HELMo Gramme

Master sustainable energy

Project - Hodgkin-Huxley Model

UE04 - Numerical methods for engineers

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1 The Hodgkin-Huxley Model

Initially, we selected the FitzHugh-Nagumo model, which is a simplified yet inaccurate version of the Hodgkin-Huxley model. The Hodgkin-Huxley model [2] offers a more comprehensive and intricate representation of action potential dynamics in neurons [3]. Consequently, we decided to utilize the latter as our ODE model.

The Hodgkin-Huxley model is considered a more realistic and accurate model for describing neuronal activity, as it takes into account the underlying biophysical mechanisms, such as the opening and closing of ion channels. However, its complexity makes mathematical and numerical analysis more difficult. The FitzHugh-Nagumo model, although a simplification, allows for the study of the fundamental properties of neuronal excitability and action potentials without the inherent complexity of the Hodgkin-Huxley model.[4]

$$\frac{dV}{dt} = \frac{1}{C}\left(I_{\text{ext}} - I_{\text{Na}} - I_{\text{K}} - I_{\text{L}}\right) \tag{1}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n \tag{2}$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m \tag{3}$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h \tag{4}$$

where :

- $V(t)$: membrane potential, representing the electrical potential difference between the inside and outside of the cell membrane [V]
- n, m, h : fraction of gates that are in the permissive state [-]
- C : membrane capacitance $[\frac{A \cdot s}{m^2 V}]$
- I_{ext} : applied external current density $[A/m^2]$
- I_{na}, I_K, I_L : ionic current density through sodium, potassium, and leak channels, respectively $[A/m^2]$
- $\alpha_n(V), \alpha_m, \alpha_h$: opening rates of ion channels as a function of membrane potential $[1/s]$
- $\beta_n(V)\beta_m(V), \beta_h(V)$: closing rates of ion channels as a function of membrane potential $[1/s]$

To simplifie the equation, we consider α_m,α_h,β_m,β_h as **constants**. We are aware that the behavior of these quantities resembles that of an inverse exponential function[5] [1]. Consequently, the equations found in the literature are inaccurate. Thus, we proceed to rewrite their equations :

$$\alpha_n = D_n \cdot e^{\frac{-V}{V_n}} \tag{5}$$
$$\beta_n = -D_n \cdot e^{\frac{-V}{V_n}} \tag{6}$$
$$\alpha_m = -\beta_m \tag{7}$$
$$\alpha_h = -\beta_h \tag{8}$$
$$\tag{9}$$

1.1 Verification to the dimensions of equations

- Equation (1): $\left[\frac{V}{s}\right] = \left[\frac{V\cdot m^2}{A\cdot s}\right] - \left(\left[\frac{A}{m^2}\right] + \left[\frac{A}{m^2}\right] + \left[\frac{A}{m^2}\right]\right) \left[\frac{V}{s}\right] = \left[\frac{V}{s}\right]$
- Equation (2): $\left[\frac{1}{s}\right] = \left[\frac{1}{s}\right] \cdot [-] - \left[\frac{1}{s}\right] \cdot [-] \left[\frac{1}{s}\right] = \left[\frac{1}{s}\right]$

1.2 What is the link between the equations and the physics of the problem ?[1]

To arrive at the mathematical formulation of the phenomena, we start by constructing an electrical circuit that represents the cellular membrane components of a neuron involved in action potentials, as shown in the figure 1 on the left. The extracellular environment is at the top, while the intracellular environment is at the bottom.

First, we insert an electrical capacitance between the two environments to represent the lipid bilayer that isolates them. Next, we represent each type of ion channel with an electrical resistance. These resistances depend on the voltage, as the channels are closed in the absence of a stimulus and open when a stimulus arrives.

Finally, we add a voltage-independent resistance for the current leakage, which represents small current charges that can escape due to the fact that the cell membrane is not completely impermeable to current even at rest. All components are arranged in parallel in the circuit, as ions can pass either through the lipid bilayer (which in practice is very rare) or through one of the ion channels but will never pass through several of these elements in series to go from one environment to another.[6]

[1] These functions were provided by Mrs. Hoffait

Terms in the equation	Signification	Electric component
V	Membrane Potential	Electrical Voltage
C	Membrane Capacity	Capacitor
I_{ext}	External applied current	Current source
I_{Na}	Sodium ion current	variable resistance (conductance) and battery
I_{K}	Potassium ion current	variable resistance (conductance) and battery
I_{L}	Leakage current	variable resistance (conductance) and battery

Table 1: Correspondence between the terms of the equations and the electrical components

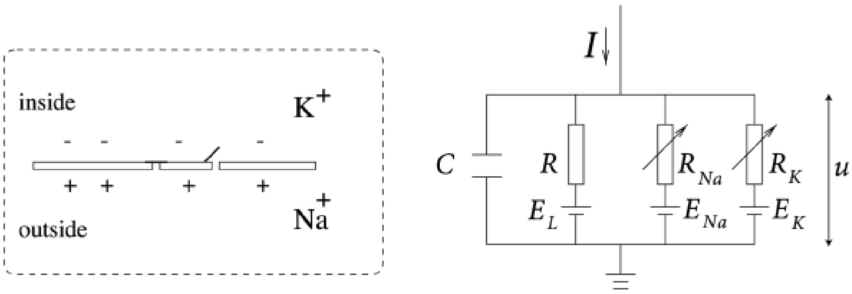

Figure 1: Hodgkin Huxley electric model

2 How does this system meet the constraints imposed by the professor ?

We must define the external current I_{ext} function as a Gaussian function so that the equations are non-autonomous. A Gaussian is quite suitable for the external current, given its physical meaning of excitation followed by de-excitation.

- The system studied is useful in a particular field : Yes, the Hodgkin-Huxley model is widely used in the fields of biophysics and neuroscience to study action potentials and neuron dynamics
- It is a Cauchy problem: Yes, the Hodgkin-Huxley model is a Cauchy problem, as one can specify initial conditions for the state variables V(0), n(0), m(0), and h(0)
- Coupled: Yes, the equations of the Hodgkin-Huxley model are coupled, as the state variables interact with one another in the different equations
- Nonlinear (or linear with non-constant coefficients): Yes, the Hodgkin-Huxley model is nonlinear due to the α_n and β_n functions, which depend on the membrane potential V(t)

- Non-autonomous with a minimum of 2 state variables: If the external current I_{ext} is a non-constant function of time, the Hodgkin-Huxley model becomes non-autonomous. The model has four state variables: $V(t)$, $n(t)$, $m(t)$, and $h(t)$

The Hodgkin-Huxley model meets all the criteria Mr. Walmag had specified. This model provides a more detailed and realistic description of neuronal activity compared to the FitzHugh-Nagumo model, although it is also more complex to analyze and simulate.

3 Transform it to a Cauchy Problem

We must define initial conditions for the four state variables. We know that at rest, and according to the graph 2, we are at -70mV for V.

- $V(0) = -70 \cdot 10^{-3}$ V

We must also define initial values for m, n, h. They represent a fraction of openness, so we can imagine that their value is when the neuron is at rest and does not receive any external excitation so they all equal 0 :

- $n = 0$
- $m = 0$
- $h = 0$

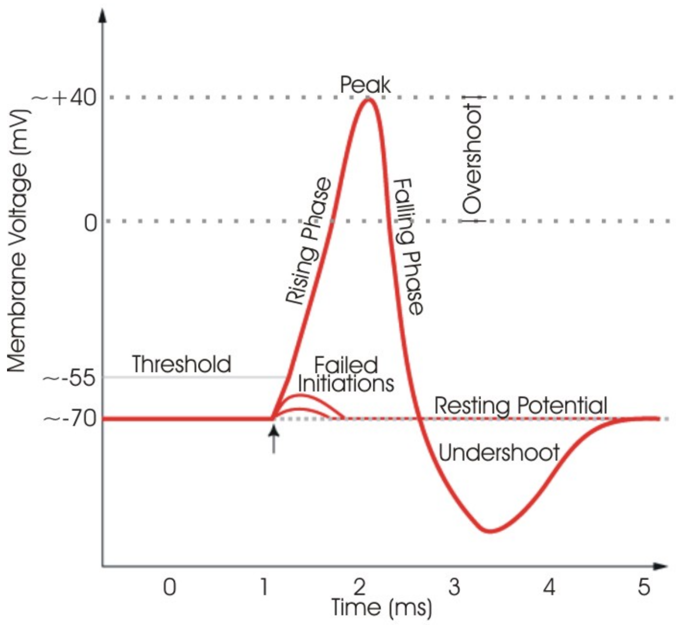

Figure 2: Membrane Voltage $f(t)$

These initial conditions place the neuron in a resting state at the beginning of the simulation. By applying an external current I_{ext}, we can then study how the membrane potential and the state variables of the ion channels evolve over time as a function of the model parameters.

4 Transformation of our autonomous equations

Our basic equations are self-contained. Indeed, they do not depend explicitly on time. In order to fit into the conditions of the project, we have to make our equations non-autonomous. To do this, we will vary the excitation current I_{ext} as a function of time. We have chosen to vary it according to a Gaussian because it is the most representative function of our problem (current pulse). We therefore have:

$$I_{ext} = A \cdot e^{-(\gamma t)^2} \tag{10}$$

5 Adimension

To non-dimensionalize the Hodgkin-Huxley model, we will first apply the Vaschy Buckingham theorem to find our non-dimension variables.This theorem can help us in this situation. We have **4 dimensions** wich are kg, m^2, s, A. We also have **16 quantities** wich are :

$$V, C, J, I_{Na}, I_K, I_L, \alpha_m, \alpha_n, \alpha_h, \beta_n, \beta_m, \beta_h, m, n, h, t \tag{11}$$

We obtain 16-4 = **12 dimensionless numbers**.

Let's start again from the basic equations :

$$\frac{dV}{dt} = \frac{1}{C}\left(A \cdot e^{-(\gamma t)^2} - I_{\mathrm{Na}} - I_{\mathrm{K}} - I_{\mathrm{L}}\right) \tag{12}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n \tag{13}$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m \tag{14}$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h \tag{15}$$

First, let's deal with time, where τ is a dimensionless coefficient :

$$\tau = \gamma \cdot t \tag{16}$$

$$\frac{d\tau}{dt} \cdot \frac{d}{d\tau} = \gamma \cdot \frac{d}{d\tau} \tag{17}$$

We pose :

$$\sigma = \frac{V}{V_0} \Leftrightarrow V = \sigma \cdot V_0 \tag{18}$$

Therefore we find 4 news dimensionless coefficients..

$$\frac{\gamma d(\sigma V_0)}{d\tau} = \frac{1}{C}(A \cdot e^{-(\gamma t)^2}) - I_{\text{Na}} - I_{\text{K}} - I_{\text{L}}) \tag{19}$$

$$\frac{d\sigma}{d\tau} = \frac{1}{C\gamma V_0}(A \cdot e^{-(\tau)^2} - \frac{1}{C\gamma V_0}(I_{\text{Na}}) - \frac{1}{C\gamma V_0}(I_{\text{K}}) - \frac{1}{C\gamma V_0}(I_{\text{L}}) \tag{20}$$

$$\frac{d\sigma}{d\tau} = \eta \cdot e^{-(\tau)^2} - \mu - \iota - \phi \tag{21}$$

$$\tag{22}$$

We can rewrite the equation 5 with the dimensionless coefficient σ :

$$\alpha_n = D_n \cdot e^{\frac{-V_0\sigma}{V_n}} \tag{23}$$

$$\beta_n = -D_n \cdot e^{\frac{-V_0\sigma}{V_n}} \tag{24}$$

$$\tag{25}$$

With these equations and the equation of τ, we can rewrite the equations as follows :

$$\frac{\gamma dn}{d\tau} = D_n e^{\frac{-V_0\sigma}{V_n}} \cdot (1-n) - D_n e^{\frac{-V_0\sigma}{V_n}} n \tag{26}$$

$$\frac{dn}{d\tau} = \frac{D_n}{\gamma} e^{-\chi} \cdot (1-2n) \tag{27}$$

$$\frac{dn}{d\tau} = \lambda e^{-\chi} \cdot (1-2n) \tag{28}$$

$$\tag{29}$$

Where λ and χ are two new dimensionless coefficients :

$$\chi = \frac{V_0 \cdot \sigma}{V_n} \tag{30}$$

$$\lambda = \frac{D_n}{\gamma} \tag{31}$$

If we rewrite the equations of m and h 12 with the adimensionnalisation of time, we find four dimensionless coefficients :

$$\frac{\gamma dm}{dt} = \alpha_m \cdot (1-m) - \beta_m m \tag{32}$$

$$\frac{dm}{d\tau} = \frac{\alpha_m}{\gamma} \cdot (1-m) + \frac{\alpha_m m}{\gamma} \tag{33}$$

$$\frac{dm}{d\tau} = \frac{\alpha_m}{\gamma} \tag{34}$$

$$\frac{dm}{d\tau} = \pi \tag{35}$$

$$\tag{36}$$

$$\frac{\gamma dh}{dt} = \alpha_h \cdot (1-h) - \beta_h h \tag{37}$$
$$\frac{dh}{d\tau} = \frac{\alpha_h}{\gamma} \cdot (1-h) + \frac{\alpha_h h}{\gamma} \tag{38}$$
$$\frac{dh}{d\tau} = \frac{\alpha_h}{\gamma} \tag{39}$$
$$\frac{dh}{d\tau} = \epsilon \tag{40}$$
$$\tag{41}$$

We can thus rewrite the equations as follows :

$$\frac{d\sigma}{d\tau} = \eta \cdot e^{-(\tau)^2} - \mu - \iota - \phi \tag{42}$$
$$\frac{dn}{d\tau} = \lambda e^{-\chi} \cdot (1-2n) \tag{43}$$
$$\frac{dm}{d\tau} = \pi \tag{44}$$
$$\frac{dh}{d\tau} = \epsilon \tag{45}$$
$$\tag{46}$$

5.1 Recap of dimensionless variables

Terms in the equation	**Equation**	**Physical interpretation**
τ	$\gamma \cdot t$	Analysis time
σ	$\frac{V}{V_0}$	Percentage of relative excitation at rest
η	$\frac{1}{C\gamma V_0} \cdot A$	Excitation current function of V_0
χ	$\frac{V_0 \cdot \sigma}{V_n}$	Percentage of relative excitation from n gate
μ	$\frac{1}{C\gamma V_0}(-I_{\text{Na}})$	Sodium current function of V_0
ι	$\frac{1}{C\gamma V_0}(-I_{\text{K}})$	Potassium current function of V_0
ϕ	$\frac{1}{C\gamma V_0}(-I_{\text{L}})$	Leak current function of V_0
λ	$\frac{D_n}{\gamma}$	opening rates of ion channels of gate n
π	$\frac{\alpha_m}{\gamma}$	opening rates of ion channels of gate m
ϵ	$\frac{\alpha_h}{\gamma}$	opening rates of ion channels of gate h
n	/	fraction of gates that are in the permissive state
m	/	fraction of gates that are in the permissive state
h	/	fraction of gates that are in the permissive state

Table 2: Correspondence between dimensionless numbers and their physical interpretation

6 Study of particular cases

The purpose of this section is to examine specific cases in our system. We will therefore analyze the behaviour of our various functions and give them a physical interpretation. For clarity, we decided to make a notebook. This allows us to easily see how changing parameters impacts our system. The notebook, with the help of a cursor, instantly returns the trace of the various functions of our system according to the adimensional parameters. We know how to vary and compare several parameters without having to recompile the code and thus see directly the impact of the changes made on our variables. You will find in the notebook the study of these cases as well as their graphs and interpretations.

7 Conclusion

To conclude, we approached the Hodgkin-Huckley model of equations. This describes neuronal activity through the opening and closing of ion channels. This is a complex model, which we had to modify slightly to meet the required specifications. We were able to understand the latter through the project. Indeed, manipulating the different equations, understanding what they refer to allowed us to become familiar with the problem and finally to understand its physical meaning. We were also able to have an approach to the Runge Kutta method and thus see the strength of the latter to solve a system of ordinary differential equations, complicated at first.

8 Annexes

8.1 FitzHugh-Nagumo model

The FitzHugh-Nagumo model is a simplified version of the Hodgkin-Huxley model that describes the dynamics of action potentials in neurons. The model is used in biophysics and neuroscience to study neuronal excitability and the propagation of electrical signals in nerve cells.

The FitzHugh-Nagumo equations are a coupled system of two ordinary differential equations:

$$\frac{dv(t)}{dt} = v(t)(a - v(t))(v(t) - 1) - w(t) + I(t)$$
$$\frac{dw(t)}{dt} = bv(t) - cw(t)$$

where :

- $v(t)$: represents the membrane potential of the neuron (state variable 1)
- $w(t)$: represents a state variable associated with the activation/inactivation of ion channels (state variable 2)
- a, b, c : positive constants
- a: represents the wave amplitude
- b:
- c: represents the velocity of the travelling wave
- $I(t)$: is an externally applied current (a function of time)

- The system studied is useful in a particular domain: Yes, the FitzHugh-Nagumo model is used in biophysics and neuroscience to study the dynamics of action potentials in neurons.
- It is a Cauchy problem: Yes, the FitzHugh-Nagumo equations are a Cauchy problem, since one can specify initial conditions for $v(0) = v_0$ and $w(0) = w_0$.
- The equations must be coupled: Yes, the FitzHugh-Nagumo equations are coupled because the change in v(t) depends on w(t) and vice versa.
- Non-linear (or linear with non-constant coefficients): Yes, the FitzHugh-Nagumo equations are non-linear due to the terms $v(t)^2$ and $v(t)^3$.

- Non-autonomous with a minimum of 2 state variables: Yes, if I(t) is a non-constant function of time, the FitzHugh-Nagumo equations become non-autonomous. The system also has two state variables: v(t) and w(t).

So, the FitzHugh-Nagumo equations therefore meet all the criteria specified in the course. This model provides valuable insights into the dynamics of action potentials and can be utilized for a range of studies in biophysics and neuroscience. We have to find academic articles about the FitzHugh-Nagumo to check the quality of our report[2].

[2] A peer-reviewed publication is also sometimes referred to as a scholarly publication. The peer-review process subjects an author's scholarly work, research, or ideas to the scrutiny of others who are experts in the same field and is considered necessary to ensure academic scientific quality

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