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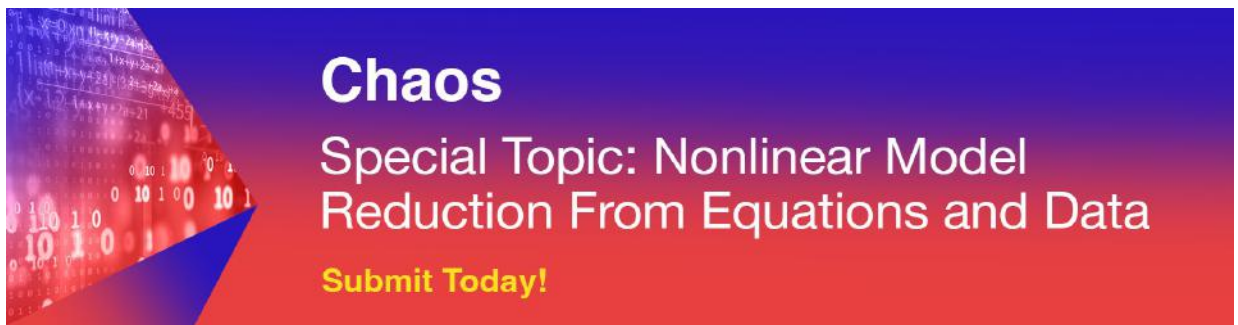
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ABSTRACT

Cognitive tasks in the human brain are performed by various cortical areas located in the cerebral cortex. The cerebral cortex is separated into different areas in the right and left hemispheres. We consider one human cerebral cortex according to a network composed of coupled subnetworks with small-world properties. We study the burst synchronization and desynchronization in a human neuronal network under external periodic and random pulsed currents. With and without external perturbations, the emergence of bursting synchronization is observed. Synchronization can contribute to the processing of information, however, there are evidences that it can be related to some neurological disorders. Our results show that synchronous behavior can be suppressed by means of external pulsed currents.

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The human brain is a complex organ responsible for cognitive processes and physiological functions. It contains about 100 billion neurons that are coupled by means of electrical and chemical synapses. The electrical synapse is a bidirectional link between two neighboring neurons. In the chemical synapse, never impulses are transferred in one way by means of neurotransmitters. In this work, we build a neuronal network based on the structural connectivity matrix of a human brain. Our network is composed of cortical regions, in which each region is described by subnetworks with small-world properties. Depending on the parameters, it is possible to observe synchronous and desynchronous behaviors. Neuronal synchronization can not only be associated with memory and consciousness, but also be related to

epilepsy and Parkinson disease. We analyze the effects of periodic and random pulsed currents in the neuronal activities. We show that pulsed currents play an important role in the emergence and suppression of neuronal synchronization.

I. INTRODUCTION

The brain is an organ located at the center of the nervous system in humans.¹ The human nervous system is responsible for receiving stimuli from sensory receptors and sending them to the brain and spinal cord, as well as to conduct impulses back to other

parts of the body.² At the cellular level, the nervous system has neurons that send signals rapidly and precisely to other cells.³ The signals are sent in the form of electrochemical impulses through axons, which can be directly transmitted to neighboring cells through electrical synapses. Also, neurotransmitters are released at chemical synapses, which can be either excitatory or inhibitory.⁴ The neurons connected to each other form a large layered network in which the different cortical layers in one hemisphere have connections with other ones in another hemisphere.⁵ Smith and Pereda⁶ demonstrated that a chemical synaptic activity modulates nearby electrical synapses. They provided evidence that chemical transmission interacts with electrical synapses to regulate the conductance. Kopell and Ermentrout⁷ reported that chemical and electrical synapses perform complementary roles in the synchronous behavior of interneuronal networks.

Subnetworks appear in the brain and they interact with each other during task accomplishing. Xu *et al.*⁸ demonstrated that multiple cognitive processes may be related to common brain regions during cognitive tasks. Sun *et al.*⁹ explored burst synchronization transitions in a neuronal network of subnetworks. They showed the effects of intra and intercoupling strength on the burst synchronization and implications on the brain plasticity.

Map-based models have been used to mimic neuronal behaviors, such as Izhikevich, Rulkov, Courbage–Nekorkin–Vdovin, and Chialvo models.¹⁰ Originally, the Izhikevich model is continuous-time,¹¹ however, it can be transformed into a map by means of Euler discretization. The Rulkov model¹² is a two-dimensional iterate map that can exhibit silent, tonic, and spiking-bursting. The Courbage–Nekorkin–Vdovin model¹³ is a phenomenological model of excitable and spiking-bursting neurons. It has similarities to the Rulkov model. In 1995, Chialvo¹⁴ proposed a map to describe the dynamics of isolated neurons. The Chialvo model shows aperiodic solutions and bursting behavior.

In our neuronal network, each node is described by the Rulkov model, which is a two-dimensional iterated map.¹² The Rulkov map is able to display a variety of dynamical regimes, as well as to produce irregular bursts which are observed in human neurons, reported by neurobiological experiments. It has been used to investigate large neuronal networks.¹⁵ The Rulkov model has been considered in a variety of studies, such as phase synchronization in clustered networks¹⁶ and suppression of burst synchronization.^{17,18}

We focus on bursting synchronization and desynchronization in a neuronal network model based on a healthy human brain obtained from Ref. 19. In our network model, we consider 83 cortical areas (subnetworks) according to Ref. 20. The subnetworks exhibit small-world properties,^{21–23} which are a high degree of clustering and a small averaged distance between vertices (nodes). In the brain, the connections between neurons are local (connections with their nearest neighbors) and non-local (long range connections).^{24,25} One manner of modeling these connections is by means of small-world networks.²⁶ The topological properties of small-world ensure the efficient generation and integration of information in the brain.²⁷ It has been observed that small-world networks can exhibit synchronous behavior with fewer connections than networks with all-to-all coupling.²⁸

Small-world properties were identified in the nematode *Caenorhabditis elegans* that has 2462 synaptic connections among

each one of the 282 neurons.²⁹ Hilgetag *et al.* demonstrated that small-world network characteristics can be observed in cortical connectivity matrices from cat and macaque monkey brains.³⁰ From human functional magnetic resonance imaging (fMRI), Bassett and Bullmore²⁷ showed that small-world models provide an approach to understand the function and structure of the brain. Lameu *et al.*³¹ studied coupled small-world networks according to the cat cerebral cortex. Without external perturbations, they showed an emergence of bursting synchronization among neurons within the visual, somatosensory-motor, and frontolimbic cognitive regions, except for the auditory area, while burst synchronization appeared in the auditory area when some perturbations were applied in the visual area. Moreover, the small-world networks have been used to analyze phase synchronization of bursting neurons.^{16,32}

In this work, our main purpose is the study of burst synchronization and desynchronization in a neuronal network model composed of 83 subnetworks available in both hemispheres of a human brain. We apply periodic and random pulses to investigate how such perturbations influence the neuronal synchronization in the network.

This paper is organized as follows: Sec. II describes the structural connectivity matrix of the human brain and the external pulsed perturbations. In Sec. III, regarding electrical and chemical synapses, we study the phase synchronization of the cortical areas. The effect of external perturbations on the synchronization is analyzed in Sec. IV. Finally, our conclusions are described in Sec. V.

II. NETWORK OF NETWORKS MODEL

The Rulkov model is a two-dimensional discrete dynamical system. It is suitable to study a variety of large neuronal networks, due to the fact that it is easier to compute than a continuous dynamical system.¹² Neurons modeled by the Rulkov model can exhibit a variety of dynamic regimes, such as tonic spikes and chaotic bursting.³³ The Rulkov model is given by

$$x_{k+1} = \frac{\alpha}{1 + x_k^2} + y_k, \quad (1)$$

$$y_{k+1} = y_k - \lambda(x_k - \beta), \quad (2)$$

where x_k is the fast variable (membrane potential) and y_k is the slow variable at the discrete time k , respectively.³⁴ The constant α is the control parameter, while λ and β describe the external influences, which are on the order of 10^{-3} . The Rulkov model is dimensionless and is able to reproduce neuronal activities. The combinations of both α and β are useful to mimic different dynamical behaviors of the neurons, such as resting, tonic spiking, and chaotic bursts.³⁵ The time series of the fast variable of the Rulkov map are shown in Fig. 1. Figures 1(a) and 1(b) display the regimes of relaxation oscillations and pieces of spikes with decreasing amplitude, respectively. In Figs. 1(c) and 1(d), the Rulkov map exhibits bursting behavior and the red circles denote the maximum value of the slow variable y_k . The chaotic bursts are observed for $\alpha > 4$.

Our network consists of 83 nodes corresponding to different cortical regions, where each node has 120 neurons described by the Rulkov model. We use a structural connectivity matrix according to the brain of a healthy individual obtained from

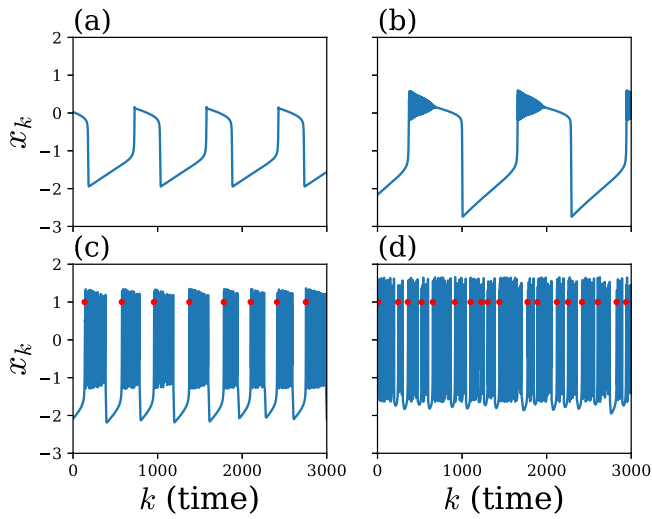


FIG. 1. Time evolution of the fast variable x_k for (a) $\alpha = 2.3$, (b) $\alpha = 3.0$, (c) $\alpha = 4.1$, and (d) $\alpha = 4.5$. The red circles show the maximum value of the slow variable y_k . We consider x_0 and y_0 randomly selected from the intervals $[-2, 2]$ and $[-4, 0]$, respectively, $\lambda = 0.001$ and $\beta = 0.001$.

<https://braingraph.org>^{20,36,37} to build a neuronal network model containing the organization of cortical connections. The connection matrix presents a weighted matrix, whose values represent the number of fibers. The symmetry adjacency matrix demonstrates the connections between the 83 cortical regions located at the cortex surface for both right and left hemispheres. The regions from 1 to 41 are related to the right hemisphere, from 42 to 82 are located at the left hemisphere, and the region with the number 83 is considered for the brainstem. By considering the matrix, we build a new matrix with only five numbers in different colors, as shown in Fig. 2. The number 0 (white) shows that there is no connection between the two cortical regions. The numbers 1 (red), 2 (green), 3 (blue), and 4 (black) represent the weak, intermediate, normal, and strong connections between the cortical areas, respectively. These numbers are based on the work published by Scannell and Young.³⁸ They reported the connectational organization of neuronal systems in the cat cerebral cortex. The regions with white, red, green, blue, and black colors have no connections, 50, 100, 150, and 200 connections with other regions, respectively. The connections are randomly selected. The numbers 1, 2, 3, and 4 have been classified according to the number of fibers in the interval $[1, 3000]$, $[3001, 6000]$, $[6001, 9000]$, and more than 9000, respectively, from the structural connectivity matrix of the brain.

Each cortical region is represented by a subnetwork with small-world properties. The small-world network has a combination of short path length comparable to a random network and high clustering as a regular network.²² According to these features, small-world networks have been applied in various research studies related to the connectivity of the nervous system.^{27,39} In the small-world network introduced by Watts and Strogatz,²² non-local links are inserted by randomly rewiring some local connections into non-local ones, while randomly selected shortcuts are added in a regular lattice

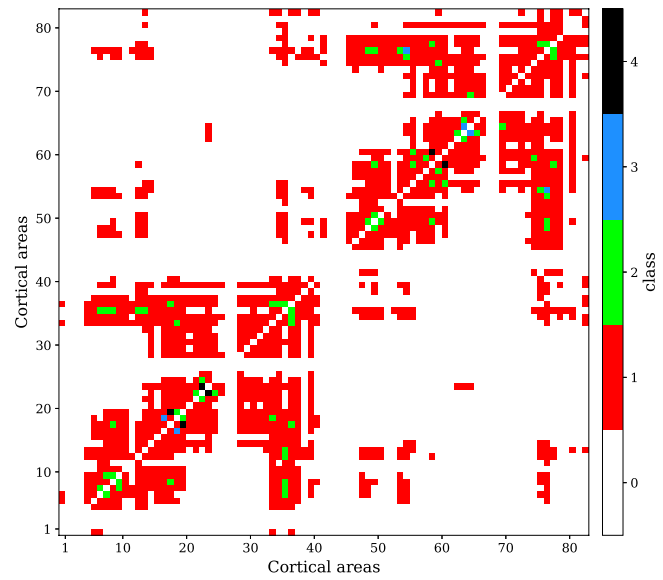


FIG. 2. Structural connection matrix related to the 83 cortical areas in the brain of a healthy human. The cortical areas start from 1 to 41 for the right hemisphere, from 42 to 82 for the left hemisphere, and with the number 83 for the brainstem.

as proposed by Newman and Watts.⁴⁰ In this work, we use the small-world network introduced by Newman and Watts to build subnetworks containing 120 neurons and 5% of shortcuts for each one. In the Newman–Watts model, there is no probability of a part of the network becomes disconnected from the rest. In the small-world subnetworks, the electrical coupling is just between the nearest neighbors (local), while the chemical connections only providing the shortcuts (non-local). In the network, the links between the small-world subnetworks follow the cortical connectome of the brain, as shown in Fig. 2.

With regard to the connections among the neurons, the couplings can be electrical or chemical. The chemical coupling can be excitatory or inhibitory. Within each small-world subnetwork, there are local and non-local connectivities that describe the electrical and chemical synapses, respectively. The connections between each subnetwork are non-local links based on the chemical synapses.

Our neuronal network is given by

$$x_{k+1}^{(nj)} = \frac{\alpha^{(nj)}}{1 + (x_k^{(nj)})^2} + y_k^{(nj)} + \frac{e}{2} (x_k^{(n-1,j)} + x_k^{(n+1,j)} - 2x_k^{(nj)}) - c \sum_{d=1}^N \sum_{f=1}^P [A_{(d,f),(n,j)} H(x_k^{(d,f)} - \theta), (x_k^{(nj)} - V_N)] + u_k, \tag{3}$$

$$y_{k+1}^{(nj)} = y_k^{(nj)} - \lambda(x_k^{(nj)} - \beta), \tag{4}$$

where the initial conditions for the variables x_k and y_k are randomly selected from $[-2, 2]$ and $[-4, 0]$, respectively. The pair (n, j) shows the neuron n ($n = 1, 2, \dots, N$) in the cortical area j ($j = 1, 2, \dots, P$),

where $N = 120$ is the number of neurons in each subnetwork and $P = 83$ is the number of cortical areas. The connectivity matrix is given by $A_{(d,f),(n,j)}$, corresponding to the chemical coupling. When the neuron (d, f) connects with the neuron (n, j) , the element of the matrix is equal to 1, otherwise is equal to zero. The $\alpha^{(n,j)}$ value is the non-linearity parameter of the Rulkov model randomly selected from [4.1, 4.4]. The values of $\alpha^{(n,j)}$ are distributed using a random uniform generator. We consider $\lambda = 0.001$ and $\beta = -1.25$. Furthermore, e and c are associated with the electrical and chemical coupling strengths, respectively. $H(x)$ is the Heaviside step function with the presynaptic threshold equal to $\theta = -1.0$ for the chemical synapse. When the presynaptic neuron voltage is greater than θ , the post-synaptic neuron receives an input. The constant V_N is described by the nature of the post-synaptic ion channels and determines the reversal potential related to the synapse. In 1984, Feldman⁴¹ reported that approximately 70%–80% of the neuronal population of the cortex is excitatory. If $V_N = 1$ or -2 , the synapse is excitatory or inhibitory, respectively. These values of V_N are randomly distributed in the whole network in such a way that 75% and 25% of connections, respectively, are excitatory and inhibitory.⁴² We consider that a single neuron does not make both excitatory and inhibitory connections with other neurons. Finally, v_k is an external pulsed perturbation that activates the spikes in the neurons. The Rulkov neurons are stimulated over time k by periodic and random pulses considered as an external pulsed current. The external perturbation v is defined as

$$v = v_0 + \Phi(k), \tag{5}$$

where v_0 is the current with constant amplitude in the interval [8, 15] and $\Phi(k)$ describes the pulses with amplitude τ which are chosen from the interval [0, 4] according to Refs. 43–45. When $\Phi(k)$ is equal to zero for all times, the current is constant, as shown in Fig. 3 (red line). The periodic pulsed currents are generated when $\Phi(k)$ assumes an on–off configuration equal to τ and 0 over time considering time intervals Δk_1 and Δk_2 in the range [1, 100] (blue line). In the random pulse (green line), the on–off transition in $\Phi(k)$ has time intervals Δk_r , randomly distributed in the interval [20, 100].

III. BURST SYNCHRONIZATION WITHOUT PULSES

In the central nervous system, bursts and oscillatory patterns of neuronal activities can be observed from slow to fast oscillations.⁴⁶ In this work, we focus on the burst phase synchronization, which is a type of neuronal synchronization.⁴⁷ It is possible to identify phase synchronization related to bursts of neuronal ensemble by means of the Kuramoto order parameter,⁴⁸ that is given by

$$R_k = \left| \frac{1}{N \times P} \sum_{n=1}^N \sum_{j=1}^P e^{i\Theta_k^{(n,j)}} \right|, \tag{6}$$

where N is the total number of neurons of each subnetwork, P is the number of cortical areas, $i = \sqrt{-1}$, and Θ_k is the phase of the neuron n in the cortical area j at time k .

To analyze the burst synchronization, we calculate the neuron phase obtained by the slow variable y_k . When y at time k represents a local maximum, a burst starts. Within each burst, a phase

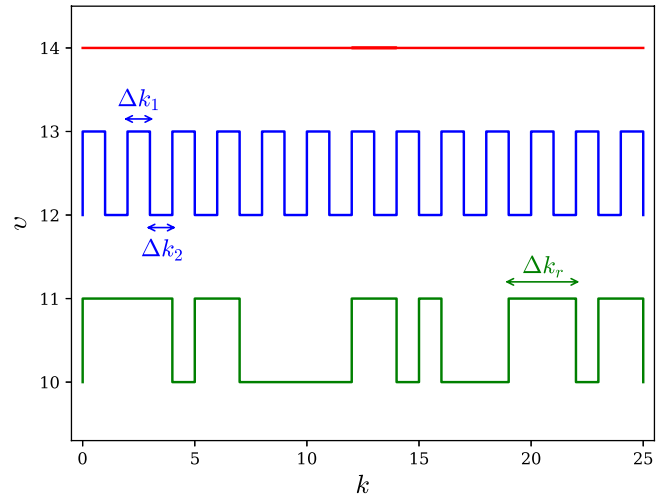


FIG. 3. Representation of external currents with constant amplitude for $v_0 = 14$ in red color, with periodic pulses for $v_0 = 12$, $\tau = 1$, and Δk_1 and Δk_2 equal to 1 in blue color, and with random pulses for $v_0 = 10$, $\tau = 1$ and Δk_r , randomly distributed in green color. We consider external currents that do not change the individual neuron behavior, namely, the neuron continues to exhibit chaotic bursts.

is described by⁴⁹

$$\Theta_k = 2\pi t + 2\pi \frac{k - k_t}{k_{t+1} - k_t}, \tag{7}$$

where $k_t < k < k_{t+1}$, k_t denotes the time when the t -th burst of the n th neuron starts and t is an integer. We investigate the role of the electrical and chemical coupling strengths by means of the

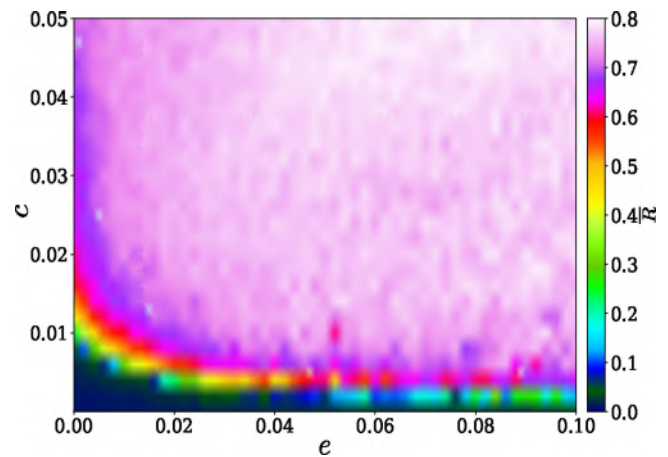


FIG. 4. Time-averaged order parameter (color bar) as a function of c (chemical synapses) in the interval [0, 0.05] and e (electrical synapses) in the range [0, 0.1] of the human’s brain cortical areas during 10^5 iterations.

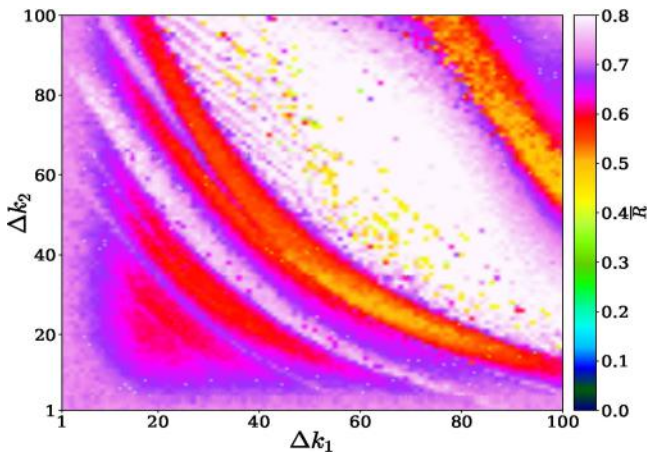


FIG. 5. Averaged order parameter of the human's brain network under a periodic pulse with $\nu_0 = 8$ and $\tau = 0.1$ in the parameter space $\Delta k_2 \times \Delta k_1$ for the synchronized point $e = 0.1$ and $c = 0.05$.

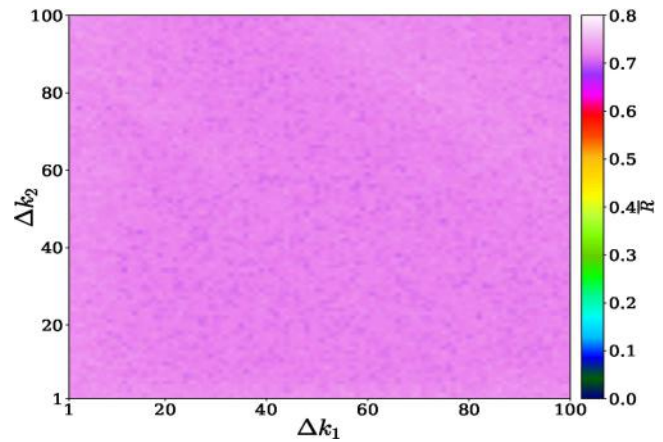


FIG. 7. Time-averaged order parameter of region 83 by considering a periodic pulsed perturbation with $\nu_0 = 8$, $\tau = 0.1$, $\Delta k_1 \in [1, 100]$, and $\Delta k_2 \in [1, 100]$ for $e = 0.1$ and $c = 0.05$ indicating the burst synchronous behavior.

time-averaged order parameter, that is given by

$$\bar{R} = \frac{1}{T} \sum_{t=1}^T R_k, \tag{8}$$

where T is the total simulation time, after a transient time. If the neurons are phase-synchronized or desynchronized, the time-averaged order parameter \bar{R} is equal to 1 or 0, respectively.³³

With regard to the neuronal network for an individual, the values of the time-averaged order parameter (color scale) as a function of the electrical and chemical coupling strengths are displayed in Fig. 4. In Fig. 4, we show the coupling strength ranges in which the network exhibits synchronous behavior. The neuronal network does

not exhibit a completely phase synchronized state ($\bar{R} = 1$), due to the fact that the neurons are not identical. According to the network synchronization diagnostic of the dynamics, the regions for $\bar{R} < 0.8$ show desynchronous behavior, while synchronous behavior occurs for $\bar{R} \geq 0.8$. The increase of the chemical coupling c leads the network to the neuronal synchronization.

IV. APPLYING EXTERNAL PULSED PERTURBATIONS IN BURSTING SYNCHRONIZATION

It has been reported that external pulsed currents can cause changes in neuronal synchronous behavior, as well as alterations in neuron spiking activities.^{50,51} With this in mind, we investigate the effect of external pulsed perturbations, as described in Eq. (5), in our brain network model considering $e = 0.1$ and $c = 0.05$, as shown in

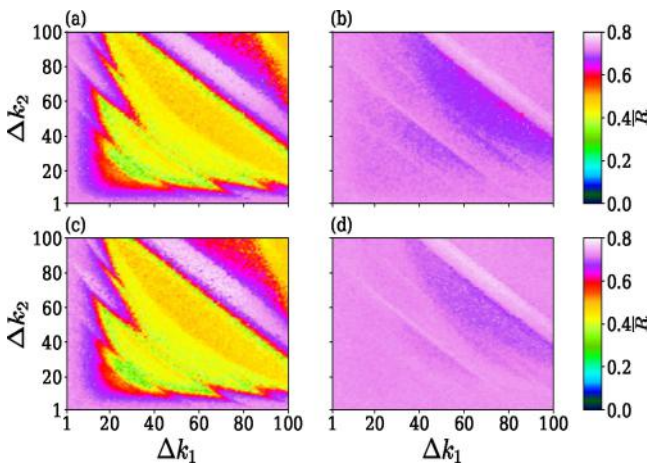


FIG. 6. Time-averaged order parameter of the whole brain network grouped into regions from (a) 1 to 34, (b) 35 to 41, (c) 42 to 75, and (d) 76 to 82. We consider a periodic pulsed current with $\nu_0 = 8$ and $\tau = 0.1$ for $e = 0.1$ and $c = 0.05$.

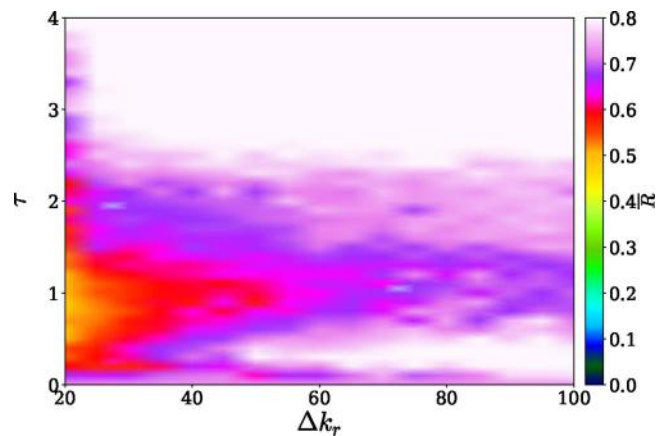


FIG. 8. Averaged order parameter of the whole brain network under a random pulsed current as a function of τ and Δk_τ for $\nu_0 = 8$, $e = 0.1$, and $c = 0.05$.

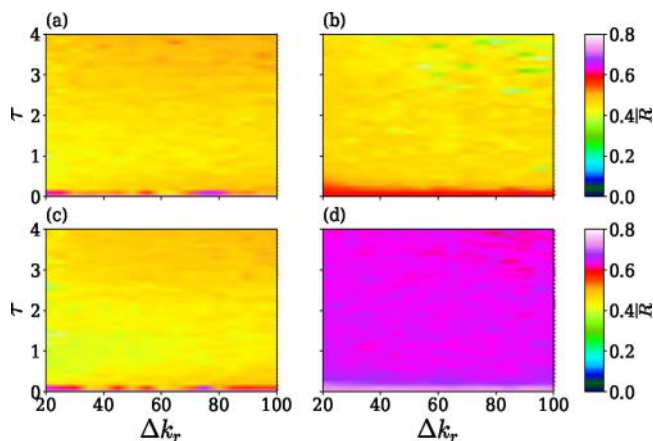


FIG. 9. Time-averaged order parameter of the four cortical regions of the brain network from (a) 1 to 34, (b) 35 to 41, (c) 42 to 75, and (d) 76 to 82, by considering a random pulsed perturbation with τ and Δk_r in the intervals $[0, 4]$ and $[20, 100]$, respectively, for $v_0 = 8$, $e = 0.1$, and $c = 0.05$.

Fig. 4. Figure 5 displays the effect of periodic pulses with $v_0 = 8$, $\tau = 0.1$, and Δk_1 and $\Delta k_2 \in [1, 100]$ ms, which represent the on and off intervals in the periodic pulse profile, respectively. The periodic perturbation induces a change in the synchronous behavior and reduces the value of the time-averaged order parameter in some areas. Our results show that alterations related to Δk_1 and Δk_2 play an important role in the synchronous patterns. In other words, depending on the combination of Δk_1 and Δk_2 , synchronization and desynchronization can emerge in all the network.

Considering the impact of the periodic pulses in the whole brain, we investigate how this external perturbation influences the synchronous behavior in the regions from 1 to 34, from 35 to 41, from 42 to 75, from 76 to 82, and 83, as exhibited in Fig. 6

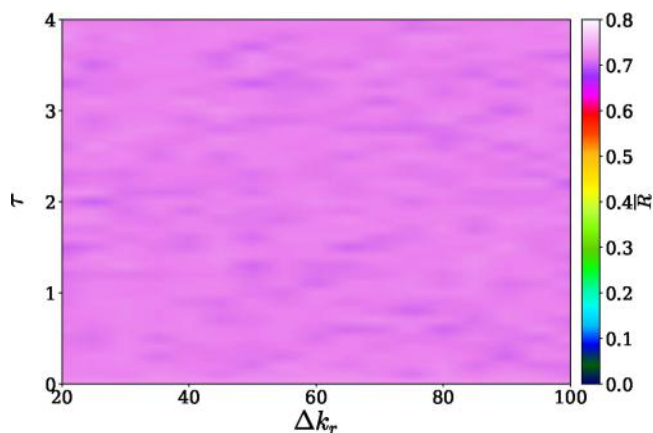


FIG. 10. Time-averaged order parameter of region 83 of the brain network under a random pulsed current for τ and Δk_r selected from the intervals $[0, 4]$ and $[20, 100]$, respectively. We consider $v_0 = 8$, $e = 0.1$, and $c = 0.05$.

from the panels (a) to (d), and Fig. 7, respectively. For the right hemisphere, Fig. 6(a) displays that, for instance, the burst desynchronization with \bar{R} about 0.4 and 0.6 starts from the time intervals greater than $\Delta k_1 \approx 20$ ms and $\Delta k_2 \approx 10$ ms, and continues until the center of the figure and around it, as well as the intervals close to 100 ms. The synchronous behavior is not suppressed when the on-off intervals change, except on some combinations of them with the time-averaged order parameter about 0.6 dispersed in Fig. 6(b). Regarding the left hemisphere, the bursting synchronization and desynchronization [Figs. 6(c) and 6(d)] are very similar to the behaviors observed in Figs. 6(a) and 6(b). In Fig. 7, neuronal synchronous behavior with \bar{R} close to 0.8 is observed.

We analyze the effect of random perturbations, as another type of external pulsed current. We consider random pulses with $v_0 = 8$, $\tau \in [0, 4]$ and Δk_r randomly distributed in the interval $[20, 100]$. To investigate the neuronal synchronous behavior in the whole brain network under a random current, we compute the time-averaged order parameter \bar{R} , as displayed in Fig. 8. Increasing τ approximately from 0.5 to 2, the bursting synchronization is suppressed for almost all the values related to Δk_r . The burst synchronous behavior does not change for $\tau > 3$ and alterations in the on-off time intervals have no substantial effect on the synchronization. For $\tau < 1$, we observe parameter regions in which synchronization appears.

In order to study the bursting synchronous behavior, we apply in the five regions an external current with random pulses. In Fig. 9, we find desynchronization (\bar{R} equal or close to 0.4 or 0.6) in the four regions exhibited in panels (a)–(d). The desynchronization occurs for all the amplitudes. Figure 9(d) shows the time-averaged order parameter greater than panels (a)–(c). Furthermore, the random perturbation applied in region 83 of the brain changes the synchronization in the whole region with \bar{R} approximately equal to 0.7, as shown in Fig. 10. The bursting synchronization does not depend on τ and Δk_r .

V. CONCLUSIONS

In this paper, we build a neuronal network model based on the healthy human brain cortical areas. We analyze the effects of various types of external pulsed perturbations on burst synchronization. We consider a small-world network of coupled Rulkov neurons for each cortical area. The network is composed of 83 subnetworks with small-world properties. In our network, each neuron can have local and non-local connections with other neurons by means of electrical and chemical synapses, respectively.

Without external pulsed currents, the neurons can exhibit synchronization between themselves due to the synaptic interaction. With regard to the external perturbation with periodic pulses, the neuronal activities depend on the pulse duration. For the random pulsed currents, we observe a reduced time-averaged order parameter when the pulse amplitude changes. Our results are robust due to the fact that we consider not only different nonlinearity parameter values in the range in which the neurons exhibit chaotic bursts, but also the initial conditions that are randomly distributed.

Our results have some similarities with the outcomes obtained by Lameu *et al.*¹⁸ for a clustered scale-free neuronal network based on the cat cortex structure. The neurons in the whole networks exhibit synchronous patterns when the coupling strength is

increased. Depending on the external perturbation, regions with synchronous behavior while others remain desynchronized are observed. We consider an external pulsed current which permits a better control on the synchronization, due to the fact that we can choose the pulse amplitude and time interval.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflicts to disclose.

Author Contributions

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DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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