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Bifurcation Analysis of a System of Morris-Lecar Neurons with Time Delayed Coupling

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Abstract:
In this study, we consider two coupled Morris-Lacer neurons and study the effect of time delay(τ) on the behavior of neuron via electrical coupling. This study focuses on the effects that the electrical coupling strength (γ), and Leakage conductance of the membrane (G_m) causes on the dynamics of the system. Stable states of the system are determined with respect to $\gamma$and τ using the appropriate phase models, and the regions of validity of the phase models in the membrane voltage signal against axonal distance plane using finite difference method estimated. Analysis of electrical coupling strength and specific membrane capacitance are analyzed. When the value of electrical coupling strength is less, it indicates a higher response to the variation of membrane voltage signal. As the electrical coupling strength increases, the voltage of the neurons decreases. When the axonal distance (x) increases, specific membrane capacitance C, also increases to optimum level then decreases after attaining axonal distance of 4nm. This shows that with appropriate choice of the voltages of $\gamma$the neurons can be made arbitrarily close in finite time and will remain that close for all subsequent time. As the current density is increased the amplitude of stable periodic responses decreases into a stable fixed point which is determined by both calcium and potassium ions. The results obtained were presented graphically and discussed.

Keywords: *Electrical coupling strength (γ), Leakage conductance of the membrane (G_m), Partial differential Equation (PDE), Crank-Nicolson Scheme (CNS), time delay (τ) Decay constant rate (κ) and membrane voltage signal*

1. Introduction and Literature Review

In this section, gap - junction coupling between neurons introduced. Related studies carried out by other scholars have also been cited. Some bsic definitions and the objectives of the study have been clearly stated.

1.1. Introduction

Neurons are the fundamental processing and information carrying units of the central nervous system, involved with sensory, cognitive, regulatory, motor, and enteric (gut) nervous system. The anatomical variation of these neurons is large, but the general morphology allows these cells to be classed as neurons. Neurons are spatially extensive, heterogeneous objects. They typically consist of a dendritic tree where the majority of inputs to the cell are received; a soma, or cell body, where these inputs are integrated, an axon hillock where the integrated inputs can cause the initiation of an action potential; and an axon where the action potential propagates along until it reaches the synaptic terminal and causes the release of neurotransmitter onto a postsynaptic cell. The type of model one uses to represent a neuron depends upon a balance between mathematical tractability and biological realism and on the issue that is

being addressed. A common technique in neuronal modeling is to represent the neuron as a single-compartment object that ignores the spatial anatomy of the cell. Although this simplification allows for greater mathematical tractability and computational efficiency, many neurons are not electrotonically compact. Thus, single-compartment models cannot be expected to fully capture the electrical behavior of neurons.

The soma; is the central cell body of the neuron. It contains the neuron's genetic material. It is responsible for maintaining the neuron's vital activity, processing incoming currents and generation of a response signal. It is surrounded by the cell membrane, which bounds the soma and defines the intracellular area. The cell membrane contains the ionic channels, which are responsible for transmission of ions and play an important role in the generation of electrical signals by the neuron.

The dendrites; are branch-like protrusions which come out of the cell body. A typical cell has a large number of the dendrites which are highly branched. They are responsible for delivering information from the other neurons and receptors to the cell.

The axon; is a long fiber-like extension of the soma. It is responsible for the transmission of a signal to another neuron. The space outside the neuron is filled by the intercellular fluid. Not all neurons necessarily fit into this analysis but structure of the vast majority of neurons will be considered only.

Electrical coupling frequently occurs between neurons of similar type and sometimes between the neurons of different types. In the case when electrical coupling occurs between the same types of neurons, it is believed to contribute to synchronization of the neuronal behavior. Chemical and electrical coupling often occur together, and in these cases they can lead to complicated behavior, for example, bistable synchronous and anti-synchronous behavior patterns.

Neurons, the building blocks of the central nervous system, are highly complex dynamical systems. To understand the way neurons interact, simplified mathematical models have been used, which aim to capture the essence of their underlying dynamics. Generic bifurcation models fall into this class of simplified neuron models. They aim to describe the underlying dynamics of the neuron by systems of ordinary differential equations. When these models are used in networks, techniques from the field of nonlinear dynamics can be applied to study phenomena of synchronization and pattern emergence. The essence of mathematical modeling is to find the right tradeoff between accuracy and simplicity. One of the most important questions in computational neuroscience is therefore which features of the complex dynamics observed in biological neurons form the essence of the specific tasks fulfilled by that neuron. Generic bifurcation models provide a promising middle way between detailed models used by experimentalists and the more simple threshold and rate models used by computational neuroscientists. This project has investigated to which extent two generic bifurcation models of different complexity grasp the essential dynamical features that play a role in cooperative neural behavior.Neurons being the fundamental unit for transmitting signals in nervous system as a biological membrane, it has played an important role in many of life's processes. Many of these processes are electrical and the different electrical behavior of nerve cells can be measured experimentally. The flow of ions across the membrane is responsible for the production of membrane potential. The mathematical formulation of the function of neuron was given firstly by H-H model. The variation of parameters of H-H equations leads to bifurcation which refers to quantitative changes in the solution structure of dynamical systems.

1.2. Signal Generation and Procession in Neuron

On the intracellular level signals are transmitted mostly in electrical form. The neuron receives an input current from the other neurons and receptors via its dendrites, processes this input electrical current and gene rates some output. An output is then transmitted via the neuron's axon in the form of a self-regenerating electrical wave, also known as an action potential or spike.

Consider a neuron in its steady state, i.e. with an absence of any input. Both the interior and exterior of the neuron contain some number of charged ions. The concentrations of ions of each type outside and inside of the neuron are different. This difference in concentrations causes a voltage drop or potential difference across the cell membrane, which are typically (between -50mV to -80 mV) depending on the type of neuron being examined. This steady state voltage drop is also known as the resting potential or the equilibrium potential of a neuron.

The energy for maintaining non-zero equilibrium potential is produced by a mechanism which is called a biological ionic pump. The biological ionic pump transfers the ions from one side of membrane to another using the power produced by burning sugar and molecular oxygen. However, there is a mechanism which acts against the biological ionic pump. The cell membrane could let in some particular types of ions through ionic channels. Each ionic channel (or gate) is responsible for its particular type of ion and could vary between an open and closed state depending on the membrane voltage and other biological properties. When an ionic channel is open, the ions governed by this channel are able to cross the membrane in the direction of their concentration and electro-chemical gradients. As the ions flow through an open channel, it changes both the membrane potential and the distribution of concentrations on the sides of the membrane.

As the membrane voltage reaches a certain value, electro-chemical and concentration gradients become balanced and ionic flow stops. This membrane voltage is called equilibrium or reversal potential for the type of ions under consideration. The term reversal is used because when the membrane potential passes through the equilibrium potential of a certain ion type the direction of flow of that type of ion reverses. As long as we consider a particular type of neuron with the preset structure of ionic channels and pumps, the equilibrium potentials of each type of ions involved in the process are determined by that structure. It is possible to compute the equilibrium potential of each type of ion by evaluating its concentration gradient using the principles of statistical mechanics and finding the corresponding membrane potential. Equilibrium potentials for each type of ion involved in the process are different.

As was mentioned above, in the absence of any external input the biological ionic pump and the ionic channels balance each other, keeping the neuron at its resting potential. If the equilibrium potential of some type of ion is greater than the resting potential of the neuron, then the flow of ions of that type would try to increase the membrane potential in case of the corresponding ionic channel

being opened. The current caused by this type of the ion is called excitatory or depolarizing current. The current depolarizes the cell membrane by making its potential more positive and excites the cell membrane by releasing the energy stored by the biological ionic pump. Otherwise the current is called hyperpolarizing or recovery current.

1.3. Literature Review

Neurons can exchange signals via two qualitatively different mechanisms; electrical coupling realized by gap-junction connections and chemical coupling provided by neurotransmitters. Early studies of neurons assumed that most of the information in higher mammals is transmitted by chemical coupling. However, newer studies suggest that gap - junctional connections in higher mammals occur more frequently than was initially assumed. Chemical and electrical coupling often occur together, and in these cases they can lead to complicated behavior, for example, bistable synchronous and anti-synchronous behavior patterns in GABAergic neurons.

Merriam, W. B. *et al* (2010) in Banks Bistable network behavior of layer interneurons in auditory cortex, The Journal of Neuroscience has noted that electrical coupling can occur between neurons separated by distances from 50μm up to 1000μm. Fukuda, T. *et al* (2000) on Gap junctions linking the dendritic network of GABAergic interneurons in the hippocampus, The Journal of Neuroscience has explained that in the latter relatively large distance may cause an effect of time delay in the signal transmission. The strength of the electrical coupling can vary as well depending on the axonal distance and with the membrane voltage. Bennett, M.V. L. *et al* (2004) has discussed electrical synapses between visualized neurons i.e. electrical coupling and neuronal synchronization in the mammalian brain. On gap- junctional coupling, recent studies have verified the existence of gap- junctional connections in neocortex, auditory cortex and hippocampus of higher mammals including humans.

Fukuda, T. *et al* (2011) analyzed gap junctions linking the dendritic network of GABAergic interneurons in the hippocampus, as a network of fast-spiking cells in the neocortex connected by electrical synapses. Functional properties of electrical synapses between inhibitory interneurons of neocortical layer where two networks of electrically coupled inhibitory neurons in neocortex, in many cases electrical and chemical coupling occur together. Gibson, J.R. *et al* (2012) studied a network of multi-polar bursting interneurons that generates frequency oscillations in neocortex. Fukuda, T. (2011) discussed gap junctions linking the dendritic network of GABAergic interneuron's in the hippocampus.

Merriam, E.B. (2008) discussed bistable network behavior of layer interneurons in auditory cortex. Electrical coupling frequently occurs between neurons of similar type. Bennett, M.V.L. and Zukin, S. (2004) analyzed electrical coupling and neuronal synchronization in the mammalian brain. Mancilla, J.G. *et al* (2009) studied synchronization of electrically coupled pairs of inhibitory interneurons in neocortex and sometimes between the neurons of different types. Gibson, J.R. *et al* (2012) analyzed two networks of electrically coupled inhibitory neurons in neocortex. In the case when electrical coupling occurs between the same types of neurons, it is believed to contribute to synchronization of the neuronal behavior. Chemical and electrical coupling often occur together, and in these cases they can lead to complicated behavior, for example, bistable synchronous and anti-synchronous behavior patterns observed in GABAergic neurons.

Merriam, E.B. *et al* (2008) discussed on bistable network behavior of layer interneurons in auditory cortex. Fukuda, T. and Kosaka, T. (2011), analyzed gap junctions linking the dendritic network of GABAergic interneurons in the hippocampus. The study will help find out how electrical coupling distance and strength relate as well in transmission. The strength of the electrical coupling can vary as well. Weak coupling is usually understood as infinitesimal coupling, or coupling that is small enough in order to be considered as a small parameter in the perturbational analysis. Strong here denotes any coupling that cannot be considered as weak. Some aspects of the relationship between strong and weak coupling in gap-junctional coupled neurons were studied by Yoshioka, M. (2006), "Chaos synchronization in gap-junction-coupled neurons".

Campbell, S.A. (2010) has discussed time delays in neural systems, also his work on Handbook of Brain Connectivity, provide an overview of the possible effects of delays on the neural systems. Type I and type II excitable systems with time delays were studied in, Buric, N. *et al* (2008) type I vs. type II excitable systems. Campbell, S.A. (2008), Introduction to delay differential equations using Terman-Wang and Fizhugh-Nagumo models. However, in this and some other papers on neural networks with time delays neurons are considered to be non-oscillating in the uncoupled state, while this project has considered inherently oscillating neurons. The setup will lead to analysis of phase models with time delay in the case of weak coupling. Studies in this area were recently done by Smith in, Smith, A. (2006) on Phase models with time delay: coupled Fitzhugh-Nagumo oscillators. However, Smith's paper considers Fithzugh-Nagumo model, which is of type II only. Those systems are of fundamental importance on describing qualitative nature of nerve impulse propagation and neural activity. In fact, this model seems rich enough, and can capture neural excitability of original H-H equation. It has assumed that signal transmission in coupled neurons is not instantaneous in general. Buric, N. *et al* (2008), analyzed type I vs. type II excitable systems with delayed coupling. Here it explains how a time delay can occur in the coupling between neurons or in a self-feedback loop. For example, synaptic communication between neurons depends on the propagation of action potentials across axons.

The finite conduction speed and the information processing time in synapses lead to a conduction delay. This project will analyze beyond weak coupling and asymptotic analysis performed on an arbitrary conductance-based model for large positive and negative values of the coupling strength. It turns out that this analysis contributes to the theory of nearly linear systems developed in Murdock, J.A. (2012) on perturbations. Theory and methods they did study provides a way to estimate a boundary between weak and strong coupling for an arbitrary gap-junctionally coupled model, and contributes to the understanding of the effects of time delay coupling on synchronization.

Applications of this work have emerged in modern equipments and devices like synchronous bistable devices e.g. clocks used primarily as an oscillator to generate periodic pulse waveforms for timing purposes, bistable multi-vibrator that is able to retain set and

reset states. It is commonly used as a basic building block for counters, registers and memories. Integrated bistable generator for wide band energy harvesting with optimized synchronous electric charge extraction circuits i.e. bistable generators have been proposed as potential solutions to the challenge of variable vibration frequencies. OSECE design technique which is used for broad board energy harvesting. Buckled spring mass (BSM) generator with OSECE circuits exhibits better performance for low coupling case or reverse sweep excitations. Best applications prospective are expected for the bistable generator with the nearly linear OSECE circuit.
The ubiquity of this bifurcation in time-delay coupled systems is suggestive of its importance, applicability, and utility in a large range of physical situations. In coupled laser systems where the time delay can be conveniently varied in experiments. The in-phase regime is one of low frequency, while the high-frequency out-of-phase regime can permit a relatively higher degree of constant output. Ecosystems where the coupling between separated communities naturally involves time delays are another area of application. For instance, it has been observed that synchronization occurs in epidemics: measles infections in different neighboring cities in the United Kingdom are known to be either in phase (Birmingham and Newcastle) or out of phase Cambridge and Norwich. In this context, analysis of the phase-flip bifurcation in ensembles of oscillators will be of interest, as also the manifestations of this phenomenon in oscillators on networks of complex topology. Studies in these directions are currently under way.

2. Mathematical Formulation
In this part we introduce the geometry to be used in solving the problem.

2.1. Geometry of the Problem
We considered two identical neurons coupled together with gap junctions by the scheme shown in figure 1. The type of connection between neurons is axon-soma, with gap junctions located at the end of the axon of each neuron.

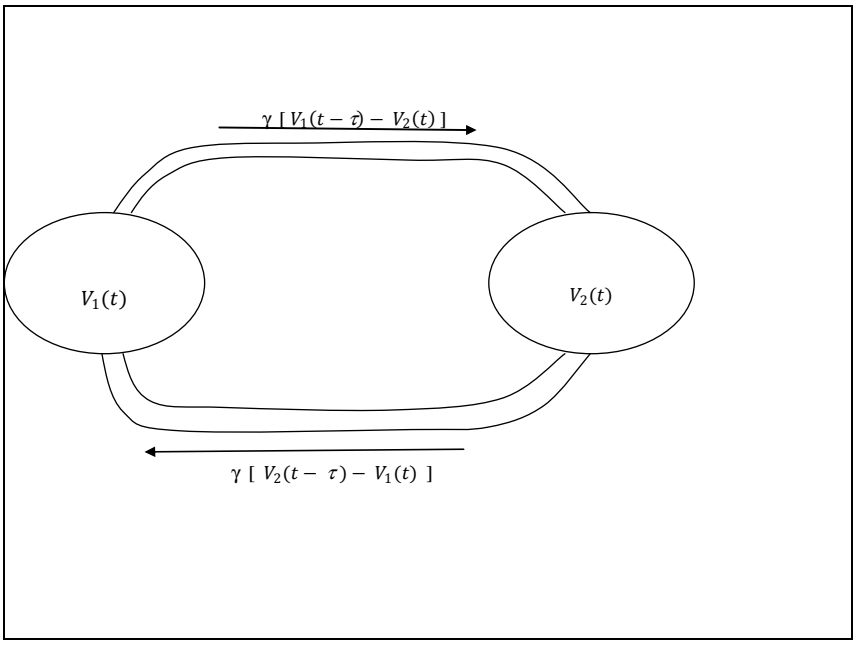

Figure 1: Scheme of two coupled neurons.

The applied current provided to each neuron is assumed to be equal for both neurons and to be at some constant value, *i* for all time. Systems of this type are popular in neuroscience, since such a setting of the model allows one to study and understand the effects of synchronization or synchronous firing in the neural networks, which are often observed in living organisms. The input, *i* represent the influence from the other elements of the network. We have focused our study on the effects of the coupling strength, λ and the time delay, τ in transmission signal on the behavior of the system. As was mentioned earlier, both λ and τ, could vary depending on the type of connection between neurons and type of the gap junction involved in the particular connection. In the present project we would try to answer the following questions: Under which conditions on λ and τ does the system admits stable synchronous solutions, and what are the type of these solutions (i.e. in-phase or anti-phase)?; When are these synchronous solutions globally attractive?

2.2. Conductance Equations
Studies of the barnacle giant muscle fiber done in 1969-1979 showed that it is represented by a conductance system consisting of two voltage dependent ionic channels, i.e. Ca^{++} and K^{+} channels respectively. These channels are considered to be independent of each other. Following the assumptions made above, the study has described a neuron by the following set of equations:

$$\begin{aligned} C\dot{V} &= -\bar{g}_L (V - V_L) - \bar{g}_{ca}\ M (V - V_{ca}) - \bar{g}_k\ W (V - V) + I \\ \dot{M} &= \bar{\lambda}_m\ \lambda_m (V) [\, M_\infty(V) - M] \\ \dot{W} &= \bar{\lambda}_W\ \lambda_W (V) [W_\infty(V) - W] \end{aligned} \qquad (1)$$

From above, equations in (1) are in the general form of a model representing an arbitrary neuron governed by two independent voltage dependent conductances. Where I is the applied current (μA/cm^2), C represents membrane capacitance (μF/cm^2), V is membrane potential(mV), while $\bar{g}_L$, $\bar{g}_{Ca}$ and $\bar{g}_K$ give the maximum instantaneous conductance values for the leak, $Ca^{++}$and K^+ pathways of the circuit respectively (Ms/cm^2). The conductance g_{Ca} and g_K govern the voltage dependent ionic pathways, and g_L represents the pathways for the natural leakage of the current.V_L, V_{Ca} and V_K are the equilibrium potentials, corresponding to the leak, Ca^{++} and K^+conductances respectively (mV). The variables M and W represent the fraction of open Ca^{++} and K^+ channels respectively (dimensionless). M_∞ (V) and $W_\infty(V)$ are the fractions of open Ca^{++} and K^+ channels at the steady state, while $\lambda_W(V)$ and $\lambda_M(V)$ are rate constants for opening Ca^{++} and K^+ channels per second (s^{-1}).

2.3. Neuron as a Mathematical Model

There are several different approaches to mathematical modeling of signal generation and transmission in neurons. Among the most widely recognized are integrate and fire, spiking, soliton conductance-based models. We have considered only single-compartment conductance-based models. These are the simple neural models where the parameters can be interpreted biophysically and measured experimentally. We will formulate a general model for a network of neurons and then determine how delays may occur in this model.

For large-scale complex networks, since the finite information transmission and computer processing speeds among complex network nodes, time-delays are compelling attention and should be considered. Time-delay coupling extremely exists in many real-world systems like on gene regulatory networks and electrical power grids. Therefore, it is quite important to investigate the synchronization of complex networks with coupling time-delay in understanding neural systems.

2.4. Equation Governing Neuron Flow

According to the model of axon-soma connection, the complete system of equations describing our problem to be studied has the following form:

$$\frac{dv}{dt} = \frac{1}{C}\ (g_{Na}(V_{Na} - V) + g_K\ (V_K - V\ ) + g_L\ (V_L - V\ ) + I) \qquad (2)$$

where, V is the membrane potential (mV), C is the specific membrane capacitance (μF/cm^2), I is an applied current (mA), V_L is the leakage reversal potential, V_K is the potassium reversal potential, V_{Na} is the sodium reversal potential, g_L is the leakage conductance density (mS/cm^2), and g_K and g_{Na} are the potassium and sodium conductance densities, which are generally functions of additional dynamical variables.

2.5. Transmission of the Information between Neuron

2.5.1. Overview of Connection Types

The mechanism which is responsible for the transmission of a signal from one neuron to another is called a synapse. The components of the neuron which generates a signal are called pre-synaptic, while the components of the neuron which receives a signal are called postsynaptic. There are two qualitatively different types of the synapses, which are called electrical and chemical synapses respectively.

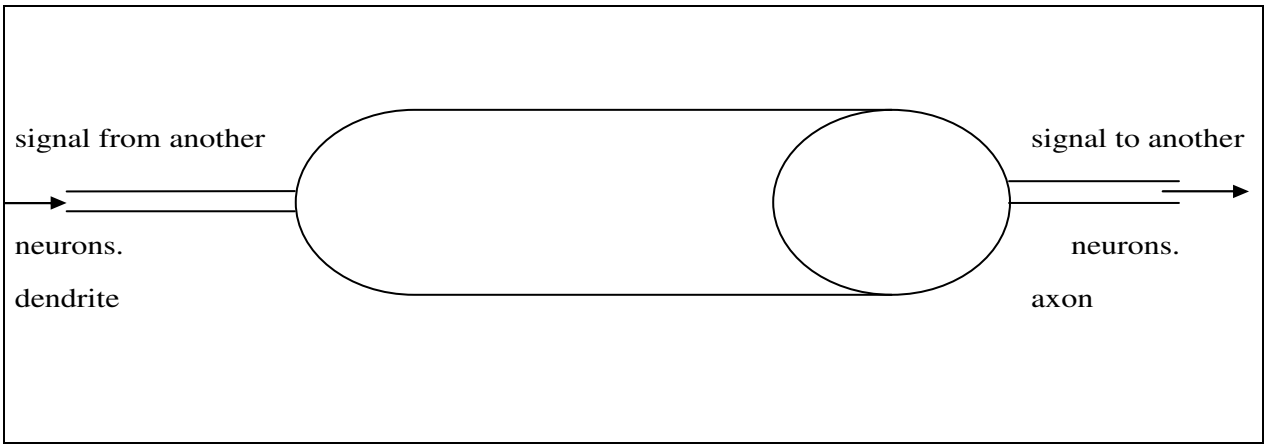

Figure 2: Schematic representation of the chemical (left) and electrical (right) synapses

Consider the structure of a typical chemical synapse first. Figure (2) provides a schematic representation of a chemical synapse. The synaptic end or terminal belongs to the axon of the pre-synaptic neuron. It contains special secretory organelles which are also called synaptic vesicles. The postsynaptic neuron is represented on the figure by the end of its dendrite. It contains the special proteins which are called receptors. The axonal synaptic terminal is separated from the dendrite receptor with the narrow gap, which is typically 20 nanometers (nm) wide and it is called a synaptic gap.

When an action potential reaches the synaptic ending, it excites synaptic vesicles and makes them release the special substances called neurotransmitters into synaptic gap. The neurotransmitters travel through the synaptic gap until they reach the dendrite receptors. As neurotransmitters reach the postsynaptic site, they bind with the receptors which make the dendrite membrane allow certain types of ions to pass through it. Activation of the dendrite receptors changes its potential and thus gives rise to a postsynaptic output signal.

The pre-synaptic and postsynaptic neurons are physically connected via special proteins which are called gap junctions. The gap junction is a channel which allows ions to pass through. Figure two schematically represents gap-junctional connection between the axon of the pre-synaptic neuron and the dendrite of the postsynaptic one. However, gap junctions can be located in any part of the pre-synaptic and post-synaptic neurons. The possible connection types are axon-dendrite, axon-soma, soma-soma, soma-dendrite or dendrite-dendrite.

The state of a gap junction generally can depend on some biophysical properties such as the concentrations of different ions on its pre-synaptic and postsynaptic sides, and is described by a synaptic conduc tance g_{syn}. The current travels both ways through a gap junction, and hence changes the voltages on the pre-synaptic and postsynaptic sides.

We note that on the contrary with the chemical synapses, the electrical synapses affect both pre-synaptic and postsynaptic sides. An effect of the gap junction on the somas of pre-synaptic and postsynaptic neurons depends on the location of the synapse. Both types of synapses are common in the neural systems of humans and different animals. Electrical synapses typically occur between neurons of the same type. Recent studies have suggested that electrical synapses are important for the synchronization of signals from different neurons.

In the following section three that follows, methods of solutions used by discretization of the equation and use of finite difference method to obtain solutions are introduced.

3. Method of Solutions

3.1. Modeling of the Electrical Synapses in Single-Compartment Conductance-Based Models

Consider the synaptic current received by a post-synaptic neuron denoted by the term I_{syn}. Any kind of synapse between neurons could then be modeled by including the term I_{syn} in the equation describing the voltage of the post-synaptic cell membrane. In order to complete the model, one needs to define I_{syn} as an explicit function of the parameters of pre- and postsynaptic cells and possibly some other biophysical quantities. Receptors are ionic channels which are sensitive to certain types of chemicals called neurotransmitters.

Consider two neurons connected by the electrical synapse. For the case of soma-soma connection, the simplest model consists of replacing the synapse by the resistor connecting the electrical circuits representing pre- and postsynaptic neurons. According to Ohm's law, in this case synaptic current could be expressed as $I_{syn} = \bar{g}_{syn}(V_{pre} - V_{post})$

The term $\bar{g}_{syn}$ represents conductance of the gap junction. In general g_{syn} could depend on some biophysical parameters, such as concentrations of some types of ions. The term

$V_{pre} - V_{post}$ expresses the voltage difference between pre- and post-synaptic cells.

According to Kirchhoff's law the sum of the currents through any junction of the circuit is equal to zero. Thus, the pre-synaptic cell is affected by the same current as a postsynaptic one, but with a different sign:

$$I_{post} = I_{pre} = -\bar{g}_{syn}(V_{pre} - V_{post})$$

It follows that electrical coupling is symmetric and there is no difference between pre- and post-synaptic cell. Thus two identical neurons coupled via a gap-junction could be described by the following system:

$$C\frac{dv_1}{dt} = f(V_1) + \bar{g}_{syn}(V_2 - V_1)$$
$$C\frac{dv_2}{dt} = f(V_2 + \bar{g}_{syn}(V_1 - V_2) \quad (3)$$

System (3) can be used in modeling axon-dendrite, axon-soma, soma-dendrite or dendrite-dendrite connections in the case when the time delay in transmission signal and losses of the signal in transmission from soma to soma are insignificant.

Consider the axon-soma connection. Due to the finite time for signal transmission along the axon, a voltage from the pre-synaptic neuron arrives to the gap junction with some time delay,τ. Due to the specific structure of the axon, the signal does not propagate backwards along the axon without weakening, and hence it is possible to neglect a signal that goes backwards in the case when an axon is long enough. Thus, the system that describes axon-soma coupled neurons has the following form:

$$C\frac{dv_{pre}(t)}{dt} = f(V_{pre}(t))$$
$$C\frac{dv_{post}(t)}{dt} = f(V_{post}(t)) + \bar{g}_{syn}(V_{pre}(t-\tau) - V_{post}(t)) \quad (4)$$

Under non - dimensionalization procedure $\bar{g}_{syn}$ is scaled by the term $\bar{g}_{ref}$. We have referred dimensionless synaptic conductance as coupling strength γ : $\gamma = \bar{g}_{syn}/\bar{g}_{ref}$. Modeling of the electrical synapse by a single resistance does not include some possible effects of the electrical synapses, such as the effect of the synaptic current being shunted by the extracellular cytoplasm. However, most of the gap junctions could be modeled by the single parameter.

3.2. Analysis of Axonal and Dendritic Signal Propagation for Morris-Lecar Neurons

The prevalent model to describe propagation of neural membrane voltage responses to ion currents is the cable equation. The cable equation is a parabolic-type partial differential equation, which is frequently studied with the use of compartmental models. The dynamics of neuron behavior is most commonly modeled by the Hodgkin-Huxley formulation, which describes the time rate of change of neural membrane voltage. The original model was based on the giant squid axon, and postulates that the membrane voltage changes due to a combination of ion currents through ion channels with voltage-dependent membrane conductance from Hodgkin, A. L. *et al* (1952)

$$\frac{dV}{dt} = \frac{1}{C}\left(g_{Na}(V_{Na} - \ ) + g_K\left(V_K - V\right) + g_L\left(V_L - V\ \right) + I\right) \quad (5)$$

Here, V is the membrane potential (mV), CS is the specific membrane capacitance (µF/cm2), I is an applied current (mA), V_L is the leakage reversal potential, V_K is the potassium reversal potential, V_{Na} is the sodium reversal potential, g_L is the leakage conductance density (mS/cm^2), and g_K and g_{Na} are the potassium and sodium conductance densities, which are generally functions of additional dynamical variables. Given initial conditions for the voltage and the other dynamical variables, the Hodgkin-Huxley equations give a fully deterministic and continuous model to describe the dynamics of a neural membrane. This model does not describe how the membrane potential propagates down the axon and dendritic structure of a neuron, and thus communicates a signal to neighboring neurons in a network.

For this, the voltage equation must be modified by an additional term, which describes the spatial dependence of the voltage. This equation is called the cable equation, by Koch, C. (1999) and is of the form

$$\frac{\partial v}{\partial t} = \frac{1}{C}\left(\frac{a}{2R}\ \frac{\partial^2 v}{\partial x^2} - g_v + \mathrm{J}\right) \quad (6)$$

Where a, is the cable (axonal or dendritic) diameter, R is the membrane resistance, and all currents (ionic and leakage) are captured in J. In general, all parameters appearing on the right hand side of this equation are functions of space and time. This equation, coupled with the Hodgkin-Huxley dynamics, then gives a full description of the dynamics of action potential propagation down an axon. Equations of the form given by equation (6) are called parabolic partial differential equations (PDEs). This type of PDE is characterized by one temporal derivative and two spatial derivatives. Without the nonlinear dynamics associated with the ion currents (J-term), the solution to equation (6) is similar to that for the more familiar heat and diffusion equations. The typical mathematical solution for parabolic PDEs is by the finite difference or finite element methods.

3.3. Finite Difference Method for Equation

The finite difference method is similar to compartmental models, but explicitly discretizes both space and time in order to reduce the system of equations to a linear algebra form. For space discretization, various methods are used which show different convergence and stability characteristics. The most basic discretization is the implicit scheme. In terms of the discrete variables the derivatives for cable equation (6) are given by

$$\frac{\partial V}{\partial t} = \frac{V_i^{t+1} - V_i^t}{\Delta t} \quad (7)$$

$$\frac{\partial^2 V}{\partial x^2} = \frac{U_{i+1,j}^{t+1} - 2V_{i+1}^{t+1} + \ V_{i-1}^{t+1}}{(\Delta x)^2} \quad (8)$$

$$gV = GV_i^{t+1} \quad (9)$$

$$J = J_i^{t+1} \quad (10)$$

3.4. Discretization of Equation

The cable equation can be discretized by substituting equations (7), (8), (9) and (10) into (6) and letting $\Delta t = \Delta x = 1$, $ECS = \frac{a}{2R} = 1, C = 5, G = 2$ as follows

$$C\frac{V_i^{t+1} - V_i^t}{\Delta t} = \frac{a}{2r}\frac{U_{i+1,j}^{t+1} - 2V_{i+1}^{t+1} + \ V_{i-1}^{t+1}}{(\Delta x)^2} - GV_i^{t+1} + J_i^{t+1} \quad (11)$$

We form the implicit scheme

$$5V_{i+1,j+1} - 2V_{i+1,j+1} - V_{i-1,j+1} = 5V_{i,j-1} - J_{i,j+1} \quad (12)$$

Taking i= 1,2,3, ……., 8 and j=1, we form the following systems of linear algebraic equations

The above algebraic equations can be written in matrix form as

$$\begin{bmatrix} 5 & -1 & 0 & 0 & 0 & 0 & 0 \\ -1 & 5 & -1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 5 & -1 & 0 & 0 & 0 \\ 0 & 0 & -1 & 5 & -1 & 0 & 0 \\ 0 & 0 & 0 & -1 & 5 & -1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 5 & -1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 5 \end{bmatrix} \begin{bmatrix} V_{11} \\ V_{21} \\ V_{31} \\ V_{41} \\ V_{51} \\ V_{61} \\ V_{71} \end{bmatrix} = \begin{bmatrix} -1.71828 \\ -6.389056 \\ -19.085 \\ -53.59 \\ -147.41 \\ -402.428 \\ -1095.63 \end{bmatrix} \quad (14)$$

Solving the above system in equation (14) using MATLAB, we get the solutions as follows

$V_{11} = -1.021796$, $V_{21} = -3.390699$, $V_{31} = -9.542641$, $V_{41} = -25.23750$

$V_{51} = -63.05487$, $V_{61} = -142.6268$, $V_{71} = -247.6514$

In section four that follows, we discuss the numerical results obtained by using tables and graphs.

4. Numerical Results and Discussion

4.1. Electrical coupling strength, ECS

By solving equation (13) using MATLAB software varying values of x, indicating the values of the results for electrical coupling strength are shown in table 1 below.

Using the initial conditions;

$$V(x,0) = 0, \text{ and } \quad V(x,t) = 1 - e^{t}. \quad (15)$$

By the boundary conditions set above, we solve equation (13) and get the results as in table 1 below.

	Electrical Coupling Strength (ECS = 1)	Electrical Coupling Strength (ECS = 2)	Electrical Coupling Strength (ECS = 3)
X = 0	-1.021796	-1.70225	-2.440079
X = 1	-3.390699	-5.098734	-6.747478
X = 2	-9.542641	-12.94879	-15.67267
X = 3	-25.23750	-30.67953	-33.90886
X = 4	-63.05487	-67.63456	-72.6456
X = 6	-142.6268	-148.6498	0.006881298
X = 7	-247.6514	-254.2414	-262.1476

Table 1: Voltage (x, t) values for varying Electrical coupling strength (ECS)

The results in the table 1 above can as well be represented graphically as shown in figure 3 below.

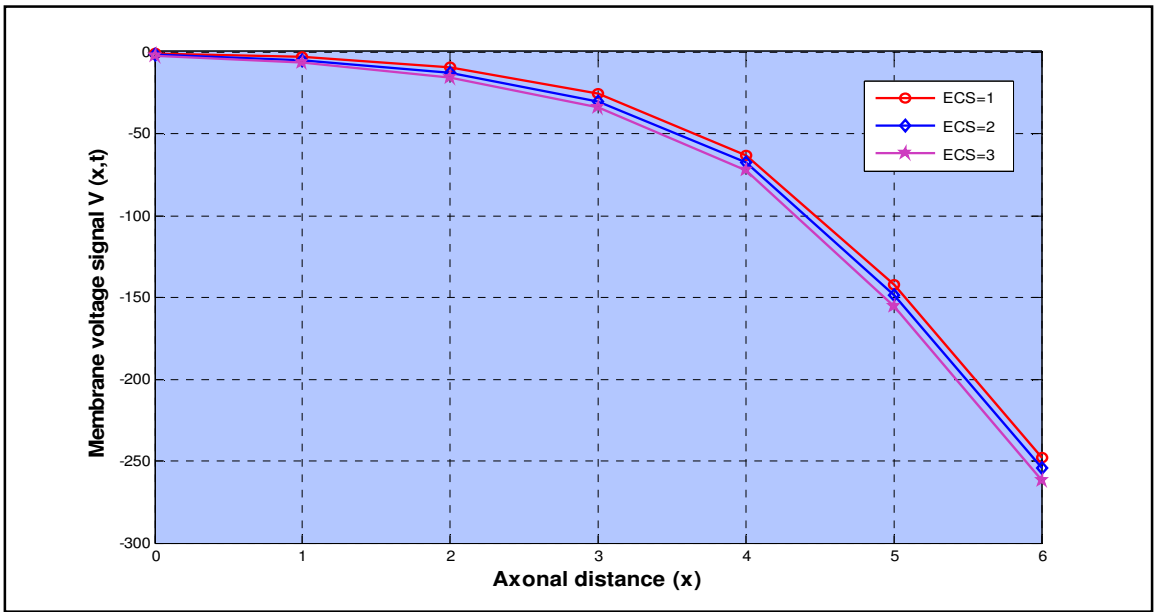

Figure 3: The changes of voltage values for varying electrical coupling strength.

Considering the stability of the equilibrium of the system, varying the parameters axonal distance and membrane voltage signal indicates different behavior as per the electrical coupling strength and it dramatically changes the behavior of the system. When the value of electrical coupling strength is less, it indicates a higher response to the variation of membrane voltage signal. As the electrical coupling strength increases, the voltage of the neurons decreases. Also when the axonal distance (x) of the neurons increases, the voltage decreases. A sudden change in the membrane potential reorientates the charges of the sensor and the kinetics of this movement depends on the energy landscape that those charges must traverse to their new position. Membrane potential becomes more negative returning towards resting potential. Therefore voltage sensitive ion channels open and close in response to changes in the membrane voltage.

4.2. Variation of specific membrane capacitance, C

By solving equation (13) using math lab software varying values of membrane capacitance with respect to x, indicating the values, the results for electrical coupling are shown in table 2 below.

	C = 5	**C = 7**	**C = 10**
X = 0	0.9029527	1.264133	1.805905
X = 1	1.354164	1.895827	2.708325
X = 2	1.544536	2.162348	3.089069
X = 3	1.617445	2.264423	3.234891
X = 4	1.63429	2.222787	3.268584
X = 5	1.587704	0.003015515	3.175411
X = 6	1.496629	2.1443281	3.033256

Table 2: Voltage (x, t) values for varying specific membrane capacitance C

The results in the table 2 above can as well be represented graphically as seen in figure 4 below.

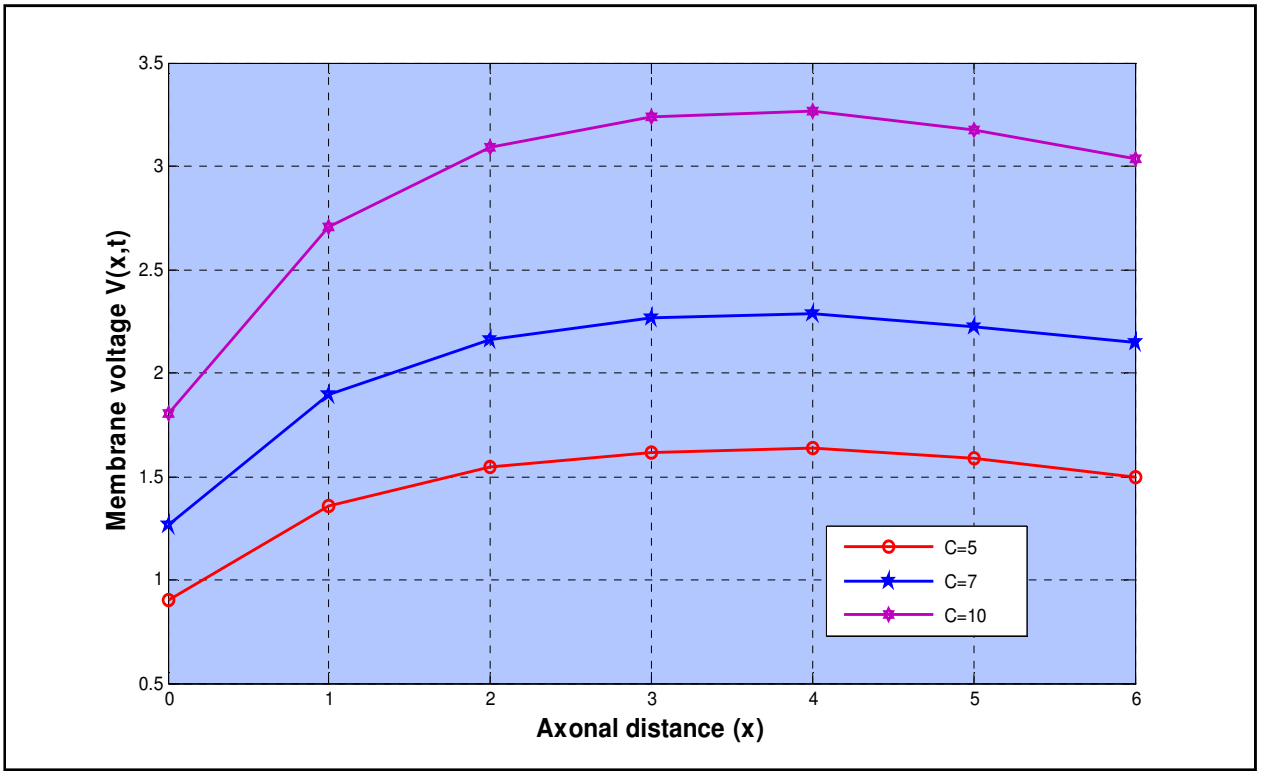

Figure 4: The changes of voltage values for varying specific membrane capacitance.

When C, increases voltage also increases to an optimum level then begins to decrease. When the axonal distance (x) increases, specific membrane capacitance C, also increases to optimum level then decreases after attaining axonal distance of 4nM. The optimum levels attained by the three graphs are different but at maximum point the axonal distance is the same. When the axonal distance (x) increases, C also increases but decreases after the optimal value of axonal distance. Time-scale τ increases with membrane resistance and capacitance. As the capacitance increases, more charge must be transferred to produce a give transmembrane voltage; as the resistance increases less charge is transferred per unit time, making the equilibration slower. When the transmembrane resistance is increased, this lowers the average leakage current across the membrane, thus increasing the conduction.

4.3. Variation of ionic leakage conductance density, G

By solving equation (13) using MATLAB software varying values of ionic leakage density G, indicating the values, the results for electrical coupling are shown in table 3 below

	G = 2	G = 4	G = 5
X = 0	0.9029527	0.9647983	1.14103
X = 1	1.324164	1.357187	1.626009
X = 2	1.544536	1.566046	1.874383
X = 3	1.617445	1.62905	1.952542
X = 4	1.63429	1.649552	1.976611
X = 5	1.607704	1.634746	1.634746
X = 6	1.576629	1.593203	1.88621

Table 3: Voltage (x, t) values for varying ionic leakage conductance density

The results in the table 3 above can as well be represented graphically as seen in figure 5 below.

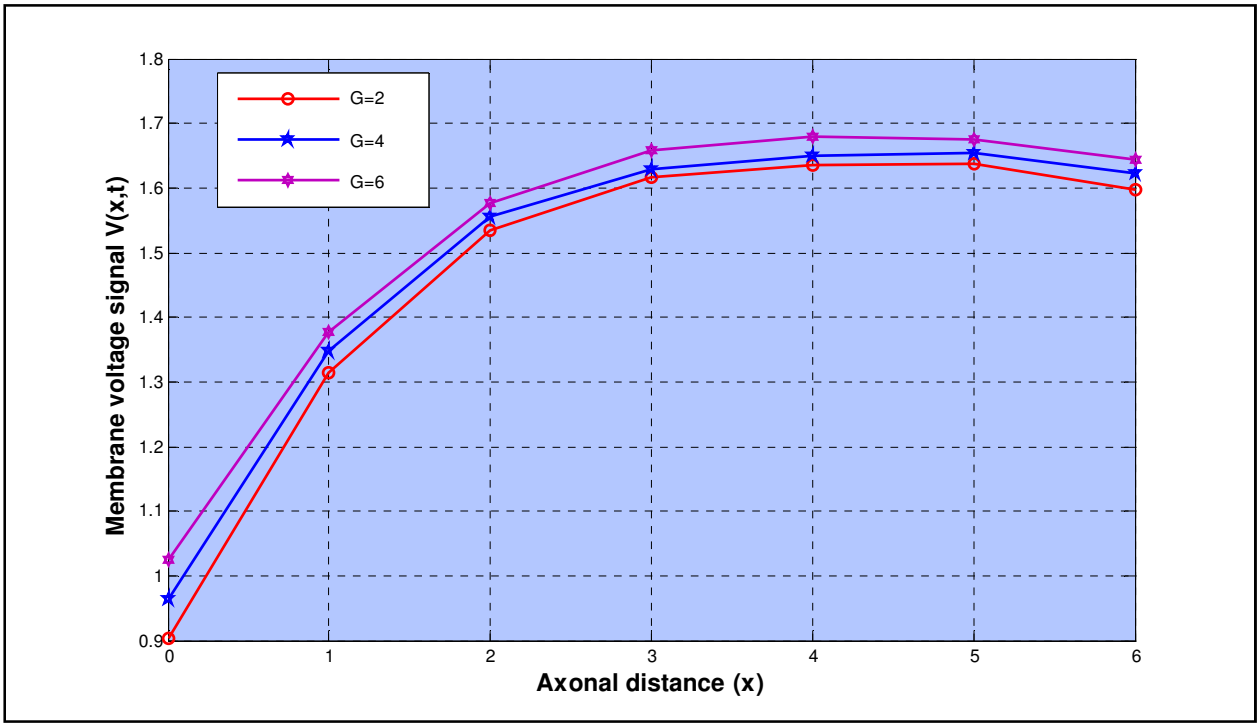

Figure 5: The changes of voltage values for varying ionic leakage conductance density.

Ionic leakage conductance increases with increase in axonal distance (x) until it attains maximum level where it does not increase any longer. As the current density is increased the amplitude of stable periodic responses decreases into a stable fixed point which is determined by both calcium and potassium ions. Changes in channel density can influence the electrical behavior of excitable membranes. Thus the role of $\bar{g}_K$ in stabilizing the resting membrane potential of the axon is taken by g_L in mammalian myelinated nerve: both maintain the stability of the resting potential, and a decrease in $\bar{g}_K$ in the H-H membrane leads to a Hopf bifurcation, from a stable membrane potential to unstable, small amplitude oscillation. If the specific channels densities are such that the membrane is close a bifurcation point, then the effects of the random open-close kinetics will be enhanced. Thus the variability of the activity of a neuron will be strongly influenced by areas of membrane where the channel density is close to a bifurcation point.

Changing channel density and total membrane capacitance affect the energy expended by neurons on restoring ion gradients across their membrane. For a cell containing ion channel from the squid giant axon of a given size, there is a channel density and an input stimulus that maximizes the energy efficiency of information coding. Changes in channel density can increase the information rate of the cell but only by sacrificing energy efficiency. The available space within cells may also constrain spike rates and consequently information rates because of the space occupied by the number of calcium or potassium ion pump needed to sustain firing of information.

In the next section that follows, we draw conclusions from the results obtained and recommendations.

5. Conclusion and Recommendations

5.1. Conclusion

The objective of this study was to investigate the effect of the electrical coupling strength and time delay on an electrically coupled neuronal network. Understanding complex neurobiological systems is one of the most difficult challenges in modern science. From the above results and discussion, we can conclude that H-H equation is the foundation of neuroscience as these parameters values are used for computational brain modeling. It removes ambiguity from theories and makes them logically consistent. In view of the above results, it has been observed that as electrical coupling strength (ECS) increases the membrane voltage decreases. As specific membrane capacitance increase it leads to increase in membrane voltage to an optimum value after which it begins to reduce uniformly. Finally also varying the ionic leakage conductance density G, at constant values of ECS = 1 and C = 10, membrane voltage increases to a maximum value after which it decreases. Same case applies with axonal distance with respect to ionic leakage conductance density.

Use of computer technology enables theories involving with a large number of elements to be investigated. Computational modeling can help to do the right experiment to solve numerically a set of biologically grounded equations describing the voltage-dependent changes. Computer modeling is an essential component of the neuroscientist's repertoire. Any variation of the H-H parameters can cause bifurcation and this analysis can solve different abnormal disorders by investigating the graphs as shown above. In the previous chapters we were able to show how time delays due to conduction along the axon or dendrite or due to transmission across the synapse could be modeled with delay differential equations. We outlined some of the tools available for analyzing such equations and reviewed some of the literature about such models. Some key observations are that: Time delays can lead to the creation of type II oscillations, especially in systems with delayed inhibitory coupling; If a system has a stable synchronous oscillation when there is no delay in the coupling, the solution remains stable for small enough delay, but may lose stability for larger delay and a system with inhibitory coupling which does not have a stable synchronous oscillation for zero delay may have one if the delay is large enough.

5.2. Recommendations

There are a number of problems which still require further study. These include: determining the effect of delay on the generation and destruction of type I oscillations (infinite period bifurcations), applying and/or extending the methods used to study synchronization in artificial neural networks to biophysical neural networks, and studying the effect of distributions of delays on biophysical neural networks. Much of the work presented in this project is explorative and the results of all of the studies should be verified and explored further. Especially the research on the representation of neocortical cell classes by generic bifurcation models can be continued in many directions. Therefore;

(i) An experimental approach to this problem is recommended in order to reduce the theoretical assumptions in this work. i.e. doing a bifurcation analysis of a more complex, realistic, neuron model and try to find out how the two relate and whether a comparison of both gives indications to possible features that are missed by the Hind marsh-Rose model.

(ii) The continuation analysis of the Hind marsh-Rose model should be completed to unravel the complete structure and organizing principle of the model i.e. properties of synchronization in networks of dynamic systems in general and of pulse coupled networks specifically are an active subject of research at all levels

(iii) The bifurcation analysis should be extended to other parameters like R, J and G upon voltage $\nu(x, t)$, although results in this work indicate that they are of less spectacular influence.

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