

1a) $v = \gamma_D / \gamma_N \ll 1 \Rightarrow \gamma_D \ll \gamma_N$

Prove: notch activity \rightarrow SS (ie $\frac{dN_i}{dt} = 0$)

$$\frac{dN_1}{dt} = F(D_2) - \gamma_N N_1$$

$\rightarrow 0, \gamma_N$ large, assume $\gamma_N N_1 \gg dN_1/dt \Rightarrow$ SS

$$\gamma_N N_1 + \frac{dN_1}{dt} = F(D_2)$$

$$\gamma_N N_1 \approx F(D_2) \Rightarrow \boxed{N_1 \approx f(D_2)} \Rightarrow \frac{dN_1}{dt} = 0$$

$$\frac{dN_2}{dt} = F(D_1) - \gamma_N N_2$$

$\rightarrow 0, \gamma_N$ large, assume $\gamma_N N_2 \gg dN_2/dt \Rightarrow$ SS

$$\frac{dN_2}{dt} + \gamma_N N_2 = F(D_1)$$

$$\gamma_N N_2 \approx F(D_1) \Rightarrow \boxed{N_2 \approx f(D_1)} \Rightarrow \frac{dN_2}{dt} = 0$$

$$\frac{dD_1}{dt} = (g(N_1) - D_1)v = [g(f(D_2)) - D_1]v$$

$$\frac{dD_2}{dt} = (g(N_2) - D_2)v = [g(f(D_1)) - D_2]v$$

b) $f(D') = \frac{F(D')}{\gamma_N} = \frac{(D')^2}{0.1 + (D')^2}$, $g(N') = \frac{G(N')}{\gamma_D} = \frac{1}{1 + 10(N')^2}$

$$\frac{dD_1}{dt} = v \left[-D_1 + \frac{1}{1 + 10 \left[\frac{D_2^2}{0.1 + D_2^2} \right]^2} \right]$$

$$\frac{dD_2}{dt} = v \left[-D_2 + \frac{1}{1 + 10 \left[\frac{D_1^2}{0.1 + D_1^2} \right]^2} \right]$$

c) Lateral inhibition work similarly as the case discussed in lecture. If D_1 & D_2 are present in equal amounts (delta in cell 1 & cell 2) the D_1 & D_2 values according to the phase portrait should reach the unstable SS (@ $D_1 = D_2 = 0.3$). In the presence of a slight perturbation of D_1 or D_2 , the system will reach a new stable SS in which one cell wins and dictates the fate of the other cell. Few active delta ligands in a cell \Rightarrow that cell wins. In this manner, in the

long-time limit the system will reach a steady state where one cell assumes primary fate and the other cell assumes secondary fate. (Notch represses primary fate).

Active notch inhibits activation of delta so low concentration of active delta strongly suggests high concentration of active notch. High concentration of active delta implies a lack of suppression of delta activation, suggesting low concentration of active notch.