In the name of God

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Principles of Biomedical Engineering
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Homework 2 - Cell potential

Solution

Problem 1.

Choose the correct answer.

1. Which of the following values is unnecessary when finding the equilibrium potential of an ion using the Nernst equation?

   a) The temperature

   b) The ratio of external and internal ion concentrations.

   c) The charge of the ion

   d) The permeability of the ion channel

   Answer: d

2. The resting membrane potential is close in value to the Nernst equilibrium potential for ——— because ———.

   a) Na^+ / there is a leakage of Na^+ ions through the membrane channels

   b) K^+ / there is a leakage of Ca^{2+} ions through the membrane channels

   c) K^+ / the membrane is very permeable to K^+ ions at rest

   d) Na^+ / due to its large driving force

   e) Cl^- / because it's the only negatively charged ion

   Answer: c

3. What effect does an intravenous injection of KCl have on behavior of neurons?

   a) Extracellular [K^+] decreases and therefore the membrane potential gets closer to Na+ equilibrium potential.

   b) The membrane potential becomes more negative and it becomes more difficult to generate action potentials.

   c) Extracellular [K^+] increases and therefore the membrane potential gets closer to Na+ equilibrium potential.

   d) None of the above is true.

   Answer: c

4. What would happen to the resting membrane potential of a neuron if sodium (Na^+) channels were normally open in the membrane, but everything else was the same?

   a) Nothing much would happen, and it would remain at approximately -65 mV.

   b) It would be less negative than the normal resting potential.

   c) It would be more negative than the normal resting potential.

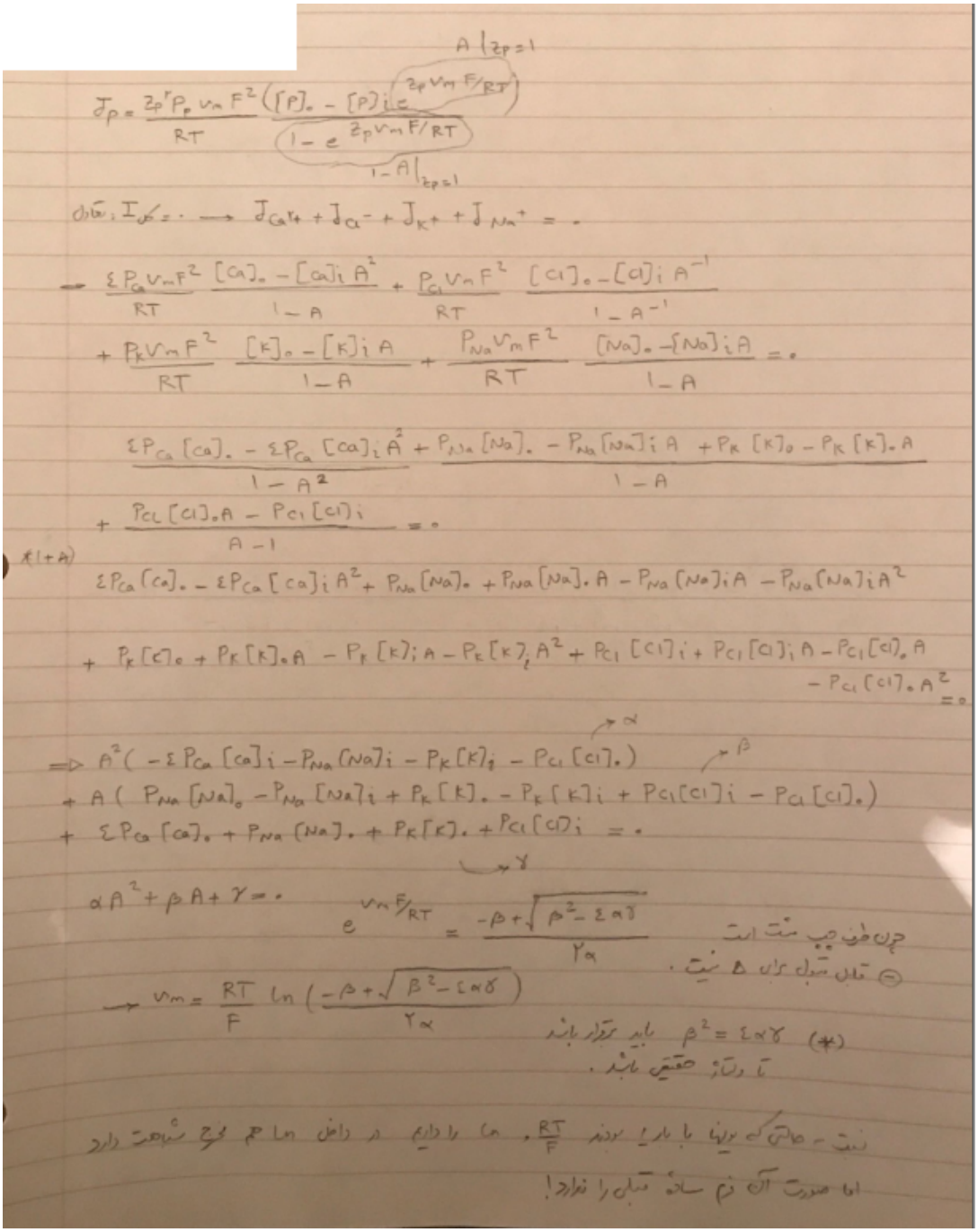
   d) It would lose its polarization and stand at exactly 0 mV (no difference between inside and outside of the neuron).

   e) None of the above.

   Answer: b

Problem 2.

Drive Goldman equation when we have four ions of Ca^{2+}, Cl^{-}, K^{+}, Na^{+}.

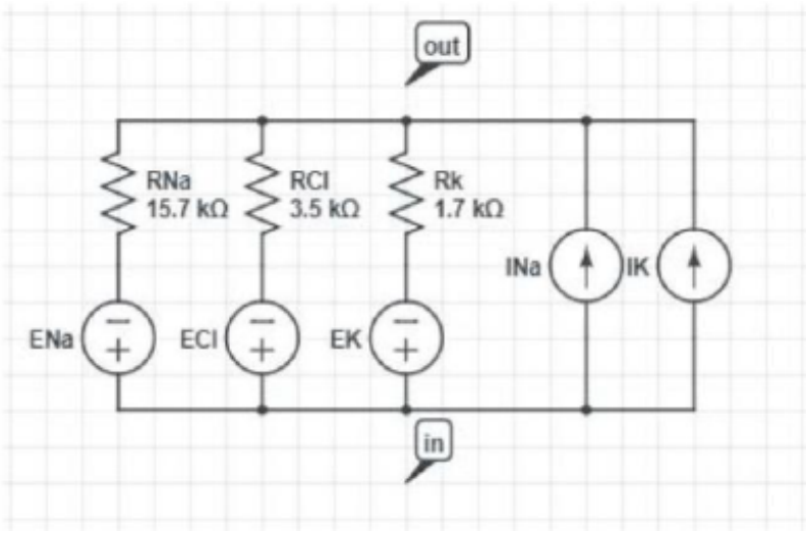


Problem 3.

Consider the following values for concentration and membrane permeability of each ion and answer the following questions.

Ion	Relative Permeability	ICF	ECF
K^+	1	300	30
Na^+	0.1	20	500
Cl^-	0.15	40	400

$R_k = 1.7$ KΩ, $R_{Na} = 15.7$ KΩ, $R_C = 3.5$ KΩ



a) If there were no active pump mechanism (i.e. the current sources were zero) what would be the resting membrane potential and ion currents according to parallel-conductance membrane model?

b) Which Nernst potential is close to resting potential of membrane?

c) If both pumps are active, can you use the Goldman equation with all ions to calculate the resting potential? Explain your answer.

a) جیب ۴ را در نظر میگیریم (منابع جریان صفت برشده از مدل)

$$E_{Na^+} = -\frac{\partial\Lambda}{z_{Na^+}} \log \frac{[Na^+]_i}{[Na^+]_o} = -\partial\Lambda \log\left(\frac{\text{۲۰}}{\partial\text{۰}}\right) = \Lambda\text{۱}^{mv}$$

$$E_{K^+} = -\frac{\partial\Lambda}{z_{K^+}} \log \frac{[K^+]_i}{[K^+]_o} = -\partial\Lambda \log\left(\frac{\text{۳۰}}{\text{۲۰}}\right) = -\partial\Lambda^{mv}$$

$$E_{Cl^-} = -\frac{\partial\Lambda}{z_{Cl^-}} \log \frac{[Cl^-]_i}{[Cl^-]_o} = \partial\Lambda \log\left(\frac{\text{۳۰}}{\text{۶۰}}\right) = -\Lambda\partial^{mv}$$

تعادل: $\sum I = \text{۰} \rightarrow V_m = \dfrac{g_K E_K + g_{Na} E_{Na} + g_{Cl} E_{Cl}}{g_K + g_{Na} + g_{Cl}}$

$$= \frac{\frac{1}{1.7^K}(-\partial\Lambda) + \frac{1}{15.7^K}(\Lambda\text{۱}) - \frac{1}{3.5^K}(\partial\Lambda)}{\frac{1}{1.7^K} + \frac{1}{15.7^K} + \frac{1}{3.5^K}} = \underline{-\text{۴}\Lambda,\text{۷}\partial^{(mv)}}$$

$$I_{Na} = g_{Na}(E_{Na} - V_m) = \frac{1}{15.7^K}(\Lambda\text{۱} + \text{۴}\Lambda,\partial\text{۷}) = \underline{\Lambda,\text{۲}\partial\ (\mu A)}$$

$$I_K = g_K(E_K - V_m) = \frac{1}{1.7^K}(-\partial\Lambda + \text{۴}\Lambda,\partial\text{۷}) = \underline{-\text{۶}\partial,\text{۶}\ (\mu A)}$$

$$I_{Cl} = g_{Cl}(E_{Cl} - V_m) = \frac{1}{3.5^K}(-\Lambda\partial + \text{۴}\Lambda,\partial\text{۷}) = \underline{-\text{۲},\text{۶۹}\ (\mu A)}$$

b) دستاز نرست مربوط به K^+ ، Cl^- هردو برابر $-\Lambda\partial^{mv}$ بوده است که نزدیک به دستاز رست است.

c) جیب کلر نداریم ← جریان کلر صفر برای Na^+ ، K^+ جریان خالص صفر

$$\hookrightarrow V_m = E_{Cl} = \frac{+\text{۲۵}}{1} \ln \frac{\text{۳۰}}{\text{۴۰}} = \underline{-\partial\text{۷},\text{۶}\partial^{(mv)}}$$

$$E_{Na} = -\text{۲۵} \ln \frac{\text{۳۰}}{\partial\text{۰۰}} = \Lambda,\text{۱۴}^{(mv)}$$

$$E_K = -\text{۲۵} \ln \frac{\text{۳۰۰}}{\text{۴}} = -\partial\text{۷},\text{۶}^{(mv)} \rightarrow I_K = \text{۰}$$

برای سدیم: $I_{Na} = -g_{Na}(E_{Na} - V_m) = -\Lambda,\text{۷۹}\ (\mu A)$: جیب

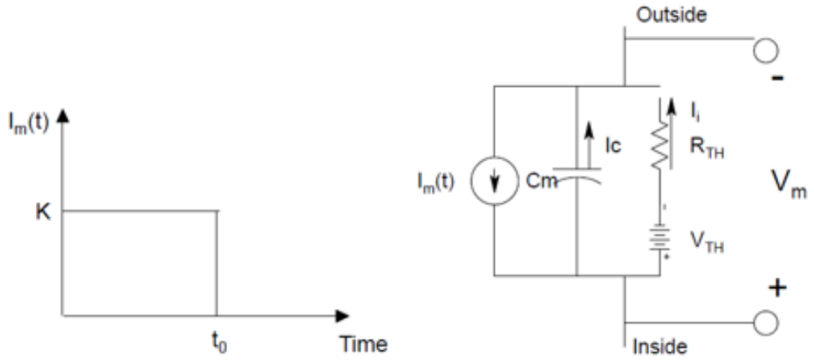
برای پتاسیم: $I_K = \text{۰}$: جیب

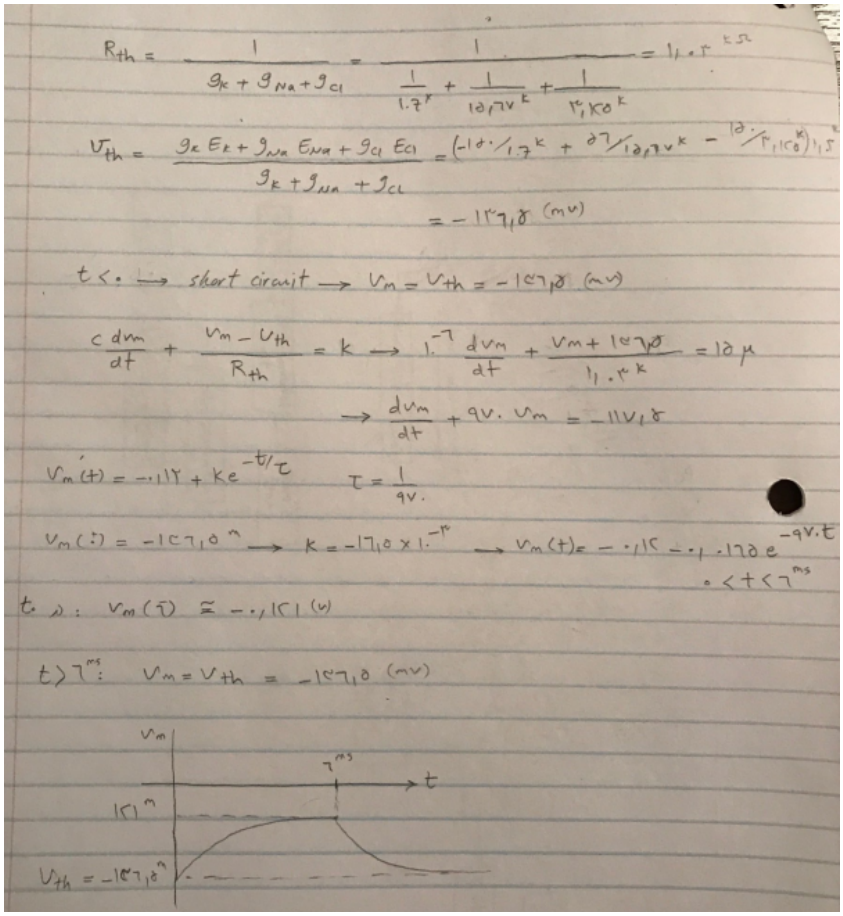
(*) معادله گلدمن یا گلدمن نیست! مدل مقاومتی تنها یا گلدمن است.

Problem 4.

Assume $I_m(t)$ is applied to cell membrane. Calculate and plot cell membrane potential. ($t_0 = 6ms$, $K = 15\mu A$)

$R_k = 1.7$ KΩ, $R_{Na} = 15.67$ KΩ, $R_C = 3.125$ KΩ
$E_k = 150$ mv, $E_{Na} = 56$ mv, $E_{Cl} = 150$ mv, $C_m = 1$ µF





Problem 5.

Equlibrium concentrations of intracellular and extracellular ions are shown for a 'normal' marine algal cell (Valonia ventricosa) in the table below. The reported membrane potential is –70 mV (negative-inside)[1] .

a) For the four ions below, sort ions based on their predicted relative permeabilities, given the reported resting voltage. Then find a way to approximate the relative permeability of each ion with respect to the most permeable ion.

Ion	Extracellular(mM)	Intracellular(mM)
Na^+	490	40
K^+	10	435
Ca^{2+}	1.0	$< 10^{-4}$
Cl^-	560	140

b) For the most permeable ion (in a), calculate the net concentration of imbalanced charge that would cause a potential of –100 mV. Valonia is a spherical cell with a diameter of 1 centimeter.

(Equations and constants are provided. Please be sure that you show units.)

Q = C . ΔE, (coulombs) = (coulombs/volt) (volt)

Charge (Q) for a spherical cell of radius r : $Q = Volume\,.\,c\,.\,F$

c is the concentration of net charge and F is the Faraday constant.

Capacitance of a spherical cell of radius r : $C = Area\,.\,C'$

C' is the capacitance per unit area. ($\simeq 1\frac{\mu F}{cm^2}$ for cells)

F = 9.649 . 10^4 (coulombs . mol^{-1})

[1]Gutknecht J (1966) Sodium, potassium, and chloride transport and membrane potentials in Valonia ventricosa. The Biological Bulletin 130:331–344.

Problem 5.

Answer:

a) We can take an indirect approach by calculating Nernst potential for the given ions and comparing to the resting potential.

	ext.	int.	E_N*	
Na^+	490	40	+63 mV	
K^+	10	435	-94 mV	
Ca^{2+}	1	10^{-4}	+115 mV	($z=2$)
Cl^-	560	140	-35 mV	

$$E_N = \frac{RT}{F} \ln \frac{C_o}{C_i}$$

Relative permeabilities:

K^+	-94 - (-70)	+24	most permeable
Cl^-	-35 - (-70)	+35	
Na^+	+63 - (-70)	+133	
Ca^{2+}	+115 - (-70)	+185	least permeable

- Now we can solve for two ions:

For example: chloride

$$V = +\frac{RT}{F} \ln \frac{P_K[K^+]_o + P_{Cl}[Cl]_i}{P_K[K^+]_i + P_{Cl}[Cl]_o} \quad \times \frac{1}{P_K} \quad \times \frac{1}{P_K}$$

$$\Rightarrow 70 = -25 \ln \frac{[K^+]_o + P_{Cl}/P_K [Cl]_o}{[K^+]_i + P_{Cl}/P_K [Cl]_o}$$

$$\Rightarrow \exp \frac{-70}{25} = \frac{10 + 140x}{435 + 560x} \Rightarrow x = 0.16 : \frac{P_{Cl}}{P_K}$$

For Calcium:

$$V = +\frac{RT}{F} \ln \frac{P_K[.1] + P_{Ca}[.1]^2}{P_K[.1435] + P_{Ca}[10^{-7}]^2} \quad \times \frac{1}{P_K} \quad \times \frac{1}{P_K}$$

$$\Rightarrow \exp -\frac{70}{25} = \frac{[.1] + x[0.001]^2}{[.1435] + x[10^{-7}]^2}$$

$$\Rightarrow x = 1.6 \times 10^4 \quad \frac{P_{Ca}}{P_K}$$

For Na:

$$V = \frac{RT}{F} \ln \frac{P_{Na}[490] + P_K[10]}{P_{Na}[40] + P_K[435]} \quad \times \frac{1}{P_K} \quad \times \frac{1}{P_K}$$

$$\exp \frac{-70}{25} = \frac{490x + 10}{40x + 435}$$

$$\Rightarrow x = 0.03 \quad \frac{P_{Na}}{P_K}$$

b)

$$r = 2 \times 10^{-2}\,(m) = 0.2\ cm \longrightarrow \begin{cases} \text{Area} = 4\pi r^2 \\ \text{Vol} = \frac{4}{3}\pi r^3 \end{cases}$$

$$Q = C \cdot \Delta E$$

Capacitance of membrane: $C = 4\pi r^2 \cdot C' = 4\pi r^2 \cdot 10^{-6}$ (r in cm, C' in F/cm^2)

$\Delta E = 6\ mV$

$$\Rightarrow \frac{4}{3}\pi r^3 \cdot c \cdot F = C \cdot \Delta E = 4\pi r^2 \cdot 10^{-6} = \pi \times 10^{-6}$$

(r = 0.2 cm)

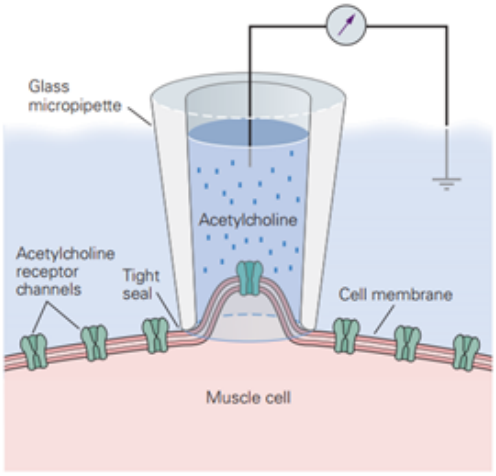
Concentration $\longrightarrow$

$$c = \frac{\pi \times 10^{-6}}{\frac{4}{3}\pi r^3 \cdot F} = \frac{3}{4} \times \frac{10^{-6}}{120 \times 10^{-9} \times 9.65 \times 10^4} = 7.71 \times 10^{-2}$$

$$= 62.17\ (\mu M)$$

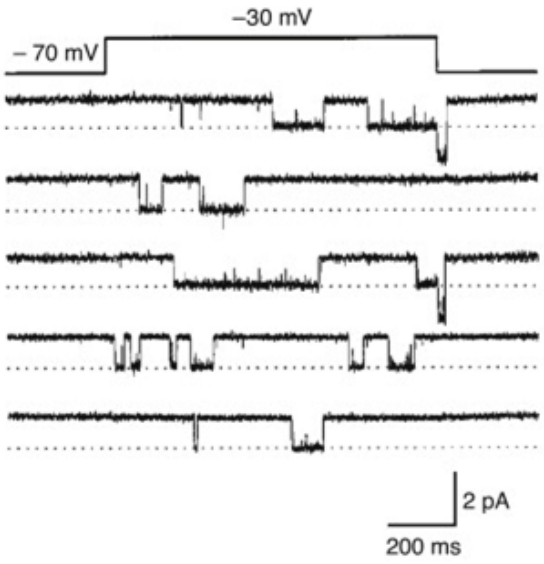
Problem 6. The Patch Clamp

The patch-clamp technique was developed in 1976 by Erwin Neher and Bert Sakmann to record current from single ion channels.



a) Explain this technique briefly.

b) It is 1976 and you developed the patch clamp technique. You obtained the following data from your first experiment. What does this tell you about the ion channel in this recording? Provide a rationale for your answer.
(The patch pipette did not contain any neurotransmitters.)



Answer:

b) The downward deflection of current indicates that this is an inward current. This recording also suggests that the time a channel is open is variable in duration (some are open for a short period of time while others are open for a longer period of time). This is shown by the variation in the duration of the current events. Each response has two conductance states, open or closed. This is shown by the sharp rise and sharp decline of the traces. They all pass the same amount of current because all of the first 3 traces are of the same magnitude. The fourth depolarization suggests that two channels have opened simultaneously since the size is twice the size of the first three. Moreover, Since the patch pipette did not contain any neurotransmitters, the ion channel in this experiment must have an inactivation mechanism. The conclusion is that this channel could be a Sodium channel.