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Effects of shift in the excitatory-inhibitory balance on firing statistics

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Abstract—It has been shown *in vivo* that the changes in the average excitatory synaptic conductance are balanced with those of inhibitory ones in cortical and spinal cord neurons. Additionally, time-constant firing irregularity is achieved when the ratio of the excitatory and inhibitory activities is constant. In this paper, we show that such ratio may fluctuate with time under the condition of neural balances. Time-changeable neural balance enables neuron to assign wide range of statistical values, and may have a possible relationship with robust neural computation in the cortex.

1. Introduction

Firing patterns of cortical neurons *in vivo* are very irregular [1, 2]. Therefore, probabilistic models are necessary to describe such patterns [3, 4]. Baker and Lemon showed that the firing patterns recorded from motor areas can be explained using a continuous-time rate-modulated gamma process [5]. The probability density function of gamma process is depicted as

$$p(T) = \frac{\lambda^{\kappa} T^{\kappa-1} \exp(-\lambda T)}{\Gamma(\kappa)}, \qquad (1)$$

where T denotes an interspike interval, λ denotes a mean firing rate, κ denotes a shape parameter, and $\Gamma(\kappa) = \int_0^\infty T^{\kappa-1}\exp(-T)dT$ is the gamma function. When $\kappa = 1$, gamma process corresponds to Poisson process, and spike train looks irregular. When κ is large, gamma process is approximated by a normal distribution, and when $\kappa \to \infty$, gamma process corresponds to perfectly regular firing. Thus, κ is a shape parameter related to regularity.

Reproducibility of statistics of real spike train variability is a key in examining the model plausibility. There are a number of statistics quantifying the variability of spike trains, and the coefficient of variation C_V is one of the most common measures which has been widely employed by many researchers [1, 6, 7]. C_V is defined as

$$C_V = \frac{1}{\overline{T}} \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (T_i - \overline{T})^2}, \qquad (2)$$

where T_i represents the ith ISI, and n the number of ISIs. C_V is a dimensionless index which indicates the spiking irregularity and takes a value 1 for infinitely long purely Poisson series of events, in which event intervals are independently exponentially distributed, and a value 0 for a perfectly periodic sequences.

C_V depends on κ in the case of constant firing rate. Baker and Lemon assumed κ to be unique to individual neurons and constant over time [5]. The assumption that κ is unique to individual neurons is also supported by other studies [8, 9]. Unique κ makes the rate of C_V constant in the case of homogeneous gamma process.

However, *in vivo*, C_V distributes widely (particularly 0.8-1.8) even though they are recorded from same neuron during same experimental condition in several studies [7, 9].

May this seemingly contradictory phenomenon be explained by varying the mean rate λ which makes the statistics C_V variable?

There are three mechanisms for making wide distribution of C_V *in vivo*: rate fluctuation, irregularity fluctuation, and statistical fluctuation.

First, rate fluctuation is a fluctuation of instantaneous firing rates during the experiment, which makes C_V distribution wide. The value of C_V is measured within a time window with a certain window size. If the time scale of the rate change is longer than the window size, C_V can exhibit various values depending on the windows.

Next, irregularity fluctuation is a fluctuation of irregularity factor of a spike generator during the experiment, which also makes C_V distribution wide. It is known that the irregularity measure varies with time during the experimental task [10]. If the irregularity is fluctuating during the experiment, the statistical values may take various values depending on the windows.

Finally, statistical fluctuation is a fluctuation that occur due to finite window size effect, and may make C_V distribution wide.

In our former study [11], we have shown that the assumption of κ to be unique to individual neurons and constant over time is too strict in gamma spike generator [12]. In this paper, we confirm this result by conductance-based neuron model, and answer to the question whether the unique κ on gamma process can reproduce such wide distribution which is often observed in *in vivo* spike data *only* by changing mean firing rates. In addition, we focus on the shift in the excitatory-inhibitory balance, which enables neuron to assign wide range of statistical values, and may have a possible relationship with robust neural computation in the cortex.

2. Numerical Analysis

2.1. Constant-balance model

Constant κ is achieved when the ratio of the excitatory and inhibitory activities is constant [13]. We show that the neuron model with such assumption cannot reproduce wide C_V distributions. We consider the single compartment model by Destexhe et al. [14], which reproduced the membrane potential of neocortical pyramidal neurons subject to an intense synaptic input.

$$\begin{aligned} C_m \frac{dV}{dt} &= -g_L(V-E_L) - I_{N_a} - I_{K_d} - I_M - \frac{1}{a} I_{syn} + I_{ext}, \\ I_{N_a} &= \bar{g}_{N_a} m^3 h (V - E_{N_a}), \\ I_{K_d} &= \bar{g}_{K_d} n^4 (V - E_K), \\ I_M &= \bar{g}_M p (V - E_K), \end{aligned} \qquad (3)$$

where C_m is the specific membrane capacitance, g_L is the leak conductance density, and E_L is the leak reversal potential, I_{N_a} is the voltage-dependent sodium current and I_{K_d} is the delayed-rectifier potassium current responsible for action potentials. I_M is a non-inactivating potassium current responsible for spike frequency adaptation, I_{ext} is an external input, a is the total membrane area and m, h, n, p are gating variables obey to first-order kinetic equations[14].

To generate realistic synaptic activity, Destexhe et al. introduced the point-conductance model. The total synaptic current, I_{syn}, was decomposed into a sum of two independent conductances:

$$I_{syn} = g_e(t)(V - E_e) + g_i(t)(V - E_i), \qquad (4)$$

where $g_e(t)$ and $g_i(t)$ are time-dependent excitatory and inhibitory conductances, respectively; E_e and E_i are their respective reversal potentials and were identical to that of the detailed biophysical model. The conductances $g_e(t)$ and $g_i(t)$ were described by a one-variable stochastic process similar to the Ornstein-Uhlenbeck process:

$$\begin{aligned} \tau_e \frac{dg_e(t)}{dt} &= -(g_e(t) - g_{e0}) + \sigma_e \eta_e(t), \\ \tau_i \frac{dg_i(t)}{dt} &= -(g_i(t) - g_{i0}) + \sigma_i \eta_i(t), \end{aligned} \qquad (5)$$

where g_{e0} and g_{i0} are average conductances, τ_e and τ_i are time constants, $\eta_e(t)$ and $\eta_i(t)$ are normalized Gaussian white noises with zero means.

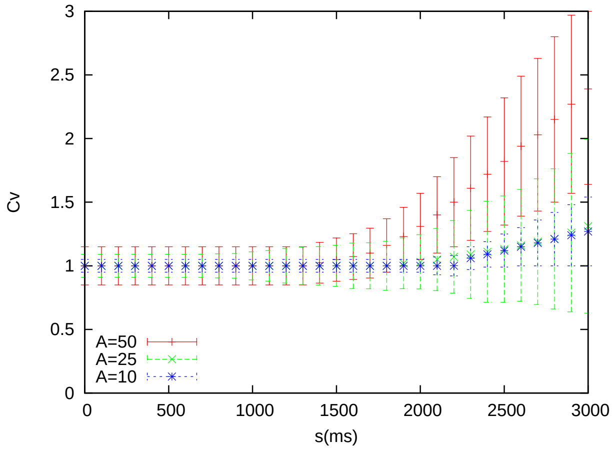

Figure 1: C_V values obtained from conductance-based model with sinusoidally varying rate. Hundred C_V rates are obtained from equation (2), and their means and variances are presented as plots and error bars. Blue, green and red plots correspond to the C_V with $A = 10$, $A = 25$ and $A = 50$, respectively. The parameters are set as $g_{e0} = 0.02$, $g_{i0} = 0.08$, $\Delta = 1000$(ms), respectively. Other parameters are same as in [14]. When the amplitude A is large (red), time scale is about $s \sim 2200$ to reproduce the C_V values of 0.8–1.8 which is obtained in several former studies [7, 9].

The excitatory and inhibitory conductances fluctuate with time, but in the former study on conductance fluctuation, noise is regarded to be weak [14]. Therefore, although the balance between excitatory and inhibitory conductance may subtly fluctuate with time, it is almost constant. We call this model "constant-balance model". In order to fluctuate the firing rate, we vary the external input I_{ext} sinusoidally with period s and its amplitude A: $I_{ext}(t) = A \sin 2\pi t/s$. We set the bin size Δ, and obtained the statistical values C_V from equation (2). The result is shown in Fig. 1.

In Fig. 1, when $A = 10$ (blue), the time scale s of over 2800 millisecond is needed to reproduce the range of C_V from the data *in vivo*, and $s \sim 2200$ for $A = 50$ (red). Such long time scales can be seen in delta wave which is a high amplitude brain wave recorded with an EEG and is usually associated with slow-wave sleep [15]. However, delta wave activity during the waking state is not common phenomenon for awake animals [15] and it is impractical to assume the presence of such long time scale dynamics in every experimental data.

From the observation of Fig. 1, if we assume the sinusoidally rate modulated external input, i.e. rate-modulated constant-balance model, the dynamics which has fairly long time scale is needed to reproduce the wide C_V distribution, which is an implausible assumption for the real experimental condition. Therefore, constant-balance model cannot reproduce wide C_V distributions, which is consistent with our former study on gamma spike generator [11].

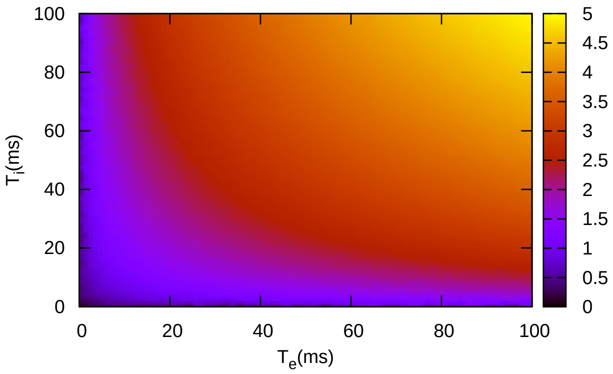

Figure 2: Maximum C_V values obtained from varable-balance model are represented with colors. Hundred C_V rates are obtained and their means are plotted for different time scale T_e and T_i respectively. The parameters are set as $g_{e0} = 0.02$, $g_{i0} = 0.08$, $\Delta = 1000$(ms), $A_e = 10$, $A_i = 10$ respectively. Other parameters are same as in [14]. In order to reproduce the maximum C_V values over 1.8 which is obtained in several former studies [7, 9], the variable-balance model can reproduce with a short time scale of T_e and T_i representing red and yellow area, which is much shorter compared with that of constant-balance model.

2.2. Variable-balance model

Next, we consider the variable-balance model, in which the firing rate and the irregularity factor κ are both modulated sinusoidally with time. In conductance-based model, κ on gamma process corresponds to varying the balance between excitatory and inhibitory conductance. We change the amplitude of g_{e0} and g_{i0} periodically as follows:

$$\begin{aligned} g_{e0}(t) &= g_{e0} + A_e \sin(2\pi t/T_e), \\ g_{i0}(t) &= g_{i0} + A_i \sin(2\pi t/T_i). \end{aligned} \tag{6}$$

Here, T_e and T_i are the periods of the sinusoidal modulation. We only assume conductance for modulation, and do not apply external inputs.

The result is in Fig. 2. As in Fig. 2, we no longer need long time scale for T_e and T_i. For example, T_e = 30(millisecond) and T_i = 30(millisecond) can reproduce the maximum C_V rate from the data *in vivo*. Such time scale can be seen in beta waves or gamma waves, which are widely observed oscillations in the frequency range of 13 to 30 Hz and 30 to 70 Hz respectively, arising from synchronous and coherent electrical activity [16, 17]. It is plausible to assume the presence of such time scale dynamics in every experimental data. Reproducing the firing statistics of the experimental data is realized by modulating the balance of excitatory and inhibitory conductances by a realistic neuron model in a plausible way.

3. Discussion

We compared the constant-balance model and variable-balance model from the viewpoint of reproducibility of wide C_V distribution. We conclude that the assumption of the constant balance between excitatory and inhibitory conductances is too strict as in the section 2.1. Instead, we proposed the variable-balance model in which the excitatory/inhibitory balance modulate with time, and in fact it has broaden the range of the statistics C_V with short time scale.

It has been shown *in vivo* that the changes in the average excitatory synaptic conductance are balanced with those of inhibitory ones in cortical and spinal cord neurons and make irregular firing [18].

According to our result, such ratio may fluctuate with time under the condition of neural balances. Several experimental evidences for such time-changeable balances can be found in recent physiological studies [19, 20]. In the modeling studies, it has shown that the leaky integrate and fire neuron model with conductance-based synapses does not require a strict balance between excitation and inhibition to achieve high irregularity of firing [21]. Time-changeable neural balance enables neuron to assign wide range of statistical values, and may have a possible relationship to robust neural computation in the cortex.

There exist several evidences that neuronal activities are changeable with time. For instance, in the case of rhythmic firing of neurons, we have to assume that the intensity of excitatory and inhibitory neurons are the same, if we assume that the balance between excitatory and inhibitory is constant. Additionally, in the case of receiving synchronous synaptic inputs, we have to assume that the intensity of excitatory and inhibitory neurons are the same as in the above mentioned case. It is a matter of course that assuming variable-balance enables neurons robust computation.

Variable-balance must be generated, at least partly, from local interconnected networks of excitatory and inhibitory neurons, but the details of the local network structure are largely unknown. It is a future problem to explore the origin of such balance as well as evaluating the effect of such mechanisms for improving neural information processing.

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