York University BPHS 4080 (Winter 2020) - HW 3 SOLUTIONS

Questions

1. A cell in a bath is subjected to changes in extracellular osmolarity the flux of the volume can be described by the equation $\phi = \mathcal{L}_V RT(C^o_\Sigma - C^i_\Sigma)$. A step change in the osmolarity of the bath produces a change in the normalized volume of the cell shown in the waveform $v(t)$ depicted below in Figure 1a. In Figure 1b, there are twelve possible normalized concentration waveforms $c(t)$.

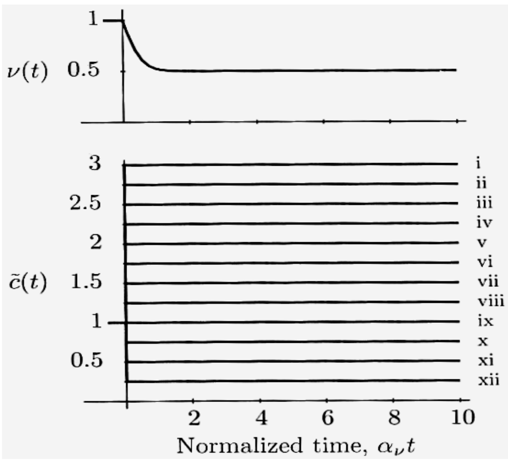


Figure 1a & b: Change in normalized volume (upper panel) in response to a change in normalized external solute concentration (lower panel) (Exercise 4.18). The normalized volume is $\nu(t) = \mathcal{V}^i(t)/\mathcal{V}^{in}$, where $\mathcal{V}^i(t)$ and $\mathcal{V}^{in}$ are the cell water volume and its isotonic value. The normalized extracellular concentration is $\tilde{c}(t) = C^o_\Sigma(t)/C^{on}_\Sigma$, where $C^o_\Sigma(t)$ and C^{on}_Σ are the total extracellular solute concentration and its isotonic value.

Assume that all solutes are impermeant and that the cell acts as an ideal osmometer such that $\mathcal{V}_c = \frac{N^i_\Sigma}{C^o_\Sigma} + \mathcal{V}'_c$, where $\mathcal{V}'_c$ represents the osmotically inactive portion of the total cell volume $\mathcal{V}_c$; it can be assumed that the active portion of the total cell volume is greater than the osmotically inactive portion.

a) From Figure 1b, which of the twelve concentration waveforms can describe the change of the normalized volume waveform in Figure 1a? Explain the choices made and the assumptions involved.

⇒ **Solution (3 points):**

At equilibrium,

$$\mathbf{V_c = \frac{N^i_\Sigma}{C^o_\Sigma} + V'_c}$$

where V'_c is the osmotically inactive portion of the total cell volume and V_c is the total cell volume; it is assumed that the total cell volume is much greater than the osmotically inactive portion. With this assumption made, it can be stated that the initial and final values of the volume are:

$$\mathbf{V_c(0) = \frac{N^i_\Sigma}{C^o_\Sigma(0)} \& V_c(\infty) = \frac{N^i_\Sigma}{C^o_\Sigma(\infty)}}$$

Since the solute is assumed to be impermeant, it can be claimed that N_{Σ}^{i} is constant throughout. Division of both equations and normalization of the concentrations gives the following results:

$$\frac{\mathbf{V_c(0)}}{\mathbf{V_c(\infty)}} = \frac{\mathbf{C_{\Sigma}^{o}(\infty)}}{\mathbf{C_{\Sigma}^{o}(0)}} \ \& \ \mathbf{\tilde{c}(\infty) = 2\tilde{c}(0)}$$

Therefore, the fifth concentration waveform can describe the change of the normalized volume waveform.

b) If the temperature of the cell and bath system was decreased by 10° C, determine mathematically if the initial slope of the normalized volume, $\frac{dv(t)}{dt}$ at $t = 0^{+}$, and the final value of the normalized volume $v(\infty)$ are either increasing, staying the same, or decreasing; ensure to explain the reasoning behind the solution

⇒ **Solution (2 points):**

The flux of water is related to the change in volume by the conservation relation gives as:

$$-\frac{\mathbf{1}}{\mathbf{A(t)}}\frac{\mathbf{dV^{i}(t)}}{\mathbf{dt}} = \phi_{\mathbf{v}} = \mathcal{L}_{\mathbf{V}}\mathbf{RT}(\mathbf{C_{\Sigma}^{o}(t)} - \mathbf{C_{\Sigma}^{i}(t)})$$

If the temperature is decreased, the magnitude of the flux will decrease, and the magnitude of the rate of change of volume will decrease. Hence, the time course of volume change will be slower. The equilibrium condition that C_{Σ}^{o} = C_{Σ}^{i} does not depend upon temperature. Therefore, the equilibrium volume will be unchanged.

2. A spherical cell is subjected to four different aqueous solutions of impermeant solutes and its equilibrium radius is measured as shown in Figure 1. The isotonic radius is 80 μm.

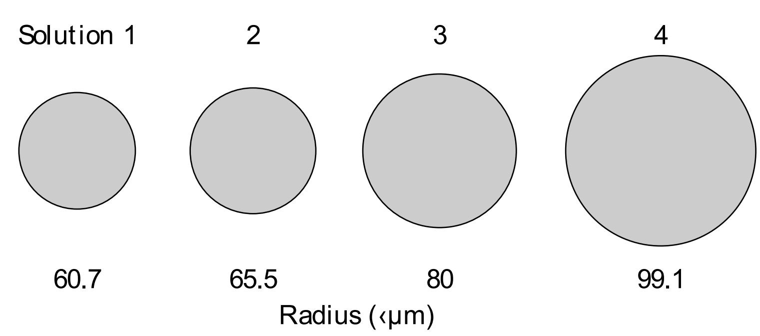


Figure 1: A spherical cell placed in four different solutions of impermeant solutes. The circles represent cross-sectional diagrams of the cell, and the numbers below the circles indicate the measured radii.

The four solutions are: 150 mmol/L NaCl, 200 mmol/L $CaCl_2$, 800 mmol/L sucrose, and 150 mmol/L xylose. The latter two solutes are sugars. You may assume that the intracellular quantity of solute does not change during these measurements.

a) Determine the compositions of Solutions 1-4

⇒ **Solution (5 points):**

If the salts are assumed to dissociate completely so that each mole of NaCl gives rise to 2 moles of ions and that each mole of $CaCl_2$ gives rise to 3 moles of ions, then the osmolarities of the 4 solutions are: NaCl, 300 mosm/L; $CaCl_2$, 600 mosm/L; sucrose, 800 mosm/L; xylose, 150 mosm/L. The order of increasing radius is in the order of decreasing osmolarity. Therefore, solution 1 must be sucrose, solution 2 must be $CaCl_2$, solution 3 must be NaCl, and solution 4 must be xylose. Since the isotonic radius is 80 μm, solution 3 must be an isotonic solution, and the isotonic concentration is therefore 300 mosm/L.

b) Find the total quantity of intracellular solute.

⇒ **Solution (5 points):**

At equilibrium

$$\mathbf{V_c = \frac{4}{3}\pi r_c^3 = \frac{N^i_\Sigma}{C^o_\Sigma} + V'_c}$$

where $\mathbf{r_c}$ is the radius of the cel. Thus, this equation is solved for two of the solutions as follows,

$$\mathbf{\frac{4}{3}\pi(99.1 \times 10^{-4})^3 = \frac{N^i_\Sigma}{150 \times 10^{-6}} + V'_c}$$
$$\mathbf{\frac{4}{3}\pi(60.7 \times 10^{-4})^3 = \frac{N^i_\Sigma}{800 \times 10^{-6}} + V'_c}$$

To find $\mathbf{N^i_\Sigma}$, subtract these two equations and solve to obtain $\mathbf{N^i_\Sigma = 5.8 \times 10^{-10}}$ mol.

c) What fraction of the isotonic volume of the cell is due to osmotically active water?

⇒ **Solution (5 points):**

For an isotonic solution,

$$\mathbf{V^n_c = \frac{N^i_\Sigma}{C^{on}_\Sigma} + V'_c}$$

Therefore, the osmotically active part of the volume is

$$\mathbf{V_c^n - V_c' = \frac{N_\Sigma^i}{C_\Sigma^{on}}}$$

which can be expressed as follows

$$\mathbf{\frac{V_c^n - V_c'}{V_c^n} = \frac{N_\Sigma^i}{C_\Sigma^{on} V_c^n} = \frac{5.8 \times 10^{-10}}{(300 \times 10^{-6})(4/3)\pi(80 \times 10^{-4})^3} \approx \frac{9}{10}}$$

3. Glucose is transported into the body by enterocytes, which are absorptive epithelial cells that line the small intestine. The following figure shows a schematic representation of an enterocyte.

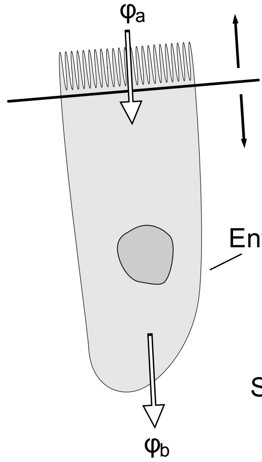


Figure 2:

The cell membrane has an apical part that separates the interior of the cell from the lumen of the intestine and a basal part that separates the interior of the cell from extracellular space on the serosal side. ϕ_a represents the flux of glucose from the lumen of the intestine through the apical part of the cell membrane and into the cell. ϕ_b represents the flux of glucose from the cell through the basal part of the cell membrane and into the extracellular serosal space.

Transport through the apical part of the cell membrane, which faces the lumen of the small intestine, is coupled to the transport of Na^+. Transport through the basolateral membrane of the cell, which faces the serosal side, is via a glucose carrier. Assume that the glucose carrier in the basolateral part of the cell can be represented by the simple, symmetric four-state carrier model. Let K represent the dissociation constant for the binding of glucose to the carrier, and let ϕ_{max} represent the maximum flux through the carriers in the basolateral part of the membrane. Let A_a and A_b represent the areas of the apical and basolateral membranes, respectively. Let V represent the volume of the cell. Assume that $A_a, A_b,$ and V are constant with respect to time. Assume that glucose is not produced, consumed, or bound by any intracellular mechanism.

a) In the steady-state the concentration of glucose in the cell is constant. Determine a relation that ϕ_a and ϕ_b must satisfy in the steady state.

⇒ **Solution (2 points):**

If the concentration of glucose in the enterocyte is constant then the net rate of influx of glucose must be zero. Therefore, $\mathbf{A_a \phi_a = A_b \phi_b}$

b) Determine a relation between ϕ_b and c_s^i and c_s^o dictated by the transport properties of the basolateral membrane, where c_S^o is the extracellular concentration of glucose on the serosal side of the membrane.

⇒ **Solution (3 points):**

Since the transport of glucose through the basolateral membrane can be represented by a simple, symmetric, four-state carrier model, the relation of efflux to concentration is

$$\mathbf{\phi_b = \phi_{max} \left(\frac{c_s^i}{c_s^i + K} - \frac{c_s^o}{c_s^o + K} \right)}$$

c) Assume that the flux ϕ_a from the lumen of the intestine into the cell is constant and that the concentration of glucose on the serosal side is zero, $c_s^o = 0$. Using the results of parts a) and b), determine an expression for $c_s^i(\infty)$ in terms of $\phi_a, \phi_{max}, K, A_a,$ and A_b.

⇒ **Solution (5 points):**

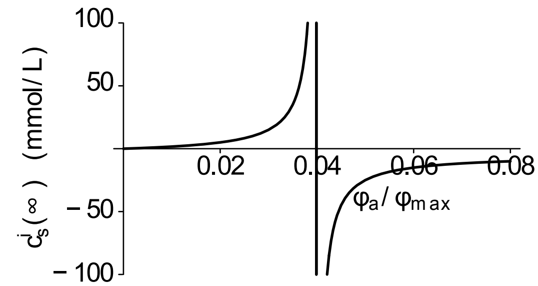
For $\mathbf{c_s^o = 0}$, combining expressions yields

$$\mathbf{A_a \phi_a = A_b \phi_{max} \left(\frac{c_s^i}{c_s^i + K} \right)}$$

To solve for $\mathbf{c_s^i}$, it is easiest to divide both sides of the equation by $\mathbf{A_b \phi_{max}}$, invert both sides of the equation and solve for $\mathbf{1/c_s^i}$ and hen take the reciprocal to obtain

$$\mathbf{c_s^i = K \frac{(A_a \phi_a / A_b \phi_{max})}{1 - (A_a \phi_a / A_b \phi_{max})}}$$

d) $c_s^i(\infty)$ is plotted versus ϕ_a/ϕ_{max} for $c_s^o = 0, K = 5$ mmol/L and for $A_a/A_b = 25$ in the following figure.



i) Explain the *physical significance* of the value of $c_s^i(\infty)$ when $\phi_a = 0$.

⇒ **Solution (5 points):**

Note when $\phi_\mathbf{a} = 0, \mathbf{c_s^i}(\infty) = 0$. This is apparent from the results of part c and is consistent with the plot shown in the problem. The physical explanation is that when the apical flux is zero, the basolateral flux is zero. Hence, for zero glucose flux through the basolateral membrane, the intracellular concentration must equal the extracellular concentration of glucose which is zero.

ii) Note from the figure that $c_s^i(\infty)$ increases rapidly as ϕ_a/ϕ_{max} increases from 0 to 0.04. Give a *physical interpretation* for this result.

⇒ **Solution (5 points):**

In steady state, as the total rate of influx of glucose in the apical region $\mathbf{A_a}\phi_\mathbf{a}$ increases, the efflux through the basolateral region increases to equal the influx. A higher efflux in the basolateral membrane occurs at higher intracellular concentrations of glucose. As the efflux is driven toward saturation, a small increment in efflux requires a large increment in intracellular glucose concentration. A steady-state solution exists provided the influx through the apical membrane is less than the maximum efflux through the basolateral membrane $\mathbf{A_b}\phi_\mathbf{max}$

iii) For $\phi_a/\phi_{max} > 0.04, c_s^i(\infty) < 0$. What is the *physical significance* of this result?

⇒ **Solution (5 points):**

When the influx exceeds the maximum efflux, i.e., when $\mathbf{A_a}\phi_\mathbf{a} > \mathbf{A_b}\phi_\mathbf{max}$, the enterocyte can no longer transport glucose out of the basolateral membrane fast enough to match the rate of influx through the apical membrane. Hence, no steady state is possible for $\phi_\mathbf{a}/\phi_\mathbf{max} > \mathbf{A_b}/\mathbf{A_a} = 1/25$. This accounts for the unphysical result in this region, which is that the equations are satisfied only for negative values of the intracellular concentration.

4. Three compartments are separated from each other by semi-permeable membranes, as illustrated in the following figure.

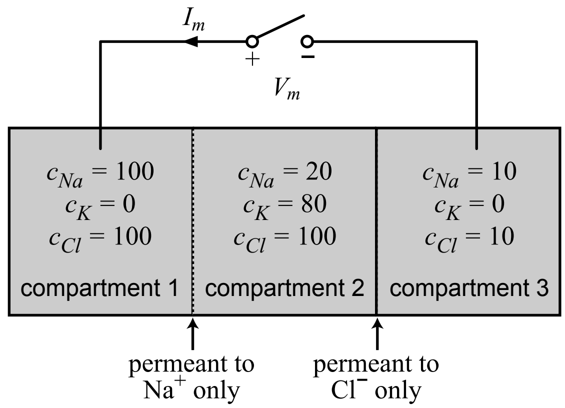


Figure 3:

Each compartment contains well-stirred solutions of sodium, potassium, and chloride ions, with concentrations indicated in the figure (in mmol/L). The membrane between compartment 1 and 2 is permeant to sodium ions only, and its specific electrical conductivity G_{Na} is 5 mS/cm^2. The membrane between compartment 2 and 3 is permeant to chloride ions only, and its specific electrical conductivity G_{Cl} is 2 mS/cm^2. Both membranes have areas $A = 10$ cm^2.The temperature T is such that $RT/(F \log e)$ = 60 mV.

a) Sketch an electrical circuit that represents the steady-state relation between current and voltage for the three compartments. Label the nodes that correspond to compartments 1, 2, and 3. Include the switch in your sketch. Label I_m, V_m and the conductances.

⇒ **Solution (5 points):**

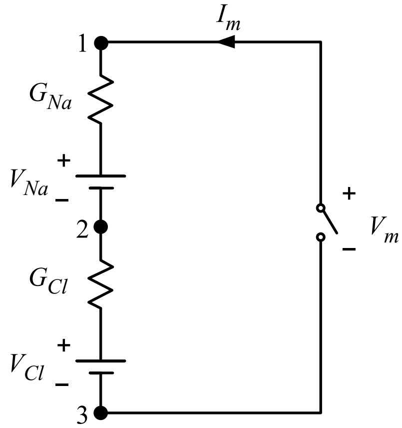


Figure 4:

b) Let V_1 and V_2 represent the steady-state potentials in compartments 1 and 2 with reference to compartment 3 when the switch is open. Calculate numerical values for V_1 and V_2

⇒ **Solution (5 points):**

$$\mathbf{V_{Na} = \frac{RT}{z_{Na}\, F\, \log e} \log_{10} \frac{c^{o}_{Na}}{c^{o}_{Na}} = (60mV)\log_{10}\frac{20}{100} = -42mV}$$

$$\mathbf{V_{Cl} = \frac{RT}{z_{Cl}\, F\, \log e} \log_{10} \frac{c^{o}_{Cl}}{c^{i}_{Cl}} = (-60mV)\log_{10}\frac{10}{100} = 60mV}$$

$$\mathbf{V_1 = V_{Na} + V_{Cl} = -42 + 60 = 18mV}$$

$$\mathbf{V_2 = V_{Cl} = 60mV}$$

c) Compute the steady-state value of the current I_m when the switch is closed.

⇒ **Solution (5 points):**

$$\mathbf{V_m = I_m R_{Na} + V_{Na} + I_m R_{Cl} + V_{Cl}}$$

$$\mathbf{\rightarrow I_m = \frac{V_m - V_{Na} - V_{Cl}}{R_{Na} + R_{Cl}}}$$

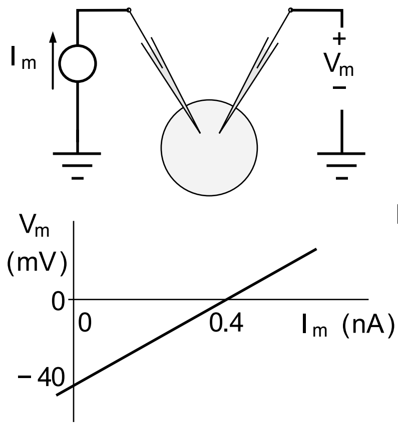
where

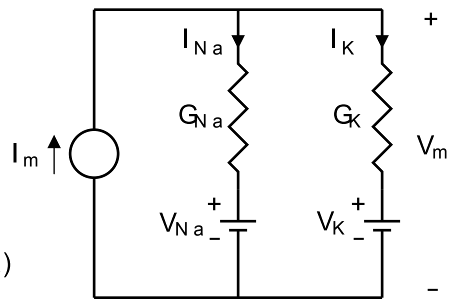
$$\mathbf{R_{Na} = \frac{1}{AG_{Na}} = \frac{1}{(10cm^2)(5mS/cm^2)} = \frac{1}{50mS} = 20\Omega}$$
$$\mathbf{R_{Cl} = \frac{1}{AG_{Cl}} = \frac{1}{(10cm^2)(2mS/cm^2)} = \frac{1}{20mS} = 50\Omega}$$

Also, when the switch is closed, $\mathbf{V_m = 0}$ so,

$$\mathbf{I_m = \frac{42mV - 60mV}{20\Omega + 50\Omega} = -0.26mA}$$

5. The ionic concentrations of a uniform isolated cell are given in the following table.





	Concentration (mmol/L	
	Inside	Outside
Potassium	150	15
Sodium	15	150

An electrode is inserted into the cell and connected to a current source so that the current through the cell membrane is I_m. The steady-state voltage across the cell membrane V_m is determined as a function of the current as shown in the following figure.
Assume that: (1) the cell membrane is permeable to only K^+ and Na^+ ions; (2) the Nernst equi- librium potentials are $V_n = (60/z_n)\, log_{10} \left(c_n^o / c_n^i\right)$ (mV); (3) ion concentrations are constant; (4) active transport processes make no contribution to these measurements.

a) Determine the equilibrium potentials for sodium and potassium ions, V_{Na} and V_K.

⇒ **Solution (5 pts):**

The Nernst equilibrium potentials are

$$\mathbf{V_K = 60 \log_{10}\left(\frac{15}{150}\right) = -60\ mV}$$

$$\mathbf{V_{Na} = 60 \log_{10}\left(\frac{150}{15}\right) = +60\ mV}$$

b) What is the resting potential of the cell with these ionic concentrations?

⇒ **Solution (5 pts):**

Note that when $\mathbf{I_m = 0, V_m = V_m^o = -40\ mV}$.

c) With the current I_m adjusted so that $V_m = V_K$, what is the ratio of the sodium current to the total membrane current, I_{Na}/I_m?

⇒ **Solution (5 pts):**

When $\mathbf{V_m = V_K, I_K = 0}$. Therefore $\mathbf{I_m = I_{Na}}$ or $\mathbf{I_{Na}/I_m = 1}$.

d) What is the total conductance of the cell membrane $\mathcal{G}_m = \mathcal{G}_{Na} + \mathcal{K}$?

⇒ **Solution (5 pts):**

The slope of the curve that relates $\mathbf{V_m}$ to $\mathbf{I_m}$ equals the total resistance of the membrane. Hence, the reciprocal is the membrane conductance.

$$\mathcal{G}_\mathbf{m} = \frac{\mathbf{0.4 \times 10^{-9}}}{\mathbf{40 \times 10^{-3}}} = \mathbf{10\ nS}$$

e) Determine $\mathcal{G}_{Na}$ and $\mathcal{G}_K$.

⇒ **Solution (5 pts):**

The resting potential of the cell is related to the ion conductances and Nernst equilibrium potentials by the relation

$$\mathbf{V_m^o} = \frac{\mathcal{G}_\mathbf{K}}{\mathcal{G}_\mathbf{K} + \mathcal{G}_\mathbf{Na}}\mathbf{V_K} + \frac{\mathcal{G}_\mathbf{Na}}{\mathcal{G}_\mathbf{K} + \mathcal{G}_\mathbf{Na}}\mathbf{V_{Na}}$$

In addition, $\mathcal{G}_\mathbf{K} + \mathcal{G}_\mathbf{Na} = \mathbf{10\ nS}$. Combining these two equations yields

$$-\frac{\mathbf{40}}{\mathbf{6}} = -\left(\mathbf{10} - \mathcal{G}_\mathbf{Na}\right) + \mathcal{G}_\mathbf{Na}$$

Hence, $\mathcal{G}_\mathbf{Na} = \mathbf{5/3\ nS}$ and $\mathcal{G}_\mathbf{K} = \mathbf{25/3\ nS}$. These results fit with the fact that the resting potential is much closer to the potassium than to the sodium equilibrium potential. Hence, we expect the potassium conductance to greatly exceed the sodium conductance.