Final Exam CHEME 5440

1. Notch-Delta
receptor ligand

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

$\frac{\partial D_1}{\partial J} = (g(N_1) - D_1)v$

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

$\frac{\partial D_2}{\partial J} = (g(N_2) - D_2)v$

N_x = Active notch in cell x
D_x = Active delta in cell x
dimensional

f [=] Activation function

g [=] Inhibition function

where $J = \gamma_N t$ and $v = \frac{\gamma_D}{\gamma_N}$

when $v = \frac{\gamma_D}{\gamma_N} << 1 \Rightarrow \gamma_D << \gamma_N$ Therefore Notch reaches steady state faster

The degradation constant for notch is much greater than delta, so it reaches a steady state faster

The the system simplifies to the following resulting dynamical equations

$\frac{\partial N_1}{\partial J} = f(D_2) - N_1 \approx 0 \quad N_1 = f(D_2) \Rightarrow \quad \frac{\partial D_1}{\partial J} = (g(f(D_2)) - D_1)v$

$\frac{\partial N_2}{\partial J} = f(D_1) - N_2 \approx 0 \quad N_2 = f(D_1) \Rightarrow \quad \frac{\partial D_2}{\partial J} = (g(f(D_1)) - D_2)v$

(b) $f(D') = \frac{F(D')}{\gamma_N} = \frac{D'^2}{0.1 + D'^2}$ (6) $\quad x_1 = D_1, \; x_2 = D_2$

$g(N) = \frac{G(N)}{\gamma_D} = \frac{1}{1 + 10N^2}$ (7)

Nullclines: $0 = \frac{\partial D_1}{\partial J} \Rightarrow D_1 = g(f(D_2))$

$0 = \frac{\partial D_2}{\partial J} \Rightarrow D_2 = g(f(D_1))$

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

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

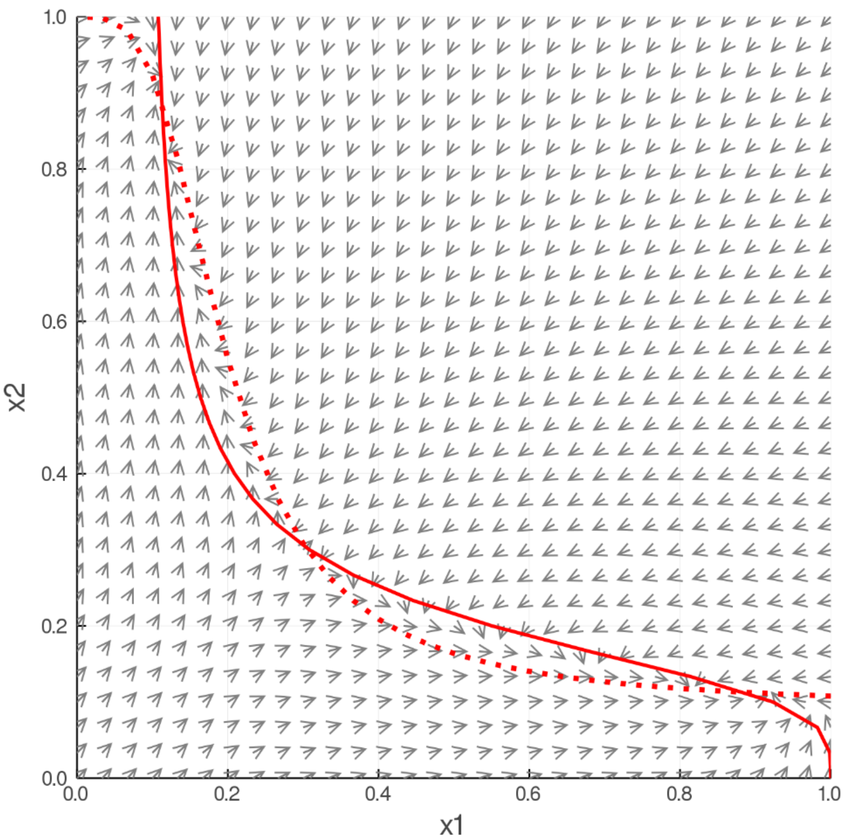
where $v << 1$, and the initial conditions are [(6,6), (0,0)]

Explanation in word document 1(b).

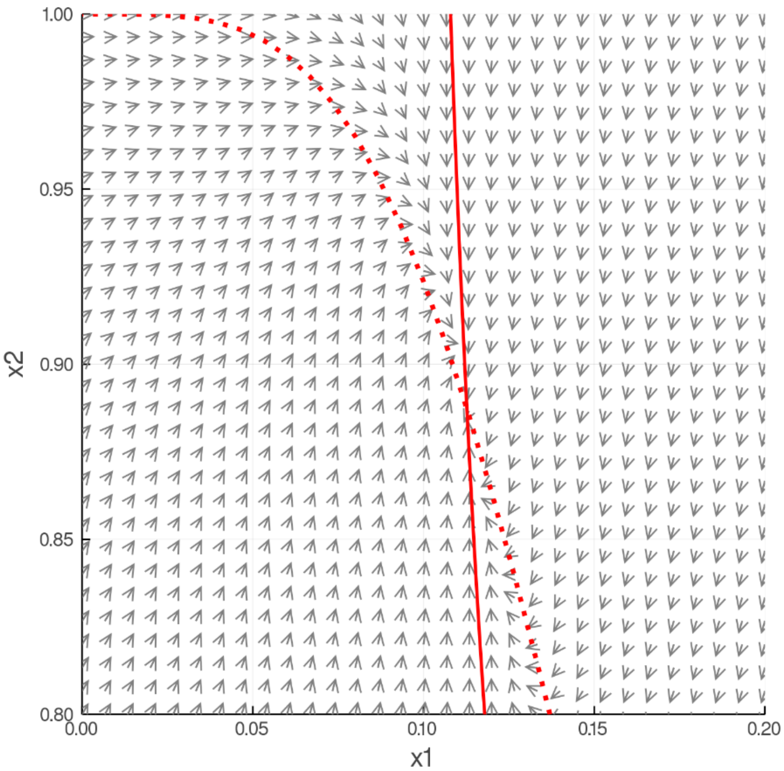
1 (b) Looking at the phase portrait, the two steady-states on the left and right appear to be stable, while the steady-state in the middle is unstable. This can be observed by looking closely at the intersections of the plots. Based on the phase portrait at long times, cell 1 assumes the primary fate and cell 2 assumes the secondary fate, or cell 2 assumes the primary fate while cell 1 assumes the secondary fate with the stable stead-state on the top left.

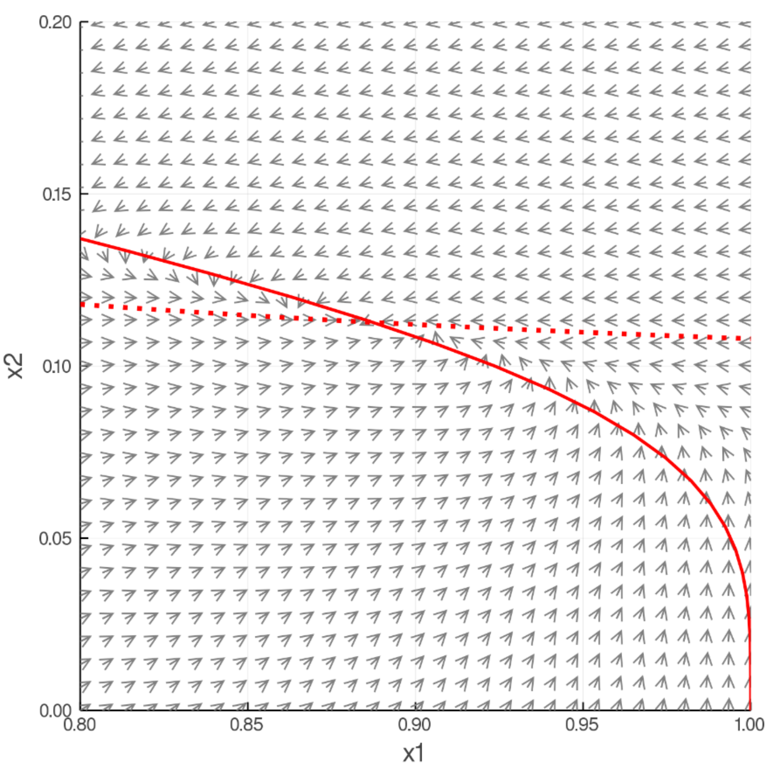
Lateral inhibition is defined as the feedback mechanism between neighboring cells that amplifies the difference between them. Lateral inhibition does work similarly to the limit in which the decay rate of delta is greater than that of notch. When the decay rate of notch is greater than that of delta, lateral inhibition causes one cell to assume the primary fate while the other assumes the secondary fate based on the steady-states observed in the phase portrait. This is similar to the case in lecture, where differences in active notch in cell 1 and cell 2 cause one to assume the primary fate and the other the secondary fate.

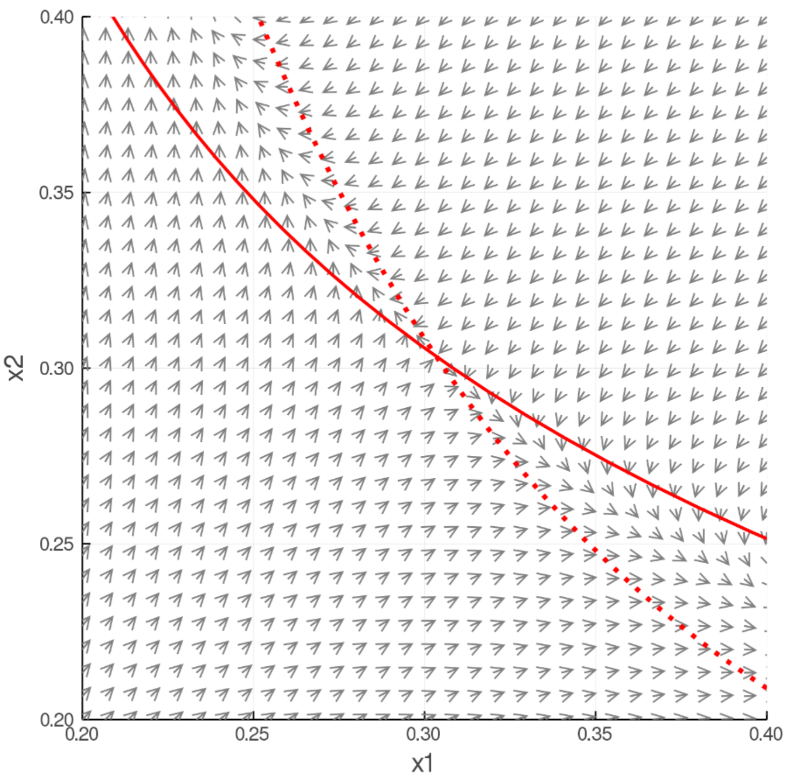
This is the phase portrait for the system where x1 is active notch in cell 1 and x2 is active notch in cell 2.



The stability of the steady states has also been showed by zooming in.


1.00
0.95
0.90
0.85
0.80
x2
0.00
0.05
0.10
0.15
0.20
x1


0.20
0.15
0.10
0.05
0.00
x2
0.80
0.85
0.90
0.95
1.00
x1


0.40
0.35
0.30
0.25
0.20
x2
0.20
0.25
0.30
0.35
0.40
x1