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A New Adaptive Method for Solving Neuron Cells Problem of Hodgkin-Huxley and Estimating Parameters

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A B S T R A C T

In this paper, a new adaptive parametrization model of fourth order neuron cells model of Hodgkin-Huxley (HH) is introduced. The adaptation algorithm design or as can be called adaptive identification algorithm of parameters of the neuron cells HH model is produced. This algorithm is theoretically and computationally proved. This introduced algorithm is basically based on Lyepunov functions and adaptive observer methods which may prove the stability of the model to obtain unique solutions. The results of the computer simulation of the identification problem are shown in the figures and the parameters are clearly coincide the real values. Some terms of the problem are defined for the measured data. It provides an observation model to determine the most informative data for a specific parameter, and find the best fit model. In the HH model of neural cells, the consistency of the differential equations of the adaptation model with the observers of cell's activation is shown by fitting the observed data to the real data within the high accuracy of estimating the parameters.

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1. Introduction

The most complex systems existing is the dynamic of neuron cells of human brain. In order to understand how the human brain is physically working, massive mathematical and biological studies have been published for many years. Moreover, it is studied to create its mathematical models and to redesign its construction [1,2]. Although there may exists different complexities to simplify models, studying the dynamic models of the brain has been recently started and successively developed [3,4]. The biological neuron models are based on the class of ordinary differential equations of the Hodgkin–Huxley model (HH) and its simplifications' models. These models have considered as Hindmarsh– Rose (HR), FitzHugh–Nagumo (FHN), Morris–Lecar (ML), etc. Most of the biological neuron's dynamical behavior of spiking or bursting cells is simplicity exhibited in the HH model [5].

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The activity of neurons has been recently studied by Wang N. [6] and the neurons are known “neural mass models”. These are dominated by the parameters of the models which have physical meaning for the cells’ actions. To state and parameters estimation for neural cells models, a number of methods are used such as, but not limited to, network [7,8], observer methods [9,10] and least square methods [11], etc.

The identification of the model parameters based on the neuron state measurements. Many methods base on adaptation observers and learning data. Identification of HH model dynamics was studied by Centofanti et al. [12], employing the operator learning techniques. The HH model was transformed in [13] and additive noise in voltage data was reduced, then analyzing the source of this noise reduction is analytically employed for parameter estimations. By applying Model Predictive Control, Fröhlich F. and Jezernik S. [14] showed the possibility of influencing the shape of the resulting control signal via tunable controller parameters, and to take into account biophysical constraints on the input signals and state variables. The HH model was reduced in [15] into only one ordinary differential equation (ODE), and the deep learning was employed to identify the dynamics of the approximation system. A simple approach for solving the problem of identifying states and parameters of HH problem were proposed [16] using Machine Learning Methods. Bougandoura et al [17] found that the HH model can be contribute to easier modeling and implementation of reversible electroporation dynamics, providing an effective tool for kind of exploration of electroporation for cancer therapy. Simple model for the HH model was proposed by embedding noise parameter in neural response, see [18]. In [19], an adaptive observer for asymptotical estimation of the parameters and states of the model was presented. The method proposed is to find explicit representation of periodic solutions of HH problem since this problem, however, does not have analytical solutions. Identifying the parameters allows a better understanding of the mechanisms underlying biological meaning of the neuran phenomena. The Markov chain Monte Carlo (MCMC) was the best method which helped Wang YC et al [20] to propose a method for parameter identification and uncertainty quantification in a Bayesian framework. This allows to incorporate more knowledges about the parameters of the model (as probability distributions) and to get less error of distribution of parameters informed by the measured data.

In this paper, the HH neuron model is illustrated. In order to solve identification problem of HH, the speed gradient (SG) method is used with the relative theory of feedback Kalman–Yakubovich lemma (FKYL) as it is proposed in [21,22]. The convergence statement of the estimated parameters to their true values was modeled in different form, and the proof is given. The results of the identification of the parameters are given by the computer simulation and shown in figures.

The paper is organized as follows. In Section 2, the problem statement is presented in details. The design of the adaptation algorithm is clearly presented in section 3 presents. The main results are given in Section 4, and then in section 5, the computer simulation results and valued of parameters are described. Concluding of this paper is given in section 6.

2. Problem Statment

Consider the classical Hodgkin-Huxley (HH) neuron model [23]:

$$\dot{x}_1 = \frac{1}{C}\left(I - g_{Na} x_3^3 x_4 x_1 + 120\, x_3^3 x_4 E_{Na} - g_k x_2^4 x_1 + 36\, x_2^4 E_k - g_L\left(x_1 - E_L\right)\right)$$

$$\dot{x}_2 = \left(\frac{0.01\left(x_1 + v_1\right)}{e^{-0.1\left(x_1 + v_1\right)} - 1} - 0.125\, e^{-\frac{x_1 + v_2}{80}}\right) x_2 + \frac{0.01\left(x_1 + v_1\right)}{1 - e^{-0.1\left(x_1 + v_1\right)}}$$

$$\dot{x}_3 = \left(\frac{0.1\left(x_1 + v_3\right)}{e^{-0.1\left(x_1 + v_3\right)} - 1} - 4\, e^{-0.0556\left(x_1 + v_4\right)}\right) x_3 + \frac{0.1\left(x_1 + v_3\right)}{1 - e^{-0.1\left(x_1 + v_3\right)}}$$

(1)

$$\dot{x}_4 = \left(0.07e^{-0.05(x_1+v_5)} - \frac{1}{1+e^{-0.1(x_1+v_6)}}\right)x_4 + v_7 e^{-0.05(x_1+v_5)}$$

$$y(t) = x_1(t)$$

where $x_1(t)$ is the measured voltage, $x_2(t)$, $x_3(t)$, $x_4(t)$ are the giant variables and y is the output of system (1). This model describes the change of the voltage x(t) in the electrical potential in the neuron cells over time depending on some parameters C, E_k, E_{Na}, E_L, g_k, g_{Na}, I, g_L, v_1, v_2, v_3, v_4, v_5, v_6, v_7. Some of these parameters are assumed to be known: $I, g_{Na}, E_{Na}, g_k, E_k, g_L, E_L, v_1, v_3, v_7$; however, other parameters may vary from cell to another, thus these are considered as unknown.

The variables $x_1(t)$, $x_2(t)$, $x_3(t)$, $x_4(t)$ are assumed to be experimentally measured. In order to estimate the unknown parameters of the HH neuron model (1), the adaptive model is introduced here as follow [19]:

$$\dot{z}_1 = \frac{1}{C}\left(I - \hat{g}_{Na} z_3^3 z_4 x_1 + 120\, z_3^3 z_4 \hat{E}_{Na} - \hat{g}_k z_2^4 x_1 + 36\, x_2^4 \hat{E}_k - \hat{g}_L x_1 + \hat{g}_L \hat{E}_L\right) - l(x_1(t) - z_1(t))$$

$$\dot{z}_2 = \left(\frac{0.01(x_1+v_1)}{e^{-0.1(x_1+v_1)}-1} - 0.125\, e^{-\frac{x_1+v_2}{80}}\right)z_2 + \frac{0.01(x_1+v_1)}{1-e^{-0.1(x_1+v_1)}} \quad (2)$$

$$\dot{z}_3 = \left(\frac{0.1(x_1+v_3)}{e^{-0.1(x_1+v_3)}-1} - 4\, e^{-0.0556(x_1+v_4)}\right)z_3 + \frac{0.1(x_1+v_3)}{1-e^{-0.1(x_1+v_3)}}$$

$$\dot{z}_4 = \left(0.07e^{-0.05(x_1+v_5)} - \frac{1}{1+e^{-0.1(x_1+v_6)}}\right)z_4 + 0.07e^{-0.05(x_1+v_5)}$$

where $z_1(t)$, $z_2(t)$, $z_3(t)$, $z_4(t)$ are the state variables and the term $l\big(x_1(t) - z_1(t)\big)$ is the stabilizing term of the adaptive model (2).

For simplicity and having particular regular and observation systems to build another model, parameters such as $v_1, v_2, v_3, v_4, v_5, v_6$ in some terms of big brackets must be defined.

Assume that the vector of the unknown parameters is denoted as $\theta = [\theta_1, \theta_2, \theta_3, \theta_4, \theta_5, \theta_6, \theta_7, \theta_8, \theta_9, \theta_{10}]^T$, where $\theta_1 = \hat{I}$, $\theta_2 = \hat{g}_{Na}$, $\theta_3 = \hat{E}_{Na}$, $\theta_4 = \hat{g}_k$, $\theta_5 = E_k$, $\theta_6 = \hat{g}_L$, $\theta_7 = \hat{g}_L \hat{E}_L$, $\theta_8 = \hat{v}_1$, $\theta_9 = \hat{v}_3$, $\theta_{10} = \hat{v}_7$. Then, the adaptation algorithm design for θ should insure and satisfy that:

$$\lim_{t\to\infty} |x(t) - z(t)| = 0 \quad (3)$$

$$\lim_{t\to\infty} |\theta(t) - \tilde{\theta}| = 0 \quad (4)$$

where $\tilde{\theta} = \left[I, g_{Na}, E_{Na}, g_k, E_k, g_L, g_L E_L, v_1, v_3, v_7\right]^T$, and it is assumed that v_2, v_4, v_6, C are known and have the real values $v_2 = 60$, $v_4 = 60$, $v_5 = 60$, $v_6 = 30$, $C = 1$.

3. Adaptive Algorithm Design

Equations Consider the state estimation error function $e(t) = x(t) - z(t)$ as follows

$$\dot{e} = A_l\, e + B_1\left(I - g_{Na} x_3^3 x_4 x_1 + 120 E_{Na} x_3^3 x_4 x_1 - g_k x_2^4 x_1 + 36 E_k x_2^4 x_1 - g_L x_1 + g_L E_L x_1\right) + B_2\left(\theta_8 \left(\frac{0.01}{1 - e^{-0.1(x_1+50)}}\right)\right)$$

$$+ B_3\left(\theta_9 \left(\frac{0.1}{1 - e^{-0.1(x_1+35)}}\right)\right) + B_4\left(\theta_{10}\, e^{-0.05(x_1+60)}\right)$$

$$= A_l\, e + B_1\left(\theta_1 - \theta_2 x_3^3 x_4 x_1 + 120\, \theta_3 x_3^3 x_4 x_1 - \theta_4 x_2^4 x_1 + 36\, \theta_5 x_2^4 x_1 - \theta_6 x_1 + \theta_7 x_1\right) + B_2\left(\theta_8 \left(\frac{0.01}{1 - e^{-0.1(x_1+50)}}\right)\right)$$

$$+ B_3\left(\theta_9 \left(\frac{0.1}{1 - e^{-0.1(x_1+35)}}\right)\right) + B_4\left(\theta_{10}\, e^{-0.05(x_1+60)}\right) \qquad (5)$$

where $A_l = \begin{pmatrix} -l & 0 & 0 & 0 \\ \alpha_1 & \beta_1 & 0 & 0 \\ \alpha_2 & 0 & \beta_2 & 0 \\ 0 & 0 & 0 & \beta_3 \end{pmatrix}$;

such that

$$\alpha_1 = \frac{0.01}{1 - e^{-0.1(y(t)+50)}}, \quad \alpha_2 = \frac{0.1}{1 - e^{-0.1(y(t)+35)}}, \quad \beta_1 = \left(\frac{0.01(y(t)+50)}{e^{-0.1(y(t)+50)} - 1} - 0.125\, e^{-\frac{y(t)+60}{80}}\right),$$

$$\beta_2 = \left(\frac{0.1(y(t)+35)}{e^{-0.1(y(t)+35)} - 1} - 4\, e^{-0.0556(y(t)+60)}\right), \quad \beta_3 = \left(0.07 e^{-0.05(y(t)+60)} - \frac{1}{1 + e^{-0.1(y(t)+60)}}\right)$$

and

$$B_1 = (1,0,0,0)^T, \quad B_2 = (0,1,0,0)^T, \quad B_3 = (0,0,1,0)^T, \quad B_4 = (0,0,0,1)^T$$

The speed gradient method [24] is used for the adaptation algorithm design. In this case, the quadratic goal function $\Psi(e) = e^T \Phi e$ is used, where $\Phi = \Phi^{\mathrm{T}} > 0$ is a positive definite matrix which will be determined later. Then, the systems (1) and (2) are replaced with the error Eq.5 as the last one depends only on the error variable e. Using the speed gradient method leads to have the following equations:

$$\dot{\theta}_1 = -\delta_1 e^T Q B_1 \,.\, 1$$

$$\dot{\theta}_2 = -\delta_2 e^T Q B_1 \,(-x_3^3 x_4 x_1)$$

$$\dot{\theta}_3 = -\delta_3 e^T Q B_1 \,(x_3^3 x_4 x_1)$$

$$\dot{\theta}_4 = -\delta_4 e^T Q B_1 \,(-x_2^4 x_1) \qquad (6)$$

$$\dot{\theta}_5 = -\delta_5 e^T Q B_1 \,(x_2^4 x_1)$$

$$\dot{\theta}_6 = -\delta_6 e^T Q B_1 \,(-x_1)$$

$$\dot{\theta}_7 = -\delta_7 e^T Q B_1 (x_1)$$

$$\dot{\theta}_8 = -\delta_8 e^T Q B_2 \left(\frac{0.01}{1 - e^{-0.1(x_1 + 50)}} \right)$$

$$\dot{\theta}_9 = -\delta_9 e^T Q B_3 \left(\frac{0.1}{1 - e^{-0.1(x_1 + 35)}} \right)$$

$$\dot{\theta}_{10} = -\delta_{10} e^T Q B_4 (e^{-0.05(x_1 + 60)})$$

4. Main Theories

Solutions of the adaptive model and the true one are coincided and have the convenient convergence corresponding to the following theories:

Theorem 1. The goal Eqs.3 and 4 are hold for any initial conditions of the systems (1), (2) and (6), for $l > 0$, $\delta > 0$.

Proof: the proof is based on the Lyapunov function:

$$V(e) = e^T \Phi e + \frac{|\theta|^2}{\delta} \tag{7}$$

The derivative of Eq.7 is evaluated along the systems (1), (2) and (6), then:

$$\dot{V}(e) = e^T\left(A_l^T\Phi + \Phi A_l\right)e + 2e^T\Phi B_1\left(\theta_1 - \theta_2 x_3^3 x_4 x_1 + 120\,\theta_3 x_3^3 x_4 x_1 - \theta_4 x_2^4 x_1 + 36\,\theta_5 x_2^4 x_1 - \theta_6 x_1 + \theta_7 x_1\right)$$
$$+ 2e^T\Phi B_2\left(\theta_8\left(\frac{0.01}{1 - e^{-0.1(x_1+50)}}\right)\right) + 2e^T\Phi B_3\left(\theta_9\left(\frac{0.1}{1 - e^{-0.1(x_1+35)}}\right)\right) + 2e^T\Phi B_4\left(\theta_{10} e^{-0.05(x_1+60)}\right) + \sum_{i=1}^{10} \frac{\theta_i \dot{\theta}_i}{\delta} \tag{8}$$

Substituting equations of system (6) in (8) results $\dot{V}(e) = e^T\left(A_l^T\Phi + \Phi A_l\right)e$. The required condition $\dot{V}(e) < 0$ has to be satisfied for all e: $e \neq 0$, such that:

$$A_l^T \Phi + \Phi A_l = -P \tag{9}$$

where $\Phi = \Phi^T > 0$. Since A_l has negative real parts of eigenvalues and Lyapanov Eq.9 has the solution Φ.

We can prove that $V(e(t))$ is bounded which obtain then the solutions of the system (1) are bounded, and the error equation is also bounded.

Definition 1. *Time-varying function* $g : [0,\infty] \rightarrow \mathbb{R}^n$ *is persistent excitation (PE) if it is bounded and there exists* $t_T > 0$ *and* $\mathcal{E}, K > 0$ *such that:*

$$\int_t^{t+t_T} g(\tau) g^T(\tau) d\tau \geq \varepsilon K \tag{10}$$

In other words, persistent excitation of vector of functions $F(t)$ is equivalent to the existence of $\varepsilon, t_T, t_0 > 0$ such that for all $\tau \in \mathbb{R}$; $|\tau| = 1$, $t > t_0$ to satisfy that $\max_{[t, t+T]} |F^T(t)\ \tau| > \varepsilon$ [24].

Now, let us suppose

$f_1(x)=\left[1\ ,-x_3^3x_4x_1\ ,\ x_3^3x_4x_1\ ,\ -x_2^4x_1\ ,\ x_2^4x_1\ ,\ -x_1\ ,\ x_1\ \right]^T,\ f_2(x)=\dfrac{0.01}{1-e^{-0.1(x_1+50)}}\ ,\ f_3(x)=\dfrac{0.1}{1-e^{-0.1(x_1+35)}}\ ,\ f_4(x)=e^{-0.05(x_1+60)}$

and have theorem 2.

Theorem 2. *If the solutions of the systems (1) and (2) are bounded which leads to that $e(t)$, $\theta(t)$ are also bounded. This means all roots of $\left|A_l-\lambda I\right|$ have negative real parts. Then the functions $f_1(x), f_2(x), f_3(x), f_4(x)$ are PE and the unknown parameters converge to the real values by satisfying Eqs. 3 and 4.*

To prove the PE condition of each vector, it is satisfied that at some moment t,

$$\left[1\ ,-x_3^3x_4x_1\ ,\ 120x_3^3x_4x_1\ ,\ -x_2^4x_1\ ,\ 36x_2^4x_1\ ,\ -x_1\ ,\ x_1\right]t=0$$

if and only if

$$h_1-x_3^3x_4x_1h_2+120\,x_3^3x_4x_1h_3-x_2^4x_1h_4+36\,x_2^4x_1h_5\ -x_1h_6+\ x_1h_7=0$$

which has no more than one solution for x_1 depending on x_2, x_3, x_4. Satisfying PE of the rest of equation:

$f_2(x)h=\dfrac{0.01}{1-e^{-0.1(x_1+50)}}\ h=0 \quad \Rightarrow x_1+50=100$ has one solution,

$f_3(x)h=\dfrac{0.1}{1-e^{-0.1(x_1+35)}}\ h=0 \quad \Rightarrow x_1+35=10$ has one solution,

$f_4(x)h=e^{-0.05(x_1+60)}\ h=0 \quad \Rightarrow x_1+60=-20$ has one solution.

In Fradkov [21] specifically in Theorem 5.1 the main conditions for proving Eqs.4 and 5 are considered in details. Then the same proof can be derived for the problem of interest of this research.

4. Results and Discussion

The formulated system of equations in (6) is conducted to show if the method adequately meets the problem in (1). The method may observe different dynamical behavior of x_1, x_2, x_3, x_4, as shown in Figs. 1 and 2.

Actual values of the parameters $(I=0.1, g_Na=120, E_Na=55.17, g_k=36, E_k=-110.14, g_L=0.3, E_L=49.49, v_1=50, v_3=35, v_7=0.07)$ [20] where HH has periodic trajectory. However, it doesn't have periodic trajectories for various values for the parameters v_2, v_4, v_5, v_6 as shown in the figure's captions, so these parameters are assumed to be known. Moreover, the relative error is calculated instead of the error and shown in Fig 3. It is clear that the relative error converges to zero as $t\to\infty$.

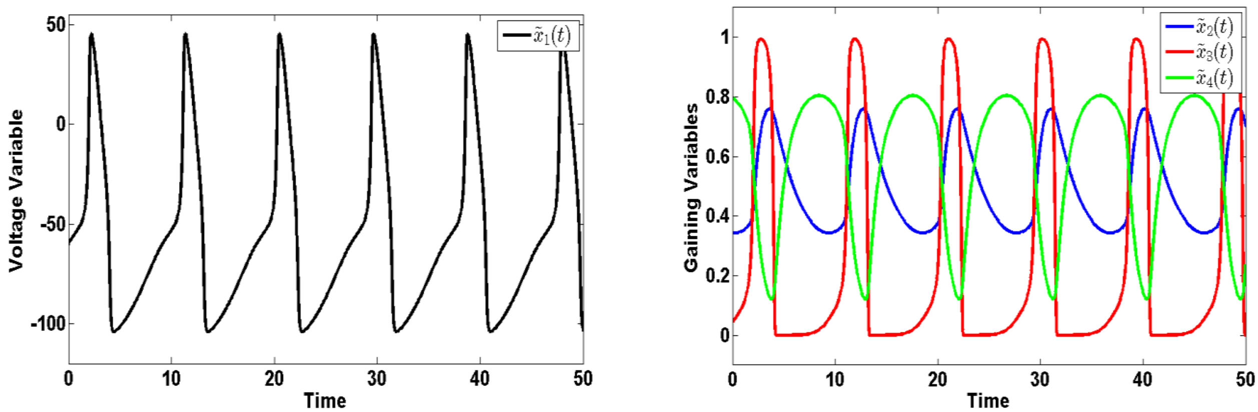


Fig. 1 – The right and left panels show periodic solutions of $x_1(t)$, $x_2(t)$, $x_3(t)$, $x_4(t)$ evaluated at the estimated values $\tilde{\theta}$ when $v_2 = 60, v_4 = 60, v_5 = 60, v_6 = 30$.

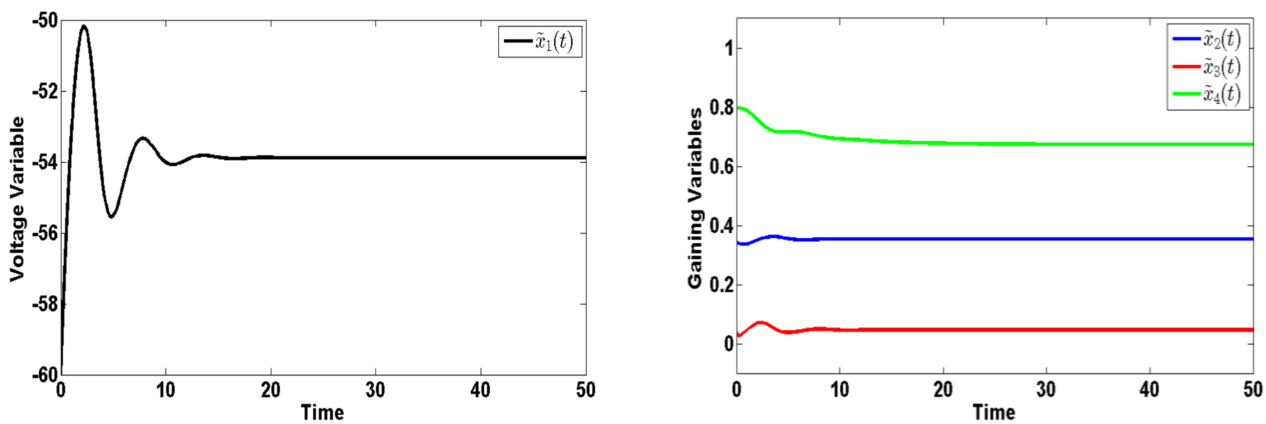


Fig. 2 –The right and left panels show solutions of $x_1(t)$, $x_2(t)$, $x_3(t)$, $x_4(t)$ evaluated at the estimated values $\tilde{\theta}$ when $v_2 = 45, v_4 = 50, v_5 = 45, v_6 = 20$.

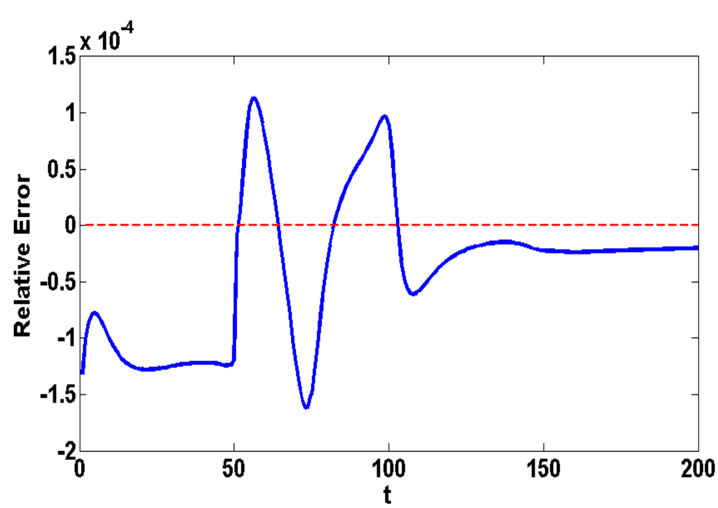
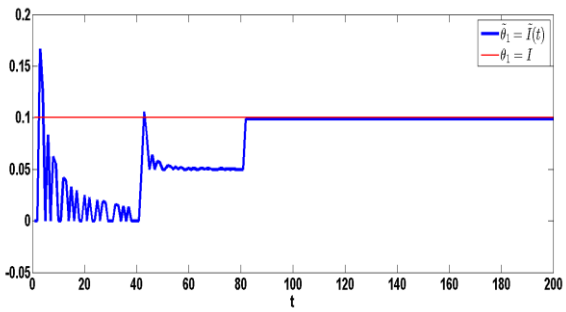
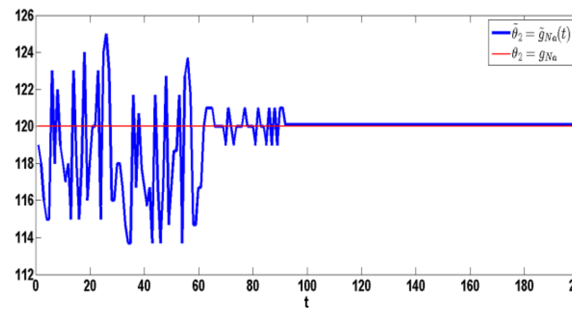


Fig. 3 – Relative error $E(t) = \dfrac{y(t) - \tilde{x}_1(t, \tilde{\theta})}{\|y\|_{\infty, [t_0, t_0 + \infty]}}$ **as a function of *t*;** $\|y(t)\|_{\infty} = max\{y(t_i)\}_{i=1}^{N}; N = 200.$

The identification process by system (6) was basically performed by modelling the error of the systems (1) and (2). The adaptation algorithm was used to calculate the parameters of the observer, $\theta(t)$. Panels of Fig.4 (i-x) show the convergence of the observer parameters to the real neuron parameters.



(i)



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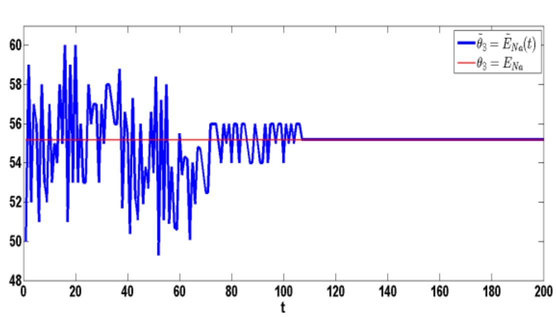

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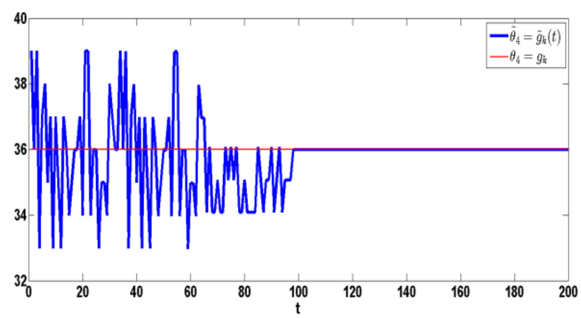

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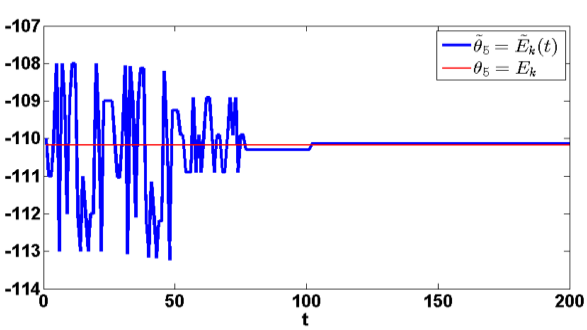

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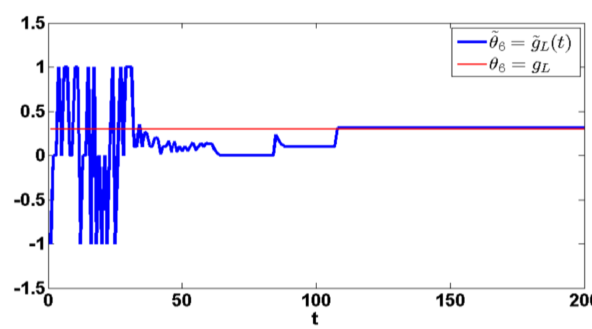

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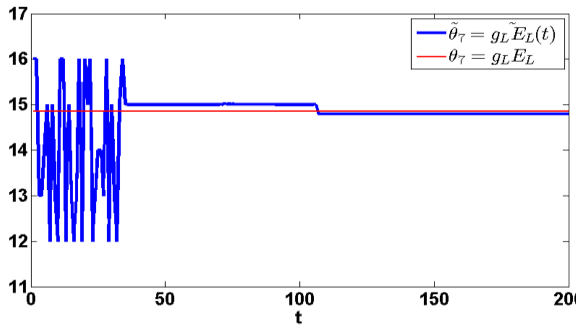

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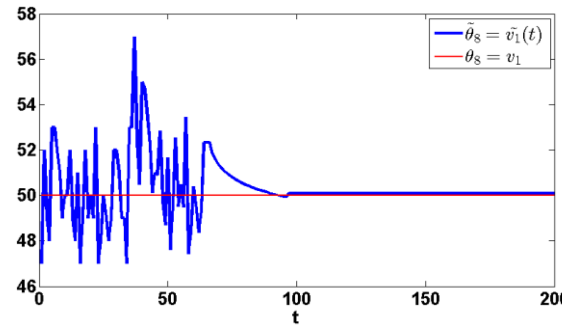

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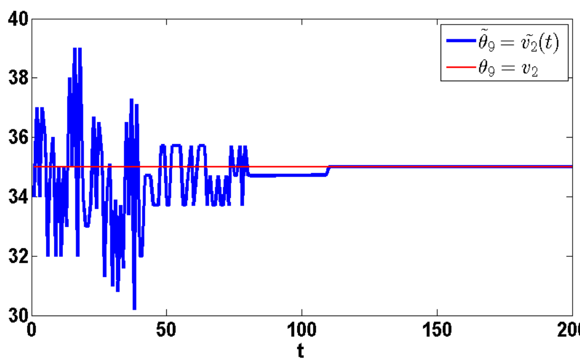

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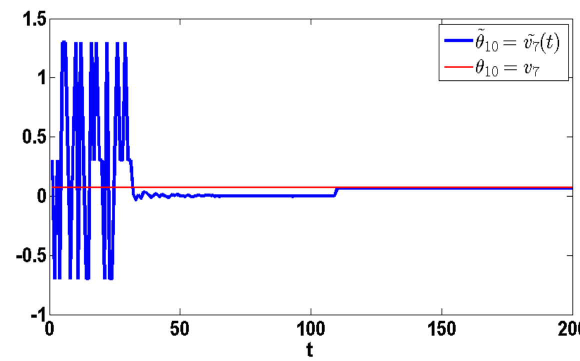

(x)

Fig. 4 – Identification process of $\tilde{\theta}=\left[I, g_{Na}, E_{Na}, g_k, E_k, g_L, g_L E_L, v_1, v_3, v_7\right]^T$; $\delta=1$, shown in panels (i-x). Estimated values and true values θ are shown in blue curves and red lines, respectively.

It spent approximately 10 minutes on a standard PC in Matlab R2020. The proposed technique returns the estimates of the initial condition and the unknown parameters which are nonlinearly included in the right-hand side of the system. In this regard, it would fairly compare the time spent calculating the integrals of the dynamical system (6) with the error in Eq.5 with other functions like, for example, sensitivity functions.

4. Conclusion

This paper proposed a new framework model especially for solving the fourth order differential equations of HH neuron cells model. This model represented the solutions of HH model couple of systems, the error function in Eq.5 and systems of ordinary differential equations of the parameters in system (6). The new model of neural cells system of the HH model showed very high performance for the method as showed in the figures. This design of the model introduced fast solutions and then fast estimation for the unknown parameters. The technique employed ideas of using using the speed grediant design to express and represent measured trajectories as explicit functions for unknown parameters. Then, it considered fast and efficient model evaluations by computation techniques in Matlab, and introduced like integral form to inverse problems that may match variables and parameters that are nonlinearly entering the right-hand side of the model to be explicitly estimated. This could reduce the dimensionality of the parametrized problem to have more accurate estimations. Moreover, the results of estimations in the example showed how the method is highly effective in solving systems of nonlinear equations with estimating large numbers of unknown parameters without needing crucial conditions of other methods like Newton and Newton-Raphson.

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