~ Elec436 HW3 ~

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2. Channel probabilities n, m, and h: Write a formula that can be used to determine the value of each one of the quantities listed. The result should depend on the parameters given in Table 13.2, the state variables of Table 13.3, and the results of any preceding items on the list.

   a. v_m, the transmembrane potential relative to the resting value.

   $v_m = V_m + 60$

   b. α_n, the rate constant for n for opening channels.

   $\alpha_n = 0.01 \cdot (10 - v_m) / (\exp((10 - v_m)/10) - 1)$

   c. β_n, the rate constant for n for closing channels.

   $\beta_n = 0.125 e^{(-v_m/80)}$

   d. α_m, the rate constant for m for opening channels.

   $\alpha_m = 0.1 \cdot (25 - v_m) / (e^{\frac{(25 - v_m)}{10}} - 1)$

   e. β_m, the rate constant for m for closing channels.

   $\beta_m = 4 \cdot e^{(-v_m/18)}$

   f. α_h, the rate constant for h for opening channels.

   $\alpha_h = 0.07 \cdot e^{(-v_m/20)}$

   g. β_h, the rate constant for h for closing channels.

   $\beta_h = 1 / (e^{\frac{(30 - v_m)}{10}} + 1)$

   h. $\dot{n} \equiv dn/dt$ at $t = t_0$, the time derivative of n evaluated at $t = t_0$.

   $\dot{n} \equiv \frac{dn}{dt} = \alpha_n (1 - n) - n \beta_n$

   i. $\dot{m} \equiv dm/dt$ at $t = t_0$, the time derivative of n at $t = t_0$.

   $\dot{m} \equiv \frac{dm}{dt} = \alpha_m (1 - m) - m \beta_m$

   j. $\dot{h} \equiv dh/dt$ at $t = t_0$, the time derivative of n at $t = t_0$.

   $\dot{h} \equiv \frac{dh}{dt} = \alpha_h (1 - h) - h \beta_h$

$\bar{g}_K = 36 \ mS/cm^2$

5. Conductivity and current: Find the numerical value (with units) of each of the following, using the parameter values given in Table 13.2 and the values for the state variables of set A, which are given in Table 13.3. For this illustrative example, use Δt equal to 50 μsec. A Δt of 50 μsec works well for hand calculations and for initial computer runs done for testing algorithms. When accurate results become the goal, a smaller Δt of 1 to 10 μsec is more frequently chosen, because the time integration is then done more precisely. In these initial exercises the emphasis is on instruction, so a larger Δt is used, thus making the nature of the step by step evolution more obvious.

   a. g_K, the K^+ conductivity.

   $g_K = \bar{g}_K n^4 = (36 mS/cm^2)(0.378)^4 = 0.73497 \ mS/cm^2$

   b. g_{Na}, the Na^+ conductivity.

   $g_{Na} = m^3 h \bar{g}_{Na} = (0.417)^3 (0.477)(120 mS/cm^2) = 4.15057 \ mS/cm^2$

   c. V_K, the transmembrane voltage relative to E_K.

   $V_K = V_m - E_K = (-11.5 - (-72.1)) = +60.6 mV$

   d. V_{Na}, the transmembrane voltage relative to E_{Na}.

   $V_{Na} = V_m - E_{Na} = (-11.5 - (+52.4)) = -63.9 mV$

   c. I_K, the K^+ current.

   $I_K = g_K (V_m - E_K) = (0.73497 mS/cm^2)(-11.5 + 72.1 \ mV) = 44.54 \ \mu A/cm^2$

   d. I_{Na}, the Na^+ current.

   $I_{Na} = g_{Na} (V_m - E_{Na}) = (4.15057 mS/cm^2)(-11.5 - 52.4 mV) = -265.2 \ \mu A/cm^2$

   e. I_L, the leakage current.

   $I_L = g_L (V_m - E_L) = (0.3 mS/cm^2)(-11.5 + 49.2 mV) = 11.3 \ \mu A/cm^2$

   f. I_{ion}, the total ionic current.

   $I_{ion} = I_K + I_{Na} + I_L = -209.4 \ \mu A/cm^2$

   g. $V_{dot} \equiv \dot{V}_m$, the time derivative of V_m, evaluated at t_0.

   $\dot{V}_m = V_{dot} = \frac{I_s - I_{ion}}{C_m} = \frac{0 + 209.4 \ \mu A/cm^2}{1.0 \ \mu F/cm^2} = 209.4 \ volts/sec$

6. Channel probabilities n, m, and h: Find values for each of the quantities listed. The result should depend on the parameters given in Table 13.2, the state variables of Table 13.3, and, as needed, the results of any preceding items on the list.

a. v_m, the transmembrane potential relative to the resting value.

$= V_m - V_r = (-11.5 - (-60)) = 48.5\,mV$ ✓

b. α_n, the rate constant for n for opening channels.

$= 0.01(10 + 11.5)/(\exp((10 + 11.5)/10) - 1) = 0.393371\ msec^{-1}$

c. β_n, the rate constant for n for closing channels.

$= 0.125 \exp(11.5/80) = 0.068174\ msec^{-1}$

d. α_m, the rate constant for m for opening channels.

$= 0.1(25 + 11.5)/(\exp((25 + 11.5)/10) - 1) = 2.597745\ msec^{-1}$

e. β_m, the rate constant for m for closing channels.

$= 4 \exp(11.5/18) = 0.27032\ msec^{-1}$

f. α_h, the rate constant for h for opening channels.

$= 0.07 \exp(11.5/20) = 0.27032\ msec^{-1}$

g. β_h, the rate constant for h for closing channels.

$= 1/(\exp((30 + 11.5)/10) + 1) = 0.864127\ msec^{-1}$

h. $\dot{n} \equiv dn/dt$ at $t = t_0$, the time derivative of n at $t = t_0$.

$= \alpha_n(1-n) - n\beta_n = 0.21891\ msec^{-1}$

i. $\dot{m} \equiv dm/dt$ at $t = t_0$, the time derivative of n at $t = t_0$.

$= \alpha_m(1-m) - m\beta_m = 1.40176\ msec^{-1}$

j. $\dot{h} \equiv dh/dt$ at $t = t_0$, the time derivative of n at $t = t_0$.

$= \alpha_h(1-h) - h\beta_h = -0.40895\ msec^{-1}$

7. Time shift Δt: Use the results of Exs. 5 and 6 to find values for each of the following for the interval Δt beginning at time $t = t_0$. Assume that Δt is small enough that derivatives retain their initial values throughout the interval.

a. ΔV_m, the change of V_m from $t = t_o$ to $t = t_0 + \Delta t$.

$= V_{dot} \cdot \Delta t = (209.4\ volts/sec)(50\ \mu sec) = 10.47\ mV$

b. Δn, the change of probability n from $t = t_o$ to $t = t_0 + \Delta t$.

$= \frac{dn}{dt}\Delta t = (0.21891\ msec^{-1})(50\ \mu sec) = 0.010945$ no units

c. Δm, the change of probability m from $t = t_o$ to $t = t_0 + \Delta t$.

$= \frac{dm}{dt}\Delta t = (1.40176\ msec^{-1})(50\ \mu sec) = 0.070088$

d. Δh, the change of probability h from $t = t_o$ to $t = t_0 + \Delta t$.

$= \frac{dh}{dt}\Delta t = (-0.40895\ msec^{-1})(50\ \mu sec) = -0.020447$

e. $V_m(t_0 + \Delta t)$, the value of V_m at $(t_0 + \Delta t)$.

$= V_m + \Delta V_m = -11.5\,mV + 10.47\,mV = -1.03\,mV$

f. $n(t_0 + \Delta t)$, the value of n at $(t_0 + \Delta t)$.

$= n + \Delta n = 0.378 + 0.010945 = 0.388945$

no units

g. $m(t_0 + \Delta t)$, the value of m at $(t_0 + \Delta t)$.

$= m + \Delta m = 0.417 + 0.070088 = 0.487088$

h. $h(t_0 + \Delta t)$, the value of h at $(t_0 + \Delta t)$.

$= h + \Delta h = 0.477 - 0.020447 = 0.456553$

Exercise 15 deals with the initial depolarizing current, a stimulus current. Stimuli are analyzed at length in a later chapter. Here the topic is examined only as needed for some relatively simple exercises.

15. Suppose one considers again Eq. (5.39) from the text, which is essentially

$$C_m \frac{dV_m}{dt} + I_{ion} = I_m$$

A stimulus is applied to a membrane having the characteristics of Table 13.2. Thus $I_m = I_s$ (and thereby has a nonzero amplitude), and during the period the stimulus is applied. By the convention used here, the stimulus starts at $t = t_0$. Unless specified otherwise, $I_s = 50$ μA/cm^2, and the membrane is at rest. Examine the instant after the stimulus begins.

a. What is dV_m/dt?

$= \frac{I_s - I_{ion}}{C_m} = \frac{50\ \mu A/cm^2}{1.0\ \mu F/cm^2} = 50\ mV/msec$

b. What is dV_m/dt if $I_s = -50$ μA/cm^2 ?

$= \frac{I_s - I_{ion}}{C_m} = \frac{-50\ \mu A/cm^2}{1.0\ \mu F/cm^2} = -50\ mV/msec$

c. What is ΔV_m for the first 100 msec after the stimulus starts, if dV_m/dt retains its initial value throughout that interval?

$\Delta V_m = Vdot \cdot \Delta t = 50 \frac{mV}{msec} \cdot 100 msec = \underline{\underline{5V}}$

d. What is dV_m/dt if the membrane is in state A (i.e., as given in Table 13.3)?

$259.4 \frac{mV}{msec}$

e. What is dV_m/dt if the membrane is in state B (i.e., as given in Table 13.4)?

$9.27915 \frac{mV}{msec}$

d)

$Vdot = \frac{dV_m}{dt} = \frac{I_s - I_{ion}}{C_m}$

$I_{ion} = I_K + I_{Na} + I_L$

$= 44.52 - 265.2 + 11.3 = -209.4\ \mu A/cm^2$

$\frac{dV_m}{dt} = \frac{(50 - (-209.4))\ \mu A/cm^2}{1.0\ \mu F/cm^2} = 259.4 \frac{mV}{msec}$

e)

$g_K = \bar{g}_K n^4 = (36\ mS/cm^2)(0.759)^4 = 11.9473\ mS/cm^2$

$g_{Na} = m^3 h \bar{g}_{Na} = (0.955)^3 (0.104)(120\ mS/cm^2) = 10.87\ mS/cm^2$

$I_K = g_K (V_m - E_K) = 724.0061\ \mu A/cm^2$

$I_{Na} = g_{Na} (V_m - E_{Na}) = -694.5852\ \mu A/cm^2$

$I_L = 11.3\ \mu A/cm^2$

$I_{ion} = I_K + I_{Na} + I_L = 40.7208\ \mu A/cm^2$

$\frac{dV_m}{dt} = \frac{I_s - I_{ion}}{C_m} = \frac{(50 - 40.7208)\ \mu A/cm^2}{1.0\ \mu F/cm^2} = 9.27915\ mV/msec$

28. Sketch an action potential for nerve.

a. Indicate periods of rest and action.

b. On the sketch, indicate the periods when sodium current has higher magnitude than potassium or leakage.

→ Time interval 1~2. • Starts with voltage exceeds threshold and ends with repolarization.

c. On the sketch, indicate the periods when potassium current has twice or more the magnitude of leakage.

→ Time interval 2 to 3.

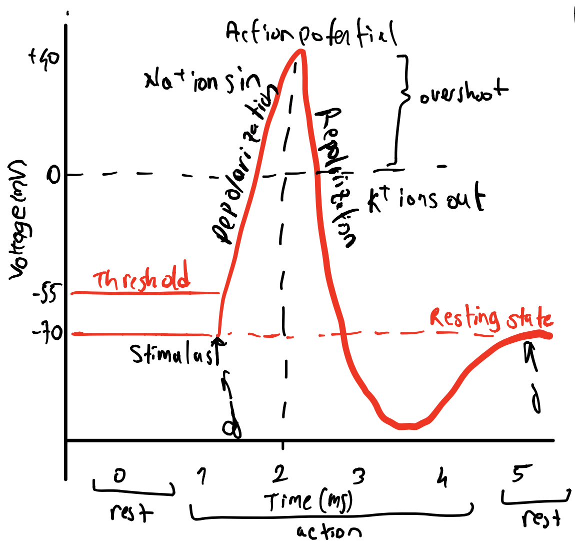
d. On the sketch, use labeled arrows to identify a time when n has the value of n_∞ and n at rest. In two sentences, justify using n_∞ as the value of n at rest by explaining the circumstances when doing so is acceptable, and when not.

d) Living membrane exists continuously throughout its life time, so it has no fixed starting points. The fact that time "0" is simply chosen to embody more physiological meaning than it has. Starting conditions for each of state variables normally are chosen as those that exist at rest.

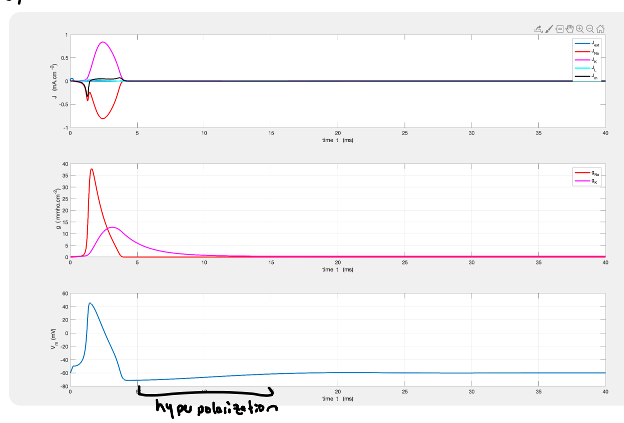
$$n_0 = n_\infty = \alpha_n/(\alpha_n+\beta_n)$$

where α, β evaluated using $v_m = 0$, cor. $V_m = V_r$. V_m, m, h hold their initialized values through $t<0$.

a)



b, c)



An action potential is a rapid rise and subsequent fall in voltage or membrane potential across a cellular membrane with a characteristic pattern. Sufficient current is required to initiate a voltage response in cell membrane; if current is insufficient to depolarize the membrane to the threshold level, an action potential will not fire.

Stimulus starts the rapid change in action potential. Sufficient current must be administered to the cell in order to raise the voltage above the threshold voltage to start membrane depolarization. Depolarization is caused by rapid rise in membrane potential opening of Na^+ channels in the cellular membrane, resulting in a large influx of Na^+ ions.

Membrane Repolarization results from rapid Na^+ channel inactivation as well as large efflux of K^+ ions resulting from activated K^+ channels.

Hyperpolarization is lowered membrane potential caused by efflux of K^+ ions and closing of the K^+ channels.

Resting state is when membrane potential returns to the resting voltage that occured before the stimulus occured.

Voltage Clamp Exercises. The voltage clamp experimental setup provided an innovative platform for determining membrane properties. Understanding the voltage clamp allows one to review carefully the experimental data from which membrane properties are understood, and also allows one to enjoy some concepts that have been abstracted from the voltage clamp experiments.

29. Which one of the following is the objective of the voltage clamp:

    a. Confuse students by introducing an unnecessarily large number of electrodes.

    b. Hold membrane current constant while measuring changing V_m.

    c. Hold V_m constant to stabilize the membrane current and thereby get an accurate measurement.

    d. Hold V_m constant and measure membrane current with time.

    e. Obtain a dynamic record of changes in V_m with membrane current.

30. In a few sentences, explain how a voltage clamp experiment is conducted: What is controlled, and how, and what is measured?

The voltage clamp is an experimental method to measure ionic current through membranes of excitable cells, such as neurons, while holding membrane voltage at a set level (controlled). A basic voltage clamp will iteratively measure the membrane potential, and then change voltage to desired value by adding necessary current. This "clamps" the cell membrane at at desired constant voltage, allowing voltage clamp to record what currents are delivered. Since the currents applied to cell must equal to current going across cell membrane at the set voltage, recorded current indicate how the cell reacts to changes in membrane potential.

31. A voltage clamp from rest (Table 13.2) to $v_m = 20$ mV is applied to a resting squid axon. What is the ratio of the potassium conductance that results after a long time divided by the potassium conductance just after the voltage transition. (Provide this ratio based on analysis using the HH equations. A computer simulation is unnecessary.)

$n = 0.378$ after voltage transition. so $g_k = \bar{g}_k \cdot n^4 = \underline{0.73497 \text{ mS/cm}^2}$ question 5

V_m is 20 mV so

$\alpha_n = 0.01(10-20)/(\exp((10-20)/10) - 1) = 0.1582$

$\beta_n = 0.125\exp(-20/80) = 0.0975$

$n_\infty = \alpha_n/(\alpha_n+\beta_n) = 0.619$

$g_{k\text{-new}} = \bar{g}_k (n_\infty)^4 = 5.29 \text{ mS/cm}^2$

$\dfrac{g_{k\text{new}}}{g_{k\text{int}}} = \dfrac{5.29}{0.73497} = \underline{\underline{7.2}}$

Exercises 38–42 refer to Figure 5.9, which shows ionic current following a voltage clamp. For 37 and 38 focus on the 91-mV trace. For 40–42 focus on the 117-mV trace.

38. The flow of what ion dominates the curve during the period from 1 to 2 msec?

→ Na^+ ion dominates. | During period from 1 to 2 msec the flow of Na^+ ion dominates curve. The a.p. is a result of a large increase in ~~Na~~ Na^+ permeability.

39. In which direction is the net current flow from 1 to 2 msec?

→ inward | Given Na^+ Nernst potential is 57 mV. The voltage clamp is 91 mV, The diff. from resting potential gives 91 − 60 = 31 mV, which gives inward driving force.

40. Which ion dominates the curve during the period from 3 to 4 msec?

→ Na^+ ion dominates. | From 3 to 4 msec current is rising. Driving force on Na^+ is outward and Na^+ dominates curve.

41. Why does this trace fail to fall below the horizontal axis?

→ The sodium Nernst potential is reached with a step change of 117 mV. ($V_r = -60$, $E_{Na} = 57$ mV) This implies Na^+ equilibrium condition. Due to the early inward current is 0, trace does not fall below horizontal axis. Driving force in Na^+ ~w

42. What is the time period during which Na^+ flow dominates this trace?

Current starts to increase, K^+ starts to affects after 1 msec. Thus 0–1 msec current dominates comes from Na^+.