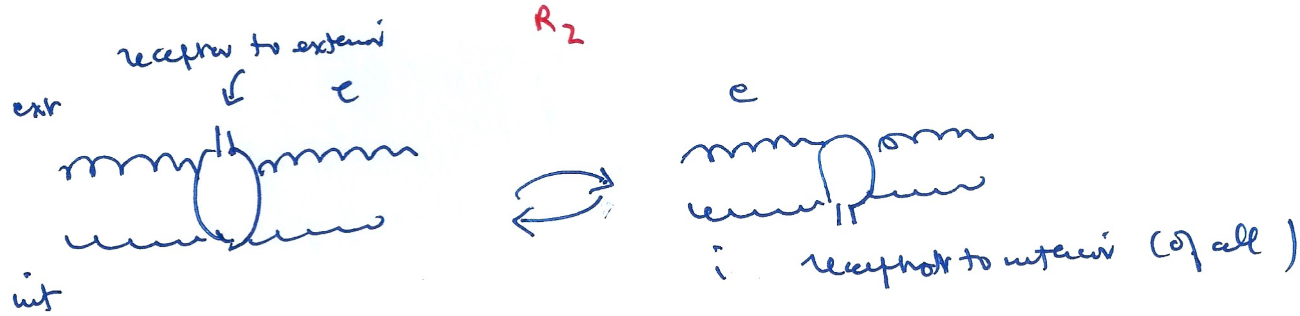
C5.12 (old C8.1b) Math Physiol 2014 q2

2)

(a)

$$S_i + C_i \underset{k_-}{\overset{\overset{R_1}{k_+}}{\rightleftharpoons}} P_i \underset{k_2}{\overset{\overset{R_3}{k_1}}{\rightleftharpoons}} P_e \underset{k_+}{\overset{\overset{R_4}{k_-}}{\rightleftharpoons}} S_e + C_e$$

$$C_i \underset{\underset{R_2}{k_4}}{\overset{k_3}{\rightleftharpoons}} C_e$$



S_i interior ~~bed~~ binds to C_i interior receptor → complex switches to exterior receptor complex releases exterior substrate

Law of mass action $A+B \xrightarrow{r} C$ rate of formation of C is $\propto AB$

(b) As in the question, overall rates as indicated in diagram above & then

$$\dot{s}_i = R_1 \qquad (1)$$

$$\dot{c}_i = R_1 + R_2 \qquad (2)$$

$$\dot{p}_i = -R_1 + R_3 \qquad (3)$$

$$\dot{p}_e = -R_3 + R_4 \qquad (4)$$

$$\dot{s}_e = -R_4 \qquad (5)$$

$$\dot{c}_e = -R_4 - R_2 \qquad (6)$$

c_2

$c_i + c_e + p_i + p_e$:

Add (2) (6) (3) (4)

$$\Rightarrow \dot{(c_i + c_e + p_i + p_e)} = R_4 + R_2 - R_4 - R_2 - R_1 + R_3 - R_3 + R_4 = 0$$

So $c_i + c_e + p_i + p_e$ is constant

$$\dot{(s_i + s_e + p_i + p_e)} = [(1) + (5) + (3) + (4)]$$
$$R_1 - R_4 - R_1 + R_3 - R_3 + R_4 = 0$$

So $s_i + s_e + p_i + p_e$ = constant

p_i, c_i, p_e, c_e quasi-steady

$$\Rightarrow R_1 + R_2 = -R_1 + R_3 = -R_3 + R_4 = -R_4 - R_2 = 0$$

so $\underline{R_1 = -R_2 = R_3 = R_4}$

(c) $k_\pm \to \varepsilon k_\pm$:

$$R_1 = \varepsilon[-k_+ s_i c_i + k_- p_i]$$
$$R_4 = \varepsilon[-k_- p_e + k_+ s_e c_e]$$
$$R_2 = k_4 c_e - k_3 c_i$$
$$R_3 = -k_1 p_i + k_2 p_e$$

we have $\dot{s}_e = -R_4 = -\varepsilon[k_+ s_e c_e - k_- p_e]$

So approximately

$$c_i = \frac{k_4}{k_3} c_e \quad , \quad p_i = \frac{k_2}{k_1} p_e \qquad (*)$$

Also $c_i + c_e + p_i + p_e =$ constant

$s_i + s_e + p_i + p_e =$ constant

And $\dot{s}_e = \varepsilon [k_- p_e - k_+ c_e s_e]$

The sneaky bit here is to spot that with $R_1 \approx R_4$

$$\dot{s}_i + \dot{s}_e = R_1 - R_4 \approx 0$$

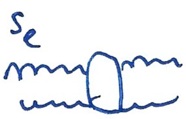
So $s_i + s_e \approx$ constant

$\Rightarrow p_i + p_e \approx$ constant $\Rightarrow p_i, p_e$ constant

$\Rightarrow c_i + c_e \approx$ constant $\Rightarrow c_i, c_e$ constant

(due to (*))

So then $\dot{s}_e = \varepsilon [k_- p_e - k_+ c_e s_e]$ is a single equation for s_e.



(ii) The pump acts against its gradient

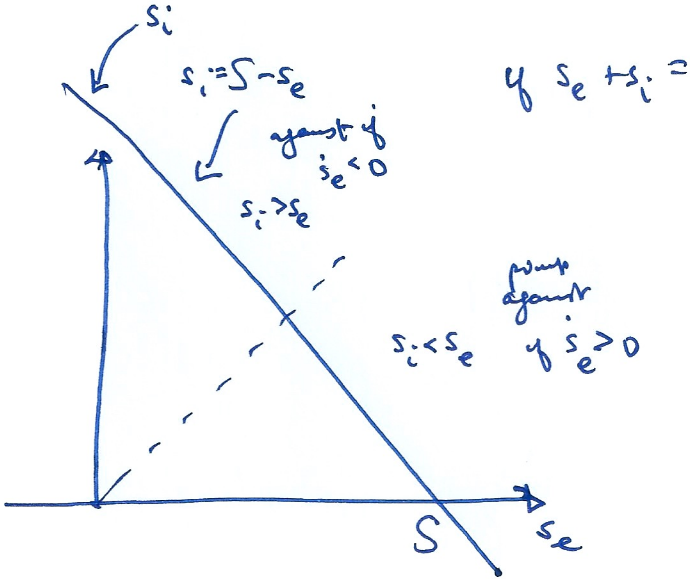
if $\dot{s}_e > 0$ when $s_e > s_i$

Well this is obviously possible depend on values of

$s_i + s_e = S$, $p_i + p_e = P$, $c_i + c_e = C$

Since $s_e \to \frac{k_- p_e}{k_+ c_e} = s_\infty$

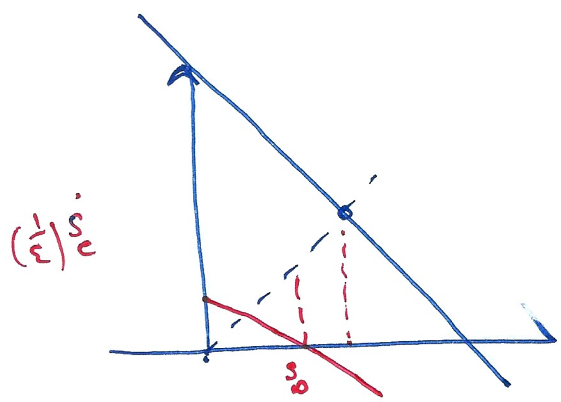
if $s_e + s_i = S$



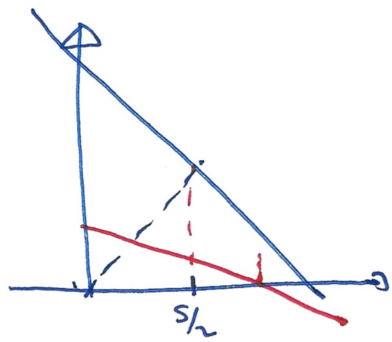
pump is against gradient if $\dot{s}_e > 0$ when $s_e > s_i$
or $\dot{s}_e < 0$ when $s_e < s_i$

3 ~~2~~ cases

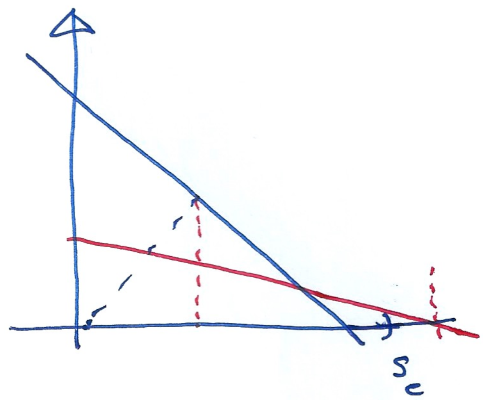
$s_\infty = \dfrac{k_- p_e}{k_+ c_e} < S/2$



$S/2 < s_\infty < S$



$s_\infty > S$



$s_\infty < \frac{1}{2}S$ pumps against for $s_\infty < s_e < \frac{1}{2}S$

$\frac{1}{2}S < s_\infty < S$ " $\frac{1}{2}S < s_e < s_\infty$

$s_\infty > S$ " $\frac{1}{2}S < s_e < s_\infty$

So in all cases pump is against the gradient if s_e is between $\frac{1}{2}S$ and s_∞.

iii Now $k_3 \to \varepsilon^2 k_3$

so $R_1 = \varepsilon[-k_+ s_i c_i + k_- p_i]$

$R_4 = \varepsilon[-k_- p_e + k_+ s_e c_e]$

$R_2 = k_4 c_e - \varepsilon^2 k_3 c_i$

$R_3 = -k_1 p_i + k_2 p_e$

$R_1 \propto -R_2 = R_3 = R_4$

$c_i + c_e + p_i + p_e \simeq$ constant

$s_i + s_e + p_i + p_e \simeq$ constant

As before $\dot{s}_i + \dot{s}_e \simeq R_1 - R_4 \simeq 0$

$s_i + s_e = S$ constant

$c_i + c_e = C$ constant

$p_i + p_e = P$ constant

$R_1, R_4 = O(\varepsilon) \Rightarrow R_2, R_4 = O(\varepsilon)$

$\Rightarrow p_i = \frac{k_2}{k_1} p_e \Rightarrow p_i, p_e$ constant

$R_2 = O(\varepsilon) = c_e = O(\varepsilon)$

$\Rightarrow c_i \simeq C$ constant

$\dot{s}_e = -R_4 = \varepsilon[k_- p_e - k_+ s_e c_e]$

$\simeq \varepsilon[k_- p_e + O(\varepsilon)]$

Depends on p_e: if $P = O(\varepsilon)$ then it will be eventually ok

otherwise $s_e \uparrow$ until $s_e = O(\frac{1}{\varepsilon})$, $s_e = \frac{1}{\varepsilon} S_e \Rightarrow \dot{S}_e \simeq \varepsilon[k_- p_e - k_+ S_e(\frac{c_e}{\varepsilon})]$

but then this requires $S_e = O(\frac{1}{\varepsilon})$ $c_e = \varepsilon C_e$

& so we would have $(R_1 \to \varepsilon R_1$ but $R_4 = -\varepsilon[k_- P_e + k_+ S_e C_e]$

$\dot{s}_i = \varepsilon R_1$

etc..

This is a bit open-ended since we are not told much about S, P etc.

Simple answer is it doesn't work straightforwardly.