CHEME 7770: Biomolecular

Homework #5

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1.

With recycling :

$$\frac{dR_s}{dt} = -k_f L R_s + k_r R_s^* - k_e R_s + V_s + k_{rec} R_i \quad \text{—} \quad (1)$$

$$\frac{dR_s^*}{dt} = k_f L R_s - k_r R_s^* - k_e^* R_s^* + k_{rec} R_i^* \quad \text{—} \quad (2)$$

$$\frac{dR_i^T}{dt} = k_e R_s + k_e^* R_s^* - k_{deg} R_i^T - k_{rec} R_i^T \quad \text{—} \quad (3)$$

$$\frac{dR_i^*}{dt} = k_e^* R_s^* - k_{deg} R_i^* - k_{rec} R_i^* \quad \text{—} \quad (4)$$

Equating (3) to 0 and rearranging,

$$k_{deg} R_i^T = k_e R_s + k_e^* R_s^* - k_{rec} R_i^T$$

Adding (1) + (2) + (3) we get

$$V_s = k_{deg} R_i^T$$

$$\Rightarrow V_s = k_e R_s + k_i^* R_s^* - k_{rec} R_i^T$$

$$\therefore R_s = \frac{V_s + k_{rec} R_i^T - k_e^* R_s^*}{k_e}$$

Substituting in (2),

$$k_f L \left(\frac{V_s + k_{rec} R_i^T - k_e^* R_s^*}{k_e} \right) - k_r R_s^* - k_e^* R_s^* + k_{rec} R_i^* = 0$$

Taking in terms of R_s^* and other terms,

we get

$$R_s^* = \left(\frac{K_{ss} L}{1 + K_{ss} L}\right)\left[\frac{V_s}{k_e^*} + \frac{k_{rec} R_i^*}{k_e^*}\right] + \frac{k_{rec} R_i^*}{(k_e^* + k_r)}\left[\frac{1}{1 + K_{ss} L}\right]$$

From (4), we get

$$R_i^* = \frac{k_e^* R_s^*}{k_{deg} + k_{rec}}$$

Total active receptor $\quad R_{tot}^* = R_s^* + R_i^*$

$$= R_s^*\left[1 + \frac{k_e^*}{k_{deg} + k_{rec}}\right]$$

$$= \left[\frac{1}{k_e^*} + \frac{1}{(k_{deg} + k_{rec})}\right]^* \left[\left(\frac{K_{ss} L}{1 + K_{ss} L}\right)\left[V_s + k_{rec} R_i^*\right] + \left(\frac{1}{1 + K_{ss} L}\right)\left(\frac{k_{rec} k_e^* R_i^*}{k_e^* + k_r}\right.\right.$$

$R_{i,total}^*$ is max when $L \gg 1$, i.e. when ligand conc. is very high.

$$R_{i,tot}^{*\,max} = \left[\frac{1}{k_e^*} + \frac{1}{k_{deg} + k_{rec}}\right]\left(V_s + k_{rec} R_i^*\right)$$

This ~~mean~~ means that as $k_{rec} \uparrow$, i.e. recycling increases, total active receptors increase.

2.

a)
$$\frac{dC_a}{dt} = -d_a C_a + \frac{\gamma_{0a} + \gamma_a C_a^2}{1 + C_a^2 + C_r^2}$$

$$\frac{dC_r}{dt} = -C_r + \frac{\gamma_{0r} + \gamma_r C_a^2}{1 + C_a^2}$$

~~A is an activator for both A & R~~

~~R is an inhibitor for both A & R~~

A is an activator for both A & R

R is an inhibitor for A only.

b) When A conc. is low, production of A gets activated and conc. of A increases, as does R. When R conc reaches certain thresholds, it starts inhibiting A, and A conc. starts decreasing. At very large R, conc. of A is very low and then activation of R by A stops. Then R conc. starts falling. This way, system gets back into original state. This process ~~continues~~ then starts again. This is the 'oscillator' element of a biological system.

Parts (b, c, e) appended at the end.

3.

$$\frac{du}{dt} = \frac{\alpha}{1+v^n} - u = f(u, v)$$

$$\frac{dv}{dt} = \frac{\alpha}{1+u^n} - v = g(u, v)$$

a) Here,

(i) $\longrightarrow$ v is repressor for u

u is repressor for v

ii) α is effective rate of synthesis.

iii) n is cooperativity of repression

iv) $(+1)$ is degradation rate const. for repressor.

b) From plot,

For $n=1$, 1 steady state sol^n exists.

$n=2$, 3 steady state sol^{n}s exist.

By increasing n (cooperativity of repression), we see that no. of steady state sol^{n}s ~~exist~~ increase.

c) For $n=1$, the only steady state is stable.

$n=2$, 2 sol^{n}s are stable.

the sol^n at $(2.5, 2.5)$ is a saddle point, i.e. unstable.

d) $$\bar{J} = \begin{bmatrix} \frac{\partial f}{\partial u} & \frac{\partial f}{\partial v} \\ \frac{\partial g}{\partial u} & \frac{\partial g}{\partial v} \end{bmatrix} = \begin{bmatrix} -1 & -\frac{\alpha}{(1+v^n)^2} \times n v^{n-1} \\ -\frac{\alpha n u^{n-1}}{(1+u^n)^2} & -1 \end{bmatrix}$$

For a centre where $u = v = u_s = v_s$

$$\bar{J} = \begin{bmatrix} -1 & -\frac{n\alpha u_s^{n-1}}{(1+u_s^n)^2} \\ -\frac{n\alpha u_s^{n-1}}{(1+u_s^n)^2} & -1 \end{bmatrix}$$

~~Let eigenvalues be λ~~

$$\cancel{(-1-\lambda)^2 - \left\{-\frac{n\alpha u_s^{n-1}}{(1+u_s^n)^2}\right\}^2}$$

$Tr(\bar{J}) = -2$

$Det(\bar{J}) = 1 - \left[\frac{n\alpha u_s^{n-1}}{(1+u_s^n)^2}\right]^2$

$\therefore$ Eigen values ~~of~~ λ are given by

$$\lambda = \frac{tr(\bar{J}) \pm \sqrt{tr(\bar{J})^2 - 4\det(\bar{J})}}{2}$$

$$= \frac{-2 \pm \sqrt{4\left(1 - 1 + \left(\frac{n\alpha U_s^{n-1}}{(1+U_s^n)^2}\right)^2\right)}}{2}$$

$$= \frac{-2 \pm 2\frac{n\alpha U_s^{n-1}}{(1+U_s^n)^2}}{2}$$

$$\lambda = -1 \pm \frac{n\alpha U_s^{n-1}}{(1+U_s^n)^2}$$

If $n=1$, $\lambda = -1 \pm \frac{\alpha}{(1+U_s)^2}$

$n=2$, $\lambda = -1 \pm \frac{2\alpha U_s}{(1+U_s^2)^2}$

e~~d~~) For $u = v = 2.5$, $\alpha = 10$

For $n=1$, $\lambda = -1 \pm \frac{10}{3.5^2}$

$= -1.816$, -0.183

For $n=2$, $\lambda = -1 \pm \dfrac{20 \times 2.5}{\cancel{8}(1+2.5^2)^2}$

$= -1 \pm \dfrac{50}{7.25^2}$

$= -1.951, \underline{\underline{-0.04}}$

f) 1)

$k_f L R_1 - k_r R_1^* = 0$

$R_1^* = \dfrac{k_f L R_1}{k_r} = K_{ss} L R_1$

$k_f^{ND} N_1 D_2 - k_r^{ND} N_1^* = 0$

$N_1^* = \cancel{k} K_S^{ND} N_1 D_2$

$k_D R_1^* = \gamma_D D_1$

$k_D R_2^* = \gamma_D D_2$

$\rightarrow D_2 = \dfrac{k_D R_2^*}{\gamma_D} = \dfrac{k_D K_{ss} L R_2}{\gamma_D}$

$\underline{N_1^* = K_{ss}^{ND} N_1 \dfrac{k_D K_{ss} L R_2}{\gamma_D}}$

$\dfrac{dR_1}{dt} = \dfrac{\beta^n}{k^n + N_1^{*n}} - \gamma_R R_1$

$\therefore \dfrac{dR_1}{dt} = \dfrac{\beta^n}{k^n + (\delta) R_2^n} - \gamma_R R_1 \rightarrow f(R_1, R_2)$

$\dfrac{dR_2}{dt} = \dfrac{\beta^n}{k^n + \delta R_1^n} - \gamma_R R_2 \rightarrow g(R_1, R_2)$

Similar to Collins toggle eq^{n}s.