2015-03-01

A Mathematical Model of Amoeboid Cell Motion as a Continuous-Time Markov Process

Lynnae Despain
Brigham Young University - Provo

A Mathematical Model of Amoeboid Cell Motion as a

Continuous-Time Markov Process

Lynnae Despain

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science

John Dallon, Chair
Emily Evans
Christopher Grant
William Smith

Department of Mathematics

Brigham Young University

March 2015

ABSTRACT

A Mathematical Model of Amoeboid Cell Motion as a
Continuous-Time Markov Process

Lynnae Despain
Department of Mathematics, BYU
Master of Science

Understanding cell motion facilitates the understanding of many biological processes such as wound healing and cancer growth. Constructing mathematical models that replicate amoeboid cell motion can help us understand and make predictions about real-world cell movement. We review a force-based model of cell motion that considers a cell as a nucleus and several adhesion sites connected to the nucleus by springs. In this model, the cell moves as the adhesion sites attach to and detach from a substrate. This model is then reformulated as a random process that tracks the attachment characteristic (attached or detached) of each adhesion site, the location of each adhesion site, and the centroid of the attached sites. It is shown that this random process is a continuous-time jump-type Markov process and that the sub-process that counts the number of attached adhesion sites is also a Markov process with an attracting invariant distribution. Under certain hypotheses, we derive a formula for the velocity of the expected location of the centroid.

Keywords: cell motion, Markov process

Contents

Chapter 1. Introduction

Amoeboid cell motion is a crawling type of movement of a single cell that occurs as the cytoplasm changes shape by protruding and retracting extensions, known as pseudopods. These pseudopods form via actin polymerization and act as adhesion sites, interacting with and attaching to the extracellular matrix (ECM). Contraction occurs, causing locomotion of the cell. Finally, the adhesive bonds release and the pseudopods detach and retract into the advancing cell body [4]. This type of motion is exhibited by protozoan amoebae, slime molds such as *Dictyostelium discoideum*, some human cells such as leukocytes, and some tumor cells. Understanding cell motion can help us understand complex biological processes such as wound healing [8], immune response [4], and metastasis [9].

To introduce some mathematical understanding of amoeboid cell motion, we review a force-based model of a single cell that considers a cell as several adhesion sites connected to the nucleus by springs. The attachment characteristic of each site (attached or detached) is determined by random switching terms. When a site attaches, it does so at a location that is some random perturbation of the location of the cell center. The attached sites exert forces on the nucleus, causing cell motion.

This force-based model is presented in [3]. Numerical simulations in [3] suggest cell speed is independent of force and is greatly influenced by the binding dynamics of the cell. We seek to verify these observations analytically. As such, our primary goal is to find a formula to predict the expected velocity of the cell under such motion.

Using ideas from the force-based mode, we construct a model of amoeboid cell motion as a stochastic process. This process considers the attachment characteristic of each adhesion site, the location of each adhesion site, and the location of the centroid of the attached sites. We show that, under our formulation, this stochastic process is a continuous-time Markov process from which we can determine the time derivative of the expected location of the centroid.

Before formulating and discussing our model, we first look at the projected process of counting the number of attached adhesion sites. This projected process is a continuous-time Markov process, and we examine its transition rate matrix and stationary distribution.

In developing the Continuous-time Centroid Model, we begin by presenting definitions and introducing notation that will be used throughout this paper. We define several functions and measures that will be used to construct the transition kernel μ and the rate function c for our stochastic process. We then construct the corresponding rate kernel α, and show that our stochastic process is actually a Markov process generated by α.

Next, we formulate the previously discussed projected process in terms of measures and kernels and rigorously prove that it is a Markov process and that it has an attracting invariant distribution. Finally, we show that if we begin with an initial distribution for the full Markov process that when projected gives the invariant distribution for the projected process, then we have a time-invariant formula for the time derivative of the expected location of the centroid.

To generalize this result, we consider what happens when the perturbation of an adhesion site from the centroid is governed by a distribution that is space-dependent. Under these conditions, we derive a similar result to predict the velocity of the expected location of the centroid. This allows us to extend our model to more complex biological situations such as modeling chemotaxis.

Chapter 2. The Differential Equation Model

This section reviews a model of amoeboid cell motion established in [3] that we call the Differential Equation Model. This model considers the forces involved in amoeboid cell motion in a simplified manner. We think of a cell as multiple integrin-based adhesion sites that interact with an external substrate and exert forces on the cell's nucleus, or the cell center. In this model, it is as if the adhesion sites are connected to the cell center with springs. That is, the force an adhesion site exerts on the cell center is proportional to the distance between the cell center and the adhesion site.

Because the nucleus is surrounded by cytoplasm, there is a drag force on the cell center. To model this, we assume the cell center is a sphere moving through a liquid with low Reynolds number and that the drag is proportional to the velocity of the cell center.

Let $\mathbf{x}$ denote the location in $\mathbb{R}^N$ of the cell center. Suppose there are n adhesion sites. Let ℓ_j denote the rest length of the spring attaching site j to the cell center and let β_j denote the corresponding spring constant. Let $\psi_j(t)$ be a random variable that takes the values of 0 and 1 to indicate whether or not site j is attached to the substrate at time t. Let $t_{p,j}$ be the time that site j becomes attached for the pth time. Let $\mathbf{v}_j$ give the location in $\mathbb{R}^N$ of site j. Then

$$\mathbf{v}_j(t) = \mathbf{x}(t_{p,j}^-) + \mathbf{b}_{p,j} \qquad \text{for } t \in [t_{p,j}, t_{p+1,j})$$

where $x(t_{p,j}^-) = \lim_{t \to t_{p,j}^-} x(t)$ and $\mathbf{b}_{p,j}$ is a random variable governed by some distribution η that gives the perturbation of the location of site j from the cell center. Notice, then, that when site j attaches it does so at a distance $\|\mathbf{b}_{p,j}\|$ from the cell center. It remains at that location until the site detaches.

The force-based model uses Newton's second law of motion: $F = m\mathbf{a}$, where F is the total force exerted on the cell center, m is the mass of the cell center, and $\mathbf{a}$ is the acceleration of the cell center. However, due to the low Reynolds number, the acceleration term can be ignored, leaving $F = 0$. Letting γ denote the drag coefficient, the drag force is $\gamma\mathbf{x}'$. The total force exerted by the adhesion sites is

$$\sum_{j=1}^{n} \beta_j(\|\mathbf{x} - \mathbf{v}_j\| - \ell_j)\frac{\mathbf{x} - \mathbf{v}_j}{\|\mathbf{x} - \mathbf{v}_j\|}\psi_j$$

Thus, the equation of motion for the cell center is

$$\gamma\mathbf{x}' = -\sum_{j=1}^{n} \beta_j(\|\mathbf{x} - \mathbf{v}_j\| - \ell_j)\frac{\mathbf{x} - \mathbf{v}_j}{\|\mathbf{x} - \mathbf{v}_j\|}\psi_j$$

If we assume the rest lengths of the springs are zero, this simplifies to

$$\gamma \mathbf{x}' = -\sum_{j=1}^{n} \beta_j (\mathbf{x} - \mathbf{v}_j)\psi_j$$

For further analysis and numerical results of the Differential Equation Model, see [3].

Chapter 3. The Continuous-time Centroid Model

The Differential Equation Model can be approximated by tracking the location of the centroid of the cell, rather than the cell center. Informally, we consider the limit of the differential equation model as the spring constants β_j become large. Under such conditions, it is expected that the nucleus no longer moves smoothly between positions but rather that the centroid jumps from position to position. Such a problem was examined in [2] as a discrete-time Markov process where the time steps were taken to be the event times. We now formulate this problem as a continuous-time Markov process that also includes inter-event times and call it the Continuous-time Centroid Model.

In compliance with the differential equation model, we assume that when an adhesion site attaches, it does so at a location that is some random displacement from the centroid of the previously attached adhesion sites. For simplicity, we assume that when an adhesion site detaches it does not change location. Furthermore, at each attachment or detachment event we consider the movement of the centroid to be instantaneous. We also assume that attachment and detachment events occur independently of one another and at random and allow only one attachment or detachment event at a time.

Chapter 4. A Projected Process: Counting Attached Sites

Before discussing the full Continuous-time Centroid Model, we first examine a simpler process $\hat{X}$ that counts the number of attached sites. We do so using the familiar context of a transition rate matrix and distribution vectors.

To begin, fix a number $n \in \mathbb{N}$, where n is the number of adhesion sites. The state space of $\hat{X}$ is $\{0, 1, \ldots, n\}$. Fix two positive constants θ_a and θ_d. Assume that the wait time for a detached site to attach is exponentially distributed with parameter θ_a and that the wait time for an attached site to detach is exponentially distributed with parameter θ_d.

It is a standard result in probability that the minimum of m independent exponentially distributed random variables is itself an exponentially distributed random variable whose parameter is the sum of the parameters of the m independent exponential random variables.

Suppose there are i sites attached. The wait time for any detachment to occur is the minimum of the wait times for each of the attached sites to detach. Since there are i sites attached, it follows that the wait time for a detachment to occur is exponentially distributed with parameter $i\theta_d$. Similarly, there are $(n-i)$ detached sites, so the wait time for an attachment to occur is exponentially distributed with parameter $(n-i)\theta_a$.

To simplify this process, we assume it is memoryless. That is, the number of attached sites at the next event depends only on the number of sites that are currently attached and not on any information about previous times. This implies that the wait times between events are exponentially distributed.

Consider a state $i \in \{0, 1, \ldots, n\}$. Since only one attachment or detachment event occurs at a time, we only allow transitions from state i to state $i-1$ or $i+1$, corresponding to a detachment or attachment event, respectively. The generator, or transition rate matrix, Q for $\hat{X}$ is the matrix with entries q_{ij} given by

$$q_{i,i-1} = i\theta_d, \qquad q_{i,i} = -((n-i)\theta_a + i\theta_d), \quad q_{i,i+1} = (n-i)\theta_a,$$

and $q_{i,j} = 0$ otherwise.

Let $\tau_1, \tau_2, \ldots$ be the jump times of $\hat{X}$. Let $\hat{Y}$ be the embedded discrete-time Markov chain, called the jump chain of $\hat{X}$, given by $\hat{Y}_k = \hat{X}_t$ for $t \in [\tau_k, \tau_{k+1})$. Let $R = (r_{ij})$ be the transition probability matrix for $\hat{Y}$, so that the jump chain $\hat{Y}$ has transition probabilities

r_{ij}. Then the jump probabilities are given by

$$r_{ij} = \begin{cases} -\frac{q_{ij}}{q_{ii}}, & j \neq i \\ 0, & j = i \end{cases}$$

So $r_{ij} > 0$ if $j \in \{i-1, i+1\}$ and $r_{ij} = 0$ otherwise. Let $r_{ij}^{(k)}$ be the k-step transition probability for $\hat{Y}$. We prove two properties of $\hat{Y}$.

Proposition 4.1. *The Markov chain $\hat{Y}$ described above is irreducible.*

Proof. If $i > j$, then

$$r_{ij}^{(i-j)} \geq r_{i,i-1} r_{i-1,i-2} \ldots r_{j+1,j} > 0$$

If $i < j$, then

$$r_{ij}^{(j-i)} \geq r_{i,i+1} r_{i+1,i+2} \ldots r_{j-1,j} > 0$$

If $i = j \neq n$, then

$$r_{ii}^{(2)} \geq r_{i,i+1} r_{i+1,i} > 0$$

If $i = j = n$, then

$$r_{ii}^{(2)} \geq r_{i,i-1} r_{i-1,i} > 0$$

So i communicates with j and j communicates with i for all states i, j. Thus, $\hat{Y}$ is irreducible.

□

Proposition 4.2. *$\hat{Y}$ is a recurrent Markov chain.*

Proof. We show that every state is recurrent for $\hat{Y}$. Since the state space $S = \{0, 1, 2, \ldots, n\}$ is finite, by Corollary 7.2.3 in [7] there is at least one recurrent state. Because Proposition 4.1 gives that $\hat{Y}$ is irreducible, it then follows by Corollary 7.2.1 of [7] that all the states are recurrent. □

We show that $\hat{X}$ has a stationary distribution ζ and that it is attracting, where ζ is as given in Proposition 4.3.

Proposition 4.3. *The distribution vector ζ given by*

$$\zeta_k = \frac{1}{(\theta_d + \theta_a)^n} \binom{n}{k} \theta_d^{n-k} \theta_a^k, \quad k = 0, 1, \ldots, n$$

is a stationary distribution for $\hat{X}$. If $\{p_{ij}(t)\}$ are the transition probabilities of $\hat{X}$, then $p_{ij}(t) \to \zeta_j$ as $t \to \infty$.

Proof. For ζ to be a stationary distribution of $\hat{X}$ it must satisfy $\zeta Q = 0$. Let $(\zeta Q)_j$ denote the j^{th} entry of the row vector ζQ. We find that

$$(\zeta Q)_j = \begin{cases} -n\theta_a \zeta_0 + \theta_d \zeta_1, & \text{if } j = 0 \\ (n-(j-1))\theta_a \zeta_{j-1} - ((n-j)\theta_a + j\theta_d)\zeta_j + (j+1)\theta_d \zeta_{j+1}, & \text{if } 1 \leq j \leq n-1 \\ \theta_a \zeta_{n-1} - n\theta_d \zeta_n, & \text{if } j = n \end{cases}$$

So

$$(\zeta Q)_0 = -n\theta_a \left(\frac{1}{(\theta_d + \theta_a)^n} \theta_d^n \right) + \theta_d \left(\frac{n}{(\theta_d + \theta_a)^n} \theta_d^{n-1} \theta_a \right) = 0$$

and

$$(\zeta Q)_n = \theta_a \left(\frac{n}{(\theta_d + \theta_a)^n} \theta_d \theta_a^{n-1} \right) - n\theta_d \left(\frac{1}{(\theta_d + \theta_a)^n} \theta_a^n \right) = 0$$

For $1 \leq j \leq n-1$,

$$
\begin{aligned}
(\zeta Q)_j &= \frac{1}{(\theta_d+\theta_a)^n}\left[(n-(j-1))\theta_a\binom{n}{j-1}\theta_a^{j-1}\theta_d^{n-(j-1)} - (n-j)\theta_a\binom{n}{j}\theta_a^j\theta_d^{n-j}\right. \\
&\qquad\qquad \left. -j\theta_d\binom{n}{j}\theta_a^j\theta_d^{n-j} + (j+1)\theta_d\binom{n}{j+1}\theta_a^{j+1}\theta_d^{n-(j+1)}\right] \\
&= \frac{1}{(\theta_d+\theta_a)^n}\left[\frac{n!}{(j-1)!(n-j)!}\theta_a^j\theta_d^{n-j+1} - \frac{n!}{j!(n-j-1)!}\theta_a^{j+1}\theta_d^{n-j}\right. \\
&\qquad\qquad \left. -\frac{n!}{(n-j)!(j-1)!}\theta_a^j\theta_d^{n-j+1} + \frac{n!}{(n-j-1)!j!}\theta_a^{j+1}\theta_d^{n-j}\right] \\
&= 0
\end{aligned}
$$

So $\zeta Q = 0$ and ζ is a stationary distribution for $\hat{X}$.

By Propositions 4.1 and 4.2, we know that $\hat{Y}$ is irreducible and recurrent. Since $\hat{Y}$ is the jump chain of $\hat{X}$, we have that $\hat{X}$ is an irreducible continuous-time Markov process with a recurrent jump chain. By Theorem 7.4.5 of [7], the transition probabilities converge to the stationary probabilities. That is, $p_{ij}(t) \to \zeta_j$ as $t \to \infty$, and we say that ζ is attracting.

□

We will revisit the process $\hat{X}$ in Section 8 and will formulate it in terms of measures and rate kernels. Under this new construction, results corresponding to Propositions 4.1 and 4.3 are given in Lemma 8.5 and Proposition 8.7, respectively. We will also discuss the relationship between the transition rate matrix Q and the rate kernel $\hat{\alpha}$ (to be defined in Section 5) and the relationship between their corresponding invariant distributions (see comments following Propositions 8.4 and 8.7).

Chapter 5. Formulation of the Continuous-time Centroid Model

We introduce definitions and notations that will be used hereafter. To begin, fix two numbers $n, N \in \mathbb{N}$, where n is the number of adhesion sites and N is the dimension of the space in which the cell moves. We will consider the adhesion sites as being uniquely labeled with the integers $0, 1, \ldots, n-1$. Fix positive constants θ_a, θ_d and a Borel probability measure η on $E := \mathbb{R}^N$ such that $\int_E \mathbf{x}\, d\eta(\mathbf{x})$ is well-defined and finite. Assume that the wait time for a detached adhesion site to attach is exponentially distributed with parameter θ_a and the wait time for an attached adhesion site to detach is exponentially distributed with parameter θ_d. We choose η such that when a detached adhesion site attaches, its new location is a perturbation of the old centroid governed by the distribution η.

We will make use of the following definitions and notations:

- For two sets A, B, define A^B to be the set of functions from B to A.

- For $k \in \mathbb{N}$, define $[k] := \{0, 1, 2, \ldots, k-1\}$.

- For $\psi \in \{0,1\}^{[n]}$, define $|\psi| := \sum_{i \in [n]} \psi(i)$. We use ψ to indicate the attachment characteristic of the cell. So

$$\psi(i) = \begin{cases} 0, & \text{if site } i \text{ is detached} \\ 1, & \text{if site } i \text{ is attached} \end{cases}$$

  Since ψ gives the attachment characteristic of the cell, $|\psi|$ gives the number of adhesion sites that are attached.

- Define a space $\mathsf{X} := \left\{ \{0,1\}^{[n]} \times E^{[n+1]} : \sum_{i \in [n]} \psi(i)(\mathbf{v}(i) - \mathbf{v}(n)) = 0 \right\}$. For $\mathbf{v} \in E^{[n+1]}$, $\mathbf{v}(i)$ gives the location of site i for $i \in [n]$, and $\mathbf{v}(n)$ gives the centroid of the attached adhesion sites. A point $(\psi, \mathbf{v}) \in \mathsf{X}$ describes the attachment characteristic of the cell, the location of the adhesion sites, and the location of the centroid. The condition in the definition of X ensures that $\mathbf{v}(n)$ is, in fact, the centroid of the attached sites.

- Endow $\{0,1\}$ with the discrete topology, E with the Euclidean topology, $\{0,1\}^{[n]} \times E^{[n+1]}$ with the corresponding product topology, and X with the corresponding subspace topology.

- Let $\mathcal{B}(\cdot)$ denote the Borel σ-algebra of a topological space.

- Given $\mathbf{a}, \mathbf{b} \in E$ and $a, b \in \mathbb{R}$, define a function $S_{(\mathbf{a},\mathbf{b},a,b)} : E \times E \to E \times E$ by $S_{(\mathbf{a},\mathbf{b},a,b)}(\mathbf{x}, \mathbf{y}) := (a(\mathbf{x} - \mathbf{a}), b(\mathbf{y} - \mathbf{b}))$. This function scales and translates a point in $E \times E$.

- For each $i \in [n]$:

  - Define $r_i : \{0,1\}^{[n]} \to [0,1]$ by

  $$r_i(\psi) := \frac{\theta_d \psi(i) + \theta_a(1 - \psi(i))}{\theta_d\,|\psi| + \theta_a(n - |\psi|)}$$

  We will show in Claim 6.1 that $r_i(\psi)$ is the probability that the next event involves site i.

  - Define $s_i : \{0,1\}^{[n]} \to \{0,1\}^{[n]}$ so that $s_i(\psi)$ agrees with ψ except on $\{i\}$. Technically speaking,

  $$s_i(\psi) := \big(\psi \setminus \{(i, \psi(i))\}\big) \cup \{(i, 1 - \psi(i))\}$$

  When site i changes state, the overall attachment characteristic of the cell goes from ψ to $s_i(\psi)$.

  - Define P_i to be the partition of $[n+1]$ consisting of singletons except for $\{i, n\}$. That is,

  $$P_i := \Big\{\{j\} : j \in [n] \setminus \{i\}\Big\} \cup \{i, n\}$$

So

$$P_i = \Big\{\{0\},\{1\},\dots,\{i-1\},\{i+1\},\dots,\{n-1\},\{i,n\}\Big\}$$

Note that the elements of $\{i,n\}$ identify the values of $\mathbf{v}$ that can change when site i changes state, namely the location $\mathbf{v}(i)$ of site i and the centroid $\mathbf{v}(n)$.

- Define $G_i : E \to E^{\{i\}}$ by $G_i(\mathbf{y}) := \{(i,\mathbf{y})\}$. So $G_i(\mathbf{y})$ is a function that maps $i \mapsto \mathbf{y}$. However, we prefer to think of $G_i(\mathbf{y})$ as the single-element set $G_i(\mathbf{y}) = \{(i,\mathbf{y})\}$.
- Define $F_i : E \times E \to E^{\{i,n\}}$ by $F_i(\mathbf{y}_1,\mathbf{y}_2) := \{(i,\mathbf{y}_1),(n,\mathbf{y}_2)\}$.
- Given $(\psi,\mathbf{v}) \in \{0,1\}^{[n]} \times E^{[n+1]}$, define the measure $\mu^{(\psi,\mathbf{v})}_{\{i\}}$ on $E^{\{i\}}$ by $\mu^{(\psi,\mathbf{v})}_{\{i\}} := \delta_{\mathbf{v}(i)} \circ G_i^{-1}$, where $\delta_{\mathbf{v}(i)}$ is the standard point-mass measure on E.

  The formula for $\mu^{(\psi,\mathbf{v})}_{\{i\}}$ reflects the fact that site i does not move when site j changes state, $j \neq i$. We provide further explanation following Claim 6.3
- Define the measure $\mu^{(\psi,\mathbf{v})}_{\{i,n\}}$ on $E^{\{i,n\}}$ by

$$\mu^{(\psi,\mathbf{v})}_{\{i,n\}} := \begin{cases} \big(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\big) \circ F_i^{-1}, & \text{if } |\psi| = \psi(i) = 1 \\ \big(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\big) \circ S^{-1}_{(\mathbf{0},(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1),1,1)} \circ F_i^{-1}, & \text{if } |\psi| > \psi(i) = 1 \\ (\eta \times I) \circ S^{-1}_{(-\mathbf{v}(n),-(|\psi|+1)\mathbf{v}(n),1,1/(|\psi|+1))} \circ F_i^{-1}, & \text{if } \psi(i) = 0 \end{cases}$$

  where $I : E \times \mathcal{B}(E) \to [0,1]$ is the inclusion kernel defined by $I(\mathbf{x},S) := \delta_{\mathbf{x}}(S)$, so

$$(\eta \times I)(A \times B) = \int_A \eta(d\mathbf{x}) I(\mathbf{x},B) = \int_A \eta(d\mathbf{x})\delta_{\mathbf{x}}(B) = \int_{A\cap B} \eta(d\mathbf{x}) = \eta(A \cap B)$$

  The formula for $\mu^{(\psi,\mathbf{v})}_{\{i,n\}}$ reflects the different ways the centroid and the location of site i change when site i changes state. We expound on this following Claim 6.4.

- Define $\tilde{\mu} : \mathsf{X} \times \mathcal{B}\left(\{0,1\}^{[n]} \times E^{[n+1]}\right) \to \mathbb{R}$ by

$$\tilde{\mu}((\psi, \mathbf{v}), \cdot) := \sum_{i \in [n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi,\mathbf{v})} \right)$$

  Note that $\tilde{\mu}((\psi, \mathbf{v}), A)$ is the probability that the configuration at the next event is in A. We justify this in Remark 6.5.

- Define $\mu : \mathsf{X} \times \mathcal{B}(\mathsf{X}) \to \mathbb{R}$ to be the restriction of $\tilde{\mu}$ to $\mathsf{X} \times \mathcal{B}(\mathsf{X})$. Thus, given a starting configuration $\mathsf{x} \in \mathsf{X}$, $\mu(\mathsf{x}, A)$ is the probability that the configuration at the next event is in A. By restricting $\tilde{\mu}$ to $\mathsf{X} \times \mathcal{B}(\mathsf{X})$ we are creating a measure μ that is only concerned with sets of acceptable configurations, rather than sets of arbitrary configurations.

- Define $\hat{\mu} : [n+1] \times \mathcal{P}([n+1]) \to \mathbb{R}$ by

$$\hat{\mu}(i, \cdot) := \frac{\theta_d i \delta_{i-1} + \theta_a(n-i)\delta_{i+1}}{\theta_d i + \theta_a(n-i)}$$

- Define $\hat{c} : [n+1] \to (0, \infty)$ by $\hat{c}(i) := \theta_d i + \theta_a(n-i)$.

- Define $c : \mathsf{X} \to (0, \infty)$ by $c(\psi, \mathbf{v}) := \hat{c}(|\psi|)$. We discuss c and $\hat{c}$ further at the end of Section 6.

- Define $\alpha : \mathsf{X} \times \mathcal{B}(\mathsf{X}) \to [0, \infty)$ by $\alpha((\psi, \mathbf{v}), A) := c(\psi, \mathbf{v})\mu((\psi, \mathbf{v}), A)$

- Define $\hat{\alpha} : [n+1] \times \mathcal{P}([n+1]) \to [0, \infty)$ by $\hat{\alpha}(i, \hat{A}) := \hat{c}(i)\hat{\mu}(i, \hat{A})$. We will discuss $\hat{\alpha}$ more following Proposition 8.4.

Chapter 6. Properties and Explanations

In this section, we explore some properties of the above defined mappings and measures.

Claim 6.1. *Suppose the attachment characteristic of a cell is given by $\psi \in \{0,1\}^{[n]}$. Then for $i \in [n]$, $r_i(\psi)$ is the probability that the next event involves site i.*

Proof. Fix $i \in [n]$. Consider the n independent exponentially distributed random variables $\xi_0, \xi_1, \dots, \xi_{n-1}$, where ξ_j is the wait time for site j to change state. By assumption, ξ_j is exponentially distributed with parameter λ_j, where

$$\lambda_j = \begin{cases} \theta_d, & \text{if site } j \text{ is attached} \\ \theta_a, & \text{if site } j \text{ is detached} \end{cases} = \begin{cases} \theta_d, & \text{if } \psi(j) = 1 \\ \theta_a, & \text{if } \psi(j) = 0 \end{cases} = \theta_d \psi(j) + \theta_a (1 - \psi(j))$$

Notice that the wait time ξ for the next event to occur is the minimum of the wait times for the next event at each site. So $\xi = \min\{\xi_j : j \in [n]\}$. Because $\xi_0, \xi_1, \dots, \xi_{n-1}$ are independent exponential random variables with parameters $\lambda_0, \lambda_1, \dots, \lambda_{n-1}$, respectively, it follows that ξ is exponentially distributed with parameter $\lambda := \sum_{j \in [n]} \lambda_j$. (The proof of this is a standard exercise in probability.) Observe,

$$\begin{aligned} \lambda &= \sum_{j \in [n]} \lambda_j \\ &= \sum_{j \in [n]} (\theta_d \psi(j) + \theta_a (1 - \psi(j))) \\ &= \theta_d \sum_{j \in [n]} \psi(j) + \theta_a \Big(n - \sum_{j \in [n]} \psi(j) \Big) \\ &= \theta_d \, |\psi| + \theta_a (n - |\psi|) \end{aligned}$$

Since i is fixed, let $\xi' := \min\{\xi_j : j \neq i\}$. Then ξ' is an exponential random variable with parameter $\lambda' := \sum_{j \in [n] \setminus \{i\}} \lambda_j$, or equivalently $\lambda' = \lambda - \lambda_i$. Note that ξ' and ξ_i are independent.

The occurrence that the next event involves site i is $\{\xi = \xi_i\}$. This is the same as $\{\xi_j > \xi_i : j \neq i\}$, or equivalently $\{\xi' > \xi_i\}$. So the probability that the next event involves site i is $\mathbb{P}(\xi' > \xi_i)$.

We have two independent exponential random variables ξ' and ξ_i with parameters λ' and λ_i, respectively. It is a standard exercise in probability that

$$\mathbb{P}(\xi' > \xi_i) = \frac{\lambda_i}{\lambda' + \lambda_i}$$

Since $\lambda = \lambda' + \lambda_i$, this gives

$$\mathbb{P}(\xi' > \xi_i) = \frac{\lambda_i}{\lambda} = \frac{\theta_d \psi(i) + \theta_a(1 - \psi(i))}{\theta_d \,|\psi| + \theta_a(n - |\psi|)} = r_i(\psi)$$

Therefore, $r_i(\psi)$ represents the probability that the next event involves site i.

$\square$

The next claim and the comments following it give the updated configuration if the cell starts with configuration $(\psi, \mathbf{v})$, more than one adhesion site is attached, site i attached, and site i detaches.

Claim 6.2. *If* $(\psi, \mathbf{v}) \in \mathsf{X}$ *and* $|\psi| > \psi(i) = 1$, *then* $(s_i(\psi), \mathbf{v}_{[n]} \cup \{(n, \mathbf{v}(n) - \frac{1}{|\psi|-1}(\mathbf{v}(i) - \mathbf{v}(n)))\}) \in \mathsf{X}$.

Proof. Since $(\psi, \mathbf{v}) \in \mathsf{X}$, we have

$$\sum_{j \in [n]} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) = 0.$$

Isolating the i^{th} term gives

$$\sum_{j \in [n] \setminus \{i\}} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) = -(\mathbf{v}(i) - \mathbf{v}(n))$$

By the definition of $s_i(\psi)$ we have

$$\sum_{j \in [n] \setminus \{i\}} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) = \sum_{j \in [n]} s_i(\psi)(j)(\mathbf{v}(j) - \mathbf{v}(n))$$

Notice that there are $|\psi| - 1$ nonzero values of $s_i(\psi)$. Thus,

$$\begin{aligned}
\sum_{j\in[n]} s_i(\psi)(j)(\mathbf{v}(j) - \mathbf{v}(n)) &= \sum_{j\in[n]\setminus\{i\}} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) \\
&= -\left(\mathbf{v}(i) - \mathbf{v}(n)\right) \\
&= -\left(|\psi| - 1\right)\frac{\mathbf{v}(i) - \mathbf{v}(n)}{|\psi| - 1} \\
&= -\sum_{j\in[n]} s_i(\psi)(j)\frac{(\mathbf{v}(i) - \mathbf{v}(n))}{|\psi| - 1}
\end{aligned}$$

Therefore,

$$\sum_{j\in[n]} s_i(\psi)(j)\left(\mathbf{v}(j) - \left(\mathbf{v}(n) - \frac{(\mathbf{v}(i) - \mathbf{v}(n))}{|\psi| - 1}\right)\right) = 0$$

So $(s_i(\psi), \mathbf{v}_{[n]} \cup \{(n, \mathbf{v}(n) - \frac{1}{|\psi|-1}(\mathbf{v}(i) - \mathbf{v}(n)))\}) \in \mathsf{X}$.

$\square$

If $(\psi, \mathbf{v})$ gives the current configuration of the cell, site i is attached, and there is more than one attached adhesion site, then when site i detaches, the new attachment characteristic is given by $s_i(\psi)$ and the locations of all the adhesion sites remain as they were. Suppose the new configuration is given by $(s_i(\psi), \mathbf{w})$. Then $\mathbf{w}|_{[n]} = \mathbf{v}|_{[n]}$. Since $\mathbf{w}(n)$ is the new location of the centroid, we know that $\sum_{j\in[n]} s_i(\psi)(j)(\mathbf{w}(j) - \mathbf{w}(n)) = 0$. Since $\mathbf{w}|_{[n]} = \mathbf{v}|_{[n]}$, this gives

$$\sum_{j\in[n]} s_i(\psi)(j)(\mathbf{v}(j) - \mathbf{w}(n)) = 0$$

Because $(s_i(\psi), \mathbf{v}_{[n]} \cup \{(n, \mathbf{v}(n) - \frac{1}{|\psi|-1}(\mathbf{v}(i) - \mathbf{v}(n)))\}) \in \mathsf{X}$, we know that

$$\sum_{j\in[n]} s_i(\psi)(j)\left(\mathbf{v}(j) - \left(\mathbf{v}(n) - \frac{(\mathbf{v}(i) - \mathbf{v}(n))}{|\psi| - 1}\right)\right) = 0$$

Thus,

$$\sum_{j\in[n]} s_i(\psi)(j)(\mathbf{v}(j)-\mathbf{w}(n)) = \sum_{j\in[n]} s_i(\psi)(j)\left(\mathbf{v}(j)-\left(\mathbf{v}(n)-\frac{(\mathbf{v}(i)-\mathbf{v}(n))}{|\psi|-1}\right)\right)$$

Since there are $|\psi|-1$ nonzero values of $s_i(\psi)$ we then get

$$-(|\psi|-1)\mathbf{w}(n)+\sum_{j\in[n]} s_i(\psi)(j)\mathbf{v}(j) = -(|\psi|-1)\left(\mathbf{v}(n)-\frac{(\mathbf{v}(i)-\mathbf{v}(n))}{|\psi|-1}\right)+\sum_{j\in[n]} s_i(\psi)(j)\mathbf{v}(j)$$

Solving for $\mathbf{w}(n)$ gives

$$\mathbf{w}(n) = \mathbf{v}(n)-\frac{(\mathbf{v}(i)-\mathbf{v}(n))}{|\psi|-1}$$

Hence, the new location of the centroid is $\mathbf{v}(n)-\frac{(\mathbf{v}(i)-\mathbf{v}(n))}{|\psi|-1}$ and the new configuration of the cell is $(s_i(\psi), \mathbf{v}_{[n]} \cup \{(n, \mathbf{v}(n)-\frac{1}{|\psi|-1}(\mathbf{v}(i)-\mathbf{v}(n)))\})$.

Next, we explore the definitions of the measures $\mu^{(\psi,\mathbf{v})}_{\{i\}}$ and $\mu^{(\psi,\mathbf{v})}_{\{i,n\}}$.

Claim 6.3. *For* $(\psi,\mathbf{v}) \in \mathsf{X}$ *and* $i \in [n]$, $\mu^{(\psi,\mathbf{v})}_{\{i\}} = \delta_{\mathbf{v}|_{\{i\}}}$.

Proof. Recall that $\mu^{(\psi,\mathbf{v})}_{\{i\}}$ is a measure on $E^{\{i\}}$. For $B \in \mathcal{B}(E^{\{i\}})$ we have

$$\begin{aligned}
\mu^{(\psi,\mathbf{v})}_{\{i\}}(B) &= \left(\delta_{\mathbf{v}(i)} \circ G_i^{-1}\right)(B) \\
&= \delta_{\mathbf{v}(i)}\big(G_i^{-1}(B)\big) \\
&= \delta_{\mathbf{v}(i)}\big(\{\mathbf{y} \in E : G_i(\mathbf{y}) \in B\}\big) \\
&= \delta_{\mathbf{v}(i)}\big(\{\mathbf{y} \in E : \{(i,\mathbf{y})\} \in B\}\big) \\
&= \begin{cases} 0, & \text{if } \{(i,\mathbf{v}(i))\} \notin B \\ 1, & \text{if } \{(i,\mathbf{v}(i))\} \in B \end{cases} \\
&= \delta_{\mathbf{v}|_{\{i\}}}(B)
\end{aligned}$$

□

Conceptually, when site $j \neq i$ changes state (from attached to detached or vice versa) the location of site i should not change. Accordingly, if site $j \neq i$ changes state and site i is no longer associated with the location $\mathbf{v}(i)$, then $\mu_{\{i\}}^{(\psi,\mathbf{v})}$ returns a value of 0, indicating that this is not an acceptable configuration. The measure $\mu_{\{i\}}^{(\psi,\mathbf{v})}$ returns a value of 1 when site i is associated with location $\mathbf{v}(i)$, indicating an acceptable location for site i. So the formula for $\mu_{\{i\}}^{(\psi,\mathbf{v})}$ reflects the fact that site i does not move when site j changes state for $j \neq i$.

Claim 6.4. *For $(\psi, \mathbf{v}) \in \mathsf{X}$ and $i \in [n]$,*

$$\mu_{\{i,n\}}^{(\psi,\mathbf{v})} = \begin{cases} \delta_{\mathbf{v}|_{\{i,n\}}}, & \textit{if } |\psi| = \psi(i) = 1 \\ \delta_{\{(i,\mathbf{v}(i)),(n,\mathbf{v}(n)-(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1))\}}, & \textit{if } |\psi| > \psi(i) = 1 \\ (\eta \times I)\left(\left\{(\mathbf{x},\mathbf{y}) : \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)\right\} \in \cdot\right\}\right), & \textit{if } \psi(i) = 0 \end{cases}$$

Proof. Let $B \in \mathcal{B}(E^{\{i,n\}})$. There are three cases.

Case 1: $|\psi| = \psi(i) = 1$. Then

$$\begin{aligned} \mu_{\{i,n\}}^{(\psi,\mathbf{v})}(B) &= \left(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\right) \circ F_i^{-1}(B) \\ &= \left(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\right)\left(F_i^{-1}B\right) \\ &= \left(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\right)\left(\left\{(\mathbf{y}_1,\mathbf{y}_2) \in E \times E : \{(i,\mathbf{y}_1),(n,\mathbf{y}_2)\} \in B\right\}\right) \\ &= \begin{cases} 1, & \text{if } \{(i,\mathbf{v}(i)),(n,\mathbf{v}(n))\} \in B \\ 0, & \text{otherwise} \end{cases} \\ &= \delta_{\mathbf{v}|_{\{i,n\}}}(B) \end{aligned}$$

Case 2: $|\psi| > \psi(i) = 1$. Observe that

$$S_{(\mathbf{0},(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1),1,1)}(\mathbf{x},\mathbf{y}) = \left(\mathbf{x},\, \mathbf{y} - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)$$

So for $|\psi| > \psi(i) = 1$,

$$\begin{aligned}
\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(B) &= \big(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\big) \circ S^{-1}_{(\mathbf{0},(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1),1,1)} \circ F_i^{-1}(B) \\
&= \big(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\big) \left(\left\{(\mathbf{x},\mathbf{y}) : \left(\mathbf{x},\, \mathbf{y} - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right) \in F_i^{-1}(B)\right\}\right) \\
&= \big(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\big) \left(\left\{(\mathbf{x},\mathbf{y}) : \left\{(i,\mathbf{x}), \left(n, \mathbf{y} - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right\} \in B\right\}\right) \\
&= \begin{cases} 1, & \text{if } \left\{(i,\mathbf{v}(i)), \left(n, \mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right\} \in B \\ 0, & \text{otherwise} \end{cases} \\
&= \delta_{\{(i,\mathbf{v}(i)),(n,\mathbf{v}(n)-(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1))\}}(B)
\end{aligned}$$

Case 3: $\psi(i) = 0$. Notice that

$$\begin{aligned}
S_{(-\mathbf{v}(n),-(|\psi|+1)\mathbf{v}(n),1,1/(|\psi|+1))}(\mathbf{x},\mathbf{y}) &= \left(\mathbf{x}+\mathbf{v}(n), \frac{1}{|\psi|+1}(\mathbf{y}+(|\psi|+1)\mathbf{v}(n))\right) \\
&= \left(\mathbf{x}+\mathbf{v}(n), \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)
\end{aligned}$$

So

$$\begin{aligned}
\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(B) &= (\eta \times I) \circ S^{-1}_{(-\mathbf{v}(n),-(|\psi|+1)\mathbf{v}(n),1,1/(|\psi|+1))} \circ F_i^{-1}(B) \\
&= (\eta \times I)\left(\left\{(\mathbf{x},\mathbf{y}) \in E \times E : \big(\mathbf{x}+\mathbf{v}(n), \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\big) \in F_i^{-1}(B)\right\}\right) \\
&= (\eta \times I)\left(\left\{(\mathbf{x},\mathbf{y}) \in E \times E : \left\{\big(i, \mathbf{x}+\mathbf{v}(n)\big), \left(n, \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)\right\} \in B\right\}\right)
\end{aligned}$$

□

Suppose $(\psi, \mathbf{v}) \in \mathsf{X}$ is the current configuration of the cell. If site i is the only one attached, then we are in Case 1. The only possible event involving site i is for site i to detach. When this happens, the locations of site i and the centroid do not change, so they are given by $\mathbf{v}(i)$ and $\mathbf{v}(n)$, respectively. Thus, $\mu^{(\psi,\mathbf{v})}_{\{i,n\}} = \delta_{\mathbf{v}|_{\{i,n\}}}$ indicates whether or not we have an acceptable configuration.

If site i is attached but is not the only attached site, then we are in Case 2. When site i detaches, the attachment characteristic is given by $s_i(\psi)$. All the adhesion sites remain at their current locations, and the new centroid is $\mathbf{v}(n) - \frac{1}{|\psi|-1}(\mathbf{v}(i) - \mathbf{v}(n))$. So the configuration of the cell is $(s_i(\psi), \mathbf{v}_{[n]} \cup \{(n, \mathbf{v}(n) - \frac{1}{|\psi|-1}(\mathbf{v}(i) - \mathbf{v}(n)))\})$. Thus, $\mu^{(\psi,\mathbf{v})}_{\{i,n\}} = \delta_{\{(i,\mathbf{v}(i)),(n,\mathbf{v}(n)-(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1))\}}$ indicates whether or not we have an acceptable configuration for this situation.

If site i is detached, then we are in Case 3. In this situation, site i must attach when it changes state. The possible new locations for site i (and their various likelihoods) are perturbations of the old centroid that are governed by η. Additionally, the new centroid moves to accommodate the newly attached site i.

Having explored the definitions of $\mu^{(\psi,\mathbf{v})}_{\{i\}}$ and $\mu^{(\psi,\mathbf{v})}_{\{i,n\}}$, we then combine them to form $\tilde{\mu}$. Recall that

$$\tilde{\mu}((\psi, \mathbf{v}), \cdot) = \sum_{i\in[n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p\in P_i} \mu^{(\psi,\mathbf{v})}_p \right)$$

Remark 6.5. *For $(\psi, \mathbf{v}) \in \mathsf{X}$ and $A \in \mathcal{B}\left(\{0,1\}^{[n]} \times E^{[n+1]}\right)$, $\tilde{\mu}((\psi, \mathbf{v}), A)$ is the probability that the configuration at the next event is in A.*

For some basic set $B \in \mathcal{B}\left(\{0,1\}^{[n]} \times E^{[n+1]}\right)$ given by $B = B' \times \bigtimes_{p\in P_i} B_p$ we get from knowledge of general products that

$$\begin{aligned}
\tilde{\mu}((\psi, \mathbf{v}), B) &= \left(\sum_{i\in[n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p\in P_i} \mu^{(\psi,\mathbf{v})}_p \right) \right) \left(B' \times \bigtimes_{p\in P_i} B_p \right) \\
&= \sum_{i\in[n]} \left(r_i(\psi)\delta_{s_i(\psi)}(B') \prod_{p\in P_i} \mu^{(\psi,\mathbf{v})}_p(B_p) \right)
\end{aligned}$$

Note that for a given i:

- $r_i(\psi)$ is the probability that the next event involves site i
- $\delta_{s_i(\psi)}(B')$ returns a value of 1 when $s_i(\psi) \in B'$ and returns 0 otherwise

- For $p \in P_i$, the measure $\mu_p^{(\psi,\mathbf{v})}(B_p)$ returns a nonzero value only if the adhesion sites and the centroid are in an acceptable configuration when site i changes state.

So for a given i, the value $r_i(\psi)\delta_{s_i(\psi)}(B') \prod_{p \in P_i} \mu_p^{(\psi,\mathbf{v})}(B_p)$ is the probability that the next event involves site i and the new configuration is in B. Summing over all $i \in [n]$ gives the probability that the configuration at the next event is in B.

Since a set $A \in \mathcal{B}(\{0,1\}^{[n]} \times E^{[n+1]})$ is the union or intersection of basic sets in $\mathcal{B}(\{0,1\}^{[n]} \times E^{[n+1]})$ and $\tilde{\mu}$ is a measure, it follows that $\tilde{\mu}((\psi, \mathbf{v}), A)$ is the probability that the configuration at the next event is in A.

Recall that $\mu = \tilde{\mu}|_{\mathsf{X} \times \mathcal{B}(\mathsf{X})}$. For a starting configuration $\mathsf{x} \in \mathsf{X}$ and a set $A \in \mathsf{X} \times \mathcal{B}(\mathsf{X})$ of acceptable cell configurations, $\mu(\mathsf{x}, A)$ is the probability that, starting at x, the configuration at the next event is in A.

We now turn our attention to the mappings $\hat{c}$ and c. Recall from the proof of Claim 6.1 that, given the system has configuration $(\psi, \mathbf{v}) \in \mathsf{X}$, the wait time ξ for the next event to occur is exponentially distributed with parameter $\lambda = \theta_d |\psi| + \theta_a(n - |\psi|)$. So

$$E(\xi) = \frac{1}{\lambda} = \frac{1}{\theta_d |\psi| + \theta_a(n - |\psi|)} = \frac{1}{c(\psi, \mathbf{v})}$$

Thus, $c(\psi, \mathbf{v})$ gives the reciprocal of the expected wait time until the next event, given a starting configuration $\mathsf{x} = (\psi, \mathbf{v})$.

If $|\psi| = i$ then

$$E(\xi) = \frac{1}{\theta_d i + \theta_a(n - i)} = \frac{1}{\hat{c}(i)}$$

So $\hat{c}(i)$ gives the reciprocal of the expected wait time until the next event, given that there are i adhesion sites currently attached.

The following results will be utilized when proving the results of Section 8. We prove that many of the maps defined in Section 5 are measurable.

Lemma 7.1. *For each $i \in [n]$, r_i is measurable.*

Proof. Fix $i \in [n]$. For $\psi \in \{0,1\}^{[n]}$ we have

$$r_i(\psi) = \frac{\theta_d \psi(i) + \theta_a(1-\psi(i))}{\theta_d |\psi| + \theta_a(n-|\psi|)}$$

Define a map $\pi_i : \{0,1\}^{[n]} \to \{0,1\}$ by $\pi_i(\psi) = \psi(i)$. For open $V \subset \{0,1\}$, we have

$$\pi_i^{-1}(V) = \begin{cases} \emptyset, & \text{if } V = \emptyset \\ \{0,1\}^{[n]}, & \text{if } V = \{0,1\} \\ \{\psi \in \{0,1\}^{[n]} : \psi(i) = 0\}, & \text{if } V = \{0\} \\ \{\psi \in \{0,1\}^{[n]} : \psi(i) = 1\}, & \text{if } V = \{1\} \end{cases}$$

Notice that in the last two cases, $\pi_i^{-1}(V)$ is a cylinder set in $\{0,1\}^{[n]}$, which is open. Thus, $\pi_i^{-1}(V)$ is a measurable set, so π_i is measurable.

By construction we have a map $|\cdot|$ defined on $\{0,1\}^{[n]}$ by $|\psi| = \sum_{i\in[n]} \psi(i)$. So $|\psi| = \sum_{i\in[n]} \pi_i(\psi)$. Since the sum of measurable functions are measurable, we know that $|\cdot|$ is measurable.

We can rewrite r_i as

$$r_i = \frac{\theta_d \pi_i + \theta_a(1-\pi_i)}{\theta_d |\cdot| + \theta_a(n-|\cdot|)}$$

So r_i is measurable.

□

Lemma 7.2. *For each $i \in [n]$, the maps F_i and G_i are measurable.*

Proof. Fix $i \in [n]$. Observe that $E^p = \mathcal{P}(p \times E)$ for $p \in P_i$. So G_i and F_i are set-valued maps from E to $\mathcal{P}(\{i\} \times E)$ and from $E \times E$ to $\mathcal{P}(\{i, n\} \times E)$, respectively, denoted $G_i : E \rightsquigarrow \{i\} \times E$ and $F_i : E \times E \rightsquigarrow \{i, n\} \times E$. For G_i and F_i to be measurable, we require $\{i\} \times E$ and $\{i, n\} \times E$ to be complete separable metric spaces and

$$
\begin{aligned}
G_i^{-1}(U) &:= \{\mathbf{x} \in E : G_i(\mathbf{x}) \cap U \neq \emptyset\} \in \mathcal{B}(E) \\
F_i^{-1}(V) &:= \{(\mathbf{x}_1, \mathbf{x}_2) \in E \times E : F_i(\mathbf{x}_1, \mathbf{x}_2) \cap V \neq \emptyset\} \in \mathcal{B}(E \times E)
\end{aligned}
$$

for every open $U \subset \{i\} \times E$ and open $V \subset \{i, n\} \times E$. (See Definition 8.1.1 in [1].) We show this is the case.

We know that $E = \mathbb{R}^N$ is a complete separable metric space. Therefore $\{i\} \times E$ is a complete separable metric space. We show that G_i is measurable.

Let $U \subset \{i\} \times E$ be open. Then either $U = \emptyset \times U'$ or $U = \{i\} \times U'$ for some open $U' \subset E$. If $U = \emptyset \times U' = \emptyset$, then $G_i^{-1}(U) = G_i^{-1}(\emptyset) = \emptyset$, which is measurable. If $U = \{i\} \times U'$, then

$$
\begin{aligned}
G_i^{-1}(U) &= \{\mathbf{x} \in E : G_i(\mathbf{x}) \cap U \neq \emptyset\} \\
&= \{\mathbf{x} \in E : \{(i, \mathbf{x})\} \cap U \neq \emptyset\} \\
&= \{\mathbf{x} \in E : (i, \mathbf{x}) \in U\} \\
&= \{\mathbf{x} \in E : \mathbf{x} \in U'\} \\
&= U'
\end{aligned}
$$

Since $U' \in \mathcal{B}(E)$, we have that G_i is measurable.

Next we show that F_i is measurable. First note that $\{i, n\} \times E = (\{i\} \times E) \cup (\{n\} \times E)$. Since both $\{i\} \times E$ and $\{n\} \times E$ are complete separable metric spaces, it follows that $\{i, n\} \times E$ is a complete separable metric space.

Let $V \subset \{i, n\} \times E$ be open. Then $V = \bigcup_{j=i}^{\infty} V_j \times W_j$ for some open $V_j \subset \{i, n\}$ and open

$W_j \subset E$. Notice that

$$
\begin{aligned}
F_i^{-1}(V) &= \{(\mathbf{x}_1, \mathbf{x}_2) \in E \times E : \{(i, \mathbf{x}_1), (n, \mathbf{x}_2)\} \cap V \neq \emptyset\} \\
&= \{(\mathbf{x}_1, \mathbf{x}_2) \in E \times E : (i, \mathbf{x}_1), (n, \mathbf{x}_2) \in V\}
\end{aligned}
$$

For $\mathbf{x} \in E$, let

$$
\begin{aligned}
\mathcal{V}_{\mathbf{x}} &= \{W_j : (i, \mathbf{x}) \in V_j \times W_j\} \\
\mathcal{W}_{\mathbf{x}} &= \{W_j : (n, \mathbf{x}) \in V_j \times W_j\}
\end{aligned}
$$

Let

$$
V_{\mathbf{x}} = \bigcup_{V' \in \mathcal{V}_{\mathbf{x}}} V' \quad \text{and} \quad W_{\mathbf{x}} = \bigcup_{W' \in \mathcal{W}_{\mathbf{x}}} W'
$$

Then $V_{\mathbf{x}}$ and $W_{\mathbf{x}}$ are open. Let

$$
V^* = \bigcup_{\mathbf{x} \in E} V_{\mathbf{x}} \quad \text{and} \quad W^* = \bigcup_{\mathbf{x} \in E} W_{\mathbf{x}}
$$

So V^* and W^* are also open. We show that $F_i^{-1}(V) = V^* \times W^*$.

Suppose $(\mathbf{x}_1, \mathbf{x}_2) \in V^* \times W^*$. Then $(i, \mathbf{x}_1) \in V_j \times W_j$ for some j, and $(n, \mathbf{x}_2) \in V_k \times W_k$ for some k. So $(i, \mathbf{x}_1), (n, \mathbf{x}_2) \in V$. Thus, $(\mathbf{x}_1, \mathbf{x}_2) \in F_i^{-1}(V)$, and $V^* \times W^* \subset F_i^{-1}(V)$.

Now suppose $(\mathbf{x}_1, \mathbf{x}_2) \in F_i^{-1}(V)$. Then $(i, \mathbf{x}_1), (n, \mathbf{x}_2) \in V$, so $(i, \mathbf{x}_1) \in V_j \times W_j$ and $(n, \mathbf{x}_2) \in V_k \times W_k$ for some j, k. This gives $(\mathbf{x}_1, \mathbf{x}_2) \in V^* \times W^*$. So $F_i^{-1} \subset V^* \times W^*$.

We now have that $F_i^{-1} = V^* \times W^*$. Since V^* and W^* are open, it follows that $F_i^{-1}(V)$ is open, so F_i is measurable.

$\square$

Lemma 7.3. *For $\mathbf{a}, \mathbf{b} \in E$ and $a, b \in \mathbb{R}$, the map $S_{(\mathbf{a}, \mathbf{b}, a, b)}$ is measurable.*

Proof. Let $\mathbf{a}, \mathbf{b} \in E$ and $a, b \in \mathbb{R}$. Observe that

$$S^{-1}_{(\mathbf{a},\mathbf{b},a,b)}(B) = \{(\mathbf{x}, \mathbf{y}) : (a(\mathbf{x} - \mathbf{a}), b(\mathbf{y} - \mathbf{b})) \in B\}$$

If $a = 0$ and $b = 0$, then

$$S^{-1}_{(\mathbf{a},\mathbf{b},0,0)}(B) = \{(\mathbf{x}, \mathbf{y}) : (\mathbf{0}, \mathbf{0}) \in B\} = \begin{cases} \emptyset, & \text{if } (\mathbf{0}, \mathbf{0}) \notin B \\ E \times E, & \text{if } (\mathbf{0}, \mathbf{0}) \in B \end{cases}$$

So $S^{-1}_{(\mathbf{a},\mathbf{b},0,0)}(B) \in \mathcal{B}(E \times E)$.

Suppose that exactly one of a and b is nonzero. Without loss of generality, suppose $a = 0$ and $b \neq 0$. Then $(\mathbf{x}, \mathbf{y}) \in B$ if and only if $(\mathbf{0}, \frac{1}{b}\mathbf{y} + \mathbf{b}) \in S^{-1}_{(\mathbf{a},\mathbf{b},0,b)}(B)$. So $S^{-1}_{(\mathbf{a},\mathbf{b},0,b)}(B)$ is a combination of translations and dilations of B. Since translations and dilations of Borel subsets of Euclidean space are again Borel subsets of Euclidean space, it follows that $S^{-1}_{(\mathbf{a},\mathbf{b},0,b)}(B) \in \mathcal{B}(E \times E)$. Similarly, if $a \neq 0$ and $b \neq 0$, then $(\mathbf{x}, \mathbf{y}) \in B$ if and only if $(\frac{1}{a}\mathbf{x} + \mathbf{a}, \frac{1}{b}\mathbf{y} + \mathbf{b}) \in S^{-1}_{(\mathbf{a},\mathbf{b},a,b)}(B)$. Again, $S^{-1}_{(\mathbf{a},\mathbf{b},a,b)}(B)$ is a combination of translations and dilations of B, so $S^{-1}_{(\mathbf{a},\mathbf{b},a,b)}(B) \in \mathcal{B}(E \times E)$. Hence, $S_{(\mathbf{a},\mathbf{b},a,b)}$ is measurable.

□

Chapter 8. Main Results

In this section, we prove the existence of a continuous-time jump-type Markov process generated by the rate kernel α. This process is our Continuous-time Centroid Model that describes cell motion. We also examine the projected process that counts the number of attached adhesion sites (as in Section 4) and derive results analogous to Propositions 4.1 and 4.3. We end with Theorem 8.9, which gives the time derivative of the expected location of the centroid.

To construct the desired continuous-time jump-type Markov process X, we start by proving that μ is a probability kernel. Using μ, we show that there is a discrete-time Markov process Y with transition kernel μ. The Markov chain Y will serve as the jump chain for X. Since μ is a probability kernel, we have that $\alpha = c\mu$ is also a kernel. Using the kernel α, the jump chain Y, and i.i.d. exponentially distributed wait times, we construct X as a continuous-time jump-type Markov process.

Proposition 8.1. *The map μ is a probability kernel from X to X.*

Proof. Fix $i \in [n]$. By construction,

$$r_i(\psi) = \frac{\theta_d \psi(i) + \theta_a(1 - \psi(i))}{\theta_d |\psi| + \theta_a(n - |\psi|)}$$

is clearly nonnegative. By Lemma 7.1 we know that r_i is measurable.

Now we show that the map $((\psi, \mathbf{v}), A) \mapsto r_i(\psi)\delta_{s_i(\psi)}(A)$ is a kernel from X to $\{0,1\}^{[n]}$. Let $\nu_i : \mathsf{X} \times \mathcal{B}\left(\{0,1\}^{[n]}\right) \to \overline{\mathbb{R}}_+$ be given by

$$\nu_i((\psi, \mathbf{v}), A) = r_i(\psi)\delta_{s_i(\psi)}(A)$$

Fix $(\psi, \mathbf{v}) \in \mathsf{X}$. Then $r_i(\psi) \geq 0$ is constant. Since $\delta_{s_i(\psi)}$ is a measure on $\mathcal{B}\left(\{0,1\}^{[n]}\right)$, it follows that $r_i(\psi)\delta_{s_i(\psi)} = \nu_i((\psi, \mathbf{v}, \cdot))$ is a measure on $\mathcal{B}\left(\{0,1\}^{[n]}\right)$.

Now fix $A \in \mathcal{B}\left(\{0,1\}^{[n]}\right)$. Let $D_{i,A} : \{0,1\}^{[n]} \to \overline{R}_+$ be given by $D_{i,A}(\psi) = \delta_{s_i(\psi)}(A)$. Then $D_{i,A}$ is measurable, and since r_i is measurable it follows that $r_i D_{i,A} = \nu_i(\cdot, A)$ is measurable.

Since $\nu_i((\psi, \mathbf{v}, \cdot))$ is a measure on $\mathcal{B}\left(\{0,1\}^{[n]}\right)$ and $\nu_i(\cdot, A)$ is measurable in $\mathsf{x} \in \mathsf{X}$, it follows that ν_i is a kernel from X to $\{0,1\}^{[n]}$. That is, the map $((\psi, \mathbf{v}), A) \mapsto r_i(\psi)\delta_{s_i(\psi)}(A)$ is a kernel from X to $\{0,1\}^{[n]}$.

Next we show that each μ_p^{x} is a kernel from X to E^p for each $i \in [n]$ and $p \in P_i$. From Lemma 7.2 we know that G_i and F_i are measurable for each $i \in [n]$.

We first show that $\mu^{\times}_{\{i\}}$ is a kernel from X to $E^{\{i\}}$ for each $i \in [n]$. Let $g_i : \mathsf{X} \times E \to E^{\{i\}}$ be given by $g_i((\psi, \mathbf{v}), \mathbf{x}) = G_i(\mathbf{x})$. Then g_i is a measurable function. Define $d_i : \mathsf{X} \times \mathcal{B}(E) \to [0,1]$ by $d_i((\psi, \mathbf{v}), B) = \delta_{\mathbf{v}(i)}(B)$. Then d_i is a probability kernel from X to E. By Lemma 1.41(ii) in [5] we then have that

$$d_i\left((\psi, \mathbf{v}), \left(g_i((\psi, \mathbf{v}), \cdot)\right)^{-1}\right) = \delta_{\mathbf{v}(i)} \circ G_i^{-1}$$

is a kernel from X to $E^{\{i\}}$. So $\mu^{\times}_{\{i\}}$ is a kernel from X to $E^{\{i\}}$.

To show $\mu^{\times}_{\{i,n\}}$ is a kernel from X to $E^{\{i,n\}}$, we show it in each of the three cases. Let $f_i : \mathsf{X} \times (E \times E) \to E^{\{i,n\}}$ be given by $f_i((\psi, \mathbf{v}), (\mathbf{x}_1, \mathbf{x}_2)) = F_i(\mathbf{x}_1, \mathbf{x}_2)$. Then f_i is measurable. Define $d_{i,n} : \mathsf{X} \times \mathcal{B}(E \times E) \to [0,1]$ by $d_{i,n}((\psi, \mathbf{v}), B) = (\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)})(B)$. Then $d_{i,n}$ is a probability kernel from X to $E \times E$. Again, by Lemma 1.41 in [5] it follows that

$$d_{i,n}\left((\psi, \mathbf{v}), \left(f_i((\psi, \mathbf{v}), \cdot)\right)^{-1}\right) = (\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}) \circ F_i^{-1}$$

is a kernel from X to $E \times E$.

We know from Lemma 7.3 that $S_{(\mathbf{a}, \mathbf{b}, a, b)}$ is measurable for any $\mathbf{a}, \mathbf{b} \in E$ and $a, b \in \mathbb{R}$. Since both F_i and $S_{(\mathbf{0}, (\mathbf{v}(i) - \mathbf{v}(n))/(|\psi|-1), 1, 1)}$ are measurable, we have that

$$f_i((\psi, \mathbf{v}), S_{(\mathbf{0}, (\mathbf{v}(i) - \mathbf{v}(n))/(|\psi|-1), 1, 1)}(\cdot))$$

is a measurable mapping. Thus,

$$\delta(i,n)\left((\psi, \mathbf{v}), \left(S^{-1}_{\left(\mathbf{0}, \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}, 1, 1\right)} \circ \left(f_i((\psi, \mathbf{v}), \cdot)\right)^{-1}\right)\right) = (\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}) \circ S^{-1}_{\left(\mathbf{0}, \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}, 1, 1\right)} \circ F_i^{-1}$$

is a kernel from X to $E^{\{i,n\}}$.

Recall that η is a Borel probability measure and I is a kernel. This implies $\eta \times I$ is a kernel. Thus,

$$(\eta \times I) \circ S^{-1}_{\left(-\mathbf{v}(n), -(|\psi|+1)\mathbf{v}(n), 1, \frac{1}{|\psi|+1}\right)} \circ F_i^{-1}$$

is a kernel from X to $E^{\{i,n\}}$. Therefore, $\mu^{\times}_{\{i,n\}}$ is a kernel from X to $E^{\{i,n\}}$.

We now have that $\mu^{\times}_p$ is a kernel from X to E^p for every $p \in P_i$ and $i \in [n]$. One more application of Lemma 1.41 from [5] gives that the map

$$((\psi, \mathbf{v}), A) \mapsto \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi,\mathbf{v})} \right)(A)$$

is a kernel from X to $\{0,1\}^{[n]} \times E^{[n+1]}$.

Since sums of kernels are again kernels, it follows that $\tilde{\mu}$ given by

$$((\psi, \mathbf{v}), A) \mapsto \sum_{i \in [n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi,\mathbf{v})} \right)(A)$$

is a kernel from X to $\{0,1\}^{[n]} \times E^{[n+1]}$.

Note that X is a Borel subset of $\{0,1\}^{[n]} \times E^{[n+1]}$. By construction $\tilde{\mu}(\mathsf{x}, \cdot)$ is a measure. Since the restriction of a measure to the measurable subsets of a measurable set is a measure, it follows that $\mu(\mathsf{x}, \cdot) = \tilde{\mu}(\mathsf{x}, \cdot)\big|_{\mathcal{B}(\mathsf{X})}$ is a measure. Therefore, μ is a kernel from X to X.

It remains to show that $\mu((\psi, \mathbf{v}), \mathsf{X}) = 1$ for every $(\psi, \mathbf{v}) \in \mathsf{X}$. Fix $(\psi, \mathbf{v}) \in \mathsf{X}$ and $i \in [n]$. Let $\lambda_i := \delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi,\mathbf{v})}$. We proceed by cases to show that λ_i is a probability measure on X.

Case 1: If $|\psi| = \psi(i) = 1$, then $s_i(\psi) = \varphi$ where $\varphi \in \{0,1\}^{[n]}$ is identically zero. Also,

$$\lambda_i(\cdot) = \begin{cases} 1, & (s_i(\psi), \mathbf{v}) \in \cdot \\ 0, & \text{otherwise} \end{cases}$$

So $\lambda_i = \delta_{(\varphi,\mathbf{v})}$. Since $\sum_{i \in [n]} \varphi(i)(\mathbf{v}(i) - \mathbf{v}(n)) = 0$ we have that $(\varphi, \mathbf{v}) \in \mathsf{X}$. So $\lambda_i(\mathsf{X}) = \delta_{(\varphi,\mathbf{v})}(\mathsf{X}) = 1$ and λ_i is a probability measure on X.

Case 2: If $|\psi| > \psi(i) = 1$, let $\mathbf{w} \in E^{[n+1]}$ such that $\mathbf{w} = \mathbf{v}$ on $[n]$ and

$$\mathbf{w}(n) = \mathbf{v}(n) - \frac{1}{|\psi| - 1}(\mathbf{v}(i) - \mathbf{v}(n))$$

Then $\lambda_i = \delta_{(s_i(\psi),\mathbf{w})}$. Observe,

$$\begin{aligned}
\sum_{j\in[n]} s_i(\psi)(j)(\mathbf{w}(j)-\mathbf{w}(n)) &= \sum_{j\in[n]\setminus\{i\}} \psi(j)\left(\mathbf{v}(j)-\left(\mathbf{v}(n)-\frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right) \\
&= \sum_{j\in[n]\setminus\{i\}} \psi(j)(\mathbf{v}(j)-\mathbf{v}(n)) + (\mathbf{v}(i)-\mathbf{v}(n)) \\
&= \sum_{j\in[n]} \psi(j)(\mathbf{v}(j)-\mathbf{v}(n)) \\
&= 0
\end{aligned}$$

So $(s_i(\psi),\mathbf{w}) \in \mathsf{X}$, giving $\lambda_i(\mathsf{X}) = \delta_{(s_i(\psi),\mathbf{w})}(\mathsf{X}) = 1$. Thus, λ_i is a probability measure on X.

Case 3: If $\psi(i) = 0$, we examine $(\eta \times I)$. Since η is a probability measure and I is the inclusion kernel, we have that $\eta \times I$ is a probability measure on $E \times E$. We show that $\eta \times I$ is concentrated on the diagonal of $E \times E$.

For $(\mathbf{x},\mathbf{y}) \in E \times E$, notice that

$$(\eta \times I)(\{(\mathbf{x},\mathbf{y})\}) = (\eta \times I)(\{\mathbf{x}\} \times \{\mathbf{y}\}) = \eta(\{\mathbf{x}\} \cap \{\mathbf{y}\})$$

If $(\eta \times I)(\{(\mathbf{x},\mathbf{y})\}) \neq 0$, it must be that $\mathbf{y} = \mathbf{x}$. So single-point sets of nonzero measure must lie on the diagonal of $E \times E$. For some $B \subset E \times E$ we have that

$$(\eta \times I)(B) = (\eta \times I)\Big(\bigcup_{(\mathbf{x},\mathbf{y})\in B} \{(\mathbf{x},\mathbf{y})\}\Big) \leq \sum_{(\mathbf{x},\mathbf{y})\in B} (\eta \times I)(\{(\mathbf{x},\mathbf{y})\})$$

If B contains no points from the diagonal of $E \times E$, then $(\eta \times I)(B) = 0$. So $\eta \times I$ is concentrated on the diagonal of $E \times E$.

Recall that

$$\begin{aligned}
&S^{-1}_{(-\mathbf{v}(n),-(|\psi|+1)\mathbf{v}(n),1,(|\psi|+1)^{-1})} \circ F^{-1}(\cdot) \\
&\qquad = \left\{(\mathbf{x},\mathbf{y}) \in E \times E : \left\{(i,\mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{y}}{|\psi|+1}+\mathbf{v}(n)\right)\right\} \in \cdot\right\}
\end{aligned}$$

Let

$$A := \left\{ \left\{ (i, \mathbf{x}), \left(n, \frac{\mathbf{x} + |\psi| \, \mathbf{v}(n)}{|\psi| + 1} \right) \right\} : \mathbf{x} \in E \right\}$$

Then

$$F_i^{-1}(A) = \big\{ (\mathbf{x}, \mathbf{y}) : \{(i, \mathbf{x}), (n, \mathbf{y})\} \in A \big\} = \left\{ (\mathbf{x}, \mathbf{y}) : \mathbf{y} = \frac{\mathbf{x} + |\psi| \, \mathbf{v}(n)}{|\psi| + 1} \right\}$$

So

$$\begin{aligned}
S^{-1}_{\left(-\mathbf{v}(n), -(|\psi|+1)\mathbf{v}(n), 1, \frac{1}{|\psi|+1}\right)}(F_i^{-1}(A)) &= \left\{ (\mathbf{x}, \mathbf{y}) : \left(\mathbf{x} + \mathbf{v}(n), \frac{\mathbf{y} + (|\psi| + 1)\mathbf{v}(n)}{|\psi| + 1} \right) \in F_i^{-1}(A) \right\} \\
&= \left\{ (\mathbf{x}, \mathbf{y}) : \frac{\mathbf{y} + (|\psi| + 1)\mathbf{v}(n)}{|\psi| + 1} = \frac{\mathbf{x} + \mathbf{v}(n) + |\psi| \, \mathbf{v}(n)}{|\psi| + 1} \right\} \\
&= \left\{ (\mathbf{x}, \mathbf{y}) : \frac{\mathbf{y} + (|\psi| + 1)\mathbf{v}(n)}{|\psi| + 1} = \frac{\mathbf{x} + (|\psi| + 1)\mathbf{v}(n)}{|\psi| + 1} \right\} \\
&= \{ (\mathbf{x}, \mathbf{y}) : \mathbf{y} = \mathbf{x} \}
\end{aligned}$$

So $S^{-1}_{(-\mathbf{v}(n), -(|\psi|+1)\mathbf{v}(n), 1, 1/(|\psi|+1))}(F_i^{-1}(A))$ is precisely the diagonal of $E \times E$. Since $(\eta \times I)$ is concentrated on the diagonal of $E \times E$, it follows that $(\eta \times I) \circ S^{-1}_{(-\mathbf{v}(n), -(|\psi|+1)\mathbf{v}(n), 1, 1/(|\psi|+1))} \circ F_i^{-1}$ is concentrated on A. That is, $\mu^{(\psi, \mathbf{v})}_{\{i,n\}}$ is concentrated on A when $\psi(i) = 0$.

Recall that for $j \neq i$ we have $\mu^{(\psi, \mathbf{v})}_{\{j\}} = \delta_{\mathbf{v}|_{\{j\}}}$. So $\mu^{(\psi, \mathbf{v})}_{\{j\}}$ is a point mass measure. So λ_i is a product of $\mu^{(\psi, \mathbf{v})}_{\{i,n\}}$ and several point mass measures. Therefore, λ_i is a probability measure on $\{0, 1\}^{[n]} \times E^{[n+1]}$. We show that λ_i is a probability measure on X.

Define a set W by

$$W = \big\{ \mathbf{w} \in E^{[n+1]} : \mathbf{w} = \mathbf{v} \text{ on } [n+1] \setminus \{i, n\} \text{ and } \{(i, \mathbf{w}(i)), (n, \mathbf{w}(n))\} \in A \big\}$$

where A is the set defined previously. Then $\mathbf{w}(n) = \frac{1}{|\psi|+1}(\mathbf{w}(i) + |\psi| \, \mathbf{w}(n))$ for $\mathbf{w} \in W$.

Since $\delta_{s_i(\psi)}$ is concentrated on $s_i(\psi)$, $\mu^{(\psi, \mathbf{v})}_{\{j\}}$ is concentrated on $\{(j, \mathbf{v}(j)\}$ for $j \neq i$, and $\mu^{(\psi, \mathbf{v})}_{\{i,n\}}$ is concentrated on A, it follows that λ_i is concentrated on $\big\{ \big(s_i(\psi), \mathbf{w} \big) : \mathbf{w} \in W \big\}$.

We show that $(s_i(\psi), \mathbf{w}) \in \mathsf{X}$ for $\mathbf{w} \in W$. Since $(\psi, \mathbf{v}) \in \mathsf{X}$, we know that

$$\sum_{j \in [n]} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) = 0$$

Additionally, by hypothesis $\psi(i) = 0$. We show that $\sum_{j \in [n]} s_i(\psi)(j)(\mathbf{w}(j) - \mathbf{w}(n)) = 0$. Observe,

$$\begin{aligned}
\sum_{j \in [n]} s_i(\psi)(j)(\mathbf{w}(j) - \mathbf{w}(n)) &= \mathbf{w}(i) - \frac{\mathbf{w}(i) + |\psi|\,\mathbf{v}(n)}{|\psi| + 1} + \sum_{j \in [n]} \psi(j) \left(\mathbf{v}(j) - \frac{\mathbf{w}(i) + |\psi|\,\mathbf{v}(n)}{|\psi| + 1} \right) \\
&= \frac{|\psi|\,\mathbf{w}(i) - |\psi|\,\mathbf{v}(n)}{|\psi| + 1} - \frac{|\psi|\,\mathbf{w}(i)}{|\psi| + 1} + \sum_{j \in [n]} \psi(j) \left(\mathbf{v}(j) - \frac{|\psi|\,\mathbf{v}(n)}{|\psi| + 1} \right) \\
&= -\frac{|\psi|\,\mathbf{v}(n)}{|\psi| + 1} + \sum_{j \in [n]} \psi(j) \left(\mathbf{v}(j) - \frac{|\psi|\,\mathbf{v}(n)}{|\psi| + 1} \right) \\
&= \sum_{j \in [n]} \psi(j) \left(\mathbf{v}(j) - \frac{|\psi|\,\mathbf{v}(n)}{|\psi| + 1} - \frac{\mathbf{v}(n)}{|\psi| + 1} \right) \\
&= \sum_{j \in [n]} \psi(j) \left(\mathbf{v}(j) - \mathbf{v}(n) \right) \\
&= 0
\end{aligned}$$

So $(s_i(\psi), \mathbf{w}) \in \mathsf{X}$ for all $\mathbf{w} \in W$. Thus, $\big\{ \big(s_i(\psi), \mathbf{w}\big) : \mathbf{w} \in W \big\} \subset \mathsf{X}$. Since λ_i is concentrated on a subset of X, it follows that λ_i is a probability measure on X.

In all three cases, λ_i is a probability measure on X. Notice that

$$r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi, \mathbf{v})} = r_i(\psi)\lambda_i$$

So

$$\mu((\psi, \mathbf{v}), \cdot) = \sum_{i \in [n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p \in P_i} \mu_p^{(\psi, \mathbf{v})} \right) = \sum_{i \in [n]} r_i(\psi)\lambda_i$$

Since each λ_i is a probability measure on X and $\sum_{i\in[n]} r_i(\psi) = 1$ we have

$$\mu((\psi, \mathbf{v}), \mathsf{X}) = \sum_{i\in[n]} r_i(\psi)\lambda_i(\mathsf{X}) = \sum_{i\in[n]} r_i(\psi) = 1$$

Since we also know that $r_i(\psi) \geq 0$ for each i, it follows that $\mu((\psi, \mathbf{v}), \cdot)$ is a probability measure on X. Therefore, μ is a probability kernel from X to X.

□

As noted previously, since μ is a probability kernel, it follows that $\alpha = c\mu$ is a kernel. Additionally, since μ is a probability kernel, we can use it as the transition kernel for a discrete-time Markov process.

Proposition 8.2. *For any Borel probability measure ρ on X, there is a discrete-time Markov process Y on X with transition kernel μ such that Y_0 is ρ-distributed.*

Proof. Since ρ is a measure and μ is a probability kernel from X to X, by Theorem 3.4.1 in [6] there is a stochastic process Y on X^∞ that is measurable with respect to $(\mathcal{B}(\mathsf{X}))^\infty$ and a probability measure P_ρ such that $\mathsf{P}_\rho(B)$ is the probability of the set $\{Y \in B\}$ and for each n and $A_i \subset \mathsf{X}$ we have

$$\begin{aligned}&\mathsf{P}_\rho(Y_0 \in A_0, Y_1 \in A_1, \ldots, Y_n \in A_n)\\ &\qquad= \int_{\mathsf{y}_0\in A_0}\int_{\mathsf{y}_1\in A_1}\cdots\int_{\mathsf{y}_{n-1}\in A_{n-1}} \rho(d\mathsf{y}_0)\mu(\mathsf{y}_0, d\mathsf{y}_1)\ldots\mu(\mathsf{y}_{n-1}, A_n)\end{aligned}$$

By the Theorem 3.4.1 in [6], we have that Y is actually a discrete-time Markov process with initial distribution ρ and transition probability kernel μ.

□

Using α as the rate kernel and Y as the jump chain, we now construct our desired continuous-time jump-type Markov process X.

Proposition 8.3. *For every Borel probability measure ρ on X, there is a pure jump-type continuous-time Markov process X on X with rate kernel α such that X_0 is ρ-distributed. If Y is as defined in Proposition 8.2 and (γ_i) is a sequence of i.i.d. exponential random variables with mean 1 that are independent of Y, then X can be defined by the formula $X_t = Y_k$ for $t \in [\tau_k, \tau_{k+1})$, where $\tau_k := \sum_{i=1}^{k}(\gamma_i/c(Y_{i-1}))$.*

Proof. By Proposition 8.1 we know that μ is a kernel from X to X. Notice that $c(\psi, \mathbf{v}) = \theta_d\,|\psi| + \theta_a(n - |\psi|)$ is positive and measurable. Thus, $\alpha = c\mu$ is a kernel from X to X.

For each $i \in [n]$ we know that $s_i(\psi)(i) \neq \psi(i)$. So $\delta_{s_i(\psi)}(\{\psi\}) = 0$. This implies $\mu((\psi, \mathbf{v}), \{(\psi, \mathbf{v})\}) = 0$, giving $\alpha((\psi, \mathbf{v}), \{(\psi, \mathbf{v})\}) = c(\psi, \mathbf{v})\mu((\psi, \mathbf{v}), \{(\psi, \mathbf{v})\}) = 0$ for all $(\psi, \mathbf{v}) \in \mathsf{X}$.

Given a Borel probability measure ρ on X, let Y be as in Proposition 8.2. Let $\gamma = (\gamma_k)$ be a sequence of i.i.d. exponential random variables with mean 1 such that γ and Y are independent. That such a sequence exists is a consequence of the Ionescu Tulcea Theorem (see comment after Theorem 6.17 in [5]).

We show that $\sum_k \gamma_k/c(Y_{k-1}) = \infty$ a.s. Suppose to the contrary that $\sum_k \gamma_k/c(Y_{k-1})$ converges. Notice that $c \leq n(\theta_d + \theta_a)$, so c is bounded. Observe,

$$\sum_{k=1}^{m} \gamma_k = n(\theta_d + \theta_a) \sum_{k=1}^{m} \frac{\gamma_k}{n(\theta_d + \theta_a)} \leq n(\theta_d + \theta_a) \sum_{k=1}^{m} \frac{\gamma_k}{c(Y_{k-1})}$$

Since $\sum_k \gamma_k/c(Y_{k-1})$ converges, so does its sequence of partial sums. Thus, the sequence $\{\sum_{k=1}^{m} \gamma_k\}$ is bounded by a convergent sequence and, therefore, converges. This implies that the partial sums $\sum_{k=1}^{m} \gamma_k$ are bounded by some $M \in \mathbb{R}_+$. So

$$\frac{1}{m} \sum_{k=1}^{m} \gamma_k \leq \frac{1}{m} M \to 0 \quad \text{as } m \to \infty$$

So $\frac{1}{m} \sum_{k=1}^{m} \gamma_k \to \infty$ as $m \to 0$.

Since the γ_k are i.i.d. with mean 1, the Strong Law of Large Numbers gives

$$\frac{1}{m}\sum_{k=1}^{m}\gamma_k \to 1 \quad \text{a.s.}$$

a contradiction.

So it must be that $\sum_k \gamma_k/c(Y_{k-1}) = \infty$ a.s. The desired result now follows from Theorem 12.18 in [5]. □

Because of its significance to our final result, we now formulate and examine the projected process $\hat{X} := \pi \circ X$. Recall that for $(\psi, \mathbf{v}) \in \mathsf{X}$, $\pi((\psi, \mathbf{v})) = |\psi|$ gives the number of attached adhesion sites when the cell has configuration $(\psi, \mathbf{v})$. So $\hat{X}$ counts the number of attached adhesion sites at each stage of the process X. This projected process was discussed in Section 4 using a transition rate matrix. Previously, we assumed $\hat{X}$ is a Markov process, but we now rigorously prove that this is true under our formulation.

Proposition 8.4. *If X is as in Proposition 8.3, then $\hat{X} := \pi \circ X$ is a pure jump-type continuous-time Markov process with rate kernel $\hat{\alpha}$ and initial distribution $\rho \circ \pi^{-1}$.*

Proof. Recall that $\pi : \mathsf{X} \to [n+1]$ is defined by $\pi(\psi, \mathbf{v}) = |\psi|$. Since X has initial distribution ρ, we have that $P(X_0 \in \cdot) = P \circ X_0^{-1} = \rho$. Then

$$P(\hat{X}_0 \in \cdot) = P \circ \hat{X}_0^{-1} = P \circ (\pi \circ X_0)^{-1} = P \circ X_0^{-1} \circ \pi^{-1} = \rho \circ \pi^{-1}$$

So $\hat{X}$ has initial distribution $\rho \circ \pi^{-1}$.

Let Y be as in Proposition 8.2. Since X is as in Proposition 8.3, we have that $X_t = Y_k$ for $t \in [\tau_k, \tau_{k+1})$, where $\tau_k := \sum_{i=1}^{k} \gamma_i/c(Y_{i-1})$.

Let $\hat{Y} = \pi \circ Y$. Notice that

$$c(\psi, \mathbf{v}) = \hat{c}(|\psi|) = \hat{c}(\pi(\psi, \mathbf{v}))$$

So $c(Y_k) = \hat{c}(\pi(Y_k)) = \hat{c}(\hat{Y}_k)$. So we also have $\tau_k = \sum_{i=1}^{k} \gamma_i / \hat{c}(\hat{Y}_{i-1})$. Additionally, for $t \in [\tau_k, \tau_{k+1})$ we get $\hat{X}_t = \pi \circ X_t = \pi \circ Y_k = \hat{Y}_k$.

Notice that

$$\hat{\mu}(i, \{i\}) = \frac{\theta_d i \delta_{i-1}(\{i\}) + \theta_a (n-i)\delta_{i+1}(\{i\})}{\theta_d i + \theta_a (n-i)} = 0$$

So $\hat{\alpha}(i, \{i\}) = \hat{c}(i)\hat{\mu}(i, \{i\}) = 0$ for all $i \in [n+1]$.

From these observations, the desired result will follow from Theorem 12.18 in [5] if $\hat{Y}$ is a discrete-time Markov process with transition kernel $\hat{\mu}$. We use Dynkin's Criterion for discrete-time Markov processes (see Appendix Theorem A.1) to show this is the case.

Note that π is a continuous surjection. Let $\mathbf{z}$ be the zero element of $E^{[n+1]}$ and consider $\mathbf{1}_{[i]} \in \{0,1\}^{[n]}$. Define $g : [n+1] \to \mathsf{X}$ by $g(i) := (\mathbf{1}_{[i]}, \mathbf{z})$. Then g is continuous and

$$(\pi \circ g)(i) = \pi(\mathbf{1}_{[i]}, \mathbf{z}) = \left|\mathbf{1}_{[i]}\right| = i$$

So g is a continuous right-inverse of π.

Now we must show that $\mu((\psi, \mathbf{v}), \pi^{-1}(\hat{A})) = \hat{\mu}(\pi((\psi, \mathbf{v})), \hat{A})$ for all $(\psi, \mathbf{v}) \in \mathsf{X}$ and $\hat{A} \in \mathcal{P}([n+1])$. We first show the result for sets of the form $\{j\}$.

Let

$$J = \{\varphi \in \{0,1\}^{[n]} : (\varphi, \mathbf{w}) \in \mathsf{X} \text{ for some } \mathbf{w} \in E^{[n+1]} \text{ and } |\varphi| = j\}$$

$$W = \{\mathbf{w} \in E^{[n+1]} : (\varphi, \mathbf{w}) \in \mathsf{X} \text{ for some } \varphi \in \{0,1\}^{[n]} \text{ with } |\varphi| = j\}$$

Then $\pi^{-1}(\{j\}) = J \times W$. Notice that for $\psi \in \{0,1\}^{[n]}$,

$$\delta_{s_i(\psi)}(J) = \begin{cases} 0, & \text{if } |s_i(\psi)| \neq j \\ 1, & \text{if } |s_i(\psi)| = j \end{cases}$$
$$= \delta_{|s_i(\psi)|}(\{j\})$$

Since $J \times W \subset \mathsf{X}$, we know that $\bigtimes_{p \in P_i} \mu_p^{(\psi, \mathbf{v})}(W) = 1$ for all $i \in [n]$ and $(\psi, \mathbf{v}) \in \mathsf{X}$. So for $(\psi, \mathbf{v}) \in \mathsf{X}$ we have

$$
\begin{aligned}
\mu((\psi,\mathbf{v}),\pi^{-1}(\{j\})) &= \sum_{i\in[n]} \left(r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes_{p\in P_i} \mu_p^{(\psi,\mathbf{v})} \right) \left(\pi^{-1}(\{j\})\right) \\
&= \sum_{i\in[n]} r_i(\psi)\delta_{|s_i(\psi)|}(\{j\}) \\
&= \sum_{i\in\psi^{-1}(\{1\})} r_i(\psi)\delta_{|s_i(\psi)|}(\{j\}) + \sum_{i\in\psi^{-1}(\{0\})} r_i(\psi)\delta_{|s_i(\psi)|}(\{j\}) \\
&= \sum_{i\in\psi^{-1}(\{1\})} r_i(\psi)\delta_{|\psi|-1}(\{j\}) + \sum_{i\in\psi^{-1}(\{0\})} r_i(\psi)\delta_{|\psi|+1}(\{j\}) \\
&= \sum_{i\in\psi^{-1}(\{1\})} \frac{\theta_d\, \delta_{|\psi|-1}(\{j\})}{\theta_d\,|\psi| + \theta_a(n-|\psi|)} + \sum_{i\in\psi^{-1}(\{0\})} \frac{\theta_a\, \delta_{|\psi|+1}(\{j\})}{\theta_a\,|\psi| + \theta_a(n-|\psi|)} \\
&= \frac{\theta_d\,|\psi|\;\delta_{|\psi|-1}(\{j\}) + \theta_a(n-|\psi|)\delta_{|\psi|+1}(\{j\})}{\theta_a\,|\psi| + \theta_a(n-|\psi|)} \\
&= \hat{\mu}(|\psi|\,,\{j\}) \\
&= \hat{\mu}(\pi(\psi,\mathbf{v}),\{j\})
\end{aligned}
$$

Notice, for $k \in [n+1]$, that δ_k is additive. This implies $\hat{\mu}(|\psi|\,,\cdot)$ is additive. That is, $\hat{\mu}(|\psi|\,,\hat{A}) = \sum_{j\in\hat{A}} \hat{\mu}(|\psi|\,,\{j\})$ for $\hat{A} \in \mathcal{P}([n+1])$. Since $\mu((\psi,\mathbf{v}),\cdot)$ is a measure, it is also additive.

Therefore,

$$
\begin{aligned}
\mu((\psi,\mathbf{v}),\pi^{-1}(\hat{A})) &= \mu\left((\psi,\mathbf{v}),\pi^{-1}\left(\bigcup\nolimits_{j\in\hat{A}}\{j\}\right)\right) \\
&= \mu\left((\psi,\mathbf{v}),\bigcup\nolimits_{j\in\hat{A}}\pi^{-1}(\{j\})\right) \\
&= \sum_{j\in\hat{A}} \mu((\psi,\mathbf{v}),\pi^{-1}(\{j\})) \\
&= \sum_{j\in\hat{A}} \hat{\mu}(\pi(\psi,\mathbf{v}),\{j\}) \\
&= \hat{\mu}\left(\pi(\psi,\mathbf{v}),\bigcup\nolimits_{j\in\hat{A}}\{j\}\right) \\
&= \hat{\mu}(\pi(\psi,\mathbf{v}),\hat{A})
\end{aligned}
$$

Now by Dynkin's Criterion we have that $\hat{\mu}$ is a probability kernel and $\hat{Y}$ is a discrete-time Markov process with transition kernel $\hat{\mu}$. The desired result then follows from Theorem 12.18 in [5].

□

In Section 4, we presented $\hat{X}$ as the Markov process generated by the transition rate matrix Q. In Proposition 8.4, we generate $\hat{X}$ using the rate kernel $\hat{\alpha}$. Since these processes are the same, we want to know how Q and $\hat{\alpha}$ are related. Notice that

$$\hat{\alpha}(i,\{j\}) = \begin{cases} \theta_d i, & \text{if } j = i-1 \\ \theta_a(n-i), & \text{if } j = i+1 \\ 0, & \text{otherwise} \end{cases}$$

giving $\hat{\alpha}(i,\{j\}) = q_{ij}$ for $j \neq i$. These correspondences are due to the fact that both $\hat{\alpha}$ and Q describe the rate at which $\hat{X}$ transitions from one state to another.

By construction, $\hat{Y}$ is the jump chain of $\hat{X}$. Thus, we can prove analogous results to those presented in Section 4. Accordingly, the following result corresponds to Proposition 4.1.

Lemma 8.5. *A Markov chain with transition kernel $\hat{\mu}$ is irreducible.*

Proof. Let $\hat{W}$ be a Markov chain with transition kernel $\hat{\mu}$. Then $P(\hat{W}_1 = j|\hat{W}_0 = i) = \hat{\mu}(i,\{j\})$ for $i,j \in [n+1]$. Let $w_{ij} = \hat{\mu}(i,\{j\})$ and $w_{ij}^{(k)} = P(\hat{W}_k = j|\hat{W}_0 = i)$. Then $\hat{W}$ is irreducible if for each pair $i,j \in [n+1]$ we have $w_{ij}^{(k)} > 0$ for some $k \in \mathbb{N}$. We show this is the case.

Notice that

$$w_{ij} = \hat{\mu}(i,\{j\}) = \begin{cases} \dfrac{\theta_d i}{\theta_d i + \theta_a(n-i)}, & j = i-1 \\ \dfrac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)}, & j = i+1 \\ 0, & \text{otherwise} \end{cases}$$

So $w_{ij} > 0$ if $j \in \{i-1, i+1\}$ and $w_{ij} = 0$ otherwise.

Fix $i, j \in [n+1]$. The Chapman-Kolmogorov relation gives $w_{ij}^{k+\ell} = \sum_m w_{im}^k w_{mj}^\ell$ for $k, \ell \in \mathbb{N}$. If $i > j$, then

$$w_{ij}^{(i-j)} \geq w_{i,i-1} w_{i-1,i-2} \ldots w_{j+1,j} > 0$$

If $i < j$, then

$$w_{ij}^{(j-i)} \geq w_{i,i+1} w_{i+1,i+2} \ldots w_{j-1,j} > 0$$

If $i = j \neq n$, then

$$w_{ii}^{(2)} \geq w_{i,i+1} w_{i+1,i} > 0$$

If $i = j = n$, then

$$w_{ii}^{(2)} \geq w_{i,i-1} w_{i-1,i} > 0$$

So there is some $k \in \mathbb{N}$ such that $w_{ij}^{(k)} > 0$. Therefore $\hat{W}$ is irreducible.

$\square$

Since $\hat{Y}$ has transition kernel $\hat{\mu}$, the preceding result gives that $\hat{Y}$ is irreducible. The following result gives the stationary distribution, or invariant measure, for $\hat{\mu}$. This will be used to derive an invariant measure for $\hat{X}$.

Lemma 8.6. *The measure ω on $\mathcal{P}([n+1])$ given by*

$$\omega = \sum_{k \in [n+1]} \left(\binom{n-1}{k-1} \theta_a^{k-1} \theta_d^{n-k+1} + \binom{n-1}{k} \theta_a^k \theta_d^{n-k} \right) \delta_k$$

is an invariant measure for $\hat{\mu}$.

Proof. First note that for $b < 0$ or $b > a$ we take $\binom{a}{b} := 0$.

For ω to be an invariant measure for $\hat{\mu}$ we need $\int \hat{\mu}(k, B) \omega(dk) = \omega(B)$ for $B \in \mathcal{P}([n+1])$. Letting

$$\omega_k = \binom{n-1}{k-1} \theta_a^{k-1} \theta_d^{n-k+1} + \binom{n-1}{k} \theta_a^k \theta_d^{n-k}$$

we can write $\omega = \sum_{k\in[n+1]} \omega_k \delta_k$. Then $\int \hat{\mu}(k,B)\omega(dk) = \sum_{k=0}^{n} \omega_k \hat{\mu}(k,B)$. Hence, for ω to be invariant for $\hat{\mu}$ we want to show that $\omega = \sum_{k=0}^{n} \omega_k \hat{\mu}(k,\cdot)$. Since $\omega = \sum_{k=0}^{n} \omega_k \delta_k$ and

$$\hat{\mu}(k,\cdot) = \frac{\theta_d k \delta_{k-1} + \theta_a (n-k)\delta_{k+1}}{\theta_d k + \theta_a (n-k)}$$

it is sufficient to show that

$$\sum_{k=0}^{n} \omega_k \delta_k = \sum_{k=0}^{n} \omega_k \frac{\theta_d k \delta_{k-1} + \theta_a (n-k)\delta_{k+1}}{\theta_d k + (n-k)\theta_a} \tag{8.1}$$

The coefficient for δ_0 on the right of (8.1) is

$$\omega_1 \frac{\theta_d}{\theta_d + (n-1)\theta_a} = (\theta_d^n + (n-1)\theta_a \theta_d^{n-1}) \frac{\theta_d}{\theta_d + (n-1)\theta_a} = \theta_d^n = \omega_0$$

which is the coefficient for δ_0 on the left.

For $0 < k < n$, the coefficient for δ_k on the right of (8.1) is

$$\omega_{k-1} \frac{(n-k+1)\theta_a}{(k-1)\theta_d + (n-k+1)\theta_a} + \omega_{k+1} \frac{(k+1)\theta_d}{(k+1)\theta_d + (n-k-1)\theta_a}$$

Observe that

$$\begin{aligned}
\omega_{k-1} \frac{(n-k+1)\theta_a}{(k-1)\theta_d + (n-k+1)\theta_a} &= \frac{\left(\binom{n-1}{k-2}\theta_a^{k-2}\theta_d^{n-k+2} + \binom{n-1}{k-1}\theta_a^{k-1}\theta_d^{n-k+1}\right)(n-k+1)\theta_a}{(k-1)\theta_d + (n-k+1)\theta_a} \\
&= \frac{(n-1)!\theta_a^{k-1}\theta_d^{n-k+1}\left((k-1)\theta_d + (n-k+1)\theta_a\right)(n-k+1)}{(k-1)!\,(n-k+1)!\,((k-1)\theta_d + (n-k+1)\theta_a)} \\
&= \frac{(n-1)!}{(k-1)!\,(n-k)!}\theta_a^{k-1}\theta_d^{n-k+1} \\
&= \binom{n-1}{k-1}\theta_a^{k-1}\theta_d^{n-k+1}
\end{aligned}$$

and

$$
\begin{aligned}
\omega_{k+1}\frac{(k+1)\theta_d}{(k+1)\theta_d+(n-k-1)\theta_a} &= \frac{\left(\binom{n-1}{k}\theta_a^k\theta_d^{n-k}+\binom{n-1}{k+1}\theta_a^{k+1}\theta_d^{n-k-1}\right)\,(k+1)\theta_d}{(k+1)\theta_d+(n-k-1)\theta_a} \\
&= \frac{(n-1)!\theta_a^k\theta_d^{n-k}((k+1)\theta_d+(n-k-1)\theta_a)\,(k+1)}{(k+1)!\,(n-k-1)!((k+1)\theta_d+(n-k-1)\theta_a)} \\
&= \frac{(n-1)!}{k!\,(n-k-1)!}\theta_a^k\theta_d^{n-k} \\
&= \binom{n-1}{k}\theta_a^k\theta_d^{n-k}
\end{aligned}
$$

So for $0<k<n$, the coefficient for δ_k on the right of (8.1) is

$$
\binom{n-1}{k-1}\theta_a^{k-1}\theta_d^{n-k+1}+\binom{n-1}{k}\theta_a^k\theta_d^{n-k}=\omega_k
$$

The coefficient on the right of (8.1) for δ_n is

$$
\begin{aligned}
\omega_{n-1}\frac{\theta_a}{(n-1)\theta_d+\theta_a} &= \frac{((n-1)\theta_a^{n-2}\theta_d^2+\theta_a^{n-1}\theta_d)\theta_a}{(n-1)\theta_d+\theta_a} \\
&= \frac{\theta_a^{n-1}\theta_d((n-1)\theta_d+\theta_a)}{(n-1)\theta_d+\theta_a} \\
&= \theta_a^{n-1}\theta_d \\
&= \omega_n
\end{aligned}
$$

So the coefficient for δ_k on the left side of (8.1) and the coefficient for δ_k on the right side of (8.1) are equal for all $k\in[n+1]$. Thus, ω is an invariant measure for $\hat{\mu}$.

$\square$

Using the previous result, we can derive an invariant measure for $\hat{X}$. The following result is analogous to Proposition 4.3.

Proposition 8.7. *The unique invariant distribution σ for the rate kernel $\hat{\alpha}$ is given by*

$$\sigma := \frac{1}{(\theta_d + \theta_a)^n} \sum_{k \in [n+1]} \binom{n}{k} \theta_d^{n-k} \theta_a^k \delta_k$$

If $\hat{Z}$ is a pure jump-type continuous-time Markov process with rate kernel $\hat{\alpha}$, then the distribution of $\hat{Z}_t$ converges to σ as $t \to \infty$, regardless of the distribution of $\hat{Z}_0$.

Proof. From Lemma 8.6 we know that

$$\omega = \sum_{k \in [n+1]} \left(\binom{n-1}{k-1} \theta_a^{k-1} \theta_d^{n-k+1} + \binom{n-1}{k} \theta_a^k \theta_d^{n-k} \right) \delta_k$$

is an invariant measure for the transition kernel $\hat{\mu}$. Recall that $\hat{c}(k) = k\theta_d + (n-k)\theta_a$. We show that $\hat{c} \cdot \sigma$ is invariant for $\hat{\mu}$, where $(\hat{c} \cdot \sigma)(A) := \int_A \hat{c}\, d\sigma$. To do this, we show that $\hat{c} \cdot \sigma$ is proportional to ω. First notice that

$$(\hat{c} \cdot \sigma)(A) = \int_A \hat{c}\, d\sigma = \int_A \hat{c}(k)\sigma(dk) = \sum_{k \in A} \hat{c}(k)\sigma_k = \sum_{k \in [n+1]} \hat{c}(k)\sigma_k \, \delta_k$$

where we take $\sigma = \sum_{k \in [n+1]} \sigma_k \delta_k$.

We then have

$$\begin{aligned}
\hat{c}(k)\sigma_k &= (k\theta_d + (n-k)\theta_a) \frac{1}{(\theta_a + \theta_d)^n} \binom{n}{k} \theta_d^{n-k} \theta_a^k \\
&= \frac{1}{(\theta_a + \theta_d)^n} \left(\binom{n}{k} k \theta_d^{n-k+1} \theta_a^k + \binom{n}{k} (n-k) \theta_d^{n-k} \theta_a^{k+1} \right) \\
&= \frac{1}{(\theta_a + \theta_d)^n} \left(\frac{n!}{(k-1)!(n-k)!} \theta_d^{n-k+1} \theta_a^k + \frac{n!}{k!(n-k-1)!} \theta_d^{n-k} \theta_a^{k+1} \right) \\
&= \frac{n\theta_a}{(\theta_a + \theta_d)^n} \left(\frac{(n-1)!}{(k-1)!(n-k)!} \theta_a^{k-1} \theta_d^{n-k+1} + \frac{(n-1)!}{k!(n-k-1)!} \theta_a^k \theta_d^{n-k} \right) \\
&= \frac{n\theta_a}{(\theta_a + \theta_d)^n} \left(\binom{n-1}{k-1} \theta_a^{k-1} \theta_d^{n-k+1} + \binom{n-1}{k} \theta_a^k \theta_d^{n-k} \right) \\
&= \frac{n\theta_a}{(\theta_a + \theta_d)^n} \omega_k
\end{aligned}$$

So $\hat{c}(k)\sigma_k$ is proportional to ω_k, with the same proportionality constant for each k. Therefore, $\hat{c}{\cdot}\sigma$ is proportional to ω, which implies $\hat{c}{\cdot}\sigma$ is an invariant measure for $\hat{\mu}$. By Proposition 12.23 of [5], σ is an invariant measure for $\hat{\alpha}$.

Since

$$\sigma([n+1]) = \frac{1}{(\theta_d+\theta_a)^n} \sum_{k\in[n+1]} \binom{n}{k} \theta_d^{n-k}\theta_a^k = 1$$

we have that σ is actually a probability measure, so σ is an invariant distribution corresponding to the rate kernel $\hat{\alpha}$.

By Lemma 8.5 we know that $\hat{\mu}$ is irreducible, which implies $\hat{\alpha}$ is also irreducible. By Proposition 12.25 in [5], it follows that σ is the unique invariant distribution for $\hat{\alpha}$, and it is attracting.

□

Recall from Proposition 4.3 that the row vector ζ with entries

$$\zeta_k = \frac{1}{(\theta_d+\theta_a)^n} \binom{n}{k} \theta_d^{n-k}\theta_a^k, \quad k = 0, 1, \ldots, n$$

is the invariant distribution for the transition matrix Q. We proved in Proposition 8.7 that

$$\sigma = \frac{1}{(\theta_d+\theta_a)^n} \sum_{k\in[n+1]} \binom{n}{k} \theta_d^{n-k}\theta_a^k \delta_k$$

is the invariant distribution for the rate kernel $\hat{\alpha}$. These are related by

$$\sigma(\{k\}) = \frac{1}{(\theta_d+\theta_a)^n} \binom{n}{k} \theta_d^{n-k}\theta_a^k = \zeta_k$$

The following result will be used several times in the proof of Theorem 8.9.

Lemma 8.8. *Suppose $f : \mathsf{X} \to [0,\infty]$ is measurable and $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$. Then*

$$\int_{\mathsf{X}} f(\mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) = \sum_{i \in \psi^{-1}(\{1\})} r_i(\psi) f(s_i(\psi), \mathbf{v})$$
$$+ \sum_{i \in \psi^{-1}(\{0\})} r_i(\psi) \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x} + \mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right) d\eta(\mathbf{x}) \tag{8.2}$$

for $|\psi| \le 1$ and

$$\int_{\mathsf{X}} f(\mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) = \sum_{i \in \psi^{-1}(\{1\})} r_i(\psi) f\left(s_i(\psi), \mathbf{v}|_{[n]} \cup \left\{\left(n, \mathbf{v}(n) - \frac{\mathbf{v}(i) - \mathbf{v}(n)}{|\psi| - 1}\right)\right\}\right)$$
$$+ \sum_{i \in \psi^{-1}(\{0\})} r_i(\psi) \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x} + \mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right) d\eta(\mathbf{x}) \tag{8.3}$$

for $|\psi| > 1$.

Proof. By definition of μ, for $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$ we have

$$\begin{aligned}
\int_{\mathsf{X}} f(\mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) &= \int_{\mathsf{X}} f(\mathsf{y}) \left(\sum_{i\in[n]} r_i(\psi)\delta_{s_i(\psi)} \times \bigtimes\nolimits_{p \in P_i} \mu_p^{(\psi,\mathbf{v})}\right)(d\mathsf{y}) \\
&= \sum_{i\in[n]} r_i(\psi) \int_{\mathsf{X}} f(\mathsf{y}) \left(\delta_{s_i(\psi)} \times \bigtimes\nolimits_{p \in P_i} \mu_p^{(\psi,\mathbf{v})}\right)(d\mathsf{y}) \\
&= \sum_{i\in[n]} r_i(\psi) \int_{E^{[n+1]}} f(s_i(\psi), \mathbf{w}) \left(\bigtimes\nolimits_{p \in P_i} \mu_p^{(\psi,\mathbf{v})}\right)(d\mathbf{w}) \\
&= \sum_{i\in[n]} r_i(\psi) \int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z}) \mu_{\{i,n\}}^{(\psi,\mathbf{v})}(d\mathbf{z})
\end{aligned} \tag{8.4}$$

If $|\psi| = \psi(i) = 1$, then $\mu_{\{i,n\}}^{(\psi,\mathbf{v})} = \delta_{\mathbf{v}|_{\{i,n\}}}$. So

$$\int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z}) \mu_{\{i,n\}}^{(\psi,\mathbf{v})}(d\mathbf{z}) = f(s_i(\psi), \mathbf{v}) \tag{8.5}$$

If $|\psi| > \psi(i) = 1$, then $\mu^{(\psi,\mathbf{v})}_{\{i,n\}} = \delta_{\{(i,\mathbf{v}(i)),(n,\mathbf{v}(n)-(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1))\}}(\mathbf{z})$. This gives

$$\int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z})\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(d\mathbf{z}) = f\left(s_i(\psi), \mathbf{v}|_{[n]} \cup \left\{\left(n, \mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right\}\right) \tag{8.6}$$

If $\psi(i) = 0$, then

$$\mu^{(\psi,\mathbf{v})}_{\{i,n\}} = (\eta \times I)\left(\left\{(\mathbf{x},\mathbf{y}) : \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)\right\} \in \cdot\right\}\right)$$

This gives

$$\begin{aligned}
&\int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z})\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(d\mathbf{z}) \\
&= \int_{E\times E} f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right)(\eta\times I)(d(\mathbf{x},\mathbf{y})) \\
&= \int_E \eta(d\mathbf{x}) \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{y}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right) I(\mathbf{x}, d\mathbf{y}) \\
&= \int_E \eta(d\mathbf{x}) f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right) \\
&= \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right)\eta(d\mathbf{x})
\end{aligned} \tag{8.7}$$

Using equations (8.5) and (8.7), we have that for $|\psi| \le 1$,

$$\begin{aligned}
\sum_{i\in[n]} r_i(\psi) \int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z})\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(d\mathbf{z}) = \sum_{i\in\psi^{-1}(\{1\})} r_i(\psi) f(s_i(\psi), \mathbf{v}) \\
+ \sum_{i\in\psi^{-1}(\{0\})} r_i(\psi) \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{1}{|\psi|+1}\mathbf{x} + \mathbf{v}(n)\right)\right\}\right) \eta(d\mathbf{x})
\end{aligned} \tag{8.8}$$

Equation (8.2) now follows from equations (8.4) and (8.8). From equations (8.6) and (8.7) we find that

$$\begin{aligned}
&\sum_{i\in[n]} r_i(\psi) \int_{E^{\{i,n\}}} f(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \mathbf{z})\mu^{(\psi,\mathbf{v})}_{\{i,n\}}(d\mathbf{z}) \\
&= \sum_{i\in\psi^{-1}(\{1\})} r_i(\psi) f\left(s_i(\psi), \mathbf{v}|_{[n]} \cup \left\{\left(n, \mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right\}\right) \\
&+ \sum_{i\in\psi^{-1}(\{0\})} r_i(\psi) \int_E f\left(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x}+\mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}\right) \eta(d\mathbf{x})
\end{aligned} \tag{8.9}$$

Combining equations (8.4) and (8.9) gives equation (8.3).

□

We now proceed to our main result. In it, we prove a formula for the time derivative of the expected value of the centroid location. That is, we prove a formula that gives the rate of change of the expected location of the centroid over time.

Theorem 8.9. *For each $i \in [n+1]$, let $f_i : \mathsf{X} \to E$ be defined by $f_i(\psi, \mathbf{v}) := \mathbf{v}(i)$. Let σ be as in Proposition 8.7 and let ρ be a distribution on X such that $\sigma = \rho \circ \pi^{-1}$ and such that f_i is ρ-integrable for every i. Let X be as in Proposition 8.3. Let $\|\cdot\|$ be the ∞-norm in E, and assume η is supported on $\{\mathbf{x} \in E : \|\mathbf{x}\| \leq R\}$ for some $R > 0$. Then for every $i \in [n+1]$ and $t \geq 0$, $\mathbb{E}(f_i(X_t))$ is well-defined and finite, and*

$$\frac{\partial}{\partial t^+}\mathbb{E}(f_n(X_t)) = \frac{\bar{\eta}\theta_d}{(\theta_d+\theta_a)^n}((\theta_d+\theta_a)^n - \theta_d^n), \tag{8.10}$$

where $\partial/\partial t^+$ denotes the right-hand derivative and $\bar{\eta} := \int_E \mathbf{x}\, d\eta(\mathbf{x})$.

Proof. Define $g : \mathsf{X} \to [0,\infty)$ by the formula $g(\mathsf{x}) = \max\{\|f_i(\mathsf{x})\| : i \in [n+1]\}$. Let $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$. We use Lemma 8.8 on $\mathbf{1}_{\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\leq R\}}$ to find $\mu(\mathsf{x}, \{\mathsf{y} : g(\mathsf{y}) - g(\mathsf{x}) \leq R\})$.

If $|\psi| > 1$, then for $i \in \psi^{-1}(\{1\})$, we know that

$$\sum_{j\in[n]} s_i(\psi)(j)\left(\mathbf{v}(j) - \left(\mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right) = 0$$

So

$$-(|\psi|-1)\left(\mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right) + \sum_{j\in[n]} s_i(\psi)(j)\mathbf{v}(j) = 0$$

and

$$\mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1} = \sum_{j\in[n]} \frac{s_i(\psi)(j)}{|\psi|-1}\mathbf{v}(j)$$

Since $\frac{s_i(\psi)(j)}{|\psi|-1} \geq 0$ for each $j \in [n]$ and $\sum_{j\in[n]} \frac{s_i(\psi)(j)}{|\psi|-1} = 1$, we have that $\mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}$ is in the convex hull of $\{\mathbf{v}(j) : j \in [n]\}$. Therefore,

$$\left\|\mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right\| \leq \max\{\|\mathbf{v}(j)\| : j \in [n]\}$$

so that

$$g\left(s_i(\psi), \mathbf{v}|_{[n]} \cup \left\{\left(n, \mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\right)\right\}\right) = \max\{\|\mathbf{v}(j)\| : j \in [n]\}$$

Notice that since $\mathsf{x} \in \mathsf{X}$, we know that $\sum_{j\in[n]} \psi(j)(\mathbf{v}(j) - \mathbf{v}(n)) = 0$. Isolating $\mathbf{v}(n)$ gives $\mathbf{v}(n) = \sum_{j\in[n]} \frac{\psi(j)}{|\psi|}\mathbf{v}(j)$. This means $\mathbf{v}(n)$ is in the convex hull of $\{\mathbf{v}(j) : j \in [n]\}$, giving

$$\|\mathbf{v}(n)\| \leq \max\{\|\mathbf{v}(j)\| : j \in [n]\}$$

Thus, if $g(\mathsf{x}) = \|\mathbf{v}(n)\|$, then there is some $j_0 \in [n]$ such that $g(\mathsf{x}) = \|\mathbf{v}(j_0)\|$. Hence,

$$g\Big(s_i(\psi), \mathbf{v}|_{[n]} \cup \Big\{\Big(n, \mathbf{v}(n) - \frac{\mathbf{v}(i)-\mathbf{v}(n)}{|\psi|-1}\Big)\Big\}\Big) = g(\mathsf{x})$$

so

$$g\Big(s_i(\psi), \mathbf{v}|_{[n]} \cup \Big\{\Big(n, \mathbf{v}(n) - \frac{\mathbf{v}(i) - \mathbf{v}(n)}{|\psi| - 1}\Big)\Big\}\Big) - g(\mathsf{x}) = 0 < R$$

and

$$\mathbf{1}_{\{\mathsf{y}: g(\mathsf{y}) - g(\mathsf{x}) \le R\}}\Big(s_i(\psi), \mathbf{v}|_{[n]} \cup \Big\{\Big(n, \mathbf{v}(n) - \frac{\mathbf{v}(i) - \mathbf{v}(n)}{|\psi| - 1}\Big)\Big\}\Big) = 1 \tag{8.11}$$

If $|\psi| \le 1$, then

$$g(s_i(\psi, \mathbf{v})) = \max\{\|\mathbf{v}(j)\| : j \in [n+1]\} = g(\mathsf{x})$$

which gives

$$\mathbf{1}_{\{\mathsf{y}: g(\mathsf{y}) - g(\mathsf{x}) \le R\}}(s_i(\psi), \mathbf{v}) = 1 \tag{8.12}$$

In either case, for $\mathbf{x} \in E$

$$\|\mathbf{x} + \mathbf{v}(n)\| - g(\mathsf{x}) \le \|\mathbf{x}\| + \|\mathbf{v}(n)\| - g(\mathsf{x}) \le \|\mathbf{x}\|$$

and

$$\left\|\frac{\mathbf{x}}{|\psi| + 1} + \mathbf{v}(n)\right\| - g(\mathsf{x}) \le \left\|\frac{\mathbf{x}}{|\psi| + 1}\right\| + \|\mathbf{v}(n)\| - g(\mathsf{x}) \le \left\|\frac{\mathbf{x}}{|\psi| + 1}\right\| \le \|\mathbf{x}\|$$

So

$$g\Big(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \Big\{(i, \mathbf{x} + \mathbf{v}(n)), \Big(n, \frac{\mathbf{x}}{|\psi| + 1} + \mathbf{v}(n)\Big)\Big\}\Big) - g(\mathsf{x}) \le R$$

if $\|\mathbf{x}\| \le R$. Therefore

$$\begin{aligned}\int_E \mathbf{1}_{\{\mathsf{y}: g(\mathsf{y}) - g(\mathsf{x}) \le R\}}\Big(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \Big\{(i, \mathbf{x} + \mathbf{v}(n)), \Big(n, \frac{\mathbf{x}}{|\psi| + 1} + \mathbf{v}(n)\Big)\Big\}\Big)\eta(d\mathbf{x}) \\ \ge \int_E \mathbf{1}_{\{\mathbf{x} \in E: \|\mathbf{x}\| \le R\}}\eta(d\mathbf{x})\end{aligned}$$

Notice that

$$\int_E \mathbf{1}_{\{\mathbf{x} \in E: \|\mathbf{x}\| \le R\}}\eta(d\mathbf{x}) = \eta(\{\mathbf{x} \in E : \|\mathbf{x}\| \le R\}) = 1$$

Hence,

$$\int_E \mathbf{1}_{\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\}}\Big(s_i(\psi),\mathbf{v}|_{[n+1]\setminus\{i,n\}}\cup\Big\{(i,\mathbf{x}+\mathbf{v}(n)),\Big(n,\frac{\mathbf{x}}{|\psi|+1}+\mathbf{v}(n)\Big)\Big\}\Big)\eta(d\mathbf{x})\ge 1 \quad (8.13)$$

By Lemma 8.8 with $\mathbf{1}_{\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\}}$ and using equations (8.11), (8.12), and (8.13), we find that

$$\begin{aligned}
\mu(\mathsf{x},\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\}) &= \int_{\mathsf{y}\in\mathsf{X}} \mathbf{1}_{\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\}}(\mathsf{y})\mu(\mathsf{x},d\mathsf{y})\\
&\ge \sum_{i\in\psi^{-1}(\{1\})} r_i(\psi)+\sum_{i\in\psi^{-1}(\{0\})} r_i(\psi)\\
&= \sum_{j\in[n]} r_i(\psi)\\
&= 1
\end{aligned}$$

However, we know that μ is a probability measure, so $\mu(\mathsf{x},\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\})\le 1$. Thus,

$$\mu(\mathsf{x},\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\})=1 \tag{8.14}$$

Let Y be as in Proposition 8.2, fix a whole number k, and let λ be the distribution of Y_k. By Proposition 8.2 in [5], the distribution of (Y_k,Y_{k+1}) is $\lambda\times\mu$, so equation (8.14) implies

$$\begin{aligned}
\mathbb{P}(g(Y_{k+1})-g(Y_k)\le R) &= (\lambda\times\mu)\big(\{(\mathsf{x},\mathsf{y})\in\mathsf{X}\times\mathsf{X}:g(\mathsf{y})-g(\mathsf{x})\le R\}\big)\\
&= \int_{\mathsf{x}\in\mathsf{X}}\lambda(d\mathsf{x})\mu(\mathsf{x},\{\mathsf{y}:g(\mathsf{y})-g(\mathsf{x})\le R\})\\
&= \int_{\mathsf{x}\in\mathsf{X}}\lambda(d\mathsf{x})\\
&= 1
\end{aligned}$$

This means $g(Y_{k+1})\le g(Y_k)+R$ almost surely. By induction, it follows that for every whole number k

$$g(Y_k) \leq g(Y_0) + kR \tag{8.15}$$

almost surely.

We now show that $\mathbb{E}(f_i(X_t))$ is well-defined and finite for all $i \in [n+1]$ and $t \geq 0$. Fix $t \geq 0$. Equation (8.15) implies

$$\begin{aligned}
\mathbb{E}(g(X_t)) &= \sum_{k=0}^{\infty} \mathbb{E}(g(X_t)|t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})) \\
&= \sum_{k=0}^{\infty} \mathbb{E}(g(Y_k)|t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})) \\
&\leq \sum_{k=0}^{\infty} \mathbb{E}(g(Y_0) + kR|t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})) \\
&= \sum_{k=0}^{\infty} \mathbb{E}(g(Y_0)|t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})) + R\sum_{k=0}^{\infty} k\mathbb{P}(t \in [\tau_k, \tau_{k+1})) \\
&= \mathbb{E}(g(Y_0)) + R\sum_{k=0}^{\infty} k\mathbb{P}(t \in [\tau_k, \tau_{k+1})) \\
&\leq \mathbb{E}(g(Y_0)) + R\sum_{k=0}^{\infty} k\mathbb{P}(t \geq \tau_k) \\
&= \mathbb{E}(g(X_0)) + R\sum_{k=0}^{\infty} k\mathbb{P}(t \geq \tau_k) \qquad (8.16)
\end{aligned}$$

By hypothesis, each f_i is ρ-integrable, giving $\int_{\mathsf{X}} \|f_i\| \, d\rho < \infty$ for each $i \in [n+1]$. Since X_0 is ρ-distributed, we see that

$$\mathbb{E}(g(X_0)) = \int_{\mathsf{X}} g \, d\rho < \infty$$

since $g(\mathsf{x}) = \max\{\|f_i(\mathsf{x})\| : i \in [n+1]\}$. Additionally, notice that

$$c(i) = i\theta_d + (n-i)\theta_a \leq i\theta + (n-i)\theta = n\theta$$

where $\theta = \max\{\theta_a, \theta_d\}$. So

$$\tau_k = \sum_{j=1}^{k} \frac{\gamma_j}{c(Y_{j-1})} \geq \sum_{j=1}^{k} \frac{\gamma_j}{n\theta}$$

Furthermore, since $\gamma_1, \ldots, \gamma_k$ are i.i.d. exponential random variables with mean 1, we know that γ_j has density function $x \mapsto e^{-x}$. So $\sum_{j=1}^{k} \gamma_j$ has density function $x \mapsto \frac{e^{-x}x^{k-1}}{\Gamma(k)} = \frac{e^{-x}x^{k-1}}{(k-1)!}$. Therefore, equation (8.16) implies

$$\begin{aligned}
\mathbb{E}(g(X_t)) &\leq \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} k\mathbb{P}(t \geq \tau_k) \\
&= \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} k\mathbb{P}\big(t \geq \frac{1}{n\theta}\sum_{j=1}^{k}\gamma_j\big) \\
&= \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} k\int_0^{tn\theta} \frac{e^{-x}x^{k-1}}{(k-1)!}\,dx \\
&\leq \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} k\int_0^{tn\theta} \frac{x^{k-1}}{(k-1)!}\,dx \\
&= \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} k\frac{(tn\theta)^k}{k!} \\
&= \mathbb{E}(g(X_0)) + R\sum_{k=1}^{\infty} \frac{(tn\theta)^k}{(k-1)!} \\
&= \mathbb{E}(g(X_0)) + Rtn\theta\sum_{k=0}^{\infty} \frac{(tn\theta)^k}{k!} \\
&= \mathbb{E}(g(X_0)) + Rtn\theta e^{tn\theta} \\
&< \infty
\end{aligned}$$

Since $\mathbb{E}(g(X_t)) < \infty$ and $g(X_t) \geq f_i(X_t)$, we have $\mathbb{E}(f_i(X_t)) < \infty$ for all $i \in [n+1]$. Varying t gives that $\mathbb{E}(f_i(X_t))$ is well-defined and finite for all $i \in [n+1]$ and $t \geq 0$.

Suppose ν_t is the distribution of X_t and $\hat{X}$ is as in Proposition 8.4. Since X_0 is ρ-distributed and $\sigma = \rho \circ \pi^{-1}$, we have that $\hat{X}_0$ is σ-distributed. By Proposition 8.7, we know that σ is an invariant distribution for $\hat{X}$, so it must be that $\hat{X}_t$ is also σ-distributed for all $t \geq 0$. Thus, $\sigma = \nu_t \circ \pi^{-1}$ for all $t \geq 0$. We now have that each ν_t satisfies the hypothesis for ρ. Since X is time-homogeneous, we could, in essence, restart the process at each time t

and expect the same behavior. Therefore, (8.10) holds for all $t \geq 0$ if it holds when $t = 0$. We show this is the case.

Given $(i, j) \in [n+1] \times [n+1]$, recall that (Y_0, Y_1) is $(\rho \times \mu)$-distributed. Therefore,

$$\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = j) = (\rho \times \mu)(\pi^{-1}(\{i\}) \times \pi^{-1}(\{j\})) = \int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \int_{\pi^{-1}(\{j\})} \mu(\mathsf{x}, d\mathsf{y}) \tag{8.17}$$

If $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$, then for $\ell \in [n]$ and $\mathbf{w} \in E^{[n+1]}$,

$$\mathbf{1}_{\pi^{-1}(\{j\})}(s_\ell(\psi), \mathbf{w}) = \mathbf{1}_{\{j\}}(\pi(s_\ell(\psi), \mathbf{w})) = \mathbf{1}_{\{j\}}(|s_\ell(\psi)|)$$

Letting $\mathbf{w} = \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \left\{(i, \mathbf{x} + \mathbf{v}(n)), \left(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\right)\right\}$ for $\mathbf{x} \in E$ gives

$$\int_E \mathbf{1}_{\pi^{-1}(\{j\})}(s_\ell(\psi), \mathbf{w}) d\eta(\mathbf{x}) = \int_E \mathbf{1}_{\{j\}}(|s_\ell(\psi)|) d\eta(\mathbf{x}) = \mathbf{1}_{\{j\}}(|s_\ell(\psi)|)\eta(E) = \mathbf{1}_{\{j\}}(|s_\ell(\psi)|)$$

Using Lemma 8.8 with $\mathbf{1}_{\pi^{-1}(\{j\})}$ gives

$$\begin{aligned}
\int_{\pi^{-1}(\{j\})} \mu(\mathsf{x}, d\mathsf{y}) &= \int_{\mathsf{X}} \mathbf{1}_{\pi^{-1}(\{j\})}(\mathsf{y}) \mu(\mathsf{x}, d\mathsf{y}) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} r_\ell(\psi) \mathbf{1}_{\{j\}}(|s_\ell(\psi)|) + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi) \mathbf{1}_{\{j\}}(|s_\ell(\psi)|) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} r_\ell(\psi) \mathbf{1}_{\{j+1\}}(|\psi|) + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi) \mathbf{1}_{\{j-1\}}(|\psi|) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} \frac{\theta_d \, \mathbf{1}_{\{j+1\}}(|\psi|)}{\theta_d \, |\psi| + \theta_a(n - |\psi|)} + \sum_{\ell \in \psi^{-1}(\{0\})} \frac{\theta_a \, \mathbf{1}_{\{j-1\}}(|\psi|)}{\theta_d \, |\psi| + \theta_a(n - |\psi|)} \\
&= \frac{|\psi| \, \theta_d \, \mathbf{1}_{\{j+1\}}(|\psi|)}{\theta_d \, |\psi| + \theta_a(n - |\psi|)} + \frac{(n - |\psi|)\theta_a \, \mathbf{1}_{\{j-1\}}(|\psi|)}{\theta_d \, |\psi| + \theta_a(n - |\psi|)} \\
&= \frac{(j+1)\theta_d \, \mathbf{1}_{\pi^{-1}(\{j+1\})}(\mathsf{x})}{\theta_d(j+1) + \theta_a(n - (j+1))} + \frac{(n - (j-1))\theta_a \, \mathbf{1}_{\pi^{-1}(\{j-1\})}(\mathsf{x})}{\theta_d(j-1) + \theta_a(n - (j-1))}
\end{aligned}$$

Since $\sigma = \rho \circ \pi^{-1}$ it follows that

$$\begin{aligned}
&\int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \int_{\pi^{-1}(\{j\})} \mu(\mathsf{x}, d\mathsf{y}) \\
&= \int_{\pi^{-1}(\{i\})} \left(\frac{(j+1)\theta_d \, \mathbf{1}_{\pi^{-1}(\{j+1\})}(\mathsf{x})}{\theta_d(j+1) + \theta_a(n-(j+1))} + \frac{(n-(j-1))\theta_a \, \mathbf{1}_{\pi^{-1}(\{j-1\})}(\mathsf{x})}{\theta_d(j-1) + \theta_a(n-(j-1))} \right) \rho(d\mathsf{x}) \\
&= \frac{(j+1)\theta_d \ \rho(\pi^{-1}(\{j+1\}) \cap \pi^{-1}(\{i\}))}{\theta_d(j+1) + \theta_a(n-(j+1))} + \frac{(n-(j-1))\theta_a \ \rho(\pi^{-1}(\{j-1\}) \cap \pi^{-1}(\{i\}))}{\theta_d(j-1) + \theta_a(n-(j-1))} \\
&= \frac{(j+1)\theta_d \ (\rho \circ \pi^{-1})(\{j+1\} \cap \{i\})}{\theta_d(j+1) + \theta_a(n-(j+1))} + \frac{(n-(j-1))\theta_a \ (\rho \circ \pi^{-1})(\{j-1\} \cap \{i\})}{\theta_d(j-1) + \theta_a(n-(j-1))} \\
&= \frac{(j+1)\theta_d \ \sigma(\{j+1\} \cap \{i\})}{\theta_d(j+1) + \theta_a(n-(j+1))} + \frac{(n-(j-1))\theta_a \ \sigma(\{j-1\} \cap \{i\})}{\theta_d(j-1) + \theta_a(n-(j-1))} \\
&= \begin{cases} \dfrac{i\theta_d}{\theta_d i + \theta_a(n-i)} \sigma(\{i\}), & \text{if } i = j+1 \\ \dfrac{(n-i)\theta_a}{\theta_d i + \theta_a(n-i)} \sigma(\{i\}), & \text{if } i = j-1 \\ 0, & \text{otherwise} \end{cases}
\end{aligned}$$

Combining this with equation (8.17) gives

$$\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = j) = \begin{cases} \dfrac{i\theta_d}{\theta_d i + \theta_a(n-i)} \sigma(\{i\}), & \text{if } i = j+1 \\ \dfrac{(n-i)\theta_a}{\theta_d i + \theta_a(n-i)} \sigma(\{i\}), & \text{if } i = j-1 \\ 0 & \text{otherwise} \end{cases} \tag{8.18}$$

Define $h : \mathsf{X} \times \mathsf{X} \to E^{[n+1]}$ by $h(\mathsf{x}, \mathsf{y}) = f_n(\mathsf{y}) - f_n(\mathsf{x})$. Letting $J_i = \{i-1, i+1\} \cap [n+1]$, we then have that

$$\begin{aligned}
\mathbb{E}(f_n(X_t) - f_n(X_0)) &= \mathbb{E}(h(X_0, X_t)) \\
&= \sum_{i \in [n+1]} \sum_{j \in J_i} \mathbb{E}(h(X_0, X_t) | \pi(Y_0) = i, \pi(Y_1) = j) \mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = j)
\end{aligned} \tag{8.19}$$

Conditioning further gives

$$
\begin{aligned}
&\mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = j) \\
&= \sum_{k=0}^{\infty} \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&= \sum_{k=0}^{\infty} \mathbb{E}(h(Y_0, Y_k)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&= \sum_{k=2}^{\infty} \mathbb{E}(h(Y_0, Y_k)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\quad + \mathbb{E}(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_1, \tau_2))\mathbb{P}(t \in [\tau_1, \tau_2)|\pi(Y_0) = i, \pi(Y_1) = j) \qquad (8.20)
\end{aligned}
$$

We first compute the last term in equation (8.20) and then estimate the sum preceding it.

By construction, $\tau_1 = \frac{\gamma_1}{c(Y_0)}$ and $\tau_2 = \frac{\gamma_1}{c(Y_0)} + \frac{\gamma_2}{c(Y_1)}$. If $\pi(Y_0) = i$ and $\pi(Y_1) = j$, then $c(Y_0) = \hat{c}(\pi(Y_0)) = \hat{c}(i)$ and $c(Y_1) = \hat{c}(\pi(Y_1)) = \hat{c}(j)$. Since Y is independent of $\gamma_1, \gamma_2, \ldots$ we then find that

$$
\begin{aligned}
&\mathbb{E}(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_1, \tau_2)) \\
&\quad = \mathbb{E}\left(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j, \frac{\gamma_1}{c(Y_0)} \le t < \frac{\gamma_1}{c(Y_0)} + \frac{\gamma_2}{c(Y_1)}\right) \\
&\quad = \mathbb{E}\left(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j, \frac{\gamma_1}{\hat{c}(i)} \le t < \frac{\gamma_1}{\hat{c}(i)} + \frac{\gamma_2}{\hat{c}(j)}\right) \\
&\quad = \mathbb{E}(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j) \qquad (8.21)
\end{aligned}
$$

Because (Y_0, Y_1) is $(\rho \times \mu)$-distributed, we have

$$
\begin{aligned}
&\mathbb{E}(h(Y_0, Y_1)|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\quad = (\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = j))^{-1} \int_{\pi^{-1}(\{i\}) \times \pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y})\, d(\rho \times \mu)(\mathsf{x}, \mathsf{y}) \\
&\quad = (\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = j))^{-1} \int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \int_{\pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y}) \mu(\mathsf{x}, d\mathsf{y}) \qquad (8.22)
\end{aligned}
$$

For $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$, we know that

$$0 = \sum_{\ell \in [n]} \psi(\ell)(\mathbf{v}(\ell) - \mathbf{v}(n)) = \sum_{\ell \in \psi^{-1}(\{1\})} (\mathbf{v}(\ell) - \mathbf{v}(n))$$

If $|\psi| > 1$ then by Lemma 8.8 with $h(\mathsf{x}, \mathsf{y})\mathbf{1}_{\pi^{-1}(\{j\})}$ and by the previous statement,

$$\begin{aligned}
&\int_{\pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) = \int_{\mathsf{X}} h(\mathsf{x}, \mathsf{y})\mathbf{1}_{\pi^{-1}(\{j\})}\mu(\mathsf{x}, d\mathsf{y}) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} r_\ell(\psi)\left(\left(\mathbf{v}(n) - \frac{\mathbf{v}(\ell) - \mathbf{v}(n)}{|\psi| - 1}\right) - \mathbf{v}(n)\right)\mathbf{1}_{\{j\}}(|s_\ell(\psi)|) \\
&\qquad\qquad + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi)\int_E \left(\left(\frac{\mathbf{x}}{|\psi| + 1} + \mathbf{v}(n)\right) - \mathbf{v}(n)\right)\mathbf{1}_{\{j\}}(|s_\ell(\psi)|)\,d\eta(\mathbf{x}) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} r_\ell(\psi)\left(-\frac{\mathbf{v}(\ell) - \mathbf{v}(n)}{|\psi| - 1}\right)\mathbf{1}_{\{j+1\}}(|\psi|) + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi)\frac{\mathbf{1}_{\{j-1\}}(|\psi|)}{|\psi| + 1}\int_E \mathbf{x}\,d\eta(\mathbf{x}) \\
&= -\frac{\theta_d}{\theta_d\,|\psi| + \theta_a(n - |\psi|)}\frac{\mathbf{1}_{\{j+1\}}(|\psi|)}{|\psi| - 1}\sum_{\ell \in \psi^{-1}(\{1\})}(\mathbf{v}(\ell) - \mathbf{v}(n)) + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi)\frac{\mathbf{1}_{\{j-1\}}(|\psi|)}{|\psi| + 1}\bar{\eta} \\
&= 0 + \frac{(n - |\psi|)\theta_a}{\theta_d\,|\psi| + \theta_a(n - |\psi|)}\mathbf{1}_{\{j-1\}}(|\psi|)\,\frac{\bar{\eta}}{|\psi| + 1} \\
&= \frac{(n - \pi(\mathsf{x}))\theta_a}{\theta_d\pi(\mathsf{x}) + \theta_a(n - \pi(\mathsf{x}))}\mathbf{1}_{\{j-1\}}(\pi(\mathsf{x}))\,\frac{\bar{\eta}}{j}
\end{aligned}$$

If $|\psi| \leq 1$, then

$$\begin{aligned}
&\int_{\pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) = \int_{\mathsf{X}} h(\mathsf{x}, \mathsf{y})\mathbf{1}_{\pi^{-1}(\{j\})}\mu(\mathsf{x}, d\mathsf{y}) \\
&= \sum_{\ell \in \psi^{-1}(\{1\})} r_\ell(\psi)((\mathbf{v}(n) - \mathbf{v}(n))\mathbf{1}_{\{j\}}(|s_\ell(\psi)|) \\
&\qquad\qquad + \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi)\int_E \left(\left(\frac{\mathbf{x}}{|\psi| + 1} + \mathbf{v}(n)\right) - \mathbf{v}(n)\right)\mathbf{1}_{\{j\}}(|s_\ell(\psi)|)\,d\eta(\mathbf{x}) \\
&= \sum_{\ell \in \psi^{-1}(\{0\})} r_\ell(\psi)\frac{\mathbf{1}_{\{j-1\}}(|\psi|)}{|\psi| + 1}\int_E \mathbf{x}\,d\eta(\mathbf{x}) \\
&= \frac{(n - |\psi|)\theta_a}{\theta_d\,|\psi| + \theta_a(n - |\psi|)}\mathbf{1}_{\{j-1\}}(|\psi|)\,\frac{\bar{\eta}}{|\psi| + 1} \\
&= \frac{(n - \pi(\mathsf{x}))\theta_a}{\theta_d\pi(\mathsf{x}) + \theta_a(n - \pi(\mathsf{x}))}\mathbf{1}_{\{j-1\}}(\pi(\mathsf{x}))\,\frac{\bar{\eta}}{j}
\end{aligned}$$

So

$$\int_{\pi^{-1}(\{j\})} h(\mathsf{x},\mathsf{y})\mu(\mathsf{x},d\mathsf{y}) = \frac{(n-\pi(\mathsf{x}))\theta_a}{\theta_d\pi(\mathsf{x})+\theta_a(n-\pi(\mathsf{x}))}\,\mathbf{1}_{\{j-1\}}(\pi(\mathsf{x}))\,\frac{\bar{\eta}}{j} \tag{8.23}$$

Using equation (8.23), we then find that

$$\begin{aligned}
&\int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \int_{\pi^{-1}(\{j\})} h(\mathsf{x},\mathsf{y})\mu(\mathsf{x},d\mathsf{y}) \\
&\qquad = \int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x})\frac{(n-\pi(\mathsf{x}))\theta_a}{\theta_d\pi(\mathsf{x})+\theta_a(n-\pi(\mathsf{x}))}\,\mathbf{1}_{\{j-1\}}(\pi(\mathsf{x}))\,\frac{\bar{\eta}}{j} \\
&\qquad = \begin{cases} \rho(\pi^{-1}(\{i\}))\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\,\dfrac{\bar{\eta}}{i+1}, & \text{if } i=j-1 \\ 0, & \text{otherwise} \end{cases} \\
&\qquad = \begin{cases} \sigma(\{i\})\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\,\dfrac{\bar{\eta}}{i+1}, & \text{if } i=j-1 \\ 0, & \text{otherwise} \end{cases}
\end{aligned}$$

Plugging this into equation (8.22) and using equation (8.18) gives

$$\begin{aligned}
&\mathbb{E}(h(Y_0,Y_1)|\pi(Y_0)=i,\pi(Y_1)=j) \\
&\quad = \begin{cases} (\mathbb{P}(\pi(Y_0)=i,\pi(Y_1)=j))^{-1}\sigma(\{i\})\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\,\dfrac{\bar{\eta}}{i+1}, & \text{if } i=j-1 \\ 0, & \text{if } i=j+1 \end{cases} \\
&\quad = \begin{cases} \dfrac{\theta_d i+\theta_a(n-i)}{(n-i)\theta_a\sigma(\{i\})}\sigma(\{i\})\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\,\dfrac{\bar{\eta}}{i+1}, & \text{if } j=i+1 \\ 0, & \text{if } j=i-1 \end{cases} \\
&\quad = \begin{cases} \dfrac{\bar{\eta}}{i+1}, & \text{if } j=i+1 \\ 0, & \text{if } j=i-1 \end{cases}
\end{aligned} \tag{8.24}$$

Combining equations (8.21) and (8.24) gives

$$\mathbb{E}(h(Y_0,Y_1)|\pi(Y_0)=i,\pi(Y_1)=j,t\in[\tau_1,\tau_2)) = \begin{cases} \dfrac{\bar{\eta}}{i+1}, & \text{if } j=i+1 \\ 0, & \text{if } j=i-1 \end{cases} \tag{8.25}$$

Because $\gamma_1,\gamma_2,\ldots$ are i.i.d. exponentially distributed with mean 1 and are independent of Y, for $j = i \pm 1$ we have

$$
\begin{aligned}
\mathbb{P}(t \in [\tau_1, \tau_2) | \pi(Y_0) = i, \pi(Y_1) = j) &= \mathbb{P}\left(\frac{\gamma_1}{c(Y_0)} \leq t < \frac{\gamma_1}{c(Y_0)} + \frac{\gamma_2}{c(Y_1)} |, \pi(Y_0) = i, \pi(Y_1) = j \right) \\
&= \mathbb{P}\left(\frac{\gamma_1}{\hat{c}(i)} \leq t < \frac{\gamma_1}{\hat{c}(i)} + \frac{\gamma_2}{\hat{c}(j)} | \pi(Y_0) = i, \pi(Y_1) = j \right) \\
&= \mathbb{P}\left(\frac{\gamma_1}{\hat{c}(i)} \leq t < \frac{\gamma_1}{\hat{c}(i)} + \frac{\gamma_2}{\hat{c}(j)} \right) \\
&= \mathbb{P}\left(\gamma_1 \leq t\hat{c}(i), \gamma_2 > \left(t - \frac{\gamma_1}{\hat{c}(i)} \right) \hat{c}(j) \right) \\
&= \int_0^{t\hat{c}(i)} \int_{\left(t - \frac{x}{\hat{c}(i)}\right)\hat{c}(j)}^{\infty} e^{-x} e^{-y} \, dy \, dx \\
&= \int_0^{t\hat{c}(i)} e^{-t\hat{c}(j)} e^{-\left(1 - \frac{\hat{c}(j)}{\hat{c}(i)}\right)x} \, dx \\
&= \frac{\hat{c}(i)}{\hat{c}(j) - \hat{c}(i)} \left(e^{-t\hat{c}(i)} - e^{-t\hat{c}(j)} \right) \qquad (8.26)
\end{aligned}
$$

Combining equations (8.25) and (8.26) gives

$$
\begin{aligned}
&\mathbb{E}(h(Y_0, Y_1) | \pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_1, \tau_2)) \mathbb{P}(t \in [\tau_1, \tau_2) | \pi(Y_0) = i, \pi(Y_1) = j) \\
&\qquad = \begin{cases} \dfrac{\bar{\eta}}{i+1} \dfrac{\left(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)}\right)\hat{c}(i)}{\hat{c}(i+1) - \hat{c}(i)}, & \text{if } j = i+1 \\ 0, & \text{if } j = i-1 \end{cases} \qquad (8.27)
\end{aligned}
$$

We now proceed to estimate the sum in (8.20). Using equation (8.15), we see that

$$
\|h(Y_0, Y_k)\| = \|f_n(Y_k) - f_n(Y_0)\| \leq g(Y_k) + g(Y_0) \leq 2g(Y_0) + kR
$$

This, together with an argument similar to that which showed the finiteness of $\mathbb{E}(g(X_t))$, gives

$$
\begin{aligned}
&\left\| \sum_{k=2}^{\infty} \mathbb{E}(h(Y_0, Y_k)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \right\| \\
&\leq \sum_{k=2}^{\infty} \mathbb{E}(\|h(Y_0, Y_k)\||\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\leq \sum_{k=2}^{\infty} \mathbb{E}(2g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\qquad + \sum_{k=2}^{\infty} \mathbb{E}(kR|\pi(Y_0) = i, \pi(Y_1) = j, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\leq 2\mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = j) \sum_{k=2}^{\infty} \mathbb{P}(t \geq \tau_k|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\qquad + R \sum_{k=2}^{\infty} k\mathbb{P}(t \geq \tau_k|\pi(Y_0) = i, \pi(Y_1) = j) \\
&\leq 2\mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = j)(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)
\end{aligned}
\tag{8.28}
$$

From equations (8.20) and (8.27) we have

$$
\begin{aligned}
&\sum_{k=2}^{\infty} \mathbb{E}(h(Y_0, Y_k)|\pi(Y_0) = i, \pi(Y_1) = i+1, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = i+1) \\
&\qquad = \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i + 1) - \frac{\bar{\eta}}{i+1} \frac{(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)})\hat{c}(i)}{\hat{c}(i+1) - \hat{c}(i)}
\end{aligned}
$$

and

$$
\begin{aligned}
&\sum_{k=2}^{\infty} \mathbb{E}(h(Y_0, Y_k)|\pi(Y_0) = i, \pi(Y_1) = i-1, t \in [\tau_k, \tau_{k+1}))\mathbb{P}(t \in [\tau_k, \tau_{k+1})|\pi(Y_0) = i, \pi(Y_1) = i-1) \\
&\qquad = \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i - 1)
\end{aligned}
$$

Combining these with equation (8.28) gives

$$\left\| \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i+1) - \frac{\bar{\eta}}{i+1} \frac{e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)}}{\hat{c}(i+1) - \hat{c}(i)} \hat{c}(i) \right\| \\ \leq 2\mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = i+1)(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1) \quad (8.29)$$

and

$$\|\mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i-1)\| \\ \leq 2\mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = i-1)(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1) \quad (8.30)$$

From equation (8.19) we have

$$\mathbb{E}(h(X_0, X_t)) = \sum_{i=0}^{n-1} \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i+1)\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = i+1) \\ + \sum_{i=1}^{n} \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i-1)\mathbb{P}(\pi(Y_0) = i, \pi(Y_1) = i-1)$$

Letting $M_{i,j} = \mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = j)$ and putting the previous result together with equations (8.18), (8.29), and (8.30) gives

$$\left\| \mathbb{E}(h(X_0, X_t)) - \sum_{i=0}^{n-1} \frac{\bar{\eta}}{i+1} \frac{(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)})\hat{c}(i)}{\hat{c}(i+1) - \hat{c}(i)} \frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right\| \\ \leq \sum_{i=0}^{n-1} \left\| \mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i+1) - \frac{\bar{\eta}(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)})\hat{c}(i)}{(i+1)(\hat{c}(i+1) - \hat{c}(i))} \right\| \frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \\ + \sum_{i=1}^{n} \|\mathbb{E}(h(X_0, X_t)|\pi(Y_0) = i, \pi(Y_1) = i-1)\| \frac{\theta_d i\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \\ \leq \sum_{i=0}^{n-1} (2M_{i,i+1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \\ + \sum_{i=1}^{n} (2M_{i,i-1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \frac{\theta_d i\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \quad (8.31)$$

Notice that $M_{i,j}$ is independent of t, so

$$\lim_{t\to 0^+} \frac{(2M_{i,i+1}(e^{tn\theta}-1-tn\theta)+Rtn\theta(e^{tn\theta}-1))\left(\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\right)}{t} = 0$$

and

$$\lim_{t\to 0^+} \frac{(2M_{i,i-1}(e^{tn\theta}-1-tn\theta)+Rtn\theta(e^{tn\theta}-1))\left(\frac{\theta_d i\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\right)}{t} = 0$$

This gives

$$\begin{aligned}\lim_{t\to 0^+} \frac{1}{t}\Bigg[\sum_{i=0}^{n-1}(2M_{i,i+1}(e^{tn\theta}-1-tn\theta)+Rtn\theta(e^{tn\theta}-1))\left(\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\right)\\ +\sum_{i=1}^{n}(2M_{i,i-1}(e^{tn\theta}-1-tn\theta)+Rtn\theta(e^{tn\theta}-1))\left(\frac{\theta_d i\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\right)\Bigg] = 0 \quad (8.32)\end{aligned}$$

Additionally,

$$\begin{aligned}&\lim_{t\to 0^+}\frac{1}{t}\sum_{i=0}^{n-1}\frac{\bar\eta}{i+1}\frac{(e^{-t\hat c(i)}-e^{-t\hat c(i+1)})\hat c(i)}{\hat c(i+1)-\hat c(i)}\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\\
&=\sum_{i=0}^{n-1}\frac{\bar\eta}{i+1}\frac{(-\hat c(i)+\hat c(i+1))\hat c(i)}{\hat c(i+1)-\hat c(i)}\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\\
&=\sum_{i=0}^{n-1}\frac{\bar\eta}{i+1}\hat c(i)\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i+\theta_a(n-i)}\\
&=\sum_{i=0}^{n-1}\frac{\bar\eta}{i+1}(\theta_d i+\theta_a(n-i))\frac{\theta_a(n-i)}{\theta_d i+\theta_a(n-i)}\frac{1}{(\theta_d+\theta_a)^n}\binom{n}{i}\theta_d^{n-i}\theta_a^i\\
&=\sum_{i=0}^{n-1}\frac{\bar\eta\,\theta_a(n-i)}{i+1}\frac{1}{(\theta_d+\theta_a)^n}\frac{n!}{i!(n-i)!}\theta_d^{n-i}\theta_a^i\\
&=\sum_{i=0}^{n-1}\frac{\bar\eta\,\theta_d}{(\theta_d+\theta_a)^n}\frac{n!}{(i+1)!(n-i-1)!}\theta_d^{n-i-1}\theta_a^{i+1}\\
&=\frac{\bar\eta\,\theta_d}{(\theta_d+\theta_a)^n}\sum_{i=0}^{n-1}\binom{n}{i+1}\theta_d^{n-i-1}\theta_a^{i+1}\\
&=\frac{\bar\eta\,\theta_d}{(\theta_d+\theta_a)^n}((\theta_d+\theta_a)^n-\theta_d^n) \quad (8.33)\end{aligned}$$

We know from equations (8.31) and (8.32) that

$$\begin{aligned}
\lim_{t\to 0^+} \frac{1}{t} &\left\| \mathbb{E}(h(X_0, X_t)) - \sum_{i=1}^{n-1} \frac{\bar{\eta}}{i+1} \frac{(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)})\hat{c}(i)}{\hat{c}(i+1) - \hat{c}(i)} \frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right\| \\
&\le \lim_{t\to 0^+} \frac{1}{t} \left[\sum_{i=0}^{n-1} (2M_{i,i+1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \left(\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right) \right. \\
&\qquad \left. + \sum_{i=1}^{n} (2M_{i,i-1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \left(\frac{\theta_d i\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right) \right] \\
&= 0
\end{aligned}$$

Combining this with equation (8.33) and using $h(X_0, X_t) = \mathbb{E}(f_n(X_t) - f_n(X_0))$ gives

$$\lim_{t\to 0^+} \left\| \frac{\mathbb{E}(f_n(X_t) - f_n(X_0))}{t} - \frac{\bar{\eta}\,\theta_d}{(\theta_d + \theta_a)^n}((\theta_d + \theta_a)^n - \theta_d^n) \right\| = 0$$

Thus,

$$\lim_{t\to 0^+} \frac{\mathbb{E}(f_n(X_t)) - \mathbb{E}(f_n(X_0))}{t} = \frac{\bar{\eta}\,\theta_d}{(\theta_d + \theta_a)^n}((\theta_d + \theta_a)^n - \theta_d^n)$$

which implies

$$\frac{\partial}{\partial t^+}\mathbb{E}(f_n(X_0)) = \frac{\bar{\eta}\,\theta_d}{(\theta_d + \theta_a)^n}((\theta_d + \theta_a)^n - \theta_d^n)$$

□

Theorem 8.9 tells us that if η has compact support then, in essence, the expected velocity of the cell is given by equation (8.10).

Chapter 9. Space-dependent Perturbations

Recall that when an adhesion site attaches, its new location is a perturbation of the old centroid governed by the distribution η. In this section, we examine what happens when η becomes space-dependent.

For each $\mathbf{y} \in E$, let $\eta_{\mathbf{y}}$ be a Borel probability measure on E such that $\int_E \mathbf{x} d\eta_{\mathbf{y}}(\mathbf{x})$ is well-defined and finite. Then define $\mu_{\{i,n\}}^{(\psi,\mathbf{v})}$ by

$$\mu_{\{i,n\}}^{(\psi,\mathbf{v})} := \begin{cases} \left(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\right) \circ F_i^{-1} & \text{if } |\psi| = \psi(i) = 1 \\ \left(\delta_{\mathbf{v}(i)} \times \delta_{\mathbf{v}(n)}\right) \circ S^{-1}_{(\mathbf{0},(\mathbf{v}(i)-\mathbf{v}(n))/(|\psi|-1),1,1)} \circ F_i^{-1} & \text{if } |\psi| > \psi(i) = 1 \\ \left(\eta_{\mathbf{v}(n)} \times I\right) \circ S^{-1}_{(-\mathbf{v}(n),-(|\psi|+1)\mathbf{v}(n),1,1/(|\psi|+1))} \circ F_i^{-1} & \text{if } \psi(i) = 0 \end{cases}$$

So we now have that for $(\psi, \mathbf{v}) \in \mathsf{X}$, the measure $\mu_{\{i,n\}}^{(\psi,\mathbf{v})}$ uses $\eta_{\mathbf{v}(n)}$. That is, the perturbation of a newly attached adhesion site from the previous centroid is governed by a distribution that is dependent on the previous location of the centroid.

All the properties and results up to Lemma 8.8 follow exactly as before since whenever we use μ or $\mu_{\{i,n\}}^{\mathsf{x}}$, we first fix $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$, which then fixes our choice of the distribution $\eta_{\mathbf{v}(n)}$. In place of Lemma 8.8 we now have

Lemma 8.8*. *Suppose $f : \mathsf{X} \to [0, \infty]$ is measurable and $\mathsf{x} = (\psi, \mathbf{v}) \in \mathsf{X}$. Then*

$$\begin{aligned} \int_{\mathsf{X}} f(\mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) &= \sum_{i \in \psi^{-1}(\{1\})} r_i(\psi) f(s_i(\psi), \mathbf{v}) \\ &+ \sum_{i \in \psi^{-1}(\{0\})} r_i(\psi) \int_E f\Big(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \Big\{(i, \mathbf{x} + \mathbf{v}(n)), \Big(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\Big)\Big\}\Big) d\eta_{\mathbf{v}(n)}(\mathbf{x}) \end{aligned} \tag{8.2*}$$

for $|\psi| \leq 1$ and

$$\begin{aligned} \int_{\mathsf{X}} f(\mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) &= \sum_{i \in \psi^{-1}(\{1\})} r_i(\psi) f\Big(s_i(\psi), \mathbf{v}|_{[n]} \cup \Big\{\Big(n, \mathbf{v}(n) - \frac{\mathbf{v}(i) - \mathbf{v}(n)}{|\psi| - 1}\Big)\Big\}\Big) \\ &+ \sum_{i \in \psi^{-1}(\{0\})} r_i(\psi) \int_E f\Big(s_i(\psi), \mathbf{v}|_{[n+1]\setminus\{i,n\}} \cup \Big\{(i, \mathbf{x} + \mathbf{v}(n)), \Big(n, \frac{\mathbf{x}}{|\psi|+1} + \mathbf{v}(n)\Big)\Big\}\Big) d\eta_{\mathbf{v}(n)}(\mathbf{x}) \end{aligned} \tag{8.3*}$$

for $|\psi| > 1$.

Note that the only change is that the integrals are now with respect to $\eta_{\mathbf{v}(n)}$. Theorem

8.9 becomes the following:

Theorem 8.9*. *For each $i \in [n+1]$, let $f_i : \mathsf{X} \to E$ be defined by $f_i(\psi, \mathbf{v}) := \mathbf{v}(i)$. Let σ be as in Proposition 8.7 and let ρ be a distribution on X such that $\sigma = \rho \circ \pi^{-1}$ and such that f_i is ρ-integrable for every i. Let X be as in Proposition 8.3. Let $\|\cdot\|$ be the ∞-norm in E. Assume there is some $R > 0$ such that $\eta_{\mathbf{y}}$ is supported on $\{\mathbf{x} \in E : \|\mathbf{x}\| \le R\}$ for every $\mathbf{y} \in E$. Then for every $i \in [n+1]$ and $t \ge 0$, $\mathbb{E}(f_i(X_t))$ is well-defined and finite, and*

$$\frac{\partial}{\partial t^+}\mathbb{E}(f_n(X_t)) = \sum_{i \in [n]} \frac{\theta_a(n-i)}{i+1} \int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x}) \tag{8.10*}$$

where $\bar{\eta}(\mathsf{x}) := \int_E \mathbf{x}\, d\eta_{f_n(\mathsf{x})}(\mathbf{x})$.

Proof. Using Lemma 8.8* in place of Lemma 8.8, the proof proceeds as in the proof of Theorem 8.9 up to equation (8.23) since anything involving Lemma 8.8 or μ either uses a fixed $\mathsf{x} \in \mathsf{X}$, uses the uniform bound R on the support of $\eta_{\mathbf{y}}$, or gives something that does not involve $\eta_{\mathbf{y}}$. Using $h(\mathsf{x}, \mathsf{y}) = f_n(\mathsf{y}) - f_n(\mathsf{x})$, equation (8.23) becomes

$$\int_{\pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) = \frac{(n - \pi(\mathsf{x}))\theta_a}{\theta_d \pi(\mathsf{x}) + \theta_a(n - \pi(\mathsf{x}))} \mathbf{1}_{\{j-1\}}(\pi(\mathsf{x})) \frac{\bar{\eta}(\mathsf{x})}{j} \tag{8.23*}$$

We then get

$$\begin{aligned}
&\int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \int_{\pi^{-1}(\{j\})} h(\mathsf{x}, \mathsf{y})\mu(\mathsf{x}, d\mathsf{y}) \\
&\qquad = \int_{\pi^{-1}(\{i\})} \rho(d\mathsf{x}) \frac{(n - \pi(\mathsf{x}))\theta_a}{\theta_d \pi(\mathsf{x}) + \theta_a(n - \pi(\mathsf{x}))} \mathbf{1}_{\{j-1\}}(\pi(\mathsf{x})) \frac{\bar{\eta}(\mathsf{x})}{j} \\
&\qquad = \begin{cases} \dfrac{(n-i)\theta_a}{\theta_d i + \theta_a(n-i)} \dfrac{1}{i+1} \displaystyle\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x}), & \text{if } i = j-1 \\ 0, & \text{otherwise} \end{cases}
\end{aligned}$$

which gives

$$
\begin{aligned}
&\mathbb{E}(h(Y_0,Y_1)|\pi(Y_0)=i,\pi(Y_1)=j)\\
&=\begin{cases}(\mathbb{P}(\pi(Y_0)=i,\pi(Y_1)=j))^{-1}\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\dfrac{1}{i+1}\displaystyle\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x}), & \text{if } i=j-1\\ 0, & \text{if } i=j+1\end{cases}\\
&=\begin{cases}\dfrac{\theta_d i+\theta_a(n-i)}{(n-i)\theta_a\sigma(\{i\})}\dfrac{(n-i)\theta_a}{\theta_d i+\theta_a(n-i)}\dfrac{1}{i+1}\displaystyle\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x}), & \text{if } j=i+1\\ 0, & \text{if } j=i-1\end{cases}\\
&=\begin{cases}\dfrac{1}{\sigma(\{i\})(i+1)}\displaystyle\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x}), & \text{if } j=i+1\\ 0, & \text{if } j=i-1\end{cases}
\end{aligned}
\tag{8.24*}
$$

We then get

$$
\begin{aligned}
&\mathbb{E}(h(Y_0,Y_1)|\pi(Y_0)=i,\pi(Y_1)=j,t\in[\tau_1,\tau_2))\\
&\qquad=\begin{cases}\dfrac{1}{\sigma(\{i\})(i+1)}\displaystyle\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x}), & \text{if } j=i+1\\ 0, & \text{if } j=i-1\end{cases}
\end{aligned}
\tag{8.25*}
$$

so that

$$
\begin{aligned}
&\mathbb{E}(h(Y_0,Y_1)|\pi(Y_0)=i,\pi(Y_1)=j,t\in[\tau_1,\tau_2))\mathbb{P}(t\in[\tau_1,\tau_2)|\pi(Y_0)=i,\pi(Y_1)=j)\\
&\qquad=\begin{cases}\dfrac{\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)}\dfrac{\left(e^{-t\hat{c}(i)}-e^{-t\hat{c}(i+1)}\right)\hat{c}(i)}{\hat{c}(i+1)-\hat{c}(i)}, & \text{if } j=i+1\\ 0, & \text{if } j=i-1\end{cases}
\end{aligned}
\tag{8.27*}
$$

Then

$$
\begin{aligned}
&\left\|\mathbb{E}(h(X_0,X_t)|\pi(Y_0)=i,\pi(Y_1)=i+1)-\frac{\int_{\pi^{-1}(\{i\})}\bar{\eta}(\mathsf{x})\,d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)}\frac{\left(e^{-t\hat{c}(i)}-e^{-t\hat{c}(i+1)}\right)\hat{c}(i)}{\hat{c}(i+1)-\hat{c}(i)}\right\|\\
&\qquad\le 2\mathbb{E}(g(Y_0)|\pi(Y_0)=i,\pi(Y_1)=i+1)(e^{tn\theta}-1-tn\theta)+Rtn\theta(e^{tn\theta}-1)
\end{aligned}
\tag{8.29*}
$$

and so

$$\left\| \mathbb{E}(h(X_0, X_t)) - \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)} \frac{\left(e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)}\right)\hat{c}(i)}{\hat{c}(i+1) - \hat{c}(i)} \frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right\|$$
$$\leq \sum_{i=0}^{n-1} (2M_{i,i+1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \left(\frac{\theta_a(n-i)\sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right)$$
$$+ \sum_{i=1}^{n} (2M_{i,i-1}(e^{tn\theta} - 1 - tn\theta) + Rtn\theta(e^{tn\theta} - 1)) \left(\frac{\theta_d i \sigma(\{i\})}{\theta_d i + \theta_a(n-i)} \right) \tag{8.31*}$$

where $M_{i,j} = \mathbb{E}(g(Y_0)|\pi(Y_0) = i, \pi(Y_1) = j)$. Therefore,

$$\lim_{t\to 0^+} \frac{1}{t} \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)} \frac{e^{-t\hat{c}(i)} - e^{-t\hat{c}(i+1)}}{\hat{c}(i+1) - \hat{c}(i)} \hat{c}(i) \frac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)} \sigma(\{i\})$$
$$= \lim_{t\to 0^+} \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)} \frac{-\hat{c}(i)e^{-t\hat{c}(i)} + \hat{c}(i+1)e^{-t\hat{c}(i+1)}}{\hat{c}(i+1) - \hat{c}(i)} \hat{c}(i) \frac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)} \sigma(\{i\})$$
$$= \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)} \frac{-\hat{c}(i) + \hat{c}(i+1)}{\hat{c}(i+1) - \hat{c}(i)} \hat{c}(i) \frac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)} \sigma(\{i\})$$
$$= \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{\sigma(\{i\})(i+1)} \hat{c}(i) \frac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)} \sigma(\{i\}))$$
$$= \sum_{i=0}^{n-1} \frac{\int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})}{i+1} (\theta_d i + \theta_a(n-i)) \frac{\theta_a(n-i)}{\theta_d i + \theta_a(n-i)}$$
$$= \sum_{i\in[n]} \frac{\theta_a(n-i)}{i+1} \int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x}) \tag{8.33*}$$

and we get

$$\frac{\partial}{\partial t^+} \mathbb{E}(f_n(X_0)) = \sum_{i\in[n]} \frac{\theta_a(n-i)}{i+1} \int_{\pi^{-1}(\{i\})} \bar{\eta}(\mathsf{x})\, d\rho(\mathsf{x})$$

□

By allowing the perturbations of newly attached adhesion sites to depend on the position of the centroid, we are able to expand our model to incorporate more biological applications.

For instance, our model can be used to predict the velocity of a cell in the presence of chemical attractants, so we can better model chemotaxis.

Chapter 10. Discussion and Conclusion

In summary, we formulated a model of amoeboid cell motion of a single cell on a substrate. In this model, we consider the cell as a nucleus attached by springs to several adhesion sites. We then track the location of each adhesion site as well as the location of the centroid of the adhesion sites that are currently attached to the substrate.

We examined a random process that tracks how many adhesion sites are attached at time t using the assumption that it is a Markov process. We showed, in the context of a transition rate matrix and distribution vectors, that this process has an attracting stationary distribution.

Next, we formalized our model using transition kernels. We then rigorously proved that our model is a continuous-time jump-type Markov process. We then derived a time-invariant result to predict the time derivative of the expected location of the centroid. This result can be used analytically and in numerical simulations to predict the velocity of a cell.

As a modification of our main result, we considered what happens when the perturbation of an adhesion site from the centroid is governed by a distribution that is space-dependent. Under these circumstances, we derived a result to predict the velocity of a cell. This extends our model to more complex biological situations such as chemotaxis.

Appendix A. Additional Theorems

Theorem A.1. (Dynkin's Criterion for Discrete-time Markov Processes on Topological Spaces) *Let T_1 and T_2 be topological spaces and $f : T_1 \to T_2$ a continuous surjection with a continuous right-inverse. Let $Q_1 : T_1 \times \mathcal{B}(T_1) \to [0,1]$ be a probability kernel, and let $Q_2 : T_2 \times \mathcal{B}(T_2) \to [0,1]$ be a function satisfying $Q_1(x, f^{-1}(A)) = Q_2(f(x), A)$ for every*

$x \in T_1$ and $A \in \mathcal{B}(T_2)$.

Then Q_2 is a probability kernel, and for every probability measure ρ on $\mathcal{B}(T_1)$ and every discrete-time Markov process Φ with initial distribution ρ and transition kernel Q_1, the discrete-time stochastic process $f \circ \Phi$ is a Markov process with initial distribution $\rho \circ f^{-1}$ and transition kernel Q_2

Proof. We first show that Q_2 is a probability kernel. By hypothesis, there is some continuous right-inverse g of f. Since f is surjective, for $y \in T_2$ there is some $x \in T_1$ with $f(x) = y$. Notice that for $A \in \mathcal{B}(T_2)$

$$Q_2(y, A) = Q_2(f(x), A) = Q_1(x, f^{-1}(A)) = (Q_1(x, \cdot) \circ f^{-1})(A)$$

So $Q_2(y, \cdot) = Q_1(x, \cdot) \circ f^{-1}$. Since f is continuous, we know that f is measurable. Furthermore, $Q_1(x, \cdot)$ is a measure because Q_1 is a probability kernel. Thus, $Q_2(y, \cdot)$ is a measure. Additionally,

$$Q_2(y, T_2) = Q_1(x, f^{-1}(T_2)) = Q_1(x, T_1) = 1$$

since Q_1 is a probability kernel. So $Q_2(y, \cdot)$ is a probability measure.

Let $A \in \mathcal{B}(T_2)$. For $y \in T_2$, we know that $(f \circ g)(y) = y$. So

$$Q_2(y, A) = Q_2(f(g(y)), A) = Q_1(g(y), f^{-1}(A)) = (Q_1(\circ, f^{-1}(A)) \circ g)(y)$$

That is, $Q_2(\circ, A) = Q_1(\circ, f^{-1}(A)) \circ g$. We know that g is measurable since it is continuous. Moreover, $Q_1(\cdot, f^{-1}(A))$ is measurable since Q_1 is a probability kernel. Thus, $Q_2(\circ, A)$ is measurable. So Q_2 is a probability kernel.

Let ρ be a probability measure on $\mathcal{B}(T_1)$, and let Φ be a discrete-time Markov process with initial distribution ρ and transition kernel Q_1. Let $\Psi = f \circ \Phi$ and $\nu = \rho \circ f^{-1}$. Take any $k \in \mathbb{N}$ and $A_0, A_1, \ldots, A_k \in \mathcal{B}(T_2)$. Since Φ is a Markov process with initial distribution

ρ and transition kernel Q_1 we know that

$$P(\Phi_0 \in B_0, \dots, \Phi_k \in B_k) = \int_{x_0 \in B_0} \dots \int_{x_{k-1} \in B_k} \rho(dx_0) Q_1(x_0, dx_1) \dots Q_1(x_{k-1}, B_k)$$

for any $B_0, \dots, B_k \in \mathcal{B}(T_1)$ (see Theorem 3.4.1 [6]). Using $y_i = f(x_i)$, we then get

$$\begin{aligned}
&P(\Psi_0 \in A_0, \dots, \Psi_k \in A_k) \\
&\qquad = P(f(\Phi_0) \in A_0, \dots, f(\Phi_k) \in A_k) \\
&\qquad = P(\Phi_0 \in f^{-1}(A_0), \dots, \Phi_k \in f^{-1}(A_k)) \\
&\qquad = \int_{x_0 \in f^{-1}(A_0)} \dots \int_{x_{k-1} \in f^{-1}(A_{k-1})} \rho(dx_0) Q_1(x_0, dx_1) \dots Q_1(x_{k-1}, f^{-1}(A_k)) \\
&\qquad = \int_{y_0 \in A_0} \dots \int_{y_{k-1} \in A_{k-1}} \rho(f^{-1}(dx_0)) Q_2(y_0, dy_1) \dots Q_2(y_{k-1}, A_k) \\
&\qquad = \int_{y_0 \in A_0} \dots \int_{y_{k-1} \in A_{k-1}} \nu(dx_0) Q_2(y_0, dy_1) \dots Q_2(y_{k-1}, A_k)
\end{aligned}$$

This implies $\Psi = f \circ \Psi$ is a Markov process with initial distribution $\nu = \rho \circ f^{-1}$ and transition kernel Q_2.

□

Notation

$\mathcal{F} \vee \mathcal{G} := \sigma\{\mathcal{F}, \mathcal{G}\}$ for σ-algebras $\mathcal{F}, \mathcal{G}$.

$A \perp\!\!\!\perp B$ means A and B are independent.

$A \perp\!\!\!\perp_C B$ means A and B are conditionally independent given C.

θ_t is the shift operator, so that $(\theta_t X)_s = X_{s+t}$

Theorem A.2. *(Theorem 12.18 [5]) For any kernel $\alpha = c\mu$ on S with $\alpha(x, \{x\}) \equiv 0$, consider a Markov chain Y with transition kernel μ and some i.i.d. exponentially distributed random variables $\gamma_1, \gamma_2, \dots \perp\!\!\!\perp Y$ with mean 1. Assume that $\sum_n \gamma_n / c(Y_{n-1}) = \infty$ a.s. under* *every initial distribution for Y. Then*

$$X_t = Y_n,\ t \in [\tau_n, \tau_{n+1}),\ n \in \mathbb{Z}_+ \tag{A.1}$$

$$\tau_n = \sum_{k=1}^{n} \frac{\gamma_k}{c(Y_{k-1})},\ n \in \mathbb{Z}_+ \tag{A.2}$$

define a pure jump-type Markov process with rate kernel α.

Proof. Let P_x be the distribution of the sequences $Y = (Y_n)$ and $\Gamma = (\gamma_n)$ when $Y_0 = x$. For convenience, we may regard (Y, Γ) as the identity mapping on the canonical space $\Omega = S^\infty \times \mathbb{R}^\infty$. Construct X from (Y, Γ) as in (1) and (2), with $X_t = s_0$ arbitrary for $t \geq \sum_n \tau_n$. Then X is a pure jump-type process with jump times $\tau_1, \tau_2, \ldots$. Introduce the filtrations $\mathcal{G} = (\mathcal{G}_n)$ induced by (Y, γ) and $\mathcal{F} = (\mathcal{F}_t)$ induced by X. So $\mathcal{G}_n = \sigma\{(Y_k, \gamma_k) : k \leq n\}$ and $\mathcal{F}_t = \sigma\{X_s : s \leq t\}$. It suffices to prove the Markov property $P_x[\theta_t X \in \cdot | \mathcal{F}_t] = P_{X_t}\{X \in \cdot\}$, since the rate kernel may then be identified via Theorem 12.17 [5].

Fix any $t \geq 0$ and $n \in \mathbb{Z}_+$, and define

$$\kappa = \sup\{k : \tau_k \leq t\},\ \ \beta = (t - \tau_n)c(Y_n)$$

Let

$$T^m(Y, \Gamma) = \{(Y_k, \gamma_{k+1}) : k \geq m\}, \quad (Y', \Gamma') = T^{n+1}(Y, \Gamma), \quad \text{and } \gamma' = \gamma_{n+1}.$$

We show that $\mathcal{F}_t = \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$ on $\{\kappa = n\}$. To prove this, we prove the following:

- $X_t = Y_n$ on $\{\kappa = n\}$
- $\{\kappa = n\} \in \mathcal{F}_t \cap (\mathcal{G}_n \vee \sigma\{\gamma' > \beta\})$
- $\mathcal{G}_n = \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$ on $\{\kappa = n\}$
- $\mathcal{F}_t \subseteq \mathcal{G}_n$ on $\{\kappa = n\}$
- $\mathcal{G}_n \subseteq \mathcal{F}_t$ on $\{\kappa = n\}$

First note that if $\kappa = n$, then $\sup\{k : \tau_k \leq t\} = n$. This means $\tau_n \leq t$ and $\tau_{n+1} > t$. So $t \in [\tau_n, \tau_{n+1})$, giving $X_t = Y_n$ on $\{\kappa = n\}$.

Next, we show that $\{\kappa = n\} \in \mathcal{F}_t \cap (\mathcal{G}_n \vee \sigma\{\gamma' > \beta\})$. By construction X is a pure jump-type process with jump times $\tau_1, \tau_2, \ldots$. On p. 237 of [5] we are given that the jump times τ_k are optional with respect to the filtration $\mathcal{F} = (\mathcal{F}_s)$ induced by X. This means that for each $k \in \mathbb{Z}_+$ we have $\{\tau_k \leq s\} \in \mathcal{F}_s$ for all $s \in \mathbb{Z}_+$. In particular, this gives $\{\tau_n \leq t\}, \{\tau_{n+1} \leq t\} \in \mathcal{F}_t$.

Observe,

$$\begin{aligned}
\{\kappa = n\} &= \{\sup\{k : \tau_k \leq t\} = n\} \\
&= \{\tau_n \leq t,\, \tau_{n+1} > t\} \\
&= \{\tau_n \leq t\} \cap \{\tau_{n+1} > t\} \\
&= \{\tau_n \leq t\} \cap \{\tau_{n+1} \leq t\}^c
\end{aligned}$$

Since $\{\tau_n \leq t\}, \{\tau_{n+1} \leq t\} \in \mathcal{F}_t$, we have that $\{\kappa = n\} \in \mathcal{F}_t$.

To show $\{\kappa = n\} \in \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$, use (A.2) to get

$$\tau_n = \sum_{k=1}^{n} \frac{\gamma_k}{c(Y_{k-1})} = \frac{\gamma_n}{c(Y_{n-1})} + \sum_{k=1}^{n-1} \frac{\gamma_k}{c(Y_{k-1})} = \frac{\gamma_n}{c(Y_{n-1})} + \tau_{n-1}$$

So

$$\{\tau_n \leq t\} = \left\{ \frac{\gamma_n}{c(Y_{n-1})} + \tau_{n-1} \leq t \right\} = \{\gamma_n \leq (t - \tau_{n-1})c(Y_{n-1})\}$$

Let $\beta' = (t - \tau_{n-1})c(Y_{n-1})$. Then

$$\{\tau_n \leq t\} = \{\gamma_n \leq \beta'\} = \{\gamma_n \in [0, \beta']\} = \gamma_n^{-1}([0, \beta'])$$

Since $[0, \beta'] = (\beta', \infty)^c \in \mathcal{B}$, where $\mathcal{B}$ is the σ-algebra generated by the Borel sets of $\overline{\mathbb{R}}_+$, and γ_n is $\mathcal{G}_n/\mathcal{B}$-measurable, it follows that $\gamma_n^{-1}([0, \beta']) \in \mathcal{G}_n$. So $\{\tau_n \leq t\} \in \mathcal{G}_n$. Thus, $\{\tau_n \leq t\} \in \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$.

By a similar argument we get

$$\{\tau_{n+1} > t\} = \{\gamma_{n+1} > (t - \tau_n)c(Y_n)\} = \{\gamma_{n+1} > \beta\} = \{\gamma' > \beta\}$$

So $\{\tau_{n+1} > t\} \in \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$. Therefore,

$$\{\tau_n \leq t\} \cap \{\tau_{n+1} > t\} \in \mathcal{F}_t \cap (\mathcal{G}_n \vee \sigma\{\gamma' > \beta\})$$

giving

$$\{\kappa = n\} \in \mathcal{F}_t \cap (\mathcal{G}_n \vee \sigma\{\gamma' > \beta\})$$

Now we show that on $\{\kappa = n\}$ we have $\mathcal{G}_n \vee \sigma\{\gamma' > \beta\} = \mathcal{G}_n$. Notice that $\{\kappa = n\} \subseteq \{\gamma' > \beta\}$. By definition, $\sigma\{\gamma' > \beta\}$ is the smallest σ-algebra containing $\{\gamma' > \beta\}$. That is,

$$\sigma\{\gamma' > \beta\} = \{\emptyset, \{\gamma' > \beta\}, \{\gamma' > \beta\}^c, \Omega\}$$

Observe,

$$\begin{aligned}
\emptyset \cap \{\kappa = n\} &= \emptyset \\
\{\gamma' > \beta\} \cap \{\kappa = n\} &= \{\kappa = n\} \\
\{\gamma' > \beta\}^c \cap \{\kappa = n\} &= \emptyset \\
\Omega \cap \{\kappa = n\} &= \{\kappa = n\}
\end{aligned}$$

So $\sigma\{\gamma' > \beta\} \cap \{\kappa = n\} = \{\emptyset, \{\kappa = n\}\}$. Since $\{\kappa = n\} \subseteq \{\tau_n \leq t\}$ and $\{\tau_n \leq t\} \in \mathcal{G}_n$, it follows that $\{\tau_n \leq t\} \cap \{\kappa = n\} = \{\kappa = n\}$. So $\{\kappa = n\} \in \mathcal{G}_n \cap \{\kappa = n\}$, giving $\sigma\{\gamma' > \beta\} \cap \{\kappa = n\} \subseteq \mathcal{G}_n \cap \{\kappa = n\}$. Thus, when restricted to $\{\kappa = n\}$, we have

$$\mathcal{G}_n \vee \sigma\{\gamma' > \beta\} = \mathcal{G}_n$$

We now show that $\mathcal{F}_t \subseteq \mathcal{G}_n$ on $\{\kappa = n\}$. Recall that on $\{\kappa = n\}$ we have $X_t = Y_n$. Thus

$$\mathcal{F}_t = \sigma\{X_s : s \leq t\} = \sigma\{Y_m : m \leq n\}$$

By definition, $\sigma\{Y_m : m \leq n\}$ is the smallest σ-algebra such that Y_m is measurable for each $m \leq n$. Since each $Y_m, m \leq n$, is measurable on $\mathcal{G}_n$, it follows that $\sigma\{Y_m : m \leq n\} \subseteq \mathcal{G}_n$. So $\mathcal{F}_t \subseteq \mathcal{G}_n$ on $\{\kappa = n\}$.

Next, we show that $\mathcal{G}_n \subseteq \mathcal{F}_t$ on $\{\kappa = n\}$. We do this by showing Y_m and γ_m are $\mathcal{F}_t$-measurable for each $m \leq n$. We begin by proving that γ_m is $\mathcal{F}_t$-measurable on $\{\kappa = n\}$ for all $m \leq n$. By construction,

$$\tau_m = \sum_{k=1}^{m} \frac{\gamma_k}{c(Y_{k-1})} = \sum_{k=1}^{m-1} \frac{\gamma_k}{c(Y_{k-1})} + \frac{\gamma_m}{c(Y_{m-1})}.$$

Thus,

$$\gamma_m = \left(\tau_m - \sum_{k=1}^{m-1} \frac{\gamma_k}{c(Y_{k-1})} \right) c(Y_{m-1}) = (\tau_m - \tau_{m-1}) c(Y_{m-1})$$

When given Y_{m-1}, the value of $c(Y_{m-1})$ is completely determined. This means that $E_{Y_{m-1}}[c(Y_{m-1})] = c(Y_{m-1})$. Thus,

$$E_{Y_{m-1}}[\gamma_m] = E_{Y_{m-1}}[(\tau_m - \tau_{m-1}) c(Y_{m-1})] = c(Y_{m-1}) E_{Y_{m-1}}[(\tau_m - \tau_{m-1})]$$

By hypothesis, $\gamma_m \perp\!\!\!\perp Y_{m-1}$ and $E[\gamma_m] = 1$, so $E_{Y_{m-1}}[\gamma_m] = E[\gamma_m] = 1$. Thus,

$$1 = E_{Y_{m-1}}[\gamma_m] = c(Y_{m-1}) E_{Y_{m-1}}[(\tau_m - \tau_{m-1})]$$

which gives

$$c(Y_{m-1}) = \frac{1}{E_{Y_{m-1}}[(\tau_m - \tau_{m-1})]}$$

We then have that

$$\gamma_m = \frac{\tau_m - \tau_{m-1}}{E_{Y_{m-1}}[(\tau_m - \tau_{m-1})]}$$

But $\gamma_m \perp\!\!\!\perp Y_{m-1}$, so

$$\gamma_m = \frac{\tau_m - \tau_{m-1}}{E[\tau_m - \tau_{m-1}]}$$

So γ_m is $\mathcal{F}_t$-measurable if τ_m and τ_{m-1} are $\mathcal{F}_t$-measurable. By the definition of measurable real-valued functions, τ_m is $\mathcal{F}_t$-measurable if $\{\tau_m \leq s\} \in \mathcal{F}_t$ for all $s \in \overline{\mathbb{R}}_+$. We prove this is the case.

For $s \leq t$, we have $\mathcal{F}_s \subseteq \mathcal{F}_t$ by construction. Additionally, $\{\tau_m \leq s\} \in \mathcal{F}_s$ since τ_m is optional. Thus, $\{\tau_m \leq s\} \in \mathcal{F}_t$ for $s \leq t$.

For $s > t$, it is always true that $\tau_m \leq s$ for $m \leq n$ since $\tau_m < \tau_n \leq t < s$ on $\{\kappa = n\}$. So $\{\tau_m \leq s\} \in \mathcal{F}_t$ for $s > t$ on $\{\kappa = n\}$.

Therefore, $\{\tau_m \leq s\} \in \mathcal{F}_t$ for all s on $\{\kappa = n\}$. Hence, τ_m is $\mathcal{F}_t$-measurable on $\{\kappa = n\}$ for all $m \leq n$. This implies γ_m is $\mathcal{F}_t$-measurable on $\{\kappa = n\}$ for all $m \leq n$.

Since $X_s = Y_m$ for $s \in [\tau_m, \tau_{m+1})$, $\mathcal{F}_s \subseteq \mathcal{F}_t$ for $s \leq t$, and $X_t = Y_n$, it follows that Y_m is $\mathcal{F}_t$-measurable on $\{\kappa = n\}$ for all $m \leq n$. Therefore $\mathcal{G}_n \subseteq \mathcal{F}_t$ on $\{\kappa = n\}$.

Hence,

$$\mathcal{F}_t = \mathcal{G}_n = \mathcal{G}_n \vee \sigma\{\gamma' > \beta\} \quad \text{on } \{\kappa = n\}$$

Now we want to prove the Markov property for X, namely that $P_x[\theta_t X \in \cdot|\mathcal{F}_t] = P_{X_t}\{X \in \cdot\}$. It is enough by Lemma 6.2 in [5] to prove that

$$P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r|\mathcal{G}_n, \gamma' > \beta] = P_{Y_n}\{T(Y, \Gamma) \in \cdot, \gamma_1 > r\}.$$

To justify this, we use Lemma 6.2 [5] to show that

$$P_x[\theta_t X \in \cdot|\mathcal{F}_t] = P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r|, \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}]$$

and we show that

$$P_{X_t}\{X \in \cdot\} = P_{Y_n}\{T(Y,\Gamma) \in \cdot,\ \gamma_1 > r\}$$

First, we show that $\{\theta_t X \in \cdot\} = \{(Y', \Gamma') \in \cdot,\ \gamma' - \beta > r\}$ on $\{\kappa = n\}$. Notice that

$$(Y', \Gamma') = T^{n+1}(Y,\Gamma) = \{(Y_k, \gamma_{k+1}) : k \geq n+1\}$$

So

$$\begin{aligned}
\{(Y', \Gamma') \in \cdot, \gamma' - \beta > r\} &= \{(Y_k, \gamma_{k+1})_{k \geq n+1} \in \cdot, \gamma_{n+1} > \beta + r\} \\
&= \{(Y_k, \gamma_k)_{k \geq n+1} \in \cdot\} \\
&= \{(Y_k, \gamma_k)_{k > n} \in \cdot\} \\
&= \{(X_s)_{s > t} \in \cdot\} \\
&= \{\theta_t X \in \cdot\}
\end{aligned}$$

where the fourth equality holds since (Y, Γ) determines X and $X_t = Y_n$ on $\{\kappa = n\}$. (Note that we are changing set spaces at pretty much every step of the above calculations.)

This implies $1\{\theta_t X \in \cdot\} = 1\{(Y', \Gamma') \in \cdot, \gamma' - \beta > r\}$ on $\{\kappa = n\}$. We now have $\{\kappa = n\} \in \mathcal{F}_t \cap (\mathcal{G}_n \vee \sigma\{\gamma' > \beta\})$ with $\mathcal{F}_t = \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}$ and $1\{\theta_t X \in \cdot\} = 1\{(Y', \Gamma') \in \cdot, \gamma' - \beta > r\}$ on $\{\kappa = n\}$. By Lemma 6.2 [5] it follows that

$$\begin{aligned}
P_x[\theta_t X \in \cdot | \mathcal{F}_t] &= E_x[1\{\theta_t X \in \cdot\} | \mathcal{F}_t] \\
&= E_x[1\{(Y', \Gamma') \in \cdot, \gamma' - \beta > r\} | \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}] \\
&= P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r | \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}]
\end{aligned}$$

We also find that on $\{\kappa = n\}$

$$\begin{aligned}
P_{Y_n}\{T(Y,\Gamma) \in \cdot,\, \gamma_1 > r\} &= P_{Y_n}\{(Y_k, \gamma_{k+1})_{k\geq 1} \in \cdot,\, \gamma_1 > r\} \\
&= P_{Y_n}\{(Y_k, \gamma_k)_{k\geq 1} \in \cdot\} \\
&= P_{Y_n}\{(Y,\Gamma) \in \cdot\} \\
&= P_{X_t}\{X \in \cdot\} \text{ since } X \text{ is determined by } (Y,\Gamma) \text{ and } Y_n = X_t
\end{aligned}$$

(Note that, again, we are changing set spaces at pretty much each step.)

Thus, to prove $P_x[\theta_t X \in \cdot|\mathcal{F}_t] = P_{X_t}\{X \in \cdot\}$, it is sufficient to prove

$$P_x[(Y',\Gamma') \in \cdot, \gamma' - \beta > r|\mathcal{G}_n \vee \sigma\{\gamma' > \beta\}] = P_{Y_n}\{T(Y,\Gamma) \in \cdot,\, \gamma_1 > r\}$$

We show that $\gamma' \perp\!\!\!\perp (\mathcal{G}_n, Y', \Gamma')$ and that $(Y',\Gamma') \perp\!\!\!\perp_{\mathcal{G}_n} (\gamma', \beta)$. By hypothesis we know that $\gamma_1, \gamma_2, \ldots$ are i.i.d. and $\gamma_1, \gamma_2, \ldots \perp\!\!\!\perp Y$. Since $\mathcal{G}_n = \sigma\{(Y_k, \gamma_k) : k \leq n\}$ and $\gamma_{n+1} \perp\!\!\!\perp (Y_k, \gamma_k)$ for $k \neq n+1$, it follows that $\gamma' \perp\!\!\!\perp \mathcal{G}_n$.

A conceptual description of conditional independence is that A and B are conditionally independent given C if and only if B contains no information about A that is not contained in C (see Proposition 6.6 in [5]). By definition $(Y', \Gamma') = \{(Y_k, \gamma_{k+1}) : k \geq n+1\}$. Conceptually, we see that $\sigma(Y', \Gamma')$ contains no information about $\sigma(\gamma')$, so $\sigma(Y', \Gamma')$ contains no information about $\sigma(\gamma')$ that is not contained in $\mathcal{G}_n$. Thus $\gamma' \perp\!\!\!\perp_{\mathcal{G}_n} (Y', \Gamma')$. We now have that $\gamma' \perp\!\!\!\perp \mathcal{G}_n$ and $\gamma' \perp\!\!\!\perp_{\mathcal{G}_n} (Y', \Gamma')$. By Proposition 6.8 in [5] this gives $\gamma' \perp\!\!\!\perp (\mathcal{G}_n, Y', \Gamma')$.

By definition

$$\beta = (t - \tau_n)c(Y_n) = \left(t - \sum_{k=1}^{n} \frac{\gamma_k}{c(Y_{k-1})}\right) c(Y_n)$$

So $\sigma(\beta)$ contains no information about $\sigma(\gamma')$ that is not contained in $\mathcal{G}_n$, giving $\gamma' \perp\!\!\!\perp_{\mathcal{G}_n} \beta$.

Note that $\sigma(Y_n) \subseteq \mathcal{G}_n$, so $\mathcal{G}_n$ contains all the information about Y_n. Since Y is Markov, we know that $Y_{n+1}, Y_{n+2}, \ldots$ are independent of $Y_1, Y_2, \ldots Y_n$ given Y_n. This, along with the fact that $\mathcal{G}_n$ contains no information about $Y_{n+1}, Y_{n+2}, \ldots$, implies $\sigma(\beta)$ contains no information about $\sigma(Y', \Gamma')$ that is not contained in $\sigma(\mathcal{G}_n, \gamma')$. Therefore $\beta \perp\!\!\!\perp_{\mathcal{G}_n, \gamma'} (Y', \Gamma')$.

Since $(Y', \Gamma') \perp\!\!\!\perp_{\mathcal{G}_n} \gamma'$ and $(Y', \Gamma') \perp\!\!\!\perp_{\mathcal{G}_n, \gamma'} \beta$. It then follows by Proposition 6.8 [5] that $(Y', \Gamma') \perp\!\!\!\perp_{\mathcal{G}_n} (\gamma', \beta)$.

Next we show that

$$P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r | \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}] = P_{Y_n}\{T(Y, \Gamma) \in \cdot,\ \gamma_1 > r\}$$

First, note that $\{(Y', \Gamma') \in \cdot\} \perp\!\!\!\perp_{\mathcal{G}_n} \{\gamma' - \beta > r\}$ since $(Y', \Gamma') \perp\!\!\!\perp_{\mathcal{G}_n} (\gamma', \beta)$. Additionally, $\{\gamma' - \beta > r\} \subseteq \{\gamma' > \beta\}$ for $r \geq 0$.

It is a simple exercise in probability to show that if A, B, C, D are events with $A \perp\!\!\!\perp_C B$ and $B \subseteq D$ with $P(C), P(C \cap D) \neq 0$, then

$$P(A \cap B | C \cap D) = P(A|C) \frac{P(B|C)}{P(D|C)}$$

This implies

$$P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r | \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}] = P_x[(Y', \Gamma') \in \cdot | \mathcal{G}_n] \frac{P_x[\gamma' - \beta > r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]}$$

Observe that

$$\frac{P_x[\gamma' - \beta > r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]} = \frac{P_x[\gamma' > \beta + r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]}$$

By hypothesis we have that $\gamma_1, \gamma_2, \ldots \perp\!\!\!\perp Y$ are i.i.d. exponentially distributed with mean 1. Thus, $\gamma' \perp\!\!\!\perp_{\mathcal{G}_n} \beta$. We also know that $\gamma' \perp\!\!\!\perp \mathcal{G}_n$. Hence,

$$\frac{P_x[\gamma' > \beta + r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]} = \frac{e^{-(\beta + r)}}{e^{-\beta}} = e^{-r}$$

Therefore,

$$\frac{P_x[\gamma' - \beta > r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]} = e^{-r} = P_{Y_n}[\gamma_1 > r]$$

By construction, $T(Y, \Gamma) = \{(Y_k, \gamma_{k+1}) : k \geq 1\}$. So

$$
\begin{aligned}
P_x[(Y', \Gamma') \in \cdot | \mathcal{G}_n] &= P_x[\{(Y_k, \gamma_{k+1}) : k \geq n+1\} \in \cdot | \mathcal{G}_n] \\
&= P_x[\theta_n \{(Y_k, \gamma_{k+1}) : k \geq 1\} \in \cdot | \mathcal{G}_n] \\
&= P_{Y_n}[\{(Y_k, \gamma_{k+1}) : k \geq 1\} \in \cdot] \text{ since } Y \text{ is Markov, by Prop. 8.9 [5]} \\
&= P_{Y_n}[T(Y, \Gamma) \in \cdot]
\end{aligned}
$$

Note that $\gamma_1 \perp\!\!\!\perp T(Y, \Gamma)$. Thus,

$$
P_{Y_n}[T(Y, \Gamma) \in \cdot, \gamma_1 > r] = P_{Y_n}[T(Y, \Gamma) \in \cdot] P_{Y_n}[\gamma_1 > r]
$$

Therefore,

$$
\begin{aligned}
P_x[(Y', \Gamma') \in \cdot, \gamma' - \beta > r | \mathcal{G}_n \vee \sigma\{\gamma' > \beta\}] &= P_x[(Y', \Gamma') \in \cdot | \mathcal{G}_n] \frac{P_x[\gamma' - \beta > r | \mathcal{G}_n]}{P_x[\gamma' > \beta | \mathcal{G}_n]} \\
&= P_{Y_n}[T(Y, \Gamma) \in \cdot] P_{Y_n}[\gamma_1 > r] \\
&= P_{Y_n}[T(Y, \Gamma) \in \cdot, \gamma_1 > r]
\end{aligned}
$$

as desired. Thus, $P_x[\theta_t X \in \cdot | \mathcal{F}_t] = P_{X_t}\{X \in \cdot\}$, so X is a Markov process.

By construction, X is a pure jump-type process. To prove that $\alpha = c\mu$ is the rate kernel for X, we prove that

$$
(E_x[\tau_1])^{-1} P_x[X_{\tau_1} \in B] = c(x)\mu(x, B)
$$

Recall that μ is the transition kernel for Y, so that $\mu(x, B) = P_x[Y_1 \in B]$. By construction, $X_{\tau_1} = Y_1$, so $\mu(x, B) = P_x[X_{\tau_1} \in B]$. Letting $\tau_0 = 0$, we also have

$$
(E_x[\tau_1])^{-1} = (E_{Y_0}[\tau_1 - \tau_0])^{-1} = c(Y_0) = c(x)
$$

Thus, $(E_x[\tau_1])^{-1} P_x[X_{\tau_1} \in B] = c(x)\mu(x, B)$ as desired, and $\alpha = c\mu$ is the rate kernel of X.

$\square$

Bibliography

[1] Jean-Pierre Aubin and Hélène Frankowska. *Set-valued analysis*. Modern Birkhäuser Classics. Birkhäuser Boston, Inc., Boston, MA, 2009. Reprint of the 1990 edition [MR1048347].

[2] J. C. Dallon, E. J. Evans, Christopher P. Grant, and W. V. Smith. Cell speed is independent of force in a mathematical model of amoeboidal cell motion with random switching terms. *Math. Biosci.*, 246(1):1–7, 2013.

[3] J. C. Dallon, Matthew Scott, and W. V. Smith. A force based model of individual cell migration with discrete attachment sites and random switching terms. *Journal of Biomechanical Engineering*, 135(7):071008–1–071008–10, 2013.

[4] Peter Friedl, Stefan Bormann, and Eva-B. Bröcker. Amoeboid leukocyte crawling through extracellular matrix: lessons from the dictyostelium paradigm of cell movement. *Journal of Leukocyte Biology*, 70(4):491–509, 2001.

[5] Olav Kallenberg. *Foundations of modern probability*. Probability and its Applications (New York). Springer-Verlag, New York, second edition, 2002.

[6] Sean Meyn and Richard L. Tweedie. *Markov chains and stochastic stability*. Cambridge University Press, Cambridge, second edition, 2009. With a prologue by Peter W. Glynn.

[7] Peter Olofsson. *Probability, statistics, and stochastic processes*. Wiley-Interscience [John Wiley & Sons], Hoboken, NJ, 2005.

[8] Kandice Tanner, Donald R. Ferris, Luca Lanzano, Herhan Mandefro, William W. Mantulin, David M. Gardiner, Elizabeth L. Rugg, and Enrico Gratton. Coherent movement of cell layers during wound healing by image correlation spectroscopy. *Biophysical Journal*, 97(7):2098–2106, 2009.

[9] Mahmut Yilmaz and Herhard Christofori. Mechanisms of motility in metastasizing cells. *Molecular Cancer Research*, 8(5):629–642, 2010.