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Research Article

Analysis of parameter changes of a neuronal network model using transfer entropy

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ABSTRACT

Understanding the dynamics of coupled neurons is one of the fundamental problems in the analysis of neuronal model dynamics. The transfer entropy (TE) method is one of the primary analyses to explore the information flow between the neuronal populations. We perform the TE analysis on the two-neuron conductance-based Hodgkin-Huxley (HH) neuronal network to analyze how their connectivity changes due to conductances. We find that the information flow due to underlying synaptic connectivity changes direction by changing conductances individually and/or simultaneously as a result of TE analysis through numerical simulations.

1. Introduction

Neuronal action potentials are the basic units of brain activity but how millions of neurons adjust their interactions remains an open problem. Different patterns of synchronization behavior have been observed by the excitable cells after an applied stimulation or during spontaneous activity [1-3]. These synchronizations have been observed in different sensory tasks including visual [4], auditory [5] as well as in the motor system [6]. Some pathological conditions in brain activity are related to the disturbance of the synchronization patterns [7]. Once the dynamics of the synchronization changes, the pattern activity between neurons change mostly due to the communication between the ion channels. However, the effects of the ion channels on the information transfer are still unclear. We approach this question with a statistical measure called transfer entropy.

Transfer entropy is a non-parametric statistical measure capable of capturing nonlinear source-destination relations between multi-variate time series [8-9]. Data recorded from neurons involve generally one or more variables and the interactions between these variables are highly nonlinear. So, applying the transfer entropy method is fit to analyze these types of neuronal data. Directed information methods like transfer entropy reveal an analytical difference between the direction of the information flow between the neurons in a network. We perform the TE analysis on the two-neuron conductance-based Hodgkin-Huxley (HH) neuronal network to obtain how their connectivity changes due to conductances.

It has been shown that the relationship between the parameters including ionic conductances, applied current, or coupling constant of a neuron affects the pattern of synchronization [10-11]. However, analyzing the roles of intrinsic ionic conductances in information transfer is limited. Most neurons involve voltage-gated currents together with background 'passive' currents and we will be focusing on their influence on information flow [12]. To the best of our knowledge there have been no works detailing how ionic conductances can tune the direction of information flow between the neurons in a neuronal network.

Conductance-based models have been used to generate the spiking activity of electrically excitable cells including heart cells, pancreatic-beta cells and neurons and it has proved itself as a very successful tool to mimic the spiking activity and analyze the systems deeply [13-15].

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Mathematical models of the neurons can contain many free parameters that drive the activity pattern such as the maximal conductances of the different ionic currents, applied current, the coupling constant, or noise strength [16]. These parameters should be determined either by experimental measurements or by simulations of complex optimization problems until the model performs truly. However, conductances of real neurons are not constant parameter, they can change with the changing activity of the cell according to the intrinsic dynamics of the currents [17]. We focus on the effects of the maximal conductances in a coupled Hodgkin-Huxley neuronal network that we defined. In our model, the coupling is defined from Neuron 1 to Neuron 2 and in the system, while Neuron 1 is spiking due to the applied current, Neuron 2 is spiking due to the coupling from Neuron 1. In this network, there are two negative feedback variables for each neuron. The activation of a K^+ current (n) responsible for the upstroke of an impulse together with the inactivation of the Na+ currents (h) provides negative feedback to the system. On the other hand, Na^+ current activation (m) responsible for starting the spiking activity provides positive feedback for each neuron in our network model.

Here, we explore the activities of voltage-gated Na^+, K^+ channels, and passive leak ion channels using a Hodgkin-Huxley-type model network. For a coupled HH model, we show that the activities due to the changes in the conductance parameters of these channels manifest themselves as variations of the synchrony of the action potentials and the spike intervals of the coupled system. Due to these changes, the roles of the affecting and the affected neurons can easily switch, causing a change of direction in coupling. In order to explore this phenomenon from data, we propose the utilization of transfer entropy, which is a non-parametric information theoretic quantity used to detect the direction of the statistical interactions between two variables, even if they are nonlinearly dependent as in this application. We show that we can detect any change in the direction between the affected and the affecting neurons and demonstrate this as a function of changing conductance values.

Our findings are important in terms of understanding the changes in channel activation/inactivation properties as a result of changes in channel densities which can reveal the physiological or pathological situations affecting the neuronal network activity in the way neurons respond to changes in conductances.

2. Methods

In this work, we focus on the analysis of a network of two coupled neurons using the HH model system and apply the transfer entropy method to this model with changing maximal conductances. We studied the effects of varied potassium, sodium, and leak conductances on transfer entropy in two populations of conductance-based model neurons.

2.1 Transfer Entropy

An effective mathematical modeling of a physical phenomenon is of utmost importance to better understand and describe the factors and their relationships causing it. In statistics and machine learning, many methods, such as regression and neural networks, have been utilized in science and engineering for this purpose. In addition to modeling, information theory has let us to quantify the interactions between different variables and/or model parameters using data. In particular, Shannon entropy is an information theoretical quantity to describe the average uncertainty of a system, model or a parameter and it is defined by the following equation:

$$H(V) = -\sum_{v\in V} p(v)\log\big(p(v)\big). \qquad (1)$$

where H denotes the entropy of a random variable "V" and p(v) represents its probability density function (pdf). Using this main concept, other information theoretical quantities, like the Shannon entropy, Mutual Information (MI), Kullback-Leibler divergence and Transfer Entropy (TE), are defined in the literature [18-19]. Among these, MI is used to quantify the "amount of information" obtained about one random signal through observing the other random signal, which can be expressed by the following equation:

$$MI(V_1, V_2) = \sum_{v_1\in V}\sum_{v_2\in V} p(v_1, v_2)\log\frac{p(v_1,v_2)}{p(v_1)p(v_2)}, \quad (2)$$

where $MI(V_1, V_2)$ denotes the mutual information between random variables V_1 and V_2. Above, it is observed that this quantity is defined in terms of the pdf of random variables and becomes zero for the statistical independence case, i.e. p (v_1, v_2) =p(v_1)p(v_2). MI can be utilized to identify nonlinear relationships among random variables, whereas the correlation coefficient ρ is optimal as long as there is a linear relationship. MI between two variables can also be expressed as a summation of Shannon entropies as shown below:

$$MI(V_1, V_2) = H(V_1) + H(V_2) - H(V_1, V_2), \qquad (3)$$

where $H(V_1, V_2)$ is the joint Shannon entropy. Here, we note that $MI(V_1, V_2) = MI(V_2, V_1)$, meaning that MI is a symmetric measure. Therefore, if we would like to identify the direction of information flow from one variable to another, MI is not a sufficient approach. Instead, Schreiber [19] proposed another information theoretical quantity, called Transfer Entropy, which is capable of detecting the direction, i.e. either V_1 effects V_2, or V_2 effects V_1, for two variables. In the literature, the affecting variable is generally known as the "source" and the affected variable is known as the "target" variable. The TE in two directions are calculated from data by using the following equations:

$$TE_{V_1V_2} = T\left(V_{2(i+1)}\middle|\boldsymbol{V_{2(i)}^{(k)}}, \boldsymbol{V_{1(i)}^{(l)}}\right) = \sum_{v_{2(i+1)}, \boldsymbol{v_{2(i)}^{(k)}}, \boldsymbol{v_{1(i)}^{(l)}}} p\left(v_{2(i+1)}, \boldsymbol{v_{2(i)}^{(k)}}, \boldsymbol{v_{1(i)}^{(l)}}\right) \log_2 \frac{p\left(v_{2(i+1)}|\boldsymbol{v_{2(i)}^{(k)}}, \boldsymbol{v_{1(i)}^{(l)}}\right)}{p\left(v_{2(i+1)}|\boldsymbol{v_{2(i)}^{(k)}}\right)}, \quad (4)$$

$$TE_{V_2V_1} = T\left(V_{1(i+1)}\middle|\boldsymbol{V_{1(i)}^{(k)}}, \boldsymbol{V_{2(i)}^{(l)}}\right) = \sum_{v_{1(i+1)}, \boldsymbol{v_{1(i)}^{(k)}}, \boldsymbol{v_{2(i)}^{(l)}}} p\left(v_{1(i+1)}, \boldsymbol{v_{1(i)}^{(k)}}, \boldsymbol{v_{2(i)}^{(l)}}\right) \log_2 \frac{p\left(v_{1(i+1)}|\boldsymbol{v_{1(i)}^{(k)}}, \boldsymbol{v_{2(i)}^{(l)}}\right)}{p\left(v_{1(i+1)}|\boldsymbol{v_{1(i)}^{(k)}}\right)}, \quad (5)$$

where $(i+1)$ is an index for the leading time instant and (i) is an index for the current time. Above, $\boldsymbol{v_{1(i)}^{(k)}} = \left\{v_{1(i)}, \dots, v_{1(i-k+1)}\right\}$ shows the vector including the value of V_1 at time instant (i) and its values at $(k-1)$ preceeding time instants. Similarly, $\boldsymbol{v_{2(i)}^{(l)}} = \left\{v_{2(i)}, \dots, v_{2(i-l+1)}\right\}$ denotes the vector including the value of V_2 at time instant (i) and its values at $(l-1)$ leading time instants. Here, V_1 shows the k-th order and V_2 shows the l-th order Markov processes. In the literature, k and l are also referred as the embedding dimensions. In our simulations, one past value of each signal is taken into consideration by assuming $k = l = 1$ during TE analysis. In this case, TE can be estimated by the marginal and joint Shannon entropies as follows:

$$TE_{V_2V_1} = T\left(V_{1(i+1)}\middle|\boldsymbol{V_{1(i)}}, \boldsymbol{V_{2(i)}}\right) = H\left(V_{1(i)}, V_{2(i)}\right) - H\left(V_{1(i+1)}, V_{1(i)}, V_{2(i)}\right) + H\left(V_{1(i+1)}, V_{1(i)}\right) - H\left(V_{1(i)}\right) \quad (6)$$

In order to analyze the effect of change in conductance parameters, we utilize TE as defined above. In these equations, we note that the pdf's of variables need to be estimated from data first. Here, utilized histogram based estimations to infer the multivariate pdf's given above. To do this, both source and target data are separated into certain number of bins and the frequency of data in each volume element is used as the pdf estimate [20-21]. As an example, we illustrate the joint probability density estimate , $\hat{p}\left(V_{1(i)}, V_{2(i)}\right)$, of two action potential data, using 10 and 100 bins for the marginal and joint histograms, respectively, in Figure 1.In order to judge if the estimated values are significant, we utilize a surrogate data testing with a p-value of 0.05.

The rest of the approach proceeds as follows: The probability density function of each term in (6) is estimated by the illustrated histogramming given above and the following entropy terms are obtained using (1) and its multivariate versions:
$H\left(V_{1(i)}, V_{2(i)}\right), H\left(V_{1(i+1)}, V_{1(i)}, V_{2(i)}\right), H\left(V_{1(i+1)}, V_{1(i)}\right),$ $H\left(V_{1(i)}\right)$. Finally, TE from $V_2 to\, V_1$ is computed by the substitution of these in (6). The procedure is shown in the Figure 2.

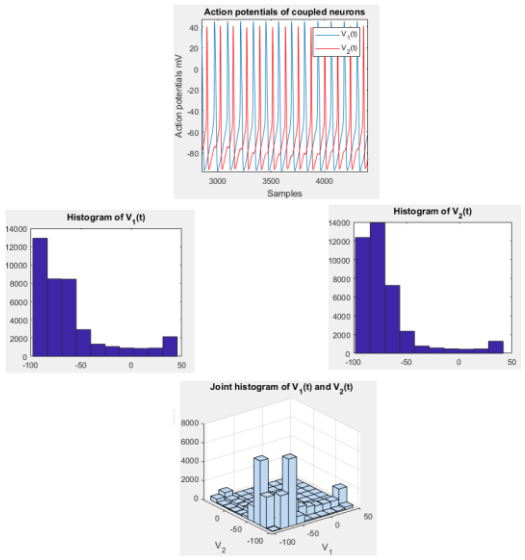

Figure 1. Probability density estimation from neuron action potential data using histograms.

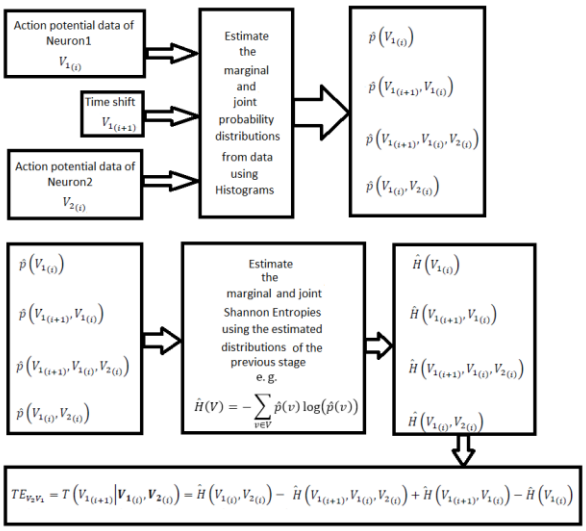

Figure 2. The block diagram of the proposed approach.

2.2 Model

Neurons are electrically excitable cells and responsible for the information transfer in our body through electrical signals called action potentials or spikes. Hodgkin and Huxley (HH) defined a first mathematical model that explains the generation of spikes using a nonlinear differential equation system [22]. K^+ and Na^+ ions together with the Cl^- ions are mainly responsible for the electrical behavior of the HH system. We consider a Hodgkin-Huxley type model describing the activity of two coupled neuronal network with coupling corresponds to that of an electrical synapse as shown in Figure 3. Electrical synapses are specific sites where gap junction channels bridge the plasma membrane of two neurons. Gap junction is a gap between the pre- and post-synaptic neurons and impulse in here are transmitted in both directions [23]. So we define the coupling is proportional to the difference between the pre-synaptic and postsynaptic membrane potentials.

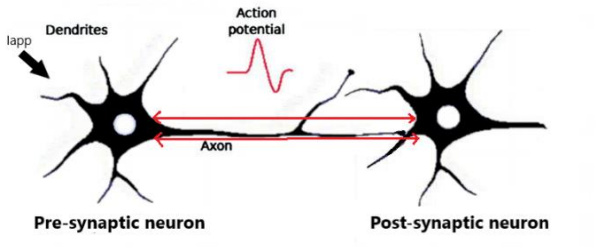

Figure 3. Model configuration for two-neuron Hodgkin-Huxley network

The differential equations for the rate of change of voltage V_1 and V_2 for these neurons are given as follows:

$$C_m \frac{dV_1}{dt} = I_{app} - I_{Na,1} - I_{K,1} - I_{L,1}, \quad (7)$$

$$C_m \frac{dV_2}{dt} = -I_{Na,2} - I_{K,2} - I_{L,2} - k(V_1 - V_2) \quad (8)$$

where C_m is the membrane capacitance, I_{app} is the applied current. Here, $I_{Na,i}$ is the fast sodium current, $I_{K,i}$ is the delayed rectifying potassium current and $I_{L,i}$ is the leak current that all measured in $\frac{\mu A}{cm^2}$ for $i = 1,2$. Coupling between the two neurons is simply defined by voltage difference as $k(V_1 - V_2)$ and coupling strength is k.

In our HH network model, ionic currents for each neuron $x = 1,2$ are defined as follows:

$$I_{Na,x} = \overline{g_{Na,x}} m^3 h (V_x - V_{Na}), \quad (9)$$

$$I_{K,x} = \overline{g_{K,x}} n^4 (V_x - V_K), \quad (10)$$

$$I_{L,x} = \overline{g_{L,x}} (V_x - V_L). \quad (11)$$

V_{Na}, V_K, V_L are the reversal potentials associated with the currents. Here m represents the Na^+ activation and h represents the inactivation of the channel. n is the activation variable of the K^+ current. Here $\overline{g_x}$ denotes the maximal conductances. Gating functions of the ion channels defined with activation and inactivation dynamics and changing with time according to the differential equations below:

$$\frac{dx}{dt} = \frac{x_\infty(V) - x}{\tau_x(V)}, \quad x = m, h, n. \quad (12)$$

The equilibrium activation and inactivation functions are defined as follows;

$$x_\infty(V) = \frac{\alpha_x(V)}{\alpha_x(V) + \beta_x(V)}, \quad x = m, h, n, \quad (13)$$

where (τ_x) shows the time that the channel needs to reach the equilibrium. Time constants in our network model are defined as:

$$\tau_x(V) = \frac{1}{\alpha_x(V) + \beta_x(V)}, \quad x = m, h, n. \quad (14)$$

Table 1 contains the information on the transition rates α_x and β_x and the parameter values used to simulate the network.

Table 1. Transition rates and parameter values for the coupled two-neuron network model.

Transition rates (ms^{-1})		
α_m	$0.1(40+V)/(1-\exp(-(55+V)/10)$	
β_m	$4\exp(-(65+V)/18)$	
α_h	$0.07\exp(-(65+V)/20)$	
β_h	$1/(1+\exp(-(35+V))$	
α_n	$0.01(55+V)/(1-\exp(-(10V+55))$	
β_n	$0.125\exp(-(V+65)/80)$	
Parameter values		
$C_m = 1\ \mu F$	$V_{Na} = 50\ mV$	$g_{Na} = 120\ \mu S$
$I_{app} = 8\ mA$	$V_K = -77\ mV$	$g_K = 36\ \mu S$
$k = 0.25$	$V_L = -54.4\ mV$	$g_L = 0.3\ \mu S$

2.3 Simulation:

Model network is solved by XPPAUT software [24] using a 4th order Runge-Kutta solver with a time step of 0.001ms and the application of the transfer entropy method is simulated by the MATLAB software. Initial values for the simulations are considered as: $V_1 = V_2 = -65$, $m_1 = m_2 = 0.05$, $h_1 = h_2 = 0.6$ and $n_1 = n_2 = 0.317$.

3. Results

Varying ionic conductances have an effect on the cell's electrical activity and understanding the underlying reason is biologically crucial. Here, we investigate this by focusing on three conductances that are available in the Hodgkin-Huxley neuronal network model. Here, the defined coupled neurons show phase-locked spiking. By definition, the Neuron 1 is spiking due to applied current and the Neuron 2 is spiking due to the coupling from Neuron 1. So originally the direction of the information flow is defined from Neuron 1 to Neuron 2 (1-to-2). We both independently change the conductances of each current separately and the same currents' conductances simultaneously under the observation of the amount of information flow. For all cases, we simulate transfer entropy analysis over the ranges of g_x parameters for which the model network exhibits tonic spiking and analyzes whether the order of the information flow changes due to the strength of the maximal conductances or not.

3.1 The effects of changing maximal potassium conductances in the model

Altering the kinetic properties of K^+ current in the HH model is known to alter the spike duration and interspike interval [15]. And the maximal K^+ conductances g_{K1} and g_{K2} in our coupled two-neuron network model measures the amount of subtractive feedback to the system from each neuron. So here we ask whether the information flow changes the direction by changing the amount of subtractive feedback with altering the conductances separately (g_{K1} or g_{K2}) and simultaneously (g_{K1} and g_{K2}).

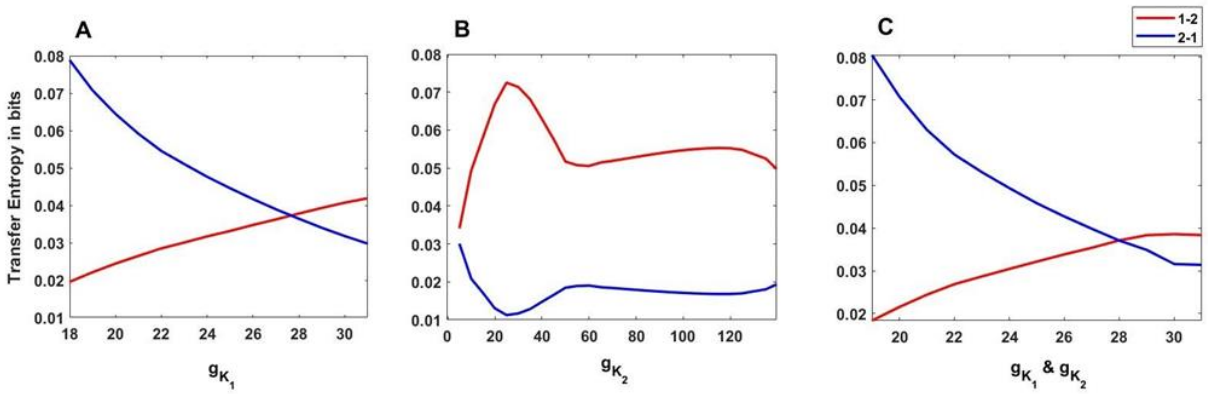

Figure 4. Transfer entropy results with changing a) g_{K1}, maximal conductance of K^+ current for Neuron 1 b) g_{K2}, maximal conductance of K^+ current for Neuron 2 and c) g_{K1} & g_{K2}, maximal conductances of K^+ currents for Neuron 1 and Neuron 2 simultaneously with the same ratio.

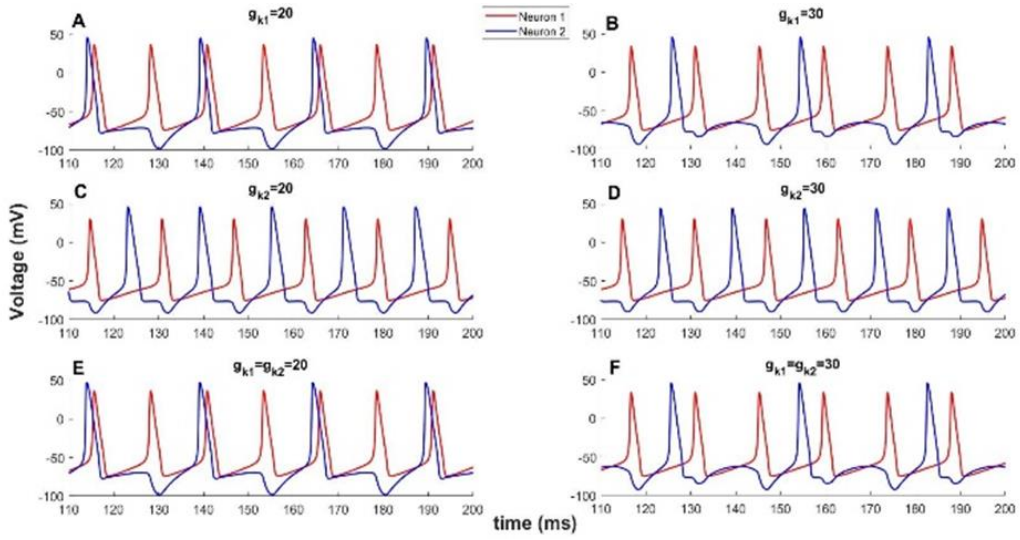

Figure 5. Pattern of spiking activity of Neuron 1 and Neuron 2 when A) g_{K1}=20, g_{K2}=36; B) g_{K1}=30, g_{K2}=36; C) g_{K1}=36, g_{K2}=20; D) g_{K1}=36, g_{K2}=30; E) $g_{K1} = g_{K2} = 20$; F) $g_{K1} = g_{K2} = 30$.

Figure 4 shows the effects of changing g_{K1} (panel A), changing g_{K2}(panel B), and changing g_{K1} and g_{K2} together (panel C) on information flow as a result of transfer entropy simulation. Information flow from Neuron 1 to Neuron 2 is shown as 1-to-2 and the information flow from Neuron 2 to Neuron 1 is shown as 2-to-1. Figure 5 shows the effect of the changing maximal conductances on the output signal in terms of the synchrony, spike duration, and interspike interval. We can see that, the direction of flow changes with the increasing g_{K1} conductance in Figure 4A. Even though our coupling is defined as 1-to-2, before g_{K1} around 27, the TE results of 2-to-1 is higher. This can be explained as the g_{K1} arranges the amount of the subtractive feedback and when the amount of subtractive feedback is high enough for Neuron 1, the frequency of Neuron 1 is decreasing by increasing the interspike interval as shown in Figures 5A and 5B.

As a result, input coming to Neuron 2 from Neuron 1 dominates the information flow and causes the change of the direction from 1-to-2 to 2-to-1 (Figure 4A).

The characteristic of the TE curves for varying g_{K2} does not cross each other meaning that the information flow does not change direction according to the strength of the subtractive feedback due to K^+ current of Neuron 2 [25]. To be able to change the information flow in this coupled system, we should support Neuron 2, but increasing g_{K2} will do the inverse and the phase locked system is not affected as illustrated in Figure 5C&5D.

Once we start to increase the K^+ conductance of each neuron together with the same ratio, we observe a similar effect of increasing the K^+ conductance of Neuron 1. For lower values of maximal K^+ conductances (g_{K1} and g_{K2}) information is transferred from Neuron 2 to Neuron 1. But there is a threshold value around $g_{K1} = g_{K2} = 28$, that the information changes the direction to 1-to-2. Figure 5E and 5F shows the spiking behavior and how the phase-locked system is affected by the changes of both K^+ conductances.

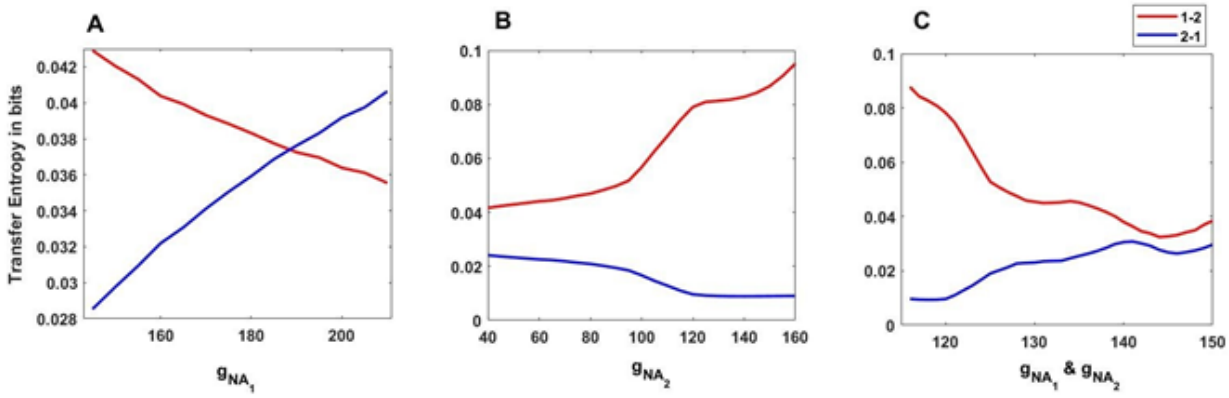

Figure 6. Transfer entropy results with changing a) g_{Na1}, maximal conductance of Na^+ current for Neuron 1 b) g_{Na2}, maximal conductance of Na^+ current for Neuron 2 and c) g_{Na1} & g_{Na2}, maximal conductances of Na^+ currents for Neuron 1 and Neuron 2 simultaneously with the same ratio.

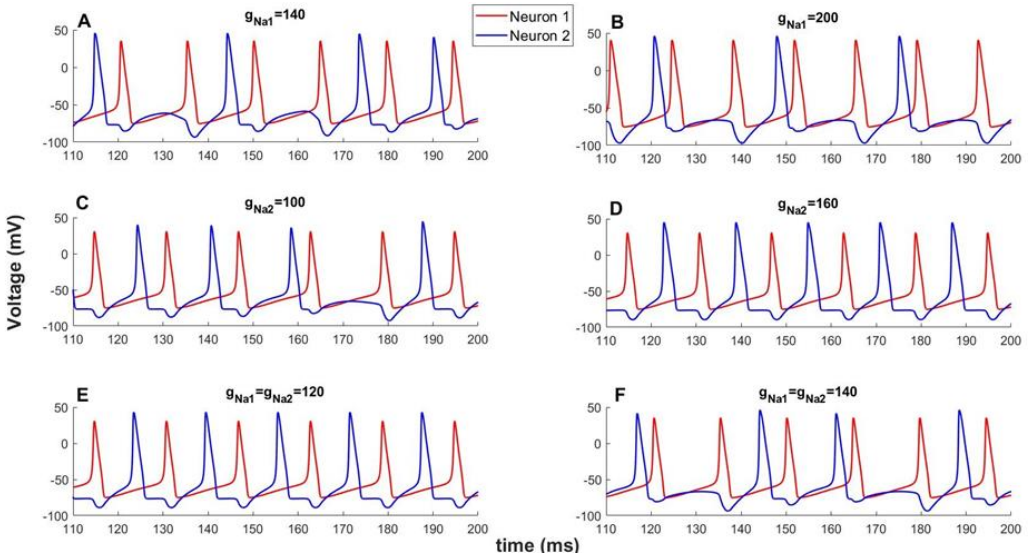

Figure 7. Pattern of spiking activity of Neuron 1 and Neuron 2 when A) g_{Na1}=140, g_{Na2}=120; B) g_{Na1}=200, g_{Na2}=120; C) g_{Na1}=120, g_{Na2}=100; D) g_{Na1}=120, g_{Na2}=160; E) $g_{Na1} = g_{Na2} = 120$; F) $g_{Na1} = g_{Na2} = 140$.

Since the system is highly nonlinear, forecasting the direction of the flow according to current strength is almost impossible without further analysis like we applied here with Transfer Entropy.

3.2 The effects of changing maximal sodium conductances in the model

The activity pattern that our model network displays are also controlled by Na^+ conductances g_{Na1} and g_{Na2} providing positive feedback to the related neurons. Additional Na^+ conductance supports the neuron to act more profoundly to equivalent input current as we can see in Figure 7.

Increasing the Na^+ current for Neuron 1 without increasing the K^+ current can cause the model network to drive into a more depolarized state and that is why information transfer changes direction from 1-to-2 to 2-to-1 (Figure 6A).

Once we compare the results of Na^+ and K^+ conductance effect on the TE as shown in the Figure 6A and Figure 4A, we observe an opposite behavior since they support the system adversely. On the other hand, increases in g_{Na2} conductance only have an inverse effect against the g_{Na1} results. The amount of information flow builds up from Neuron 1 to Neuron 2 and the direction of the information flow stays stable (Figure 6B). Increasing both Na^+ currents by increasing the maximal conductances g_{Na1} and g_{Na2} together have a similar effect in our coupled network and transfer entropy curves do not cross each other and the information flow stays the same.

The gating dynamics responsible for channel activations and inactivations are highly nonlinear especially for the Na+ conductance. Na^+ channel simulates the dynamics with two gates; activation and inactivation. While the activation of the Na^+ channel supports the system positively, inactivation of the channel provides negative feedback to the system [26].

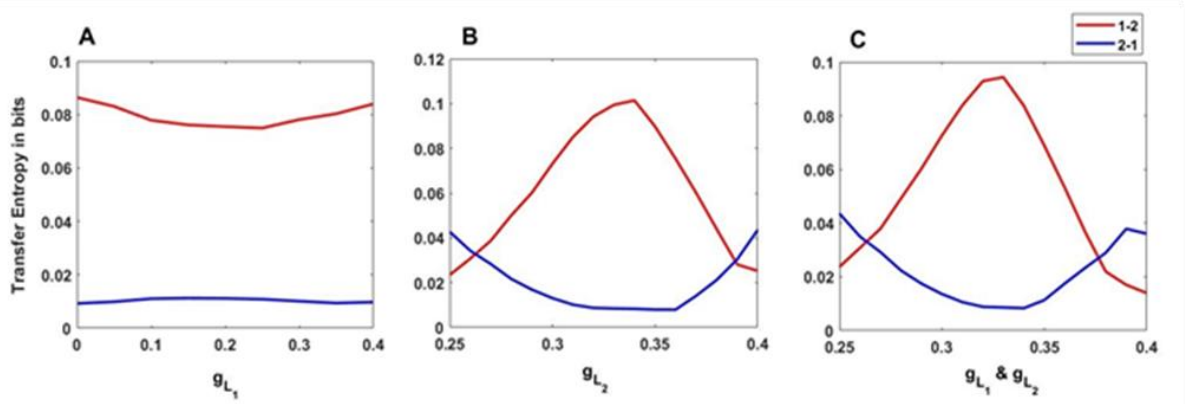

Figure 8: Transfer entropy results with changing a) g_{L1}, maximal conductance of leak current for Neuron 1 b) g_{L2}, maximal conductance of leak current for Neuron 2 and c) g_{L1}&g_{L2}, maximal conductances of leak currents for Neuron 1 and Neuron 2 simultaneously with the same ratio.

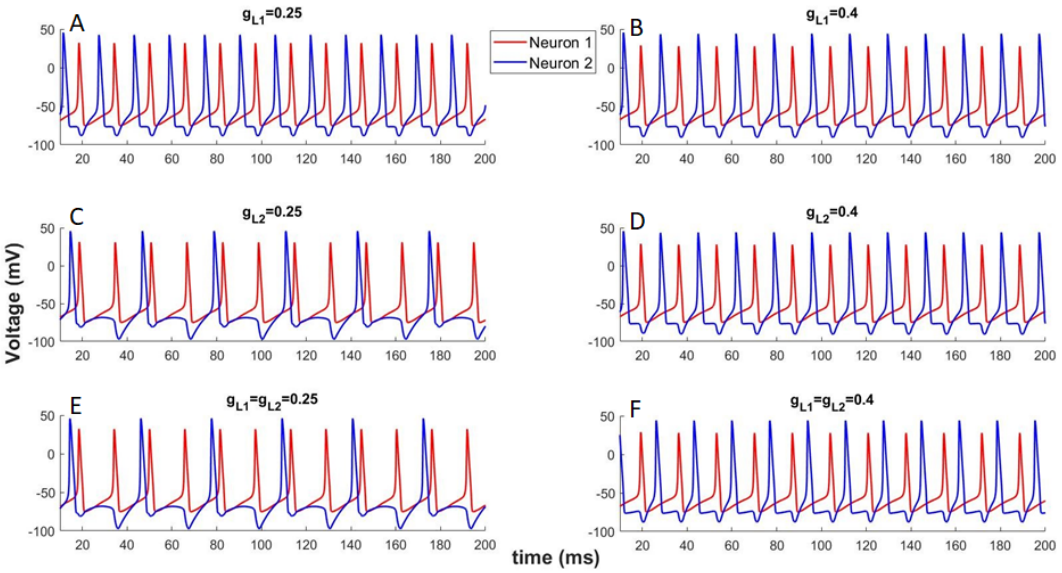

Figure 9: Pattern of spiking activity of Neuron 1 and Neuron 2 when A) g_{L1}=0.25, g_{L2}=0.3; B) g_{L1}=0.4, g_{L2}=0.3; C) g_{L1}=0.3, g_{L2}=0.25; D) g_{L1}=0.3, g_{L2}=0.4; E) g_{L1}=g_{L2}=0.25; F) g_{L1}=g_{L2}=0.4.

So, our study reveals unexpected information transfer changes following changes in sodium conductance.

3.3 The effects of changing maximal Leak conductances in the model

Leak channels provide a background synaptic activity and how they influence the information flow for the coupled system is also important to analyze. Altering the leak conductance by changing the g_L parameters also alter the intrinsic cell dynamics. However, it is not yet established if it changes the information flow. To analyze the change in information flow, we simply increase the maximal leak conductances of each neuron separately and together in the network model.

The presence of the added leak conductance for Neuron 1 does not have any impact on the flow of information as we can see in Figure 5A. Transfer entropy results for both directions are not affected by the changes in g_{L1}. The phase-locked system is not affected by the changes in g_{L1} as shown in Figure 9A&9B that supports the stability in TE results.

Neuron 2 does not have an applied input and excitability is due to the coupling from Neuron 1. So increasing or decreasing the leak conductance causes a corresponding increase/decrease in the frequency of action potentials affecting the direction of the information flow as we can see in Figure 9B and 9C.

Interspike interval for Neuron 2 decreases as g_{L2} increases and 2-to-1 coupling turns to the 1-to-2 coupling between neurons. During this change in the coupling, the direction of the information flow also changes. Similar results are observed once both the leak conductances are perturbed as shown in Figure 8C and Figure 9E&F. So conductance-based networks can show both ways of information flow according to the strength of the leak conductance.

While the information flow occurs from Neuron 2 to Neuron 1 for smaller g_L values, the direction oscillates with an increasing g_{L2} value. These results suggest that the interaction between the coupled network dynamics critically changes by the effects of leak conductance by changing the interspike variability and as a result the direction of the information flow changes between the neurons.

4. Conclusion

The objective of this study is to determine the effects of changing conductances on the two –neuron HH network by using the transfer entropy which is an information-theoretical quantity. Our defined model involves two synchronized neurons due to the coupling defined from Neuron 1 to Neuron 2. Firstly, we observe a strong correlation between the maximal conductances of the ion channels g_{Na}, g_K and g_L, the action potential duration and interspike interval. Once we perturb these parameters, the pattern of synchronization for the neuronal networks also changes dramatically. That is why it is crucial to analyze the ambiguity of the parameters in the network model. In order to understand the population behavior of neurons, we should understand the relations under the nonlinear dynamics involved in the AP network. Here, to understand how neural systems integrate, encode, and compute information, we use transfer entropy, which is capable of catching the nonlinear interactions between the variables. For the two-neuron HH network, the TE analysis reveals that information transfer changes direction with the maximum conductances against the coupling defined originally. This coupling between neurons is modeled by the nonlinear equation system of (7) and (8), where it is not obvious that the first neuron can also be affected by the second. However, using TE, we show that the latter statement can also come true as a result of changing conductances. For example, from Figure 2A, we can conclude that the direction of coupling (information flow) is from neuron 2 to neuron 1 for conductance levels up to $g_{K1} \cong 27$ as the probability of predicting the current values of neuron 2's action potential by using its own past values and the past values of neuron 1 is higher than the probability of the predictability of that of neuron 1 from its own past and neuron 2's past. In other words, for this conductance zone, $TE_{V_2V_1} > TE_{V_1V_2}$. Similarly, we note that this directionality is reversed as the conductance values exceed 27 for this case.

We observe these changes with each maximal conductance including the leak channel. Either having a very strong or very weak leak for Neuron 2 changes the information flow. We observe that there is an interval for g_{L2} that holds the network stable as is defined. On the other hand, Na^+ channel activation provides a positive feedback to the network and once we increase the maximal conductance of the Neuron 1 there is a threshold that changes the information flow from 1-to-2 to 2-to-1 due to the strong positive feedback flows from Neuron 1 to Neuron 2. K^+ channel activation, on the other hand, provides negative feedback to the system and we observe an opposite behavior once we perturb the K^+ maximal conductance as we expect. This time, for lower values of the g_{K1}, information flow changes direction from 1-to-2 to 2-to-1 due to the strong negative feedback flow from Neuron 1 to Neuron 2.

Depending on the ion channels property, changing the maximal conductance of either each neuron separately or together, can change the amount of information flow against the coupling. This result highlights that since different data sets can closely optimize the experimental data and the flow of the direction changes with the changing maximal conductances, the chosen parameter set is matter even though it can mimic the data well.

The main effect of the perturbation of conductances is to change the synchrony with either changing the interspike interval or spike duration. According to the perturbed parameter we observe the disruption of the synchronized network. The TE analysis is defined for inspecting the information transfer between the signals. For neuronal spikes simulated by our defined network, TE analysis reveals useful information about the parameters of the involved ion channels. Since the network is highly nonlinear, the effect of adding or subtracting a conductance can change the different intrinsic properties like the values of other parameters. That is why we need deeper analysis to better understand the underlying behavior of neuronal networks.

This work presents a complementary analysis to our previous effort on the full network investigation of a coupled two neuron HH model where the effects of additional noise are examined.

Declaration

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The author(s) also declared that this article is original, was prepared in accordance with international publication and research ethics, and ethical committee permission or any special permission is not required.

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