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Controlling neuronal sensitivity to synchronous input

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Abstract

Neurons in vivo are continuously bombarded by synaptic input—so how can they detect particular inputs against this background of synaptic activity? We study how modulating background synaptic input can change neuronal sensitivity to a subset of synchronized inputs. We find that changes in net excitation or inhibition vary both the probability of detecting synchronous input and also the probability of a false-positive response. Varying the level of background input can modulate probability of synchrony detection independently of false-positive probability.

Keywords: Background activity; Noise; Signal detection; Receiver-operating characteristic curve; Efficacy

1. Introduction

Neurons in vivo receive a continuous barrage of synaptic input [4]. One method of embedding a signal within this synaptic bombardment is to encode it as a subset of synchronous synaptic inputs. An unanswered question is how neurons detect particular inputs, in this case the synchronized inputs, against a background of synaptic activity. Understanding what factors control how well neurons perform this task is important for understanding how information, in particular about the timing of a stimulus, is encoded and transmitted.

Background synaptic input affects neural responses in a number of ways, including increasing response variability, enhancing responsiveness, and changing the gain of neuronal responses [1–3,5–7]. Here we examine how background synaptic activity

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affects neuronal sensitivity to synchronized synaptic inputs. We focus on examining how background synaptic input affects the ability of specific inputs to evoke an action potential in a neuron within a specified window of time, and how changing this background activity modulates the efficacy of these inputs. In this way we characterize how neuronal sensitivity to synchronous input can be modulated.

2. Model

We used an integrate-and-fire neuron with a threshold potential of -52 mV and a reset potential of -70 mV. The membrane potential (V) was given by

$$\tau \frac{dV}{dt} = V_{rest} - V + g_K(E_K - V) + g_{Ex}(E_E - V) + g_{In}(E_I - V),$$

where $V_{rest} = -70$ mV is the resting membrane potential and $\tau = 10$ ms is the membrane time constant. Constant current (referred to in the text as driving current) was injected into the neuron where noted in the text.

A short refractory period was generated after each action potential by increasing a potassium conductance, g_K, to three times the resting membrane conductance of the neuron. Between action potentials, g_K exponentially decayed to zero with a time constant of 5 ms. The reversal potential was $E_K = -80$ mV.

Excitatory and inhibitory synaptic conductances, g_{Ex} and g_{In} were generated from incoming Poisson spike trains. In the $1X$ condition, the underlying rates of these spike trains were 1500 Hz for excitatory inputs and 1318 Hz for inhibitory inputs. With each presynaptic spike, the synaptic conductance was increased by 8% (for excitatory inputs) and 24% (for inhibitory inputs) of the resting membrane conductance. Between presynaptic events, the synaptic conductances decayed towards zero with a time constant of 5 ms. $E_E = 0$ mV and $E_I = -80$ mV were the excitatory and inhibitory reversal potentials, respectively.

At a specific time in each trial ($t = 0$ in Fig. 1A), a single EPSC was injected into the neuron. This was an instantaneous rise in injected current which decayed exponentially over time with a time constant of 5 ms. In the text, the size of the EPSC is given as the peak of the EPSP resulting from this EPSC injected in the absence of any additional synaptic input. For this reason, the EPSC size is given in mV.

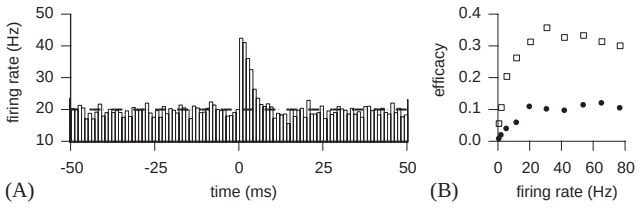

Fig. 1. (A) An example firing rate histogram in response to an EPSC injected at time $t = 0$. The dashed line represents the baseline firing rate. (B) EPSC efficacy for 2 (filled circles) and 6 mV (open squares) EPSCs as a function of postsynaptic baseline firing rate.

3. Results

The goal of this study was to examine how background synaptic input can modulate the efficacy of individual and groups of synchronously arriving synaptic inputs. We model these as a single EPSC injected into the model neuron at a specific time ($t =$ 0 ms) in each trial. To measure the efficacy of this input, we created a firing rate histogram by binning spike times, collected over many trials, relative to EPSC onset. The baseline firing rate (r_0–see dashed line in Fig. 1A), which is equal to the average firing rate of the neuron in the absence of an injected EPSC, was subtracted from each bin in the firing rate histogram. The cumulative sum of the resulting histogram was measured

$$\text{cumulative sum at time } t = \sum_{t'=0}^{t} (r(t') - r_0)\Delta t,$$

where $r(t)$ is the size of the firing rate histogram bin representing time t and Δt is the width of each bin in the histogram. The peak of the cumulative sum is a measure of the elevation in firing rate above baseline resulting from the injected EPSC, and is equal to the probability that the injected EPSC will elicit an action potential.

We first examined the relationship between EPSC efficacy and baseline firing rate (see Fig. 1B). We injected different levels of driving current (see Methods) and measured EPSC efficacy at the resulting different baseline firing rates. For two sizes (2 and 6 mV) of injected EPSC, efficacy was affected by baseline firing rate, particularly for lower baseline firing rates.

These results indicate that EPSC efficacy can be modulated by simply adding either excitation or inhibition, suggesting that a neuron can be made more sensitive to an EPSC by increasing the baseline firing rate. However, when measuring the neuron's performance as an EPSC detector, it is important to consider not only the probability that the neuron will fire in response to the EPSC (the detection probability or the neuron's hit rate), but also the probability that the neuron will fire in the absence of an EPSC (the probability of a false-positive response, or the neuron's false-alarm rate).

Increasing the baseline firing rate of the neuron effectively increases the overall probability that the neuron will fire at any point in time. Thus not only did the probability that the neuron will fire an action potential in response to an EPSC, the hit rate, increase, but so did the probability that a neuron will fire in the absense of an ESPC, the false-alarm rate. One way to illustrate this effect is by plotting the receiver operating characteristic (ROC) curve for the neuron. Such curves are drawn in Fig. 2. For Fig. 2, 6 mV EPSCs were used. These stimuli may be thought of as arising from 6 or more synaptic inputs perfectly synchronized in time. The y-axis of each panel is the hit rate (β), the probability that the neuron fired an action potential within 10 ms after the injected EPSC. The x-axis is the false-alarm rate (α), the probability that the neuron fired an action potential within a 10 ms window when no EPSC was injected. The area under each curve is a measure of the neuron's performance as a synchronous input detector. If the neuron always detects the EPSC, the hit rate always equals one and the area under the ROC curve is also one. The ROC curve of a random detector (where the hit rate equals the false-alarm rate) will have an area of 0.5 under it.

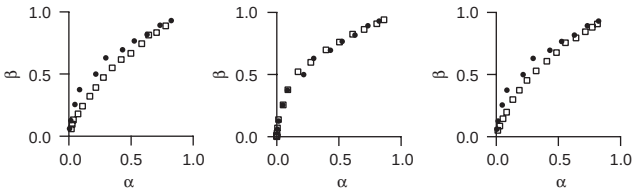

Fig. 2. Each ROC curve is made up of hit rate (β) plotted against false-alarm rate (α) for many different baseline firing rates. Left: performance in the $1X$ (filled circles) and the $3X$ condition (open squares). Center: performance in the $1X$ condition (filled circles) and with the same input noise but with conductance equivalent to the $3X$ condition (open squares). Right: performance in the $1X$ condition (filled circles) and with the same conductance but input noise equivalent to the $3X$ condition (open squares).

The curve traced by the filled circles in each panel represent the responses of the neuron in the $1X$ condition. For each point, the driving current injected into the neuron was adjusted to drive the neuron at a different baseline firing rate. As baseline firing rate is increased, the curve moves upward and to the right because both the hit rate β and the false-alarm rate α increase. This is analagous to changing the threshold that the neuron uses to detect an EPSC, or the strategy that the neuron uses to detect an EPSC.

The open squares in the left panel of Fig. 2 represent the responses of the neuron in the $3X$ condition. Here we see that tripling the rate of excitatory and inhibitory inputs (the $3X$ condition) decreases the area under the ROC curve, decreasing the performance of the neuron. This indicates that EPSC efficacy may be changed in a manner independent of baseline firing rate by changing the rate of background synaptic input. Changing the overall conductance of the neuron does not have this effect (open squares in the center panel of Fig. 2). The performance of the neuron with additional conductance is identical to the performance of the neuron in the $1X$ condition. Increasing the input noise (defined here as the variance of the background synaptic current) without changing the conductance changes the shape of the ROC curve and hence the performance of the neuron at detecting the EPSC (open squares in the right panel of Fig. 2).

4. Discussion

Our results show that the ability of an input (or multiple synchronous inputs) to elicit an action potential can be controlled either through manipulations that affect the baseline firing rate of a neuron or through manipulations that change the input noise to a neuron. These two different manipulations have different effects on the neuron's responses. Changing the baseline firing rate of the neuron is analagous to decreasing the discrimination threshold of the neuron in that it increases both input efficacy as well as false-alarm rate. Varying the input noise to the neuron can control input efficacy independently of baseline firing rate and affects the performance of the neuron as an input detector.

Manipulations that change the input noise to a neuron have also been shown to change neuronal response gain, measured as slope of the steady-state firing rate in response to constant injected current [1,2]. These results, combined with those shown here, suggest a relationship between EPSC efficacy and steady-state neuronal response gain. Work in progress will characterize the relationship between these two measurements of neuronal responsivity.

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