Neural Networks and Biological Modeling

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ANSWERS TO QUESTION SET 2

Exercise 1: Nernst equation

1.1 We plug the given values into the Nernst equation and compute E_{rev}. Pay attention to signs!

For Ca^{2+} we get:

$$E_{Ca^{2+}rev} = -\frac{1.38 \cdot 10^{-23} \, \text{J/K} \cdot 310 \text{K}}{+2 \cdot 1.60 \cdot 10^{-19} C} \cdot ln(\frac{10^{-4} \, mol \, m^{-3}}{1.5 \, mol \, m^{-3}}) = +0.1284 \frac{J}{C} = 128.4 mV$$

ion	C_{int}	C_{ext}	E_{rev}
K^+	140	5	-89.0 mV
Na^+	10	145	71.4 mV
Ca^{2+}	10^{-4}	1.5	128.4 mV

1.2 The current is given by $I = g(u - E_{\text{rev}})$ where g is the conductance and E_{rev} the reversal potential for the ion under consideration, and u is the membrane potential. For constant conductance, the current-voltage relationship is a straight line. Note: in the plot below, the Ca current has been multiplied by 100 in order to increase readability and to emphasize the non-negative slope.

By convention, an *inward* current has negative sign, and corresponds to the movement of positively charged particles from the outside to the inside of the cell. For a resting potential of -65 mV, sodium and calcium ions generate inward currents, while potassium ions generate an outward current. If the conductances are varied, the slope of the lines will change accordingly, but the reversal potentials are unaffected.
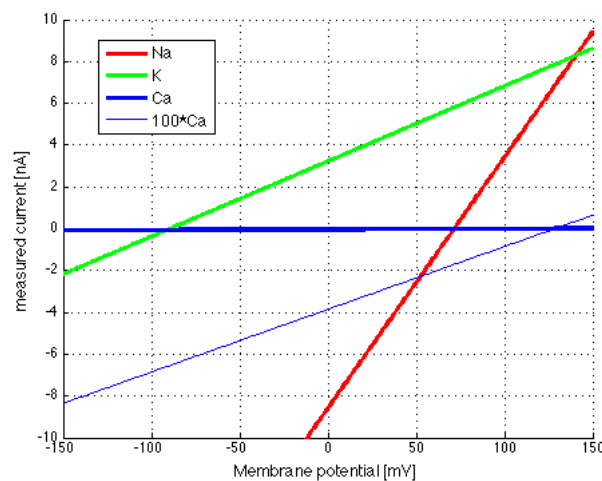

Figure 1: Clamped voltage and measured current for different channels

Exercise 2: Model of an ion channel

2.1 r is the fraction of open channels (or, equivalently, the probability that a single channel is open). $1 - s$ is the fraction of inactivated channels. The fact that r stands for activation and s for inactivation is due to the differences in the time constants (the channel must activate before it inactivates). g_{ion} is the maximal conductance for the ion under consideration (g_{ion} = conductance of a single channel $\times$ total number of channels), and u_{ion} its reversal potential.

2.2 The two gating variables r and s approach their target value r_0 and s_0 (see last week exercises for a discussion of the linear diff.eq.). We read the following values from the given figures: r grows with $\tau_r = 1ms$ from 0 to 1 (or maybe a little less if you take u' from the figure rather than from the text which specifies $\epsilon << 1$). s decays from 1 to 0.2 with $\tau_s = 15ms$. When computing $I_{ion}(t)$ don't forget to take the gating variables to the power n1 or n2 as given in the exercise.

- For $t < 0$, the channel is closed because $r = 0$.

- At $t = 1$ ms, the channel is partially open because $r_0 \simeq 1$ and $\tau_r = 1$ ms (so that $r \simeq 1 - e^{-1} \simeq 0.6$).

- At $t = 3$ ms, the channel is almost completely open because $r \simeq 1$ but $s \simeq 1$ due to its long time constant (15 ms).

- At $t = 20$ ms, the channel is partially closed because $s_0 \simeq 0.2$ and $\tau_s = 15$ ms.

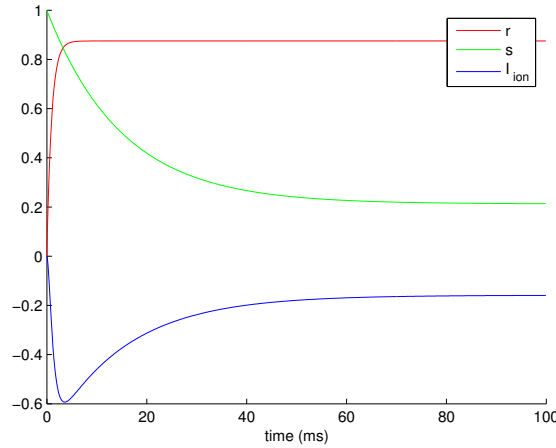- At $t = 100$ ms, the channel is almost completely closed because $s \simeq 0.2$.

Figure 2: Evolution of the gating variables r and s and of the associated ionic current I_{ion} for parameter values $u_1 = -50$ mV, $u_2 = -30$ mV, $u' = -32.5$ mV, $g_{\text{ion}} = 0.03$ nS, and $E_{\text{ion}} = 0$ mV.

Exercise 3: Dynamics of conductances

3.1 For $t < 0$, n is at its resting value $n_\infty(0) = 0$. If the membrane potential instantaneously jumps to a value u_0, $n(t)$ approaches its new resting value exponentially with time constant $\tau_n(u_0)$:

$$n(t) = n_\infty(u_0)(1 - e^{-t/\tau_n(u_0)})$$

3.2 We observe that for $u_0 = 10$mV and 20 mV, the two resulting curves are just scaled versions of each other (same time constant $\tau_n(u) = 5$ms). For $u_0 = 40$mV we see not only a larger final value but a much faster growth because $\tau_n(u)$ is 1ms.
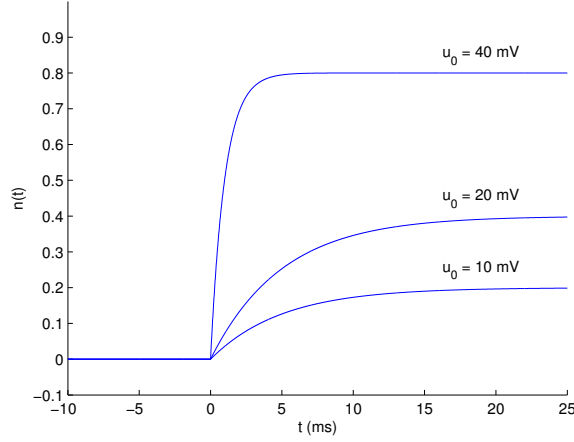

3.3 Note the qualitative difference: only for n^1 we see the typical exponential decay to the target value, whereas when taking the small values (n is smaller than 1 and very small for $t << \tau_n$) to some power, the curves are "starting flat". We can quantify this observation by linearizing n(t) around t=0 and find the following first degree Taylor polynomial $P_1(t)$:
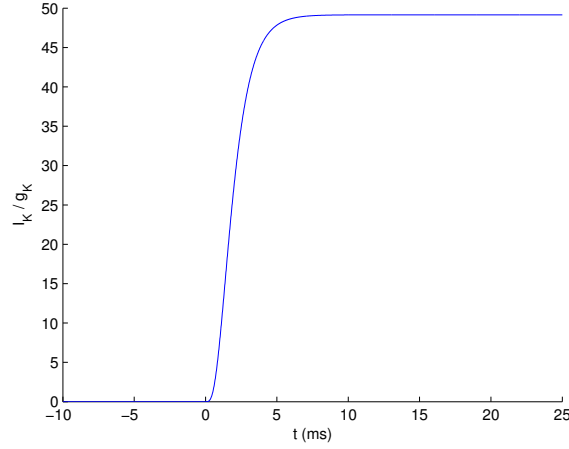
$$n(t) = n_\infty(u_0)(1 - e^{-t/\tau_n(u_0)}) \approx P_1(t) = n(0) + n'(0)(t - 0) = 0 + n_\infty(u_0)\frac{1}{\tau}e^{-0/\tau_n(u_0)}(t - 0) = n_\infty(u_0)\frac{t}{\tau_n(u_0)}$$

whereas for $[n(t)]^k, k \geq 2$ we find $P_1(t) = ... = 0$ as you can see again from the Taylor expansion:

$$[n(t)]^k = [n_\infty(u_0)(1 - e^{-t/\tau_n(u_0)})]^k$$

$$\approx [n_\infty(u_0)(1 - e^{-0/\tau_n(u_0)})]^k + k[n_\infty(u_0)(1 - e^{-0/\tau_n(u_0)})]^{k-1} \times (n_\infty(u_0)\frac{1}{\tau}e^{-0/\tau_n(u_0)}) \times (t - 0)$$

$$= 0 + k[0]^{k-1} \times n_\infty(u_0)\frac{t}{\tau_n(u_0)} = 0$$
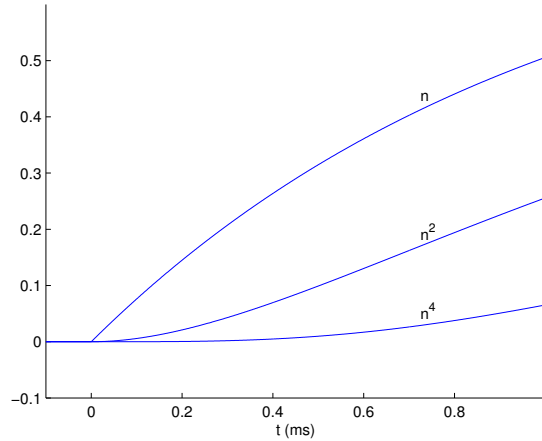
3.4 With $E_K = -80$ mV, we obtain

3.5 The exponent p is measured by fitting the power-law behaviour of $I_K(t)$ for small t. The activation curve n_∞ is obtained by plotting the maximal value of I_K for each voltage step against the value of the voltage, and the time constant τ_n can be deduced from the slope of $\sqrt[p]{I_K}$ for small times, or by fitting an exponential to $\sqrt[p]{I_K}$.

Exercise 4: Gating dynamics – two equivalent mathematical descriptions

The two descriptions of the gating dynamics are equivalent. The formulation introduced in this exercise is typically used in chemistry. See chapter 2.2.2 in http://neuronaldynamics.epfl.ch/online/Ch2.S2.html for more information.

4.1 By rearranging the terms on the right hand side of Eq. (2) to a form that corresponds to Eq. (3) we see that to make these dynamics equal we have to choose: $m_0(u) = \frac{\alpha_m(u)}{\alpha_m(u)+\beta_m(u)}$ and $\tau_0(u) = \frac{1}{\alpha_m(u)+\beta_m(u)}$

4.2 Assuming $\alpha = \beta^{-1}$ (we neglect indices and the voltage dependence for simplicity), we arrive at

$$m_0 = (1 + \frac{1}{\alpha^2})^{-1}.$$

We further notice that by using $\tanh(x) = \frac{1-e^{-2x}}{1+e^{-2x}}$ we can simplify $0.5(1 + \tanh[x]) = (1 + e^{-2x})^{-1}$. Then we can solve for α as

$$\begin{aligned}
(1 + \frac{1}{\alpha^2})^{-1} = m_0 &= (1 + e^{-2\gamma(u-\theta)})^{-1} \\
\alpha^2 &= e^{2\gamma(u-\theta)} \\
\alpha &= e^{\gamma(u-\theta)}.
\end{aligned}$$

4.3 We know that $\tau = (\alpha + \beta)^{-1}$. Using the assumptions and the form for α we just calculated we get:

$$\tau = (\alpha + \beta)^{-1} = \left(e^{\gamma(u-\theta)} + e^{-\gamma(u-\theta)}\right)^{-1} = 0.5\,\mathrm{sech}(\gamma(u-\theta)).$$