Neural Networks and Biological Modeling

Professor Wulfram Gerstner
Laboratory of Computational Neuroscience

Question set 2

Exercise 1: Model of an ion channel

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

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

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

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

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

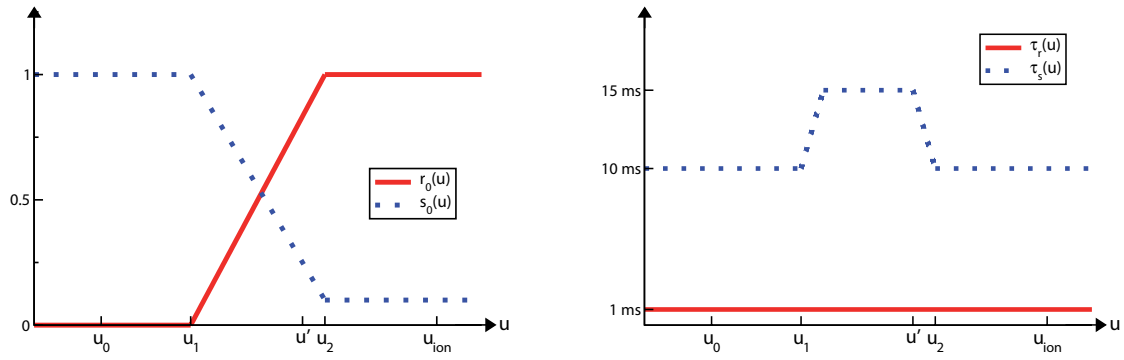


Figure 1: Graphical representation of the variables r_0, s_0, τ_r and τ_s.

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

r : .....

s : .....

g_{ion} : .....

u_{ion} : .....

1.2 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 2: Nernst equation

Using the Nernst equation,

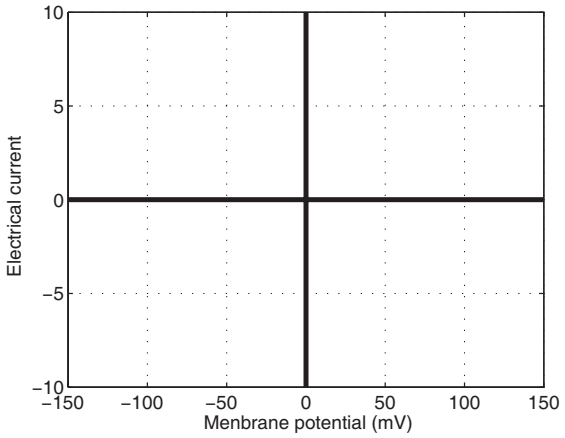
$$E_{\text{rev}} = -\frac{kT}{ze} \log\left(\frac{C_{\text{int}}}{C_{\text{ext}}}\right) , \tag{1}$$

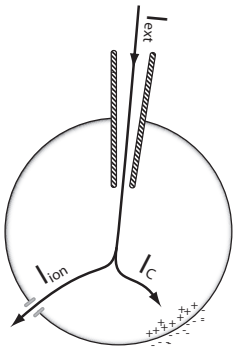
where $k \simeq 1.4e^{-23}$J/K is the Boltzmann constant, T is the absolute temperature, e is the electron's charge, and z is the valence of the ion species.

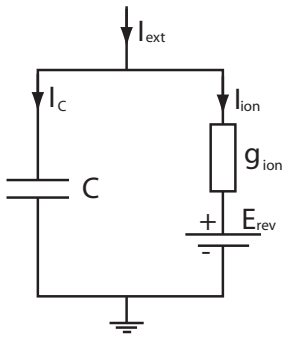
2.1 Calculate the reversal potential for Na^+, K^+ and Ca^{2+} assuming the following concentrations:

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

2.2 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 $I_{\text{ion}} = g(u - E_{\text{rev}})$, $g_{\text{Na}} = 120\text{nS}$, $g_{\text{K}} = 36\text{nS}$, $g_{\text{Ca}} = 0.3\text{nS}$.







2.3 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 3: Dynamics of conductances

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

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

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 obey 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:

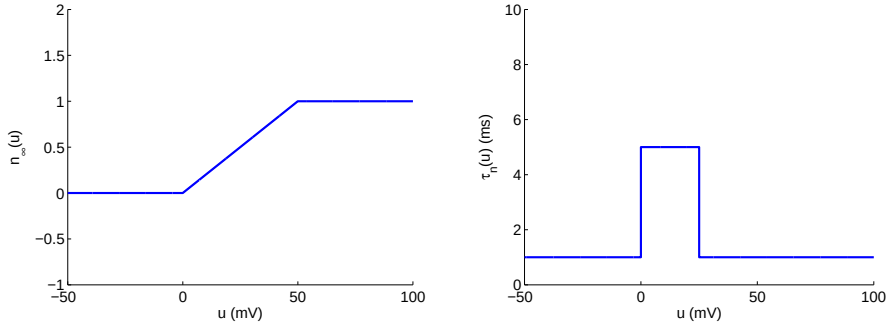
$$\tau_n(u) = \begin{cases} 1 \text{ ms} & \text{if} \quad u \leq 0 \\ 5 \text{ ms} & \text{if} \quad 0 < u \leq 25 \\ 1 \text{ ms} & \text{if} \quad u > 25 \end{cases}$$

and

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

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 Voltages steps of various amplitudes, how can we determine p, $\tau_n(u)$ and $n_\infty(u)$?

Exercise 4: Model of a synapse

The arrival of a presynaptic action potential at a synapse triggers the release of neurotransmitter, which is then taken up by specialized receptors on the postsynaptic membrane. The activation of these receptors triggers the opening of ion channels in the postsynaptic membrane. As a result, an electrical current flows accross the membrane and provokes a transient change in membrane potential, called a postsynaptic potential.

The opening of ion channels can be modeled by a transient increase in conductance, resulting in a postsynaptic current of the form

$$I^{\text{ion}} = g(t - t_0)(u - E_0) \tag{2}$$

where t_0 is the time of arrival of the presynaptic spike and E_0 the reversal potential for the synapse. We suppose that the time course of the conductance increase can be modeled by an α-function:

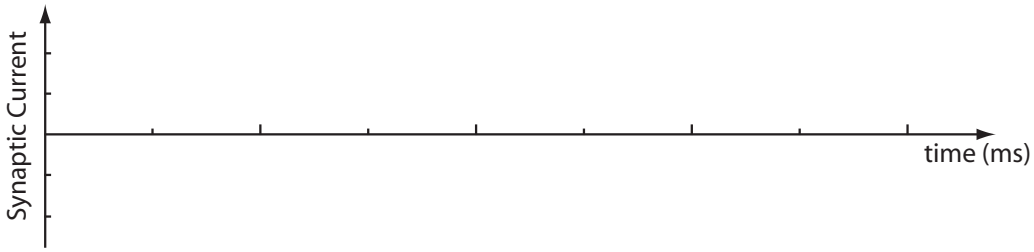
$$g(t) = g_0 \frac{t}{\tau} e^{-t/\tau}\,. \tag{3}$$

Consider excitatory and inhibitory synapses with the following parameters:

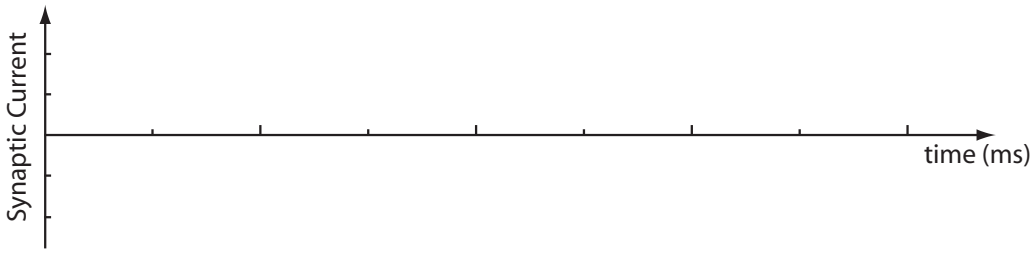
excitatory synapse : $g_0^{\text{exc}} = 1$ nS, $\tau^{\text{exc}} = 1$ ms, $E_0^{\text{exc}} = 0$ mV

inhibitory synapse : $g_0^{\text{inh}} = 10$ nS, $\tau^{\text{inh}} = 10$ ms, $E_0^{\text{inh}} = -70$ mV

4.1 Suppose that the membrane potential is clamped at -60 mV, and that an excitatory synapse is activated at time $t = 5$ms and an inibitory one at time $t = 20$ms. Sketch the form of the postsynaptic current in the following graph.



4.2 Same as in 4.1, but $u = -72$ mV.



4.3 What happens if $u = -70$ mV?

Exercise 5: Numerical Integration of H.-H. model of the Squid Axon

Make sure you have correctly installed ipython. In case you have any doubt ask any of the assistants. Download HH.py from the course's webpage on moodle. HH.py is a python module containing 4 main functions: HH_Step, HH_Ramp, HH_Sinus and HH_ForwardEuler. The later is a subroutine used by the first 3 to perform the numerical integration. With those, you can simulate a step current, a ramp current of a sinusoidal current injected in the squid axon. The specific formulas implemented are described in p. 36 of 'Spiking Neuron Models'. Once you have started ipython -pylab in the directory containing HH.py, simply type:

```
>> import HH
```

to port HH.py onto your current session. Then you can simulate a step current in a Hodgkin-Huxley model by typing:

```
>> HH.HH_Step()
```

which should trigger a plot with three panels. To have information on the arguments of the function, simply type:

```
>> HH.HH_Step?
```

or open HH.py in any text editor.

5.1 What is the lowest step current amplitude for generating at least one spike?

5.2 What is the lowest step current amplitude to generate repetitive firing?

5.3 What is the minimum current required to make a spike when the current is slowly increased (ramp current waveform) instead of being increased suddenly?

5.4 What is the current threshold for repetitive spiking if the density of sodium channels is increased by a factor of 1.5?

Hint: You can change the parameters of the model in the appropriate section of HH.py; use any text editor to save the change. To actualize the change you have saved, you must type in your current ipython workspace:

```
>> reload HH
```

5.5 Look at HH_Step(I_amp = -5) and HH_Step(I_amp = -1). What is happening here? To which gating variable do you attribute this rebound spike?