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Effects of Exogenous Noise in a Silent Neuron Model: Firing Induction and EM Signal Detection

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***Abstract*— Neuronal intrinsic noise has already shown to play a constructive role in stimuli detection. Here, an exogenous noise, applied to the neuron model as a random membrane voltage perturbation, has been considered. Properly choosing its frequency band, such a noise is able to induce firing activity in a silent neuron and to enhance the detectability of an exogenous signal, representative of an electromagnetic stimulation, through the phenomenon known as stochastic resonance.**

I. Introduction

Electrical responses of excitable cells are affected by biological noise generated by different stochastic phenomena underlying cell functioning. The major sources of intrinsic noise in nervous system are the apparent randomness in the time sequence of action potentials in presynaptic neurons, the stochastic behavior of synaptic mechanisms, and the probabilistic gating of both voltage-dependent and ligand-dependent ion channels (channel noise) [1].

Recently, such an endogenous electrical noise has been widely studied, in order to evaluate its role on neuronal encoding of stimuli, evidencing that noise may enhance neuron signal detectability through the stochastic resonance (SR) phenomenon [2], [3].

In this context, recent studies conducted by the authors have evidenced the SR mechanism both in a single neuron membrane patch [4], [5] and in a myelinated nerve fiber [6], considering the stimulus as an exogenous voltage signal, representative of an external electromagnetic (EM) field stimulation. In the neuron, channel noise was accounted in a realistic way by modeling voltage-gated ion channels as a Markov process, whereas in the fiber, all sources of internal noise were modeled as a unique generator of a white Gaussian stochastic process.

Results of such studies have identified the existence of an optimum noise level, dependent on amplitude and frequency of the applied sinusoidal EM signal, which maximizes signal encoding on neuronal firing [6]. Nevertheless, such an optimum noise level, in real neurons, cannot be varied or controlled, being related to neuron typology and operating conditions. Therefore, it is worthwhile to explore the possibility that similar results can be obtained by applying to the system an exogenous amount of noise, in order to excite the neuron and to make it more responsive to a well defined exogenous EM signal.

If so, noise could be furnished from the outside to those neuronal systems where the activation threshold has raised or the endogenous noise level has lowered, due to the aging or to degenerative diseases. This possibility opens the way to suggestive medical applications, such as the optimization of the information transfer by a cochlear implant, through the noise level tuning [7].

In present work, the authors show that even exogenous noise, as long as it presents a well defined degree of correlation, may induce firing activity in a silent neuron and maximize the information transferred from the EM signal to the output spike sequence, through a SR-like phenomenon. In order to evaluate such a correlation, and thus the optimum spectral features of exogenous noise, results of studies into frequency sensitivity of both ionic channels [8] and nervous cells [9] have been taken into account.

II. Model and Methods

The used neuron model is a Hodgkin and Huxley one (HH) [10], encompassing, besides stimulation and leakage currents, sodium and potassium ones, responsible for the action potential generation. The circuital equivalent scheme, thus composed by the parallel combination of membrane capacitance, stimulation current generator, and three branches representing leakage, sodium, and potassium currents, leads to a differential equation numerically solved with time step of $1\ \mu s$.

The model presents two stable states: the resting state and the firing one, depending on the level of stimulation current I_0, being $I_0=6.3\ \mu A/cm^2$ the threshold value above which a stable firing occurs.

An exogenous EM field has been assumed to induce an additive perturbation over the membrane potential [6], [11], according to relation:

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$$\Delta V_{EM}(\theta) = \frac{1.5 ER\cos(\theta)}{\left[1+(\omega\tau)^2\right]^{\frac{1}{2}}} \quad (1)$$

being E, ω and θ, respectively, the amplitude, the angular frequency, and the direction of the exogenous EM field, R the radius of the cell, and τ the time constant of the cell membrane. In such a hypothesis, the EM signal can be considered, in the circuital representation, as a voltage generator in series with the components describing neuron model.

In order to account for the noise, two different configurations have been considered. In the first one, a current generator of a white Gaussian random process is placed in parallel with the circuital neuron model and represents the endogenous sources of noise which induces stochastic current fluctuations. In the latter one, a random voltage generator, representative of the exogenous noise, is placed in series with the neuron circuital model, as for the exogenous EM signal (Fig. 1). In both cases, the noise level is given by $(2D)^{1/2}\xi(t)$, being $\xi(t)$ a Gaussian process with unitary variance, measured in $(\mu A/cm^2)^2$ for the current noise and in mV^2 for the voltage one.

In this regard, it should be noticed that the two different modalities of inserting noise in the model will act in different ways on the membrane voltage fluctuations, which determine the action potential generation when a threshold value is crossed. Actually, current fluctuations are filtered by the parallel of capacitance and conductances of the equivalent circuit, whereas the voltage noise is directly superimposed on the membrane voltage. Therefore, in order to apply an effective exogenous noise, which does not short-circuit the membrane capacitance, the white Gaussian process should be properly filtered.

Moreover, since admittance functions of sodium and potassium channels present a low pass behavior (Fig. 2 only for sodium channel) with cut-off frequency dependent on operating membrane voltage [8], it seems advisable to excite the system with a noise having a spectral content including all the frequencies the ionic channels are sensitive to.

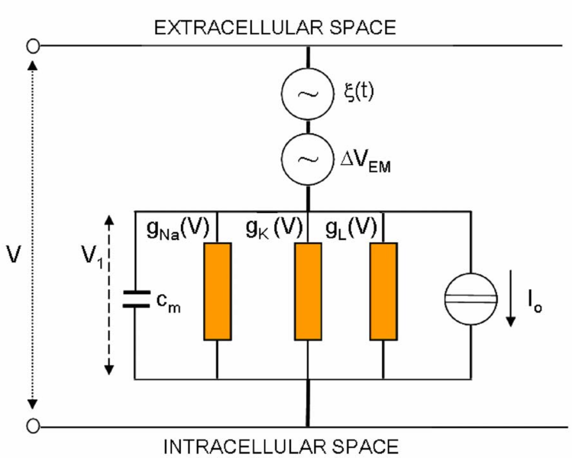

Fig. 1. Electric circuit representing neuron excitable membrane. The EM signal ΔV_{EM} is introduced as an additive perturbation over membrane voltage, as well as the exogenous noise $\xi(t)$.

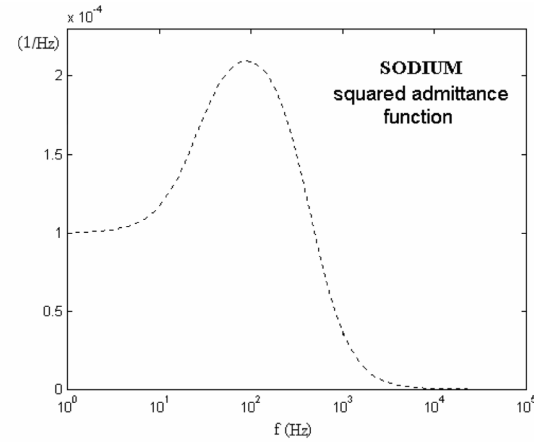

Fig. 2. Squared admittance function $|Y(f)|^2$ of sodium channel for an operating membrane voltage V=-40 mV.

In order to evaluate the EM signal detectability versus the exogenous noise level, first, time course of the membrane voltage (V) over 1 second was converted into a time series of square pulses $U(t)$, each corresponding to a spike, having height $U_H = 1$ and width 2 ms, while $U(t) = U_L = 0$ in no-firing states [2], [6]. The mean power spectral density (PSD), averaged over 200 runs of the signal $U(t)$, was calculated to extract the value of its component at the input signal frequency. Finally, such values, calculated for each exogenous noise level, were compared.

III. Results

A. Without the exogenous EM signal

Simulations of the model in the absence of the EM signal have evidenced that the exogenous noise, applied as a voltage generator driven by a white Gaussian process, is not able to induce the activity of the neuron in subthreshold conditions (I_0=6 $\mu A/cm^2$), even for high values of D (order of hundreds of mV^2). On the other hand, the effect of the same exogenous white noise on the activity of the neuron in suprathreshold conditions (I_0=7 $\mu A/cm^2$) is a complete firing inhibition for D values just above 3 mV^2 (result not shown). Therefore, as expected from previous considerations about the channels sensitivity and the time constant of the neuronal circuit model, an uncorrelated voltage perturbation does not induce firing activity, but even disrupts it.

Nevertheless, if white Gaussian noise is previously filtered with a Lorentzian filter having a cut-off angular frequency above the band of channel sensitivity (ω_c=5 kHz), a low intensity of it (D=5 mV^2) is enough to trigger off an irregular firing in a neuron stimulated with I_0=6 $\mu A/cm^2$ (Fig. 3).

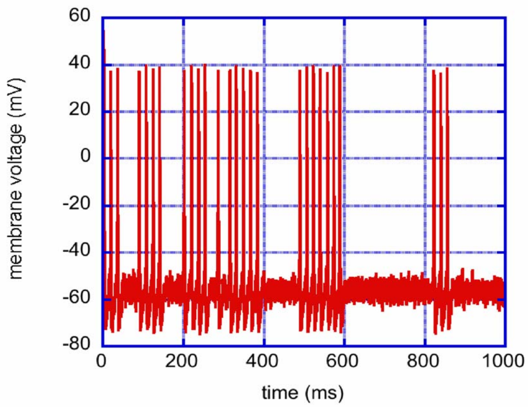

Fig. 3. Time course of the neuron membrane voltage, evidencing an irregular sequence of spikes (26 per second) induced by an exogenous voltage noise ($D=5\ mV^2$) filtered at $\omega_c=5\ kHz$, for $I_0=6\ \mu A/cm^2$.

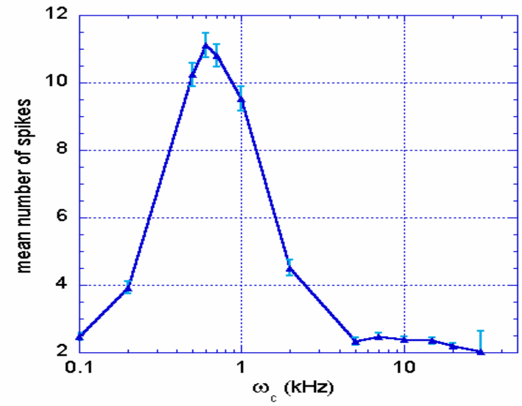

Fig. 4. Mean number of spikes and standard error, calculated over 200 membrane voltage traces *1 s* long, induced by colored voltage oscillations ($D=1\ mV^2$) on a silent neuron ($I_0=6\ \mu A/cm^2$), versus the cut-off angular frequency of the filter used to color noise.

Thus, a deeper study has been conducted over 200 membrane voltage traces in order to evaluate the effectiveness of the voltage noise in neuron excitability with respect to the cut-off angular frequency (ω_c) of the filter applied to the noise. Fig. 4, representing the mean number of induced spikes with its standard error, shows a bell-shaped behaviour, with a maximum value for ω_c equal to *600 Hz*. Such a value is coincident with the resonance frequency of PSD of subthreshold neuron voltage oscillations (see Fig. 5 reported in [12]). The shown behaviour (Fig. 4) may be explained considering that filters with low cut-off frequency remove spectral components the neuron is more sensitive to [12], whereas, for high cut-off frequencies, the neuron membrane itself filters a great part of the colored noise power.

Therefore, in order to verify that the exogenous noise may play the same role of the endogenous one [2], [3], a study has been carried out on the neuron excitability versus the noise intensity *D*, with two different choices of cut-off angular frequency. On the one hand, $\omega_c=600\ Hz$ has been chosen since the obtained colored noise is more effective in firing induction (Fig. 4); on the other hand, referring to the aforementioned PSD (Fig. 5 in [12]), an angular frequency ($\omega_c=7\ kHz$) has been considered, including all spectral components of neuronal voltage fluctuations whose power density is above 10^{-4} of the maximum value.

B. With the exogenous EM signal

Studies conducted into frequency sensitivity of HH neuron model, in the absence of noise, have evidenced different ranges of frequency (windows), related to neuron proper oscillations [3], [13], where an applied EM signal is more effective in the induction of neuronal firing.

In particular, considering a neuron stimulated with $I_0=6\ \mu A/cm^2$, the threshold amplitude for the firing generation is equal to *4 mV* for a *50 Hz* sinusoidal signal [13]. Therefore, for a sinusoidal *50 Hz* input signal with amplitude *0.7 mV*, the neuron will stay in the resting state; nevertheless, the addition of a weak colored noise makes the system fire. Moreover, as reported in Fig. 5 for a noise of $D=14\ mV^2$ ($\omega_c=7\ kHz$), the spike sequence *U(t)* presents, besides the main peak at $f_{max}=62\ Hz$, a clear component at *50 Hz*, carrying the signal information, unlike the output sequence obtained with the noise alone.

Fig. 6 reports the values of such spectral components versus the noise variance *D*, for a sinusoidal EM signal (*50 Hz* of frequency; *0.7 mV* of amplitude) and for the two chosen ω_c. As evident from the figure, in both cases, suitable levels of exogenous noise exist which optimize information transfer from input to output. In particular, for the same sinusoid amplitude, the noise filtered at $\omega_c=600\ Hz$, not only allows a better signal detection (higher maximum value of the blue line in Fig. 6), but also for lower noise variance levels. Therefore, such a colored noise, which is the most effective in firing induction (Fig. 4) seems to be also a suitable one for optimizing signal detection using minimum noise power levels.

IV. Conclusions

In this work, detectability of an exogenous EM signal has been studied in the presence of an exogenous Gaussian noise hypothesized, as well as the EM signal, to induce a perturbation over membrane voltage.

Results of such a study have shown that, unlike the endogenous noise, modeled as a random current fluctuation, a white exogenous noise is not able to excite the firing in a silent neuron.

Nevertheless, if a degree of correlation is introduced in the noise through a filtering with a suitable cut-off angular

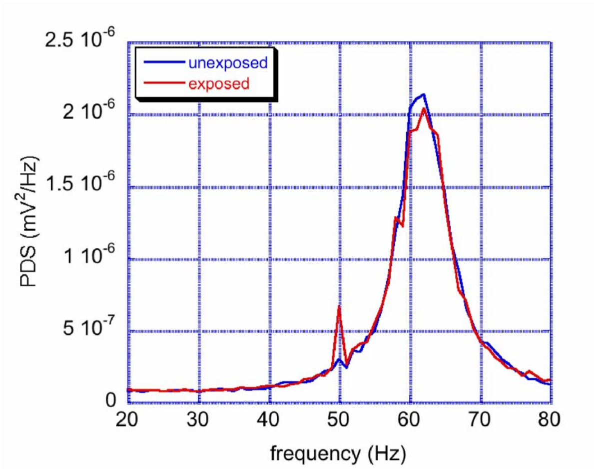

Fig. 5. Comparison of the mean PSDs of the output pulse sequences *U(t)*, calculated in the presence and in the absence of the EM signal ($f = 50$ Hz; $\Delta V_{EM} = 0.7$ mV), with an exogenous noise ($D = 14$ mV^2; $\omega_c = 7$ kHz) and $I_0 = 6$ $\mu A/cm^2$.

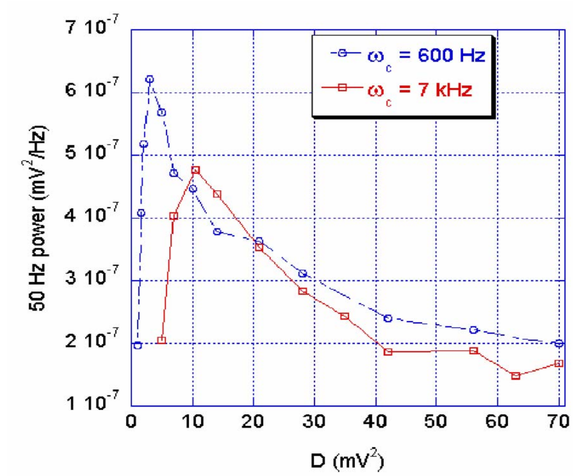

Fig. 6. Value of the component at 50 Hz of the PSD of the output spike train, for a sinusoidal signal ($f = 50$ Hz; $\Delta V_{EM} = 0.7$ mV) and two different cut-off angular frequencies ($\omega_c = 600$ Hz, $\omega_c = 7$ kHz), versus the variance D of the exogenous noise.

frequency, the exogenous noise not only induces firing activity, but also allows the frequency information about the input EM signal to transfer into the output spike train, as evidenced from spectral components of its PSD.

Moreover, an optimum noise level exists, strongly dependent on its correlation degree, that enhances such an information transfer, and thus the capability of the system to detect the EM input signal.

These results confirm the feasibility of suggestive medical applications where a suitable amount of exogenous noise is furnished to neuronal systems in order to enhance stimuli detectability [7], [14] and open the way to a more accurate design of stimulation parameters of biomedical devices.

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