Diffusion on a tree with stochastically gated nodes

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Abstract. We consider diffusion on a tree with nodes that randomly switch between allowing and prohibiting particles to pass. We find exact expressions for various splitting probabilities and mean first passage times for a single diffusing particle and show how the many parameters in the problem, such as the node gating statistics and tree topology, contribute to these exit statistics. We also consider a concentration of particles that can always pass through interior branch nodes and determine how an intermittent source at one end of the tree affects the flux at the other end. The latter problem is motivated by applications to insect respiration.

1. Introduction

Biological systems often employ branched tree structures in order to distribute nutrients from a single source to many destinations or to gather nutrients from many sources. Examples include plant roots, river basins, neuronal dendrites, and cardiovascular and tracheal systems. Motivated by such systems, a number of recent works in theoretical biology study diffusion in a tree [1, 2, 3]. In this paper, we consider diffusion in a tree with stochastically-gated nodes. We suppose that a Markov jump process controls whether or not particles can pass through the nodes of the tree, and we find exact expressions for various splitting probabilities and mean first passage times (MFPTs) for a particle diffusing through the tree. Our exact calculations show how the many parameters in the problem (node gating statistics, tree topology, tree edge length, etc.) contribute to these exit statistics. We also consider a concentration of particles diffusing in a tree. We suppose that particles can always pass through interior branch nodes, but that they are intermittently supplied at one end of the tree. In the case of nutrient transport through a tree, one would like to know how much the flux at the opposite end of the tree decreases as a result of an intermittent supply compared to a constant supply. We determine this decrease exactly and find that it depends crucially on where the intermittent source is located.

One such example of diffusive flow from an intermittent source through a branched network is insect respiration. Insects breathe through a branched network of tracheal tubes that allows oxygen to diffuse to their cells [4]. Oxygen is intermittently supplied to this network through valves (called spiracles) in the exoskeleton, which rapidly open and close during the so-called flutter phase [5]. Determining how the opening and closing decreases oxygen uptake would help sort out the competing hypotheses for the purpose of this curious behavior [6]. A previous model that ignored tracheal branching showed that rapid opening and closing of the spiracles allows the insect to maintain high oxygen uptake during the flutter phase [7]. We show that this result still holds in the more realistic case of a branching tracheal network. In fact, we find that branching strengthens this result. That is, branching allows the insect to maintain an even higher oxygen uptake during the flutter phase. Our work is also motivated by medical applications. The state of the art in respiratory physiotherapy includes various machines and devices, and almost all of them rely on supplying air to a patient's lungs intermittently at high frequency [8].

The paper is organized as follows. In section 2, we use the results of [9, 10] to collect some facts on diffusion in an interval with switching boundaries. We then use these results to study diffusion in an interval with switching at interior points (section 3). There, we find the splitting probability that a diffusing particle will exit out one end of the interval given a set of randomly opening and closing gates in the interior. We also determine the mean first passage time (MFPT) to escape and find a homogenized diffusion coefficient in the case of many gates that rapidly open and close. Armed with these results, we move to the full problem of diffusion in a tree with switching at the nodes in sections 4 and 5. In section 4 we find the splitting probability that a diffusing particle will exit out any particular terminal node given that all the nodes of the tree randomly open and close, and we also find the MFPT to escape. In section 5, we consider an intermittent supply of a concentration of particles diffusing through a tree. We conclude with a brief discussion.

2. Boundary switching on an interval

In order to study the full problem of diffusion in a tree with stochastically-gated nodes, we first consider diffusion in an interval with switching boundaries. We will formulate the problem from the so-called *particle perspective*, in which the boundaries do not physically change but their effective permeability depends on the conformational state of the diffusing Brownian particle, see Fig. 1(a). The dynamics is described by a stochastic differential equation (SDE) with switching boundaries. An alternative formulation is the so-called *gate perspective*, in which each boundary switches between a closed and open state, see Fig. 1(b). The dynamics is now represented by a partial differential equation (PDE) with switching boundaries, namely, the diffusion equation for particle concentration. The two perspectives are mathematically equivalent if and only if all boundaries are perfectly correlated. We will focus mainly on the particle perspective, but consider the gate perspective in section 5. Throughout the paper, we refer to a switching boundary as a *stochastic gate*, irrespective of whether it is the particle or boundary that physically switches.

Consider a Brownian particle diffusing in an interval $[0, L]$ that switches conformational state according to a continuous-time Markov jump process $n(t) \in \{0, 1\}$ with fixed transition rates μ and ν

$$0 \underset{\mu}{\overset{\nu}{\rightleftharpoons}} 1 \tag{2.1}$$

Suppose that both boundaries are absorbing when $n(t) = 0$ and reflecting otherwise. Let $X_t \in [0, L]$ denote the position of the particle at time t. Define $p(x, t)$ to be the probability density for the stochastic process X_t and set $p_n(x, t) = \mathbb{E}[p(x, t)1_{n(t)=n}]$. The densities p_n evolve according to the differential Chapman-Kolmogorov (CK) equation

$$\frac{\partial p_n(x,t)}{\partial t} = \frac{\partial^2 p_n(x,t)}{\partial x^2} + \sum_{m=0,1} A_{nm} p_m(x,t), \tag{2.2}$$

with $\mathbf{A}$ the matrix

$$\mathbf{A} = \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix}. \tag{2.3}$$

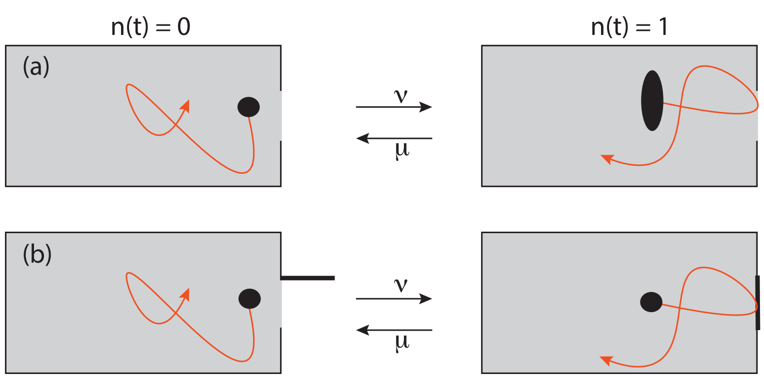

Figure 1: Switching barrier from (a) the particle perspective and (b) the gate perspective.

We have fixed units so that the diffusion coefficient is unity. Equation (2.2) is supplemented by the boundary conditions

$$p_0(0,t) = p_0(L,t) = 0, \qquad \left.\frac{\partial p_1(x,t)}{\partial x}\right|_{x=0} = \left.\frac{\partial p_1(x,t)}{\partial x}\right|_{x=L} = 0,$$

and the initial condition

$$p_n(x,0) = \delta(x-y)\rho_n,$$

where ρ_n is the stationary measure of the ergodic two-state Markov process generated by the matrix $\mathbf{A}$,

$$\sum_{m=0,1} A_{nm}\rho_m = 0, \quad \rho_0 = \frac{\mu}{\mu+\nu}, \quad \rho_1 = \frac{\nu}{\mu+\nu}. \tag{2.4}$$

Following [9, 10] we now determine the splitting probability for being absorbed at $x=0$ rather than $x=L$, say, and the mean first passage time (MFPT) for being absorbed at either end. Both quantities can be defined in terms of the stopping time‡

$$\tau = \inf\big\{t \geq 0 : \{X_t \in \{0,L\}\} \cap \{n(t)=0\}\big\}.$$

2.1. Splitting probability

Define the splitting probability for escaping at the end $x=0$ by

$$q_n(x) := \mathbb{P}(X_\tau = 0 \cap n(0) = n \,|\, X_0 = x),$$

By constructing the backwards CK equation, it can be shown that q_n satisfies the ordinary differential equation (ODE)

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} q_0 \\ q_1 \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix}\begin{pmatrix} q_0 \\ q_1 \end{pmatrix},$$

where Δ denotes the 1-D Laplacian d^2/dx^2 and the boundary conditions are

$$q_0(0) = \rho_0, \quad q_0(L) = 0,$$
$$q_1'(0) = 0, \quad q_1'(L) = 0.$$

Adding the equations for q_0 and q_1, and setting $q(x) = q_0(x) + q_1(x)$ gives

$$\Delta q(x) = 0, \quad q(0) = \rho_0 + q_1(0), \quad q(L) = q_1(L). \tag{2.5}$$

with $q_1(x)$ satisfying the equation

$$\Delta q_1(x) - (\mu+\nu)q(x) = -\nu q(x). \tag{2.6}$$

It is straightforward to solve this boundary value problem (BVP) and obtain

$$q(x) := q_0(x) + q_1(x) = \frac{\rho_0\xi(L-x) + e^{\xi L}(\rho_0(L\xi - x\xi - 1) + 1) + \rho_0 - 1}{\rho_0(L\xi+2) + e^{\xi L}(\rho_0(L\xi - 2) + 2) - 2}, \tag{2.7}$$

where $\xi = \sqrt{\mu+\nu}$.

Two related quantities will be needed in section 5. The first is the probability of escape through the end $x=L$ when the particle is in state i, given that $x=L$ is always open:

$$r^i(x) = r_0^i(x) + r_1^i(x),$$

‡ A stopping time τ is a random variable whose value is interpreted as the time (finite or infinite) at which a given stochastic process is terminated according to some stopping rule that depends on current and past states. A classical example of a stopping time is a first passage time.

where

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} r_0^i \\ r_1^i \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} r_0^i \\ r_1^i \end{pmatrix},$$

with boundary conditions

$$r_0^i(0) = \partial_x r_1^i(0) = r_{1-i}^i(L) = 0, \quad r_i^i(L) = \rho_i.$$

We note that

$$r_1^0(0) = \frac{\rho_1\rho_0(\sinh(L\xi) - L\xi)}{L\rho_0\xi\cosh(L\xi) + \rho_1\sinh(L\xi)} \tag{2.8}$$

$$\text{and} \quad r_1^1(0) = \frac{\rho_1(\rho_1\sinh(L\xi) + L\rho_0\xi)}{L\rho_0\xi\cosh(L\xi) + \rho_1\sinh(L\xi)}. \tag{2.9}$$

The second quantity is the probability that the particle is in state i when it first reaches $x = L$ assuming that $x = 0$ is always reflecting:

$$a^i(x) = a_0^i(x) + a_1^i(x),$$

where

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} a_0^i \\ a_1^i \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} a_0^i \\ a_1^i \end{pmatrix},$$

with boundary conditions

$$\partial_x a_0^i(0) = \partial_x a_1^i(0) = a_{1-i}^i(L) = 0, \quad a_i^i(L) = \rho_i.$$

We note that

$$a_0^0(0) = \rho_0(\rho_0 + \rho_1\mathrm{sech}(L\xi)) \tag{2.10}$$

$$a_0^1(0) = a_1^0(0) = \rho_1\rho_0(1 - \mathrm{sech}(L\xi)) \tag{2.11}$$

$$\text{and} \quad a_1^1(0) = \rho_1(\rho_1 + \rho_0\mathrm{sech}(L\xi)). \tag{2.12}$$

2.2. MFPTs

Defining the MFPT to escape at either end according to

$$v_n(x) := \mathbb{E}[\tau 1_{\{n(0)=n\}} \,|\, X_0 = x],$$

it can be shown that v_n satisfies the ODE [10, 11]

$$-\begin{pmatrix} \rho_0 \\ \rho_1 \end{pmatrix} = \Delta \begin{pmatrix} v_0 \\ v_1 \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} v_0 \\ v_1 \end{pmatrix},$$

with boundary conditions

$$v_0(0) = 0, \quad v_0(L) = 0,$$
$$\partial_x v_1(0) = 0, \quad \partial_x v_1(L) = 0.$$

It is straightforward to solve this BVP and obtain

$$v(x) := v_0(x) + v_1(x) = \frac{1}{2}\Big(x(L-x) + \frac{L\rho_1\coth\left(\frac{L\xi}{2}\right)}{\rho_0\xi}\Big) \tag{2.13}$$

For later use, we note that if we replace L by $2L$, then

$$v_0^{(2)}(L) = \frac{L\left(L\rho_0\xi + 2\rho_1\tanh\left(\frac{L\xi}{2}\right)\right)}{2\xi}. \tag{2.14}$$

Another useful quantity is the MFPT to escape from the end $x = L$, say, given that the other end $x = 0$ is always closed:

$$u(x) := u_0(x) + u_1(x),$$

where

$$-\begin{pmatrix} \rho_0 \\ \rho_1 \end{pmatrix} = \Delta \begin{pmatrix} u_0 \\ u_1 \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} u_0 \\ u_1 \end{pmatrix},$$

with boundary conditions

$$\partial_x u_0(0) = 0, \quad u_0(L) = 0,$$
$$\partial_x u_1(0) = \partial_x u_1(L) = 0.$$

We note that

$$u(x) = \frac{1}{2}\Big(L^2 + \frac{2L\rho_1 \coth(L\xi)}{\rho_0 \xi} - x^2\Big). \tag{2.15}$$

3. Series of stochastic gates

Recently, the problem of diffusion through a 1-D domain with multiple switching gates within the interior of the domain has been analyzed from the gate perspective [12]. In this section, we formulate the corresponding steady-state particle perspective problem in terms of splitting probabilities and mean first passage times, and use probabilistic arguments to find the solutions. Consider a single particle diffusing in the interval $[0, NL]$ and suppose that it switches conformational state according to a continuous-time Markov jump process $n(t) \in \{0, 1\}$ with fixed transition rates μ and ν

$$0 \underset{\alpha}{\overset{\nu}{\rightleftharpoons}} 1.$$

Suppose that the particle can diffuse freely through the interval when $n(t) = 0$, but cannot pass through $x = l_k := kL$ when $n(t) = 1$ for $1 \le k \le N - 1$. (We could equivalently have assumed that the gates switch states provided all the gates are perfectly correlated.) We also assume that the particle can be absorbed at $x = 0$ and $x = L$ only when $n(t) = 0$, otherwise it is reflected.

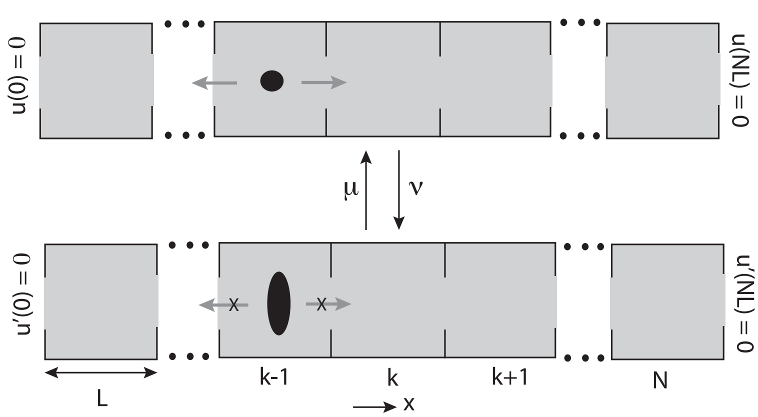

Figure 2: Series of stochastic gates in the particle perspective.

3.1. Splitting probabilities

Let $X_t \in [0, NL]$ denote the position of the particle and define the stopping time

$$\mathcal{T} = \inf\big\{t \geq 0 : \{X_t \in \{0, NL\}\} \cap \{n(t) = 0\}\big\}. \tag{3.1}$$

Assume $\mathbb{P}(n(0) = 0) = \rho_0$. For $n \in \{0, 1\}$, let

$$\pi_n(x) = \mathbb{P}(X_{\mathcal{T}} = 0 \,|\, \{X_0 = x\} \cap \{n(0) = n\}). \tag{3.2}$$

One can show (see [9, 11]) that π_n satisfies the ODEs

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} \pi_0 \\ \pi_1 \end{pmatrix} + \begin{pmatrix} -\nu & \nu \\ \mu & -\mu \end{pmatrix} \begin{pmatrix} \pi_0 \\ \pi_1 \end{pmatrix}, \tag{3.3}$$

with exterior boundary conditions

$$\begin{aligned} &\pi_0(0) = 1 \quad \pi_0(NL) = 0 \\ &\pi_1'(0) = 0 \quad \pi_1'(NL) = 0, \end{aligned}$$

and the interior boundary conditions at the k-th gate, $l_k := kL$, are

$$\begin{aligned} &\pi_0(l_k-) = \pi_0(l_k+), \\ &\pi_0'(l_k-) = \pi_0'(l_k+), \\ &\pi_1'(l_k-) = \pi_1'(l_k+) = 0. \end{aligned}$$

A simple rescaling shows that

$$p_n(x) := \rho_n \pi_n(x) = \mathbb{P}(X_{\mathcal{T}} = 0 \cap n(0) = n \,|\, X_0 = x) \tag{3.4}$$

satisfies the ODEs

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} p_0 \\ p_1 \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} p_0 \\ p_1 \end{pmatrix}, \tag{3.5}$$

with exterior boundary conditions

$$\begin{aligned} &p_0(0) = \rho_0, \quad p_0(NL) = 0, \\ &p_1'(0) = 0, \quad p_1'(NL) = 0, \end{aligned}$$

and the same interior boundary conditions as π_n.

By the definition of p_n, we have that

$$p(x) := p_0(x) + p_1(x) = \mathbb{P}(X_{\mathcal{T}} = 0 \,|\, X_0 = x). \tag{3.6}$$

By the strong Markov property§, if $0 \leq k \leq N - 1$ and $x \in (l_k, l_{k+1})$, then

$$p(x) = \frac{1}{\rho_0}\Big(q(s) p_0(l_k) + (1 - q(s)) p_0(l_{k+1})\Big), \tag{3.7}$$

where $s = x - l_k$ and

$$q(s) = \mathbb{P}(X_{\tau_k} = l_k \,|\, X_0 = s),$$

is given in (2.7) since all the cells have length L, and τ_k is the stopping time

$$\tau_k = \inf\big\{t \geq 0 : \{X_t \notin (l_k, l_{k+1})\} \cap \{n(t) = 0\}\big\}.$$

To see why (3.7) holds, let $\{\mathcal{F}_t\}_{t \geq 0}$ be the filtration generated by the strong Markov process $\{(X_t, n(t))\}_{t \geq 0}$. Let $\mathbb{E}_x$ denote the expectation conditioned on $X_0 = x$ and

§ Recall that a stochastic process has the Markov property if the conditional probability distribution of future states of the process (conditional on both past and present states) depends only upon the present state, not on the sequence of events that preceded it. The term strong Markov property is similar to the Markov property, except that the "present" is defined in terms of a stopping time.

$\mathbb{P}(n(0)=0)=\rho_0$. Similarly, let $\mathbb{E}_{x,n}$ denote the expectation conditioned on $X_0=x$ and $n(0)=n$. Then, by the tower property of conditional expectation and the fact that the random variable $1_{X_{\tau_k}=l_k}$ is measurable with respect to $\mathcal{F}_{\tau_k}$, we have that

$$\begin{aligned} p(x) &= \mathbb{E}_x[1_{X_{\mathcal{T}}=0}] = \mathbb{E}_x\big[\mathbb{E}_x[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{\tau_k}]\big] \\ &= \mathbb{E}_x\big[1_{X_{\tau_k}=l_k}\mathbb{E}_x[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{\tau_k}]\big] + \mathbb{E}_x\big[1_{X_{\tau_k}=l_{k+1}}\mathbb{E}_x[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{\tau_k}]\big]. \end{aligned}$$

Applying the strong Markov property to both terms and using the linearity of expectation yields

$$\begin{aligned} p(x) &= \mathbb{E}_x[1_{X_{\tau_k}=l_k}]\mathbb{E}_{l_k,0}[1_{X_{\mathcal{T}}=0}] + \mathbb{E}_x[1_{X_{\tau_k}=l_{k+1}}]\mathbb{E}_{l_{k+1},0}[1_{X_{\mathcal{T}}=0}] \\ &= q(s)\pi_0(l_k) + (1-q(s))\pi_0(l_{k+1}). \end{aligned}$$

Applying the definition of p_0 in (3.4) gives (3.7).

Since

$$p_0(l_0)=\rho_0, \quad p_0(NL)=0, \tag{3.8}$$

it follows that $p(x)$ is determined by the remaining $N-1$ constants

$$p_0(l_1),\dots,p_0(l_{N-1}).$$

As the cells are evenly spaced, we find that each of these constants is the average of its neighbors

$$p_0(l_k)=\frac{1}{2}\big(p_0(l_{k-1})+p_0(l_{k+1})\big), \tag{3.9}$$

for $k=1,\dots,N-1$. To see why (3.9) holds, define the stopping time

$$s_k=\inf\big\{t\geq 0:\{X_t\notin(l_{k-1},l_{k+1})\}\cap\{n(t)=0\}\big\}. \tag{3.10}$$

Observe that

$$\begin{aligned} \pi_0(l_k) &= \mathbb{E}_{l_k,0}[1_{X_{\mathcal{T}}=0}] = \mathbb{E}_{l_k,0}[\mathbb{E}_{l_k,0}[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{s_k}]] \\ &= \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}\mathbb{E}_{l_k,0}[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{s_k}]] + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}\mathbb{E}_{l_k,0}[1_{X_{\mathcal{T}}=0}|\mathcal{F}_{s_k}]]. \end{aligned}$$

As above, the strong Markov property and linearity imply that $\pi_0(l_k)$ is

$$\begin{aligned} &\mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}]\mathbb{E}_{l_{k-1},0}[1_{X_{\mathcal{T}}=0}] + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}]\mathbb{E}_{l_{k+1},0}[1_{X_{\mathcal{T}}=0}] \\ &\quad = \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}]\pi_0(l_{k-1}) + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}]\pi_0(l_{k+1}). \end{aligned}$$

By symmetry, $\mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}]=\mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}]=1/2$. Applying the definition of p_0 in (3.4) gives (3.9).

Rearranging (3.9), we see that the constants satisfy a discretized Laplace's equation

$$p_0(l_{k-1})-2p_0(l_k)+p_0(l_{k+1})=0, \tag{3.11}$$

for $k=1,\dots,N-1$, with (3.8) serving as boundary conditions. Solving this system and applying (3.7) and (2.7) yields $p(x)$.

3.2. Mean first passage times

Consider the same diffusing particle scenario as in section 3.1 above, but now we seek the expected absorption time (MFPT) of the particle to either of the switching boundaries

$$w_n(x)=\mathbb{E}_x[\mathcal{T}1_{\{n(0)=n\}}]. \tag{3.12}$$

One can show (see [9, 11]) that w_n satisfies the ODEs

$$-\begin{pmatrix} \rho_0 \\ \rho_1 \end{pmatrix} = \Delta \begin{pmatrix} w_0 \\ w_1 \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} w_0 \\ w_1 \end{pmatrix}, \tag{3.13}$$

with exterior boundary conditions

$$\begin{aligned} &w_0(0) = 0 \quad w_0(NL) = 0 \\ &w_1'(0) = 0 \quad w_1'(NL) = 0, \end{aligned}$$

and the same interior boundary conditions as π_n.

By the definition of w_n, we have that

$$w(x) := w_0(x) + w_1(x) = \mathbb{E}_x[\mathcal{T}]. \tag{3.14}$$

By the strong Markov property, if $0 \le k \le N-1$ and $x \in (l_k, l_{k+1})$, then

$$w(x) = v(s) + \frac{1}{\rho_0}\Big(q(s)w_0(l_k) + (1-q(s))w_0(l_{k+1})\Big), \tag{3.15}$$

where $s = x - l_k$, the exit time $v(x)$ is given in (2.13), and the splitting probability $q(s)$ is given in (2.7). To see why (3.15) holds, observe that by the tower property and the fact that the random variables $1_{X_{\tau_k}=l_k}$ and τ_k are measurable with respect to $\mathcal{F}_{\tau_k}$, we have

$$\begin{aligned} w(x) &= \mathbb{E}_x[\mathcal{T}] = \mathbb{E}_x[\tau_k] + \mathbb{E}_x[\mathbb{E}_x[\mathcal{T} - \tau_k | \mathcal{F}_{\tau_k}]] \\ &= \mathbb{E}_x[\tau_k] + \mathbb{E}_x[1_{X_{\tau_k}=l_k} \mathbb{E}_x[\mathcal{T} - \tau_k | \mathcal{F}_{\tau_k}]] + \mathbb{E}_x[1_{X_{\tau_k}=l_{k+1}} \mathbb{E}_x[\mathcal{T} - \tau_k | \mathcal{F}_{\tau_k}]]. \end{aligned}$$

Applying the strong Markov property to the last two terms and using the linearity of expectation yields

$$\begin{aligned} w(x) &= \mathbb{E}_x[\tau_k] + \mathbb{E}_x[1_{X_{\tau_k}=l_k}]\mathbb{E}_{l_k,0}[\mathcal{T}] + \mathbb{E}_x[1_{X_{\tau_k}=l_{k+1}}]\mathbb{E}_{l_{k+1},0}[\mathcal{T}] \\ &= v(s) + q(s)\mathbb{E}_{l_k,0}[\mathcal{T}] + (1-q(s))\mathbb{E}_{l_{k+1},0}[\mathcal{T}]. \end{aligned}$$

Applying the definition of w_0 in (3.12) gives (3.15).

Since $w_0(l_0) = w_0(NL) = 0$, it remains to determine the $N-1$ constants

$$w_0(l_1), \dots, w_0(l_{N-1}).$$

Since the cells are evenly spaced, we have that

$$w_0(l_k) = V + \frac{1}{2}\big(w_0(l_{k-1}) + w_0(l_{k+1})\big), \tag{3.16}$$

for $k = 1, \dots, N-1$, where $V = v_0^{(2)}(L)$ is given in (2.14). To see why (3.16) holds, observe that $w_0(l_k) = \rho_0 \mathbb{E}_{l_k,0}[\mathcal{T}]$ and thus

$$\begin{aligned} \frac{w_0(l_k)}{\rho_0} &= \mathbb{E}_{l_k,0}[s_k] + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}} \mathbb{E}_{l_k,0}[\mathcal{T} - s_k | \mathcal{F}_{s_k}]] \\ &\quad + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}} \mathbb{E}_{l_k,0}[\mathcal{T} - s_k | \mathcal{F}_{s_k}]]. \end{aligned}$$

As before, applying the strong Markov property to the second two terms and using linearity gives

$$\begin{aligned} \frac{w_0(l_k)}{\rho_0} &= \mathbb{E}_{l_k,0}[s_k] + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}]\mathbb{E}_{l_{k-1},0}[\mathcal{T}] \\ &\quad + \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}]\mathbb{E}_{l_{k+1},0}[\mathcal{T}]. \end{aligned} \tag{3.17}$$

By symmetry, $\mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k-1}}] = \mathbb{E}_{l_k,0}[1_{X_{s_k}=l_{k+1}}] = 1/2$. We further have that $\rho_0 \mathbb{E}_{l_k,0}[s_k] = V$ by the reflection principle for Brownian motion. Multiplying (3.17) by

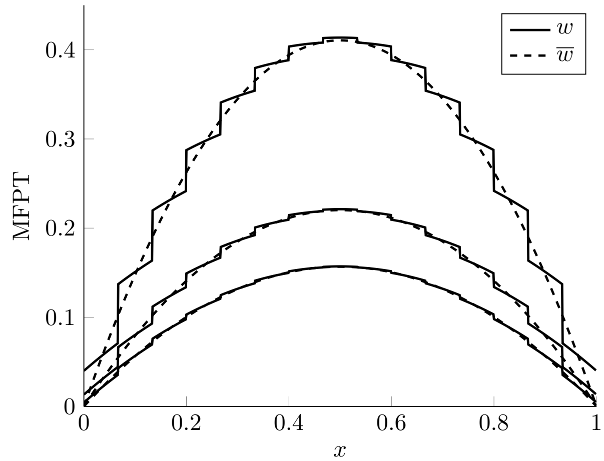

Figure 3: Homogenized diffusion. We plot the MFPT to escape from an interval with many fast switching gates ($w(x)$ in (3.14)) and the MFPT to escape an interval with homogenized diffusion coefficient (3.20), which is $\overline{w}(x)$ in (3.19). The three pairs of curves correspond to $\rho_0 = 1/4$, $1/2$, and $3/4$, with higher curves corresponding to lower values of ρ_0. We note that $w(x)$ has jump discontinuities at gates which we plot as vertical lines. In all plots, we take the number of gates to be $N = 15$ and $a = 1$. The $w(x)$ and $\overline{w}(x)$ plots become indistinguishable for larger values of N.

ρ_0 gives (3.16). Rearranging (3.16), we notice that these constants satisfy a discretized Poisson equation

$$w_0(l_{k-1}) - 2w_0(l_k) + w_0(l_{k+1}) = -2V, \tag{3.18}$$

for $k = 1, \ldots, N-1$, and $w_0(l_0) = w_0(NL) = 0$ can be interpreted as boundary conditions. Solving this system yields $w(x)$.

3.3. Limit of many gates and fast switching

Let $L = 1/N \ll 1$ and $\xi = 2N/a$ for some $a > 0$. From (3.18) and (2.14), we have

$$N^2\big(w_0(l_{k-1}) - 2w_0(l_k) + w_0(l_{k+1})\big) = -2N^2V = -(\rho_0 + \rho_1 a \tanh(1/a)).$$

Taking the continuum limit of the left-hand side and noting that $w_1 \approx (\rho_1/\rho_0)w_0$ for fast switching, we have $w(x) \approx \overline{w}(x)$ with $\overline{w}(x)$ the solution to the BVP

$$\Delta\overline{w}(x) = -\big(1 + a\tanh(1/a)\frac{\nu}{\mu}\big), \quad \overline{w}(0) = \overline{w}(1) = 0. \tag{3.19}$$

The latter yields the classical MFPT for a diffusing particle with diffusion coefficient

$$\Big[1 + a\tanh(1/a)\frac{\nu}{\mu}\Big]^{-1}. \tag{3.20}$$

to escape from the interval $(0, 1)$. We illustrate the accuracy of this approximation in Fig. 3.

4. Stochastic gates at the nodes of a tree

Consider a finite regular tree Γ consisting of N_v nodes or vertices and N_e line segments or edges of length L (see Fig. 4a). The nodes $\alpha \in \Gamma$ of the network may be classified as either branching or terminal (excluding the primary node). Let $\mathcal{B}$ denote the set of branching nodes, and let $\mathcal{O}$ denote the set of terminal nodes. The first branch node opposite the primary node is denoted by α_0. For every other branching node $\alpha \in \mathcal{B}$ and terminal node $\alpha \in \mathcal{O}$ there exists a unique direct path from α_0 to α (one that does not traverse any line segment more than once). We can label each node $\alpha \neq \alpha_0$ uniquely by the index k of the final segment of the direct path from α_0 to α so that the branch node corresponding to a given segment label k can be written $\alpha(k)$. We

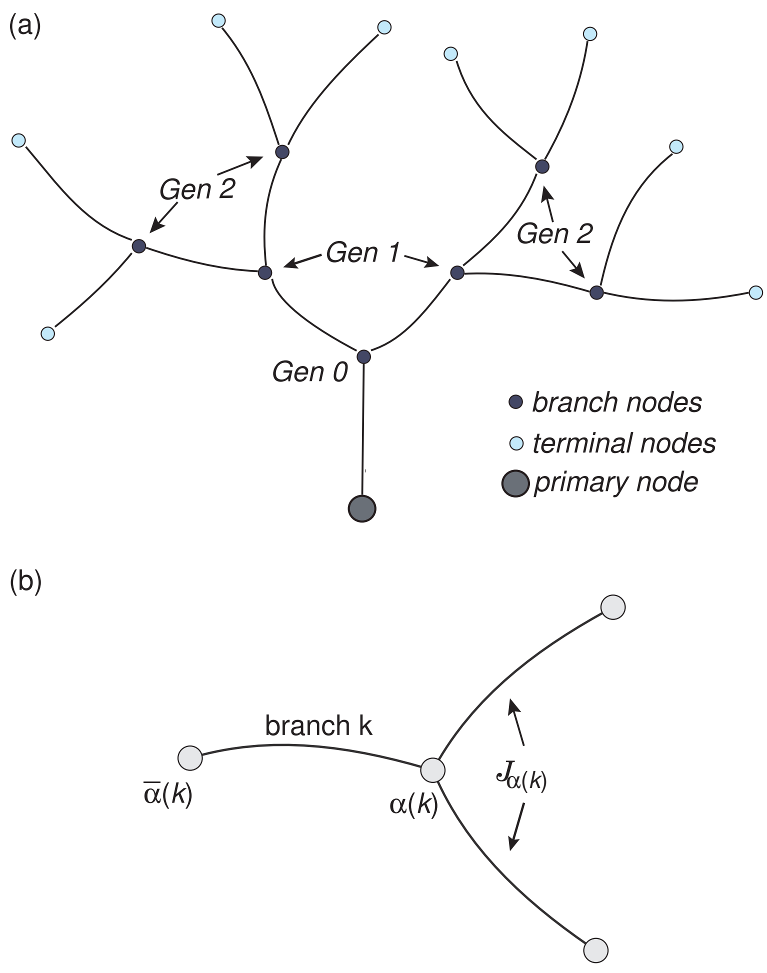

Figure 4: Labeling scheme for a regular tree Γ with coordination number $z = 3$. (a) Sketch of a tree with $N = 3$ generations (Gen) of branch nodes, a primary node, and $2(N+1)$ terminal nodes. (b) The branch node $\alpha(k)$ is shown in relation to the neighboring branch node $\overline{\alpha}(k)$ closest to the primary node. The branch segments extending out from $\alpha(k)$ in the positive direction together comprise the set $\mathcal{J}_{\alpha(k)}$.

denote the other node of segment k by $\overline{\alpha}(k)$. For example, $\overline{\alpha}_0$ is the primary node. We can also introduce a direction on each segment of the tree such that every direct path from $\overline{\alpha}_0$ always moves in the positive direction. Finally, we introduce the prameterised local coordinate $x_k(s)$, $s \in [0, L]$ for each segment k such that

$$\lim_{s\to L} x_k(s) = \alpha(k), \quad \lim_{s\to 0} x_k(s) = \overline{\alpha}(k). \tag{4.1}$$

Consider a single branching node $\alpha \in \mathcal{B}$ and label the set of segments radiating from it by $\mathcal{I}_\alpha$. Let $\mathcal{J}_\alpha$ denote the set of line segments $k \in \mathcal{I}_\alpha$ that radiate from $\alpha \in \mathcal{B}$ in a positive direction (see Fig. 4b). If we denote the total number of segments radiating from any branch node α by the coordination number z, then the number of elements of $\mathcal{J}_\alpha$ is $z - 1$. (In this paper we take the coordination number of every branch point to be the same. However, the analysis could be generalized to the case of a variable coordination number. For the sake of illustration, we take the coordination number of the tree to be $z = 3$ in Fig. 4.) Using these various definitions, we can introduce the idea of a generation. Take α_0 to be the zeroth generation. The first generation then consists of the set of nodes (or corresponding edges) $\Sigma_1 = \{\alpha(k), k \in \mathcal{J}_{\alpha_0}\}$, the second generation is $\Sigma_2 = \{\alpha(l), l \in \mathcal{J}_\alpha, \alpha \in \Sigma_1\}$ etc. Let N denote the generation of the most downstream branch nodes, that is, N is the smallest integer for which Σ_{N+1} only includes terminal nodes.

We can now formulate the particle perspective problem on a tree. Consider a single particle diffusing on the tree Γ and suppose that it switches conformational state according to a continuous-time Markov jump process $n(t) \in \{0, 1\}$ with fixed transition rates μ and ν

$$0 \underset{\mu}{\overset{\nu}{\rightleftharpoons}} 1.$$

The particle can diffuse freely through the branch nodes $\alpha \in \mathcal{B}$ when $n(t) = 0$, but cannot pass through any of them when $n(t) = 1$. We also assume that the particle can be absorbed at one of the terminal nodes $\alpha \in \mathcal{O}$ only when $n(t) = 0$, otherwise it is reflected. We will consider different boundary conditions for the primary node.

4.1. Splitting probability to escape through a specific terminal node

First, suppose that the primary node also acts as a switching boundary, that is, the particle can be absorbed at $\overline{\alpha}_0$ if $n(t) = 0$, otherwise it is reflected. Let $X_t \in \Gamma$ denote the position of the particle on Γ and define the stopping time

$$\mathcal{T} = \inf\big\{t \geq 0 : \{X_t \in \mathcal{O} \cup \{\overline{\alpha}_0\}\} \cap \{n(t) = 0\}\big\}.$$

Assume $\mathbb{P}(n(0) = 0) = \rho_0$. For $n \in \{0, 1\}$ and $\gamma \in \mathcal{O}$, let

$$\pi_n^\gamma(x) = \mathbb{P}(X_\mathcal{T} = \gamma \,|\, X_0 = x \cap n(0) = n).$$

Generalizing the 1D case [9, 11], one can show that π_n^γ satisfies

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} \pi_0^\gamma \\ \pi_1^\gamma \end{pmatrix} + \begin{pmatrix} -\nu & \nu \\ \mu & -\mu \end{pmatrix} \begin{pmatrix} \pi_0^\gamma \\ \pi_1^\gamma \end{pmatrix}, \tag{4.2}$$

with exterior boundary conditions

$$\pi_0^\gamma(\alpha) = \delta_{\alpha,\gamma}, \quad \partial_x \pi_1^\gamma(\alpha) = 0, \quad \alpha \in \mathcal{O} \cup \{\overline{\alpha}_0\}, \tag{4.3a}$$

and interior boundary conditions at the branch points $\alpha(k) \in \mathcal{B}$. In particular, π_0^γ satisfies the continuity conditions

$$\pi_0^\gamma(x_k(L)) = \pi_0^\gamma(x_j(0)), \quad j \in \mathcal{J}_\alpha, \tag{4.3b}$$

and the flux conservation condition

$$\partial_x \pi_0^\gamma(x_k(L)) + \sum_{j\in\mathcal{J}_\alpha} \partial_x \pi_0^\gamma(x_j(0)) = 0. \tag{4.3c}$$

Note that for the upstream segment k the flux flows into the branch node, whereas for the remaining $z-1$ downstream segments $j \in \mathcal{J}_\alpha$ the flux flows out of the branch node. On the other hand, π_1^γ satisfies the reflecting boundary conditions

$$\partial_x \pi_1^\gamma(x_k(L)) = \partial_x \pi_1^\gamma(x_j(0)) = 0, \quad j \in \mathcal{J}_\alpha \tag{4.3d}$$

A simple rescaling shows that

$$p_n^\gamma(x) := \rho_n \pi_n^\gamma(x) = \mathbb{P}(X_{\mathcal{T}} = \gamma \cap n(0) = n \,|\, X_0 = x) \tag{4.4}$$

satisfies the ODEs

$$\begin{pmatrix} 0 \\ 0 \end{pmatrix} = \Delta \begin{pmatrix} p_0^\gamma \\ p_1^\gamma \end{pmatrix} + \begin{pmatrix} -\nu & \mu \\ \nu & -\mu \end{pmatrix} \begin{pmatrix} p_0^\gamma \\ p_1^\gamma \end{pmatrix}, \tag{4.5}$$

with exterior boundary conditions

$$p_0^\gamma(\alpha) = \rho_0 \delta_{\alpha,\gamma}, \quad \partial_x p_1^\gamma(\alpha) = 0, \quad \alpha \in \mathcal{O} \cup \{\overline{\alpha}_0\}, \tag{4.6}$$

and the same interior boundary conditions as π_n^γ. By the definition of p_n^γ, we have that

$$p^\gamma(x) := p_0^\gamma(x) + p_1^\gamma(x) = \mathbb{P}(X_{\mathcal{T}} = \gamma \,|\, X_0 = x).$$

As in (3.7), if $x = x_k(s)$, $s \in (0, L)$, then by the strong Markov property

$$p^\gamma(x) = \frac{1}{\rho_0}\Big(q(s) p_0^\gamma(x_k(0)) + (1 - q(s)) p_0^\gamma(x_k(L))\Big), \tag{4.7}$$

where

$$q(s) = \mathbb{P}(X_{\tau_k} = x_k(0) \,|\, X_0 = x_k(s)),$$

is given in (2.7) since all the edges have length L, and τ_k is the stopping time

$$\tau_k = \inf\big\{t \ge 0 : \{X_t \in \{x_k(0), x_k(L)\}\} \cap \{n(t) = 0\}\big\}.$$

Introduce the set of constants evaluated at the nodes

$$\Phi_{\gamma\alpha(k)} \equiv p_0^\gamma(x_k(L)) = p_0^\gamma(x_j(0)), \quad j \in \mathcal{J}_\alpha. \tag{4.8}$$

As in (3.9), we have that each of these constants is the average of its neighbors

$$\Phi_{\gamma\alpha(k)} = \frac{1}{z}\left(\Phi_{\gamma\overline{\alpha}(k)} + \sum_{j\in\mathcal{J}_\alpha} \Phi_{\gamma\alpha(j)}\right), \quad k \in \bigcup_{j=0}^{N} \Sigma_j. \tag{4.9}$$

Rearranging this equation, we see that the constants satisfy a discretized Laplace's equation on the tree

$$\Phi_{\gamma\overline{\alpha}(k)} - z\Phi_{\gamma\alpha(k)} + \sum_{j\in\mathcal{J}_\alpha} \Phi_{\gamma\alpha(j)} = 0, \quad k \in \bigcup_{j=0}^{N} \Sigma_j \tag{4.10}$$

with boundary conditions determined by equation (4.6):

$$\Phi_{\gamma\overline{\alpha}_0} = 0, \quad \Phi_{\gamma\alpha(j)} = \rho_0 \delta_{\alpha(j),\gamma}, \quad j \in \Sigma_{N+1}. \tag{4.11}$$

Our strategy for solving this set of iterative equations will be to start at the final generation Σ_N of branch nodes and work inward to the primary node solving recursively. (An analogous iterative scheme was previously used to determine the

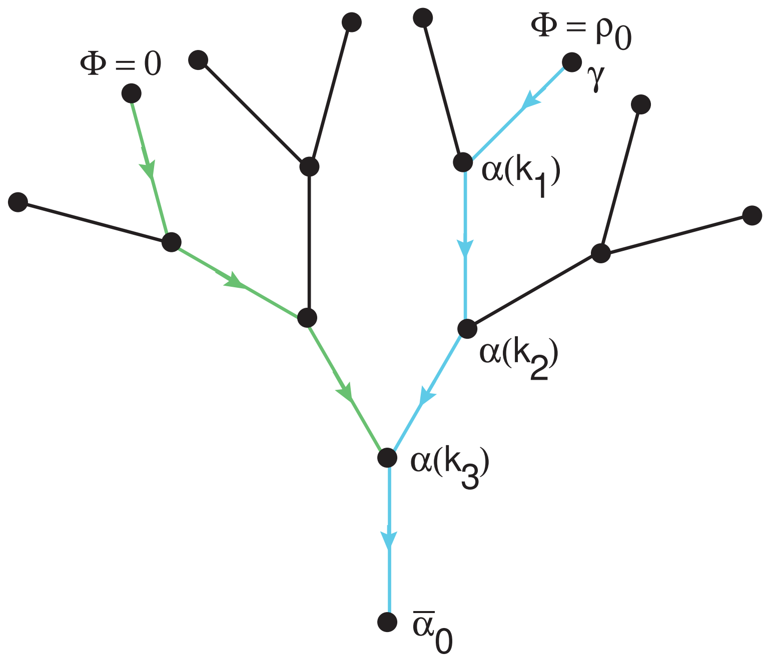

Figure 5: Direct path $\mathcal{A}_\gamma$ from terminal node γ to the primary node $\overline{\alpha}_0$ (indicated by blue). Here γ is the labelled node where the particle is absorbed. There are three generations of branch nodes ($N = 2$). Also shown is a path (indicated by green) from another terminal node that joins $\mathcal{A}_\gamma$ at $\alpha(k_3)$, which means that $r = 3$.

Green's function of the advection-diffusion equation on a tree [1].) Let $\{k_m,\ m = 1, 2, \cdots, N+1\}$ be a sequence of segments starting at a node $\alpha(k_1) \in \Sigma_N$ and proceeding along a direct path toward the primary node with $\alpha(k_{N+1}) = \alpha_0$. For ease of notation, set $\Phi_j = \Phi_{\gamma\alpha(k_j)}$ and $\overline{\Phi}_j = \Phi_{\gamma\overline{\alpha}(k_j)}$.

First consider the case that $\gamma \in \mathcal{J}_{\alpha(k_1)}$ and denote the corresponding path to the primary node by $\mathcal{A}_\gamma$, see Fig. 5. Starting at the outer branch node $\alpha(k_1)$ we have

$$\Phi_1 = \frac{1}{z}\left(\rho_0 + \Phi_2\right),$$

which we can rewrite as

$$\Phi_1 = \frac{\rho_0}{H_1(z)} + \frac{\overline{\Phi}_1}{H_1(z)}, \quad H_1(z) = z. \tag{4.12}$$

The next iteration is

$$\Phi_2 = \frac{1}{z}\left(\Phi_1 + (z-2)\widehat{\Phi}_1 + \Phi_3\right),$$

where $\widehat{\Phi}_1$ is evaluated on any branch node $\alpha \in \Sigma_N$ such that $\alpha \neq \alpha(k_1)$. It follows that $\widehat{\Phi}_1 = \Phi_2/z$ so that

$$\Phi_2 = \frac{1}{z}\left(\frac{1}{z}\left(\rho_0 + \Phi_2\right) + \frac{z-2}{z}\Phi_2 + \Phi_3\right),$$

which on rearranging gives

$$\Phi_2 = \frac{\rho_0}{H_1(z)H_2(z)} + \frac{\overline{\Phi}_2}{H_2(z)}, \quad H_2(z) = H_1(z) - \frac{z-1}{H_1(z)}.$$

We can thus establish the general recurrence relation

$$\Phi_m = \frac{\rho_0}{G_m(z)} + \frac{\overline{\Phi}_m}{H_m(z)}, \tag{4.13}$$

with the functions $H_m(z)$ defined recursively:

$$H_m(z) = z - \frac{z-1}{H_{m-1}(z)}, \quad m = 2, \ldots, N+1, \tag{4.14}$$

and

$$G_m(z) = \prod_{j=1}^{m} H_j(z). \tag{4.15}$$

Note that iterating equation (4.14) leads to a finite continued fraction. For example, in the case of three generations ($N = 3$), we have

$$H_{\alpha_0}(z) = z - \cfrac{z-1}{z - \cfrac{z-1}{z - \cfrac{z-1}{z}}}. \tag{4.16}$$

One way to derive the general recurrence relation (4.13) is to use proof by induction. That is, suppose equation (4.13) holds for $m = n-1 > 2$. Use the fact that

$$\Phi_n = \frac{1}{z}\left(\Phi_{n-1} + (z-2)\widehat{\Phi}_{n-1} + \Phi_{n+1}\right),$$

with the path from Σ_{N+1} to $\widehat{\Phi}_{n-1}$ not intersecting $\mathcal{A}_\gamma$. It follows that $\widehat{\Phi}_{n-1}$ satisfies equation (4.13) with $\rho_0 = 0$. Hence,

$$z\Phi_n = \frac{\rho_0}{G_{n-1}(z)} + \frac{\Phi_n}{H_{n-1}(z)} + (z-2)\frac{\Phi_n}{H_{n-1}(z)} + \Phi_{n+1},$$

Rearranging this equation yields equation (4.13) for $m = n$. It is also straightforward to write down the modified recurrence relation starting from a terminal node for which $\Phi = 0$. Suppose $\gamma \notin \mathcal{J}_{\alpha(k_1)}$ such that $k_m \notin \mathcal{A}_\gamma$ for $0 < m < r$ and $k_m \in \mathcal{A}_\gamma$ for $r \leq m \leq N+1$ with $1 < r \leq N+1$. (If $r = 1$ then we recover the path $\mathcal{A}_\gamma$.) It follows that

$$\Phi_m = \frac{\overline{\Phi}_m}{H_m(z)} \quad (0 < m < r), \quad \Phi_m = \frac{\rho_0}{G_m(z)} + \frac{\overline{\Phi}_m}{H_m(z)} \quad (r \leq m \leq N+1). \tag{4.17}$$

Given the recursive equations for Φ_m we can now start from the primary node $\overline{\alpha}_0$ with $\overline{\Phi}_{N+1} \equiv \Phi_{\gamma\overline{\alpha}_0} = 0$, and iterate forwards along the tree using $\overline{\Phi}_{m-1} = \Phi_m$. Thus

$$\begin{aligned}
\Phi_{N+1} &= \frac{\rho_0}{G_{N+1}(z)}. \\
\Phi_m &= \frac{\rho_0}{G_m(z)} + \frac{\Phi_{m+1}}{H_m(z)}, \quad (r \leq m \leq N) \\
\Phi_m &= \frac{\Phi_{m+1}}{H_m(z)}, \quad (0 < m < r)
\end{aligned}$$

If $r = 1$, then we have

$$\Phi_m = \rho_0 \left[\frac{1}{G_m(z)} + \frac{1}{G_{m+1}(z) H_m(z)} + \frac{1}{G_{m+2}(z) H_m(z) H_{m+1}(z)} + \dots \right. \\ \left. + \frac{1}{G_{N+1}(z) H_m(z) H_{m+1}(z) \cdots H_N(z)} \right]. \tag{4.18}$$

for all $1 \leq m \leq N$. Similarly, if $r > 1$ then Φ_m satisfies equation (4.18) for $r \leq m \leq N$ and

$$\Phi_m = \frac{\Phi_r}{H_{r-1}(z) \cdots H_m(z)}. \tag{4.19}$$

for $0 < m < r$. Finally, we can substitute our solution into equation (4.7) expressed in the form

$$p^\gamma(x) = \frac{1}{\rho_0} \Big(q(s) \Phi_{k-1} + (1 - q(s)) \Phi_k \Big), \; x = x_k(s), \; s \in (0, L). \tag{4.20}$$

4.2. MFPT to escape through a terminal node

We now seek the MFPT of the particle to be absorbed at any of the terminal nodes $\alpha \in \mathcal{O}$, assuming the primary node is always closed. Define

$$w_n(x) = \mathbb{E}[\mathcal{T} 1_{\{n(0)=n\}} \,|\, X_0 = x]. \tag{4.21}$$

One can show (see [9, 11]) that w_n satisfies

$$- \left(\begin{array}{c} \rho_0 \\ \rho_1 \end{array} \right) = \Delta \left(\begin{array}{c} w_0 \\ w_1 \end{array} \right) + \left(\begin{array}{cc} -\nu & \mu \\ \nu & -\mu \end{array} \right) \left(\begin{array}{c} w_0 \\ w_1 \end{array} \right), \tag{4.22}$$

with exterior boundary conditions

$$\begin{aligned} w_0(\alpha) \quad &= \partial_x w_1(\alpha) = 0, \quad \alpha \in \mathcal{O}, \\ \partial_x w_0(\alpha) &= \partial_x w_1(\alpha) = 0, \quad \alpha = \overline{\alpha}_0, \end{aligned}$$

and the same interior boundary conditions (4.3*b*)–(4.3*d*) as π_n. By the definition of w_n, we have that

$$w(x) := w_0(x) + w_1(x) = \mathbb{E}[\mathcal{T} \,|\, X_0 = x]. \tag{4.23}$$

Suppose that the particle starts on a segment k (not the primary segment). As in (3.15), if $x = x_k(s)$, $s \in (0, L)$, then by the strong Markov property

$$w(x) = v(s) + \frac{1}{\rho_0} \Big(q(s) w_0(x_k(0)) + (1 - q(s)) w_0(x_k(L)) \Big), \tag{4.24}$$

where the exit time $v(s)$ is given in (2.13) and the splitting probability $q(s)$ is given in (2.7). On the other hand, if the particle starts on the primary segment, then it can only exit via the branch point α_0 so that

$$w(x) = u(s) + \frac{w_0(\alpha_0)}{\rho_0}, \tag{4.25}$$

where $u(s)$ is given in (2.15). Introducing the following set of constants evaluated at the nodes

$$\Psi_{\alpha(k)} \equiv w_0(x_k(L)) = w_0(x_j(0)), \quad j \in \mathcal{J}_\alpha, \tag{4.26}$$

we see that, as in equation (3.16),

$$\Psi_{\alpha(k)} = V + \frac{1}{z} \left(\Psi_{\overline{\alpha}(k)} + \sum_{j \in \mathcal{J}_\alpha} \Psi_{\alpha(j)} \right), \quad k \in \bigcup_{j=0}^{N} \Sigma_j,$$

with $V = v_0^{(2)}(L)$ given by equation (2.14). Rearranging this equation, shows that the constants satisfy a discretized Poisson equation on the tree

$$\Psi_{\overline{\alpha}(k)} - z\Psi_{\alpha(k)} + \sum_{j\in\mathcal{J}_\alpha} \Psi_{\alpha(j)} = -zV, \quad k \in \bigcup_{j=0}^{N} \Sigma_j \tag{4.27}$$

with boundary conditions

$$\Psi_\alpha = 0, \quad \alpha \in \mathcal{O}. \tag{4.28}$$

From equation (4.25),

$$\Psi_{\overline{\alpha}_0} = u_0(0) + \Psi_{\alpha_0}. \tag{4.29}$$

We can solve the discrete equation (4.27) using a similar recursive method to the analysis of equation (4.10). Since $\Psi_\alpha = 0$ for all $\alpha \in \mathcal{O}$, it follows from symmetry that $\Psi_{\alpha(k)}$ only depends on the generation of the segment k. Thus, let $\{k_m,\ m = 1, 2, \cdots, N+1\}$ be any sequence of segments starting at a node $\alpha(k_1) \in \Sigma_N$ and proceeding along a direct path toward the primary node with $\alpha(k_{N+1}) = \alpha_0$. For ease of notation, set $\Psi_j = \Psi_{\alpha(k_j)}$ and $\overline{\Psi}_j = \Psi_{\overline{\alpha}(k_j)}$. Starting from any terminal node in Σ_{N+1}, we see that

$$\Psi_1 = V + \frac{\Psi_2}{z},$$

which we can rewrite as

$$\Psi_1 = V + \frac{\overline{\Psi}_1}{H_1(z)}, \quad H_1(z) = z. \tag{4.30}$$

Then, as we continue inwards we find that

$$\Psi_m = \frac{V}{F_m(z)} + \frac{\overline{\Psi}_m}{H_m(z)}, \tag{4.31}$$

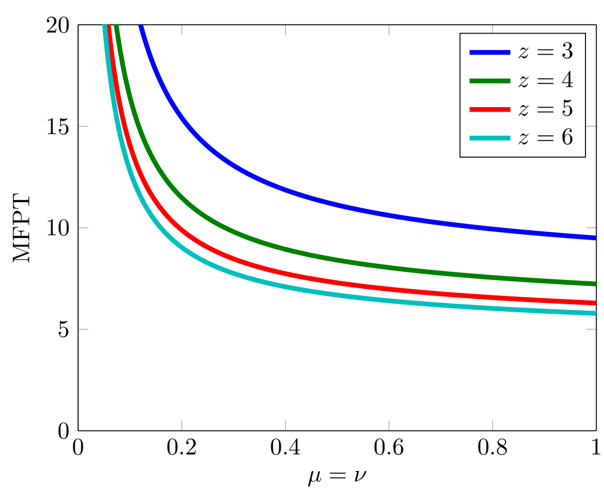

Figure 6: Fast switching and increased coordination number z both decrease MFPT to terminal nodes. We plot the MFPT $w(\overline{\alpha}_0)$ against the switching rate $\mu = \nu$. Increasing the switching rate decreases the MFPT. Increasing the coordination number z decreases the MFPT since more branching tends to push the particle towards the terminal nodes. In all plots, $N = 2$ and $L = 1$.

with

$$\frac{1}{F_m(z)} = z\left(\frac{1}{H_m(z)} + \frac{z-1}{H_m(z)H_{m-1}(z)} + \frac{(z-1)^2}{H_m(z)H_{m-1}(z)H_{m-2}(z)} + \dots \right.$$
$$\left. + \frac{(z-1)^{m-1}}{H_m(z)H_{m-1}(z)\cdots H_1(z)}\right). \tag{4.32}$$

We now move forward through the tree starting from the primary branch node α_0 using $\overline{\Psi}_m = \Psi_{m+1}$:

$$\Psi_m = V\left[\frac{1}{F_m(z)} + \frac{1}{F_{m+1}(z)H_m(z)} + \frac{1}{F_{m+2}(z)H_m(z)H_{m+1}(z)} + \dots \right.$$
$$\left. + \frac{\Psi_{N+1}}{H_m(z)H_{m+1}(z)\cdots H_N(z)}\right]. \tag{4.33}$$

for all $1 \leq m \leq N$. We can determine Ψ_{N+1} by substituting $\overline{\Psi}_{N+1} = u_0(0) + \Psi_{N+1}$ into equation (4.31) for $m = N+1$, that is,

$$\Psi_{N+1} = \frac{V}{F_{N+1}(z)} + \frac{u_0(0) + \Psi_{N+1}}{H_{N+1}(z)},$$

which can be rearranged to give

$$\Psi_{N+1} = \frac{1}{H_{N+1}(z)-1}\left(\frac{H_{N+1}(z)V}{F_{N+1}(z)} + u_0(0)\right). \tag{4.34}$$

Finally, we substitute into equation (4.24), rewritten as

$$w(x) = v(s) + \frac{1}{\rho_0}\Big(q(s)\Psi_{k-1} + (1-q(s))\Psi_k\Big) \tag{4.35}$$

for $x = x_k(s)$, $s \in (0, L)$. If x is on the primary segment, then

$$w(x) = u(s) + \frac{\Psi_{N+1}}{\rho_0}. \tag{4.36}$$

In Fig. 6, we plot the MFPT $w(\overline{\alpha}_0)$ as a function of the switching rate for different values of the coordination number, z. It can be seen that increasing z decreases the MFPT. This is because, as the analysis above shows, the symmetry in the problem reduces it to a one-dimensional random walk on the generation number with probability of hopping to a larger generation equal to $(z-1)/z$ and probability of hopping to a smaller generation equal to z^{-1}. Thus, increasing z tends to push the particle towards terminal nodes. This is consistent with the well-known result that for a discrete-time symmetric random walk on a tree, the distance from the primary node is described by a random walk with a computable drift away from the primary node for any coordination number $z > 2$.

5. Flux through a tree with stochastically-gated nodes

Driven by the biological applications described in the Introduction, we now take the gate perspective and keep track of the concentration of particles diffusing in a tree Γ with permanently open branch nodes and randomly switching primary or terminal nodes. We begin in section 5.1 by calculating the flux without any switching nodes, and quickly find the flux in the case that either the primary node or terminal nodes switch between being a source (inhomogeneous Dirichlet condition) and a sink (homogeneous Dirichlet condition). In section 5.2, we suppose that the primary node is an intermittent source (switches between an inhomogeneous Dirichlet condition and a no flux Neumann condition) and calculate the flux through the terminal nodes. In section 5.3, we consider the reverse situation in which the terminal nodes are intermittent sources and find the flux through the primary node.

5.1. Non-switching case and intermittent sink/source

We first analyze the case without any switching nodes. Let $\eta > 0$ and consider the concentration $\pi^\eta(x,t)$ of particles diffusing in a tree Γ satisfying

$$\frac{\partial \pi^\eta}{\partial t} = \Delta \pi^\eta, \quad x \in \Gamma, t > 0, \tag{5.1}$$

with exterior boundary conditions

$$\pi^\eta(\alpha, t) = \eta > 0, \quad \forall\, \alpha \in \mathcal{O}, \tag{5.2}$$

$$\pi^\eta(\overline{\alpha}_0, t) = 0, \tag{5.3}$$

and interior boundary conditions

$$\pi^\eta(x_k(L)) = \pi^\eta(x_j(0)), \quad j \in \mathcal{J}_\alpha, \tag{5.4}$$

$$\partial_x \pi^\eta(x_k(L)) + \sum_{j \in \mathcal{J}_\alpha} \partial_x \pi^\eta(x_j(0)) = 0. \tag{5.5}$$

Defining the steady-state solution $\pi^\eta(x) \equiv \lim_{t\to\infty} \pi^\eta(x,t)$ and introducing the constants $\Theta_{\alpha(k)} = \pi^\eta(\alpha(k))$, we solve the steady-state diffusion equation on each segment k according to

$$\pi^\eta(x_k(s)) = \frac{s}{L}[\Theta_{\alpha(k)} - \Theta_{\overline{\alpha}(k)}] + \Theta_{\overline{\alpha}(k)}. \tag{5.6}$$

We can solve for $\Theta_{\alpha(k)}$ recursively by imposing current conservation at each branching node, that is,

$$\Theta_{\overline{\alpha}(k)} - \Theta_{\alpha(k)} - \sum_{j \in \mathcal{J}_{\alpha(k)}} [\Theta_{\overline{\alpha}(j)} - \Theta_{\alpha(j)}] = 0. \tag{5.7}$$

The exit flux through the primary node per each terminal node source can then be determined according to

$$\widehat{J} = \frac{\partial_x \pi^\eta(x)|_{x=\overline{\alpha}_0}}{L(z-1)^{N+1}} = \frac{\Theta_{\alpha_0}}{L(z-1)^{N+1}},$$

where $(z-1)^{N+1}$ is the number of terminal nodes.

Since all terminal nodes satisfy the same boundary condition, it follows from symmetry that $\Theta_{\alpha(k)}$ only depends on the generation of the segment k. Thus, let $\{k_m,\ m = 1, 2, \cdots, N+1\}$ be any sequence of segments starting at a node $\alpha(k_1) \in \Sigma_N$ and proceeding along a direct path toward the primary node with $\alpha(k_{N+1}) = \alpha_0$. For ease of notation, set $\Theta_j = \Theta_{\alpha(k_j)}$ and $\overline{\Theta}_j = \Theta_{j+1} = \Theta_{\overline{\alpha}(k_j)}$. Starting from any terminal node in Σ_{N+1}, current conservation implies that

$$\Theta_2 - \Theta_1 = (z-1)(\Theta_1 - \eta),$$

which we can rewrite as

$$\Theta_1 = \frac{\Theta_2 + (z-1)\eta}{z}. \tag{5.8}$$

Then, as we continue inwards we find that

$$\Theta_m = \frac{\overline{\Theta}_m}{H_m(z)} + \frac{(z-1)^m \eta}{G_m(z)} \tag{5.9}$$

with H_m and G_m defined according to equations (4.14) and (4.15). The final step is to move forward through the tree starting from the primary branch node α_0 using the boundary condition $\overline{\theta}_{N+1} = 0$. We thus find that the flux through the primary node per each terminal node source is

$$\widehat{J} = \frac{1}{L} \frac{\eta}{G_{N+1}(z)}. \tag{5.10}$$

Finally, setting $\eta = 1$ and $\widetilde{\pi} = 1 - \pi^1$, it follows that

$$J = -(z-1)^{N+1} \partial_x \widetilde{\pi}(\alpha), \quad \alpha \in \mathcal{O}, \tag{5.11}$$

is the steady-state exit flux through the $(z-1)^{N+1}$ open terminal nodes given that the boundary condition at the primary node is $\widetilde{\pi}(\overline{\alpha}_0, t) = 1$.

Now suppose that the boundary conditions at the terminal nodes switch between a homogeneous and inhomogeneous Dirichlet conditions. That is, suppose $u(x,t)$ satisfies the PDE (5.1) with interior boundary conditions (5.4) and (5.5), boundary condition at the primary node (5.3) and randomly switching boundary conditions at terminal nodes

$$u(\alpha, t) = 1 \quad \text{and} \quad u(\alpha, t) = 0, \quad \forall \alpha \in \mathcal{O},$$

depending on whether $n(t) = 0$ or 1, respectively, where $n(t)$ is as in (2.1). Following [9], we introduce the first moment of the solution to the stochastic PDE according to

$$V_n(x,t) = \mathbb{E}[u(x,t) 1_{n(t)=n}]. \tag{5.12}$$

such that

$$\frac{\partial V_0}{\partial t} = \Delta V_0 - \nu V_0 + \mu V_1 \tag{5.13a}$$

$$\frac{\partial V_1}{\partial t} = \Delta V_1 + \nu V_0 - \mu V_1 \tag{5.13b}$$

with exterior boundary conditions

$$V_0(\overline{\alpha}_0, t) = V_1(\overline{\alpha}_0, t) = 0, \quad V_0(\alpha, t) = \rho_0, \quad V_1(\alpha, t) = 0, \, \forall \, \alpha \in \mathcal{O} \tag{5.14}$$

and the same interior boundary conditions as u.

We would like to calculate the steady-state solution of equations (5.13a) and (5.13b). First, note that

$$\mathbb{E}[u(x,t)] = V_0(x,t) + V_1(x,t). \tag{5.15}$$

Since there exists a globally attracting steady-state, it follows that

$$\lim_{t \to \infty} \mathbb{E}[u(x,t)] = V(x) \equiv \sum_{n=0,1} V_n(x), \tag{5.16}$$

where $V_n(x) \equiv \lim_{t \to \infty} V_n(x,t)$. Adding equations (5.13$a$) and (5.13$b$) then gives

$$\Delta V(x) = 0, \quad x \in \Gamma \tag{5.17}$$

with exterior boundary conditions

$$V(\overline{\alpha}_0) = 0, \quad V(\alpha) = \rho_0, \, \forall \, \alpha \in \mathcal{O}. \tag{5.18}$$

Thus, replacing η by ρ_0 we see that $V(x)$ is given by $\pi^{\rho_0}(x)$. In particular, replacing η by ρ_0 in (5.10) shows that switching between homogeneous and inhomogeneous Dirichlet conditions at the terminal nodes reduces the flux to the primary node by the proportion of time the condition is inhomogeneous. It is straightforward to check that this same relation holds for the flux to the terminal nodes if we switch between homogeneous and inhomogeneous Dirichlet conditions at the primary node. We will see below in sections 5.2 and 5.3 that this simple relation no longer holds if we switch between Dirichlet and Neumann conditions.

All of the above has a direct probabilistic interpretation from the particle perspective. Let X_t denote the position of a particle diffusing on Γ that can freely pass through all branch nodes and can be absorbed at any terminal node. Define the absorption time

$$\tau = \inf\big\{t \geq 0 : X_t \in \mathcal{O} \cup \{\overline{\alpha}_0\}\big\}.$$

If $\eta = 1$, then the resulting BVP for $\pi^1(x)$ implies that $\pi^1(x)$ is the splitting probability

$$\pi^1(x) = \mathbb{P}_x(X_\tau \in \mathcal{O}). \tag{5.19}$$

And of course

$$\widetilde{\pi}(x) := 1 - \pi^1(x) = \mathbb{P}_x(X_\tau = \overline{\alpha}_0) \tag{5.20}$$

satisfies the same BVP as $\pi^1(x)$, but with the inhomogeneous condition at the primary node. The case of switching inhomogeneous/homogeneous Dirichlet conditions at the primary node is thus immediate. Further, the conservation equation (5.7) follows from the same probabilistic argument that yielded (4.9). Finally, letting $n(t)$ be as in (2.1) we see that

$$\begin{aligned} V(x) &= \mathbb{P}_x(X_\tau \in \mathcal{O} \cap n(\tau) = 0) = \mathbb{P}_x(X_\tau \in \mathcal{O})\mathbb{P}_x(n(\tau) = 0) \\ &= \rho_0 \pi^1(x) = \pi^{\rho_0}(x), \end{aligned}$$

by independence. On the other hand (see below), if terminal nodes switch between absorbing and reflecting boundary conditions, then X_t and $n(t)$ are no longer independent and the analysis is much more delicate.

5.2. Flux through a tree with a stochastically-gated primary node

In our next example, we assume that the primary node is an intermittent source (switches between an inhomogeneous Dirichlet condition and a no flux Neumann condition) and calculate the flux through the open terminal nodes. The particle concentration $u(x,t)$ satisfies the diffusion equation (5.1), interior boundary conditions (5.4)-(5.5), boundary conditions at the terminal nodes

$$u(\alpha, t) = 0 \quad \forall\, \alpha \in \mathcal{O},$$

and a boundary condition at the primary node that randomly switches between

$$u(\overline{\alpha}_0, t) = 1 \quad \text{and} \quad \partial_x u(\overline{\alpha}_0, t) = 0,$$

depending on whether $n(t) = 0$ or 1, respectively, where $n(t)$ is as in (2.1). As in the previous example, section 5.1, $V_n(x,t)$ is defined according to equation (5.12), which satisfies (5.13*a*)-(5.13*b*) with modified exterior boundary conditions

$$V_0(\overline{\alpha}_0, t) = \rho_0,\ \partial_x V_1(\overline{\alpha}_0, t) = 0, \quad V_0(\alpha, t) = V_1(\alpha, t) = 0,\ \forall\, \alpha \in \mathcal{O} \tag{5.21}$$

and interior boundary conditions (5.4)-(5.5). Finding the expected value of u at large time amounts to finding $V_n(x) := \lim_{t\to\infty} V_n(x,t)$.

We will use the probabilistic arguments of previous sections to find $V_n(x)$. Consider a single particle diffusing on Γ that can always diffuse freely through branch nodes and be absorbed at terminal nodes. Assume that the particle can be absorbed at the primary node only when $n(t) = 0$, otherwise it is reflected. Let $X_t \in \Gamma$ denote the position of the particle at time t and define the absorption time

$$\mathcal{T} = \inf\Big\{t \geq 0 : \{X_t \in \mathcal{O}\} \cup \big\{\{X_t = \overline{\alpha}_0\} \cap \{n(t) = 0\}\big\}\Big\},$$

so that $V_n(x)$ has the probabilistic interpretation

$$V_n(x) = p_n(x) := \mathbb{P}(\{X_{\mathcal{T}} = \overline{\alpha}_0\} \cap \{n(0) = n\} \,|\, X_0 = x).$$

By the strong Markov property, or from the BVP satisfied by $V(x)$, it follows that

$$p(x) := p_0(x) + p_1(x) = \widetilde{\pi}(x)\big(\rho_0 + p_1(\overline{\alpha}_0)\big),$$

for $x \in \Gamma$, where $\widetilde{\pi}(x)$ is the splitting probability computed above in (5.20). From the equivalent deterministic interpretation of $\widetilde{\pi}(x)$ in section 5.1, the expected flux to the terminal nodes with an intermittent source at the primary node is thus reduced by the factor

$$\kappa = \rho_0 + p_1(\overline{\alpha}_0), \tag{5.22}$$

compared to the case where the concentration at the primary node is always unity. That is, the expected flux is

$$F := \kappa J, \quad \alpha \in \mathcal{O}, \tag{5.23}$$

where J is the flux with a constant source given in (5.11).

It thus remains to find $p_1(\overline{\alpha}_0)$. We will proceed by solving for p_0 and p_1 evaluated at all the nodes. First, from continuity, we introduce a constant vector for each segment k of the form

$$\chi_{\alpha(k)} := \begin{pmatrix} p_0(x_k(L)) \\ p_1(x_k(L)) \end{pmatrix} = \begin{pmatrix} p_0(x_j(0)) \\ p_1(x_j(0)) \end{pmatrix}, \quad j \in \mathcal{J}_{\alpha(k)}. \tag{5.24}$$

By symmetry, $\chi_{\alpha(k)}$ only depends on the generation of the segment k, so let $\{k_m : m = 0, 1, \ldots, N+1\}$ be any sequence of segments starting at a node $\alpha(k_0) \in \Sigma_{N+1}$ and proceeding along a direct path toward the primary node with $\alpha(k_{N+1}) = \alpha_0$. For ease, let $\chi_j = \chi_{\alpha(k_j)}$ and $\overline{\chi}_j = \chi_{\overline{\alpha}(k_j)}$ and denote the components of χ_j by (χ_j^0, χ_j^1).

Let $\mathbb{P}_{x,n}$ denote the probability measure conditioned on $X_0 = x \in \Gamma$ and $n(0) = n \in \{0, 1\}$. Define the stopping time

$$s_m = \inf\big\{t \geq 0 : \{X_t = \alpha(k_{m-1})\} \cup \{X_t = \alpha(k_{m+1})\}\big\}.$$

For $n \in \{0, 1\}$ and $m \in \{1, \ldots, N\}$, the strong Markov property shows that

$$\begin{aligned} \frac{\chi_m^n}{\rho_n} &= \mathbb{P}_{\alpha(k_m),n}(X_{\mathcal{T}} = \overline{\alpha}_0) \\ &= \mathbb{P}_{\alpha(k_{m-1}),0}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m-1}) \cap n(s_m) = 0) \\ &\quad + \mathbb{P}_{\alpha(k_{m-1}),1}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m-1}) \cap n(s_m) = 1) \\ &\quad + \mathbb{P}_{\alpha(k_{m+1}),0}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m+1}) \cap n(s_m) = 0) \\ &\quad + \mathbb{P}_{\alpha(k_{m+1}),1}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m+1}) \cap n(s_m) = 1). \end{aligned} \tag{5.25}$$

By symmetry, we have that for $i \in \{0, 1\}$

$$\begin{aligned} &\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m\pm1}) \cap n(s_m) = 1 - i) \\ &= \mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m\pm1}))\mathbb{P}_{\alpha(k_m),n}(n(s_m) = 1 - i). \end{aligned}$$

Furthermore,

$$\mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m-1})) = \frac{z-1}{z}$$
$$\text{and} \quad \mathbb{P}_{\alpha(k_m),n}(X_{s_m} = \alpha(k_{m+1})) = \frac{1}{z},$$

and

$$\mathbb{P}_{\alpha(k_m),n}(n(s_m) = 1-i) = \frac{a_n^{1-i}}{\rho_n},$$

where a_n^{1-i} is given in (2.10)-(2.12). Rewriting equation (5.25) in matrix notation gives

$$\chi_m = \mathbf{B}\Big(\frac{1}{z}\overline{\chi}_m + \frac{z-1}{z}\chi_{m-1}\Big), \tag{5.26}$$

where $\mathbf{B}$ is the matrix

$$\mathbf{B} = \left(\begin{array}{cc} \dfrac{a_0^0(0)}{\rho_0} & \dfrac{a_0^1(0)}{\rho_1} \\ \\ \dfrac{a_1^0(0)}{\rho_0} & \dfrac{a_1^1(0)}{\rho_1} \end{array}\right).$$

Using the fact that χ_0 is the zero vector, we solve this system iteratively as in previous sections and find that

$$\chi_m = \big(\mathcal{H}_m(z)\big)^{-1}\chi_{m+1}, \tag{5.27}$$

with $\mathcal{H}_1(z) = z\mathbf{B}^{-1}$ and $\mathcal{H}_m(z)$ is defined recursively

$$\mathcal{H}_m(z) = z\mathbf{B}^{-1}\Big[I - \frac{z-1}{z}\mathbf{B}\big(\mathcal{H}_{m-1}(z)\big)^{-1}\Big], \quad m = 2,\ldots,N+1.$$

Note that $\mathcal{H}_m(z)$ reduces to (4.14) in the case that $\mathbf{B}$ is just the scalar 1.

Finally, it can be seen that $\overline{\chi}_{N+1}^0 = \rho_0$ and, by the strong Markov property,

$$\begin{aligned} \frac{\overline{\chi}_{N+1}^1}{\rho_1} &= \mathbb{P}_{\overline{\alpha}_0,1}(X_{\mathcal{T}} = \overline{\alpha}_0) \\ &= \mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \overline{\alpha}_0) + \mathbb{P}_{\alpha_0,0}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \alpha_0 \cap n(s_0) = 0) \\ &\quad + \mathbb{P}_{\alpha_0,1}(X_{\mathcal{T}} = \overline{\alpha}_0)\mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \alpha_0 \cap n(s_0) = 1), \end{aligned} \tag{5.28}$$

where s_0 is the stopping time

$$s_0 = \inf\Big\{t \geq 0 : \big\{\{X_t = \overline{\alpha}_0\} \cap \{n(t) = 0\}\big\} \cup \big\{X_t = \alpha_0\big\}\Big\}.$$

Now,

$$\mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \overline{\alpha}_0) = 1 - \frac{(r_1^0(0) + r_1^1(0))}{\rho_1}$$
$$\mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \overline{\alpha}_0 \cap n(s_0) = 0) = \frac{r_1^0(0)}{\rho_1}$$
$$\mathbb{P}_{\overline{\alpha}_0,1}(X_{s_0} = \overline{\alpha}_0 \cap n(s_0) = 1) = \frac{r_1^1(0)}{\rho_1}.$$

where r_1^i is given in (2.8)-(2.9). Equation (5.28) can be rewritten in matrix notation as

$$\overline{\chi}_{N+1} = c + \mathbf{C}\chi_{N+1}, \tag{5.29}$$

with the vector $c = (\rho_0,\ \rho_1 - r_1^0(0) - r_1^1(0))$ and $\mathbf{C}$ is the matrix

$$\mathbf{C} = \begin{pmatrix} 0 & 0 \\ \\ \dfrac{r_1^0(0)}{\rho_0} & \dfrac{r_1^1(0)}{\rho_1} \end{pmatrix}.$$

Combining equations (5.26), (5.27), and (5.29), we find that

$$\overline{\chi}_{N+1} = \Big[I - \big[\mathbf{C}[I - \frac{z-1}{z}\mathbf{B}(\mathcal{H}_N(z))^{-1}\big]^{-1}\frac{1}{z}\mathbf{B}\Big]^{-1} c. \tag{5.30}$$

The sum of the components of (5.30) give the flux reduction factor κ of equation (5.22). In Figs. 7 and 8, we plot κ and the expected flux through the terminal nodes F of equation (5.23). As expected, Fig. 7 shows that increasing the switching rate $\mu = \nu$ increases both κ and F. However, it is interesting that the tree topology affects κ and F differently: if the coordination number z increases, then κ decreases and $F = \kappa J$ increases. We expect that increasing z increases J as this is analogous to the fact that increasing z decreases the MFPT to a terminal node (see Fig. 6). The fact that increasing z increases F, however, shows that even though more branching decreases κ, the increase in J is great enough so that $F = \kappa J$ increases. The situation is reversed in section 5.3 below.

5.3. Flux through a tree with stochastically-gated terminal nodes

Finally, suppose that the intermittent sources are at the terminal nodes and consider the flux to the primary node. The analysis is analogous to section 5.2 above, so we only sketch it briefly. The particle concentration $u(x,t)$ satisfies the diffusion equation (5.1), interior boundary conditions (5.4)-(5.5), boundary conditions at the primary node

$$u(\overline{\alpha}_0, t) = 0,$$

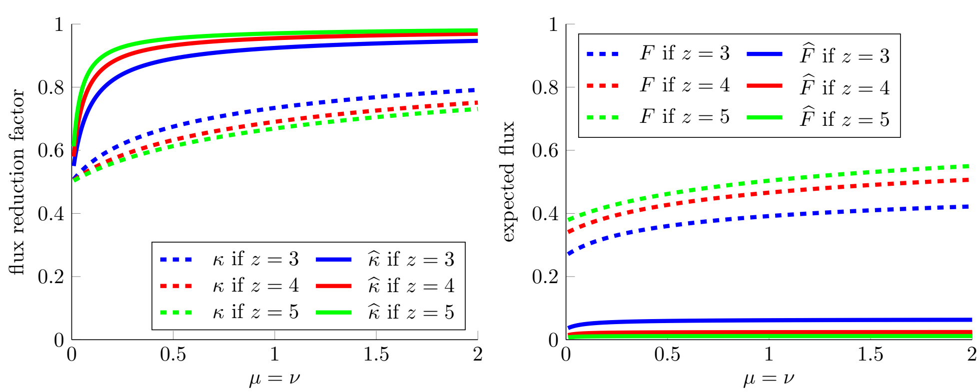

Figure 7: The effect of tree topology on the flux reduction factor and the expected flux for different placements of the intermittent source. We plot κ of (5.22) and $\widehat{\kappa}$ of (5.31) in the left figure and we plot F of (5.23) and $\widehat{F}$ of (5.32) in the right figure, all as functions of the switching rate $\mu = \nu$. In all cases, increasing the switching rate $\mu = \nu$ increases κ, F, $\widehat{\kappa}$, and $\widehat{F}$ (we note that κ and $\widehat{\kappa}$ both converge to 1 as $\mu = \nu \to \infty$). However, increasing the coordination number z decreases κ and increases F, and increases $\widehat{\kappa}$ and decreases $\widehat{F}$. In all plots, $N = 2$ and $L = 1$.

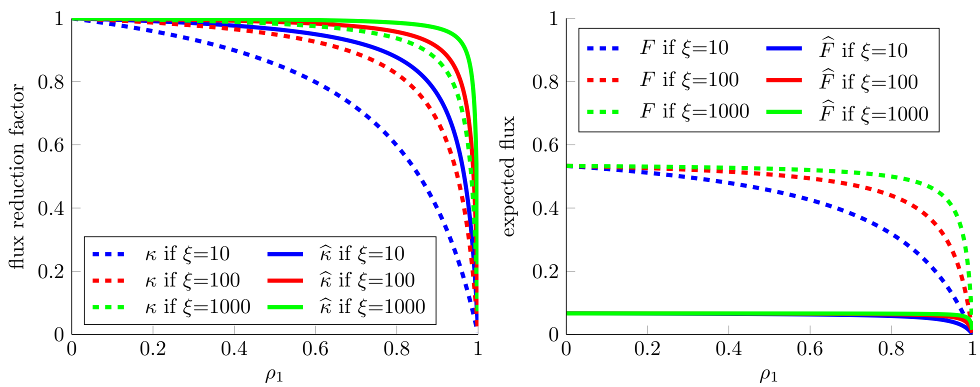

Figure 8: The effect of switching rate parameters, $\rho_1 = \nu/(\mu+\nu)$ and $\xi = \sqrt{\mu+\nu}$, on the flux reduction factor and the expected flux for different placements of the intermittent source. We plot κ of (5.22) and $\widehat{\kappa}$ of (5.31) in the left figure and we plot F of (5.23) and $\widehat{F}$ of (5.32) in the right figure, all as functions of the proportion of time in the closed state, $\rho_1 \in (0,1)$. In all cases, increasing ξ and/or decreasing ρ_1 increases κ, F, $\widehat{\kappa}$, and $\widehat{F}$. We note that κ and $\widehat{\kappa}$ both converge to 1 as $\xi \to \infty$ for any $\rho_1 \in (0,1)$. Thus, the source can be closed almost all of the time, and yet the flux reduction factor can be close to 1 if ξ is taken sufficiently large. In all plots, $N = 2$, $L = 1$, and $z = 3$.

and a boundary condition at the terminal nodes that randomly switches between

$$u(\alpha,t) = 1 \quad \text{and} \quad \partial_x u(\alpha,t) = 0 \quad \forall\, \alpha \in \mathcal{O},$$

depending on whether $n(t) = 0$ or 1, respectively, where $n(t)$ is as in (2.1).

As above, we define $V_n(x,t)$ according to (5.12) and use probabilistic arguments to find $V_n(x) := \lim_{t\to\infty} V_n(x,t)$. Consider a single particle diffusing on Γ that can always diffuse freely through branch nodes and be absorbed at the primary node. Assume that the particle can be absorbed at the terminal nodes only when $n(t) = 0$, otherwise it is reflected. Let $X_t \in \Gamma$ denote the position of the particle at time t and define the absorption time

$$\mathcal{T} = \inf\Big\{t \geq 0 : \{X_t = \overline{\alpha}_0\} \cup \big\{\{X_t \in \mathcal{O}\} \cap \{n(t) = 0\}\big\}\Big\}.$$

so that

$$V_n(x) = p_n(x) := \mathbb{P}(X_{\mathcal{T}} \neq \overline{\alpha}_0 \cap n(0) = n \,|\, X_0 = x).$$

By the strong Markov property, if $x \in \Gamma$, then

$$p(x) := p_0(x) + p_1(x) = \pi^1(x)\big(\rho_0 + p_1(\alpha)\big), \quad \alpha \in \mathcal{O},$$

where $\pi^1(x)$ is the splitting probability computed above in (5.19). From the equivalent deterministic interpretation of $\pi^1(x)$ in section 5.1, the expected flux to the primary node with intermittent sources at the terminal nodes is reduced by the factor

$$\widehat{\kappa} = \rho_0 + p_1(\alpha), \quad \alpha \in \mathcal{O}, \tag{5.31}$$

compared to the case where the concentration at the terminal nodes $\alpha \in \mathcal{O}$ is always unity. That is, the expected flux (per each terminal node source) is

$$\widehat{F} := \widehat{\kappa}\widehat{J}, \tag{5.32}$$

where $\widehat{J}$ is the flux with a constant source given in (5.10).

To find $p_1(\alpha)$ for $\alpha \in \mathcal{O}$, we define $\chi_{\alpha(k)}$ by (5.24) and let $\{k_m : m = 0, 1, \dots, N+1\}$ be any sequence of segments starting at the primary branch node $\alpha(k_0)$ and proceeding along a direct path toward any terminal node $\alpha \in \mathcal{O}$. As above, let $\chi_j = \chi_{\alpha(k_j)}$ and $\overline{\chi}_j = \chi_{\overline{\alpha}(k_j)}$ and denote the components of χ_j by (χ_j^0, χ_j^1). By the same argument as in section 5.2, one finds that $\{\chi_m\}_{m=0}^{N+1}$ satisfy (5.26) with $1/z$ and $(z-1)/z$ swapped. Solving this system, establishes that if $\alpha \in \mathcal{O}$, then $\widehat{\kappa} = \rho_0 + p_1(\alpha)$ is given by the sum of the components of

$$\Big[I - \big[\mathbf{C}[I - \frac{1}{z}\mathbf{B}(\mathcal{J}_N(z))^{-1}\big]^{-1}\frac{z-1}{z}\mathbf{B}\Big]^{-1}c,$$

where $\mathbf{B}$, $\mathbf{C}$, and c are as in section 5.2 and $\mathcal{J}_m(z)$ defined recursively

$$\mathcal{J}_m(z) = \frac{z}{z-1}\mathbf{B}^{-1}\Big[I - \frac{1}{z}\mathbf{B}\big(\mathcal{J}_{m-1}(z)\big)^{-1}\Big], \quad m = 2, \dots, N+1,$$

with $\mathcal{J}_1(z) = \frac{z}{z-1}\mathbf{B}^{-1}$.

In Figs. 7 and 8, we plot the flux reduction factor $\widehat{\kappa}$ of equation (5.31) and the expected flux through the primary node $\widehat{F}$ of equation (5.32). In contrast to section 5.2 above, Fig. 7 shows that if the coordination number z increases, then $\widehat{\kappa}$ increases and $\widehat{F} = \widehat{\kappa}\widehat{J}$ decreases.

6. Discussion

In this paper, we considered diffusion in a tree with stochastically-gated nodes. We found exact expressions for various splitting probabilities and mean first passage times (MFPTs) for a single particle diffusing through a tree. Prompted by applications to respiration, we also considered a concentration of particles diffusing in a tree. Supposing that particles can always pass through interior branch nodes but that they are intermittently supplied at one end of the tree, we calculated the flux at the other end of the tree. Our examples in section 5 extend the insect respiration model in [7] which ignored tracheal branching. The model in [7] sought to explain the rapid opening and closing of respiratory valves (spiracles) in an insect's exoskeleton (see Fig. 9) by showing that rapid opening and closing allows an insect to maintain high oxygen uptake. Our work establishes that this result still holds in the more realistic case of branching trachea. In fact, branching trachea allow the insect to maintain an even higher level of oxygen uptake.

Future work will include comparing these model predictions with experimental data. In order to make a closer comparison with such data, it will be necessary to take account of the fact that the different levels of trachea and tracheoles have ever decreasing diameters, so that our simplifying assumption of a homogeneous tree will need to be modified. That is, we assumed throughout that all branches have the same length L and the same diffusion coefficient D (which we set to unity). Here we briefly sketch how to extend the analysis of section 5 in order to incorporate changes in branch diameter. The first step is to note that the diffusion coefficient D becomes smaller as the branch diameter decreases so that D will depend on the generation, $D \to D_m$, $m = 0, \dots, N$, where N is the number of generations excluding the primary branch. (We still assume that all branches of a given generation are identical.) It follows that the Laplacian in equation (5.1) must be multiplied by D_m for $x = x_k(s)$, $0 < s < L$, and $k \in \Sigma_m$ (branch k belongs to the m-th generation). The only modification in the

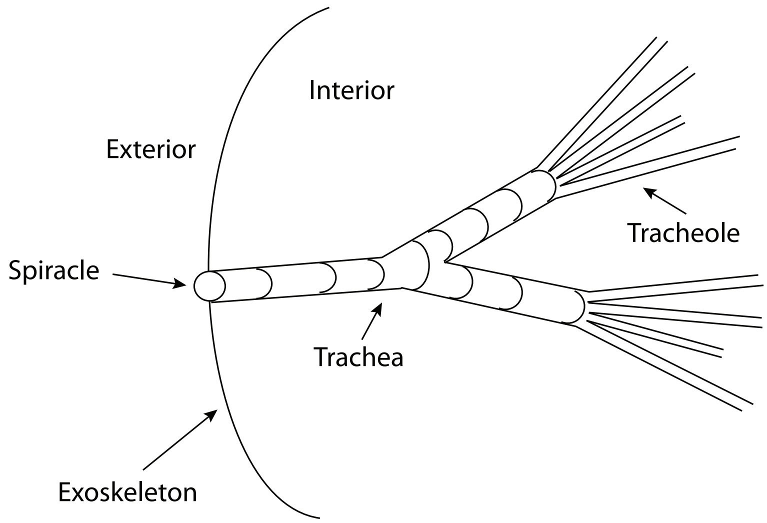

Figure 9: Sketch of a simple insect tracheal system. Insects use a different system for respiration than vertebrates. Instead of lungs, they have a series of branching tubes (trachea and tracheoles) through which oxygen flows from the atmosphere to individual cells or small groups of cells. Carbon dioxide then travels back out along the same tubes. Air enters the insect's body through valve-like openings in the exoskeleton. These openings (called spiracles) are located laterally along the thorax and abdomen of most insects, usually one pair of spiracles per body segment.

steady-state equations of section 5.1 is that the current conservation equation (5.5) becomes

$$D_m \partial_x \pi^\eta(x_k(L)) + D_{m+1} \sum_{j \in \mathcal{J}_\alpha} \partial_x \pi^\eta(x_j(0)) = 0, \quad k \in \Sigma_m,$$

which implies that the iterative equation (5.7) becomes

$$\Theta_{\overline{\alpha}(k)} - \Theta_{\alpha(k)} - C_m \sum_{j \in \mathcal{J}_{\alpha(k)}} [\Theta_{\overline{\alpha}(j)} - \Theta_{\alpha(j)}] = 0, \quad k \in \Sigma_m$$

with $C_m = D_{m+1}/D_m$. Solving this iterative equation will then require keeping track of the coefficients C_m, and this will lead to more complicated expressions for the generation-dependent functions $H_m(x)$ and $G_m(x)$. Turning to the more involved examples of sections 5.2 and 5.3, the presence of r-dependent diffusion coefficients means that one has to modify the symmetry conditions listed below equation (5.25), resulting in a more complicated matrix equation than equation (5.26), for example.

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