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Stochastic resonance in feedforward-loop neuronal network motifs in astrocyte field

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HIGHLIGHTS

- The FFL network motifs are modeled in astrocyte field with mutual neuron–astrocyte interactions.
- The stochastic behaviors of the proposed network motifs are studied.
- Astrocytes improve the performance of signal processing via stochastic resonance.
- The functional roles of astrocytes are discussed.

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ABSTRACT

Elucidating the underlying dynamical properties of neuronal network motifs, statistically significant patterns of interconnections, is essential to understand the dynamics of the whole networks. Besides, the brain is intrinsically noisy. Various noise-induced dynamical behaviors, in particular, the stochastic resonance (SR), have been found in both neuronal systems and neuronal network motifs. However, the effect of astrocytes, active partners in neuronal signal processing, has not yet received much attention. In this paper, we study the effect of astrocytes on the stochastic behaviors of the typical triple-neuron feedforward-loop (FFL) neuronal network motifs. The neurons are described by the Hodgkin–Huxley model, while the astrocytes are modeled by extending the Li–Rinzel model to a two-dimensional field with the effect of diffusion. The mutual neuron–astrocyte interactions are established correspondingly. Simulation results indicate that the stochastic behaviors of the FFL motifs show bell-shaped dependence on the intensities of both noise and astrocyte–neuron coupling. Moreover, in the presence of astrocytes, the performance of the FFL motifs on weak signal transmission in both noisy and noise-free environments can be significantly improved. From this point of view, the astrocytes can be regarded as a possible internal source of "noise", which assist the neurons in signal processing.

1. Introduction

Complex networks are ubiquitous in nature. In addition to the well-known small-world effect and scale-free property, a large number of complex networks also have recurring patterns of interconnections, termed as "network motifs", which are statistically more significant than those in randomized networks with the same degree sequence (Milo et al., 2002; Shen-Orr et al., 2002; Reigl et al., 2004; Wuchty et al., 2003; Sporns and Kotter, 2004; Li et al., 2007; Li and Li, 2008). Especially, in the study of biological neuronal networks, motifs have also been found (Milo et al., 2002; Reigl et al., 2004; Song et al., 2005). In addition, it has been discovered that, the connections among neurons in the network motifs tend to be stronger than other connections, which implies that the motifs are linked to each other in a way that tends to keep the independent functions of each motif (Song et al., 2005; Alon, 2007). So, the network motifs can be seen as basic building blocks of the networks, and uncovering their dynamical properties and specific functions is essential to understand the behaviors of the whole networks. Currently, several interesting functions and dynamical properties have been found in neuronal network motifs, such as the acceleration and delay of response and long- and short-term memory (Li, 2008; Ren et al., 2010; Franović and Miljković, 2010).

Neurons are fundamental elements for constituting neuronal network motifs. They can generate electrical signals in response to chemical and other inputs, and then transmit them to other neurons. Besides, the brain is intrinsically noisy. Suitable noise in brain can enrich the stochastic dynamics of neuronal ensembles and induce various complex behaviors (Rolls and Deco, 2010;

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Destexhe and Rudolph, 2012; Li et al., 2006). The stochastic resonance (SR), a counterintuitive phenomenon that a proper noise can enhance the output of nonlinear dynamical systems to an optimal level, is considered as one of the most important mechanisms for neuronal information transmission. Originally, the SR was used to describe the noise-enhanced complex behaviors only when the power of a signal is weaker than that of the noise. Currently, it has been extended to characterize the occurrence of any kind of enhanced signal processing by noise (either internally or externally). In particular, it can also be used to describe a SR-like firing behavior, which is caused by the intrinsic “stochastic” effect of excitable nonlinear systems even in the absence of external noise. In this case, the internal chaotic behaviors of the excitable system can serve as an internal noise for exhibiting SR. To make a difference with the SR induced by external noise, such stochastic behavior is named as “intrinsic stochastic resonance” (ISR) (Manjarrez et al., 2002; Chik et al., 2001; Gammaitoni et al., 1998; Hu et al., 1993; Wang et al., 1998; Braun et al., 1994; Anishchenko et al., 1993). Currently, many studies on SR/ISR of different neuronal systems have been reported (Manjarrez et al., 2002; Chik et al., 2001; Collins et al., 1995; Douglass et al., 1993; Longtin, 1995; Levin and Miller, 1996; Guo and Li, 2012; Gailey et al., 1997). In addition, the SR in some neuronal network motifs has also been found (Guo and Li, 2009).

On the other hand, in most parts of the brain, neurons are outnumbered by glial cells. So, a more realistic picture of brain tissue is a mass of glial cells with neurons embedded. The glial cells can be in general classified into two categories: the microglia and the macroglia cells. The former mainly functions in phagocytosis that protects the neurons of the central nervous system against infections. In addition to fulfilling the classical supportive roles as the microglia cells (Fields and Stevens-Graham, 2000, 2002; Haydon, 2001; Newman, 2003), the macroglia cells have been gradually evidenced to be active partners in neuronal signal processing in different brain areas, although they are unable to generate action potentials. The star-shaped astrocytes are the most numerous type and the best-studied macroglia cells (Haydon and Carmignoto, 2006). Experimental results have shown that astrocytes can listen to the neuronal chatter, respond to it and then talk back to the neurons. In other words, there exist bidirectional communications between neurons and astrocytes (Allegrini et al., 2009; Valenza et al., 2011; Nadkarni and Jung, 2004, 2007; Wade et al., 2011). Considering this, it is more reasonable to study the stochastic behaviors of neuronal network motifs by taking the effect of astrocytes into account.

Following this motivation, the effects of astrocytes on the stochastic behaviors of neuronal network motifs are systematically studied in this paper. Similar to Guo and Li (2009), the most significant triple-neuron feedforward-loop (FFL) neuronal network motifs are studied. But different from Guo and Li (2009), the effects of astrocytes and the corresponding astrocyte–neuron interactions are also considered here. In our model, the neurons are modeled by the Hodgkin–Huxley (HH) neuron model, while the astrocytes are modeled by extending the well-known Li–Rinzel model to a two-dimensional astrocyte field with the effect of diffusion among astrocytes. Then, the bidirectional neuron–astrocyte interactions are defined. Four typical FFL motifs with different combinations of excitatory and inhibitory neurons are discussed, and the impacts of astrocytes on SR in these network motifs are discussed.

The rest of this paper is organized as follows. In Section 2, structural configuration of the neuronal network motifs, as well as the models of neurons, astrocytes, and mutual neuron–astrocyte interactions, is introduced. In Section 3, a series of simulations is performed and the influence of astrocytes on the stochastic behaviors of network motifs is discussed. Finally, conclusion and discussion are given in Section 4.

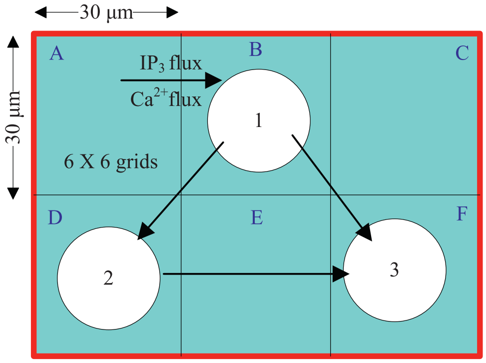

Fig. 1. Scheme of the network motif in astrocyte field. Each circle denotes a neuron and each square stands for an astrocyte with 30 μm × 30 μm. Each square is then divided into 6 × 6 grids. Astrocytes are coupled by intercellular flux conditions to form a two-dimensional sheet, and on their boundaries, the flux conditions for both Ca^{2+} and IP_3 fluxes are assumed. The boundary of the whole astrocyte field is represented by the red line. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)

2. Model

In this paper, we model the neuronal network motifs in a two-dimensional astrocyte field with mutual neuron–astrocyte interactions. Similar to Guo and Li (2009), the triple-neuron feedforward-loop (FFL) network motif, the most significant motif in neuronal networks, is focused. Fig. 1 schematically shows the architecture of this motif, in which neuron 1 drives neuron 2, and both neurons 1 and 2 drive neuron 3. In this architecture, the neurons 1 and 3 can be regarded as the input and output neurons of the FFL motif, respectively. In addition to the neurons, six astrocytes, represented by an array of square cells with each cell located at a specific point of a regular lattice, are included. There are two reasons for formulating such a network configuration. Firstly, in the real human cortex, the ratio of astrocytes to neurons is about 1.4:1 (Nedergaard et al., 2003). So, in the simulation, it is more realistic to set the ratio of astrocytes to neurons close to the nature. Secondly, to avoid the influence of unsymmetric diffusion of the gliotransmitters from neuron 1 on neurons 2 and 3 (more details will be given in Section 3.1), neurons 2 and 3 are distributed with the same distance to neuron 1.

The calcium (Ca^{2+}) is an essential element for establishing bidirectional neuron–astrocyte interaction. On the one hand, some glutamate (Glu) can be released from the presynaptic neuron into the synaptic cleft, when a presynaptic neuron fires an action potential. Part of glutamate can bind to the metabotropic glutamate receptors (m-GluRs) on astrocytes, triggering the release of inositol 1,4,5-triphosphate (IP_3) in the intracellular space of astrocytes. The production of IP_3 in turn leads to the IP_3-dependent Ca^{2+} release from endoplasmic reticulum (ER) and Ca^{2+}-dependent Ca^{2+} release (CICR) from ER. On the other hand, if the calcium concentration inside the astrocyte exceeds a certain threshold, astrocyte can feedback to neuron by a depolarization current. In such a manner, the bidirectional signaling way between neuron and astrocyte can be established (Porter and McCarthy, 1996; Parpura and Haydon, 2000; Araque et al., 1998; Nedergaard, 1994). In the following, the models for neuron and astrocyte are illustrated in detail.

2.1. Hodgkin and Huxley neuron model

The dynamics of each neuron in the network motif is described by the Hodgkin–Huxley neuron model, which is a typical paradigm for describing the spiking behavior and refractory properties of real neurons based on nonlinear conductance of ion channels.