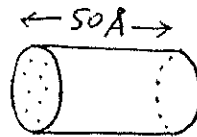


MCB 166 Problem Set #1

1. A Na-selective ion channel that produces a single-channel current of 1.6 pA ($1 \text{ pA} = 10^{-12} \text{ amps}$) under a voltage of 90 mV has a conductance of 17.8 pS. Say that this channel is a membrane-spanning circular cylinder (50 Angstrom long) filled with a typical biological electrolyte solution (resistivity, $\rho = 60 \text{ ohm-cm}$). Find the internal diameter of the pore. You will get a reasonable value for macromolecular pore, but would expect a Na-ion-selective pore to have a larger or smaller internal diameter? Draw a channel shape (not a uniform diameter cylinder) which can have the observed conductance as well as selectivity. (Hint: The molecular current picture of a channel profile would have a separate 'vestibule' region and a 'selectivity filter').

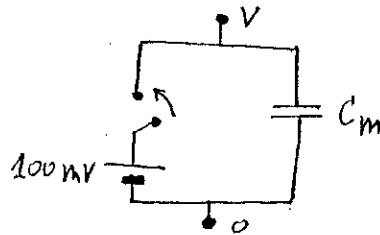


$$A = \pi r^2$$

$$R = \rho l / A$$

$$1 \text{ pA} = 10^{-12} \text{ Amps}$$

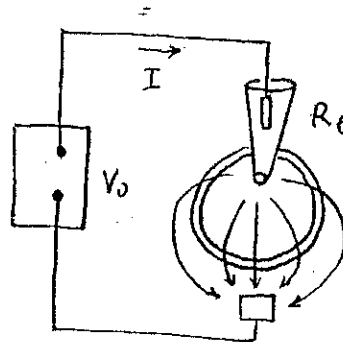
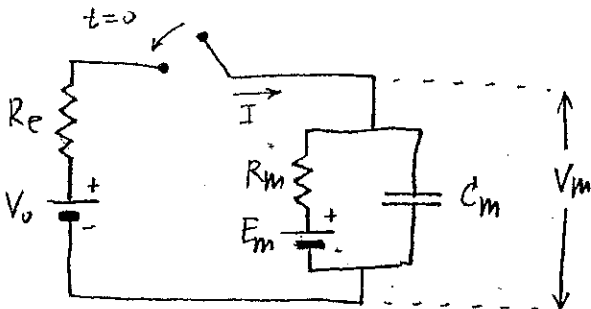
2. The amplitude of a nerve action is about a 100 mV displacement of the membrane potential caused by an influx of Na^+ ions. How many moles of a monovalent ion must cross the membrane to set up a potential of this magnitude? ($C = 1 \text{ microfarad per square centimeter of membrane}$). A squid giant axon has a diameter of 1 mm, and the axoplasm has a ionic concentration of about 0.5 M. Compare the number of ions needed to maintain a 100 mV potential in 1 cm^2 of membrane to the number in the axon cylinder enclosed by a 1 cm^2 of membrane. A garfish olfactory nerve is 1 micrometer in diameter (10^{-3} mm). Do the same comparison for it. What does this calculation tell you about the running down of nerve batteries by the firing of action potentials?



$$Q = CV$$

$$C_m = 1 \mu\text{F}/\text{cm}^2$$

3. Consider the membrane equivalent circuit shown in class. Instead of constant-current generator, the cell is now stimulated by a battery of potential V_0 via a high-resistance microelectrode, $R_e = 1/g_e$. (For a typical glass microelectrode, $R_e = 10^7 \text{ ohm}$).



- a) Write the differential equation for the membrane potential as a function of time after V_0 is instantaneously switched on.

That is, apply Kirchoff's laws* to the circuit having parallel leak and capacitance currents. Because of the large resistance of the microelectrode, the applied pulse will be characterized by two time constants, the membrane time constant, $T_m = R_m C_m = 10^{-3}$ sec independent of the size of the cell, and an additional 'access-resistance' time constant, $T_e = R_e C_m$, which will depend on the size of the cell (for a cell of area 100 square microns, $C_m = 10^{-6}$ farads/cm² $\times 100 \times 10^{-8}$ cm² = 10^{-12} farads; hence for this particular cell, $T_e = 10^7$ ohms $\times 10^{-12}$ farads = 10^{-5} sec). This means when an experimenter applies a fast step of voltage to the electrode the membrane potential V_m cannot follow instantaneously and does not reach a value equal to the applied potential.

In fact, I'll even give you the answer, but you must show the steps to get there.

$$\frac{dV_m}{dt} + \frac{V_m}{T} = \frac{V_o}{T_e} + \frac{E_m}{T_m} \quad (1)$$

where $T_e = R_e C_m = C_m / g_m$, $T_m = R_m C_m = C_m / g_m$, $1/T = 1/T_e + 1/T_m$

b) Verify that Eqn (2) below is the solution to Eqn (1) satisfying the initial condition that $V_m = E_m$ until the switch is thrown.

$$V_m(t) = [(R_m V_o + R_e E_m) / (R_m + R_e)] (1 - \exp(-t/T)) + E_m \exp(-t/T) \quad (2)$$

or $V_m(t) - E_m = (R_m / (R_e + R_m)) (V_o - E_m) (1 - \exp(-t/T))$

c) For our cell at rest, $R_m = 10^3$ ohm-cm²/10⁻⁶ cm² = 10⁹ ohm. Find $V_m(\infty)$ compared to V_o . Say during excitation, the membrane resistance drops by a factor of 100. What happens to $V_m(\infty)$ for a fixed V_o ? Is our battery still a constant-voltage source in this case?

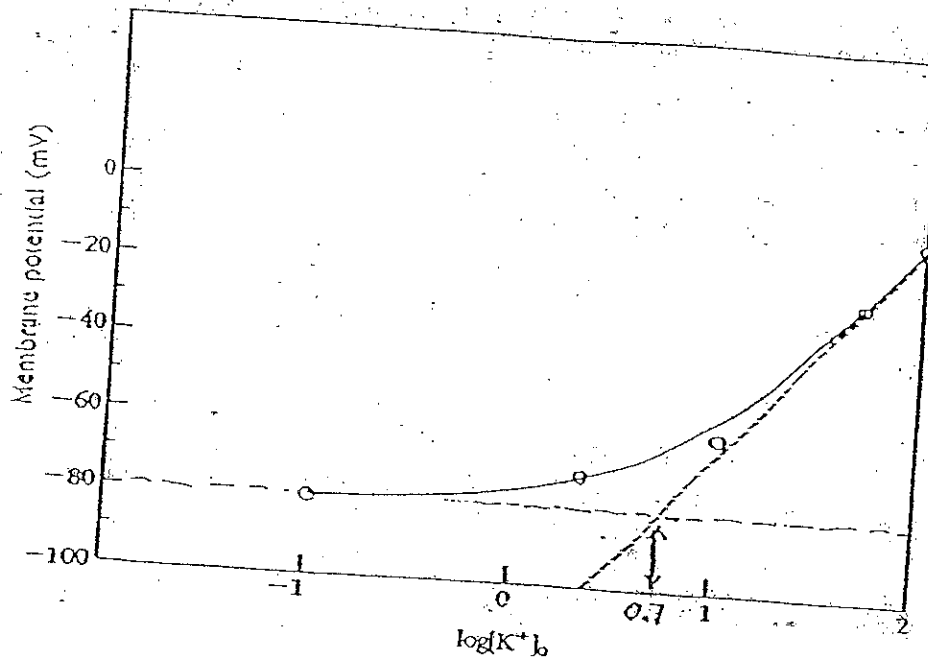
* Kirchoff's laws

1. The algebraic sum of the currents which meet at a junction point in an electric circuit is zero.
2. The algebraic sum of the electromotive forces and potential drops around any closed path of an electric circuit is zero.

4. The figure shows data for a cell with Na⁺ and K⁺ as the only permeable ions. For this case, the Goldman equation can be written as

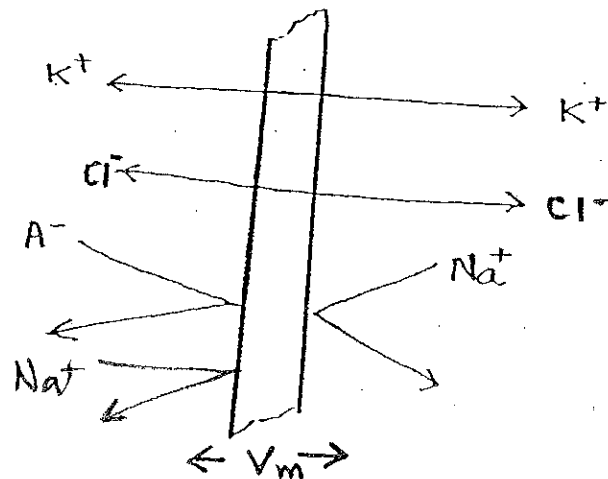
$$V_m = \frac{(kT/e) \ln [(P_k [K^+]_o + P_{Na} [Na^+]_o) / (P_k [K^+]_i + P_{Na} [Na^+]_i)]}{60 \log_{10} [([K^+]_o + r [Na^+]_o) / ([K^+]_i + r [Na^+]_i)]}$$

where $r = P_{Na}/P_k$ is the relative permeability. For this cell, the external Na is held fixed at 50 mM. Find r from the data given. (Hint: one way to solve this problem is to notice that the dashed line represents data for which the Na⁺ contribution is negligible since it has the slope appropriate to perfect K⁺ selectivity. The horizontal line is asymptotic to the condition $[K]_o = 0$. The two lines intersect $\log_{10} ([K]_o)$ or $[K]_o = 5$ mM).



5. The membrane situation shown is a Donnan equilibrium. The external permeant ion concentrations given as $[K^+]_o = 10 \text{ mM}$ and $[Cl^-]_o = 200 \text{ mM}$ and impermeant $[Na^+]_o = 190 \text{ mM}$. The internal impermeant (monovalent) anion concentration is $[A^-] = 100 \text{ mM}$. Find the concentrations $[K^+]_i$ and $[Cl^-]_i$ and find the Donnan equilibrium potential across the membrane. Recall that the internal and external solutions are electroneutral; there is osmotic equilibrium; and the permeant ions must be at equilibrium at the same membrane potential (Donnan condition).

$[K^+]_i = ?$	$[K^+]_o = 10 \text{ mM}$
$[Cl^-]_i = ?$	$[Cl^-]_o = 200 \text{ mM}$
$[A^-]_i = 100 \text{ mM}$	$[Na^+]_o = 190 \text{ mM}$
$[Na^+]_i = ?$	
$V_m = ?$	



Physical Constants

N_A = Avogadro's number = 6.023×10^{23} molecules/mol

F = Faraday's constant = 9.648×10^4 C/mol

ϵ_0 = the permittivity constant = 8.85×10^{-12} F/m

k = Boltzmann's constant = 1.381×10^{-23} joule/ $^{\circ}$ K

R = gas constant = 1.987 cal/mol- $^{\circ}$ K

e = elementary electrical charge = 1.602×10^{-19} C

$^{\circ}$ K = absolute temperature = $^{\circ}$ C + 273.16