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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 #5   Issued: October 14, 2004
                                               Due: October 21, 2004

Reading
    Lecture 17 — Volume 2: Chapter 1
    Lecture 18 — Volume 2: 2.1-2.4.2
    Lecture 19 — Volume 2: 2.4.3-2.5

Announcements

The recitation on October 19 is cancelled so that we can meet that evening for a Writing Clinic. The Writing Clinic will be held from 7:30 to 9:30 PM. Please return your written critiques of your peer's laboratory report at that time. You will also receive critiques from the technical and writing staffs.

Exercise 1. 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 2. Describe the distinctions between the following terms that refer to ion transport across a cellular membrane: electrodiffusive equilibrium, steady-state, resting conditions, and cellular quasi-equilibrium.

Exercise 3. Figure 1 shows measurements of the resting potential of a glial cell for different values of extracellular potassium concentration (left panel). These measurements are to be interpreted in terms of the network model shown in the right panel of the same figure. Assume that $c_{Na}^o = 150$
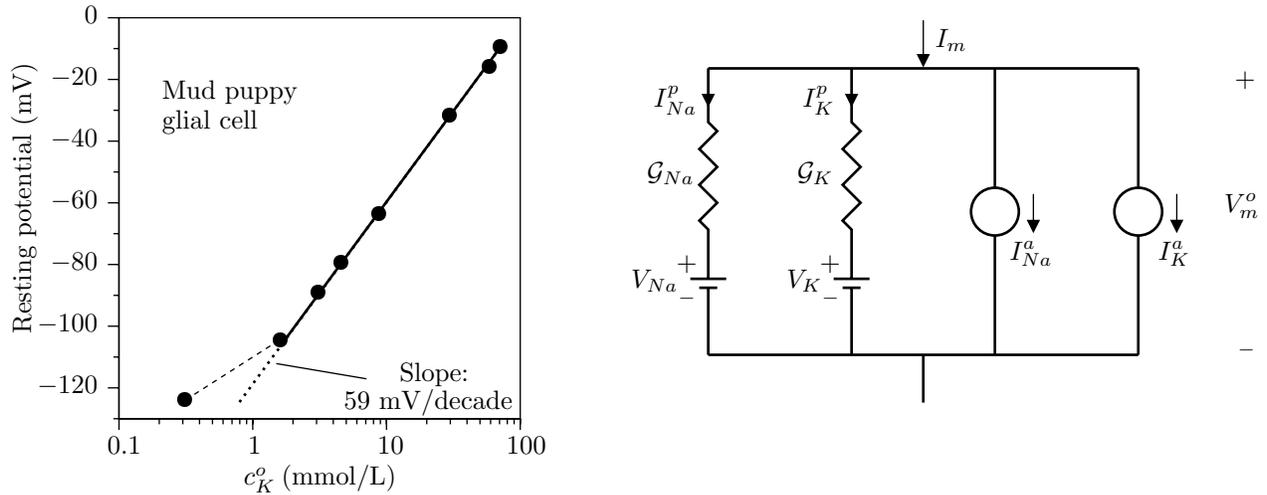
Figure 1: Measurements and model of electrical responses of a glial cell.

mmol/L, $c_{Na}^i = 15$ mmol/L and that the external solution is maintained isotonic with the cytoplasm by controlling impermeant solutes. Assume that sodium and potassium concentrations are constant, except for c_K^o, and that the pump system, which consists of I_{Na}^a and I_K^a, is nonelectrogenic.

a) Consider only the region for which the data are well fit by the straight line of slope 59 mV/decade. Indicate whether the following statements are true or false and give a brief reason for each answer.

    i) $I_m = 0$.

    ii) $V_m^o \approx V_K$.

    iii) $\mathcal{G}_{Na} \gg \mathcal{G}_K$.

    iv) $V_{Na} > V_K$.

    v) $c_K^i = 100$ mmol/L.

    vi) $I_K^a = -I_{Na}^a$.

    vii) $I_K^p = -I_{Na}^p$.

    viii) $I_{Na}^a = -\mathcal{G}_{Na}(V_m^o - V_{Na})$.

b) It is proposed that deviation of the data from the straight line for the lowest c_K^o is a result of a change in $\mathcal{G}_K$ that occurs when $V_m^o < -110$ mV. For the data shown, is this a reasonable hypothesis? Does it require that $\mathcal{G}_K$ for $V_m^o = -125$ mV is larger or smaller than $\mathcal{G}_K$ for $V_m^o > -100$ mV? Explain.

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.
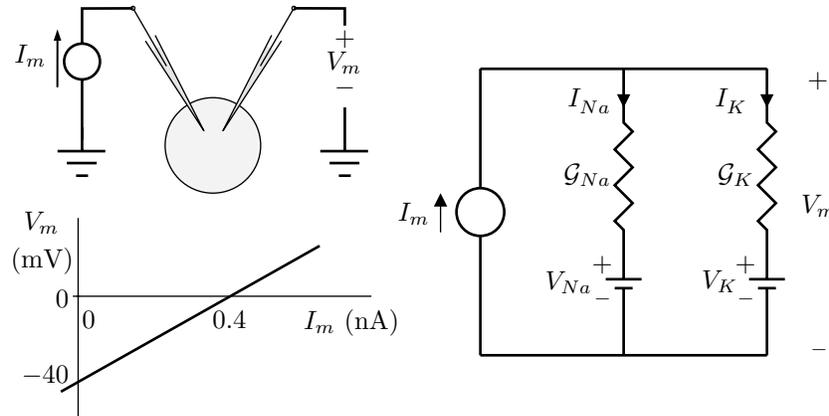
Assume that: (1) the cell membrane is permeable to only K^+ and Na^+ ions; (2) the Nernst equilibrium potentials are $V_n = (60/z_n) \log_{10}(c_n^o/c_n^i)$ (mV); (3) ion concentrations are constant; (4) active transport processes make no contribution to these measurements.

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. The resting membrane potential, V_m^o, of two uniform, isolated cells is measured as a function of the external concentration of potassium, c_K^o, with the sodium concentration held fixed at its normal value, c_{Na}^{on}, and then as a function of the external sodium concentration, c_{Na}^o, with the potassium concentration held fixed at its normal value, c_K^{on}. The results for these two cells are shown in the following figure.
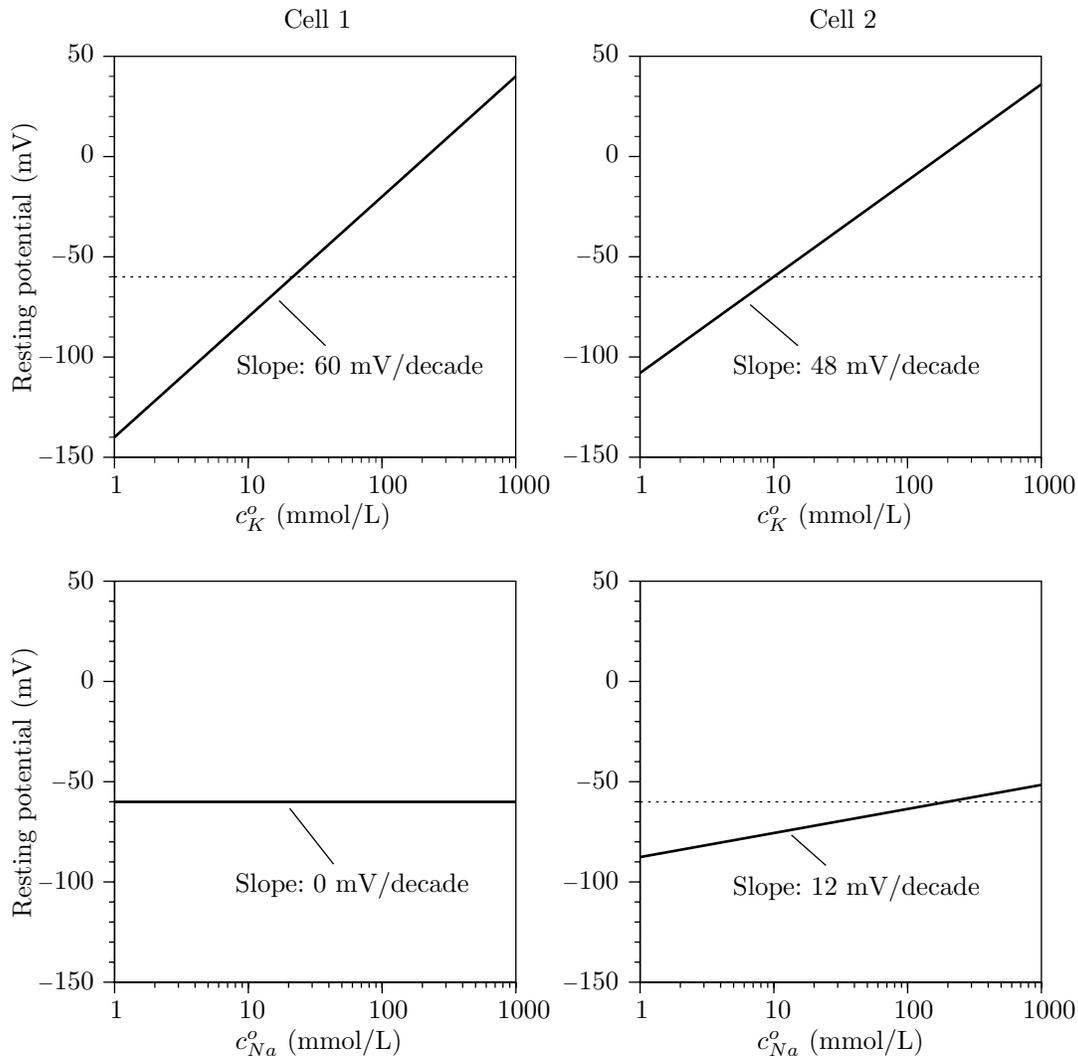
You may assume that for each cell: (1) external solutions are isotonic; (2) the membranes are impermeable to ions other than potassium and sodium; (3) the internal concentrations of potassium and sodium are maintained constant by a non-electrogenic active transport mechanism; (4) the total membrane conductance is 10 nS; (5) the normal resting potential is −60 mV; (6) the internal concentration of sodium is 20 mmol/L.

a) For each cell, determine the total conductance of the membrane to potassium and to sodium, $\mathcal{G}_K$ and $\mathcal{G}_{Na}$, respectively. If either value is indeterminate from the information given, describe what additional information would be needed.

b) For each cell, determine the internal and external concentrations of potassium and the external concentration of sodium at the normal resting potential (−60 mV). If the value is indeterminate from the information given, describe what additional information would be needed.

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c) For each cell, determine the simplest equivalent electric network model that relates the dependence of the resting potential of the cell on the ion concentrations. Indicate the values of all elements in the network.

Problem 2. The membrane of a cell is known to be permeable to Na^+ and K^+ only, with passive ionic conductances of $G_{Na} = 10^{-6}$ S/cm^2 and $G_K = 10^{-3}$ S/cm^2, and contains a $(Na^+- K^+)$ATPase active transport mechanism that transports 3 molecules of Na^+ outward and 2 molecules of K^+ inward through the membrane for each molecule of ATP split into ADP and phosphate. In the experiment shown in Figure 2, the cell is kept at a temperature of $24°C$. For
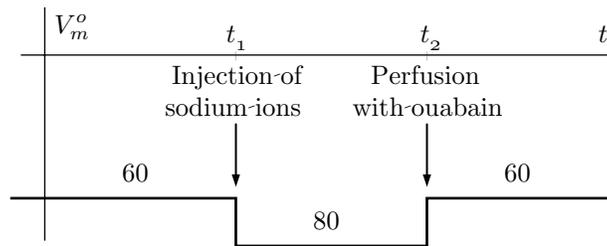
Figure 2: Effect of sodium injection and ouabain on resting potential.

$t < t_1$, the cell is in its normal resting state with resting potential $V_m^o \approx -60$ mV, and resting ion concentrations shown in the following table.

Ion	Concentration (mmol/L)	
	Internal	External
Sodium	15	135
Potassium	156	15

At $t = t_1$, Na^+ is injected rapidly into the cell interior, without the passage of any current through the membrane, to double the intracellular sodium concentration. When the injection is completed, the membrane potential hyperpolarizes to approximately -80 mV. At $t = t_2$ ouabain, a blocker of the active transport mechanism, is applied to the cell and the membrane potential returns to approximately its normal resting value.

a) Is the active transport mechanism electrogenic or nonelectrogenic? Explain!

b) Does the active transport mechanism contribute appreciably to the resting potential for $t < t_1$? Explain!

c) How many moles of ATP are split per second by a cm^2 of membrane during the interval (t_1, t_2)?

Problem 3. 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 4. Consider the model of a cell shown in the following figure.
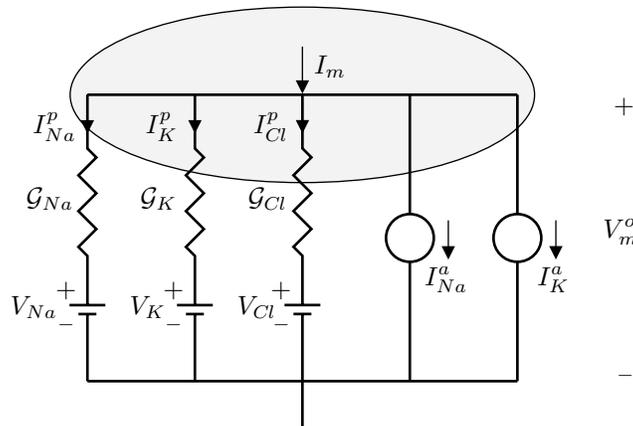
The cell has channels for the passive transport of sodium, potassium, and chloride as well as a pump that actively transports sodium out of the cell and potassium into the cell. The pump ratio is $I_{Na}^a/I_K^a = -1.5$. The following table shows the intracellular and extracellular concentrations, Nernst equilibrium potentials, and conductance ratios for sodium and potassium. Some information is also given for chloride; blank entries represent unknown quantities.

	c_n^i	c_n^o	V_n	$\mathcal{G}_n/\mathcal{G}_K$
	(mmol/L)		(mV)	
Na$^+$	10	140	$+68$	0.1
K$^+$	140	10	-68	1
Cl$^-$		150		1

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.

a) Choose one of the following statements and explain why it is true.

    i) The cell resting potential depends on $\mathcal{G}_{Cl}$.

    ii) The cell resting potential depends on V_{Cl}.

    iii) The cell resting potential depends on both $\mathcal{G}_{Cl}$ and V_{Cl}.

    iv) The cell resting potential does not depend on $\mathcal{G}_{Cl}$.

    v) The cell resting potential does not depend on V_{Cl}.

    vi) The cell resting potential does not depend on either $\mathcal{G}_{Cl}$ or V_{Cl}.

b) Determine V_m^o.

c) 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.

    i) 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.

    ii) Determine $V_m^o(\infty)$, the value of the membrane potential after the cell has equilibrated.

    iii) Determine $c_{Cl}^i(\infty)$, the intracellular chloride concentration after the cell has equilibrated.

    iv) Give a physical interpretation of your results in i), ii), and iii).

    v) Discuss the validity of the assumptions that the sodium and potassium concentrations in the cell are constant and that the volume does not change.