Front Dynamics in a Reaction-Diffusion Model for Tumor Growth

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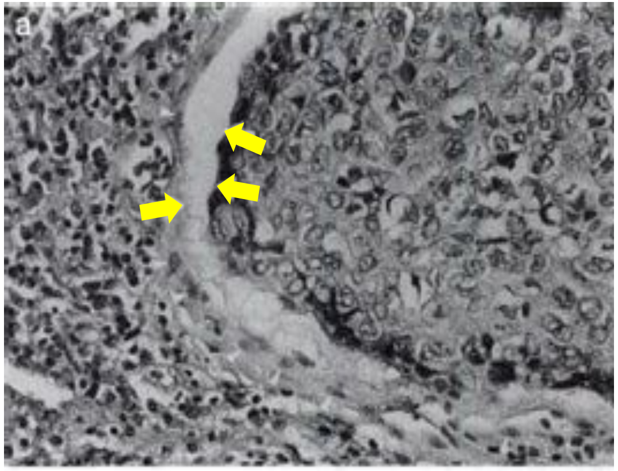
Introduction

- We want to understand cancer tumor dynamics phenomenologically
- Much mathematical analysis of tumor growth is done in one spatial dimension
- We can capture new behaviors by incorporating an additional dimension



Tumor Growth Model (Gatenby-Gawlinski)

n_1 normal cells

n_2 cancer cells

L acid produced by cancer cells

D is a small constant;
approximate with D=0

$$\begin{cases} (n_1)_\tau &= \overbrace{n_1(1-n_1) - \delta_1 L n_1}^{F(n_1,n_2,L)} + \cancel{D\Delta n_1} \\ (n_2)_\tau &= \overbrace{\varrho n_2(1-n_2)(n_2-a) - \delta_2 L n_2}^{G(n_1,n_2,L)} + \nabla\cdot((1+\kappa-n_1)\nabla n_2) \\ L_\tau &= \overbrace{\delta_3(n_2-L)}^{H(n_1,n_2,L)} + \frac{1}{\varepsilon^2}\Delta L \end{cases}$$

Fast-Slow Analysis

Fast component describes the “fast” dynamics (spatially) and slow component describes the “slow” dynamics

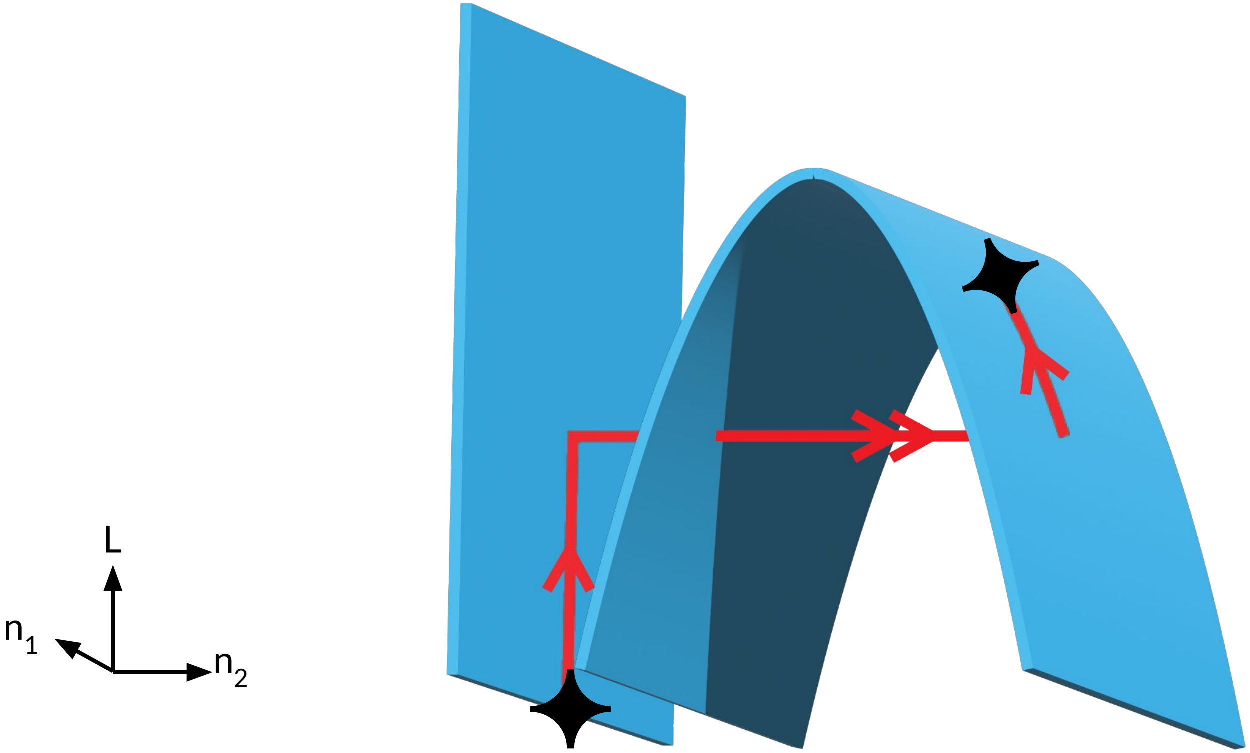
$$\textbf{Fast} \quad \left({}' = \frac{d}{d\xi}\right)$$

$$\begin{cases} n_1' &= -\frac{n_1}{c}\left(1 - n_1 - \delta_1 L\right) \\ n_2' &= \frac{r}{1+\kappa-n_1} \\ r' &= -\frac{cr}{1+\kappa-n_1} - \varrho n_2(1-n_2)(n_2-a) + \delta_2 L n_2 \end{cases}$$

$$\textbf{Slow} \quad \left(\epsilon\xi = \tau,\ {}' = \frac{d}{d\tau}\right)$$

$$\begin{cases} L' &= s \\ s' &= -\delta_3(n_2 - L). \end{cases}$$

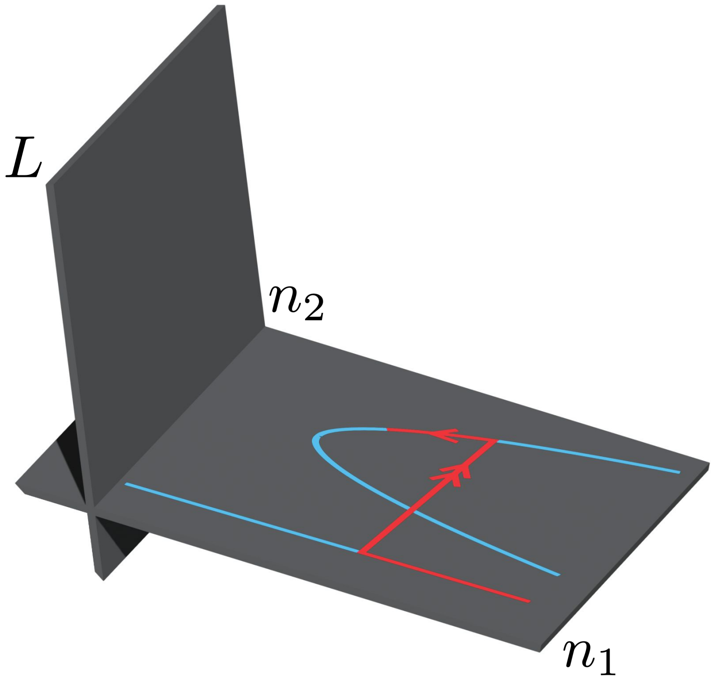
Construction of the Traveling Front



Benign vs. Malignant

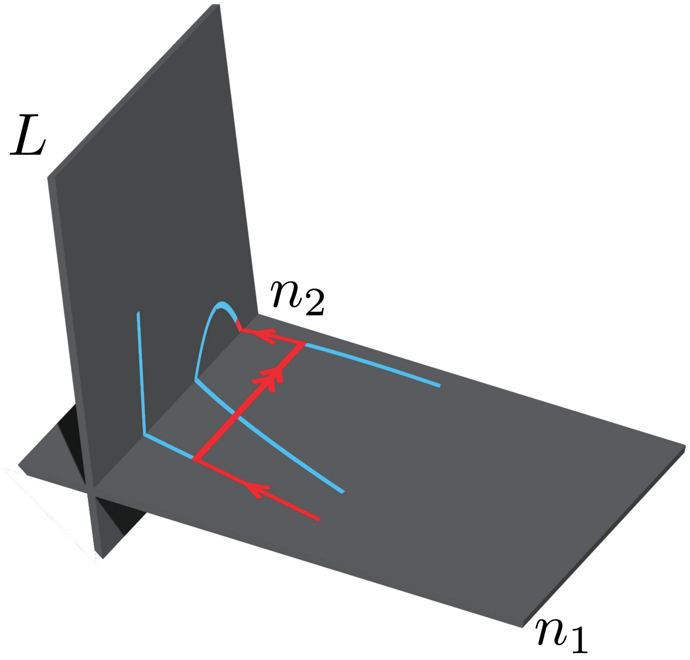
In the benign case, there is a stable fixed point where

$$n_1 = 1 - \delta_1 L^\star > 0$$

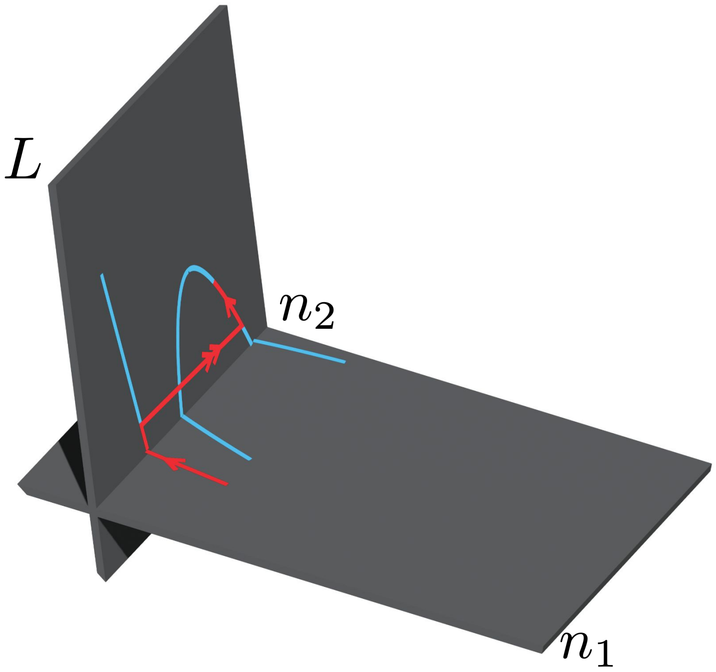


Benign vs. Malignant

Two possibilities for malignant case:

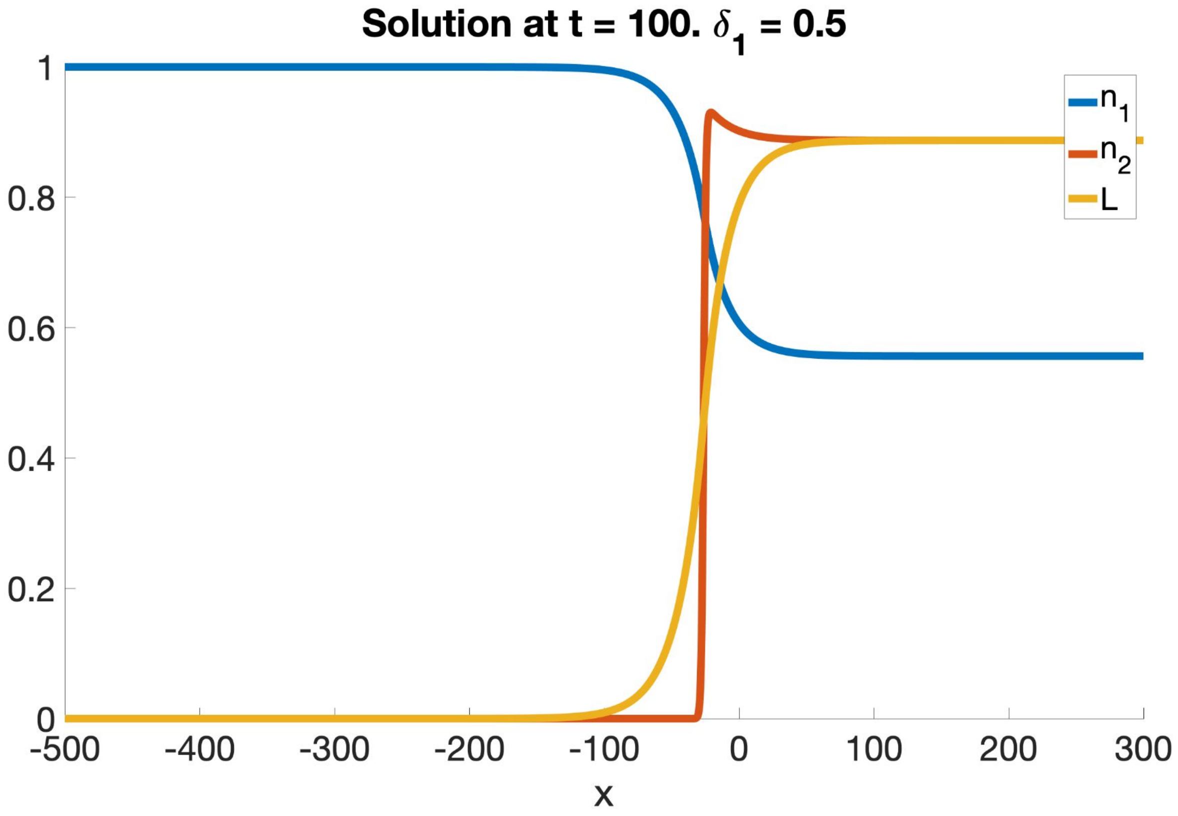


n_2 increases before $n_1 \downarrow 0$



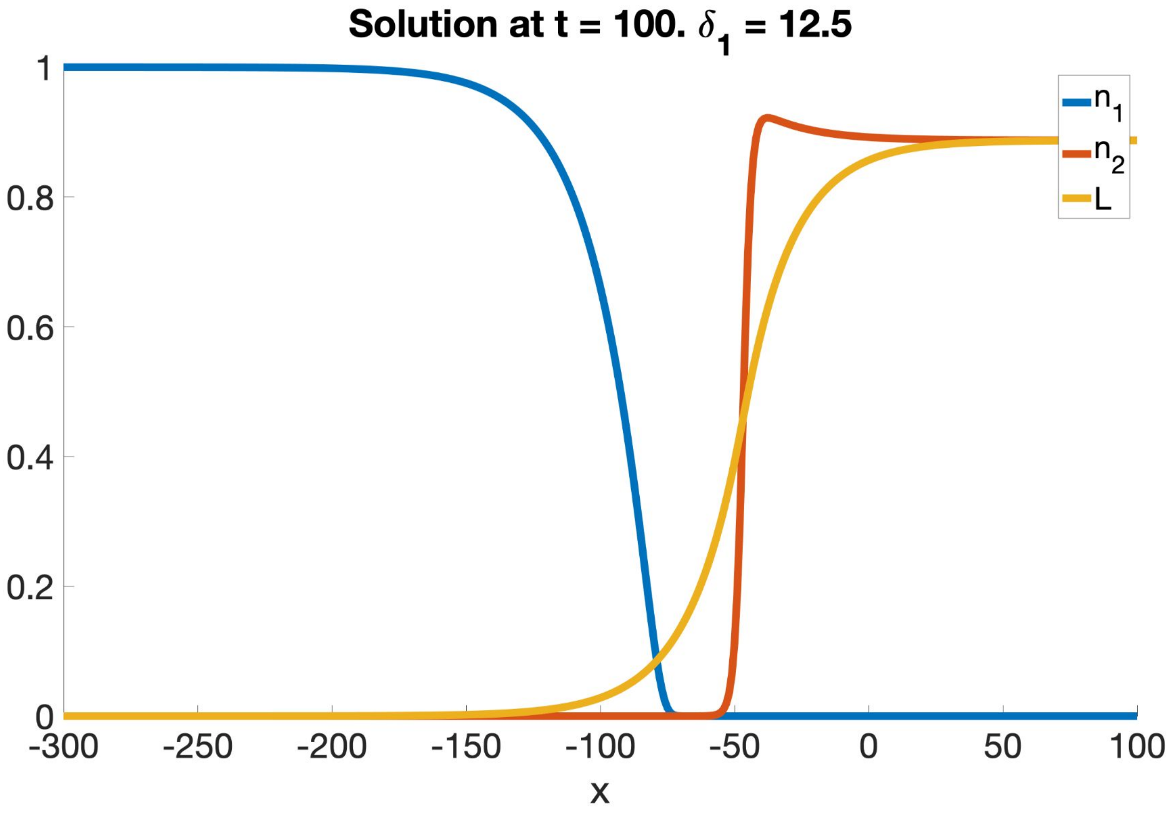
$n_1 \downarrow 0$ before n_2 increases

No Gap



Solution at t = 100. δ_1 = 0.5
1
0.8
0.6
0.4
0.2
0
-500
-400
-300
-200
-100
0
100
200
300
x
n_1
n_2
L

Gap



Solution at t = 100. δ_1 = 12.5
1
0.8
0.6
0.4
0.2
0
-300
-250
-200
-150
-100
-50
0
50
100
x
n_1
n_2
L

Stability Analysis of the Traveling Front

In the traveling wave frame, we have

$$0 = D(n_1)_{\xi\xi} + c(n_1)_\xi + F(n_1, n_2, L)$$
$$0 = ((1 + \kappa - n_1)(n_2)_\xi)_\xi + c(n_2)_\xi + G(n_1, n_2, L)$$
$$0 = \frac{1}{\varepsilon^2} L_{\xi\xi} + cL_\xi + H(n_1, n_2, L)$$

Stability Analysis of the Traveling Front

Linearize about traveling wave solution:

$$(n_1, n_2, L) = (n_1^\star, n_2^\star, L^\star)(\xi) + e^{\lambda\tau + i\ell y}(\overline{n_1}, \overline{n_2}, \overline{L})(\xi)$$

$$\mathbb{L}(\xi)\begin{pmatrix}\overline{n_1}\\ \overline{n_2}\\ \overline{L}\end{pmatrix} = \lambda\begin{pmatrix}\overline{n_1}\\ \overline{n_2}\\ \overline{L}\end{pmatrix} + \ell^2\begin{pmatrix}D & & \\ & 1+\kappa-n_1^\star & \\ & & \frac{1}{\varepsilon^2}\end{pmatrix}\begin{pmatrix}\overline{n_1}\\ \overline{n_2}\\ \overline{L}\end{pmatrix}$$

where

$$\mathbb{L}(\xi) = \begin{pmatrix} D\frac{d^2}{d\xi^2} + c\frac{d}{d\xi} + F_{n_1} & 0 & F_L \\ -(n_2^\star)_{\xi\xi} - (n_2^\star)_\xi\frac{d}{d\xi} & (1+\kappa-n_1^\star)\frac{d^2}{d\xi^2} + c\frac{d}{d\xi} + G_{n_2} - (n_1^\star)_\xi\frac{d}{d\xi} & G_L \\ 0 & H_{n_2} & \frac{1}{\varepsilon^2}\frac{d^2}{d\xi^2} + H_L + c\frac{d}{d\xi} \end{pmatrix}$$

Instability Criterion

- We expect $\lambda_c(\ell) = \lambda_{c,2}\ell^2 + \mathcal{O}(\ell^4)$
- Solvability condition:

$$\left\langle \lambda_{c,2} \begin{pmatrix} (n_1^\star)_\xi(\xi) \\ (n_2^\star)_\xi(\xi) \\ (L^\star)_\xi(\xi) \end{pmatrix} + \begin{pmatrix} D(n_1^\star)_\xi(\xi) \\ (1+\kappa-n_1^\star)(n_2^\star)_\xi(\xi) \\ \frac{1}{\varepsilon^2}(L^\star)_\xi(\xi) \end{pmatrix}, \begin{pmatrix} (\overline{n_1}^c)^A(\xi) \\ (\overline{n_2}^c)^A(\xi) \\ (\overline{L}^c)^A(\xi) \end{pmatrix} \right\rangle = 0$$

$$\implies \lambda_{c,2} = -\frac{\int_{\mathbb{R}} D(n_1^\star)_\xi(\overline{n_1}^c)^A + (1+\kappa-n_1^\star)(n_2^\star)_\xi(\overline{n_2}^c)^A + \frac{1}{\varepsilon^2}(L^\star)_\xi(\overline{L}^c)^A \, d\xi}{\int_{\mathbb{R}}(n_1^\star)_\xi(\overline{n_1}^c)^A + (n_2^\star)_\xi(\overline{n_2}^c)^A + (L^\star)_\xi(\overline{L}^c)^A \, d\xi}$$

Instability Criterion

- Sign of

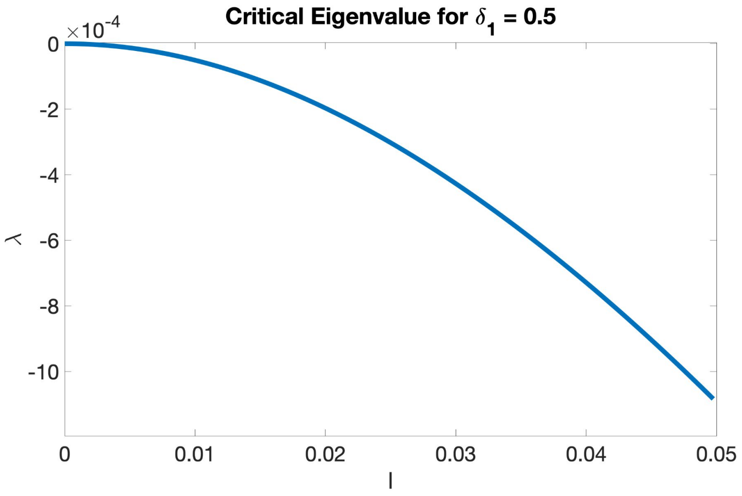
$$\lambda_{c,2} = -\frac{\int_{\mathbb{R}} D(n_1^\star)_\xi (\overline{n_1}^c)^A + (1+\kappa - n_1^\star)(n_2^\star)_\xi (\overline{n_2}^c)^A + \frac{1}{\varepsilon^2}(L^\star)_\xi (\overline{L}^c)^A \, d\xi}{\int_{\mathbb{R}} (n_1^\star)_\xi (\overline{n_1}^c)^A + (n_2^\star)_\xi (\overline{n_2}^c)^A + (L^\star)_\xi (\overline{L}^c)^A \, d\xi}$$

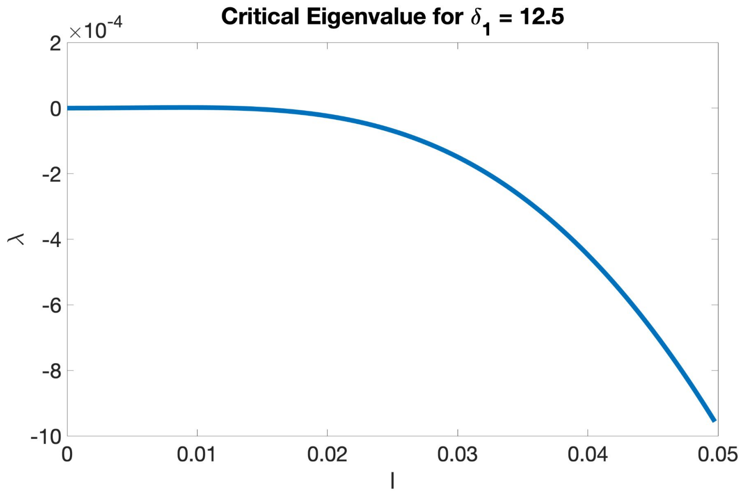
  determines stability

- Using the slow-fast structure, we compute

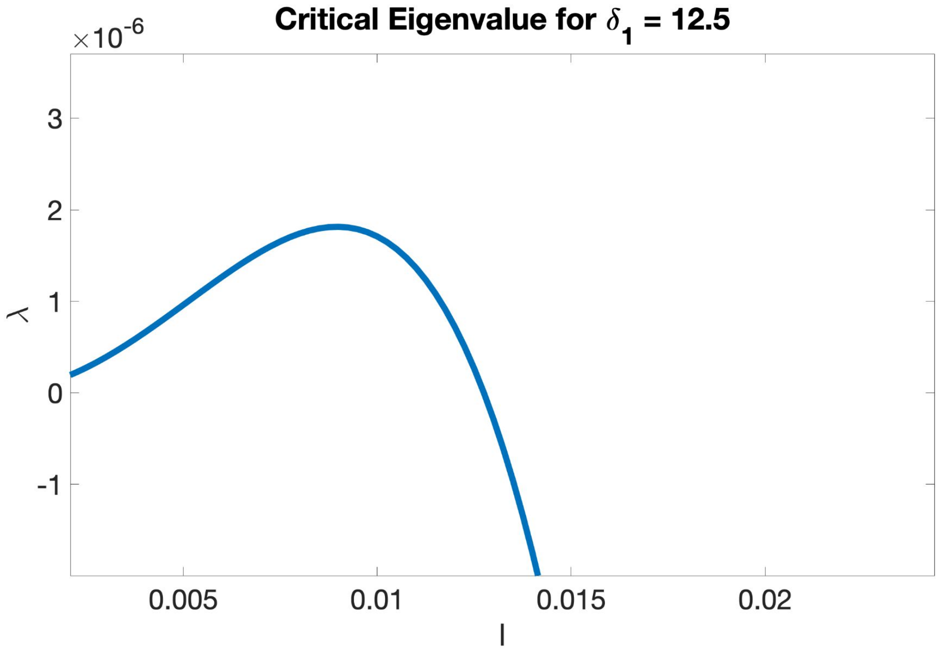
$$\operatorname{sgn}(\lambda_{c,2}) = \operatorname{sgn}\left(\int_{\mathbb{R}} \delta_1 \overline{n_1} n_1^\dagger + \delta_2 n_2^\dagger (n_2^\dagger)_\xi e^{\left(\frac{c}{1+\kappa - n_1^\star}\right)\xi} \, d\xi \right)$$

Critical Eigenvalues



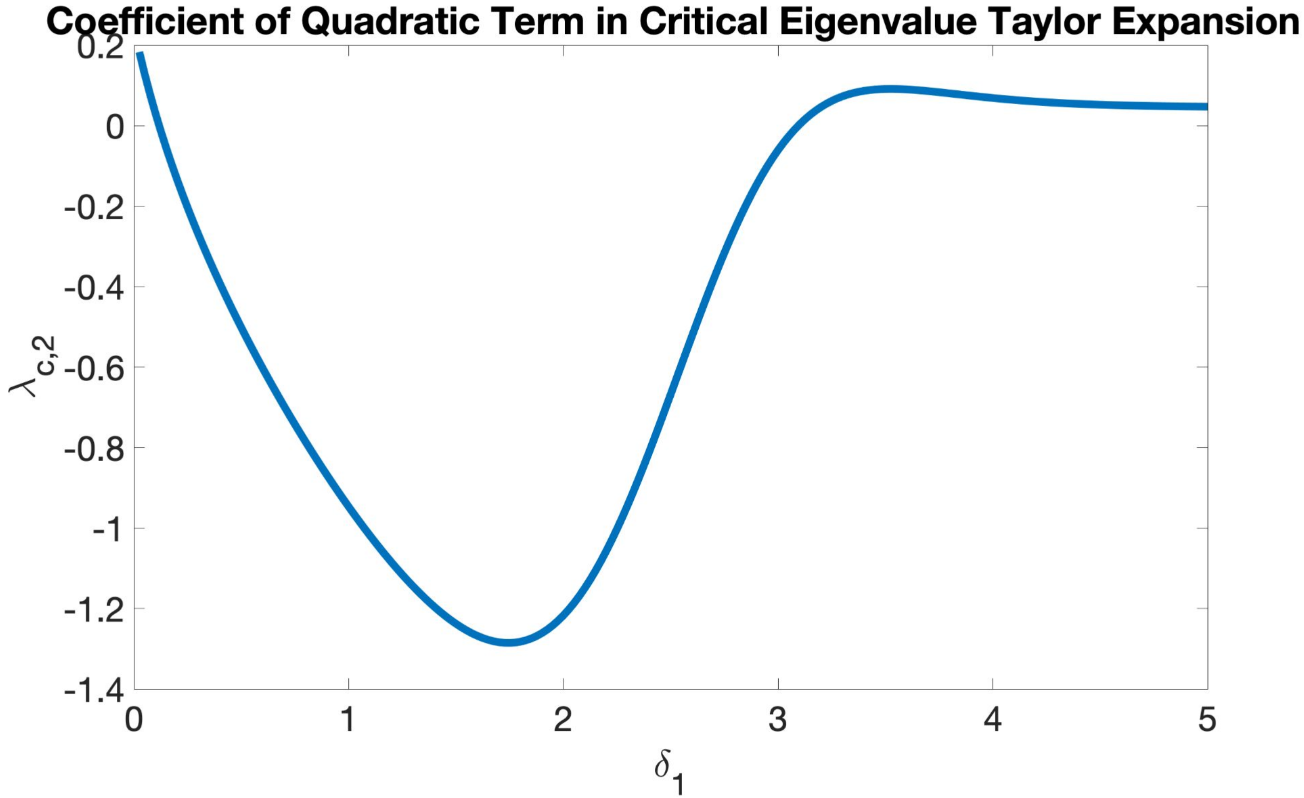


Zooming in on Case with Instability



Convexity Graph

$$\lambda_c(\ell) = \lambda_{c,2}\ell^2 + \mathcal{O}(\ell^4)$$



Thank you!

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2D Wave