Diffusion into a biological cell.

Diffusion is an important means of transport of many nutrients and other substances into the intracellular fluid (ICF or cytoplasm) from the surrounding extracellular fluid (ECF). It is usually called passive transport. We assume for simplicity that the cell is spherical, and adopt spherical polar coordinates \((r, \theta, \phi)\), related to Cartesians \((x, y, z)\) by

\[
x = r \sin(\theta) \cos(\phi), \quad y = r \sin(\theta) \sin(\phi), \quad z = r \cos(\theta)
\]

Here \(r \geq 0, \quad 0 \leq \theta \leq \pi, \quad 0 \leq \phi < 2\pi\).

Now the concentration is described by a function \(c(r, \theta, \phi, t)\).
Spherical Polar Coordinates

\[0 \leq r < \infty\]
\[0 \leq \theta \leq \pi\]
\[0 \leq \phi \leq 2\pi\]
In spherical polars, we find that

\[ \nabla^2 c = \frac{1}{r} \frac{\partial^2 [rc]}{\partial r^2} + \frac{1}{r^2 \sin \theta} \frac{\partial}{\partial \theta} \left( \sin \theta \frac{\partial c}{\partial \theta} \right) + \frac{1}{r^2 \sin^2 \theta} \frac{\partial^2 c}{\partial \phi^2} . \]

Let’s suppose that we have a spherically symmetric situation, where \( c \) does not depend on \( \theta \) or \( \phi \), so we have \( c(r, t) \).

We see that the 3-D diffusion equation reduces to

\[ \frac{\partial c(r,t)}{\partial t} = D \frac{1}{r} \frac{\partial^2 [rc(r,t)]}{\partial r^2} . \]

The flux vector now has only a component in the (outward) radial direction, given by

\[ J_r(r, t) = -D \frac{\partial c(r,t)}{\partial r} . \]
Consider firstly diffusion through the wall of a spherical cell. Let the cell radius be $R$ and the wall thickness be $a \ll R$. Suppose the ECF and ICF have concentrations of diffusate $c_o$ and $c_i$, respectively. The concentration gradient across the wall, in the outward radial direction, is

$$\frac{\partial c}{\partial r} \approx \frac{c_i-c_o}{a}.$$ 

Applying Fick’s first equation, we find that $\mathcal{J}$, the flux of diffusate across unit area of cell wall per unit time, in the outward radial direction, is therefore given approximately by $\frac{D}{a} (c_i - c_o)$, that is

$$\mathcal{J} \approx P(c_i - c_o). \quad (6.1)$$
ECF
\[ c = c_0 \]

ICF
\[ c = c_i \]
Here $P = \frac{D}{a}$ is called the **permeability** of the cell wall.

Note that $D$ here is the diffusion coefficient within the cell wall, and may be much smaller than in the ECF or ICF. Furthermore, the concentrations $c_o$ and $c_i$ should be, but cannot easily be measured inside the wall, near its boundaries, where they may be smaller or larger than the corresponding values just outside the wall boundaries.

For these reasons, (6.1) is commonly applied in practice using the concentrations just *outside* the wall boundaries, with $P$ taken to be a characteristic constant for the cell wall, to be determined experimentally, and with the wall width $a$ effectively set equal to 0.
Example: Oxygen consumption by a cell.

- A spherical cell of radius $R$ consumes oxygen at a rate proportional to the local concentration within its ICF, with rate constant $k > 0$. Oxygen diffuses across the cell wall from the ECF, which is effectively an infinite sea, and then diffuses within the ICF while being consumed.

Let the diffusion coefficient in the ECF be $D_E$, and that in the ICF be $D_I$. Let the permeability of the cell wall be $P$.

Consider a steady state situation, where the concentration of oxygen in the ECF, far from the cell, has the constant value $C_\infty$.

Denote the concentrations in the ICF and ECF by $c(r)$, $C(r)$, respectively.
In the ECF:–

\[ \frac{\partial C}{\partial t} = D_E \frac{1}{r} \frac{\partial^2 [rC]}{\partial r^2}, \]

reducing to

\[ \frac{d^2 [rC(r)]}{dr^2} = 0 \implies C(r) = A + \frac{B}{r}, \quad r > R \]

The condition that \( C(r) \to C_\infty \) as \( r \to \infty \) fixes \( A = C_\infty \), so

\[ C(r) = C_\infty + \frac{B}{r}, \quad r > R, \quad (6.2) \]

with \( B \) still to be determined.
In the ICF:–

\[ \frac{\partial c}{\partial t} = D I r \frac{1}{r} \frac{\partial^2 [r c]}{\partial r^2} - k c, \text{ reducing to } \frac{d^2 [r c(r)]}{dr^2} = \beta^2 [r c(r)] , \quad \beta = \sqrt{\frac{k}{D I}} \]

\[ \Rightarrow r c(r) = G e^{\beta r} + H e^{-\beta r} , \quad 0 < r < R . \]

Thus \( c(r) = \frac{G e^{\beta r} + H e^{-\beta r}}{r} \), and finiteness of \( c \) at \( r = 0 \) requires \( H = -G \), so

\[ c(r) = G e^{\beta r} - e^{-\beta r} , \quad 0 < r < R, \quad (6.3) \]

with \( G \) still to be determined.

[Note that \( G e^{\beta r} - e^{-\beta r} \rightarrow 2 \beta G \) as \( r \rightarrow 0 \).]
The constants $B, G$ are determined by the boundary conditions at the cell wall, where the flux must be continuous, since there is no creation or consumption of oxygen within the wall. Thus

$$-D_I c'(R) = -D_E C''(R) = J,$$ where $J = P(c(R) - C(R))$.

Then

$$-D_I G \left\{ \frac{\beta(e^{\beta R} + e^{-\beta R})}{R} - \frac{e^{\beta R} - e^{-\beta R}}{R^2} \right\} = P \left\{ G \frac{e^{\beta R} - e^{-\beta R}}{R} - C_\infty - \frac{B}{R} \right\}, \quad (6.4)$$

and

$$-D_E B \left\{ -\frac{1}{R^2} \right\} = P \left\{ G \frac{e^{\beta R} - e^{-\beta R}}{R} - C_\infty - \frac{B}{R} \right\}. \quad (6.5)$$
Solving these two equations for the two unknowns \( B, G \) we substitute into our solution

\[
c(r) = G \frac{e^{\beta r} - e^{-\beta r}}{r}, \quad 0 < r < R \quad \text{and} \quad C(r) = C_\infty + \frac{B}{r}, \quad r > R.
\]

Although the structure of the equations (6.4), (6.5) that determine \( B, G \) is quite simple, the expressions for \( B, G \) in terms of the given parameters \( R, D_E, D_I, C_\infty \) and \( P \) are *very* complicated:
There is a lesson here!

To proceed, note firstly that $(1 - \beta R)e^{\beta R} - (1 + \beta R)e^{-\beta R}$ is negative. (Check it!)

It then follows from (6.6),(6.7) that $B$ has the opposite sign to $G$, and also that the term $\{-\ldots\}$ on the LHS of (6.4) is positive.
Suppose that $B$ is positive and $G$ is negative. Then the RHS of (6.4) would be negative and the LHS would be positive - a contradiction. Thus $B$ is negative and $G$ is positive.

Now we see from (6.5) that $C(R) - c(R) = -D_E B/PR^2 > 0$. From these results we can see the general form of the solution, which is as shown in the next picture.
• Having found the solution, we can answer questions like:

**Qu:**
At what rate is the cell consuming oxygen in order to maintain the steady state?

**Ans:**
Rate (\(= \text{amount/unit time}\)) \(= -4\pi R^2 J = 4\pi R^2 P[C(R) - c(R)]\)

\[= -4\pi D_E B.\]

We can write this as \(k^*V C_\infty\), where \(V = 4\pi R^3/3\) is the cell volume and \(k^*\) is an “effective rate constant” \(k^* = r k\), with dimensionless \(r > 0\):

\[r = \frac{3P[1-\beta R]}{\{D_I(1-\beta R)-P(1-[1-\beta R][D_I/D_E])\}}e^{\beta R}-\{D_I(1+\beta R)-P(1-[1+\beta R][D_I/D_E])\}e^{-\beta R}\]
What about time-dependent (transient) cases? Consider for example the case when the cell has initially $c(r, t = 0) = H(r)$ in the ICF $0 < r < R$, for some given $H(r)$, and is placed at time $t = 0$ in an effectively infinite sea $r > R$ of ECF containing oxygen at concentration $C(r, t = 0) = C_\infty$.

Can we find the subsequent concentration profile inside and outside the cell, as the steady state is approached?

It is not too hard to formulate the mathematical problem, but to solve it exactly is getting tough!
The mathematical problem:

Solve

\[
\begin{align*}
\frac{\partial C(r,t)}{\partial t} &= D_E \frac{1}{r} \frac{\partial^2 [rC(r,t)]}{\partial r^2}, & r > R, \ t > 0 \\
\frac{\partial c(r,t)}{\partial t} &= D_I \frac{1}{r} \frac{\partial^2 [rc(r,t)]}{\partial r^2} - kc(r,t), & 0 < r < R, \ t > 0
\end{align*}
\]

subject to the IC

\[
\begin{align*}
C(r, 0) &= C_\infty, & r > R \\
c(r, 0) &= H(r), & 0 < r < R
\end{align*}
\]
and the BCs for $t > 0$

\[
\begin{align*}
-D_E \frac{\partial C(r,t)}{\partial r} \bigg|_{r=R} &= -D_I \frac{\partial c(r,t)}{\partial r} \bigg|_{r=R} = P[c(R,t) - C(R,t)], \\
C(r,t) \to C_\infty, & \quad r \to \infty; \quad c(0, t) \text{ finite}.
\end{align*}
\]

An exactly solvable problem?