} \right) \right\} \\
+ \left( e^{-\frac{2q\Delta}{\tau}}(x_0^2 - 3\bar{x}^2 - 3\sigma^2) - (x_0^2 - \bar{x}^2 - \sigma^2) \right) \\
+ \frac{1}{2\sqrt{2}\pi}(3e^{-\frac{2q\Delta}{\tau}} - 1) \left( (x_0 + \bar{x})e^{-\frac{(x_0 + \bar{x})^2}{2\sigma^2}} - \bar{x}e^{-\frac{\bar{x}^2}{2\sigma^2}} \right) \right].
\]

(12)

For case (ii) the initial position \( x \) follows the steady state distribution in Eq. (5) The mean first passage time is then written as

\[
\int_0^{x_0} dxP(x)T(x) = \int_0^{x_0} dx \left[ P_0 + \alpha P_0(e^{-\frac{2q\Delta}{\tau}} - 1) \left( c(x) - P_0 \int_0^L c(x) dx \right) \right] [T_0(x) + \alpha T_1(x)].
\]

(13)

For a Gaussian form of \( c(x) \) the \( \alpha \) order term becomes

\[
T_1^{(s)} = P_0 \int_0^{x_0} dxT_1(x) + P_0 \left( e^{-\frac{2q\Delta}{\tau}} - 1 \right) \int_0^{x_0} dx e^{-\frac{(x-x_0)^2}{2\sigma^2}}T_0(x)
\]

\[
- P_0 \left( e^{-\frac{2q\Delta}{\tau}} - 1 \right) \text{Erf} \left( \frac{x_0}{\sqrt{2}\sigma} \right) \int_0^{x_0} dxT_0(x),
\]

(14)

where \( T_0(x) \) and \( T_1(x) \) are defined in Eqs. (10) and (11). After straightforward algebra the \( \alpha \) order term in first passage time with the steady state initial condition becomes

\[
T_1^{(s)} = \frac{2qP_0}{v^2 \tau} \left[ \frac{1}{2} \left\{ \text{Erf} \left( \frac{\bar{\tau} - x_0}{\sqrt{2}\sigma} \right) - \text{Erf} \left( \frac{\bar{x} - x_0}{\sqrt{2}\sigma} \right) \right\} \\
+ \left( e^{-\frac{2q\Delta}{\tau}}(x_0^2 - 2\bar{x}^2 - 2\sigma^2) - (x_0^2 - \bar{x}^2 - \sigma^2) \right) \\
+ \frac{\sigma}{\sqrt{2}\pi} \left( 2e^{-\frac{2q\Delta}{\tau}} - 1 \right) \left( (x_0 + \bar{x})e^{-\frac{(x_0 + \bar{x})^2}{2\sigma^2}} - \bar{x}e^{-\frac{\bar{x}^2}{2\sigma^2}} \right) \right] \\
- \frac{P_0x_0^2}{3} \left( 2e^{-\frac{2q\Delta}{\tau}} - 1 \right) \text{Erf} \left( \frac{\bar{x}}{\sqrt{2}\sigma} \right).
\]

(15)
In a time interval \( dt \) and \( c \) and compare the result with above analytical calculation. In the next section, we measure the first passage time in simulation and compare the result with above analytical calculation.

The results in Eqs 11, 12 and 15 are for an impulse response kernel \( R(t) = \alpha \delta(t - \Delta) \), and these can be easily generalized for any arbitrary response function. In the next section, we measure the first passage time in simulation and compare the result with above analytical calculation.

**IV. SIMULATION RESULTS ON FIRST PASSAGE TIME**

We perform a Monte Carlo simulation on a one dimensional box of size \( L \), with reflecting boundary walls at the two ends. In a time interval \( dt \) the bacterium moves by a distance \( vdt \). At the end of each time step, we compute the tumbling probability, as in Eq. 1. For an impulse response function \( R(t) = \alpha \delta(t - \Delta) \), the tumbling probability at time \( t \) is given by \( dt/\tau (1 - (\alpha c[x(t - \Delta)]) \), where \( x(t - \Delta) \) is the position of the bacterium at a time \( \Delta \) back in the past and \( c[x(t - \Delta)] \) is the concentration experienced by the bacterium at that past instant of time. At the end of one time step the bacterium attempts to tumble with this probability. If the tumbling attempt is unsuccessful, it continues to move in the same direction with same velocity \( v \), and if the tumbling attempt is successful, the bacterium changes its direction (in this one-dimensional case, it reverses the sign of \( v \)) with probability \( q \). Starting from a given initial position \( x \) at \( t = 0 \), we measure the first passage time at a position \( x_0 \) and average over different trajectories. In order to avoid the region with rapid spatial variation of the concentration field, we consider a target which is one mean free path away from the Gaussian peak in the same direction as the starting position of the bacterium: \( x_0 = \overline{\pi} - v\tau \).

In Fig. 2 we show the variation of \( T_1(x) \) with \( \sigma \) (discrete symbols) and compare it with our analytical result in Eq. 11 (solid lines). We find reasonably good agreement between our simulation and analytical calculation. For very small \( \sigma \) the concentration variation can be perceived only within a very narrow region around the peak \( \overline{\pi} \). Hence the bacterial trajectory starting from \( x \) and ending at \( x_0 \), which does not cross the peak at \( \overline{\pi} \), consists of isotropic diffusion for the most part. As a result, in the limit of small \( \sigma \) the mean first passage time is given by that for an ordinary Brownian motion and is equal to \( T_0(x) \) in Eq. 11 and the first order term \( T_1(x) \) goes to zero. Similarly, in the limit of very large \( \sigma \) the profile is almost flat, and even in this case the motion is close to isotropic diffusion and \( T_1(x) \) vanishes. Our simulation and analytical calculation are consistent with this simple argument.

For intermediate \( \sigma \) values, \( T_1(x) \) must show a non-monotonic variation, since it vanishes for small and large \( \sigma \). We find a minimum for \( T_1(x) \) at a particular width \( \sigma^* \). In other words, there exists an optimal width \( \sigma^* \) when the first passage time at the nutrient-rich region becomes shortest and the bacterium becomes the most efficient searcher. The bottom right and top right insets in Fig. 2 show the variation of the optimal width \( \sigma^* \) as a function of the initial position \( x \) and the memory \( \Delta \) of the bacterium, respectively. Note that even in the Markovian limit, when the bacterium does not have any memory, and does not accumulate in the nutrient-rich region in the long time limit [15], its first passage properties still show the existence of an optimal width when the search is most efficient.
is very slow, and during the time interval of the first passage at the target, the width of \( c \) depends on \( \sigma \).

In this limit, therefore, one expects results similar to those in a static concentration profile. Our simulation data starts, and \( D \) is the nutrient diffusivity.

The bacterial motion will depend on \( \sigma_0 \) and \( D \), depending on the time scale \( t_c \). For \( t < t_c \) the motion depends on \( \sigma_0 \), and for \( t > t_c \) the motion is mainly controlled by \( D \). In the limit of very small \( D \), therefore, one would expect the first passage time to be a function of \( \sigma_0 \) alone. In fact this is the limit when the nutrient diffusion is very slow, and during the time interval of the first passage at the target, the width of \( c(x, t) \) changes very little. In this limit, therefore, one expects results similar to those in a static concentration profile. Our simulation data

\[ c(x, t) = \exp \left( -\frac{(x-\mu)^2}{2(\sigma_0^2 + 2Dt)} \right) / \sqrt{2\pi(\sigma_0^2 + 2Dt)} \]

\( \sigma_0 \) is the width at the time when the chemotaxis motion starts, and \( D \) is the nutrient diffusivity.

\[ \frac{c(x, t)}{\sigma_0^2 / D} \sim \frac{\alpha}{\sqrt{\pi}} \exp \left( -\frac{(x-\mu)^2}{2\sigma_0^2} \right) / \sqrt{2\pi(\sigma_0^2 + 2Dt)} \]

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The bacterial motion will depend on \( \sigma_0 \) and \( D \), depending on the time scale \( t_c \). For \( t < t_c \) the motion depends on \( \sigma_0 \), and for \( t > t_c \) the motion is mainly controlled by \( D \). In the limit of very small \( D \), therefore, one would expect the first passage time to be a function of \( \sigma_0 \) alone. In fact this is the limit when the nutrient diffusion is very slow, and during the time interval of the first passage at the target, the width of \( c(x, t) \) changes very little. In this limit, therefore, one expects results similar to those in a static concentration profile. Our simulation data
in Fig. 4A indeed show that for small $D$ there is an optimum width $\sigma_0$ where $T_1(x)$ becomes minimum. As $D$ increases, $t_\epsilon$ becomes smaller when $T_1(x)$ does not show much variation with $\sigma_0$ and the minimum becomes less and less pronounced. In Fig. 4A we verify this.

In Fig. 4B we show the variation of $T_1(x)$ against $D$ for fixed $\sigma_0$ values. For very large $D$ the Gaussian profile quickly flattens out, and the bacterial motion becomes an isotropic diffusion. In this limit $T_1(x)$ becomes zero. For very small $D$ values, the limit for a static Gaussian profile is recovered, and (as shown in our data in Fig. 2 main plot) $T_1(x)$ has a negative value that depends on $\sigma_0$. Therefore, for a given $\sigma_0$, as $D$ is varied, $T_1(x)$ starts from a negative value at small $D$ and becomes zero at large $D$. Whether this variation is monotonic or not depends on the choice of $\sigma_0$. Our data in Fig. 4B show that for large $\sigma_0$ the variation is monotonic but for small $\sigma_0$ a minimum is reached at a particular $D$; that is, there is an optimum diffusivity of the nutrient when the search is most efficient. For our various choice of $\sigma_0$ values over a wide range (full data set not presented here), we also notice that an optimum diffusivity is observed whenever $\sigma_0$ is fixed at a value smaller than $\sigma^*$, the optimum width for the static concentration profile (see Fig. 2 main plot). For $\sigma_0 > \sigma^*$, on the other hand, $T_1(x)$ increases monotonically with $D$.

The above observation tentatively indicates that it may be possible to describe the results for the time-dependent nutrient concentration in terms of a static concentration profile with an ‘effective width’ $\sigma_e$. For a given value of $\sigma_0$ and $D$ the width of $c(x,t)$ keeps increasing during bacterial motion: at the start of the motion the width is $\sigma_0$, and at the end of the first passage the average width is $\sqrt{\sigma_0^2 + 2D T_1(x)}$. Let us assume that $\sigma_e$ is some measure of the average or effective width experienced by the bacterium during this process. Obviously, $\sigma_e$ is a function of both $\sigma_0$ and $D$: for a fixed $\sigma_0$, as $D$ is varied, $\sigma_e \approx \sigma_0$ for very small $D$, and as $D$ becomes very large, so does $\sigma_e$. In the course of this variation, if $\sigma_e$ crosses $\sigma^*$, then $T_1(x)$ shows a minimum and if $\sigma_0 > \sigma^*$ such that $\sigma_e$ never reaches $\sigma^*$ (because $\sigma_e$ can never fall below $\sigma_0$), then $T_1(x)$ shows a monotonic increase with $D$. The above picture explains our numerical data well. However, we would like to mention that we do not yet have any mathematical expression for $\sigma_e$ in terms of $\sigma_0$ and $D$. It would be interesting to directly verify the mechanism proposed above.

VI. CONCLUSION

In this paper, we have considered the chemotaxis motion of a bacterium in a medium where the nutrient is also undergoing diffusion and its concentration profile is given by a Gaussian whose width increases with time. We have measured the mean first passage time of the bacterium at the neighborhood of the Gaussian peak. In the limit when the nutrient diffusion is slow compared to the bacterial motion, the bacterium experiences an effectively static concentration profile, a Gaussian with a fixed width, and in this regime we calculate the mean first passage time analytically, within a coarse-grained formalism. We find that the mean first passage time shows a minimum as a function of the width of the Gaussian, which means that the search process becomes most efficient at a certain optimum width. Our numerical simulation matches the analytical result well.

For a time-dependent concentration profile, i.e., in the regime in which the nutrient diffusion occurs over a time-scale comparable to bacterial motion, we find that the first passage time is a function of nutrient diffusivity $D$ and the width $\sigma_0$ of the Gaussian at the onset of chemotaxis motion. When $D$ is held fixed at a small value, the mean first passage time shows a minimum against variation of $\sigma_0$, as in the static case. But for large $D$ the minimum becomes less pronounced. As a function of $D$, the mean first passage time shows a minimum if $\sigma_0$ is held fixed at a small value. But no such minimum is observed when $\sigma_0$ is set at a large value.
The existence of an optimal width of the nutrient concentration profile that makes the search process most efficient is an interesting result. Apart from the mean first passage time, we have also examined our conclusion by measuring the most probable first passage time. Note that for a general process described by an equation of the form given in Eq. 2, the probability distribution for first passage time shows a long tail which makes the mean first passage time much larger than the typical (or most probable) one. Our numerical simulations (data not shown here) show that the typical first passage time also becomes minimum at a particular width whose value is very close to the one for which the mean showed a minimum.

In [16] the chemotactic efficiency was characterized by a quantity called ‘uptake’ (defined as the total amount of nutrient encountered by the bacterium up to a certain time). It was shown that under harsh environmental conditions, when the nutrient is scarce, the long time uptake can be maximized for a particular shape of the response kernel. In contrast, we consider a given response kernel and vary the parameter(s) characterizing the concentration gradient of the nutrient in the medium to find the minimum first passage time. In other words, for a given response kernel we find the optimum environmental conditions for the fastest search process. It is easy to argue that the long time uptake does not show any maximum in our case, when the response kernel is fixed and the environmental conditions are varied. The long time uptake decreases monotonically as the concentration gradient is decreased.

Finally, it would be interesting to verify our conclusions in experiments. Recently, E.coli chemotaxis has been studied in a micro-fluidic channel whose width is comparable to the bacterial mean free path \([17,19]\). In such a setup, the motion of the bacterium can be considered to be effectively one-dimensional. It is possible to generate a Gaussian chemical concentration profile using techniques of diffusive microfluidics \([23]\). The motion of the bacterium can be tracked to measure its first passage properties. Our model predicts that for a static Gaussian profile of width \(\sigma \approx 50 \mu m\), wild-type E.coli have shortest first passage time. However, it can be experimentally challenging to verify our results for a time-dependent nutrient concentration profile. Most common chemoattractants such as aspartate and serine have diffusivity \(D \approx 1000 \mu m^2/s\) which is much larger than bacterial diffusivity. As a result, the chemical diffuses very quickly in the medium, and initially localized concentration quickly flattens out. Thus the bacterium experiences a very weak concentration gradient and the chemotactic correction \(T_1\) to its first passage time may become too small for experimental detection.

VII. ACKNOWLEDGMENT

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