Crusher

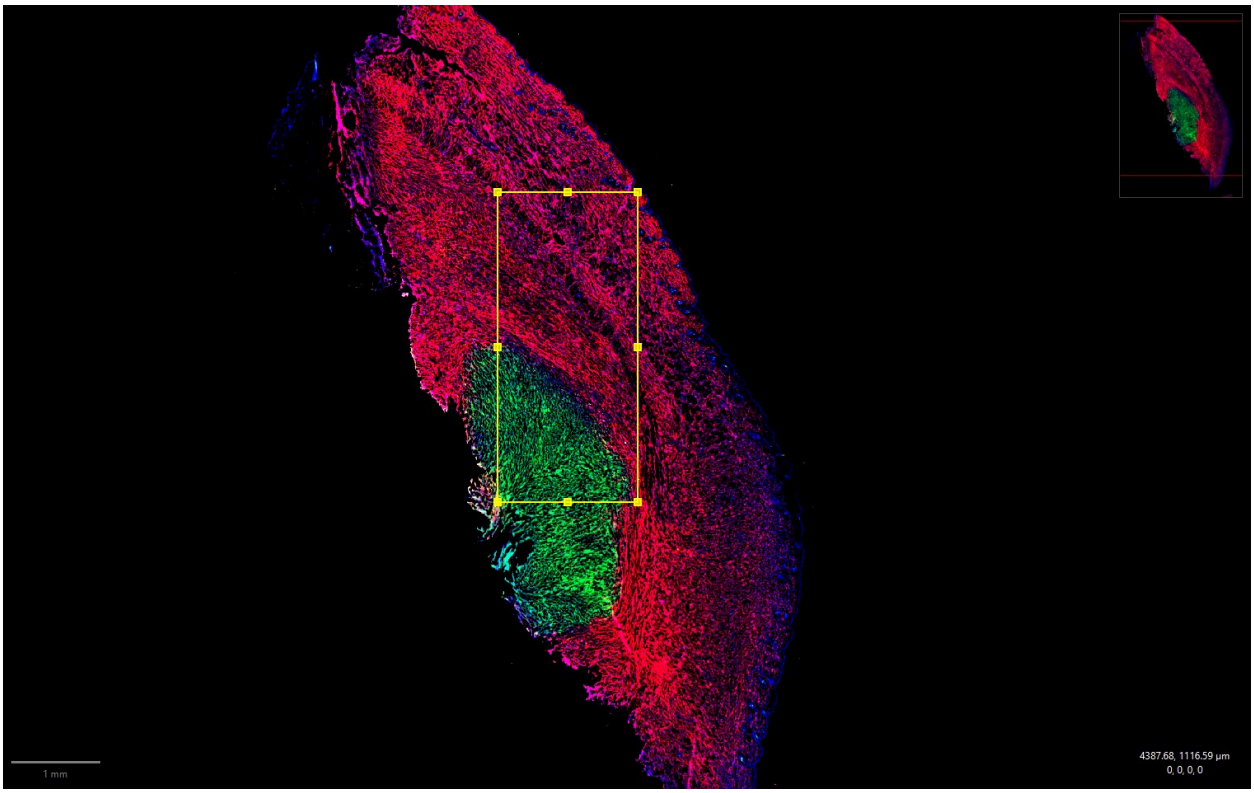
Date	@March 7, 2025
tags	1D

- Decided to go back to 1D for now.
- Motivation was because of what appears to be a clear separation of the T-cells in the 10mm tumor.
- Added the 2D data to the 1D simulation repository.
- Created a crusher file which project all points onto some line I defined.
- Plots all the points as well as the line to get an idea of what the projection will look like.
- Also plots a pdf of all the projected points.

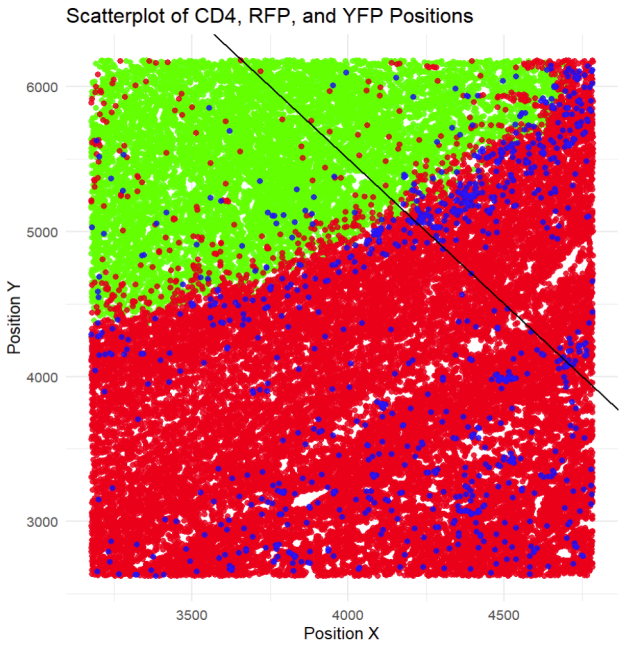
Info

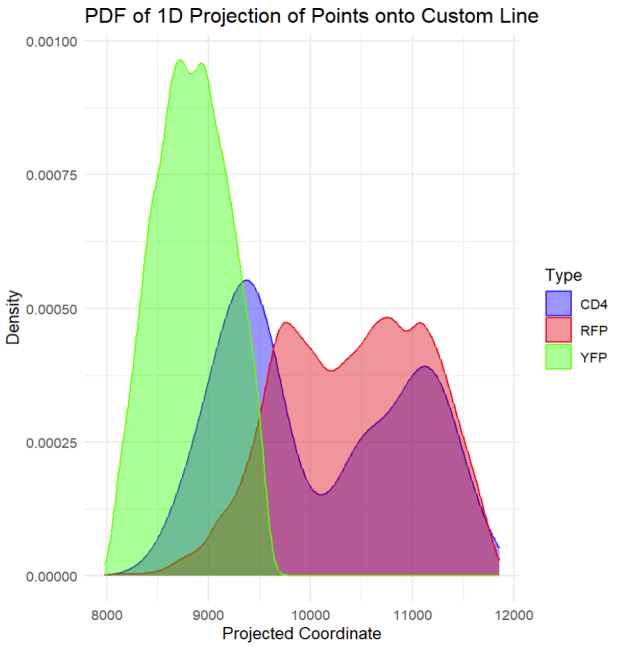
- There's a weird warning, saying that a reached elapsed time limit.
- Takes a weird amount of time to load.
- Jiggling the plot window seems to make it load better, idk why.

10mm_tumor:



- Chose $y = -2m + 13500$





- Seems pretty legit for now.

1D simulation pt2

Date	@March 7, 2025
Files & media	chemoking_gradient_calc.pdf
tags	1D

- Going back because modeling the T-cell movement in 2D seems to be a little weird right now, hopefully will go back eventually.
- Will be making a change where T-cells will have a velocity that will be influenced by the gradient.

The Setup:

- b_{min}, b_{max} : smallest and largest positions observed across the entire dataset.
- Let $X_i(0)$ denote the position of t-cell i at time step 0:

$$X_i(0) \sim Uniform(b_{min}, b_{max})$$

- Let $V_i(0)$ denote the velocity of t-cell i at time step 0:

$$V_i(0) \sim Uniform(-1, 1)$$

- Let $X_i(t), V_i(t)$ denote the position and velocity of T-cell i at time step t

$$X_i(t) = X_i(t-1) + V_i(t-1)$$

The Behaviors:

> 💡 Note
>
> - These are subject to change

Chemokine Gradient

- Let $c(x)$ denote the concentration of chemokine at position x:
  - For n cancer cells, x_i denotes the position and M_i denotes the heat of cancer cell i
  - D denotes the diffusion constant of the chemokines.
  - δ denotes the decay constant of the chemokines

$$c(x) = \sum_{i=1}^{n} \frac{M_i}{2\sqrt{D\delta}} e^{-\sqrt{\delta/D}(|x-x_i|)}$$

- Can see the derivation for it in the pdf `chemokine_gradient_calc.pdf`.
- Can pull out some constants for faster computation

$$c(x) = \frac{1}{2\sqrt{D\delta}} \sum_{i=1}^{n} M_i e^{-\sqrt{\delta/D}(|x-x_i|)}$$

- Let $\nabla c(x)$ denote the concentration gradient at position x
  - Will point in the direction of greater concentration.

$$\nabla c(x) = -\frac{1}{2D}\sum_{i=1}^{n} M_i e^{-\sqrt{\delta/D}(|x-x_i|)} \cdot sgn(x-x_i)$$

- Additionally, let $|\nabla c(x)|$ denote the magnitude of said gradient.

- Not sure what to call this, will refer to it as the **logistic function**
- Will be used to determine how the gradient will influence the velocity.

$$\sigma_\alpha(y) = \frac{e^{\alpha y}}{1+e^{\alpha y}}$$

- The larger that α is, the stronger that the gradient will influence the velocity.
- Will also have a speed term v

Chemokine Visualization 10mm Tumor

Behavior 0: Logistic Always Update

- The Cancer Cells will always listen to the gradient.
- So
- If $\nabla c(X_i(t)) > 0$

$$V_i(t) = \sigma_\alpha(|\nabla c(X_i(t))|) \cdot v$$

- If $\nabla c(X_i(t)) < 0$

$$V_i(t) = -\sigma_\alpha(|\nabla c(X_i(t))|) \cdot v$$

Behavior 1: Probability becomes the velocity

- The logistic function will be used as a probability that the T-cells respond to the gradient.
- let $p \sim uniform(0,1)$
- The gradient will affect the velocity if

$$p < \sigma_\alpha(|\nabla c(X_i(t))|)$$

- The velocity update:
  - If $\nabla c(X_i(t)) > 0$

$$V_i(t) = \sigma_\alpha(|\nabla c(X_i(t))|) \cdot v$$

  - If $\nabla c(X_i(t)) < 0$

$$V_i(t) = -\sigma_\alpha(|\nabla c(X_i(t))|) \cdot v$$

- When the gradient isn't affected:

$$V_i(t) = V_i(t-1)$$

results

Chemokine Visualization 10mm Tumor

- Green Represents YFP Cancer Cells Distribution
- Red Represents RFP Cancer Cells Distribution
- Black Represents the Concentration/Gradient scale is on the right

💡 Takeaways

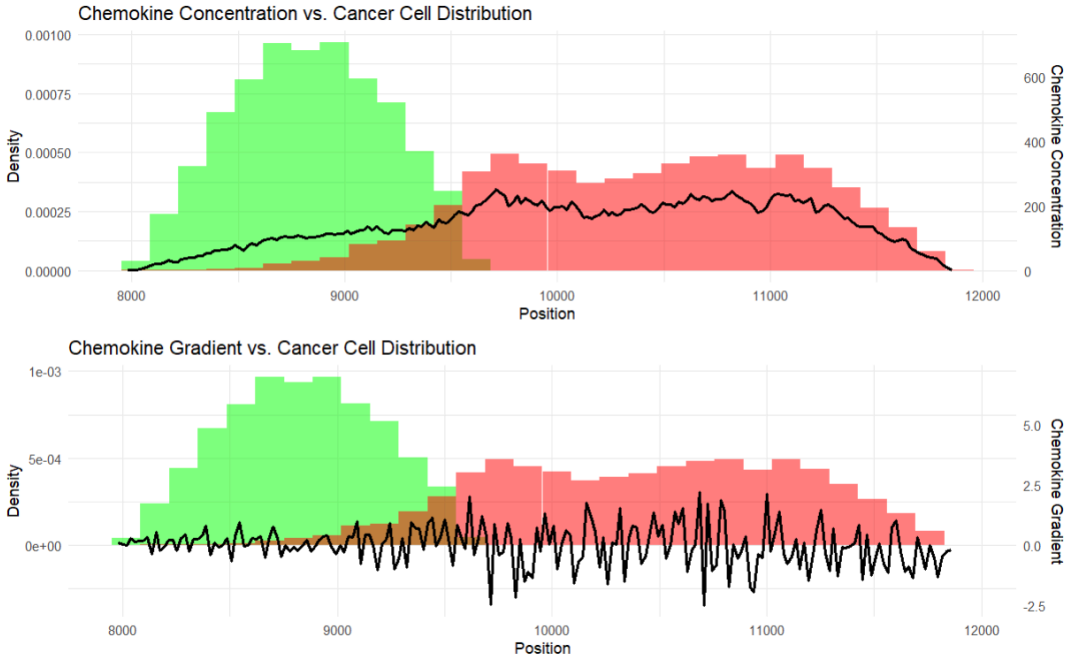
- For the RFP, YFP heat ratio, the smaller the ratio the longer it will take for a T-cell to exit it's region.
  - I think anything above a 1-2 ratio and below like 10 is reasonable.
- For Diffusion/Decay:
  - Higher diffusion/Smaller Decay should be used if we want the T-cells to reach the two noticed clusters in Crusher for the 10mm Tumor
  - Smaller Diffusion/Greater Decay should be used to have the T-cells be more spread out.
  - I think Diffusion 10/ Decay 0.1, is good if we want T-cells to be more spread out
  - I think Diffusion 10/ Decay 0.01, is good if we want T-cells to focus more at those peaks.

Modifying YFP RFP Heat Ratios

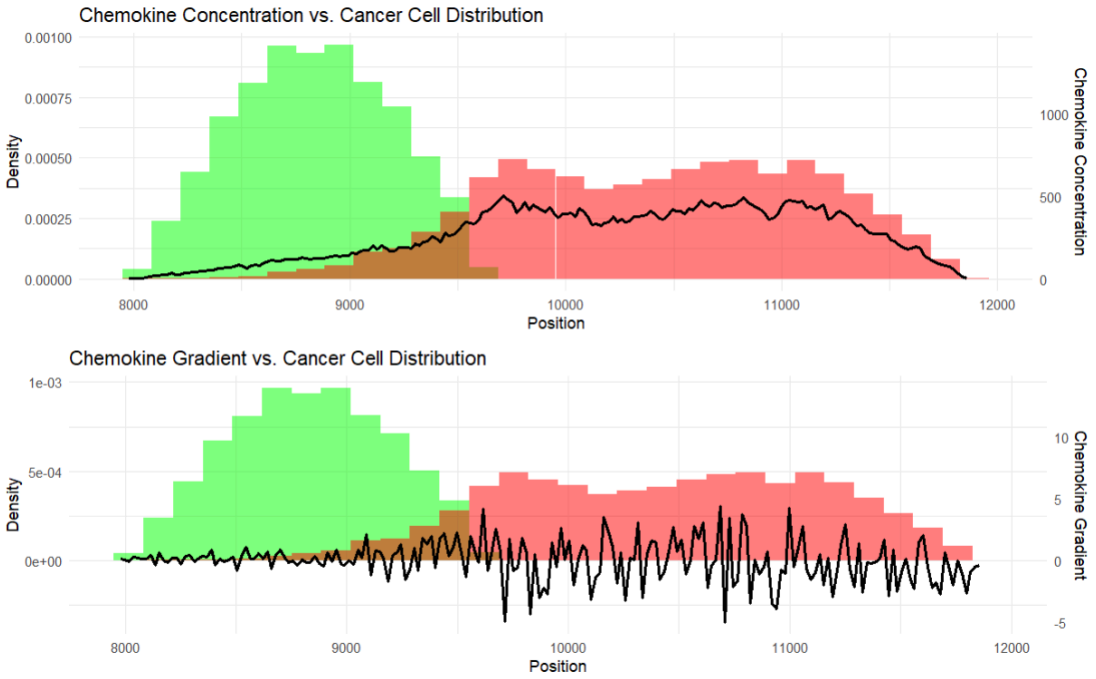
- Diffusion = 10
- Delta = 0.1

Modifying YFP RFP Heat Ratios

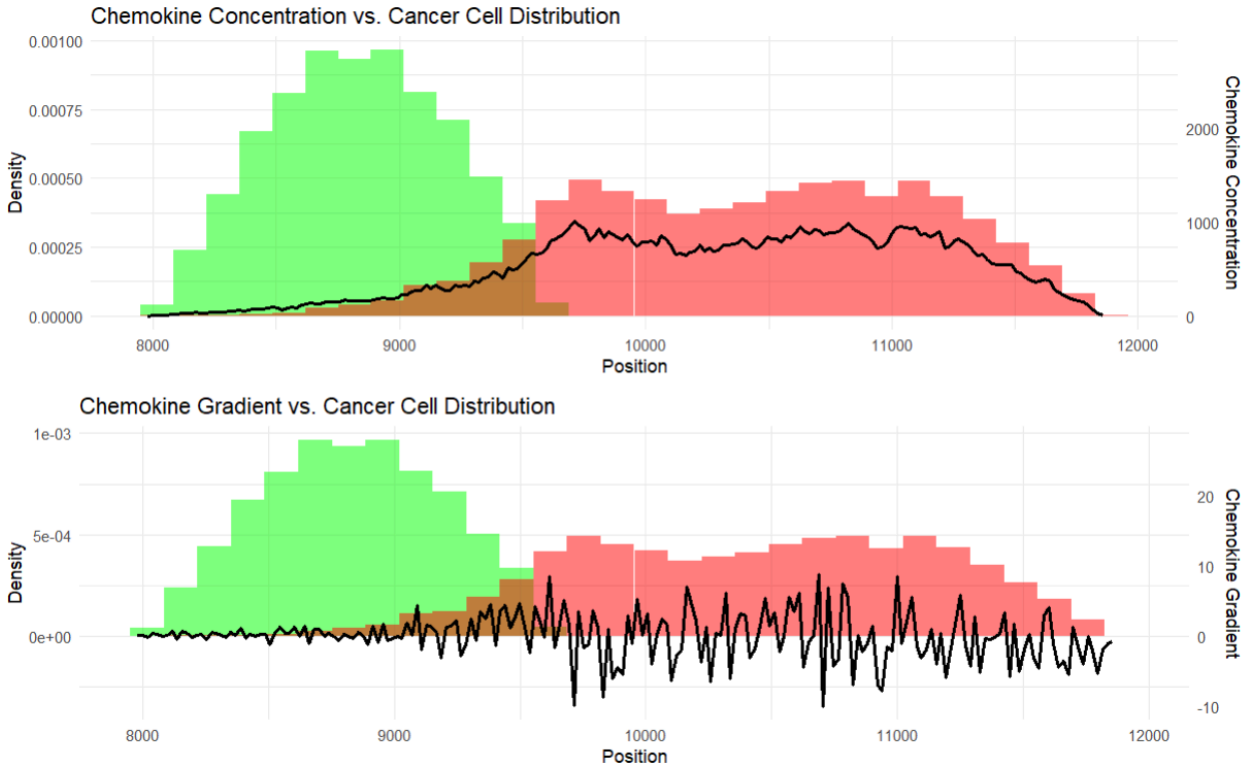
- Diffusion = 10
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 2



- Diffusion = 10
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 4

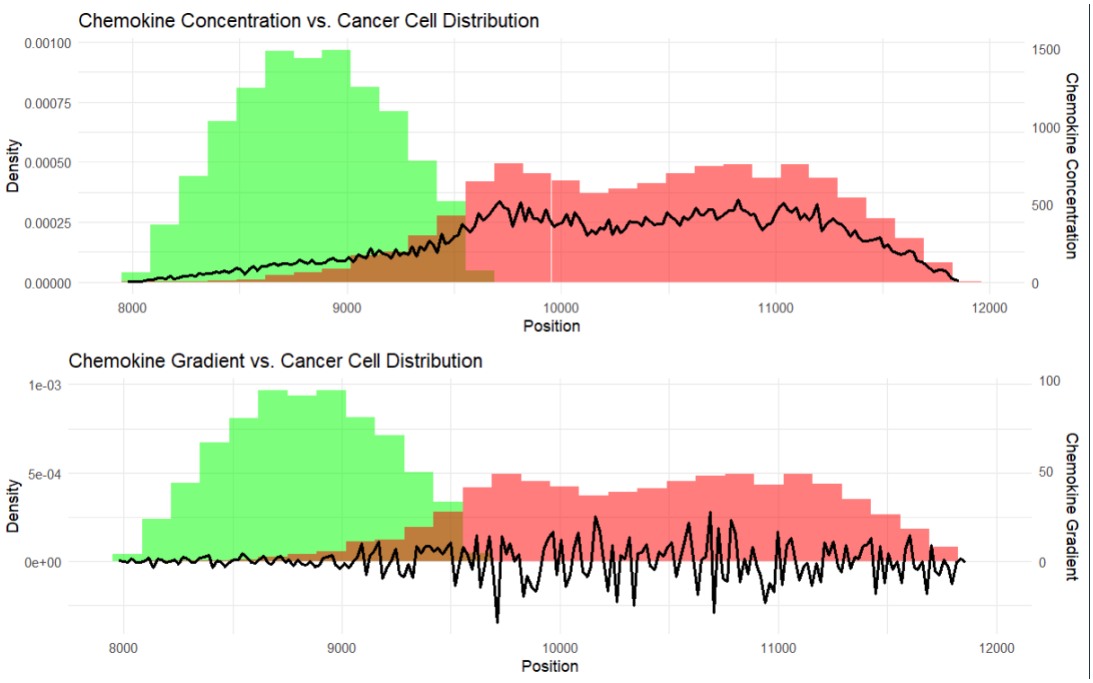


- Diffusion = 10
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 8

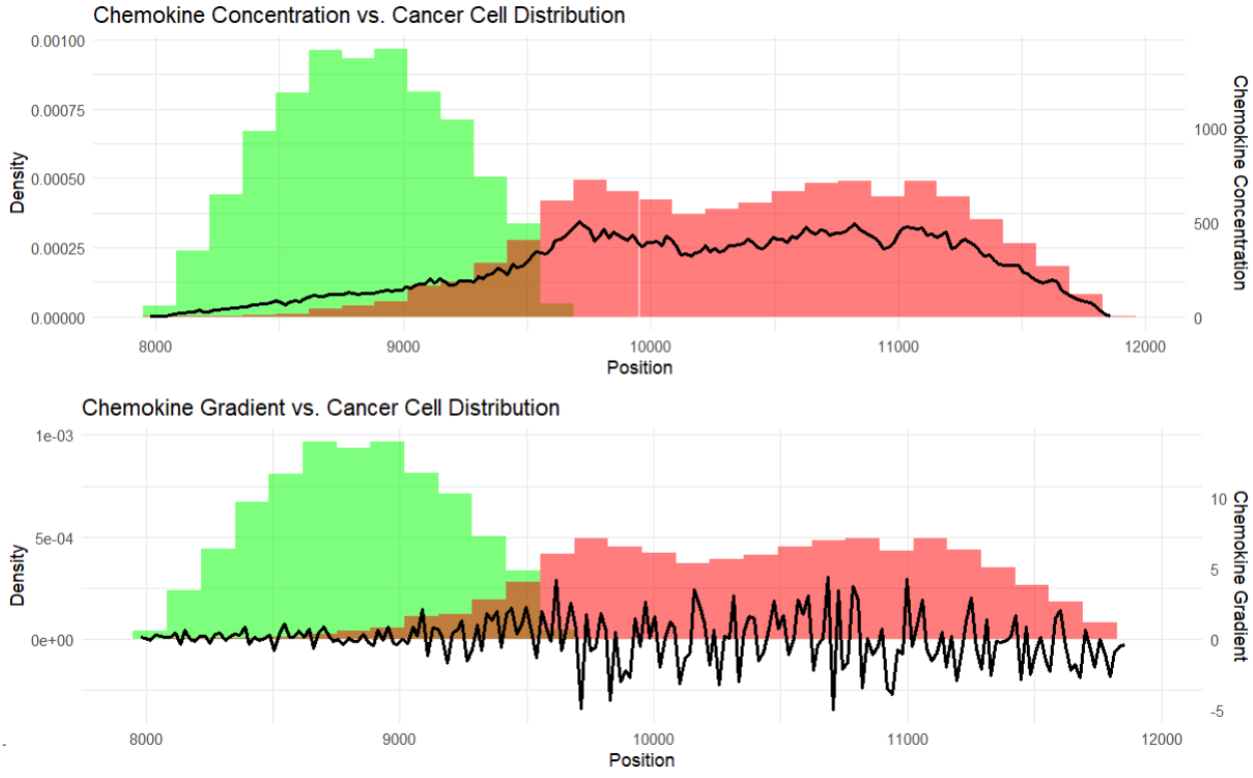


Modifying Diffusion

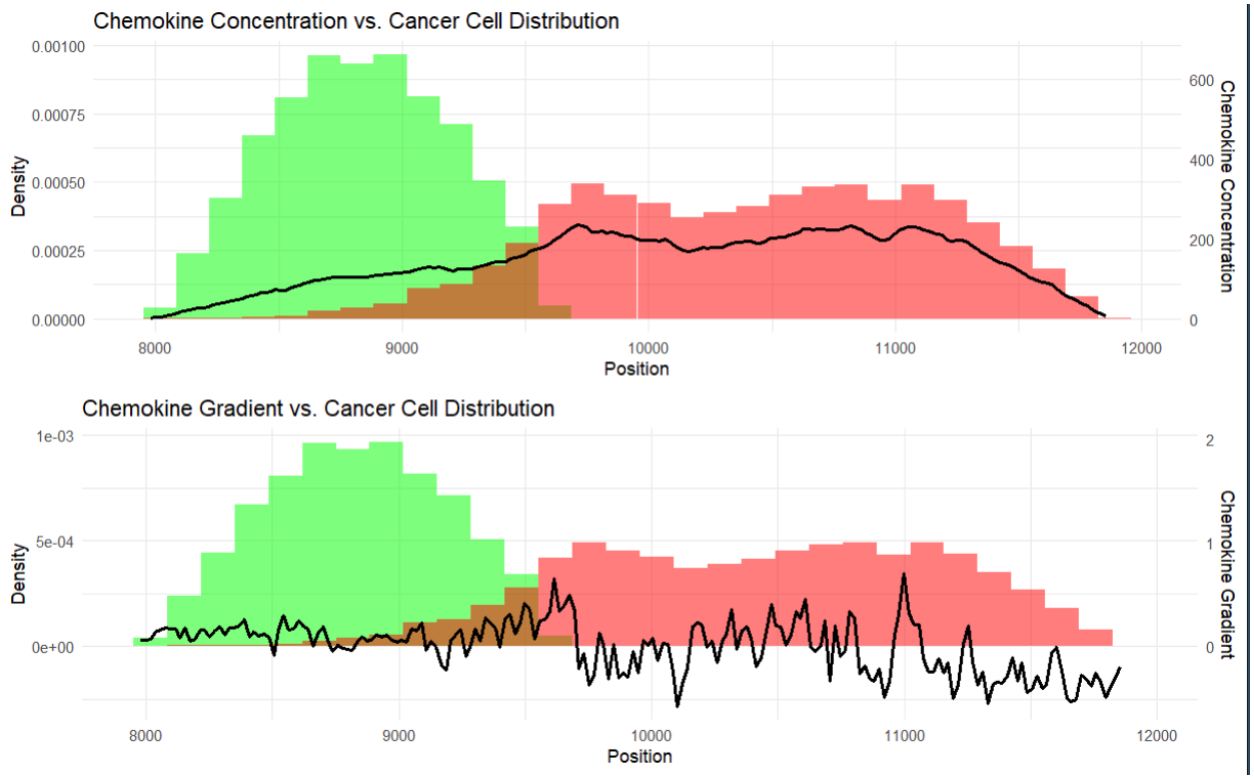
- Diffusion = 1
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 4



- Diffusion = 10
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 4

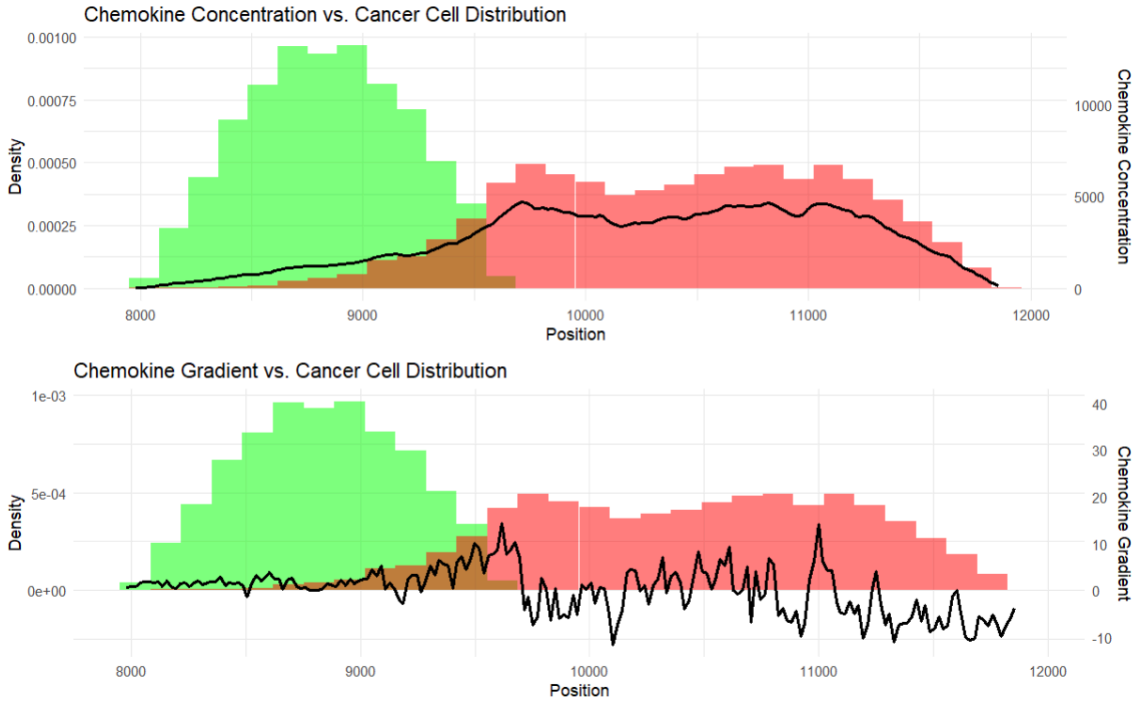


- Diffusion = 100
- Delta = 0.1
- YFP Heat = 1
- RFP Heat = 4

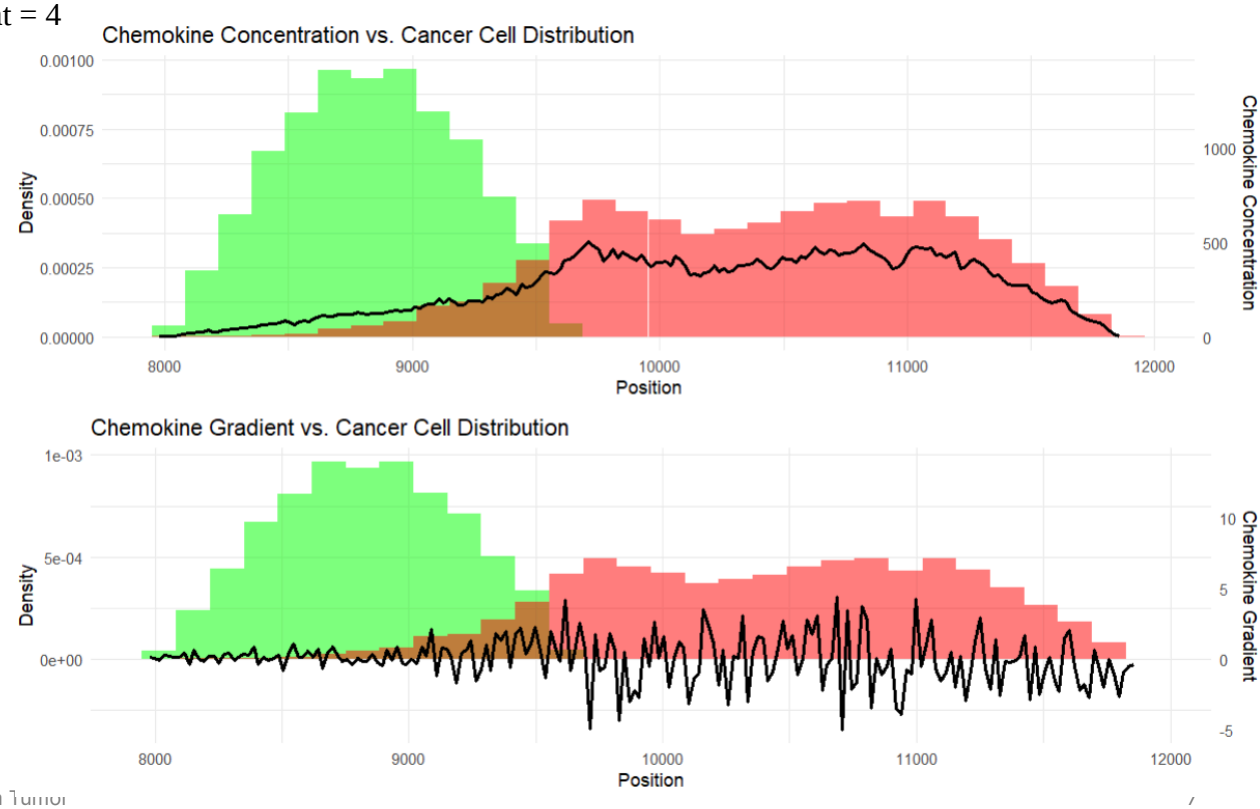


Modifying Decay

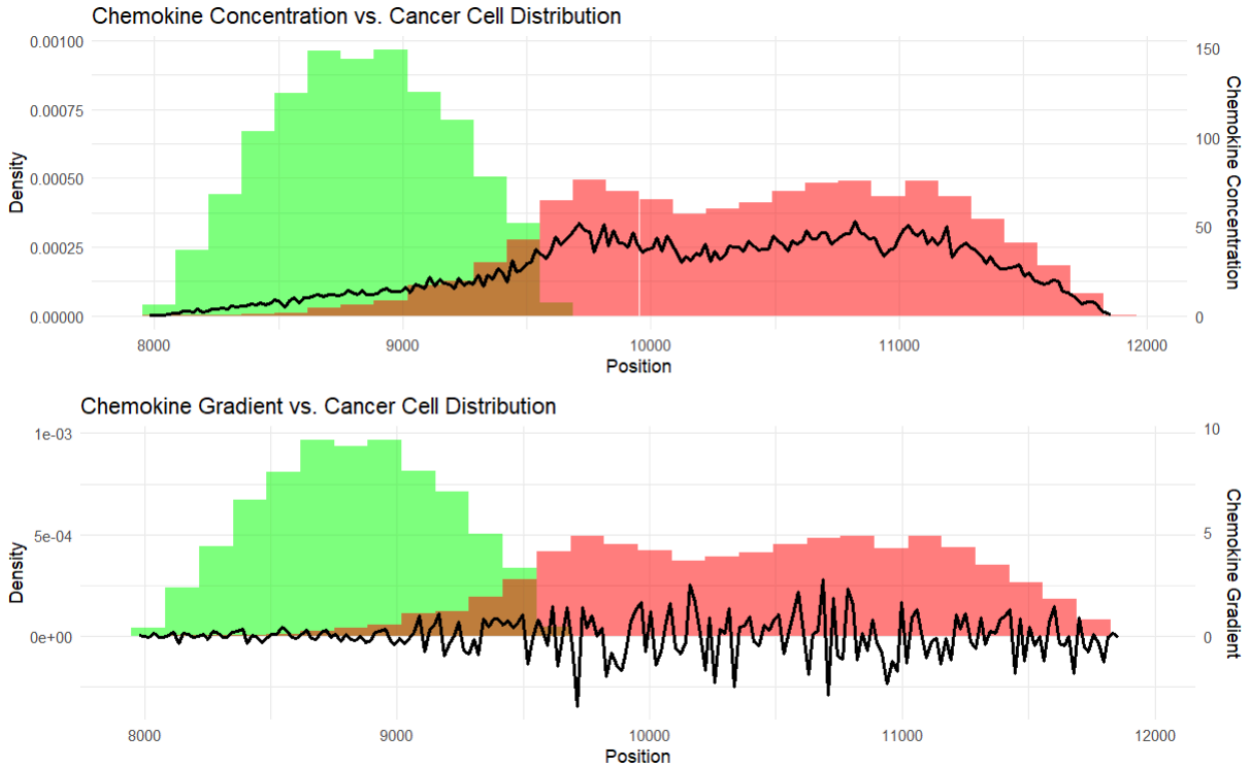
- Diffusion = 10
- Delta = 0.01
- YFP Heat = 1
- RFP Heat = 4



- Diffusion = 10
- Delta = 1
- YFP Heat = 1
- RFP Heat = 4



- Diffusion = 10=
- Delta = 1=
- YFP Heat = 1=
- RFP Heat = 4

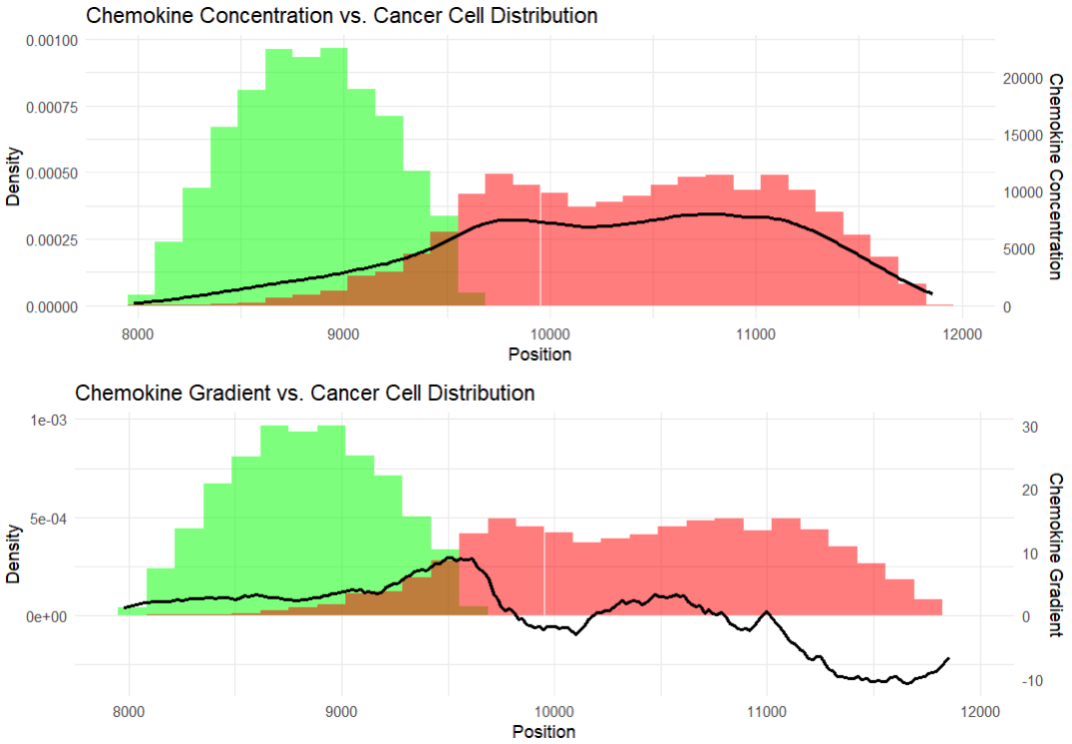


Paper Constants

Simulation Constant Searching

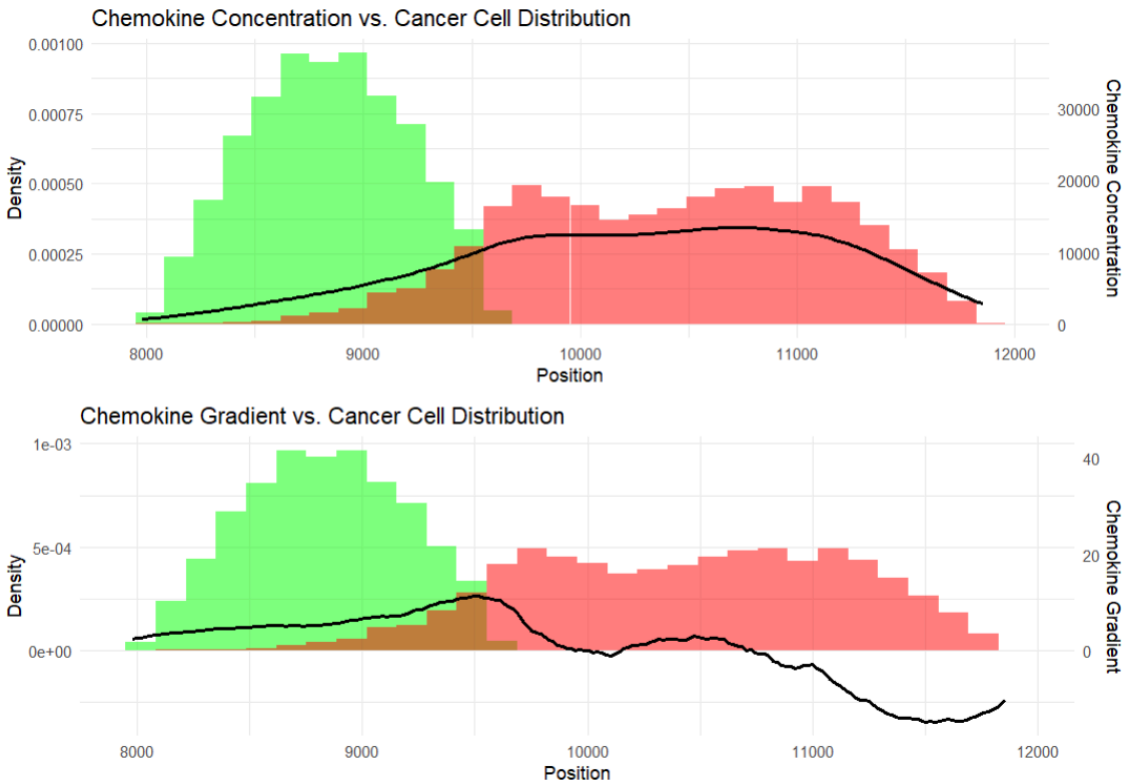
CCL21

- $d_{1/2} = 128.0$
- $K = 0.00542$
- YFP Heat = 1
- RFP Heat = 4



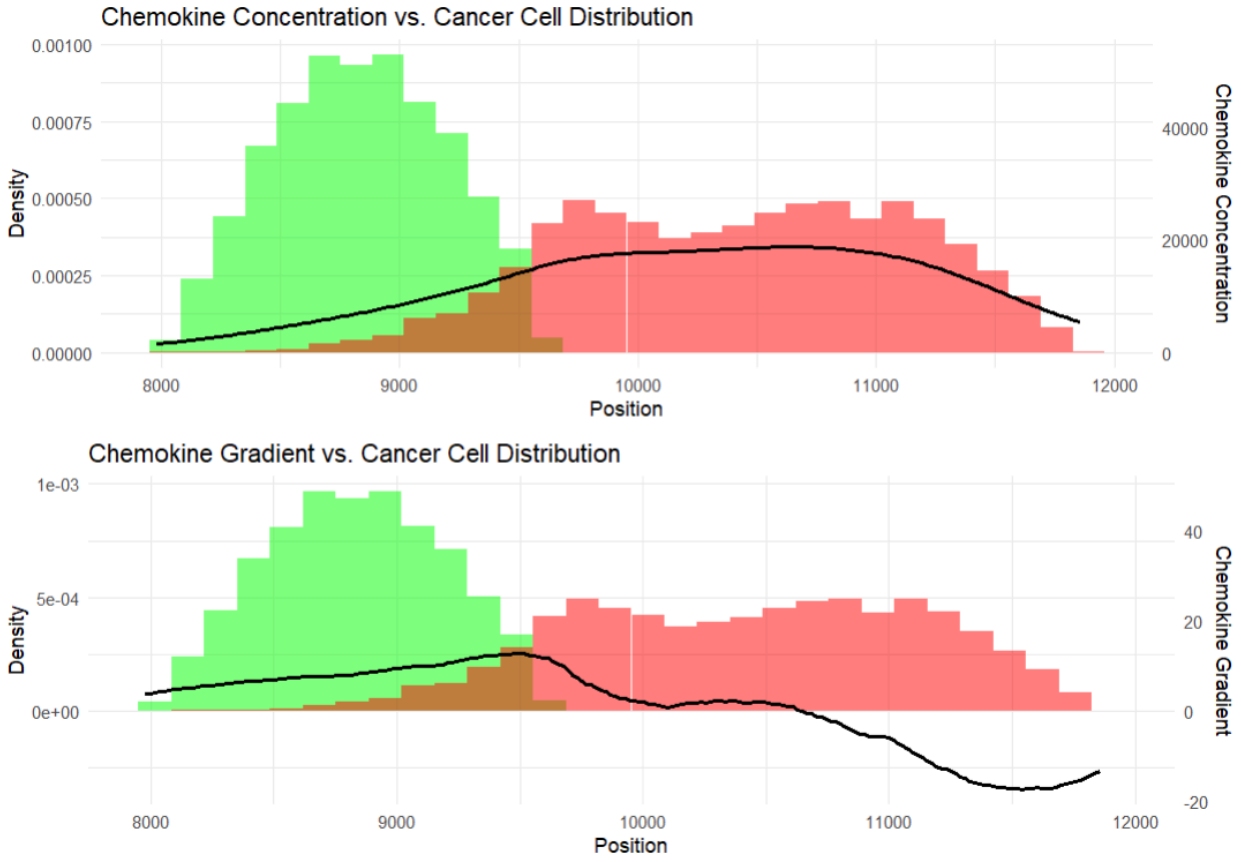
CCL19

- $d_{1/2} = 226.4$
- $K = 0.00306$
- YFP Heat = 1
- RFP Heat = 4



CCL21trunc

- $d_{1/2} = 338.6$
- $K = 0.00205$
- YFP Heat = 1
- RFP Heat = 4



results

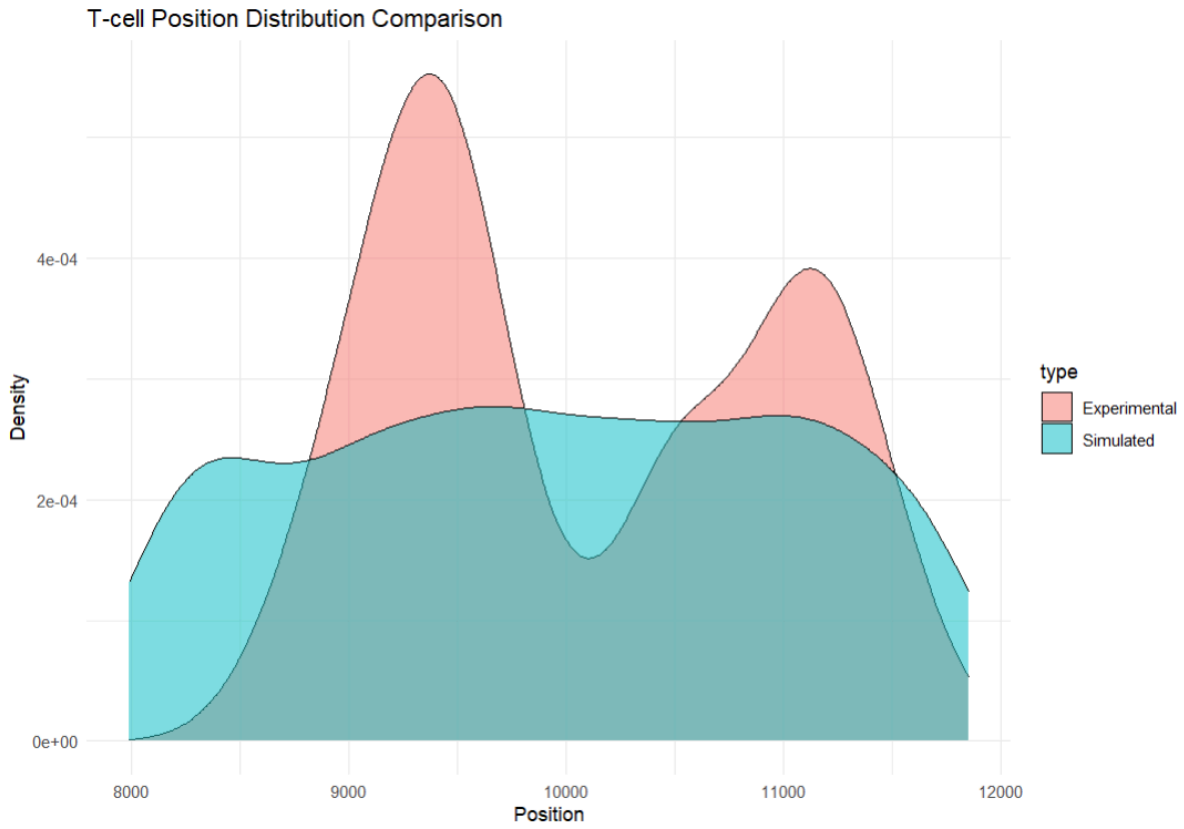
Info

- Anything greater than alpha = 0 does not appear to have change.

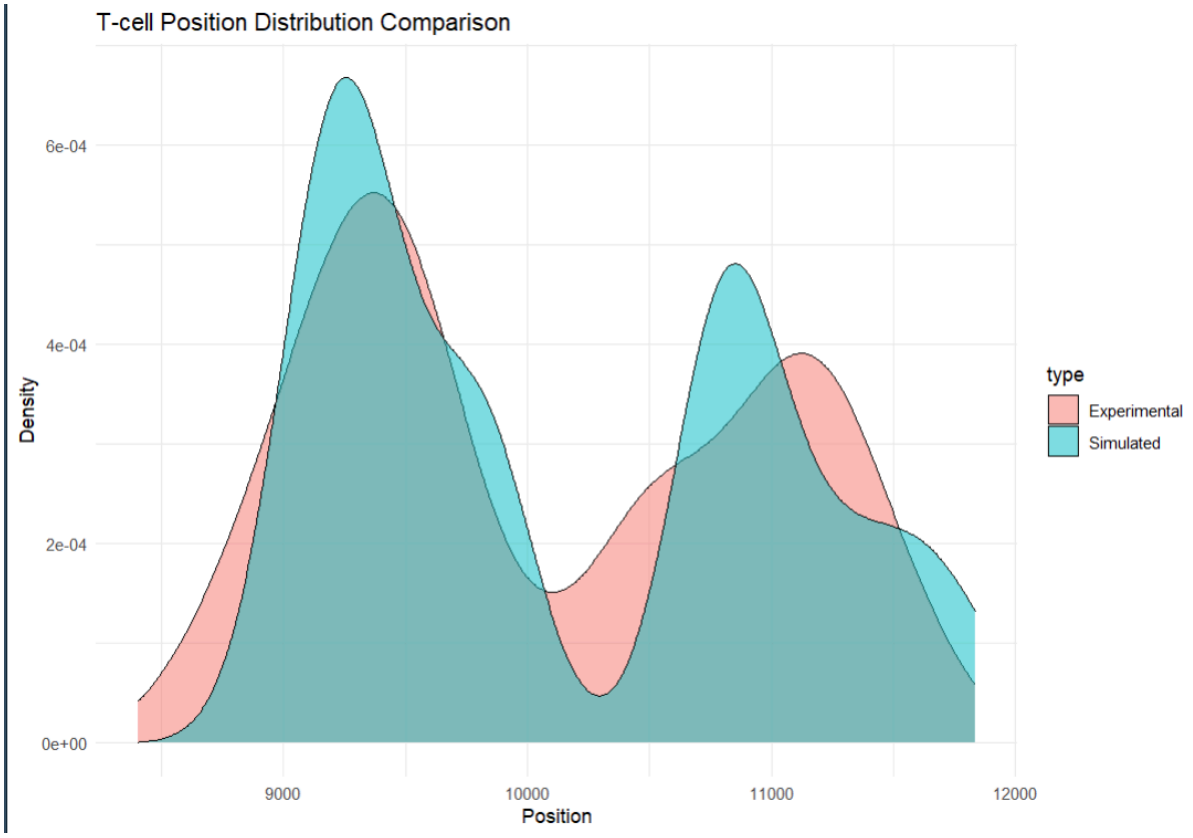
CCL21

Behavior 0

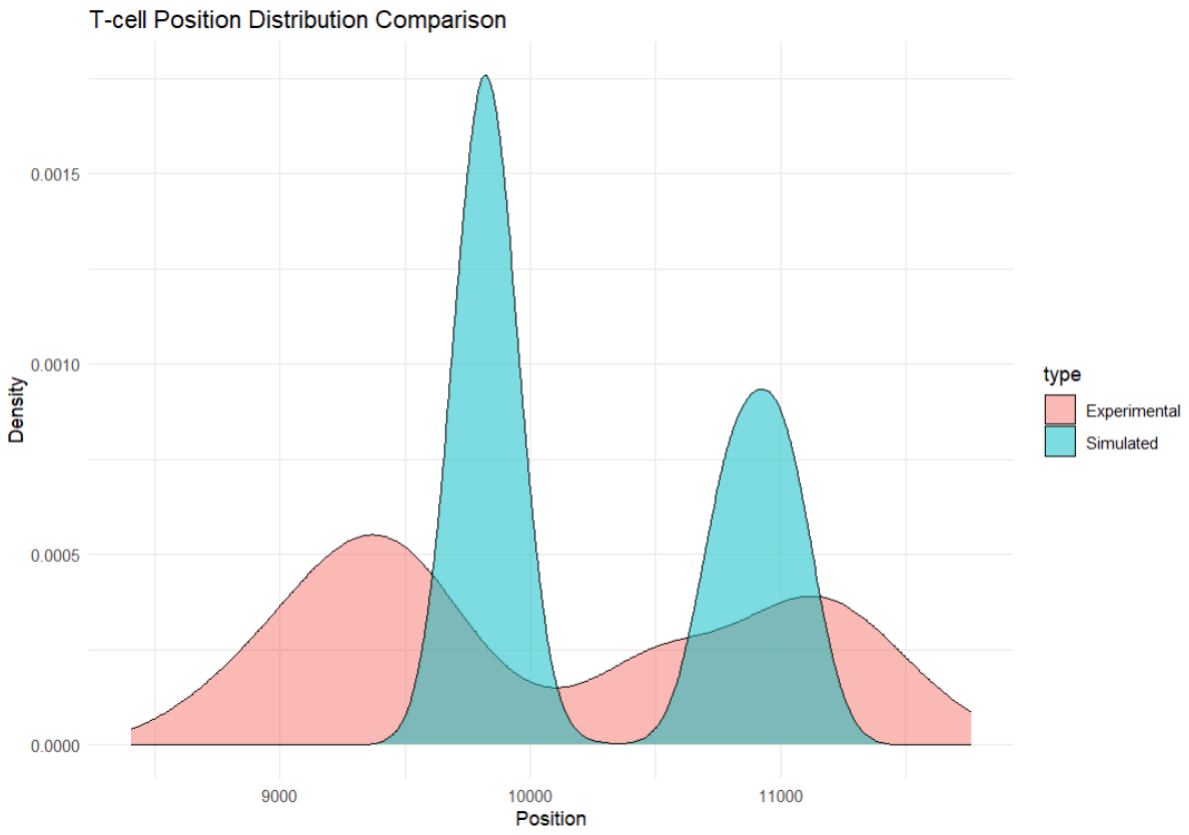
- alpha = -10
- speed = 2
- num-steps = 10000



- alpha = -1
- speed = 2
- num-steps = 10000

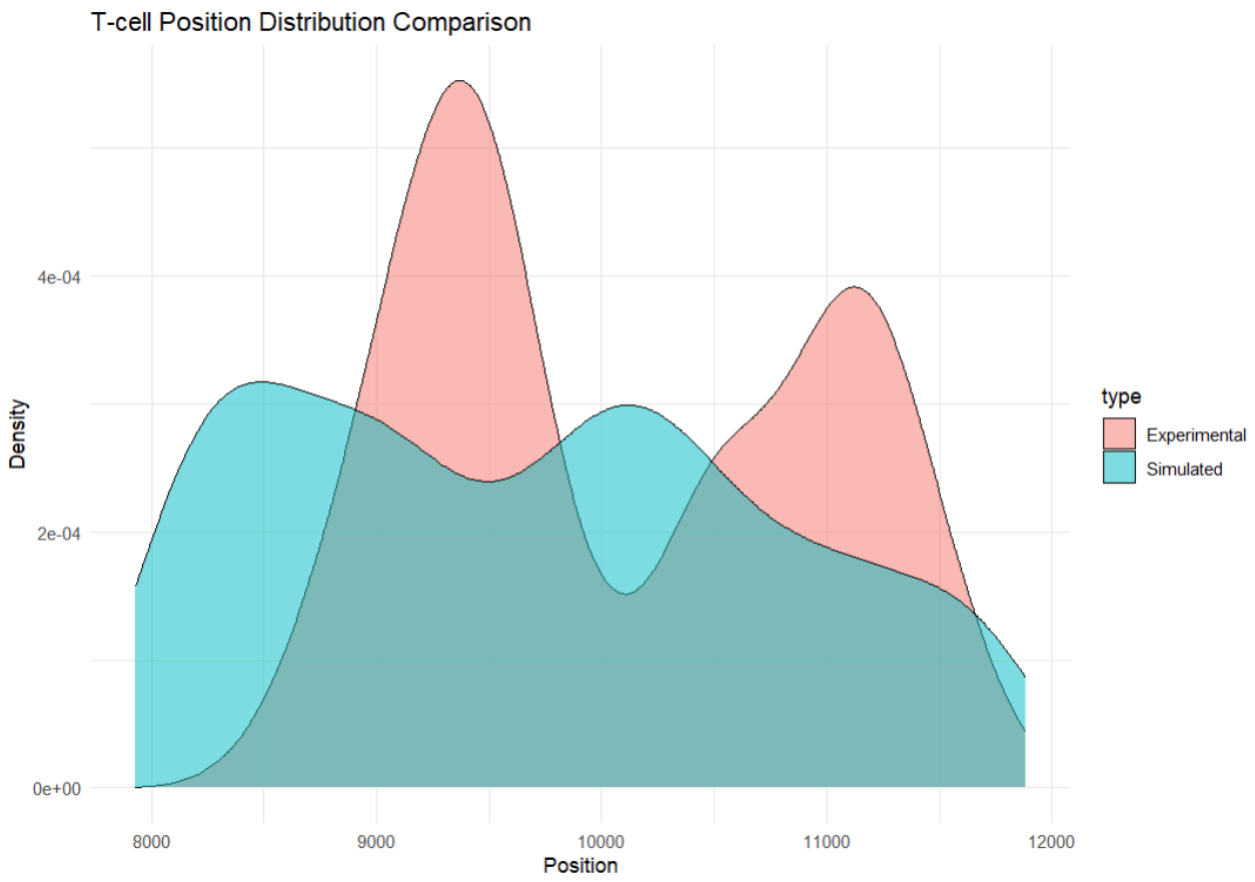


- alpha = 1e-6
- speed = 2
- num-steps = 10000

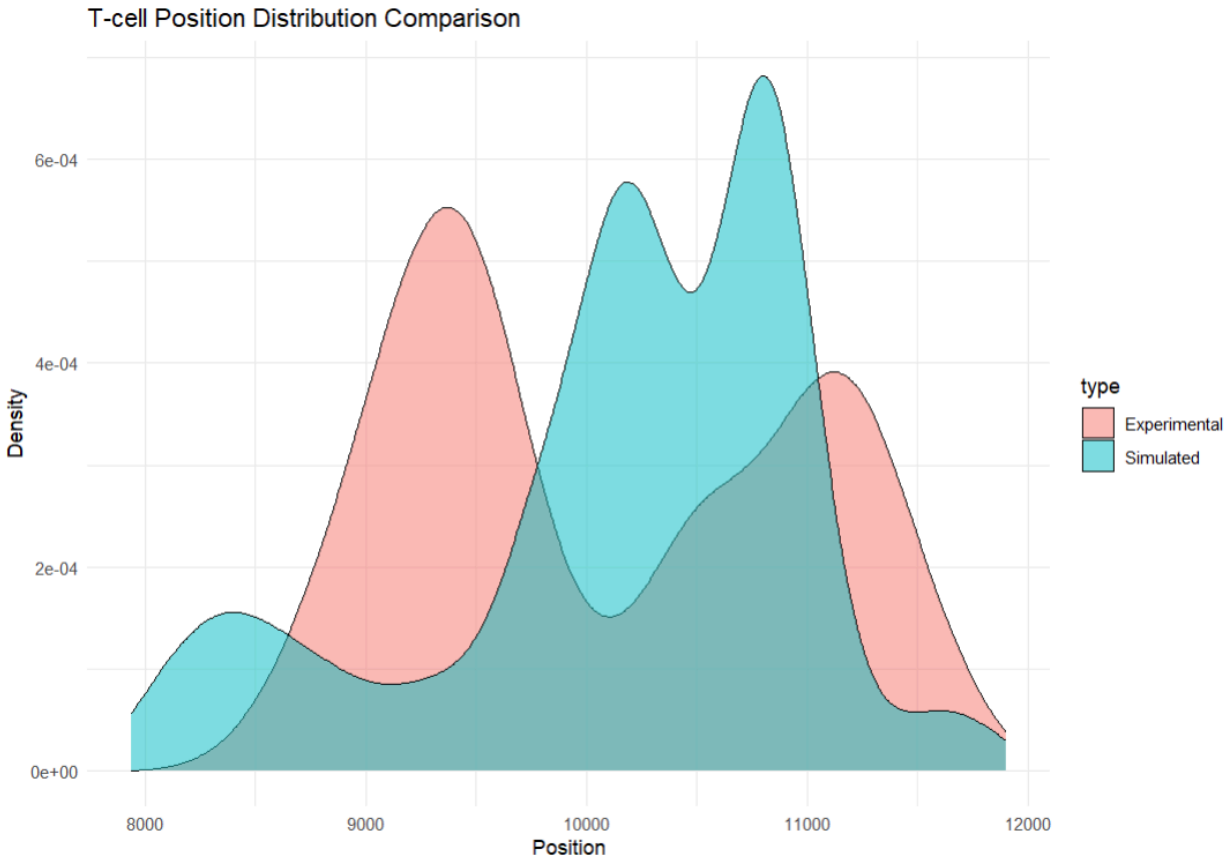


Behavior 1

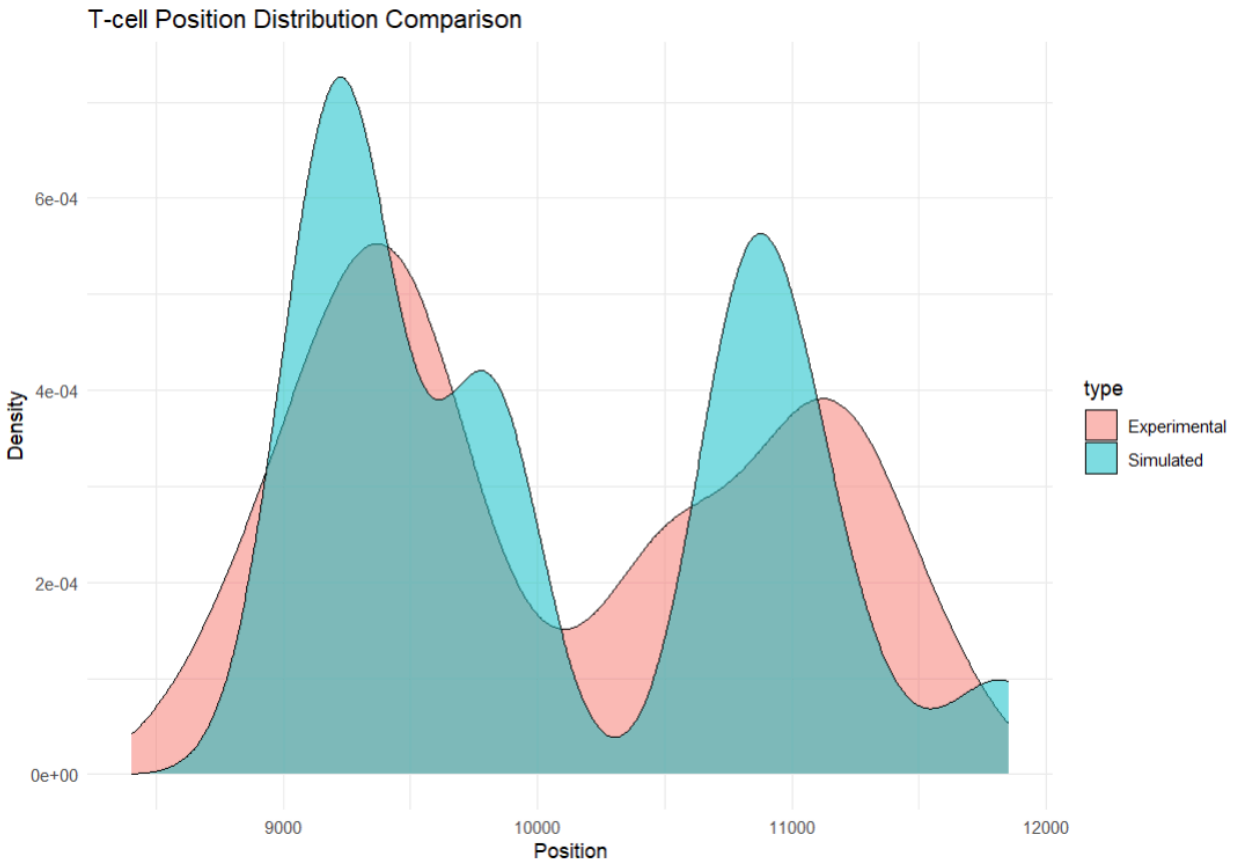
- alpha = -100
- speed = 2
- num-steps = 10000



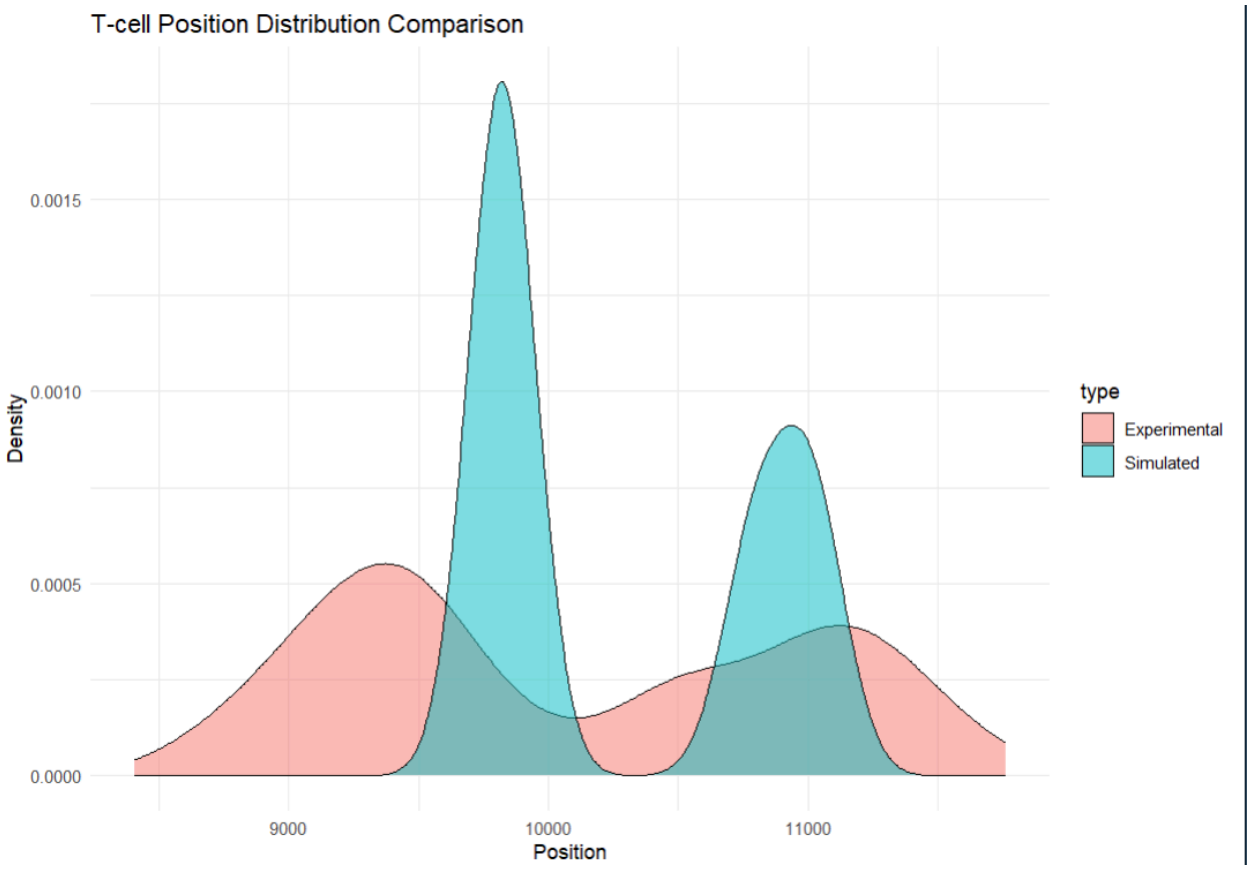
- alpha = -10
- speed = 2
- num-steps = 10000



- alpha = -1
- speed = 2
- num-steps = 10000


T-cell Position Distribution Comparison
Density
6e-04
4e-04
2e-04
0e+00
9000
10000
11000
12000
Position
type
Experimental
Simulated

- alpha = 1e-6


T-cell Position Distribution Comparison
Density
0.0015
0.0010
0.0005
0.0000
9000
10000
11000
Position
type
Experimental
Simulated

Steady-State Diffusion with Degradation in 2D

1 Introduction

We aim to derive and solve the steady-state diffusion equation for chemokine concentration in a two-dimensional space with degradation. We assume a system where chemokines diffuse outward from cancer cells while simultaneously degrading at a constant rate.

2 Deriving the 2D Diffusion Equation

2.1 Fick's First Law

Fick's First Law states that the diffusion flux $\mathbf{J}$ is proportional to the negative gradient of the concentration:

$$\mathbf{J} = -D\nabla c, \tag{1}$$

where:

- $\mathbf{J} = (J_x, J_y)$ is the diffusion flux (amount of substance per unit area per unit time),
- D is the diffusion coefficient,
- $c(x, y, t)$ is the chemokine concentration,
- ∇c is the concentration gradient.

In Cartesian coordinates, this expands to

$$J_x = -D\frac{\partial c}{\partial x}, \quad J_y = -D\frac{\partial c}{\partial y}. \tag{2}$$

2.2 Fick's Second Law

Applying the principle of mass conservation, we obtain Fick's Second Law:

$$\frac{\partial c}{\partial t} = -\nabla \cdot \mathbf{J}. \tag{3}$$

Expanding the divergence in two dimensions:

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right). \tag{4}$$

If chemokines degrade at a constant rate δ, we introduce a decay term:

$$\frac{\partial c}{\partial t} = D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right) - \delta c. \tag{5}$$

2.3 Steady-State Approximation

For a steady-state solution, we set $\partial c/\partial t = 0$:

$$D\left(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}\right) = \delta c. \tag{6}$$

Dividing by D:

$$\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} = \frac{\delta}{D} c. \tag{7}$$

3 Conversion to Polar Coordinates

Since the problem is radially symmetric, we use polar coordinates (r, θ), where

$$x = r\cos\theta, \quad y = r\sin\theta.$$

The Laplacian in polar coordinates (assuming no θ dependence) simplifies to

$$\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} = \frac{\delta}{D}\, c.$$

Define

$$\lambda^2 = \frac{\delta}{D} \quad \Longrightarrow \quad \lambda = \sqrt{\frac{\delta}{D}}.$$

The steady-state radial equation then becomes:

$$\frac{d^2 c}{dr^2} \; + \; \frac{1}{r}\frac{dc}{dr} \; - \; \lambda^2\, c = 0.$$

4 Substitution $\boldsymbol{\rho = \lambda\, r}$

To transform the above ODE into the standard modified Bessel equation of order 0, we set

$$\rho = \lambda\, r \quad \Longrightarrow \quad r = \frac{\rho}{\lambda}.$$

Using the chain rule:

1. First derivative:
$$\frac{d}{dr} = \frac{d\rho}{dr}\frac{d}{d\rho} = \lambda\,\frac{d}{d\rho}.$$

2. Second derivative:
$$\frac{d^2}{dr^2} = \frac{d}{dr}\left(\lambda\frac{d}{d\rho}\right) = \lambda^2\,\frac{d^2}{d\rho^2}.$$

Substitute these into

$$\frac{d^2 c}{dr^2} + \frac{1}{r}\frac{dc}{dr} - \lambda^2\, c = 0.$$

We get:

$$\lambda^2\frac{d^2 c}{d\rho^2} + \frac{1}{r}\left(\lambda\frac{dc}{d\rho}\right) - \lambda^2\, c = 0.$$

Since $r = \rho/\lambda$, we have $\frac{1}{r} = \frac{\lambda}{\rho}$, so

$$\lambda \frac{1}{r} \frac{dc}{d\rho} = \lambda^2 \frac{1}{\rho} \frac{dc}{d\rho}.$$

Hence,

$$\lambda^2 \Big[\frac{d^2c}{d\rho^2} + \frac{1}{\rho} \frac{dc}{d\rho} - c \Big] = 0.$$

Dividing by λ^2 (which is nonzero), we obtain the **modified Bessel equation** of order 0:

$$\frac{d^2c}{d\rho^2} + \frac{1}{\rho} \frac{dc}{d\rho} - c = 0.$$

4.1 Solution via Modified Bessel's Equation

This is recognized as a modified Bessel's equation of order zero. By letting $\rho = \lambda r$, we rewrite the ODE in the standard form of the modified Bessel equation:

$$\frac{d^2c}{d\rho^2} + \frac{1}{\rho} \frac{dc}{d\rho} - c = 0. \tag{8}$$

The general solution is a linear combination of $I_0(\rho)$ and $K_0(\rho)$, the modified Bessel functions of the first and second kind of order zero :

$$c(\rho) = A\, I_0(\rho) + B\, K_0(\rho). \tag{9}$$

Reverting to r, we have

$$c(r) = A\, I_0(\lambda r) + B\, K_0(\lambda r). \tag{10}$$

4.2 Applying Boundary Conditions

Decay at Infinity. As $r \to \infty$, $I_0(\lambda r)$ grows exponentially, while $K_0(\lambda r)$ decays exponentially . To ensure $c(r) \to 0$ at large r, we must set $A = 0$. Hence, the solution simplifies to

$$c(r) = B\, K_0(\lambda r). \tag{11}$$