

1. (10 points)

The time course of one-dimensional diffusion of a solute from a point source in space and time has the form

$$c_n(x, t) = \frac{n_0}{\sqrt{4\pi Dt}} e^{-x^2/4Dt}$$

where n_0 is the number of moles of solute per unit area placed at $x = 0$ at $t = 0$. $c_n(x, t)$ is computed for locations x_a and x_b as shown in Fig.1.

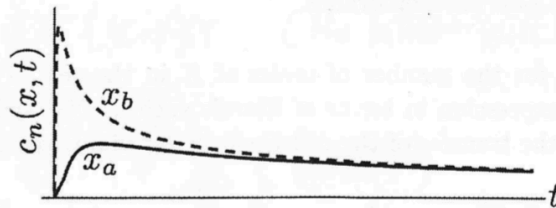


Figure 1:

- 5] a. Is $x_a > x_b$ or is $x_a < x_b$? Explain.

$$x_a > x_b$$

$\max(c_n(x_b, t))$ occurs sooner than $\max(c_n(x_a, t))$ indicating x_b is closer to site of release

- 5] b. Describe briefly how this picture would change if D was increased.

- peak amplitude decreases
- peak at a given spatial location is reached faster

2. (25 points)

An experiment is performed to determine the permeability, P_X , of the membrane of a cell to solute X . The cell is spherical and has a radius of $72 \mu\text{m}$. It is placed in a solution containing solute X for a sufficient time to load the cell with N_X moles of X . A set of identical vials containing identical solutions that do not contain the solute X are prepared. The cell is then immersed successively in the series of these vials for $T = 10$ minutes per vial, i.e., 10 minutes in vial 1, followed by 10 minutes in vial 2, followed by 10 minutes in vial 3, etc., as shown in Fig.2.

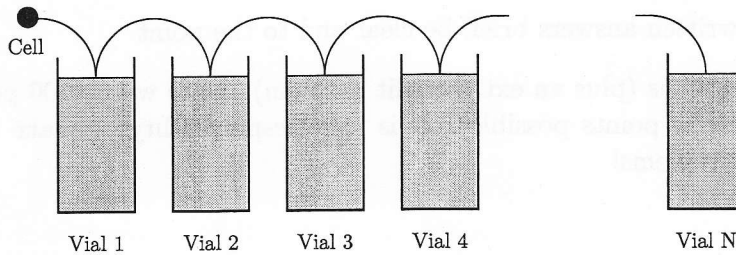


Figure 2:

The number of moles of solute X in vial k , is $n_X(k)$. Assume that the volume of the cell is constant and negligible compared with the volume of a vial, and hence, the concentration of solute in a vial is always negligible compared to that in the cell. The solute permeates the membrane according to Ficks Law for membranes.

- 13 a. Determine an expression for the number of moles of X in the cell as a function of time, $n_i^X(t)$. You may write this expression in terms of literals such as N_X and a suitably defined time constant. Assume that the transfer of the cell from vial to vial takes no time.

• must have initially $n_i^X(0) = N_X$ (initial condition)

• rate of change of amount of solute will be given as:

r - cell radius
 A - cell surface area
 C_x - concentration inside or outside
 V - cell volume

$$\frac{d}{dt} n_i^X = -AP_X [C_x^i(t) - C_x^o(t)] \cong -AP_X C_x^i \quad (\text{since } C_x^o \cong 0)$$

$$= -\frac{AP_X}{V} n_i^X$$

• so $\frac{d}{dt} n_i^X = -\frac{AP_X}{V} n_i^X = -\frac{3P_X}{r} n_i^X \rightarrow n_i^X(t) = N_X e^{-t/\tau}$

NOTE: Assumed the shape and radius of the cell stayed constant

where $\tau \equiv \frac{r}{3P_X}$

12 b. Determine an expression for the total quantity of X in the k 'th vial, $n_X(k)$ in terms of literals such as N_X , T , and a suitably defined time constant.

- Each time the cell is moved (every 10 min.), there will be less and less solute to diffuse out. The # of moles diffused will equal what left the cell during the interval $(k-1)T < t < kT$ ($T = 10$ min.), which is the same as the difference between what is in the cell at ~~time~~ $t = kT$ versus $t = (k-1)T$ (the latter will be the larger one!)

$$\rightarrow n_X(k) = -n_i^X(kT) + n_i^X((k-1)T)$$

$$= N_X \left[e^{-(k-1)T/\tau} - e^{-kT/\tau} \right]$$

$$= N_X e^{-kT/\tau} \left[e^{T/\tau} - 1 \right] = n_X(k)$$

3. (20 points)

Three compartments filled with aqueous solutions are separated by semipermeable membranes as shown in Fig.3.

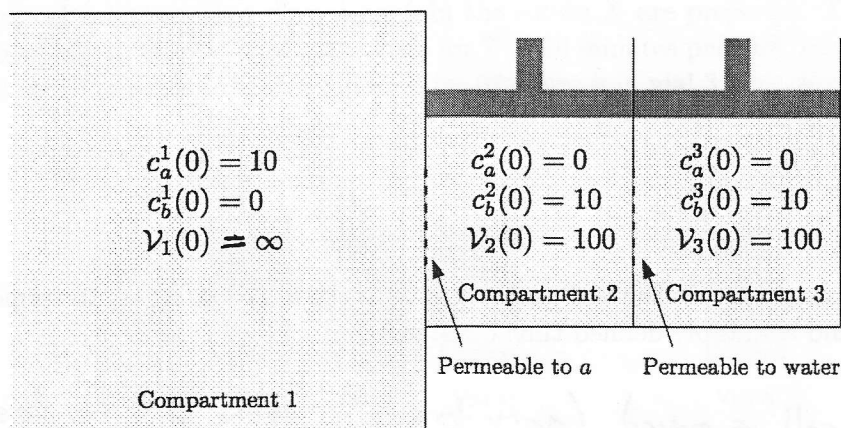


Figure 3:

Two non-electrolyte solutes *a* and *b* are contained in the solutions. Initial concentrations of each solute (in mmol/L) and initial volumes (in cm³) are given in the figure. The membrane separating compartments 1 and 2 is permeable to solute *a* only and not permeable either to solute *b* or to water. The membrane separating compartments 2 and 3 is permeable to water only and not permeable to either solutes *a* or *b*. The volume of compartment 1, V_1 , is much larger than that of the other compartments. You may assume that it has an infinite volume. Compartments 2 and 3 contain pistons with frictionless bearing surfaces. Therefore, the hydraulic pressure in these compartments is zero.

- 3 a. Is the system in diffusive equilibrium at $t = 0$? Explain.

No. The concentration difference of solute *a* between C_1 and C_2 , along w/ the permeability in the separating membrane means that *a* will move between the two.

Compartment #1
↓

- 3 b. Is the system in osmotic equilibrium at $t = 0$? Explain.

Yes. Since the membrane separating C_2 and C_3 is permeable only to water AND the osmolarities are the same between the two, no water will move (at least initially).

14 c. Determine the equilibrium concentrations $[c_1^a(\infty), c_1^b(\infty), c_2^a(\infty), c_2^b(\infty), c_3^a(\infty), \text{ and } c_3^b(\infty)]$ and volumes ($V_2(\infty)$ and $V_3(\infty)$).

• Because solute a will move from C1 to C2, after $t=0$ the system will no longer be in osmotic equilibrium.

• In the long run, we can already see the following:

$$c_1^a(\infty) = \frac{1000}{L} = c_2^a(\infty) \quad \leftarrow \text{because eventually C1 and C2 will reach diffusive equilibrium due to the memb. permeability}$$

$$c_1^b(\infty) = 0 = c_3^a(\infty) \quad \leftarrow \text{no solute a can make it over to C3}$$

• Due to water movement across C2 and C3, we need a few extra steps to get the other values, noting that:

- at $t=\infty$, the system will be in osmotic (and diffusive!) equilibrium

- the total volume of C2 and C3 stays const., i.e. $V_2(\infty) + V_3(\infty) = 200 \text{ cm}^3$

• the final osmolarity must satisfy the following: $\rightarrow V_3(\infty) = 200 - V_2(\infty)$

$$\overbrace{10 + \frac{c_2^b(0) \cdot V_2(0)}{V_2(\infty)}}^{\text{comp. 2}} = \overbrace{\frac{c_3^b(0) \cdot V_3(0)}{V_3(\infty)}}^{\text{comp. 3}}$$

final concentr. of solute a
final concentr. of solute b
final concentration of solute b

$$\rightarrow 10 + \frac{1000}{V_2(\infty)} = \frac{1000}{V_3(\infty)} = \frac{1000}{200 - V_2(\infty)} \rightarrow V_2(\infty)^2 - 2000 = 0$$

so $V_2(\infty) = 141 \text{ cm}^3$ and thereby $V_3(\infty) = 59 \text{ cm}^3$

• Then $c_2^b(\infty) = \frac{1000}{V_2(\infty)} = 7.1 \text{ mmol/L}$

$$c_3^b(\infty) = \frac{1000}{V_3(\infty)} = 17.1 \text{ mmol/L}$$

$$c_1^a(\infty) = 10 \frac{\text{mmol}}{\text{L}}, c_1^b(\infty) = 0$$

$$c_2^a(\infty) = 10, c_2^b(\infty) = 7.1, V_2(\infty) = 141$$

$$c_3^a(\infty) = 0, c_3^b(\infty) = 17.1, V_3(\infty) = 59$$

4. (25 points)

To understand how metabolic rate might affect glucose concentration in cells, we wish to analyze a simple model. Assume that glucose is transported across the cell membrane by a process that can be represented by a simple, symmetric, four-state carrier model, so that the flux of glucose crossing the membrane is given by

$$\phi_s = \phi_m \left(\frac{c_s^i}{c_s^i + K} - \frac{c_s^o}{c_s^o + K} \right)$$

where K represents the dissociation constant for the binding of glucose to the carrier and ϕ_m represents the maximum flux through the carriers. Assume that the cell is surrounded by fluid that contains glucose and that the extracellular concentration is constant, i.e., $c_s^o = C$. Assume that the cell is metabolizing (consuming) glucose at a constant rate α mol/s. Assume that these conditions persist, and a steady-state condition is reached in which the intracellular concentration of glucose c_s^i is a constant. Assume that the surface area A and volume V of the cell are constant.

+6

a. Determine the steady state relation between the rate of glucose consumption α and the flux of glucose ϕ_s through the cell membrane. [Hint: Consider the units of α and ϕ_s]

$$[\phi_s] = \frac{\text{amount}}{\text{area} \cdot \text{time}} = \frac{\text{mol}}{\text{m}^2 \cdot \text{s}}, \quad [\alpha] = \frac{\text{amount}}{\text{time}} = \frac{\text{mol}}{\text{s}}$$

- At steady-state, the intracellular concentration (c_s^i) must be constant. Put another way: ^{the rate for} what comes into the cell (i.e. $A\phi_s$) must be directly proportional (w/ a const. of -1) to the rate at which it is consumed

$$\alpha = -A\phi_s$$

- 10 b. In the steady state, the concentration of glucose in the cell is constant. Determine an expression for this concentration (c_s^i) in terms of the rate of glucose consumption α and constant parameters of this system.

$$q_s = q_m \left(\frac{c_s^i}{c_s^i + k} - \frac{c}{c + k} \right) = - \frac{\alpha}{A}$$

Now need to solve for c_s^i

$$\frac{c_s^i}{c_s^i + k} = \frac{c}{c + k} - \frac{\alpha}{q_m A}$$

$$c_s^i \left[1 - \frac{c}{c + k} + \frac{\alpha}{q_m A} \right] = \frac{kc}{c + k} - \frac{k\alpha}{q_m A}$$

$$c_s^i = \frac{\frac{k}{c + k} \left[c - \frac{\alpha}{q_m A} (c + k) \right]}{\frac{1}{c + k} \left[c + k - c + \frac{\alpha}{q_m A} (c + k) \right]} = k \frac{\frac{1}{q_m A} [c q_m A - \alpha (c + k)]}{\frac{1}{q_m A} [k q_m A + \alpha (c + k)]}$$

$$\rightarrow c_s^i = k \frac{[c q_m A - \alpha (c + k)]}{[k q_m A + \alpha (c + k)]} = \frac{\frac{kc}{c + k} - \frac{k\alpha}{q_m A}}{1 - \frac{c}{c + k} + \frac{\alpha}{q_m A}}$$

The solution to the equation developed in Part b is plotted in Fig.4 for the special case $K = C$.

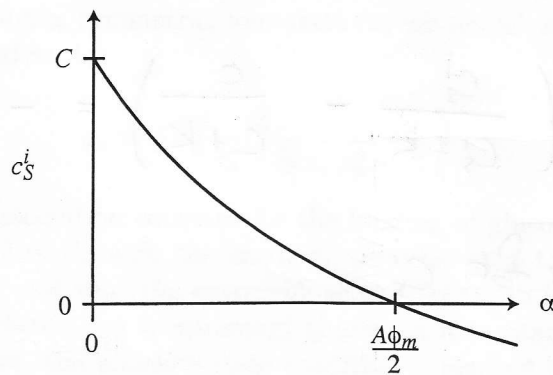


Figure 4:

+3 c1. Provide a *physical interpretation* of the result shown for $\alpha = 0$.

When $\alpha = 0$, no glucose is being consumed and the steady-state flux is zero. This occurs when $C_s^i = C_s^o = C$

+3 c2. Provide a *physical interpretation* of the result shown for $0 < \alpha = A\phi_m/2$. ← printing error!

As α increases, the flux (inwards) must also increase.

Since $C_s^o = C = \text{const.}$, the only way for the flux to increase is via a larger concentration difference (i.e. $C_s^i < C_s^o$)

+3 c3. Provide a *physical interpretation* of the result shown for $\alpha > A\phi_m/2$.

Negative concentration = not physical

The cell cannot consume glucose faster than the rate at which it can be transported across (which occurs when $C_s^i = 0$)

5. (20 points)

47

Two compartments of a fluid-filled chamber are separated by a membrane as shown in Fig.5. The

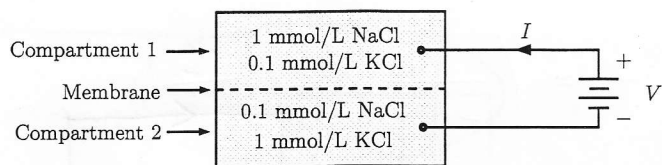


Figure 5:

$1 \text{ L} = 10^3 \text{ cm}^3$

area of the membrane is 100 cm^2 and the volume of each compartment is 1000 cm^3 . The solution in compartment 1 contains 1 mmol/L NaCl and 0.1 mmol/L KCl . The solution in compartment 2 contains 0.1 mmol/L NaCl and 1 mmol/L KCl . The temperatures of the solutions are 24°C . The membrane is known to be permeable to a single ion, but it is not known if that ion is sodium, potassium, or chloride. Electrodes connect the solutions in the compartments to a battery. The current I was measured with the battery voltage $V = 0$ and was found to be $I = -1 \text{ mA}$.

a. Identify the permeant ion species. Explain your reasoning.

ions disassociate such that: $C_{\text{Na}}^1 = 1 \text{ mmol}$, $C_{\text{K}}^1 = 0.1 \text{ mmol}$, $C_{\text{Cl}}^1 = 1.1 \text{ mmol}$
 $C_{\text{Na}}^2 = 0.1 \text{ mmol}$, $C_{\text{K}}^2 = 1 \text{ mmol}$, $C_{\text{Cl}}^2 = 1.1 \text{ mmol}$

- chlorine is in diffusive equilibrium, so no net diffusion of Cl^-
- if Na^+ were permeant, it would go from comp. 1 to 2 (i.e. the current would be positive)
- if K^+ were permeant, it would go from comp. 2 to 1 (because $C_{\text{K}}^2 > C_{\text{K}}^1$), thereby leading to a negative current

→ Since $I < 0$, K⁺ must be the permeant ion

+10

b. Draw an equivalent circuit for the entire system, including the battery. Indicate values for those components whose values can be determined.

• Nernst potential for K^+ :

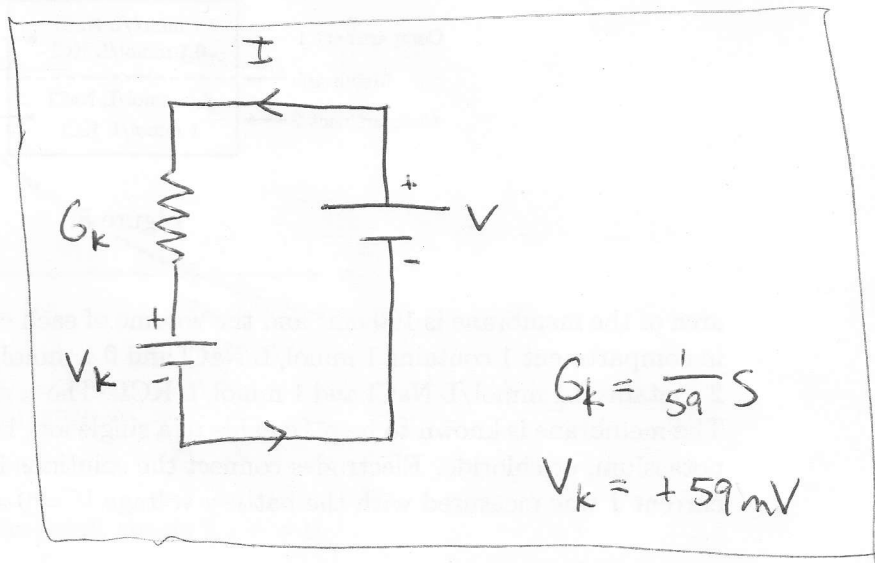
$$V_K = \frac{RT}{F} \ln \frac{C_K^o}{C_K^i}$$

$$= 59 \text{ mV} \cdot \log\left(\frac{1}{0.1}\right) = +59 \text{ mV}$$

• From Ohm's Law

$$\Delta V = IR = \frac{I}{G}$$

$$\rightarrow G = \frac{I}{\Delta V} = \frac{I}{V - V_K} = \frac{-1 \text{ mA}}{-59 \text{ mV}} = \frac{1}{59} \text{ S}$$



$$G_K = \frac{1}{59} \text{ S}$$

$$V_K = +59 \text{ mV}$$

+3

c. Determine the current I that would result if the battery voltage were set to 1 V. Explain your reasoning.

$$I = G\Delta V = G(V - V_K) = \frac{1}{59}(1 - 0.059)$$

$$= 15.9 \text{ mA}$$

Extra Credit (15 Points):

Consider the model of a cell shown in Fig.6 The cell has channels for the passive transport of

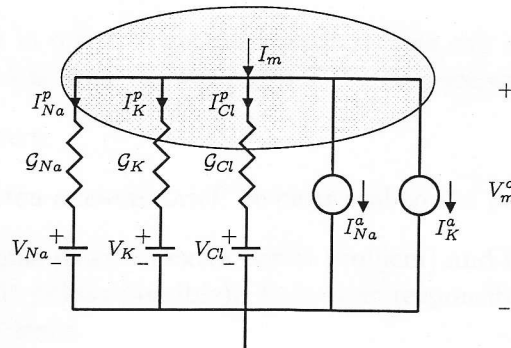


Figure 6:

sodium, potassium, and chloride as well as a pump that actively transports sodium out of the cell and potassium into the cell. The pump ratio is $I_{Na}^a/I_K^a = -1.5$. The following table shows the intracellular and extracellular concentrations, Nernst equilibrium potentials, and conductance ratios for sodium and potassium. Some information is also given for chloride; blank entries represent unknown quantities. The cell also contains impermeant intracellular ions. Assume that the cell is in equilibrium at $t = 0$, i.e., assume that at $t = 0$ the cell has reached a condition for which all solute concentrations, the cell volume, and the membrane potential are constant.

	c_n^i	c_n^o	V_n	G_n/G_K
	(mmol/L)		(mV)	
Na ⁺	10	140	+68	0.1
K ⁺	140	10	-68	1
Cl ⁻		150		1

Figure 7:

+6 a. Determine V_m^o .

• Equilibrium implies no net flux of either Na⁺ or K⁺

$$\left. \begin{aligned} G_{Na} (V_m^o - V_{Na}) + I_{Na}^a &= 0 \\ G_K (V_m^o - V_K) + I_K^a &= 0 \end{aligned} \right\} \rightarrow \frac{G_{Na} (V_m^o - V_{Na})}{G_K (V_m^o - V_K)} = \frac{I_{Na}^a}{I_K^a}$$

• $\frac{I_{Na}^a}{I_K^a} = -1.5$ (given), $\frac{G_{Na}}{G_K} = 0.1$ (table), $V_{Na} = 68 \text{ mV} = -V_K$

So $\frac{V_m^o - 68}{V_m^o + 68} = -1.5 \rightarrow \boxed{V_m^o = -59.5 \text{ mV}}$

[+4]

b. At $t = 0$, the external concentration of chloride is reduced from 150 mmol/L to 50 mmol/L by substituting an isosmotic quantity of an impermeant anion for chloride. Assume that the concentrations of sodium and potassium both inside and outside the cell remain the same and that the volume of the cell does not change. Determine $V_m^o(0^+)$, the value of the membrane potential immediately after the change in solution. You may ignore the effect of the membrane capacitance.

• Nernst potential for Cl^- changes as follows

$$\Delta V_{\text{Cl}} = -\frac{RT}{F} \ln\left(\frac{50}{c_{\text{Cl}}^i(0^+)}\right) - \left(-\frac{RT}{F} \ln\left(\frac{150}{c_{\text{Cl}}^i(0^-)}\right)\right) = \frac{RT}{F} \ln\left(\frac{150}{50}\right)$$

$$= 28 \text{ mV}$$

assuming $c_{\text{Cl}}^i(0^+) = c_{\text{Cl}}^i(0^-)$

• By superposition, the change in V_m^o due to the change in ΔV_{Cl} is given by

$$\Delta V_m^o = \frac{G_{\text{Cl}}}{G_m} \Delta V_{\text{Cl}} = \frac{1}{1+1+0.1} \cdot 28 = 13.3 \text{ mV}$$

$$\rightarrow V_m^o(0^+) = -59.5 + 13.3 = \boxed{-46.2 \text{ mV}}$$