Fast Response to Small Signals with Noise in Neurons

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Abstract. Neurons in the brain receive synaptic inputs delivered as random trains. Mathematical theory was developed to relate the rate of threshold crossings with statistics of membrane fluctuations evoked by random point input process. Integrate-and-fire neuronal model was used to check validity of theoretical results. Mathematical theory approximated firing rate for low level of activity and showed that dependence of threshold crossings on mean rate of membrane potential change brings about very fast response to small signals.

Keywords: neuron, stochastic process, firing rate.

1 Introduction

Communication between neurons takes place via stochastic spike trains. Since synaptic transmission itself is random [1], the processing in neuronal systems unavoidably becomes stochastic. Indeed, intracellular recordings *in vivo* have revealed strong stochastic membrane potential fluctuations [2, 3]. To understand the principles of neuronal information processing it is necessary to describe the influence which stochastic signals have on the statistical properties of membrane potential and firing.

This problem was introduced several decades ago, when simplified integrate-and-fire models of neurons receiving stochastic inputs were analyzed [4].

Later work steadily broadened the scope of analysis by introducing leaky integrate-and-fire models [5], by applying techniques for calculation of firing statistics [6], and recently by analyzing nonstationary inputs [7] and correlated inputs [8]. The question of how the signal detection depends on the properties of noise was intensively studied in a range of natural and artificial systems [9, 10] including neurons [11]. In this work, we investigated how the detection of single postsynaptic potential is influenced by the strength of noise in the model of integrate-and-fire neurons. It was shown that a population of similar neurons can response very fast to small signals imbedded in noise.

2 Model Definition and Mathematical Description

We used a system of simplified one-compartment model neurons in which spike generation occurs when the fluctuating membrane potential crosses a threshold level. Although simple, threshold crossings in such a leaky integrate-and-fire system can be made similar to the firing of more realistic neuronal models with Hodgkin-Huxley spike generating mechanism [12]. Our simplified system was governed by equations that described the dynamics of neuronal membrane potential, V, (as deviation from the resting potential):

$$dV/dt = -V/\tau_m + \eta(t)/C. \tag{1}$$

Here, τ_m is the membrane time constant (ms), C is the neuron's capacitance (μF), and input $\eta(t) = \sum_j a_i s(t - t_j)$. The function $s(t - t_j)$ describes the time course of unitary synaptic current as an exponential, $\exp\left[-(t-t_j)/\tau_s\right]$, where τ_s is the synaptic time constant; $s(t - t_j)$ is equal to 0 if $t < t_j$. The random amplitude of synaptic current is a, and t_j is the arrival time of the synaptic event, j.

The probability to cross a given threshold level, V_{th}, from below with some rate of potential change, $V' \equiv dV/dt$, is equal to $w_1(V', V_{th})\delta V \delta V'$, where w_1 is the joint probability density for membrane potential and its rate of change. After noticing that $\delta V = V'\delta t$, we can obtain an expression for the rate of

threshold crossings from below [13, 14]:

$$f_1 = \int_0^\infty w_1(V', V_{th}) V' dV'.$$

Let us consider a case when the neuron receives a single synaptic input with amplitude A, "signal", embedded in stationary random input. The rate of threshold crossings, f_1, also describes a response of a pool of similar neurons receiving single synaptic input as a shared input. Deterministic "signal" changes the threshold for action potential and mean rate of membrane potential change, but leaves other statistics of the membrane potential unchanged. For stationary stochastic input, the membrane potential and its rate of change are independent variables; thus, w_1 is equal to a product of two probability densities. When the total synaptic input rate is high, these probability densities may be approximated by Gaussian function [8]. After taking the integral the expression for the rate of threshold crossings becomes:

$$\begin{aligned}
f_1 = &\frac{1}{\sqrt{2\pi}\sigma_V} \exp\left[-\frac{(V_{th} - r)^2}{2\sigma_V^2} \right] \\
&\times \frac{1}{\sqrt{2\pi}\sigma_{V'}} \left[\sigma_{V'}^2 \exp\left(-\frac{r'^2}{2\sigma_{V'}^2} \right) + r'\sigma_{V'}\sqrt{\frac{\pi}{2}} \mathrm{erfc}\left(-\frac{r'}{\sqrt{2}\sigma_{V'}} \right) \right].
\end{aligned} \tag{2}$$

In the latter equation σ_V and $\sigma_{V'}$ are standard deviations for membrane potential and the rate of change accordingly, r is the postsynaptic potential in response to "signal" synaptic input, and erfc is the complementary error function. Postsynaptic potential, r, can be calculated by integrating equation (1). For synaptic current s the postsynaptic potential:

$$\nu = \tau_s \tau_m \left[\exp(-\{t - t_0\}\tau_s) - \exp(-\{t - t_0\}/\tau_m) \right] / \left[C(t_s - t_m) \right],$$

and $r = A\nu$.

The standard deviation for V and V' can be obtained from auto-correlation function. The membrane potential correlation function, $k(t_1, t_2)$, was calculated previously [8] by comparing characteristic functionals [14, 15] derived for membrane potential as a continuous stochastic process and as a random

point process generated by input trains [8]:

$$
\begin{aligned}
k(t_1, t_2) = &(a_s^2 + \sigma_s^2) \int_0^T g_1(t)\nu(t_1 - t)\nu(t_2 - t)dt \\
&+ a_s^2 \int_0^T \int_0^T g_2(t', t'')\nu(t_1 - t')\nu(t_2 - t'')dt'dt'',
\end{aligned}
\tag{3}
$$

where a_s and σ_s are mean and standard deviation for synaptic amplitudes with normal distribution, g_1 is the total input rate, and g_2 is correlation function for the input trains. In case when the input trains are stationary and uncorrelated [8]:

$$
k(\tau) = \sigma_V^2 \left[\tau_s \exp\left(- |\tau|/\tau_s \right) - \tau_m \exp\left(- |\tau|/\tau_m \right) \right],
$$

where $\tau = t_1 - t_2$ and

$$
\sigma_V = \tau_m \tau_s \left[(a_s^2 + \sigma_s^2)g_1/(2\{\tau_m + \tau_s\}) \right]^{1/2} /C.
$$

Consequently, the standard deviation for V': $\sigma_{V'} = \sigma_V/(\tau_m \tau_s)^{1/2}$.

Simulations were done in order to check applicability of the analytical results. Neuronal model had leak conductance equal to $2nS$, membrane time constant was 5 ms, and synaptic time constant was 3 ms. The total synaptic input rate was 10 kHz. The distribution for synaptic amplitudes was normal and had mean equal to 0; thus, mean membrane potential was the same as at rest. The standard deviation value was changed to get different noise strength. The "signal" synaptic input with the amplitude $A = 0.03586$ nA was injected with the period of 50 ms. Equation (1) was solved numerically using the implicit trapezoidal scheme [16] with a time step of 0.05 ms. Synaptic input was simulated by generating continuous stochastic process with Gaussian probability density and exponentially decaying correlation function [17]. The correlation function was calculated by using equation (3) with s substituted for ν according to the theoretical description of the process for the net synaptic input [8]. In these simulations, spike event was registered when the membrane potential crossed the threshold level equal to 15 mV. The crossings also evoked

hyperpolarizing current by activating conductance with the reversal potential of -30 mV and with decay time constant of 5 ms. The conductance amplitude was equal to the leak conductance. Runs of 5000 s were simulated to collect statistics for firing rate.

3 Influence of Strength of Noise on the Response

To investigate how the integration of small signals in neurons depends on the strength of noise we calculated the rate of threshold level crossings. Small "signal" synaptic input causing postsynaptic response with the amplitude of 5 mV was injected (Fig. 1, lower panel). The strength of noise was changed by choosing different values for the standard deviation of synaptic amplitude.
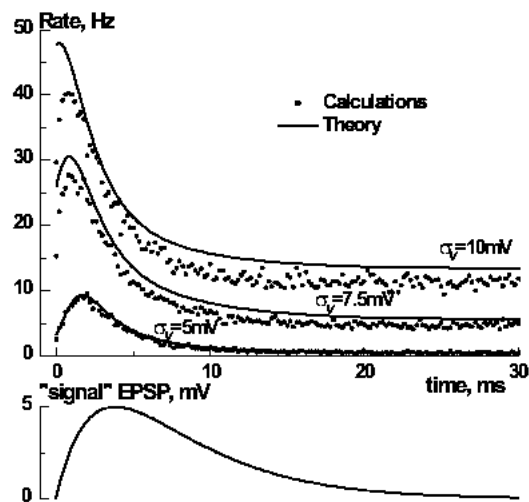

Fig. 1. Dependence of the firing rate on time after injection of "signal" synaptic input (lower panel). Different strength of the noise was achieved by changing standard deviation of the synaptic amplitude. Note very fast response in case of stronger noise.

As can be seen from Fig. 1 the dependency of firing rate on time changed with different strength of the noise. For weak noise, the change of firing rate

in time was reminiscent of evoked "signal" postsynaptic membrane potential (Fig. 1, lower panel); although, the maximum of firing rate occurred earlier. For stronger noise, the rate jumped just at the moment of injection of "signal" synaptic input when mean membrane potential was not changed yet. In agreement with equation (2), this means that the threshold crossings are strongly dependent on the mean rate of potential change.

From a physical point of view this can be explained as follows. In case of stronger noise membrane potential fluctuations occur near the threshold quite often. However, because the firing rate is still low, fluctuations approach the threshold with a low rate. At the moment of injection of "signal" input, the mean rate of potential change jumps to a new value, and, thus, the probability to cross the threshold increases very sharply.

Equation (2) not only describes the mechanism for the fast response, but also approximates the firing rate quite well. The approximation was better for very low firing rate since the model neuron included spike afterhyperpolarization, which repolarized membrane potential below the threshold level. For faster firing rates this brought about discrepancy with the mathematical prediction because some threshold crossings were eliminated.

The results presented suggest that ubiquitous spontaneous activity in the brain could serve several functions: first, the noise can help in detecting small subthreshold signals; second, fluctuations of membrane potential could keep neurons ready for very fast response to subthreshold signals.

4 Discussion

We used a simple integrate-and-fire neuronal model without resetting. Such threshold model was investigated before and equations for the rate of threshold crossings were derived for periodical input [18]. However, in the brain, unitary synaptic currents transfer information between neurons. In this study we analyzed temporal dependency of probability to fire in response to a single synaptic current imbedded in noise. We noticed that a very fast increase in firing probability takes place after the onset of a single synaptic current.

Changes of firing rate in response to single synaptic currents were analyzed theoretically in integrate-and-fire neurons for high firing rates [19]. The theory

derived required numerical solution of integral equations [19] and did not allow explicit analysis of firing rate dependency on stimulus parameters. In our study, the derived equation (2) describes a relation between the probability to cross the threshold and the rate of change of mean membrane potential induced by a synaptic current. Although fast firing response to the step onset of injected current was reported previously [20], a possibility for a single synaptic current to cause fast changes in mean firing rate was not acknowledged.

5 Conclusions

The derived mathematical relations together with modeling results suggest that a population of neurons receiving stochastic input can respond to a subthreshold shared synaptic input with a very fast increase of the mean firing rate. The effect is brought about by stochastic membrane fluctuations near the firing threshold at the moment of onset of the shared input.

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