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Modeling of time delay-induced multiple synchronization behavior of interneuronal networks with the Izhikevich neuron model

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Abstract: The synchronization behavior of the networks of fast-spiking interneurons is investigated by using one of the phenomenological neural network models, the Izhikevich model. Since electrical and chemical synapses exist within the same networks of inhibitory cells, delayed inhibitory and fast electrical synapses are coupled in the simulations. The effects of hybrid synapses in promoting synchronous activity in neural networks are investigated with short and long time delays. The distinct frequency bands observed in electroencephalography and magnetoencephalography signals are determined using the raster plots of neural networks. For quantitative comparison of activities in networks, the degree of synchrony in the network is calculated. The influences of several network parameters such as inhibitory synaptic strength, electrical synaptic strength, synaptic time constant, and time delay on the network activity are investigated. It is observed that the coupling of electrical and chemical synapses promotes multiple synchronous behaviors in the network. Another important finding is that even though the synchronization measure is highly dependent on inhibitory synaptic strengths at low electrical synaptic strength and synaptic time constant, not much dependence on inhibitory synaptic strengths is observed at high electrical synaptic strength.

Key words: Fast-spiking neuron, Izhikevich neuron model, frequency bands, synchronization

1. Introduction

Synchronization of networks is an important phenomenon since most neural networks rely on a synchronous behavior for proper functioning, such as pattern recognition, information transmission, and learning. The synchronization in a network may also lead to some diseases such as Parkinson disease and epilepsy [1]. For example, abnormal synchronous bursting behavior of neuronal networks is a sign of epileptic activity. The synaptic mechanisms have profound influences on synchronization [2].

The synchronized activity of a network of neurons exhibits oscillations. These oscillations have characteristic frequencies ranges from 0.1 Hz to $>$100 Hz and are related to different brain functions such as sleeping and waking stages. The oscillations at a variety of frequencies are observed in electroencephalography (EEG), which is an electrophysiological monitoring method to record electrical activity of the brain. EEG is used to diagnose epilepsy, sleep disorders, coma, and brain death. In addition, magnetoencephalography (MEG), a functional neuroimaging technique, is used for mapping brain activity. The signals measured in EEG and MEG can be decomposed into distinct frequency bands such as 1–3 Hz (delta), 4–7 Hz (theta), 8–15 Hz (alpha), 16–31 Hz (beta), and 32–70 Hz (gamma). There is a correlation between these rhythms and behaviors [3].

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For brain functions, communication between neurons is required. Interneuronal communication primarily takes place at synapses, where information is carried from one neuron to a second neuron. There are two main modalities of synaptic transmission: chemical and electrical. Both chemical and electrical synapses are structurally complex and functionally dynamic. Interactions between these two forms of interneuronal communication are required for normal brain development and function [4].

Electrical and chemical synapses exist within the same networks of inhibitory cells, resulting in hybrid coupled networks, and each kind of synapse is able to assist the synchrony among oscillating neurons [4,5].

Modeling the dynamic behavior of a network has attracted much attention in recent years [4–22]. Gibson et al. [6] showed by paired-cell recordings that while the same type of inhibitory neurons were strongly interconnected by electrical synapses, electrical synapses between different inhibitory cell types were rare. In coupled interneurons, the electrical synapses were strong enough to synchronize spikes. Between fast-spiking (FS) cells, inhibitory chemical synapses are also common.

Several works in the literature used only chemical synaptic currents in the investigation of the synchronization behavior of networks [2,7–10]. In the wok by Kudela et al. [2], a conductance-based model was used to study the networks of synaptically connected neurons generating action potentials. The network consisted of excitatory and inhibitory neurons. Each neuron in the network had a defined number of inhibitory and excitatory synapses on its input. Only inhibitory synaptic current was used in the simulations. The effects of time delay on the local and global synchronization in small-world neuronal networks with chemical synapses were investigated in the work by Yu et al. [10]. It was shown that the information transmission delay can always induce synchronization transitions of spiking neurons in small-world networks for both excitatory and inhibitory coupling types.

Garbo et al. [11] investigated synchronization properties using several biophysical

models of FS interneurons and in particular the Wang and Buzsaki model [12]. Their main findings were that the synchronization properties are model-dependent and the reversal potential of the inhibitory synapses affects the synchronization properties

A simple mass model was described considering the model of Jansen and Rit [13] by Olivier and Friston [14]. It was shown that the whole spectrum of MEG/EEG signals can be reproduced within the oscillatory regime of this model by changing the population kinetics. It was shown that MEG/ EEG signals depend upon the kinetics of both inhibitory and excitatory neural populations [14].

In this work, the synchronization behavior of interneuronal networks is investigated using the Izhikevich model by coupling chemical and electrical synapses. In the literature, there are some works that used both synapses for synchronization behavior of neurons with different scale neuron models. In these works, the dynamics of FS interneurons were described either by the Wang-Buzsaki model [12] or by conductance-based model [2], and some other works used Hodgkin–Huxley type models [11,15]. To the best of my knowledge, the modeling capabilities of the Izhikevich model in terms of synchronization have not been investigated. In this work, the Izhikevich model is used by coupling the chemical and electrical synapses with and without delays. Not only the behavior at short time delay but also the effect of long time delay is considered with various electrical and chemical synaptic strengths. The distinct frequency bands observed in EEG and MEG signals are determined using the raster plots of neural networks. For quantitative comparison of activities in networks, the degree of synchrony in the network is calculated as well. The influences of several network parameters on the synchronization behavior of interneuronal networks are investigated. It is shown that both types of synapses play an important role in the synchronization of the network. By increasing the inhibitory synaptic

delay, a transition from regular to mixed oscillatory patterns is observed. Another important finding is that the dependence of synchronization measure on time delay decreases when the inhibitory synaptic strength is strong enough.

2. Izhikevich neuron model

The phenomenological Izhikevich neuron model is used to investigate the synchronization behavior of interneuronal networks. Two-dimensional systems of differential equations of the Izhikevich neuron model are in the form given in Eq. (1).

$$\begin{aligned} \dot{v} &= 0.04v^2 + 5v + 140 - u + I \\ \dot{u} &= a(bv - u) \end{aligned} \tag{1}$$

Here, v and u represent the membrane potential of the neuron and membrane recovery, respectively. They are dimensionless variables. v and u account for the activation of K^+ ionic currents and inactivation of Na^+ ionic currents, respectively [16]. a and b are dimensionless parameters. The last term, I, in Eq. (1) denotes currents that consist of two parts: externally applied current and synaptic current, ($I = I^{out} + I^{syn}$). The externally applied current represents the effect of inputs coming from outside of the network. Applied external current is modeled as $I^{out} = I_o + \beta\alpha_i(t)$, where I_o is constant, α(t) is white noise with mean value of 1 mA, and $\beta = 0.025$. After the spike reaches its apex (+30 mV), the membrane voltage and the recovery variable are reset according to Eq. (2).

$$v \geq 30 \quad \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases} \tag{2}$$

Here, c and d are dimensionless parameters.

Since many FS cell pairs display both an electrical synapse and a chemical inhibitory synapse in at least one direction [4], the internal synaptic current consists of two terms, which are electrical and chemical synapses for each neuron, as given in Eq. (3) [22].

$$I_i^{syn}(t) = \sum_j r_{ij}\left[E_{inh} - V_i\right] + \sum_k g_{ik}\left[V_k - V_i\right] \tag{3}$$

Here, the reversal potential for inhibitory synapses is E_{inh} = –80 mV. V_i and V_k denote the membrane potential of neurons i and j, respectively. r_{ij} decreases exponentially with a time constant, τ_s, as given in Eq. (4).

$$\tau_s \dot{r}_{ij} = -r_{ij} \tag{4}$$

For each spiked neuron (the jth connected to ith neuron), the connection between these neurons is updated as $r_{ij} \leftarrow r_{ij} + \omega_{ij}$ after time delay τ_{ij}. ω_{ij} is the inhibitory synaptic strength from neuron j to neuron i. g_{ik} is the electrical synaptic strength from neuron k to i. It is constant throughout the paper [22].

The degree of synchrony in the network is calculated according to the method developed by Hansel and Sompolinsky [23]. The synchronization measure is computed as in Eq. (5).

$$S = \frac{\Delta_N}{\Delta} \tag{5}$$

Time fluctuations of the average membrane potential are defined as in Eq. (6).

$$\Delta_N = \left\langle A_N(t)^2 \right\rangle_t - \left\langle A_N(t) \right\rangle_t^2 \tag{6}$$

Here, the sign $\langle\rangle_t$ denotes the average over time. $A_N(t)$ is the average membrane potential in the network at time t given as $A_N(t) = \sum_{i=1}^{N} V_i(t)/N$.

The population averaged variance of single neuron activity is determined according to Eq. (7).

$$\Delta = \frac{1}{N}\sum_{i=1}^{N}\left(\langle V_i(t)^2\rangle_t - \langle V_i(t)\rangle_t^2\right) \tag{7}$$

3. Simulation results

3.1. Synchronization of FS interneurons with coupled chemical and electrical synapses

The network comprises 300 FS neurons, which are connected by inhibitory chemical and electrical synapses. It is assumed that all electrical synapses are fast; delays are only considered by the inhibitory synapses. Connection probability is $pr_c = 0.1$ for chemical and $pr_e = 0.05$ for electrical synapses. Chemical synapses are bidirectional. The two-dimensional system of differential equations of the Izhikevich neuron model is integrated numerically using the Euler method with a fixed time step of $h = 0.01$ ms. The influences of several network parameters on the network activity are analyzed and discussed. The network activity is defined as $\sum_i n_i(t)$ where $n_i(t)$ is the number of spiked neurons in the network in a short time interval.

First, FS interneurons are connected by inhibitory chemical synapses. The influences of inhibitory synaptic strength (ω_{ij}) and electrical synaptic strength (g_{ij}) are investigated. Simulations are done for 1500 ms. However, for a detailed view, the raster plots are depicted for only the last 300 ms. Apart from delayed chemical synapses, the networks can be coupled by fast electrical synapses, so-called gap-junctions. They are thought to be involved in the synchronization behavior of neurons. The raster plots for various inhibitory synaptic delays (τ = 0, 5, 15, 25, 50, 60 ms) with only chemical synapses and with chemical and electrical synapses are depicted in Figures 1a and 1b, respectively. In these simulations, inhibitory synaptic strength is $\omega = 0.025$ and the time constant is τ_s =10 ms.

Figure 1a reveals that when there is only a chemical synapse and fixed spike transmission delay, which is an inhibitory synaptic delay, τ is zero and the synchronization cannot be achieved. When time delay is introduced, the network exhibits synchronous behaviors. Increasing time delay leads to multiple synchronous behaviors in the network.

As observed from Figure 1b, introducing electrical synapses promotes the synchronization. Even without time delay, synchronization is induced. Similar to Figure 1a, multiple synchronous behaviors are observed by induced time delay. With increasing time delay, the pattern changes from a single bar to a multiple bar structure. Compared to the effect of chemical synapses, it is observed that the electrical one has prominent effects on synchronization.

The reasons for observing multiple synchronous behaviors can be explained as follows:

- Neurons fire at a specific frequency with an externally applied current without any inhibition. Constant initial current I_o is selected as 8.5 pA to maintain the firing of FS neurons at frequencies of around 100 Hz. The time between two spikes in the neurons that fire in this frequency is 10 ms. If time delay is less than this period, delayed inhibition in other neurons reaches one neuron in less than 10 ms. Therefore, the respective neuron spikes only once. Firing is delayed since the current I decreases due to inhibition. Depending on time constant τ_s, the inhibition decreases with time. After inhibition, the neuron spikes again, and since the other neurons spike approximately at the same time, firing is seen as a single bar in the raster plots.

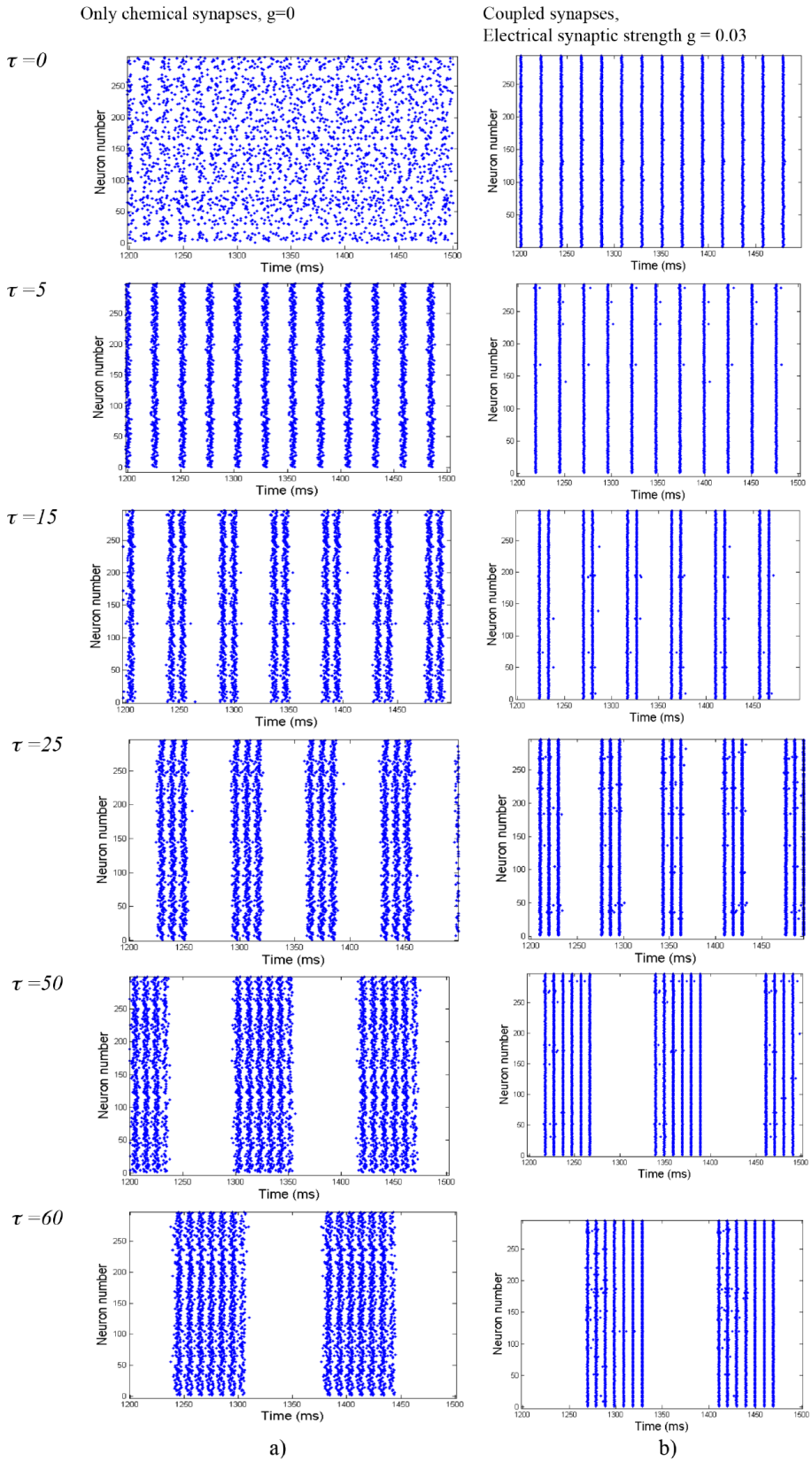

Figure 1. The raster plots of the network with (a) only chemical synapses and (b) coupled synapses for different inhibitory synaptic delays (τ = 0, 5, 15, 25, 50, 60 ms). ω = 0.025, the time constant τ_s = 10 ms.

- If time delay is bigger than the firing period, before receiving inhibition from other neurons, any neuron can spike more than once. This situation can be seen clearly in the raster plots. For example, as seen in Figures 1 and 2, at τ =50 ms and τ_s =10 ms, since the effect of inhibition in a neuron is reached after 50 ms, the neuron spikes six times before inhibition. This behavior is observed as 6 bars in the raster plots.
- If the time delay is longer than the firing period, two different frequencies are observed in the raster plot. Frequencies observed in the simulations revealed in Figure 1a are given in the Table.

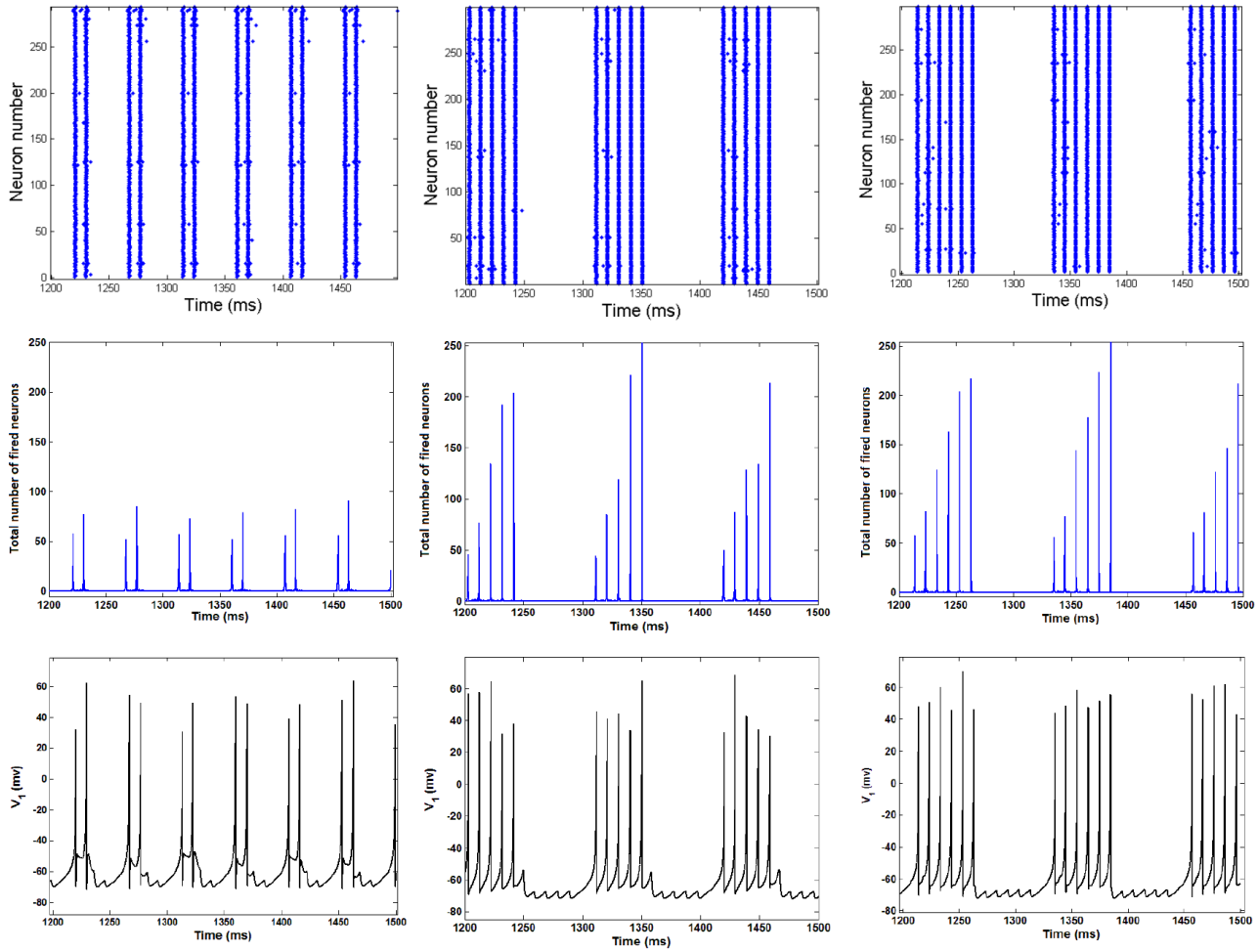

Figure 2. Raster plots, network activity, and membrane potential of the first neuron for coupled synapses for time delay τ = 15, 47, and 50 ms. g = 0.03, ω = 0.025.

It is found that interneuronal networks can be synchronized by coupled synapses within the gamma frequency range for low time delays. When time delay is varied, the neuronal firing frequencies change monotonically and cover a frequency range from alpha to gamma bands.

In Figure 2, for comparison, raster plots, network activity, and membrane potential of any neuron versus time curves with coupled synapses for three time delays, τ = 15, 47, and 50 ms, are depicted. These three time delays are selected to depict the behaviors at beta (τ = 15 ms) and alpha frequencies (τ = 47 and 50 ms) (see the Table). The network activity, which is defined as the total number of spiked neurons in the network

Table. Frequencies obtained when coupled synapses are present.

Time delay, τ(ms)	Lower frequency, f (Hz)	Distinct frequency bands	Higher frequency, f_1 (Hz)
5	40	Gamma	Not observed
15	20	Beta	100
25	15	Alpha	100
50	10	Alpha	100
60	8	Alpha	100

at any time, is calculated. As seen in Figure 2, the number of the neurons that spike first is lower, and then it is increasing with time. The reason for this behavior is decreased inhibition. Since the effect of inhibition is decreasing, more neurons spike with time.

As observed in Figure 2, even though each neuron in the network is the FS type, bursting type membrane potential is observed. Neuronal activity alternates between a silent phase (resting mode) and an active phase of fast repetitive spiking. As seen in the membrane potential graphs of the first neuron, when the time delay is increased, the number of spikes increases. For example, while 5 spikes are observed at 47 ms of time delay, when the time delay is changed to 50 ms, 6 spikes are obtained.

3.2. The synchronization measure

To compare the neural activities in networks quantitatively, the degree of synchrony in the network is calculated according to Eqs. (5)–(7). As seen from Figure 1, time delay and electrical and chemical synapses have influences on the synchronous behavior of networks. The synchronization measure, S, versus inhibitory synaptic delay, τ, is plotted in Figure 3 for various inhibitory synaptic strengths. In these simulations, only chemical synapses are considered (g = 0).

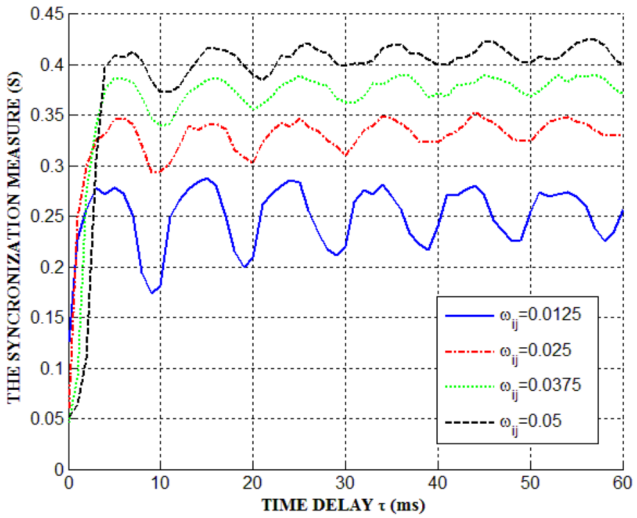

Figure 3. The synchronization measure, S, versus inhibitory synaptic delay, τ, for various inhibitory synaptic strengths. g = 0.

Figure 3 reveals that increasing inhibitory synaptic strength promotes the synchronization. Lower synaptic strength exhibits oscillation in synchronization measure S with time delay. It is also observed that when time delay is increased, the magnitude of oscillation in synchronization measure is decreasing. However, at

high synaptic strengths, the oscillatory behavior observed in synchronization measure decreases. It is observed that the dependence of synchronization measure in time delay is decreasing when inhibitory synaptic strength is strong.

As observed from Figure 3, the synchronization measure is the highest at time delays of 5, 15, 25, 50, and 60 ms. When these time delays are used in the simulations, the bars in the raster plots are obtained clearly and the exact determination of frequencies is possible. Therefore, in the Table, the aforementioned time delays are considered.

In the next simulations, by keeping inhibitory synaptic strength constant ($\omega = 0.025$), the delay-induced synchronization behavior is modeled in networks composed of inhibitory neurons for different electrical synaptic strengths (g). Synchronization measure S versus inhibitory synaptic delay τ for various electrical synaptic strengths (g) is depicted in Figure 4.

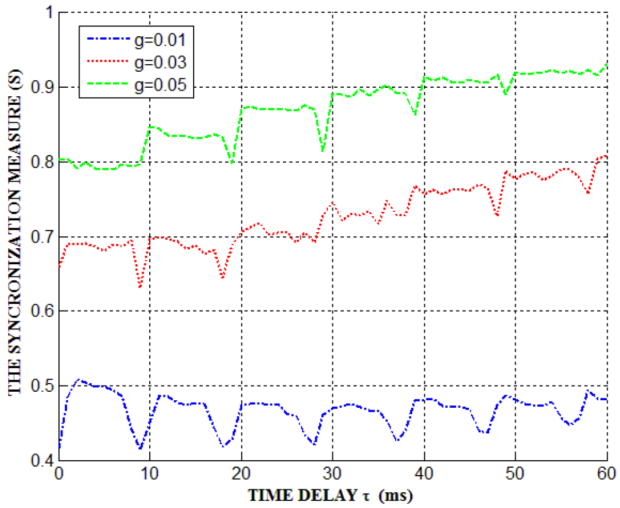

Figure 4. The synchronization measure, S, versus inhibitory synaptic delay, τ, for various electrical synaptic strengths. $\omega = 0.025$.

It is seen in Figure 4 that introducing electrical synapses promotes the synchronization measure. For example, while g = 0.05 at $\tau = 60$ ms, S is approaching one, which means that full synchrony, S, is only 0.325 at the same time delay when g = 0, as seen in Figure 3. In these simulations, synaptic time constant $\tau_s = 10$ ms. Synchronization measure is decreasing at almost multiples of the firing period and then starts to increase. Synchronization is highly dependent on the synaptic strength. It is observed that without introducing electrical synapses, reaching high synchronization measures is not possible.

As can be seen from Figures 3 and 4, the synchronization measure for time delays near multiples of the firing period (in our case, it is 10 ms without inhibition) is lower than other values of τ. This can be explained as follows: at τ near multiples of the firing period of FS neurons, some neurons fire but some neurons are still inhibited so they cannot fire. Therefore, the synchronization is low. At τ values different than multiples of the firing period, all neurons are inhibited or not inhibited.

Dependence of synchronization measure S on synaptic time constant τ_s for different inhibitory synaptic strengths is investigated and S versus τ_s is plotted in Figure 5 for different strengths. Electrical synapses are zero here. Since in Figure 3 it is observed that at almost multiples of 5 ms (10 ms), S reaches the maximum (minimum) for each strength, the next simulations are done for synaptic delays $\tau = 5$ ms and $\tau = 10$ ms.

As seen from Figure 5, at shorter synaptic time constants, S is changing significantly with τ_s. The

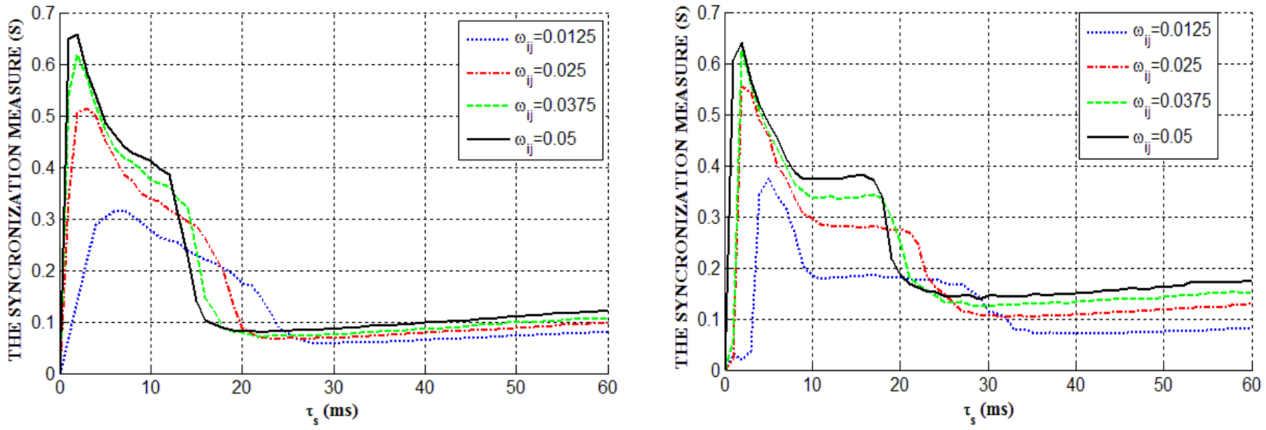

Figure 5. The synchronization measure, S, versus synaptic time constant, τ_s, for various inhibitory synaptic strengths. g = 0.

increase in S is followed by a decrease and then an almost constant S is obtained. To investigate the reasons for low S at high τ_s, the raster plot of the network for $\tau_s = 50$, ($\tau = 5$, $\omega_{ij} = 0.05$, and g = 0), the membrane potential and the current of the 25th neuron are depicted in Figure 6. The 25th neuron is selected due to its interesting dynamics: it spikes and stays in a resting position.

Analyses show that in the case of long τ_s, once a presynaptic neuron spikes, its inhibition effect on the postsynaptic neuron continues for a long time. As a result of this, the postsynaptic neuron cannot spike due

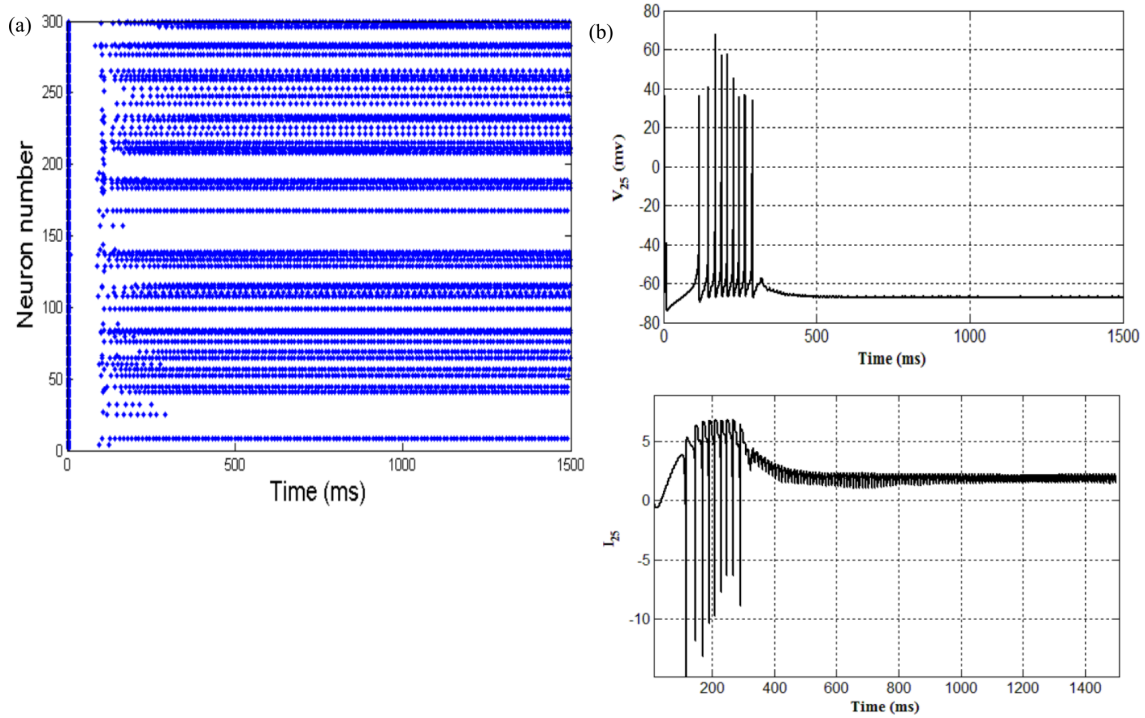

Figure 6. (a) The raster plot of network and (b) the membrane potential and current of the 25th neuron for $\tau_s = 50$, $\tau = 5$, $\omega_{ij} = 0.05$, and g = 0.

to the decreased current as long as the inhibition effect continues. For this reason, many neurons cannot spike; therefore, synchronization decreases.

In Figure 7, the influences of synaptic time constant on S are depicted when coupled synapses are used in the simulations. As observed from Figure 7, for higher electrical synaptic strength and low synaptic time constant, the synchronization measure reaches 1. When the synaptic time constant is increased, S starts to decrease and reaches an almost constant value. When Figures 7a and 7b are compared, it is observed that at low electrical synaptic strength S highly depends on inhibitory synaptic strengths while at high electrical synaptic strength, not much dependence on inhibitory synaptic strengths is found.

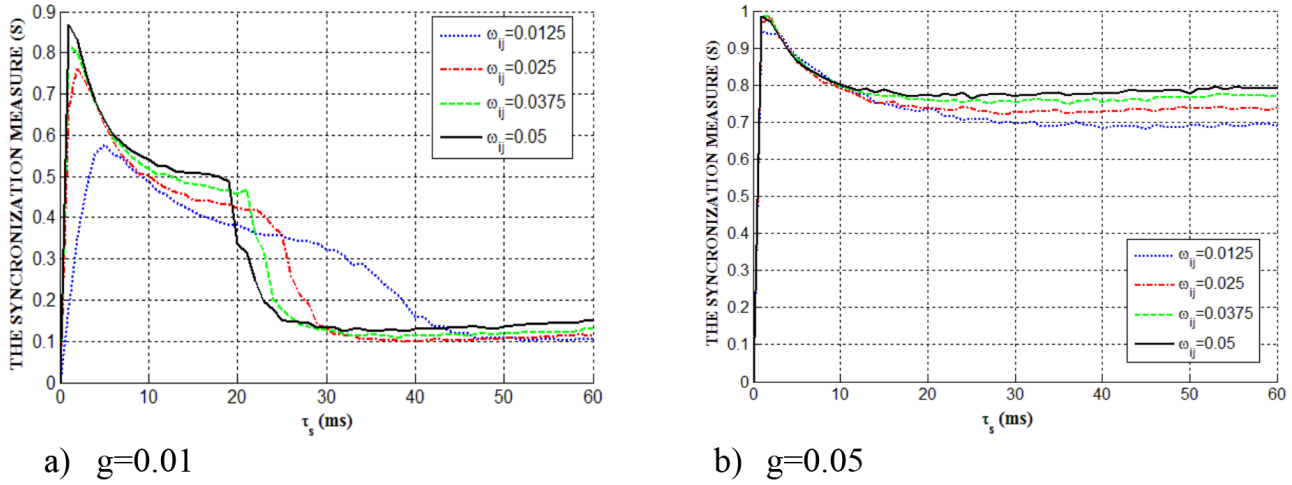

Figure 7. The synchronization measure, S, versus synaptic time constant, τ_s, for various inhibitory synaptic strengths. $\tau = 5$ ms.

4. Conclusions

The effects of coupled synapses and time delay in promoting synchronous activity in neural networks are investigated using the phenomenological neural network model, the Izhikevich model. Dependence of synchronization on synapses parameters is investigated and results are analyzed. Inhibitory synapses with zero time delay do not induce synchronization even at high inhibitory synaptic strength. However, when inhibitory synapses are coupled with chemical ones, synchronization is induced even without time delay. Increasing time delay leads to multiple synchronization patterns. Time delay and the synaptic time constant have significant effects on synchronous behavior as strengths. It is observed that the synchronization measure is highly dependent on inhibitory synaptic strengths at low electrical synaptic strength. However, not much dependence on inhibitory synaptic strengths is found at high electrical synaptic strength. A wide range of frequencies is covered depending upon time delays. The detailed analysis of these frequencies will be done as a future work.

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