Gain modulation and frequency locking under conductance noise

Michael Rudolph*, Alain Destexhe

Unité de Neurosciences Intégratives et Computationnelles, CNRS, UPR-2191, Bat. 33, Avenue de la Terrasse 1, 91198 Gif-sur-Yvette, France

Abstract

In the intact cortical network, neurons process information while receiving thousands of synaptic inputs. We investigated how this noise modulates the ability to resolve constant and oscillatory stimulation by using simplified neuron models. The cellular response was precise and reliable for a broad range of model parameters, while the output rate depended on the stimulus amplitude. The results suggest that both temporal and rate coding schemes are not exclusive but rather encode different aspects of the input at the same time. Conductance noise was found to play a modulating role, suggesting that high-conductance noise confers advantageous computational properties to neurons.
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1. Introduction

Cortical neurons in vivo are subject to a tremendous synaptic "noise" which was shown to markedly impact on the electrophysiological properties and the cellular response [8,5,9]. Recently, in the context of the general neural coding debate, neural responses to various more complex stimuli were investigated (for a review see [1]). Here, theoretical models and experiments suggest that cortical neurons are capable of precise and reliable spike responses even in the presence of noise (see e.g. [7]). However, these results were mainly obtained in low-conductance states, and it is not known if precise and reliable responses can be obtained in high-conductance states resembling in vivo conditions.

* Corresponding author.
E-mail address: michael.rudolph@iaf.cnrs-gif.fr (M. Rudolph).

Here we address this question by using simplified Hodgkin–Huxley type models of cortical neurons subject to conductance noise and additional synaptic inputs. We show that the neuronal response shows differences depending on the type of noise, and we conclude that high-conductance noise confers advantageous computational properties to neurons, including the possibility of modulating their response between temporal and rate coding.

2. Methods

Simulations were performed using a simplified point-conductance model of cortical neurons [2], described by the membrane equation

$$C_m \dot{V}(t) = -g_{leak}(V(t) - E_{leak}) - \sum_{int} I_{int}(t) - I_{syn}(t) + I_{stim}(t),$$

where $V(t)$ denotes the membrane voltage ($C_m = 1 \ \mu F/cm^2$ specific membrane capacity, $g_{leak} = 4.52 \times 10^{-5} \ s/cm^2$ leak conductance, $E_{leak} = -80 \ mV$ reversal potential), and $\sum_{int} I_{int}(t)$ denotes the sum over intrinsic voltage-dependent currents. A fast Na^+, a delayed-rectifier K^+ current and a V_m-dependent K^+ current were included and described by Hodgkin–Huxley models.

$I_{syn}(t) = g_e(t)(V(t) - E_e) + g_i(t)(V(t) - E_i)$ denotes the membrane current due to synaptic noise, decomposed into excitatory $g_e(t)$ and inhibitory $g_i(t)$ time-dependent conductances (reversal potentials $E_e = 0 \ mV$ and $E_i = -75 \ mV$). Both were described by one-variable stochastic processes similar to the Ornstein–Uhlenbeck process: $\frac{dg_{i,e}(t)}{dt} = -\frac{1}{\tau_{i,e}}(g_{i,e}(t) - g_{i,e0}) + \sqrt{2/\tau_{i,e}}\,\sigma_{i,e}W_{i,e}$, where $g_{i,e0}$ are mean conductances, $\tau_{i,e}$ are time constants ($\tau_e = 10.49 \ ms$, $\tau_i = 2.728 \ ms$), $\sigma_{i,e}$ denote the standard deviation (SD) of $g_{i,e}(t)$. $W_{i,e}$ denotes Gaussian white noise of unit standard deviation and zero mean for inhibition and excitation, respectively. Background parameters were altered between 10% and 200% around standard values of $g_{e0} = 0.0121 \ \mu s$, $g_{i0} = 0.057 \ \mu s$, $\sigma_e = 0.012 \ \mu s$, $\sigma_i = 0.0264 \ \mu s$. Stimulations were either an individual excitatory synaptic event with amplitude g_{amp} or (sinusoidal) excitatory conductance waveforms $I_{stim}(t) = -g_{amp}[1 + \sin(2\pi\nu_{stim}t)](V(t) - E_e)$, $0 \ ns \leqslant g_{amp} \leqslant 30 \ ns$.

The responses for a fixed number of repetitions of a stimulus were accumulated in *peri-stimulus time histograms* (PSTHs) and the background subtracted, yielding reduced PSTHs (Fig. 1B). For single conductance pulses, the integrated reduced PSTH yields the probability for evoking spikes explicitly by the stimulus. For sinusoid stimuli the reduced PSTH contained statistically significant peaks (Fig. 1B), and the average SD of these events defined the precision of the response [6]. The reliability was defined as the ratio between the number of spikes in all events obtained from the reduced PSTHs and the total number of spikes during the stimulus.

3. Results

We first investigated the impact of various background properties on the response of the cell to an excitatory synaptic stimulus. The probability obtained by integration
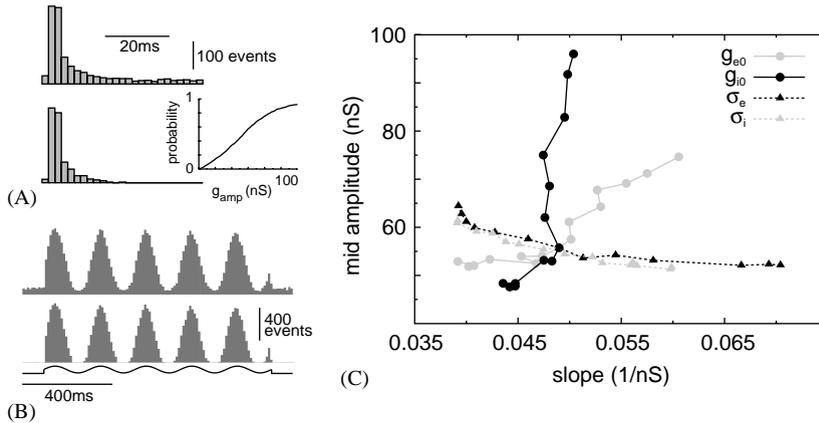
Fig. 1. Cellular response and gain modulation. (A) PSTH (upper plot) and reduced PSTH (lower plot) obtained from excitatory stimuli ($g_{amp} = 60$ ns, 1000 repetitions). Integration of the reduced PSTH yields the probability for spikes specifically evoked by the stimulus, which shows a sigmoidal behavior as a function of g_{amp} (inset). (B) PSTH (upper plot) and reduced PSTH (lower plot) obtained for sinusoidal excitatory conductance stimuli ($g_{amp} = 12$ ns, $v_{stim} = 5$ Hz, 1000 repetitions). (C) Gain modulation by background noise. The mid-amplitude and slope were obtained from sigmoidal fits to probability-g_{amp} plots (inset in A). Parameters of the background were changed between 10% and 200% of the standard values (see Methods).

of the reduced PSTHs shows a sigmoidal behavior as a function of the stimulation amplitude (Fig. 1A). From this, the amplitude g_{amp}^{mid} at which the probability reaches 0.5 as well as the slope at g_{amp}^{mid} can be defined. The phase plot (Fig. 1C) reveals that g_{i0} is the most effective parameter to change g_{amp}^{mid} and, thus, the *working point* of the cell. On the other hand, σ_e and σ_i impact mainly on the slope, this way modulating the sensitivity or *gain* of the cell. The mean excitatory conductance g_{e0} shows an effect on both measures.

Recently we have shown that simplified model neurons (see Methods) subject to oscillating current injection with fixed frequency were capable to respond with a high reliability and precision in the presence of both current as well as conductance noise in a broad range of model parameters. In accordance with previous experimental studies [3], a phase locking behavior was observed for a broad range of driving frequencies and noise levels. Two different modes of frequency locking can be distinguished: *spike-rate locking*, preferably observed for low noisy current, where cell phase locked to the external stimulus by modulating its firing rate, and *spike-time locking*, preferably in models with conductance noise, where the cell phase locked to the stimulus by an adjustment of individual spike times without change in its firing rate. Interestingly, changing the amplitude of the noise allowed to continously switch between both modes.

We next investigated the reliability and precision of high-frequency input signals. We calculated the response to sinusoid conductance waveforms with low stimulus amplitude g_{amp} in the presence of conductance noise. For increasing g_{amp}, the output frequency as well as the reliability increased monotonically (Fig. 2A). The mean excitatory and
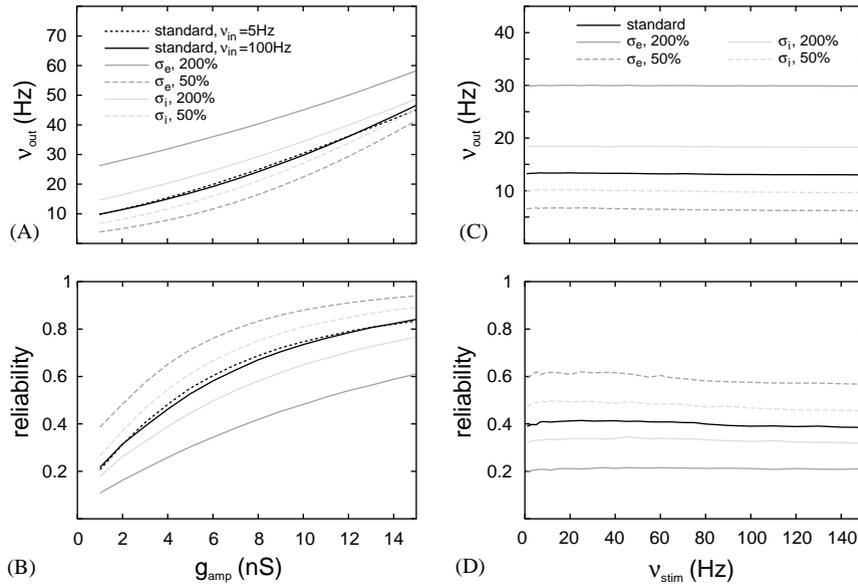
Fig. 2. Cellular response for different background parameters (relative to standard values, see Section 2). (A) Response frequency v_{out} as a function of stimulation amplitude g_{amp} for fixed input frequencies. (B) Reliability as a function of g_{amp} (legend as in A). (C) and (D) v_{out} (C) and reliability (D, for legend see C) as a function of v_{in} for fixed stimulation amplitude ($g_{amp} = 3$ nS).

inhibitory conductances had opposite effects on v_{out} and the reliability, with an increase in v_{out} and decrease in reliability with increasing g_{e0}. In the investigated parameter range, excitatory conductance was more efficient to evoke comparable changes in v_{out} or the reliability. This was also true for the effect of the noise SD, but here an increase in both σ_e and σ_i led to an increase in v_{out} (Fig. 2A) and overall decrease in the reliability (Fig. 2B).

The temporal resolution of the input, quantified by the mean SD of the output events, was low (< 2 ms) and decreased only slightly with increasing stimulation amplitude. Suprisingly, even large changes in the background parameters only minimally impacted on the ability to resolve weak periodic stimuli (Fig. 3A). Moreover, only minimal differences in the reliability and v_{out} were found when the input frequency was altered (see Fig. 2A and B, dotted lines).

For fixed stimulation amplitude, the cell locked to the sinusoid stimulus even for very high frequencies. In contrast, for cells subject to current noise, locking was lost after reaching a critical frequency (usually below 100 Hz for comparable stimulus and noise amplitudes). No dependence of the output frequency on v_{in} was found (spike-time locking, Fig. 2C). Indications for spike-rate locking could only be evidenced for very strong stimuli ($g_{amp} > 80$ nS). Noise showed a modulating impact similar to that found in simulations with variable g_{amp}, by shifting v_{out} and reliability (Fig. 2C and D). As expected, the SD of the output events decreased with increasing stimulus frequency,
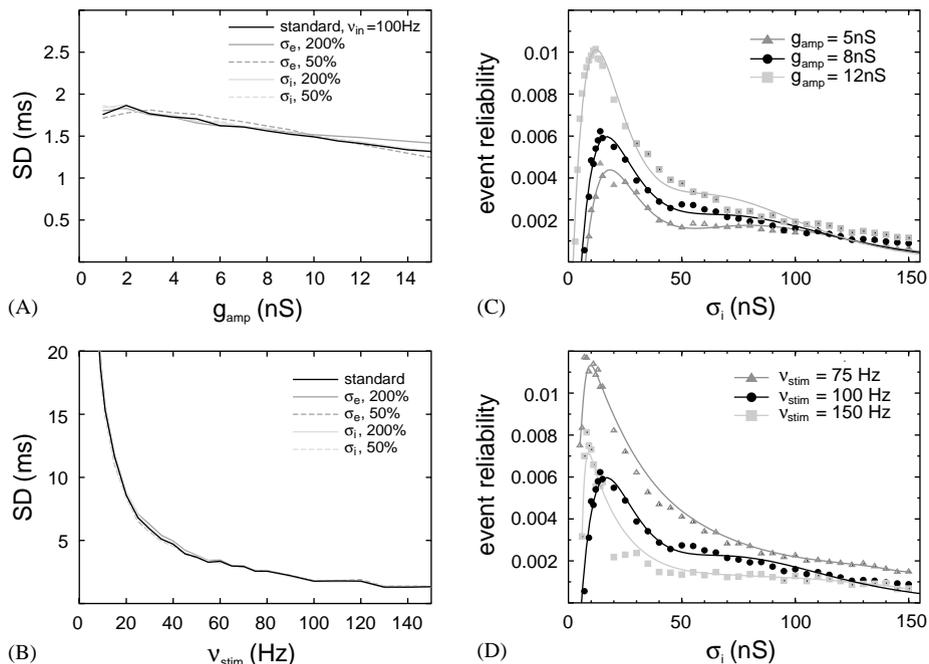
Fig. 3. (A) and (B) Average SD of the response as function of stimulation amplitude for fixed input frequencies (A), or stimulation frequency v_{in} ($g_{amp} = 3$ ns, B) for different background parameters (given relative to standard values, see Section 2). (C) and (D) Reliability for the first event in the reduced PSTHs for $v_{in} = 100$ Hz and various amplitudes (C) as a function of the noise amplitude, and for fixed stimulation amplitudes (8 ns) but different v_{in} (D). In all cases $\sigma_e = 0.4\sigma_i$.

following the stimulus time course, but was nearly unaffected by the background parameters (Fig. 3B).

To investigate further the impact of the background noise on the ability to resolve high stimulation frequencies, we continuously changed σ_e and σ_i while keeping the ratio between both parameters as well as other model parameters fixed. Whereas the precision of the response was very high and nearly unaffected by the noise and stimulation properties (not shown), the reliability of the first event was optimal only for a narrow range of noise amplitudes for both various stimulation amplitudes (Fig. 3C) and frequencies (Fig. 3D). This behavior is similar to stochastic resonance.

4. Conclusions

We investigated the impact of synaptic noise on the cellular response using a simplified models of cortical neurons. We found marked differences between the modulating effect of noise modeled as current or conductance. In the presence of conductance noise, the cell was able to resolve stimulating frequencies in the whole tested range

(up to 150 Hz and beyond) with high precision and reliability, while keeping the average firing frequency nearly constant. This corresponds to a coding scheme built on the precise timing of spikes.

On the other hand, the strength of the input translated into a change of the firing rate, with the input frequency showing only minimal impact. This suggests that both coding dimensions are not exclusive but simultaneously present to encode different aspects of the input, a view also supported by recent experimental results [4]. Conductance noise showed a modulating effect on the firing rate and reliability, while keeping the precision nearly unaffected. How these effects impact on information processing on the network level remains to be answered (research supported by CNRS and NIH).

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