1a.

1a) Using Eqn 1 from Lecture on May 5th and May 7th

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

$$\frac{dD_1}{dt} = G(N_1) - \gamma_D D_1$$

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

$$\frac{dD_2}{dt} = G(N_2) - \gamma_D D_2$$

let $\tau' = t\gamma_D$ and $\nu' = \frac{\gamma_N}{\gamma_D}$

$\nu = \frac{\gamma_D}{\gamma_N} << 1$ then $\nu' >> 1$

$$\frac{dN_1}{d\tau'} = \left(S(D_2) - N_1\right)\nu'$$

$$\frac{dD_1}{d\tau'} = g(N_1) - D_1$$

etc.

then $$\frac{1}{\nu'}\frac{dN_1}{d\tau'} = \nu'\frac{dN_1}{dt} = S'(D_2) - N_1 \simeq 0$$

and $$\frac{1}{\nu'}\frac{dN_2}{d\tau'} = \nu'\frac{dN_2}{d\tau'} = S'(D_1) - N_2 \simeq 0$$

this result indicates that notch will reach a pseudo steady state regardless of the concentration of notch and delta quickly.

This result can then be applied to equations 2-5

At steady state which was shown to occur with $\nu \ll 1$

$$\frac{dN_1}{d\tau} = f(D_2) - N_1 = 0 \rightarrow N_1 = f(D_2)$$

$$\frac{dN_2}{d\tau} = f(D_1) - N_2 = 0 \rightarrow N_2 = f(D_1)$$

Substitute into 3 and 5

$$\boxed{\begin{aligned} \frac{1}{\nu}\frac{dD_1}{d\tau} &= \left(g(f(D_2)) - D_1\right) \\ \frac{1}{\nu}\frac{dD_2}{d\tau} &= \left(g(f(D_1)) - D_2\right) \end{aligned}}$$

$$\frac{1}{\nu}\frac{dD_1}{d\tau} = \frac{1}{1 + 10\left(\frac{D_2^2}{0.1 + D_2^2}\right)^2} = D_1$$

$$\frac{1}{\nu}\frac{dD_2}{d\tau} = \frac{1}{1 + 10\left(\frac{D_1^2}{0.1 + D_1^2}\right)^2} = D_1$$

1b. This plot was created by running ToggleMono.jl in conjunction with PhasePortrait.jl

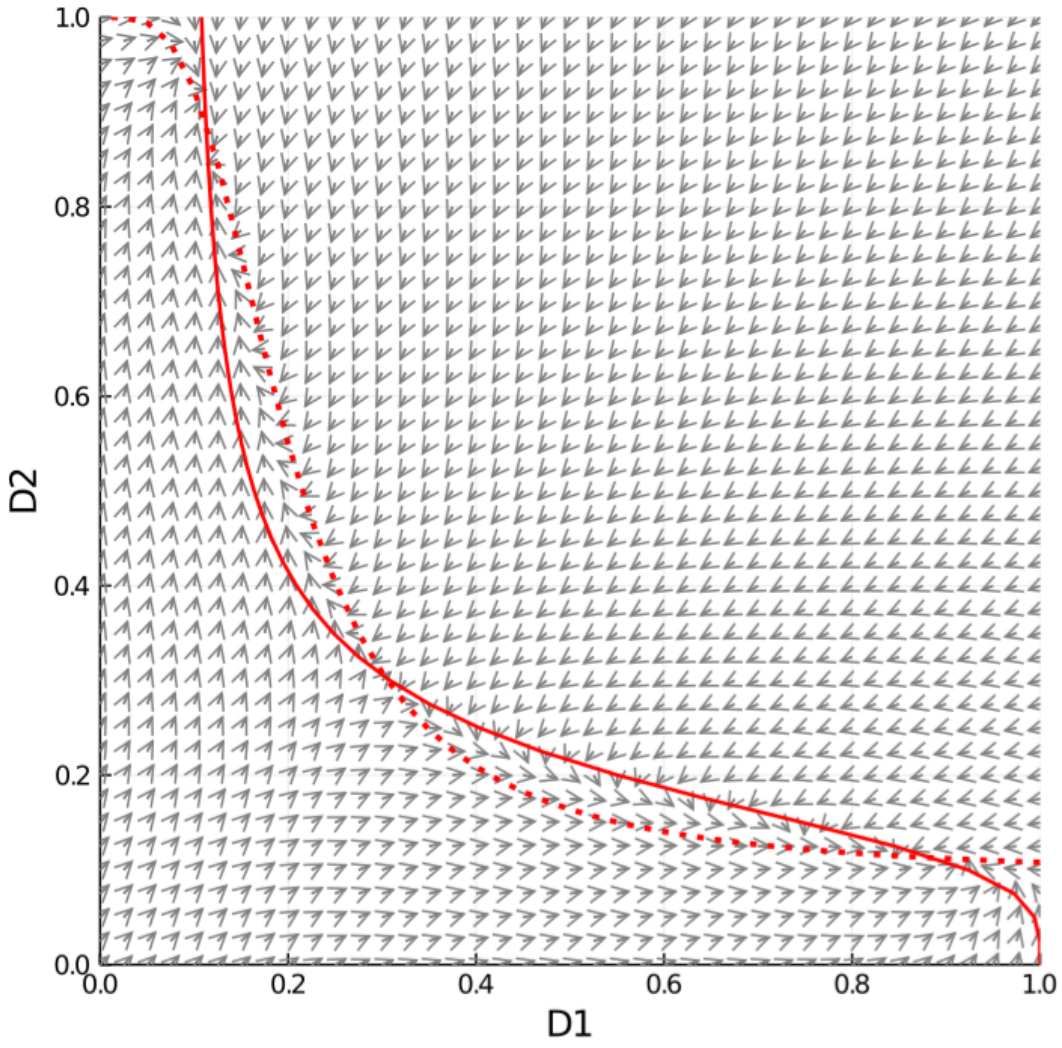
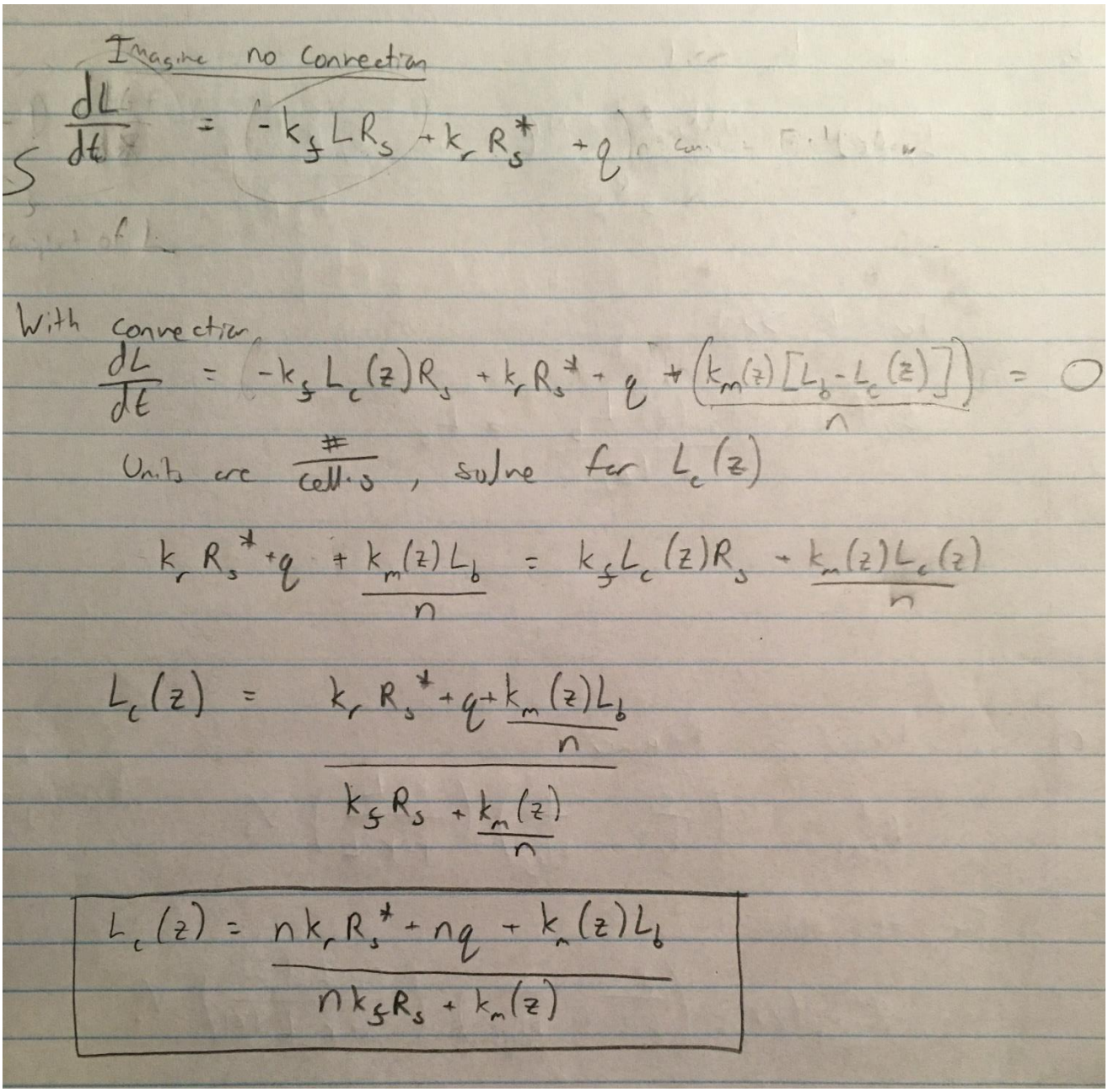



**Figure 1:** Phase portrait of the concentration of delta in cell 2 vs. the in cell 1. Three fixed points are present with two of them being stable and the central one being unstable

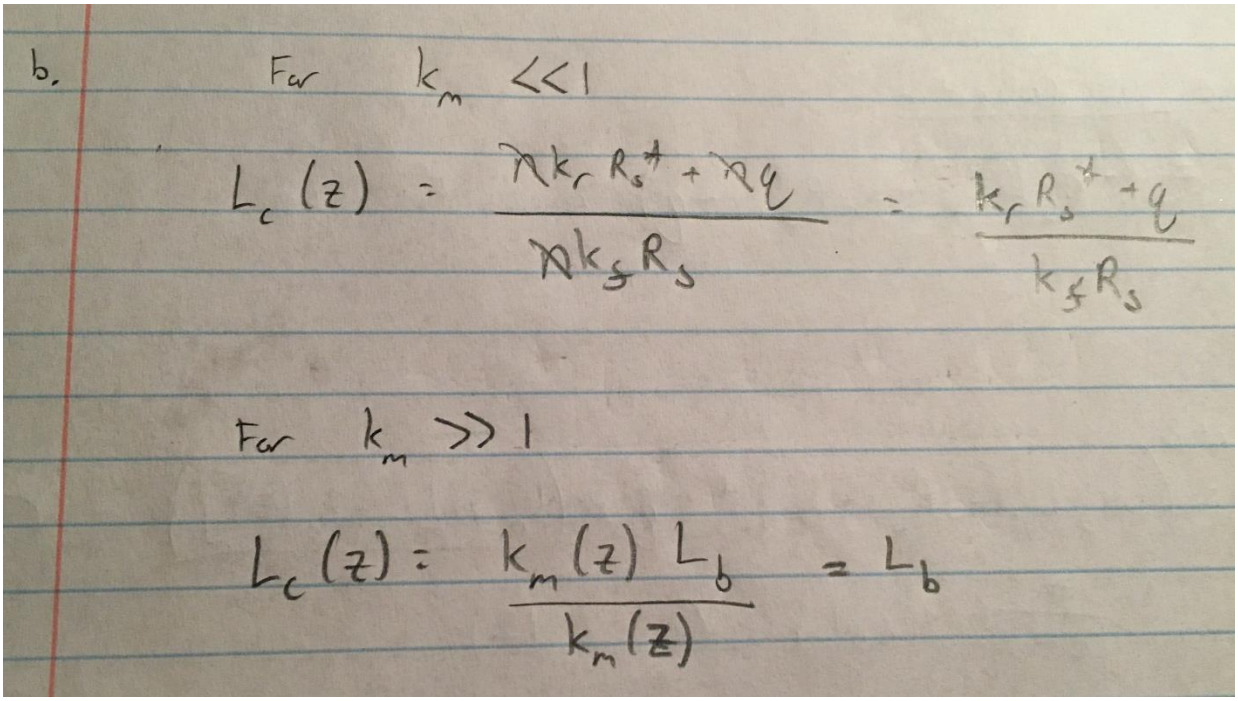
This phase portrait shows three steady states, with the central fixed point being unstable while the other fixed points are stable. The two stable points at either end of $D_1$ and $D_2$ values indicate the two different fates that can occur. Higher $D_1$ indicates cell 2 winning, or achieving the primary fate, while a higher $D_2$ indicates cell 1 winning. Lateral inhibition does work similarly, however the change is much sharper than when the decay rate of Delta is much greater than

Notch. This means that to move the system from one stable point to another point that will eventually converge to the other stable point a much smaller change is necessary in this system than in the one discussed in class.

2a.

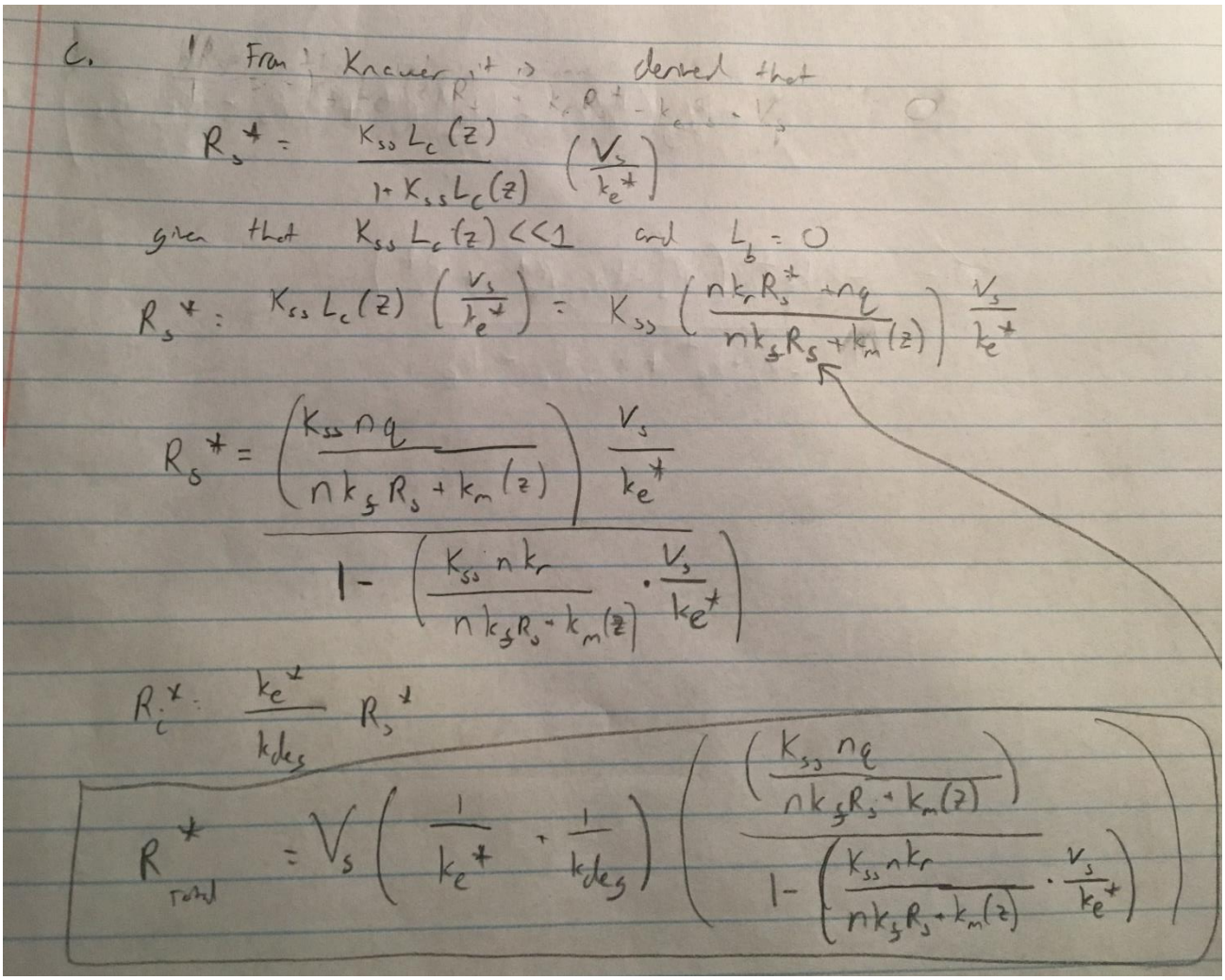


2b.




For a very small mass transfer coefficient the EGF concentration is not dependent at all on the bulk concentration but is dependent on cell production and the rate of the forward and reverse reaction. Due to a small mass transfer coefficient there would be little EGF being brought from the bulk to the cell surface, therefore the influential component would be the cell activity towards producing EGF. For a very large mass transfer coefficient, the transfer is so high that the concentration within the convective current is similar to that in the bulk and the cellular component does not play a significant part in EGF concentration. This is intuitive as at a high mass transfer coefficient there should be no difference between the flowing component and the reservoir and the bulk value should be much more influential than the cellular component.

2c.


c. From Knower, it is derived that
$R_s^* = \frac{K_{ss} L_c(z)}{1 + K_{ss} L_c(z)} \left(\frac{V_s}{k_e^*}\right)$
given that $K_{ss} L_c(z) << 1$ and $L_b = 0$
$R_s^* = K_{ss} L_c(z) \left(\frac{V_s}{k_e^*}\right) = K_{ss} \left(\frac{n k_r R_s^* + nq}{n k_s R_s + k_m(z)}\right) \frac{V_s}{k_e^*}$
$R_s^* = \frac{\left(\frac{K_{ss} nq}{n k_s R_s + k_m(z)}\right) \frac{V_s}{k_e^*}}{1 - \left(\frac{K_{ss} n k_r}{n k_s R_s + k_m(z)} \cdot \frac{V_s}{k_e^*}\right)}$
$R_c^* = \frac{k_e^*}{k_{des}} R_s^*$
$R_{Total}^* = V_s \left(\frac{1}{k_e^*} + \frac{1}{k_{des}}\right) \left(\frac{\left(\frac{K_{ss} nq}{n k_s R_s + k_m(z)}\right)}{1 - \left(\frac{K_{ss} n k_r}{n k_s R_s + k_m(z)} \cdot \frac{V_s}{k_e^*}\right)}\right)$

where

$$\frac{dR_s^*}{dt} = k_f L_c(z) R_s - k_r R_s^* - k_e^* R_s^* = 0$$

$$k_f \left( \frac{n k_r R_s^* + nq}{n k_f R_s + k_m(z)} \right) R_s - k_r R_s^* - k_e^* R_s^* = 0$$

solve for $R_s$

$$\frac{n k_f}{n k_r R_s^* + nq} + \frac{k_m(z)}{(n k_r R_s^* + nq) R_s} = \left( \left( \frac{k_r + k_e}{k_f} \right) R_s^* \right)^{-1}$$

$$R_s = \frac{k_m(z)}{n k_r R_s^* + nq} \left( \left( \left( \frac{k_r + k_e}{k_f} \right) R_s^* \right)^{-1} - \frac{n k_f}{n k_r R_s^* + nq} \right)^{-1}$$

2d. This plot was created by running 2d.jl

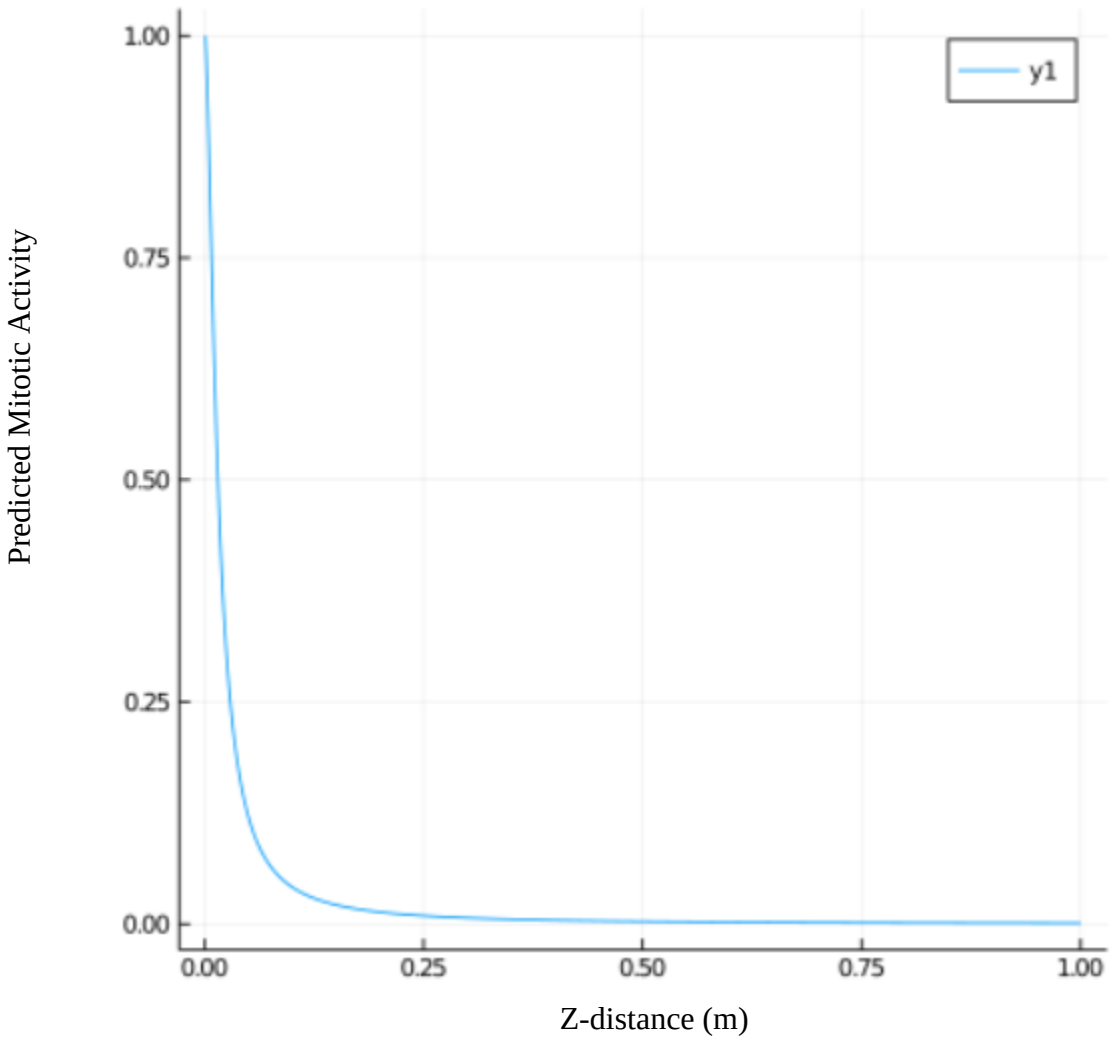
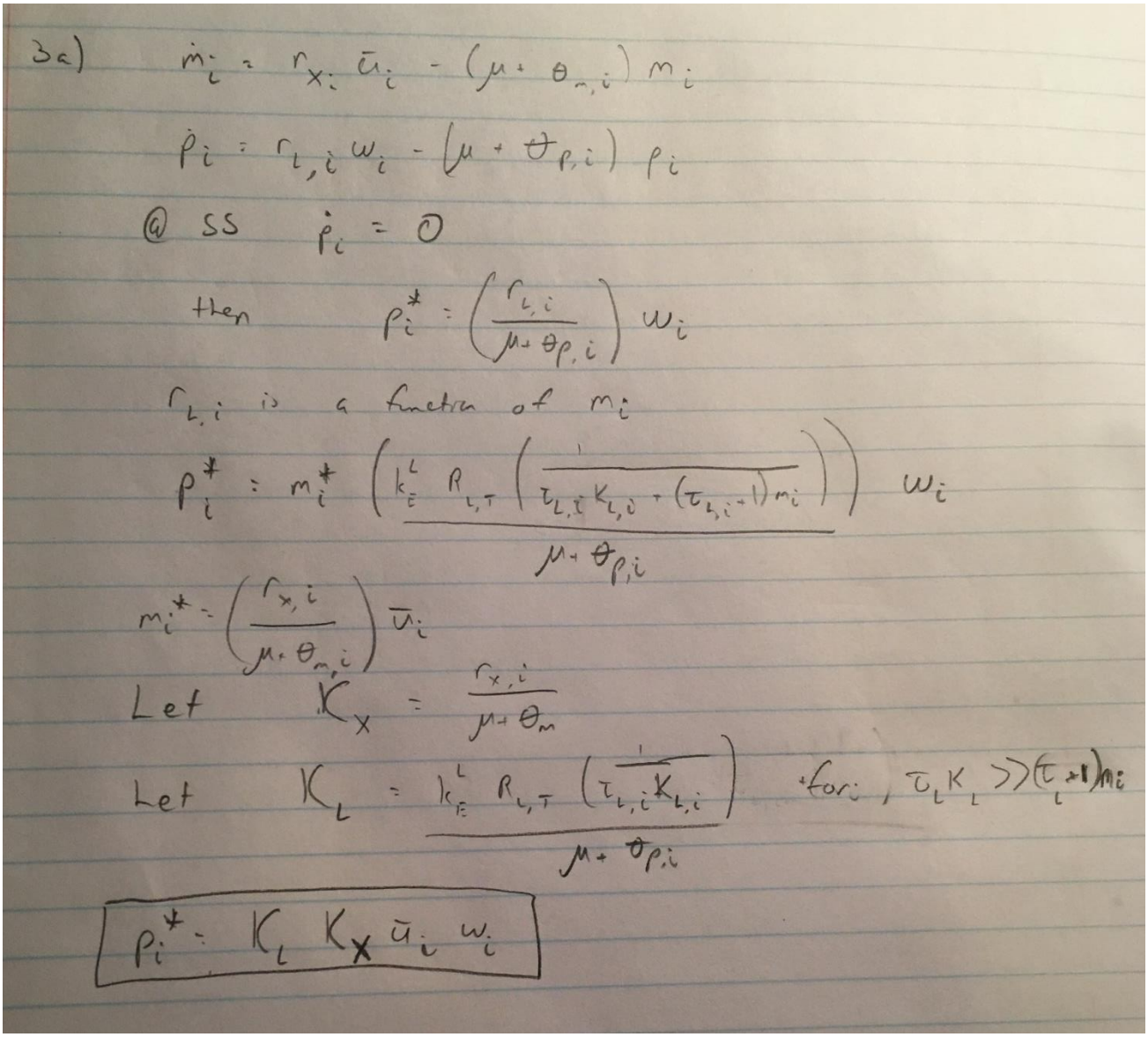



**Figure 2:** Plot of predicted mitotic activity vs. Z-distance. The prediction was made by normalizing the total active receptor.

3a.


3a)
$\dot{m}_i = r_{x,i}\,\bar{u}_i - (\mu + \theta_{m,i})\,m_i$
$\dot{\rho}_i = r_{L,i}\,w_i - (\mu + \theta_{\rho,i})\,\rho_i$
@ SS $\dot{\rho}_i = 0$
then $\rho_i^* = \left(\frac{r_{L,i}}{\mu + \theta_{\rho,i}}\right) w_i$
$r_{L,i}$ is a function of $m_i$
$\rho_i^* = m_i^* \left( \frac{k_i^L\, R_{L,T}\left(\frac{1}{\tau_{L,i} K_{L,i} + (\tau_{L,i}+1) m_i}\right)}{\mu + \theta_{\rho,i}} \right) w_i$
$m_i^* = \left(\frac{r_{x,i}}{\mu + \theta_{m,i}}\right) \bar{u}_i$
Let $K_x = \frac{r_{x,i}}{\mu + \theta_m}$
Let $K_L = \frac{k_i^L\, R_{L,T}\left(\frac{1}{\tau_{L,i} K_{L,i}}\right)}{\mu + \theta_{\rho,i}}$ for, $\tau_L K_L >> (\tau_L + 1) m_i$
$\rho_i^* = K_L\, K_x\, \bar{u}_i\, w_i$

3b and 3c. Plot created by running 3d.jl

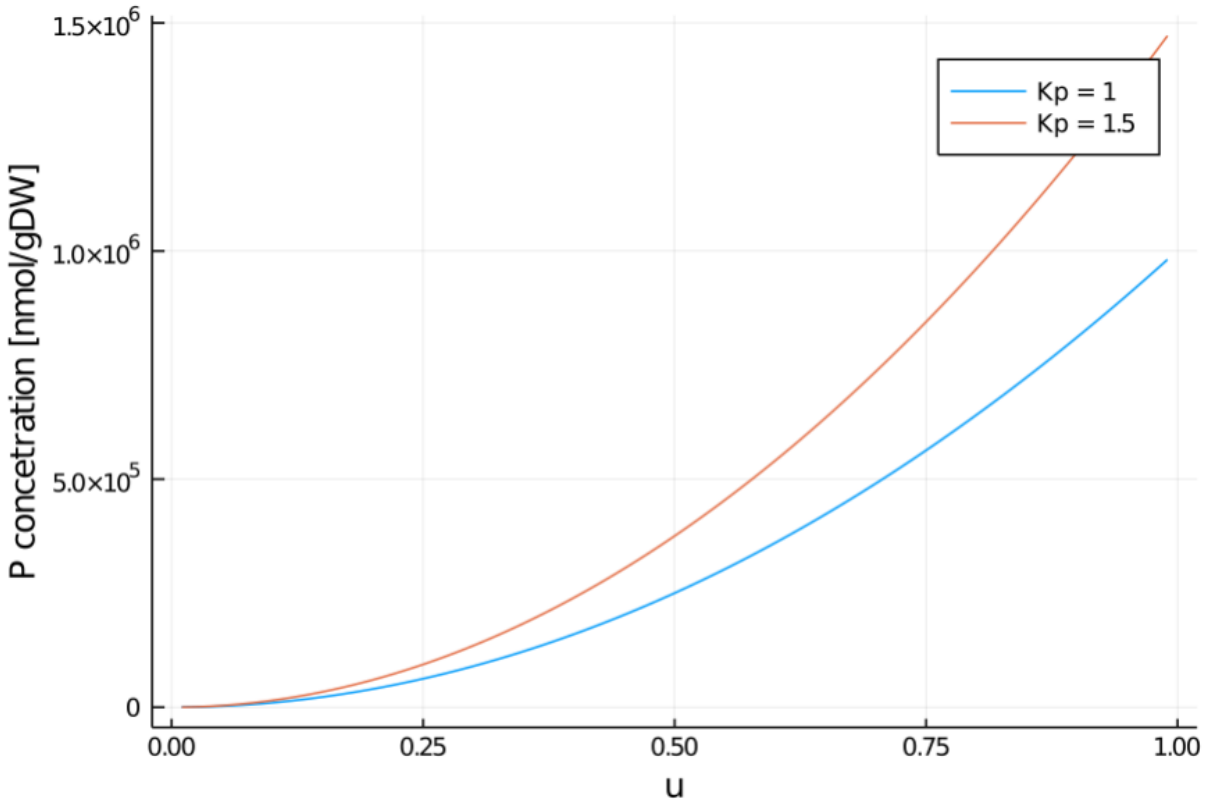



**Figure 3:** This figure is a plot of the concentration of P vs. the control function u. One line is the predicted values if the polysome amplification constant is 1, the other is if the polysome amplification constant is greater than 1

For 3b.

| Variable | Value | Reference |
|---|---|---|
| Cell doubling time | 40 (minutes) | Given |
| Cell volume | 1 (um^3) | Given |
| Cell volume in Liters | 1e-15 (L) | Calculated from Cell_volume which was given |
| Cell weight | 4.3e-13 (g) | Given |
| Water (% cell that is water) | 70% | Given |
| Characteristic intracellular enzyme concentration | 0.3 uM or 2.326 nmol/gDW | Given or calculated from given |
| Protein half life | 24 hours | Given |
| Translational initiation time | 1.5 seconds or 0.0004167 hours | Given or calculated from given |
| Translational saturation coefficient | 200 uM or 1550.4 nmol/gDW | Given or calculated from given |

| | | |
|---|---|---|
| $k_I$ | 2400 1/hr | Calculated from translational initiation time which was given |
| Protein degradation | 1.73 1/hr | Calculated from protein half-life which was given |
| Dilution | 1.04 1/hr | Calculated from cell doubling time which was given |
| Characteristic protein length | 333 aa | Given |
| Protein length | 300 aa | Given |
| $k_e$ | 18 aa/s | Given |
| Ribosomes | 26.3e3 ribosomes/cell | BIND: 100059 |
| Ribosome concentration | 338.7 nmol/gDW | Calculated from value taken from BIND: 100059 |
| Average Elongation Constant | 194.6 1/h | Calculated from given values |
| Protein Elongation Constant | 175.3 1/h | Calculated from given values |
| Tau | 0.07304 (unitless) | Calculated from given values |
| Vmax | 59371 nmol/(gDW*hr) | Calculated from given values or values derived from BIND: 100059 |
| $K_X$ | 0.575 nmol/gDW | Taken from Prelim 1 |
| $R_L$ | 301.4 1/hr | Calculated from given values and equation taken from lecture |
| $K_L$ | 189.1 (unitless) | Calculated from given values and equation taken from lecture |
| $K_P$ | 1.5 | Arbitrary value greater than 1 as requested in the question |

For 3c. As the polysome amplification constant increases, the curve moves upwards as more copies of P are produced for the same value of u.

4a. All equations, and code for 4 can be found in q4.jl

W1 was found to be 0.045, while W2 was found to be 98.95. The assumption was made that the last given value of overall rate was nearly equivalent to the asymptotic value. Though this can be

visually confirmed to be untrue it was believed that the difference would be small and therefore not significantly affect results.

4b. K was estimated to be 0.5 mM while n was estimated to be 3.25. These values were determined by using a visual guess of what was the best fit rather than use a least-square regression.

4c.

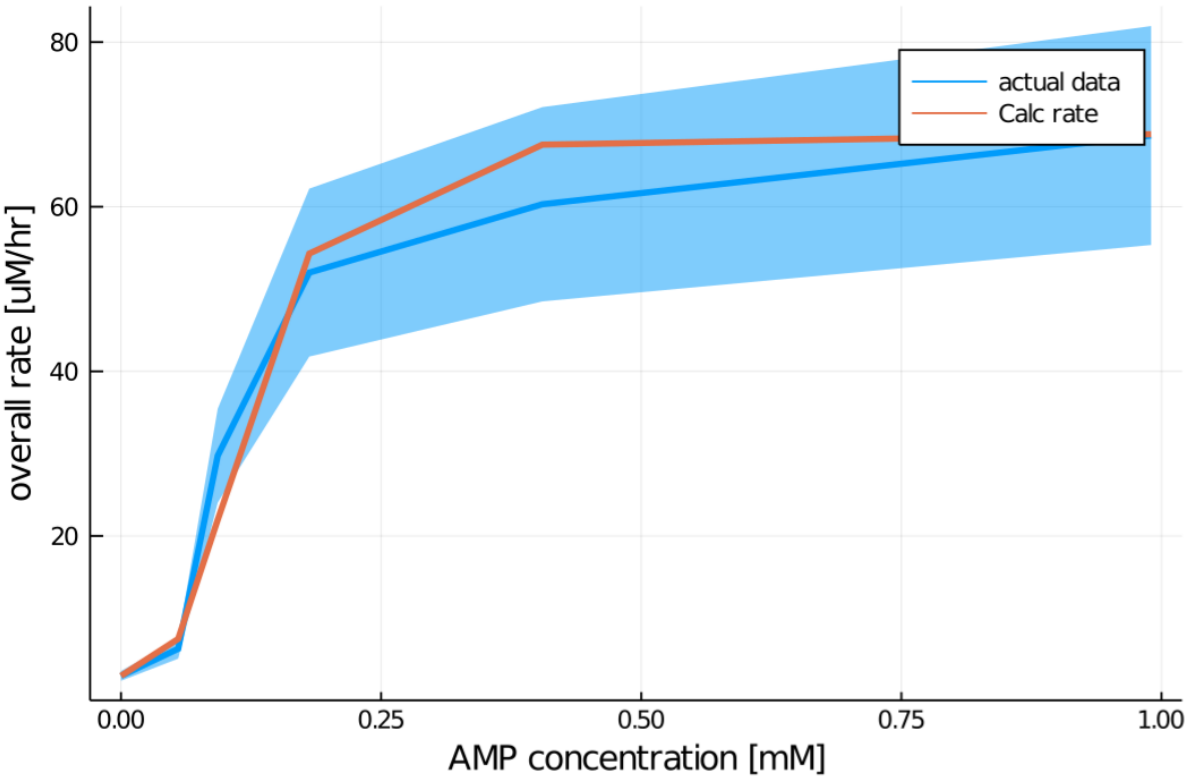



**Figure 4:** The overall reaction rate vs. the AMP concentration. The shaded region encompasses the 95% confidence interval. The orange line is the predicted rate while the blue line is the actual rate

The predicted rate matches the actual rate very well at lower values of AMP. However, this model was unable to match the same asymptotic plateau that occurred in the actual data. This was not significant as no portion of the calculated rate falls out of the 95% confidence interval. It

is possible that the previous assumptions of the asymptotic value of the rate could have affected this outcome, along with not using a least-square regression to find values of K and n.