Introduction to Computational Neuroscience

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Resumen

This document introduces fundamental concepts in computational neuroscience, with a particular focus on the role of modeling in understanding brain function. The purpose is to get enough deep to create new insights by the hand of investigation.

Índice

1. Generalities

1. Santiago Ramón y Cajal established that the brain is composed of discrete units—neurons—rather than forming a continuous fluid.

2. **Neuron**: A neuron is an electrically excitable cell that processes and transmits information through signals. It has three main components:

   - **Dendrites**: Receive input signals from other neurons.
   - **Soma (cell body)**: Acts as a nonlinear integrator. If the combined input exceeds a certain threshold, the neuron emits a spike.
   - **Axon**: Conducts the output spike to other neurons, often over long distances.

3. **Synaptic Communication**:

   - Synapses are the junctions where a presynaptic neuron communicates with a postsynaptic neuron.
   - **Action Potentials**: Given a big amount of inputs (e.g. 10.000), the membrane potential crosses a threshold, and an electrical event known as an action potential is generated. Its shape and amplitude remain constant as it travels down the axon.
   - A sequence of action potentials generated by a neuron over time is known as a **spike train**.

2. Model 1: Nernst Potential

The Nernst potential arises from the interplay between diffusion and electrostatics at equilibrium. When ions diffuse from a region of high concentration to low concentration—e.g., K^+ moving out of a neuron—the net movement carries positive charge away, leaving behind excess negative charge. This charge imbalance generates an electric potential that increasingly opposes the diffusion. At equilibrium, the chemical and electrical driving forces exactly cancel. The resulting voltage is the Nernst potential, so $n(x) = Np(x)$

$$p(x) \propto \exp(-B \cdot u(x)) \quad \Rightarrow \quad \frac{n_1(x)}{n_2(x)} = \exp(-B \cdot \Delta u)$$

Solving for the potential difference:

$$\Delta u = \frac{1}{B} \log\left(\frac{n_2(x)}{n_1(x)}\right)$$

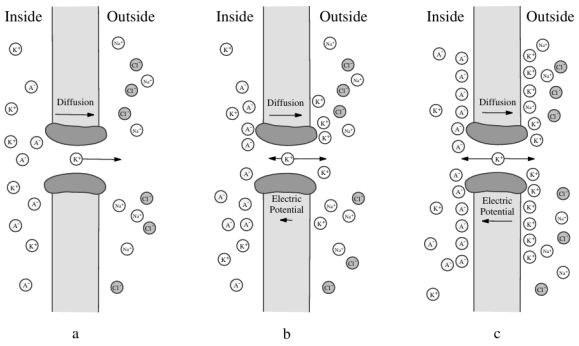

Figura 1: Visualization of membrane with two densities and equilibrium of two forces.

In biophysical terms, this yields the Nernst equation $E = k_B T \log\left(\frac{[\text{ion}]_{\text{out}}}{[\text{ion}]_{\text{in}}}\right)$ which is valid for a single ion type.

Insight: We model the system under thermal equilibrium, which balances the diffusive and electrical forces. What about the case out of equilibrium? How to model it?

3. Model 2: Hodgkin-Huxley Model

The Hodgkin Huxley (H-H) model improves the real neurons understanding. First, it describes the membrane potential as an electrical circuit consisting of a capacitor in parallel, where ion channels act as voltage-dependent gates. This arises non-equilibrium behavior.

Main Assumption: The action potential is the macroscopic answer to the sum of all the individual currents done by the ion channels. These channels arises are modeled as gates with RC dynamics.

1. **Capacitor - Membrane:** The neuron's membrane is modeled as a capacitor that stores energy in the form of an electric field:

$$C = \frac{Q}{U}$$

The capacitor current is nonzero only when the membrane potential changes over time, using Ohm's law:

$$I_C(t) = C\frac{du(t)}{dt}$$

2. **Current Conservation (Kirchhoff's Law):** The total membrane current $I(t)$ splits and sums:

$$I(t) = I_C(t) + \sum_k I_k(t)$$

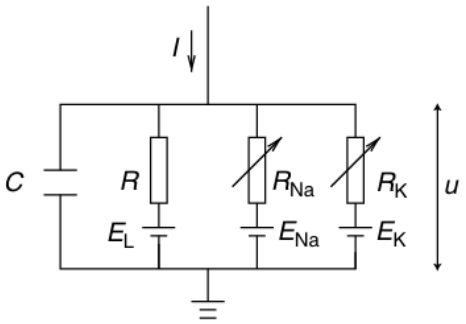

Figura 2: Electrical circuit representation of the Hodgkin-Huxley model showing membrane capacitance and gates dynamics.

Ionic Currents: Each ion species contributes to the total current based on its own gate:

$$\sum_k I_k = g_L(u - E_L) + g_{Na} \cdot m^3 h \cdot (u - E_{Na}) + g_K \cdot n^4 \cdot (u - E_K)$$

Gate Dynamics: Each gating variable $x \in \{m, h, n\}$ evolves over time as a first-order differential equation. Gating is sensitive to the membrane potential, so gates are classified as active or inactive. This mechanism is modeled by the probability that an active gate is open m (or n for K^+ channels) and the probability that an inactive gate is open is h. Then, a proportion of open & close channels is given by $p = m^a h^b$

$$\dot{x} = \frac{1}{\tau_x(u)}(x - x_0(u))$$

There are two figures important to understand the H-H model:

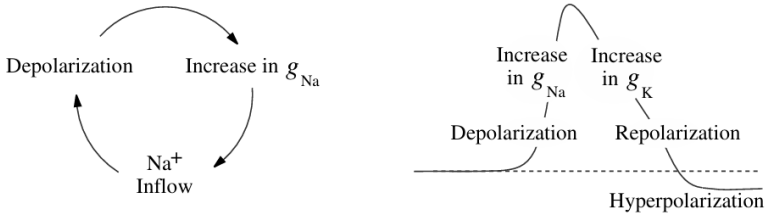

Figure 2.16: Positive and negative feedback loops resulting in excited (regenerative) behavior in neurons.

Figura 3: Figure taken from Izhikevich's book

The Hodgkin-Huxley model exhibits two key feedback loops: (1) A fast positive feedback loop where Na^+ channels open rapidly causing depolarization, and (2) A slower negative feedback loop where K^+ channels gradually open to repolarize the membrane. The temporal difference between these loops creates the characteristic spike. The spikes will depend on the parameters of the gates.

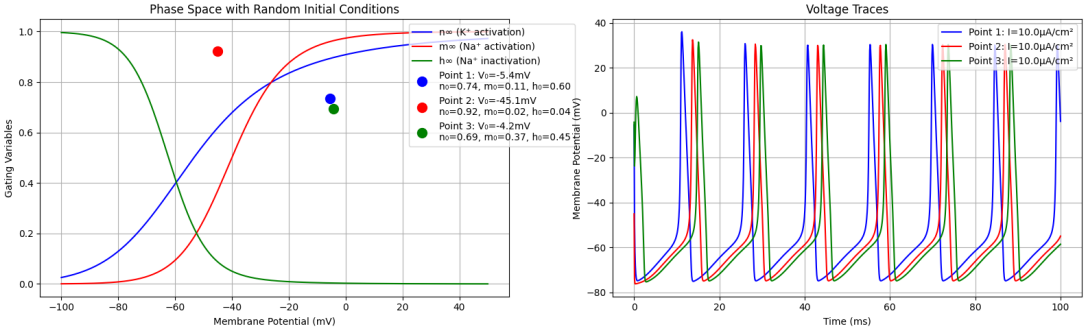

Figura 4: Spikes of the Hodgkin-Huxley model for different parameters.

4. Integrate and Fire Models

4.1. Perfect Integrate and Fire (IF)

In practice H-H model is computationally expensive, if we neglect the gates dynamics, the model can be simplified to an **Integrate and Fire** model. This model is simpler and focus in the linear integration of the inputs and the membrane represented as a voltage.

$C\frac{du}{dt} = I(t)$

Then the membrane potential grows linearly until it reaches a threshold θ and then it resets to a resting potential u_{rest}. At firing time $(t_f) - > u(t_f^-) = \theta$ and $u(t_f^+) = u_{rest}$. This model just integrates the input current and when the threshold is reached, it fires a spike and resets.

Clearly, we don't capture the spike decay. Then, to improve the phenomena, we can add a leaky term.

4.2. Leaky Integrate and Fire Model (LIF)

Building our neuron, it is important to capture the spike decay. Then, adding a leaky term to the equation will help us. Note that, we can imagine that the membrane as an RC circuit,

$C\frac{du}{dt} = -g_L(U - U_R) + I(t)$

Note that $-g_L(U - U_R)$ is the leaky term. To solve it, we can use the method of integrating factors.

1. Notation

$$\tau_m = RC \implies \tau_m \frac{dU}{dt} = -\big(U - U_R\big) + R\,I(t) \tag{1}$$

$$\frac{dU}{dt} + \frac{1}{\tau_m} U = \frac{U_R}{\tau_m} + \frac{R}{\tau_m} I(t) \tag{2}$$

2. Integrating factor. We assumed the derivative of the product.

$$P(t) = \frac{1}{\tau_m} \implies \mu(t) = e^{\int P(t)\,dt} = e^{\,t/\tau_m} \tag{3}$$

$$\frac{d}{dt}\big[e^{\,t/\tau_m}\,U(t)\big] = e^{\,t/\tau_m}\frac{U_R}{\tau_m} + e^{\,t/\tau_m}\frac{R}{\tau_m} I(t) \tag{4}$$

3. Integrate from t_0 to t

$$e^{\,t/\tau_m}\,U(t) = \int_{t_0}^{t}\Big[e^{\,s/\tau_m}\frac{U_R}{\tau_m} + e^{\,s/\tau_m}\frac{R}{\tau_m} I(s)\Big]\,ds \tag{5}$$

$$\boxed{U(t) = U_R + \frac{R}{\tau_m}\int_{t_0}^{t} e^{-\,(t-s)/\tau_m}\,I(s)\,ds} \tag{6}$$

4. Threshold and reset

Given a firing time $t_f : U(t_f^-) = \theta$ and (7)

Inmediatly after t_f we reset, so: $U(t_f^+) = U_R$, (8)

* Note that, the expression (6) is the solution of the LIF model. The key part of the solution is the convolution, in which the kernel is $e^{-\,(t-s)/\tau_m}$ and works as a memory of the past inputs $I(s)$. If τ_m is big, the memory is longer, and if τ_m is small, the memory is shorter.

4.3. Exponential Integrate and Fire Model (EIF)

The spiking of LIF model is not very realistic, since the spikes grows slowly compared with the real neuron spikes. To improve the model, we can use an exponential function to spike fastly. Then,

$$C\frac{du}{dt} = -g_L(U - U_R) + g_L \cdot \Delta_t \cdot \exp\left(-\frac{U - U_{th}}{\Delta_t}\right) + I(t) \tag{9}$$

where Δ_t is the slope of the spike, U_{th} is the effective threshold (marks when to grows exponentially). The solution will be implemented numerically.

4.4. Refractory Integrate and Fire Model (RIF).

LIF model is too linear, and neurons are not linear. Curiously, from experimental data we can infer a non-linear function $f(u)$.

$$\tau_m \frac{du}{dt} = f(u) + R \cdot I(t) \quad \text{rewriting} \quad \frac{f(u)}{\tau_m} = \frac{du}{dt} - \frac{R}{\tau_m} \cdot I(t) \tag{10}$$

The RHS can be measured, so the LHS can be inferred from data.

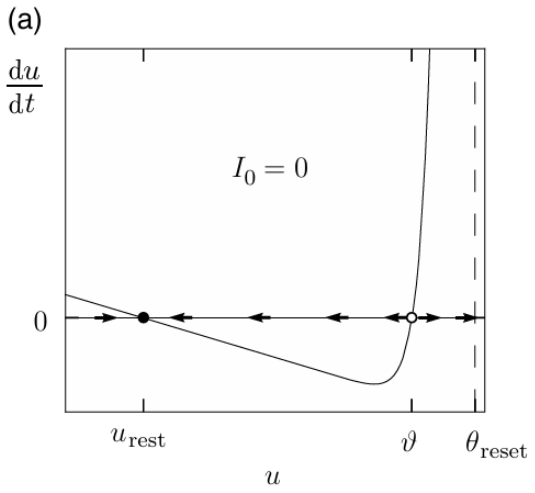

Figura 5: Infered shape from experimental data.

4.4.1. Typical form of $f(u)$

There exist two fixed points: u_{rest} (stable) and u_{th} (unstable). That dominates the dynamics of the system.

4.4.2. Adding refractory

When an spike is generated, the sodium channels inactivate, and other channels are active. Then, the shape of $f(u)$ is modified. In specific, the u_{th} moves temporarily higher, and the slope of $f(u)$ also changes. In other words, the u_{th} is moves temporarily higher, that is all.
Perfect, let's see the results of Integrate and Fire models.

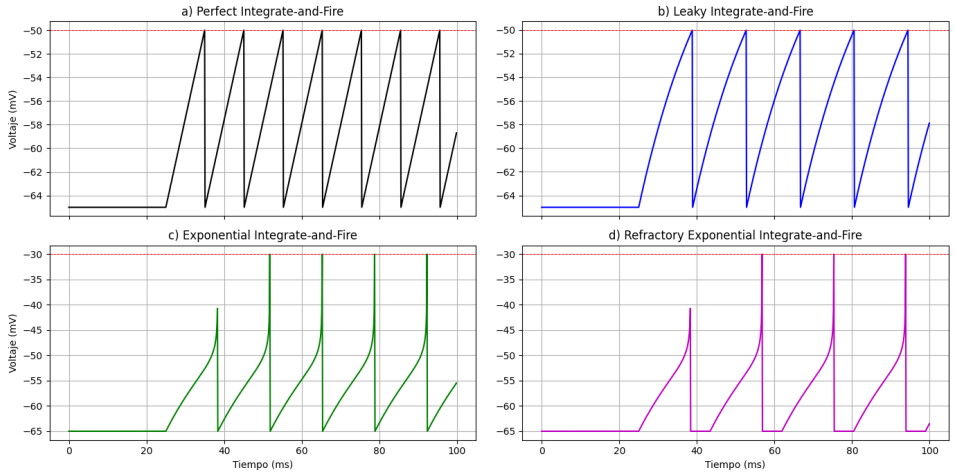

Figura 6: Comparison of IF models.

4.5. Adaptative Integrate and Fire

From experiments, it is clear how neurons change the distance between spikes after some time lapse, at begging they are short latter they are longer. This process is called adaptation. To implement adapatation, we need to add a new variable to the model w, so

$$\tau_m \frac{du}{dt} = f(u) + R \cdot I(t) - R \sum_k w_k \delta(t - t_k)$$
$$\tau_w \frac{dw}{dt} = \underbrace{-w}_{\text{decay}} + \underbrace{a\,(u - u_{\text{rest}})}_{\text{depolarization coupling}} \underbrace{+ b\,\tau_w \sum_f \delta(t - t_f)}_{\text{spike-triggered jump}} \tag{11}$$

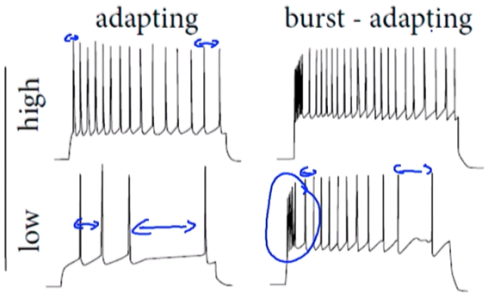

Figura 7: Adaptation of the neuron.

The Adaptive Exponential (AdEx) model incorporates an adaptation variable w coupled to the membrane potential. The parameter a governs subthreshold coupling, increasing w as the membrane departs from rest. The parameter b sets the spike-triggered increment of w. Adaptation accumulates through both mechanisms, doing difficult for the membrane potential to reach the threshold.

Just look how the patterns increased with another variable:

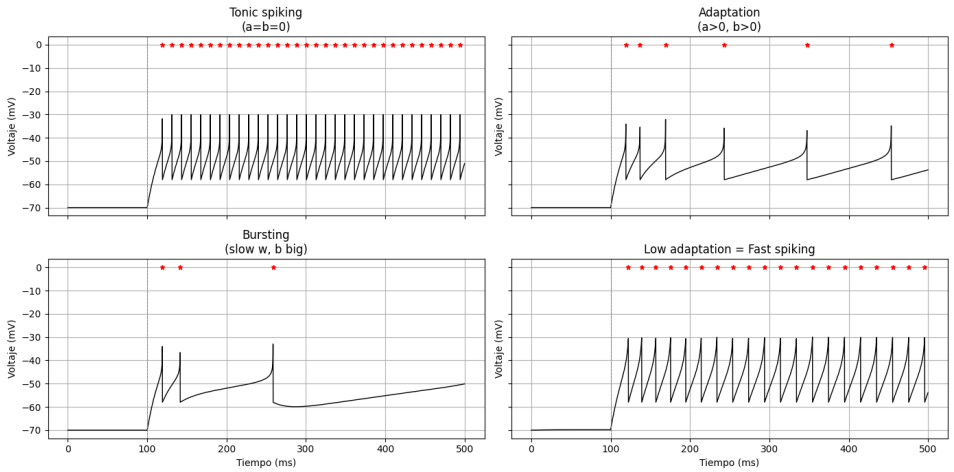

Figura 8: Different patterns of adaptation controlled by a, τ_k and b.

5. Spike train statistics

Hodgkin–Huxley-type models is compu tationally prohibitive, since we can simulate only a handful of neurons in real time. In contrast, using an integrate-and-fire model is computa tionally effective, but the model is unrealistically simple and incapable of producing rich spiking

Lectures:

1. The Computational Neuroscience of the Brain