MCB 166 Problem Set #2

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1. Threshold-switch model of excitation.

A resting membrane is mainly potassium selective with a resting membrane potential $E_r = -70$ mV. The membrane is stimulated by steps of constant current. When the membrane potential is depolarized to a threshold voltage,
($V^* = -50$ mV) a large Na conductance isswitched on , so that the membrane equilibrium potential is now near the Na reversal potential, $E_{Na} = +50$mV. Say that $G_r = 10^{-6}$ mho, $G_{Na} = 10^{-4}$ mho, $C = 10^{-9}$ farads.

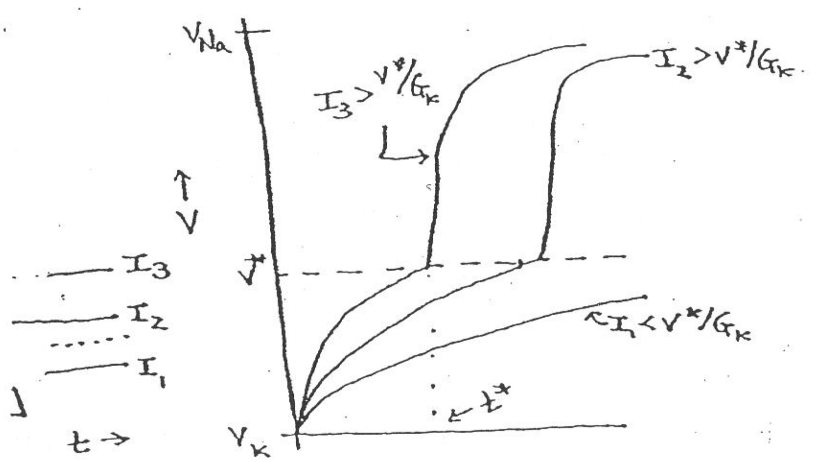
The voltage follows the differential equation

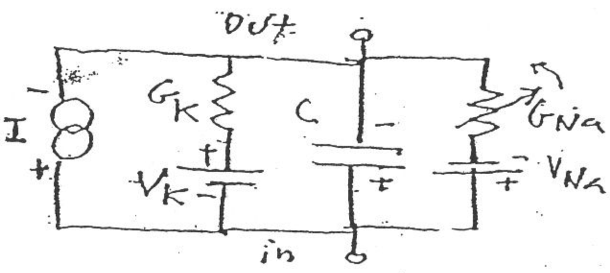
$$I = C\, dV/dt + G_K (V - V_K) + S(V - V^*)\, G_{Na} (V - V_{Na}),$$

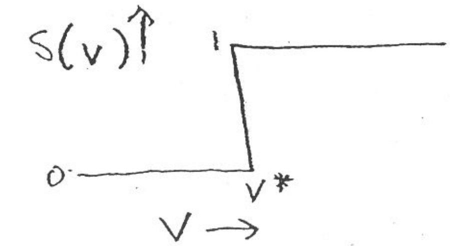
where $S(V-V^*)$ is a step functionof voltage centered about threshold, $S(x) = 0$ for $x < 0$, $S(x) = 1$ for $x > 0$. This is a nicer way to write the pair of equations we did in cl ass.

(a) Solve for the voltage for 3 different values of stimulus,
$I = 0.5\, I_{Rh}$, $1.5\, I_{Rh}$, and $2 I_{Rh}$.
Here $I_{Rh} = G_r (V^* - E_r) = 2 \times 10^{-8}$ amp is the miniumun current needed to reach threshold. Use t^* as the time when $V(t)$ reaches V^*. Recall that both equations (above and below threshold) have solutions of the form $V(t) = A + B\, e^{-ct}$, where A,B and c are obtained from the initial and steady-state conditions for each solution and one switches equations at $t = t^*$ which becomes the initial time for the 'excited' phase. Plot the three solutions on the same V-t graph.

(b) Plot the steady state current-voltage relation under constant voltage (voltage-clamp) conditions (ie. the current voltage relation obtained by setting $dV/dt = 0$).







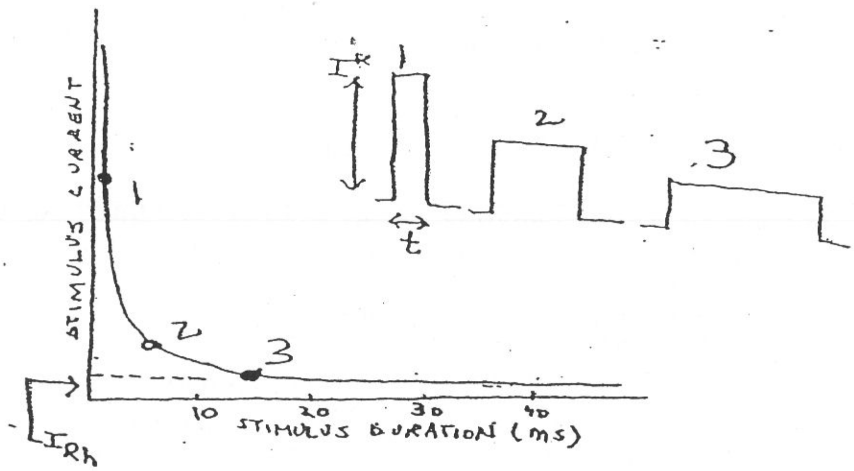
2. <u>Strength-Duration Relation</u> (Lapique's Law)

For constant-current stimuli, the amplitude and duration of the stimulating current step are related by Lapique's Law ,

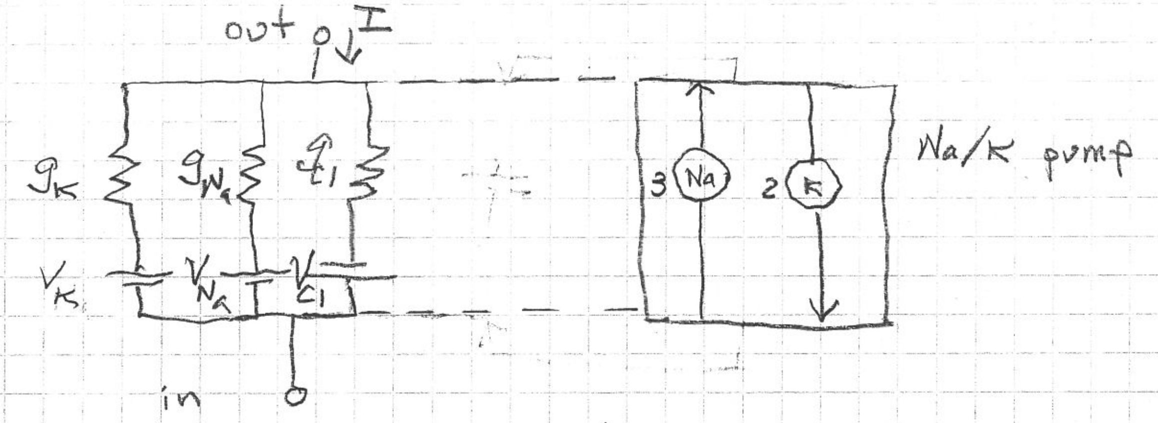
$$I^* = I_{Rh} / (1 - \exp(-t^*/T).$$

I_{Rh}, called the rheobase is the minimum current which can cause excitation. T is the membrane the characteristic membrane time constant.

Using the current-clamp response to to different current steps (ie. the results of prob. 1), derive Lapique's law (ie. calculate the time it takes for the voltage to reach V* as a function of stimulus amplitude, I* and the. time to reach threshold for that particular stimulus, t*).



3. EQUIVALENT CIRCUIT WITH ELECTROGENIC PUMP



The figure shows the equivalent circuit for an axon at rest in parallel with an equivalent constant-current source representing the Na/K-ATPase pump.

a) Write an expression for the reversal potential (in the absence of the pump) in terms of V_K, V_{Na}, V_{Cl} and the <u>relative</u> conductances

$$\alpha = g_{Na}/g_K \quad \text{and} \quad \beta = g_{Cl}/g_K$$

Is this situation, $I_L = I_K + I_{Na} + I_{Cl} = 0$, an equilibrium?

If not, why not?

b) Now introduce the pump

$$I_{pump} = I_{Na-pump} + I_{K-pump},$$

$$I_{Na-pump} = -3/2\ I_{K\ pump}$$

Write the expression for the new resting potential in terms of the batteries and (new) <u>relative</u> permeabilities

Use the equilibrium conditions:

$$I_{Na} = I_{Na-leak} + I_{Na-pump} = 0$$

$$I_K = I_{K-leak} + I_{K-pump} = 0$$

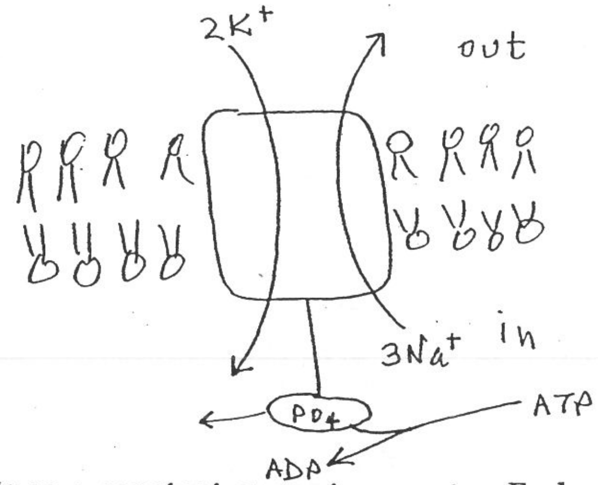
$$I_{Cl} = 0 \qquad \text{(Hint: similar formula with } \alpha \text{ changed)}$$

c) Show that the formula you derived is still valid when you ignore the chloride terms (as I did in the worked example*). Explain this by working out the relation between the equilibrium concentrations of Cl^- and the membrane potential.

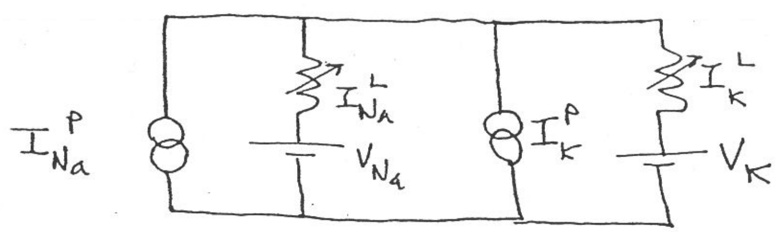
* over 2

worked example for prob. 3

Active Transport-- Na - K exchange pump.



The pump acts as a constant-current generator. Each pump cycle exchanges 3 Na+ for 2 K+ thus producing an outward current which makes the membrane potential more negative.



$I_K = I_{K\text{-}L} + I_{K\text{-}P}$ $\qquad$ $I_{Na} = I_{Na\text{-}L} + I_{Na\text{-}P}$

pump exchange, $I_{Na\text{-}P} = -m I_{K\text{-}P}$, $\quad m = 3/2$

Now at eq., $I_K = 0$ <u>and</u> $I_{Na} = 0$.

$I_{K\text{-}L} = -I_{K\text{-}P}$, $I_{Na\text{-}L} = -I_{Na\text{-}P} = m I_{K\text{-}P} = -m I_{K\text{-}L}$.

$$m I_{K\text{-}L} + I_{Na\text{-}L} = 0$$

$I_{K\text{-}L} = P_K f(v)(K_i \exp(v) - K_o) + PNa\, f(v)(Na_i \exp(v) - Na_o) = 0.$

$v_m = \ln[(K_o + r' Na_o)/(K_i + r' Na_i)]$, $\quad r' = P_{Na}/(m P_K)$