Model for Coupling Scheme and its Impact on Neurons Behaviour

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Abstract

Collective oscillations is typical phenomena observed in the systems biology including neurons. Investigating the mechanisms for which it occurs in neural networks evokes a significant interest among neuroscientists. From mathematical point of view, the coupling schemes rule the neuron's behaviours ranging from microscopic to macroscopic scales. This paper aims to study the impacts of coupling scheme in a minimal network of two fully coupled identical oscillators (e.g., neurons). We proceed the research by employing the numerical approach and time-series analysis. We consider both Kuramoto-like oscillator and Leaky integrate-and-fire neuron as the objects of study. In the former case, we found the phase of two oscillators are perfectly locked and stable if their frequency are identical as stated by the main theorem. In the latter case, the membrane potentials of two neurons are perfectly synchronized, characterized by the same firing rate, due to the effect of excitatory delta pulses.

Keywords: *Biological Neurons; Coupling Scheme; Signal Transmission; Pulse*

1. Introduction

As explained in the elementary books of physiology, the very simple structure of biological neuron consists of three main components namely dendrite, soma, and axon [1]. The dendrites collect all signals and transmit them to the soma where a summation process is performed. If the total incoming inputs exceed a certain value, then a pulse (or equivalently "spike") is generated as the output signal. The signal travels along the axon up to the axon terminal button and triggers the release of neurotransmitters into the gap between the presynaptic (sender) and postsynaptic (receiver) neurons [2].

The neuron communicates by sending and receiving the pulses. The effect of the pulse on neuron dynamics is encoded in the so-called inter-spike interval (ISI), i.e. the time length between any two consecutive spikes [3]. In the absence of any coupling, the neuron fires the pulse at a constant rate[1] $1/\text{ISI}_0$, if it operates above the threshold [2] [4]. Contrarily, the presence of coupling affects the firing as well as the ISI of single neuron [5]. The incoming excitatory pulses accelerates the firing rate of postsynaptic neuron, while the inhibitory one decelerates the firing rate.

In order for the coupling to take a role on the neuron dynamics, it is necessary to introduce a connection between the two neurons. Mathematically, the connectivity of any two "nodes" can be represented in term of adjacency matrix $G = (g_{i,j})$ where i and j denote the source and target nodes, respectively. The matrix element $g_{i,j} = 1$ if there is a connection from i to j; otherwise it is 0 [6]. In this study we works with only two neurons, meaning that the matrix G is two dimensional with zero components in the main diagonal following the fact that the self-connectivity is excluded.

From mathematical neuroscience point of view, the question of how the two neurons do interact to each other (e.g., coupling scheme) and its impacts are very central [7] [8]. For instance, in which conditions the regular and irregular firing behaviours do exist in the biological neurons? [9].

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[1] The rate of neuronal firing is defined as a ratio of $1/\text{ISI}$. The subscript 0 means that the ISI is constant.

Numerous experimental and computational studies have been devoted to investigate such dynamics. As for instance, the phase locking synchronization in the original Kuramoto model is characterized by a zero phase-lag of oscillators which is induced by a sufficiently strong coupling strength [10]. The finding is consistent to that have been observed in the real experimental setup of brain stimulation [11]. Meanwhile, the synchronous state in the populations of neurons is characterized by strong correlations of the pulses in single neuron level [12]. In the cortical neurons, the presence of cortico-thalamo-cortical feedback loops may contribute to the synchronization of cortical activities [13].

In this paper we discuss the impact of coupling schemes on the neuron dynamics. In contrast to the original model for large-scale neurons studied in most computational studies, here we limit ourselves on two mutually coupled oscillators to carefully illustrate physically the emergence of periodic synchronous regime under the control of coupling schemes. At first, we consider phase difference, a simplest scheme in the sinusoidally coupled Kuramoto oscillators which have a widespread application in many natural systems [14]. We state the main results in the form of theorem and prove the existence of phase-locked dynamics and its stability. Next, we focus on the pulse as an elementary unit in the signal transmission amongst neurons. The neuron model used here is one-dimensional leaky integrate-and-fire (LIF) neuron with a delta pulse. The LIF neuron is selected as it is widely used and applicable for numerical and analytical treatments.

2. Methods

This study uses a descriptive-type quantitative design. The data is collected through numerical integration methods, while the time series analysis is carried out to characterize the emerging dynamical regimes. More specifically, the research procedures consist of three main steps: model formulation, numerical simulation, and bifurcation analysis as described below.

2.1 Model formulation

In this step, we review the mathematical models describing the interaction of two neurons. The first model replicates the experimental setup of two pendulum clocks studied a long time ago by a Mathematician Christiaan Huygens. The second one describes two synaptically coupled Leaky integrate-and-fire (LIF) neurons. Here, the synaptic coupling is ruled by a delta function.

2.2 Simulations

Next, we simulate the models by making a use of Euler integration scheme implemented in C programming languages. The main point is observing the emergence of dynamical behaviour from the two interacting neurons.

2.3 Bifurcation analysis

In the final step, we analyse the emerging dynamics in terms of bifurcation theory and compare the analytical results with numerical ones. In the case of LIF neuronal model, we make a use of the synchrony measure $\sigma = \langle |u_2(t) - u_1(t)| \rangle$ where $\langle * \rangle$ denotes time averaging. If $\sigma = 0$ the two neurons are perfectly locked.

3. Results and Discussions

In this section, we introduce the neuron models and the corresponding interaction scheme. Our aim is to answer a question on which way the connectivity affects the dynamics of coupled neurons. We begin with the simplest coupling, based on the phase differences of Kuramoto oscillators [10]. Next, we present the role of pulses on neuronal dynamics, taking into account the LIF neurons as a paradigmatic model.

3.1 Phase difference

The phase difference (or phase shift) is a difference between two phases of two periodic functions. In this context, the dynamics of each single oscillator changes according to the phase difference with other oscillators. In principle, the interaction can be either *attractive* or *repulsive*. The experiment of two pendulum clocks (like in the Huygens's experiment) or metronomes attached to a common vibrating support is perhaps the oldest setup where one can observe such a type of dynamics [15]. In the context of biological neurons, the phase difference is equivalent to that of gap junction, connecting the axon terminal of presynaptic neuron and the receptor of postsynaptic one which enables direct communication amongst neurons [16].

Definition 1. Consider the following systems

$$\begin{cases} \dfrac{d\Phi_1}{dt} = \omega_1 + \mu \sin(\Phi_2 - \Phi_1) \\ \dfrac{d\Phi_2}{dt} = \omega_2 + \mu \sin(\Phi_1 - \Phi_2) \end{cases} \tag{1}$$

where Φ_1, Φ_2 and ω_1, ω_2 stands for the phases and angular frequencies of oscillator 1 and 2, respectively. The coupling term depends sinusoidally on the phase difference with $\mu > 0$ as the coupling strength.

Let us now define a phase difference $\Phi(t) = \Phi_1(t) - \Phi_2(t)$. If we take a derivative of both sides, then the coupled system of Eq. (1) can be reduced to a single equation,

$$\frac{d\Phi}{dt} = \omega - 2\mu \sin(\Phi) \tag{2}$$

where $\omega = \omega_1 - \omega_2$ defines a frequency difference. This formulation helps us to understand the behaviour of coupled systems (1) under the actions of parameter ω and μ.

Theorem 1. The equilibrium Φ^* for system (2) if it exists is not unique.

Proof. Assume that Φ^* exists and it is unique. By definition of equilibrium: any solutions $\Phi_k^* = \Phi_l^*$ implies that

$$\omega = 2\mu \sin(\Phi_k^*) = 2\mu \sin(\Phi_l^*), \tag{3}$$

for nonnegative integers k and l. Choosing $\Phi_k^* = \frac{\pi}{2}$ and $\Phi_l^* = \frac{3\pi}{2}$ contradicts the equality (3) and hence proves the non-uniqueness of Φ^*. •

Theorem 2. The equilibrium $\Phi^* = 0$ is stable, if $\omega = 0$.

Proof. Since $\omega = 0$ then $f(\Phi) = -2\mu \sin(\Phi)$. This implies $f'(0) = -2\mu \cos(0) = -2\mu < 0$ and hence $\Phi^* = 0$ is stable. •

The interpretation of Theorem 1 and Theorem 2 is shown in the Figure 2. The stable and unstable equilibrium points are denoted as solid red dots and open circles, respectively. The red cross denotes a coordinate $(0, \omega)$.
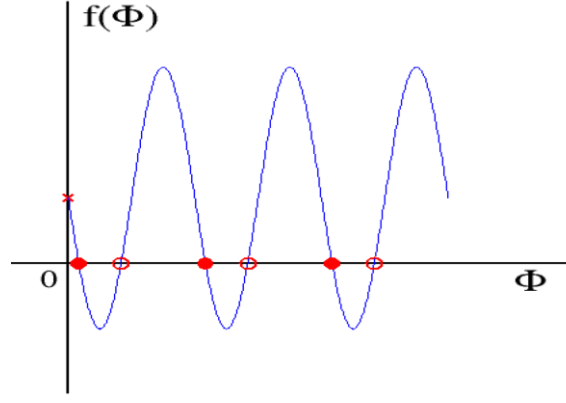
Figure 1. A graph of $\frac{d\Phi}{dt} = f(\Phi)$ of Eq. 2 for $\omega = 1$ and $\mu = 1$.

The equilibrium Φ^* for Eq. (2) can either appear or disappear as the parameter ω is varied. It exists if $-\omega_c \leq \omega \leq \omega_c$ where ω_c is a critical (bifurcation) point. A special case when the oscillators 1 and 2 have equal frequency, i.e., $\omega = 0$, the solution $\Phi^* = 0$ is stable as stated by Theorem 3.2. Therefore, they can exhibit in-phase synchronization, a regime when two oscillators move in the same direction simultaneously (see Figure 2a).

To find ω_c, let's impose a condition when the graph $f(\Phi) = \omega - 2\mu \sin(\Phi)$ is tangent to the Φ axis in correspondence of the equilibrium point. So, we have an equality

$$\omega = 2\mu \sin(\Phi) \tag{4}$$

and the corresponding derivative

$$\frac{d}{d\Phi}\omega = 2\mu \frac{d}{d\Phi}\sin(\Phi). \tag{5}$$

The Eq. (5) implies $\cos(\Phi) = 0$ for $\Phi = \frac{\pi}{2} + \ell\pi$ where ℓ is nonnegative integer. Then Eq. (4) yields $\omega_c = 2\mu$. As μ is increased, the stable equilibrium becomes closer to 0 (see again Figure 1) which means that the phase-lag becomes smaller. Here, the coupling is said to be attractive, and this explains the scenario in Figure 2b and c. To approximate μ for small Φ (i.e., $\Phi \ll 1$) impose $\sin(\Phi) \approx \Phi$, and from Eq. (4) we have $\mu = \omega/2\Phi$.
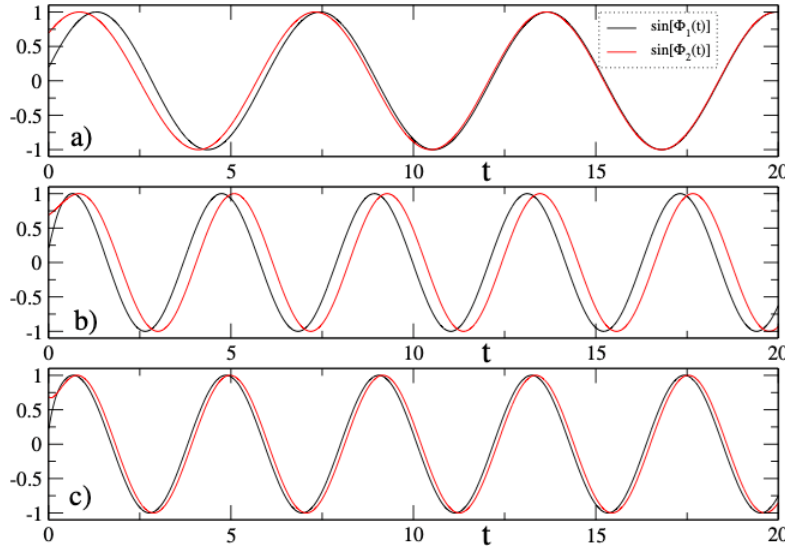

Figure 2. The time trace of phase oscillator 1 (black) and 2 (red): a) $\omega_1 = 1, \omega_2 = 1$, and $\mu = 0.1$; b) $\omega_1 = 2, \omega_2 = 1$, and $\mu = 1$; c) $\omega_1 = 2 \ \omega_2 = 1$, and $\mu = 3$.

Figure 2 compares the behaviour of the system (1) for three different values of $(\omega_1, \omega_2, \mu)$. Panel a) corresponds to $\omega_1 = 1, \omega_2 = 1$, and $\mu = 0.1$. Panel b) and c) correspond to the same frequencies $\omega_1 = 2, \omega_2 = 1$ but different coupling strength $\mu = 1, \mu = 3$ respectively. In the panel a), the two oscillators are initially different from one another with respect to their phase. As the time goes on, they become indistinguishable and their phase difference equal to zero. In contrast, panel b) and c) show a condition where the phase-lag between oscillator 1 and 2 is finite and constant. Notice that, the phase-lag in c) is smaller than that of b) due to the effect of the coupling strength.

3.2 Pulsatile coupling

In this section we discuss a situation in which the neuron is stimulated by the presynaptic spikes (pulses). The synapse can either be electrical or chemical. In the electrical synapse, the signal transmission can occur even when the membrane potential of the pre-synaptic neuron below threshold [17]. Contrarily, the signal transmission in the chemical synapse occurs when the membrane potential passed a threshold. In this study, we focus on the chemical synapse.

Definition 2. Let's consider two identical LIF neurons where $u_1(t)$ and $u_2(t)$ are used to describe the membrane potential for neuron 1 and 2, respectively. The evolution equation of membrane potentials for the two neurons is given by

$$\begin{cases} \tau_m \dfrac{du_1}{dt} = -u_1(t) + R I_1^{syn}(t) \\ \tau_m \dfrac{du_2}{dt} = -u_2(t) + R I_2^{syn}(t) \end{cases} \tag{6}$$

and combined with the reset conditions

$$u_1 \geq \vartheta \implies u_1 = u_r$$
$$u_2 \geq \vartheta \implies u_2 = u_r.$$

Whenever neuron 1 or 2 passed a threshold ϑ, it is reset to u_r and experiences a refractory time t_r for which the neuron is insensitive to the inputs.

The variables $I_1^{syn}(t)$ and $I_2^{syn}(t)$ characterize the synaptic input for neuron 1 and 2, respectively and defined as

$$I_1^{syn}(t) = \mu \sum_n s(t - t_n^2) + I_0 \tag{7}$$

$$I_2^{syn}(t) = \mu \sum_n s(t - t_n^1) + I_0. \tag{8}$$

The parameters $\mu = \mu_0/2$ and I_0 are the coupling strength and constant current, respectively. The synapse is excitatory (inhibitory) if $\mu > 0 (\mu < 0)$. The sums run over all pulses emitted by the neuron 1 and 2 at a time t_n^1 and t_n^2, respectively.

Each pulse being emitted by a single neuron is described by the function $s(t)$. The shape of a single pulse can take many forms [2]. We classify the delta-pulses which have infinitely narrow width and the pulses with the finite widths (e.g., exponential, and alpha pulses). The definition of each pulse is given below.
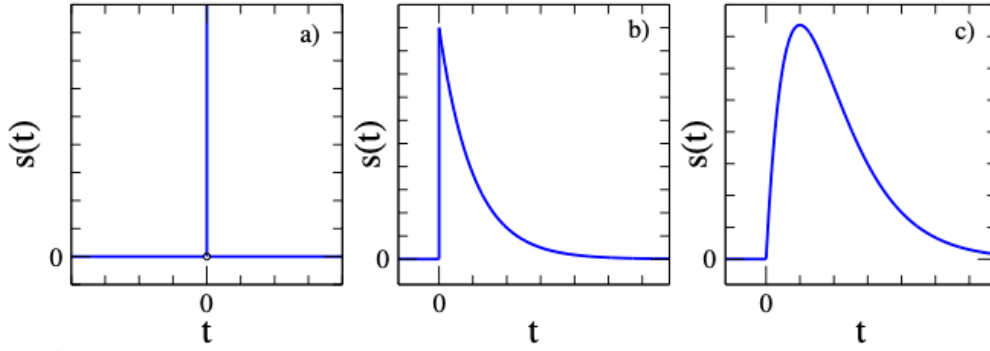
Figure 3. Pulse shape: a) delta pulse, b) exponential pulse, c) alpha pulse

Definition 3. Delta Pulse, Exponential Pulse, and Alpha Pulse:

- Delta Pulse $[s(t) = \delta(t)]$

$$\delta(t) = \begin{cases} +\infty, t = 0 \\ 0, t \neq 0 \end{cases} \tag{9}$$

- Exponential Pulse

$$s(t) = \alpha e^{-\alpha t}, t > 0 \tag{10}$$

- Alpha Pulse

$$s(t) = \alpha^2 t e^{-\alpha t}, t > 0 \tag{11}$$

The parameter $\frac{1}{\alpha}$ is the width of the exponential and alpha pulses. Notice that all pulses are normalized to area 1 so that one can easily compare the coupling strengths. The shapes of $s(t)$ are displayed in Figure 3. In all cases, the presynaptic spikes occur at time $t = 0$ while for $t < 0$, $s(t) = 0$.
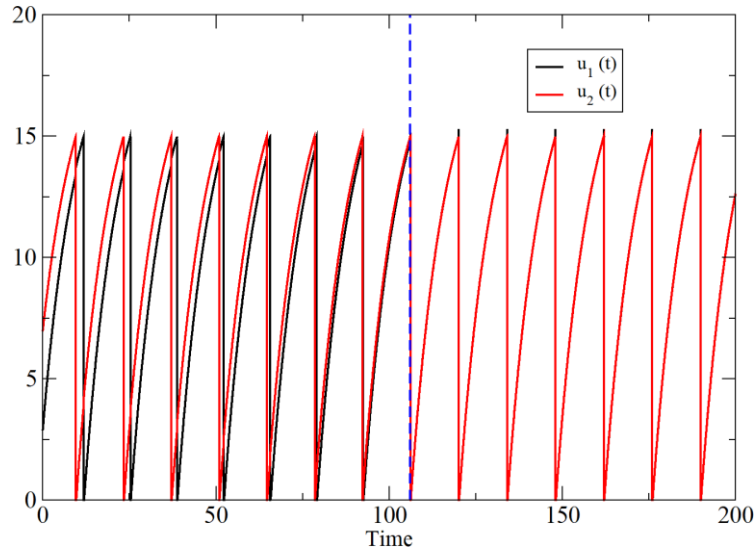

Figure 4. The time evolution of membrane potential for neuron 1 (black) and 2 (red) with mutual excitatory coupling and $\mu_0 = 0.6$. The blue dashed line corresponds to Tr

Figure 4 displays the time series of membrane potential for the two LIF neurons with delta pulses. The initial conditions for the membrane potential $u_{1,2}(0)$ are selected from uniform and random distributions. All parameter sets to produce Figure 4 are displayed in Table 1 and assumed to be identical for all neurons.

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Table 1. Parameterization

No.	Parameters		References
1.	Reset potential (u_r)	0 mV	[4]
2.	Threshold (ϑ)	15 mV	[4]
3.	Refractory time (t_r)	0.1 ms	Assumed
4.	Resistance (R)	1 Ω	[4]
5.	Constant current (I_0)	20 mV	[4]
6.	Membrane time constant (τ_m)	10 ms	[4]
7.	Coupling strength ($\mu_0 > 0$)	[0.1, 1]	Assumed

A general remark concerns on the oscillatory behaviour of the neuron 1 and 2 under the action of a constant current I_0. When $\mu_0 = 0$, the membrane potential for neuron 1 and 2 evolves independently according to Eq. (6) and have an equal period or inter-spike interval

$$T = t_r + \tau_m \ln\left(\frac{RI_0}{RI_0 - \vartheta}\right) \tag{12}$$

If $\mu_0 > 0$ we notice that for the fully excitatory connections; the firing of presynaptic neuron kicks the membrane potential of the postsynaptic neuron forward which then accelerates its firing rate. Interestingly, after a finite amount of time around $t \approx 106$ ms (see the blue dashed line in Figure 4) the phases of two neurons locked and they start to fire the pulse simultaneously because of such mutual interaction. The inter-spike interval $T \approx 13.96$ fits the formula of Eq. (12). For future reference, the time needed by the neurons to attains the phase-locking dynamics is defined by a transient time Tr.
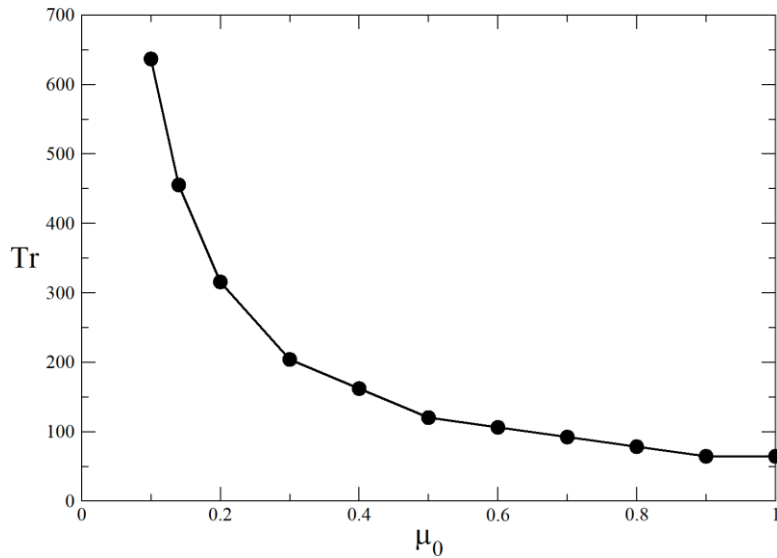
Figure 5. Transient time Tr versus coupling strength μ_0.

Practically, we compute the transient time Tr as a function of μ_0 as follows: in each integration time step the condition $\sigma(t) = |u_2(t) - u_1(t)|$ is imposed in such way that $Tr = min\{t|\sigma(t) = 0\}$. The result is displayed in Figure 5: there one can see the dependence of transients on the coupling strength. As μ_0 is increased, the rate of convergence to the periodic synchronous dynamics becomes faster.

Previous studies suggest that synchrony in neuronal networks might be associated with the neurological diseases such as epilepsy and seizures [18] [19]. It has been initially studied rigorously

by Peskin (1975) and then generalized by Mirollo and Strogatz [20] for any two pulse-coupled oscillators interacting through delta pulses. In a more complicated physiological structures such as two populations of excitatory and inhibitory neurons, the synchrony and phase-locking behaviours are robust in the presence of finite pulses [21].

4. Conclusion

In this paper, we have discussed the role of coupling schemes on neuron dynamics. First, we consider a phase difference of two sinusoidally coupled oscillators and found they becomes indistinguishable, i.e. phase difference is exactly 0, if their frequencies are identical. Meanwhile, their phase difference is not zero and finite, as long as the frequencies are not identical. Secondly, we consider two identical LIF neurons synaptically coupled through delta pulses and observe a phase-locked and perfect synchronization for the excitatory postsynaptic potential, similar to that have been found in the former case.

Finally, it is enlightful to notes some limitations of this study. Here, we are working with a minimal network of two identical oscillators (neurons), while the brain has a complex structure and it is organized into multi-layers of many interacting units. We argue the same scenario emerges in a larger system sizes under several conditions. For example, in two interacting populations of excitatory and inhibitory neurons the perfect synchronization exists if the inhibition prevails against excitation [22]. Further studies are hereby required.

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