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CHEME 5440
Final

1. Notch – Delta Signaling

(a) Two-cell Model.

$$\frac{\partial N_1}{\partial t} = F(D_2) - \gamma_N N_1$$

$$\frac{\partial D_1}{\partial t} = G(N_1) - \gamma_D D_1$$

$$\frac{\partial N_2}{\partial t} = F(D_1) - \gamma_N N_2$$

$$\frac{\partial D_2}{\partial t} = G(N_2) - \gamma_D D_2$$

N_x: active notch in cell x

D_x: active delta in cell x

F: activation function

G: inhibition function

γ: degradation constant

Non-dimensional expression

$\tau = \gamma_N \cdot t$

$\nu = \gamma_D / \gamma_N$

$$\frac{\partial N_1}{\partial \tau} = f(D_2) - N_1$$

$$\frac{\partial D_1}{\partial \tau} = (g(N_1) - D_1)\,\nu$$

$$\frac{\partial N_2}{\partial \tau} = f(D_1) - N_2$$

$$\frac{\partial D_2}{\partial \tau} = (g(N_2) - D_2)\,\nu$$

For $\nu = \gamma_D/\gamma_N \ll 1$, $\nu \to 0$

$\frac{\partial D_1}{\partial \tau} \to 0$. $\frac{\partial D_2}{\partial \tau} \to 0$

Notch N_1, N_2 quickly settle to steady state.

$$\frac{\partial N_1}{\partial \tau} = 0 \Rightarrow f(D_2) = N_1$$

$$\frac{\partial N_2}{\partial \tau} = 0 \Rightarrow f(D_1) = N_2$$

Dynamic equations for Delta:

$$\frac{\partial D_1}{\partial \tau} = (g(f(D_2)) - D_1)\,\nu$$

$$\frac{\partial D_2}{\partial \tau} = (g(f(D_1)) - D_2)\,\nu$$

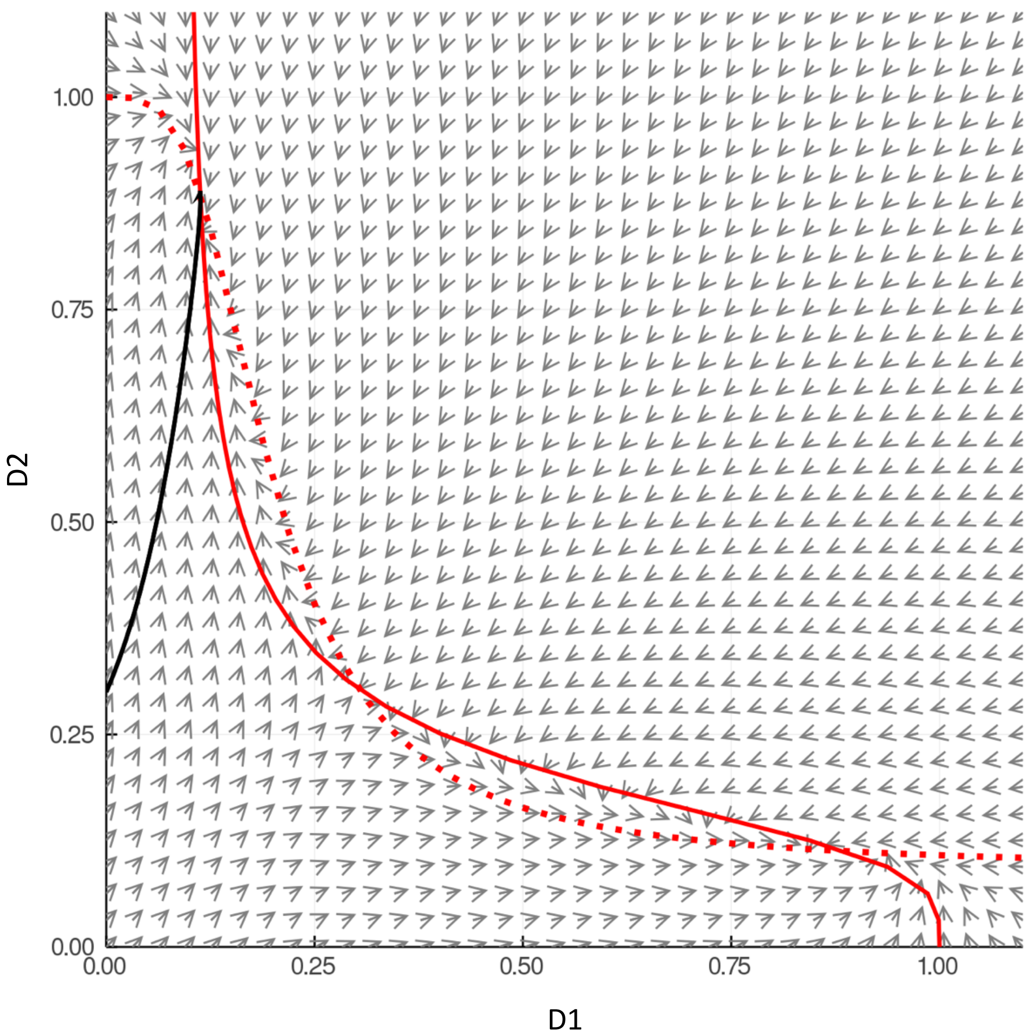
(b). Phase portrait.

From Lecture Notes $f(D') = \frac{D'^2}{0.1+D'^2}$ $g(N) = \frac{1}{1+10N^2}$

$$\frac{\partial D_1}{\partial \tau} = g(f(D_2)) - D_1 = \frac{1}{1+10\times\left(\frac{D_2^2}{0.1+D_2^2}\right)^2} - D_1$$

$$\frac{\partial D_2}{\partial \tau} = g(f(D_1)) - D_2 = \frac{1}{1+10\times\left(\frac{D_1^2}{0.1+D_1^2}\right)^2} - D_2$$

Plot phase portrait for dynamics of Delta using Julia.



From the graph generated from Julia (confirmed by Excel), we can tell that the system has 3 fixed points at (0.11,0.88), (0.3,0.3), and (0.9,0.11). Two points at (0.11,0.88) and (0.9,0.11) are stable steady states while (0.3,0.3) is an unstable steady state.

Since the two stable fixed points correspond to the situation where one cell has a large Delta activity and the other one a small Delta activity, the prediction of the model is that at long times the two cells will adopt different fates, which indicates either towards (0.11,0.88) or to (0.9,0.11). This is consistent with the conclusion discussed in class when limit $v \gg 1$.