Problem 1: Signal attenuation and amplification is signaling cascades

(a) Given eqn: $\frac{d[R^*]}{dt} = k_{on}[R][L] - k_{off}[R^*]$ (1)

$\frac{d[X^*]}{dt} = -\frac{d[X]}{dt} = \frac{V_1[X]}{k_1+[X]} - \frac{V_2[X^*]}{k_2+[X^*]}$, where $V_1 = \gamma_1[R^*]$ (2)

$\frac{d[Y^*]}{dt} = -\frac{d[Y]}{dt} = \frac{V_3[Y]}{k_3+[Y]} - \frac{V_4[Y^*]}{k_4+[Y^*]}$, where $V_3 = \gamma_3[X^*]$ (3)

$R_T = [R]+[R^*]$; (4) $\Rightarrow [R] = R_T - [R^*]$

$X_T = [X]+[X^*]$; (5) $\Rightarrow [X] = X_T - [X^*]$

$Y_T = [Y]+[Y^*]$; (6) $\Rightarrow [Y] = Y_T - [Y^*]$

Dimensionless variables & parameters:

$x^* = [X^*]/X_T \Rightarrow [X^*] = x^* X_T$; $\kappa_1 = k_1/X_T \Rightarrow k_1 = \kappa_1 X_T$

$\kappa_2 = k_2/X_T \Rightarrow k_2 = \kappa_2 X_T$; $\kappa_3 = k_3/Y_T \Rightarrow k_3 = \kappa_3 Y_T$; $\kappa_4 = k_4/Y_T \Rightarrow k_4 = \kappa_4 Y_T$;

$\kappa_0 = k_{off}/(k_{on}[L])$; $\theta_B = [R^*]/R_T \Rightarrow [R^*] = \theta_B R_T$

$V_1/V_2 = (\gamma_1\theta_B/V_2)\cdot R_T$; $V_3/V_4 = (\gamma_3 x^*/V_4)\cdot X_T$;

@ S.S: $\frac{d[R^*]}{dt} = \frac{d[X^*]}{dt} = \frac{d[Y^*]}{dt} = 0$

For (3): $\frac{d[Y^*]}{dt} = -\frac{d[Y]}{dt} = \frac{V_3[Y]}{k_3+[Y]} - \frac{V_4[Y^*]}{k_4+[Y^*]} = 0$, where $V_3 = \gamma_3[X^*]$

$\Rightarrow \frac{V_3}{V_4}\frac{Y_T - [Y^*]}{\kappa_3 Y_T + (Y_T - [Y^*])} - \frac{[Y^*]}{\kappa_4 Y_T + [Y^*]} = 0$

Since $y^* = [Y^*]/Y_T \Rightarrow [Y^*] = y^* Y_T$

$\Rightarrow \frac{V_3}{V_4}\frac{Y_T - y^* Y_T}{\kappa_3 Y_T + (Y_T - y^* Y_T)} - \frac{y^* Y_T}{\kappa_4 Y_T + y^* Y_T} = 0$

$\Rightarrow \frac{V_3}{V_4}\frac{1-y^*}{\kappa_3 + (1-y^*)} = \frac{y^*}{\kappa_4 + y^*}$

$\Rightarrow \frac{V_3}{V_4}(1-y^*)(\kappa_4+y^*) = y^*[\kappa_3 + (1-y^*)]$

$\Rightarrow \frac{V_3}{V_4}(\kappa_4 + y^* - \kappa_4 y^* - y^{*2}) = y^*\kappa_3 + y^* - y^{*2}$

$\Rightarrow \frac{V_3}{V_4}\kappa_4 + \frac{V_3}{V_4}y^* - \frac{V_3}{V_4}\kappa_4 y^* - \frac{V_3}{V_4}y^{*2} - \kappa_3 y^* - y^* + y^{*2} = 0$

$\Rightarrow \underbrace{(1-\frac{V_3}{V_4})}_{a} y^{*2} + \underbrace{(\frac{V_3}{V_4} - \frac{V_3}{V_4}\kappa_4 - \kappa_3 - 1)}_{b} y^* + \underbrace{\frac{V_3}{V_4}\kappa_4}_{c} = 0$

satisfy $a y^{*2} + b y^* + c = 0$

$$\therefore y^* = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

$$\therefore y^* = \frac{\left(1 + K_3 + \frac{V_3}{V_4}K_4 - \frac{V_3}{V_4}\right) \pm \sqrt{\left(\frac{V_3}{V_4} - \frac{V_3}{V_4}K_4 - K_3 - 1\right)^2 - 4\left(1 - \frac{V_3}{V_4}\right)\left(\frac{V_3}{V_4}K_4\right)}}{2\left(1 - \frac{V_3}{V_4}\right)}$$

where $\frac{V_3}{V_4} = \frac{\gamma_3 x^* X_T}{V_4}$

$$y^* = \frac{\left(1 + K_3 + \frac{\gamma_3 x^* X_T}{V_4}K_4 - \frac{\gamma_3 x^* X_T}{V_4}\right) \pm \sqrt{\left(\frac{\gamma_3 x^* X_T}{V_4} - \frac{\gamma_3 x^* X_T}{V_4}K_4 - K_3 - 1\right)^2 - 4\left(1 - \frac{\gamma_3 x^* X_T}{V_4}\right)\left(\frac{\gamma_3 x^* X_T}{V_4}K_4\right)}}{2\left(1 - \frac{\gamma_3 x^* X_T}{V_4}\right)}$$

For (2) $\frac{d[X^*]}{dt} = -\frac{d[X]}{dt} = \frac{V_1[X]}{K_1 + [X]} - \frac{V_2[X^*]}{K_2 + [X^*]} = 0$ where $V_1 = \gamma_1 [R^*]$

$$\Rightarrow \frac{\gamma_1 [R^*](X_T - [X^*])}{K_1 X_T + (X_T - [X^*])} = \frac{V_2 [X^*]}{K_2 X_T + [X^*]}$$

$$\Rightarrow \frac{\gamma_1 \theta_B R_T (X_T - x^* X_T)}{K_1 X_T + (X_T - x^* X_T)} = \frac{V_2 (x^* X_T)}{K_2 X_T + (x^* X_T)}$$

$$\Rightarrow \frac{\gamma_1 \theta_B R_T (1 - x^*)}{K_1 + (1 - x^*)} = \frac{V_2 x^*}{K_2 + x^*}$$

$$\Rightarrow (\gamma_1 \theta_B R_T - \gamma_1 \theta_B R_T x^*)(K_2 + x^*) = [K_1 + (1 - x^*)] V_2 x^*$$

$$\Rightarrow \gamma_1 \theta_B R_T K_2 + \gamma_1 \theta_B R_T x^* - \gamma_1 \theta_B R_T K_2 x^* - \gamma_1 \theta_B R_T x^{*2}$$

$$= K_1 V_2 x^* + V_2 x^* - V_2 x^{*2}$$

$$\Rightarrow \gamma_1 \theta_B R_T K_2 + \gamma_1 \theta_B R_T x^* - \gamma_1 \theta_B R_T K_2 x^* - \gamma_1 \theta_B R_T x^{*2} - K_1 V_2 x^* - V_2 x^* + V_2 x^{*2} = 0$$

$$\Rightarrow \underbrace{(V_2 - \gamma_1 \theta_B R_T)}_{a} x^{*2} + \underbrace{(\gamma_1 \theta_B R_T - \gamma_1 \theta_B R_T K_2 - K_1 V_2 - V_2)}_{b} x^* + \underbrace{\gamma_1 \theta_B R_T K_2}_{c} = 0$$

satisfy $a x^{*2} + b x^* + c = 0$ $\quad x^* = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$

$$\Rightarrow x^* = \frac{(V_2 + K_1 V_2 + \gamma_1 \theta_B R_T K_2 - \gamma_1 \theta_B R_T) \pm \sqrt{(\gamma_1 \theta_B R_T - \gamma_1 \theta_B R_T K_2 - K_1 V_2 - V_2)^2 - 4(V_2 - \gamma_1 \theta_B R_T)\gamma_1 \theta_B R_T K_2}}{2(V_2 - \gamma_1 \theta_B R_T)}$$

$$\Rightarrow x^{*} = \frac{\left(1 + \mathcal{K}_1 + \frac{V_1}{V_2}\mathcal{K}_2 - \frac{V_1}{V_2}\right) \pm \sqrt{\left(\frac{V_1}{V_2} - \frac{V_1}{V_2}\mathcal{K}_2 - \mathcal{K}_1 - 1\right)^2 - 4\left(1-\frac{V_1}{V_2}\right)\left(\frac{V_1}{V_2}\mathcal{K}_2\right)}}{2\left(1-\frac{V_1}{V_2}\right)}$$

where $\frac{V_1}{V_2} = \frac{\gamma_1 \theta_B R_T}{V_2}$

For (1) $\frac{d[R^*]}{dt} = k_{on}[R][L] - k_{off}[R^*] = 0$

$$\Rightarrow \frac{k_{on}[R][L]}{k_{on}[L]} - \frac{k_{off}(\theta_B R_T)}{k_{on}[L]} = 0$$

$$\Rightarrow [R] - \mathcal{K}_D(\theta_B R_T) = 0 \Rightarrow R_T - [R^*] - \mathcal{K}_D(\theta_B R_T) = 0$$

$$\Rightarrow R_T - \theta_B R_T - \mathcal{K}_D(\theta_B R_T) = 0 \Rightarrow 1 - \theta_B - \mathcal{K}_D \theta_B = 0$$

$$\Rightarrow \boxed{\theta_B = \frac{1}{1+\mathcal{K}_D}}$$

Final Answer

Plug $\theta_B = \frac{1}{1+\mathcal{K}_D}$ into x^* above.

then:
$$x^* = \frac{\left(V_2 + \mathcal{K}_1 V_2 + \frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D} - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right) \pm \sqrt{\left(\frac{\gamma_1 R_T}{1+\mathcal{K}_D} - \frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D} - \mathcal{K}_1 V_2 - V_2\right)^2 - 4\left(V_2 - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right)\frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D}}}{2\left(V_2 - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right)}$$

where $\mathcal{K}_D = k_{off}/(k_{on}[L])$

plug x^*

$$x^* = \frac{\left(V_2 + \mathcal{K}_1 V_2 + \frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D} - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right) \pm \sqrt{\left(\frac{\gamma_1 R_T}{1+\mathcal{K}_D} - \frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D} - \mathcal{K}_1 V_2 - V_2\right)^2 - 4\left(V_2 - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right)\frac{\gamma_1 R_T \mathcal{K}_2}{1+\mathcal{K}_D}}}{2\left(V_2 - \frac{\gamma_1 R_T}{1+\mathcal{K}_D}\right)}$$

where $\mathcal{K}_D = k_{off}/(k_{on}[L])$ $\mathcal{K}_D$ containing input $[L]$

into the y^*:

$$y^* = \frac{\left(1 + \mathcal{K}_3 + \frac{\gamma_3 x^* X_T}{V_4}\mathcal{K}_4 - \frac{\gamma_3 x^* X_T}{V_4}\right) \pm \sqrt{\left(\frac{\gamma_3 x^* X_T}{V_4} - \frac{\gamma_3 x^* X_T}{V_4}\mathcal{K}_4 - \mathcal{K}_3 - 1\right)^2 - 4\left(1 - \frac{\gamma_3 x^* X_T}{V_4}\right)\left(\frac{\gamma_3 x^* X_T}{V_4}\mathcal{K}_4\right)}}{2\left(1 - \frac{\gamma_3 x^* X_T}{V_4}\right)}$$

Then we get the output y^* as a function of $[L]$