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Washout Filter Based Control of Two Hodgkin-Huxley Neurons Coupled By Electrical Synapses

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Abstract :

The purpose of this work is to present a bifurcation control of a coupled Hodgkin-Huxley model. The structure of the model is like a master-slave mechanism where two neurons are coupled by an electrical synaptic conductance. Fundamental aim is to stop the bursts generated due to Hopf bifurcations arisen from the injection of external current to the master (first) neuron. The bifurcations are analyzed and detected using the MATLAB based MATCONT toolbox and various Andronov-Hopf conditions are detected. The synaptic conductance appears to affect the occurrence of the Hopf conditions. Higher conductances lead to lesser number of Hopf points. The control of these bifurcations are performed by washout filter aided by linear quadratic projective control theory. The washout filter processes the membrane potentials only and projective control generates a gain to transform the filtered output to a current injection to the slave neuron. A detailed numerical example for one case and summary of all cases are presented. Simulations and graphical results are presented for the detailed example. Success of other cases are summarized as a table. It appears that, too small synaptic conductance values renders it difficult to attain a stable control of the bifurcations. However, one has a successful outcome for most conductance values.

Keywords: Hodgkin-Huxley neurons; Electrical synapses; Andronov-Hopf bifurcations; Washout filters; Linear quadratic regulators; Projective control

1. INTRODUCTION

The Hodgkin-Huxley Model [16] of the real neurons 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 [25] and external electric field [18, 26]. Bifurcation are problematic is biological neural networks since the diseases such as Parkinson's [19], epilepsy [21] and schizophrenia [2, 20] have some connections with the instabilities in the neural cell dynamic. In addition, various cardiac and muscle diseases possess chaotic behaviors [14] during the course of a particular disease. Because of that, controlling bifurcation 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 [6]. One of the mostly met bifurcation type is 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 [4, 5], nonlinear feedback [1] and washout filters [23, 24, 15]. 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 [25] 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.

This work is an extension of the previous studies [11, 9, 10, 12, 8]. Its purpose is to perform a bifurcation control for a coupled Hodgkin-Huxley neuron pair instead of a single one. The feedback will be received from the membrane potentials of both neurons but the control will be applied only to one of them.

First of all, we will use the MATCONT toolbox [7] on MATLAB to detect the possible one parameter bifurcation points in the coupled Hodgkin-Huxley dynamics. Secondly a washout filter is developed that is to process the membrane potentials. The output of the filter will be fed back to one of the neurons as an external current. The stable operation of the washout filter and neural dynamics combination will require a linear gain to be inserted between the filter's output and input of the neural dynamics. This gain will be evaluated using linear quadratic projective control approach. [27]. Simulations are performed to assess the closed loop performance.

2. MATERIALS AND METHODS

2.1. The Hodgkin-Huxley Model of the Squid Giant Axon

The traditional Hodgkin-Huxley model in [16] is a highly nonlinear 4^{th} order model aiming at the quantitative description of a single neuron membrane or more truly speaking, the giant axon of the European squid. It includes the dynamical properties of the membrane potential and the permeabilities of the sodium, potassium and leakage (mainly chloride) ion channels. That also has one external input which represents the current due to a possible stimulus or a test input (voltage clamp etc.). One can define it mathematically as:

$$\begin{aligned} C\frac{\mathrm{d}v}{\mathrm{d}t} &= I_{ext} - g_{Na}m^3h(v-v_{Na}) - g_Kn^4(v-v_K) - g_L(v-v_L) \\ \frac{\mathrm{d}m}{\mathrm{d}t} &= \alpha_m(v)(1-m) - \beta_m(v)m \\ \frac{\mathrm{d}n}{\mathrm{d}t} &= \alpha_n(v)(1-n) - \beta_n(v)n \\ \frac{\mathrm{d}h}{\mathrm{d}t} &= \alpha_h(v)(1-h) - \beta_h(v)h \end{aligned} \tag{1}$$

where v is the membrane potential in mV, m and h are the activation and inactivation variables of the sodium channel respectively and n is the activation of the potassium channel. The variables m, n, h are dimensionless and varies in the range $[0, 1]$. The model can be externally stimulated by an input current represented by I_{ext}. In the above equation there are also three conductance parameters g_{Na}, g_K and g_L which represents the lumped conductances of sodium, potassium and leakage channels respectively. In addition all channels have an equilibrium potential that are represented by v_{Na}, v_K and v_L for sodium, potassium and leakage channels respectively. α_j and β_j are nonlinear functions in sigmoidal forms. As we are interested in the coupled Hodgkin-Huxley equations, the details together with the synaptic coupling will be discussed in the next section.

2.2. The Coupled Hodgkin-Huxley Models

In this work, we are dealing with a coupled neural model formed by synaptically coupling two identical Hodgkin-Huxley neurons. Here, the synapse is represented by an electrical conductance g_c and the coupling is performed through electrical current inputs. As a result, one can express the coupled Hodgkin-Huxley equations as:

$$\begin{aligned} C_1\frac{\mathrm{d}v_1}{\mathrm{d}t} &= I_1 - g_{Na_1}m_1^3h_1(v_1-v_{Na}) - g_{K_1}n_1^4(v_1-v_K) - g_{L_1}(v_1-v_L) - g_c(v_1-v_2) \\ C_2\frac{\mathrm{d}v_2}{\mathrm{d}t} &= I_2 - g_{Na_2}m_2^3h_2(v_2-v_{Na}) - g_{K_2}n_2^4(v_2-v_K) - g_{L_2}(v_2-v_L) - g_c(v_2-v_1) \\ \frac{\mathrm{d}m_1}{\mathrm{d}t} &= \alpha_m(v_1)(1-m_1) - \beta_m(v_1)m_1 \\ \frac{\mathrm{d}m_2}{\mathrm{d}t} &= \alpha_m(v_2)(1-m_2) - \beta_m(v_2)m_2 \\ \frac{\mathrm{d}n_1}{\mathrm{d}t} &= \alpha_n(v_1)(1-n_1) - \beta_n(v_1)n_1 \\ \frac{\mathrm{d}n_2}{\mathrm{d}t} &= \alpha_n(v_2)(1-n_2) - \beta_n(v_2)n_2 \\ \frac{\mathrm{d}h_1}{\mathrm{d}t} &= \alpha_h(v_1)(1-h_1) - \beta_h(v_1)h_1 \\ \frac{\mathrm{d}h_2}{\mathrm{d}t} &= \alpha_h(v_2)(1-h_2) - \beta_h(v_2)h_2 \end{aligned} \tag{2}$$

where,

$$\begin{aligned} \alpha_n(v_i) &= \frac{0.1-0.01v_i}{\exp(1-0.1v_i)-1} \\ \alpha_m(v_i) &= \frac{2.5-0.1v_i}{\exp(2.5-0.1v_i)-1} \\ \alpha_h(v_i) &= 0.07\exp\left\{\frac{-v_i}{20}\right\} \\ \beta_n(v_i) &= 0.125\exp\left\{\frac{-v_i}{80}\right\} \\ \beta_m(v_i) &= 4\exp\left\{\frac{-v_i}{18}\right\} \\ \beta_h(v_i) &= \frac{1}{\exp(3-0.1v_i)+1} \end{aligned} \tag{3}$$

The definitions of the state variables in (2) can be seen in **Table 1**. The definitions of the physical parameters and their nominal values are available in **Table 2**.

Table 1: The definitions and units of the state variables and inputs in (2)

Variable	Definition	Unit
v_1	The membrane potential of the master neuron	mV
v_2	The membrane potential of the slave neuron	mV
m_1	Represents the proportion of the activating molecules of the sodium channels on the membrane of the master neuron	Dimensionless and varies between 0 and 1
m_2	Represents the proportion of the activating molecules of the sodium channels on the membrane of the slave neuron	Dimensionless and varies between 0 and 1
n_1	Represents the proportion of the activating molecules of the potassium channels on the membrane of the master neuron	Dimensionless and varies between 0 and 1
n_2	Represents the proportion of the activating molecules of the potassium channels on the membrane of the slave neuron	Dimensionless and varies between 0 and 1
h_1	Represents the proportion of the inactivating molecules of the sodium channels on the membrane of the master neuron	Dimensionless and varies between 0 and 1
h_2	Represents the proportion of the inactivating molecules of the sodium channels on the membrane of the slave neuron	Dimensionless and varies between 0 and 1
I_1	External current injection to master neuron	$\mu A/cm^2$
I_2	External current injection to slave neuron	$\mu A/cm^2$

Table 2: The definitions and units of the state variables and inputs in (2)

Variable	Definition	Value	Unit
C_1	Membrane capacitance of the master neuron	0.91	$\mu F/cm^2$
C_2	Membrane capacitance of the slave neuron	0.91	$\mu F/cm^2$
g_{Na1}	Lumped conductance of the sodium channels of the master neuron	120	mS/cm^2
g_{Na2}	Lumped conductance of the sodium channels of the slave neuron	120	mS/cm^2
g_{K1}	Lumped conductance of the potassium channels of the master neuron	36	mS/cm^2
g_{K2}	Lumped conductance of the potassium channels of the slave neuron	36	mS/cm^2
g_{L1}	Lumped conductance of the leakage channels of the master neuron	0.3	mS/cm^2
g_{L2}	Lumped conductance of the leakage channels of the slave neuron	0.3	mS/cm^2
v_{Na1}	Lumped equilibrium potential of the sodium channels of the master neuron	115	mV
v_{Na2}	Lumped equilibrium potential of the sodium channels of the slave neuron	115	mV
v_{K1}	Lumped equilibrium potential of the potassium channels of the master neuron	-12	mV
v_{K2}	Lumped equilibrium potential of the potassium channels of the slave neuron	-12	mV
v_{L1}	Lumped equilibrium potential of the leakage channels of the master neuron	10.6	mV
v_{L2}	Lumped equilibrium potential of the leakage channels of the slave neuron	10.6	mV
g_c	Conductance of the electrical synapse	0.3 (varied)	mS

In **Figures 1** and **2**, one can see a typical response pattern of the model in (2) with nominal parameters in **Table 2**.

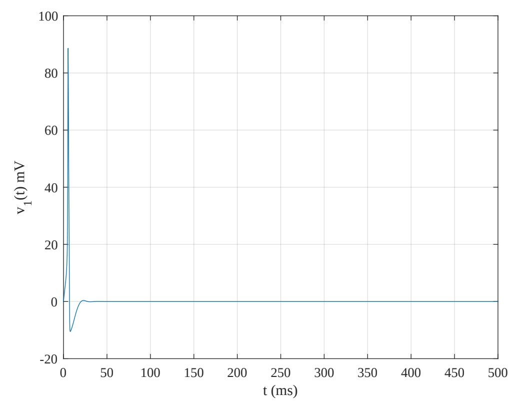

Figure 1: A typical response of the model in (2) with nominal parameters in **Table 2**. Here, the inputs are $I_1 = 0$ and $I_2 = 0$. This is the membrane potential of the master neuron $v_1(t)$.

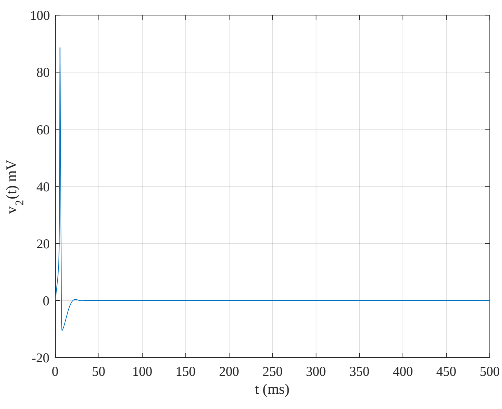

Figure 2: A typical response of the model in (2) with nominal parameters in **Table 2**. Here, the inputs are $I_1 = 0$ and $I_2 = 0$. This is the membrane potential of the master neuron $v_2(t)$.

2.3. Bifurcation Phenomenon

Bifurcations are the qualitative changes in the dynamical properties of a nonlinear system due to a parameter drift [6]. In bifurcation theory, there are two general types of bifurcations:

Local Bifurcations: These are analysed entirely through changes in the local stability properties of equilibria, periodic orbits or other invariant sets as parameters cross through critical thresholds.

Global Bifurcations: This may appear when larger invariant sets of the system 'collide' with each other, or with equilibria of the system. It is not easy to detect them just by the stability analysis of fixed points (equilibria).

In this work we will discuss the local bifurcations of the equilibrium points of the coupled Hodgkin-Huxley model in (2). Consider a general nonlinear system of the following form:

$$\dot{x} = f(x,p) \tag{4}$$

with x_e being its equilibrium i.e. $f(x_e,p) = 0$ and p is a parameter. The Jacobian of (4) will be:

$$A(x_e,p_0) = \left.\frac{\partial f(x,p)}{\partial x}\right|_{x=x_e,p=p_0} \tag{5}$$

Note that, the above derivative is evaluated at the equilibrium $x = x_e$ and the parametric setting $p = p_0$. The local bifurcations in continuous time dynamical systems may appear in the following forms:

Andronov-Hopf Bifurcation (H): Hopf bifurcation [3] a condition where a limit cycle erupts from an equilibrium in dynamical systems generated by ODEs. In this type of a bifurcation, the equilibrium changes stability via a pair of purely imaginary eigenvalues. In other words $\lambda[A(x_e,p_0)]$ should at least have one pair of $\pm j\omega$. In that case, p_0 becomes the Hopf bifurcating parameter.

Limit Point (LP): A limit point or saddle-node bifurcation [17] appears when two equilibria in a dynamical system collide and disappear. Mathematically speaking, this occurs when the critical equilibrium has one zero eigenvalue. In other words $\lambda[A(x_e,p_0)]$ should have one 0. In that case, p_0 becomes the Limit Point bifurcating parameter.

Neutral Saddle (NS): Though not considered as a bifurcation, most bifurcation software such as MATCONT detects this as a critical point. A saddle point [22] is a situation where there are two eigenvalues of the Jacobian at the respective equilibrium point appear with opposite signs. In other words $\lambda[A(x_e,p_0)]$ should at least have one pair of $\pm\gamma$ where $\gamma \in \mathcal{R}$.

The detection of above conditions by analytical derivations is a very cumbersome task. Because of that, we prefer numerical approaches. One can numerically solve the equilibrium points, evaluate the Jacobian matrices and trace the eigenvalues against varying parameter (p) in a particular range of values. Software packages such as AUTO [13] or MATCONT [7] can successfully achieve this goal. In this work we will employ MATCONT package as it is very easy to integrate with MATLAB.

2.4. Washout Filter Design

The washout filters are of high – pass nature which only allows the transient portions of the input signals. Consider the linear system below:

$$\begin{aligned}\dot{z} &= A_w z + B_w \xi \\ \psi &= A_w z + B_w \xi\end{aligned} \tag{6}$$

where $z \in \mathbb{R}^p$, $\psi \in \mathbb{R}^p$, $\xi \in \mathbb{R}^p$, $A_w \in \mathbb{R}^{p\times p}, and\, B_w \in \mathbb{R}^{p\times p}$. Here, ξ is the input of the filter. If the above dynamics is expressed in the Laplace domain the following result can be obtained:

$$G(s) = \frac{\psi(s)}{\xi(s)} = A_w\left[sI_{p\times p} - A_w\right]^{-1} B_w + B_w \tag{7}$$

where $G(s)$ is the multi-input and multi-output transfer function from input ξ to output ψ. It is clearly noted here that the following limit tends to zero.

$$\lim_{s\to 0} G(s) \to 0 \tag{8}$$

The above result means that the system in (6) blocks the steady state inputs. This property is the core part of the control mechanisms aided with a washout filter. When combined with a nonlinear system, washout filters should retain its original equilibrium points.

2.5. Linear Quadratic Projective Control Theory

The projective control approach [27] is a linear control technique that approximates an output feedback controller from an equivalent full state feedback design. This is performed through a transformation from full state feedback eigenspace to that of the output feedback by orthogonal projection. Before going into the details one needs to review a full state feedback control technique. In this work, we will prefer linear quadratic full state feedback technique. Consider a linear system depicted by:

$$\dot{x} = Ax + Bu \tag{9}$$

where $x \in \mathbb{R}^n$, $u \in \mathbb{R}^m$, $A \in \mathbb{R}^{n\times n}$, $B \in \mathbb{R}^{n\times m}$. If one designs a full state feedback controller as $u = -Kx$ the closed loop dynamics will be $\dot{x} = (A - BK)x$. Here $K \in \mathbb{R}^{m\times n}$. A practical way to derive the full state feedback controller gain K is to apply linear quadratic full state feedback (LQSF) control. That is the minimization of a quadratic performance index defined below:

$$J = \int_0^\infty \left(x^T Q x + u^T R u\right) dt \tag{10}$$

by an input defined as $u = -Kx$. In the above $Q \in \mathbb{R}^{n\times n}$ and $R \in \mathbb{R}^{m\times m}$. The solution to the above problem is obtained using the positive definite symmetric solution $P \in \mathbb{R}^{n\times n}$ of the following Algebraic Riccati Equation (ARE):

$$A^T P + PA - PBR^{-1}B^T P + Q = 0 \tag{11}$$

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The control gain K can be evaluated by the following:

$$K = R^{-1} B^T P \tag{12}$$

MATLAB can solve the above problem using the command `K=lqr(A,B,Q,R)`. The eigenspectrum of this closed loop dynamics is defined by the equation shown below:

$$(A - BK)\, V = V\Lambda \tag{13}$$

where Λ is the diagonal matrix with the entries of eigenvalues of the closed loop dynamics (or the eigenvalues $A - BK$) and V is the matrix of the corresponding eigenvectors. If one is thinking of making a static output feedback from $y = Fx$ with $F \in \mathbb{R}^{q\times n}$, $y \in \mathbb{R}^q$ as $u = -K_o y = -K_o F x$. If this feedback is assumed to retain q eigenvalues out of Λ(denote this as Λ_e and corresponding eigenvectors from V as V_q) the following should also be written:

$$(A - BKF)\, V_q = V_q \Lambda_q \tag{14}$$

Combining (13) and (14) the following can be written:

$$(A - BK)\, V = (A - BK_o F)\, V_q \tag{15}$$

This allows one to solve for K_o as:

$$K_o = K V_q F V_q^{-1} \tag{16}$$

For the nonlinear systems a linearization approach should be applied first to obtain a linear model. In local bifurcation analysis generally this will be a Jacobian based linearization. Application to the washout filter theory requires the augmentation of the linearized model in the bifurcated state and the washout filter in (6). Consider a non-autonomous nonlinear system in the following form:

$$\dot{x} = f(x, p) + Bu \tag{17}$$

and its Jacobian linearized form at bifurcated equilibrium $x = x_b$ and parameter $p = p_b$ will be:

$$\dot{\hat{x}} = A_b \hat{x} + Bu \tag{18}$$

where $u \in \mathbb{R}$ is an input to (17) and $\hat{x} = x - x_b$. In (18) can be evaluated by:

$$A_b = \left.\frac{\partial f(x,p)}{\partial x}\right|_{x=x_b, p=p_b} \tag{19}$$

When one augments (18) by (6) the following can be written:

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix}\hat{x}\\ z\end{bmatrix} = \begin{bmatrix}A_b & 0\\ B_w & A_w\end{bmatrix}\begin{bmatrix}\hat{x}\\ z\end{bmatrix} + \begin{bmatrix}B\\ 0\end{bmatrix} u \tag{20}$$

The above assumes that we are washout filtering the state vector of the bifurcated system (i.e. $\xi = \hat{x}$). The output of the filter should also be taken into account:

$$\psi = A_w z + B_w \hat{x} = \begin{bmatrix}B_w & A_w\end{bmatrix}\begin{bmatrix}\hat{x}\\ z\end{bmatrix} \tag{21}$$

In the view of projective control theory, one should have a feedback from ψ to u as $u = -K_o \psi$.

2.6. Application to Coupled Hodgkin-Huxley Model

In order to apply the theory developed so far to our coupled Hodgkin-Huxley model, we should first obtain the Jacobian of the model in (2). This can be performed from the following:

$$A_b = \begin{bmatrix}
\frac{\partial \dot{v}_1}{\partial v_1} & \frac{\partial \dot{v}_1}{\partial v_2} & \frac{\partial \dot{v}_1}{\partial m_1} & \frac{\partial \dot{v}_1}{\partial m_2} & \frac{\partial \dot{v}_1}{\partial n_1} & \frac{\partial \dot{v}_1}{\partial n_2} & \frac{\partial \dot{v}_1}{\partial h_1} & \frac{\partial \dot{v}_1}{\partial h_2}\\
\frac{\partial \dot{v}_2}{\partial v_1} & \frac{\partial \dot{v}_2}{\partial v_2} & \frac{\partial \dot{v}_2}{\partial m_1} & \frac{\partial \dot{v}_2}{\partial m_2} & \frac{\partial \dot{v}_2}{\partial n_1} & \frac{\partial \dot{v}_2}{\partial n_2} & \frac{\partial \dot{v}_2}{\partial h_1} & \frac{\partial \dot{v}_2}{\partial h_2}\\
\frac{\partial \dot{m}_1}{\partial v_1} & \frac{\partial \dot{m}_1}{\partial v_2} & \frac{\partial \dot{m}_1}{\partial m_1} & \frac{\partial \dot{m}_1}{\partial m_2} & \frac{\partial \dot{m}_1}{\partial n_1} & \frac{\partial \dot{m}_1}{\partial n_2} & \frac{\partial \dot{m}_1}{\partial h_1} & \frac{\partial \dot{m}_1}{\partial h_2}\\
\frac{\partial \dot{m}_2}{\partial v_1} & \frac{\partial \dot{m}_2}{\partial v_2} & \frac{\partial \dot{m}_2}{\partial m_1} & \frac{\partial \dot{m}_2}{\partial m_2} & \frac{\partial \dot{m}_2}{\partial n_1} & \frac{\partial \dot{m}_2}{\partial n_2} & \frac{\partial \dot{m}_2}{\partial h_1} & \frac{\partial \dot{m}_2}{\partial h_2}\\
\frac{\partial \dot{n}_1}{\partial v_1} & \frac{\partial \dot{n}_1}{\partial v_2} & \frac{\partial \dot{n}_1}{\partial m_1} & \frac{\partial \dot{n}_1}{\partial m_2} & \frac{\partial \dot{n}_1}{\partial n_1} & \frac{\partial \dot{n}_1}{\partial n_2} & \frac{\partial \dot{n}_1}{\partial h_1} & \frac{\partial \dot{n}_1}{\partial h_2}\\
\frac{\partial \dot{n}_2}{\partial v_1} & \frac{\partial \dot{n}_2}{\partial v_2} & \frac{\partial \dot{n}_2}{\partial m_1} & \frac{\partial \dot{n}_2}{\partial m_2} & \frac{\partial \dot{n}_2}{\partial n_1} & \frac{\partial \dot{n}_2}{\partial n_2} & \frac{\partial \dot{n}_2}{\partial h_1} & \frac{\partial \dot{n}_2}{\partial h_2}\\
\frac{\partial \dot{h}_1}{\partial v_1} & \frac{\partial \dot{h}_1}{\partial v_2} & \frac{\partial \dot{h}_1}{\partial m_1} & \frac{\partial \dot{h}_1}{\partial m_2} & \frac{\partial \dot{h}_1}{\partial n_1} & \frac{\partial \dot{h}_1}{\partial n_2} & \frac{\partial \dot{h}_1}{\partial h_1} & \frac{\partial \dot{h}_1}{\partial h_2}\\
\frac{\partial \dot{h}_2}{\partial v_1} & \frac{\partial \dot{h}_2}{\partial v_2} & \frac{\partial \dot{h}_2}{\partial m_1} & \frac{\partial \dot{h}_2}{\partial m_2} & \frac{\partial \dot{h}_2}{\partial n_1} & \frac{\partial \dot{h}_2}{\partial n_2} & \frac{\partial \dot{h}_2}{\partial h_1} & \frac{\partial \dot{h}_2}{\partial h_2}
\end{bmatrix} \tag{22}$$

The partial derivatives in (22) are available in **Appendix A**. In the application we will filter the membrane potentials v_1 and v_2 but apply the input to one of the neurons only. If we apply the input to the second neuron (i.e. I_2 is the input):

$$B = \begin{bmatrix}0\\ \frac{1}{C_2}\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\end{bmatrix} \tag{23}$$

The linearized form of the neuron model will be then:

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix}\hat{v}_1\\ \hat{v}_2\\ \hat{m}_1\\ \hat{m}_2\\ \hat{n}_1\\ \hat{n}_2\\ \hat{h}_1\\ \hat{h}_2\end{bmatrix} = A_b \begin{bmatrix}\hat{v}_1\\ \hat{v}_2\\ \hat{m}_1\\ \hat{m}_2\\ \hat{n}_1\\ \hat{n}_2\\ \hat{h}_1\\ \hat{h}_2\end{bmatrix} + BI_2 \tag{24}$$

As we filter both membrane potentials, we will need a second order washout filter which can be expressed as shown below:

$$\begin{aligned}
\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} &= \begin{bmatrix}a_{w11} & a_{w12}\\ a_{w21} & a_{w22}\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}b_{w11} & b_{w12}\\ b_{w21} & b_{w22}\end{bmatrix}\begin{bmatrix}v_1\\ v_2\end{bmatrix} = A_w \begin{bmatrix}z_1\\ z_2\end{bmatrix} + B_w \begin{bmatrix}v_1\\ v_2\end{bmatrix}\\
\begin{bmatrix}y_1\\ y_2\end{bmatrix} &= A_w \begin{bmatrix}z_1\\ z_2\end{bmatrix} + B_w \begin{bmatrix}v_1\\ v_2\end{bmatrix}
\end{aligned} \tag{25}$$

Concerning stability, one should ensure that A_w should be Hurwitz. One needs to augment the linearized model in (24) with the second order washout filter in (25) and form the following:

$$\frac{\mathrm{d}}{\mathrm{d}t}\begin{bmatrix}\hat{v}_1\\ \hat{v}_2\\ \hat{m}_1\\ \hat{m}_2\\ \hat{n}_1\\ \hat{n}_2\\ \hat{h}_1\\ \hat{h}_2\\ z_1\\ z_2\end{bmatrix} = \begin{bmatrix}
\frac{\partial \dot{v}_1}{\partial v_1} & \frac{\partial \dot{v}_1}{\partial v_2} & \frac{\partial \dot{v}_1}{\partial m_1} & \frac{\partial \dot{v}_1}{\partial m_2} & \frac{\partial \dot{v}_1}{\partial n_1} & \frac{\partial \dot{v}_1}{\partial n_2} & \frac{\partial \dot{v}_1}{\partial h_1} & \frac{\partial \dot{v}_1}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{v}_2}{\partial v_1} & \frac{\partial \dot{v}_2}{\partial v_2} & \frac{\partial \dot{v}_2}{\partial m_1} & \frac{\partial \dot{v}_2}{\partial m_2} & \frac{\partial \dot{v}_2}{\partial n_1} & \frac{\partial \dot{v}_2}{\partial n_2} & \frac{\partial \dot{v}_2}{\partial h_1} & \frac{\partial \dot{v}_2}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{m}_1}{\partial v_1} & \frac{\partial \dot{m}_1}{\partial v_2} & \frac{\partial \dot{m}_1}{\partial m_1} & \frac{\partial \dot{m}_1}{\partial m_2} & \frac{\partial \dot{m}_1}{\partial n_1} & \frac{\partial \dot{m}_1}{\partial n_2} & \frac{\partial \dot{m}_1}{\partial h_1} & \frac{\partial \dot{m}_1}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{m}_2}{\partial v_1} & \frac{\partial \dot{m}_2}{\partial v_2} & \frac{\partial \dot{m}_2}{\partial m_1} & \frac{\partial \dot{m}_2}{\partial m_2} & \frac{\partial \dot{m}_2}{\partial n_1} & \frac{\partial \dot{m}_2}{\partial n_2} & \frac{\partial \dot{m}_2}{\partial h_1} & \frac{\partial \dot{m}_2}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{n}_1}{\partial v_1} & \frac{\partial \dot{n}_1}{\partial v_2} & \frac{\partial \dot{n}_1}{\partial m_1} & \frac{\partial \dot{n}_1}{\partial m_2} & \frac{\partial \dot{n}_1}{\partial n_1} & \frac{\partial \dot{n}_1}{\partial n_2} & \frac{\partial \dot{n}_1}{\partial h_1} & \frac{\partial \dot{n}_1}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{n}_2}{\partial v_1} & \frac{\partial \dot{n}_2}{\partial v_2} & \frac{\partial \dot{n}_2}{\partial m_1} & \frac{\partial \dot{n}_2}{\partial m_2} & \frac{\partial \dot{n}_2}{\partial n_1} & \frac{\partial \dot{n}_2}{\partial n_2} & \frac{\partial \dot{n}_2}{\partial h_1} & \frac{\partial \dot{n}_2}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{h}_1}{\partial v_1} & \frac{\partial \dot{h}_1}{\partial v_2} & \frac{\partial \dot{h}_1}{\partial m_1} & \frac{\partial \dot{h}_1}{\partial m_2} & \frac{\partial \dot{h}_1}{\partial n_1} & \frac{\partial \dot{h}_1}{\partial n_2} & \frac{\partial \dot{h}_1}{\partial h_1} & \frac{\partial \dot{h}_1}{\partial h_2} & 0 & 0\\
\frac{\partial \dot{h}_2}{\partial v_1} & \frac{\partial \dot{h}_2}{\partial v_2} & \frac{\partial \dot{h}_2}{\partial m_1} & \frac{\partial \dot{h}_2}{\partial m_2} & \frac{\partial \dot{h}_2}{\partial n_1} & \frac{\partial \dot{h}_2}{\partial n_2} & \frac{\partial \dot{h}_2}{\partial h_1} & \frac{\partial \dot{h}_2}{\partial h_2} & 0 & 0\\
b_{w11} & b_{w12} & 0 & 0 & 0 & 0 & 0 & 0 & a_{w11} & a_{w12}\\
b_{w21} & b_{w22} & 0 & 0 & 0 & 0 & 0 & 0 & a_{w21} & a_{w22}
\end{bmatrix}\begin{bmatrix}\hat{v}_1\\ \hat{v}_2\\ \hat{m}_1\\ \hat{m}_2\\ \hat{n}_1\\ \hat{n}_2\\ \hat{h}_1\\ \hat{h}_2\\ z_1\\ z_2\end{bmatrix} + \begin{bmatrix}0\\ \frac{1}{C_2}\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\end{bmatrix} I_2$$

$$= \dot{\hat{x}}_p = A_p\hat{x}_p + B_p I_2 \tag{26}$$

The filter's output equation should also be taken into account:

$$\begin{bmatrix}y_1\\ y_2\end{bmatrix} = \begin{bmatrix}b_{w11} & b_{w12} & 0 & 0 & 0 & 0 & 0 & 0 & a_{w11} & a_{w12}\\ b_{w21} & b_{w22} & 0 & 0 & 0 & 0 & 0 & 0 & a_{w21} & a_{w22}\end{bmatrix}\begin{bmatrix}\hat{v}_1\\ \hat{v}_2\\ \hat{m}_1\\ \hat{m}_2\\ \hat{n}_1\\ \hat{n}_2\\ \hat{h}_1\\ \hat{h}_2\\ z_1\\ z_2\end{bmatrix}$$

$$= y = F_p\hat{x}_p \tag{27}$$

The filter output should be further processed by a linear gain and supplied to the input of the neuron model in (25). As we apply the control to the second input I_2 one has:

$$I_2 = -K_o y = -\begin{bmatrix}k_{o1} & k_{o2}\end{bmatrix}\begin{bmatrix}y_1\\ y_2\end{bmatrix} \tag{28}$$

where K_o is found as a result of projective control operation in **Section 2.5**. In the application one should substitute $A = A_p$, $B = B_p$ and $F = F_p$ in the equations (9), (13), (14), (15) and (16).

3. NUMERICAL APPLICATION

In this section we will present a numerical example on the application of the theory presented up to this section. We will first present the bifurcation analysis results of the model in (2) using MATCONT with the parametric settings given in **Table 2**. After that, one is eligible to see a worked example for one of the cases. Finally we will present the brief results for all the detected cases. The results will be in both tabulated and graphical forms.

3.1. The Bifurcation Analysis of Coupled HH Model

The coupled Hodgkin-Huxley model in (25) with the nominal parameters presented in **Table 2** has the following equilibrium point:

$$\begin{aligned}
v_1(\infty) &= 0.00362066881426504\\
v_2(\infty) &= 0.00362066881426504\\
m_1(\infty) &= 0.0529550868130468\\
m_2(\infty) &= 0.0529550868130468\\
n_1(\infty) &= 0.317732399760811\\
n_2(\infty) &= 0.317732399760811\\
h_1(\infty) &= 0.595994124739176\\
h_2(\infty) &= 0.595994124739176
\end{aligned} \tag{29}$$

The result shows that a very little current flows from one neuron to other due to small steady state membrane potentials. Running MATCONT continuer module starting from the above steady states for each parameter in **Table 2** will yield the results presented in **Table 3**. As a detailed example one can choose the case with $g_c = 0.3$ mS. In this case one has two bifurcations with the following equilibrium values (Current injection I_1 is also given for convenience):

$$\begin{array}{rr}
I_1 = 14.847857 & I_1 = 152.501844\\
v_1(\infty) = 6.540453 & v_1(\infty) = 21.529094\\
v_2(\infty) = 1.236544 & v_2(\infty) = 3.477715\\
n_1(\infty) = 0.420835 & n_1(\infty) = 0.638219\\
m_1(\infty) = 0.110655 & m_1(\infty) = 0.408833\\
h_1(\infty) = 0.366123 & h_1(\infty) = 0.073653\\
n_2(\infty) = 0.336785 & n_2(\infty) = 0.372046\\
m_2(\infty) = 0.061175 & m_2(\infty) = 0.079055\\
h_2(\infty) = 0.552325 & h_2(\infty) = 0.471831
\end{array} \tag{30}$$

An uncontrolled neural dynamics with $I_2 = 0$ and $I_1 = 14.847857$ $^{\mu A}/_{cm^2}$ will yield the responses shown in **Figures 3-10**.

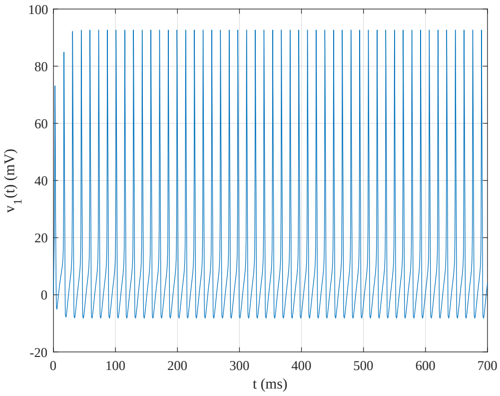

Figure 3: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The membrane potential v_1 of the master neuron.

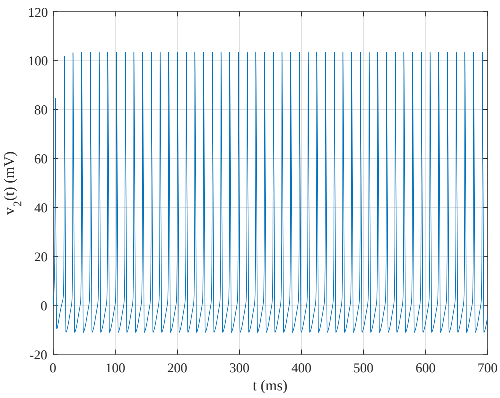

Figure 4: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The membrane potential v_2 of the slave neuron.

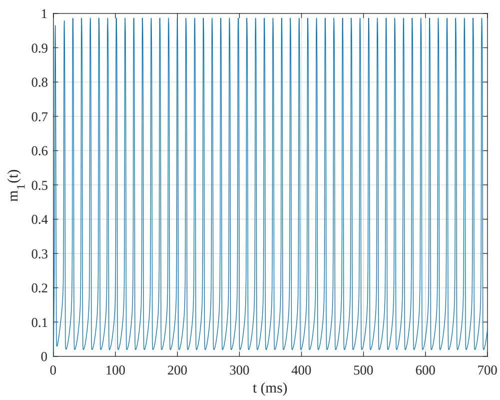

Figure 5: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The sodium channel activation m_1 of the master neuron.

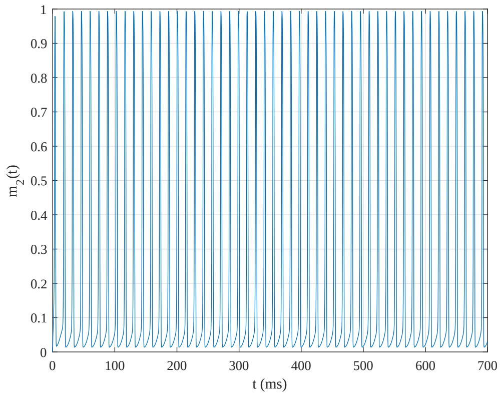

Figure 6: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The sodium channel activation m_2 of the slave neuron.

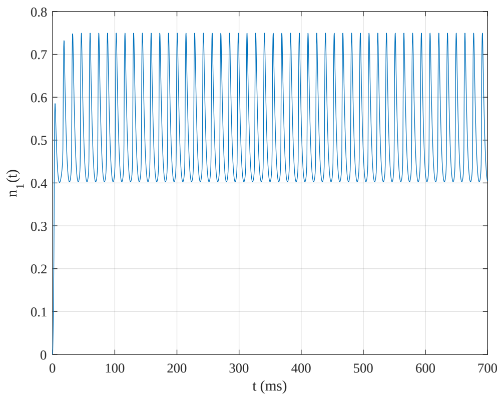

Figure 7: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The potassium channel activation n_1 of the master neuron.

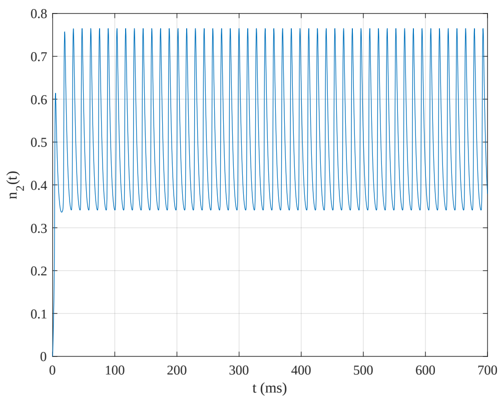

Figure 8: Uncontrolled response of (25) when $I_1 = 14.847857\ ^{\mu A}/_{cm^2}$ and $I_2 = 0$. The potassium channel activation n_2 of the slave neuron.

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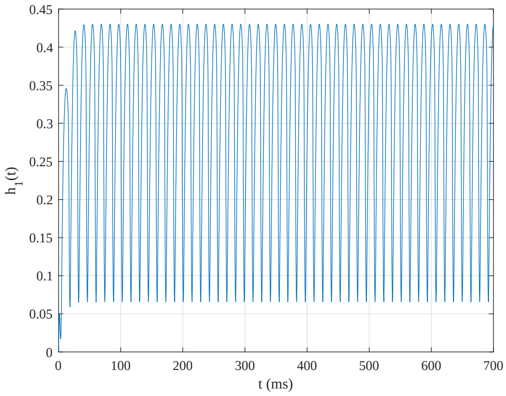

Figure 9: Uncontrolled response of (25) when $I_1 = 14.847857$ $^{\mu A}/_{cm^2}$ and $I_2 = 0$. The sodium channel inactivation h_1 of the master neuron.

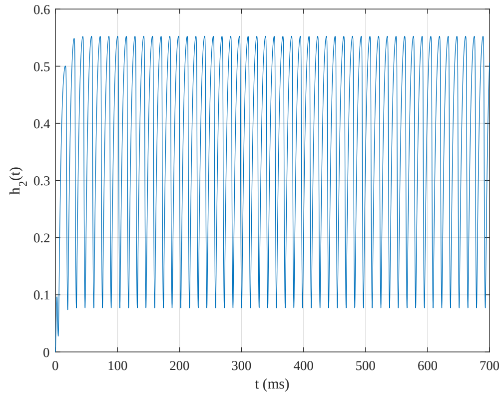

Figure 10: Uncontrolled response of (25) when $I_1 = 14.847857$ $^{\mu A}/_{cm^2}$ and $I_2 = 0$. The sodium channel inactivation h_2 of the slave neuron.

Table 3: Detected bifurcations/critical points and their associated equilibria when there is an external current injection I_1 to the master neuron. Information about the headings: H: Hopf, NS: Neutral Saddle, LP: Limit Point, Value: Value of the effected parameter I_1. The results are presented for different synaptic conductance values. It appears that, external current injection leads to Hopf bifurcations.

g_c	$v_1(\infty)$	$v_2(\infty)$	$n_1(\infty)$	$m_1(\infty)$	$h_1(\infty)$	$n_2(\infty)$	$m_2(\infty)$	$h_2(\infty)$	Value	Type
0.001	5.255025	0.008116	0.400335	0.096297	0.409347	0.317801	0.052983	0.595837	9.539644	H
0.001	21.924066	0.022362	0.643033	0.419208	0.070495	0.31802	0.053072	0.595339	154.217281	H
0.005	21.918011	0.096427	0.64296	0.419048	0.070542	0.319156	0.053537	0.592745	154.193624	H
0.01	21.910463	0.18705	0.642868	0.41885	0.070601	0.320547	0.054112	0.589564	154.163631	H
0.05	5.58047	0.228802	0.405527	0.099776	0.398213	0.321189	0.054378	0.588097	10.680526	H
0.05	21.850976	0.844242	0.642147	0.417284	0.071068	0.33069	0.058444	0.566322	153.911338	H
0.1	5.85971	0.450684	0.409981	0.102845	0.388757	0.324605	0.055814	0.580277	11.741288	H
0.1	21.779144	1.534038	0.641273	0.415396	0.071636	0.341424	0.063322	0.541667	153.582469	H
0.3	6.540453	1.236544	0.420835	0.110655	0.366123	0.336785	0.061175	0.552325	14.847857	H
0.3	21.529094	3.477715	0.638219	0.408833	0.073653	0.372046	0.079055	0.471831	152.501844	H
0.8	6.802367	2.444945	0.425007	0.113787	0.357587	0.355716	0.070315	0.508908	17.587794	H
0.8	21.331211	6.174167	0.635786	0.403653	0.075292	0.414996	0.106394	0.378225	155.743859	H
1.5	6.597305	3.266742	0.421741	0.111329	0.364262	0.368701	0.077196	0.47938	18.433365	H
1.5	22.106992	8.505227	0.645244	0.424027	0.069082	0.452024	0.135941	0.304745	177.975522	H
3	6.218991	4.027507	0.415711	0.106908	0.376734	0.380779	0.084081	0.452258	18.835379	H
3	23.786192	11.647292	0.66497	0.468506	0.057474	0.50092	0.185416	0.221266	227.573322	H
10	5.65089	4.810824	0.40665	0.100543	0.395819	0.393252	0.091713	0.424723	19.009216	H
10	24.479281	16.654449	0.672813	0.486882	0.053332	0.57429	0.287578	0.127447	284.652612	H
20	5.466247	5.019982	0.403705	0.098543	0.402107	0.396587	0.093848	0.417458	19.025163	H
30	5.397554	5.093747	0.402609	0.097808	0.404456	0.397763	0.094611	0.414907	19.028261	H
50	5.339721	5.154305	0.401686	0.097192	0.406438	0.398729	0.095241	0.412816	19.02988	H

3.2. Bifurcation Control of Coupled Hodgkin-Huxley Model

The next step is to derive the Jacobian of the coupled Hodgkin-Huxley neuron's in (22) and (23). These are shown below:

$$A_b = \begin{bmatrix} -1.9656 & 0.3297 & -218.6639 & 192.3526 & 19.3785 & 0.0000 & 0.0000 & 0.0000 \\ 0.3297 & -1.1850 & 0.0000 & 0.0000 & 0.0000 & -80.0118 & 93.0265 & 3.4345 \\ 0.0032 & 0.0000 & -0.1989 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 \\ 0.0370 & 0.0000 & 0.0000 & -3.1274 & 0.0000 & 0.0000 & 0.0000 & 0.0000 \\ -0.0045 & 0.0000 & 0.0000 & 0.0000 & -0.1379 & 0.0000 & 0.0000 & 0.0000 \\ 0.0000 & 0.0029 & 0.0000 & 0.0000 & 0.0000 & -0.1856 & 0.0000 & 0.0000 \\ 0.0000 & 0.0283 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -3.9778 & 0.0000 \\ 0.0000 & -0.0043 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -0.1191 \end{bmatrix} \tag{31}$$

$$B_b = \begin{bmatrix} 0.0000 \\ 1.0989 \\ 0.0000 \\ 0.0000 \\ 0.0000 \\ 0.0000 \\ 0.0000 \\ 0.0000 \end{bmatrix} \tag{32}$$

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Now, one needs to construct a washout filter as guided by (25). For the sake of simplicity A_w can be chosen as a diagonal but Hurwitz matrix. So one can propose a second order washout filter of the form:

$$\begin{aligned}\begin{bmatrix}\dot{z}_1\\ \dot{z}_2\end{bmatrix} &= \begin{bmatrix}-0.1 & 0\\ 0 & -0.1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}1 & 0\\ 0 & 1\end{bmatrix}\begin{bmatrix}v_1\\ v_2\end{bmatrix}\\ \begin{bmatrix}y_1\\ y_2\end{bmatrix} &= \begin{bmatrix}-0.1 & 0\\ 0 & -0.1\end{bmatrix}\begin{bmatrix}z_1\\ z_2\end{bmatrix} + \begin{bmatrix}1 & 0\\ 0 & 1\end{bmatrix}\begin{bmatrix}v_1\\ v_2\end{bmatrix}\end{aligned} \tag{33}$$

Now the augmented linearized system as shown in (20) and (21) will be obtained as:

$$\begin{aligned}A_p &= \begin{bmatrix}-1.9656 & 0.3297 & -218.6639 & 192.3526 & 19.3785 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000\\ 0.3297 & -1.1850 & 0.0000 & 0.0000 & 0.0000 & -80.0118 & 93.0265 & 3.4345 & 0.0000 & 0.0000\\ 0.0032 & 0.0000 & -0.1989 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000\\ 0.0370 & 0.0000 & 0.0000 & -3.1274 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000\\ -0.0045 & 0.0000 & 0.0000 & 0.0000 & -0.1379 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000\\ 0.0000 & 0.0029 & 0.0000 & 0.0000 & 0.0000 & -0.1856 & 0.0000 & 0.0000 & 0.0000 & 0.0000\\ 0.0000 & 0.0283 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -3.9778 & 0.0000 & 0.0000 & 0.0000\\ 0.0000 & -0.0043 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -0.1191 & 0.0000 & 0.0000\\ 1.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -0.1000 & 0.0000\\ 0.0000 & 1.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & 0.0000 & -0.1000\end{bmatrix}\\ B_p &= \begin{bmatrix}0\\ 1.0989\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\end{bmatrix}\\ F_p &= \begin{bmatrix}1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -0.1 & 0\\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -0.1\end{bmatrix}\end{aligned} \tag{34}$$

One needs to apply a linear quadratic design on A_p and B_p as discussed in (9), (10), (11) and (12). This can be done using MATLAB's `lqr(Aw,Bw,Q,R)` command. Here, one can choose a diagonal Q and R matrices for the sake of simplicity. For example:

$$\begin{aligned}Q &= 100I_{10\times 10}\\ R &= 1\end{aligned} \tag{35}$$

When one invokes the MATLAB's `lqr` command with the above settings ((34) and (35)), the following full state feedback gain K is obtained:

$$K = \begin{bmatrix}6.2992 & 10.0357 & 993.6238 & 275.3479 & -109.0120\\ -70.7955 & 63.0255 & 3.0168 & 1.1181 & 8.6447\end{bmatrix} \tag{36}$$

The above feedback will generate the following closed loop eigenvalues of $(A_p - B_pK)$:

$$\begin{aligned}&-0.0999999999999999 + j0.00000000000000\\ &-0.109788467900073 + j0.649031197939546\\ &-0.109788467900073 - j0.649031197939546\\ &-0.119137469271643 + j0.00000000000000\\ &-0.144962621418435 + j0.00000000000000\\ &-0.185519318403883 + j0.00000000000000\\ &-1.01251661131442 + j0.00000000000000\\ &-3.85311621948766 + j0.00000000000000\\ &-5.22045764353346 + j0.00000000000000\\ &-11.2701812870012 + j0.00000000000000\end{aligned} \tag{37}$$

As we receive the output y from a second order washout filter (namely, we have two outputs), one can only retain 2 eigenvalues from the above. If we attempt to retain the last two (i.e. $\lambda_q = [-5.22045764353346, -11.2701812870012]$) we will need to use the corresponding eigenvector block V_q as shown in the following:

$$V_q = \begin{bmatrix}-0.98063 & 0.03859\\ 0.03662 & -0.99526\\ 0.00062 & -0.00001\\ 0.01732 & -0.00018\\ -0.00087 & 0.00002\\ -0.00002 & 0.00026\\ -0.00083 & 0.00386\\ 0.00003 & -0.00038\\ 0.19151 & -0.00346\\ -0.00715 & 0.08910\end{bmatrix} \tag{38}$$

Applying (16) using $F = F_p$ will yield the projected feedback gain K_o as:

$$K_o = \begin{bmatrix}0.5573 & 8.801\end{bmatrix} \tag{39}$$

When this gain applied as $I_2 = -K_o y$ with y defined in (28), the output feedback closed loop eigenvalues should be obtained as:

$$\begin{aligned}&-11.2701812870012 + j0.00000000000000\\ &-5.22045764353346 + j0.00000000000000\\ &-3.62452553259496 + j0.00000000000000\\ &-0.0374010987824154 + j0.656505366266219\\ &-0.0374010987824154 - j0.656505366266219\\ &-0.0170171483163279 + j0.00000000000000\\ &-0.197312057426063 + j0.00000000000000\\ &-0.144979527546607 + j0.00000000000000\\ &-0.100000000000000 + j0.00000000000000\\ &-0.119368771442084 + j0.00000000000000\end{aligned} \tag{40}$$

The first two eigenvalues above are the retained ones (so the projection operation worked as expected). The other eigenvalues are obtained at stable locations. So we have a successful outcome in linear domain. In order to have a realistic test, we will need to perform a simulation with the original nonlinear model in (25). When one performs a simulation with original coupled HH dynamics in (25), the washout filter in (33) and the feedback gain in (39) one will be able to see the results in **Figures 11-18**. One can also see the required level of the current I_2 in **Figure 19**.

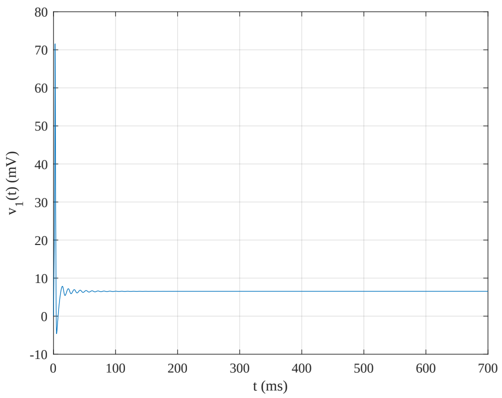

Figure 11: Controlled variation of membrane potential of the master neuron v_1 with the washout filter in (33) and the feedback gain in (39).

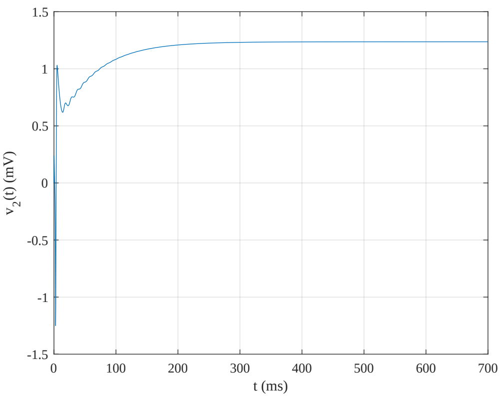

Figure 12: Controlled variation of membrane potential of the slave neuron v_2 with the washout filter in (33) and the feedback gain in (39).

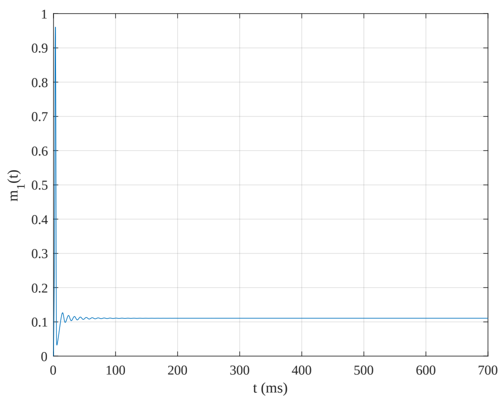

Figure 13: Controlled variation of sodium channel activation of the master neuron m_1 with the washout filter in (33) and the feedback gain in (39).

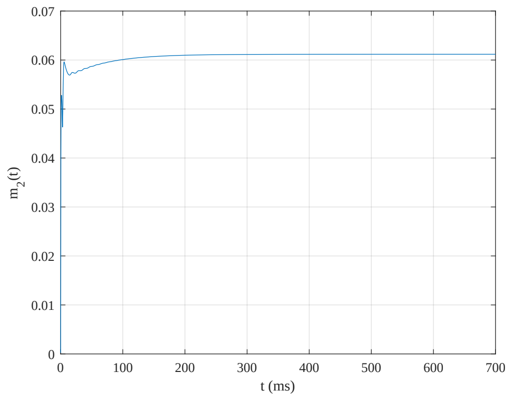

Figure 14: Controlled variation of sodium channel activation of the slave neuron m_2 with the washout filter in (33) and the feedback gain in (39).

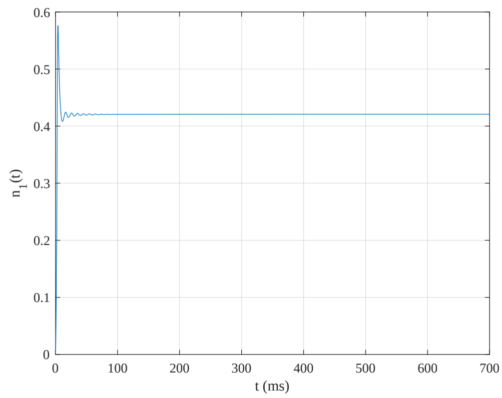

Figure 15: Controlled variation of potassium channel activation of the master neuron n_1 with the washout filter in (33) and the feedback gain in (39).

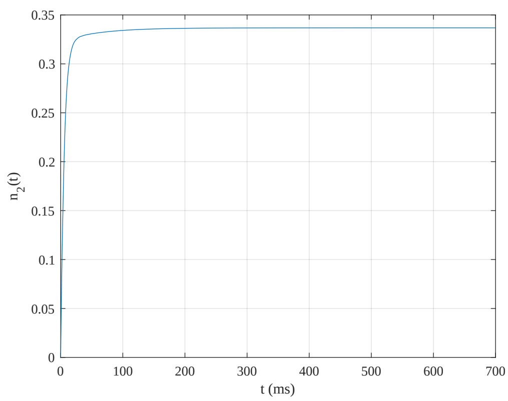

Figure 16: Controlled variation of potassium channel activation of the slave neuron n_2 with the washout filter in (33) and the feedback gain in (39).

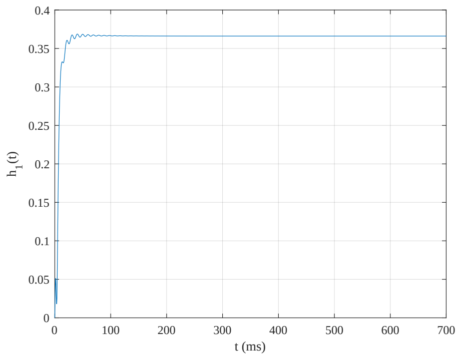

Figure 17: Controlled variation of sodium channel inactivation of the master neuron h_1 with the washout filter in (33) and the feedback gain in (39).

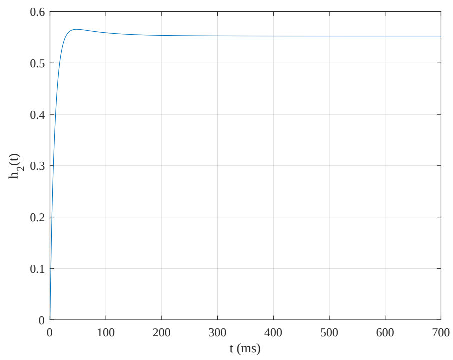

Figure 18: Controlled variation of sodium channel inactivation of the slave neuron h_2 with the washout filter in (33) and the feedback gain in (39).

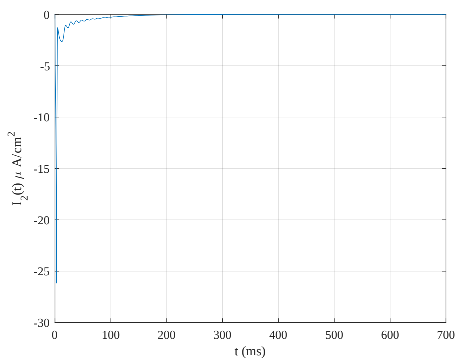

Figure 19: The required level of current injection to the slave neuron I_2 with the washout filter in (33) and the feedback gain in (39).

The final state of the membrane potentials, activations and inactivations are obtained from simulation as:

$$\begin{aligned} v_1(\infty) &= 6.5405 \\ v_2(\infty) &= 1.2365 \\ m_1(\infty) &= 0.11066 \\ m_2(\infty) &= 0.061175 \\ n_1(\infty) &= 0.42083 \\ n_2(\infty) &= 0.33678 \\ h_1(\infty) &= 0.36612 \\ h_2(\infty) &= 0.55233 \end{aligned} \tag{41}$$

Comparing with (30), one can deduce that our washout filter design worked qıuite successfully and retained the original equilibrium points of bifurcation when $I_1 = 14.848$.

3.3. Results of Bifurcation Control for Other Cases

In this section, we will present the brief results of bifurcation control for all other cases in **Table 3** (i.e. all cases other than the example in **Section 3.2**). The results are presented in **Table 4**. One can see, which cases are successful and the Q and R settings that leads to a successful result. In addition the Q matrix is formed mostly as a more generic diagonal form as shown below:

$$Q = \begin{bmatrix} q_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & q_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \tag{42}$$

In the case of other options such as $Q = qI_{10\times 10}$ it is indicated in the table.

4. DISCUSSION & CONCLUSION

In this research a method is presented to develop a control algorithm for stabilizing the bifurcations existing in a coupled Hodgkin-Huxley dynamics. The two neurons are coupled by an electrical synaptic conductance. The bifurcations are due to an injection of external current to the master (first) neuron. In order to detect all the bifurcations we first employed the MATCONT software (a free MATLAB toolbox by [7]) and it revealed that we have one or two Andronov-Hopf cases depending on the strength of the synapse (i.e. the level of synaptic conductance). Very high synaptic conductance such as $g_c > 20$ mS leads to a single occurrence of a Hopf phenomenon (see **Table 3**). However, in most of the cases one has two cases with one small external current injection in the range $9 < I_1 < 20$ $^{\mu A}/_{\text{cm}^2}$ and with one higher current injection in the range $150 < I_1 < 300$ $^{\mu A}/_{\text{cm}^2}$. Concerning the bifurcation control attempts one can state that, lower conductance values such as $g_c = 0.001$ mS leads to problems in stabilization of the neural couple. In the case of $g_c = 0.05$ mS and $g_c = 0.1$ mS there exists a small level of chattering (or oscillations). When the conductance g_c has higher values, it seems much easier to find stable controls. In addition to all those, having $g_c > 0.8$ mS leads to a stable outcome with the same Q and R settings regardless of the value of g_c.

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Table 4: Brief results of bifurcation control of coupled Hodgkin-Huxley neurons in (25). The bifurcating parameter is the external current injection to master neuron (I_1). The control is applied to slave neuron (to I_2). The order of cases are same as that of **Table 3**. The linear quadratic matrix settings are also given (Q, R). In all cases $R = 1$ unless otherwise noted.

g_c	Settings for Q and R	Success?
0.001	Not Found	No. Very difficult to stabilize. Oscillations does not cease.
0.001	Not Found	No. Very difficult to stabilize. Oscillations does not cease.
0.005	Diagonal $Q = 100I_{10\times10}$	Yes. Works with slight level of chattering at the steady state.
0.01	Diagonal $Q = 100I_{10\times10}$ and $R = 0.1$	Yes. Works with slight level of chattering at the steady state.
0.05	Q as (42) with $q_1 = 10000$, $q_2 = 100$	Yes
0.05	Q as (42) with $q_1 = 20000$, $q_2 = 100$	Yes
0.1	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
0.1	Q as (42) with $q_1 = 20000$, $q_2 = 100$	Yes
0.3	Q as (42) with $q_1 = 10000$, $q_2 = 100$	Yes
0.3	Q as (42) with $q_1 = 10000$, $q_2 = 100$	Yes
0.8	Q as (42) with $q_1 = 10000$, $q_2 = 100$	Yes
0.8	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
1.5	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
1.5	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
3	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
3	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
10	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
10	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
20	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
30	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes
50	Q as (42) with $q_1 = 5000$, $q_2 = 100$	Yes

A. JACOBIAN PARTIAL DERIVATIVES

$$\frac{\partial \dot{v}_1}{\partial v_1} = -\frac{g_{Na\,1}\, h_1\, {m_1}^3 + g_{K\,1}\, {n_1}^4 + g_c + g_{L\,1}}{C_1}$$

$$\frac{\partial \dot{v}_1}{\partial v_2} = \frac{g_c}{C_1}$$

$$\frac{\partial \dot{v}_1}{\partial m_1} = -\frac{3\, g_{Na\,1}\, h_1\, {m_1}^2\, (v_1 - v_{Na\,1})}{C_1}$$

$$\frac{\partial \dot{v}_1}{\partial m_2} = 0$$

$$\frac{\partial \dot{v}_1}{\partial n_1} = -\frac{4\, g_{K\,1}\, {n_1}^3\, (v_1 - v_{K\,1})}{C_1}$$

$$\frac{\partial \dot{v}_1}{\partial n_2} = 0$$

$$\frac{\partial \dot{v}_1}{\partial h_1} = -\frac{g_{Na\,1}\, {m_1}^3\, (v_1 - v_{Na\,1})}{C_1}$$

$$\frac{\partial \dot{v}_1}{\partial h_2} = 0$$

$$\frac{\partial \dot{v}_2}{\partial v_1} = \frac{g_c}{C_2}$$

$$\frac{\partial \dot{v}_2}{\partial v_2} = -\frac{g_{Na\,2}\, h_2\, {m_2}^3 + g_{K\,2}\, {n_2}^4 + g_c + g_{L\,2}}{C_2}$$

$$\frac{\partial \dot{v}_2}{\partial m_1} = 0$$

$$\frac{\partial \dot{v}_2}{\partial m_2} = -\frac{3\, g_{Na\,2}\, h_2\, {m_2}^2\, (v_2 - v_{Na\,2})}{C_2}$$

$$\frac{\partial \dot{v}_2}{\partial n_1} = 0$$

$$\frac{\partial \dot{v}_2}{\partial n_2} = -\frac{4\, gk_2\, {n_2}^3\, (v_2 - v_{K\,2})}{C_2}$$

$$\frac{\partial \dot{v}_2}{\partial h_1} = 0$$

$$\frac{\partial \dot{m}_1}{\partial h_2} = -\frac{g_{Na\,2}\, {m_2}^3\, (v_2 - v_{Na\,2})}{C_2}$$

$$\frac{\partial \dot{v}_2}{\partial v_1} = \frac{2\, m_1\, e^{-\frac{v_1}{18}}}{9} + \frac{m_1 - 1}{10\, \left(e^{\frac{5}{2} - \frac{v_1}{10}} - 1\right)} + \frac{e^{\frac{5}{2} - \frac{v_1}{10}}\, \left(\frac{v_1}{10} - \frac{5}{2}\right)\, (m_1 - 1)}{10\, \left(e^{\frac{5}{2} - \frac{v_1}{10}} - 1\right)^2}$$

$$\frac{\partial \dot{m}_1}{\partial v_2} = 0$$

$$\frac{\partial \dot{m}_1}{\partial m_1} = \frac{\partial \dot{m}_1}{\partial v_2} = \frac{\frac{v_1}{10} - \frac{5}{2}}{e^{\frac{5}{2} - \frac{v_1}{10}} - 1} - 4\, e^{-\frac{v_1}{18}}$$

$$\frac{\partial \dot{m}_1}{\partial m_2} = 0$$

$$\frac{\partial \dot{m}_1}{\partial n_1} = 0$$

$$\frac{\partial \dot{m}_1}{\partial n_2} = 0$$

$$\frac{\partial \dot{m}_1}{\partial h_1} = 0$$

$$\frac{\partial \dot{m}_1}{\partial h_2} = 0$$

$$\frac{\partial \dot{m}_2}{\partial v_1} = 0$$

$$\frac{\partial \dot{m}_2}{\partial v_2} = \frac{2\, m_2\, e^{-\frac{v_2}{18}}}{9} + \frac{m_2 - 1}{10\, \left(e^{\frac{5}{2} - \frac{v_2}{10}} - 1\right)} + \frac{e^{\frac{5}{2} - \frac{v_2}{10}}\, \left(\frac{v_2}{10} - \frac{5}{2}\right)\, (m_2 - 1)}{10\, \left(e^{\frac{5}{2} - \frac{v_2}{10}} - 1\right)^2}$$

$$\frac{\partial \dot{m}_2}{\partial m_1} = 0$$

$$\frac{\partial \dot{m}_2}{\partial m_2} = 0\, \frac{\frac{v_2}{10} - \frac{5}{2}}{e^{\frac{5}{2} - \frac{v_2}{10}} - 1} - 4\, e^{-\frac{v_2}{18}}$$

$$\frac{\partial \dot{m}_2}{\partial n_1} = 0$$

$$\frac{\partial \dot{m}_2}{\partial n_2} = 0$$

$$\frac{\partial \dot{m}_2}{\partial h_1} = 0$$

$$\frac{\partial \dot{m}_2}{\partial h_2} = 0$$

$$\frac{\partial \dot{n}_1}{\partial v_1} = \frac{n_1\, e^{-\frac{v_1}{80}}}{640} + \frac{n_1 - 1}{100\, \left(e^{1 - \frac{v_1}{10}} - 1\right)} + \frac{e^{1 - \frac{v_1}{10}}\, \left(\frac{v_1}{100} - \frac{1}{10}\right)\, (n_1 - 1)}{10\, \left(e^{1 - \frac{v_1}{10}} - 1\right)^2}$$

$$\frac{\partial \dot{n}_1}{\partial v_2} = 0$$

$$\frac{\partial \dot{n}_1}{\partial m_1} = 0$$

$$\frac{\partial \dot{n}_1}{\partial m_2} = 0$$

$$\frac{\partial \dot{n}_1}{\partial n_1} = \frac{\frac{v_1}{100} - \frac{1}{10}}{e^{1 - \frac{v_1}{10}} - 1} - \frac{e^{-\frac{v_1}{80}}}{8}$$

$$\frac{\partial \dot{n}_1}{\partial n_2} = 0$$

$$\frac{\partial \dot{n}_1}{\partial h_1} = 0$$

$$\frac{\partial \dot{n}_1}{\partial h_2} = 0$$

$$\frac{\partial \dot{n}_2}{\partial v_1} = 0$$

$$\frac{\partial \dot{n}_2}{\partial v_2} = 0\frac{n_2\, e^{-\frac{v_2}{80}}}{640} + \frac{n_2 - 1}{100\, \left(e^{1-\frac{v_2}{10}} - 1\right)} + \frac{e^{1-\frac{v_2}{10}}\, \left(\frac{v_2}{100} - \frac{1}{10}\right)\, (n_2 - 1)}{10\left(e^{1-\frac{v_2}{10}} - 1\right)^2}$$

$$\frac{\partial \dot{n}_2}{\partial m_1} = 0$$

$$\frac{\partial \dot{n}_2}{\partial m_2} = 0$$

$$\frac{\partial \dot{n}_2}{\partial n_1} = 0$$

$$\frac{\frac{\partial \dot{n}_2}{\partial n_2} = \frac{v_2}{100} - \frac{1}{10}}{e^{1-\frac{v_2}{10}} - 1} - \frac{e^{-\frac{v_2}{80}}}{8}$$

$$\frac{\partial \dot{n}_2}{\partial h_1} = 0$$

$$\frac{\partial \dot{n}_2}{\partial h_2} = 0$$

$$\frac{\partial \dot{h}_1}{\partial v_1} = \frac{7\, e^{-\frac{v_1}{20}}\, (h_1 - 1)}{2000} - \frac{h_1\, e^{3-\frac{v_1}{10}}}{10\left(e^{3-\frac{v_1}{10}} + 1\right)^2}$$

$$\frac{\partial \dot{h}_1}{\partial v_2} = 0$$

$$\frac{\partial \dot{h}_1}{\partial m_1} = 0$$

$$\frac{\partial \dot{h}_1}{\partial m_2} = 0$$

$$\frac{\partial \dot{h}_1}{\partial n_1} = 0$$

$$\frac{\partial \dot{h}_1}{\partial n_2} = 0$$

$$\frac{\partial \dot{h}_1}{\partial h_1} = -\frac{7\, e^{-\frac{v_1}{20}}}{100} - \frac{1}{e^{3-\frac{v_1}{10}} + 1}$$

$$\frac{\partial \dot{h}_1}{\partial h_2} = 0$$

$$\frac{\partial \dot{h}_2}{\partial v_1} = 0$$

$$\frac{\partial \dot{h}_2}{\partial v_2} = \frac{7\, e^{-\frac{v_2}{20}}\, (h_2 - 1)}{2000} - \frac{h_2\, e^{3-\frac{v_2}{10}}}{10\left(e^{3-\frac{v_2}{10}} + 1\right)^2}$$

$$\frac{\partial \dot{h}_2}{\partial m_1} = 0$$

$$\frac{\partial \dot{h}_2}{\partial m_2} = 0$$

$$\frac{\partial \dot{h}_2}{\partial n_1} = 0$$

$$\frac{\partial \dot{h}_2}{\partial n_2} = 0$$

$$\frac{\partial \dot{h}_2}{\partial h_1} = 0$$

$$\frac{\partial \dot{h}_2}{\partial h_2} = -\frac{7\, e^{-\frac{v_2}{20}}}{100} - \frac{1}{e^{3-\frac{v_2}{10}} + 1}$$

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