

Attached is my submission for the 5440-Final.

It includes written work and the various plots that were necessary to complete the problems.

All the plots can be created based on the Julia code and excel work books included in the attached files. The files for each problem are in the folder associated with that problem.

Problem 1:

These plots can be created by executing the **NotchDeltaPhasePortrait.jl** file, each one is created by uncommenting one of the specified initial state vectors (further details can be found with that problem)

Problem 2:

The plot was created using the **Problem 2 Part D** excel workbook.

Problem 3:

Both the plot for part B and C were created using the **Plotting for Part B** excel workbook with each being created using a different sheet.

Problem 4:

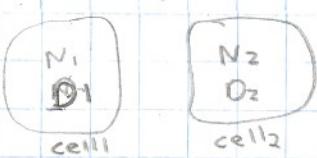
The plot for this problem was created using the **Problem 4 excell workbook** file.

-Rachel Eichman

Rge32

Problem 1

Part A:



The equations for the two cell model of Notch and Delta are

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

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

$$\frac{\partial D_1}{\partial z} = (g(N_1) - D_1) v \quad (3)$$

$$\frac{\partial D_2}{\partial z} = (g(N_2) - D_2) v \quad (5)$$

Where $z = \gamma_N t$ $v = \gamma_D / \gamma_N$ and N_x is active Notch in cell X

↓

These are degredchen

D_x is active delta in cell X

$f(D)$ → activah fun $= F(D) / \gamma_N$

$g(N)$ → inhibith fun $G(N) / \gamma_D$

To argue that notch activity quickly settles into a steady state we must argue that

$$\frac{\partial N_1}{\partial z} \approx 0 = f(D_2) - N_1 \quad N_1 \approx f(D_2)$$

In order to do this I will choose a diffat set of variab with which to non-dimensionalize the system. we will choose $z' = \gamma_D t$ $v = \gamma_D / \gamma_N$

Dimensional equations:

$$\frac{\partial N_1}{\partial z} = F(D_2) - \gamma_N N_1 \rightarrow \gamma_D \frac{\partial N_1}{\partial z'} = F(D_2) - \gamma_N N_1 \xrightarrow{\gamma_D \frac{\partial N_1}{\partial z'} = (f(D_2) - N_1) \gamma_N} \frac{\partial N_1}{\partial z'} = f(D_2) - N_1$$

$$\frac{\partial D_1}{\partial z} = G(N_1) - \gamma_D D_1 \quad \gamma_D \frac{\partial D_1}{\partial z'} = G(N_1) - \gamma_D D_1 \xrightarrow{\frac{\partial D_1}{\partial z'} = g(N_1) - D_1}$$

$$\frac{\partial N_2}{\partial z} = F(D_1) - \gamma_N N_2 \quad \gamma_D \frac{\partial N_2}{\partial z'} = F(D_1) - \gamma_N N_2 \xrightarrow{\gamma_D \frac{\partial N_2}{\partial z'} = (f(D_1) - N_2) \gamma_N} \frac{\partial N_2}{\partial z'} = (f(D_1) - N_2) \gamma_N$$

$$\frac{\partial D_2}{\partial z} = G(N_2) - \gamma_D D_2 \quad \gamma_D \frac{\partial D_2}{\partial z'} = G(N_2) - \gamma_D D_2 \xrightarrow{v \frac{\partial D_2}{\partial z'} = g(N_2) - D_2} v \frac{\partial D_2}{\partial z'} = g(N_2) - D_2$$

The four equations that describe

this system with the diffat choice of $z' = \gamma_D t$ are

$$v \frac{\partial N_1}{\partial z'} = f(D_2) - N_1 \quad (2^*) \quad \text{in the case that } v = \frac{\gamma_D}{\gamma_N} \ll 1$$

$$\frac{\partial D_1}{\partial z'} = g(N_1) - D_1 \quad (3^*) \quad (2^*) \quad v \frac{\partial N_1}{\partial z'} \approx 0 = f(D_2) - N_1$$

The notch

activity

$$v \frac{\partial N_2}{\partial z'} = f(D_1) - N_2 \quad (4^*)$$

$$(4^*) \quad v \frac{\partial N_2}{\partial z'} \approx 0 = f(D_1) - N_2$$

quickly

settling

$$\frac{\partial D_2}{\partial z'} = g(N_2) - D_2 \quad (5^*)$$

$N_2 = f(D_1)$ a quasi

steady state.

as shown by the each,

even in the diffnt time system we come to the result that $f(D_2) \approx N_1$ and $N_2 \approx f(D_1)$ suggests steady state beha for Notch in both cells.
 we can then write the resulting dynamical equatn that desrcle delta beha.

I will do this in the z' domain so as to not have a γ in my final equat.

we have (3*) and (5*) Based on Quasi Steady state
 $N_1 \approx f(D_2) \quad N_2 \approx f(D_1)$

$$(3*) \quad \frac{\partial D_1}{\partial z'} = g(N_1) - D_1$$

$$\boxed{\frac{\partial D_1}{\partial z'} = g[f(D_2)] - D_1}$$

$$(5*) \quad \frac{\partial D_2}{\partial z'} = g(N_2) - D_2$$

$$\boxed{\frac{\partial D_2}{\partial z'} = g[f(D_1)] - D_2}$$

Part B

The g and f functions given in lecture were

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

we can plug these equations into the dynamics equan for active delta,

$$\boxed{\frac{\partial D_1}{\partial z'} = \frac{1}{1 + 10 \left(\frac{D_2}{0.1 + D_2^2} \right)^2} - D_1 \quad \text{and}}$$

$$\boxed{\frac{\partial D_2}{\partial z'} = \frac{1}{1 + 10 \left(\frac{D_1^2}{0.1 + D_1^2} \right)} - D_2}$$

we will now plot the behavior of these equations in a phase portrait in Julia,

which can be recreated by running the Notch Delta Phase Portrat.jl file which uses PhasePortratV2.jl

(the perturbations)

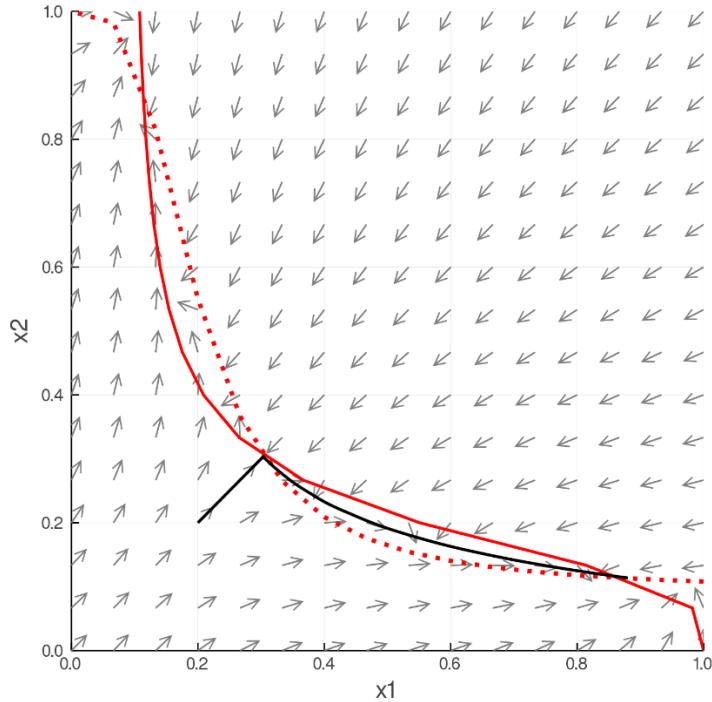
i.e. the
eyslightly
openEJ↑
slightly

In all four of the shown examples if the system is perturbed from the $D_1 = D_2$ state it will move in longt to a state where the omat $D_1 \neq D_2$ and one is signifn larger than the other indicative of one cell adopting the primary fate and the other adopting a secondary st if one cell achieves any slight advantage. (Although these plots don't show this the initial unsteady state whe $D_1 = D_2$ if the system were initly there and perturbed in anyway in long time the end beha will be the same with one cell adoptng a primary fate and the other a secondary fate).

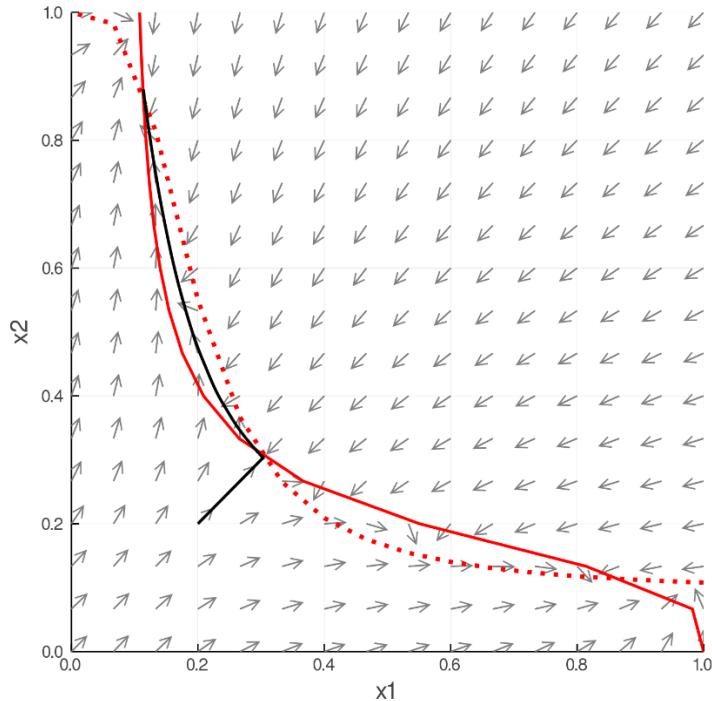
→ The system we discussed in lectur had the same net result where one cell adopt a primary fate and the other a secondary fate this time as result of diff. & active notch levels.

The four phase portraits were made by executing NotchDeltaPhasePortrait.jl, and uncommenting one of the four initial state vectors. In lines 28-31.

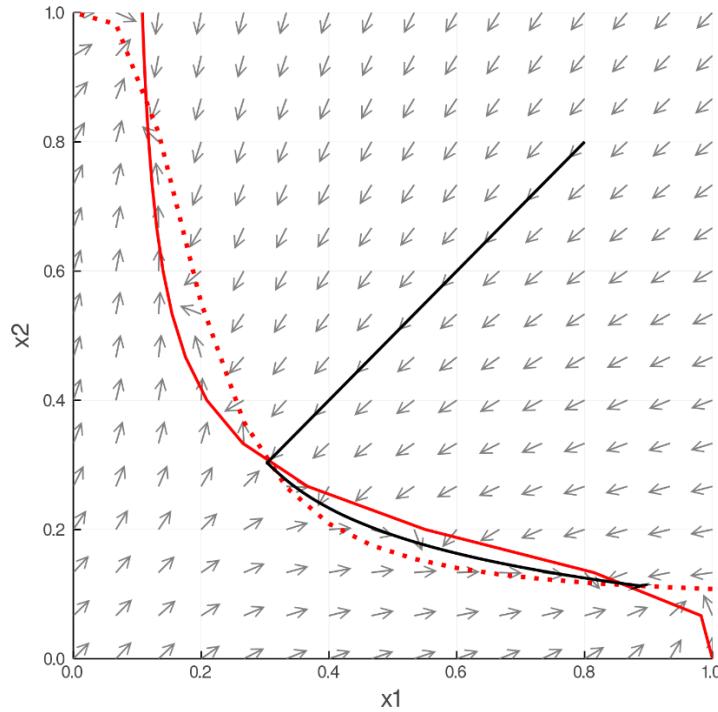
D1=D2=0.2perturbD1 (this plot was made by uncommenting line 28, and generating a phase portrait for the corresponding x_0 vector)



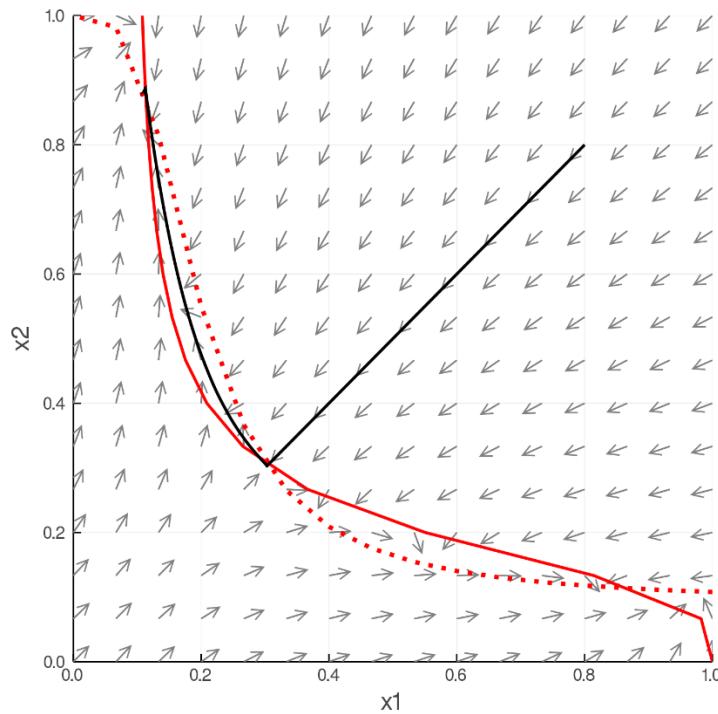
D1=D2=0.2perturbD2 (this plot was made by uncommenting line 29, and generating a phase portrait for the corresponding x_0 vector)



D1=D2=0.8perturbD1 (this plot was made by uncommenting line 30, and generating a phase portrait for the corresponding x0 vector)

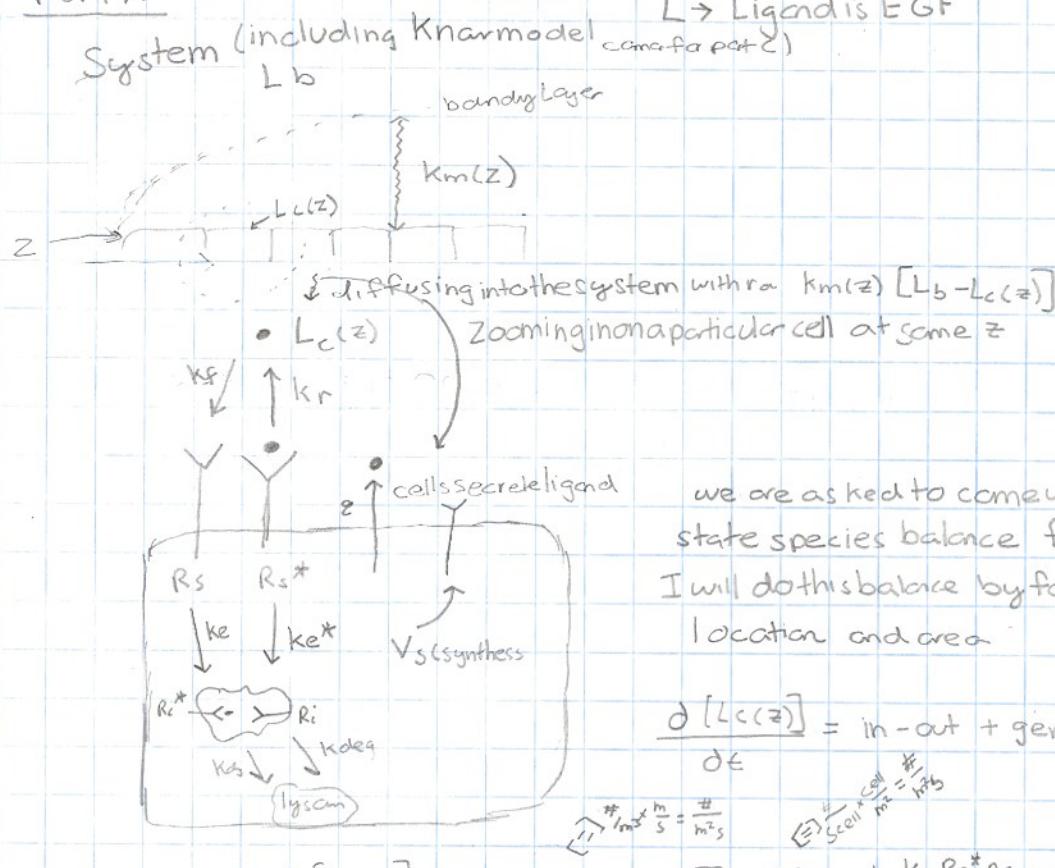


D1=D2=0.8perturbD2 (this plot was made by uncommenting line 31, and generating a phase portrait for the corresponding x0 vector)



Problem 2

Part A



we are asked to come up with a steady state species balance for EGF

I will do this balance by focusing on a particular location and area

$$\frac{\partial [L_c(z)]}{\partial t} = \text{in-out} + \text{generation}$$

$$\frac{\#}{m^3 \cdot s} = \frac{\#}{m^2 \cdot s}$$

$$\frac{\#}{m^2 \cdot s} = \frac{\#}{m^2 \cdot s}$$

$$\Delta z \times \frac{\partial [L_c(z)]}{\partial t} = km(z) [L_b - L_c(z)] + \varepsilon \times n_c + k_r R_s^* n_c - k_f L_c(z) R_s n_c$$

$$m \times \frac{\#}{s} = \frac{\#}{m \cdot s}$$

$$\frac{1}{s} \times \frac{\#}{cell} \times \frac{cell}{m^2} = \frac{\#}{m^2 \cdot s}$$

$$\frac{m^2}{s} \times \frac{\#}{m^2} \times \frac{\#}{cell} \times \frac{cell}{m^3} = \frac{\#}{m^3 \cdot s}$$

$$\text{at steady state } \frac{\partial [L_c(z)]}{\partial t} = 0$$

$$0 = km(z) [L_b - L_c(z)] + \varepsilon n_c + k_r R_s^* n_c - k_f L_c(z) R_s n_c$$

we now need to solve for $L_c(z)$

$$(\#) \quad 0 = km(z) L_b - L_c(z) km(z) + \varepsilon n_c + k_r R_s^* n_c - k_f R_s n_c L_c(z)$$

$$L_c(z) [km(z) + k_f R_s n_c] = km(z) L_b + \varepsilon n_c + k_r R_s^* n_c$$

$$\boxed{L_c(z) = \frac{km(z) * L_b + \varepsilon n_c + k_r R_s^* n_c}{km(z) + k_f R_s n_c}}$$

Part B

In the transport limited regime K_m is small

if we assume $K_m \ll k_f R_s n_c$ then the expression is simplified to

$$L_c(z) = \frac{K_m(z) L_b + \varepsilon n_c + k_r R_s * n_c}{k_f R_s n_c}$$

in the binding limited regime K_m is large

if we assume $K_m \gg k_f R_s n_c$

$$L_c(z) = \frac{K_m(z) L_b + \varepsilon n_c + k_r R_s * n_c}{K_m(z)}$$

$$L_c(z) = L_b + \frac{\varepsilon + k_r R_s * n_c}{K_m(z)}$$

In the case of small K_m the equation can be simplified even further to

$$\rightarrow L_c(z) \approx \frac{\varepsilon + k_r R_s * n_c}{k_f R_s} \quad \text{transport limited}$$

and similarly if K_m is very large the equation can be simplified further to

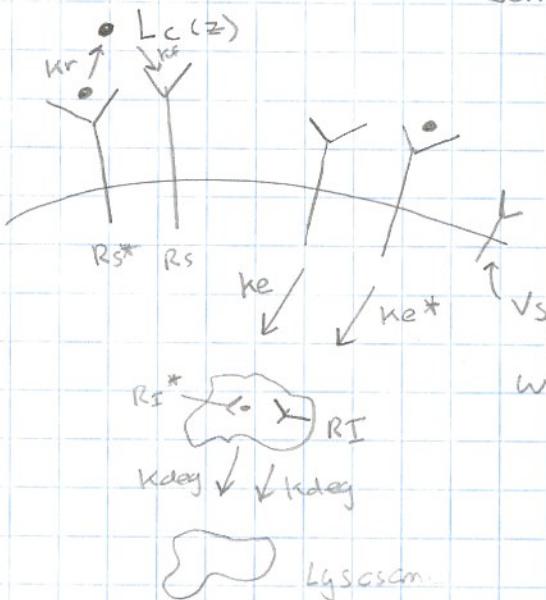
$$L_c(z) \approx L_b \quad \text{binding limited}$$

Based on these equations the system when binding is limited behaves as if the concentration in the cell is the bulk concentration. Since anything rapidly diffuses away, the transport limited case behaves in such a way that there is no oxygen diffusion and anything produced stays in the neighbourhood of the cell instead of diffusing away.

DontC

We will now incorporate the results for the local EGF concentration into the linear model (not including recycling)

Model: for a cell at some location z



where $R_s \rightarrow$ inactive surface area

$R_s^* \rightarrow$ active surface area

$R_I \rightarrow$ inactive internal receptor

$R_I^* \rightarrow$ active internal receptor

We can then write species balances on the system

Mass Balances:

(1)

$$\text{free surface receptor: } \frac{\partial R_s}{\partial t} = -k_f L_c(z) R_s + k_r R_s^* - k_{e*} R_s^* - k_v s$$

$$\text{bound (active) surface receptor: } \frac{\partial R_s^*}{\partial t} = k_f L_c(z) R_s - k_r R_s^* - k_e^* R_s^* \quad (2)$$

$$\text{total internal receptor: } \frac{\partial R_I^*}{\partial t} = k_e R_s + k_e^* R_s^* - k_{deg} R_I^* \quad (3)$$

$$\text{where } R_I^* = R_{I,s} + R_{I,*} \quad \frac{\partial R_I^*}{\partial t} = k_e R_s - k_{deg} R_I^*$$

$$\text{internal active receptor: } \frac{\partial R_I^*}{\partial t} = k_e^* R_s^* - k_{deg} R_I^* \quad (4)$$

$$@ S.S \quad \frac{\partial R_s}{\partial t} = \frac{\partial R_s^*}{\partial t} = \frac{\partial R_I^*}{\partial t} = \frac{\partial R_I^*}{\partial t} = 0$$

Solving this system leads to the same result as in class (w/o $L = L_c(z)$)

$k_r L_c(z) / V_s \downarrow$ other

$$K_f L R_s = (k_e^* + k_r) R_s^*$$

$$R_s = \frac{(k_e^* + k_r)}{K_f L} R_s^*$$

$$k_r R_s^* + V_s = (k_e + K_f L) R_s$$

$$k_r R_s^* + V_s = \frac{(k_e + K_f L)(k_e^* + k_r)}{K_f L} R_s^*$$

$$V_s = R_s^* \left(\frac{(k_e + K_f L)(k_e^* + k_r)}{K_f L} - k_r \right)$$

$$V_s = R_s^* \left(\frac{k_e k_e^* + k_e k_r + K_f L k_e^*}{K_f L} \right)$$

$$\frac{K_{ss} L_c}{1 + K_{ss}}$$

conce

$L_c(z)$

$$R_s^* = \frac{K_f L}{(k_e k_e^* + k_e k_r) + K_f L k_e^*} V_s$$

$$R_s^* = \frac{K_f L}{(k_e k_e^* + k_e k_r) + K_f L} \frac{V_s}{k_e^*}$$

$$R_s^* = \left(\frac{K_{ss} L}{1 + K_{ss}} \right) \frac{V_s}{k_e^*}$$

$$K_{ss} = \frac{K_f k_e^*}{k_e (k_e^* + k_r)}$$

$$R_{\text{Total}}^* = R_s^* + R_i^*$$

(3) und (4)

$$K_e^* R_s^* = K_{\text{deg}} R_i^* \quad K_e R_s = K_{\text{deg}} R_i$$

$$R_i^* = \frac{K_e^*}{K_{\text{deg}}} R_s^* \quad R_i = \frac{K_e}{K_{\text{deg}}} R_s$$

(1)

$$-k_f L_c(z) R_s + k_r R_s^* - K_e R_s + V_s = 0$$

$$k_f L_c(z) R_s - k_r R_s^* - K_e R_s^* = 0 \rightarrow (k_r + K_e) R_s^* = k_f L_c(z) R_s$$

if $L_b = 0$ (H) is also (when K_C and K_m are ref(z))

$$0 = -L_c K_m + \varepsilon n_c + k_r R_s^* n_c - k_f L_c(z) R_s n_c$$

$$0 = -L_c K_m + \varepsilon n_c + k_r R_s^* n_c - (k_r + K_e) R_s^* n_c$$

$$0 = -L_c K_m + \varepsilon n_c + n_c (k_r R_s^* - k_r R_s^* - K_e R_s^*)$$

$$L_c K_m = \varepsilon n_c + n_c (-K_e R_s^*)$$

$$L_c \frac{K_m}{n_c} = \varepsilon - K_e R_s^*$$

Based on the derivation in class we have

$$R_s^* = \frac{K_{ss} L_c}{1 + K_{ss} L_c} \left(\frac{V_s}{K_e^*} \right) \quad \text{assume } K_{ss} L_c \ll 1$$

$$R_s^* = K_{ss} L_c \left(\frac{V_s}{K_e^*} \right)$$

$$R_s^* = K_{ss} \left(\frac{n_c}{K_m} \right) \left(\varepsilon - K_e^* R_s^* \right) \frac{V_s}{K_e^*}$$

$$R_s^* = \frac{K_{ss} n_c \varepsilon V_s}{K_e^* K_m} - \frac{K_{ss} n_c V_s}{K_m} R_s^*$$

$$R_s^* \left(1 + \frac{K_{ss} n_c V_s}{K_m} \right) = \frac{K_{ss} n_c \varepsilon V_s}{K_e^* K_m}$$

$$R_s^* = \frac{\frac{K_{ss} n_c \varepsilon V_s}{K_e^* K_m}}{1 + \frac{K_{ss} n_c V_s}{K_m}} = \frac{\frac{K_{ss} n_c V_s}{K_m}}{1 + \frac{K_{ss} n_c V_s}{K_m}} \cdot \frac{\varepsilon}{K_e^*} = \frac{K_c}{K_m + K_c} \cdot \frac{\varepsilon}{K_e^*}$$

$$K_c = K_{ss} L_c V_s$$

Similarity to the case in lecture
 - ε
 - $\frac{1}{K_{\text{deg}}}$
 - $\frac{1}{K_e^*}$

Part D

Plot mitotic rate as a function of z

We will use the given Sherwood number correlation to find the behavior of $K_m(z)$

$$S_{hz} = \frac{K_m(z)}{D_L/z} = \left(\frac{\gamma z^2}{D_L} \right)^{1/3}$$

$$\rightarrow \left(\frac{\gamma}{D_L} \right)^{1/3} D_L \frac{z^{2/3}}{z}$$

$$K_m(z) = \left(\frac{\gamma z^2}{D_L} \right)^{1/3} \frac{D_L}{z}$$

Mitotic rate is proportional to R^*_{total}

$$\text{mitotic rate} = \overset{\text{mitogenic signal}}{\gamma} \cdot R^*_{\text{Total}}$$

since this is a linear response we will plot R^*_{Total} vs. z .

In the excel sheet, in the problem 2 folder

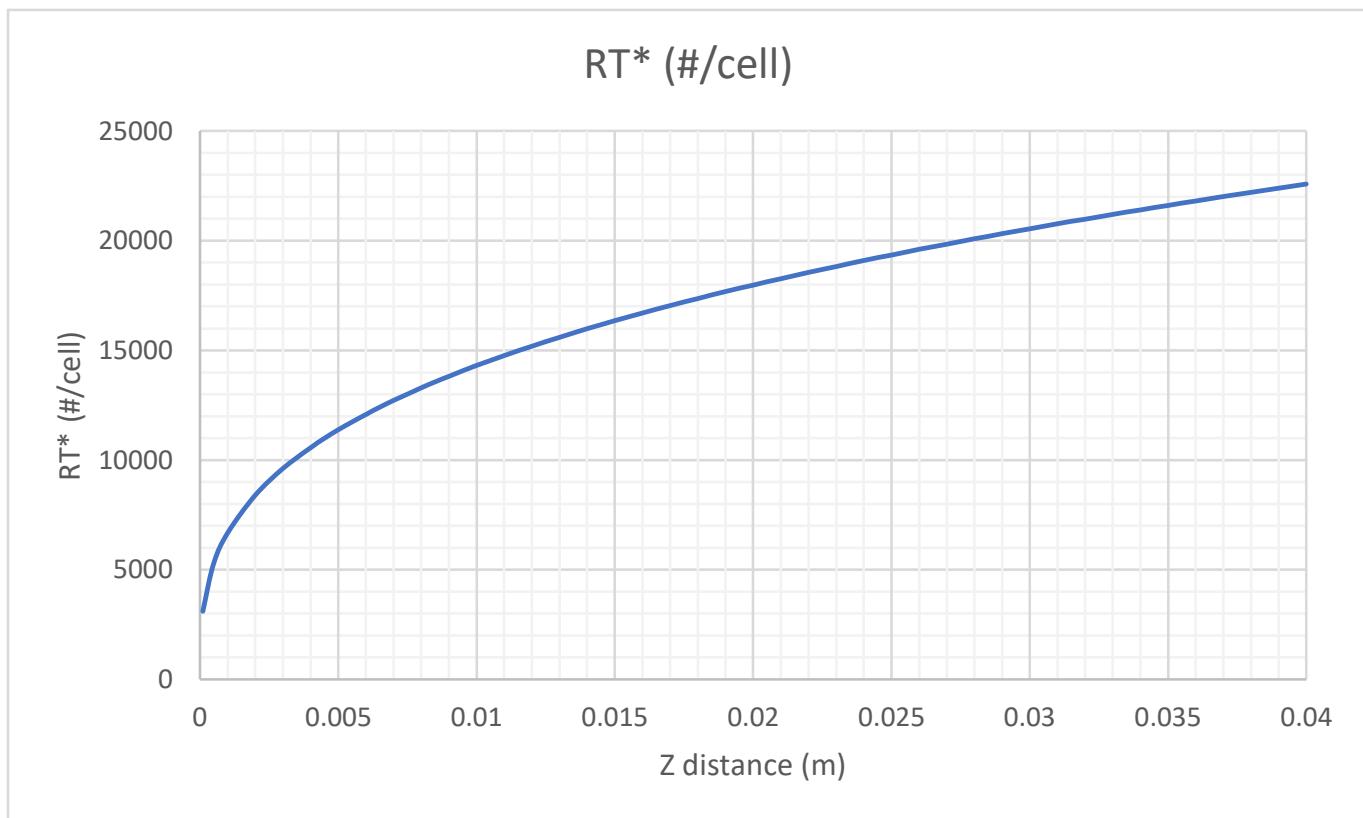
$$R^*_{\text{Total}} = \underbrace{\left(\frac{1}{k_e^*} + \frac{1}{k_{deg}} \right)}_{\text{"resistive term}} \underbrace{\left(\frac{k_c}{K_m(z) + k_c} \right)}_{\text{"Board fraction"}} z \quad \text{is plotted for various } z \text{ values}$$

I made these two assumptions regarding the given values:

a) Given as $k_f = 5.14 \times 10^{-21} \text{ m}^3/\text{s}$ Should have units of $\text{m}^3/\text{s}/\#$

b) Given as $V_S = 18 \text{ s}^{-1} \text{ cm}^{-1}$ \rightarrow is the chg of #/skell.

Problem 2 Part D



Problem 3

Part A:

$$@ S.S., \overset{e^{\mu}}{z} = \overset{e^{\mu}}{(z)} = 0$$

$$0 = r_{X,i} \bar{u}_i - (\mu + \Theta_{m,i}) m_i$$

$$0 = r_{L,i} w_i - (\mu + \Theta_{p,i}) p_i$$

$$m_i^* = \frac{r_{X,i}}{(\mu + \Theta_{m,i})} \bar{u}_i$$

$K_{X,i}$

$$m_i^* = K_{X,i} \bar{u}_i$$

$$K_{X,i} = \frac{r_{X,i}}{(\mu + \Theta_{m,i})}$$

$$p_i^* = \frac{r_{L,i}}{(\mu + \Theta_{p,i})} w_i$$

according to course notes

 $r_{L,i}$ can be written as

$$r_{L,i} = K_{E,i}^L R_{L,T} \left(\frac{m_i^*}{Z_{L,i} K_{L,i} + (Z_{L,i} + 1) p_i^*} \right)$$

using assumption 7

the denominator can be approximated as $Z_{L,i} K_L$

so

$$r_{L,i} = \frac{K_{E,i}^L R_{L,T} m_i^*}{Z_{L,i} K_{L,i}}$$

we can then plug this back in above

$$\begin{aligned} p_i^* &= \frac{r_{L,i}}{(\mu + \Theta_{p,i})} w_i \\ &= \frac{K_{E,i}^L R_{L,T}}{(\mu + \Theta_{p,i})(Z_{L,i} K_{L,i})} m_i^* w_i \\ &= \frac{K_{E,i}^L R_{L,T}}{(\mu + \Theta_{p,i})(Z_{L,i} K_{L,i})} K_{X,i} \bar{u}_i \end{aligned}$$

$$p_i^* = K_{L,i} K_{X,i} \bar{u}_i$$

$$\begin{aligned} K_{L,i} &\text{ is the translation gain} \\ &= \frac{K_{E,i}^L R_{L,T}}{(\mu + \Theta_{p,i})(Z_{L,i} K_{L,i})} \\ &\quad \begin{array}{l} \uparrow \text{elongation rate per} \\ \uparrow \text{pitch of inter} \\ \uparrow \text{total ribosome concn} \end{array} \\ &\quad \downarrow \text{transactive const.} \\ &\quad \downarrow \text{translsh sat. const.} \end{aligned}$$

The data driven value of K_X can be found by

looking @ high inducer concn when expression saturates

 $m^* e (I = 0.216 \text{ mM}) = K_X$ based on my calculations forConverting the units for $\langle n \rangle$ K_X has a value of

$$m^* e = \langle n_i \rangle \times \left(\frac{1 \times 10^9}{6.022 \times 10^{23}} \right) \Rightarrow n_i = 93$$

$$I = 0.216 \quad m^* e = 1.197 \rightarrow 1.20 \text{ this is the}$$

value of K_X we will use for this problem

Part B

We need to estimate ρ_i^* which means estimating all of the parameters. Some parameter require calculation those calculation are summarized below

$$K_I = \frac{1}{\text{charachteristic time}} = \frac{1}{1.5 \text{ s}} = 0.666 \text{ s}^{-1}$$

We have to convert the units of RLT to μM from #/cell

$$\text{RLT} = \frac{26,300 \text{ ribosomes}}{\text{cell}} \left(\frac{1 \text{ cell}}{1 \mu\text{m}^3} \right) \left(\frac{10^{15} \mu\text{m}^3}{1 \text{ L}} \right) \left(\frac{1 \text{ mol}}{6.022 \times 10^{23} \text{ molecules}} \right) \left(\frac{10^6 \mu\text{M}}{1 \text{ mol}} \right) = 43.7 \mu\text{M}$$

Based on the value of e_L (avg rate of elongation of 18 aa/s)

$$k_{E,i}^L = e_L \times \frac{1}{L} = \frac{18 \text{ aa}}{\text{s}} \times \frac{1}{333 \text{ aa}} = 0.05405 \text{ s}^{-1}$$

We can then calculate $\Sigma_{L,i}$ for the system, $\Sigma_{L,i} = \frac{k_A + k_E k_i}{K_I}$ assume $k_A \ll k_E k_i$

$$\Sigma_{L,i} = \frac{k_E L}{K_I} = \frac{0.05405 \text{ s}^{-1}}{0.666 \text{ s}^{-1}} = 0.0811$$

We can then calculate μ and θ_{P_i} by the doubling time and half-life.

$$r_{deg} = \theta_{P_i} \rho_i^* \quad t_{1/2} = \frac{\ln(2)}{\theta_{P_i}} \quad \theta_{P_i} = \frac{\ln(2)}{t_{1/2}} = \frac{\ln(2)}{24 \text{ hr}} \times \frac{1 \text{ hr}}{60 \text{ min}} \times \frac{1 \text{ min}}{60 \text{ s}} \\ = 8.02 \times 10^{-6} \text{ s}^{-1}$$

For μ , the doubling time is the time it takes for cell volume to double which would dilute by a factor of $1/2$ so it is also one effective half-life of the protein

$$\mu = \frac{\ln(2)}{t_0} = \frac{\ln(2)}{40 \text{ min}} \left(\frac{1 \text{ min}}{60 \text{ s}} \right) = 2.89 \times 10^{-4} \text{ s}^{-1}$$

Based on the values in the table we can calculate a value for $K_{L,i}$

$$K_{L,i} = \frac{k_{E,i}^L \text{ RLT}}{(\mu + \theta_{P_i}) (\Sigma_{L,i} K_I)} = \frac{0.05405 \text{ s}^{-1} \times 43.7 \mu\text{M}}{(2.89 \times 10^{-4} + 8.02 \times 10^{-6}) \text{ s}^{-1} \times (0.0811) (200 \mu\text{M})} = 490$$

$$\rho_i^* = K_{L,i} K_{X,i} \bar{u}_i \bar{w}_i$$

This is plotted with \bar{u}_i vs \bar{w}_i

Part C

with the polysac

$$P_i^* = K_{L,i} K_{X,i} w_i \bar{u}_i$$

$$P_i^{*'} = \frac{K_p}{P_i^*} K_{L,i} K_{X,i} w_i \bar{u}_i$$

$$P_i^{*'} = P_i^* K_p$$

Based on the plot it shifts the
curve upward.

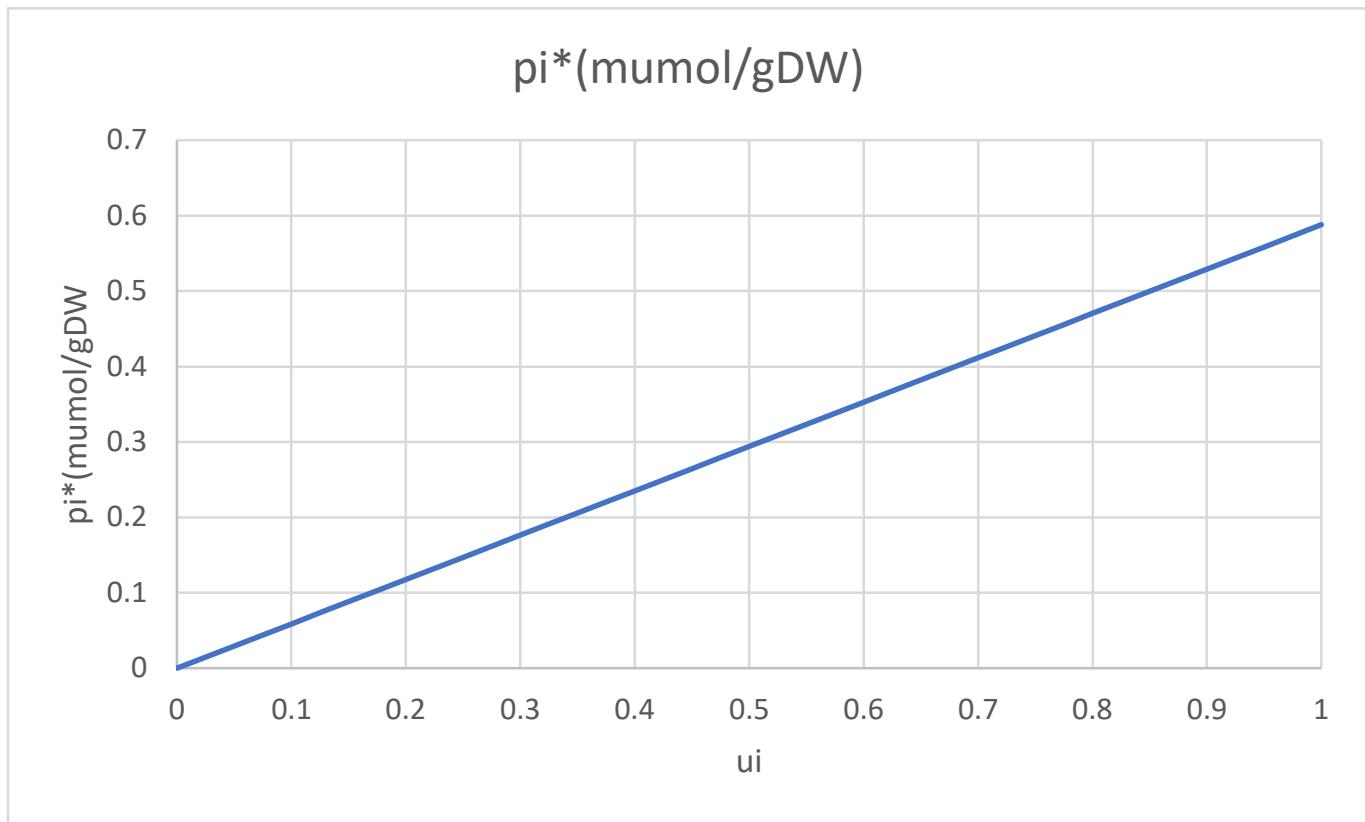
Problem 3 Parameters

Parameter	Value	units	Source	
Kxi (transcription gain)	1.20	nmol/gDW	Prelim 1 Q1 Solutions	*for all values with calculations see written work for how the calculations were done
ui	(between 0 and 1)	unitless		
wi		1 unitless	Problem statement	

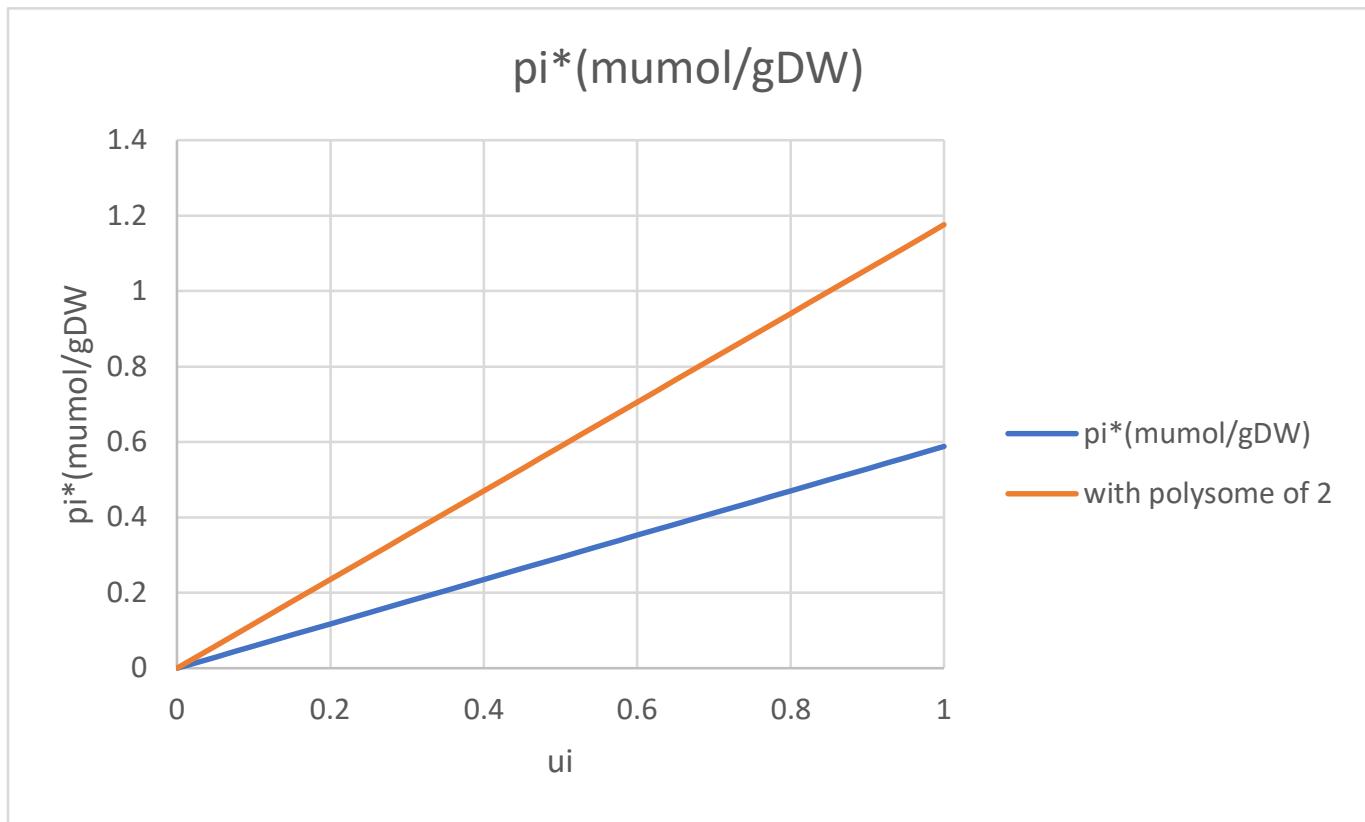
Params to calculate KLi

protein half life	24 hr	Problem statement
doubling time	40 min	Problem statement
mu	0.000289 s^-1	Calculated
theta Pi	0.00000802 s^-1	Calculated
Tau Li	0.0811 unitless	Calculated (kI/kEL) assuming kA << kEL
Kli	200 muM	Problem statement
RLT (Total Ribosome Concentration)	26300 ribosomes/cell	Bionumber: 101441 (see link on bionumbers for the value at appropriate doubling time.)
e. coli cell volume	1 um^3	problem statement
RLT (muM)	43.7 muM	Calculated
kLEi	0.05405 s^-1	Calculated
n (length of protein)	333 aa	Problem statement
Avg elongation rate for protein (eL)	18 aa/s	Bionumber: 101441 (see link on bionumbers for the value at appropriate doubling time.)
charachteristic translation initiaton time	1.5 s	problem statement * this is actually the same table as was used for RLT
kI (rate of initiaiton)	0.6667 s^-1	calculated
KLi	490 unitless	calculated

Part B

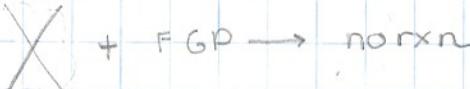


Part C



Problem 4

no enzyme

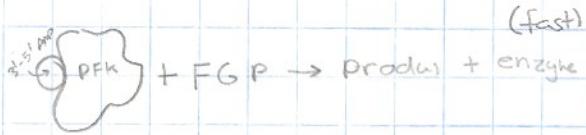


microstate weight

1



W_1



$W_2 f_{3'-5' \text{AMP}}$

} rxn

Based on these micro states v is as follows

$$v = \frac{W_1 + W_2 f_{3'-5' \text{AMP}}}{1 + W_1 + W_2 f_{3'-5' \text{AMP}}} \quad \text{where } f_{3'-5' \text{AMP}} = \frac{([3'-5' \text{AMP}] / K_D)^n}{1 + ([3'-5' \text{AMP}] / k_g)^n}$$

Part A

we will estimate the parameters for W_1 and W_2 based on the dataset

$$\hat{r}_j = r_j v$$

we need to calculate the kinetic limit of the rxn r_j

$$r_j = k_{\text{cat}} E_1 \left(\frac{\text{FDP}}{K_{\text{FDP}} + \text{FDP}} \right) \left(\frac{\text{ATP}}{K_{\text{ATP}} + \text{ATP}} \right)$$

we can plugin all the the parameter values given in the problem

$$r_j = 6.4 \text{ s}^{-1} (0.12 \mu\text{M}) \left(\frac{0.1 \mu\text{M}}{0.11 \mu\text{M} + 0.1 \mu\text{M}} \right) \left(\frac{2.3 \mu\text{M}}{0.42 \mu\text{M} + 2.3 \mu\text{M}} \right)$$

$$r_j = 0.0193 \mu\text{M/s}$$

the given data has units of $\mu\text{M/hr}$ so we will convert r_j

$$r_j = \frac{0.0193 \mu\text{M}}{\text{s}} \times \frac{60 \text{s}}{1 \text{min}} \times \frac{60 \text{min}}{1 \text{hr}} = 69.48 \mu\text{M/hr}$$

we can calculate W_1 using the datapoint when $[3'-5' \text{AMP}] = 0$

at this point $f_{3'-5' \text{AMP}} = 0$ and

$$\hat{r}_j = r_j v = r_j \frac{W_1}{1 + W_1}$$

$$\hat{r}_j (\text{AMP}=0) = 3.0003 \frac{\mu\text{M}}{\text{hr}} = \frac{69.48 \mu\text{M}}{\text{hr}} \left(\frac{W_1}{1 + W_1} \right)$$

Based on this W_1 is 0.0452

we can calculate W_2 at the othelimit of the dataset.

when $3'-5' \text{Amp} = 0.99 \text{ mM}$ $\hat{r}_i = 68.653 \mu\text{M}/\text{hr}$

at this point $\hat{r}_i = r_i \sqrt{V}$

$$V = \frac{\hat{r}_i}{r_i} = \frac{68.653}{69.48} = 0.988$$

if we assume at this point $f_{3'-5' \text{Amp}} \approx 1$

$$V = \frac{W_1 + W_2}{1 + W_1 + W_2}$$

$$0.988 = \frac{0.0452 + W_2}{1 + 0.0452 + W_2}$$

Based on this W_2 is $1.03266 + 0.988W_2 = 0.0452 + W_2$

$$0.98746 = 0.012W_2$$
$$\boxed{W_2 = 82.3}$$

Part B

K_D and n in the $F_{3'-5' \text{Amp}}$ expression were calculated using a non-linear least square fit of the data in excel, where the error in the calculated \hat{r}_i and mean \hat{r}_i is minimized. This was done using excel solver.

Based on the solver solution with the above value of W_1 and W_2

$$\boxed{K_D = 0.685 \text{ mM}} \quad \boxed{n = 2.49}$$

Part C

See plot. Given the large error bars, and the two curves in the plot, I would say the model adequately describes the given system and well within the large error bars.

Problem 4 excell workbook

