

Washout filter based control for the Hodgkin-Huxley nerve cell dynamics

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Abstract

In this work we present a washout filter based control approach for stabilizing the oscillations in Hodgkin-Huxley type neurons. The oscillations occur due to the bifurcations that arise from the potassium and sodium channel conductance deviations. The MATCONT toolbox software environment was used for analysis of the bifurcation points in conjunction with MATLAB. The simulations of the Hodgkin-Huxley (HH) model at those points are provided to validate the results obtained from the MATCONT software. Then a washout filter is proposed to stabilize the oscillations occur at the Hopf bifurcation points where the external current injection is used to provide the control actuation. A second simulation set is provided to demonstrate the action of the washout filter.

Key Words: Hopf bifurcation, saddle bifurcation, Hodgkin-Huxley equation, potassium channel, sodium channel

1. Introduction

The Hodgkin-Huxley nonlinear model [1] of a real neuron (giant squid axon at first) is one of the biggest challenges in the electrophysiology field in the near history. The cell membrane potential is modeled using the basic circuit theory and some chemical kinetics. As a result a fourth order highly nonlinear differential equation is obtained. This model possesses a rich set of bifurcations due to the additional current injection as described by [2] and external electric fields [3,4]. Bifurcations are problematic in biological neural networks since the diseases such as Parkinson's [5], epilepsy [6] and schizophrenia [7, 8] have some connections with the instabilities in the neural cell dynamics. In addition, various cardiac and muscle diseases possess chaotic behaviors [9] during the course of a particular disease. Because of that, controlling bifurcations in the neuron dynamics may bring some new insights in the treatment of some neurological disorders. Local bifurcation analysis is an important branch of the nonlinear system theory where the properties of the equilibrium points of a nonlinear system changes due to a single parameter deviation [10]. One of the mostly met bifurcation type is the Hopf type bifurcation where

the equilibrium point loses its stability as a result of a single pair of purely complex eigenvalues arising from a parameter drift. There are also other critical points such as the saddle point where there is a real pair of eigenvalues one of which is on the left hand side and the other is the right hand side of the complex plane (with equal values). In order to solve the stability issue in such a case, several studies have been proposed. Some of those methods are the linear delayed feedback [11, 12], nonlinear feedback [13] and washout filters [14, 15, 16]. The advantage of the washout filters is that they do not change the equilibrium points of the uncontrolled (open loop) nonlinear system. The washout filter is originally a high-pass filter which does not pass steady state inputs (only allows the transients). An application of the washout filters for the Hodgkin-Huxley type nerve cell dynamics are presented in [2] for the bifurcations existent in the neuron model where the variable parameter is the possible external current injection (from the cell environment) into the nerve cell. That attempts to control the bifurcations by applying an external current stimulus. In this work we present another bifurcation control mechanism based on the extended washout filter for the bifurcations resulting from the deviations in the sodium and potassium channel conductances. In the first attempt, the MATCONT toolbox [17] is used to detect particular Hopf bifurcation points in the Hodgkin-Huxley nerve cell dynamics. Secondly, the points are simulated in MATLAB in order to verify the oscillations occurred at the detected parameter sets. The approach of extended washout filter is applied to the nerve cell dynamics by driving the external current input and the MATLAB simulations are repeated in order to check whether the oscillations decrease or not. In addition to the simulations, a bifurcation analysis of the closed loop against the washout filter coefficients by the MATCONT package is performed in order to investigate the stability of the HH-Washout Filter combination.

2. Hodgkin-Huxley model

The Hodgkin-Huxley model is a fourth order nonlinear differential equation derived for representing the action potential dynamics of the giant squid axon. The presented model is explained in detail in the resource [1]. In this section only the resultant equations are given with the nominal parameter values:

$$\begin{aligned}
 C_m \frac{dV}{dt} &= -g_{Na}m^3h(V - V_{Na}) - g_Kn^4(V - V_K) - g_L(V - V_L) + I_{ext} \\
 \frac{dn}{dt} &= \alpha_n(1 - n) - \beta_n n \\
 \frac{dm}{dt} &= \alpha_m(1 - m) - \beta_m m \\
 \frac{dh}{dt} &= \alpha_h(1 - h) - \beta_h h
 \end{aligned} \tag{1}$$

$$\alpha_n = \frac{0.1 - 0.01V}{\exp(1 - 0.1V) - 1}, \quad \beta_n = 0.125 \exp\left(-\frac{V}{80}\right)$$

$$\alpha_m = \frac{2.5 - 0.1V}{\exp(2.5 - 0.1V) - 1}, \quad \beta_m = 4 \exp\left(-\frac{V}{18}\right)$$

$$\alpha_h = 0.07 \exp\left(-\frac{V}{20}\right), \quad \beta_h = \frac{1}{\exp(3 - 0.1V) + 1}$$

Definitions of the parameters are:

V_{is} the displacement of the cell membrane potential from its resting value in mV;

n is a dimensional variable which can vary between 0 and 1 representing the proportion of activating molecules of the potassium channel;

m is same type of variable as n which represents the proportion of the activating molecules of the sodium channel;

h same type of variable as n which represents the proportion of the inactivating molecules of the sodium channel;

I_{ext} denotes the external current injection, in units of $\mu A/cm^2$;

g_{Na} denotes the sodium channel conductance, in units of mS/cm^2 ;

g_k denotes the potassium channel conductance, in units of mS/cm^2 ;

g_L denotes the current leakage conductance, in units of mS/cm^2 (due to the chloride and other ions);

C_m denotes the membrane capacitance, in units of $\mu F/cm^2$;

V_{Na} denotes the sodium channel resting potential, in units of mV;

V_K denotes the potassium channel resting potential, in units of mV;

V_L denotes the the level of potential where the leakage current reduces to zero.

The following values were used in the simulations:

$$\begin{aligned}
 g_K &= 36mS/cm^2 \\
 g_{Na} &= 120mS/cm^2 \\
 g_L &= 0.3mS/cm^2 \\
 V_K &= -12mV \quad . \\
 V_{Na} &= 115mV \\
 V_L &= 10.613mV \\
 C_m &= 0.91\mu F/cm^2
 \end{aligned} \tag{2}$$

In this work the external current injection is set to zero by default. It is to be used as an external stimulus for stabilizing the neuron with the washout filter. In the next section the Hopf bifurcation analysis results produced by the MATCONT toolbox are presented for the variations occurred in the sodium and potassium channel conductance parameters.

3. Bifurcation analysis results

The bifurcation analysis is done by first finding an equilibrium point of the dynamical system given in (1) by simulating with zero external current ($I_{ext} = 0$). According to the simulation results the Hodgkin-Huxley model with the nominal parameters in (2) the following equilibrium point is found:

$$\begin{aligned}
 V &= 0.003620359468 \\
 n &= 0.31773241094 \\
 m &= 0.0529551709 \\
 h &= 0.5959943932.
 \end{aligned}
 \tag{3}$$

Starting the MATCONT continuer using the above as the initial conditions some points are found as the saddle and Hopf bifurcations. The following results are found by tracing over the potassium or sodium channel conductance while holding the other one at its nominal value. In the following table, the bifurcation points found by the MATCONT software is presented.

Table 1. Bifurcation analysis results derived by the MATCONT software.

Case	1	2	3
Parameter & Prop	$g_K = 20.041$ $g_{Na} = 120$	$g_K = 13.8$ $g_{Na} = 120$	$g_K = 7.89$ $g_{Na} = 120$
Eigenvalues	$\lambda_1 = -4.61532$ $\lambda_2 = -0.131416$ $\lambda_3 = j0.360138$ $\lambda_4 = -j0.360138$	$\lambda_1 = -4.7913$ $\lambda_2 = -0.152529$ $\lambda_3 = 0.152529$ $\lambda_4 = 0.425965$	$\lambda_1 = -7.03698$ $\lambda_2 = -0.331413$ $\lambda_3 = 0.331413$ $\lambda_4 = 1.23876$
Equilibrium Points	$V = 2.6939079$ $n = 0.3596422$ $m = 0.072340538$ $h = 0.49994929$	$V = 5.8511661$ $n = 0.4098447$ $m = 0.10274964$ $h = 0.389045$	$V = 25.621793$ $n = 0.68536241$ $m = 0.51701021$ $h = 0.047222083$
Type of Condition	Hopf Bifurcation	Saddle Point	Saddle Point

Case	4	5	6
Parameter & Prop	$g_K = 3.8229$ $g_{Na} = 120$	$g_{Na} = 210.16$ $g_K = 36$	$g_{Na} = 311.35163$ $g_K = 36$
Eigenvalues	$\lambda_1 = -5.57594$ $\lambda_2 = -0.422727$ $\lambda_3 = j1.15984$ $\lambda_4 = -j1.15984$	$\lambda_1 = -5.04953$ $\lambda_2 = -0.125772$ $\lambda_3 = j0.369568$ $\lambda_4 = -j0.369568$	$\lambda_1 = -5.71663$ $\lambda_2 = -0.137406$ $\lambda_3 = 0.137406$ $\lambda_4 = 0.64287$
Equilibrium Points	$V = 35.333876$ $n = 0.77395955$ $m = 0.74063787$ $h = 0.0186268$	$V = 0.95529707$ $n = 0.33241241$ $m = 0.059205632$ $h = 0.56236738$	$V = 2.8902874$ $n = 0.36274397$ $m = 0.073974298$ $h = 0.49288875$
Type of Condition	Hopf Bifurcation	Hopf Bifurcation	Saddle Point

Case	7	8	9
Parameter & Prop	$g_{Na} = 370 \ g_K = 36$	$g_{Na} = 539.014 \ g_K = 36$	$g_{Na} = 1057.516 \ g_K = 36$
Eigenvalues	$\lambda_1 = -8.15906$ $\lambda_2 = -0.176176$ $\lambda_3 = 0$ $\lambda_4 = 2.70059$	$\lambda_1 = -18.43536$ $\lambda_2 = 2.32620$ $\lambda_3 = 0.33965$ $\lambda_4 = -0.33965$	$\lambda_1 = -26.24354$ $\lambda_2 = j1.61188$ $\lambda_3 = -j1.61188$ $\lambda_4 = -0.42966$
Equilibrium Points	$V = 8.9984957$ $n = 0.45979811$ $m = 0.14295607$ $h = 0.29038163$	$V = 26.273054$ $n = 0.692306$ $m = 0.534022$ $h = 0.044102$	$V = 35.693744$ $n = 0.776670$ $m = 0.747283$ $h = 0.018066$
Type of Condition	Limit Point	Saddle Point	Hopf Bifurcation

In order to show the bifurcation characteristics of the model in (1) it will be convenient to show the bifurcation diagrams obtained by the MATCONT software for the varying values of the potassium and sodium conductance (g_K and g_{Na}). These are given in Figures 1 and 2.

The responses of the equation (1) in the conditions presented in Table 1 are given in the Figures 3–11. In all cases the external current injection is zero.

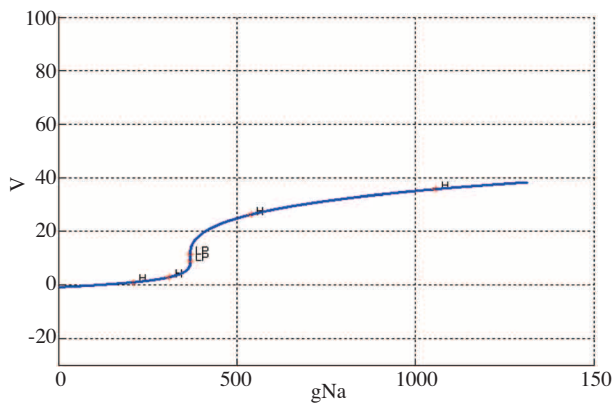


Figure 1. The bifurcation diagram for sodium conductance (g_{Na}) variation.

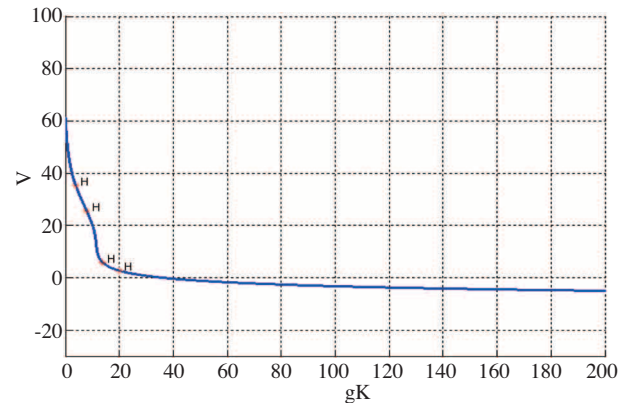


Figure 2. The bifurcation diagram for potassium conductance (g_{K}) variation.

It can be said that the bifurcation analysis results produced by MATCONT package for HH model shares similar outcome with the research in [18]. This situation can be considered as a verification of the MATCONT algorithms for a high order nonlinear system.

4. Washout filter theory

The washout filters are linear filtering systems that obey a high pass filter property in which only the transient signals are allowed (since they have an higher frequency) and the steady state inputs are rejected. Its connection with the nonlinear systems is an interesting point which leads to the preservation of the equilibrium points of the original system.

Mathematically, the washout filter is a high pass system which can be presented in transfer function form as [16]:

$$G(s) = \frac{Y(s)}{X(s)} = \frac{s}{s+d}$$

$$\lim_{s \rightarrow 0} G(s) \rightarrow 0 \quad (4)$$

where the constant d is the reciprocal of the time constant of the filter which is also an important parameter for the application. In the state space form,

$$\dot{z} = x - dz$$

$$y = x - dz \quad (5)$$

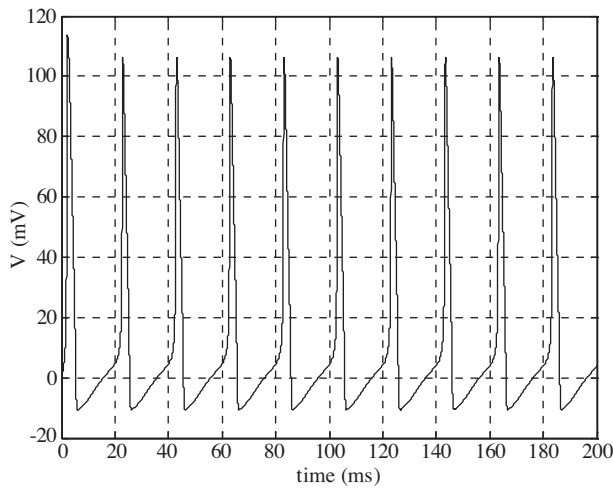


Figure 3. Results of the open loop simulation for the case $g_K = 20.041, g_{Na} = 120$.

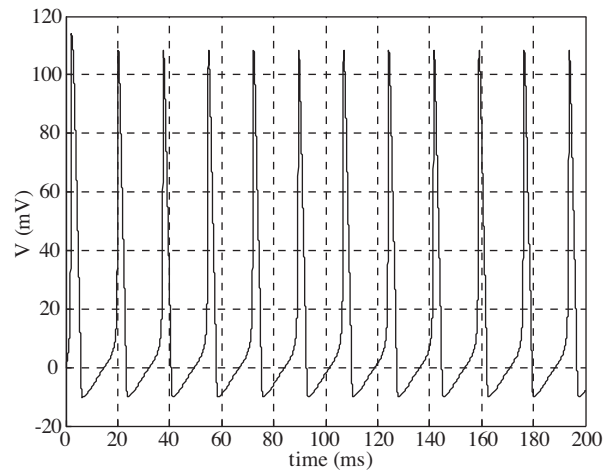


Figure 4. Results of the open loop simulation for the case $g_K = 13.8, g_{Na} = 120$.

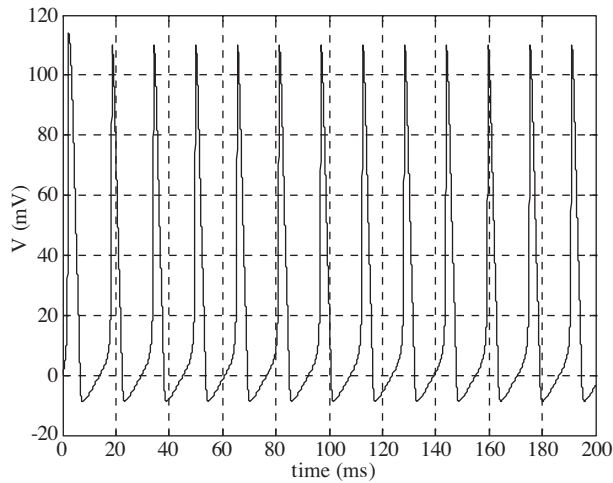


Figure 5. Results of the open loop simulation for the case $g_K = 7.89, g_{Na} = 120$.

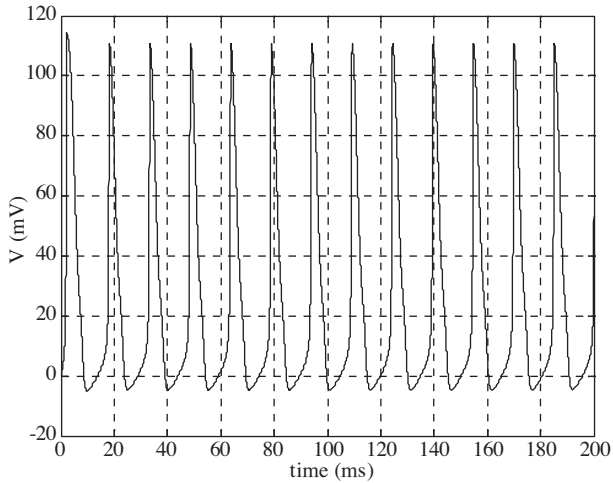


Figure 6. Results of the open loop simulation for the case $g_K = 3.8229, g_{Na} = 120$.

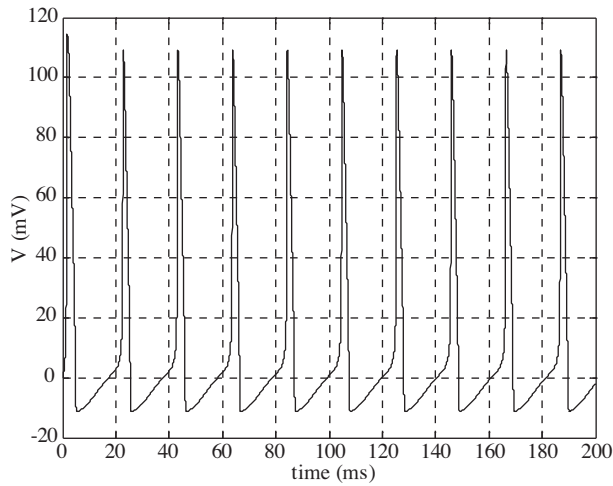


Figure 7. Results of the open loop simulation for the case $g_K = 36, g_{Na} = 210.16$.

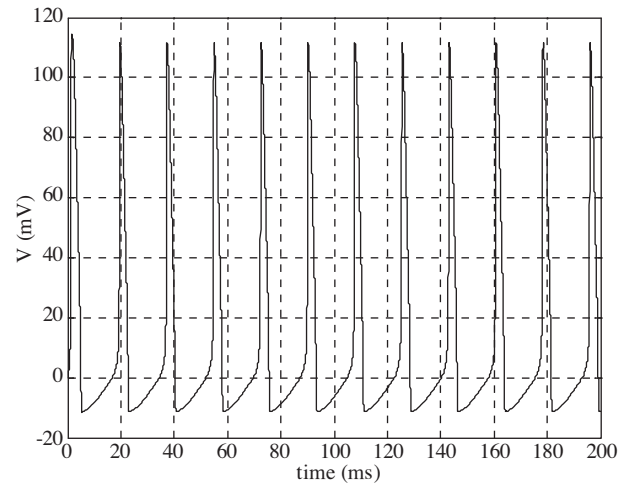


Figure 8. Results of the open loop simulation for the case $g_K = 36, g_{Na} = 311.35$.

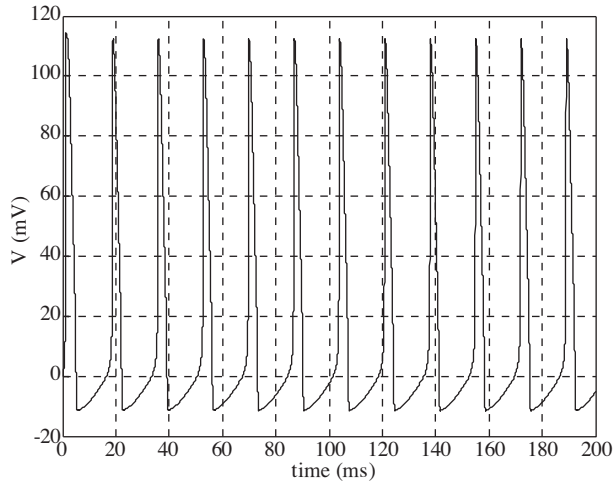


Figure 9. Results of the open loop simulation for the case $g_K = 36, g_{Na} = 370$.

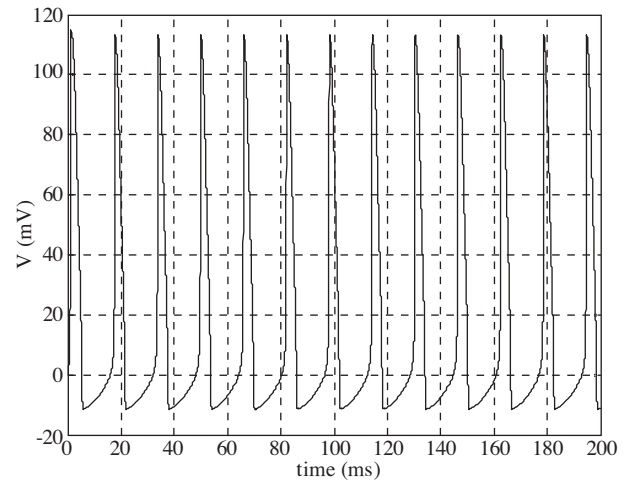


Figure 10. Results of the open loop simulation for the case $g_K = 36, g_{Na} = 539.014$.

where z is the state variable of the system in (4) and y is the output variable. The application of the above filter to a nonlinear system like (1) requires that a control gain should be introduced to the filter output. In this case, the above function will be

$$\begin{aligned} \dot{z} &= \mathbf{C}\mathbf{x} - dz \\ y &= K(\mathbf{C}\mathbf{x} - dz) \end{aligned} \quad (6)$$

Now the output variable y can be applied directly to the input of the nonlinear system in consideration. In the above, the state variable x is now considered as a state vector where the measurable variables are fed back to the filter through a selector matrix, $\mathbf{C} \in \mathbb{R}^{1 \times n}$.

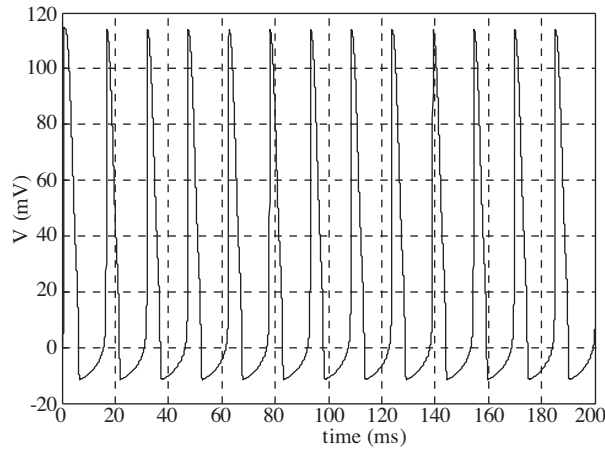


Figure 11. Results of the open loop simulation for the case $g_K = 36, g_{Na} = 1056.516$.

When a nonlinear system $\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, u)$ is linearized around a certain equilibrium point the linearized state equation is (including the higher order remaining terms)

$$\dot{\mathbf{x}} = \mathbf{A}\mathbf{x} + \mathbf{B}u + \mathbf{h}(\mathbf{x}, u). \tag{7}$$

Interconnection of the above with (6) yields:

$$\begin{aligned} \dot{\mathbf{x}} &= \mathbf{A}\mathbf{x} + \mathbf{B}u + \mathbf{h}(\mathbf{x}, u) \\ \dot{z} &= \mathbf{C}\mathbf{x} - dz \\ u &= K(\mathbf{C}\mathbf{x} - dz) \end{aligned} \tag{8}$$

The resultant equations present the closed loop controller formed by an output feedback. The closed loop state equation can be written as

$$\underbrace{\begin{bmatrix} \dot{\mathbf{x}} \\ \dot{z} \end{bmatrix}}_{\dot{\mathbf{x}}_c} = \underbrace{\begin{bmatrix} \mathbf{A} + \mathbf{B}\mathbf{K}\mathbf{C} & -\mathbf{B}\mathbf{K}d \\ \mathbf{C} & -d \end{bmatrix}}_{\mathbf{A}_c} \underbrace{\begin{bmatrix} \mathbf{x} \\ z \end{bmatrix}}_{\mathbf{x}_c}. \tag{9}$$

In bifurcation theory [15], it is known that only the quadratic and cubic terms affect the stability of them. So a possible extension of the above design can be helpful. In this case, the control gain is given to the quadratic and cubic functions of the output variable y . So in this case (8) will be reshaped as

$$\begin{aligned} \dot{\mathbf{x}} &= \mathbf{A}\mathbf{x} + \mathbf{B}u + \mathbf{h}(\mathbf{x}, u) \\ \dot{z} &= \mathbf{C}\mathbf{x} - dz \\ y &= \mathbf{C}\mathbf{x} - dz \\ u &= K_2y^2 + K_3y^3 \end{aligned} \tag{10}$$

This should be a better control system to cope with the bifurcations occurring in especially higher order nonlinear systems like that of the (1). In the next section the application of the above presentation to the Hodgkin-Huxley equation is described.

5. Washout filter control of the Hodgkin-Huxley equation

For the Hodgkin-Huxley equation in (1) only the membrane voltage variable V is measurable because of that the controller structure of (10) will be in the following form:

$$\begin{aligned}
C_m \frac{dV}{dt} &= -g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_{ext} \\
\frac{dn}{dt} &= \alpha_n (1 - n) - \beta_n n \\
\frac{dm}{dt} &= \alpha_m (1 - m) - \beta_m m \\
\frac{dh}{dt} &= \alpha_h (1 - h) - \beta_h h \\
\dot{z} &= -V - dz \\
y &= -V - dz \\
I_{ext} &= K_2 y^2 + K_3 y^3
\end{aligned} \tag{11}$$

For the sake of computational complexity reduction, the quadratic term gain K_2 is taken as zero. The complete system in (11) is analyzed for possible bifurcations using MATCONT toolbox in MATLAB. The analysis is performed for each bifurcation case presented in Table 1. As expected, the equilibrium potential V remains constant throughout the analysis (as washout filter should result). Its value is equal to the equilibrium value of the respective bifurcation condition (The values given in Table 1). During the trace of the parameter d additional saddle points are detected by the MATCONT software which are shown in Table 2. The new bifurcations are due to the interaction of the new eigenvalue brought by the washout filter with the original eigenvalues in the respective bifurcation condition (i.e. the ones given in Table 1). The trace of the parameter K_3 doesn't result any critical condition (neither a Hopf and saddle point).

It should be noted here that the value of K_3 is kept at 10. For holding $d = 0.001$ and tracing K_3 between -1000 and 1000, MATCONT does not provide any single parameter bifurcation results. The 7th case of Table 1 (limit point or LP) cannot be solved by MATCONT as it has an eigenvalue exactly at the origin. The algorithm gets stuck and cannot converge to a solution.

6. Simulation of the Washout Filter – HH model combination

First simulations performed used $d = 0.001$ and $K_3 = 10$ as the washout filter parameters. The first results show that this combination presents stable responses for all of the cases presented in Table 1 except the 7th. Graphical representations of the associated results are presented in Figures 12–20. In the graphs, both the membrane potential response and the required electrical stimulation current levels are shown. In addition, the initial transient behavior of membrane potential and stimulation current are shown in order to prove that there is no initial jump in the responses and current profile as the original graphs (in the left column) give this impression to the readers at a first look. To indicate this, the abbreviation IR (initial region) is used next to the title of the subplots.

Table 2. The results of the MATCONT analysis for the closed loop.

Case	2	2	3
Value of d	$d = 0.1518$	$d = 0.4270$	$d = 0.3314$
Eigenvalues	$\lambda_1 = -0.1518$	$\lambda_1 = -0.4270$	$\lambda_1 = -0.3314$
	$\lambda_2 = -4.79144$	$\lambda_2 = -4.79144$	$\lambda_2 = -7.03698$
	$\lambda_3 = 0.42696$	$\lambda_3 = 0.4270$	$\lambda_3 = -0.331413$
	$\lambda_4 = 0.15180$	$\lambda_4 = 0.15180$	$\lambda_4 = 0.331413$
	$\lambda_5 = -0.15254$	$\lambda_5 = -0.15254$	$\lambda_5 = 1.23876$
Type of Condition	Saddle Point	Saddle Point	Saddle Point

Case	6	8	
Value of d	$d = 0.1374$	$d = 0.3397$	
Eigenvalues	$\lambda_1 = -0.1374$	$\lambda_1 = -0.3397$	
	$\lambda_2 = -5.71663$	$\lambda_2 = -18.43536$	
	$\lambda_3 = -0.137406$	$\lambda_3 = 2.32620$	
	$\lambda_4 = 0.137406$	$\lambda_4 = 0.3397$	
	$\lambda_5 = 0.64287$	$\lambda_5 = -0.3397$	
Type of Condition	Saddle Point	Saddle Point	

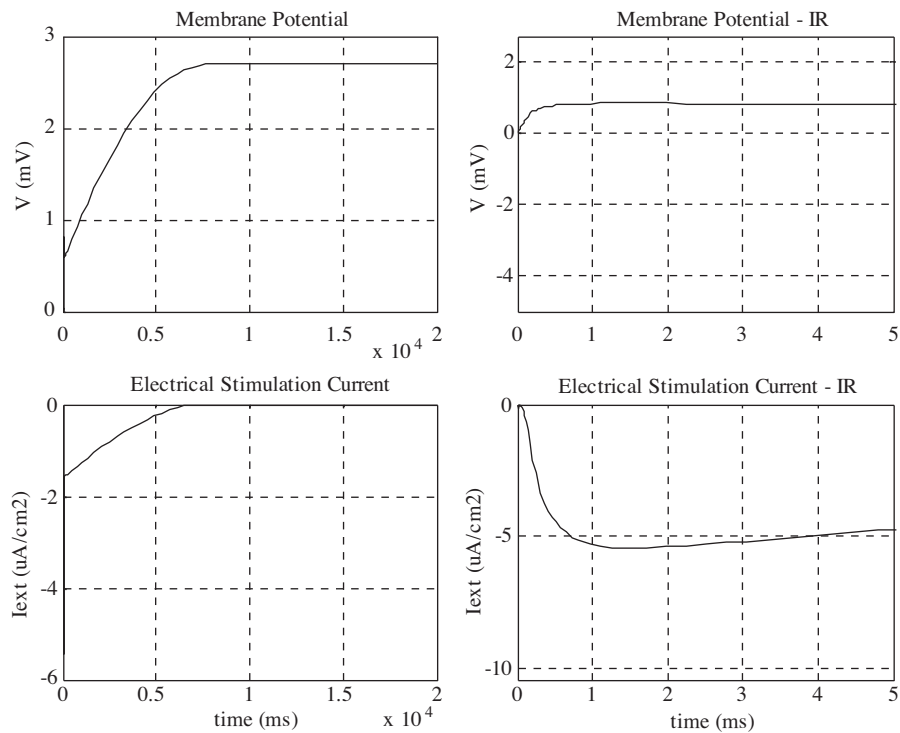


Figure 12. The response of the closed loop WF-HH system for $g_K = 20.041, g_{Na} = 120$.

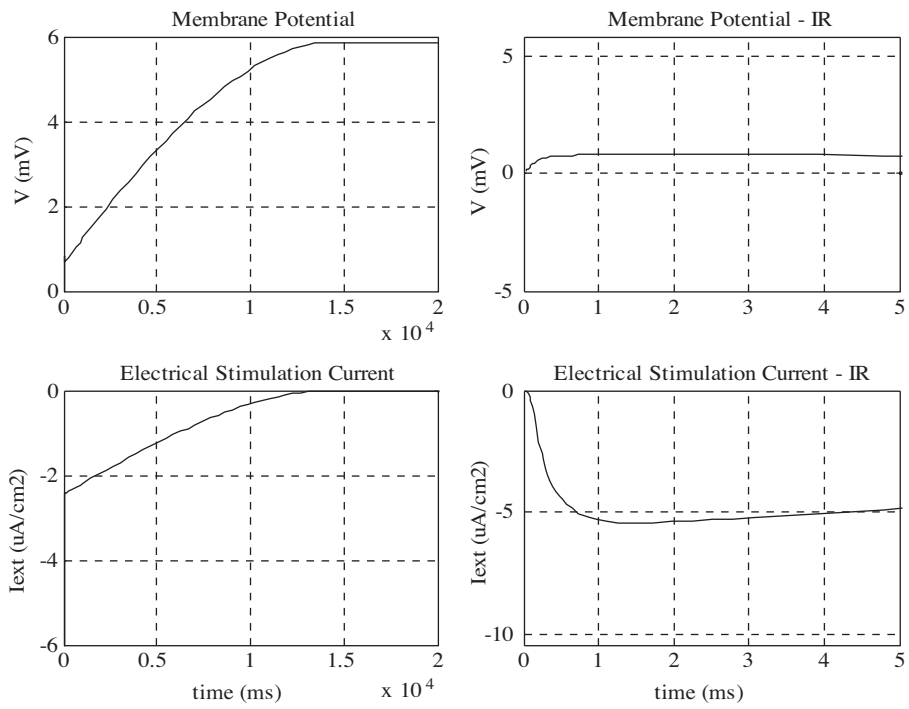


Figure 13. The response of the closed loop WF-HH system for $g_K = 13.8, g_{Na} = 120$.

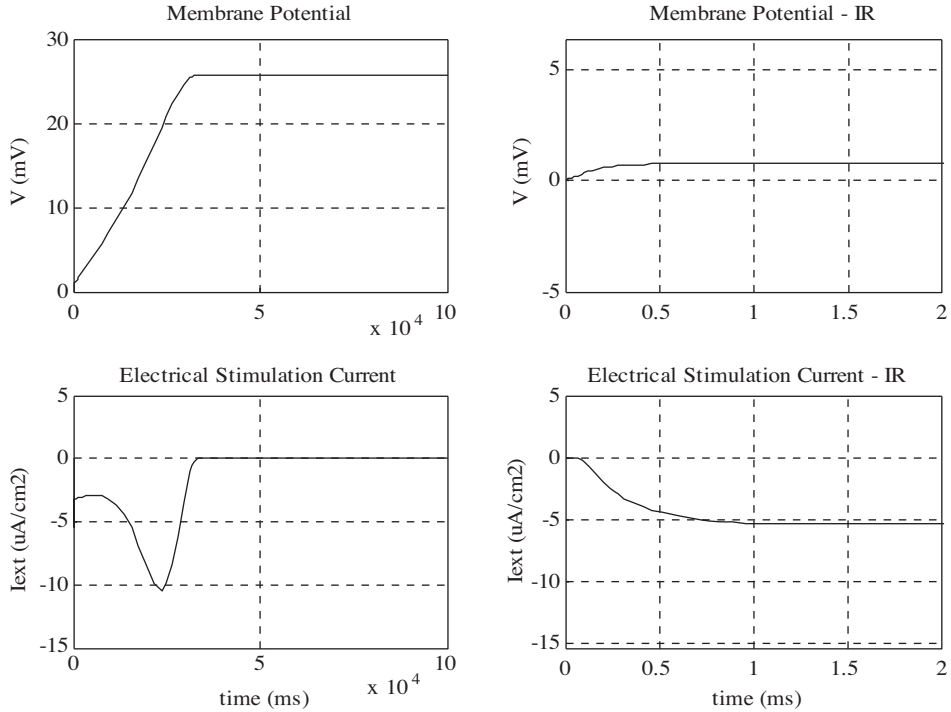


Figure 14. The response of the closed loop WF-HH system for $g_K = 7.89, g_{Na} = 120$.

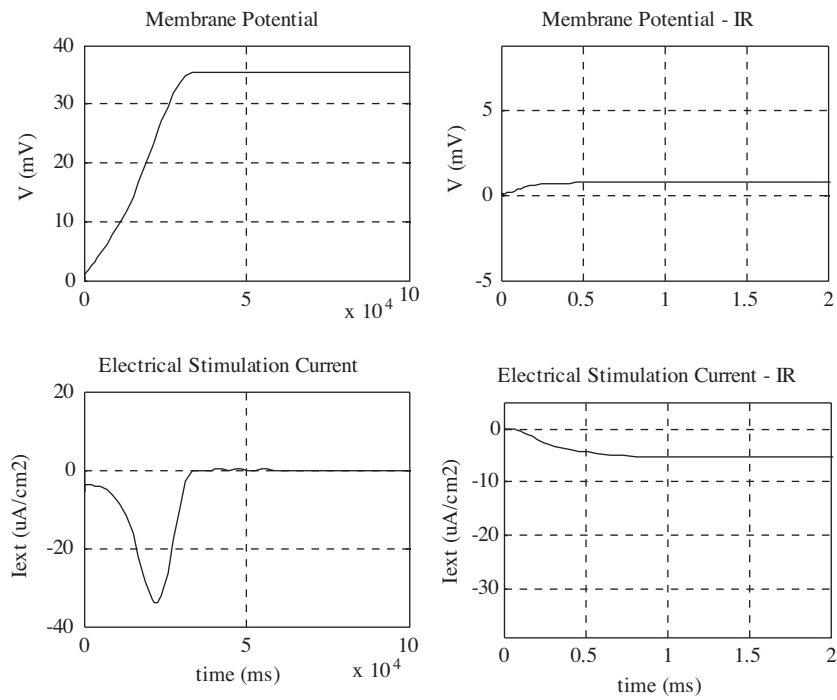


Figure 15. The response of the closed loop WF-HH system for $g_K = 3.8229, g_{Na} = 120$.

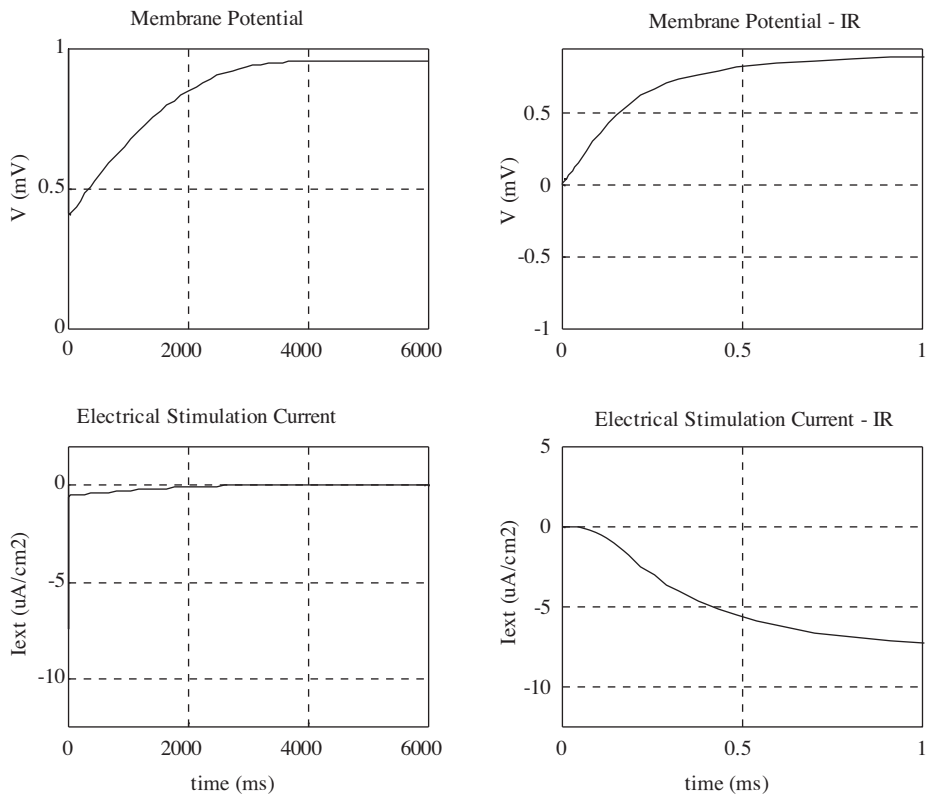


Figure 16. The response of the closed loop WF-HH system for $g_K = 36, g_{Na} = 210.16$.

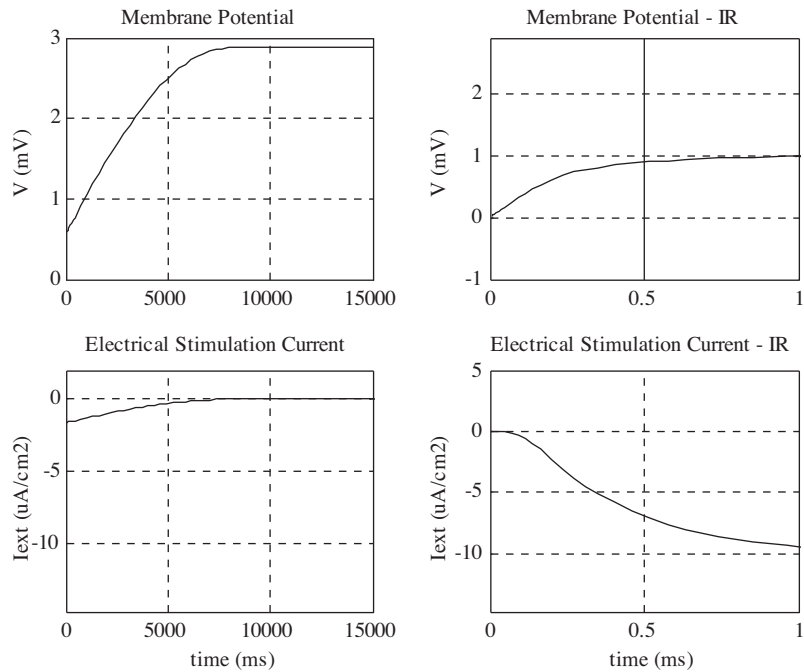


Figure 17. The response of the closed loop WF-HH system for $g_K = 36, g_{Na} = 31.35163$.

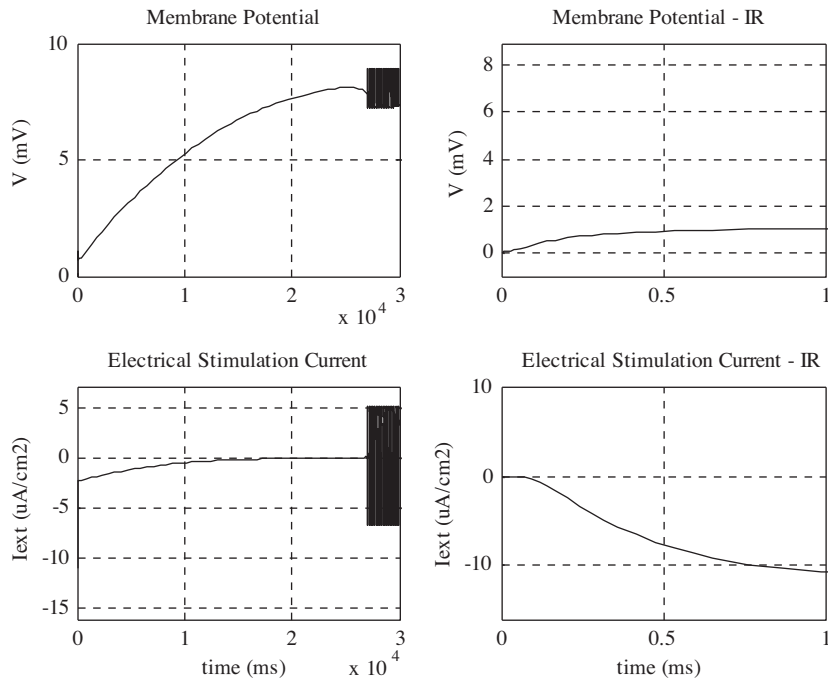


Figure 18. The response of the closed loop WF-HH system for $g_K = 36, g_{Na} = 370$.

As it can be understood from Figure 18, Case 7 of Table 1 cannot be stabilized with the current configuration. This is an expected result as washout filters are not recommended for the models having an equilibrium point with a complete zero eigenvalue. However, it is interesting to note that a combination of

$d = 0.00001$, $K_3 = 1000$ leads to a stable result as shown in Figure 21. Nevertheless, the settling time increases considerably when compared to the other cases of Table 1 (other than 7). Another observation up to this point is the increase in the absolute level of the stimulation current with the increasing sodium channel conductance.

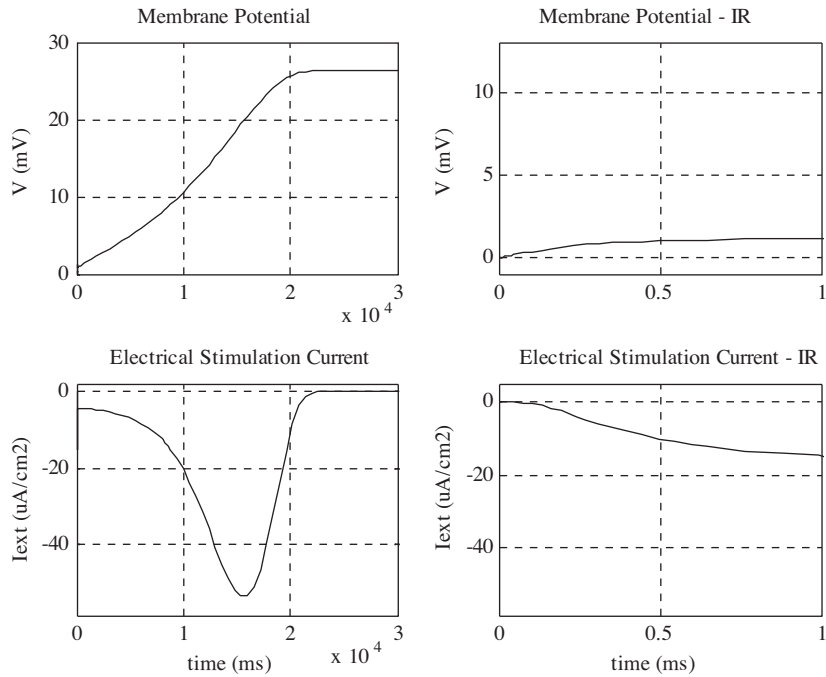


Figure 19. The response of the closed loop WF-HH system for $g_K = 36$, $g_{Na} = 539.014$.

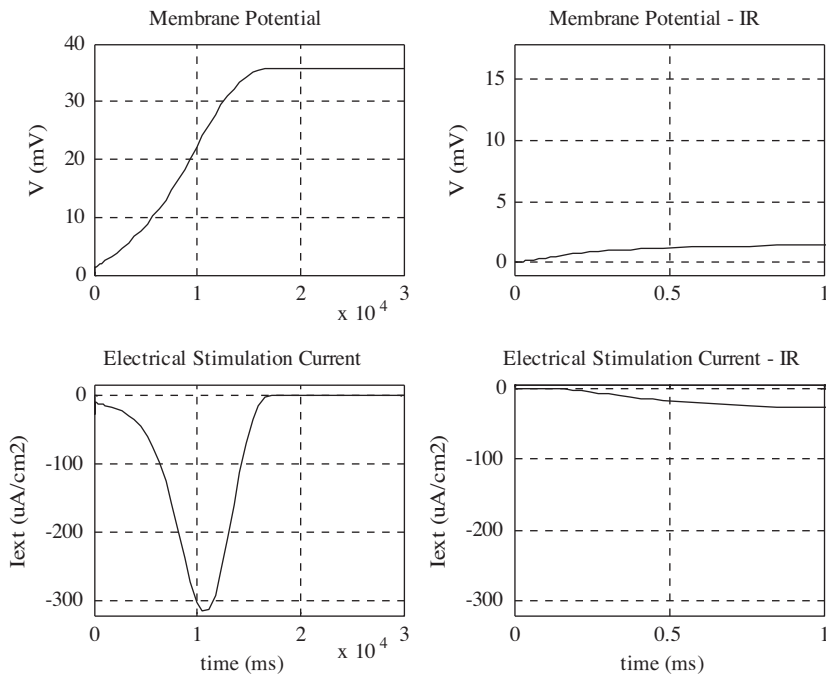


Figure 20. The response of the closed loop WF-HH system for $d = 0.00001$, $K_3 = 1000$.

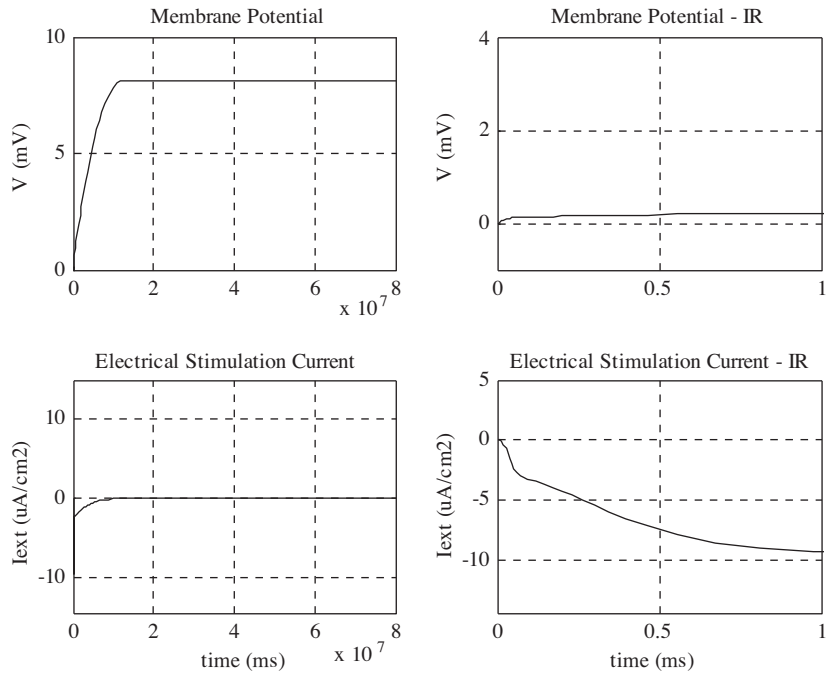


Figure 21. Stabilized case 7 of Table 1, with the selection $g_K = 0.00001, g_{Na} = 1000$.

In Table 2, it is stated that the value of d leads to a new saddle point as the additional pole created by the washout filter interacts with the original eigenvalues. In Figure 22, the membrane potential response of the closed loop at $g_{Na} = 311.351$ with $d = 0.1374, K_3 = 10$ is given for convenience. This example corresponds to the information given in the 4th column of Table 2.

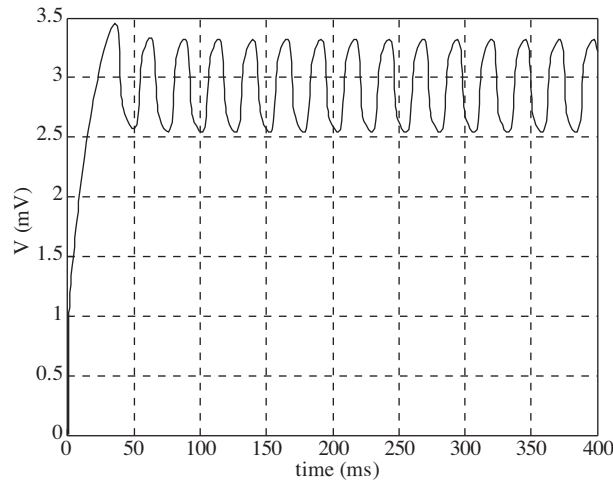


Figure 22. The closed loop response corresponding to Case 6 of Table 1 with $d = 0.1374, K_3 = 10$.

As expected the new saddle point is unstable with an oscillation at 40 Hz whereas the original oscillation corresponding to the information in the 6th column of Table 1 has a frequency of 59 Hz. The frequencies are not that much different however the amplitudes are considerably different as easily inferred from Figures 8 and 22. When the value of parameter d is increased the amplitude of oscillations increases. In Figure 23,

an example response is given for $d = 0.5$. Note that there is a considerable level of increase in the oscillation amplitude. With the increasing K_3 the oscillation amplitude seems to decrease however the closed loop may not be stabilized. This effect is demonstrated in Figure 24 as the amplitude drops under 1 mV when K_3 is increased to the value $K_3 = 1000$. Lastly, with a decreasing d , the amplitude of oscillation is decreasing and after some value the oscillation ceases. As a result, it can be said that washout filter can either stabilize an equilibrium point (oscillations terminated) or change its amplitude (or frequency). To have a stable result out of a washout filter application on a HH type nerve fiber one should choose the value of filter time constant d as small as possible, such as $d = 0.001$. The value of K_3 is then adjusted according to the transient behavior and level of stimulation current. However, too high values should be avoided so as not to experience solver difficulties.

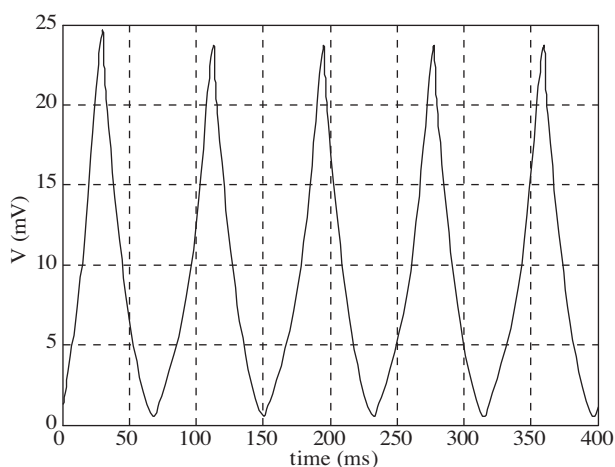


Figure 23. The closed loop response corresponding to Case 6 of Table 1 with $g_K = 0.05, g_{Na} = 10$.

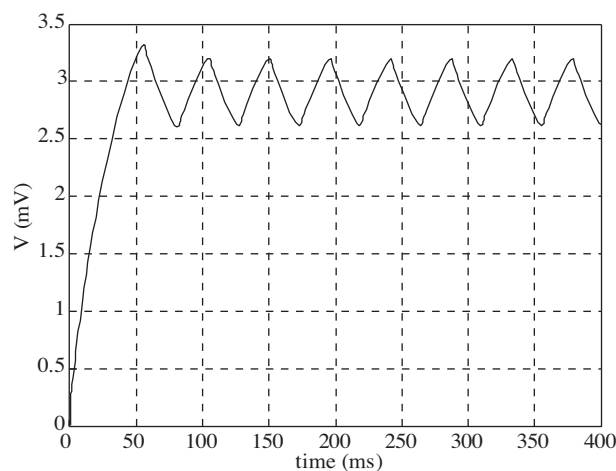


Figure 24. The closed loop response corresponding to Case 6 of Table 1 with $d = 0.5, K_3 = 1000$.

7. Discussion and conclusion

In this research, a single parameter bifurcation analysis of the oscillating Hodgkin-Huxley type nerve fiber and a cure for the instabilities are presented. The purpose is to stop the oscillations which correspond to the repetitive firings in the view of biophysics. First of all, possible single parameter bifurcations are detected using the MATLAB based MATCONT numerical continuation package. The potassium and sodium channel have several Hopf and Saddle points at various levels of conductances. The first results show that, the increasing level of sodium and decreasing level of potassium conductances lead to at least two Hopf bifurcations which are the main cause of oscillations in the fiber. Not only the Hopf points but also the saddle points can be the causes of oscillations in the HH type nerve fibers. To control the oscillations a first order washout filter is integrated to the HH model which will adjust the level of the stimulation current automatically by measuring the membrane potential. The washout filter is of extended type which interacts with the cubic nonlinearities in HH model which may be affiliated with the bifurcations. The simulation results show that the time constant of the filter should be chosen as small as possible to have a stable outcome. Increased level of the filter time constant can lead to additional saddle points due to the interaction of the filter pole with the eigenvalues corresponding to the model. In addition, the amplitude of the oscillations is quite sensitive to the value of the filter time constant.

With its increasing value, the amplitude of the oscillation increases. The output of the filter is amplified by a gain which affects especially the duration of the transient behavior. Higher the gain, smaller is the amplitudes of the oscillations. Gain values too high may lead to solver difficulties during application. Thus, as with the filter time constant, the designer should select the gain's value as small as possible. The stimulation current variation increases with the increasing sodium channel conductance as understood from the graphical results. In the literature, it is indicated that the washout filters are not suitable for the cases with a complete zero eigenvalue. In this research, however the HH model is stabilized by the washout filter by selecting an extremely small filter time constant and a higher gain. This is one of the most interesting results of this work.

A study focused on controlling a nerve fiber can be useful in brain neurophysiologic studies as repetitive firings correspond to the bifurcations in the basic and advance HH type models. However, the behavior of the nerve fibers may be different in a realistic situation as the cells operate in a network where each cell affects the other's activities. Therefore, bifurcation conditions can be very different. However, this study may constitute a prototype for similar research on the networked cells. This is one of the topics for future research. In addition the nonlinear analysis of the washout filter-HH model combination can be another direction for a related future study.

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