Recitation #2

**Fick's first law**

\[ \phi(x,t) = -D \frac{\partial c(x,t)}{\partial x} \]

**Continuity equation**

\[ -\frac{\partial \phi(x,t)}{\partial x} = \frac{\partial c(x,t)}{\partial t} \]

**Diffusion equation**

\[ \frac{\partial c(x,t)}{\partial t} = D \frac{\partial^2 c(x,t)}{\partial x^2} \]

**Steady state solution**: Time-invariant

\[ \left( \frac{\partial c}{\partial t} = 0, \frac{\partial \phi}{\partial t} = 0 \right) \]

\[ \phi(x,t) = \phi_o \text{ (constant flux)} \]

\[ c(x,t) = -\frac{\phi_o}{D} x + \phi_o \]

**Equilibrium**: Zero flux + time invariant

\[ \phi_o = 0 \]

\[ c(x,t) = \text{constant} \]

\[ \Rightarrow \text{uniform distribution} \]

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**Impulse Response**

Given \( c(x,0) = n_o \delta(x) \) at \( t=0 \)

Solve \( \frac{\partial c_{x,t}}{\partial t} = D \frac{\partial^2 c_{x,t}}{\partial x^2} \) for \( t>0 \)

\[ c(x,t) = \frac{n_o}{\sqrt{4\pi Dt}} e^{-x^2/(4Dt)} \]

Gaussian function

mean = 0

\( \sigma = \sqrt{2Dt} \)

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**How long till half the solute diffuses to \( |x| > x_{1/2} \)**

\[ \frac{x_{1/2}}{\sqrt{2Dt}} \geq \frac{2}{3} \]

\[ \frac{2}{3} \sqrt{2Dt} \geq x_{1/2} \]

\[ \frac{4}{9} 2Dt \geq x_{1/2}^2 \]

\[ t \geq \frac{x_{1/2}^2}{D} = t_{1/2} \]
Problem 1. Consider a cell composed of a cell body to which is attached a long thin tubular “process” (e.g., the axon of a neuron or the flagellum of a sperm cell) of length \( l \) cm (Figure 1). Suppose some substance \( n \) (e.g., a metabolite) is generated in the cell body and diffuses along the process, all along which the substance is consumed at a constant uniform rate, \( \alpha_n \) mol/s per unit length. The continuity equation for the substance thus becomes

\[
\frac{\partial c_n}{\partial t} = - \frac{\partial \phi_n}{\partial x} - \frac{\alpha_n}{A}
\]

where \( A \) is the (assumed constant) cross-sectional area of the process.

a) Combine the modified continuity equation given above with Fick’s Law to obtain a modified form of the diffusion equation that must be satisfied by \( c_n \).

b) Show that a solution of this equation in the steady-state \((\partial c_n/\partial t = \partial \phi_n/\partial t = 0)\) is

\[
c_n(x) = \frac{\alpha_n}{2DA} x^2 + a_\circ x + b_\circ
\]

and find values of the constants \( a_\circ \) and \( b_\circ \) corresponding to the boundary conditions \( c_n(0) = C_\circ \) and \( \phi_n(l) = 0 \).

c) Show that the requirement that \( \alpha_n \) mol/(s·cm) be consumed uniformly along the process sets an upper limit (if \( C_\circ, D, A, \) and \( \alpha_n \) are fixed) on the possible length \( l \) of the process, and find a formula for this upper bound.
1. Substance $n$ generated $\Rightarrow$ diffuse $(e.g. \text{ ATP})$

$\alpha_n$: consumption rate $(\text{mol/s per unit length})$

[Continuity equation]

$$\frac{\partial C_n}{\partial t} = -\frac{\partial \phi_n}{\partial x} - \frac{\alpha_n}{A}$$

- Increase rate of local concentration
- Spatial gradient in flux
- Reaction loss

a) Fick's law $\phi_n = -D_n \frac{\partial C_n}{\partial x}$

$$\therefore \quad \frac{\partial C_n}{\partial t} = +D_n \frac{\partial^2 C_n}{\partial x^2} - \frac{\alpha_n}{A}$$

b) In the steady state $(\frac{\partial}{\partial t} \to 0)$

$$D_n \frac{d^2 C_n(x)}{dx^2} - \frac{\alpha_n}{A} = 0$$

$$\frac{d^2 C_n(x)}{dx^2} = \frac{\alpha_n}{D_n A}$$
general solution \( \Rightarrow \quad C_n(x) = \frac{\alpha_n}{2DA} x^2 + a_0 x + b_0 \)

\((a_0, b_0 : \text{constants})\)

Boundary conditions

\[
\begin{align*}
C_n(0) &= C_0 : \text{meaning?} \\
&\quad \text{(intracellular concentration is maintained.)}
\end{align*}
\]

\(\phi_n(l) = 0\)

At the end of process,

\(\text{(molecules cannot go further)}\)

\[C_n(0) = C_0 \Rightarrow b_0 = C_0.\]

\[
\phi_n(l) = -D_n \frac{\partial C_n}{\partial x} \bigg|_{x=l} = -D_n \left( \frac{\alpha_n}{D_n A} x + a_0 \right) = 0
\]

\[\therefore a_0 = -\frac{\alpha_n l}{D_n A}\]

\[C_n(x) = \frac{\alpha_n}{2DA} x^2 - \frac{\alpha_n l}{D_n A} x + C_0\]

C) What is the minimum concentration?

Where does it happen? \(\Rightarrow x=l\).

\[C_n(l) = \frac{\alpha_n}{2DA} l^2 - \frac{\alpha_n l^2}{D_n A} + C_0\]

\[= C_0 - \frac{\alpha_n l^2}{2D_n A}\]

Since negative concentration does not make sense,

\[C_0 \geq \frac{\alpha_n l^2}{2D_n A} \quad l^2 \leq \frac{2D_n A C_0}{\alpha_n}\]

If this is violated (If the process becomes longer)

\(\Rightarrow\) End of the process cannot get the molecule at all.
Problem 2. As your first assignment at Tinyfluidics Inc., you are asked to design a microfluidic device that will remove small molecules from a sample of fluid that contains both large molecules and small molecules. After some thinking, you design the laminar flow device shown below.

The sample is injected in a port with width $\delta$. The sample flow is surrounded by buffers injected on both sides of the sample. The combined flow then passes through a channel that has width $W$ and length $L$ after which the fluids are separated into a desired filtrate output (in a channel of width $d$) and two waste outputs. Assume that the fluid moves with the same speed $v$ in all parts of the microfluidic device (although this is not generally true, it is a convenient starting point). Assume that $\delta << d$, and that $W$ is sufficiently large that it can be taken to be infinity.

To test the device, you mix a solution that contains equal concentrations of 2 proteins, A and B. The diffusivity of solute B is four times that of solute A.

Part a. Briefly explain how this device takes advantage of differences in diffusivities to achieve separation.

Part b. Let $f_A$ represent the ratio of the amount of solute A found in the filtrate divided by the amount of solute A in the sample. Determine an expression for $f_A$. Determine an expression for the analogous ratio $f_B$ for solute B.

The following figure shows a plot of the dependence of $f_A$ and $f_B$ on $L$, when $\delta = 1\mu m$, $d = 20\mu m$, $v = 1\text{ mm/s}$, and $D_A = 10^{-7}\text{ cm}^2/\text{s}$.

![Graph showing the relationship between $f_A$ and $f_B$ and $L$.]

Part c. Which curve (dashed or solid) represents $f_A$? Explain.

Part d. Determine $L_0$, the value of $L$ that maximizes the difference between $f_A$ and $f_B$. Briefly explain why this difference is smaller when $L << L_0$ and when $L >> L_0$. 

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Two proteins A and B

\[ 4D_A = D_B \]

a) As the narrow sample stream enters the device, proteins will get diffused in the lateral (x) dimension. The larger the diffusivity, the farther it will diffuse.

At the entrance

At the outlet
(b) \[ f_A = \frac{\text{Amount of } A \text{ recovered}}{\text{Amount of } A \text{ injected}} \]

Initial \[ \Rightarrow \] final recovered

\[ C_A(x) = \frac{n_A}{S(x)} \Rightarrow C_A(x, t) = \frac{n_A}{\sqrt{4\pi Dt_0}} e^{-\frac{x^2}{4Dt_0}} \]

(at \( t = 0 \))

(at injection)

(\( t = t_0 \))

What is \( t_0 \)? \( \Rightarrow \) \( v t_0 = L \Rightarrow t_0 = \frac{L}{v} \).

\[ f_A = \frac{\int_{-\frac{L}{2}}^{\frac{L}{2}} \left( \frac{n_A}{\sqrt{4\pi Dt_0}} e^{-\frac{x^2}{4Dt_0}} \right) dx}{\int_{-\infty}^{\infty} \frac{n_A S(x)}{dx} dx} \]

\[ = \int_{-\frac{L}{2}}^{\frac{L}{2}} \frac{\sqrt{\frac{1}{\frac{L}{2}}}}{\sqrt{4\pi Dt_0}} \frac{e^{-\frac{x^2}{4Dt_0}}}{dx} dx \]

If \( \frac{d}{2} = \sqrt{4DAt_0} \Rightarrow f_A = 0.68 \)

\( = 2\sqrt{4DAt_0} \Rightarrow f_A = 0.95 \).

(c) Since B diffuses faster, dotted line represents B.

(d) One can estimate (from the graph) that \( L_0 \) should be about \( \approx 1.5 \text{mm} \).