MCB166 — Fall 2017— Problem Set 2

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1. <u>Threshold-switch model of excitation</u>

2. Strength-Duration Relation (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 the 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*).

To solve this problem, we start with:

$$V(t_\theta) = V_\theta = E_r + \frac{I}{G_r}\left(1 - e^{\frac{-t_\theta}{\tau}}\right)$$

Which I will rewrite as:

$$V* = E_r + \frac{I*}{G_r}\left(1 - e^{\frac{-t*}{T}}\right)$$

$$V* - E_r = \frac{I*}{G_r}\left(1 - e^{\frac{-t*}{T}}\right)$$

$$G_r\left(V* - E_r\right) = I*\left(1 - e^{\frac{-t*}{T}}\right)$$

From problem 1, we were given that:

$$I_{Rh} = G_r\left(V* - E_r\right)$$

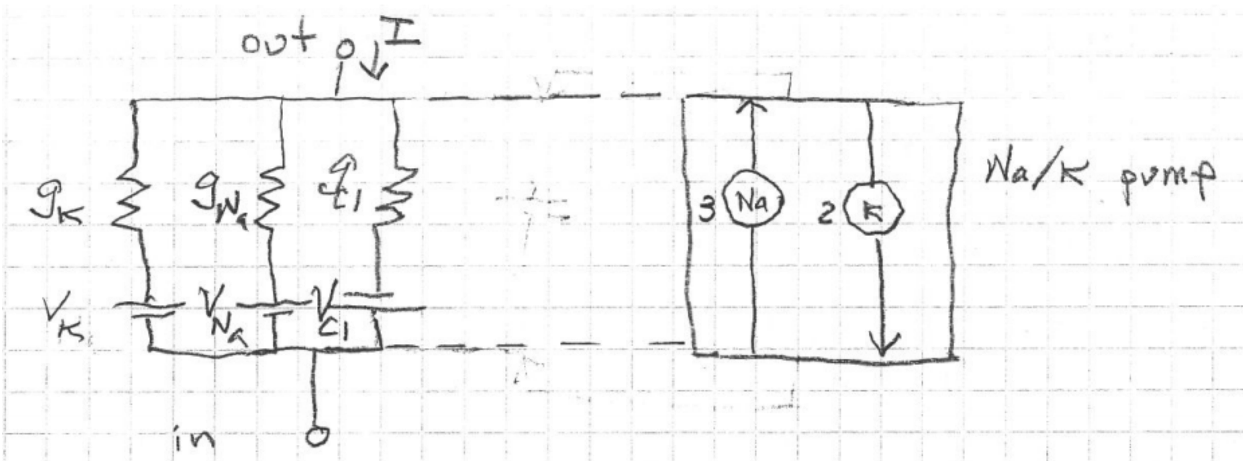
Therefore, we can rewrite the equation as:

$$I_{Rh} = I*\left(1 - e^{\frac{-t*}{T}}\right)$$

$$I* = \frac{I_{Rh}}{1 - e^{\frac{-t*}{T}}}$$

Therefore, we have derived Lapique's law using the current-clamp response to different current steps.

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 relative conductances

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

Is this situation, $I_L = I_K + I_{Na} + I_{Cl} = 0$, an equilibrium? If not, why not?

To solve this problem, we start with:

$$I_{total} = G_K(V_r - E_K) + G_{Na}(V_r - E_{Na}) + G_{Cl}(V_r - E_{Cl}) = 0$$

$$G_K V_r - G_K E_K + G_{Na} V_r - G_{Na} E_{Na} + G_{Cl} V_r - G_{Cl} E_{Cl} = 0$$

$$G_K V_r + G_{Na} V_r + G_{Cl} V_r = G_K E_K + G_{Na} E_{Na} + G_{Cl} E_{Cl}$$

Dividing both sides by G_K gives us:

$$\frac{G_K V_r + G_{Na} V_r + G_{Cl} V_r}{G_K} = \frac{G_K E_K + G_{Na} E_{Na} + G_{Cl} E_{Cl}}{G_K}$$

$$V_r + \frac{G_{Na}}{G_K} V_r + \frac{G_{Cl}}{G_K} V_r = E_K + \frac{G_{Na}}{G_K} E_{Na} + \frac{G_{Cl}}{G_K} E_{Cl}$$

Substituting in $\alpha = \frac{g_{Na}}{g_K}$ and $\beta = \frac{g_{Cl}}{g_K}$ gives us:

$$V_r + \alpha V_r + \beta V_r = E_K + \alpha E_{Na} + \beta E_{Cl}$$

$$V_r = \frac{E_K + \alpha E_{Na} + \beta E_{Cl}}{1 + \alpha + \beta}$$

If

(b) Now introduce the pump

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

$$I_{\mathrm{Na}-pump} = -\frac{3}{2} I_{\mathrm{K}-pump}.$$

Write the expression for the new resting potential in terms of the batteries and (new) relative permeabilities. Use the equilibrium conditions:

$$I_{\mathrm{Na}} = I_{\mathrm{Na}-leak} + I_{\mathrm{Na}-pump}$$

$$I_{\mathrm{K}} = I_{\mathrm{K}-leak} + I_{\mathrm{K}-pump},$$

$$I_{\mathrm{Cl}} = 0$$

To solve this problem, we start with:

$$I_{pump} = I_{\mathrm{Na}-pump} + I_{\mathrm{K}-pump}$$

$$I_{pump} = I_{\mathrm{Na}-leak} + I_{\mathrm{Na}-pump} + I_{\mathrm{K}-leak} + I_{\mathrm{K}-pump} = 0$$

$$I_{\mathrm{Na}-leak} + \left(-\frac{3}{2} I_{\mathrm{K}-pump}\right) + I_{\mathrm{K}-leak} + I_{\mathrm{K}-pump} = 0$$

$$I_{\mathrm{Na}-leak} - \frac{1}{2} I_{\mathrm{K}-pump} + I_{\mathrm{K}-leak} = 0$$

$$I_{\mathrm{Na}-leak} + \frac{1}{2} I_{\mathrm{K}-leak} + I_{\mathrm{K}-leak} = 0$$

$$I_{\mathrm{Na}-leak} + \frac{3}{2} I_{\mathrm{K}-leak} = 0$$

This equation can be rewritten as:

$$G_{\mathrm{Na}}\left(V_r - E_{\mathrm{Na}}\right) + \frac{3}{2} G_{\mathrm{K}}\left(V_r - E_{\mathrm{K}}\right) = 0$$

$$G_{\mathrm{Na}} V_r - G_{\mathrm{Na}} E_{\mathrm{Na}} + \frac{3}{2} G_{\mathrm{K}} V_r - \frac{3}{2} G_{\mathrm{K}} E_{\mathrm{K}} = 0$$

$$G_{\mathrm{Na}} V_r + \frac{3}{2} G_{\mathrm{K}} V_r = G_{\mathrm{Na}} E_{\mathrm{Na}} + \frac{3}{2} G_{\mathrm{K}} E_{\mathrm{K}}$$

$$V_r = \frac{G_{\mathrm{Na}} E_{\mathrm{Na}} + \frac{3}{2} G_{\mathrm{K}} E_{\mathrm{K}}}{G_{\mathrm{Na}} + \frac{3}{2} G_{\mathrm{K}}}$$

(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.

To solve this problem, we start with:

$$I_{\mathrm{Cl}} = 0$$

This equation can be rewritten as:

$$G_{\mathrm{Cl}}\left(V_r - E_{\mathrm{Cl}}\right) = 0$$

Dividing both sides by G_{Cl} gives us:

$$\frac{G_{\mathrm{Cl}}\left(V_r - E_{\mathrm{Cl}}\right)}{G_{\mathrm{Cl}}} = \frac{0}{G_{\mathrm{Cl}}}$$

$$V_r - E_{\mathrm{Cl}} = 0$$

$$V_r = E_{\mathrm{Cl}}$$