5440 Final exam
Part 2 Question 1

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a) from notes $\tau = \gamma_N t$, $\nu = \gamma_D, \gamma_N$

$$\frac{\partial N_1}{\partial \tau} = f(D_2) - N_1 \quad (2)$$

$$\frac{\partial D_1}{\partial \tau} = (g(N_1) - D_1)\nu \quad (3)$$

$$\frac{\partial N_2}{\partial \tau} = f(D_1) - N_2 \quad (4)$$

$$\frac{\partial D_2}{\partial \tau} = (g(N_2) - D_2)\nu \quad (5)$$

given $\gamma_D / \gamma_N = \nu << 1$

from (3) and (5) we get

$$\frac{\partial D_1}{\partial \tau} \simeq 0 , \quad \frac{\partial D_2}{\partial \tau} \simeq 0$$

as $\nu \ll 1$
and ν multiplies
across all terms.

$\therefore$ $D_1, D_2 \simeq$ constant

$\therefore$ $f(D_1), f(D_2) \simeq$ constant

looking @ (1) if $N_1 > f(D_2)$ then $\frac{\partial N_1}{\partial t} < 0$ causing N_1 to decrease until it reaches S.S. @ $N_1 = f(D_2)$.

if $N_1 < f(D_2)$ then $\frac{\partial N_1}{\partial t} > 0$ causing N_1 to increase until it reaches S.S. @ $N_1 = f(D_2)$.

1a continued

The Same can be said looking @ eqn (3) as because $\frac{\partial D_1}{\partial t} \approx 0$ $f(D_1) \approx$ constant $\therefore$

if $N_2 > f(D_1)$ then $\frac{\partial N_2}{\partial \tau} < 0$ and N_2 decreases until it reaches S.S. @ $N_2 = f(D_1)$.

if $N_2 < f(D_1)$ then $\frac{\partial N_2}{\partial \tau} > 0$ and N_2 increases until it reaches S.S. @ $N_2 = f(D_1)$.

$\therefore$ if $\nu = \frac{\gamma_D}{\gamma_N} << 1$ both the delta and Notch activity approach a S.S.$\therefore$

And we get

$$\frac{\partial D_1}{\partial \tau} = \nu(g(N_1) - D_1) \approx 0, \quad \frac{\partial D_2}{\partial \tau} = \nu(g(N_2) - D_2) \approx 0$$

$$g(N_1) \approx D_1, \quad g(N_2) \approx D_2$$

$\therefore$

$$\frac{\partial N_1}{\partial \tau} = f(g(N_2)) - N_1, \quad \frac{\partial N_2}{\partial \tau} = f(g(N_1)) - N_2$$

and because $D_i \approx$ constant $\rightarrow g(N_i) \approx$ constant and $\therefore f(g(N_i)) \approx$ constant and thus N_i goes to approx. S.S. and $\therefore f(g(N_i)) \approx$ constant and thus N_i also goes to approx. S.S.

$\therefore$ as described above $\frac{\partial D_1}{\partial \tau}, \frac{\partial D_2}{\partial \tau}, \frac{\partial N_1}{\partial \tau}, \frac{\partial N_2}{\partial \tau} \approx 0$

ADDENDUM to Problem 1 (why we can assume $g(N_i) \simeq D_i$)

$$\frac{\partial D_i}{\partial \tau} = \left(g(N_i) - D_i\right)\nu, \quad \nu = \frac{\gamma_D}{\gamma_N}$$

for $\nu \ll 1$

$$\frac{1}{\nu}\frac{\partial D_i}{\partial \tau} = g(N_i) - D_i$$

Note 1 D_i must be non-negative

Note 2 $g(N_i)$ has a range of $[0, 1]$

$\therefore$ $\frac{1}{\nu}\frac{\partial D_i}{\partial \tau}$ has a max of 1

(if $g(N_i) = 1$, $D_i = 0$)

Because $\nu \ll 1 \rightarrow \frac{1}{\nu} \gg 1$

$\therefore$ $\frac{\partial D_i}{\partial \tau}$ must be $\ll 1$ such that

$$\frac{1}{\nu}\frac{\partial D_i}{\partial \tau} = 1 \text{ @ max}$$

$\therefore$ $\frac{\partial D_i}{\partial \tau} \simeq 0$ and both

D_1, D_2 can be assumed to be @ S.S.

as this analysis applies to both.

if $D_i > g(N_i)$

↳ $\frac{\partial D_i}{\partial \tau} < 0$, $\therefore$ $\frac{\partial D_i}{\partial \tau}$ is either $\simeq 0$ or causes D_i to plummet until $D_i = g(N_i)$ and $\therefore$ $\frac{\partial D_i}{\partial \tau} = 0$ irrespective of

if $D_i < g(N_i)$

↳ $\frac{\partial D_i}{\partial \tau} > 0$, $\therefore$ $\frac{\partial D_i}{\partial \tau}$ is either $\simeq 0$ or causes D_i to rise until $D_i = g(N_i)$.

$\boxed{1B}$

from notes

D of other cell

$$f(D') = \frac{F(D')}{\gamma_N} = \frac{D'^2}{0.1 + D'^2} \qquad (6)$$

N of the same cell

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

$$\therefore \frac{\partial N_1}{\partial \tau} = f\left(g(N_2)\right) - N_1 = f\left(\frac{1}{1+10N_2^2}\right) - N_1$$

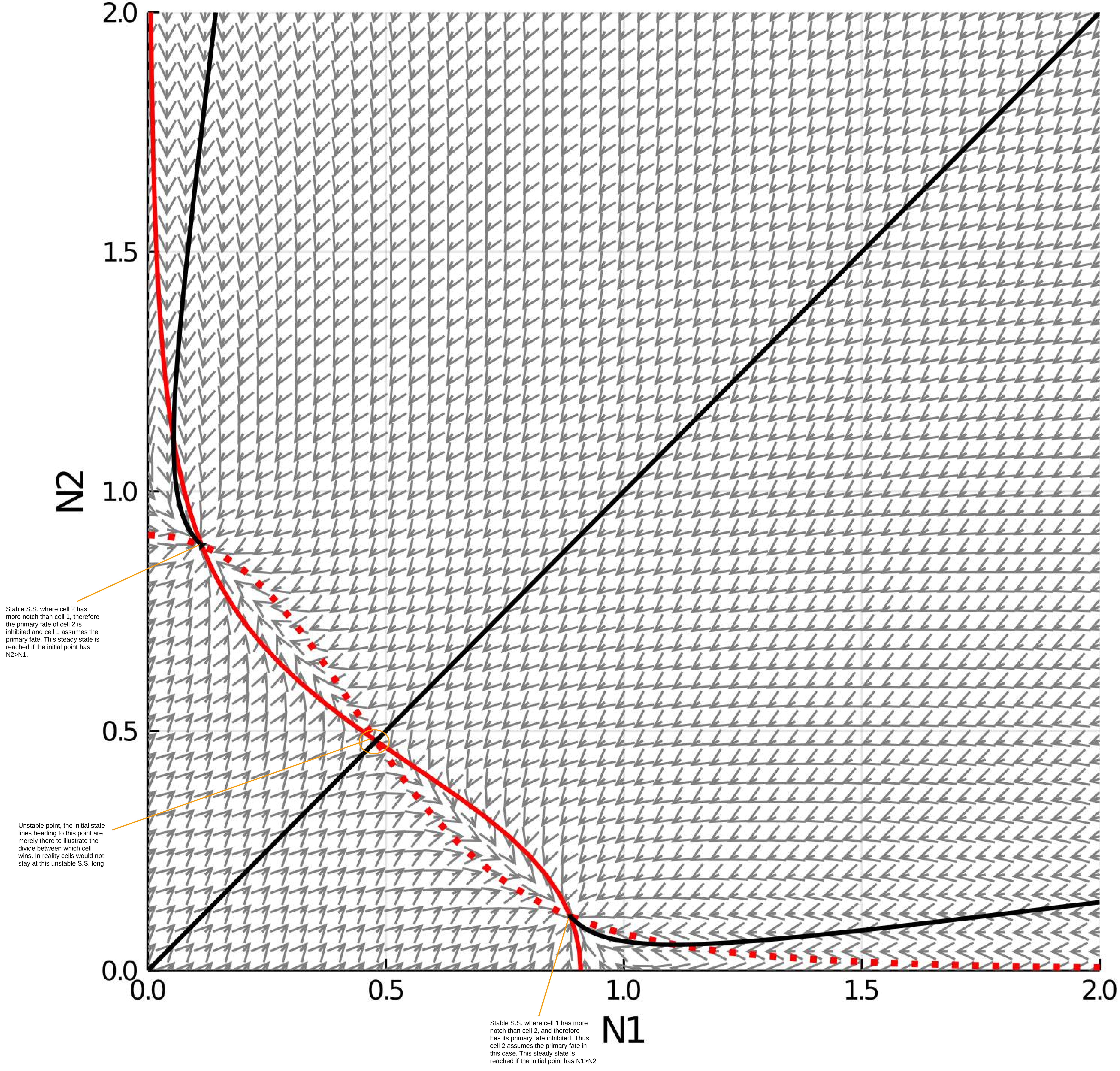
$$\frac{\partial N_1}{\partial \tau} = \frac{\left(\frac{1}{1+10N_2^2}\right)^2}{0.1 + \left(\frac{1}{1+10N_2^2}\right)^2} - N_1 \qquad (E1)$$

$$\frac{\partial N_2}{\partial \tau} = f(g(N_1)) - N_2 = f\left(\frac{1}{1+10N_1^2}\right) - N_2$$

$$\frac{\partial N_2}{\partial \tau} = \frac{\left(\frac{1}{1+10N_1^2}\right)}{0.1 + \left(\frac{1}{1+10N_1}\right)^2} - N_2 \qquad (E2)$$

Took E1, and E2 and Plugged them into Atum, Please see the Problem 1 file.

It appears as if lateral inhibition works exactly the same when $\nu \ll 1$ or $\nu \gg 1$.


2.0
1.5
1.0
0.5
0.0
N2
0.0
0.5
1.0
1.5
2.0
N1
Stable S.S. where cell 2 has more notch than cell 1, therefore the primary fate of cell 2 is inhibited and cell 1 assumes the primary fate. This steady state is reached if the initial point has N2>N1.
Unstable point, the initial state lines heading to this point are merely there to illustrate the divide between which cell wins. In reality cells would not stay at this unstable S.S. long
Stable S.S. where cell 1 has more notch than cell 2, and therefore has its primary fate inhibited. Thus, cell 2 assumes the primary fate in this case. This steady state is reached if the initial point has N1>N2