1. Eq^{n}s. with recycling

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

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

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

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

@ S.S.

Adding (1), (2) and (3) we get

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

From (3) we get $k_{deg} R_i^T = k_e R_s + k_e^* R_s^* - k_{rec} R_i^T$

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

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

Substituting above value of R_s in (2) we get

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

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

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

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

Now, from (4) $(k_{rec}+k_{deg})R_i^* = k_e^* R_s^* \cancel{-k_{rec}}$

$$\Rightarrow \boxed{R_i^* = \frac{k_e^* R_s^*}{(k_{deg}+k_{rec})}}$$

Total active receptor

$$R^*_{total} = R_s^* + R_i^*$$

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

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

$$\boxed{R^*_{i_{tot}} = \left[\frac{1}{k_e^*}+\frac{1}{(k_{deg}+k_{rec})}\right]\left[\left(\frac{K_{ss}L}{K_{ss}L+1}\right)\left[V_s+k_{rec}R_i^T\right]+\frac{k_{rec}R_i^* k_e^*}{(k_e^*+k_r)}\left[\frac{1}{K_{ss}L+1}\right]\right]}$$

Maximum total active receptor concⁿ is obtained when Ligand concⁿ is very high i.e. $L>>1 \Rightarrow K_{ss}L>>1$

$$\therefore \boxed{R^{*\,max}_{i_{total}} = \left(\frac{1}{k_e^*}+\frac{1}{(k_{deg}+k_{rec})}\right)\left[V_s+k_{rec}R_i^T\right]}$$

∴ Recycling increases amount of total active receptors

∴ for No recycle case $R^{*\,max}_{i_{total}} = \left(\frac{1}{k_e^*}+\frac{1}{k_{deg}}\right)\left[V_s\right]$

2. (a)

$$\frac{dc_a}{dt} = -d_a c_a + \frac{r_{0a}+r_a c_a^2}{1+c_a^2+c_r^2}$$

$$\frac{dc_r}{dt} = -c_r + \frac{r_{0r}+r_r c_a^2}{1+c_a^2}$$

A is an activator of A and an activator of R.

R is an inhibitor of A and has no effect on R.

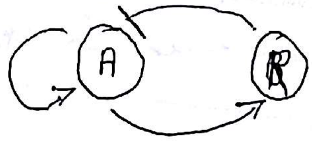
d_a is the first order degradation constant of A.

2.(b) The fixed point is unstable, as soon as the point is encountered the system changes rapidly.

2. (d) Initially when the concⁿ of A is low, production of A gets activated and increases with increasing concⁿ of A. As A increases, concentration of R increases too. When the concentration of R reaches a certain concentration, it starts inhibiting the production of A. As R keeps increasing, A keeps decreasing and finally at very high R there is a sharp decrease in amount of A which brings the system back to its original state as A can no longer activate R. Same cycle continues in a loop and hence the system ~~is~~ represents an oscillator.

The black line traces the path of a point which goes around in a loop.

The arrows represent the same observation.



3.(a)

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

$$\frac{dv}{dt} = \frac{\alpha}{1+u^n} - v = g(u,v) \quad -(2)$$

3. (a) (i) v acts as a repressor for u
u acts as a repressor for v

(ii) α gives the effective rate of synthesis

(iii) n = cooperativity of repression

(iv) +1 is the degradation rate const. for both repressors.

3 (b) 1 steady state solution exists for $n=1$

3 steady state solutions exists for $n=2$

Increasing degree of cooperativity increases number of steady state sol^{n}s!

3 (c) For $n=1$ 1 steady state sol^n exists. It is a stable sol^n since all arrows direct to that point. It is a <u>sink</u>

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

The point at around $(2.5, 2.5)$ is a <u>saddle point</u>

The points near the axis are ~~un~~<u>stable spirals</u>

Increase in n introduces unstability.

3 (d)

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

For a centre $u_s = v_s$

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

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

Eigen values at centre point are given by.

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

$$\lambda_\pm = \frac{-2 \pm \sqrt{4 - 4[\{n^2\alpha^2 u_s^{n-1}(1+u_s^n)^{-2}\}^2 + 1]}}{2}$$

$$\Rightarrow \lambda_\pm = \frac{-1 \pm \sqrt{(n\alpha u_s^{n-1}(1+u_s^n)^{-2})^2}}{}$$

$$\Rightarrow \lambda_\pm = -1 \pm n\alpha u_s^{n-1}(1+u_s^n)^{-2}$$

When $n=1$, $\lambda_\pm = -1 \pm \alpha u_s^0(1+u_s)^{-2} = -1 \pm \alpha(1+u_s)^{-2}$

$n=2$, $\lambda_\pm = -1 \pm 2\alpha u_s(1+u_s^2)^{-2}$

For $u_s \ll 1$, $n=1$ is unstable, $n=2$ is stable, $u_s \gg 1$; $n=1$ is stable, $n=2$ is unstable

3 (d) For $u = v = 2.5$

~~Kcrit~~ At $n=1$, Eigen values are $-1.8163, -0.1837$

Stable

$n=2$, Eigen values are $-5.0816, 3.0816$

Unstable.

At same conc^n, increasing cooperativity makes the system unstable.

~~(a)~~ 3(e) for $u = v = 2.5$

$n=1$, $K_{crit} = 12.25$

$n=2$, $K_{crit} = 2.45$.