@ Steady State : $\frac{d[\,]}{dt} = 0$

$Y^* = [Y^*]/Y_T$ $\qquad$ $Y_T = Y + Y^*$

$\frac{dY^*}{dt} = \frac{V_3[Y]}{K_3+[Y]} - \frac{V_4[Y^*]}{K_4+[Y^*]}$ $\qquad$ $V_3 = \gamma_3[X^*]$

(1)
@ S.S.

$0 = k_{on}[R][L] - k_{off}[R^*]$

$k_{off}[R^*] = k_{on}[R][L] \Rightarrow k_{off}[R^*] = k_{on}(R_T - [R^*])[L]$

$k_{off}[R^*] = (k_{on}R_T - k_{on}[R^*])[L]$

$k_{off}[R^*] + k_{on}[R^*][L] = k_{on}R_T[L]$

$[R^*](k_{off} + k_{on}[L]) = k_{on}R_T[L]$

$$[R^*] = \frac{k_{on}R_T[L]\,/k_{off}}{(k_{off}+k_{on}[L])\,/k_{off}}$$

$[R^*] = \theta_B R_T$

$\Downarrow$

$V_1 = \gamma_1[R^*]$

$V_1 = \gamma_1\theta_B R_T$

$$[R^*] = \frac{\frac{1}{K_D}R_T}{1+\frac{1}{K_D}} \cdot \frac{K_D}{K_D} \Rightarrow \frac{R_T}{K_D+1}$$

(2)
@ S.S.

$$0 = \frac{V_1[X]}{K_1+[X]} - \frac{V_2[X^*]}{K_2+[X^*]}$$

$$\frac{V_2[X^*]}{K_2+[X^*]} = \frac{V_1[X]}{K_1+[X]} \Rightarrow V_2[X^*](K_1+[X]) = V_1[X](K_2+[X^*])$$

$V_2[X^*](K_1+[X]) = V_1[X]K_2 + V_1[X][X^*] \longrightarrow$

$V_1 = \gamma_1 \theta_B * R_T$

v_1

$V_2[X^*](K_1+[X]) = V_1[X]K_2 + V_1[X][X^*]$

$V_2[X^*]K_1 + V_2[X^*][X] = V_1[X]K_2 + V_1[X][X^*]$

$V_2[X^*]K_1 - V_1[X]K_2 = [X][X^*](V_1 - V_2)$

$V_2[X^*]K_1 - V_1K_2X_T + V_1K_2[X^*] = X_T[X^*](V_1-V_2) - [X^*]^2(V_1-V_2)$

$[X^*]^2(V_1-V_2) + [X^*](V_2K_1 + V_1K_2 - X_T(V_1-V_2)) - V_1K_2X_T = 0$

$$\cancel{\frac{-(V_1K_2 - X_T(V_1-V_2)) \pm \sqrt{(V_1K_2 - X_T(V_1-V_2))^2 - 4(V_1-V_2)(V_1K_2X_T)}}{2(V_1-V_2)}}$$

$$\cancel{[X^*]_{r,i} = \frac{-V_1K_2 + X_T(V_1-V_2) \pm \sqrt{(V_1K_2)^2 - 2V_1K_2X_T(V_1-V_2) + X_T^2(V_1-V_2)^2 - 4(V_1-V_2)V_1K_2X_T}}{2(V_1-V_2)}}$$

$[X^*]x^*(V_1-V_2) + x^*(V_2K_1 + V_1K_2 - X_T(V_1-V_2)) - V_1K_2 = 0$

$\frac{1}{(V_2X_T)}$ $\quad K_1+$

$x^{*2}\left(\frac{V_1}{V_2}-1\right) + x^*\left(\frac{V_1}{V_2}K_2 - \frac{V_1}{V_2} + 1\right) - \frac{V_1}{V_2}K_2 = 0$

(3)
@ s.s.

$$0 = \frac{V_3[Y]}{K_3 + [Y]} - \frac{V_4[Y^*]}{K_4 + [Y^*]}$$

*similar process as (2) @ s.s. . . .

$$[Y^*]^2(V_3 - V_4) + [Y^*](V_4K_3 + V_3K_4 - Y_T(V_3 - V_4)) - V_3K_4Y_T = 0$$

$$[Y^*]\,y^*(V_3 - V_4) + y^*(V_4K_3 + V_3K_4 - Y_T(V_3 - V_4)) - V_3K_4 = 0$$

$$[Y^*]\,y^*(V_3 - V_4) + y^*V_4K_3 + y^*V_3K_4 - y^*Y_T(V_3 - V_4) - V_3K_4 = 0$$

$$y^{*2}(V_3 - V_4) + y^*V_4\mathcal{K}_3 + y^*V_3\mathcal{K}_4 - y^*(V_3 - V_4) - V_3\mathcal{K}_4 = 0$$

$$Y^{*2}V_3 - y^{*2}V_4 + y^*V_4\mathcal{K}_3 + y^*V_3\mathcal{K}_4 - y^*V_3 + y^*V_4 - V_3\mathcal{K}_4 = 0$$

$$y^{*2}V_3/V_4 - y^{*2} + y^*\mathcal{K}_3 + y^*V_3/V_4\,\mathcal{K}_4 - y^*V_3/V_4 + y^* - V_3/V_4\,\mathcal{K}_4 = 0$$

$$y^{*2}(V_3/V_4 - 1) + y^*(\mathcal{K}_3 + V_3/V_4\,\mathcal{K}_4 - V_3/V_4 + 1) - V_3/V_4\,\mathcal{K}_4 = 0$$

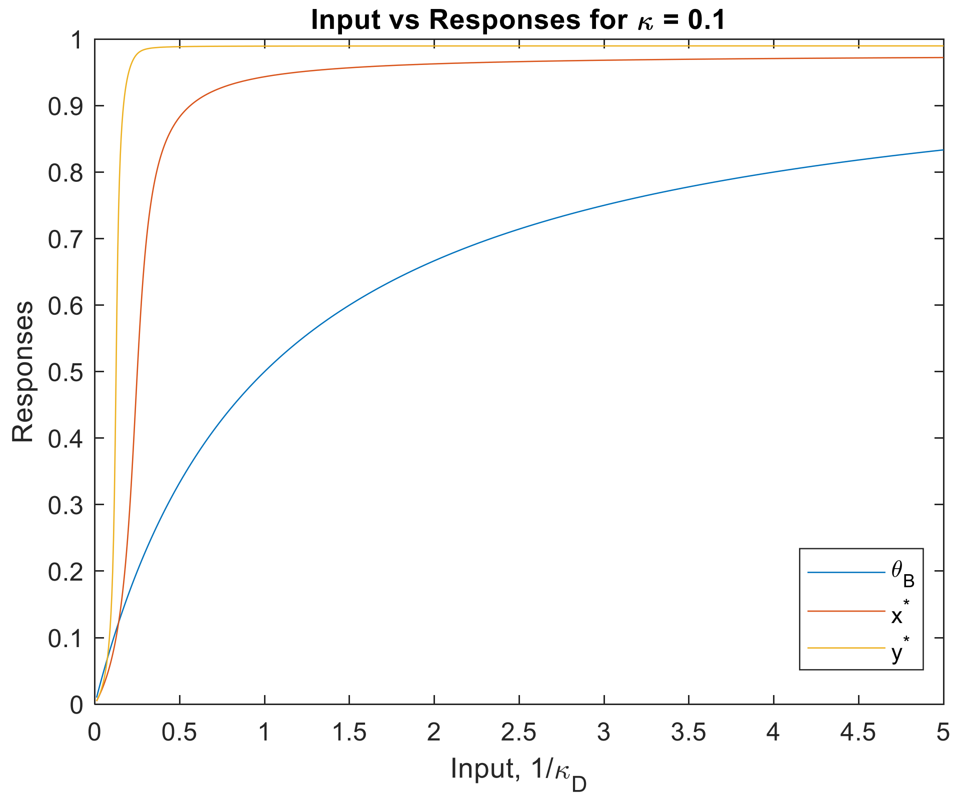
$$y^{*2}[(\gamma_3 x^*/V_4)X_T - 1] + y^*[\mathcal{K}_3 + (\gamma_3 x^*/V_4)X_T\mathcal{K}_4 - (\gamma_3 x^*/V_4)X_T + 1] - (\gamma_3 x^*/V_4)X_T\mathcal{K}_4 = 0$$

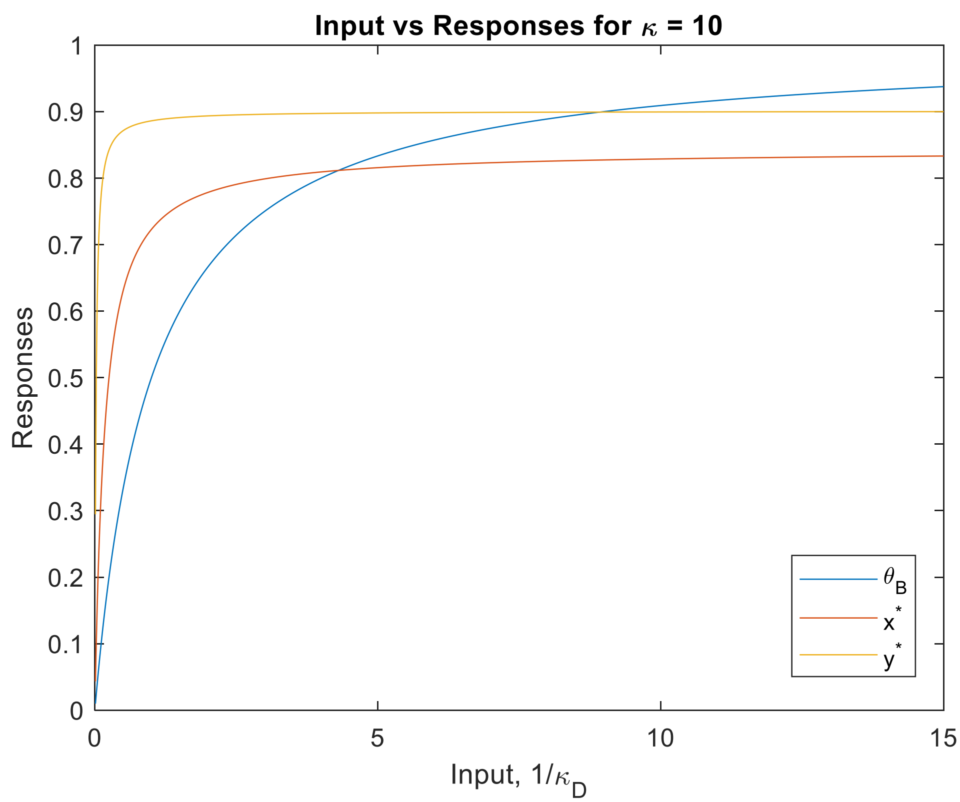
$$x^{*2}[(\gamma_1\theta_B/V_2)R_T - 1] + x^*[\mathcal{K}_1 + (\gamma_1\theta_B/V_2)R_T\mathcal{K}_2 - (\gamma_1\theta_B/V_2)R_T + 1] - (\gamma_1\theta_B/V_2)R_T\mathcal{K}_2 = 0$$

$$\theta_B = \frac{1}{\mathcal{K}_D + 1}$$ -OR- (re-written) $\Longrightarrow$ $$\theta_B = \frac{1/\mathcal{K}_D}{1 + 1/\mathcal{K}_D}$$

Allison Nestor
*Everything not done on lined paper was done with MATLAB code

1. A) *on lined paper
   B)





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*Everything not done on lined paper was done with MATLAB code

C) kappa = 0.1 Θ_B Hill coefficient: n = 1, (other parameter in eq: c = 1)

X* Hill coefficient: n = 3.053, (other parameter in eq: c = 0.251)

Y* Hill coefficient: n = 7.315, (other parameter in eq: c = 0.124)

kappa = 10 Θ_B Hill coefficient: n = 1, (other parameter in eq: c = 1)

X* Hill coefficient: n = 0.642, (other parameter in eq: c = 0.260)

Y* Hill coefficient: n = 0.608, (other parameter in eq: c = .0202)

D) kappa = 0.1 Θ_B % change: 43.478%

X* % change: 101.826%

Y* % change: 402.580%

kappa = 10 Θ_B % change: 43.478%

X* % change: 27.966%

Y* % change: 5.6566%

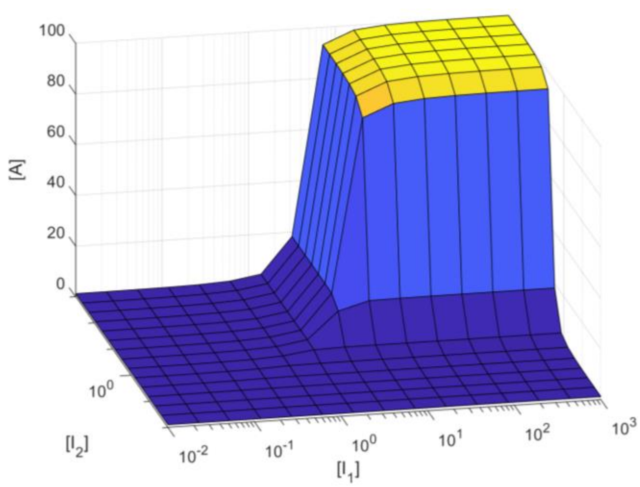
E) *on lined paper

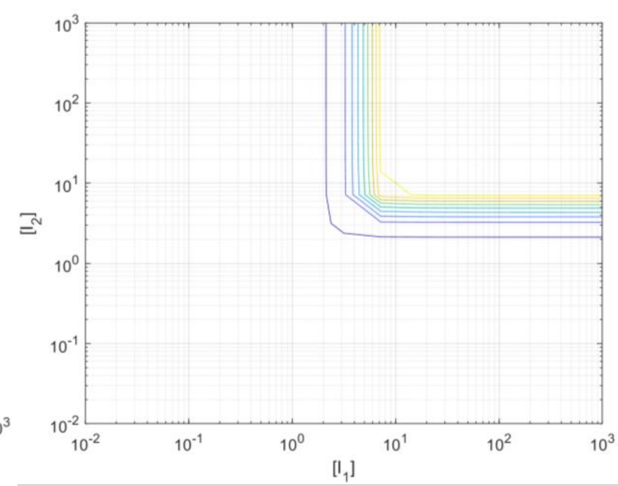
2. A) [A] = 1.1097

[B] = 49.4451

[C] = 49.4451

B)

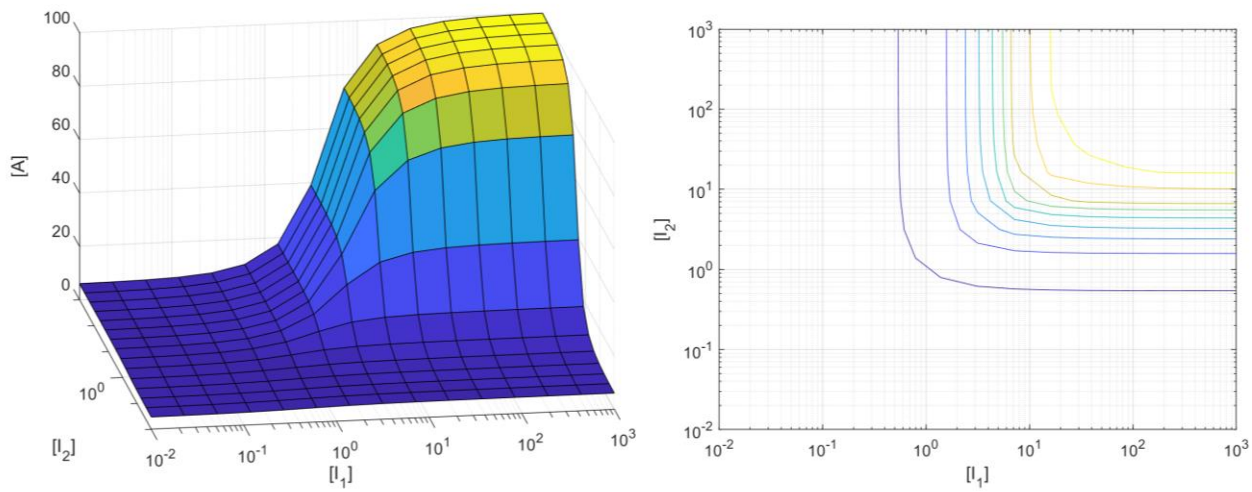




C) AND Logic Gate

Allison Nestor
*Everything not done on lined paper was done with MATLAB code

D)



This might be referred to as a "fuzzy" operator since the [A] values are not as close to 0 as they were when K_{si} values were 5 units. Plus, as the concentrations of the inhibitors reached higher values, the switch-like response with the AND logic operation was less defined when K_{si} values were 35 units.

E) *on lined paper

1.e) Parameter tuning is important because parameter tuning allows for dimensionality reduction, meaning that random variables are reduced to obtain a set of principal variables. For example, parameter tuning was important to help obtain the Hill coefficients that fits the θ_B, x^*, & y^* plots. In order to fit properly with the Hill equation, parameter tuning was needed. Then, zero-order ultrasensitivity is important because it is a great representation of signal responses that are operating close to saturation and are very sensitive to subtle changes for the input. The Hill equation curve fits ~~with~~ when $n > 1$ would be ultrasensitive. These two components (parameter tuning & zero-order ultrasensitivity) allow for accurate amplification of input signals since random variables that might be magnified will be reduced with parameter tuning, and any important change in the input signal will be amplified into a large change in output with zero-order ultrasensitivity. The same circuit can amplify signals based on parameter values by changing the input protein concentrations or manipulating reaction rates via the environment (changing temperature, pH., etc.)

2.e) Zero-order ultrasensitivity is important in the operation of the gate since such sensitivity provides a switch-like response that can be easily represented with logic gates, like "AND" or "OR." As discussed in Goldbeter & Koshland (1981), sigmoidal, ultrasensitive responses are commonplace in cell signaling, and when zero-order (or close to saturation), the response shows both a threshold and an abrupt leveling off at maximal response, resulting in a steeply sigmoidal input-output relationship.