MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Department of Electrical Engineering and Computer Science,
Department of Mechanical Engineering,
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Quantitative Physiology: Cells and Tissues
2.791J/2.794J/6.021J/6.521J/BE.370J/BE.470J/HST.541J

Homework Assignment #2 Issued: September 16, 2004
Due: September 23, 2004

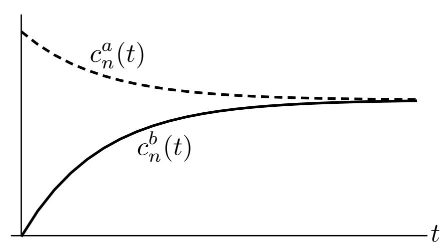
Reading

Lecture 5 — Volume 1: 3.8-3.8.5
Lecture 6 — Volume 1: 4.1-4.3.2.3 4.4-4.5.1.2
Lecture 7 — Volume 1: 4.7-4.7.1.2
Lecture 8 — Volume 1: 4.7.2-p.230 Fig.4.26 Fig.4.28 4.8.2-4.8.3

Exercise 1. Describe the *dissolve-diffuse theory* for diffusion through cellular membranes.

Exercise 2. Two time constants are involved in two-compartment diffusion through a membrane: the steady-state time constant of the membrane (τ_{ss}) and the equilibrium time constant for the two compartments (τ_{eq}). Without the use of equations, describe these two time constants.

Exercise 3. A solute n diffuses through a membrane that separates two compartments that have different initial concentrations. The concentrations in the two compartments as a function of time, $c_n^a(t)$ and $c_n^b(t)$, are shown in the following figure.



The volumes of the two compartments are $\mathcal{V}_a$ and $\mathcal{V}_b$. Is $\mathcal{V}_a > \mathcal{V}_b$ or is $\mathcal{V}_a < \mathcal{V}_b$? Explain.

Exercise 4. Define *osmolarity*.

Exercise 5. The following three formulas for the sugar (trisaccharide) raffinose (found in sugar beets) were proposed:

$$C_{12}H_{28}O_{14},$$
$$C_{18}H_{42}O_{21},$$
$$C_{36}H_{84}O_{42}.$$

De Vries (1888) used a plant cell to determine that plasmolysis occurred with a solution containing 59.4 grams of raffinose per liter of water whereas plasmolysis occurred in a solution of sucrose at a concentration of 0.1 mol/L. Based on these measurements, de Vries determined the correct formula for raffinose. Which formula would you choose and why would you choose it?

Problem 1. Consider diffusion through a thin membrane that separates two otherwise closed compartments. As illustrated in Figure 1, the membrane and both compartments have cross sectional areas $A = 1$ cm^2. Compartment 1 has length $L_1 = 50$ cm, compartment 2 has length $L_2 = 10$

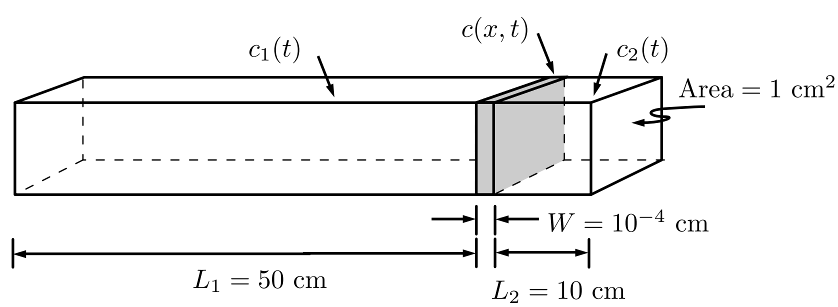


Figure 1: Two compartments separated by a membrane.

cm, and the membrane thickness is $W = 10^{-4}$ cm. Assume that (1) the compartments contain sugar solutions and that both compartments are well stirred so that the concentration of sugar in compartment 1 can be written as $c_1(t)$ and that in compartment 2 can be written as $c_2(t)$; (2) the concentration of sugar in the membrane can be written as $c(x,t)$, where x represents distance through the membrane; (3) the diffusivity of sugar in the membrane is $D_{sugar} = 10^{-5}$ cm^2/s and the membrane:water partition coefficient $k_{m:w}$ is 1; (4) the concentration of sugar in the membrane has reached steady state at time $t = 0$ and that $c_1(0) = 1$ mol/L and $c_2(0) = 0$ mol/L.

a) Compute the flux of sugar through the membrane at time $t = 0$, $\phi_s(0)$.

b) Compute the final value of concentration of sugar in compartment 1, $c_1(\infty)$.

c) Let τ_{eq} characterize the amount of time required to reach equilibrium. What would happen to τ_{eq} if the diffusivity of sugar in the membrane were doubled? Explain your reasoning.

Problem 2. A thin membrane and a thick membrane, that are otherwise identical, are used to separate identical solutions of volume $\mathcal{V} = 1\,\text{cm}^3$ (Figure 2). All the membrane surfaces facing the solutions have area $A = 1\,\text{cm}^2$. The thin membrane has thickness $d_s = 10^{-4}\,\text{cm}$; the thick membrane has thickness $d_l = 1\,\text{cm}$. For $t < 0$ the aqueous solutions on both sides of the membrane are identical and do not contain solute n. At $t = 0$ a small concentration of solute n is added to the solution on side 1 of the membrane. You may assume that there is no water flow across the membrane. The diffusion coefficient and membrane:solution partition coefficient of n in both membranes are $D_n = 10^{-5}\,\text{cm}^2/\text{s}$ and $k_n = 2$, respectively.

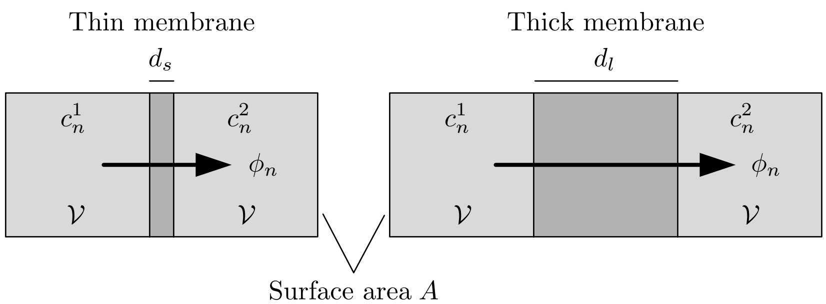


Figure 2: Schematic diagrams of thin and thick membranes.

a) For each membrane, estimate the time τ_{ss} that it takes for the concentration profile in the membrane to reach its steady-state spatial distribution.

b) For each membrane, find the time τ_{eq} that it takes for the solutions on the two sides of the membrane to come to equilibrium assuming that the spatial distribution of solute in the membrane is the steady-state distribution.

c) Is it reasonable to assume that Fick's Law for membranes applies for the thin membrane at each instant in time, i.e., does

$$\phi_n(t) = P_s(c_n^1(t) - c_n^2(t))\ ?$$

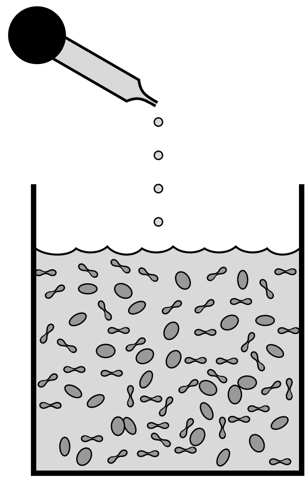
where P_s is the permeability of the thin membrane.

d) Is it reasonable to assume that Fick's Law for membranes applies for the thick membrane at each instant in time, i.e., does

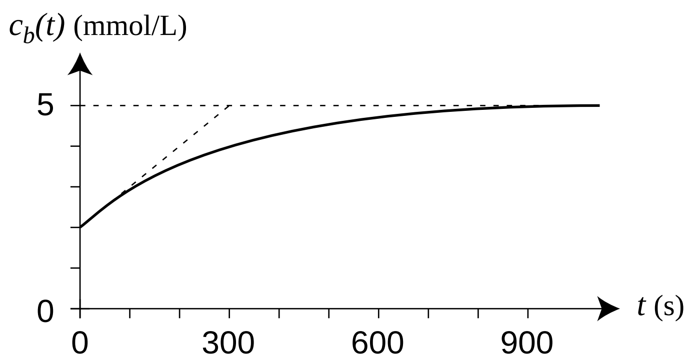
$$\phi_n(t) = P_l(c_n^1(t) - c_n^2(t))\ ?$$

where P_l is the permeability of the thick membrane.

Problem 3. Glucose is dripped at a constant rate $R = 2\mu$mol/s into a bath that contains 10^{12} identical red blood cells, as shown in the following figure.



Assume that each red blood cell has a volume $\mathcal{V}_C = 25$ $(\mu\text{m})^3$ and a surface area $\mathcal{A}_C = 80$ $(\mu\text{m})^2$, and that neither of these changes over the time interval considered in this problem. Assume that the volume of the bath is 1 L, and that the bath is well stirred. (You may assume that the amount of water dripped into the bath is negligibly small.) The concentration of glucose in the bath, $c_b(t)$, if found to increase as a function of time t, as shown in the following plot.



Part a. Is the following logic True or False?

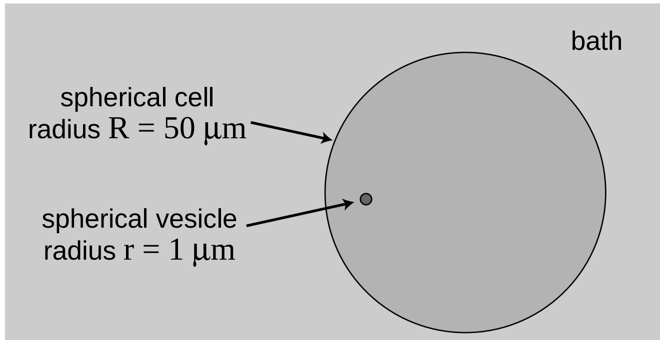
> The flux of glucose through each of the cell membranes cannot be constant over the time $0 < t < 900$ s, because if it were, the concentration $c_b(t)$ would be a linear function of time.

If the truthfulness of this statement cannot be determined from the information provided, describe what additional information is needed.

Part b. Determine the flux of glucose through the membrane of each cell at time $t = 900$ s. Use our normal convention that outward flux (i.e., flux leaving the cell) is positive and inward flux is negative. Determine the numerical value (or numerical expression) **and units**. If you cannot determine the numerical value from the information provided, describe what additional information is needed.

Part c. Determine the flux of glucose through the membrane of each cell at time $t = 0$ s. Use our normal convention that outward flux (i.e., flux leaving the cell) is positive and inward flux is negative. Determine the numerical value (or numerical expression) **and units**. If you cannot determine the numerical value from the information provided, describe what additional information is needed.

Problem 4. All cells are surrounded by a cell membrane. The cytoplasm of most cells contains a variety of organelles that are also enclosed within membranes. Assume that a spherical cell with radius $R = 50\mu$m contains a spherical organelle called a vesicle, with radius $r = 1\mu$m, as shown in the following figure.



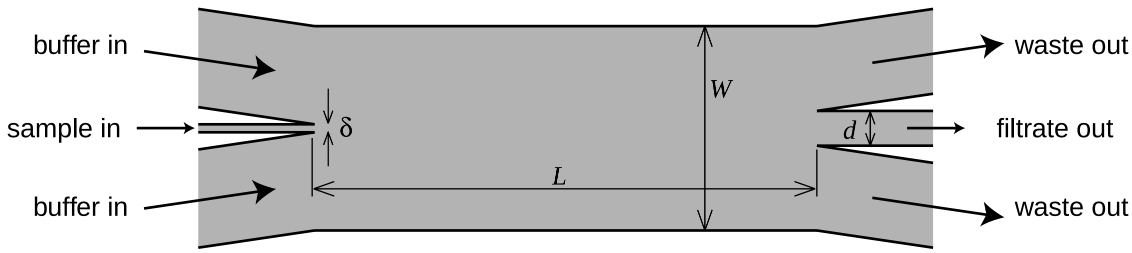
Assume that the membranes surrounding the cell and vesicle are uniform lipid bilayers with identical compositions and the same thickness $d = 10$ nm. Assume that solute X is transported across both the cell and vesicle membrane via the dissolve and diffuse mechanism. Assume that X dissolves equally well in the bath and in the aqueous interiors of the vesicle and cell. Assume that the solute X dissolves 100 times less readily in the membrane (i.e., the partitioning coefficient is 0.01). Assume the diffusivity of X in the membranes is 10^{-7}cm^2/s.

Initially, the concentration of X is zero inside the cell and inside the vesicle. At time $t = 0$, the cell is plunged into a bath that contains X with concentration 1 mmol/L.

a) Estimate the time that is required for the concentration of X in the cell to reach 0.5 mmol/L. Find a numerical value or explain why it is not possible to obtain a numerical value with the information that is given.

b) Estimate the time that is required for the concentration of X in the vesicle to reach 0.5 mmol/L. Find a numerical value or explain why it is not possible to obtain a numerical value with the information that is given.

Problem 5. 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.

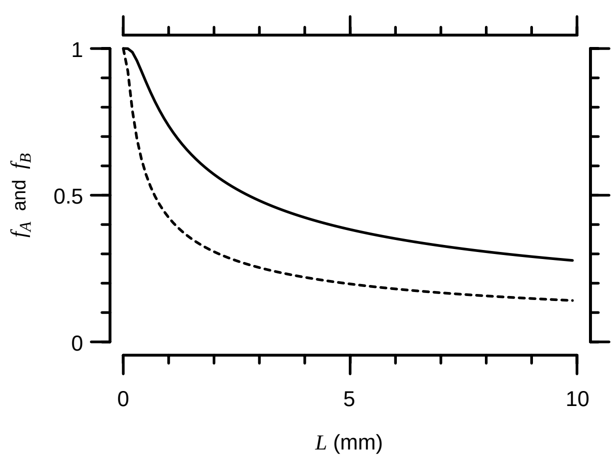


The sample is injected in a port with width δ. The sample flow is surrounded by buffers injected on both sides of the sample. The combined flow then passes through a channel that has width W and length L after which the fluids are separated into a desired filtrate output (in a channel of width d) and 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, $v = 1$ mm/s, and $D_A = 10^{-7}$ cm^2/s.



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 $L >> L_0$.