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Highly irregular spike trains generated from weakly fluctuated inputs

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Abstract—The irregular firing of a cortical neuron is believed to emerge from a highly fluctuating drive generated by a balance between excitatory and inhibitory synaptic inputs. A previous study reported a strange response of the Hodgkin-Huxley neuron to the fluctuated inputs where an irregularity of spike trains is inversely proportional to an input irregularity. In the current study, we investigated the origin of this strange response using the map-based models. The map-based model reproduced the strange response in the dynamics Subcritical Hopf bifurcations. In the this case, the map-based model shows a bistability of resting state and repetitive firing state, indicating that the bistability is the origin of the strange Input-Output relationship. Our results show that the irregular firing can be emerged even from a weakly fluctuating drive under the existence of the bistability. Spike correlations in cortex are considerably smaller than expected based on the amount of shared presynaptic input. Such decorrelation of the spike trains are important substrate for information processing. The fact that the weakly fluctuating drive is capable to induce highly irregular firing would contribute to an efficient neural processing.

1. Introduction

Cortical neurons generate irregular spike trains including highly variable intervals [28, 11, 25]. The irregular spiking has received much attention because it offers functionally important roles in the neural information processing [7, 8, 10, 14]. The origin of the irregularity is intrinsic noises, e.g. synaptic unreliability [2] and ion-channel noise [34], and a highly fluctuating drive generated by a balance between excitatory and inhibitory synaptic inputs to the neurons [22, 31, 33, 1, 27, 17]. The response of the neuron has been classically characterized by its frequency-current relationship [15, 18], but knowing the frequency-current relationship is not sufficient to understand neuronal responses to the fluctuated inputs. Several studies have shown the responses of the neurons to the fluctuated inputs and reported reactive differences among the neuron models [3, 12, 9, 26, 21, 4, 5, 16, 17].

Regarding the response to the fluctuated inputs, an interesting phenomenon has been reported [20]:

> The variability of output spike trains of the Hodgkin-Huxley (HH) neuron model decreases as the input variance increases.

This inverse relationship between input and output variances is seemingly counterintuitive. Here we call it the "strange response." The schematic representation of the strange response is shown in Fig.1. The authors concluded their report by providing a possible underlying mechanism suggesting that the strange response of the HH may originate from the subthreshold oscillation of the membrane potential. In fact, the input-output (I-O) relationship for a leaky integrate-and-fire neuron model (LIF), which does not possess the subthreshold oscillation, is proportional (Fig.1B). A similar phenomenon was observed in also an experimental study [30].

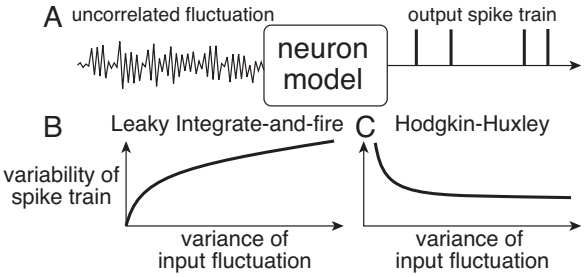

Figure 1: Schematic representation of the strange response of the Hodgkin-Huxley model [20]. (A) A neuron model receives the uncorrelated fluctuation mimicing balancing synaptic inputs and generates the output spike train. (B) The variability of the spike train is shown as a function of the variance of the input fluctuation. For the leaky integrate-and-fire model, the variability of the spike train increases as the input variance increases. (C) For the Hodgkin-Huxley model, the variability of the spike train decreases as the input variance increases.

Although their finding is important and fundamental, further analysis is required, because the comparison was performed using models whose dynamics are largely different from each other. Numerous differences exist between the HH and LIF, including the complexity of dynamics, the number of variables, and the number of parameters. Moreover, the HH is too complicated to find the origin of the strange response. Therefore, we cannot acknowledge that, as the authors concluded, the subthreshold oscillation is the origin of the strange response. Other components may

cause the strange response. The purpose of this study was to reveal the origin of the strange response. We show the map-based model possessing the bistability reproduced the strange response, while the model without bistability did not. This indicates that the irregular firing can be emerged even from a weakly fluctuating drive under the existence of the bistability.

2. Methods

2.1. The Map-based models

2.1.1. The bistable Rulkov model

The discrete-time dynamical systems as valid phenomenological models of neurons are known as the map-based models. The Rulkov model is the map-based model replicating spiking-bursting neural activity [19]. The bifurcation of the fixed point on this model is the subcritical Andronov-Hopf [23]. This model is therefore capable to possess the bistability [13]. We will refer to this model as the bistable Rulkov model for clarity. The bistable Rulkov model is described as follows:

$$\begin{cases} x_{n+1} = F_{\mathrm{sub}}(x_n, y_n), & (1) \\ y_{n+1} = y_n + (-x_n + s + I_n)/\tau. & (2) \end{cases}$$

x_n is the fast and y_n is the slow dynamical variable. Slow time evolution of y_n is due to a large value of the parameter τ; $\tau = 100$ in this study. I_n describes an external input applied to the model (section 2.2). s is the control parameter to select the regime of individual behavior. s was set to $1 - \sqrt{\frac{\alpha}{1-1/\tau}}$ to make bifurcation occur at $I_n = 0$. In its original formulation [19], the Rulkov model uses $s' = s + 1$. $F_{\mathrm{sub}}(x, y)$ is a function that represents the subthreshold behavior of the membrane potential, and also includes a threshold and reset mechanism to produce spikes:

$$F_{\mathrm{sub}}(x, y) = \begin{cases} \dfrac{\alpha}{(1-x)} + y, & \text{if } x \le 0, \\ \alpha + y, & \text{if } 0 < x < \alpha + y, \\ -1, & \text{if } x \ge \alpha + y. \end{cases}$$

where $\alpha = 4$ in this study.

2.1.2. The supercritical Rulkov model

As the map-based model which does not exhibit the bistability, the model proposed by Shilnikov and Rulkov was employed [24]. The bifurcation of the fixed point on this model is the supercritical Andronov-Hopf. This model exhibit the small amplitude subthreshold oscillation. We will refer to this model as the supercritical Rulkov model. This model is described as follows:

$$\begin{cases} x_{n+1} = F_{\mathrm{sup}}(x_n, y_n), & (3) \\ y_{n+1} = y_n + (-x_n + s + I_n)/\tau, & (4) \end{cases}$$

where

$$F_{\mathrm{sup}}(x, y) = \begin{cases} \dfrac{-\alpha^2}{4} - \alpha + y, & \text{if } x < -1 - \alpha/2, \\ \alpha x + (x+1)^2 + y, & \text{if } -1 - \alpha/2 \le x \le 0, \\ 1 + y, & \text{if } 0 < x < 1 + y, \\ -1, & \text{if } x \ge 1 + y. \end{cases}$$

$\tau = 100$, and $\alpha = 1$ in this study. s was set to $-\{1 + 1/\tau + \alpha\}/2$ to make bifurcation occur at $I_n = 0$. I_n describes an external input applied to the model (section 2.2).

2.2. Input fluctuation

The inward current to a cell body, I_n in Eqs.(2) and (4), is described by the form

$$I_n = \mu + \sigma\xi_n,$$

where ξ_n is white Gaussian noise. The parameters μ and σ control the mean and fluctuation of inputs, respectively. This fluctuated input is based on the following assumption: a cortical neuron receives thousands of synaptic contacts; if incoming inputs through synapses were assumed to be independent, the sum of a large number of independent excitatory and inhibitory inputs can be approximated to an uncorrelated fluctuation [32].

2.3. ISI statistics

Output spike trains were evaluated based on two statistics of ISIs: the mean ISI ($\overline{T}$) and the coefficient of variation (Cv), defined respectively as

$$\overline{T} = \frac{1}{n}\sum_{i=1}^{n} T_i,$$

$$\mathrm{Cv} = \sqrt{\overline{(T_i - \overline{T})^2}}/\overline{T},$$

where T_i represents an ISI. Cv evaluates irregularity of the spike trains. If the spike train is completely regular, that is, all ISIs are constant, Cv corresponds to 0. If the spike train is completely random, indicating a Poisson process, Cv corresponds to 1. Because Cv is a dimensionless quantity, we can directly compare Cv for the various models. In contrast, $\overline{T}$ is not a dimensionless value. We therefore use the ratio of $\overline{T}$ to membrane time constant, $\overline{T}/\tau$, for comparison. We estimated ($\overline{T}/\tau$, Cv) from a finite ISI sequence consisting of $10,000$ ISIs obtained by a numerical simulation.

3. Results

3.1. The Map-based models

3.1.1. The bistable Rulkov model reproduces the strange response

We hypothesized that the strange response depends on the bistability. The bistable Rulkov model shows the bistability with appropriate parameters (section 2.1.1)[19]. The

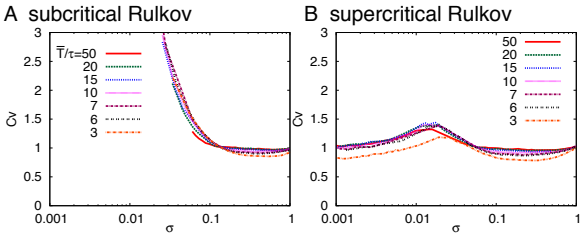

Figure 2: Relationship between input variance σ and output variance Cv

ISI statistics of the bistable Rulkov model are depicted in Fig.2A. The bistable Rulkov model reproduces the strange response: regardless of the value of $\overline{T}/\tau$, Cv was larger than 2 for $\sigma < 0.04$; as σ increased, Cv declined and converged to 1.

3.1.2. The supercritical Rulkov model does not reproduce the strange response

To investigate if the map-based model without bistability fails to reproduce the strange response, the ISI statistics of the supercritical Rulkov model were calculated (section 2.1.2, Fig.2B). The supercritical Rulkov model did not reproduce the strange response: regardless of the value of $\overline{T}/\tau$, Cv was almost constant for any value of σ; Cv slightly increased for σ around 0.02.

3.2. Spike trains with large Cv values

To investigate how the bistability produces the highly irregular spike trains, spike trains of the bistable and supercritical Rulkov model are depicted in Fig.3. The spike train with large Cv value (Cv = 2) contained burst-like spikes, i.e., successive occurrence of spikes (Fig.3A, enlargement). $\overline{T}$ of the spike train is small due to the burst-like spikes, while the variance of ISIs are relatively large compared with $\overline{T}$ due to the inter-burst interval. This results in the large Cv value. As the input variance increases, the number of spikes included in single burst-like spikes gradually decreases, the spike trains settled eventually to the Poisson spike train (Fig.3B, Cv= 1). On the supercritical Rulkov model, the burst-like spike trains were not generated. Only small clusters of spikes were included in the spike trains of which Cv is larger than 1 (Fig.3C, Cv= 1.4). As the input variance decreases, the spikes were more likely to occur at the top of subthreshold oscillation (Fig.3D, enlargement). The probability of the spike generation was stochastic due to the input fluctuation. This spike train corresponds to the discrete Poisson process, whose Cv value is 1.

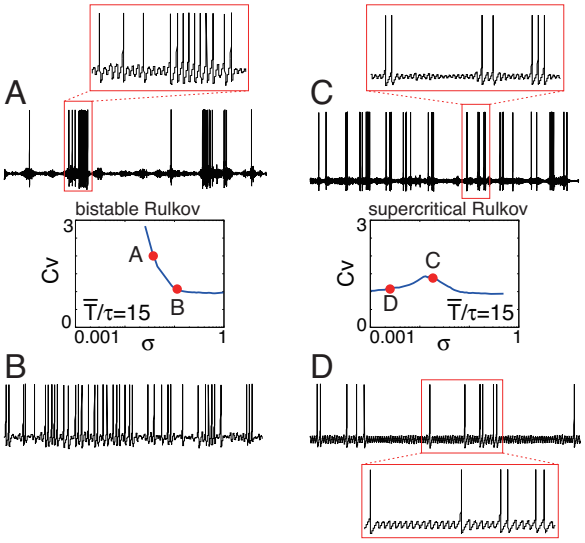

Figure 3: Example spike trains of the map-based models of which $\overline{T}/\tau = 15$. (A) The spike train of the bistable Rulkov model of which Cv = 2. Enlargement of one of the burst-like spikes is depicted in the upper red box. (B) The spike train of the bistable Rulkov model of which Cv = 1. (C) The spike train of the supercritical Rulkov model of which Cv = 1.4. Three of the clustering spikes are enlarged in the upper red box. (D) The spike train of the supercritical Rulkov model of which Cv = 1. Enlargement in the lower red box shows the spikes being phase-locked to the top of the subthreshold oscillation.

4. Discussion

We demonstrated that the map-based model with bistability reproduced the strange I-O relationships. This indicates that the origin of the strange I-O relationship is the bistability of the resting state and repetitive firing state. Our results show that the bistability enables the neuronal spike trains irregular even with the small fluctuation of the inputs. Recent studies demonstrate that spike correlations in recurrent neural networks are considerably smaller than expected based on the amount of shared presynaptic input, and decorrelation of the spike trains are important substrate for information processing. The fact that the weakly fluctuating drive is capable to induce highly irregular firing would contribute to an efficient neural processing.

The bistability of resting state and repetitive firing state have been observed in biological neurons in the entorhinal cortex of the brain [6]. In these neurons, activity-dependent changes of a Ca^{2+}-sensitive cationic current plays a critical role. The entorhinal cortex is the main interface between the hippocampus and cortex, and is known for the substrate of the conscious memory. The strange response may play some role in the memory formation in the entorhinal cortex.

In this study, the bistability of resting states and repetitive firing state was realized using an intrinsic bifurcation mechanism of the HR. On the other hand, the bistability can be realized based on the Up/Down states of the membrane potential [29]. The Up/Down state is two distinct levels of membrane potentials of neurons. In cortical neurons, the membrane potential stays around -65 mV in Down states and -45 mV in Up states. Firing probability in the

Up state is much higher than the Down state. The cortical neurons often exhibits spontaneous transitions between Up and Down states. The Up/Down state can be considered the bistability of attractors. The strange response due to the Up/Down states may be observed in the whole neocortex.

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