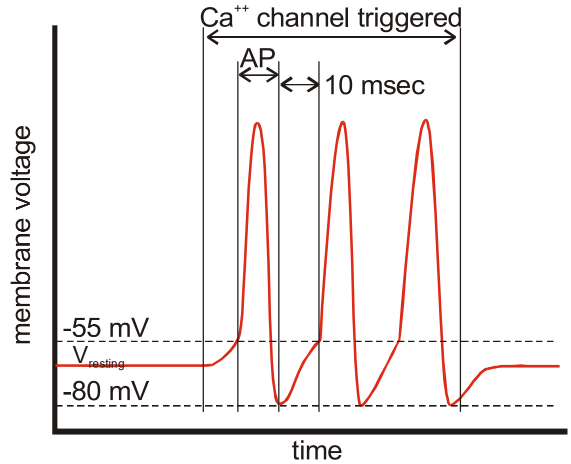
Quantitative Physiology I / Molecular and Cellular Systems; BMEN E4001x
HW4: Channels and potentials,
Due Nov. 12, 2025, 11:00PM

1) Design of an action potential burst cell (20 points)

Assume your lab has cells with excitable membranes, equipped with voltage sensitive Na^+ and K^+ channels sufficient to produce action potentials. Your task is to modify these cells such that they produce a train of action potentials at set time intervals on demand. You plan to do this by introducing a new Ca^{++} channel. When triggered, these channels increase Ca^{++} conductance, altering the cells' electrical properties.

Your mission in this problem is to specify the conductance of these Ca^{++} channels that would induce a pulse train in which action potentials start every 20 ms.



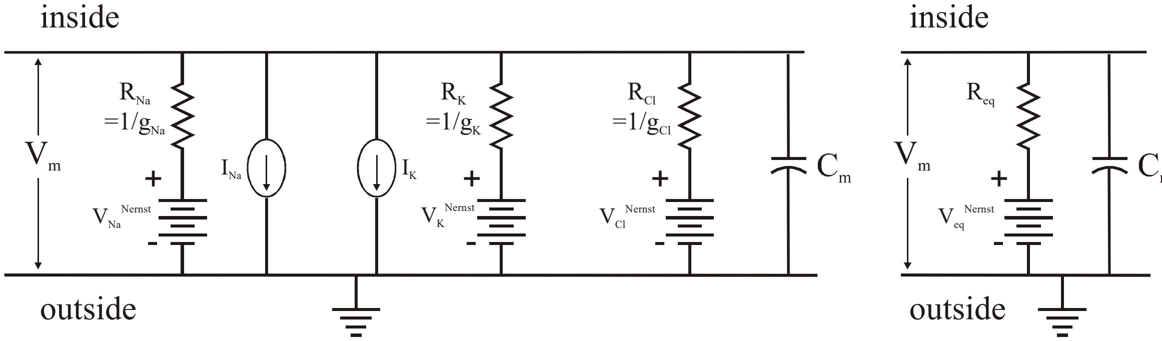
Assume:

ion	internal conc. (mM)	external conc. (mM)	pump rate (absolute value) ($\mu A/cm^2$)	V^{Nernst} (mV)	conductance (S/cm^2)
Na^+	15	145	1.356	60.605 mV	1.0×10^{-5}
K^+	120	5	0.9898	-84.898 mV	1.0×10^{-4}
Cl^-	7	116	--	-75.00 mV	2.0×10^{-5}
Ca^{++}	1×10^{-4}	1.2	--	(to be calculated)	0 when inactive, for you to specify when active

- Membrane capacitance is 1 $\mu F/cm^2$.
- The Ca^{++} channels allow passage of only Ca^{++} ions during the trigger signal.
- Note that the Ca^{++} ion has two positive charges.
- Each action potential:
  - is started when the membrane voltage increases to –55 mV,
  - lasts 10 ms; the goal is to design a 10 ms period between the end of one action potential and beginning of the next,
  - terminates with instantaneous closure of the repolarizing K^+ channels. Membrane voltage at this point = –80 mV (this is a simplifying assumption), and
  - is mediated by channels whose conductance overwhelms the resting conductance during the action potential but are completely off outside of the 10 ms action potential.
- Constants and units:
  - T = 310 K;
  - 1 Siemens = 1 Amp / Volt
  - 1 Volt = 1 J / C = 1 N*m/C; (C = Coulombs)
  - 1 Amp = 1 C/sec
  - 1 F * 1 Ω = 1 sec; 1 S = 1 1/Ω ; 1Ω=1V/A

Part A - Electrical Equivalence (5 points)

1.1) Consider the membrane to be modeled as the pump-leak model with a capacitor element. Derive that, in terms of the electrical equivalence circuit, the right schematic is equivalent to the left circuit, with the specified values of equivalent resistance and voltage source.



$$R_{eq} = \left(\frac{1}{R_{Na}} + \frac{1}{R_K} + \frac{1}{R_{Cl}} \right)^{-1} \quad \text{(or alternatively)} \quad g_{eq} = g_{Cl} + g_K + g_{Na}$$

$$V_{eq}^{Nernst} = \frac{-I_{Na} - I_K + g_{Na} V_{Na}^{Nernst} + g_K V_K^{Nernst} + g_{Cl} V_{Cl}^{Nernst}}{g_{Na} + g_K + g_{Cl}}$$

1.2) What is the resting potential for this system?

Part B – Design of Electrical Response (15 points)

Now consider the membrane with channels that provide a Ca^{++} conductance of g_{Ca}. (That is, consider the system with the channels triggered to be open).

1.3) Expand the model from Part 1 to include the new Ca^{++} channel. Provide an expression for a new resting potential as a function that includes g_{Ca}. Assume that the membrane is not excitable, so approaching this new potential does not initiate an action potential.

1.4) For an experiment in which the membrane voltage is first clamped to -80 mV and then released, provide an equation describing membrane voltage as a function of time. Provide numbers for key voltages. As in part 1.3, assume here that the membrane is not excitable.

1.5) Provide an expression for how long it takes after release (unclamping) for the membrane voltage to reach -55 mV. That is, for an excitable membrane, how long will it take before a new action potential is initiated?

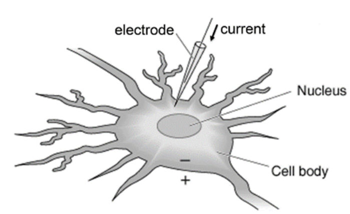
1.6) What Ca^{++} conductance is needed to provide a 10 ms gap between the hyperpolarization phase and initiation of a new action potential?

2) Rescue a cell (10 points)

This Question focuses on the same cell as Question 1, with the parameters listed above. In addition, assume the cell has a surface area of 1000 $\mu m^2 = 1 \times 10^{-5}$ cm^2.

2.1) At time t=0, the cell is subjected to ouabain, a toxin that selectively blocks the Na^+/K^+ pump. What is the cell's new resting potential?

2.2) You want to offset the effect of ouabain on membrane voltage by inserting a transmembrane electrode into the affected cell. Update the expressions in HW4Q1 for R_{eq} and V_{eq}^{Nernst} to include the effect of the electrode. Consider a flow of positive charges into the cell as a positive current. *This is opposite for what we assigned for channels and pumps.*



2.3) What electrode current (in Amperes) is needed to maintain the membrane voltage at -75 mV? Remember, ouabain is still present, inhibiting the pump.