M2 Biology **08/10/20**

TD1: Models of Neurons I

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The goal of this series of problems is to investigate various dynamical properties of the simplest type of single neuron models: point neurons. In these models, a neuron's complex morphology is simplified to a single point, characterised by its membrane potential V, which is the difference in potential between the interior and the exterior of the neuron.

In the following we will consider the parameters:

C_m	g_l	E_l	V_{th}	V_{reset}
100 pF	10 nS	-70 mV	-50 mV	-80 mV

1 LIF neurons

1.1 Preliminary maths

Consider the following differential equation for a variable x evolving with the time t:

$$\tau \frac{\mathrm{d}x}{\mathrm{d}t} = -x(t) + c(t) \tag{1.1}$$

where the initial condition is given by $x(t=0) = x_0$.

1. Compute the time evolution of $x(t)$ when $c(t)$ is constant, equal to c_0.
2. For an arbitrary function $c(t)$, verify that a formal and general solution to the differential equation is given by:

$$x(t) = e^{-\frac{t}{\tau}} \left[x_0 + \frac{1}{\tau} \int_0^t c(t')\, e^{\frac{t'}{\tau}}\, \mathrm{d}t' \right]. \tag{1.2}$$

1.2 Leaky neuron

Neuron membranes are permeable to ions, therefore differences in ion concentration and in electric potential between the interior and the exterior of the neuron result in a flow of ions across the membrane (through dedicated channels), according to:

$$I = -g_l(V_m - E_l) \tag{1.3}$$

where g_l is the leak conductance and the leak potential E_l is the value of the membrane potential V_m for which there is no current across the membrane. This current results in the accumulation of charge Q close to the membrane of the neuron that acts as a capacitor, itself resulting in a membrane potential:

$$Q = C_m V_m \tag{1.4}$$

where C_m is the membrane capacitance.

3. Knowing the current I corresponds to the variation in time of charge Q in the neuron, obtain a differential equation governing the time course of the membrane potential V_m. Solve this equation for any initial condition V_0, introducing a time constant τ_m.
4. Depending on its initial value V_0, how does the membrane potential V_m behave in time?

1.3 Leaky Integrate-and-Fire model

The LIF model is a good starting point for simulating neurons. It reproduces some qualitative features of the membrane potential dynamics, and introduces a framework on which we can build more realistic models.

The LIF model is a differential equation for the membrane potential of a neuron with a capacitance and a leak term combined with an additional tweak: when the membrane potential reaches a particular value, called the threshold, a spike is emitted and the membrane potential is returned to a reset value.

The dynamical equation for the membrane potential is:

$$C_m \frac{\mathrm{d}V_m}{\mathrm{d}t} = g_l(E_l - V_m) + I_{app} \tag{1.5}$$

$$\text{if } V_m > V_{th} \text{ , then } V_m = V_{reset} \tag{1.6}$$

with I_{app} a constant applied current.

As we can observe on the simulations, there are different regimes depending on the injected current.

5. Can you find the condition on which the neuron is able to spike starting from a potential $V_0 < V_{th}$? Deduce the threshold current for which this condition is verified. Plot the corresponding bifurcation diagram in the 1D I_{app} space.

1.4 Euler Method

Any real function f of a variable t that is infinitely differentiable can be written as a Taylor expansion in $t + \Delta t$:

$$f(t + \Delta t) = f(t) + \sum_{n=0}^{\infty} \frac{f^{(n)}(t)}{n!}(\Delta t)^n$$

with $f^{(n)}(t)$ the n^{th} derivative of $f(t)$. For Δt small enough, up to first order:

$$f(t + \Delta t) = f(t) + f'(t)\,\Delta t + \mathcal{O}(\Delta t^2) \tag{1.7}$$

6. Using this formula, can you elaborate a method to simulate the differential equation of the membrane potential obtained in question 1? And for the LIF model?
7. **num** This numerical scheme is called the Euler method. Implement it in Python to get the evolution of V_m without the reset mechanism and compare with your solution obtained at question 3 for different values of I_{app}. Now add the reset mechanism, what do you observe?

Note: All the equations above were dependent on the time variable t. The same ideas can be transferred to functions of space coordinates x, y... or any other type of variable.

Parenthesis: stiff equations A stiff equation is a differential equation for which certain numerical methods for solving the equation are numerically unstable, unless the step size is taken to be extremely small. With the Euler method, even simple linear equations can be stiff, such as:

$$f'(t) = -15f(t) \qquad x(0) = 1 \tag{1.8}$$

8. What is the analytical solution of this equation?

9. **num** What will be the problem with the Euler method? Can you numerically verify it?

1.5 Firing rate as a function of current (f-I curve)

When the applied current is held fixed, the time for the neuron membrane potential to increase from its reset value to the threshold can be calculated.

10. **num** Compute the inter-spike interval T_{ISI} as well as the firing rate f of the neuron. Numerically compute the firing rate for different values of I_{app} and compare.

11. Study the limits of this formula depending on I_{app}. Can you highlight a limit of the LIF model?

1.6 Response to an oscillating input current

We now inject of a small oscillating current $I_{app}(t) = 2I_0 \cos(\omega t)$ which we can also write as $I_{app}(t) = I_0 \left[e^{i\omega t} + e^{-i\omega t}\right]$. The membrane potential integrates this current, therefore when it reaches its steady state, it oscillates at the same frequency with a certain time lag given by a phase ϕ. We can therefore write the steady-state membrane potential as:

$$V_m(t) = E_l + A\left[e^{i(\phi+\omega t)} + e^{-i(\phi+\omega t)}\right] \tag{1.9}$$

12. Show that:

$$A\exp(i\phi) = \frac{I_0}{g_l + i\,C_m\omega} \tag{1.10}$$

13. Compute the amplitude A and phase ϕ of the response. Provide an explanation of the limiting behaviours at low ($\omega \ll g_l/C_m$) and high frequency ($\omega \gg g_l/C_m$). Does the membrane response show a peak at a particular non-zero frequency?

Note: Instead of writing $2\cos(\omega t) = e^{i\omega t} + e^{-i\omega t}$ *we could have written* $\cos(\omega t) = \Re(e^{i\omega t})$. *This way, we could have used a complex oscillating current* $I_{app}(t) = I_0 \cdot e^{i\omega t}$ *(which has no physical meaning) and take the real parts of the equations.*