**M2 Biology** **30/09/21**

# TD2: Models of Neurons II

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TD material is available at:

`https://github.com/Elieoriol/2122_UlmM2_ThNeuro/tree/master/TD2`

In the first tutorial, we have developed the most basic model of a spiking neuron: the LIF neuron. In this tutorial, we will underline the inability of this model to account for a fundamental property of real neurons that is post-spiking refractoriness. We will also be interested in the modeling of two more features of biological neurons: adaptation and shunting inhibition. Finally, we will introduce the QIF model, richer in behavior than the LIF one.

## 1 Refractory period

Additional rules can be added to account for other observed features of real spikes, also called action potentials. One of the observed features is a refractory period; immediately after a spike the neuron cannot produce another spike for a short period of time called the refractory period. The refractory period can be included in models of neurons in a number of ways.

### 1.1 Forced voltage clamp

The voltage is fixed at its reset value following a spike for the duration of the refractory period $\tau_{ref}$.

1. What is the maximal firing rate $f$ with this method?

   A disadvantage of this method is that as the firing rate of the neuron increases, the neuron spends a greater proportion of its time in the refractory period with the membrane potential at its low reset value. Therefore, the mean membrane potential decreases with increased input in such a model, in contrast to the behavior of real neurons.

### 1.2 Refractory conductance

A solution closer to biology is to add a large conductance $g_K$ at spike time, producing an outward hyperpolarizing current. In real neurons, such a late current can most often be related to potassium channels.

2. Explain why a large conductance can replace the LIF reset mechanism. Propose a differential equation for $g_K$ to enable the neuron to spike again after the refractory period. Does this model solve the previous problem?

*Note: This is a first step towards the Hodgkin-Huxley model of spiking neurons. The difference resides in that instead of roughly adding a decaying conductance at spike time, this conductance is made non-linearly voltage-dependent: when the membrane potential reaches high values, this conductance becomes large and brings the potential down.*

### 1.3 Raised threshold

A third alternative could be to consider that the neuron does not really go into a refractory period but instead becomes less prone to spiking by raising its threshold.

3. By analogy with the previous method, can you think of a way to implement a raised threshold method?
4. **num** Implement numerically the three previous methods.

## 2 Firing rate adaptation

A well-known property of neurons is adaptation. For instance, driven by an injected current, a decrease in time of the firing rate of a neuron to a steady-state value can be observed.

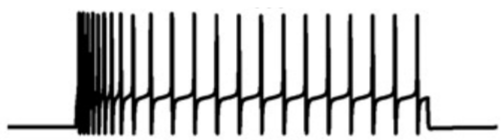

Figure 1: Example of firing rate adaptation in response to an injected current.

We are going to model this phenomenon by considering the effect of ion channels which open whenever a neuron fires a spike and let in negative current, such that:

$$\tau_m \frac{\mathrm{d}V}{\mathrm{d}t} = -V - W + I \tag{1}$$

where, after each spike occurring at $V_{th}$, $W$ is increased by $W_R$ and $V$ is reset to 0. Between spikes, $W$ decays back to zero with time constant $\tau_w$:

$$\tau_w \frac{\mathrm{d}W}{\mathrm{d}t} = -W \tag{2}$$

### 2.1 First approximation

We first make the approximation that $W$ is constant between spikes. A constant current $I_{syn} > V_{th}$ is injected into the neuron.

1. Discuss qualitatively what happens after the first spike.
2. At which value of $W$ does the model stop spiking? Show that the total number of spikes emitted is roughly $(I_{syn} - V_{th})/W_R$.
3. Compute the duration of an interspike interval (ISI) as a function of $W$ in that interval.

### 2.2 General firing rate

It is no longer possible to ignore the decay of $W$ if the ISI becomes comparable to the time constant of the decay $\tau_w$.

4. Can you explain why? Is it possible for the neuron to stop spiking?

We therefore consider that the system has reached its equilibrium firing rate and fires spikes with a period $T$.

5. Compute the time course of $W$ between two successive spikes, assuming that immediately after the first of the two spikes $W(t=0) = W_0$.
6. Show that $W_0$ is given by:
$$W_0 = \frac{W_R}{1 - \exp(-T/\tau_w)}. \tag{3}$$
7. We assume that $T \ll \tau_w$, such that $W$ can be approximated by its average value during the whole interspike interval. Show that the period $T$ of spike emission is given by:
$$T = \tau_m \cdot \log\left(\frac{I - W_R\tau_w/T}{I - V_{th} - W_R\tau_w/T}\right). \tag{4}$$
8. Show that, as the injected current increases, the neuron firing rate $r(I)$ behaves as:
$$r(I) \sim aI \tag{5}$$
with $a = [\tau_w W_R + \tau_m V_{th}]^{-1}$.
9. How does this compare to an integrate-and-fire neuron without firing rate adaptation?

## 3 Non linear models

Linear models cannot reproduce all the behaviors of biological neurons. We propose to study a nonlinear model of neurons and show how it can display a richer repertoire of behaviors.

The model we consider is the *quadratic integrate and fire* (QIF) model:

$$\begin{aligned} \frac{\mathrm{d}V}{\mathrm{d}t} &= V^2 + b \\ \text{if } V > V_{peak} &\text{ , then } V \to V_{reset} \end{aligned} \tag{6}$$

We consider here the potential $V$ and the quantity $b$ to be adimensional (through normalization for instance). $b$ can be a function of time (a varying current), but we consider it constant for the moment.

1. Would you describe $V_{peak}$ as a threshold?

### 3.1 $b > 0$

2. Describe the behavior of the neuron in this case.

### 3.2 $b < 0$

3. Can you characterize the steady states of the neuron? Plot the graph of these steady states against $b$.

4. Depending on $V_{reset}$ and $b < 0$, what are the different behaviors of the neuron regarding excitation?

### 3.3 Bifurcation diagram

5. Plot the bifurcation diagram of the system, in the $V_{reset}$ and $b$ space.

6. We consider $V_{reset} > \sqrt{|b|}$. Can you compute the period of the oscillations? We note that the solution of the differential equation in this case is:

$$V(t) = \sqrt{|b|}\, \frac{1 + \exp\left(2\sqrt{|b|}(t + t_0)\right)}{1 - \exp\left(2\sqrt{|b|}(t + t_0)\right)}$$

with $t_0 = \dfrac{1}{2\sqrt{|b|}} \log\left(\dfrac{V_{reset} - \sqrt{|b|}}{V_{reset} + \sqrt{|b|}}\right)$.

### 3.4 Analogy with "theta neurons"

The theta model is described by the following equation:

$$\frac{\mathrm{d}\theta}{\mathrm{d}t} = 1 - \cos\theta(t) + [1 + \cos\theta(t)] \cdot I(t) \tag{7}$$

We consider that a spike is emitted when $\theta$ reaches the value $\pi$.

7. Show that for $I < 0$ there are two equilibria for the system, a stable and an unstable one. Show that if $\theta$ is not initially equal to the unstable equilibrium, it converges to the stable equilibrium.

8. In the case $I > 0$, show that there is no equilibrium. Conclude that the trajectories are periodic orbits with regular spiking.

9. Can you see a link with the quadratic model? What happens when $I = 0$?

## 4 Conductance-based synapses and shunting inhibition

Another interesting phenomenon is shunting inhibition. Experimentally, one can observe that the effects of inhibition and excitation do not necessarily sum in a linear fashion, such that inhibition can "shunt" the effect of excitation. This effect particularly applies with excitatory synapses spanning the dendritic tree and inhibitory synapses closer to the soma.

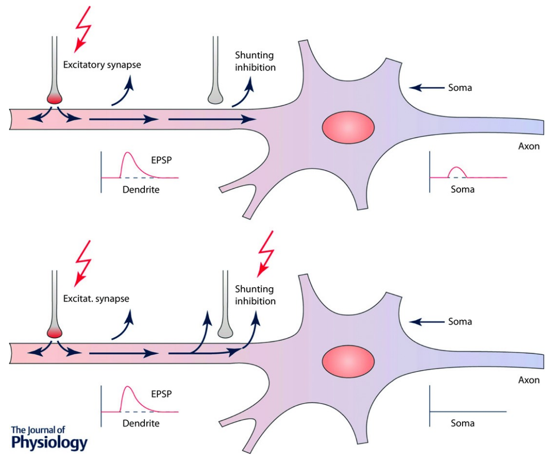


Figure 2: Shunting inhibition.

We consider a neuron well below the threshold for action potential initiation. The neuron is described by its membrane potential $V(t)$ that obeys the equation:

$$C_m \frac{\mathrm{d}V}{\mathrm{d}t} = -g_L(V - V_L) - g_E(t)(V - V_E) - g_I(t)(V - V_I) \tag{8}$$

with:

- $C_m$ the membrane capacitance
- $g_L$ the leak conductance and $V_L$ the resting membrane potential
- $g_E(t)$, $g_I(t)$ the time-dependent excitatory/inhibitory synaptic conductances
- $V_E$, $V_I$ the excitatory/inhibitory reversal potentials

In real neurons, $V_L \sim -70$mV, $V_I \sim -70$mV or lower, $V_E \sim 0$ mV. For the sake of simplicity we set here the resting potential to be $V_L = 0$mV, and we set $V_I = V_L$.

We consider the situation in which the voltage is $V = 0$ at $t = 0$, and investigate the effects of various combinations of excitatory and inhibitory conductances on the voltage response.

1. Rewrite (8) in terms of the membrane time constant $\tau_m = C_m/g_L$, rescaled conductances $\tilde{g}_E(t) = g_E(t)/g_L$, $\tilde{g}_I(t) = g_I(t)/g_L$, and $V_E$.

2. Show that (8) can be rewritten as:

$$\tau_{eff}(t) \frac{\mathrm{d}V}{\mathrm{d}t} = -V + V_{eff}(t) \tag{9}$$

   where $\tau_{eff}(t)$ and $V_{eff}(t)$ are functions of $\tau_m$, $\tilde{g}_E(t)$, $\tilde{g}_I(t)$, and $V_E$.

### 4.1 Excitation only

We consider a situation in which there is no inhibition. The (rescaled) excitatory conductance opens abruptly at $t = 0$, and closes abruptly at $t = \tau_E$,

$$\tilde{g}_E(t) = \begin{cases} 0 & t < 0 \\ g_E & t \in [0, \tau_E] \\ 0 & t > \tau_E \end{cases} \tag{10}$$

3. Compute the response of the voltage (EPSP, excitatory post-synaptic potential) in both intervals $t \in [0, \tau_E]$ and $t > \tau_E$. Sketch qualitatively the shape of the EPSP.

4. What is the amplitude of the peak of the EPSP? Discuss qualitatively how it depends on $g_E$, $V_E$ and the ratio of time constants $\tau_E/\tau_m$.

### 4.2 Inhibition only

We consider the reverse situation in which there is no excitation, and the (rescaled) inhibitory conductance opens abruptly at $t = 0$, and closes abruptly at $t = \tau_I$,

$$\tilde{g}_I(t) = \begin{cases} 0 & t < 0 \\ g_I & t \in [0, \tau_I] \\ 0 & t > \tau_I \end{cases} \tag{11}$$

5. Compute the response of the voltage (IPSP, excitatory post-synaptic potential). What does it look like?

### 4.3 Both

We now consider the situation in which there is a tonic inhibitory conductance, $g_I(t) = g_I$. The excitatory conductance again opens abruptly at $t = 0$ and closes abruptly at $t = \tau_E$.

6. Repeat the steps of section 1. Compare what happens with and without inhibition. Does the system sum linearly excitatory and inhibitory inputs?