

Controlling Neuronal Sensitivity to Synchronous Input

Frances S. Chance¹ and Alex D. Reyes

Center for Neural Science, New York University, New York, NY 10003

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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 [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, 7]. 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

¹denotes corresponding author. current address: Department of Neurobiology and Behavior, University of California, 2205 McGaugh Hall, Irvine CA 92697-4550

neuronal sensitivity to synchronous input can be modulated.

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 , 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

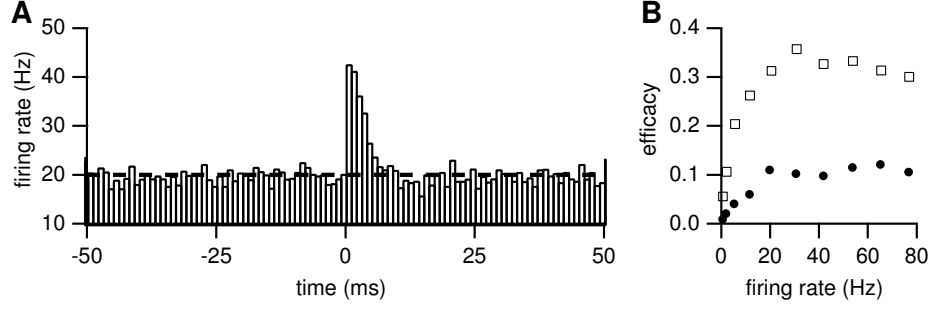


Figure 1: (A) An example firing rate histogram in response to an EPSC injected at time $t = 0$. The dashed line represents the baseline firing rate. (B) EPSC efficacy for 2 mV (filled circles) and 6 mV (open squares) EPSPs as a function of postsynaptic baseline firing rate.

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. For both sizes 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 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 absence of an EPSC, 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 figure 2. For figure 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 there was no EPSC injected. The area under each curve is a measurement 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.

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 analogous 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 figure 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, or decreases 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

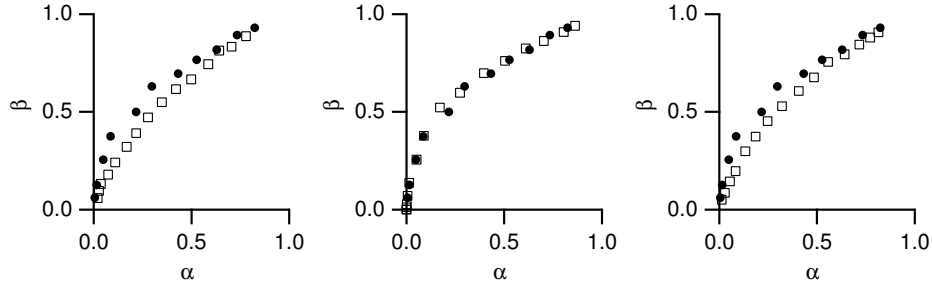


Figure 2: Each ROC curve is made up of hit rate (β) plotted against false-alarm rate (α) for many different baseline firing rates. Left: performance in the 1X (filled circles) and the 3X condition (open squares). Center: performance in the 1X condition (filled circles) and with the same input noise but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

have this effect (open 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 (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 figure 2).

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 analogous 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 [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 responsiveness.

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Frances Chance uses both computational modeling and slice electrophysiology in her research to study how the response properties of neurons recorded *in vivo* arise from the underlying neural circuitry. She holds a Ph.D. from Brandeis University and was a Sloan/Swartz Foundation post-doctoral fellow in the Center for Neural Science at New York University. She is currently a faculty member in the Department of Neurobiology and Behavior at the University of California, Irvine).

Alex Reyes is an assistant professor at the Center for Neural Science at New York University. He uses a combination of multiple whole-cell recordings *in vitro* and computer simulations to examine how an individual neuron and a small network of neurons process signals.