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Deriving Behaviour of Hodgkin Huxley model with fever dynamics: A computational study

Hasan Eskalen[1] *and Sukru Ozgan*[2]

[1] Graduate School of Natural and Applied Science, Kahramanmaras Sutcu Imam University, Turkey
[2] Department of Physics Kahramanmaras Sutcu Imam University, Turkey

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Abstract: A single neuron can be modeled by the set of differential equations. Hodgkin-Huxley (HH) model, the one of the most famous neuron model, can be considered as a dynamical system with four independent variables. Here we studied to reduce the number of differential equation required for conductance based HH model under strong inhibitory noise. Exponential Integrate and Fire (EIF) model, one independent variable, is used as a reduced model of HH model by using current-voltage (I-V) curve of the original model. The required reduction parameters are determined from this curve. The behaviour of HH model and its reduced EIF (rEIF) model are in good agreement in sub-threshold level. Above-threshold behaviour of reduced EIF model and original model compared in terms of threshold voltage under strong inhibitory noise. Our numerical simulations clearly show that sub-threshold behaviour of HH model perfectly reduced to rEIF model.

Keywords: Hodgkin-Huxley, exponential integrate and fire, I-V curve, reduction.

1 Introduction

Perception, behaviour, memories and other complex human being skills organized by the brain and individual nerve cells are basic blocks of it. At the inside of this complex machine, some 10^{11} neurons that each can be connected to 10^4 other neurons, exist [8]. Mathematical models illustrating the dynamics of single neurons are crucial to understanding complex neural network behaviour. Although it is a simple algorithm that a neuron collects all inputs come from other neurons and fire if the certain threshold level achieved, it is required more complex formulation to model spike generation mechanism of a realistic neuron. Conductance based HH had been considered as one of the most significant models in mathematical neuroscience since its discovery in 1952 [7]. In HH model, the dimension is described by voltage gated channels which are nothing but coupled nonlinear ordinary differential equations [13]. In neural modeling, the more detailed biophysical models, the higher model dimension is required and dimension is described by voltage gated channels [2]. Easy computability and generating firing pattern like real biological neurons are two main feature of good single neuron model [10]. Even though, HH model can accomplish generating desired firing pattern; it is not computationally effective. In fact, it is cost lot, about 1200 operation per one ms is needed. On the other hand, Integrate and Fire (IF) model that require only 5 operations per one ms, is easy to simulate but it can not generate some important feature of real neurons [11].

Deriving biophysical models and its parameters from real noisy neural data have recently attracted much attention in the field of computational neuroscience. By the help of the recent advance in patch clamp and dynamical clamp techniques, the neural activity can be observed with high spatial and temporal resolutions [9]. In literature, HH model parameters

* Corresponding author e-mail: heskalen@gmail.com

were estimated by using dual extended Kalman filtering [12]. Recently, the required linear and nonlinear parameter for biophysical HVC model were extracted from electrophysiological data [14]. Badel et. al. measured activity of neocortical brain slices. From the result of this measurement, they modeled real neurons activity by using EIF model [1]. Extracting required neural model parameters from experimental data techniques can be modified as detailed biophysical neuron model might be reduced to more simpler neural model. Badel et. al. reduced 2-dimensional Wang-Buzsaki neural model to 1-dimensional EIF model [2].

As we have already known that dynamical problems are generally non-lineer and most of non-lineer systems are impossible to solve analytically[15]. Although the simplest numerical method for solving differential equations is Euler's method, various different solution techniques with superior properties, such as Perturbation iteration method, variational iteration method, and Adomian decomposition method existed[16,17,18,19]. In this, article, solutions of differential equations were obtained by using the ode45 function (implements fourth order Runge-Kutta numerical integration algorithms) in MATLAB software (R2012b).

The aim of this study is that obtaining required reduction parameters needed for EIF model from HH model and examine sub-threshold and spiking mechanism of HH and its reduced model under random strong inhibitory noise.

2 Models and methods

2.1 Hodgin-Huxley model

In our study to simulate behaviour of neurons, we choose famous Hodgin-Huxley (HH) model that consists of Sodium, Potassium and Leak currents. The model used in our study similar to the model used by Ermentrout [4]. The model is given by four nonlinear coupled equations:

$$C_m \frac{dV}{dt} = -(I_L + I_{Na} + I_K + I_{noise}) + Iapp \tag{1a}$$

$$I_{Na} = g_{Na} m^3 h (V - E_{Na}) \tag{1b}$$

$$I_K = g_K n^4 (V - E_K) \tag{1c}$$

$$I_L = g_L (V - E_L) \tag{1d}$$

where C_m, I_{noise} and I_{app} represent membrane capacitance, noise current and constant applied current respectively. The constant, g_{Na}, g_K and g_L are maximum conductance of related ions and E_{Na}, E_K and E_L represent reversal potentials of corresponding ions. The first nonlinear equation represents voltage, V, and the other three, m, n, h represent gating variables.

$$\frac{dx}{dt} = \alpha_x(V)(1-V) - b_x(V)x, \;\; x = m,n,h \tag{2a}$$

$$\alpha_m(V) = 0.32(54+V)/(1-exp(-(V+54)/4)) \tag{2b}$$

$$b_m(V) = 0.28(V+27)/(exp((V+27)/5)-1) \tag{2c}$$

$$\alpha_h(V) = 0.128exp(-(50+V)/18) \tag{2d}$$

$$b_h(V) = 4/(1+exp(-(V+27)/5)) \tag{2e}$$

$$\alpha_n(V) = 0.032(52+V)/(1-exp(-(V+52)/5)) \tag{2f}$$

$$b_n(V) = 0.5exp(-(57+V)/40) \tag{2g}$$

General expression for gating variables are given in Equation *2.2a*, $\alpha_m(V)$, $\alpha_h(V)$, $\alpha_n(V)$, $b_m(V)$, $b_h(V)$ and $b_n(V)$ are

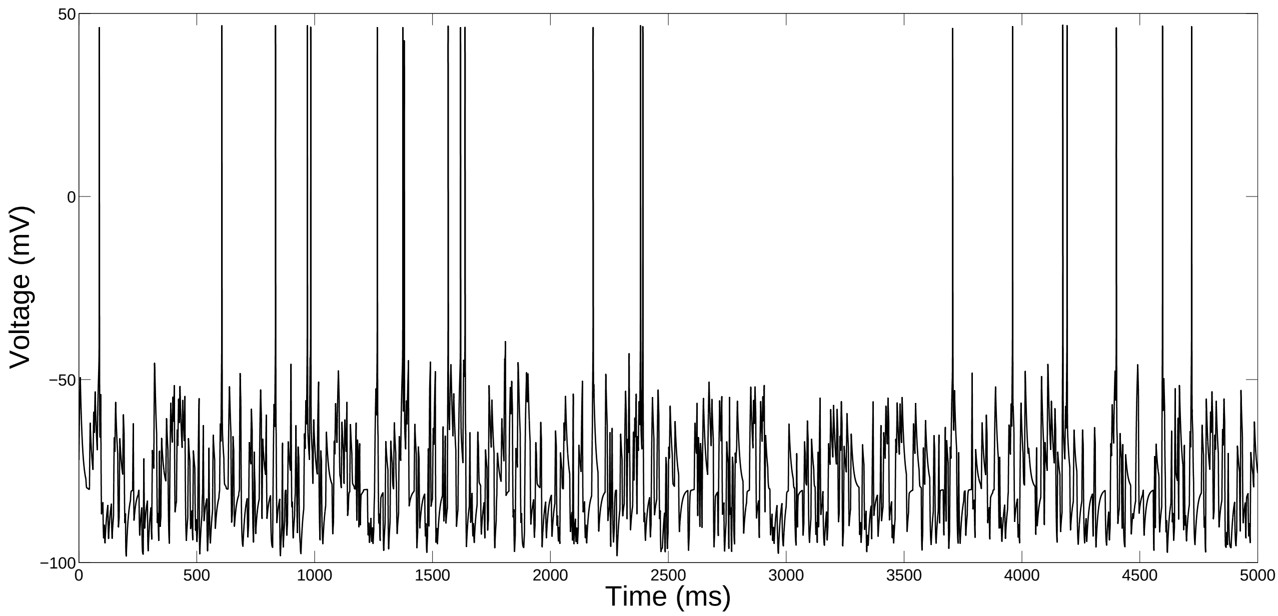

Fig. 1: Voltage-time graph of HH model under strong inhibitory noise.

specific functions of gating variables [4]. An arbitrary strong inhibitory noise is used at our study. Strong inhibitory noise provides to examine sub-threshold behavior more deeply. The behavior of HH model under strong inhibitory noise is shown in Figure 1. As it can be inferred from this figure neuron generally oscillated at the sub-threshold level and some time fire without any pattern. The used parameters are given in Table 1 and the membrane capacitance C_m, and applied current $Iapp$ is taken as 1 nF and -0.5 μA sequentially

Table 1: The values of HH model parameters

	Sodium	Potasium	Leak
Conductance (μ S)	g_{Na}=40	g_K=3	g_L=0.1
Reversal Potentials (mV)	E_{Na}=50	E_K=-100	E_L=-75

2.2 Exponential integrate and fire model

The simplest form of linear Integrate and Fire Model consists of only passive leakage current and by applying external current neurons behave as an integrator, and when the cell reaches a certain threshold the potential of cell reset to predetermined level.

$$C_m \frac{dV}{dt} = I_L + I_{app} + I_{noise} \tag{3}$$

At the Equation 3, C_m shows membrane capacitance, I_L implies passive leakage current, I_{app} indicates external applied current and I_{noise} represents the noise current. Linear Integrate and Fire Model (LIF) can not exactly express the behavior of neurons at the action potential level. Fourcaud-Trocme et. al. mention this problem and introduce new IF model which is called Exponential Integrate and Fire Model [5]. EIF model can be expressed as;

$$C_m \frac{dV}{dt} = I_L + F(V) + I_{app} + I_{noise} \tag{4}$$

Exponential Integrate and Fire model actually similar to LIF model. The leak current, applied current and noise current are the same for both models but in the EIF model there are also, $F(V)$ function which generates the difference between them. $F(V)$ represents a function of voltage which describes spike generating currents. LIF model expresses a special form of EIF model in which the function of F equal to zero. $F(V)$ function can be express as,

$$F(V) = \frac{1}{\tau_m}(E_L - V + \triangle_T e^{(V-V_T)/\triangle_T}) \tag{5}$$

In the Equation 5, τ_m is called time constant of neuron and it is also equal to g_L/C_m. V_T represents the spike threshold and $\triangle_T$ shows the spike width.

2.3 Obtaining I-V curve

The four parameters that are needed for rEIF model, are obtained from the I-V curve of HH neural model. The method of parameter optimization is similar to the method of Badel et. al. [1,2]. At first, we stimulate HH neural model under strong inhibitory noise, after than sub-threshold voltage domain divided into small voltage pieces. Then, the corresponding average currents of the specific voltage pieces are calculated. Finally, the obtained average currents versus corresponding voltages are plotted. The simulations were performed with Matlab R2014a. In our study, we focus on the voltage interval of -90 mV to -43 mV, after this upper boundary voltage, current values of neuron getting increased exponentially, because of up strike mechanism of the spike. In this study, voltage range equally divided 48 parts and the average current values of each of this parts are separately calculated.

Parameters	Resting Potential	Spike Threshold	Time Constant	Spike Width
Symbols	E_L	V_T	τ_m	$\triangle_T$
Values	-79.98	-50.12	9.84	2.33

Table 2: Calculated values of Reduced EIF model parameters

Figure 2 shows the I-V curve of HH model. Insert plot indicates an example of some specific voltage values and how many times overlapped depend on time. The only up strike behavior of neural oscillations are considered when the average currents are calculated. As an example, about ten different currents are found and their average is calculated for -50 mV over 1200 ms in Figure 2 insert.

After obtaining I-V curve, rEIF model parameters are calculated by using, The Matlab R2014a function *lsqcurvefit* (solving nonlinear curve fitting problems in least-squares style). Four unknown parameters found from 48 equation easily by using this built-in function.

3 Results

In order to compare HH model and reduced EIF model, the four unknown parameters are obtained from I-V curve of HH model. The obtained rEIF parameters are given in Table 2. The rEIF model and HH model stimulated under same strong

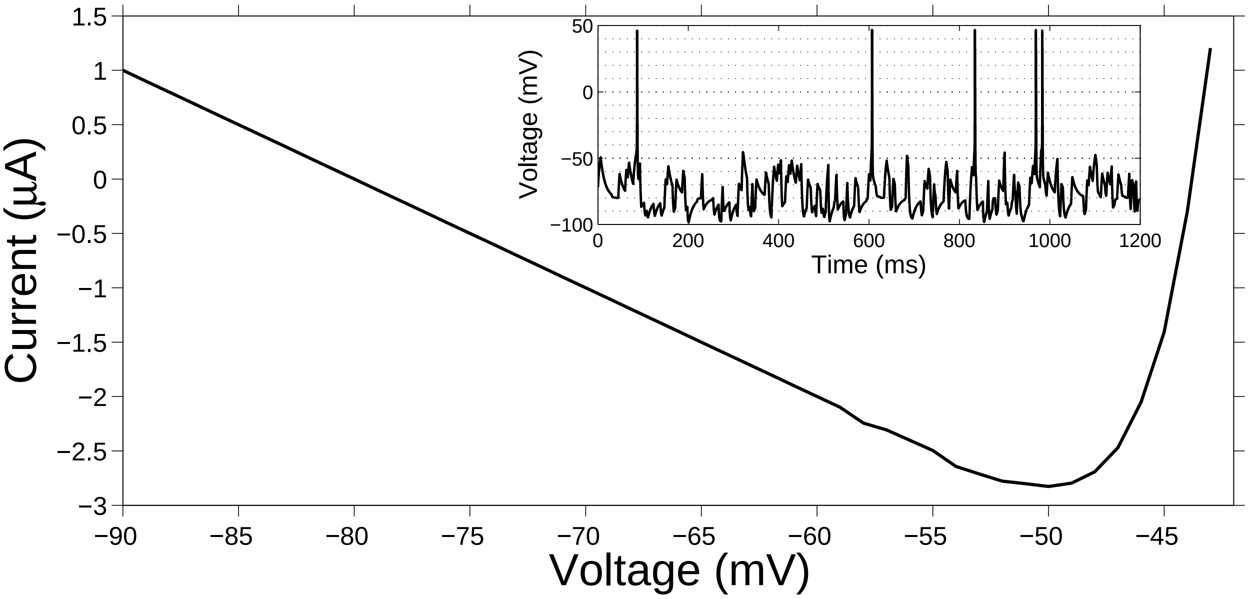

Fig. 2: The Current vs Voltage curve of HH neural model

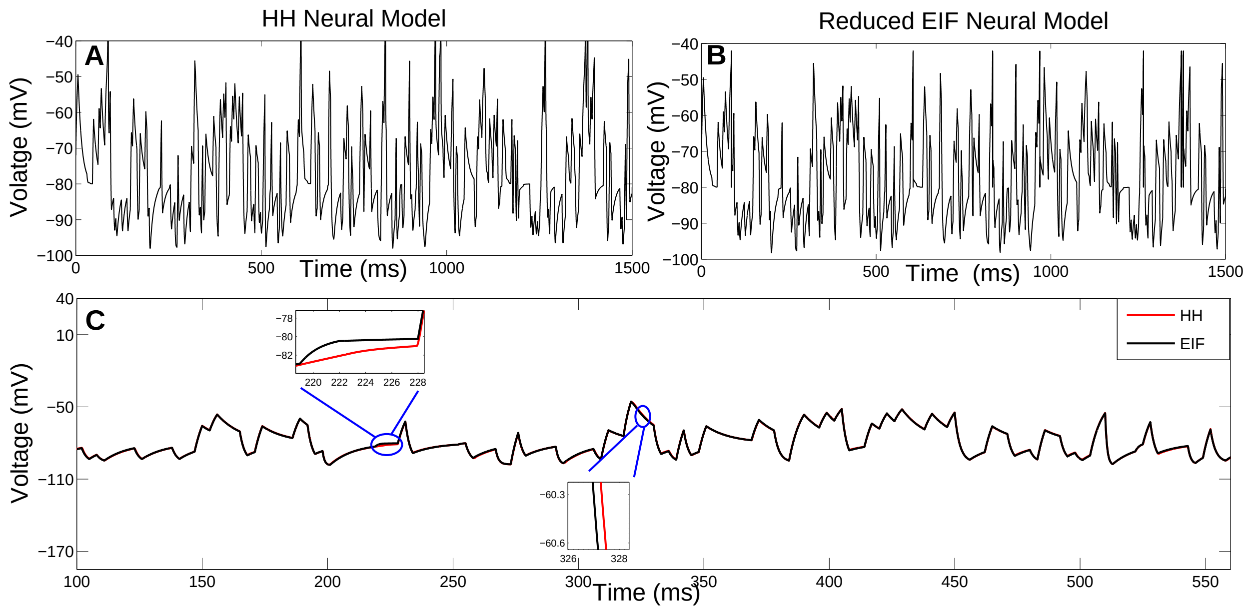

Fig. 3: Sub-threshold behavior of HH and rEIF model

inhibitory noise by using obtained four parameters at the Table2. Figure 3-A shows the sub-threshold behaviour of HH neural model in a more detail over a time interval of 1500 ms. The voltage trace of the rEIF model behaviour is given in Figure 3-B. As it can be seen from these figures neural voltage trace strictly similar for both original model and its reduced model in the sub-threshold level. In the Figure 3-C, voltage trace of both HH and rEIF model are drawn together from 100 ms to 560 ms. Red line implies HH model trace and black line represent rEIF model trace as indicated in the figure. Although voltage traces are seen in one color, black, with the naked eye. It actually composes of two different colors. Two different areas of this figure zoomed in to show behaviour of voltage traces of both models in more detail. As it can be seen from this zoomed figures HH neural model and its rEIF neural model are very close to each other, there are only tiny differences between them and these difference are barely seen with naked eye. As a result of Figure 3, its clean that sub-threshold behaviour of HH neural model perfectly reduced to EIF model, it is hard to see differences with out zoom in. Figure 4-A represents the voltage-time graph of HH neural model over the time interval of 1000 ms. As

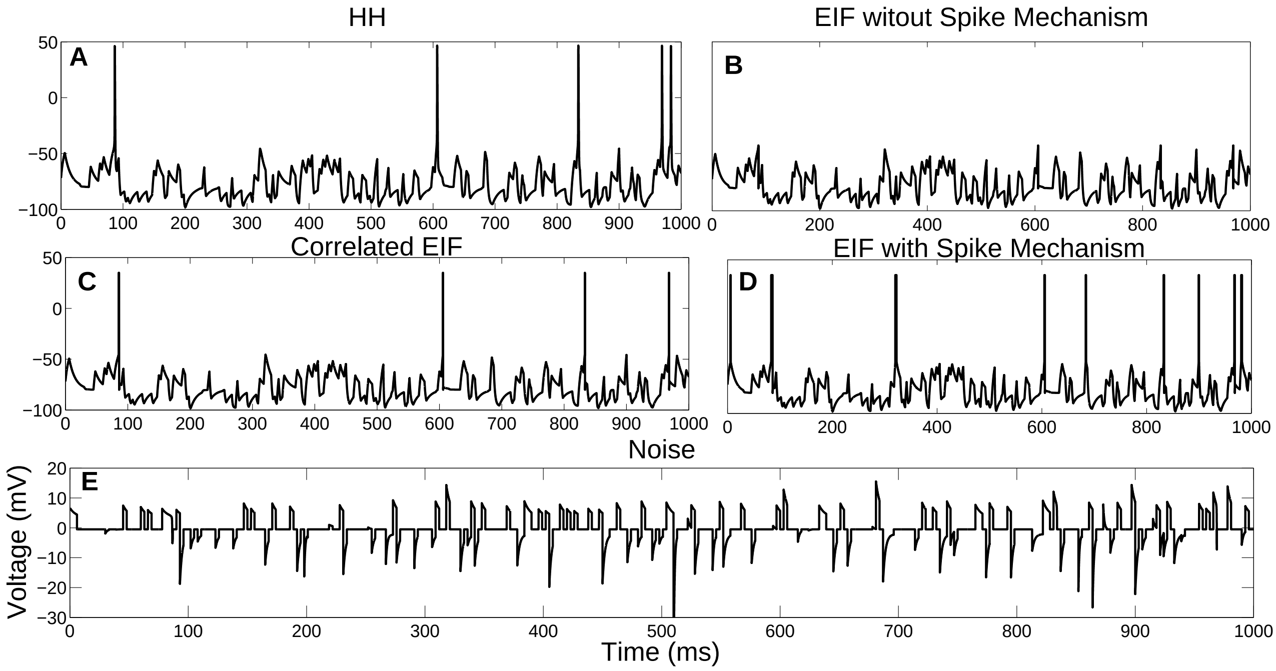

Fig. 4: Behaviour of original HH, reduced rEIF and crEIF model and given noise

seen from the figure HH model fire 5 times over this time. Figure 4-B shows reduced EIF neural model without spike mechanism derived from I-V curve of HH neural model. EIF neural model with spike mechanism given in Figure 4-D and in this graph, parameter of the spike threshold calculated from I-V curve; see Table 2. As seen from the Figure 4-D reduced EIF model make 9 spikes. Although original HH model fire 5 times, reduced EIF model fire 9 times. We assume that the reason of this problem is originated from two main reasons. The first reason is nature of EIF model and the second reason is the used noise matrix. The arbitrary strong inhibitory noise is used in our simulations. Figure 4-E shows the used noise. Generally, noise is negative; indicate strong inhibition; and it fluctuates from -20 mV to 8 mV. During some part of simulation noise push up the voltage trace above spike threshold and then suddenly push down the voltage trace below it. This type of behaviour of noise at the original HH model some time trigger the action potential, spike, some times cause sub-threshold oscillation but in the EIF model, all voltage values above threshold level assumed to cause the spike. This problem can easily solve by increasing spike threshold voltage by %10 per cent. Figure 4-C indicates rEIF model with threshold voltage %10 per cent more than in the Table 2. This new rEIF model could called as correlated reduced EIF (crEIF) model. crEIF implies increasing spike threshold and in this study this critical values are taken %10 per cent above the original values. Over the time interval of 1000 ms, the only one spike miss at the correlated EIF model compared to original HH neural model.

Time Interval(ms)	HH	EIF	crEIF
0-1000	5	9	4
1000-2000	6	16	6
2000-3000	3	6	3
3000-4000	2	3	2
4000-5000	5	10	5
0-5000	21	44	20

Table 3: Spike Statistics of HH and its reduced models

4 Discussion

Obtained electrophysiological data from real neurons that used to derive mathematical neuron model parameters is the hot topic in the field of computational neuroscience. Reducing detailed neural model by using its I-V curve to simple neural model becoming one of the studying areas of this field. Here we have shown that original Hodgin Huxley model reduced to EIF model by using I-V curve of HH model. I-V curve actually gives us to examine HH model in the different point of view i.e. this curve does not depend on time. From this curve, the necessary parameters of EIF model are obtained. As seen in Figure 2, this curve consists of linear and exponential parts. I-V curve behaves linearly between -90 mV to -50 mV and behaves exponentially after -50 mV. The Equation 4 is also composed of linear and exponential parts. From I-V curve, the four parameters of Equation 5 are found by using least squares approximation.

The result of reduction perfectly suitable with original HH model at the sub-threshold level. Both models voltage-time trace almost behave in the same manner but the spike mechanism of the original model is not matched with EIF model. We assume that nature of EIF model and random strong inhibitory noise matrix cause this problem. In the EIF model, spike variability is not an issue to mention, this model has only fix spike threshold and if the voltage reaches the threshold, then neuron get fire [11]. To overcome this problem we propose crEIF model. EIF and crIEF model actually same model but in the crEIF model, spike threshold is modificated. Spike threshold found from I-V curve of HH model, used in EIF, is increased by 5 mV at crEIF model to ignore noises that are exceeding spike threshold. As a result, HH neural model and our proposed crEIF models behave very closed to each other at the not only sub-threshold level but also above the threshold. This method of reducing original HH neural model to EIF neural model can be used to simulate large neural network because of computational efficiency.

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors have contributed to all parts of the article. All authors read and approved the final manuscript.

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