

Bifurcation Control of Fitzhugh-Nagumo Models

Reşat Özgür DORUK^{*1}, Hamza IHNISH²

^{1,2}Atılım Üniversitesi, Mühendislik Fakültesi, Elektrik ve Elektronik Mühendisliği Bölümü, 06836, Ankara

(Alınış / Received: 10.11.2017, Kabul / Accepted: 01.08.2018, Online Yayınlanma / Published Online: 11.09.2018)

Keywords

Fitzhugh-Nagumo neurons,
Bifurcation,
Washout filter,
Projective control,
Nonlinear control

Abstract: A theoretical bifurcation control strategy is presented for a single Fitzhugh-Nagumo (FN) type neuron. The bifurcation conditions are tracked for varying parameters of the individual FN neurons. A MATLAB package called as MATCONT is utilized for this purpose and all parameters of the neuron is analyzed one-by-one. Analysis by MATCONT revealed five Hopf (H) and one Limit-Point/Saddle Point (LP) bifurcation. The Hopf type of bifurcations are controlled by a washout filter supported by projective control theory. Washout filters are designed as first and second order. First order washout filter which is also physically applicable appeared to be more advantageous than the second order version. It appeared that, the LP case could not be stabilized by the aid of a washout filter. To solve this issue, a nonlinear controller is proposed. The only drawback associated with that is its inability to keep the original equilibrium point. Simulations are also provided to validate the research done.

Fitzhugh-Nagumo Modelleri İçin Çatallanma Denetimi

Anahtar Kelimeler

Fitzhugh-Nagumo nöronları,
Çatallanma,
Arındırma filtreleri,
İzdüşümsel denetim,
Doğrusal olmayan denetim

Özet: Bu yazıda tekil Fitzhugh-Nagumo (FN) nöron modelleri için teorik bir çatallanma denetim çalışması sunulmaktadır. Değişmekte olan parametreler için çatallanma analizleri MATLAB üzerinde çalışan MATCONT uygulaması ile yapılmıştır. Söz konusu analizde 5 Hopf (H) ve 1 adette Sınır Noktası/Eyer Düğümü (LP) olgusuna rastlanmıştır. Hopf tipi çatallanmalar izdüşümsel denetim ile desteklenmiş arındırma süzgeçleri kullanılarak sağlanmıştır. Arındırma süzgeçleri birinci ve ikinci derece olarak uygulanmıştır. Birinci derece süzgeç ikinci dereceye göre daha avantajlı olduğu anlaşılmıştır. Birinci derece süzgeç hem daha uygulanabilir olmakta hem de daha hızlı davranmaktadır. LP türü çatallanmalar için derecesinden bağımsız olarak arındırma süzgecinden yapılan çıktı geri beslemesi başarılı olamamakta ve bu nedenle birinci derece süzgeçle beraber birde zar potansiyelinden ek bir geri besleme alınmaktadır. Bunun dezavantajı süzgecin yüksek geçiren niteliğinin bozulmasına neden olmakta ve LP denge noktasının korunmasına olanak vermemektedir. Bu soruna çözüm olması için doğrusal olmayan bir denetleyici tasarımıda gösterilmektedir. Bunun tek dezavantajı orjinal denge noktaları korunmaktadır. Sonuçlar benzetimlerle desteklenmektedir.

1. Introduction

1.1. General introduction and literature survey

Modeling biological neurons by differential equations is a popular subject of research in the last two decades. The Nobel prize winner Hodgkin-Huxley (HH) model [1] is a result of a voltage-clamp based research on the squid giant axon. This is a quite nonlinear and computationally complex neuron model but it is important due to its ability to describe the behavior of a realistic neuron. In order to simplify the models certain attempts are made. [2] and [3] are some related well known examples. These are simplified order reduced models. The Fitzhugh-Nagumo model coined in [2, 4] is somehow different in appearance

as it does not refer to any physical terms other than the membrane potential. The behavior of ion channels are merged into a single recovery variable. In this view, it can be compared to a continuous time recurrent neural network. Although it is mathematically different, it does have a set of bifurcations like the other two ([1] and [3]). There are numerous studies that are concentrated on analysis of bifurcations in Fitzhugh-Nagumo neurons. Some related works can be given as [5–11]. According to these sources, the main bifurcation condition seen in Fitzhugh-Nagumo type neurons is the single parameter Andronov-Hopf (or simply Hopf) bifurcation [12–16]. Basically, this is a situation where a limit cycle erupts from an equilibrium point of a dynamical system due to the change in its stability through a pair of complex conjugate eigenvalues. This event ap-

* Corresponding author: resat.doruk@atilim.edu.tr

pears when a parameter change occurs which yields pure complex conjugate eigenvalues. In addition the stability of the resultant limit cycle determines the criticality of the Hopf bifurcation. If it is a supercritical bifurcation, one has a stable limit cycle where as there will be an unstable limit cycle in case of a subcritical bifurcation. Another type of a bifurcation that occurs in FN models is the Saddle Node or Limit Point bifurcation [12, 17, 18]. This is the vanishing of an equilibrium point due to the collision of two equilibria in a dynamical system. The parameter change that leads to this situation results in a single zero eigenvalue in the Jacobian of the system. Bifurcations can be harmful in physical systems due to instability or high-amplitude oscillations. Thus, controlling a bifurcation is beneficial. Control of a bifurcation [19] can be performed by various methods. These can be a regular control system like linear quadratic regulator [20], washout filters [21, 22] and local feedback [23]. There are some advanced techniques such as delayed feedback [24] are also seen in the literature. Control of Fitzhugh-Nagumo models are met in the neuroscience and nonlinear systems literature. Some related studies focusing on this are [11, 25–30]. Most of these studies are related to chaotic synchronization or controlling of the chaos phenomenon itself.

1.2. Summary of this work

In this research, we will concentrate on a pure bifurcation control study. The target action of the controllers is to stabilize a particular bifurcating equilibrium point by implementing a feedback from membrane potential or from the full state (membrane potential and recovery variable) of a Fitzhugh-Nagumo neuron. The controllers are mainly based on washout filter theory [21, 22] designed through output feedback approaches. Using output feedback approaches are quite beneficial as the feedback from the output of the washout filter can be thought of an output feedback from the combined dynamics of the washout filter and FN neuron. The washout filter is naturally a high-pass filter that blocks the steady state and only allows transient portion of the signals. In nonlinear systems, application of a washout filter will keep the location of the equilibrium points. This is beneficial concerning the neurological dimension of the study because the membrane potential will not be shifted which might lead to certain conditions especially when applied to neuromuscular junction.

In the case that washout filters are not successful (unstable or not working as expected), one can apply other linear or nonlinear techniques. This may especially be necessary at the Limit Point case.

Some peculiarities in an application of bifurcation control is the necessity of the knowledge of the parameters. In the real life these parameters are often unknown or vaguely known. Because of this fact, an initial system identification process should be applied. This goal can be achieved by various methodologies such as combined state and parameter estimation methodologies [31–33], least squares techniques [34–36] and possible maximum likelihood estimation methods [37–39]. A similar approach is the minimization of the mean square error between the measured membrane potential and the one generated by the model

neuron. In this research, we will also demonstrate how successful a minimum mean square optimization is in the detection of the bifurcated parameters.

1.3. Outline of this work

One can examine the developmental steps of this research as shown below:

1. First of all, the dynamical model of a Fitzhugh-Nagumo neuron [4] is introduced. The information includes the mathematical details of the model (including its linearization) and numerical values of the parameters (in **Section 2.1**).
2. An introduction to bifurcation theory is presented. Here one will be able to meet the qualitative and mathematical definitions of the Saddle Points, Hopf and Saddle Node (Limit Point) bifurcations [12] (**Section 2.2**).
3. A bifurcation analysis of Fitzhugh-Nagumo neuron model is performed and associated results are presented. The analysis is performed by MATCONT which is a MATLAB based software package. We provide tables that reveal types of bifurcation (Hopf, Limit Point etc.), value of the bifurcating parameter, the corresponding equilibrium points and the associated eigenvalues of system Jacobian (**Section 2.2.4**).
4. In this work, our desire is to stabilize each bifurcated equilibrium point by applying a properly designed feedback control law that measures the neuron membrane potential. Major methodologies are based on washout filter theory [21] and nonlinearity cancellation [40]. Since washout filters are linear filters, their utilization in bifurcation control will require the development of linear control techniques. In this study, we will benefit from linear quadratic theory (LQR). The washout filters are integrated with the linearized neuron model and filter the membrane potential. However, the control law is generated from a signal which is the linear combination of the washout filter states. So, we will have a feedback from a subset of the combined state vector (linearized neuron and washout filter). This corresponds to an output feedback and thus one can implement output feedback control approaches such as projective control theory [41]. The linear techniques will especially be beneficial for the Hopf bifurcation cases (**Section 3.1** and **3.2**). In the case that linear techniques are not successful, a nonlinearity cancellation based approach is also provided **Section 4.4.1**.
5. Application of the bifurcation control theory to the Fitzhugh-Nagumo neurons are presented. The Hopf bifurcations are stabilized by washout filter based feedback. Two examples washout filter based control are presented. One only implements a feedback from the membrane potential whereas the other one implements a feedback from the full state of the neuron. The Limit Point bifurcation is controlled by a nonlinear methodology as washout filter based approaches failed **Section 4**.

6. A minimum mean square based parameter estimation [42] approach is also introduced as a last part of this research. As the parameters of a neuron is actually very difficult to know one will need to perform an experiment to identify the numerical values of its parameters. This is also beneficial as one will be able to estimate the bifurcating parameter if applied to a bifurcating neuron. In a realistic environment (in vivo or in vitro) only the membrane potential information is available. Thus, the estimation procedure should rely on a trace of membrane potential measured. For the optimization purposes, MATLAB Optimization Toolbox is utilized (Section 4.5).
7. Numerical examples and simulation results are presented in Section 5.

1.4. Concerning realistic problems

In this research, we are talking about bifurcation control of a neuron model. Of course some questions may rise regarding the realistic extension of the developments here. We can make the following comments on this manner:

1. Rather than physical features, Fitzhugh-Nagumo models are originally developed to reflect the dynamical features of a biological neuron. This mainly includes firing and bursting. But, this does not mean that it is not suitable for a realistic application.
2. The neuron may be utilized in a realistic application if its parameters can be properly determined in a realistic environment. In Section 4.5, we discussed an approach to achieve this goal.
3. In a mammalian nervous system, not every fiber can be directly accessible. In other words, touching with an electrode to the neural membrane may detrimentally alter its operation. In such cases, one can either place the electrodes a nearby location to the neuron and record the action potential peaks and record the neural spiking events (peaks of the action potentials occurred) and train the model using a point process maximum likelihood (similar to that of [43]). The controller will then be designed. This type of problems are met when we are dealing with the modeling of sensory neurons.
4. The problem that is addressed in this research is about the control of a bifurcation event (merely to stop an oscillation of the membrane potential). This may be considered as a representative of a medical condition such as Parkinson’s disease [44] or bipolar disorder [45]. These can be considered as a moderate or low frequency oscillation generated by a large group of neurons. After performing a suitable parameter identification one can implement a feedback mechanism to stop these oscillations which can be thought as a treatment. Here attaching an electrode to a neural membrane may still be an issue. One can place the electrode to a nearby location and using the current flow through the conductance of the surrounding medium to measure the variations in the membrane

potential of the interested neuron(s). A current sensing mechanism might be necessary here.

2. Fitzhugh-Nagumo Models and Their Bifurcation Analysis

2.1. Mathematical details of the model

Fitzhugh-Nagumo models [4] are second order nonlinear differential equations bearing the membrane potential (V) and a recovery variable (W). A FN neuron can be excited by an external current injection (I). The mathematical equation is shown below (form in [4, 7, 46]):

$$\begin{aligned} \dot{V} &= V - dV^3 - W + I \\ \dot{W} &= cV + a - bW \end{aligned} \tag{1}$$

where (a, b, c, d) are specific neuron parameters, (V) is in mV’s, (I) is in $\mu A/cm^2$. In addition the above equation assumes that the time variable t is in milliseconds. Table 1 shows the nominal values of the specific parameters of (1).

Table 1. The nominal parameters of the FN model in (1). These are evaluated using the information from [7].

Parameter	Value
a	0.08
b	0.056
c	0.064
d	0.333

The variation of the membrane potential with the parameters in Table 1 will be similar to that of Figure 1. Based on the simulation results, we can write the steady state or equilibrium point corresponding to the nominal parameters in Table 1 as shown below:

$$\begin{aligned} V_\infty &= -1.5369 \\ W_\infty &= -0.3279 \end{aligned} \tag{2}$$

Equilibrium points (or the solutions of ($\dot{V} = 0$ & $\dot{W} = 0$)) may also be found by finding the roots of the following polynomial:

$$bdV^3 + (c - b)V + a = 0 \tag{3}$$

and then substituting the result V_∞ to the following equation:

$$W_\infty = V_\infty - V_\infty^3 \tag{4}$$

Using the values in Table 1 and solving the equations (3) and (4) using MATLAB roots([]) command one will have one real values solution that is exactly the same as that of (2).

From (3) it is pretty obvious that, the equilibrium point strictly depends on the values of the model parameters (a, b, c, d). The change of one or more parameters of the model will lead to a relocation of the respective equilibrium points of (1). As that is a nonlinear system, the deviation of equilibrium points may lead to a change in the qualitative behavior of the model in (1). These phenomena are called as bifurcation [12] in nonlinear systems theory and may be detrimental for physical systems.

The purpose of this work is to develop control laws that will stabilize the dynamics of (1) around the bifurcated equilibrium points. Development of linear controllers around equilibrium points require the linearization of the nonlinear model in (1). If $x = [V, W]^T$ and if (1) is written as

$$\dot{x} = f(x, I, \theta) \quad (5)$$

with $\theta \in \mathcal{R}$ being a system parameter, one can write the Jacobian linearized system as:

$$\dot{\hat{x}} = \nabla_x f(x, I, \theta)|_{(x=x_\infty, I=I_\infty)} \hat{x} + \nabla_I f(x, I, \theta)|_{(x=x_\infty, I=I_\infty)} \hat{I} \quad (6)$$

where $\hat{x} = x - x_\infty$, $\hat{I} = I - I_\infty$ and $\nabla_x f$ corresponds to the gradient of f with respect to x . One can rewrite (6) as:

$$\dot{\hat{x}} = A_\infty \hat{x} + B_\infty \hat{I} \quad (7)$$

where $A_\infty = \nabla_x f(x, I, \theta)|_{(x=x_\infty, I=I_\infty)}$ and $B_\infty = \nabla_I f(x, I, \theta)|_{(x=x_\infty, I=I_\infty)}$.

Considering the model in (1), these matrices will be:

$$A_\infty = \begin{bmatrix} 1 - 3dV^2 & -1 \\ c & -b \end{bmatrix} \quad (8)$$

$$B_\infty = \begin{bmatrix} 1 \\ 0 \end{bmatrix}$$

The eigenvalues of A_∞ is important in determining the local stability properties of (1) at $x = x_\infty$ and thus it is critical in bifurcation discussion.

2.2. Parameter drifts and bifurcations

In the previous section we stated that nonlinear systems (all physical systems are nonlinear in nature) may exhibit different behaviors when an equilibrium point moves due to a change in one or more parameter of the considered nonlinear system.

In two dimensional (planar) systems, the most common single parameter bifurcations are of Hopf [14] or Saddle Node/Limit Point [17] type. There is also a critical point called as a Saddle Point which has nothing to do with the saddle node/limit point cases and thus it is not considered as a bifurcation.

In this research, we will discuss the bifurcations exhibited by (1) against deviations in parameters $\theta = [a, b, c, d]$ so we will suppose that $I = 0$ in the analysis stage. It will be treated as an input when we discuss the bifurcation control in Section 4.

With $I = 0$ (5) can be rewritten as:

$$\dot{x} = f(x, \theta) \quad (9)$$

and its Jacobian will be A_∞ in (7) and (8) with I being substituted as $I = 0$.

Suppose also that $x = x_\infty^n$ is the equilibrium point of (9) when the parameters are at their nominal values. So the effected parameter θ is also at its nominal value as $\theta = \theta_n$. So one can write $f(x_\infty^n, \theta_n) = 0$. When θ deviates from $\theta = \theta_n$, a bifurcation may appear. In the foregoing sections we will discuss the qualitative and numerical details of the bifurcation conditions met in this research.

2.2.1. Hopf bifurcation

Suppose that at a certain parameter $\theta = \theta_h$ the properties of a stable equilibrium point $x_\infty^h [f(x_\infty^h, \theta_h) = 0]$ changes such that a limit cycle occurs around the equilibrium point. In this case, we will have an oscillation around the equilibrium $x = x_\infty^h$. This situation is called as Hopf bifurcation [47] and revealed by a single pair of pure complex eigenvalues of A_∞ at $x = x_\infty^h$ and $\theta = \theta_h$.

The stability of erupted limit cycle is also an important concern in Hopf bifurcation discussions. If there is a stable limit cycle, one has a supercritical Hopf bifurcation otherwise the bifurcation is subcritical which yields an unstable limit cycle [14].

The criticality of Hopf bifurcations are mathematically characterized by a numerical parameter called as First Order Lyapunov Coefficient (FOLC) $l_1(0)$. This parameter is derived from Taylor series expansion of $f(x, \theta)$ up to the third degree. FOLC can be evaluated by software packages such as MATCONT [48, 49]. If it is positive, we have a subcritical and if it is negative we have a supercritical bifurcation respectively.

2.2.2. Limit Point or Saddle Node bifurcation

Limit Point (LP) or Saddle Node bifurcation [18] refers to a condition where the stability of two equilibria changes due to their collision. Suppose that this collision occurs at $\theta = \theta_l$ with the state equilibrium at $x = x_\infty^l$. At this point, one will have one eigenvalue of the system Jacobian A_∞ at origin.

2.2.3. Neutral Saddle Points

Suppose that the system Jacobian A_∞ at $\theta = \theta_s$ and at the corresponding equilibrium $x = x_\infty^s$ has a pair of eigenvalues with opposite signs and equal magnitudes ($\pm \lambda_s$). Because of its characteristic it is generally not considered as a bifurcation.

2.2.4. Situation in Fitzhugh-Nagumo models

Fitzhugh-Nagumo models exhibit mainly Hopf and Limit Point bifurcations as obtained from analysis by MATCONT package [48, 49]. In Table 2 numerical details concerning the bifurcation profile of FN neuron modeled in (1). As indicated by Table 2, the FN model in (1) has 5 Hopf and 1 Limit Point bifurcations. In order to have an idea on what is happening when the cases in Table 2 are encountered, one can refer to the Figure 3-7

3. Bifurcation Control Approaches

3.1. Washout filter theories

Washout filters [21, 22] are naturally a type of high-pass filter which blocks the steady-state responses of systems but do allow the transient part of the signal. This behavior helps to preserve the natural equilibrium of a physical system. Mathematically, it can be shown as a state space equation of the form as shown below:

$$\begin{aligned} \dot{z} &= A_w z + B_w y \\ I &= A_w z + B_w y \end{aligned} \quad (10)$$

Table 2. Bifurcation analysis results for FN model in (1) with the parameters in **Table 1**. The condition column indicates only the affected parameter all other parameters are same as **Table 1**. FOLC stands for First Order Lyapunov Coefficient which is critical in determination of the criticality of the Hopf bifurcations.

Case	Condition	Type	Equilibrium & Other Information	Eigenvalues
1	$a = 0.024906$	Hopf	$(v = -0.972082, w = -0.666201)$ FOLC= 3.46×10^{-01} Criticality: Subcritical	$(j0.2467, -j0.2467)$
2	$a = -0.024906$	Hopf	$(v = 0.972082, w = 0.666201)$ FOLC= 3.46×10^{-01} Criticality: Subcritical	$(j0.2467, -j0.2467)$
3	$b = -0.022854$	Hopf	$(v = -1.011869, w = -0.666871)$ FOLC= -8.15×10^{-01} Criticality: Supercritical	$(j0.2519, -j0.2519)$
4	$c = 0.120676$	Hopf	$(v = -0.972081, w = -0.666201)$ FOLC= -4.48×10^{-02} Criticality: Supercritical	$(j0.3428, -j0.3428)$
5	$d = 0.032276$	Hopf	$(v = -3.122398, w = -2.139884)$ FOLC= 3.35×10^{-02} Criticality: Subcritical	$(j0.3428, -j0.3428)$
6	$d = -0.000212$	Limit Point	$(v = -15.000000, w = -15.714286)$	$(1.0871, -0.0000)$

where $z \in \mathfrak{R}^p$ is the state of the washout filter, y which is a scalar or a vector is the measured output of the controlled system (i.e. the neuron) and $I \in \mathfrak{R}$ is the output of the washout filter which is the control input to the controlled system. Here, $A_w \in \mathfrak{R}^{p \times p}$ and B_w has p rows and specified number of columns depending on the size of y . As washout filter is a type of linear dynamical system one can augment it to the original nonlinear system and apply state feedback control techniques. The matrix A_w should be Hurwitz.

3.2. Linear quadratic regulators and projective control

3.2.1. Linear quadratic full state feedback control

Linear quadratic regulators are well known full state feedback control techniques based on the optimization of a quadratic performance index such as:

$$J = \frac{1}{2} \int_0^{\infty} (x^T Q x + u^T R u) dt \quad (11)$$

such that $\dot{x} = Ax + Bu$. In the above, $x \in \mathfrak{R}^n$ is the state of the linear plant, $u \in \mathfrak{R}$ is the input of the linear plant, $Q \in \mathfrak{R}^{n \times n}$ and $R \in \mathfrak{R}$ are the quadratic performance index coefficients. Here the plant is designated by $\dot{x} = Ax + Bu$ with $A \in \mathfrak{R}^{n \times n}$ and $B \in \mathfrak{R}$. The control law is generated as $u = -R^{-1}B^T P x$ where $P \in \mathfrak{R}^{n \times n}$ is a symmetric and positive definite unique solution of the algebraic Riccati equation $A^T P + PA - PBR^{-1}B^T P + Q = 0$.

3.2.2. Projective control theory

Knowing the fact that full state feedback generates a control law of the form $u = -Kx$ where the gain $K = R^{-1}B^T P$ processes all the elements of the state vector x from the plant of the form $\dot{x} = Ax + Bu$. In several control problems from realistic applications, one often appears to have cases

where all elements of the state vector can not be physically measured. This led to studies such as [41, 50, 51] which utilizes orthogonal projection theorems to obtain an output feedback $u = -K_o y$ where y has the physically measurable inputs or the output signals to be involved in feedback. K_o is computed from an orthogonal projection from the full state space to a subspace generated from the measurable elements of the state vector. Now, if one writes the full plant equation as:

$$\begin{aligned} \dot{x} &= Ax + Bu \\ y &= Cx \end{aligned} \quad (12)$$

where $y \in \mathfrak{R}^r$ is the output where the feedback is taken from, $C \in \mathfrak{R}^{n \times r}$ is the matrix relating the outputs of the plant to the state and r is the number of available feedback lines, namely the size of the output. The feedback is formed as $u = -K_o y$. To implement the projective control one has to find the full state feedback closed loop spectrum:

$$\dot{x} = (A - BK)x = A_c x \quad (13)$$

and let the diagonal eigenvalue matrix and stacked eigenvectors of A_c are denoted as Λ and Ψ as shown below:

$$\Lambda = \begin{bmatrix} \lambda_1 & 0 & 0 & \dots & 0 \\ 0 & \lambda_2 & 0 & \dots & 0 \\ 0 & 0 & \lambda_3 & \dots & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & \dots & \lambda_n \end{bmatrix}, \Psi = [v_1 \ v_2 \ v_3 \ \dots \ v_n] \quad (14)$$

where λ_i are the sorted eigenvalues of A_c and v_i are the eigenvectors associated with λ_i . The output feedback will also have n eigenvalues however they will not completely be the same as that of Λ_c instead only r number of eigenvalues from Λ_c will be the same. These are called as the retained eigenvalues. The remaining $n - r$ eigenvalues can appear anywhere in the complex plane. So projective

control will not guarantee a stable output feedback closed loop. In these cases the dynamical version of the projective control might be an alternative. The designer should first decide which eigenvalues from Λ_c should be retained. That decision is often critical concerning the stability of the final closed loop.

Suppose that the designer wants to retain r eigenvalues $\Lambda_r = \text{diag}(\lambda_1^r, \lambda_2^r, \dots, \lambda_n^r)$ from Λ_c . Here λ_i^r will have the same values as λ_i but only r number of them will be as such. The corresponding eigenvectors from Ψ will be denoted as Ψ_r . The projective control can now be obtained by applying the orthogonal projection equation to the full state feedback gain K :

$$K_o = K\Psi_r(C\Psi_r)^{-1} \quad (15)$$

where $K_o \in \mathfrak{R}^{1 \times r}$ is the output feedback gain. The closed loop dynamics of the output feedback gain is $\dot{x} = (A - BK_o C)x$ and its closed loop eigenvalues should have Λ_r exactly and $n - r$ additional manipulatable eigenvalues which may or may not be at stable locations.

3.2.3. Projective control approaches in bifurcation control

As the washout filter and the bifurcated plant will form a higher order dynamical system, projective control might be utilized to form a washout filter based bifurcation controller by applying feedback from the output of the washout filter directly. So y will be the output of the washout filter which will be processed by the projective output feedback gain K_o . The bifurcated plant should of course be linearized prior to the augmentation by the washout filter's dynamics. So one can progress as follows: For a nonlinear system of the form $\dot{x} = f(x, u)$

$$A_p = \left. \frac{\partial f}{\partial x} \right|_{x=\tilde{x}, u=\tilde{u}}, B_p = \left. \frac{\partial f}{\partial u} \right|_{x=\tilde{x}, u=\tilde{u}} \quad (16)$$

where p denotes plant. Here \tilde{x} and \tilde{u} are the equilibrium values of the nonlinear plant $\dot{x} = f(x, u)$ which means $f(\tilde{x}, \tilde{u}) = 0$ at the condition of any bifurcation. So the linearized nonlinear plant together with the washout filter will be expressed as:

$$\begin{aligned} \dot{\hat{x}} &= A_p \hat{x} + B_p \hat{u} \\ \dot{z} &= A_w z + B_w H \hat{x} \end{aligned} \quad (17)$$

where H is a matrix for selecting the measurable entries of the state vector \hat{x} . It will have ones and zeros as entries. The output of the system in (17) will be:

$$y = A_w z + B_w H \hat{x} \quad (18)$$

and the designed control law is $\hat{u} = -K_o y = -K_o (A_w z + B_w H \hat{x})$. In the above $C = [B_w H \ A_w]$, so (15) can directly be used for deriving K_o .

4. Bifurcation Controllers for Fitzhugh-Nagumo Models

4.1. Derivation of the linearized model for bifurcation control

In **Section 2.1**, we discussed the derivation of the linearized version of (1). The procedure is repeated below

for convenience. Before proceeding one has to derive the Jacobians of the Fitzhugh-Nagumo neurons. These will be:

$$\begin{aligned} \frac{\partial \dot{V}}{\partial V} &= 1 - 3dV^2 \\ \frac{\partial \dot{V}}{\partial W} &= -1 \\ \frac{\partial \dot{W}}{\partial V} &= c \\ \frac{\partial \dot{W}}{\partial W} &= -b \end{aligned} \quad (19a)$$

$$A_p = \begin{bmatrix} 1 - 3dV^2 & -1 \\ c & -b \end{bmatrix}, B_p = \begin{bmatrix} 1 \\ 0 \end{bmatrix} \quad (19b)$$

Here, the linearized state vector is $\hat{x} = [\hat{V}, \hat{W}]^T$ and the bifurcating equilibrium values \tilde{V} and \tilde{W} are given in **Table 2**. The control law is the injected current I to the nonlinear neuron model in (1). Considering the washout filter augmentation one may consider two cases. These will be:

1. The washout filter will only filter the membrane potential V resulting in a first order filter. This case is physically more practical.
2. In this case, it is assumed that both states of the neuron can be measured or observed. The washout filter will filter both the membrane potential V and the recovery variable W . This will yield a second order filter.

In the next stages we will cover the two cases discussed above.

4.2. Case 1: First Order Washout Filter

In this case as we will only implementing a feedback from the membrane potential V , we will only need a first order washout filter represented by:

$$\begin{aligned} \dot{z} &= \alpha_w z + \beta_w V \\ y &= \alpha_w z + \beta_w V \end{aligned} \quad (20)$$

where $\alpha_w < 0$ is required for stability and β_w is arbitrary. It can be equal to unity. So the augmented model will be:

$$\begin{bmatrix} \dot{\hat{V}} \\ \dot{\hat{W}} \\ \dot{z} \end{bmatrix} = \begin{bmatrix} 1 - 3dV^2 & -1 & 0 \\ c & -b & 0 \\ \beta_w & 0 & \alpha_w \end{bmatrix} \begin{bmatrix} \hat{V} \\ \hat{W} \\ z \end{bmatrix} + \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} I \quad (21)$$

The output (measurement for feedback) relationship will be given by:

$$y = [\beta_w \ 0 \ \alpha_w] \begin{bmatrix} \hat{V} \\ \hat{W} \\ z \end{bmatrix} \quad (22)$$

which means $C = [\beta_w \ 0 \ \alpha_w]$. From this point, one can apply to the methodologies presented in **Section 3.2.2**.

4.3. Case 2: Second Order Washout Filter

In this case, we assume that both membrane potential V and recovery variable W are observable. Thus, one will need a second order washout filter as shown below:

$$\begin{aligned} \begin{bmatrix} \dot{z}_1 \\ \dot{z}_2 \end{bmatrix} &= \begin{bmatrix} \alpha_w(1,1) & \alpha_w(1,2) \\ \alpha_w(2,1) & \alpha_w(2,2) \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} \beta_w(1,1) & \beta_w(1,2) \\ \beta_w(2,1) & \beta_w(2,2) \end{bmatrix} \begin{bmatrix} V \\ W \end{bmatrix} \\ y &= \begin{bmatrix} \alpha_w(1,1) & \alpha_w(1,2) \\ \alpha_w(2,1) & \alpha_w(2,2) \end{bmatrix} \begin{bmatrix} z_1 \\ z_2 \end{bmatrix} + \begin{bmatrix} \beta_w(1,1) & \beta_w(1,2) \\ \beta_w(2,1) & \beta_w(2,2) \end{bmatrix} \begin{bmatrix} V \\ W \end{bmatrix} \end{aligned} \quad (23)$$

The above can be rewritten shortly as:

$$\begin{aligned} \dot{Z} &= A_w Z + B_w X \\ Y &= A_w z + B_w X \end{aligned} \quad (24)$$

with $A_w = \begin{bmatrix} \alpha_w(1,1) & \alpha_w(1,2) \\ \alpha_w(2,1) & \alpha_w(2,2) \end{bmatrix}$, $B_w = \begin{bmatrix} \beta_w(1,1) & \beta_w(1,2) \\ \beta_w(2,1) & \beta_w(2,2) \end{bmatrix}$, $Z = [z_1, z_2]^T$ and $X = [V, W]^T$.

Here the most important criterion is the stability of A_w . It should be Hurwitz as stated in the discussion of washout filters. So the augmented model will be:

$$\begin{bmatrix} \dot{\hat{V}} \\ \dot{\hat{W}} \\ \dot{z} \end{bmatrix} = \begin{bmatrix} 1-3dV^2 & -1 & 0 & 0 \\ c & -b & 0 & 0 \\ \beta_w(1,1) & \beta_w(1,2) & \alpha_w(1,1) & \alpha_2(1,2) \\ \beta_w(2,1) & \beta_w(2,2) & \alpha_w(2,1) & \alpha_2(2,2) \end{bmatrix} \begin{bmatrix} \hat{V} \\ \hat{W} \\ z \end{bmatrix} + \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} U \quad (25)$$

The output (measurement for feedback) relationship will be given by:

$$y = \begin{bmatrix} \beta_w(1,1) & \beta_w(1,2) & \alpha_w(1,1) & \alpha_2(1,2) \\ \beta_w(2,1) & \beta_w(2,2) & \alpha_w(2,1) & \alpha_2(2,2) \end{bmatrix} \begin{bmatrix} \hat{V} \\ \hat{W} \\ z_1 \\ z_2 \end{bmatrix} \quad (26)$$

which means $C = \begin{bmatrix} \beta_w(1,1) & \beta_w(1,2) & \alpha_w(1,1) & \alpha_2(1,2) \\ \beta_w(2,1) & \beta_w(2,2) & \alpha_w(2,1) & \alpha_2(2,2) \end{bmatrix}$.

From this point, one can apply to the methodologies presented in **Section 3.2.2**. In order that (26) to be fed back to the FN neuron it should be processed by a gain which also converts it to a scalar control law.

4.4. Other options

In general a combined washout filter/projective control approach should be adequate to implement a bifurcation controller. However, in certain cases such an arrangement does not yield stable controllers. We will see in the Limit Point case neither the first nor the second order washout filter yielded a stable closed loop. Thus one will need a different controller. This fact may appear in severe cases such as Limit Point (LP). For that, a nonlinear controller is expected to be beneficial. This type of controllers often involve an internal nonlinearity cancellation and a linear feedback.

4.4.1. Nonlinearity cancellation

Nonlinearity cancellation is the elimination of certain nonlinear terms (powers of a variable, trigonometric functions

etc.) in a dynamical system by applying an interim control law to its input. The remaining system may or may not be linear depending on the existence of available terms for cancellation. Considering the Fitzhugh-Nagumo model in (1) if we apply a nonlinear control law as:

$$I = -V + dV^3 + U \quad (27)$$

to:

$$\begin{aligned} \dot{V} &= V - dV^3 - W + I \\ \dot{W} &= cV + a - bW \end{aligned} \quad (28)$$

we will obtain:

$$\begin{aligned} \dot{V} &= -W + U \\ \dot{W} &= cV + a - bW \end{aligned} \quad (29)$$

It is obvious that the above system is linear except the constant term a . It has a linear input term U . We can apply a linear feedback law as shown below:

$$U = k_1 V + k_2 W \quad (30)$$

The closed loop dynamics will now be:

$$\begin{aligned} \dot{V} &= k_1 V + k_2 W - W \\ \dot{W} &= cV + a - bW \end{aligned} \quad (31)$$

In state space form:

$$\begin{bmatrix} \dot{V} \\ \dot{W} \end{bmatrix} = \begin{bmatrix} k_1 & k_2 - 1 \\ 0 & -b \end{bmatrix} \begin{bmatrix} V \\ W \end{bmatrix} + \begin{bmatrix} 0 \\ a \end{bmatrix} \quad (32)$$

In the above, it is obvious that we have a constant term which somewhat violates the standard state space equations we see in the literature. However, as also revealed from the same equation (32) the constant term can be separated as a external input to the closed loop. The stability then can be analyzed through the notion of Bounded-Input and Bounded-Output (BIBO) stability which is described in the theorem below:

Theorem 4.1 (Bounded Input/Bounded Output (BIBO) Stability). *Consider a linear system shown by the state equation:*

$$\begin{aligned} \dot{x} &= Ax + Bu \\ y &= Cx + Du \end{aligned} \quad (33)$$

The above system is said to be bounded-input/bounded-output stable if and only if the eigenvalues of A is on the left half region of the complex plane.

Note that as a is a constant parameter in reality, it can be considered as a bounded input to (32) of which characteristic equation is:

$$\Delta(s) = \det(sI_{2 \times 2} - A) = (s - k_1)(s + b) \quad (34)$$

The roots of above are $s = k_1$ and $s = -b$. As $b > 0$, only condition required is $k_1 < 0$ per **Theorem 4.1**. Here, k_2 may be an arbitrary finite gain including $k_2 = 0$. The latter leads to a feedback only from membrane potential (V) which is beneficial as V is the only physical variable. The only bad side of this design is its inability to preserve the original equilibrium values of (1).

4.5. Problem of unknown parametrics

Most of the time, the system parameters (a, b, c, d) are not known exactly or vaguely known. A system identification should be performed prior to activation of a bifurcation controller. For models with small parameter sets like the FN neuron, it will be beneficial to try the minimum mean square estimation approaches. If one calls the parameters to be estimated as $\theta = [a, b, c, d]$ and the actual membrane potential as V_a , the following can be written:

$$J(\theta) = \int_0^{T_f} (V(\theta) - V_a)^2 dt \quad (35)$$

The above is the cost function to minimize. It is a function of unknown parameter θ . The term $V(\theta)$ refers to the computed membrane potential using the a particular estimate of the parameters θ and T_f is the duration of data collection. Basically the estimate of θ which is $\hat{\theta}$ can be found by minimizing $J(\theta)$ w.r.to the parameter θ as shown below:

$$\hat{\theta} = \underset{\theta}{\operatorname{argmin}} J(\theta) \quad (36)$$

which means:

$$\left. \frac{\partial J(\theta)}{\partial \theta} \right|_{\theta=\hat{\theta}} = 0 \quad (37)$$

Using MATLAB[®] `fmincon` function from its optimization toolbox this operation can simply be done. The cost function can be generated by recording a measurement of membrane potential and integrating the model equation using the current estimate of the parameter θ . The two data arrays are subtracted, squared and re-integrated prior to supplying `fmincon` script. In the next section, we will present the results of the application of the theory presented in this section to the bifurcation control of an FN neuron.

5. Results

The numerical simulations in this section make use of the information given in **Table 1** and **Table 2** in the development of the control laws. Before proceeding to the projective control section one will have to initialize the washout filter coefficients according to the guidelines given in **Section 3.1**. For first order washout filters we will use $\alpha_w = -0.1$ and $\beta_w = 1$. On the other hand, the second order washout filters will require matrix coefficients which can be written as $A_w = -0.1I_{2 \times 2}$ and $B_w = I_{2 \times 2}$. The full state feedback optimal control coefficients will be initialized as $Q = 50I_{3 \times 3}$ and $R = 1$ for first order washout filter case and $Q = 50I_{4 \times 4}$ and $R = 1$ for the second order filter respectively.

5.1. Results for control by a first order washout filter

Table 3 summarizes the results of the first order washout filter and projective control applied on the FN nonlinear neuron. It is understood from the simulations that LP case does not yield a stable outcome. We will need to design an alternative controller for this case. The information in

Section 4.4 will be utilized for this purpose. The graphical results showing the variation of the membrane potential for each case in **Table 2** are shown in **Figure 8-12**. The results associated with Case 6 will not be shown here as it is solved by another controller.

5.2. Results for control by a second order washout filter

Table 4 summarizes the results of the second order washout filter and projective control applied on the FN nonlinear neuron. The situation is same for the Limit Point bifurcation case so the approach proposed in **Section 4.4** seems the only solution from the alternatives presented in this research. The graphical results showing the variation of the membrane potential under control by a second order washout filter for each case in **Table 2** are shown in **Figure 13-17**.

5.3. Results of nonlinear control

In the simulations associated with the nonlinear control described in section **Section 4.4** will be utilized. The gain k_2 will be taken as zero so that only a feedback from membrane potential V is established which is meaningful in physical sense. The results are given for Case 6 with a few different values of the gain k_1 . The results are presented graphically in **Figure 18-23**. The figures reveal stable outcomes from the nonlinear control of Case 6 of **Table 2**. The only peculiarity of the nonlinear approach is that the original equilibrium values in Case 6 are not preserved. More truly speaking they are dependent on the level of the parameter k_1 .

5.4. Estimation of the neuron parameters prior to bifurcation controller

Using the theory presented in **Section 4.5** one will be able to perform a parameter determination study prior to an application of a bifurcation control as the parameters of the FN neuron should not be expected to be known at the time of implementation. Assuming the neuron is in a condition of a particular bifurcation case from **Table 2** one can apply the least squares technique for a predetermined length of samples obtained from measurement. In **Table 5**, one will be able to see what happens when one has a parameter estimation attempt for Case 1 of **Table 2** with the indicated length of samples.

As one can see from **Table 5**, the parameter estimation results are quite accurate. Thus, for other cases we will only present the results of the identification process with a sample size of 20ms for the cases 2, 3, 4 and 5 (except the Limit Point case which fails for sample sizes longer than 7ms). One can see the related results in **Table 6**.

In a realistic application, the measurement of the membrane potential will most probably have a noise accumulation due to the instrumentation. This issue should also be addressed at least in simulation level. In a simulation, the noise can be modeled by a normally distributed noise signal which modifies the measured membrane potential as shown below:

$$V_{meas} = V(1 + n_m) \quad (38)$$

Table 3. Numerical results of the bifurcation control by first order washout filter and projective control feedback. Chosen to be retained eigenvalues are shown in bold face. The columns are as follows: Case of bifurcation according to **Table 2**, eigenvalues obtained from full state LQ feedback plus washout filter, gain obtained from projective control, closed loop eigenvalues of washout filter and projective control together, indication whether the application is successful or not. It is understood from the simulations that LP case does not yield a stable outcome. This situation is same for various Q and R values and regardless of the retained eigenvalue configuration.

Case	$\lambda(A - BK)$	K_o	$\lambda(A - BK_oC)$	Success?
1 (H)	-0.0563 -1.0189 -6.9891	6.9534	-0.0194 -0.0449 -6.9891	Yes
2 (H)	-0.0563 -1.0189 -6.9891	6.9534	-0.0194 -0.0449 -6.9891	Yes
3 (H)	-0.0237 -1.0189 -6.9889	0.9537	-0.0174 + j0.0770 -0.0174 - j0.0770 -1.0189	Yes
4 (H)	-0.0569 -1.0255 -6.9800	6.9524	-0.0362 + j0.0193 -0.0362 - j0.0193 -6.9800	Yes
5 (H)	-0.0563 -1.0189 -6.9891	6.9534	-0.0194 -0.0449 -6.9891	Yes
6 (LP)	-0.0562 -1.0053 -7.0836	8.1196	0.0000 -0.0488 -7.0836	No

Table 4. Numerical results of the bifurcation control by second order washout filter and projective control feedback. Chosen to be retained eigenvalues are shown in bold face. The columns are as follows: Case of bifurcation according to **Table 2**, eigenvalues obtained from full state LQ feedback plus washout filter, gain obtained from projective control, closed loop eigenvalues of washout filter and projective control together, indication whether the application is successful or not. It is understood from the simulations of this case that LP case does not yield a stable outcome also with a second order washout filter. This situation is same for various Q and R values and regardless of the retained eigenvalue configuration.

Case	$\lambda(A - BK)$	K_o	$\lambda(A - BK_oC)$	Success?
1 (H)	-0.0850 -0.1 -1.0168 -6.9890	[7.9067, 103.2779]	-0.000856 -0.1 -1.0168 -6.9890	Yes
2 (H)	-0.0850 -0.1 -1.0168 -6.9890	[7.9067, 103.2779]	-0.000856 -0.1 -1.0168 -6.9890	Yes
3 (H)	-0.06796 -0.1 -1.0168 -6.9889	[7.9066, 112.9834]	-0.000893 -0.1 -1.0168 -6.9889	Yes
4 (H)	-0.1 -0.1330 -1.0183 -6.97999	[7.8999, 54.3666]	0.00165 -0.1 -1.0183 -6.979997	Yes
5 (H)	-0.08504 -0.1 -1.0168 -6.98907	[7.90672, 103.27787]	-0.000856 -0.1 -1.0168 -6.9890	Yes
6 (LP)	-0.0850 -0.1000 -1.0032 -7.0837	[9.0740, 104.7991]	0.0000 -0.1000 -1.0032 -7.0837	No

Table 5. The estimation results for Case 1, with the sample sizes of 5, 10, 20, 30, 60, 100, 200 ms. Note the accuracy of the results. They are closed to each other because of that a sample size of 20ms should be adequate for parameter estimation.

Case	Duration of Sample (ms)	Estimated Parameter
1	5	0.0248828873543579 0.0541595399754002 0.0643981171770769 0.332802074466949
1	10	0.0249053211554153 0.0559716655533597 0.0639958673724777 0.333003057532591
1	20	0.0249059650965805 0.0559990655943327 0.0639996669177282 0.333000444781839
1	30	0.0249059597528729 0.055999674670891 0.063999809211686 0.332999988106763
1	60	0.0249333237710483 0.0558442287975565 0.0639359319592352 0.333320749124625
1	100	0.0248905826017205 0.0559886210413623 0.0639896144231157 0.33332701550163
1	200	0.0248922500965174 0.0559884129068148 0.0639861951765453 0.333184343851034

Table 6. The estimation results for Case 1, with the sample sizes of 5, 10, 20, 30, 60, 100, 200 ms. Note the accuracy of the results. They are closed to each other thus a sample size of 20ms should be adequate for parameter estimation. This advantage breaks down for the Limit Point case due its instability which led to failure of the optimization algorithm.

Case	Duration of Sample (ms)	Estimated Parameter
2	20	-0.0249059788937565 0.0559999350469946 0.0639999797258641 0.332999887147072
3	20	0.0799998757229137 -0.0228554604746678 0.0639999084949137 0.333000277595704
4	20	0.0799998043439862 0.0559994633933543 0.120675620713213 0.333000317084924
5	20	0.0799998700190393 0.0559986628701682 0.0639995625151964 0.0322760438424776
6	5	0.0799536147174537 0.0550240563232576 0.0641215940465237 -0.00021357812004974

Table 7. The estimation results when a measurement noise is present on membrane potential. The noise is modeled by (38). The standard deviation of the noise chosen as 0.1 which corresponds to 10% noise level according to (38). The optimization algorithms are same but the computation is repeated 50 times to have statistically adequate data. The mean of parameter and their mean square error are presented.

Case	Duration of Sample (ms)	Mean Parameter	Mean Square Error
1	20	0.024904	$8.3758e-09$
		0.055796	$8.2639e-07$
		0.063938	$3.8784e-08$
		0.3332	$3.48e-09$
2	20	-0.024896	$5.5248e-08$
		0.055427	$2.3359e-05$
		0.063831	$2.8581e-06$
		0.33322	$4.36e-06$
3	20	0.080351	$1.2293e-07$
		-0.018982	$1.499e-05$
		0.064007	$4.4807e-11$
		0.33339	$1.5137e-07$
4	20	0.079826	$3.0205e-08$
		0.055006	$9.885e-07$
		0.12022	$2.078e-07$
		0.33413	$1.2761e-06$
5	20	0.080618	$3.8249e-07$
		0.060448	$1.9781e-05$
		0.065618	$2.6171e-06$
		0.032079	$3.8668e-08$
6	5	0.084227	$1.7871e-05$
		0.17428	0.01399
		0.033162	0.000951
		0.00037758	$3.4761e-07$

where n_m is a normally distributed random variable with zero mean and 0.10 standard deviation. So this noise will lead to a random modification of the membrane potential in a percentage level generated by the random number generator (i.e. `normrnd(mu, sigma, m, n)` in MATLAB). In Table 7, one can see the related results of parameter estimation with noisy measurement. The results in this table are generated by repeating the optimization 50 times to have statistically adequate data. As one can observe from Table 7 in the cases where we have an Hopf bifurcation, the noise does not bring a considerable level of difficulty. The mean square errors of the estimated parameters are quite low at the levels of 10^{-5} 's. However, the Limit Point case due to its unstable behavior one has to use a very short duration sample which led to higher level of errors as one can understand from the table. Concerning the bifurcation control, the utilization of the estimated parameters in the bifurcation controller designs are not expected to generate any hassles. However, the LP case should be treated specifically here because of the estimation errors.

6. Discussion and Conclusion

In this paper, we have presented a bifurcation analysis and control study on a single Fitzhugh-Nagumo neurons. The bifurcation analysis has been performed by a MATLAB package called as MATCONT. Utilizing this software speeds up the analysis process. MATCONT reveals five Hopf and one Limit Point bifurcation. For the Hopf bifurcation cases, we have developed first and second order

washout filter based bifurcation controllers. First order washout filter filters measures only the membrane potential whereas the second order version receives the membrane potential and recovery variable information (namely all states of the neuron). First order washout filter appeared to be more advantageous than the second order version. Besides its closeness to an experimental application, the first order filter yields a faster response than its second order counterpart. The Limit Point (LP) case resulted unsuccessful under washout filter based control. To remedy that, a nonlinear controller is designed. The results revealed that the nonlinear controller can successfully cure the instability associated with the Limit Point. The only issue with that is the variation of the equilibrium/steady-state value of the membrane potential with the control gain k_1 .

The unknown parameters at the time of bifurcation are estimated by an algorithm based on the minimum mean square (least squares) error based approach. It is concluded that when we have Hopf bifurcation in the FN neuron even there is noise the parameter estimation algorithm works quite satisfactorily even there is noise in measurement. However, for the LP case one can not say the same as the error levels seem to be considerably higher than the Hopf cases.

Acknowledgments

This study is partially supported by Government of Libya by providing a grant to the co-author.

References

- [1] Hodgkin, A. L., Huxley, A. F., 1952. Propagation of electrical signals along giant nerve fibres, *Proceedings of the Royal Society of London. Series B, Biological Sciences*, 177–183.
- [2] Fitzhugh, R., 1960. Thresholds and plateaus in the hodgkin-huxley nerve equations, *The Journal of general physiology*, 43(5), 867–896.
- [3] Morris, C., Lecar, H., 1981. Voltage oscillations in the barnacle giant muscle fiber., *Biophysical journal*, 35(1), 193.
- [4] FitzHugh, R., 1961. Impulses and physiological states in theoretical models of nerve membrane, *Biophysical journal*, 1(6), 445.
- [5] Binczak, S., Kazantsev, V., Nekorkin, V., Billbault, J., 2003. Experimental study of bifurcations in modified fitzhugh-nagumo cell, *Electronics Letters*, 39(13), 1.
- [6] Gaiko, V. A., 2011. Multiple limit cycle bifurcations of the fitzhugh–nagumo neuronal model, *Nonlinear Analysis: Theory, Methods & Applications*, 74(18), 7532–7542.
- [7] Izhikevich, E. M., FitzHugh, R., 2006. Fitzhugh-nagumo model, *Scholarpedia*, 1(9), 1349.
- [8] Rocsoreanu, C., Georgescu, A., Giurgiteanu, N., 2012. The FitzHugh-Nagumo model: bifurcation and dynamics, volume 10, Springer Science & Business Media.
- [9] Sweers, G., Troy, W. C., 2003. On the bifurcation curve for an elliptic system of fitzhugh–nagumo type, *Physica D: Nonlinear Phenomena*, 177(1), 1–22.
- [10] Tanabe, S., Pakdaman, K., 2001. Dynamics of moments of fitzhugh-nagumo neuronal models and stochastic bifurcations, *Physical Review E*, 63(3), 031911.
- [11] Wang, Q., Lu, Q., Chen, G., Duan, L., et al., 2009. Bifurcation and synchronization of synaptically coupled fhn models with time delay, *Chaos, Solitons & Fractals*, 39(2), 918–925.
- [12] Crawford, J. D., 1991. Introduction to bifurcation theory, *Reviews of Modern Physics*, 63(4), 991.
- [13] Hassard, B. D., Kazarinoff, N. D., Wan, Y.-H., 1981. Theory and applications of Hopf bifurcation, volume 41, CUP Archive.
- [14] Kuznetsov, Y. A., 2006. Andronov-hopf bifurcation, *Scholarpedia*, 1(10), 1858.
- [15] Marsden, J. E., McCracken, M., 2012. The Hopf bifurcation and its applications, volume 19, Springer Science & Business Media.
- [16] Rinzel, J., Keener, J. P., 1983. Hopf bifurcation to repetitive activity in nerve, *SIAM Journal on Applied Mathematics*, 43(4), 907–922.
- [17] Kuznetsov, Y. A., 2006. Saddle-node bifurcation, *Scholarpedia*, 1(10), 1859.
- [18] Zhou, T., 2013. Saddle-node bifurcation, in *Encyclopedia of Systems Biology*, 1889–1889, Springer.
- [19] Chen, G., Moiola, J. L., Wang, H. O., 2000. Bifurcation control: theories, methods, and applications, *International Journal of Bifurcation and Chaos*, 10(03), 511–548.
- [20] Doruk, R. O., 2010. Feedback controlled electrical nerve stimulation: A computer simulation, *Computer methods and programs in biomedicine*, 99(1), 98–112.
- [21] Hassouneh, M. A., Lee, H.-C., Abed, E. H., 2004. Washout filters in feedback control: Benefits, limitations and extensions, in *American Control Conference*, 2004. Proceedings of the 2004, volume 5, 3950–3955, IEEE.
- [22] Chen, D., Wang, H. O., Chen, G., 1998. Anti-control of hopf bifurcations through washout filters, in *Decision and Control*, 1998. Proceedings of the 37th IEEE Conference on, volume 3, 3040–3045, IEEE.
- [23] Abed, E. H., Fu, J.-H., 1986. Local feedback stabilization and bifurcation control, i. hopf bifurcation, *Systems & Control Letters*, 7(1), 11–17.
- [24] Balanov, A. G., Janson, N. B., Schöll, E., 2004. Control of noise-induced oscillations by delayed feedback, *Physica D: Nonlinear Phenomena*, 199(1), 1–12.
- [25] Aqil, M., Hong, K.-S., Jeong, M.-Y., 2012. Synchronization of coupled chaotic fitzhugh–nagumo systems, *Communications in Nonlinear Science and Numerical Simulation*, 17(4), 1615–1627.
- [26] Luo, X. S., Zhang, B., Qin, Y. H., et al., 2010. Controlling chaos in space-clamped fitzhugh–nagumo neuron by adaptive passive method, *Nonlinear Analysis: Real World Applications*, 11(3), 1752–1759.
- [27] Mishra, D., Yadav, A., Ray, S., Kalra, P. K., 2006. Controlling synchronization of modified fitzhugh-nagumo neurons under external electrical stimulation, *NeuroQuantology*, 4(1).
- [28] Rajasekar, S., Murali, K., Lakshmanan, M., 1997. Control of chaos by nonfeedback methods in a simple electronic circuit system and the fitzhugh-nagumo equation, *Chaos, Solitons & Fractals*, 8(9), 1545–1558.
- [29] Vaidyanathan, S., 2015. Adaptive control of the fitzhugh-nagumo chaotic neuron model, *International Journal of PharmTech Research*, 8(6), 117–127.
- [30] Zhang, T., Wang, J., Fei, X., Deng, B., 2007. Synchronization of coupled fitzhugh–nagumo systems via mimo feedback linearization control, *Chaos, Solitons & Fractals*, 33(1), 194–202.
- [31] Liu, J., West, M., 2001. Combined parameter and state estimation in simulation-based filtering, in *Sequential Monte Carlo methods in practice*, 197–223, Springer.
- [32] Dochain, D., 2003. State and parameter estimation

in chemical and biochemical processes: a tutorial, *Journal of process control*, 13(8), 801–818.

- [33] Evensen, G., 2009. The ensemble kalman filter for combined state and parameter estimation, *IEEE Control Systems*, 29(3), 83–104.
- [34] Ding, F., 2014. Combined state and least squares parameter estimation algorithms for dynamic systems, *Applied Mathematical Modelling*, 38(1), 403–412.
- [35] Johnson, M. L., Faunt, L. M., 1992. [1] parameter estimation by least-squares methods, *Methods in enzymology*, 210, 1–37.
- [36] Strejc, V., 1980. Least squares parameter estimation, *Automatica*, 16(5), 535–550.
- [37] Sharman, K., 1988. Maximum likelihood parameter estimation by simulated annealing, in *Acoustics, Speech, and Signal Processing, 1988. ICASSP-88., 1988 International Conference on*, 2741–2744, IEEE.
- [38] Rauch, H. E., Striebel, C., Tung, F., 1965. Maximum likelihood estimates of linear dynamic systems, *AIAA journal*, 3(8), 1445–1450.
- [39] Ghahramani, Z., Hinton, G. E., 1996. Parameter estimation for linear dynamical systems, Technical report, Technical Report CRG-TR-96-2, University of Toronto, Dept. of Computer Science.
- [40] Isidori, A., 2013. *Nonlinear control systems*, Springer Science & Business Media.
- [41] MEDANIĆ, J., USKOKOVIĆ, Z., 1983. The design of optimal output regulators for linear multivariable systems with constant disturbances, *International Journal of Control*, 37(4), 809–830.
- [42] Nguyen, N. T., 2018. Least-squares parameter identification, in *Model-Reference Adaptive Control*, 125–149, Springer.
- [43] Doruk, R. O., Zhang, K., 2018. Fitting of dynamic recurrent neural network models to sensory stimulus-response data, *Journal of Biological Physics*, .
- [44] Asai, Y., Nomura, T., Sato, S., Tamaki, A., Matsuo, Y., Mizukura, I., Abe, K., 2003. A coupled oscillator model of disordered interlimb coordination in patients with parkinson's disease, *Biological Cybernetics*, 88(2), 152–162.
- [45] Nana, L., 2009. Bifurcation analysis of parametrically excited bipolar disorder model, *Communications in Nonlinear Science and Numerical Simulation*, 14(2), 351–360.
- [46] Nagumo, J., Arimoto, S., Yoshizawa, S., 1962. An active pulse transmission line simulating nerve axon, *Proceedings of the IRE*, 50(10), 2061–2070.
- [47] Andronov, A. A., 1971. *Theory of bifurcations of dynamic systems on a plane*, volume 554, Israel Program for Scientific Translations; [available from the US Dept. of Commerce, National Technical Information Service, Springfield, Va.].
- [48] Dhooze, A., Govaerts, W., Kuznetsov, Y. A., 2003.

Matcont: a matlab package for numerical bifurcation analysis of odes, *ACM Transactions on Mathematical Software (TOMS)*, 29(2), 141–164.

- [49] Govaerts, W., Kuznetsov, Y. A., Sautois, B., 2006. *Matcont*, Scholarpedia, 1(9), 1375.
- [50] WISE, K., Deylami, F., 1991. Approximating a linear quadratic missile autopilot design using an output feedback projective control, in *AIAA Guidance, Navigation and Control Conference*, New Orleans, LA, 114–122.
- [51] Wise, K. A., Nguyen, T., 1992. Optimal disturbance rejection in missile autopilot design using projective controls, *IEEE Control Systems*, 12(5), 43–49.

Appendix

A. Graphical Illustrations

A.1. Nominal Response of the Model in (1)

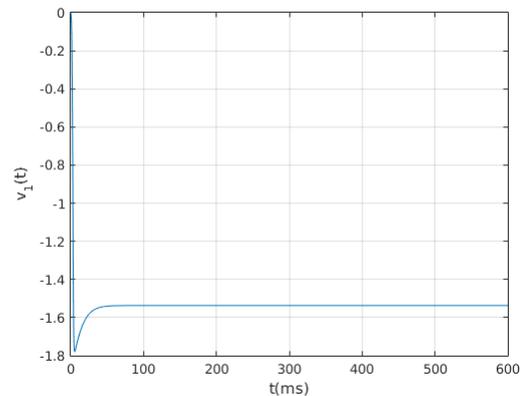


Figure 1. Variation of the membrane potential

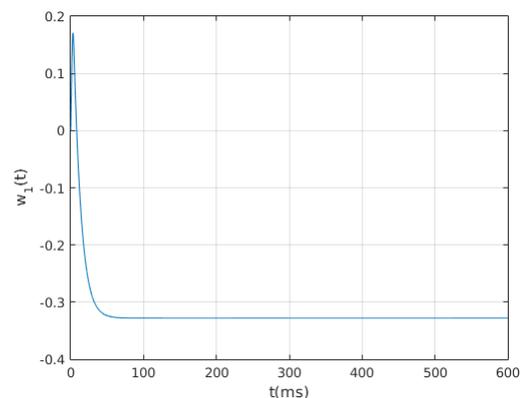


Figure 2. Variation of the recovery variable

A.2. Variation of the membrane potential under the bifurcated cases presented in Table 2.

Note the temporary decaying behavior in **Figure 5 and 6** which is an indicative of supercritical (stable limit cycle) Hopf bifurcation. Case 6 is completely unstable thus it is not explicitly displayed below.

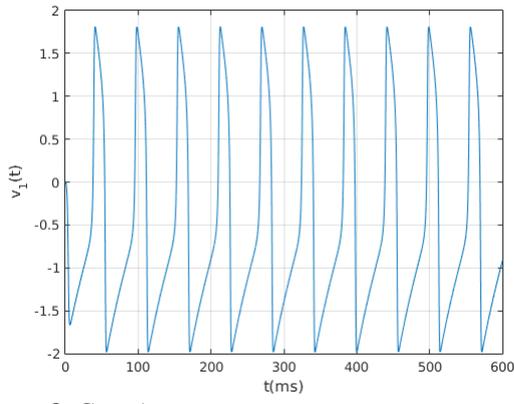


Figure 3. Case 1

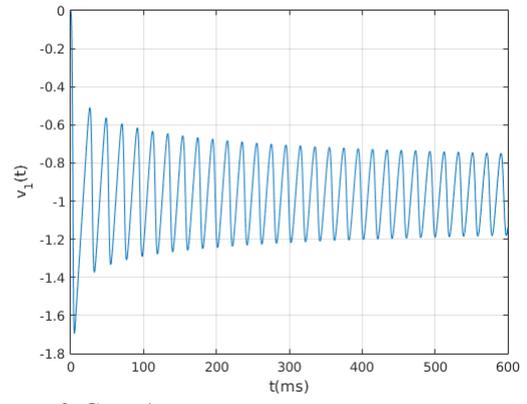


Figure 6. Case 4

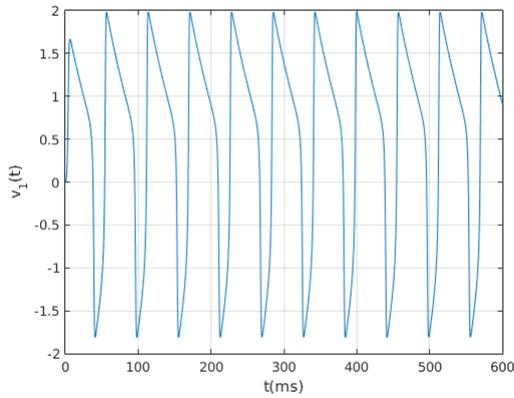


Figure 4. Case 2

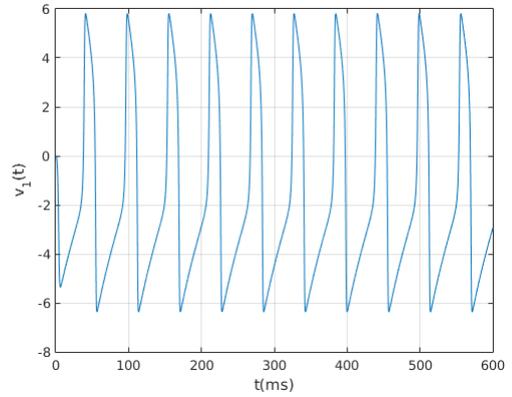


Figure 7. Case 4

A.3. Variation of the membrane potential under the controlled bifurcated cases presented in Table 2 except Case 6.

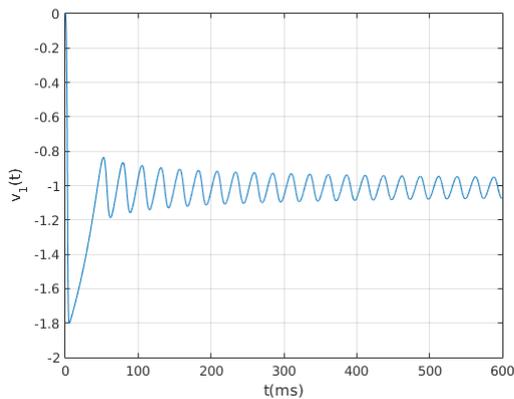


Figure 5. Case 3

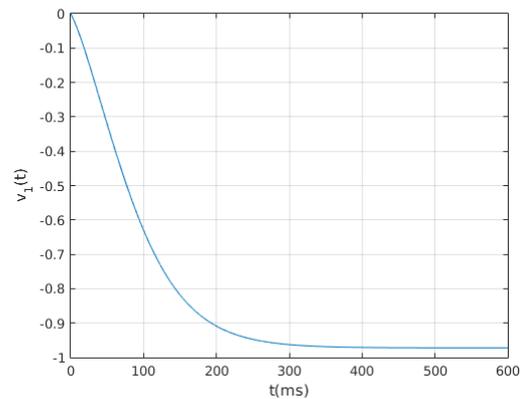


Figure 8. Case 1

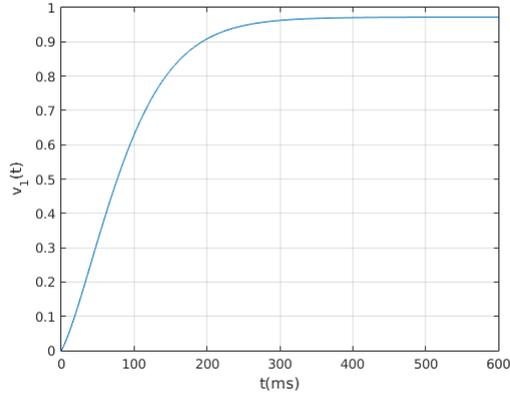


Figure 9. Case 2

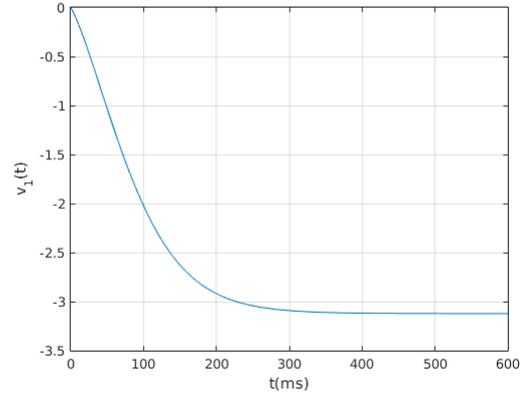


Figure 12. Case 5

A.4. Variation of the membrane potential under the controlled bifurcated cases presented in Table 4.

Case 6 is not considered here because designing a second order washout filter based controller has no considerable advantage. Note the elongation of the durations required for the membrane potentials to settle down.

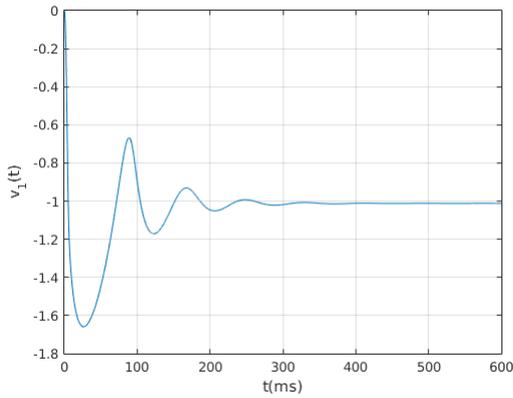


Figure 10. Case 3

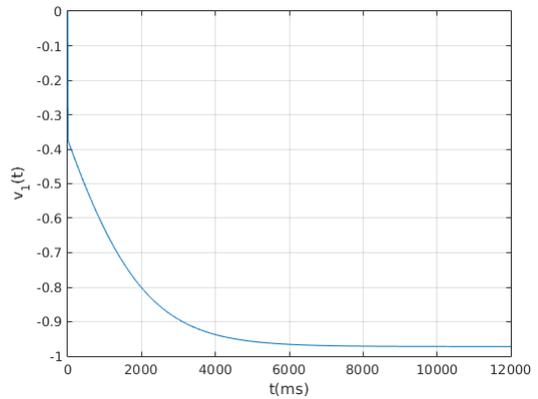


Figure 13. Case 1

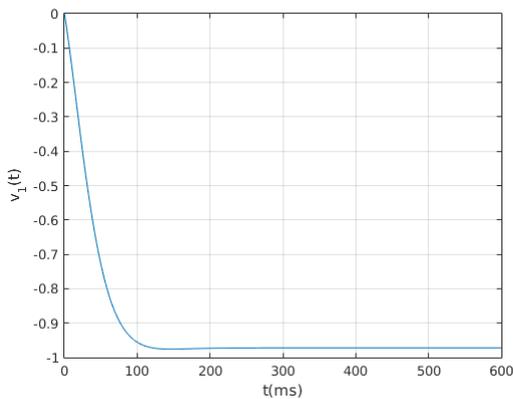


Figure 11. Case 4

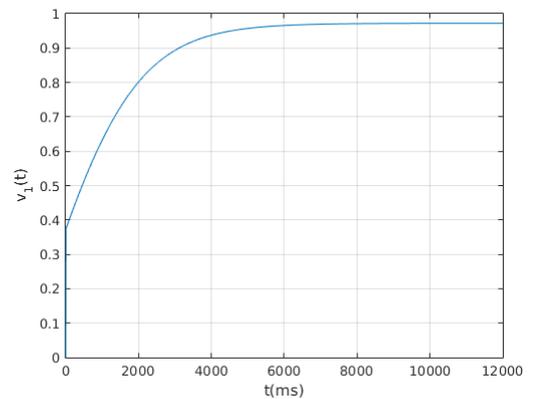


Figure 14. Case 2

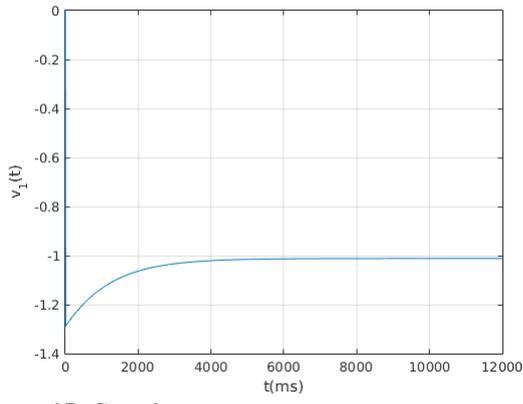


Figure 15. Case 3

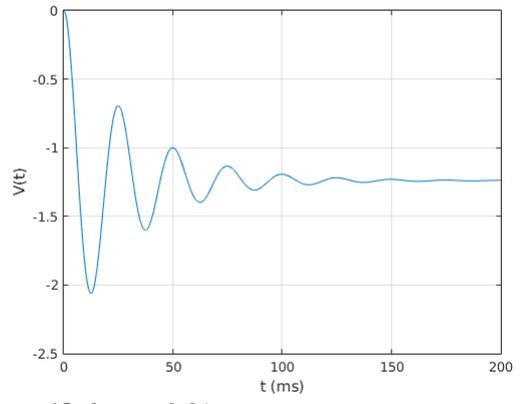


Figure 18. $k_1 = -0.01$

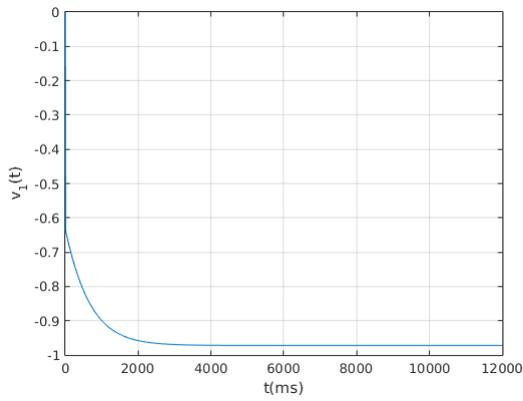


Figure 16. Case 4

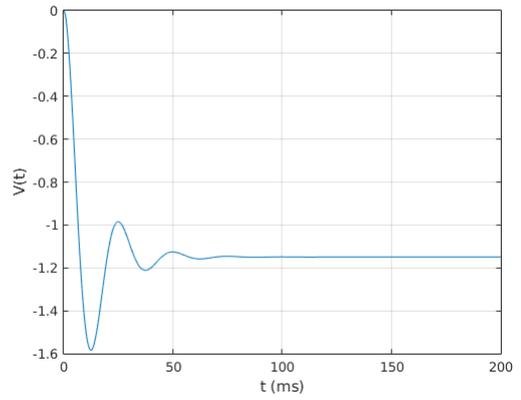


Figure 19. $k_1 = -0.1$

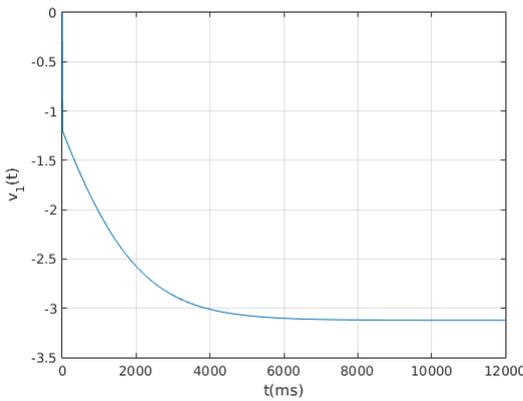


Figure 17. Case 5

A.5. The results associated with the nonlinear controller

The control gain $k_2 = 0$ so that the feedback is taken from membrane potential variable $V(t)$ only. The simulations are performed for different k_1 values which are $k_1 = \{-0.01, -0.1, -0.5, -1, -2, -5\}$.

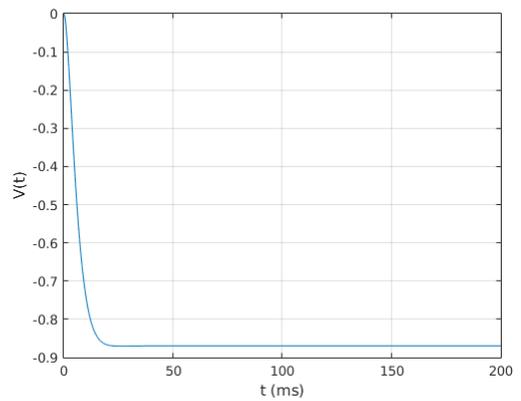


Figure 20. $k_1 = -0.5$

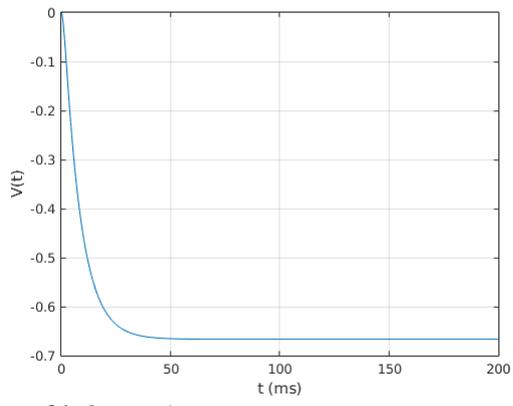


Figure 21. $k_1 = -1$

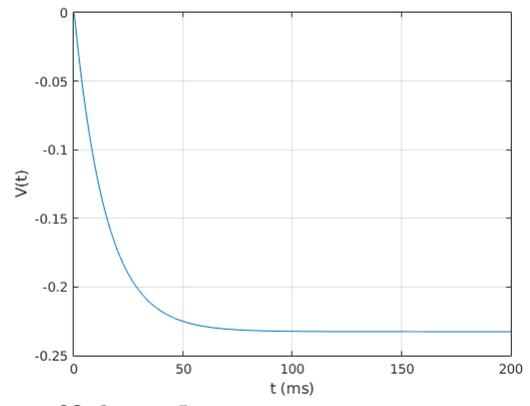


Figure 23. $k_1 = -5$

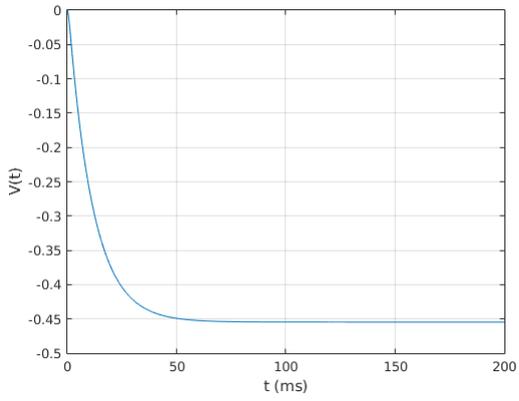


Figure 22. $k_1 = -2$