Problem Sheet 1

1)
$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} E + P$$

The law of mass action gives

$$\frac{dS}{dt} = k_{-1} C - k_1 S E \quad ①$$

$$\frac{dE}{dt} = (k_{-1} + k_2) C - k_1 S E \quad ②$$

$$\frac{dC}{dt} = k_1 S E - (k_2 + k_{-1}) C \quad ③$$

$$\frac{dP}{dt} = k_2 C \quad ④$$

Conservation law: $E + C = \text{constant} = E_0$ (assuming $C = 0$ initially)

And P decouples.

This reduces the system to two ODEs:

$$\frac{dS}{dt} = k_{-1} C - k_1 S (E_0 - C)$$

$$\frac{dC}{dt} = k_1 S (E_0 - C) - (k_2 + k_{-1}) C$$

Which can be solved subject to suitable initial conditions

$S = S_0$, $C = 0$ at $t = 0$

1.2

Non-dimensionalize : $S = S_0 s$, $C = E_0 c$, $t = \frac{t'}{k_1 E_0}$

to obtain

$$\frac{ds}{dt'} = -s + c(s + k - \lambda)$$

$$\varepsilon \frac{dc}{dt'} = s - (s+k)c$$

with $s(0) = 1$, $c(0) = 0$.

$$k = \frac{k_{-1} + k_2}{k_1 S_0}$$

$$\lambda = \frac{k_2}{k_1 S_0}$$

$$\varepsilon = \frac{E_0}{S_0} \ll 1$$

because we only need a small amount of enzyme

$t' = \varepsilon T$, $\frac{ds}{dT} = 0$ ①

$\frac{dc}{dT} = s - (s+k)c$ ②

to leading order in ε.

① ⇒ $s = \text{constant} = 1$. (Initial value)

② ⇒ $\frac{dc}{dT} = 1 - (1+k)c$

⇒ $c = \frac{1 - e^{-(1+k)T}}{1+k}$

as $T \to \infty$, $c \to \frac{1}{1+k}$.

$t' = O(1)$, $\quad \frac{ds}{dt'} = -s + c(s+k-\lambda)$ ③

$\frac{dc}{dt'} = 0$ ④ to leading order in ε

④ $\Rightarrow \quad s - (s+k)c = 0 \quad \Rightarrow \quad c = \frac{s}{s+k}$

③ $\Rightarrow \quad \frac{ds}{dt'} = \frac{-\lambda s}{s+k}$

$$\Rightarrow \quad t' = -\int_1^s \frac{\tilde{s}+k}{\lambda \tilde{s}} \, d\tilde{s}$$

$$t' = -\frac{(s-1) + k\log(s)}{\lambda}$$

Note for small time (but longer than $O(\varepsilon)$) set $s = 1 + \delta f$, $t = \delta \tau$, $\varepsilon \ll \delta \ll 1$ to get $\frac{df}{d\tau} = -\frac{\lambda}{1+k}$ to leading order in δ and so for early enough time, s falls linearly

For $t \gg 1$, $s \ll 1$, so $t' \sim -\frac{k}{\lambda} \log(s)$

$$s \sim e^{-kt'/\lambda}$$

So concentration falls exponentially and never reaches zero.

2). $2A + B \underset{k_-}{\overset{k_+}{\rightleftharpoons}} C$

The law of mass action gives a forward rate $k_+ A^{\textcircled{2}} B$ and a backwards rate $k_- C$.

because two molecules of A react.

This gives $\frac{dC}{dt} = k_+ A^2 B - k_- C$ ①

Similarly, $\frac{dA}{dt} = -2(k_+ A^2 B - k_- C)$ ②

because two molecules of A react

$\frac{dB}{dt} = -(k_+ A^2 B - k_- C)$ ③

2x ① + ③ $\Rightarrow$ $2C + A =$ constant

~~2x~~ ① + ② $\Rightarrow$ ~~2~~$C + B =$ constant

$A(0) = A_0$, $B(0) = B_0$, $C(0) = 0$ $\Rightarrow$ $A + 2C = A_0$

$B + C = B_0$

Equilibrium concentration is reached when $dC/dt = 0$

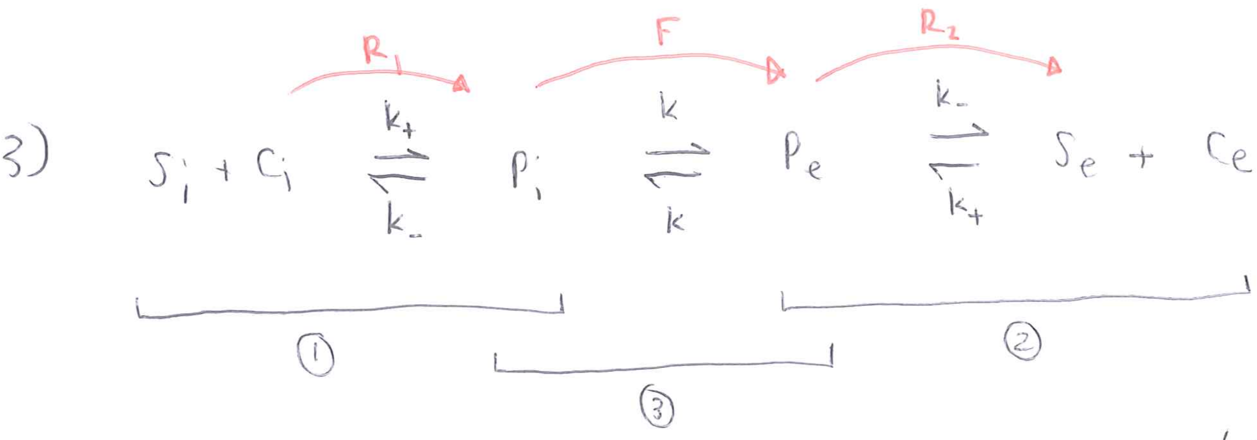
2.2

$\Rightarrow \quad k_+(A_0 - 2c^*)^2(B_0 - c^*) - k_- c^* = 0$ from ①

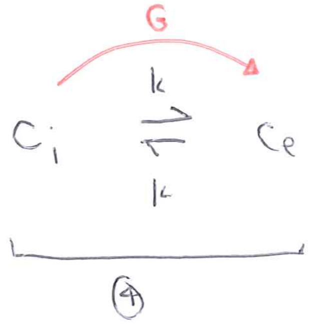
if $k_- = 0$ then equlibrium is $k_+(A_0 - 2c^*)^2(B_0 - c^*) = 0$.

$\frac{dc}{dt}$ will reach zero when $C = \frac{A_0}{2}$ or B_0, whichever

is the lowest value.



3) $$S_i + C_i \underset{k_-}{\overset{k_+}{\rightleftharpoons}} P_i \underset{k}{\overset{k}{\rightleftharpoons}} P_e \underset{k_+}{\overset{k_-}{\rightleftharpoons}} S_e + C_e$$



$$C_i \underset{k}{\overset{k}{\rightleftharpoons}} C_e$$

(All of this page is in the lectures I gave written exactly like this.)

C_i, C_e are states with binding sites exposed to the interior and exterior, respectively.

① : C_i can bind with a substrate molecule in the interior S_i to make a product P_i with rate k_+. The reverse reaction takes place at a rate k_-.

② : The same reaction as ① but in the exterior (and same reaction rates)

③ : P_i can turn into P_e and vice versa. This is the carrier doing its 'rotation'.

④ : this is the carrier site 'rotating' without any substrate on. We assume this happens at the same rate as a rotation with substrate on, ③ The reaction rates are

$$R_1 = k_+ S_i C_i - k_- P_i$$

$$R_2 = k_- P_e - k_+ S_e C_e$$

$$F = k P_i - k P_e$$

$$G = k C_i - k C_e$$

(All of this page is in the lectures I gave written exactly like this.)

and

$$\frac{dS_i}{dt} = -R_1 - J \qquad (*1)$$

$$\frac{dC_i}{dt} = -R_1 - G \qquad (*2)$$

$$\frac{dP_i}{dt} = R_1 - F \qquad (*3)$$

$$\frac{dP_e}{dt} = F - R_2 \qquad (*4)$$

$$\frac{dS_e}{dt} = R_2 + J \qquad (*5)$$

$$\frac{dC_e}{dt} = R_2 + G \qquad (*6)$$

Where J is the flux of

In equilibrium, set $\frac{d}{dt}$'s $= 0$. This gives

$$J = -R_1 = G = -R_2 = -F$$

$= C_i(t=0)$ if $P_i(0) = P_e(0) = C_e(0) = 0$.

$(*2) + (*3) + (*4) + (*6) \Rightarrow$ $P_i + P_e + C_i + C_e =$ constant, A
(conservation of carrier)

$(*3) + (*4) + (*1) + (*6) \nRightarrow$ $P_i + P_e + S_i + S_e =$ constant, B.
(conservation of substrate)

$$J = -R_1 = G = -R_2 = -F$$

$$\Rightarrow \quad J \overset{①}{=} k_- P_i - k_+ S_i C_i \qquad\qquad J \overset{③}{=} k_+ S_e C_e - k_- P_e$$

$$J \overset{②}{=} k C_i - k C_e \qquad\qquad J \overset{④}{=} k P_e - k P_i$$

$$④ \Rightarrow \quad P_e = P_i + \frac{J}{k} \qquad ⑤$$

$$② \Rightarrow \quad C_e = C_i - \frac{J}{k} \qquad ⑥$$

$$P_i + P_e + C_i + C_e = A$$

$$\Rightarrow \quad 2(P_i + C_i) = A$$ using ⑤ and ⑥.

$$\Rightarrow \quad P_i = \frac{A}{2} - C_i$$

Substituting ⑦ into ① gives $$C_i = \frac{k_- \frac{A}{2} - J}{k_- + k_+ S_i} \qquad ⑧$$

Substitute ⑥ and ⑦ into ③ and rearranging for J gives

$$J\left[1 + \frac{k_+ S_e}{k} + \frac{k_-}{k}\right] = -k_- \frac{A}{2} + (k_- + k_+ S_e)\, C_i$$

Substituting for C_i using ⑧ gives

$$J\left[\frac{k_+(K_m + S_e)}{k}\right] = -\frac{k_- A}{2} + \left(\frac{K_m - K_d + S_e}{K_m - K_d + S_i}\right)\left(\frac{k_- A}{2} - J\right)$$

Rearranging for J gives

$$J = \boxed{\frac{k k_- A}{2 k_+}} \; \frac{S_e - S_i}{\left[(K_m + S_i)(K_m + S_e) - K_d^2\right]}$$

define as k^*

4).

$$\begin{tikzcd}
S_0 \arrow[r, shift left, "N\alpha"] \arrow[r, bend left=60, "R_1"] & S_1 \arrow[l, shift left, "\beta"] \arrow[r, shift left, "(N-1)\alpha"] \arrow[r, bend left=60, "R_2"] & \cdots \arrow[l, shift left, "2\beta"] \arrow[r, shift left, "\alpha"] \arrow[r, bend left=60, "R_N"] & S_N \arrow[l, shift left, "N\beta"]
\end{tikzcd}$$

The reaction rates are

$$R_1 = N\alpha S_0 - \beta S_1$$

$$R_2 = (N-1)\alpha S_1 - 2\beta S_2$$

$$\vdots$$

$$R_i = (N-i+1)\alpha S_{i-1} - i\beta S_i$$

$$R_N = \alpha S_{N-1} - N\beta S_N$$

and

$$\frac{dS}{dt} = -R_1$$

$$\frac{dS_i}{dt} = R_i - R_{i+1} \qquad 1 \leq i \leq N-1$$

$$\frac{dS_N}{dt} = R_N$$

Conservation law comes from adding all ODEs to give

$S_0 + S_1 + \dots + S_N =$ constant $= 1$. (since these represent the fractions of gates open so sum to 1)

Suppose that $S_j = {}^N C_j \, n^j (1-n)^{N-j}$

Then

$$R_j = (N-j+1)\alpha \frac{N!}{(N-j+1)!\,(j-1)!} n^{j-1}(1-n)^{N-j+1)}$$

$$- \frac{j\beta N!}{(N-j)!\,j!} n^j (1-n)^{N-j}$$

$$= \frac{N!\,\alpha\, n^{j-1}(1-n)^{N-j+1}}{(N-j)!\,(j-1)!} - \frac{\beta N!}{(N-j)!(j-1)!} n^j (1-n)^{N-j}$$

$$= \frac{N!\, n^{j-1}(1-n)^{N-j}}{(N-j)!(j-1)!}\left(\alpha(1-n) - \beta n\right) \quad (*)$$

Now

$$\frac{dS_j}{dt} = \frac{N!}{(N-j)!\,j!}\left[j n^{j-1}(1-n)^{N-j} - (N-j) n^j (1-n)^{N-j-1}\right]\frac{dn}{dt}$$

$$= \frac{N!}{(N-j)!\,(j-1)!} n^{j-1}(1-n)^{N-j} \frac{dn}{dt} - \frac{N!}{(N-j-1)!\,j!} n^j (1-n)^{N-j-1} \frac{dn}{dt}$$

$$= \frac{(R_j - R_{j+1}) \frac{dn}{dt}}{\alpha(1-n) - \beta n}$$ substituting (*)

So if $\frac{dn}{dt} = \alpha(1-n) - \beta n$ then $\frac{dS_j}{dt} = R_j - R_{j+1}$

as required

4.3

For $N = 2$,

$$\frac{dS_0}{dt} = -R_1 \qquad R_1 = 2\alpha S_0 - \beta S_1$$

$$\frac{dS_2}{dt} = R_2 \qquad R_2 = \alpha S_1 - 2\beta S_2$$

$$S_0 + S_1 + S_2 = 1$$

So

$$\frac{dS_0}{dt} = -2\alpha S_0 + \beta(1 - S_1 - S_2).$$
$$= \beta - (2\alpha + \beta) S_0 - \beta S_2$$

$$\frac{dS_2}{dt} = \alpha(1 - S_1 - S_2) - 2\beta S_2,$$
$$= \alpha - \alpha S_0 - (\alpha + 2\beta) S_2$$

Put $S_0 = (1-n)^2 + y_0$,

$S_2 = n^2 + y_2$

Linearizing gives

$$\frac{d}{dt}\begin{pmatrix} y_0 \\ y_2 \end{pmatrix} = - \underbrace{\begin{pmatrix} 2\alpha + \beta & \beta \\ \alpha & \alpha + 2\beta \end{pmatrix}}_{\underline{M}} \begin{pmatrix} y_0 \\ y_2 \end{pmatrix}$$

Eigenvalues : $((2\alpha + \beta) - \lambda)((\alpha + 2\beta) - \lambda) - \alpha\beta = 0$

$$\lambda^2 + 3(\alpha + \beta) + 2(\alpha + \beta)^2 = 0$$

$$\lambda = -2(\alpha + \beta), \quad -(\alpha + \beta)$$

$\therefore$ stable with solutions $y_0, y_2 \propto e^{\lambda t}$.