Variability of postsynaptic responses depends on the number of synaptic inputs

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Abstract

A conductance-based model for synaptic transmission and postsynaptic integration reveals that the variability of postsynaptic responses depends on the number of synaptic inputs in a non-linear way. Increasing the number of excitatory and inhibitory inputs increases the total synaptic conductance. In consequence, the total excitatory and inhibitory currents become anti-correlated although the individual inputs vary independently from each other and the resulting membrane potential stays close to the resting potential. The postsynaptic variability is determined by the interacting effects of increasingly more independent inputs and the anti-correlation of the excitatory and inhibitory currents. These findings lead to an intuitive explanation why correlated inputs can increase the variability of neuronal responses.

Introduction

In many experimental studies it was shown that neuronal responses to a repeatedly presented stimulus can be amazingly variable. A main source of neuronal variability is the synaptic input impinging onto a neuron (e.g. [1, 10]). The variability is particularly high if a neuron receives balanced excitatory and inhibitory synaptic inputs (review: [6]).The second factor that can increase the variability of postsynaptic responses significantly is correlated input (e.g. [8, 2, 7, 5])

With a conductance-based one-compartment model of synaptic transmission and postsynaptic integration we show that the variability of postsynaptic responses depends in addition to these factors in a non-linear way on the number of active synaptic inputs. As we will show this non-linear dependence is influenced significantly by an anti-correlation between total excitatory and inhibitory currents that occurs although the individual inputs are uncorrelated.

Model

We model a neuron that is synaptically connected to N_{syn} input neurons. Not all of these inputs are active at a given time. Those input elements that are not active do not contribute to the postsynaptic response. This input organization may, for instance, mimic a visual interneuron being activated by a stimulus that is smaller than the neuron's receptive field. In this situation, the neuron is assumed to receive input only from those elements that are activated by the stimulus. The other input elements are assumed to be silent in this situation. This simplifying assumption does not take into account that noise may be generated continuously not only during stimulation [9].

In our model simulation the neuron receives up to 1000 excitatory and 1000 inhibitory synaptic inputs that are all independent from each other. The membrane potentials of the presynaptic neurons fluctuate stochastically with statistical properties as they were determined experimentally in fly motion sensitive neurons [3]. Excitation and inhibition are balanced, with all parameter values being identical for excitatory and inhibitory synaptic transmission. Analogous to the graded information transfer in many sensory systems such as fly visual neurons, retinal bipolar cells, or mitral cells in the olfactory bulb (review: [4]) we use a model of graded synaptic transmission. The graded de- and hyperpolarizations of the presynaptic membrane potential induce via a sigmoidal transfer function conductance changes of the individual synapses. The resulting postsynaptic potentials are integrated and transformed into spike trains with a model of spike generation [3]. Both the postsynaptic potentials and the spike trains are analyzed with respect to their mean and variance.

Results

The fluctuations of the postsynaptic potential as well as the mean and the variance of the postsynaptic spike count depend in a non-linear way on the number of independent synaptic inputs. For an increasing number of synaptic inputs the variance of the postsynaptic potentials first increases, then reaches a maximum and decreases again. This qualitative feature was found for all combinations of parameter values, although the postsynaptic potential variance depends quantitatively on parameters like the maximum synaptic conductance. Mean and variance of the postsynaptic spike count depend on the number of active synaptic inputs qualitatively in the same way as the variance of the integrated postsynaptic potentials.

The non-linear relation between the number of synaptic inputs transmitting independent noise signals and the variability of the postsynaptic responses is induced by a combination of two effects:

i) The total synaptic conductance increases with increasing number of active synaptic inputs. This increase causes the total inhibitory and excitatory currents to become anti-correlated, although the individual synaptic conductances vary independently from each other. This anti-correlation occurs because the excitatory and the inhibitory currents both depend on the actual postsynaptic potential value. When the postsynaptic potential approaches the excitatory reversal potential, the excitatory current decreases and the inhibitory current increases. This push-pull relationship keeps the membrane potential close to the resting potential, especially if the anti-correlation between the total excitatory and inhibitory currents is strong. This is the case for large total conductances.

ii) When the total synaptic conductance is held constant by scaling the synaptic conductances with the number of active synapses N_{syn}, the variability of the postsynaptic response decreases by $1/N_{syn}$. The postsynaptic neuron basically averages the impinging independent noise inputs. This finding refers to the comparison of different neurons with the same maximum total conductance. A neuron with more inputs with low synaptic conductance responds less variable than a cell with fewer but stronger inputs.

The relationship between both effects determines the variability of the postsynaptic responses. When the anti-correlation between the excitatory and inhibitory currents increases more than proportional to the number of inputs, the fluctuations of the postsynaptic membrane potential become larger and the mean and variance of the postsynaptic spike count increase. This is the case when a neuron receives a small number of synaptic inputs. When more synaptic inputs are active, the correlation function becomes shallower and the variability of the postsynaptic responses reaches a maximum and decreases again.

Our finding has implications for the topic of correlated synaptic inputs. When input signals are correlated, the correlation between the postsynaptic currents does not change significantly compared to uncorrelated input. It is mainly determined by the total synaptic conductance. On the other hand, correlations between inputs reduce the effective number of independent synaptic processes that are transmitted to the postsynaptic neuron. For example two totally correlated inputs have the same effect on the postsynaptic response as one of them with twice the synaptic conductance would have. Therefore, correlations between inputs increase the postsynaptic variability in the same way as a reduction of the number of independent inputs would do while the total synaptic conductance is kept constant (see ii). To induce highly variable postsynaptic responses, the number of independent synaptic inputs must be relatively low for most parameter combinations. This can be achieved either by a low total number of active inputs or by correlated inputs.

Conclusion

In summary, the variability of postsynaptic potentials and spike responses depends strongly on the number of active synaptic inputs. It is determined by the ratio between the correlation between excitatory and inhibitory currents and the number of independent inputs. The resulting postsynaptic variability is maximal for a particular number of inputs that depends on the chosen parameter values. Correlations between inputs can induce a higher variability because they can shift the effective number of independent inputs towards this maximum.

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