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2.791J/2.794J/6.021J/6.521J/20.370J/20.470J/HST.541J

Quantitative Physiology: Cells and Tissues

Homework Assignment #5

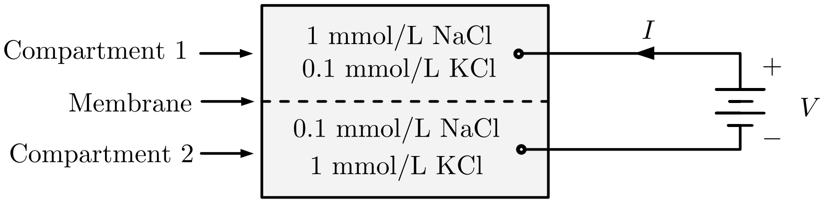
Issued: October 13, 2006
Due: October 26, 2006

This homework assignment covers two weeks of lectures and recitations.

Exercise 1. Define the Nernst equilibrium potential and briefly explain its physical basis.

Exercise 2. Active ion transport is said to have a *direct* and an *indirect* effect on the resting potential of a cell. Define both effects and discuss the distinction between the two effects.

Exercise 3. Two compartments of a fluid-filled chamber are separated by a membrane as shown in the following figure.



The 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 $I = -1$ mA.

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

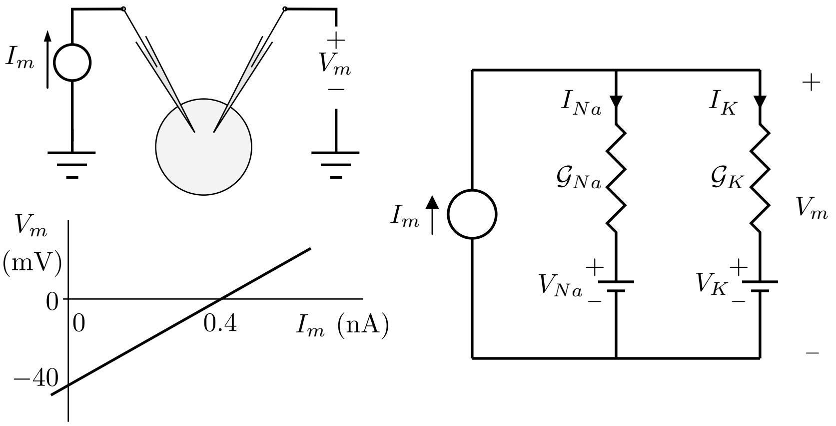
b) Draw an equivalent circuit for the entire system, including the battery. Indicate values for those components whose values can be determined.

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

Exercise 4. 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 equilibrium potentials are $V_n = (60/z_n)\log_{10}(c_n^o/c_n^i)$ (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.

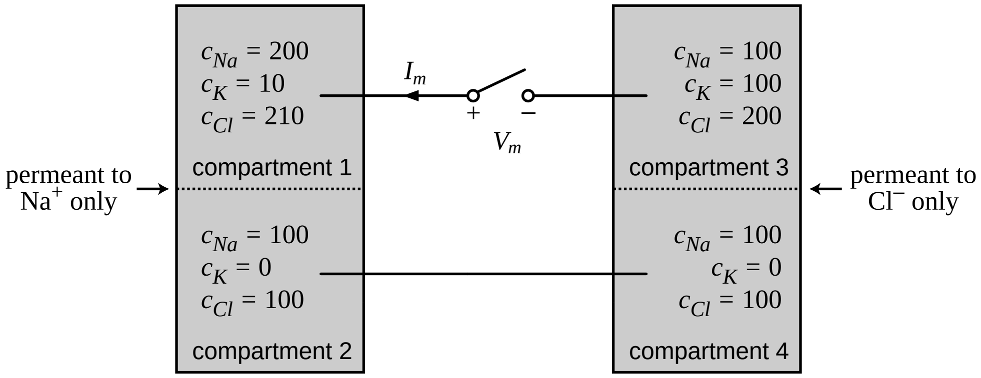
b) What is the resting potential of the cell with these ionic concentrations?

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?

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

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

Problem 1. Two chambers are each divided into two parts by semi-permeable membranes, as illustrated in the following figure.



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 3 and 4 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. Electrodes in chambers 2 and 4 are connected via a wire. Electrodes in chambers 1 and 3 are connected through a switch with wires.

a) Sketch an electrical circuit that represents the steady-state relation between current and voltage for the four compartments. Label the nodes that correspond to compartments 1, 2, 3, and 4. Include the switch in your sketch. Label I_m, V_m, and the conductances.

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.

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

Problem 2. The membrane of a cell contains an active transport mechanism that pumps three sodium ions out of the cell for every two potassium ions that it pumps into the cell. The membrane also supports the passive transport of sodium and potassium ions, but is impermeant to all other ions and is impermeant to water. The sodium conductivity is 10^{-5} S/cm^2 and the potassium conductivity is 10^{-4} S/cm^2. The cell is allowed to come to steady state and its membrane potential is -52.5 mV. The Nernst equilibrium potential for sodium is 60 mV and the Nernst equilibrium potential for potassium is -60 mV. The net outward current density due to active transport is $\frac{3}{8}$ μA/cm^2.

a) Draw an electrical circuit to represent ionic transport across the membrane of this cell. Include labels for each of the 6 numbered parameters provided in the problem statement.

b) Is the cell at rest? If yes, prove that it is at rest. If no, explain why not.

c) Is the cell in quasi-equilibrium? If yes, prove that it is at quasi-equilibrium. If no, explain why not.

d) Is the active transport mechanism electrogenic? Explain.

Problem 3. A uniform, isolated, small cell has a membrane that is permeable to sodium and potassium ions only and contains an active transport mechanism that transports 3 sodium ions outward and 2 potassium ions inward for every molecule of ATP split into ADP and phosphate. Summed over the entire membrane of this cell, the active transport system splits 10^{-17} moles of ATP per second. Assume that the cell is at quasi-equilibrium so that the concentrations of all ions are constant. The cell has a total membrane conductance of 10^{-10} siemens. The temperature is 24°C. The ionic concentrations of sodium and potassium across the membrane are given in the following table.

Ion	Concentration (mmol/L)	
	Internal	External
Sodium	15	106
Potassium	150	3

The potassium conductance exceeds the sodium conductance of this cell.

a) Determine the value of the component of the resting membrane potential, V_m^o, that is attributable directly to active transport.

b) Determine the value of the resting membrane potential, V_m^o.

c) Determine the values of the sodium, $\mathcal{G}_{Na}$, and potassium, $\mathcal{G}_K$, conductances of the membrane.

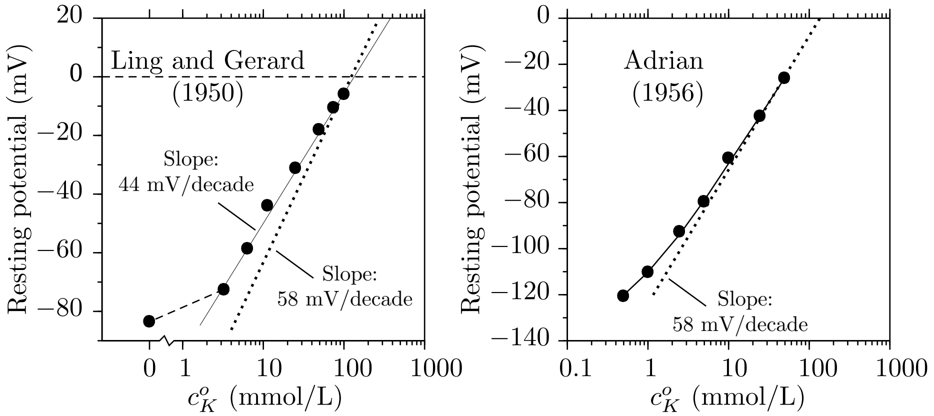


Figure 1: Two sets of measurements [Ling and Gerard, 1950; Adrian, 1956] of the dependence of the resting potential of frog sartorius muscle fibers on external potassium concentration c_K^o. The dashed lines have slopes predicted for a perfect potassium electrode.

Problem 4. Figure 1 shows two sets of measurements of the resting potential of frog sartorius muscle fibers as a function of the potassium concentration in the extracellular Ringer's solution. One set of measurements [Ling and Gerard, 1950] were among the first measurements obtained with intracellular micropipets, the other measurements [Adrian, 1956] were obtained later. In both experiments, the potassium concentration was varied by substituting equimolar quantities of KCl for NaCl in the Ringer's solution bathing the muscle. While the two sets of measurements are qualitatively similar, there are quantitative differences. For example, the slopes of the measurements at large c_K^o differ; the data of Ling and Gerard fall on a line with a slope of 44 mV/decade, whereas those of Adrian approach a line with a slope of 58 mV/decade as would be expected for a perfect potassium electrode.

Assume that the total membrane conductance of the sartorius muscle fiber is $\mathcal{G}_m = 2 \times 10^3$ S, and that the intracellular concentration of ions did not change during the measurements shown in Figure 1.

a) For Adrian's measurements:

   i) Estimate the potassium conductance $\mathcal{G}_K$ for large values of c_K^o;

   ii) Estimate the intracellular concentration of potassium c_K^i.

b) For the purposes of this part of the problem, assume that the measurements of Adrian accurately represent the relation between resting potential and extracellular potassium concentration for frog sartorius muscle fibers. The purpose of this part is to evaluate the hypothesis that in the measurements of Ling and Gerard penetration of the muscle cell membrane by a micropipet introduced an appreciable leakage path between the inside and the outside of the muscle cell. This leakage path was assumed to be caused by the hole in the membrane created by, but not filled by, the micropipet.

   i) For the measurements of Ling and Gerard, construct an electric network model that consists of two conductances and two batteries and that takes the possibility of the leakage path into account. Explain what each element represents.

ii) Determine all 4 elements from the measurements at high c_K^o. For all elements whose values are constant, evaluate the constant. For all elements whose values are not constant, simplify the expression as much as possible.

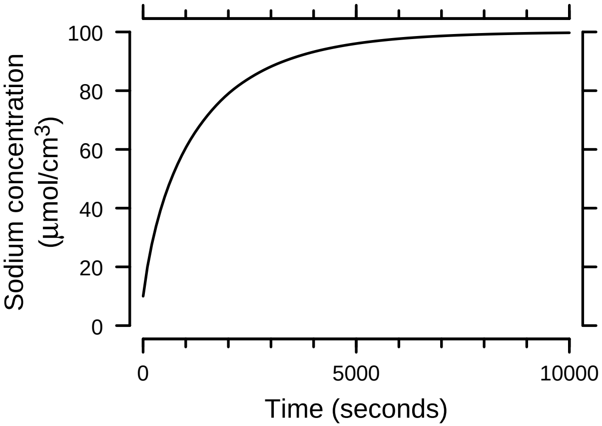
iii) Discuss whether or not your calculations support or contradict the hypothesis about the Ling and Gerard measurements.

iv) Which features of the measurements, if any, will your model not explain?

Problem 5. The membrane of a uniform cell is known to transport sodium, potassium, and chloride ions by passive electrodiffusion. The specific sodium and potassium conductances, G_{Na} and G_K, are equal (both have units of S/cm^2). The specific chloride conductance is G_{Cl}. The membrane is permeable to water: the hydraulic conductivity is $\mathcal{L}_{\mathcal{V}}$ [cm/s]. The membrane also has symmetric pumps that each transport 1 sodium ion out of the cell and 1 potassium ion into the cell on every cycle. The pumping rate for each pump is α cycles per second. The density of pumps is $\mathcal{N}$ pumps per cm^2. The cell contains only potassium ions (100 mmol/L), sodium ions (10 mmol/L), and chloride ions (110 mmol/L). It is placed in a large bath (volume much greater than that of the cell) that contains only potassium ions (10 mmol/L), sodium ions (100 mmol/L), and chloride ions (110 mmol/L). The cell membrane is freely distensible and can support no hydraulic pressure difference between the inside and outside of the cell. The cell is spherical and has a radius a. Assume that the temperature is such that $(RT)/(F \log e)$ is 60 mV.

Part a. Assume that the cell is in quasi-equilibrium with the bath. Determine V_m. Also, determine an expression for the pump rate α in terms of the other cell parameters.

Part b. At $t = 0$, ouabain is added to the bath, and the pump is immediately blocked (α goes to zero). Sodium concentration inside the cell begins to increase, as shown in the plot below.



Determine the sodium conductance G_{Na}.

Part c. With the pump blocked, an impermeant, uncharged protein is injected into the cell so that its concentration is 50 μmol/cm^3 at $t = 0$. Can this cell reach equilibrium? If yes, what are V_m, c_K^i, c_{Na}^i, and c_{Cl}^i at equilibrium? If no, why not?

References

[Adrian, 1956] Adrian, R. H. (1956). The effect of internal and external potassium concentration on the membrane potential of frog muscle. *J. Physiol.*, 133:631–658.

[Ling and Gerard, 1950] Ling, G. and Gerard, R. W. (1950). External potassium and membrane potential of single muscle fibres. *Nature*, 165:113–114.