Neural Differential Equations for Hudgkin-Huxley Model

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Abstract — Hudgkin-Huxley Model are important tool in neuronal modelling, it captures the detailed gating properties of the ion channel in the cell membrane. It describes how action potential initiated and propagated through neurons, the neuronal unit of communication. Neuronal Modelling can be computationally expensive, specially when modelling with the high resolution level models. It becomes even more challenging when considering tuning many parameters that changes with the biological properties of each sample, making the large-scale modelling big challenge in the field. Neural differential equations can propose a promising direction as data-driven differential solvers, these models can combine the current advance of machine learning with the domain knowledge of the systems. In this project, neural differential equation models are represented to solve Hodgkin-Huxley equations by combination of neural networks Approximators for gating variables of ion channels and the differential equation of how voltage is changing cross cell membrane.

1 Introduction

A neuron is a complex computational unit, it performs and generate dexterous behaviours as a nonlinear dynamical system. Our complex behaviour though comes from the interconnection of a huge network of neurons. In order for neuron to interact in this network, it needs an efficient way to communicate with each other. Neurons do this with electrical spikes called action potential. Hodgkin and Huxley had introduced a mathematical model that can describe and model how the action potential is initiated and propagated. [2] The model is a set of nonlinear equations that approximate the electrical characteristics of a neuron cell. For an efficient large-scale simulation and a lower-dimensional mathematical insight into the dynamics, a simplified version of neuronal model was proposed by FitzHugh [1] as a 2D dynamical system of action potential in a neuron.

Hodgkin–Huxley model still model in a detailed the behaviour of activation and de-activation gating of the Na and k ion channels, which represent how they change during the action potential. The model yet required them an intensive tuning of variables to fit the biological properties of each channel types. These parameters was analytically assumed, but these parameters can change between different ion-specific channels, channel types, and different neuron types and so on. So modelling complex systems of different neurons will lead to differences between the model and reality. Substituting these parts with a data-driven approach might help avoid the extensive work of biological cell properties assumptions. Neural network Differential equations methods provides us with tools to deal with that. Beside that, Large-scale simulation of groups of neurons can be computationally expensive. Having an ML approach to solve the differential equations might help accelerate the simulation. [3]

2 Methods

2.1 Hodgkin–Huxley Model

In the HH model, the properties of a neuron are described by a set of four ordinary differential equations: one for the membrane potential u ,and three others for the gating variables n,m , and h. The former is concerned with the voltage-dependent opening and closing of the potassion ion channel (K) and the latter two with the sodium ion channel (Na).

The gating variables represent the probability of the gate to be open. The equation describe the change in gating variables as follows:

$$\frac{dx}{dt} = \alpha_x(u)\,[1 - x(t)] - \beta_x(u)\,x(t)$$

$$\text{where } x \in \{n, m, h\}$$

α and β can be seen as the number of gates that changes its states from open to close state or verse versa. they are called the transition rates.

The differential equation for the membrane potential is given by combining the current passing through all the ion channels that exist in the cell membrane.

$$C\frac{du}{dt} = g_{\mathrm{Na}}m^3h(E_{\mathrm{Na}}-u)+g_{\mathrm{K}}n^4(E_{\mathrm{K}}-u)+g_{\mathrm{L}}(E_{\mathrm{L}}-u)-I_{\mathrm{inj}}$$

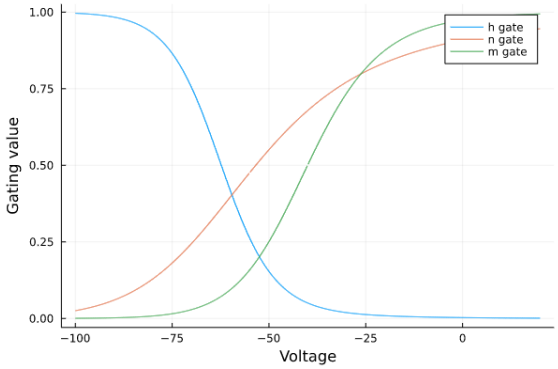

Figure 1 How the voltage-dependence gating variable response changes with different range of applied voltage

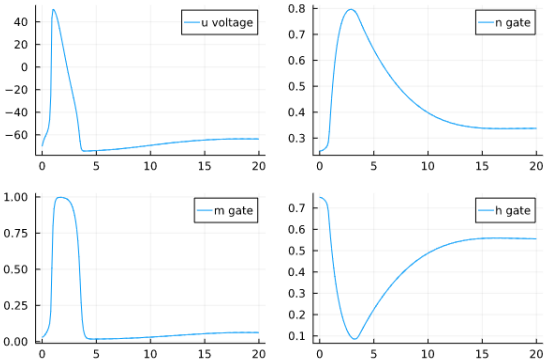

Figure 2 The trajectories of the membrane potential u and n,m,h gating variables.

The total set of equations is given by

$$\frac{dn}{dt} = \alpha_n(u)\,[1 - n(t)] - \beta_n(u)\,n(t)$$

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

$$\frac{dh}{dt} = \alpha_h(u)\,[1 - h(t)] - \beta_h(u)\,h(t)$$

$$C\frac{du}{dt} = g_{\mathrm{Na}}m^3h(E_{\mathrm{Na}}-u)+g_{\mathrm{K}}n^4(E_{\mathrm{K}}-u)+g_{\mathrm{L}}(E_{\mathrm{L}}-u)-I_{\mathrm{inj}}$$

where

$$\alpha_m(u) = \frac{2.5 - 0.1 \cdot (u + 65)}{\exp(2.5 - 0.1 \cdot (u + 65)) - 1};$$

$$\beta_m(u) = 4 \cdot \exp(-\frac{u + 65}{18})$$

$$\alpha_n(u) = \frac{0.1 - 0.01 \cdot (u + 65)}{\exp(1 - 0.1 \cdot (u + 65)) - 1};$$

$$\beta_n(u) = 0.125 \cdot \exp(-\frac{u + 65}{80})$$

$$\alpha_h(u) = 0.07 \cdot \exp(-\frac{u + 65}{20});$$

$$\beta_h(u) = \frac{1}{\exp(3 - 0.1 \cdot (u + 65)) + 1}$$

To illustrate how the different gating variables interact with the applied voltage to the cell membrane, figure 1 shows their behaviour with changing voltages.

Using numerical methods, the solution to the 4 ODE of HH model can be shown in the figure 2 as the trajectories of the membrane potential u and n,m,h gating variables. As the model describe in the equations, the channel gate of the K ion can be obtained by n^4 and

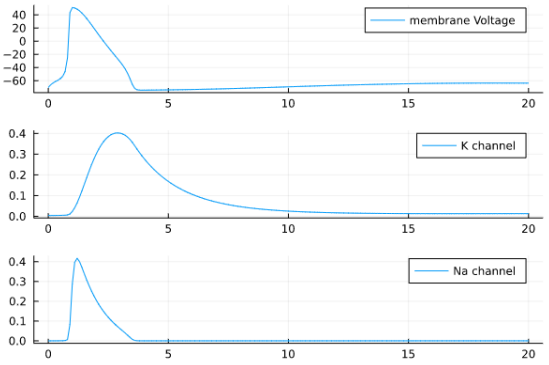

Figure 3 The trajectories of the membrane potential u and n,m,h gating variables.

the channel gate of Na are $m^3 * h$. Following the trajectories in Figure 3 of these channels we can see the biological interpretation of the action potential. When an external voltage is applied, the voltage on the membrane cell increases, which leads to open the voltage-gated channels of both K and Na, thus leading to huge flow of current, causing of the spike, then Na channel starts to close, due to the in-activation properties of h gate (decrease its gating probabilities with increasing voltage), leading to decrease the overall voltage, thus decreasing the number of opened K and Na voltage-gated channels, that returns the voltage membrane to its steady state again.

2.2 Neural Differential equations

As we see in the transition rates equations, it relies on functions and constants that has been tuned analytically to fit the data. Which is has to be different from channel to channel, ion to ion and neural region to other, To avoid this, we can use neural network model to compensate for these parts.

First we can try to use neural network to model a ion channel, to see first how it model the K ion channel

behaviour, and then incorporate it as a whole neuron system with HH Model.

For this, we are replacing gating variable equation below:

$$\frac{dx}{dt} = \alpha_x(u)\,[1 - x(t)] - \beta_x(u)\,x(t)$$

$$\text{where } x \in \{n\} \text{ in the model I used.}$$

with a neural network model that will be trained to have trajectories (solving ODE) that approximate the synthesized data from the original equation.

$$\frac{dx}{dt} = NN(u, x)$$

To have more pre-knowledge about the model, we can add another function to the differential equation that constrain the gating variable to the probabilities scheme that it already represent.

$$\frac{dx}{dt} = NN(u, x) + f(u, x)$$

$$\text{where } f(u, x) = A(1 - x) - B(x)$$

After this, we can build a model that incorporate the gating variable approximation into the whole neuron dynamic system (HH Model).

The total set of the differential equations will then given by:

$$C\frac{du}{dt} = g_{\mathrm{Na}}m^3h(E_{\mathrm{Na}}-u)+g_{\mathrm{K}}n^4(E_{\mathrm{K}}-u)+g_{\mathrm{L}}(E_{\mathrm{L}}-u)-I_{\mathrm{inj}}$$

$$\frac{dn}{dt} = NN(u, n)$$

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

$$\frac{dh}{dt} = \alpha_h(u)\,[1 - h(t)] - \beta_h(u)\,h(t)$$

After that, the best scenario would be if we could use neural network to model all the gating variable of n,m,h with 3 different neural network. In this case we can make sure that no intensive work is needed to estimate the transition rates differently in each neuron. The final differential equation will be:

$$C\frac{du}{dt} = g_{\mathrm{Na}}m^3h(E_{\mathrm{Na}}-u)+g_{\mathrm{K}}n^4(E_{\mathrm{K}}-u)+g_{\mathrm{L}}(E_{\mathrm{L}}-u)-I_{\mathrm{inj}}$$

$$\frac{dn}{dt} = NN1(u, n)$$

$$\frac{dm}{dt} = NN2(u, m)$$

$$\frac{dh}{dt} = NN3(u, h)$$

3 Results and Discussion

In this project, I have first tried to model the whole differential equation as a data-driven approach, but the result was not encouraging and the model needs a lot of training, therefore, I have decided to work on a hypbrid of both data-driven and knowledge-based approach as I showed in the methods.

The first result is the model of only single ion channel using data-driven approach. The Neural network solver was able to reconstruct the behaviour of K channel gates by training it with synthesized data from the ion channel model. The figure 4 shows the N gating variable trajectories between the numerical solution and data-driven Neural network solution, also between the training data and data that the model has not seen before - after the vertical line. the model was able to perform the behaviour that the real N gating variable will do.

Now, the second model is to use a neural network model of a n gating variable in the Hudgkin-Huxley model, to see how it interact with the induced voltage (Action potential). Replacing the differential equation of the n gating variable in the 4 HH equation should still result of the same voltage changing and behaviour in the cell membrane.

Using this approach, the result showed that with some training, the dynamics is preserved, and with more commutations capability for training, it can get accurate.

The figure 5 represents the result of the Neural differential equation model (n gating dynamics as neural network) with the trajectories of the synthesized data. The model still shows some differences in the time duration of the spike of the action potential, this shows that the model still find difficult time capturing the time-delay(analytically calculable with transition rates), but was able to approximate the steady state dynamics.

4 Conclusion

Neural differential equations can be promising tool for neural modelling. it can provide the field with a possible solutions for two important issues in Computational Neuroscience, which is at first that modelling is computationally expensive not only analytically but also numerically, and second that many detalied models requires a big pre-knowledge of the huge amount of parameters which are biologically specific for experimental approximation. In this project I have showed

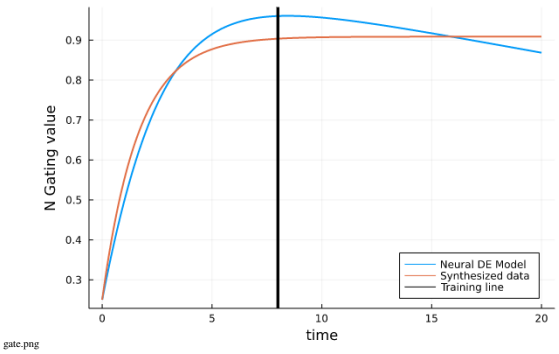

Figure 4 The N gating variable trajectories between the numerical solution and data-driven Neural network solution

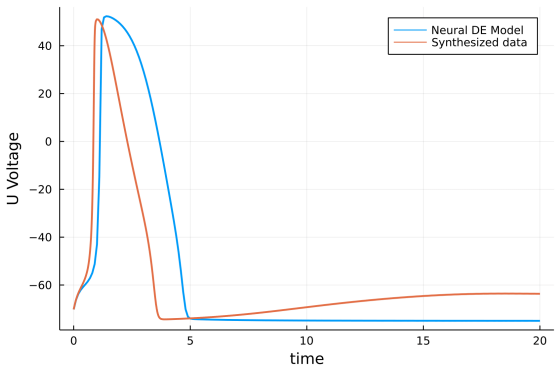

Figure 5 the N-gated Neural differential equation model with the trajectories of the synthesized data

that it is not only possible to model ion channel of cell membrane using neural differential equations e, but it is also possible to model the whole neuron membrane. And By using neural network to approximate the gating variables, you are not only gaining possible computational benefits, but also you automate the process of tuning different variables and function to make it match the specific sample you are studying. In future work, we can investigating more the possibility of using neural network to approximate all the gating variables in the system. This can be achieved in two ways depending on the proposed use of the model, if the purpose of the model is to be used on an unknown biological proprieties of the sample, then the way to go is to use 3 different neural network and train them simultaneously. But if the biological proprieties of the sample is already known and the purpose is to use it in a large-scale modeling. Then we can train every model separately, we use the knowledge of the other gating variables differential equation in the training of the approximated gating variables, and then change the second one with neural network for the second training, with making the other two knowing again and so on.

A Documentation

The code used for this project can be found at: https://github.com/AhmedAlmijbari/HodgkinModel.jl

References

[1] Richard FitzHugh. Impulses and physiological states in theoretical models of nerve membrane. *Biophysical Journal*, 1(6):445–466, July 1961.

[2] A. L. Hodgkin and A. F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, 117(4):500–544, August 1952.

[3] Chon Lok Lei and Gary R. Mirams. Neural network differential equations for ion channel modelling. *Frontiers in Physiology*, 12, 2021.