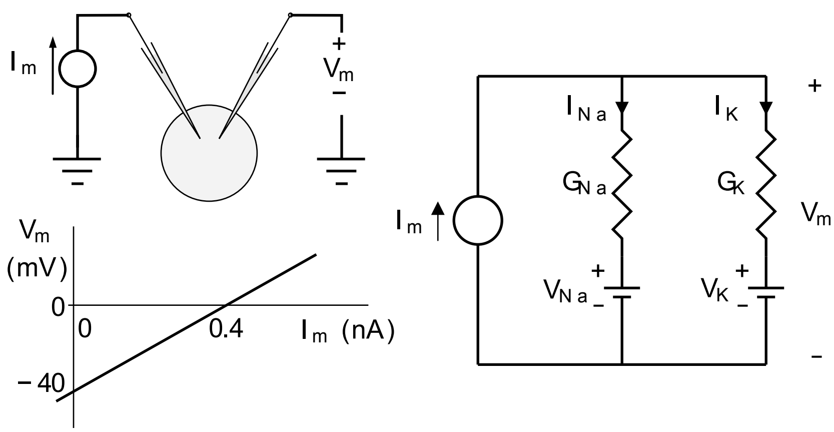
Questions

1. 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?

$\Rightarrow$ **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?

$\Rightarrow$ **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 $\mathcal{G}_m = \mathcal{G}_{Na} + \mathcal{K}$?

$\Rightarrow$ **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.

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

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

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

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

Hence, $\mathcal{G}_\mathbf{Na} = 5/3$ nS and $\mathcal{G}_\mathbf{K} = 25/3$ 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.

2. The membrane of a cell is known to contain sodium/potassium pumps and supports passive electrodiffusion of sodium, potassium, and chloride ions. The potassium conductivity is 8 times the sodium conductivity. The sodium/potassium pump drives 3 molecules of sodium outward for every 2 molecules of potassium that is driven inward. The cell is allowed to come to quasi-equilibrium in a very large bath that contains 460 mmol/L Na^+, 40 mmol/L K^+, and 500 mmol/L Cl^-. At quasi-equilibrium, the cell contains 400 mmol/L K^+ and unknown concentrations of Na^+ and Cl^-. The cells volume is constant, so there is no water transport across the cell membrane. The resting potential is -50 mV.

a) Determine the concentration of chloride ion inside the cell or explain why it cannot be determined from the available information.

⇒ **Solution (5 pts):**

Since there are no chloride pumps, there is no active transport of chloride ions. For quasi-equilibrium, it follows that the passive transport of choride ions must also be zero. Therefore, the Nernst potential for chloride must equal the resting potential of the membrane, so that

$$\mathbf{V_m^o = V_{Cl} = \frac{RT}{z_{Cl}F} \ln \frac{c_{Cl}^o}{c_{Cl}^i} = \frac{RT}{F} \ln \frac{c_{Cl}^o}{c_{Cl}^i}}$$

Assuming that the temperature is such that $(\mathbf{RT/F}) \ln(\mathbf{10}) = \mathbf{60}$ mV, then

$$\mathbf{\log \frac{c_{Cl}^i}{c_{Cl}^o} = \frac{-50 \text{ mV}}{60 \text{ mV}}}$$

Thus

$$\mathbf{c_{Cl}^i = c_{Cl}^o \times 10^{-5/6} \approx 500 \text{ mmol/L} \times 0.147 \approx 73.4 \text{ mmol/L}}$$

Notice that since the intracellular concentration of chloride is smaller than that of potassium, there must be other negative species for electroneutrality. Real cells contain significant concentrations of charged macromolecules (containing proteins and sugar groups) that are typically negatively charged. Real cells also contain specialized transport mechanisms for chloride ions, which are not considered in this problem.

b) Determine the Nernst equilibrium potential for sodium or explain why it cannot be deter- mined from the available information.

⇒ **Solution (5 pts):**

Assume that the outward current density due to sodium being pumped out of the cell is 3α and the outward current density due to potassium being pumped into the cell is -2α. If the sum of the active and passive transports of sodium is to be zero, it follows that

$$\mathbf{G_{Na} (V_m^o - V_{Na}) + 3\alpha = 0}$$

Similarly, if the sum of the active and passive transports of potassium is to be zero, it follows that

$$\mathbf{G_K\left(V_m^o - V_K\right) - 2\alpha = 0}$$

Solving each of these equations for α and then taking the ratios of the resulting equations yields

$$\mathbf{\frac{3}{2} = \frac{G_{Na}}{G_K} \times \frac{V_{Na} - V_m^o}{V_m^o - V_K}}$$

Setting the ratio of the conductances to $1/8$, $\mathbf{V_m^o} = -50$ mV, and $\mathbf{V_K} = -60$ mV (since the internal concentration is 10 times the external concentration), we can solve for $\mathbf{V_{Na}}$ to get

$$\mathbf{V_{Na} = 13\,(-50)\ \ mV\ + 12\,(60)\ \ mV\ = 70\ mV}$$

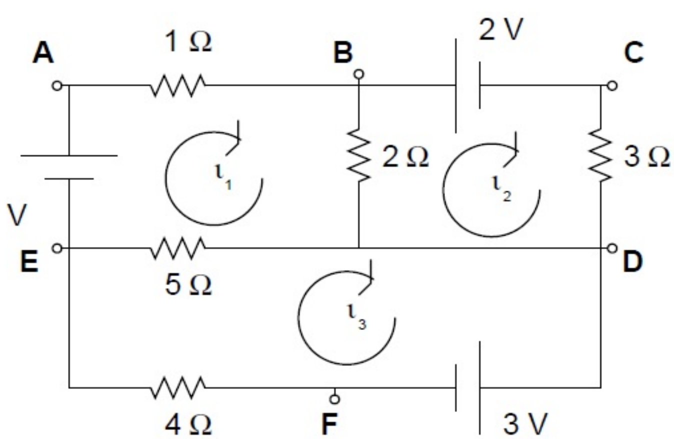
c) The pump is blocked by adding a trace concentration of ouabain to the bath. The cell quickly reaches a new resting potential. Is the new resting potential greater than, less than, or the same as the old resting potential? Explain.

⇒ **Solution (5 pts):**

Since the pump moves 3 sodium ions out of cell for every 2 potassium ions into the cell, the pump is electrogenic. Furthermore, the sum of the active currents is positive (outward). Outward active currents tend to hyperpolarize the cell membrane since

$$\mathbf{V_m^o = \sum_n \left(\frac{G_n}{G_m}\right) V_n - \frac{1}{G_m}\sum_n J_n^a}$$

3. In circuit analysis, mesh equations are used to solve any given system regardless of complexity; these equations stem from Kirchhoff's laws. Specifically, Kirchhoff's voltage laws are used to write loop equations to solve for the unknown loop currents. For the following questions, refer to the figure below:



a) Determine the mesh equations using Kirchhoff's Voltage Law by using the following defined points to form the loops (ie. the ABDE loop, the BCDB loop & EDFE loop)

⇒ **Solution (5 pts):**

For the ABDE loop, the mesh equations using Kirchhoff's Voltage Law are:

$$(\mathbf{V_A - V_B}) + (\mathbf{V_B - V_D}) + (\mathbf{V_D - V_E}) + (\mathbf{V_E - V_A}) = \mathbf{0}$$

$$\mathbf{i_1 + 2(i_1 - i_2) + 5(i_1 - i_3) + (-1V) = 0}$$

$$\mathbf{8i_1 - 2i_2 - 5i_3 = 1}$$

For the BCDB loop, the mesh equations using Kirchhoff's Voltage Law are:

$$(\mathbf{V_B - V_C}) + (\mathbf{V_C - V_D}) + (\mathbf{V_D - V_B}) = \mathbf{0}$$

$$\mathbf{(2V) + 3i_2 + 2(i_2 - i_1) = 0}$$

$$\mathbf{-2i_1 + 5i_2 = -2}$$

For the EDFE loop, the mesh equations using Kirchhoff's Voltage Law are:

$$(\mathbf{V_E - V_D}) + (\mathbf{V_D - V_F}) + (\mathbf{V_F - V_E}) = \mathbf{0}$$

$$\mathbf{5(i_3 - i_1) + (3V) + 4i_3 = 0}$$

$$\mathbf{-5i_1 + 9i_3 = -3}$$

b) Solve the created mesh equations for the currents i_1, i_2, and i_3; ensure that the solution is in accordance with the direction notation seen in the above figure (ie. the currents flow clockwise)

⇒ **Solution (5 pts):**

One way to solve the given mesh equations is to take the BCDB equation & EDFE equation and re-arrange them to put i_2 and i_3 in terms of only i_1, therefore giving you the following:

$$\mathbf{i_2 = -\frac{2}{5} + \frac{2i_1}{5}}$$

$$\mathbf{i_3 = -\frac{3}{9} + \frac{5i_1}{9}}$$

Now take the expression for i_2 and i_3 and plug them into the mesh equation for the ABDE loop, allow for the current i_1 to be solved for such that:

$$\mathbf{8i_1 - 2(-\frac{2}{5} + \frac{2i_1}{5}) - 5(-\frac{3}{9} + \frac{5i_1}{9}) = 1}$$

$$\mathbf{8i_1 + \frac{4}{5} - \frac{4i_1}{5} + \frac{15}{9} - \frac{25i_1}{9} = 1}$$

$$\mathbf{360i_1 + 36 - 36i_1 + 75 - 125i_1 = 45}$$

$$\mathbf{199i_1 = -66}$$

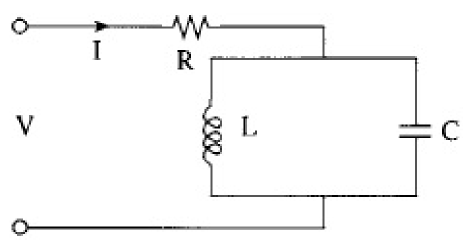
$$\mathbf{i_1 = -0.33A}$$

Now taking the expression for i_1 and plugging them back into the mesh equation for the BCDB & EDFE loops allows for the currents i_2 and i_3 to be solved for such that:

$$\mathbf{-2(-0.33A) + 5i_2 = -2 \ \& \ -5(-0.33A) + 9i_3 = -3}$$

$$\mathbf{i_2 = -0.532A \ \& \ i_3 = -0.516A}$$

4. An RLC circuit consists of a resistor, an inductor, and a capacitor, connected in series or in parallel. The circuit forms a harmonic oscillator for current and will resonate; however, the presence of the resistor forces any oscillation induced in the circuit to die away over time if it is not kept going by a source.



a) What is impedance, and what are the components that compose the real and imaginary parts of impedance? List the impedances of the components involved in the circuit shown above.

⇒ **Solution (2 pts):**

Impedance can be defined mathematically as the complex ratio of the voltage to the current in an alternating current circuit. The magnitude of impedance is the ratio of the voltage to current amplitude whereas the phase of impedance is the phase shift by which the current lags the voltage. Resistance is the real part of impedance (ie. a device with a purely resistive impedances such as a plain resistor creates no phase shift between the voltage and current), whereas reactance is the imaginary part of the impedance (ie. a component with a finite reactance induces a phase shift θ between the voltage and the current).

For the above components, the following holds true:

$$\mathbf{Z_{resistor} = R\ ,\ Z_{capacitor} = -j\frac{1}{\omega C} = \frac{1}{j\omega C}\ ,\ \&\ Z_{inductor} = j\omega L}$$

b) An AC source is now connected at the input terminals wihtin the circuit shown above; this source drives a sinusoidal voltage $v_s = V_s \cdot sin(\omega t)$, where v_s denotes the source voltage, V_s the amplitude, and ω the angular frequency of the sinusoid. What is the total impedance of the circuit shown above to the AC source?

⇒ **Solution (3 pts):**

It can be noted that when dealing with impedances, the same principle which applies to summing parallel/series resistances can be utilized. Therefore, the net impedance of the capacitor in parallel with the inductor can be expressed as:

$$\mathbf{\frac{1}{Z_{LC}} = \frac{1}{Z_L} + \frac{1}{Z_C} \;\therefore\; Z_{LC} = \frac{Z_L \cdot Z_C}{Z_L + Z_C} = \frac{j\omega L \cdot \frac{1}{j\omega C}}{\frac{1}{j\omega C} + j\omega L} = \frac{j\omega L}{1 - \omega^2 LC}}$$

Given this result, it can be added in series with the impedance of the resistor in the circuit to give the net impedance of the circuit towards the AC source

$$\mathbf{Z_{net} = R + \frac{j\omega L}{1 - \omega^2 LC}}$$

5. A number of cellular processes depend on the intracellular concentrations of ions, such as the catalytic action of certain cytoplasmic enzymes, as well as many secretory processes where the cell secretes chemical compounds into the extracellular environs.

a) Define the *Nernst equilibrium potential*, and explain its physical basis. Can an electric potential across the membrane exist without a measurable difference in the global concentration of positive and negative ions across the membrane? Explain.

⇒ **Solution (2 pts):**

The Nernst equilibrium potential defines the condition for equilibrium of an ion across a membrane permeable to that ion. The condition is given as:

$$\mathbf{V_n = \frac{RT}{z_n F} \cdot \ln\left(\frac{c_n^o}{c_n^i}\right)}$$

where V_n is the Nernst equilibrium potential defined as the inside minus the outside potential across the membrane, R is the molar gas constant, T is the absolute temperature, z_n is the valence of ion n, F is Faraday's constant, and c_n^o & c_n^i are the concentrations of ion n on the outside and inside of the membrane, respectively.

When the potential across the membrane equals the Nernst equilibrium potential, the passive flux of that ion is zero. The physical bases of the equilibrium arises because ions are transported by diffusion resulting from a difference of concentration and by drift due to the presence of an electric field across the membrane. When the fluxes due to drift and diffusion are equal and oppositely directed, the net flux is zero and equilibrium occurs.

When quantitatively analyzing any given membrane potential, electroneutrality is assumed;this implies that there is no measurable charge excess on either side of the membrane; although

there is an electric potential across the membrane due to the charge separation, there is no actual measurable difference in the overall concentration of positive and negative ions across the membrane (ie. there is no actual measurable charge excess in either side). This phenomenon occurs because the effect of charge on electrochemical potential is hugely greater than the effect of concentration; therefore, an undetectable change in concentration can create a great change on electric potential.

b) Active ion transport within an organism in a process that is capable of having a direct and an indirect effect on the resting potential of the organism. Define both effects, and explain the distinction between them.

⇒ **Solution (3 pts):**

The direct effect of active transport on the membrane potential of a cell results when the active transport mechanism transports a net current across the membrane. This contributes a component of the membrane potential that is directly attributable to active transport in the sense that if the current source is eliminated (e.g. by a specific blocker substance), the contribution of the active transport mechanism to the membrane potential goes rapidly to zero.

The indirect effect results because if the active transport mechanism is blocked, then ions will flow down their electrochemical potential gradients to reduce these gradients. Hence, ion concentrations will change which will result in changes in the Nernst equilibrium potentials of the permeable ions.

The changes in Nernst equilibrium potentials will result in a change in the resting value of the membrane potential. Because, it takes time for the ion concentrations to change appreciably, the change in potential that results from the indirect effect takes longer to be manifested than that caused by the direct effect.