Analysis of 2-Dimensional Approximation of Hodgkin-Huxley model
Computational Biology Project

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Contents

1 Introduction 2

2 Dymanics of the Hodgkin-Huxley Model 2

3 Qualitative Analysis of the 2D approximation of Hodgkin-Huxley Model 3

3.1 Trajectories 5

3.2 Equilibruim Points 6

3.3 Phase Portrait, Nullclines 8

3.4 Bifurcation With I as a Control Parameter 9

4 References 10

1 Introduction

The fundamental unit of communication in the brain is the action potential, a transient polarization of the neuron that generates an electrical charge. This process allows neurons to communicate with each other by transmitting this electrical charge.

The Hodgkin-Huxley (HH) full model is a mathematical representation that elucidates the generation of action potentials in neurons and offers an account of the ion currents involved in the electrical activity of neurons. The model considers the following types of currents: sodium, potassium, and leakage currents. The full HH model is composed of four ordinary differential equations (ODE).

$$\begin{cases} \dot{V} = \frac{-g_{Na}m^3h(V-E_{Na})-g_K n^4(V-E_K)-g_L(V-E_L+I)}{C} \\ \dot{n} = \alpha_n(1-n) - \beta_n n \\ \dot{m} = \alpha_m(1-m) - \beta_m m \\ \dot{h} = \alpha_h(1-h) - \beta_h h \end{cases}$$

2 Dymanics of the Hodgkin-Huxley Model

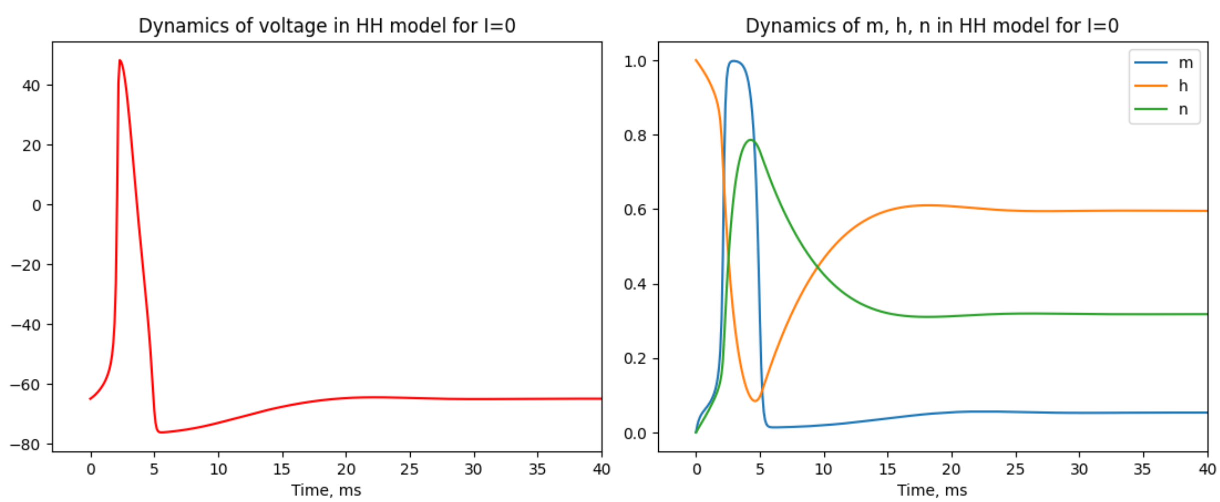

Figure 1: Trajectories without stimulus $I = 0$

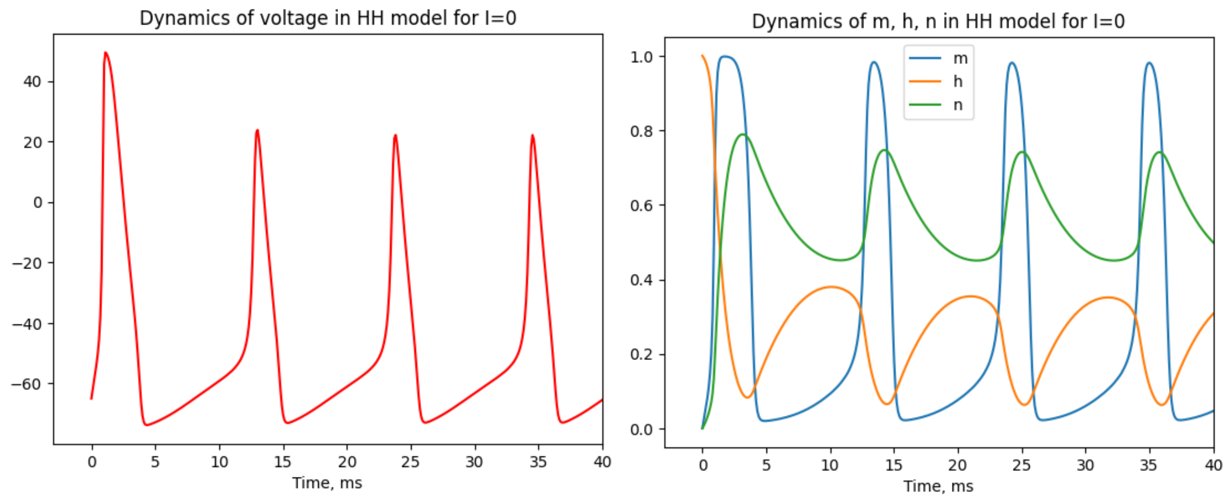

Figure 2: Trajectories with stimulus $I = 25$

For the first situation, we can see that without an external stimulus (I=0), the membrane generates only one pike, and then returns to equilibrium. While in the second condition, when a strong stimulus (I=25) is added, there will be continuous oscillations every 10 ms.

Let's take a look at how the flow of ions changes over time during an action potential. The membrane potential (voltage, red line) begins to depolarize. During depolarization, sodium channels open (m, blue line), allowing an influx of sodium ions, which makes the membrane potential more positive. Then it is repolarized as the sodium channel closes and becomes inactivated preventing the flux of ions (h, orange line). Following depolarization, potassium channels open (n, green line), leading to an efflux of potassium ions. This repolarizes the membrane, restoring it to a negative potential. After repolarization, there's a brief hyperpolarization where the membrane potential becomes more negative than the resting state, often due to prolonged potassium channel activity.

3 Qualitative Analysis of the 2D approximation of Hodgkin-Huxley Model

Analyzing a system of four differential equations, like the Hodgkin-Huxley model, can be challenging. Therefore, a switch to a system of two differential equations is necessary, known as the Reduced Hodgkin-Huxley (HH) model or the 2-Dimensional HH model.

Firstly, we assumed that the activation of sodium current has the fastest time scale. Therefore, to leading order, we approximate $m(t)$ by its steady state value $m \approx m_\infty$. The dynamics of h is similar to that of n. After a short period, transients must settle down, $h + n \approx 1$. More precisely, $1.1n + h \approx 0.89$, but we approximated $h(t) \approx 0.8 - n$. So we arrive at the following system of two differential equations:

$$\begin{cases} \dot{V} = \frac{I - g_{Na} m_\infty(V)^3 (0.8-n)(V-E_{Na}) - g_K n^4 (V-E_K) - g_L (V-E_L)}{C} \\ \\ \dot{n} = \frac{n_\infty(V) - n}{\tau_n(V)} \end{cases}$$

Where:

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}$$

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)}$$

$$\alpha_n(V) = \frac{0.01(55+V)}{1 - \exp^{\frac{-55-V}{10}}}$$

$$\alpha_m(V) = \frac{0.1(40+V)}{1 - \exp^{\frac{-40-V}{10}}}$$

$$\beta_n(V) = 0.0555 \exp^{\frac{-V}{80}}$$

$$\beta_m(V) = 0.108 \exp^{\frac{-V}{18}}$$

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

3.1 Trajectories

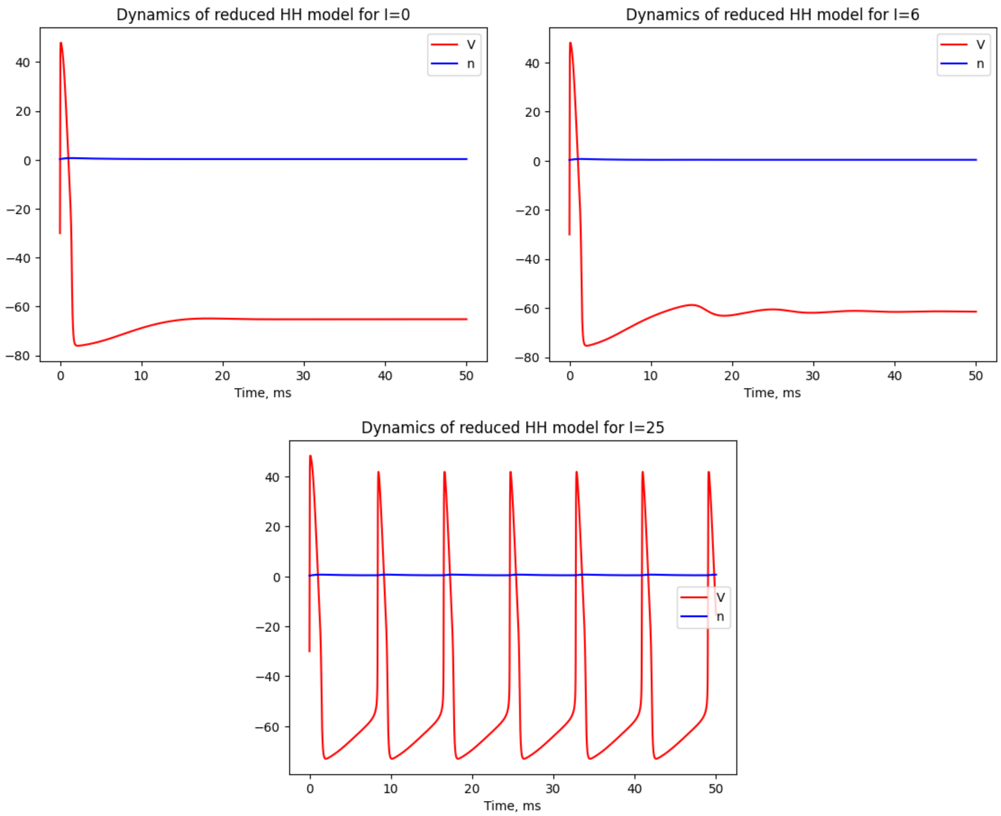

Figure 3: Trajectories of the solutions of the 2D HH model with currents: $I = 0,\ I = 6,\ I = 25$

In the initial condition, with no external input current ($I = 0$), the system tends towards its resting state, as observed in the first graph. Moving to the second graph, when a small perturbation is introduced ($I = 6$), the membrane potential leads to the generation of an action potential or spike. Lastly, in the third condition, with a sufficiently large perturbation ($I = 25$), we observe a repetitive pattern of spikes.

Therefore, the behavior of the trajectories is contingent on the strength of the external input current (I).

3.2 Equilibruim Points

We aim to investigate the long-term behavior of the system, necessitating the identification of its equilibrium points. To do this, consider the following system:

$$\begin{cases} \dot{V} = 0 \\ \dot{n} = 0 \end{cases}$$

The coordinates of the equilibruim are $(V^\star, n^\star)$ and satisfy the equations :

$$\frac{I - g_{Na} m_\infty(V^\star)^3(0.8 - n^\star)(V^\star - E_{Na}) - g_K n^{\star 4}(V^\star - E_K) - g_L(V^\star - E_L)}{C} = 0$$

$$\frac{n_\infty(V^\star) - n^\star}{\tau_n(V^\star)} = 0$$

In our case, we use numerical analysis to find these points for three different states of the system (when the parameter I is changed).

Upon determining equilibrium points, our focus shifts to assessing their stability. This involves constructing the Jacobian matrix, whose properties dictate the type of stability exhibited by the equilibrium points. The resulting Jacobian matrix is a two-dimensional array, and the eigenvalues derived from its associated characteristic polynomial provide insights into the system's stability characteristics.

$$J = \begin{pmatrix} -\frac{g_{Na} m_\infty(V)^3(0.8-n) + g_K n^4 + g_L}{C} & g_{Na} m_\infty(V)^3(V - E_{Na}) \\ \\ \frac{n_\infty(V)}{\tau_n(V)^2} & -\frac{1}{\tau_n(V)} \end{pmatrix}$$

Since it's 2D matrice, the characteristic polynomial of the Jacobian matrix is $\lambda^2 - Tr(J)\lambda + Det(J)$. There is no need to determine the eigenvalues of this matrix; it is enough to determine the signs of the determinant and trace to understand the type of stability of the equilibrium points.

$$T = Tr(J) = -\frac{\bar{g}_{Na} m_\infty(V)^3(0.8 - n) + \bar{g}_K n^4 + g_L}{C} - \frac{1}{\tau_n(V)}$$

$$D = Det(J) = -\frac{\bar{g}_{Na} m_\infty(V)^3 (0.8 - n) + \bar{g}_K n^4 + g_L}{C \tau_n(V)}$$

$(I = 0)$
In this condition, the system has an equilibrium point

$$v_{eq1} = -65.18812720535409, \quad n_{eq1} = 0.31467520370411073$$

and values of the determinant and trace are respectively

$$Det_1 : 0.213933111246806, \quad Tr_1 : -0.513303265971537$$

So, the matrix in this point has two negative eigenvalues, and this point is locally **stable**.

$(I = 6)$
In this condition, the system has an equilibrium point

$$v_{eq2} = -61.365750292077486, \quad n_{eq2} = 0.37439680975099454$$

and values of the determinant and trace are respectively

$$Det_2 : 0.385876808464135, \quad Tr_2 : -0.224733557822401$$

So, the matrix in this equilibrium point has two negative eigenvalues too, which means that this point is locally **stable**.

$(I = 25)$
In this condition, the system has an equilibrium point

$$v_{eq3} = -54.74082622244745, \quad n_{eq3} = 0.4793760929750183$$

and values of the determinant and trace are respectively

$$Det_3 : 0.762620367520092, \quad Tr_3 : 2.50325089618283$$

So, the matrix in this equilibrium point has positive eigenvalues, which means that this point is locally **unstable**.

3.3 Phase Portrait, Nullclines

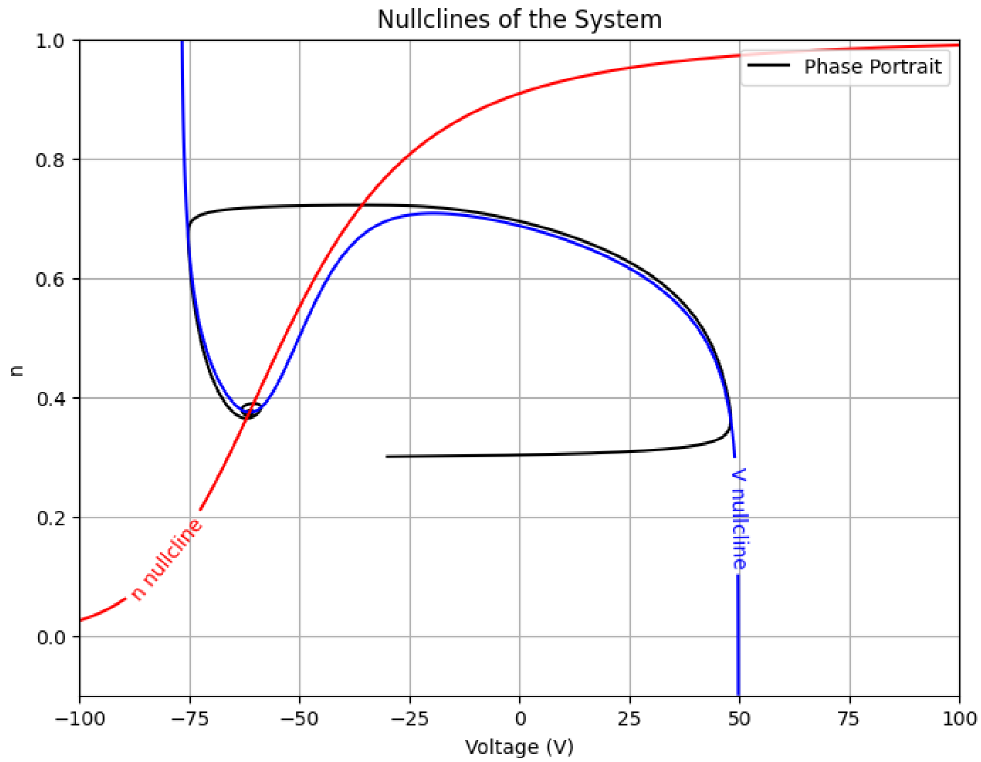

Figure 4: Nullcline of v in blue, nullcline of n in red, phase plane in black, I=0

In the Hodgkin-Huxley (HH) model, concerning its two variables, one can be regarded as fast (V), and the other as slow (n). The nullcline $\dot{V} = 0$ (depicted in blue) for the fast variable (V) takes on a cubic shape, while the nullcline $\dot{n} = 0$ (depicted in red) for the slow variable exhibits a monotonically increasing pattern. The intersection of both nullclines occurs at a single point, representing the sole steady state of the system.

Analogous to the trajectory observed in the solution (Figure 3, I=0), where a single spike is followed by a decline, the phase plane (depicted in black) commences at the initial condition and completes only one orbit.

3.4 Bifurcation With I as a Control Parameter

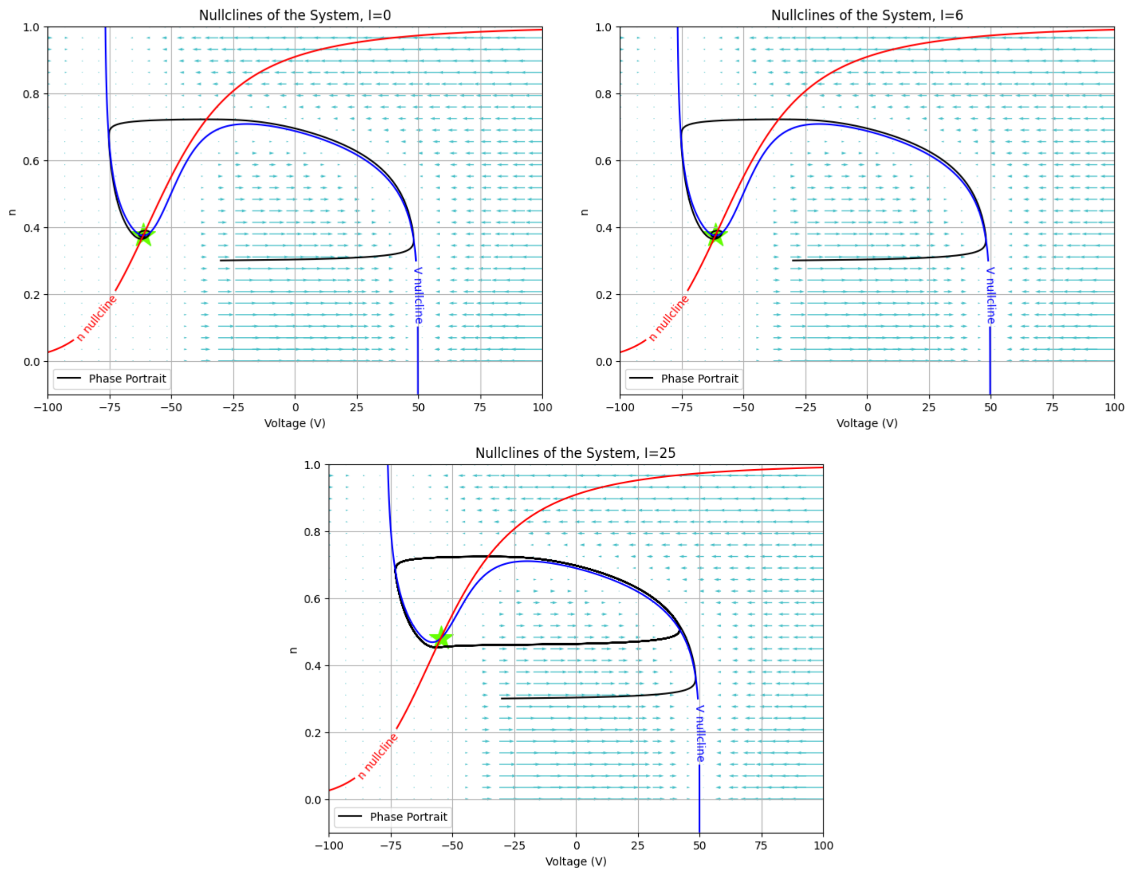

Figure 5: nullcline of v in blue, nullcline of n in red, phase plane in black, equilibrium point as green star, for I=0, I=6, I=25

In these plots, we can discern the impact of the input current on the stability of the solution. In the initial graph, lacking any external stimulus ($I = 0$), the system's solution converges towards a stable point. In the second graph, where an intermediate current ($I = 6$) is applied, insufficient strength prevents a notable deviation. However, in the final scenario with a robust stimulus ($I = 25$), the equilibrium becomes unstable, leading to a divergence in the solution.

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