

The role of background synaptic noise in striatal fast spiking interneurons

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Abstract

Striatal fast spiking (FS) interneurons provide inhibition to each other as well as to medium spiny projection (SP) neurons. They exhibit up-states synchronously with SP neurons, and receive GABAergic and AMPA synaptic input during both up- and down-states. The synaptic input during down-states can be considered noise and might affect detection of up-states. We investigate what role this background noise might play for up-state firing in a 127 compartment FS model neuron. The model has Na, KDr and KA conductances, and is activated through AMPA and GABA synapses. The model response to current injection and synaptic inputs resembled experimental data. We show that intermediate levels of noise neither facilitates nor degrades the ability of the FS neuron model to detect up-states.

Key words: Striatum, Fast Spiking Interneurons, Stochastic Resonance, Transient A current, Up states

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1 Introduction

The basal ganglia are important for the executive functions of the forebrain. Disturbances within the basal ganglia produce motor and neuropsychiatric disorders [13]. Medium spiny projection (SP) neurons, the predominant cell type in the striatum, are the first stage in cortex-basal ganglia processing and in turn control the output from the basal ganglia. In *in vivo* recordings, SP neuron membrane potential fluctuates between a "down-state" potential of -80 to -90 mV, and an "up-state" potential near -55 mV [15; 16; 12; 10], during which action potentials are generated [15; 16]. Fast spiking (FS) interneurons provide the main route of feed-forward inhibition from cortex to SP neurons [6], and might suppress SP neuron firing during up-states [7].

SP neurons and FS interneurons receive synaptic inputs during both up-states and down-states [2]. Though SP neurons have hyperpolarized down-states that prevent firing, FS interneurons have a relatively depolarized resting membrane potential and steep current-firing curve suggesting that even small excitatory inputs could translate into powerful feed-forward inhibition. Such an arrangement is also sensitive to amplification of spurious synaptic inputs. Thus, a compelling question is whether down-state activity interferes with the ability of FS interneurons to reliably signal up-states. An intriguing alternative is that down-state activity may improve signal detection in FS interneurons. The enhancement of sub-threshold periodic signals produced by low levels of noise is known as stochastic resonance (SR). In the present study, we use a computer model of an FS interneuron to investigate the effect of down-state activity on signal detection.

2 Methods

A compartmental model of a fast spiking (FS) interneuron was created using the GENESIS simulation software [3]. The morphology consisted of a soma and three primary dendrites, each with two branching points. This branching structure is a prototype of the morphology revealed by biocytin reconstructions [9], and is sufficient to reproduce electrical activity and response to synaptic inputs. Passive properties were set to reproduce the input resistance and time constants measured [2] (RM 20000 Ωcm^2 , RI 300 Ωcm and CM 0.7 $\mu\text{F}/\text{cm}^2$). Action potentials were generated by the fast Na and delayed rectifier (KDr) currents in the soma [5]. A transient K current (KA), similar to that found in SP neurons [1; 8; 14], was placed in the soma and primary dendrites to produce the experimentally observed spike latency [2]. Maximal conductances of these voltage dependent channels (Table 1, top) were optimized using the simulated annealing routine in GENESIS. The resulting frequency-current relationship

Compartment	Na^+	K_{3132}	K_{13}	KA
Soma	1149	582	1.46	333
Primary dendrite	0	0	0	90
Synapse type	E_{syn}	τ_1	τ_2	Gmax
GABA	-0.060	$1.33 \cdot 10^{-3}$	$4 \cdot 10^{-3}$	$1.131 \cdot 10^{-9}$
AMPA	0.000	$0.67 \cdot 10^{-3}$	$2 \cdot 10^{-3}$	$0.754 \cdot 10^{-9}$

Table 1

Top: Ion channel conductance density (S/m²) in each compartment type.

Bottom: Synaptic currents modeled. Ion channels activated by synapses are described by: $I_{syn} = G_{max} \cdot G_{syn}(t)(V - E_{syn})$ where E_{syn} is the reversal potential. $G_{syn}(t)$ is the synaptic conductance: $G_{syn}(t) = \frac{A_{max}}{\tau_1 - \tau_2}(\exp(\frac{-t}{\tau_1}) - \exp(\frac{-t}{\tau_2}))$ where $\tau_1 > \tau_2$ and A_{max} is adjusted to approach unity at the peak. Units in s, V and S.

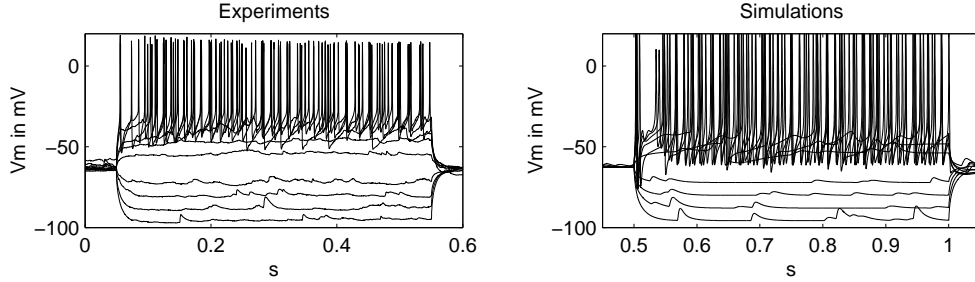


Fig. 1. Response of cultured neuron (left), and model neuron (right), to current steps increasing 0.02nA between -0.08 and +0.12 nA.

was similar to that measured in FS interneurons *in vitro* (Fig. 1 [2].)

Cortico-striatal input to the FS model neuron consisted of AMPA synaptic conductances placed in each dendritic compartment. Fast GABAergic synapses, representing local striatal inputs, were placed in the soma and proximal part of the dendritic tree at three times the density of the AMPA synapses. This distribution, and also the conductance of the synaptic channels (Table 1, bottom), produced an amplitude distribution and population reversal potential resembling that measured in triple co-cultures [2] (full manuscript in preparation). Each synapse was activated by a Poisson distributed input train with frequency varying from 0.01 to 1 Hz (or more) which encompassed the range of down-state input frequencies measured experimentally [2].

Spikes in SP neurons are the only signal transmitted out of the striatum. Since SP neurons fire only during up-states, we consider synaptic inputs during up-states to be the "signal", and synaptic inputs during the down-states to be "noise". Periodic up-states were simulated using additional Poisson input trains with periodically varying frequency to both AMPA and GABA synapses. To compare our results with other studies on neuronal information processing, we also used a more conventional signal: synchronous activation

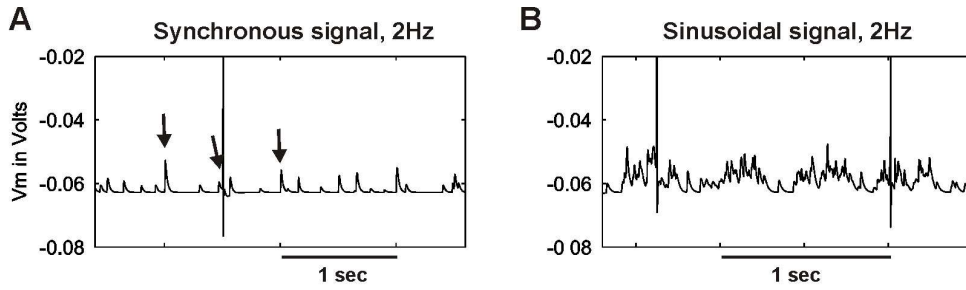


Fig. 2. Membrane potential of a model FS interneuron in response to synchronous signals is shown in (A). Arrows indicate the synchronous signal each 0.5 s inbedded in background noise. (B) shows the sinusoidal signal, here 2 Hz.

(during a time window of 5ms) of a proportion of all AMPA synapses, repeated at 2 Hz. The output signal to noise ratio (SNR) was measured in two different ways. Under the assumption that the up-state is the signal to be detected, SNR_{phase} was calculated as the ratio of up-state spikes to total spikes. We also used a more conventional measure, SNR_{rise}, based on the number of interspike intervals corresponding to the input period divided by the number of all other interspike intervals.

3 Results and discussion

Figure 2 illustrates the two different input signals that were used in the present study. The frequency of each of the input Poisson trains was either changed continuously in a sinusoidal manner (sinusoidal input) or abruptly increased for 5ms to produce synchronous subthreshold inputs. The frequency during the sinusoidal signal was set to vary from 0 to 1600 Hz [2].

The results show that the effect of down-state noise depends on the signal shape as well as the measure of SNR. An increase in noise predominantly produces a decrease in SNR, but an increase in SNR (stochastic resonance) is observed under some circumstances. Stochastic resonance is observed with the synchronous input signals when the SNR is quantified using interspike intervals (peak SNR at noise frequency = 0.5 Hz, Fig 3A). This suggests that the signal is more reliably transmitted in the presence of some noise. However, SR is not observed when the asynchronous, sinusoidal inputs signals are used (Fig 3B), regardless of the modulation frequency of the sinusoid. With sinusoids, lower frequencies correspond to longer duration up-states, which can support multiple spikes per up-state in response to intermediate noise values. Therefore the SNR_{rise} values are in general smaller for lower modulatory frequencies. SNR_{rise} also starts to decrease earlier with lower frequencies when noise is increased because of the additional interspike intervals that are smaller than the signal period. But even with high frequency sinusoids, corresponding to

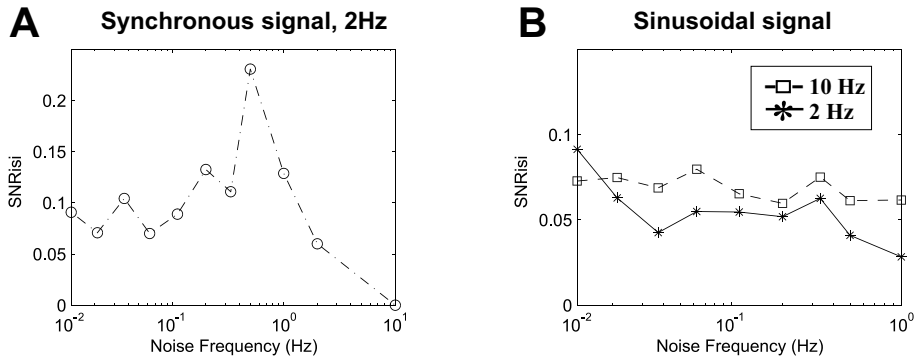


Fig. 3. SNRisi for synchronous input (A) and for asynchronous sinusoidal inputs (B). For the synchronous inputs, SNR peaks at intermediate noise values.

brief up-states (e.g. 50 ms for the 10 Hz signal), SR is not observed. Thus, the lack of SR is independent of up-state duration.

Figure 4 shows that the detection of SR depends on the method used to measure it. Because the frequency of down-state spikes is so low in the physiological noise range used here, SNRphase is close to one for all duration up-states and for the synchronous input signal, even for intermediate noise levels. For higher down-state noise, the percentage increase in noise spikes is greater than that of signal spikes; thus SNRphase starts to decrease. SNRphase does not exhibit SR for any of the input signals.

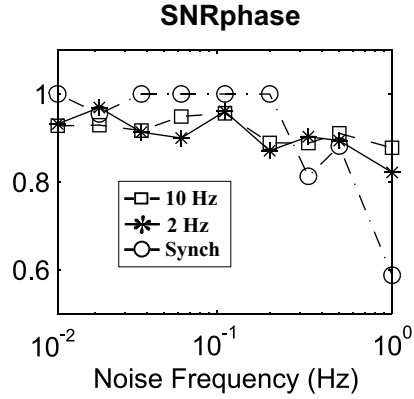


Fig. 4. Comparison of SNRphase for the synchronous and sinusoidal inputs.

Though stochastic resonance in the peripheral nervous system is well documented [4], stochastic resonance in central neurons is rare. Rudolph and Destexhe [11] demonstrated SR in a model neocortical neuron. They found that an increase in strength of the background noise, and also an increase in correlation of the input, affects the responsiveness of the system. Rudolph and Destexhe used synchronous inputs on a randomly chosen, yet time-invariant set of synaptic inputs. We confirm a similar result using the FS neuron model. We also show that the presence of SR depends on the type of signal used, as well as the measure of SNR. The synaptic inputs during up-state periods in the striatum are asynchronous and more resemble the sinusoidal signal used above. Furthermore, the up-states do not occur with a regular period, making it unlikely that ISI is the signal detected by striatal neurons. It thus is unlikely that down-state noise facilitates up-state spike generation in FS neurons.

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