Numerical and analytical approaches to an advection-diffusion problem at small Reynolds number and large Péclet number

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Abstract

Obtaining a detailed understanding of the physical interactions between a cell and its environment often requires information about the flow of fluid surrounding the cell. Cells must be able to effectively absorb and discard material in order to survive. Strategies for nutrient acquisition and toxin disposal, which have been evolutionarily selected for their efficacy, should reflect knowledge of the physics underlying this mass transport problem. Motivated by these considerations, in this paper we discuss the results from an undergraduate research project on the advection-diffusion equation at small Reynolds number and large Péclet number. In particular, we consider the problem of mass transport for a Stokesian spherical swimmer. We approach the problem numerically and analytically through a rescaling of the concentration boundary layer. A biophysically motivated first-passage problem for the absorption of material by the swimming cell demonstrates quantitative agreement between the numerical and analytical approaches. We conclude by discussing the connections between our results and the design of smart toxin disposal systems.

Keywords: first-passage problem, concentration boundary layer, advection, diffusion

(Some figures may appear in colour only in the online journal)

1. Introduction

The survival of any microorganism is dependent on its ability to control the movement of nutrients and waste between the cell interior and the external environment. Nutrients must be
easily captured and waste easily disposed with minimal metabolic exertion [1]. Factors which
determine the efficiency of any material transfer mechanism for gathering and disposing of
small molecules include the microscale flow profile surrounding the cell [2], the diffusion
coefficient of molecules being transported, and the location of transport receptors on the cell
surface [3, 4]. As with any other trait, the physical architecture of the transport receptor
arrangement is evolutionarily selected to work efficiently within the particular environment
that the organism lives. A more detailed understanding of the mass transport problem for
molecules in the extracellular fluid can yield valuable information for discerning why a given
architecture is preferable over other possible choices [5].

An example which motivates the current study is understanding the mechanism of toxin
disposal by sea urchin embryos [3, 6]. Early in development, microvilli (microscopic
cylindrical cell membrane protrusions) on the embryo grow to several microns in length, with
transport receptors localised at the tips of the microvilli. This localisation may help facilitate
more efficient toxin disposal by the embryo. By releasing molecules away from the body of
the cell, the chances are reduced that expelled toxins are reabsorbed. In this setting, the mass
transport problem for molecules in the extracellular fluid is described an advection-diffusion
equation at small Reynolds number and large Péclet number. Interestingly, the characteristic
lengthscale for the concentration boundary layer may provide a physical rationale for the
length of the microvilli involved in the toxin transport [7].

Calculating the efficiency of a material transfer mechanism requires the solution of two
distinct problems. The first problem is to determine the flow profile of the extracellular fluid.
In the present context, the Reynolds number of the flow is much smaller than one, which
justifies the use of the Stokes equation for describing microscale flows around individual cells
[8]. The second problem is to find a solution of the advection-diffusion equation using the
calculated flow profile as input. The solution of the advection-diffusion equation provides the
concentration profile governing the average motion of particles dissolved in the fluid.
Knowledge of the concentration profile leads directly to information about the probability for
a given particle to contact the outer envelope of a cell. Since the absorption of a particle
requires that it first make contact with the cell surface, the concentration profile can be used to
find a theoretical maximum absorption probability [9].

The outline for the paper is the following. In section 2 we discuss the first problem of
determining the flow profile around the cell. We discuss the small Reynolds number
approximation which allows us to obtain the flow profile using the Stokes equation. A
previously published model used to calculate the flow profile surrounding the swimming cell
is presented, which is a common model for active particles [8]. This model is chosen for
several reasons. First, it provides a model to mimic the flow around a spherical cell swimming
through a liquid. Second, since the solution for the flow profile is known, we can make
progress on an analytic approximation to the associated advection-diffusion equation.

In section 3 we discuss the second problem, determining the concentration profile around
the cell. We present an analytic approximation based on a rescaling of the concentration
boundary layer. This discussion is self-contained and does not assume any familiarity with the
associated boundary layer methods in fluid mechanics [10–15]. The pedagogical exposition is
intended so that an advanced undergraduate or first year graduate student with exposure to
boundary value problems common in a quantum mechanics or electricity and magnetism
course can follow the derivation. Our analysis of the concentration profile focuses on the first-
passage probability of a particle in the extracellular fluid being absorbed by the cell [19].

Section 4 of the paper revisits the second problem from a numerical perspective. The
difficulties faced in finding accurate analytic solutions to the advection-diffusion equation can
make numerical schemes an attractive method for finding concentration profiles [16–18]. Our
numerical results provide a benchmark to test the accuracy of the analytic approximation developed in section 3. In section 5 we compare the results of the analytical and numerical approaches, and connect the work to some of the biological motivations for the study.

2. Fluid flow

In general for a viscous fluid, the time-dependent fluid velocity \( \mathbf{v}(t) \) is described by a solution of the Navier–Stokes equation. In the present case we are interested in the flow surrounding a spherical cell of radius \( R \). Our equations for the fluid velocity will be formulated in the rest frame of the moving cell. We assume the fluid is infinite in extent and has velocity \(-\mathbf{U}(t)\mathbf{\hat{z}}\) at infinity, where \( \mathbf{U}(t) \) is the swimming speed of the cell. In the lab frame, this corresponds to a fluid that is at rest at infinity. There are several simplifications that can be made to the general form of the Navier–Stokes equation for our present application [20].

First, since the speed of the flow will be much less than the speed of sound in water, the fluid can be treated as perfectly incompressible. The incompressibility condition means that the flow is divergenceless (like the magnetic field in Maxwell’s equations),

\[
\nabla \cdot \mathbf{v} = 0.
\]

In this case, the Navier–Stokes equation governing the flow velocity \( \mathbf{v}(t) \) can be written explicitly in terms of the fluid density \( \rho \), the pressure profile \( p \), and the dynamic viscosity of the fluid \( \mu \),

\[
\frac{\partial \mathbf{v}}{\partial t} + (\mathbf{v} \cdot \nabla) \mathbf{v} = -\frac{1}{\rho} \nabla p + \frac{\mu}{\rho} \nabla^2 \mathbf{v}.
\]

Second, we consider a steady-state flow profile, in which case the explicit time derivative vanishes. Third, by considering the order of magnitude of the various terms, we see that the left-hand side of equation (2), the inertial terms, can be neglected. Let \( \mathbf{U} \) denote the cell’s average swimming speed, by considering a temporal average over a period of the fast swimming motion. The biological origin of this period corresponds to the flagellar beat cycle, or the timescale for a surface wave of cilia, depending on the cell’s particular swimming apparatus. Then the term \((\mathbf{v} \cdot \nabla) \mathbf{v}\) is of the order of magnitude \( \mathbf{U}^2 / R \), whereas \((\mu/\rho) \nabla^2 \mathbf{v}\) is of order \((\mu \mathbf{U})/(\rho R^2)\). The ratio of the two is the celebrated Reynolds number \( Re = (\rho \mathbf{U}^2 \rho)/\mu \). In the case of present interest, the Reynolds number corresponding to the flow around the cell is generally much less than one. As an example of the Reynolds numbers typically encountered for swimming microorganisms, for the green algae *Chlamydomonas Reinhardtii* we have \( R \sim 10^{-5} \) m, \( \mathbf{U} \sim 10^{-4} \) m s\(^{-1}\) and \((\mu/\rho) \sim 10^{-6} \) m\(^2\) s\(^{-1}\) which gives \( Re \sim 10^{-3} \). The small Reynolds number allows us to linearise the Navier–Stokes equation by neglecting the inertial terms. This simplification means that our flow velocity \( \mathbf{v} \) satisfies the Stokes equation

\[
\mu \nabla^2 \mathbf{v} - \nabla p = 0.
\]

In what follows, we draw on the extensive literature on small Reynolds number hydrodynamics and the associated solutions of the Stokes equation. We define spherical polar coordinates \((r, \theta, \phi)\), recalling that in the rest frame of the cell, the fluid velocity is in the \(-\mathbf{\hat{z}}\) direction at infinity. In the particular model description chosen for our application, the fluid is set into motion through axially symmetric deformations of the spherical surface of the cell. As a result of the axial symmetry, the fluid velocity will be independent of \( \phi \). At small Reynolds number the fluid motion is then determined by the no-slip boundary condition at the surface. The details for the calculation of the flow velocity can be found in [8]. Defining the dimensionless radial coordinate \( \xi = r/R \), the dimensionless, steady-state fluid velocity is
\[ u(\xi) = \frac{v(\xi)}{U} \] where
\[ u(\xi) = -\xi + \sum_{\ell=1}^{\infty} m_{\ell} u_{\ell}(\xi, \theta) + \sum_{\ell=2}^{\infty} k_{\ell} v_{\ell}(\xi, \theta). \] (4)
The defining relations for \( u_{\ell}(\xi, \theta) \) and \( v_{\ell}(\xi, \theta) \) are
\[ u_{\ell}(\xi, \theta) = \xi^{-(\ell+2)}((\ell + 1) P_{\ell}(\cos \theta) \hat{\xi} + P_{\ell}^{1}(\cos \theta) \hat{\theta}), \] (5)
\[ v_{\ell}(\xi, \theta) = \xi^{-\ell}((\ell + 1) P_{\ell}(\cos \theta) \hat{\xi} + \frac{(\ell - 2)}{\ell} P_{\ell}^{1}(\cos \theta) \hat{\theta}) \] (6)
with \( P_{\ell}(\cos \theta) \) the Legendre polynomial and \( P_{\ell}^{1}(\cos \theta) \) the associated Legendre function. This expansion is in terms of a fundamental set of solutions to the Stokes equation. The numerical coefficients \( m_{\ell} \) and \( k_{\ell} \) are the associated multipole moments. Although this expansion is for a vector valued quantity, it is conceptually quite similar to the expansion of the scalar potential students encounter when studying electrostatics. In what follows, the particular fluid model we consider is the squirming swimmer, defined in section IV. B. of [8]. The only non-zero multipole moments in this model are \( m_{1}^{2} = 1/2, m_{3} = -k_{3} = 7/48 \), and \( m_{5} = -k_{5} = -25/72 \).

3. Analytical model

With a solution for the flow profile in hand, we now turn to the second problem, determining the concentration profile \( c(\xi, \theta, \phi) \) from the advection-diffusion equation. Our eventual aim is to find the first passage probability that a molecule released at a position \( (\xi', \theta', \phi') \) reaches the inner boundary at \( \xi = 1 \). In the dimensionless radial coordinates, this inner boundary represents the surface of the spherical cell. Alternatively, the molecule can escape and reach an outer absorbing boundary. For the purposes of an analytic calculation, this outer absorbing surface can be infinitely far away. To accomplish this goal, we solve the advection-diffusion equation using the known velocity profile. In this section we first discuss an analytic approximation of the problem. Later we will compare our results to a numerical calculation.

For an incompressible fluid, the advection-diffusion equation reads as
\[ \frac{\partial C}{\partial t} + \mathbf{v} \cdot \nabla C = D \nabla^2 C, \] (7)
where \( D \) is the diffusion coefficient for the molecule of interest, \( C \) is the molecular concentration, and \( t \) is time. We define the dimensionless concentration \( c = CR^3 \) and dimensionless time \( \tau = (Dt)/R^2 \). In what follows we will work with a time independent flow velocity described earlier, in which case the Péclet number can be defined as \( Pe = (RU)/D \). The Péclét number characterises the relative importance of advection and diffusion to the transport of molecules in the extracellular fluid. Large \( Pe \) flows are dominated by advection, whereas diffusion is more important for small \( Pe \) flows. In this paper we will consider the large \( Pe \) case. The dimensionless form of equation (7) in spherical polar coordinates is
\[ \frac{\partial c}{\partial \tau} + Pe \left( -\cos \theta + \sum_{\ell=1}^{\infty} m_{\ell} \xi^{-(\ell+2)}((\ell + 1) P_{\ell}(\cos \theta) \frac{\partial c}{\partial \xi} + \sum_{\ell=2}^{\infty} k_{\ell} \xi^{-\ell}(\ell + 1) P_{\ell}^{1}(\cos \theta) \frac{\partial c}{\partial \theta} \right) \] 
\[ + Pe \left( \sin \theta + \sum_{\ell=1}^{\infty} m_{\ell} \xi^{-(\ell+2)} P_{\ell}^{1}(\cos \theta) + \sum_{\ell=2}^{\infty} k_{\ell} \xi^{-\ell}(\ell - 2) P_{\ell}^{1}(\cos \theta) \frac{\partial c}{\partial \phi} \right) = \nabla^2 c. \] (8)
We now consider an approximate analytical approach to the problem. The basic idea is to use methods common to boundary layer problems [12–15] to find the leading order solution of equation (8) with the boundary conditions given. Readers familiar with this literature will recognise the general strategy, but our exposition is intended to be entirely self-contained so that a physics student with no previous exposure to the fluids literature but exposure to boundary value problems (at an advanced undergraduate or introductory graduate level) can follow along. The general structure for the calculation is as follows. A first change of variables \((\xi \rightarrow \rho)\) defines the boundary layer equation for our problem. A second change of variables (the similarity transformation \(\rho \rightarrow \eta\)) gives us an effective radial equation. This equation is then solved using methods similar to those students are familiar with from solving boundary value equations (Green’s function).

Defining the small parameter \(\alpha = 1/Pe\), we first rescale the radial variable \(\xi = 1 + \alpha^e \rho\) to stretch out the boundary layer. The dimensionless time is rescaled as \(\tau = \alpha^n T\), but we do not rescale the angular variables \(\theta\) and \(\phi\). Dominant balance [21] determines the value of exponents \(n = 1/2\) and \(m = 1\). By making this choice of exponents, in a perturbative expansion for the concentration, \(c = \sum_{k=0}^{\infty} \alpha^{k/2} c_k\), the equation governing \(c_0\) will contain temporal, advective, and diffusive terms. The physical thickness of the concentration boundary layer is \(\ell_R^{12} a\). Inserting the perturbative expansion into equation (8) and collecting terms of the same order in \(\alpha^{1/2}\), the result is a system of coupled equations for the \(c_k\). Defining \(\mu = \cos \theta\) and using our specific choice of squirming swimmer multipole moments, the lowest order governing equation for the concentration is

\[
\frac{\partial c_0}{\partial T} + \frac{105}{16} \rho (\mu - 6 \mu^3 + 5 \mu^5) \frac{\partial c_0}{\partial \rho} - \frac{(1 - \mu^2)}{32} (29 - 140 \mu^2 + 175 \mu^4) \frac{\partial c_0}{\partial \mu} - \frac{\partial^2 c_0}{\partial \rho^2} = 0.
\]

(9)

A common method in this type of boundary layer problem [22, 23] is to define similarity variables \(\eta = \rho/g\) and \(\chi = T/g^2\), where \(g(\mu)\) encapsulates the angular dependence of the boundary layer. Making this choice, the following relationships are needed for the change of variables:

\[
\frac{\partial c_0}{\partial \rho} = \frac{1}{\varpi} \frac{\partial c_0}{\partial \eta}, \quad \frac{\partial^2 c_0}{\partial \rho^2} = \frac{1}{\varpi^2} \frac{\partial^2 c_0}{\partial \eta^2}, \quad \frac{\partial c_0}{\partial \mu} = -\frac{\varpi g}{\varpi^2} \frac{\partial c_0}{\partial \eta}.
\]

This transformation isolates the angular dependence and defines the concentration boundary layer equation for the problem,

\[
\frac{\partial c_0}{\partial \chi} + \eta \frac{\partial c_0}{\partial \eta} \left(\frac{105}{16} (\mu - 6 \mu^3 + 5 \mu^5) g^2 + \frac{(1 - \mu^2)}{32} (29 - 140 \mu^2 + 175 \mu^4) g \frac{dg}{d\mu}\right)
- \frac{\partial^2 c_0}{\partial \eta^2} = 0.
\]

(10)

Provided the term in large parenthesis is equal to a constant \(\gamma\), the equation is transformed into an effective radial equation, since all of the angular dependence disappears. The solution for the associated angular function \(g(\mu)\) which defines our similarity transformation is discussed in an appendix A. To proceed we define the time-integrated concentration

\[
C_0 = \int_{0}^{\infty} c_0 \, d\chi.
\]

(11)

The equation for \(C_0\) becomes

\[
c_0(\chi = \infty) - c_0(\chi = 0) + \gamma \eta \frac{\partial C_0}{\partial \eta} - \frac{\partial^2 C_0}{\partial \eta^2} = 0.
\]

(12)
Consider a spatial domain where all molecules released are eventually captured with probability one. The concentration is defined in the spherical shell between two perfectly absorbing surfaces, the first at the surface of the cell \( (\eta = 0) \), and a second at some prescribed distance \( (\eta = \eta_s) \). Since all molecules are eventually absorbed, \( c_0(\chi = \infty) = 0 \). If a molecule is released in the extracellular fluid at position \( (\xi', \theta', \phi') \), the corresponding initial condition is \( c_0(\chi = 0) = \delta^3(\xi - \xi') \).

Writing the initial condition in terms of \( \eta \), our effective radial equation, equation (12), becomes

\[
\frac{\partial^2 c_0}{\partial \eta^2} - 2\frac{\partial c_0}{\partial \eta} = -\frac{\delta \left( \eta - \frac{\xi' g(\mu)}{g(\mu') \eta} \right) \delta (\mu - \mu') \delta (\phi - \phi')}{\alpha^{1/2} g(\mu)(1 + \alpha^{1/2} g(\mu) \eta)^2}.
\]  

(13)

Here we have chosen a value of the constant \( \gamma = 2 \). To solve equation (13), note that the two independent solutions to the homogeneous equation are a constant and \( \text{erfi}(\eta) = \frac{2}{\sqrt{\pi}} \int_0^\eta e^z^2 dz \). Using perfectly absorbing boundary conditions at \( \eta = 0 \) and \( \eta = \eta_s \), the solution for \( C_0 \) is

\[
C_0 = \mathcal{I} \text{erfi}(\eta_s)(\text{erfi}(\eta_s) - \text{erfi}(\eta_c)).
\]  

(14)

Here \( \eta_c (\eta_s) \) is the smaller (larger) of \( \eta \) and \( \eta' \). To complete the solution, we must calculate the proper normalisation \( \mathcal{I} \). This calculation is performed in the appendix B.

In terms of the original variables, the first-passage probability is calculated as

\[
\Pi_0 = \int_0^\infty d\tau \int_0^{2\pi} d\phi \int_{-1}^1 d\mu \xi^2 \frac{\partial C_0}{\partial \xi} \bigg|_{\xi = 1}.
\]  

(15)

The result can be written in terms of the boundary layer variable \( \eta \) and the time-integrated concentration \( C_0 \) as

\[
\Pi_0 = 2\pi \alpha^{1/2} \int_{-1}^1 d\mu \ g(\mu) \frac{\partial C_0}{\partial \eta} \bigg|_{\eta = 0}.
\]  

(16)

Performing the angular integration we arrive at

\[
\Pi_0 = \frac{e^{-(\eta')^2}}{(1 + \alpha^{1/2} g(\mu') \eta')^2} \left( \frac{\text{erfi}(\eta')}{\text{erfi}(\eta_c)} \right).
\]  

(17)

Moving the outer absorber \( \eta_c \) out to infinity and writing the result back in terms of \( \xi' \) yields the final result,

\[
\Pi_0 = \frac{e^{-(\eta')^2}}{(\xi')^2}.
\]  

(18)

The angular function \( w(\mu) = g(\mu)^2 \) that appears in the result is calculated from the associated angular equation in the appendix A. Note that the final result is properly normalised as \( \Pi_0(\xi' = 1) = 1 \). The result can be compared to a much simpler calculation, the first-passage probability in the case of pure diffusion, for which \( \Pi_{\text{diffusion}} = 1/\xi' \) [19]. In words, the effect of fluid flow is an exponential suppression of the first-passage probability as compared with the purely diffusive case.
4. Numerical model

We now turn our attention to obtaining a numerical solution for the first-passage probability. Building the numerical model is generally simpler and less prone to sporadic oscillations in the solution if a grid with uniform spacing is used. This is achieved by casting equation (8) in Cartesian coordinates to obtain a numerical solution. Replacing the derivatives in equation (8) with their finite-difference counterparts yields

\[
e^{n+1}_{i,j,k} = e^n_{i,j,k} + h^2 \left[ \frac{1}{h^2} + \frac{Pe \nu_x_{i,j,k}}{2h} \right] e^n_{i-1,j,k} + \left( \frac{1}{h^2} - \frac{Pe \nu_x_{i,j,k}}{2h} \right) e^n_{i+1,j,k} + \left( \frac{1}{h^2} + \frac{Pe \nu_y_{i,j,k}}{2h} \right) e^n_{i,j-1,k} + \left( \frac{1}{h^2} - \frac{Pe \nu_y_{i,j,k}}{2h} \right) e^n_{i,j+1,k} + \left( \frac{1}{h^2} - \frac{6}{h^2} e^n_{i,j,k+1} \right).
\]

(19)

Here \(e^n_{i,j,k}\) is the value of the concentration at the location indexed by \(i, j, k\) at the time indexed by \(n\) with \(h_s\) as the time step and \(h\) as the distance between grid points. We work on a grid 10 units wide with 200 equidistant points along each axis. Here, a unit corresponds to the dimensionless distance equal to one cell radius. The average velocity field \(v_{i,j,k}\) is computed first and stored in memory for each grid point. For the sake of comparison, the same fluid model used in our analytic calculation, the squirming swimmer, is used to obtain our numerical solutions. We use an explicit finite-difference scheme where the concentration at time \(n + 1\) is computed from the concentration at time \(n\). This is continued until the percent change in the concentration field is no larger than 0.01% per iteration at any grid point, indicating that the concentration field has reached steady state.

To calculate the first-passage probability, we first compute the flux of molecules through the inner and outer boundaries of the domain. These bounding surfaces are composed of discrete square surface elements defined at each grid point. The flux density \(J_{i,j,k}\) through a surface element at a given grid point at index \((i, j, k)\) is determined by taking the derivative of the concentration field normal across each surface element at the given point. For example, the flux density \(J_{i,j,k}\) exists only for \(\hat{x}\) direction is

\[
J_{i,j,k} = -\frac{de}{dx} \bigg|_{i,j,k} = \frac{-3e_{i,j,k} + 4e_{i+1,j,k} - e_{i+2,j,k}}{2h}.
\]

(20)

Equations for the flux density normal to the \(\hat{y}\) or \(\hat{z}\) directions could be obtained by a cyclic permutation of the indices \(i, j,\) and \(k\). The total flux \(\Phi_S\) through a surface \(S\) is then the sum of each \(J_{i,j,k}\) located at each surface element \(s\) composing \(S\), multiplied by the area of the surface element \((h^2)\). This is shown explicitly in equation (21) where the flux density at a given point on the surface \(J_{i,j,k}\) is summed over the set of surface elements \(\{s\}\) which composes the entire surface \(S\).

\[
\Phi_S = \sum_{\{s\}} h^2 J_{i,j,k} = h^2 \sum_{\{s\}} J_{i,j,k}.
\]

(21)

Since the concentration field is considered to be at steady state, the first passage probability \(\Pi\) is the total flux through the inner absorbing boundary at \(\xi = 1\), denoted as \(S_1\), divided by the sum of the flux through both the inner boundary and the outer boundaries. The outer boundaries,
which are cumulatively denoted as $S_2$, constitute a large cube, with faces at $x = \pm 5$, $y = \pm 5$, and $z = \pm 5$. Because the grid points are located on a Cartesian grid, the inner boundary $S_1$ is not a perfectly smooth sphere, but is a cubically faceted approximation to one.

\[
\Pi = \frac{\Phi_{S_1}}{\Phi_{S_1} + \Phi_{S_2}} = \frac{\sum_{x=1}^{x,L} \sum_{y=1}^{y,L} J_{x,y,k}}{\sum_{x=1}^{x,L} \sum_{y=1}^{y,L} J_{x,y,k} + \sum_{x=1}^{x,L} \sum_{y=1}^{y,L} J_{x,y,k}}.
\]

(22)

Using this procedure, we have numerically calculated the first-passage probability. The results are shown for $Pe = 10$ in figure 1 and for $Pe = 100$ in figure 2.

5. Results

To make a biologically motivated comparison between the analytical approach and the numerical solution, we numerically calculate the average first-passage probability, $\langle \Pi_0 \rangle = \frac{1}{7} \int_{-1}^{1} d\zeta' \Pi_0$ from equation (18). This takes into account the fact that molecules will be released around the entire surface of the cell, with a roughly uniform angular distribution of source locations. The full set of angular results from the numerical calculation are fit to a function of the form,

\[
\Pi_{\text{fit}} = \frac{e^{-\alpha(\zeta'-1)^b}}{(\zeta')^2}
\]

(23)

using a nonlinear least squares routine in Python. Figures 3 and 4 show a comparison of the numerical result for the first-passage probability and the analytic approximation. The result for the first-passage probability is in good agreement with the numerical result, especially at large $Pe$ (see figure 3). This is reassuring as the perturbation programme is constructed based on a small parameter $Pe^{-1/2}$. As $Pe$ is reduced the agreement becomes less quantitatively accurate (see figure 4), but continues to capture the qualitative behaviour, even for source locations far outside of the concentration boundary layer.
It should be noted that there is some disagreement between the numerical and analytical solutions very close to the absorbing surface \((1 < \xi' < 1.1)\). This is likely due to the rough surface created when defining a spherical surface on a Cartesian grid. For the numerical model, the spherical absorbing surface consists of small square surfaces (of area \(h^2\)) which are arranged to mimic the curved surface of the sphere. The distance between a point on the rough surface and the ideal spherical surface is no grater than one grid spacing \((h = 0.05)\). For points very close to the surface, a disparity between the numerical and analytical solutions may emerge as we probe the space near (within a few grid points of) the absorbing surface. In the region of concern \((1 < \xi' < 1.1)\), we are within only two grid points of the surface. Thus, if greater accuracy in this region is desired, then one must use a finer grid at the cost of increased computation time. For points further away from the surface however, the rough surface will have little effect on the solution.

To make contact with the motivations for the study discussed in the introduction, note that the cost and effectiveness of the toxin transport system is an active area of experimental...
A physical microvilli length of 4 μm corresponds to a source location of 1.1 in figures 3 and 4. For a cell in a flow field (either generated by its own swimming motion or an environmental flow), designing a *smart* toxin disposal system would probably only require that the cell have knowledge of the upstream direction. In the biophysical context, the receptors responsible for effluxing toxin molecules to the exterior of the cell do not chemically modify the toxin. As a result, there is a potentially costly scenario in which effluxed molecules are reabsorbed and have to be discarded again, which is known as futile cycling. The cell could see significant gains in efficiency be either preferentially activating transport receptors downstream or actively transporting molecules tagged for export to downstream receptors. A future experiment designed to monitor receptor activity in a controlled flow environment, perhaps a microfluidic chamber, might be able to uncover whether a smart disposal mechanism similar to this has evolved naturally.

6. Conclusion

Motivated by a mass transport problem during embryonic development, we considered an active particle model for a swimming cell, the spherical squirmer. Within the context of the model, we determined the first-passage probability for an advection-diffusion equation at small Reynolds number and large Péclet number. Numerical approaches to solving the advection-diffusion equation based on explicit finite-differencing were compared to an analytic approximation based on a rescaling of the concentration boundary layer. For large Péclet number we find quantitative agreement between the approaches. As the Péclet number is reduced, the analytic approximation continues to capture the qualitative behaviour of the first-passage probability, but deviates somewhat from the numerical results. The regime of validity for the analytic approximation might be improved by continuing the perturbation programme beyond the zeroth order. This is a potential direction for future research.

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Appendix A. The angular equation for $g(\mu)$

In the main body of the text, we were able to obtain a radial equation for the first-passage probability, provided that we could find a solution to an associated angular equation for $g(\mu)$. By making the choice $\gamma = 2$, we obtain a first-order differential equation for the variable $w = g^2$,

$$\frac{dw}{d\mu} + p(\mu)w = q(\mu), \quad (24)$$

where

$$p(\mu) = \frac{420\mu(1 - 5\mu^2)}{29 - 140\mu^2 + 175\mu^4}, \quad (25)$$

$$q(\mu) = \frac{128}{29 - 169\mu^2 + 315\mu^4 - 175\mu^6}. \quad (26)$$

This equation can be solved with an integrating factor. To do so we calculate $b(\mu) = \int p(\mu)\,d\mu$ which gives

$$b(\mu) = -6 \sqrt{7} \tan^{-1}(\sqrt{7}(5\mu^2 - 2)) - 3 \log(29 - 140\mu^2 + 175\mu^4). \quad (27)$$

The desired solution is then

$$w(\mu) = e^{-b(\mu)} \left( \int_{-1}^{\mu} q(s) e^{b(s)}\,ds + K \right), \quad (28)$$

where $K$ is an integration constant. In all of the plots shown in this paper $K = 0$.

Appendix B. The first-passage normalisation

To complete the calculation of the concentration $C_0$, we determine the constant $I$ in equation (14). Obtaining the correct value is important, as it effects the normalisation of the first-passage probability. Because of the delta function source, the situation is similar to that encountered in other boundary value problems. The concentration $C_0(\eta, \eta')$ is continuous at $\eta = \eta'$, but its first derivative is discontinuous. To determine the constant $I$, we integrate both sides of the governing equation (equation (13)) $\int_0^{2\pi} d\phi \int_{-1}^{1} d\mu \, g(\mu) \int_{\eta'}^{-\epsilon} d\eta$ to determine the discontinuity in the first derivative of $C_0$,

$$\frac{\partial C_0}{\partial \eta} \bigg|_{\eta = \eta' - \epsilon} = -\frac{1}{2\pi G \alpha^{1/2}(1 + \alpha^{1/2} g(\mu')\eta'^2)^2}, \quad (29)$$

where $G = \int_{-1}^{1} d\mu \, g(\mu)$. The factor of $g(\mu)$ in the integration to determine the discontinuity was incorrectly omitted in [7]; it is needed to ensure the proper normalisation,

$$I = \frac{-e^{\alpha\nu^2}}{4(\pi \alpha)^{1/2} G(1 + \alpha^{1/2} g(\mu')\eta'^2)^2}. \quad (30)$$

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