Exercise 4: Solutions

Transport in Biological Systems

Fall 2015

1. We have two-layer blood vessel with an inner radius, R_i, an outer radius, R_o, and an interface radius of R_1; diffusion coefficients D_1 and D_2; and solute of concentrations C_i and C_o. We are asked what the effective diffusion coefficent is.

   (a) As a blood vessel is most like a hollow cylinder, and assuming steady state and no reaction given the problem statement, we start with Fick's law,

   $$\frac{dC}{dt} = D\frac{1}{r}\frac{d}{dr}\Big(r\frac{dC}{dr}\Big) = 0,$$

   and then integrate twice, using A and B as integration constants, to get

   $$\frac{dC}{dr} = \frac{A}{r}$$
   $$C = B + Aln(r).$$

   This solution generally holds for both the inner portion (let's use C_1) and the outer portion (let's use C_2).

   (b) Assuming $\Phi_1 = \Phi_2$, our boundary conditions are :

   $$C_1(R_i) = C_i$$
   $$C_2(R_o) = C_o$$
   $$C_1(R_1) = C_2(R_1)$$
   $$-D_1\frac{dC_1}{dr}\Big|_{R_1} = -D_2\frac{dC_2}{dr}\Big|_{R_1}$$

   (c) Then we can use these (and substitute) to solve for B_1 and B_2:

   $$B_1 = C_i - A_1 ln(R_i)$$
   $$B_2 = C_o - A_2 ln(R_o)$$

   And we can plug that into the third boundary condition (continuous concentration) to get a first expression for A_1:

   $$C_i + A_1 ln(R_1/R_i) = C_o + A_2 ln(R_1/R_o)$$
   $$A_1 = \frac{C_o - C_i + A_2 ln(R_1/R_o)}{ln(R_1/R_i)}$$

Plugging that back into the continuous flux boundary condition, we can say

$$\Big(\frac{C_o - C_i + A_2 ln(R_1/R_o)}{ln(R_1/R_i)}\Big)\frac{D_1}{R_1} = \frac{A_2 D_2}{R_1}$$

And after a fair bit of rearrangment, we get:

$$A_2 = \frac{D_1(C_o - C_i)}{D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o)}$$
$$A_1 = \frac{D_2(C_o - C_i)}{D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o)}$$

Which finally gives us:

$$C_1(r) = C_i + \Big(\frac{D_2(C_o - C_i)}{D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o)}\Big) ln(r/R_i)$$
$$C_2(r) = C_o + \Big(\frac{D_1(C_o - C_i)}{D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o)}\Big) ln(r/R_o)$$

(d) But then the big question is what do we do with that to get an effective diffusivity? Recalling that for a single cylinder (rearranging equation 6.7.37 from example 6.7) we can say that,

$$N_{single\_cylinder} = -\frac{D}{ln(R_{out}/R_{in})}\Big(\frac{C_{out} - C_{in}}{r}\Big)$$

where the first term is going to be our template for an effective diffusivity:

$$\Big[\frac{D}{ln(R_{out}/R_{in})}\Big]_{effective}$$

We can look at our equation for flux in the double cylinder

$$N_i = N_o = -\frac{D_2 A_2}{r} = -\frac{D_1 D_2 (C_o - C_i)}{(D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o))r}$$

and rearrange it to get something that looks like the single cylinder's second term with some other stuff that will be our effective diffusivity term:

$$N_i = N_o = -\frac{D_1 D_2}{D_2 ln(R_1/R_i) - D_1 ln(R_1/R_o)}\Big(\frac{C_o - C_i}{r}\Big)$$

So we want something that looks like an effective diffusivity... flip over that section and we can see that it is like adding resistors in parallel:

$$\Big[\frac{ln(R_{out}/R_{in})}{D}\Big]_{effective} = \frac{ln(R_1/R_i)}{D_1} + \frac{ln(R_o/R_1)}{D_2}$$

where we can (probably) generalize this for n layers:

$$\left[\frac{ln(R_{out}/R_{in})}{D}\right]_{effective} = \sum_{i=1}^{n} \frac{(ln(R_{out,i}/R_{in,i}))}{D_i}$$

The point being that if we know something about the overall geometry and the concentration difference, we can measure the effective diffusivity and then back out individual diffusivities. Note that if $D_1 = D_2$, we get back the original solution for 1 layer from Example 6.7. This should look familiar from our previous 2 membrane problem and it may seem like a lot of algebreic manipulation to get here, but this sort of solution is very powerful when you start adding new layers. Now that we have this general form, we should know what to do if we want to add another layer or so...

2. Considering drug delivery from a sphere (e.g. all those microsphere drugs on the market) and testing the idea that we can neglect polymer erosion...

   (a) From example 6.8, we learned that the release rate of drug in a non-eroding sphere was flux*surface area, $N_i\Big|_R(4\pi R^2)$ (equation 6.7.49). If we now consider polymer, we can assume that will be similar, $N_p\Big|_R(4\pi R^2)$, where p denotes polymer and i denotes drug. Note that these expressions are the change in material per time. We'll come back to the flux.

   Keeping in mind that R is now R(t), and taking the volume of a sphere, $V = \frac{4}{3}\pi R^3$, we can first write an expression for the changing volume of the polymer sphere in time,

$$\frac{dV}{dt} = \frac{4}{3}\pi\frac{d(R^3)}{dt}.$$

   If we multiply this by the concentration of solid polymer, we get change in material per time. Thus we can write the relationship between the change in geometry to the release rate,

$$-C_p\frac{4}{3}\pi\frac{d(R^3)}{dt} = N_p\Big|_R(4\pi R^2),$$
$$-C_p\frac{d(R^3)}{dt} = 3R^2N_p\Big|_R.$$

   and we have completed our first task! (Note that the negative sign is introduced as we equate loss of material with flux away in the positive r direction.)

   (b) Coming back to the flux, we have assumed steady state diffusion of polymer into the solvent (note that we are now in the solvent around the polymer), we can say that, as in Example 6.8:

$$0 = \frac{dC_p}{dt} = \nabla^2 C_p$$
$$0 = \frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dC_{p,s}}{dr}\right)$$
$$C_{p,s} = B - \frac{A}{r}$$

   Where concentration of the polymer in the solvent is $C_{p,s}$ and B and A are integration constants.

   Then we need to apply the boundary conditions. We are given the familiar $C_{p,s}(R) = \Phi_p C_p$, where Φ_p is the partition coefficient of polymer going between the solid state and into the

solvent. We have discussed that a common boundary condition is $C_{p,s}(\infty) = 0$ and it appeared in Example 6.8. Applying these, we can say that $B = 0$ and $A = -\Phi_p C_p R$. Thus,

$$C_{p,s}(r) = \frac{\Phi_p C_p R}{r}$$
$$N_{p,s}(r) = -D_{p,s}\frac{dC_{p,s}}{dr} = \frac{D_{p,s}\Phi_p C_p R}{r^2}$$
$$N_{p,s}(R) = \frac{D_{p,s}\Phi_p C_p}{R}$$

$D_{p,s}$ is the diffusion coefficient for polymer in solvent. Recall that R is a function of t and note that we are assuming steady state of the polymer concentration profile in the solvent is reached faster than R changes.

(c) So now we can put everything together from the previous sections to get the change in R with time (also known as solving Equation 6.12.4):

$$N_{p,s}\Big|_R = N_p\Big|_R$$
$$\frac{D_{p,s}\Phi_p C_p}{R} = -\frac{C_p}{3R^2}\frac{d(R^3)}{dt}$$
$$\frac{d(R^3)}{dt} = -3RD_{p,s}\Phi_p$$

It may be useful to let $u = R^3$ and then we can say that $\int u^{-1/3}du = \frac{3}{2}u^{2/3}$ in order to conclude that $u^{2/3} = R^2$. So finally we can do some rearrangement and substitution and integrate from the initial condition, $R(0) = R_0$, to the current condition, $R(t)$, we can solve for R(t):

$$\int_{R_0}^{R}\frac{d(R^3)}{R}d(R^3) = -3D_{p,s}\Phi_p\int_0^t dt$$
$$\frac{3}{2}(R^2 - R_0^2) = -3D_{p,s}\Phi_p t$$
$$R(t) = \sqrt{R_0^2 - 2D_{p,s}\Phi_p t}$$

We are given a bunch of parameters

Property	Polymer	drug
D (cm^2/s)	$1x10^{-10}$	$2x10^{-6}$
Solution solubility (mol/cm^3)	$C_{p,s}(R) = 1x10^{-10}$	$C_0 = 1x10{-}6$
Concentration (mol/cm^3)	$C_p = 1x10^{-8}$	$C_d = 1x10^{-7}$
Partition Coefficient	$\Phi_p = 0.01$	$\Phi_d = 1.00$

So, for a polymer sphere with a 0.25 cm initial radius, we can calculate that it would take $(R_0^2/2D_{p,s}\Phi_p) = 3.13x10^{10}$ s or 990 years for the polymer to completely disolve! Or it would take about 20 years for a 1% change in diameter. We can use this information to finally think about whether it was a good assumption to neglect degradation (quasi-steady-state assumption!).

What are the relevant timescales for drug then? From example 6.8, the drug release rate was $4\pi D_i C_o R$, where D_i is the diffusivity of the drug and C_o was the surface concentration, which we

are told is 10^{-6} mol/cm^3. We can calculate the total number of moles from $(4/3)\pi R_0^3 C_{initial} = 6.54x10^{-9}$, where $R(0) = R_0 = 0.25$ cm.

The release rate multiplied by time is the amount released, so we can say that:

$$fraction\_drug\_released = \frac{3D_i C_o R(t)t}{C_{initial} R_0}$$

Assuming for a minute that the radius of the polymer doesn't change (using $R(t) = R_0$), we can calculate that all of the drug will be released in $1.67x10^4$ s. Similarly, it would take 27.8 minutes for 10% of the drug to be released! Given that all of the drug will be released LONG before a 1% change in radius, I think the assumption was good! (Though that was a long process to get there!)

3. Considering a gap in the endothelium with a hemi-spherical profile with radius, b. We neglect the thickness of the endothelium and consider the semi-infinite hemisphere of underlying tissue. We are considering the transport of cholesterol in the tissue where it enters only at the damaged point (not through the endothelium). At $r = b$, $P = P_0$ and $C = C_p$. As $r \to \infty$, $P = 0$ and $C = 0$. We are asked what distributions of C, P, and v are at steady state.

   (a) We start with a solute mass balance, a momentum balance in the form of Darcy's law, and a fluid mass balance:

$$v\nabla C = D\nabla^2 C \to v\frac{dC}{dr} = \frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{dC}{dr}\right)$$
$$v = -K\nabla P \to v = -K\frac{dP}{dr}$$
$$\nabla \cdot v = 0 \to \nabla^2 P = 0 \to \frac{1}{r^2}\frac{d}{dr}\left(r^2\frac{dP}{dr}\right) = 0$$

   Where D is the diffusion coefficient and K is the hydraulic permeability.

   (b) First we integrate and apply boundary conditions for the pressure to get the velocity:

$$P = a_1 - \frac{a_2}{r} \to P = P_0\frac{b}{r}$$
$$v = \frac{KP_0 b}{r^2}$$

   Where a_1 and a_2 were integration constants equal to 0 and $\frac{-P_0}{b}$. Ok, done with the pressure and velocity. That was relatively easy. But the solute concentration will do us in.

   (c) Then we turn to the solute equation, substituting in our equation for velocity we can write:

$$\frac{KP_0 b}{r^2}\frac{dC}{dr} = \frac{D}{r^2}\frac{d}{dr}\left(r^2\frac{dC}{dr}\right)$$

   Introducing the dummy variable $A = \frac{KP_0 b}{D}$ to make things easier and then expanding the RHS:

$$A\frac{dC}{dr} = 2r\frac{dC}{dr} + r^2\frac{d^2C}{dr^2}$$
$$\frac{d^2C}{dr^2} = \frac{dC}{dr}\left(\frac{A}{r^2} - \frac{2}{r}\right)$$

Then, letting $B = \frac{dC}{dr}$,

$$\frac{dB}{dr} = B\Big(\frac{A}{r^2} - \frac{2}{r}\Big)$$
$$ln(B) = -\frac{A}{r} - 2ln(r) + a_3$$
$$B = \frac{dC}{dr} = exp\Big[-\frac{A}{r} - 2ln(r) + a_3\Big] = \frac{1}{r^2}exp\Big[a_3 - \frac{A}{r}\Big]$$

Next, letting $u = a_3 - \frac{A}{r}$, because I'm lazy, and separating variables (again), we can finally get an expression for C:

$$\frac{du}{dr} = \frac{A}{r^2}$$
$$\int dC = \int \frac{1}{r^2}exp(u)dr = \int \frac{1}{r^2}\frac{r^2}{A}exp(u)du$$
$$C = \frac{1}{A}exp(u) + a_4 = \frac{D}{KP_0b}exp\Big[a_3 - \frac{KP_0b}{Dr}\Big] + a_4$$

Where a_3 and a_4 are of course integration constants.

(d) And then we can apply the boundary conditions to solve for a_3 and a_4 and do some rearrangement to get an expression for $C(r)$:

$$C(b) = C_0 = \frac{D}{KP_0b}exp\Big[a_3 - \frac{KP_0}{D}\Big] + a_4$$
$$a_3 = ln\Big[\frac{KP_0b}{D}(C_0 - a_4)\Big] + \frac{KP_0}{D}$$
$$C(r) = (C_0 - a_4)exp\Big[\frac{KP_0}{D}(1 - \frac{b}{r})\Big] + a_4$$
$$C(\infty) = 0 = (C_0 - a4)exp\Big(\frac{KP_0}{D}\Big) + a_4$$
$$a_4 = -\frac{C_0exp(\frac{KP_0}{D})}{1 - exp(\frac{KP_0}{D})}$$
$$C(r) = C_0\Big(1 + \frac{exp(\frac{KP_0}{D})}{1 - exp(\frac{KP_0}{D})}\Big)exp\Big[\frac{KP_0}{D}(1 - \frac{b}{r})\Big] - \frac{C_0exp(\frac{KP_0}{D})}{1 - exp(\frac{KP_0}{D})}$$
$$C(r) = \frac{C_0}{1 - exp(\frac{KP_0}{D})}\Big[exp(\frac{KP_0}{D}(1 - \frac{b}{r}))\Big] - exp\Big(\frac{KP_0}{D}\Big)$$

Well. Wasn't that invigorating!

4. Comparing flow in human vs. rabbit aortas, noting that cardiac output is Q, heart rate is $1/\omega$, recalling that $\tau_{rz} = -\frac{\Delta PR}{2L}$, and making sure we have the right units:

	Human	Rabbit
Q (ml/s)	83.3	5
ω (1/s)	1.2	3.3
D (cm)	2.5	3
ν (cm^2/s)	0.04	0.04
τ (dyn/cm^2)	2.2	75
v (cm/s)	17	71
Re	1061	531
α	6.8	1.4

We see that the human and rabbit are fairly similar w.r.t. Re, though maybe more different in α and τ.

5. As you probably noted (since the first thing you did was to plot those values, right?), the relationship is not linear. Using the tube area of 3.14 cm^2, $\nu = 0.01$ cm^2/sm velocities and Reynolds numbers can be calculated (see table). If we look at $\frac{Q}{\Delta P/L}$, we see that for the first two values, they are almost the same and also that Re is relatively low. However, for the third value, we have moved into a region of transition flow moving towards turbulent flow. In this regime we do not expect Poiseuille flow because this solution was developed for laminar flow.

ΔP $(g/cm.s^2)$	L (cm)	Q (cm^3/s)	v (cm/s)	Re	$\Delta P/L$ $(g/cm^2.s^2)$	$\frac{Q}{\Delta P/L}$
1.5	5	12	3.8	764	0.3	40
3.8	5	30	9.5	1910	0.76	39.5
12	5	55	17.5	3501	2.4	22.9