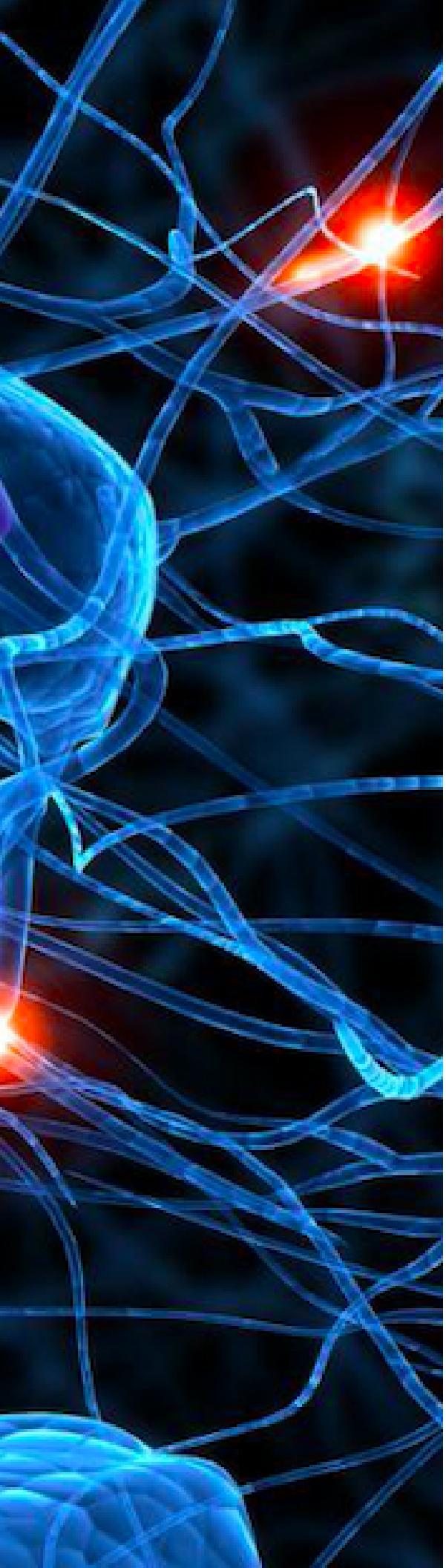

Numerical analysis of a large scale network of spiking neurons

Internship report

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Contents

1 Introduction and Motivation

Neural synchronization in the brain is the main cause of many diseases in the humans such as alzheimer and epilepsy; thus, by enhancing our knowledge about synchronization we want to contribute in this field. It is known in the literature that the synchronization behavior between any two neurons is related to the presence of a gap junction between them. The gap junction has always been modeled as a constant conductance whereas in this report, the effect of a voltage dependent gap junction between neurons in a neural network in the presence and absence of a synaptic current has been numerically studied. Further analysis can be found in [4].

2 Background studies

This section provides background knowledge required for he project. **All images and their captions are taken from the "Neural Dynamics" [5].**

2.1 Biophysics of a neuron

A neuron takes an input signal (dendrite), processes it like the CPU (soma), passes the output through a cable-like structure to other connected neurons (axon to synapse to other neurons dendrite). So a neuron is composed of four significant parts: dendrites, soma and axon, and synapse.

2.1.1 Dendrite

Dendrites are branched extensions of a neuron that get input signals from other neurons and send them to soma. In the upcoming models of this report, I have assumed that dendrites are passive, so that they cannot excite soma to generate spikes by their own.

2.1.2 Soma

soma is the part where the input signal is processed and is decided whether the neuron should spike or not.

2.1.3 Axon

neurons output signal is transferred to other neurons by its axon.

2.1.4 Synapse

Neurons axon is connected to a synapse. Synapses are the connecting points among various neurons, and the information is sent through synapses.

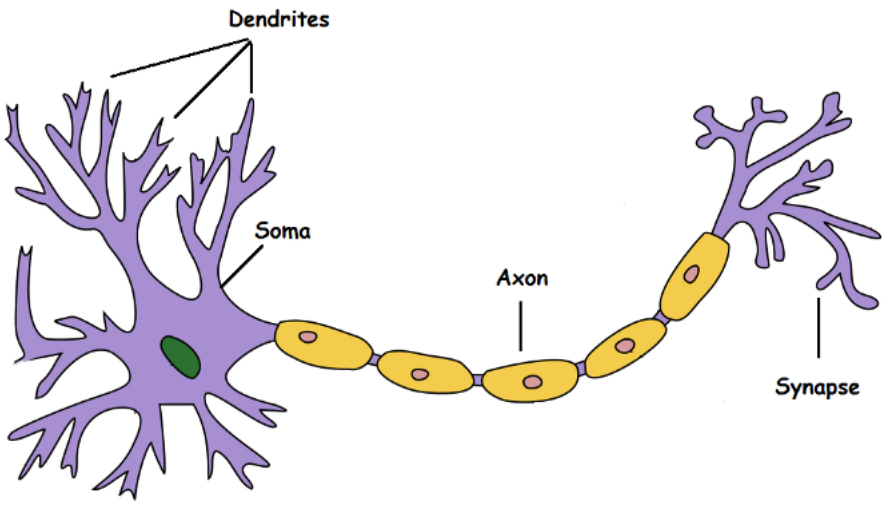

Figure 1: A simple diagram of a neuron [5]

2.2 Some basic neuronal models[1], [2]

2.2.1 Leaky integrate and fire model

The circuit shown in the figure below is the Leaky integrate and fire model of a neuron. u_{rest} is the value of the membrane potential when there is no input. If we inject a current I(t) into the neuron, or if the neuron receives synaptic input from other neurons, its potential u(t) will deviate from its initial value. A neuron is surrounded by a cell membrane. If a short current pulse I(t) is injected to the neuron, the additional electrical charge $q = \int I(t)dt$ will charge the neuron's cell membrane. Therefore, the cell membrane can be considered as a capacitor. However, the cell membrane is not completely isolated; So the charge will leak through the cell membrane gradually. So the cell membrane can be modeled by a leak resistance R.

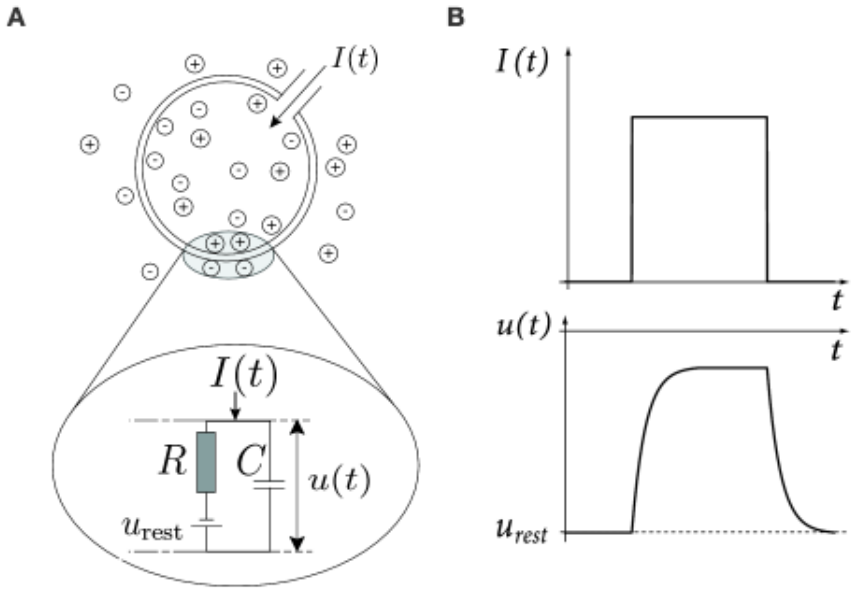

Figure 2: Electrical properties of neurons: the passive membrane. **A**. A neuron, which is enclosed by the cell membrane (big circle), receives a (positive) input current I(t) which increases the electrical charge inside the cell. The cell membrane acts like a capacitor in parallel with a resistor which is in line with a battery of potential u_{rest} (zoomed inset). **B**. The cell membrane reacts to a step current (top) with a smooth voltage trace (bottom) [5]

The mathematical equation of the circuit above is

$$\tau du/dt = -(u - u_{rest}) + RI(t)$$

. Now we have a linear equation that describes neurons membrane potential based on its input current. In order to describe spikes, we need to determine a voltage threshold. Whenever the membrane potential gets higher than that threshold, it spikes; meaning the voltage increases up to a certain value very fast, and then it goes back to its resting value.

2.2.1.1 Leaky integrate and fire model with short pulse input Let's Consider I(t) a short pulse and solve the equation mentioned above. The outcome would be: $u(t) = u_{rest} + RI_0[1 - e^{-t/\tau}]$

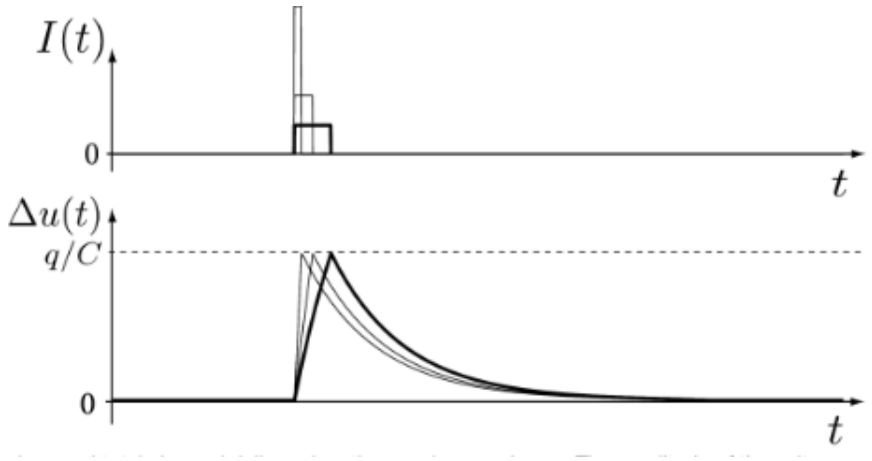

Figure 3: Short pulses and total charged delivered on the passive membrane. The amplitude of the voltage response (bottom) of a leaky integrator driven depends only on the total charge. [5]

2.2.2 Nonlinear integrate and fire model

In this model, derivative of the membrane potential is a nonlinear function of itself, so $\tau du/dt = F(u)+RI(t)$ where F(u) is a nonlinear function. I will discuss about two examples of nonlinear integrate and fire models in continue.

2.2.2.1 Exponential integrate and fire model Dynamics of this model is described by the equation below. The dynamics is linear before the threshold, and afterwards it will have an exponential behavior.

$$\tau du/dt = -(u - u_{rest}) + \Delta e^{(u-\vartheta)/\Delta} + RI$$

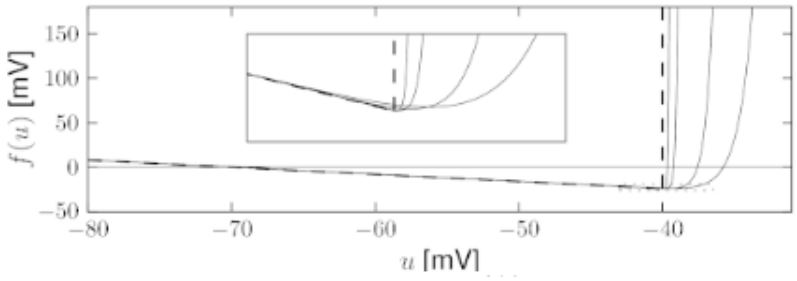

Figure 4: Exponential and leaky integrate and fire model. The function f(u) is plotted for different choices of the 'sharpness' of the threshold(Δ = 1, 0.5, 0.25. 0.05mv) in the limit Δ -¿ 0 the exponential integrate and fire model becomes equivalent to a leaky integrate and fire model (dashed line) [5]

In the absence of an external input, there are two fixed points defined by zero-crossings. The left one is stable and the right one is unstable, thus acts as a threshold. If the external input increases slowly the diagram above shifts upward until two fixed points finally merge at bifurcation point. If we increase the external current even more, the diagram will not collide the horizontal line anymore, and thus starting from any initial condition the voltage keeps increasing until the neuron spikes.

2.2.2.2 Quadratic integrate and fire model This model's dynamics is described by the equation below.

$$\tau du/dt = a_0(u - u_{rest})(u - u_c) + RI$$

Considering $a_0 > 0$ and $u_c > u_{rest}$ for $I = 0$, and initial condition $u < u_c$, the voltage decays to the resting potential. If $u > u_c$, the voltage increases until the neuron spikes. Thus, the parameter u_c can be interpreted as critical voltage for spike initiation by a short current pulse. In a neuron, instead of a quadratic nonlinearity in the suprathreshold regime, there is an exponential behavior. However, close to the threshold for repetitive firing, these two models are very similar.

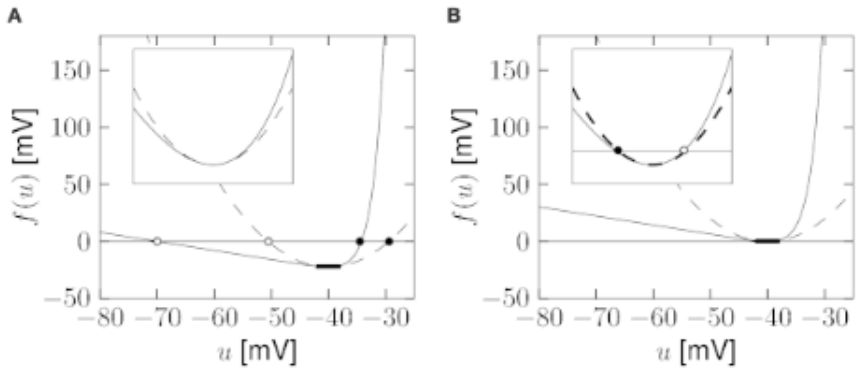

Figure 5: Quadratic integrate and fire model. **A**. The quadratic integrate and fire model compared to an exponential integrate and fire model. **B**. The quadratic integrate and fire model can be seen as an approximation of the exponential integrate and fire model depolarized to a state close to repetitive firing. [5]

2.3 Hodgkin-Huxley model [1], [2]

2.3.1 Biophysics and circuit model

There are generally three types of ion currents in a neuron, sodium, potassium, and a leak current. Specific voltage-dependent ion channels, control the flow of ions through the cell membrane. Because of continuous flows of ions through the cell membrane, the ion concentration inside the cell is different from the outside, and this difference explains the difference in potential inside and outside of the cell according to Nernst equation.

$$\frac{n_{inside}}{n_{outside}} = e^{-\frac{q(u_{outside}-u_{inside})}{KT}}.$$

The cell membrane can be modeled as a capacitor which is between the interior of the cell and its extracellular liquid. If an input current is injected to the cell, it can further charge on the capacitor, or leak through the channels in the cell membrane. Each channel type is represented as a time-dependent resistance in the figure below; When an ion channel is open, it has lower resistance and therefore an easier flow of the current inside that specific ion channel. When an ion channel is closed, its resistance is close to infinity, which means the current flow is close to zero. The Nernst potential generated by the difference in ion concentration is represented by some batteries in the figure below. The unspecific channel has a leak resistance R as shown below.

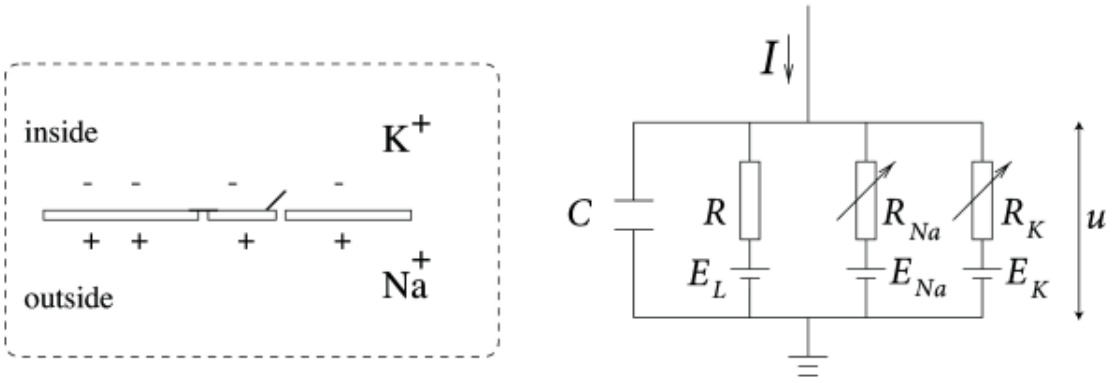

Figure 6: Hodgkin-Huxley circuit model [5]

According to the model above we have

$$cdu/dt = -\sum_k I_k(t) + I(t).$$

Assuming $g_L = 1/R$ we can write $I_L = g_L(u - E_L)$.
If all sodium and potassium channels are open, g_{Na} and g_K are the highest. However, if some of them are blocked, conductance of channels change as a function of time and voltage. For describing these changes, three additional variables were considered called m, n, h. A specific combination of m and h controls the Na+ channels while the K+ gates are controlled by n. The conductance of sodium channels is modeled as $1/R_{Na} = g_{Na}m^3h$, and the conductance of potassium is $1/R_K = g_K n^4$. So the equation of the circuit above would be:

$$\sum_k I_k = g_{Na}m^3h(u - E_{Na}) + g_K n^4(u - E_K) + g_L(u - E_L)$$

Three gating variables m, n, h evolve according to differential equations of the form $dx/dt = -1/\tau_x(u)[x - x_0(u)]$ where the dynamics of τ_x and x_0 for these gating variables are shown in the diagram below.

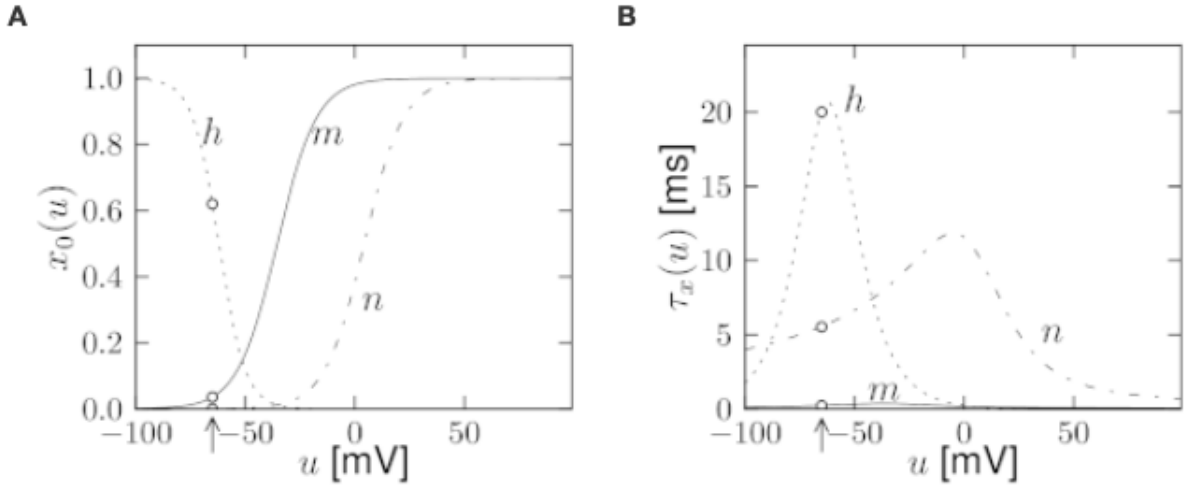

Figure 7: Dynamics of τ_x and x_0 for m,n,h as gating variables [5]

We can analyse the dynamic of the model based on the increase or decrease in membrane potential that results in the change in dynamics of m,n,h. There is no strict current or voltage threshold in this model; actually effective threshold depends on the stimulus.

2.3.2 Synapses and modeling the input current

Activation of a presynaptic neuron is conducive to releasing neurotransmitters into the synaptic cleft. The transmitter molecules activate receptors that are in the postsynaptic membrane. The activation of the receptor leads to the opening of some ion channels and thus, an excitatory or inhibitory current. The transmitter activated ion-channels can be modeled as $I_{syn}(t) = g_{syn}(t)(u(t) - E_{syn})$ Based on experiments, currents behavior can be seen as a sharp exponential rise, one fast exponential decline and one slow exponential decline that is ten times slower than the fast one. Thus we can write (sigma is over all incoming spikes)

$$g_{syn}(t) = \sum_f g[1 - e^{-(t-t(f))/\tau_{rise}}][ae^{-(t-t(f))/\tau_{fast}} + (1-a)e^{-(t-t(f))/\tau_{slow}}]\Delta(t - t(f))$$

. The current is associated with the sum of ion flows in all ion channels. Neurons on average have 200 ion channels. Hence when the current is low it means the number of open ion channels are low.

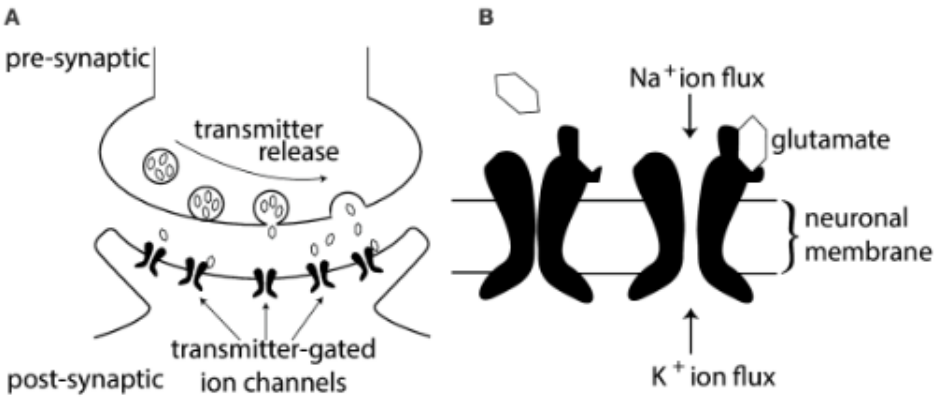

Figure 8: **A**. Schema of synaptic transmission. Upon arrival of a presynaptic spike, neurotransmitter spills into the synaptic cleft and is captured by postsynaptic receptors. **B** Schema of a postsynaptic AMPA receptor of an excitatory synapse. When glutamate is bound to the receptor, sodium and potassium ions can flow through the membrane. [5]

There are two main synapse types, Inhibitory and Excitatory synapses. Also postsynaptic receptors have various types. The Dynamics of various postsynaptic currents after a single presynaptic spike is shown in the figure below.

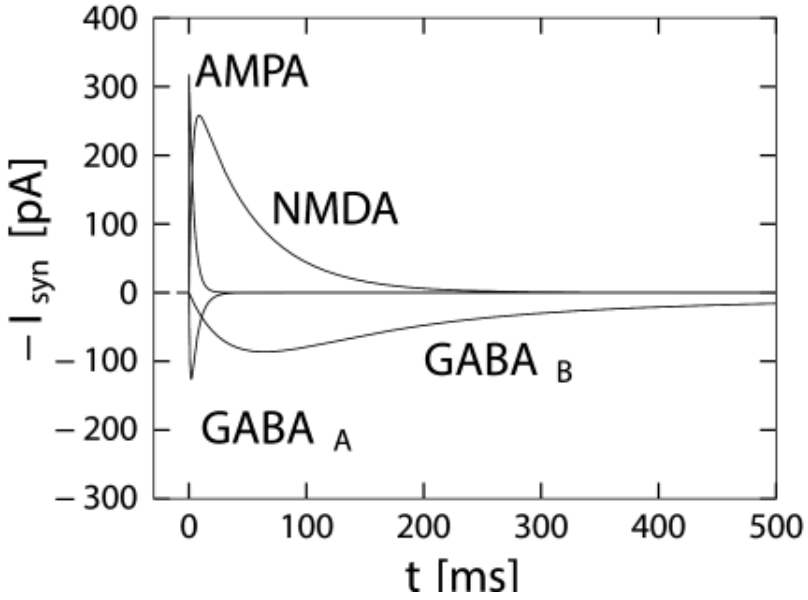

Figure 9: Spike responses of various postsynaptic receptors. [5]

2.3.3 Dendrites and the passive cable equation

Consider a piece of dendrite made of short cylindric segments with length dx. Each segment can be modeled by Hodgkin and Huxley model. The figure below shows the corresponding circuit diagram.

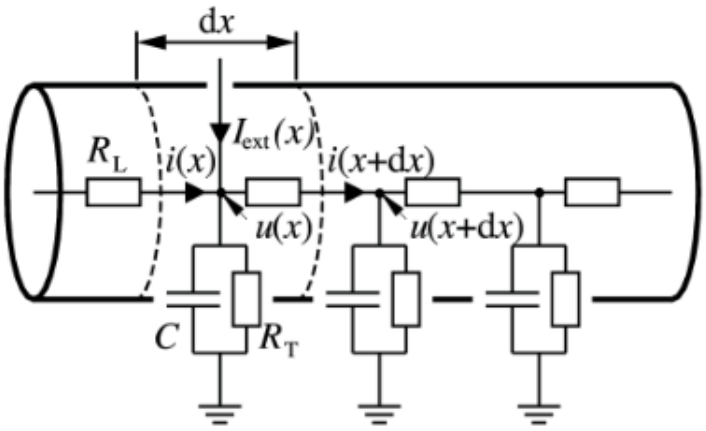

Figure 10: Part of a dendrite and the corresponding circuit diagram [5]

If we write and narrow down the equations of the circuit above we will reach the following equation where R_L, i_{ion}, c, i_{ext} are longitudinal resistance, ion current, capacitor and external current per unit length respectively.

$$\frac{\partial^2}{\partial x^2}u(t,x) = cR_L\frac{\partial}{\partial t}u(t,x) + R_L\sum_{ion} i_{ion}(t,x) - R_L i_{ext}(t,x)$$

2.3.4 Hodgkin Huxley to 2D model

A system of four equations, such as Hodgkin-Huxley model is difficult to analyze. So we perform a reduction to approximate the original model with a two dimensional model. We need two main assumptions to do this. 1- Due to small values of τ_m comparing to τ_n and τ_h dynamics of m is very fast, so we assume that m is always equal to $m_0(u)$. 2- According to the diagrams of n and h, these two variables roughly have the same speed in moving towards their fixed points; moreover, we can say $1 - h(t) = an(t) = w(t)$. Therefore, our equations will narrow down to :

$$c\frac{du}{dt} = -g_{Na}m_0(u)^3(1-w)(u-E_{Na}) - g_K(\frac{w}{a})^4(u-E_K) - g_L(u-E_L) + I(t)$$

$$\tau_w\frac{dw}{dt} = -(w - w_0(u))$$

This 2d model allows us to have phase plane analysis and therefore explain many neuron characteristics.

We can even go further, and approximate this 2D model with a 1D model. Dynamics of w which corresponds to h, n is slower than dynamics of u; so we can think of w(t) be constant in the subthreshold regime and write:

$$c\frac{du}{dt} = -g_{Na}m_0(u)^3(1-w_0(u))(u-E_{Na}) - g_K(\frac{w_0(u)}{a})^4(u-E_K) - g_L(u-E_L) + RI(t) = F(u) + RI(t)$$

So basically we have reduced the Hodgkin Huxley model to a nonlinear integrate and fire model which has a roughly similar dynamics as exponential integrate and fire model.

2.4 Adaptive exponential Integrate and fire model [1], [2]

Some neurons have special spiking patterns in response to a step current with low or high amplitude as figured below.

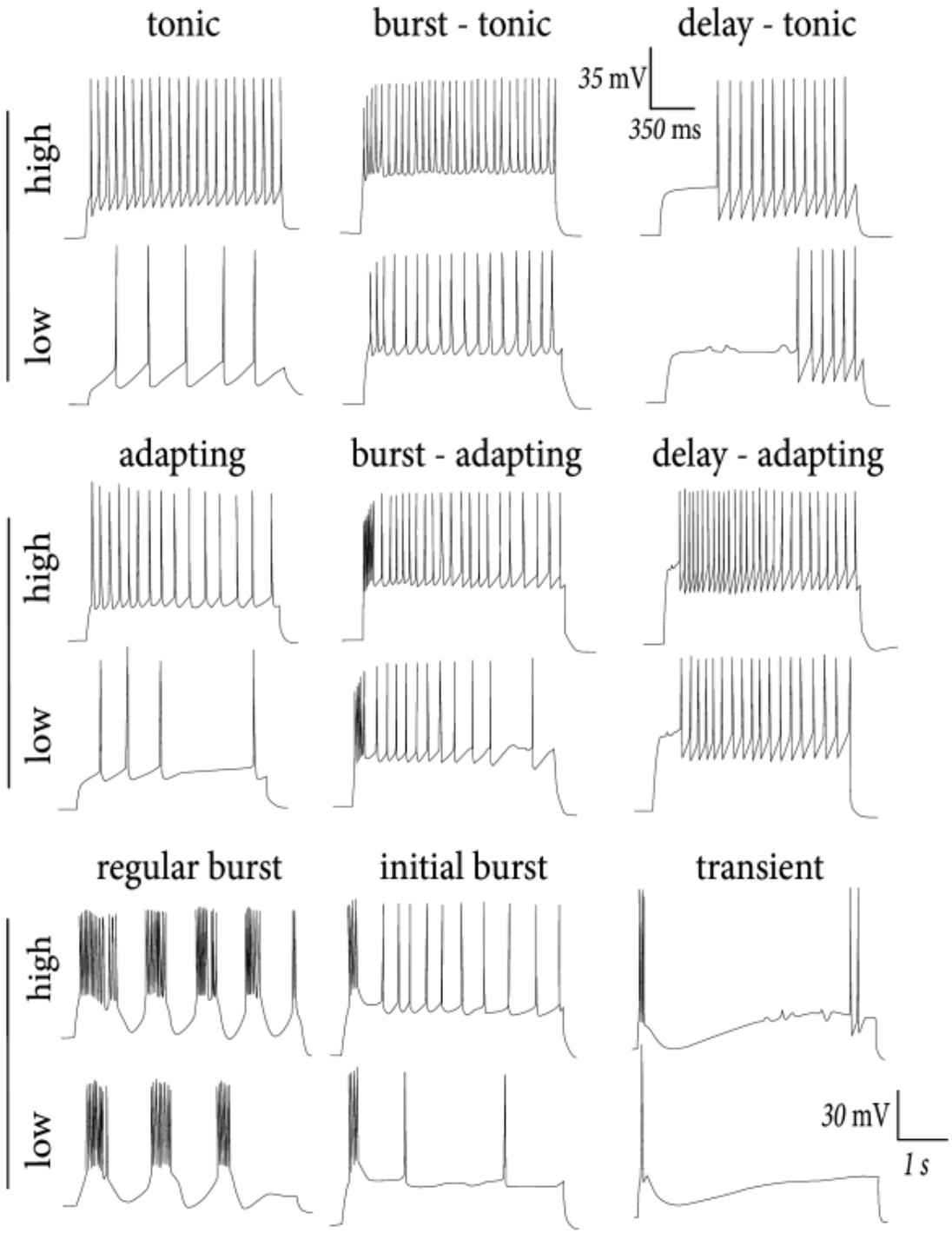

Figure 11: Various spiking patterns in neurons [5]

All of the patterns above, can be explained by an Adaptive integrate and fire model(AdEx model). This model is generated by adding adaptation variables to the exponential integrate and fire model. AdEx integrate and fire model with one additional variable is discussed in the example below.

2.4.1 One additional variable

$$\tau_m \frac{du}{dt} = -(u - u_{rest}) + \Delta e^{(u-\vartheta)/\Delta} - Rw + RI(t)$$

$$\tau_w \frac{dw}{dt} = a(u - u_{rest}) - w + b\tau_w \sum_{t^{(f)}} \delta(t - t^{(f)}).$$

Case 1- large b, a = 0

Figure 12: case 1[5]

Case 2- small b, a = 0

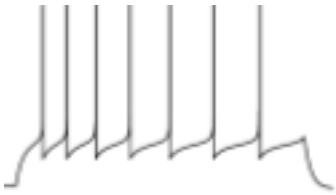

Figure 13: case 2 [5]

So as seen above, two different firing pattern arise from the same model. However, different parameters are the sources of different behavior in them. Now we can go further and consider the exponential part as a vertical line to make the equations linear. If we do so, we will reach SRM model that is described by two linear equations.

$$\tau_m \frac{du_i}{dt} = -(u_i - E_0) - R\sum_k w_k + RI_i(t)$$

$$\tau_k \frac{dw_k}{dt} = a_k(u_i - E_0) - w_k + \tau_k b_k \sum_{t^{(f)}} \delta(t - t^{(f)})$$

We can integrate from above equations and reach the following equation:

$$u(t) = \sum_f \eta(t - t^{(f)}) + \int_0^\infty \kappa(s) I_{ext}(t - s)ds + u_{rest}$$

In this model, threshold is updated after each spike so:

$$\vartheta(t) = \vartheta_0 + \int_0^\infty \theta_1(s) S(t - s)ds$$

At this model there are three linear filters that describe dynamic of neurons. The diagram of these linear blocks is illustrated below.

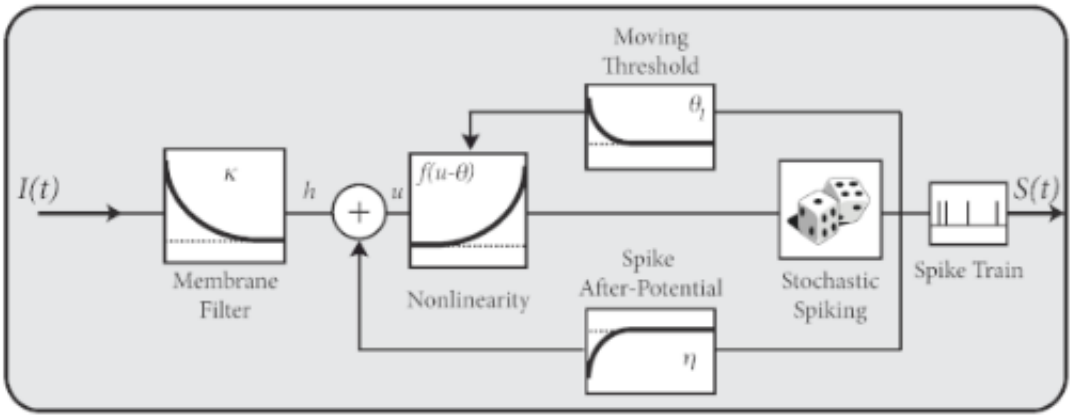

Figure 14: Spike Response Model(SRM). Input current I(t) is filtered with a filter $\kappa(s)$ and yields the input potential $h(t) = \int_0^\infty \kappa(s)I(t-s)ds$. Firing occurs if the membrane potential u reaches the threshold ϑ. S(t) is the spiking train of a neuron. Spikes $S(t) = \sum_f \delta(t - t^{(f)})$ are fed back into the threshold process in two distinct ways. Each spike causes an increase θ_1 of the threshold: $\vartheta(t) = \vartheta_0 + \int_0^\infty \theta_1(s)S(t-s)ds$. Moreover, each spike generates a voltage contribution η to the membrane potential: $u(t) = h(t) + \int_0^\infty \eta(s)S(t-s)ds$, where η captures the time course of the action potential and the spike-afterpotential. [5]

2.5 Noisy models [1], [2]

A neuron receives stochastic spikes from other neurons, so the spiking process is stochastic and the spiking time is not reliable. There are two major sources of variability. 1- intrinsic noise. 2- network noise. We can assume that the firing process has a Poisson distribution. In renewal processes, the probability of firing depends on the time that is past from the previous spike and this is why refractoriness does not happens. Knowledge of $p_0(s)$(interval distribution) is equivalent to knowing the survivor function $S_0(s)$ or the hazard $\eta_0(s)$. Knowing mentioned functions leads us to calculate the likelihood of a known spike train. Based on a real spike train, we should optimize the parameters of our model in order to maximize the log likelihood of the actual spike train. The noise model that is commonly used for this purpose is escape noise model that is an approximation of a diffusive noise model.

3 Research question

Oscillation is the main function behind the operation of many complex networks. Synchronization of neural networks refers to a time-based correlated activity of neurons.[4], [6].
Electrical synapses allow bidirectional current flows between neurons; these synapses are places at which gap-junctions connect the membranes of two neurons and initiates synchronization.
Our main objective is to study the effect of a voltage dependent gap-junction in synchronization of a large network of neurons. The recently published paper [4], has analytically [4], [7] studied the effect. This report has a numerical approach towards the same research question of the paper. At the end we will show that results found by numerical studies correspond to the analytical results reported in the paper.

4 Model and methods

In order to numerically study the effect of a voltage-dependent gap-junction and to compare that to a constant gap junction, a simulation in Matlab has been done. The simulation assumptions will be discussed below:

4.1 Network characteristics

The network is composed of two neurons. One from an excitatory population and one from an inhibitory population. The starting voltage value of the neurons is $-30mV and -55mV$. The first neuron excites the second one and the second one inhibits the first one.

4.2 Timing

The total simulation time was 10 seconds and the time step was 1 mili-seconds.

4.3 The quadratic integrate and fire model

Near the onset of firing it can be shown that the detailed dynamics of any type I conductance-based neuron model can be replaced by the reduced model:

$$c\frac{dv}{dt} = A(v - v^*)^2 + I - I_c.$$

where analytical formula can be derived to compute the effective capacitance c, the constant values of A and v^* . Using these formula one can compute these parameters numerically as functions of the biophysical parameters of the full conductance based model. I is the external current and I_c is the rheobase current- the minimal current amplitude of infinite duration (in a practical sense, about 300 milliseconds) that will result in the depolarization threshold of the cell membranes being reached, such as an action potential.
In this report we use a Quadratic integrate and fire model with parameters derived from D.Hansel and G.Mato paper[3]. Using the approach described in the paper one finds $I_c = 0.1601mA/cm^2, v^* = -59.5462mV, \bar{c} = 0.9467\mu F/cm^2$, and $A = 0.012875mS/cm^2/mV$. Also the reset and threshold voltages are determined as $v_{thresh} = -26.3462mV, v_{reset} = -64.1462mV$.
The quadratic integrate and fire model is less accurate in comparison to the HodgkinHuxley model. However, since it is less computationally expensive and is easier to implement, it has been chosen as our model for all neurons in this simulation.

4.4 External current components

- Fixed current
  To study the synchronization we will need to have a repetitive spiking pattern in the neurons; Hence, a fixed external current should be injected to the neuron. To find the minimum fixed current that will result in a repetitive spiking pattern, a Lyapunov stability analysis has been conducted in the Appendix A. Based on this analysis, in the absence of all other external currents, I_{fixed} should be greater than I_c to reach our goal. In this simulation $I_{fixed} - I_c = 1.691mA/cm^2$.

- Synaptic current
  Synaptic current is modeled by

  $$I_{syn} = \bar{g(t)}(v - E_{syn}) \rightarrow \bar{g(t)} = g[1 - e^{-\frac{(t-t(f))}{\tau_{rise}}}]e^{-\frac{(t-t(f))}{\tau_{fall}}}$$

  where $g, \tau_{rise}, \tau_{fall}$ are determined by the synapse type. E_{sync} is the potential value of the neuron at which ionic current is zero. For this simulation we have considered the inhibitory synapses to be $GABA_A$ and excitatory synapses to be $AMPA$.

- Bidirectional current(gap-junction current)
  It is known in the literature that gap-junctions play the main role in the synchronization of neurons. For a long time gap-junctions were modeled by a constant conductance; However, in this report, we want to model the gap-junctions as voltage dependent conductances and compare the effect of this approach on synchronization comparing to a constant conductance model. If the voltage-dependent coupling improves the synchronization, we can design a virtual voltage-dependent gap-junction as a controller between two neurons that we wish to synchronize them.

4.5 Measure of synchrony[3]

To characterize the degree of synchrony in a population of neurons in the simulations we measure the temporal fluctuations of the membrane potential averaged over the population[3]. The quantity

$$V(t) = \frac{1}{N}\sum_{i=1}^{N} V_i(t)$$

is evaluated over time and the variance $\sigma_V^2 =< [V(t)]^2] >_t -[< V(t) >_t]^2$ of its temporal fluctuations is computed. After normalization of σ_v to the average over the population of the single cell voltages $\sigma_V i^2 =< [Vi(t)]^2] >_t -[< Vi(t) >_t]^2$ the measure of synchrony is defined :

$$x(N) = \frac{\sigma_v^2}{\sum_{i=1}^{N} V_i(t)}$$

which is between 0 and 1. In particular, $x(N) = 1$ if the system is fully synchronized and $x(N) = 0$ in the asynchronous state.
In this simulation, we have taken account the last 1000 samples of neurons' voltages as signals to compute measure of synchrony.

5 Numerical results

As discussed before we are interested in studying the effect of voltage-dependent coupling in the synchrony of a network compared to a fixed coupling. In the voltage-dependent coupling case, the coupling can be dependent on the pre or post neuron; For each case we will study how the synchronization changes. Moreover, the simulation is conducted in both absence and presence of the synaptic currents. All in all, six different conditions are considered in the simulation.

- In the absence of synaptic currents, gap-junction conductance = g (constant coupling)

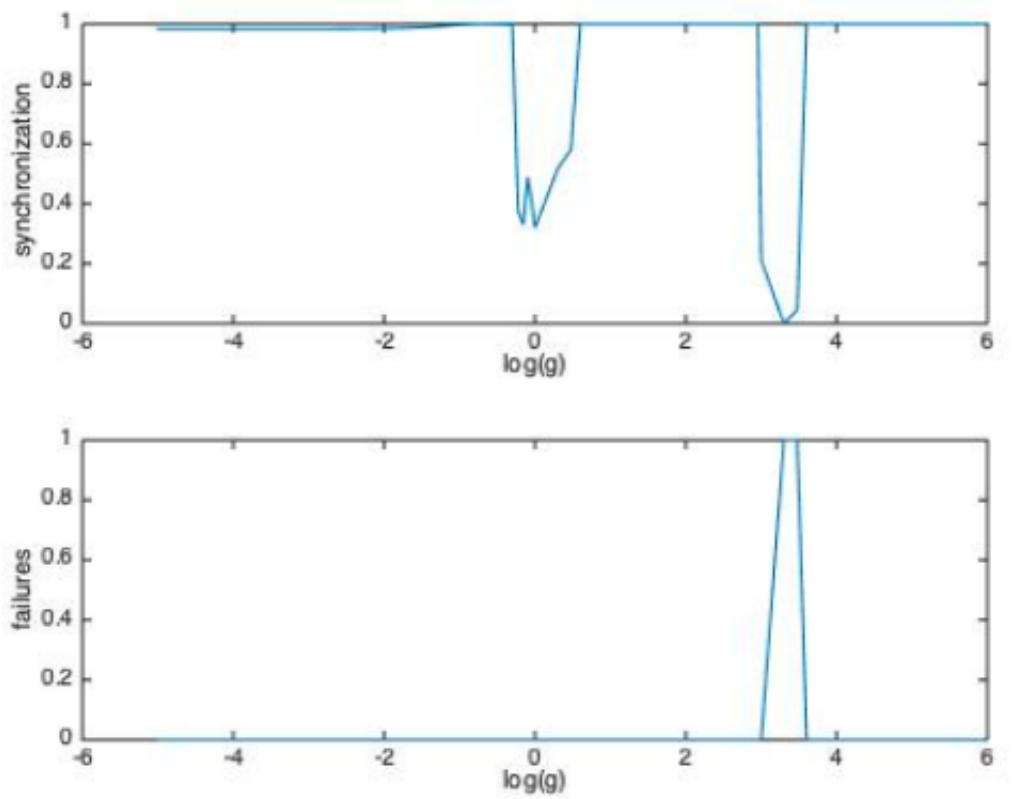

Figure 15: $\bar{g} = 0$, gap-junction conductance = g (constant coupling)

- In the absence of synaptic currents, gap-junction conductance = gv_{pre} (voltage-dependent coupling)

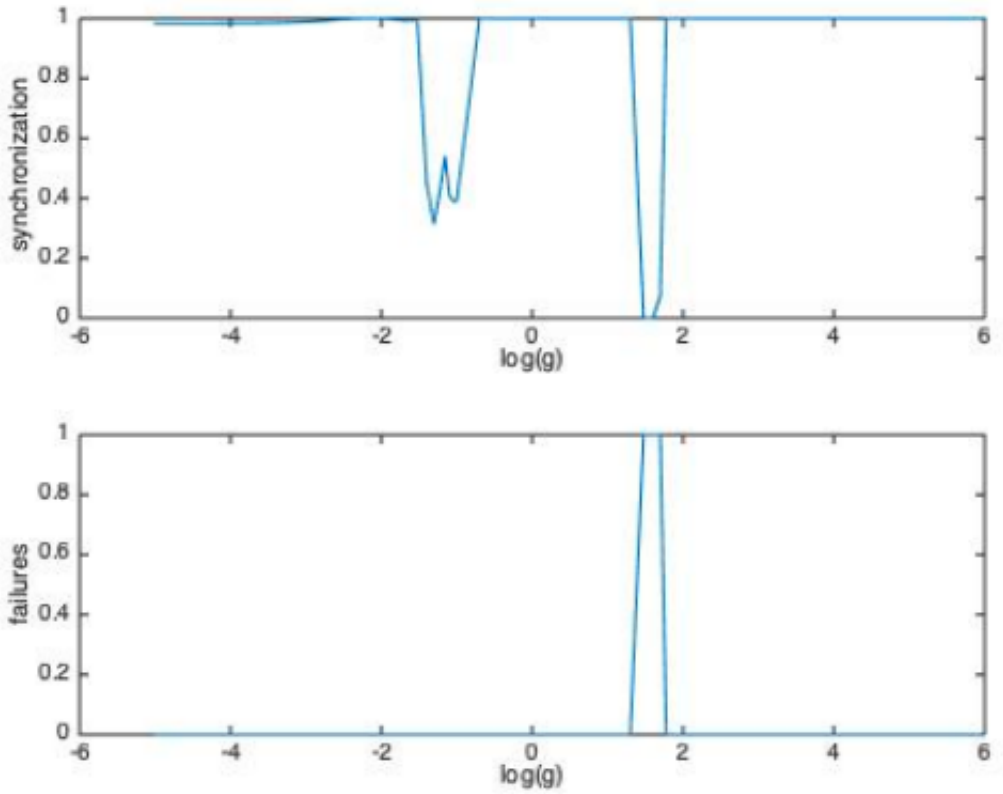

Figure 16: $\bar{g} = 0$, gap-junction conductance = gv_{pre} (voltage-dependent coupling)

- In the absence of synaptic currents, gap-junction conductance = gv_{post} (voltage-dependent coupling)

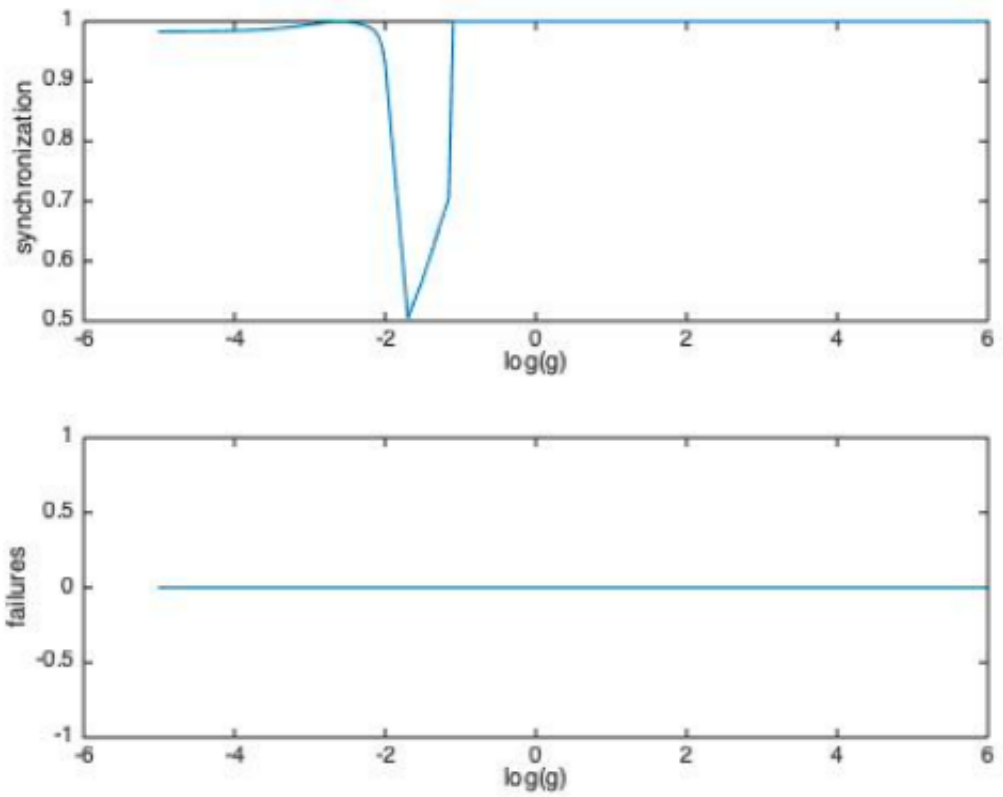

Figure 17: $\bar{g} = 0$, gap-junction conductance $= gv_{post}$ (voltage-dependent coupling)

- In the presence of $GABA_A$ and $AMPA$ Synaptic currents, gap-junction conductance $= g$ (constant coupling)

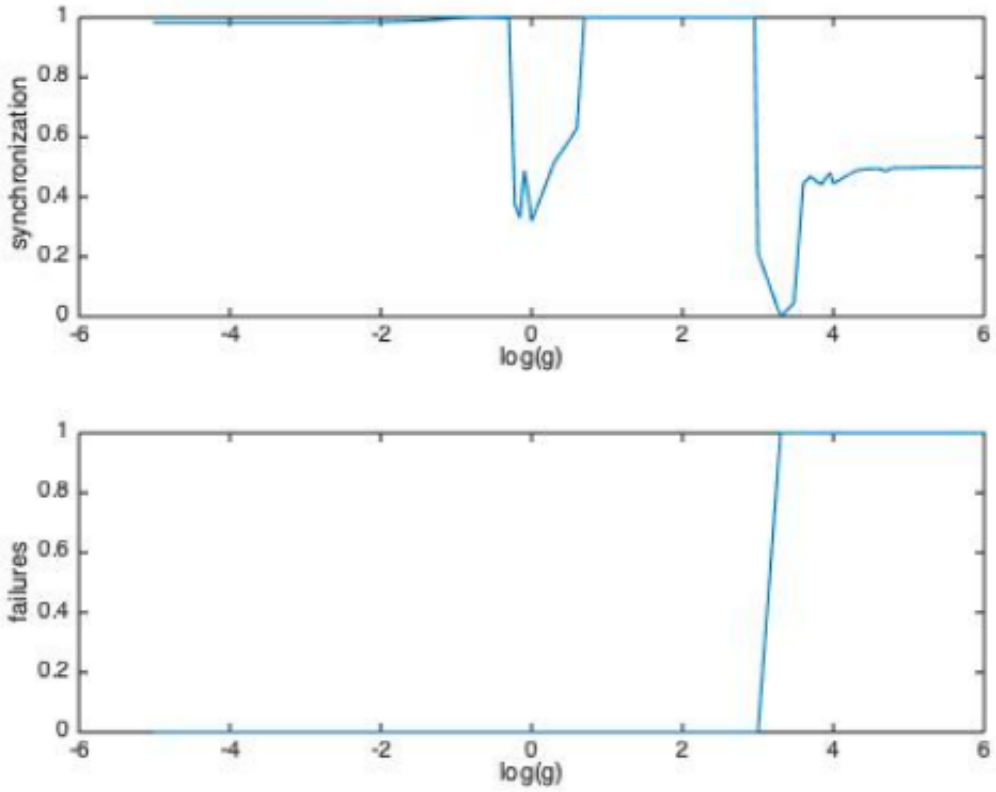

Figure 18: $\bar{g} = 0.01$, gap-junction conductance $= g$ (constant coupling)

- In the presence of $GABA_A$ and $AMPA$ Synaptic currents, gap-junction conductance $= gv_{pre}$ (voltage-dependent coupling)

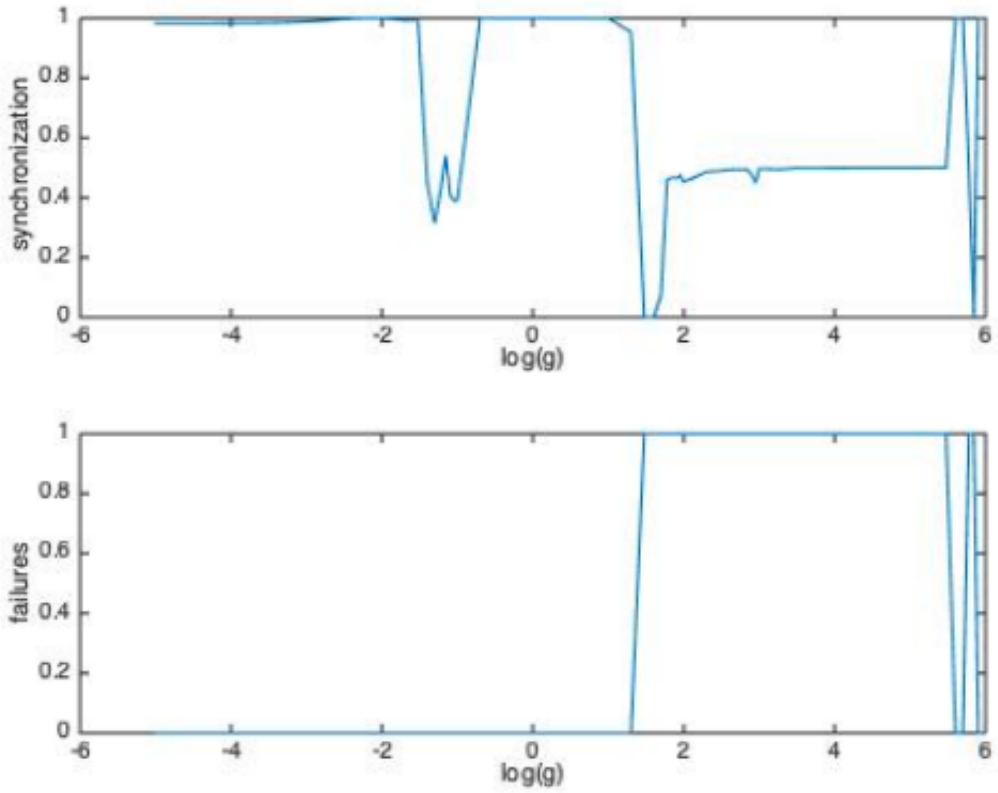

Figure 19: $\bar{g} = 0.01$, gap-junction conductance $= gv_{pre}$ (voltage-dependent coupling)

- In the presence of $GABA_A$ and $AMPA$ Synaptic currents, gap-junction conductance $= gv_{post}$ (voltage-dependent coupling)

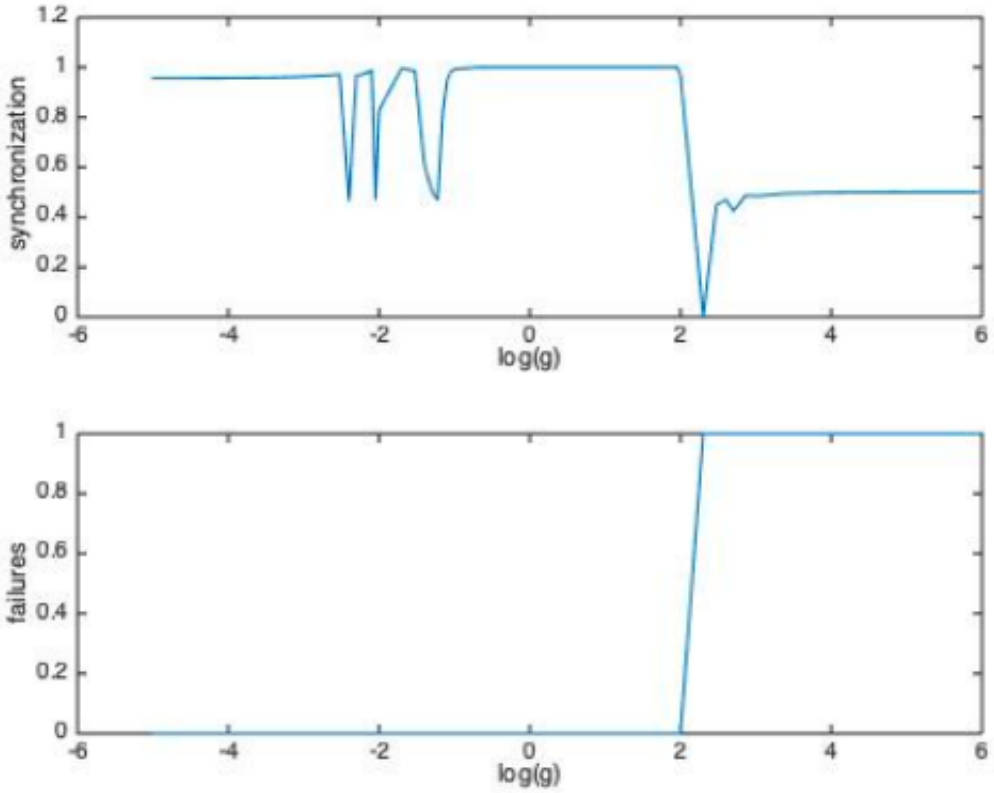

Figure 20: $\bar{g} = 0.01$, gap-junction conductance $= gv_{post}$ (voltage-dependent coupling)

6 Conclusion

In the fixed coupling conditions, both in the presence and absence of a synaptic current, for very small g values the neurons are highly synchronized. Full synchrony happens for a short range of constant g values, then for some g values($g \in [0.4, 5]$), synchronization stops. If g goes more than a particular value($g > 5$), full synchronization happens again. There is a sharp decrease in synchronization measure for $g \in [1000, 4000]$ in the first plot. This decrease is due to computational error and does not show what happens in real neurons. If we decrease simulation's time step so that it gets small enough, we will see full synchrony for all g values more than 2. In the fixed coupling condition where synaptic currents exist, if $g > 1000$, we can see a decrease in synchrony measure in the plot which is due to computational error. However, by decreasing the time step, we can assure that there is a full synchrony in the system for all g values greater than 5.

When the coupling conductance is a multiples of the first neuron's voltage, both in the presence and absence of synaptic currents, for $g < 0.02$ the system is highly synchronized. For $g \in [0.02, 0.5]$ synchronization is low, and for $g > 0.5$ there is a full synchrony in the system. System failures due to computational error is visible in the corresponding plots. When the coupling conductance is a multiples of the second neuron's voltage, in both presence and absence of synaptic currents, when $g > 0.1$, the system is fully synchronized. As analytical proof has shown, in the latter case(where the coupling conductance is a multiples of the second neuron's voltage) full synchronization starts in lower g values [4].

To sum up, In the presence or absence of synaptic currents, in the cases of voltage dependent coupling, full synchronization starts in lower g values comparing to fixed coupling conditions.

A Appendix

The quadratic integrate and fire model that we introduced has two equilibrium points, $\bar{v_1} = v^* + \sqrt{\frac{I_c}{A}}$, $\bar{v_2} = v^* - \sqrt{\frac{I_c}{A}}$. By choosing the function $V = \frac{1}{2}(v - \bar{v})^2$ for each equilibrium point as its lyapunov function, each equilibrium point is stable if $\dot{V} < 0$in a neighborhood around it.

• Stability analysis around $\bar{v_1}$: $V = \frac{1}{2}(v - \bar{v_1})^2$: $\dot{V} = \dot{v}(v - \bar{v_1}) < 0$ if and only if $v < v^* - \sqrt{\frac{I_c}{A}}$.

• Stability analysis around $\bar{v_2}$: $V = \frac{1}{2}(v - \bar{v_2})^2$: $\dot{V} = \dot{v}(v - \bar{v_2}) < 0$ if and only if $v^* - \sqrt{\frac{I_c}{A}} < v < v^* + \sqrt{\frac{I_c}{A}}$.

As a result, $\bar{v_2}$ is a stable point while $\bar{v_1}$ is an unstable point. Because we want to put the system in the mood of multiple spikes, stability is not desired. Hence, by choosing I_{fix} ,the fixed current being injected to the system, in a way that $I_{fix} > I_c$ and as a result $I_{ext} = I_{fix} - I_c > 0$, we make sure that the derivative is always positive and the system is unstable starting from any initial condition.

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