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.

INTRODUCTION

Neurons *in vivo* receive a continuous barrage of synaptic input (Holt et al, 1996). One method of embedding a signal within this synaptic bombardment is to encode it within 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 (Troyer and Miller, 1997; Hô & Destexhe, 2000; Doiron et al., 2001; Chance et al., 2002). Here we examine how background synaptic activity 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 this input. In this way we characterize how neuronal sensitivity to synchronous input can be modulated.

MODEL AND EXPERIMENTAL METHODS

We used a standard 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, by 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 figure 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 in mV, which is the peak voltage deflection resulting from injecting the EPSC into the neuron at rest, in the absence of any additional synaptic conductances.

RESULTS

The goal of this study is to examine how background synaptic input can modulate the efficacy of individual synaptic inputs and synchronous 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 figure 1A), the average firing rate of the neuron in the absence of an injected EPSC, was subtracted from each bin in the firing rate histogram, and 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 examine the relationship between EPSC efficacy and baseline firing rate (see figure 1B). We injected different levels of driving current (see Methods) and measured EPSC efficacy at

the resulting different baseline firing rates. Particularly for lower baseline firing rates, For both sizes of injected EPSC, efficacy was affected by baseline firing rate, particularly for lower baseline firing rates.

The results illustrated in figure 1C indicate that simply adding either excitation or inhibition will modulate EPSC effiacy. Neurons receive a high amount of balanced excitatory and inhibitory synaptic input *in vivo* (Softky & Koch, 1994; Shadlen & Newsome, 1994; Troyer & Miller, 1997), where net excitation approximately cancels net inhibition. We now consider the effect of balanced excitation and inhibition. We isolate the effects of balanced excitation and inhibition on EPSC efficacy from the effects of baseline firing illustrated in figure 1B by adjusting the driving current so that baseline firing was maintained at 30 Hz across all conditions.

We first examine the effects of changing the rates of background synaptic activity on EPSC efficacy (shown in figure 1C). For the 3X condition (blue squares), the rates of excitatory and inhibitory synaptic inputs were tripled from that used in the 1X condition (red circles). Varying the rate of background input had a clear effect on EPSC efficacy. Even though the baseline firing rate was held constant, raising the rate of background input significantly decreased the ability of the injected EPSC to evoke an action potential in the model neuron.

Raising the rate of background synaptic input to the neuron has two effects: it increases the overall conductance of the neuron and increases the variance of the incoming synaptic current, or input noise. We now examine the effects of each of these manipulations separately. Again, to isolate these effects from effects arising from changes in baseline firing, the driving current was adjusted so that baseline firing always remained at 30 Hz.

In figure 1D, we compare EPSC efficacies in the 1X condition (red circles) with EPSC efficacies when the synaptic conductances are tripled without changing the input noise (open blue squares). This was done by introducing additional constant excitatory and inhibitory conductances into the model without introducing any additional input noise. Surprisingly, when baseline firing rate is held constant, changing the conductance of the neuron has no significant effect on EPSC efficacy. This occurred despite the fact that the EPSP sizes were significantly reduced by the added conductance.

Figure 1E illustrates the effect of increasing input noise on EPSC efficacy. Here the red circles represent EPSC efficacies measured in the 1X condition and the blue hatched squares represent EPSC efficacies measured when the conductance of the neuron was held constant but the input noise was raised to the level in the 3X condition. Increasing input noise decreased EPSC efficacy.

EPSC efficacy can be modulated either by varying the baseline firing rate, or by changing the rate of background input, or the amount input noise received by the neuron. Although both approaches affect EPSC efficacy, they have different effects on the neuronal performance as an input detector. EPSC efficacy is essentially a measurement of the neuron's ability to detect an EPSC. However, when measuring the neuron's performance, 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 is the probability that the neuron will fire an action potential in response to an EPSC, the hit rate, increased, but so is 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

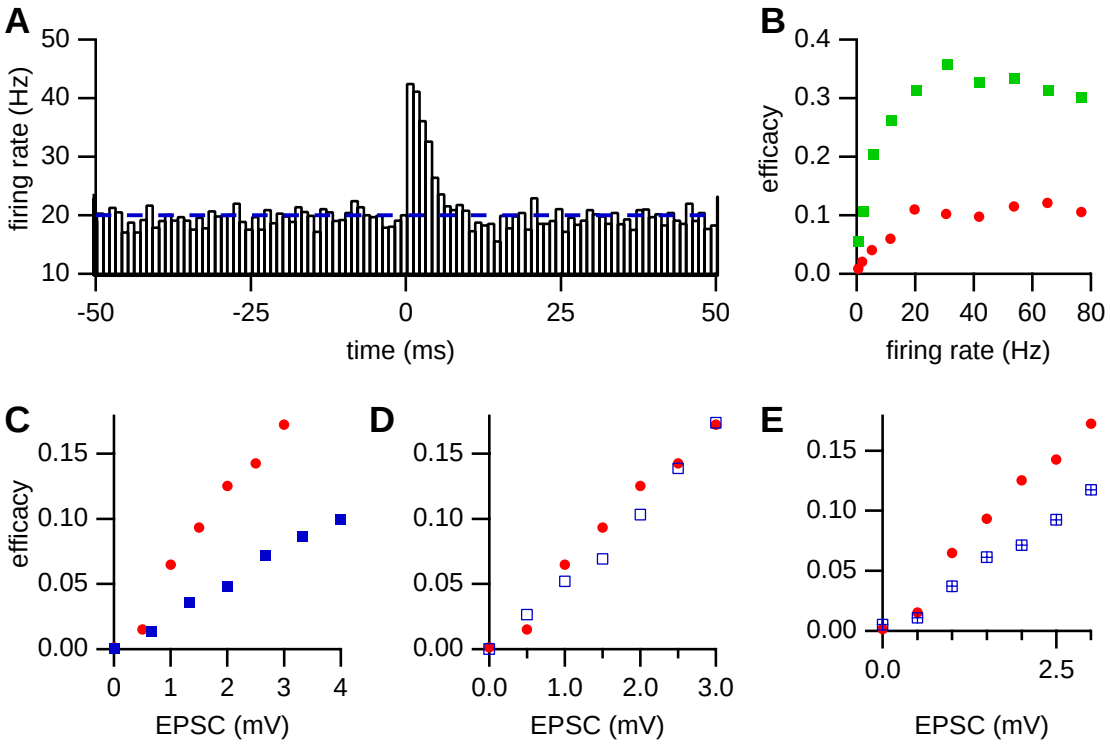

Figure 1: (A) An example firing rate histogram in response to an EPSC injected at time $t = 0$. The dashed line represents the baseline firing rate. (B) EPSC effiacy for 2 mV (red circles) and 6 mV (green squares) EPSPs as a function of postsynaptic baseline firing rate. (C) EPSC efficacy as a function of EPSC size for the 1X (red circles) and 3X (blue squares) conditions. (D) EPSC efficacy as a function of EPSC size for rate factor $= 1$ and with additional conductance equivalent to that in the rate factor $= 3$ condition (open blue squares). (E) EPSC efficacy as a function of EPSC size for rate factor $= 1$ (red circles) and with additional input noise equivalent to that in the rate factor $= 3$ condition (hatched blue squares). For (C), (D), and (E), the driving current was adjusted so that baseline firing was always 30 Hz.

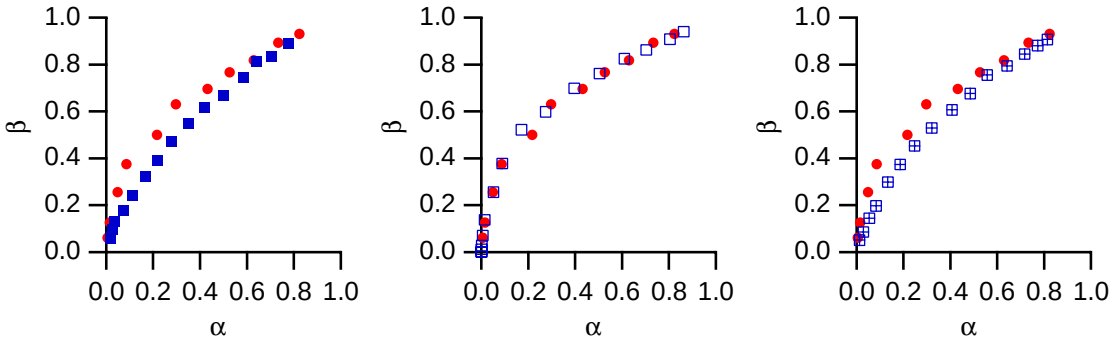

Figure 2: Each ROC curves is made up of hit rate (β) plotted against false-alarm rate (α) for a different baseline firing rate. Left: performance in the 1X (red circles) and the 3X condition (blue squares). Center: performance in the 1X condition (red circles) and with the same input noise but with conductance equivalent to the 3X condition (open blue squares). Right: performance in the 1X condition (red circles) and with the same conductance but input noise equivalent to the 3X condition (blue hatched squares).

in figure 2. For figure 2, 6 mV EPSCs were used. These EPSCs may be thought of as arising from 6 or more synchronous synaptic inputs. 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 there was no EPSC injected. The area under each curve is a measurement of the neuron's performance as a synchronous input detector.

The curve traced by the red 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 neuron moves upward and to the right along each curve because both the hit rate β and the false-alarm rate α are increased. 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 blue squares in the left panel of figure 2 represent the responses of the neuron in the 3X condition. Tripling the rate of excitatory and inhibitory input (the 3X condition) decreases EPSC efficacy in a manner that is independent of baseline firing rate (shown in figure 1D). Here we see that this manipulation decreases the area under the ROC curve, or decreases the performance of the neuron. Changing the overall conductance of the neuron (as in figure 1D) does not have this effect (open blue squares in the center panel of figure 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 to the neuron (hatched blue squares in the panel to the right) changes the shape of the ROC curve and hence the performance of the neuron at detecting the EPSC.

SUMMARY AND 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. Modulating input efficacy through these two different manipulations has 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 which 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 (Doiron et al., 2001; Chance et al., 2002). 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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