Long-Range Temporal Correlations in the Spontaneous in vivo Activity of Interneuron in the Mouse Hippocampus

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Abstract. The spontaneous in vivo firings of neuron in mouse hippocampus are generally considered as neuronal noise, where there is no any correlation in the inter-spike interval (ISI) sequences. In the present study, we investigate the nature of the ISI sequences of neuron in CA1 area of mouse hippocampus. By using the detrended fluctuation analysis (DFA), we calculated the fluctuation or scaling exponent of the ISI sequences. The results indicated that there exists the long-range power-law correlation over large time scale in the ISI sequences. To further investigate the long-range correlation of ISI, we studied the long-range correlation of ISI sequences from different types of neurons in mouse hippocampus, which are four types of interneurons categorized by their firing patterns. Our results show the presence of long-range correlations in the ISI sequence of different types of neurons. Furthermore, the shuffle surrogate data achieved by randomly shuffle the original ISI sequence is used to verify our conclusion. The application of shuffle surrogate shows that the long-range correlation is destroyed by randomly shuffle, which demonstrates that there is actually the long-range correlation in the ISI sequence. Furthermore, we also compare the long-range correlations of ISI sequence when mice are in different behavioral states, slow-wave sleep (SWS) and active exploration (AE). Our results indicated that the ISI sequences exhibit different extent of long-range correlations: the long-range correlation is significantly stronger when mice are in AE than that of ISI sequence when mice are in SWS, which demonstrated that the varied long-range correlations exhibiting in ISIs of interneurons might be associated with activities of neuronal network regulating the ongoing neuronal activity of different interneurons.

Keywords: Hippocampus, Interneuron, Long-Range Temporal Correlations, Detrended Fluctuation Analysis, Fractal.

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1 Introduction

As an important formation in the brain, hippocampus plays an important role in learning and memory. Since 1950s, hippocampus has attracted an increasing number of researchers [4, 7, 12, 13, 19]. And some researchers have investigated the long-range correlations in the neuronal models [10]. However, there are relatively less researches in the long-range correlation of the spontaneous in vivo activity of neurons in hippocampus, especially in mouse hippocampus.

Because the inter-spike interval (ISI) sequence of the spontaneous in vivo activity of neurons is irregular, ISI sequence is frequently modeled by the stochastic point process. Recently, an emerging perspective is that there exist the long-range correlations in the spontaneous spiking of neurons in the hippocampal-amygdala [3].

In recent years, there are increasing evidence indicating that many physical and biological systems exhibit long-range power-law correlations such as economics [14, 15], DNA [18, 19], human gait [8], neural receptors in biological systems [2], ion channel kinetics [11]. Detrended Fluctuation Analysis (DFA) is a scaling analysis method used to quantify long-range power-law correlations in signals [6], and the DFA method could also help distinguish distinct statues of the same system with different scaling behavior such as the healthy and sick individuals [1] as well as for waking and sleeping states [9]. To investigate the long-range correlation in neuronal spike train in mouse hippocampus, the DFA is used to characterize the presence of long-range dependence, which indicated that the spontaneous firing patterns of most of the recorded neurons could not be well described by a renewal process or by any process with short correlation; rather they present long-range power-law correlations, representing ongoing memory effects in the ISI sequence. To verify our conclusion, the shuffle surrogate dataset is achieved by randomly shuffle the original ISI sequence, thus the ISI distribution function and the mean firing rate of the shuffle surrogate is the same as the original one. By applying DFA in the shuffle surrogate dataset, we found that the long-range correlation is destroyed by randomly shuffle.

To further study the relationship between long-range correlations and behavioral states, we recorded the spontaneous in vivo activity of the neuron when mice were in different behavioral states, slow-wave sleep (SWS) and active exploration (AE), which are two significant behavioral states for mouse. After the spontaneous in vivo activities are recorded, the DFA is applied and the results indicate that 1) the ISI sequences exhibit long-range dependence when mouse are in both of these two states, and 2) the long-range correlations of the ISI sequence in SWS is significantly weaker than that of ISI sequence during mice are in AE.

2 Method

Detrended fluctuation analysis (DFA) is a modified root mean square analysis, which is widely used to the analysis of physiological data [18]. The method of DFA is briefly formulated as follows. First, the ISIs (of total length N) is integrated, $y(k)=\sum_{i=1}^{k}(X-\overline{X}), k=1,\cdots,N$, where $X(i)$ is the ith inter-spike interval (ISI) and $\overline{X}$ is the average ISI sequences. Next, the integrated time series is divided into t=int(N/n) non-overlapping boxes of length, n. In each box, a least-squares line representing the trend in that box is fit to the data, Denoted by $y_n(k)$ the y coordinate of the straight line segment time series, we detrended the integrated time series, $y_n(k)$, in each box. Subsequently, the root-mean-square fluctuation of this integrated and detrended time series is calculated by $F(n)=\left\{\frac{1}{N}\sum_{k=1}^{N}[y(k)-y_n(k)]^2\right\}^{\frac{1}{2}}$.

This computation is repeated over all time scales (box scales) in order to provide a relationship between F(n), the average fluctuation as a function of box size, and the box size n, which is the number of spikes in a box. The system with power-law correlation obeys $F(n) \propto n^{\alpha}$, where α is the slope of the line relating log F(n) and log n and is called the fluctuation or scaling exponent.

Consider an ISI sequence where the value at one ISI is completely uncorrelated from any previous values, i.e. white noise. The kinds of ISI sequence can be achieved by randomly shuffle the original ISI sequences (so-called shuffle surrogate dataset). For this type of uncorrelated data, the integrated value, y(k), corresponds to a random walk, thus $\alpha = 0.5$ [16]. For $0 < \alpha < 0.5$, ISI sequence exhibits an anti-persistent correlated process such that large and small values of the ISI sequence are more likely to alternate. And for $0.5 < \alpha \leq 1$, ISI sequences persistent long-range power-law correlations, which means a large (compared to the average) ISI is more likely to be followed by large ISI and vice versa. For $\alpha = 1$, ISI sequence corresponds to 1/f noise, which is a self-similar or scale-invariant fractal sequence. The degree of deviation of α from 0.5 toward 1 represents the strength of long-range correlation in the sequence.

3 Results

3.1 Detrended Fluctuation Analysis: Long-Range Correlations of ISI Sequences of Interneurons

The analysis of one hippocampus interneuron is shown in Fig. 1. Fig. 1A shows the original ISI sequence of an interneuron belonging to Interneuron Type III. This ISI sequence is recorded when mouse is in AE. From Fig. 1B, we can see a clear power-law scaling relationship between average fluctuation and the box size n, which exhibits the property of scale invariance. The slope, scaling exponent, is achieved by least-square fit. Also in Fig. 1B, the result of DFA in shuffle surrogate for the original ISI sequence is evidently deviated from the original one. Although it is still exhibit power-law relationship, the scale exponent for shuffle surrogate is 0.50 indicating the effectiveness of DFA. Fig. 1C shows one of the shuffle surrogates of original ISI sequence shown in Fig. 1B. And the result of DFA in this sequence is shown in Fig. 1D, in which we noticed that there is no significant difference for the scale exponent for the ISI sequence shown in Fig. 1C and its shuffle surrogate. From the result above, we conclude that the original ISI sequence does exhibit the long-range correlations.

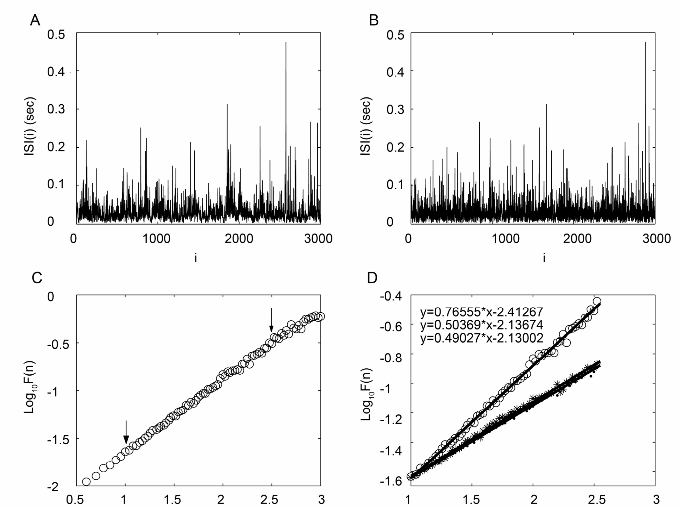

Fig. 1. DFA analysis on the ISI sequence and its shuffle surrogate

3.2 Long-Range Correlations in Different Interneurons

To further investigate the relationship between long-range correlations of ISI sequences in different firing patterns, the scale exponents of ISI sequences were estimated in two different behavioral states: SWS and AE. To maintain stable estimation, seven ISI sequences with 3000 continuous spikes were chosen from each interneuron for SWS and AE. We then statistically investigate the scale exponents of the seven sequences, and achieved the mean and standard deviation as the estimated scale exponent for each interneuron in each behavioral state. Figure 2 shows that the

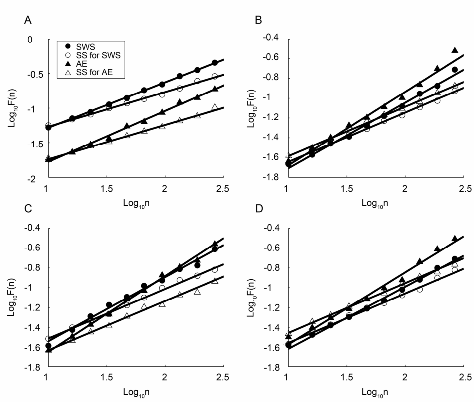

Fig. 2. The scale exponents were computed for four types of interneurons by performing DFA on 3000 ISIs during AE and SWS

Table 1. The scale exponent of recorded four types of interneurons in mouse hippocampus

Type	Scale exponent (SWS)	SS for Scale exponent (SWS)	Scale exponent (AE)	SS for Scale exponent (AE)
Type Ⅰ (n=5)	0.6567±0.0094	0.5066±0.0082	0.7373±0.0097	0.4986±0.0138
Type Ⅱ (n=7)	0.6516±0.0081	0.5046±0.0115	0.7339±0.0129	0.5069±0.0113
Type Ⅲ (n=3)	0.6506±0.0106	0.5054±0.0117	0.7538±0.0125	0.4961±0.0141
Type Ⅳ (n=9)	0.6301±0.0037	0.5002±0.0078	0.7142±0.0153	0.4981±0.0025

result of DFA analysis of the original ISI sequences of each type of interneurons and their shuffled surrogates in different behavioral states. The results showed that the scale exponents of all four types of interneurons were significantly higher than that of corresponding shuffled ISI sequences (Table 1, Figure 2). And for all four types of interneurons, the scale exponents of the ISI sequences during AE were significantly higher than that during SWS and more close to 1.

4 Discussion

To investigate the long-range correlation of the ISI sequence from these four types of interneurons, we employed the method named as DFA for the detection of long-range power-law correlations in the recorded ISI sequences. Consequently, we demonstrated that the spontaneous in vivo activity of interneuron in mouse hippocampus exhibits long-range correlations, rather than a stochastic point process. And we thus concluded that the long-range correlations of the ISI sequence indicated the presence of history effect or the memory in the firing pattern. Aside from the demonstration of the presence of long-range correlations in ISI sequences, we have further studied the relationship between the extent of long-range correlations and different behavioral states, SWS and AE.

References

1. Ashkenazy, Y., Lewkowicz, M., Levitan, J., Havlin, S., Saermark, K., Moelgaard, H.: Thomsen PEB Fractals (1999) 4(1):85-91
2. Bahar, S., Kantelhardt, J.W., Neiman, A., Rego, H.H.A., Russell, D.F., Wilkens, L., Bunde, A., Moss, F.: Long-Range Temporal Anti-Correlations in Paddlefish Eletroreceptors. Europhys. Lett. (2001) 56 (3):454-460
3. Bhattacharya, J., Edwards, J., Mamelak, A.N., Schuman, E.M.: Long-Range Temporal Correlations in the Spontaneous Spiking of Neurons in the Hippocampal-Amygdala complex of humans. Neuroscience (2005) 131:547-555
4. Burgess, N., Maguire, E.A., O'Keefe, J.: The Human Hippocampus and Spatial and Episodic Memory. Neuron (2002) 35:625-641
5. Chen, Z., Ivanov, P.C., Hu, K., Stanley, H.E.: Effect of Nonstationarities on Detrended Fluctuation Analysis. Physical Review E 65, (2002) 04117:1-15
6. Harris, K.D., Henze, D.A., Hirase, H., Leinekugel, X., Dragoi, G., Czurko, A., Buzsaki, G.: Spike Train Dynamics Predicts Theta-related Phase Precession in Hippocampal Pyramidal Cells. Nature (2002) 417:738-741

7. Hausdorff, J.M., Peng, C.K., Ladin, Z., Wei, J.Y., Goldberger, A.L.: Is Walking a Random Walk? Evidence for Long-Range Correlations in Stride Interval of Human gait. J Appl Physiol (1995) 78:349-358
8. Ivanov, P.C., Bunde, A., Amaral, L.A.N., Havlin, S., Fritsch-Yelle, J., Baevsky, R.M., Stanley, H.E.: Sleep-Wake Differences in Scaling Behavior of the Human Heartbeat: Analysis of Terrestrial and Long-Term Space Flight Data. Europhys. Lett. 48(5):594-600
9. Jackson, B.S.: Including Long-Range Dependence in Integrated-and-Fire Models of the High Interspike-Interval Variability of Cortical Neurons. Neural Computation (2004) 16:2125-2195
10. Lan, T.H., Xu, B.Q., Yuan, H.J., Lin, J.R.: Rescaled Range Analysis Applied to the Study Delayed Rectifier Potassium Channel Kinetics. Biophys Chem (2003) 106(1):67-74
11. Lin, L.N., Osan, R., Shoham, S., Jin, W.J., Zuo, W.Q., Tsien, J.Z.: Identification of Network-Level Coding Units for Real-Time Representation of Episodic Experiences in the Hippocampus. Proc. Natl. Acad. Sci. 102, (2005) No. 17:6125-6230
12. Lin, L.N., Chen, G.F., Xie, K., Zaia, K.A., Zhang, S., Tsien, J.Z.: Large-Scale Neural Ensemble Recording in the Brains of Freely Behaving Mice. J of Neurosc Methods (2006) 155:28-38
13. Liu, Y., Cizeau, P., Meyer, M., Peng, C.K., Stanley, H.E.: Correlations in Economic Time Series. Physica A (1997) 245:437-440
14. Liu, Y., Gopikrishnan, P., Cizeau, P., Meyer, M., Peng, C.K., Stanley, H.E.: Statistical Properties of the Volatility of Price Fluctuations. Phys Rev E (1999) 60(2):1390-1400
15. Montroll, E.W., Shlesinger, M.F.: Nonequilibrium Phenomena □. From Stochastics to Hydrodynamics, edited by Lebowitz JL and Montroll EW, North-Holland, Amsterdam:1-121 (1984)
16. Moruzzi, G., Magoun, H.W.: Brainstem Reticular Formation and Activation of the EEG. Electroencephal. Clin. Neurophysiol L (1949) 455-473
17. Peng, C.K., Buldyrev, S.V., Havlin, S., Simons, M., Stanley, H.E., Goldberger, A.L.: Mosaic Organization of DNA Nucleotides. Phys Rev E Stat Phys Plasmas Fluids Relat Interdiscip Topics 49 (1994) 1685-1689
18. Peng, C.K., Havlin, S., Stanley, H.E., Goldberger, A.L.: Quantification of Scaling Exponents and Crossover Phenomena in Nonstationary Heartbeat Time Series. (1995) Chaos 5: 82-87
19. Penzel, T., Kantelhardt, J.W., Grote, L., Peter, J.H., Bunde, A. Comparison of Detrended Fluctuation Analysis and Spectral Analysis for Heart Rate Variability in Sleep and Sleep Apnea. IEEE Trans Biomed Eng 50 (2003) 1143-1151