Exercise 2: Diffusion and Permeability Measurements Solutions

Transport in Biological Systems

Fall 2015

Analytical Solution of steady state 2-membrane problem

The ultimate goal of this section is to develop an expression for effective permeability of the endothelial cells on a membrane. We have 2 adjacent membranes that we assume have reached steady state and baths on either side.

Let's start by defining the things that should be labeled in your diagram (perhaps somewhat different specifics, but generally similar):

1. Let the top bath be a and the bottom b, with concentrations C_a and C_b.
2. The coordinate system starts at the top at $x = 0$.
3. Membrane 1, a.k.a. the endothelial cells, has diffusivity, concentration, partition coefficient, and thickness D_1, $C_1(x)$, Φ_2 and L_1, respectively.
4. Membrane 2 has diffusivity, concentration, partition coefficient, and thickness D_2, $C_2(x)$, Φ_2, and L_2, respectively.
5. The total thickness of the membrane is $L = L_1 + L_2$.

Now, the equations and boundary conditions. Because both membranes are at steady state, the concentration in both membranes is governed by $\frac{d^2C_i}{dt^2} = 0$, which gives us $C_1(x) = A_1x + B_1$ and $C_2(x) = A_2x + B_2$ for membranes 1 and 2. Our boundary conditions are:

1. at $x = 0$, $C_1(0) = \Phi_1 C_a$
2. at $x = L$, $C_2(L) = \Phi_2 L C_b$
3. at $x = L_1$, $\frac{C_1}{\Phi_1} = \frac{C_2}{\Phi_2}$
4. and also $N_1 = N_2$

Starting with the first two conditions, we see that $B_1 = \Phi_1 C_a$ and that $B_2 = \Phi_2 C_b - A_2 L$.

Then, turning to the flux condition, and recalling that $N_i = -D_i \frac{dC_i}{dx}$, we see that $N_1 = -D_1 A_1$ and $N_2 = -D_2 A_2$, so that $D_1 A_1 = D_2 A_2$, and thus $A_1 = \frac{D_2 A_2}{D_1}$.

Now we have everything in terms of our last unknown, A_2. Substituting in everything into the third boundary condition and doing some simplification gets us to:

$$\begin{aligned} C_a + \frac{D_2 A_2 L_1}{D_1 \Phi_1} &= C_b + \frac{A_2 L_2}{\Phi_2} \\ C_b - C_a &= \frac{D_2 A_2 L_1}{D_1 \Phi_1} + \frac{A_2 L_2}{\Phi_2} \end{aligned}$$

$$\begin{aligned}
C_b - C_a &= A_2\left(\frac{D_2\Phi_2 L_1 + D_1\Phi_1 L_2}{\Phi_1\Phi_2 D_1}\right) \\
A_2 &= \frac{\Phi_1\Phi_2 D_1}{D_2\Phi_2 L_1 + D_1\Phi_1 L_2}(C_b - C_a) \\
A_1 &= \frac{\Phi_1\Phi_2 D_2}{D_2\Phi_2 L_1 + D_1\Phi_1 L_2}(C_b - C_a)
\end{aligned}$$

You know it's right because it's pretty....

Recall that we discussed permeability for a single membrane $N_i = -\frac{D_i\Phi_i}{L}(C_L - C_0)$ and we defined $P = \frac{D_i\Phi_i}{L}$. In this case,

$$N_1 = N_2 = -\frac{\Phi_1\Phi_2 D_1 D_2}{D_2\Phi_2 L_1 + D_1\Phi_1 L_2}(C_b - C_a).$$

So then, by analogy:

$$P_{eff} = \frac{\Phi_1\Phi_2 D_1 D_2}{D_2\Phi_2 L_1 + D_1\Phi_1 L_2}.$$

We can then see that for diffusion in membranes, the permeabilities of n membranes add in series:

$$\begin{aligned}
\frac{1}{P_{eff}} &= \sum_{i=1}^{n} \frac{1}{P_i} \\
\frac{1}{P_{eff}} &= \sum_{i=1}^{n} \frac{L_i}{\Phi_i D_i}.
\end{aligned}$$

To further confirm this makes sense, if we let this be one membrane of thickness L, then $D_1 = D_2$ and $\Phi_1 = \Phi_2$ and P reduces back to $\frac{D_i\Phi_i}{L}$. As my grandfather used to say, "stick that in your pipe and smoke it."

Analytical Solution of time-dependent changes in bath concentration

The goal of this section is to understand how the baths are changing in time. Sub-goals are see the types of assumptions that are made and what types of problems allow analytical solutions. This solution generally follows a similar approach to the example in Section 6.8.4 in the book except it allows for different volumes.

For baths a and b, connected by a membrane, which we assume to be at steady state and very very thin, what are the concentrations $C_a(t)$ and $C_b(t)$?

- Let initial conditions in baths a and b be $C_a(0) = C_0$ and $C_b(0) = 0$.
- Let the bath volumes be V_a and V_b.

First, consider how the baths are changing in time relative to each other in terms of moles leaving a per time and moles entering b per time:

$$-V_a\frac{dC_a}{dt} = V_b\frac{dC_b}{dt}$$

Integrate both sides with respect to time ($\int k_1 dU(t)dt = k_1 U + k_2$, where k_1 and k_2 are constants and U is our function of time). Evaluate over time from 0 to t. This gives:

$$\begin{aligned} V_a(C_a(t) - C_0) &= -V_b(C_b(t) - 0) \\ C_a(t) &= C_0 - \frac{V_b}{V_a} C_b \end{aligned}$$

So this gives us the relationship between C_a and C_b.

Next, we know that the transport between chambers is related to the properties of the membrane and, in fact, the amount of stuff entering chamber b is equal to the flux across the membrane.

$$\begin{aligned} V_b \frac{dC_b}{dt} &= -AP(C_b - C_a) \\ V_b \frac{dC_b}{dt} &= -AP((\frac{V_b}{V_a} + 1)C_b - C_0) \end{aligned}$$

Where A is the membrane area, $P = D\Phi/L$ is permeability (or the more complex P_{eff} for 2 membranes as we saw above).

Rearrange to get

$$\frac{dC_b}{(\frac{V_b}{V_a} + 1)C_b - C_0} = -\frac{AP}{V_b} dt$$

Integrate from time 0 to t and from $C_b(0) = 0$ to $C_b(t)$, noting that the integral of $\frac{1}{ax+b}$ is $\frac{1}{a} ln|ax + b|$. Multiply through by $(\frac{V_b}{V_a} + 1)$, and rearrange the RHS to get:

$$\begin{aligned} \ln(\frac{C_0 - (\frac{V_b}{V_a} + 1)C_b}{C_0}) &= -PA(\frac{V_b + V_a}{V_a V_b})t \\ \frac{C_0 - (\frac{V_b}{V_a} + 1)C_b}{C_0} &= exp(-PA(\frac{V_b + V_a}{V_a V_b})t) \\ (\frac{V_b}{V_a} + 1)C_b &= C_0(1 - exp(\frac{V_b + V_a}{V_a V_b})t)) \\ C_b(t) &= C_0(\frac{V_a}{V_a + V_b})(1 - exp(-PA(\frac{V_b + V_a}{V_a V_b})t)) \end{aligned}$$

Note that if $V_a = V_b = V$, the first line should look a lot like the solution from section 6.8.4 (specifically, the top equation in this array should look like equation 6.8.107) in the book except that it's for the second bath so the sign is switched!

With this sort of solution, you can plug in real values and get a sense for the rate of change of the baths.

If you plug in the values, you can see that it takes about 1 second for the concentration of the top bath to change by 1%. From the simulation, the membranes appear to be equilibrating within seconds and it takes minutes for the baths to change significantly (see appended figures). Alternately, we can estimate that the relevant timescale is $t \sim \frac{x^2}{D} = 667ms$. So, basically, the membrane should be at steady state within a second and the quasi-steady state assumption is pretty good!

Concentration profile at different times around the cells and membrane