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The role of driver nodes in managing epileptic seizures: Application of Kuramoto model

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ABSTRACT

Synchronization is an important global phenomenon which could be found in a wide range of complex systems such as brain or electronic devices. However, in some circumstances the synchronized states are not desirable for the system and should be suppressed. For example, excessively synchronized activities in the brain network could be the root of neuronal disorders like epileptic seizures. According to the controllability theory of the complex networks, a minimum set of driver nodes has the ability to control the entire system. In this study, we examine the role of driver nodes in suppressing the excessive synchronization in a generalized Kuramoto model, which consists of two types of oscillators: contrarian and regular ones. We used two different structural topologies: Barabási-Albert scale-free (BASF) network and *Caenorhabditis elegans* (*C.elegans*) neuronal network. Our results show that contrarian driver nodes have the sufficient ability to break the synchronized level of the systems. In this case, the system coherency level is not fully suppressed that is avoiding dysfunctions of normal brain functions which require the neuronal synchronized activities. Moreover, in this case, the oscillators grouped in two distinct synchronized clusters that could be an indication of chaotic behavior of the system known as resting-state activity of the brain.

1. Introduction

Synchronization is an important behavior in complex systems made of many interacting oscillators. This phenomenon has several important impacts in biological, physical and technological systems (Arenas et al., 2008; Acebrón et al., 2005; Pikovsky et al., 2003; Osipov et al., 2007). In the neuronal networks, synchrony is available from the cellular level to the highest cognitive functions and dysfunctions (Arenas et al., 2008; Womelsdorf and Fries, 2007; Axmacher et al., 2006; Klimesch, 1996; Fries et al., 2002; Rodriguez et al., 1999; Uhlhaas and Singer, 2006). In many systems, synchronization behaviors are desirable; however, in some cases, these coherent oscillations can relate to some undesired situations. In the brain functions, desired synchronized activity plays a key role in neural information exchange, cognitive processing, memory, and movement (Womelsdorf et al., 2007; Haken, 2013; Kim, 2004; Cassidy et al., 2002). On the other hand, abnormal excessive neuronal synchronization is an indication of some pathological states like epilepsy and Parkinson's disease (PD) (Lehnertz et al., 2009; Hammond et al., 2007; Glass, 2001).

In order to manage these pathologic states, one strategy is to suppress the undesired coherent synchronous level. In the epileptic brain, one treatment approach is consuming the anti-epileptic drugs which seem to decrease the excitatory or increase the inhibitory neurotransmissions respectively (Vernadakis and Timiras, 2013). However, using this approach is not efficient since some patients suffer from drug-resistant epilepsy (Wendling et al., 2005). Applying Deep Brain Stimulation (*DBS*) methods using electrical discharges to the brain tissue by implanted brain pacemakers are proposed for treating seizures and restoring the normal state of the brain (Volkmann et al., 2002; Kringelbach et al., 2007; McIntyre et al., 2004a, 2004b). However, there has been some limited success in the application of this method specifically in the suitable places as stimulation sites (Conte et al., 2007).

The modeling approach is an appropriate framework to understand the mechanism of brain seizure and solve existing problems in its treatment. There are some studies on different models of epilepsy with the aim of *DBS* (McIntyre et al., 2004a, 2004b; Terman et al., 2002; Tass and Majtanik, 2006; Raiesdana and Goplayegani, 2013). The Kuramoto model is one of the well-established models applied to the neurophysiological problems (Gray et al., 1989; Schuster and Wagner, 1990; Goldwyn and Hastings, 2011; Bacelar et al., 2010; Sakaguchi and Maeyama, 2014; Murray et al., 2011). An important advantage of this

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model is its ability to achieve synchronization modes in the networks with different structures (Novikov and Benderskaya, 2014). There is some research on Kuramoto model in which the transformation of the synchronized to the desynchronized state was studied. For example, Franci et al. (2012) proposed a simplified Kuramoto model under the influence of proportional and scalar mean-field feedback (*MFF*), for the aim of *DBS*, which allows providing a desynchronized mode in the oscillatory network by introducing feedback connections. Louzada et al. (2012) proposed a strategy for suppressing the undesired synchronization in Kuramoto model by targeting random nodes. The basic of their work was in social context to avoid synchronization via political contrarians to destroy the harmony between people. They have generalized the Kuramoto model by including the contrarians which selected randomly. They also suggested that this model could be applied in neuronal networks in the sense that contrarian nodes resemble the brain pacemakers' local impacts on the neurons. We hypothesized that the topological location (*TL*) of contrarians is important in their impact on breaking the synchronization level. Previously we suggested that controllability theory could help to find important regions for managing the epileptic undesired synchronization (Bakouie et al., 2013). Controlling the complex networks is a vast framework that has been used in several research areas for various natural and technological systems (Albert et al., 1999, 2000; Nagy et al., 2010; Cohen et al., 2000; Jeong et al., 2001; Pastor-Satorras and Vespignani, 2001; Palla et al., 2005; Barabási and Albert, 1999). The purpose of controllability is to drive a dynamical system, with a suitable choice of inputs, from any initial state to desired final state within the finite time. For this goal, Liu et al. (2011) introduced the minimum number of nodes (driver nodes) which are sufficient to fully control the system's dynamics. After the proposition of structural controllability, the possibility of studying the controllability of large complex networks is provided. In the case of the structural controllability, it is essential to solving the problem of maximum matching, where the controlling input is required for every unmatched node (Hopcroft and Karp, 1973; Zhou and Ou-Yang, 2003; Zdeborová and Mézard, 2006).

The main goal of this paper is to study the effect of driver nodes in breaking the undesired synchronization in the system. For this purpose, we used the generalized Kuramoto model in which the contrarian oscillators have the significant role in breaking the level of synchronization in the system. Then, we studied the *TL* of driver nodes as contrarians on the dynamic of the network. By examining the order parameter, we evaluated the role of contrarian driver nodes, in suppressing the undesired synchronization.

2. Material and methods

2.1. Generalized Kuramoto model

In Kuramoto model, the ith oscillator is characterized by an angular phase θ_i and natural or intrinsic frequency ω_i. The dynamic of contrarian nodes in the system is:

$$\dot{\theta}_i=\omega_i+K\sum_{j=1}^{N_T}A_{ij}\sin(\theta_j-\theta_i-\tau); \tag{1}$$

where $\tau=\pi$is the degree phase shift, K is the constant coupling strength between oscillators and N_T is the total number of oscillators including contrarians and regulars. A_{ij} is the connectivity matrix of an arbitrary network.

Since the $\sin(\theta_j-\theta_i-\pi)=-\sin(\theta_j-\theta_i)$, the dynamic of the entire system could be written as:

$$\begin{cases}\dot{\theta}_i=\omega_i-K\sum_{j=1}^{N_T}A_{ij}\sin(\theta_j-\theta_i); iiscontarian\\ \dot{\theta}_i=\omega_i+K\sum_{j=1}^{N_T}A_{ij}\sin(\theta_j-\theta_i); iisregular\end{cases} \tag{2}$$

The *pi* phase shift of contrarian oscillators from their neighbors results in negative constant couplings.

The degree of phase coherence within the oscillators can be characterized by the complex order parameter defined as,

$$r=\left|\frac{1}{N_T}\sum_{j=1}^{N_T}e^{i\theta_j}\right| \tag{3}$$

The order parameter $0\leq r\leq 1$ calculates the level of synchrony between all oscillators. If the θ_i of all oscillators are identical (fully synchronized state), then $r=1$, and if all oscillators are spaced equally on the unit circle (fully desynchronized state), then $r=0$. The behavior of the model is varying based on the coupling strengths. For the lower amount of coupling strength, the dynamic of the oscillators is in a disordered state $r\ll 1$. As the coupling strength increases, beyond the critical coupling (K_c), the coherency enhanced and the system's behavior changes to partially synchronized state. Further increase of coupling strength leads to the full synchronized state.

2.2. Network construction

In this paper, we considered connected and sparse networks in all simulations. The Network of oscillators has been constructed as Barabási-albert model of scale-free networks (BASF) with size equal to 500 and the average degree equal to 4 with 82 number of driver nodes. The network of *C.elegans* neurons was constructed through data obtained from the study by Varier and Kaiser (2011). In this network, links have been established based on the interaction between neurons without their type or weight. The network size is 277 and the number of driver nodes for this network is 38. In order to find driver nodes, the framework of solving the maximum matching on the networks is done. Then, we considered the driver nodes as contrarian oscillators to apply in the model (2). We also attempt to consider the contrarians as random and high-degree nodes to compare the effect of them with regard to the driver nodes by the same fraction of contrarians. The order parameters are calculated averaged over 100 networks via autonomous runs with different initial conditions.

For calculating the order parameter versus coupling strength, the model (2) has been numerically solved using a fourth-order Runge-Kutta method with discrete time steps as dt =0.001. The remaining calculation of the model (2) has been solved with ode45 Matlab solver with the time steps dt =0.001. For all cases, the natural frequencies of oscillators have been uniformly distributed between −0.5 and 0.5 and initial phases have also been uniformly distributed between $-\pi$ and π.

3. Results

In this study connectivity pattern of the network is BASF. In the case of modeling the network with regular oscillators, the critical coupling is 0.22. For $K>$ 0.8 the system's order parameter is at steady state and model exhibits fully synchronization ($r=1$). By replacing %15 of nodes with contrarian nodes, the level of coherency reduced to 0.33 (Fig. 1, blue).

The variation of contrarians' coupling strength will change their impact on desynchronization. Fig. 1 shows that by decreasing the weight of contrarians' couplings, r increases. This means that the impact of contrarians on the synchronization suppression reduces. It also shows that applying the contrarian nodes, even with the too small connectivity strengths, is enough to break the synchronized level. In the Fig. 1, contrarians are selected randomly; however, the topological location (*TL*) of contrarians may be important in their suppression influence on the system's dynamics. Therefore, we run some experiments in which contrarians are considered as driver nodes and as high-degree nodes.