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Mixed analytical-stochastic simulation method for the recovery of a Brownian gradient source from probability fluxes to small windows

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ABSTRACT

Is it possible to recover the position of a source from the steady-state fluxes of Brownian particles to small absorbing windows located on the boundary of a domain? To address this question, we develop a numerical procedure to avoid tracking Brownian trajectories in the entire infinite space. Instead, we generate particles near the absorbing windows, computed from the analytical expression of the exit probability. When the Brownian particles are generated by a steady-state gradient at a single point, we compute asymptotically the fluxes to small absorbing holes distributed on the boundary of half-space and on a disk in two dimensions, which agree with stochastic simulations. We also derive an expression for the splitting probability between small windows using the matched asymptotic method. Finally, when there are more than two small absorbing windows, we show how to reconstruct the position of the source from the diffusion fluxes. The present approach provides a computational first principle for the mechanism of sensing a gradient of diffusing particles, a ubiquitous problem in cell biology.

1. Introduction

Recovering the source location from incomplete information about the emitting signal is a generic problem in several fields of science, such as finding an emitter in signal processing, the food source by smelling a few molecules and many more. In the context of cell biology, the question of how a cell can sample its environment and decide its final destination remains open, but it starts with the detection of an external gradient concentration that the cell must use to transform cell positional information into its genetic specialization and differentiation [30,12].

During axonal growth and guidance, the growth cone (which is the tip of a neuronal cell) uses external concentration gradients [10,25] to decide whether to continue moving or to stop, to turn right or left. Bacteria and spermatozoa can orient themselves in various chemotactical or mechanical gradients [2,11]. However, most models in the current literature that are concerned with addressing these questions rely on computing the flux to an absorbing or reflecting ball [4], an absorbing or permeable ball [9,1], or a single receptor sphere [17], all of which is insufficient to differentiate between concentrations

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to the left or right of the cell. To enable sensing of this difference, the detectors, modeled here as small absorbing windows, should be considered individually.

We compute here in the first part the steady-state fluxes of Brownian particles to small absorbing windows located on the boundary of a an infinite domain. Computing the fluxes of Brownian particles moving inside a bounded domain to small absorbing windows located on a boundary falls into the narrow escape problems [19,13,15,16,7,21] and has also been studied numerically [20]. However, the mean passage time to a small hole becomes infinite in an unbounded domain due to long excursions to infinity of Brownian trajectories. This difficulty is resolved here by computing the flux directly using two methods: first, we compute the flux of Brownian particles to small absorbers located on the half-plane, a disk in $\mathbb{R}^2$ and in a narrow band. The asymptotic computations are obtained by matched asymptotics of Laplace's equation in infinite domains.

In the second part, we develop a mixed numerical procedure to avoid tracking Brownian trajectories in the entire infinite space. We generate particles near the absorbing windows, computed from the analytical expression of the exit probability on an artificial boundary without introducing any artifacts [23,24]. This method avoids the costly computation of particle trajectories in the unbounded environment (e.g. extracellular space in the brain or cells moving in two dimensional chamber), containing large excursions away from the cell, thereby allowing direct simulations of Brownian trajectories in the region of interest close to the cell. In the absence of such a procedure, these simulations would be next to impossible to perform due to the aforementioned infinite mean passage time.

We show that the results of both independent methods (Asymptotic and numerical) agree. The local geometry and distribution of windows does matter for the reconstruction of the source position: we show that it is indeed possible to recover the source of a gradient already with three receptors. Finally, the location of the windows might also be critical for the sensitivity of detection: for example, the flux of Brownian particles to small targets depends crucially on their localization [15,14,7,21,16,19]. In summary, the manuscript is organized as follows. First, we compute asymptotically the flux of Brownian particles to receptors. Second, we introduce the mixed simulation method. In the third part, we present several applications to various geometry: half-space, a disk and a disk in a narrow band. In the fourth and last section, we apply the methods to reconstruction the source location.

2. Fluxes of Brownian particles to small targets in an open space

Brownian molecules are produced by a steady-state source located at position x_0 in an open space such as the two-dimensional real space $\mathbb{R}^2$. The steady-state distribution of particles, P_0, is the solution of the Green's function

$$-D\Delta P_0(\boldsymbol{x}) = Q\,\delta(\boldsymbol{x}-\boldsymbol{x}_0) \quad \text{for} \quad \boldsymbol{x}\in\mathbb{R}^2 \tag{1}$$

where the parameter $Q>0$ measures the injection rate of particles. We study here the flux received by an obstacle Ω containing N-small absorbing windows $\partial\Omega_1\cup\ldots\cup\partial\Omega_N$ on its boundary $\partial\Omega$. The fluxes of diffusing particles on the windows can be computed from solving the mixed boundary value problem (we now set $Q=1$) [16]

$$\begin{aligned} -D\Delta P_0(\boldsymbol{x}) &= \delta(\boldsymbol{x}-\boldsymbol{x}_0) \quad \text{for} \quad \boldsymbol{x}\in\mathbb{R}^2\setminus\Omega \\ \frac{\partial P_0}{\partial n}(\boldsymbol{x}) &= 0 \quad \text{for} \quad \boldsymbol{x}\in\partial\Omega\setminus(\partial\Omega_1\cup\ldots\cup\partial\Omega_N) \\ P_0(\boldsymbol{x}) &= 0 \ \text{for} \ \boldsymbol{x}\in\partial\Omega_1\cup\ldots\cup\partial\Omega_N \end{aligned} \tag{2}$$

The reflecting boundary condition accounts for the impenetrable walls and diffusing molecules are reflected on the surface $\partial\Omega_r=\partial\Omega\setminus(\partial\Omega_1\cup\ldots\cup\partial\Omega_N)$. The absorbing boundary condition on each window $\partial\Omega_1\cup\ldots\cup\partial\Omega_N$ represents the extreme case where the binding time of particles is fast and the particle trajectories are terminated.

Although the probability density $P_0(\boldsymbol{x})$ diverges when $|\boldsymbol{x}|\to\infty$, we are interested in the splitting probability between windows, which is the ratio of the steady-state flux at each hole divided by the total flux through all windows:

$$J_k = \frac{\displaystyle\int\limits_{\partial\Omega_k}\frac{\partial P_0(\boldsymbol{x})}{\partial \boldsymbol{n}}dS_{\boldsymbol{x}}}{\displaystyle\sum_q\int\limits_{\partial\Omega_q}\frac{\partial P_0(\boldsymbol{x})}{\partial \boldsymbol{n}}dS_{\boldsymbol{x}}}. \tag{3}$$

In two-dimensions, due to the recurrent property of the Brownian motion, the probability to hit a window before going to infinity is one, thus the total flux is one:

$$\sum_q\int\limits_{\partial\Omega_q}\frac{\partial P_0(\boldsymbol{x})}{\partial \boldsymbol{n}}dS_{\boldsymbol{x}} = 1. \tag{4}$$

We shall now compute the fluxes asymptotically for three different configurations: 1 – when the windows are distributed on a line at the boundary of the half-plane, 2 – when there are located on a disk in the entire space, and 3 – when the disk is located in a narrow band. We use the Green–Neumann's function and the method of matched asymptotics [19,21].