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FRACTAL DOUBLY STOCHASTIC BEHAVIOR OF NEURAL SPIKE TRAIN RECORDED FROM SUPRACHIASMATIC NUCLEUS OF RATS IN VITRO

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In order to identify the stochastic process underlying the firing activity of Suprachiasmatic nucleus (SCN) neurons in vitro, we use a number of statistical measures e.g., ISI histogram, periodogram, Hurst exponent, Fano factor and Allan factor. These statistics reveal the existence of 1/f-type power-law (fractal) behavior in long-duration region, while ISI histogram of each neuron is well-depicted by a gamma-r process. We demonstrate that the firing activity of SCN neurons can be well described by a gamma-r process whose firing rate modulated by fractal stochastic noise (i.e. a fractal doubly stochastic gamma point process).

(Oral presentation preferred)

Summary

The Suprachiasmatic nucleus (SCN) is known to generate circadian rhythm in mammals and govern endogenous and behavioral activities such as sleep-wake cycle, daily temperature change, etc. The firing rate of the spiking activity in SCN neurons periodically oscillates with a period of about 24 hours [1]. On a short time, however, interspike interval (ISI) firing patterns of most SCN neurons are found to be stochastic [2]. Only 10% of SCN neurons have a deterministic structure. The aim of this study is to identify the type of stochastic process underlying the firing activity of stochastic SCN neurons using several statistical measures.

EXTRACELLULAR RECORDINGS IN VITRO

Male Sprague-Dawley rats (40 – 100g) housed on a LD cycle for about two weeks were anesthetized with Nembutal (1ml/600g) before decapitation. The brain was removed to an ice-cold medium and a block of hypothalamus was cut to 130μm thick slices. Coronal tissue slices containing the SCN were transferred to a recording chamber in which the activity of single neurons was recorded extracellularly with glass micropipettes. The data recording was performed from 150 SCN neurons for 20-40min and interspike interval data were stored using pClamp software.

STOCHASTIC ANALYSIS

We employed five statistical measures: ISI histogram, periodogram, Allan factor, Fano factor and Hurst exponent, to quantify stochastic properties of SCN neurons. The *ISI histogram* exhibits the relative frequency of occurrence $p_\tau(\tau)$ of an interval of size τ. It is an estimate of the probability-density function of ISI magnitude. Although its construction yields loss of information about the order of spikes, it provides some clues about the underlying stochastic process of the ISI data. The *Periodogram* (PG) is an estimate of power spectral density (PSD) of a point process quantifying correlations between ISIs. The PG is estimated by dividing a data set into contiguous segments of equal length T (250 sec in this study) and further into M (4,096) equal bins within each segment. The number of events within each bin is counted and transformed into a PSD across frequency domain (0.004~8.19 Hertz) using a Fourier-transform method. It is well known that Fractal signals show a power-law behavior near the zero frequency, while white noise exhibits a flat PSD. The *Fano factor* (FF) is defined as the ratio of the variance of the number of events in an interval to the mean of this number, which is a function of the counting time T. It displays the degree of event clustering or anticlustering in a point process relative to homogeneous Poisson process, for which $F(\mathrm{T})=1$ for all T. For a fractal stochastic process, the FF assumes the power-law form T^{α} ($0<\alpha\leq 1$) for large T, where α is defined as the fractal exponent (scaling exponent) of the point process. The FF gives a suitable measure only for fractal exponents in the range of $0<\alpha<1$. When we assumes that the fractal exponent is greater than unity, we use the *Allan factor* (AF), which is the ratio of the event-number Allan variance to twice the mean:

$$A(T) = \frac{<[N_{i+1}(T) - N_i(T)]^2>}{2 < N_i(T) >} \tag{1}$$

It also shows long-range correlations embedded in a data set. As another measure for self-similarity, the *Hurst exponent* (H) is estimated from a power of R(k), which defined as a function of number of events in a counting block. The difference between maximum and minimum values of the accumulative sum of ISI within each block is divided by the standard deviation of the interval size. R(k) varies its power depending on the correlation property of each system; H>0.5 for positively correlated process, H<0.5 for negative one, and H=0.5 for random process.

Surrogate data method was used to help detect correlation within a dataset. Surrogate data have the same ISI histogram as the raw time series but are randomly shuffled to destroy any correlation that may be present. Significant difference of a measure of correlation between the raw data and its surrogate data indicates the presence of correlation in the raw data.

RESULTS AND DISCUSSION

ISI histograms of the ISI data from SCN neurons were found to be normally distributed (105/150) or skewed (45/150). We found that the ISI histograms of most datasets had a close similarity with those obtained from the gamma-r process (GPR), which had a probability density function as follows:

$$P_\tau(\tau) = \frac{(\mu r)^r \tau^{r-1} \exp(-\mu r \tau)}{\Gamma(r)} \tag{2}$$

The r and μ were estimated using $r_{gamma} = \frac{1}{CV_{\exp}{}^2}$ and $\mu_{gamma} = \mu_{\exp}$, where CV denotes coefficient of variation of the ISI data. The parameter ranges with which the datasets were well-fitted by the GPR were $3 < r < 25$ and $2 < \mu < 5$.

However, we found from the estimation of PG, Hurst exponent, FF and AF that the ISI data of SCN neurons exhibit 1/f-type power-law (fractal) behavior, which cannot be explained by the conventional GRP (Fig. 1). These measures commonly exhibited the same power-law values and fractal behavior above the time scale 10-50 sec. The randomly shuffled surrogate data were also analyzed and compared using the same methods. The observed high fractal exponents of the raw data dropped around zero, supporting our previous finding of the presence of long-range correlations (fractal behavior) in the ISI data of SCN neurons (Table 1).

From physiological point of view, the GRP is not realistic in that it generates a point process, relying on time-independent homogeneous firing rate μ. Yet, it is often observed that real neural spikes alternate its states irregularly between intermittent bursting and relatively less-active periods. Thus, the assumption of time-independent firing rate is far from real situations. Our results also support that the ISI data of SCN neurons have firing rates with long-duration correlation, even though their ISI histograms are very similar to those of the GRP that has no correlation.

Teich et al [3] had previously shown that a gamma-r process whose firing rate is modulated by fractal stochastic noise well described the firing patterns of the visual nervous system of the cat. From this motivation we tried to implant the long-range fractal fluctuation into the firing rate of the GRP and this rate fluctuation was constructed with sum of K alternating fractal processes with height h. To generate each constituent fractal point process, we formulated an ISI probability density function obeying a power-law behavior:

$$P(T) = cT^{-(1+\alpha)} \qquad \text{for } A< T <B \qquad (3)$$

where α is the fractal exponent, c is a normalization factor, and A and B decide the range of correlation. With these parameters (α, A, B, K, h) determined by the analysis of real ISI data of the SCN neurons, we demonstrated that a fractal binomial-noise-driven doubly stochastic gamma point process exhibited the stochastic and fractal behaviors similar to those of the ISI data of SCN neurons as illustrated in Fig. 1. This long-duration correlation might be associated with a circadian rhythm oscillating with a period of 24 hours in SCN neurons.

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TABLE 1.

	Raw data	The surrogate data	P
Periodogram Exponent	0.759 ±0.313	0.031±0.258	<0.01
Hurst Exponent	0.800±0.108	0.524±0.008	<0.01
Fano Exponent	0.635±0.225	0.082±0.178	<0.01
Allan Exponent	0.816±0.367	0.060±0.242	<0.01

Table 1. The mean values of periodogram exponent, Hurst exponent, Fano exponent, and Allan exponent with their standard deviations of raw ISI data and their surrogate data.

FIGURE LEGEND

Fig. 1 The log-log plots of (a) ISI histograms, (b) periodograms, (c) Hurst exponents, (d) Fano factors (e) Allan factors of an original data obtained from a typical SCN neuron, its surrogate and the simulated data generated by a gamma-r process whose firing rate modulated by fractal stochastic noise. The simulated data have very similar values of all measures to those of the original data.