Physics Letters A ••• (••••) •••–•••

Contents lists available at ScienceDirect

Physics Letters A

www.elsevier.com/locate/pla

Analyzing topological characteristics of neuronal functional networks in the rat brain

Hu Lu [a,c], Shengtao Yang [b], Yuqing Song [a], Hui Wei [c]

[a] School of Computer Science and Communication Engineering, Jiangsu University, Jiangsu 212003, China
[b] Institutes of Brain Science, Fudan University, Shanghai 200433, China
[c] School of Computer Science, Fudan University, Shanghai 200433, China

ARTICLE INFO

Article history:
Received 12 May 2014
Received in revised form 19 August 2014
Accepted 21 August 2014
Available online xxxx
Communicated by C.R. Doering

Keywords:
Neuronal functional networks
Complex networks
Small-world networks
Community structure
Cognitive tasks

ABSTRACT

In this study, we recorded spike trains from brain cortical neurons of several behavioral rats in vivo by using multi-electrode recordings. An NFN was constructed in each trial, obtaining a total of 150 NFNs in this study. The topological characteristics of NFNs were analyzed by using the two most important characteristics of complex networks, namely, small-world structure and community structure. We found that the small-world properties exist in different NFNs constructed in this study. Modular function Q was used to determine the existence of community structure in NFNs, through which we found that community-structure characteristics, which are related to recorded spike train data sets, are more evident in the Y-maze task than in the DM-GM task. Our results can also be used to analyze further the relationship between small-world characteristics and the cognitive behavioral responses of rats.

UNCORRECTED PROOF

1. Introduction

In recent years, complex networks based on the graph theory have been widely used to analyze the structural and functional properties of brain networks [1–3]. In brain networks, several brain areas or neurons are regarded as nodes, whereas structural or functional correlation connections are regarded as edges. Ignoring the shape, size, and other physical characteristics of the brain helps identify and analyze the likeness or difference of brain networks [4]. Edges are referred to as axons or fiber tracts in brain networks identified as structural networks. By contrast, edges are referred to as cross correlations of signals from brain areas or from single neurons in brain networks are identified as functional networks. Statistical methods can be used to calculate these correlations. Complex-network analysis methods can be used to analyze the topological characteristics of brain networks, particularly the characteristics of functional networks. Many studies have shown that the potential functional characteristics of functional networks are similar to the structural topology characteristics of brain networks [5,6]. Brain-network analysis methods have become the main methods in studying the brain system and brain diseases [7–9].

Several complex network measures, which include the clustering coefficient and the shortest path length, have been used to analyze the brain functional network. Many studies have focused on small-world network structures, which are known for their highly efficient information transmission with low transmission cost [10–12]. The results of these studies show that small-world structure changes are closely related to brain development and brain disorders [13,14]. These studies were mainly focused on the macroscopic level of connectivity and on the functional networks derived from a set of voxels from functional magnetic resonance imaging (fMRI) or from independent components of electroencephalogram (EEG) data. However, using small-world properties is only the first step in understanding the complex structure of the brain. Complex network approaches allow the quantification of other topological properties, such as modularity [15]. These measures have also been used in brain fMRI networks. Researchers have recently discovered brain network modules [16,17]. For instance, the studies partitioned pharmacological MRI and resting state fMRI networks into meaningful communities of closely interconnected voxels by using a widely used community-structure partitioning algorithm [18,19]. The cerebral cortex is a network composed of a large number of neurons. Studying the connection structures between neurons is important for understanding brain functions. However, few studies have tried to obtain the microlevel connectivity properties of neuronal functional networks (NFNs) on the level of individual neurons [20,21].

With the development of multiple electrode recording technology, spike trains from hundreds of individual neurons can be recorded simultaneously [22]. Research regarding neuron populations has proved useful in understanding population coding in neuronal populations. Population coding theory considers the

http://dx.doi.org/10.1016/j.physleta.2014.08.026
0375-9601/© 2014 Published by Elsevier B.V.

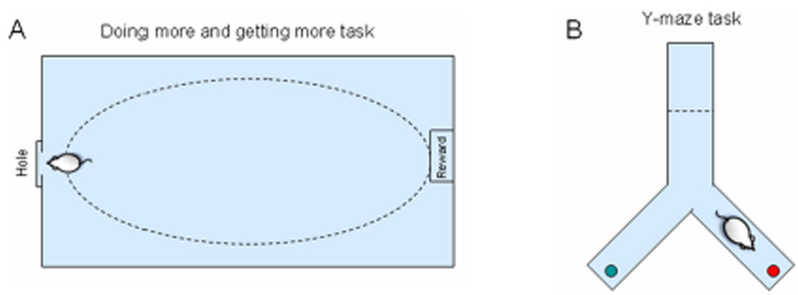

Fig. 1. Description of the processes of two different behavioral tasks. (A) Box of the DM-GM task. (B) Box of the Y-maze task.

information carried by the neuron population, instead of considering the firing rate of single neurons. New models need to be developed to understand the relationships in populations of interacting neurons. Topological analysis of the characteristics of NFNs can specifically answer questions of how the brain works. Several studies have analyzed the small-world characteristics of NFNs and have shown that NFNs have small-world properties [20,21]. In this study, we recorded the spike trains of cortical neurons of rats by using the multiple electrode recording technique. The rats performed two cognitive tasks. In the first task, the rats were trained to implement the doing more and getting more behavioral task (DM-GM, Fig. 1(A)). In the second task, the rats were trained to implement the Y-maze behavioral task (Y-maze, Fig. 1(B)). Four experimental data sets were selected from two different behavioral tasks. Each data set contains multiple trials for each rat. A single NFN was generated for each trial by using individual neurons as nodes and the correlations between the spike trains of the neurons as edges. A fully weighted and completed network was constructed for each trial. Each weighted network was converted into a binary matrix by retaining several edges with important correlations. We studied the two most important characteristics in complex networks: small-world network and community structure. Results show that small-world properties exist in different NFNs which were constructed based on the recorded neurons in this study. By using the modular function Q proposed by Newman and Girvan [15], we found that community structure characteristics depend on recorded data sets. Compared with the DM-GM cognitive task, community structure characteristics are observed in the data sets from the Y-maze cognitive task. NFNs that have community structure characteristics can be divided into different sub-structures on the basis of the modular function Q.

2. Materials and methods

2.1. Experiment data

All studies were approved by the Institutional Animal Care and Use Committee of the Fudan University. In this study, spike train data sets were selected from two different cognitive behavioral tasks. In the DM-GM task, the experimental training box was a rectangular box with bottom, but without cover (70 cm × 25 cm × 25 cm). The rats were moderately deprived of water. Rats are given water for reward when these rats run to the bottom of the box. The longer the rats stay in the top of the rectangular box, the more water they are given to drink when they returned to the bottom of the box. The training box in the Y-maze task is a Y-shaped box with bottom, but without cover. The three arms of the box have angles of 120° to each other. The rats were trained to move alternately to the left or right arm to receive juice or water as reward.

Multiple microelectrode arrays (cerebus-128 multi-channel, Blackrock Microsystems, United States) were chronically implanted in different cortical areas, such as in the anterior cingulated cortex (ACC) of the DM-GM task and in the prefrontal cortex (PFC) of the Y-maze task, in male and adulated rats. In the brain, ACC is responsible for the decision function and PFC is responsible for the memory function. DM-GM task is a decision-making memory task and Y-maze task is a working memory task. Consequently, we selected the ACC and PFC as recorded rat brain regions for this study. Signals were recorded only when the signal-to-noise ratio is larger than three. We sorted spikes on the basis of a template-match algorithm to identify spikes of single neurons when the signals exceed a threshold. A multiple neuron acquisition processor (Plexon) was used to acquire and distinguish activity from single neurons. Spike trains of neurons are composed of a sequence of spikes. All experiments were performed in accordance with animal protocols approved by the United States National Institutes of Health (NIH).

Table 1
Four spike train data sets of different cognitive tasks from multi-electrode recordings.

Task	Data sets	Neurons	Trials
DM-GM	Data 1	34	50
	Data 2	25	50
Y-maze	Data 3	20	25
	Data 4	23	25

We recorded a large population of neurons in rats, which performed two different behavioral tasks. We used four data sets of spike trains for analysis, recorded from four different rats. Two rats performed the DM-GM task and other two rats performed the Y-maze task. A total of 102 neurons were observed. Each data set of DM-GM task contained 50 trials, whereas each data set of Y-maze contained 25 trials. Each data set had different number of neurons. The number of neurons for each data set varied from 20 to 34, in which the maximum number of neurons is 34, the minimum is 20, and the mean is 25.5 (Table 1).

2.2. Functional network construction

Calculating the correlations between the spike trains of neuron pairs is the first step in constructing NFNs. Many linear methods, such as Pearson correlation coefficient and cross-correlation, were used as a measure of functional connectivity among brain networks [23,24]. Many correlation calculation methods require spike trains to be binned in small time windows, thence calculating correlations between pairs of neurons based on these bins. This method has some problems. The resulting neuronal functional networks depend on bin size. Networks generated would vary according to bin parameters. The choice of parameter is very difficult. There is no unified standard. Here, we account for this effect by directly observing each set of neuronal spike trains as a time series independent of time window. Using the function "corrcoef" in the Matlab toolbox, we applied a generalized correlation coefficient calculation to derive the correlation matrix between multiple neurons. Let $X = \{x_1, x_2, \ldots, x_i \ldots, x_n\}$, x_i represent the spike train of

Please cite this article in press as: H. Lu et al., Analyzing topological characteristics of neuronal functional networks in the rat brain, Phys. Lett. A (2014), http://dx.doi.org/10.1016/j.physleta.2014.08.026