Neural Networks and Biological Modeling

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Question set 2

Exercise 1: Nernst equation

Using the Nernst equation,

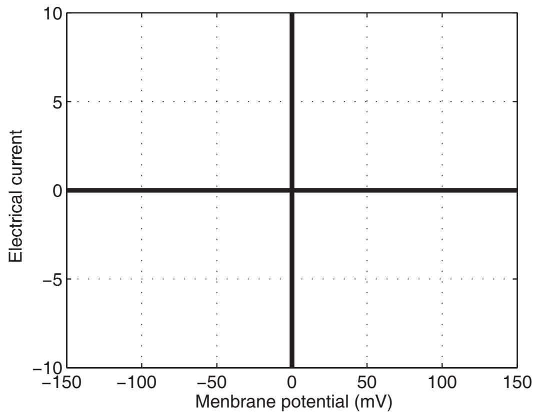
$$E_{\text{rev}} = -\frac{kT}{ze} \ln\left(\frac{C_{\text{int}}}{C_{\text{ext}}}\right) \,, \tag{1}$$

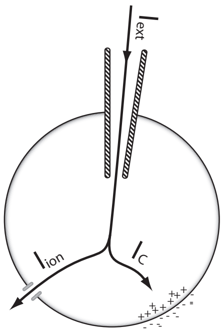
where $k \simeq 1.38 \cdot 10^{-23}$J/K is the Boltzmann constant, T is the absolute temperature, e is the elementary charge $e \simeq 1.60 \cdot 10^{-19}$ Coulomb, and z is the valence of the ion species.

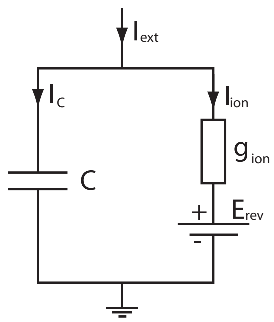
1.1 Calculate the reversal potential for Na^+, K^+ and Ca^{2+} assuming a temperature of 37 °C and the following concentrations:

ion	C_{int}	C_{ext}	E_{rev}
K^+	140	5	
Na^+	10	145	
Ca^{2+}	10^{-4}	1.5	

1.2 An experimentalist studies an ion channel by applying constant voltage while measuring the injected current. Sketch the current-voltage relationship for the three ion species in the graph below, assuming $I_{\text{ion}} = g(u - E_{\text{rev}})$, $g_{\text{Na}} = 120\text{nS}$, $g_{\text{K}} = 36\text{nS}$, $g_{\text{Ca}} = 0.3\text{nS}$.







1.3 How can one read off the reversal potential and the conductance from the graph? Assuming a resting potential of -65 mV, which type of ion generates an inward/outward current?

Exercise 2: Model of an ion channel

Consider the following model for an ion channel: the electrical current I_{ion} through the channel is given by

$$I_{ion} = g_{\text{ion}} r^{n_1} s^{n_2} (u - u_{\text{ion}})$$

where u is the membrane potential of the neuron, g_{ion} and u_{ion} are two constants, and $n_1 = 2$, $n_2 = 1$. The quantities r and s obey the equations

$$\begin{aligned} \frac{dr}{dt} &= -\frac{r - r_0(u)}{\tau_r(u)} \\ \frac{ds}{dt} &= -\frac{s - s_0(u)}{\tau_s(u)} \end{aligned}$$

with r_0, s_0, τ_r and τ_s as shown in Fig.1.

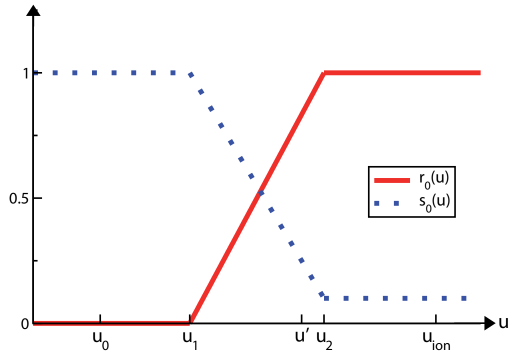
2.1 What is the *biological* interpretation of the following parameters :

r : ....

s : ....

g_{ion} : ....

u_{ion} : ....



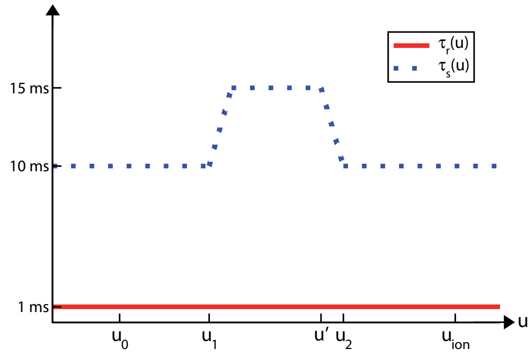


Figure 1: Graphical representation of the variables r_0, s_0, τ_r and τ_s.

2.2 How does the channel react (in terms of partial or full opening/closing) to a step change in membrane potential? Suppose that for $t < 0$, the membrane potential is clamped at a value u_0, and that at $t = 0$ it instantaneously jumps to a value $u' = u_2(1 - \varepsilon)$ with $\varepsilon \ll 1$ (see figure 1 for the values of u_0, u', u_2 and u_{ion}) where it is maintained for all $t \geq 0$.

- For $t < 0$, the channels is .... because ....
- At $t = 1$ ms, the channel is .... because ....
- At $t = 3$ ms, the channel is .... because ....
- At $t = 20$ ms, the channel is .... because ....
- At $t = 100$ ms, the channel is .... because ....

Exercise 3: Dynamics of conductances

In the Hodgkin-Huxley model, the potassium current obeys the equation:

$$I_K = \bar{g}_K n(t)^4 \left(u(t) - E_K\right)$$

where $\bar{g}_K$ is the maximal conductance, E_K the potassium reversal potential, and $n(t)^4$ is the proportion of channels that are open at time t. The quantity n obeys a first-order dynamics

$$\frac{dn}{dt} = \frac{n_\infty(u) - n}{\tau_n(u)},$$

with voltage-dependent time constant τ_n and equilibrium value n_∞.

In order to determine τ_n and n_∞, Hodgkin and Huxley pharmacologically blocked the sodium current and measured the response of the potassium current to voltage jumps of various amplitudes. The goal of this exercise is to understand this key experiment by studying a simplified version of the Hodgkin-Huxley model. Suppose τ_n and n_∞ have the following form:

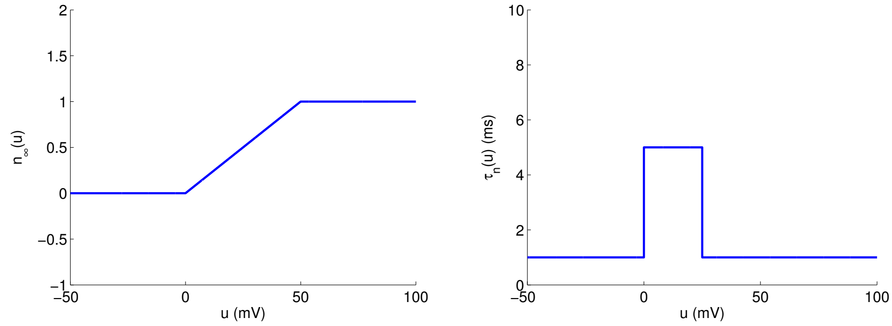
$$\tau_n(u) = \begin{cases} 1 \text{ ms} & \text{if} \quad u \leq 0\ mV \\ 5 \text{ ms} & \text{if} \quad 0 < u \leq 25\ mV \\ 1 \text{ ms} & \text{if} \quad u > 25\ mV \end{cases}$$

and

$$n_\infty(u) = \begin{cases} 0 & \text{if} \quad u \leq 0\ mV \\ u/50 & \text{if} \quad 0 < u \leq 50\ mV \\ 1 & \text{if} \quad u > 50\ mV\,. \end{cases}$$

3.1 Calculate the response of $n(t)$ to a voltage jump:

$$u(t) = \begin{cases} 0 & \text{for} \quad t < 0 \\ u_0 & \text{for} \quad t \geq 0 \end{cases}$$



3.2 Sketch the evolution of $n(t)$ for $u_0 = 10,\ 20,$ and $40\ mV$.

3.3 For $u_0 = 40$ mV, sketch the behaviour of $n(t)$, $n^2(t)$ and $n^4(t)$ assuming $t \ll \tau_n$. What is the difference between $n(t)$ and $n^4(t)$?

3.4 Plot the current $I_K(t)$ as a function of time for $u_0 = 40$ mV.

3.5 If we measure $I_K(t) = \bar{g}_K n(t)^p (u(t) - E_K)$ for voltage steps of various amplitudes, how can we determine p, $\tau_n(u)$ and $n_\infty(u)$?

Exercise 4: Gating dynamics – two equivalent mathematical descriptions

The dynamics of the gating variable m (and similarly for the other variables h and n) are often formulated as

$$\frac{dm}{dt} = \alpha_m(u)(1 - m) - \beta_m(u)m. \tag{2}$$

As a reminder, we had

$$\frac{dm}{dt} = -\frac{m - m_0(u)}{\tau_m(u)}. \tag{3}$$

4.1 Calculate $m_0(u)$ and $\tau_m(u)$ that make these dynamics equal.

4.2 Assume $\alpha_m(u) = \beta_m(u)^{-1}$. If you assume that $m_0(u) = 0.5\,(1 + \tanh\left[\gamma(u - \theta)\right])$, what is the resulting expression for $\alpha_m(u)$?

4.3 What is the resulting expression for $\tau_m(u)$?