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A Dynamical Systems View of a Neuron

1. Introduction

Neurons are the cells whose activity allows the existence of senses, thoughts, and self-consciousness.
Understanding how neurons give origin to the higher cognitive structures is arguably the main goal of neuroscience, with tremendous implications for almost every field of the human knowledge, from biology to physics to philosophy.

Although macroscopic neuroscience has made remarkable leaps forward in the last decades, the "question of consciousness" seems to require a synthesis of all the STEM fields for further progress. Computational neuroscience contributes to this effort by developing mathematical and physical models of neural behavior, allowing us to analyze and predict their interactions.

These computational models are reductionists tools, yet they prove fundamental for the analysis of our nervous system. Any process of modeling neuron interactions starts with the single neuron and its action potential, the basic unit of neural computation.

In this paper, we will briefly introduce the Hodgkin-Huxley Model, analyze its gating variables, and show what complications emerge from the model's high dimensionality. Subsequently, we will implement a standard variable reduction and study a modified version (with Na^{+} instead of Ca^{2+}) of the Morris-Lecar Model (including equilibria, stability, global phase plane, and bifurcation).
Lastly, we will build a Python Morris-Lecar simulator to gain geometric and analytical insight about the action potential of neurons.

Our goal is not to derive accurate biophysical data, rather to construct a mathematically coherent model that reduces an HH model to a ML-like model. All quantitative parameters are taken from published electrophysiological studies and are used solely for the internal consistency of the model; they are not intended to reproduce precise neuronal behavior.

2. Basic concepts and notation

2.1 Principles of neuronal electrophysiology

In order to understand the neurocomputational model, it is essential to recall the mechanism by which neurons generate electrical current. We therefore provide a brief and simplified discussion of membrane electrophysiology, propaedeutic to our mathematical model.
The expert reader may decide to skip this section: a mathematically and biologically precise description of electrophysiology is provided in section 7.

Current in axons is principally generated by the flow of two cations, Na^+ and K^+. At rest, the axon contains a greater concentration of potassium, whereas sodium is more concentrated outside the membrane.

This ionic gradient, along with selective permeability, gives origin to a resting potential across the membrane of approximately

$$u_{rest} \approx -65 \text{ mV}.$$

Neurons communicate by generating rapid spikes in the potential across the membrane, known as action potentials. Information is carried in the frequency of action potentials, not in their intensity, which is essentially invariant. Therefore, for our purposes, we consider all action potentials as having a fixed shape and amplitude.

When the potential depolarizes to a threshold value of around

$$\Theta \approx -40 \text{ mV},$$

voltage-gated sodium channels open, allowing the inflow of Na^+. This causes a further depolarization, which brings the membrane to a maximum potential of around

$$u_{max} \approx +30 \text{ mV}.$$

As sodium channels close, voltage-gated potassium channels open, permitting the outflow of K^+, causing a repolarization in the cell membrane to about

$$u_{min} \approx -80 \text{ mV}.$$

Thereafter, ion pumps and other mechanisms restore the resting potential.

2.2 Ionic currents

Without lingering on the thermodynamic and electrodynamic derivation, we recall that ionic currents arise from the electrochemical driving force, given by the difference between the membrane potential u and the Nernst equilibrium potentials of each ion species.
In a circuit representation, Nernst potentials act as fixed voltage sources, referred to as battery voltages. We will implement the standard notation E_{Na}, E_{K}, and E_{L}, for the sodium, potassium, and leakage reversal potentials, respectively.
Let G_{Na}, G_{K}, and G_L be the respective conductance and $\sum_k I_k$ the sum of the ionic currents flowing through the membrane; assuming Ohmic behavior, we get

$$\sum_{k\in\{\mathrm{Na,K,L}\}} I_k = G_{Na}(u - E_{\mathrm{Na}}) + G_{\mathrm{K}}(u - E_{\mathrm{K}}) + G_L(u - E_{\mathrm{L}}) \tag{2.1}$$

For ionic currents we will abide by the standard sign convention, with a positive sign indicating a net outflow of positive charge.

3. The Hodgkin-Huxley Model

3.1 Ionic and capacitive currents

The classical model used to describe the electrophysiological behavior of neurons is the Hodgkin-Huxley model, which consists of four coupled autonomous ODEs for the membrane potential $u(t)$ and three gating variables.
The model includes three ionic currents: sodium, potassium, and leakage, characterized by maximum conductance $\bar{g}_{\mathrm{Na}}$, $\bar{g}_{\mathrm{K}}$, and $\bar{g}_{\mathrm{L}}$.

Hodgkin and Huxley observed that the effective conductance of Na^+ and K^+ channels depends on "gating variables", emerging from the biochemical structure of the channels, represented by three dimensionless variables:

- $m(t)$: Na^+ activation
- $n(t)$: K^+ activation
- $h(t)$: Na^+ inactivation

In the HH model, the macroscopic conductance is dependent on the number of independent subunits that must be in the "open state" to allow ionic flow, represented by an appropriate power of the gating variables,

$$G_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} m^3 h$$

and

$$G_{\mathrm{K}} = \bar{g}_{\mathrm{K}} n^4.$$

$G_L = \bar{g}_L$ is considered to be constant. A biochemical explanation for the powers of the gating variables is provided in Appendix B.
Substituting these expressions in (2.1) we get the following equation for the net ionic current

$$I_{\mathrm{ion}} = \sum_{k \in \{\mathrm{Na,K,L}\}} I_k = \bar{g}_{\mathrm{Na}} m^3 h (u - E_{\mathrm{Na}}) + \bar{g}_{\mathrm{K}} n^4 (u - E_{\mathrm{K}}) + \bar{g}_L (u - E_{\mathrm{L}}). \qquad (3.1)$$

The lipid bilayer of the neuron can be considered as a capacitor with capacitance C.
Therefore, the total transmembrane current must have a capacitive current component

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

Suppose we experimentally inject a current I_{ext} into the intracellular space from outside the cell: this current is not generated by intrinsic membrane mechanisms; it is delivered by an external

amplifier. By conservation of current across the membrane circuit, we have that any current that enters the intracellular space must be balanced by either ionic flow or capacitive charging.

The externally applied current is therefore

$$I_{\text{ext}} = I_C + I_{\text{ion}}$$

Thus, the external current is

$$I_{\text{ext}} = I_C + \sum_{k\in\{\text{Na,K,L}\}} I_k = C\frac{du}{dt} + \bar{g}_{\text{Na}} m^3 h(u - E_{\text{Na}}) + \bar{g}_{\text{K}} n^4 (u - E_{\text{K}}) + \bar{g}_L (u - E_{\text{L}}) \qquad (3.2)$$

Note that when no external current is injected, i.e., $I_{\text{ext}} = 0$, the net ionic current equals the capacitive current with opposite sign, as is to be expected.
When the neuron is at rest, the potential reaches a steady state,

$$\frac{du}{dt} \approx 0$$

and

$$I_{\text{ion}} \approx 0.$$

Although originally introduced to denote injected current in experiments, the term I_{ext} more generally represents any current entering the intercellular space from outside the membrane, such as axial current arriving at a node of Ranvier during the propagation of an action potential.

3.2 Gating variables

To complete the HH model, we have to understand the ODEs that govern the gating variables. In a patch of membrane (e.g., a node of Ranvier), there is a finite number of ion channels that open and close stochastically depending on the transmembrane voltage.
The gating variables can be interpreted as the probability that a gating subunit is in the open state; for a sufficiently large number of channels, fluctuations average out and the fraction of open gates is approximated by the expected probability.

Therefore, we can assume that at any given time, in a patch with K identical sodium gating subunits, there are Km open and $K(1-m)$ closed subunits. The probability that a gate opens in a sufficiently small time Δt is given by $\alpha(u)\Delta t$, where $\alpha(u)$ is an empirically-determined probability function; the probability that a gate closes is given by $\beta(u)\Delta t$. Therefore,

$$\frac{dm}{dt} = \alpha_m(u)(1-m) - \beta_m(u)m,$$

$$\frac{dn}{dt} = \alpha_n(u)(1-n) - \beta_n(u)n, \tag{3.3}$$

$$\frac{dh}{dt} = \alpha_h(u)(1-h) - \beta_h(u)h.$$

These ODEs are the master equations that regulate a two-state continuous Markov chain.[1] A precise mathematical treatment goes beyond the scope of this paper.

For any gating variable $x \in \{m, n, h\}$, we obviously have $\alpha_x(u) > 0$ and $\beta_x(u) > 0$, and

$$\frac{dx}{dt} = \alpha_x(u)(1-x) - \beta_x(u)x.$$

The equilibrium of this ODE (i.e., $\dot{x} = 0$) is given by

$$x_\infty(u) = \frac{\alpha_x(u)}{\alpha_x(u) + \beta_x(u)}. \tag{3.4}$$

Any linear first-order ODE with a voltage-dependent equilibrium admits a relaxation form characterized by that equilibrium and a decay rate (of deviations from equilibrium), represented by $1/\tau$.
In the HH model, since x_∞ is the equilibrium value, x converges toward it with a time constant τ_x, which means

$$\frac{dx}{dt} = \frac{x_\infty(u) - x}{\tau_x}. \tag{3.5}$$

From equations (3.4) and (3.5), we immediately get

$$\tau_x(u) = \frac{1}{\alpha_x(u) + \beta_x(u)}. \tag{3.6}$$

In (3.5), x_∞ represents the steady-state probability for a gate to be open at voltage u, whereas τ_x acts as a positive time constant toward the steady state.

[1] See Norris J. R. (1998). *Markov Chains*. Cambridge University Press.

Suppose an experimenter keeps the value of u steady at equilibrium ($u = u_0 \approx -65mV$) for time $t < t_0$ and then switches the voltage to a value $u = u_1$ for $t \geq t_0$.

Our Cauchy problem becomes

$$\begin{cases} \frac{dx}{dt} = \frac{x_\infty(u_1) - x}{\tau_x(u_1)} \\ x(t_0) = x_\infty(u_0) \end{cases} \tag{3.7}$$

We can now integrate (3.7) between t_0 and t. Using the separation of variables method, we get

$$x(t) = x_\infty(u_1) + \big(x_\infty(u_0) - x_\infty(u_1)\big)e^{-\frac{t-t_0}{\tau_x(u_1)}} \tag{3.8}$$

3.3 Limits of the HH model

Despite its extreme accuracy, the HH model presents an obvious mathematical limit: its non-linearity and four-dimensionality in

$$(u(t), m(t), n(t), h(t))$$

complicate most forms of mathematical analysis on the model.
Being a non-linear system of four first-order ODEs, the HH model does not present an explicit global solution in closed form, allowing only numerical integration.

The HH model is further limited by its high dimensionality. In fact, the system of ODEs that regulates neuronal activity, like any other 4-dimensional ODE, acts as a vector field

$$X: \mathbb{R}^4 \to T\mathbb{R}^4.$$

This makes a meaningful global geometric interpretation (phase planes, nullclines, bifurcation analysis, etc.) essentially impossible. Note that, given HH regularity, a local interpretation remains feasible, but a global geometric analysis is prohibitive.
We wish to have a visual, global, low-dimensional intuition of the model, and the current form of HH does not allow it.

These complications will be partially resolved with a two-dimensional variable-reduction method, which will lead us to the Morris-Lecar Model, presented formally and analyzed in the following sections.

4. The Morris-Lecar Model

4.1 Variable reduction

The HH model now consists of the following coupled ODEs,

$$\begin{cases} C\dfrac{du}{dt} = I_{\text{ext}} - \bar{g}_{\text{Na}} m^3 h(u - E_{\text{Na}}) - \bar{g}_{\text{K}} n^4 (u - E_{\text{K}}) - \bar{g}_L (u - E_{\text{L}}) \\ \dfrac{dm}{dt} = \dfrac{m_\infty(u) - m}{\tau_m(u)} \\ \dfrac{dn}{dt} = \dfrac{n_\infty(u) - n}{\tau_n(u)} \\ \dfrac{dh}{dt} = \dfrac{h_\infty(u) - h}{\tau_h(u)} \end{cases} \tag{4.1}$$

where, for $x \in \{m, n, h\}$, x_∞ and τ_x depend on the empirically-determined Markov-chain functions $\alpha_x(u)$ and $\beta_x(u)$. Recall equations (3.4) and (3.6).
As shown in equation (3.8), x converges exponentially to x_∞ with time constant τ_x.

Experimentally, we observe that the convergence of $m(t)$ to $m_\infty(u)$ is almost instantaneous; i.e., τ_m is significantly faster than the passive-membrane time constant $\tau = {C}/{\bar{g}_L}$. Using standard values for α_m, β_m, and u, we have,

$$\frac{\tau}{\tau_m} \approx 14.^{2}$$

Therefore, we can approximate $m(t)$ by its steady-state value $m_\infty(u(t))$.
This process removes an independent dynamical variable, reducing the model's dimensions to three.

Additionally, we observe that $\tau_h(u)$ and $\tau_n(u)$ vary with voltage in a similar range, and both are much slower than τ_m. Moreover, $n_\infty(u)$ and $1 - h_\infty(u)$ exhibit similar voltage dependence. This suggests the existence of a single effective gating variable. Hence, we introduce a new variable w and empirically approximate it by either of these steady-state functions:

$$w(u) \approx a n_\infty(u) \tag{4.2}$$

for an appropriate scaling constant $a \in \mathbb{R}$.

[2] We used $u = -65mV$ and took the exponential form of $\alpha(u), \beta(u)$ directly from Hodgkin AL, Huxley AF (1952). "A quantitative description of membrane current and its application to conduction and excitation in nerve", *The Journal of Physiology.* Wiley-Blackwell.

Up to a linear rescaling, $n_\infty(u)$ and $1 - h_\infty(u)$ are essentially identical; therefore, we can find a suitable least-squares fit constant $b \in \mathbb{R}$ such that

$$an_\infty(u) \approx b\big(1 - h_\infty(u)\big). \tag{4.3}$$

Therefore, we assume that the same linear relation holds dynamically and identify

$$w(t) = an(t)$$

and

$$an(t) = b\big(1 - h(t)\big).$$

We have therefore reduced the dimensionality of the model from four to two.
To derive an explicit ODE for $\dot{w}$, we define

$$w_\infty(u) := an_\infty(u)^3 \tag{4.2'}$$

and

$$\tau_w(u) := \tau_n(u).$$

We therefore get

$$\frac{dw}{dt} = a\frac{dn}{dt} = a\frac{n_\infty(u) - n}{\tau_n(u)} = \frac{w_\infty(u) - w}{\tau_w(u)}. \tag{4.4}$$

The resulting model takes the following form,

$$\begin{cases} C\dfrac{du}{dt} = I_{\text{ext}} - \bar{g}_{\text{Na}} m_\infty^3 \dfrac{(b-w)}{b}\,(u - E_{\text{Na}}) - \bar{g}_{\text{K}}\left(\dfrac{w}{a}\right)^4 (u - E_{\text{K}}) - \bar{g}_L(u - E_{\text{L}}) \\ \dfrac{dw}{dt} = \dfrac{w_\infty(u) - w}{\tau_w(u)} \end{cases} \tag{4.5}$$

4.2 The Morris-Lecar activation curves

The following derivation will rely heavily on statistical mechanics and transition-state theory. The reader may wish to skip this technical part and consider the Morris-Lecar activation curves as given.
From equation (4.4), $w(t)$ satisfies equation (3.4) and, therefore, presents a Markov-chain form as follows,

[3] The previously-defined function $w(u)$ is defined to be identical to $w_\infty(u)$. Therefore, we will use the notation $w_\infty(u)$ in the following sections, to highlight the role of $w_\infty(u)$ with respect to $w(t)$.

$$\frac{dw}{dt} = \alpha_w(u)(1-w) - \beta_w(u)w. \tag{4.6}$$

The two states, open and closed, lie at different energies,

$$\Delta G(u) = G_{open} - G_{closed}.$$

From statistical mechanics, we know that the energy difference can be considered proportional (up to the first-order Taylor approximation) to the voltage,

$$\Delta G(u) \approx \Delta G_0 - qu,$$

where q is an effective gating charge (i.e., the net charge displacement associated with channel opening). At thermodynamic equilibrium, the probability of being in a state with free energy G is proportional to $\exp\left(-\frac{G}{k_B T}\right)$.[4] Hence,

$$\frac{P_{open}}{P_{closed}} = \exp\left(-\frac{\Delta G(u)}{k_B T}\right) \approx \exp\left(\frac{qu - \Delta G_0}{k_B T}\right). \tag{4.7}$$

Since our probability functions are the stationary distribution of a two-state Markov chain, at equilibrium we have

$$\begin{cases} \alpha_w\big(1 - w_\infty(u)\big) = \beta_w w_\infty \\ P_{open} = w_\infty(u) \\ P_{closed} = 1 - w_\infty(u) \end{cases} \tag{4.8}$$

Therefore,

$$\frac{\alpha_w(u)}{\beta_w(u)} = \frac{P_{open}}{P_{closed}} = \exp\left(\frac{qu - \Delta G_0}{k_B T}\right). \tag{4.9}$$

Morris and Lecar chose the following form of the stationary distribution functions,

$$\begin{cases} \alpha_w(u) = \phi_w \exp\left(\frac{u - U_3}{U_4}\right) \\ \beta_w(u) = \phi_w \exp\left(-\frac{u - U_3}{U_4}\right) \end{cases}.^{5} \tag{4.10}$$

[4] A full derivation of the Boltzmann distribution lies beyond the scope of this paper. For details, see e.g., Huang, K. (2008). *Statistical Mechanics* (2nd ed.). Wiley.

[5] The reason behind the choice of the subscripts is conventional and will become clearer later.

This choice produces the classical sigmoidal steady-state functions used to represent voltage-gated channels.

Equations (4.10) clearly satisfy equation (4.9). Moreover, the choice is justified by the following sum,

$$\alpha_w(u) + \beta_w(u) = 2\phi_w \cosh\left(\frac{u - U_3}{U_4}\right). \tag{4.11}$$

Recall equation (3.4). Let

$$x = \frac{u - U_3}{2U_4}.$$

We have

$$w_\infty(u) = \frac{e^x}{2\cosh x} = \frac{1}{1 + e^{-2x}} = \frac{1}{2}\left[1 + \tanh\left(\frac{u - U_3}{U_4}\right)\right]. \tag{4.12}$$

From equation (3.6), we have

$$\tau_w(u) = \frac{1}{2\phi_w \cosh\left(\frac{u - U_3}{U_4}\right)}. \tag{4.13}$$

By the same argument, we can find a similar formulation for the steady-state value $m_\infty(u)$, for which we choose

$$\begin{cases} \alpha_m(u) = \phi_m \exp\left(\dfrac{u - U_1}{U_2}\right) \\ \beta_m(u) = \phi_m \exp\left(-\dfrac{u - U_1}{2U_2}\right) \end{cases}. \tag{4.14}$$

Therefore, we get

$$m_\infty(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u - U_1}{U_2}\right)\right]. \tag{4.15}$$

No formulation of τ_m is needed because we treat it as instantaneous, as explained in section 4.1.

We have therefore reduced our model to a two-dimensional ODEs system, with specific sigmoidal functions for the steady-state variables.

4.3 Phenomenological reductions

The following section will introduce a series of modelling choices, used to simplify the geometric representation of the ODEs. Therefore, many of our approximations may seem arbitrary.
Our goal is to further simplify the model, to allow a full and meaningful analytical and geometric interpretation.
To reduce the model's complexity, we have to revise equations $(4.2')$ and (4.3) which currently state

$$w_\infty(u) = an_\infty(u) = b\big(1 - h_\infty(u)\big).$$

In our ML reduction, we decide to ignore the relation that slaves $h_\infty(u)$ to $w(u)$, to prevent h from inheriting the slow time constant τ_w. We exclusively keep the following relation,

$$w_\infty(u) = an_\infty(u).$$

We further consider

$$h(t) \approx h_\infty(u). \tag{4.16}$$

Data shows that τ_h is only slightly quicker than τ_w: our reduction cannot be fully justified physically; the reduction is purely a phenomenological modelling choice, partially allowed by empirical data. Therefore, we lose a certain degree of accuracy.

Sodium current is now modelled by

$$I_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}} m_\infty^3 h_\infty \, (u - E_{\mathrm{Na}}). \tag{4.17}$$

Therefore, we can define a single effective probability steady-state value,

$$p_\infty(u) = m_\infty^3(u) h_\infty(u). \tag{4.18}$$

Since both $m_\infty(u)$ and $h_\infty(u)$ are sigmoidal functions, their product is also a sigmoidal function. Hence, it can be approximated by the hyperbolic tangent,

$$p_\infty(u) \approx m_\infty^{\mathrm{eff}}(u) \coloneqq \frac{1}{2}\left[1 + \tanh\left(\frac{u - U_1}{U_2}\right)\right].^{6} \tag{4.19}$$

[6] We willingly use the same subscripts as equation (4.15), which we will not again use in the rest of our discussion as it is effectively replaced by equation (4.19). The constants U_1 and U_2 are refitted to match $m_\infty^{\mathrm{eff}}(u)$. Additionally, the probability must have range $[0,1]$; hence, we translate the function upward by a constant $1/2$.

Hence, we have,

$$I_{\mathrm{Na}} = \bar{g}_{\mathrm{Na}}^{\mathrm{eff}} m_{\infty}^{\mathrm{eff}} \, (u - E_{\mathrm{Na}}). \tag{4.17'}$$

Where $\bar{g}_{\mathrm{Na}}^{\mathrm{eff}}$ absorbs $\bar{g}_{\mathrm{Na}}$ with a fitting empirically-determined scaling correction.

As a last simplification, we want to reduce the power of the potassium gating variable. Recall equation (4.5), which gives us,

$$I_{\mathrm{K}} = \bar{g}_{\mathrm{K}} \left(\frac{w}{a}\right)^4 (u - E_{\mathrm{K}}). \tag{4.20}$$

We absorb a^{-4} into $\bar{g}_K$, writing $\bar{g}_{\mathrm{K}}^{\mathrm{eff}} = \bar{g}_{\mathrm{K}} a^{-4}$.

Furthermore, we observe that w^4 inherits the monotonicity and sigmoid-like shape from w. In our ML reduction, we are not interested in the probability-interpretation of w and choose to introduce a new variable, which does not alter the qualitative phase-plane shape,

$$\widehat{w}(t) = [w(t)]^4. \tag{4.21}$$

Where the steady-state function is

$$\widehat{w}_{\infty}(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u - U_3}{U_4}\right)\right].^{7} \tag{4.22}$$

Our model is therefore reduced to the following form,

$$\begin{cases} C\dfrac{du}{dt} = I_{\mathrm{ext}} - \bar{g}_{\mathrm{Na}}^{\mathrm{eff}} m_{\infty}^{\mathrm{eff}}(u)(u - E_{\mathrm{Na}}) - \bar{g}_{\mathrm{K}}^{\mathrm{eff}} \widehat{w}(t)(u - E_{\mathrm{K}}) - \bar{g}_L(u - E_{\mathrm{L}}) \\ \dfrac{d\widehat{w}}{dt} = \dfrac{\widehat{w}_{\infty}(u) - \widehat{w}}{\tau_{\widehat{w}}(u)} \end{cases}$$

[7] Again, it should be noted that we use the same subscripts as equation (4.12). This abuse of notation is justified by the fact equation (4.22) replaces equation (4.12).

4.4. Empirical values substitution

In Appendix A we explicitly determine the empirical values and steady-state functions we need to substitute. We get

$$\begin{cases} 1\left[\frac{\mu F}{cm^2}\right]\frac{du}{dt} = I_{ext} - 20\left[\frac{mS}{cm^2}\right]\left[1+\tanh\left(\frac{u+44.5\,mV}{10.7\,mV}\right)\right](u-55\,mV) - \\ \qquad -20\frac{mS}{cm^2}\,\hat{w}(t)(u+90\,mV) - 0.2\frac{mS}{cm^2}(u+65\,mV) \\ \frac{d\hat{w}}{dt} = \left(\frac{1}{2}\left[1+\tanh\left(\frac{u-4.54\,mV}{39.7\,mV}\right)\right] - \hat{w}\right)0.2\,ms^{-1}\cosh\left(\frac{u-4.54\,mV}{39.7\,mV}\right) \end{cases} . \quad (4.23)$$

We want to have the neuron model at rest when $u = -65\ \mathrm{mV}$. Therefore, we define

$$I := I_{ext} + I_{rest}. \quad (4.24)$$

Hence, when $I_{ext} = 0$, we want to have resting conditions. Computing the value for I_{rest} we get

$$I_{rest} \approx -86\ \mu A/cm^2.$$

The model becomes

$$\begin{cases} 1\left[\frac{\mu F}{cm^2}\right]\frac{du}{dt} = I - 86\left[\frac{\mu A}{cm^2}\right] - 20\left[\frac{mS}{cm^2}\right]\left[1+\tanh\left(\frac{u+44.5\,mV}{10.7\,mV}\right)\right](u-55\,mV) - \\ \qquad -20\frac{mS}{cm^2}\,\hat{w}(t)(u+90\,mV) - 0.2\frac{mS}{cm^2}(u+65\,mV) \\ \frac{d\hat{w}}{dt} = \left(\frac{1}{2}\left[1+\tanh\left(\frac{u-4.54\,mV}{39.7\,mV}\right)\right] - \hat{w}\right)0.2\,ms^{-1}\cosh\left(\frac{u-4.54\,mV}{39.7\,mV}\right) \end{cases} . \quad (4.23')$$

In the following sections, we will not rely on empirical data to analyze our model. Instead, we will keep our parameters symbolic, to allow the analytical study to be carried out in full generality.

5. Equilibrium Analysis

5.1 Nullclines

We define the following functions,

$$f(u,\widehat{w}) := \frac{1}{C}\Big(I_{\text{ext}} - \bar{g}_{\text{Na}}^{\text{eff}} m_{\infty}^{\text{eff}}(u)(u-E_{\text{Na}}) - \bar{g}_{\text{K}}^{\text{eff}}\widehat{w}(u-E_{\text{K}}) - \bar{g}_{L}(u-E_{\text{L}})\Big), \tag{5.1}$$

$$g(u,\widehat{w}) := \frac{\widehat{w}_{\infty}(u)-\widehat{w}}{\tau_{\widehat{w}}(u)}. \tag{5.2}$$

Clearly,

$$f(u,\widehat{w}) = \frac{du}{dt} \wedge g(u,\widehat{w}) = \frac{d\widehat{w}}{dt}.$$

We calculate the u-nullcline and get, for $u \neq E_{\text{K}}$,

$$f(u,\widehat{w}_{\text{nc}}) = 0,$$

$$\therefore \widehat{w}_{\text{nc}} = W(u;I_{\text{ext}}) := \frac{I_{\text{ext}} - \bar{g}_{\text{Na}}^{\text{eff}} m_{\infty}^{\text{eff}}(u)(u-E_{\text{Na}}) - \bar{g}_{L}(u-E_{\text{L}})}{\bar{g}_{\text{K}}^{\text{eff}}(u-E_{\text{K}})}. \tag{5.3}$$

The u-nullcline, for a fixed I_{ext}, is therefore the curve

$$(u, W(u;I_{\text{ext}})).$$

It clearly has a vertical asymptote for $u = E_{\text{K}}$, provided the nominator does not vanish.

We now calculate the $\widehat{w}$-nullcline; obviously,

$$\widehat{w} = \widehat{w}_{\infty}(u). \tag{5.4}$$

The $\widehat{w}$-nullcline is the curve

$$\big(u, \widehat{w}_{\infty}(u)\big).$$

Note that the $\widehat{w}$-nullcline is independent of I_{ext}.

An equilibrium $(u^*, \widehat{w}^*)$ satisfies simultaneously

$$\begin{cases} \widehat{w}^* = W(u^*, I_{\text{ext}}) \\ \widehat{w}^* = \widehat{w}_{\infty}(u^*) \end{cases}. \tag{5.5}$$

Therefore, we get

$$W(u^*;I_{\text{ext}}) = \widehat{w}_{\infty}(u^*),$$

Which is equal to

$$I_{\text{ext}} = \bar{g}_{\text{Na}}^{\text{eff}} m_{\infty}^{\text{eff}}(u^*)(u^* - E_{\text{Na}}) + \bar{g}_{\text{K}}^{\text{eff}} \hat{w}_{\infty}(u^*)(u^* - E_{\text{K}}) + \bar{g}_L(u^* - E_{\text{L}}) \tag{5.6}$$

If we define

$$F(u) := \bar{g}_{\text{Na}}^{\text{eff}} m_{\infty}^{\text{eff}}(u)(u - E_{\text{Na}}) + \bar{g}_{\text{K}}^{\text{eff}} \hat{w}_{\infty}(u)(u - E_{\text{K}}) + \bar{g}_L(u - E_{\text{L}}), \tag{5.7}$$

we get that the equilibria satisfy

$$F(u^*) = I_{\text{ext}}, \tag{5.7′}$$

with $\hat{w}^* = \hat{w}_{\infty}(u^*)$.

For a fixed choice of parameters, equilibria correspond to the intersection points between the $I-V$ function $F(u)$ and the horizontal line I_{ext}. Obviously, equilibria depend on I_{ext}; therefore, we can write $u^* = u^*(I_{\text{ext}})$ and $\hat{w}_{\infty}(u^*) = \hat{w}_{\infty}(u^*(I_{\text{ext}}))$.
Since $F(u)$ is nonlinear, consisting of a sum of sigmoidal functions and linear terms, the model allows either one or three equilibria, depending on the parameters chosen for F and the value of I_{ext}.

5.2 Linearization and local stability

Our system currently is defined as follows,

$$\begin{cases} f(u, \hat{w}) = \dfrac{du}{dt} \\ g(u, \hat{w}) = \dfrac{d\hat{w}}{dt}. \end{cases}$$

We compute the Jacobian matrix for our model,

$$\boldsymbol{J}(u, \hat{w}) = \begin{pmatrix} \dfrac{\partial f}{\partial u} & \dfrac{\partial f}{\partial \hat{w}} \\ \dfrac{\partial g}{\partial u} & \dfrac{\partial g}{\partial \hat{w}} \end{pmatrix}. \tag{5.8}$$

From equation (5.1) we get

$$\frac{\partial f}{\partial u}(u, \hat{w}) = -\frac{1}{C}\left(\bar{g}_{\text{Na}}^{\text{eff}}\left[\frac{dm_{\infty}^{\text{eff}}}{du}(u)(u - E_{\text{Na}}) + m_{\infty}^{\text{eff}}\right] + \bar{g}_{\text{K}}^{\text{eff}}\hat{w} + \bar{g}_L\right),$$

$$\frac{\partial f}{\partial \widehat{w}}(u,\widehat{w}) = -\frac{1}{C}\bar{g}_{\mathrm{K}}^{\mathrm{eff}}(u - E_{\mathrm{K}}).$$

From equation (5.2),

$$\frac{\partial g}{\partial u}(u,\widehat{w}) = \frac{\frac{d\widehat{w}_\infty}{du}\tau_{\widehat{w}}(u) - \frac{d\tau_{\widehat{w}}}{du}(\widehat{w}_\infty(u) - \widehat{w})}{[\tau_{\widehat{w}}(u)]^2},$$

$$\frac{\partial g}{\partial \widehat{w}}(u,\widehat{w}) = -\frac{1}{\tau_{\widehat{w}}(u)}.$$

We now evaluate the Jacobian J^* at an equilibrium point $(u^*, \widehat{w}^*) = \left(u^*, \widehat{w}_\infty(u^*)\right)$. Therefore, we have $\widehat{w}_\infty(u^*) - \widehat{w}^* = 0$.
Hence,

$$\boldsymbol{J}^* = \begin{pmatrix} -\frac{1}{C}\left(\bar{g}_{\mathrm{Na}}^{\mathrm{eff}}\left[\frac{dm_\infty^{\mathrm{eff}}}{du}(u^*)(u^* - E_{\mathrm{Na}}) + m_\infty^{\mathrm{eff}}\right] + \bar{g}_{\mathrm{K}}^{\mathrm{eff}}\widehat{w}_\infty(u^*) + \bar{g}_L\right) & -\frac{1}{C}\bar{g}_{\mathrm{K}}^{\mathrm{eff}}(u^* - E_{\mathrm{K}}) \\ \frac{\frac{d\widehat{w}_\infty}{du}(u^*)}{\tau_{\widehat{w}}(u^*)} & -\frac{1}{\tau_{\widehat{w}}(u^*)} \end{pmatrix} \quad (5.8')$$

According to standard planar dynamical systems theory,[8] we can characterize equilibria according to the sign of the trace and the determinant of the Jacobian matrix calculated in that point:

- $\det \boldsymbol{J} < 0$: saddle;
- $\det \boldsymbol{J} > 0 \wedge \mathrm{tr}\, \boldsymbol{J} < 0$: stable equilibrium;
- $\det \boldsymbol{J} > 0 \wedge \mathrm{tr}\, \boldsymbol{J} > 0$: unstable equilibrium;
- $\det \boldsymbol{J} > 0 \wedge \mathrm{tr}\, \boldsymbol{J} = 0$: Hopf bifurcation candidate.

We can therefore compute the determinant and the trace. We get

$$\det \boldsymbol{J}^* = \frac{1}{C\tau_{\widehat{w}}(u^*)}\left(\bar{g}_{\mathrm{Na}}^{\mathrm{eff}}\left[\frac{dm_\infty^{\mathrm{eff}}}{du}(u^*)(u^* - E_{\mathrm{Na}}) + m_\infty^{\mathrm{eff}}(u^*)\right] + \bar{g}_{\mathrm{K}}^{\mathrm{eff}}\left[\widehat{w}_\infty(u^*) + \frac{d\widehat{w}_\infty}{du}(u^*)(u^* - E_{\mathrm{K}})\right] + \bar{g}_L\right),$$

[8] For an introduction to nonlinear dynamics, see e.g., Strogatz S. H. (2015). *Nonlinear Dynamics and Chaos* (2nd ed.). CRC Press.

$$\operatorname{tr} \boldsymbol{J} = -\frac{1}{C}\left(\bar{g}_{\mathrm{Na}}^{\mathrm{eff}}\left[\frac{dm_{\infty}^{\mathrm{eff}}}{du}(u^*)(u^* - E_{\mathrm{Na}}) + m_{\infty}^{\mathrm{eff}}(u^*)\right] + \bar{g}_{\mathrm{K}}^{\mathrm{eff}}\widehat{w}_{\infty}(u^*) + \bar{g}_L\right) - \frac{1}{\tau_{\widehat{w}}(u^*)}.$$

We now compute the first derivative of F in u^*, defined by equation (5.7),

$$\frac{dF}{du}(u^*) = \bar{g}_{\mathrm{Na}}^{\mathrm{eff}}\left[\frac{dm_{\infty}^{\mathrm{eff}}}{du}(u^*)(u^* - E_{\mathrm{Na}}) + m_{\infty}^{\mathrm{eff}}(u^*)\right] + \bar{g}_{\mathrm{K}}^{\mathrm{eff}}\left[\widehat{w}_{\infty}(u^*) + \frac{d\widehat{w}_{\infty}}{du}(u^*)(u^* - E_{\mathrm{K}})\right] + \bar{g}_L.$$

Comparing it with the determinant formula, we get

$$\det \boldsymbol{J}^* = \frac{1}{C\tau_{\widehat{w}}(u^*)} \cdot \frac{dF}{du}(u^*). \tag{5.9}$$

Since C and $\tau_{\widehat{w}}(u^*)$ are positive real numbers, the sign of $\det \boldsymbol{J}^*$ depends exclusively on the sign of $F'(u)$,

$$\operatorname{sign}(\det \boldsymbol{J}^*) = \operatorname{sign}\left(\frac{dF}{du}(u^*)\right). \tag{5.9′}$$

We can therefore apply the equilibria characterization conditions directly to $F'(u^*)$.

Additionally, we note that

$$f(u, \widehat{w}_{\infty}) = \frac{1}{C}\big(I_{\mathrm{ext}} - F(u)\big), \tag{5.9″}$$

which gives us

$$\operatorname{sign}(\det \boldsymbol{J}^*) = \operatorname{sign}\left(\frac{dF}{du}(u^*)\right) = -\operatorname{sign}\left(\frac{\mathrm{d}}{du}\big[\mathrm{f}\big(u^*, \widehat{w}_{\infty}(u)\big)\big]\Big|_{u=u^*}\right). \tag{5.9‴}$$

To parametrize the equilibria by the external current, we recall equation (5.7′): assuming F is sufficiently smooth, we can apply the Inverse Function Theorem. For $F'(u^*) \neq 0$, F is a local diffeomorphism, and the equilibrium curve $I_{\mathrm{ext}} \longmapsto u^*(I_{\mathrm{ext}})$ is smooth, where u^* is here treated as a local inverse of F. Therefore, locally,

$$F^{-1}(I_{\mathrm{ext}}) = u^*(I_{\mathrm{ext}}). \tag{5.10}$$

We have hence turned the static equation (5.7) into a curve $u^*(I_{\mathrm{ext}})$. Therefore,

$$F'(u^*) = F'\big(u^*(I_{\mathrm{ext}})\big). \tag{5.11}$$

In the following section, we will study the phase plane in light of the results derived here.

6. Phase Plane and Trajectories

6.1 Phase Portrait

Recalling equations (5.1) and (5.2), our ML reduction gave rise to the following system of ODEs,

$$\begin{cases} \dot{u} = f(u, \widehat{w}; I_{\text{ext}}) \\ \dot{w} = g(u, \widehat{w}) \end{cases}.$$

We will now study the global behavior of the trajectories in the $(u, \widehat{w})$-plane for a fixed I_{ext}. The phase portrait associates a vector $\big(f(u, \widehat{w}), g(u, \widehat{w})\big)$ to each point $(u, \widehat{w})$: we can interpret it as the direction in which the system will move if perturbed.
Hence, we want to determine the sign of $f(u, \widehat{w})$ and $g(u, \widehat{w})$.

We consider the partial derivatives of f and g as derived for the Jacobian matrix in equations (5.8) and $(5.8')$. When in physiological range, $E_{\text{K}} < u$ and $\bar{g}_{\text{K}}^{\text{eff}} > 0$; therefore,

$$\frac{\partial f}{\partial \widehat{w}}(u, \widehat{w}) = -\frac{1}{C}\bar{g}_{\text{K}}^{\text{eff}}(u - E_{\text{K}}) < 0. \tag{6.1}$$

Therefore, $\frac{du}{dt}$ is strictly decreasing in $\widehat{w}$. For each u, there exists a unique $\widehat{w}_{\text{nc}}(u)$ such that $f\big(u, \widehat{w}_{\text{nc}}(u)\big) = 0$.
Hence, below the u-nullcline (i.e., $\widehat{w} < \widehat{w}_{\text{nc}}(u)$), $\dot{u}$ is positive (pointing rightwards), and above the u-nullcline, $\dot{u}$ is negative (pointing leftwards).

On the other hand, for a fixed $\widehat{w}$,

$$\frac{d\widehat{w}}{dt} = \frac{\widehat{w}_{\infty}(u) - \widehat{w}}{\tau_{\widehat{w}}(u)}.$$

Since $\tau_{\widehat{w}} > 0$,

$$\text{sign}\left(\frac{d\widehat{w}}{dt}\right) = \text{sign}(\widehat{w}_{\infty}(u) - \widehat{w}). \tag{6.2}$$

Therefore, below the $\widehat{w}$-nullcline (i.e., $\widehat{w} < \widehat{w}_{\infty}(u)$), $\frac{d\widehat{w}}{dt}$ is positive (pointing upwards), and above the $\widehat{w}$-nullcline, $\frac{d\widehat{w}}{dt}$ is negative (pointing downwards). This behavior is expected, as the $\widehat{w}$-nullcline corresponds to the graph of the steady-state equilibrium function $\widehat{w}_{\infty}(u)$.

In our introduced notation, the u-nullcline is $\big(u, \widehat{w}_{\text{nc}}(u)\big)$, whereas the $\widehat{w}$-nullcline is $\big(u, \widehat{w}_{\infty}(u)\big)$. Thus, we can rewrite equation (5.5) for equilibria as $\widehat{w}_{\infty}(u^*) = \widehat{w}_{\text{nc}}(u^*)$, which geometrically represents the intersection(s) between the u-nullcline and the $\widehat{w}$-nullcline.

6.2 Basin of attraction and separatrix

We can show that within physiological values and for a certain range of $I_{\text{ext}} \in (I_{SN1}, I_{\text{SN2}})$[9], our model presents three equilibria: the first a stable equilibrium, E; the second a saddle equilibrium, S; and the third an unstable equilibrium, U.
Generally, the stable equilibrium is for $u \approx -65\ \text{mV}$, as one would expect from our earlier biophysical observations.
We are interested in analyzing the implications of the existence of a saddle equilibrium.
The following part will rely heavily on dynamical systems results: the reader may want to consult a Nonlinear Dynamics textbook to see the proof of the theorems we use.

At a saddle equilibrium the Jacobian has two real eigenvalues of opposite sign, $\lambda_1 > 0, \lambda_2 < 0$.
We briefly recall that a solution curve (trajectory) is a function

$$t \mapsto \big(u(t), \widehat{w}(t)\big)$$

which solves the system of ODEs with initial conditions $\big(u(0), \widehat{w}(0)\big) = (u_0, \widehat{w}_0)$.
A set $S \subseteq \mathbb{R}^2$ is said to be invariant if every trajectory that starts in S stays in S for each t within its domain.
From dynamical systems theory, we know that for a saddle equilibrium we can define a stable set,

$$W^s(u^*, \widehat{w}^*) := \Big\{(u_0, \widehat{w}_0) \colon \lim_{t \to +\infty} \big(u(t), \widehat{w}(t)\big) = (u^*, \widehat{w}^*)\Big\} \tag{6.3}$$

and an unstable set

$$W^u(u^*, \widehat{w}^*) := \Big\{(u_0, \widehat{w}_0) \colon \lim_{t \to -\infty} \big(u(t), \widehat{w}(t)\big) = (u^*, \widehat{w}^*)\Big\}. \tag{6.4}$$

Clearly, both the stable and unstable sets are invariant.
From the Stable Manifold Theorem applied to our 2-dimensional vector field (which is clearly sufficiently smooth), we know that both sets can be represented as 1-dimensional curves passing through $(u^*, \widehat{w}^*)$ and tangent to the eigenvectors of $\boldsymbol{J}(u^*, \widehat{w}^*)$, associated with λ_2 for W^s and λ_1 for W^u.

Additionally, we recall that a basin of attraction of an attractor A is the set of all possible initial states that will eventually lead the system to the equilibrium; in symbols,

$$\mathcal{B}(A) := \Big\{(u_0, \widehat{w}_0) \colon \lim_{t \to +\infty} \big(u(t), \widehat{w}(t)\big) = (u^*, \widehat{w}^*)\Big\}. \tag{6.5}$$

[9] This notation will be justified with the introduction of saddle-node bifurcations in section 6.3.

For a stable equilibrium, $W^s(E) = \mathcal{B}(E)$, but a saddle clearly does not allow the existence of a basin, because a saddle is not an attractor. The only points converging to it are those on its stable curve.

To complete our mathematical machinery, we introduce the concept of limit cycle, denoted Γ. A limit cycle, with parametrization $\gamma(t)$, is an orbit such that there exists a period T for which

$$\gamma(t + T) = \gamma(t).$$

Computer simulations of our model under physiological conditions show that two basins of attraction exist: one leads to the first (stable) equilibrium E, the other to the limit cycle Γ surrounding the third (unstable) equilibrium U.
From Stable Manifold Theorem (and other dynamical systems results that go beyond the scope of this paper) applied to our model we know that

$$\partial\mathcal{B}(E) = \partial\mathcal{B}(\Gamma) = W^s(S), \tag{6.6}$$

where ∂ denotes the boundary of the set.
Clearly, $W^s(S)$ separates the two basins of attraction. Hence, we refer to it as the separatrix.

We can use the shape of the separatrix to classify neurons and explain neural behavior (see section 7): we quickly mention it here to provide a geometric and topological intuition of the separatrix.
Computer simulations show that the separatrix of bistable neurons has a closed, oval shape;[10] therefore, $\mathcal{B}(E)$ exists both on the left-hand side and on the right-hand side of the separatrix, which encloses $\mathcal{B}(\Gamma)$.
The separatrix, $W^s(S)$, of monostable neurons is open and does not enclose any region of space. Therefore, no limit cycle can exist, $\mathcal{B}(\Gamma) = \emptyset$, and the whole phase plane corresponds to $\mathcal{B}(E)$.

6.3 Bifurcations

A saddle-node bifurcation occurs when a stable equilibrium (node) and a saddle get progressively closer as a parameter changes (e.g., I_{ext}), colliding and reciprocally annihilating.
The eigenvalues of the Jacobian of a saddle-node bifurcation must be $\lambda_1 = 0 \wedge \lambda_2 \neq 0$. Therefore,

$$\det \boldsymbol{J}(u^*(I_{SN}), \widehat{w}^*) = 0 \wedge \operatorname{tr} \boldsymbol{J}(u^*(I_{SN}), \widehat{w}^*) \neq 0. \tag{6.7}$$

where I_{SN} represents a possible value of I_{ext} for which a saddle-node bifurcation occurs.

In our model, according to equations $(5.8')$ and (5.9), these conditions correspond to the following system:

[10] Rigorously, the separatrix is an 1D invariant manifold, which is topologically equivalent to S^1.

$$\begin{cases} \dfrac{dF}{du}\left(u^*(I_{SN})\right) = 0 \\ \operatorname{tr} \boldsymbol{J}^* = \dfrac{\partial f}{\partial u}\left(u^*(I_{SN})\right) + \dfrac{\partial g}{\partial \widehat{w}}\left(u^*(I_{SN})\right) \neq 0 \end{cases}. \tag{6.8}$$

It is therefore possible to compute the values I_{SN} using computer simulation methods.

The Jacobian of a Hopf bifurcation candidate at an equilibrium presents two complex-conjugate eigenvalues that cross the imaginary axis with nonzero speed as a parameter varies (e.g., I_{ext}): this causes a change in the stability of the equilibrium (from stable to unstable or the other way around).
The unstable equilibrium can then give origin to a stable or unstable limit cycle Γ_H. If the cycle is stable, we refer to the bifurcation as supercritical; if it's unstable, we refer to it as subcritical.

Since Hopf bifurcation can occur only at non-saddle equilibria, we consider the equilibria with $F'\left(u^*(I_{\text{ext}})\right) > 0$ and analyze the sign of $\operatorname{tr} \boldsymbol{J}^*$. A change of sign in $\operatorname{tr} \boldsymbol{J}^*$ gives a Hopf bifurcation candidate.

We can therefore assume there exists a value I_{ext}^H such that

$$\det \boldsymbol{J}^*\left(u^*(I_{\text{ext}}^H), \widehat{w}_\infty(u^*)\right) > 0 \wedge \operatorname{tr} \boldsymbol{J}^*\left(u^*(I_{\text{ext}}^H), \widehat{w}_\infty(u^*)\right) = 0\,. \tag{6.9}$$

Such values can be determined numerically via computer simulation.

7. Interpretation in Neuroscience

In this section, we will briefly discuss the biological interpretation of the mathematical and modelling results presented in this paper. In particular, we will focus on the role of equilibria and of bifurcations in the definition of neural behavior. We will also highlight how the Python simulator developed alongside this paper can be used to visualize the results.

7.1 Interpretation of equilibria

In section 2, we claimed that neurons have a resting potential of around $u_{rest} \approx -65\ \mathrm{mV}$. We can now make this statement more precise by using the terminology developed in sections 5 and 6: many human neurons generally present a stable equilibrium at $\left(u_{rest}, \widehat{w}_{\infty}(u_{rest})\right)$ when $I_{\mathrm{ext}} \approx 0$. Choosing sensible data, we can use our simulator to plot the phase plane and visualize the vector field and the equilibria, noticing a stable equilibrium for $u_{rest} \approx -65\ \mathrm{mV}$ as expected. Since stable equilibria act as attractors, we can affirm that neurons quickly restore the resting potential when a small fluctuation occurs, which is consistent with biological behavior.

In section 2, we further claimed that when the membrane potential crosses a certain threshold value $\Theta \approx -40\ \mathrm{mV}$, the neuron quickly depolarizes until it reaches a potential of around $u_{max} \approx +30\ \mathrm{mV}$: the membrane then polarizes again, returning to the resting potential.

We can now make this statement much more precise, distinguishing between two types of neurons: monostable and bistable.

We recall from section 6.2 that the separatrix of monostable neurons is an open 1D manifold and therefore does not enclose any region of space. Hence, no limit cycle can exist under these conditions and perturbations that push the system on the right-hand side of the separatrix cause a single spike.
It should be noted that both the stable equilibrium and the saddle lie on a globally invariant circle, which becomes a limit cycle at the saddle-node bifurcation.
Exclusively I_{ext} determines whether the neuron behaves in a single-firing or persistent-firing mode through saddle-node and Hopf bifurcations (see section 7.2).
Therefore, monostable neurons are more consistent with our initial electrophysiological explanation in section 2: the threshold value Θ gets replaced by the open separatrix.

For bistable neurons, the separatrix is a closed 1D manifold that encloses a connected region of space and separates $\mathcal{B}(E)$ from $\mathcal{B}(\Gamma)$.
If the potential is perturbed by a small value, the trajectory starts inside the basin of attraction of the stable equilibrium, $\mathcal{B}(E)$, on the left-hand side of the separatrix, and the potential quickly returns to rest.
If the potential is perturbed by a larger value, the trajectory will start inside the basin of attraction of the limit cycle, $\mathcal{B}(\Gamma)$, and the neuron will switch to a persistent-firing state.

Lastly, if the potential is perturbed by an even larger value, which surpasses the separatrix, the trajectory will once again start inside the basin of attraction of the stable equilibrium, $\mathcal{B}(E)$, and a single, stereotypical action potential will be generated.
Thus, the "threshold value" is emergent, not fixed: it corresponds to the closed separatrix, rather than to a single voltage value.

Clearly, the behavior of the action potential of bistable neurons does not only depend on I_{ext} but also on the neuron's history, i.e., whether the trajectory starts inside or outside the separatrix: such property is called hysteresis and is thought to be a necessary, but obviously not sufficient, mechanism for the existence of memory.

7.2 Interpretation of bifurcations

Saddle-node bifurcations play a significantly different role in monostable and bistable neurons.
For monostable neurons, the saddle-node occurs on an invariant circle, giving rise to a SNIC (saddle-node on invariant circle) bifurcation. The stable equilibrium and the saddle collide and annihilate on a globally invariant circle; the invariant circle immediately becomes a limit cycle, and the neuron switches from single-firing to persistent-firing mode. As $I_{\text{ext}} \to I_{\text{SN}}^{+}$, the period of the limit cycle diverges. Hence, oscillations in SNIC neurons are born with zero frequency. This provides a mathematical justification for Type-I excitability: the firing rate increases continuously from zero as the applied current I_{ext} increases.
For bistable neurons, a stable limit cycle already exists around the unstable equilibrium. Thus, when the stable equilibrium and the saddle annihilate at a saddle-node bifurcation, the only attractor remaining is Γ and the neuron can only exhibit a persistent-firing behavior.

Hopf bifurcations also regulate the behavior of neurons, but they act in a significantly different way. For simplicity, we consider a single-equilibrium regime. We need to distinguish between supercritical and subcritical Hopf bifurcations.

Before a supercritical Hopf bifurcation occurs, there is exclusively a single stable equilibrium: therefore, no fixed, stereotypical spiking orbit exists. The shape of the trajectory and the amplitude of the spike depend on the size of the perturbation: the distinction between spikes and non-spikes is not as clear as in the case of all-or-none responses.
Since the stable equilibrium is the only attractor, these neurons are monostable in this parameter regime.
When $I_{\text{ext}} > I_{\text{H}}$, the stable equilibrium becomes unstable and a stable limit cycle appears around it. Therefore, the equilibrium behavior of the neuron produces periodic oscillations with finite intrinsic frequency: as I_{ext} increases, the size of the limit cycle increases, thus making the neuron switch to repetitive-firing mode.
Before a subcritical Hopf bifurcation, a stable limit cycle already exists around the stable equilibrium. The basins of attraction of E and Γ are separated by an unstable limit cycle: if perturbations from the stable equilibrium make the system cross the unstable limit cycle, the neuron switches to repetitive firing. Hence, the neuron is clearly bistable and hysteresis occurs.

As I_{ext} increases, the unstable limit cycle shrinks and at the Hopf bifurcation it collides with the stable equilibrium, which becomes unstable. Therefore, the only attractor remaining is the stable limit cycle Γ and the neuron switches to persistent-firing mode.
Hopf bifurcations allow us to capture the underlying mechanism of Type-II excitability: the firing frequency function is discontinuous at $I_{\text{ext}} = I_H$, going from zero to a fixed positive value.

8. Conclusion

In our discussion, we have completed a phenomenological reduction of the Hodgkin-Huxley model to a two-dimensional modified Morris-Lecar model. We replaced the classic Ca^{2+} channels with Na^{+} channels, which allowed us to study the behavior of neural action potentials while maintaining some features of standard mammalian electrophysiology, regulated mostly by Na^{+} and K^{+} channels.

It is not the intention of this paper to claim novel results in neural models, rather to provide a complete and sufficiently rigorous mathematical background to fully understand and appreciate ML reductions.

We made several modelling assumptions, which inevitably reduce the biophysical accuracy of our model, but allow us to study the geometric phase plane of our system and gain useful insight about the behavior of our neurons. Neural excitability, thresholds, and firing modes emerge naturally from global phase-space geometry and bifurcation structure, as we have shown in section 7.

The Python program, developed independently and associated to this paper, allows the reader to visualize nullclines, equilibria, vector fields, and bifurcations in the phase plane: the reader can appreciate how the phase plane changes with different parameters and with increasing external current.
The time-voltage plane shows when spikes occur and provides a visually clear graphic solution to the differential equations. It is further possible to simulate trajectories with specific initial conditions and verify the difference between monostability and bistability and Type-I and Type-II excitability.

Our model is currently limited to the analysis of a single neuron, treating the external current as given without explaining its origin or interneural transmission.
Therefore, this framework could be expanded to enclose electric and chemical synapses and possibly simulate small neural networks, showing how ionic current is transmitted between neurons.

Appendix A: Derivation of ML model data

A.1 Steady-state functions

The standard "Boltzmann" form used in electrophysiology papers for activation steady-state functions is

$$x_\infty(u) = \frac{1}{1 + \exp\left(\frac{V_{1/2} - u}{k}\right)}, \qquad (A1.1)$$

where k is the slope factor and $V_{1/2}$ is the midpoint.
For inactivation steady-state functions, we have

$$x_\infty(u) = \frac{1}{1 + \exp\left(\frac{u - V_{1/2}}{k}\right)}, \qquad (A1.1')$$

Comparing $(A1.1)$ and $(A1.1')$ to (4.15) and using simple identities we get

$$U_1 = V_{1/2} \ \wedge U_2 = 2k. \qquad (A1.2)$$

Equation (4.15) for activation becomes

$$x_\infty(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u - V_{1/2}}{2k}\right)\right]. \qquad (A1.3)$$

And for inactivation,

$$x_\infty(u) = \frac{1}{2}\left[1 - \tanh\left(\frac{u - V_{1/2}}{2k}\right)\right]. \qquad (A1.3')$$

We take our data from the relevant part about basket cells in Martina & Jonas (1997).[11]
For m_∞ and h_∞ we have

$$V_{1/2}^{(m)} = -25.1 \text{ mV}$$
$$k^{(m)} = 11.5 \text{ mV}$$

$$V_{1/2}^{(h)} = -58.3 \text{ mV}$$

[11] Martina, M., & Jonas, P. (1997). Functional differences in Na+ channel gating between fast-spiking interneurons and principal neurons of rat hippocampus. *The Journal of physiology*, *505.*

$$k^{(h)} = 6.7\ \text{mV}.$$

Substituting into $(A1.3)$ and $(A1.3')$, we get

$$\begin{cases} m_\infty(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u + 25.1\ \text{mV}}{23.0\ \text{mV}}\right)\right] \\ h_\infty(u) = \frac{1}{2}\left[1 - \tanh\left(\frac{u + 58.3\ \text{mV}}{13.4\ \text{mV}}\right)\right] \end{cases}. \qquad (A1.4)$$

We therefore compute p_∞ as defined in (4.18),

$$p_\infty(u) = [m_\infty(u)]^3 h_\infty(u) = \frac{1}{16}\left[1 + \tanh\left(\frac{u + 25.1\ \text{mV}}{23.0\ \text{mV}}\right)\right]^3 \left[1 - \tanh\left(\frac{u + 58.3\ \text{mV}}{13.4\ \text{mV}}\right)\right]. \qquad (A1.5)$$

To find the parameters U_1 and U_2, as defined in equation (4.19), we use the least squares method (see the Python Code in Appendix C) over the interval $u \in [-80\ \text{mV}, -20\ \text{mV}]$ with a step size of 0.03. We choose this interval because, for $u > -20\ \text{mV}$, p_∞ loses its monotonicity due to inactivation: biologically, Na^+ are largely inactivated. Additionally, we normalize p_∞ over the interval $[0,1]$, as expected since the image of $\frac{1}{2}[1 + \tanh(\cdot)] \in [0,1]$.
We get

$$U_1 = -44.5\ \text{mV} \wedge U_2 = 10.7\ \text{mV}.$$

Substituting into (4.19),

$$p_\infty(u) \approx m_\infty^{\text{eff}}(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u + 44.5\ \text{mV}}{10.7\ \text{mV}}\right)\right]. \qquad (A1.6)$$

For equation (4.22), Ranjan et al. (2019)[12] provide data for the mammalian slow potassium channel Kv1.1,

$$V_{1/2}^{(K)} = 4.54\ \text{mV}$$
$$k^{(K)} = 19.84\ \text{mV}.$$

The paper contemplates macroscopic probabilities, therefore, we write

$$\widehat{w}_\infty(u) = \frac{1}{1 + \exp\left(\frac{V_{1/2} - u}{k}\right)} = \frac{1}{1 + \exp\left(\frac{4.54\ \text{mV} - u}{19.84\ \text{mV}}\right)}. \qquad (A1.7)$$

Using $(A1.2)$, we get

[12] Ranjan, R., Logette, E., Marani, M., Herzog, M., Tâche, V., Scantamburlo, E., Buchillier, V., & Markram, H. (2019). A Kinetic Map of the Homomeric Voltage-Gated Potassium Channel (Kv) Family. *Frontiers in cellular neuroscience*, *13*.

$$U_3 = V_{1/2}^{(K)} = 4.54\ \text{mV}$$
$$U_4 = 2k^{(K)} \approx 39.7\ \text{mV}.$$

Hence,

$$\widehat{w}_\infty(u) = \frac{1}{2}\left[1 + \tanh\left(\frac{u - 4.54\ \text{mV}}{39.7\ \text{mV}}\right)\right]. \tag{A.8}$$

From (4.13) we additionally write

$$\tau_w(u) = \frac{1}{2\phi_\text{w}\cosh\left(\frac{u - U_3}{U_4}\right)} = \frac{1}{2\phi_\text{w}\cosh\left(\frac{u - 4.54\ \text{mV}}{39.7\ \text{mV}}\right)}. \tag{A.9}$$

We once again take our data from Ranjan et al. (2019) and determine ϕ_w using the least square fit, obtaining

$$\phi_\text{w} \approx 0.10\ \text{ms}^{-1}.$$

Thus, $(A.9)$ becomes

$$\tau_w(u) = \frac{1}{0.2\ \text{ms}^{-1}\cosh\left(\frac{u - 4.54\ \text{mV}}{39.7\ \text{mV}}\right)}.^{13} \tag{A.9'}$$

A.2 Conductance and reversal potentials

The most accurate way to determine the effective maximal conductance $\bar{g}_x^{\text{eff}}$ to fit our reduced currents

$$I_x = \bar{g}_x^{\text{eff}} x_\infty(u)(u - E_x)$$

would be to perform a least-squares fit on empirical $I\text{–}V$ data.

However, finding suitable data for mammalian sodium channels or Kv1.1 channels proves to be unexpectedly difficult: many experimental papers report only normalized currents, relative activation curves, or dimensionless conductance traces. Moreover, in our reduction, the gating function p_∞ was normalized; i.e., $p_\infty(u) = [m_\infty(u)]^3 h_\infty(u) / \max\left([m_\infty(u)]^3 h_\infty(u)\right)$.
This means that $\bar{g}_x^{\text{eff}}$ can only be considered a phenomenological, macroscopic conductance.

[13] Data in Ranjan et al. (2019) is extremely scarce regarding $\tau_w(u)$. In our phenomenological model, we accept this approximation without expecting excessive biological accuracy.

For this reason, we adopt standard conductance ranges for mammalians, recognizing that this simplification could significantly distance our model from biophysically accurate results. Instead, they preserve the model's geometry and provide physiologically sensible orders of magnitude.
In fact, attempting to extract accurate values from our ML reduction would be misleading, as it is a phenomenological reduction and does not preserve the full kinetics of HH.
We choose, in order to mimic real-behavior values,

$$C = 1\frac{\mu\mathrm{F}}{\mathrm{cm}^2}.$$

$$\bar{g}_{\mathrm{Na}}^{\mathrm{eff}} = 40\ \mathrm{mS/cm^2}\,, \bar{g}_{\mathrm{K}}^{\mathrm{eff}} = 20\,\mathrm{mS/cm^2}\,, g_{\mathrm{L}} = 0.2\,\mathrm{mS/cm^2}.$$

$$E_{\mathrm{Na}} = 55\ \mathrm{mV}, \mathrm{E_K} = -90\ \mathrm{mV}, \mathrm{E_L} = -65\ \mathrm{mV}.$$

Appendix B: Gating variables and ionic channels

In section 3 we introduced gating variables (m, h, n) as the probability that a specific molecular gating subunit is in the permissive (open) state. Therefore, the gating variables are functions of time whose image is the set $[0,1]$.
We now want to gain further insight in the biomolecular reasoning behind the powers of these variables in the conductance equations summarized in (3.1),[14]

$$I_{\text{ion}} = \sum_{k\in\{\text{Na,K,L}\}} I_k = \bar{g}_{\text{Na}} m^3 h(u - E_{\text{Na}}) + \bar{g}_{\text{K}} n^4 (u - E_{\text{K}}) + \bar{g}_L (u - E_{\text{L}}).$$

It should be noted that Hodgkin and Huxley were unaware of the biomolecular structure of ionic channels, and their power choices were exclusively determined with experimental data-fitting techniques.

Current biomolecular studies show that a voltage-gated sodium channel is primarily constituted by a large α-subunit consisting of four repeated domains, denoted by DI-DIV. Simplifying the complex molecular mechanisms that would go beyond the scope of this appendix, experimental evidence shows that domains DI-DIII are mostly involved in fast (sub-milliseconds) activation, whereas DIV is mostly responsible for fast (milliseconds) inactivation. Therefore, the m^3 factor can be heuristically interpreted as representing the DI-DIII domains, while DIV is represented by h.
Clearly, our discussion is phenomenological and does not fully represent the complex biochemical reactions regulating ionic channels.

Voltage-gated potassium channels consist mainly of four α-subunits. Therefore, n can be interpreted as representing the entire α-subunit, and not just a single domain. Clearly, n is a slower variable than m, and it cannot be approximated by its steady-state function as easily as m.

The HH model assumes that every gating subunit acts independently: since every event is independent, the total probability becomes the product of the single probabilities. This assumption is possible due to the large number of ion channels present: the law of large numbers assures that the mean-field averaging corresponds to the theoretical probability for a sufficiently elevated density of ion channels (which we assume to be near-infinite).

[14] For a complete discussion of ion channels, see e.g., Hille, B. (2001). *Ion Channels of Excitable Membranes* (3rd ed.). Sinauer Associates.

Appendix C: Python Code

The entire Python code of the neuron simulator can be found on GitHub and can be downloaded, used, modified, and distributed under MIT License.