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Electromagnetic Fields Detectability in Stochastic HH-Like Neuronal Systems: Stochastic Resonance Paradigm Dependent on Biological Noise

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Abstract: - Biological noise has already been shown to play a constructive role in neuronal processing and reliability, according to a phenomenon known as stochastic resonance (SR). This phenomenon has been previously observed by the authors in the detection of electromagnetic (EM) fields in the case of an additive white Gaussian input, roughly approximating the ensemble of noise sources. Recently, attention has been devoted to channel noise which plays a significant role in neuronal processing, being at the basis of some well-known behaviors like response unreliability, missing spikes during firing, or spontaneous action potentials in resting state. Here, an HH-like neuronal model is set up and accurate channels stochastic models are adopted to investigate possible noise-induced enhancements in the detection of EM fields.

Key-Words: - EM field, signal detection, HH neuronal model, channel noise, stochastic resonance

1 Introduction

Neuronal electrical activity relies on the excitable properties of the membrane ion channels, whose strongly non linear behavior allows the basic neuronal features such as action potential generation, repolarization, adaptation and accomodation. According to the variety of neuronal morphologies, several typologies of ion channels are exhibited, which can differ on both the activation mechanism (voltage-gated or ligand-dependent) and on the selectivity to specific ion kinds. Other significant parameters are the size and density of the ion channel clusters: in some neuronal areas the channels number is relatively small, whereas in areas like nodes of Ranvier a high concentration of channels, which thus act as signal boosters, is exhibited.

Typology of ionic channels and their density in different patches of membrane are therefore responsible of specific neuronal functions.

Ion channels gating presents stochastic features, due to thermal excitation of protein macromolecules with multiple stable states, inducing ionic currents fluctuations. This behavior is experimentally observed in patch-clamp recordings, which allow the detection of both single ionic currents and whole-cell membrane potentials. The amount of such fluctuations, dependent on the number and on the typology of the channels, strongly affects the neuronal behaviour playing a crucial role in the membrane excitability.

In this work, the importance of such a kind of biological noise in the detectability of an exogenous electromagnetic (EM) field has been identified, according to the phenomenon known as stochastic resonance (SR).

2 Models and Methods

2.1 Stochastic neuron model

Moving from the Hodgkin & Huxley (HH) model [1], a stochastic neuron model has been realized, taking into account current fluctuations due to random channels gating.

In the model, stochastic features of Sodium and Potassium channels have been represented with a state machine, whose activity is described by a Markov process [2]. A numerical implementation of such a Markov chain has been adopted, based on extracting random numbers (Monte Carlo Method) to track the state of every protein subunit of each single channel [3, 4].

The neuron dynamic behavior is described by the system of differential equations (1,3):

$$C_m \frac{dV}{dt} = -I_{Na}(t) - I_K(t) - I_{leak} + I_0 \quad (1)$$

$$I_{Na} = g_{Na} \frac{N_{open}^{Na}(t)}{N_{TOT}^{Na}} (V - E_{Na}) \quad (2)$$

$$I_K = g_K \frac{N_{open}^{K}(t)}{N_{TOT}^{K}} (V - E_K) \quad (3)$$

being $N_{open}^{Na}(t)$ and $N_{open}^{K}(t)$ the istantaneuous number

of open Na and K channels calculated through the stochastic channel models. The total number of Na and K channels ($N_{TOT}^{Na}(t)$, $N_{TOT}^{K}(t)$) can be varied on the basis of the considered neuron typology. According to HH model, besides Sodium, Potassium and Leakage currents, an external current I_0 is taken into account, representative of the global synaptic stimulation coming from neighboring neurons.

2.2 Biophysical role of channel noise

Ion channels stochastic gating induces fluctuations on ionic currents, usually referred to as channel noise [5]. The amplitude of such fluctuations is strictly dependent on channels number, according to (4):

$$CV = \sqrt{\frac{1-p}{p}} \cdot \frac{1}{\sqrt{N_{TOT}}} \tag{4}$$

where the coefficient of variation CV depends on the open probability p and decreases with the number N_{TOT} of channels. For sake of simplicity all simulations in this paper are compared fixing the channels density (ρ_K=18 channels/μm^2, ρ_{Na}=60 channels/μm^2), so that variations in the number N_{TOT} correspond to different areas of the considered membrane patch.

Channel noise has been shown to be responsible for a variety of biophysical neuronal behaviors such as missing spikes during firing, spontaneous action potentials during rest and subthreshold intrinsic oscillations [6]. During suprathreshold stimulations, the stochastic HH model displays a firing activity, with occasional missing spikes, not observed with deterministic (noise-free) model. During subthreshold stimulations, the model exhibits a noisy baseline around the resting potential, but occasional spontaneous spikes are generated (Fig. 1).

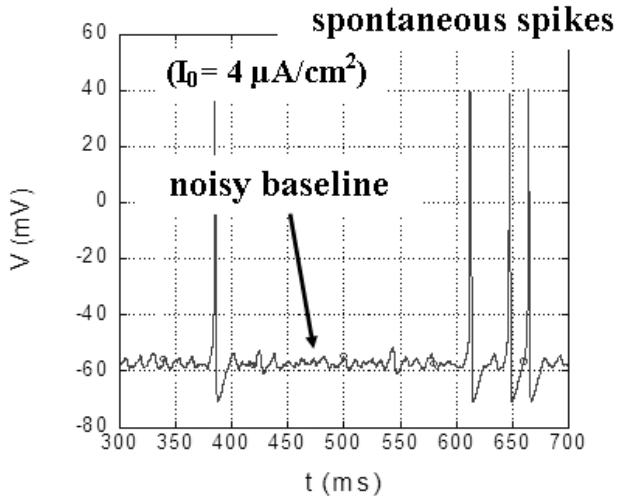

Fig. 1: Noisy baseline and spontaneous spikes in a subthreshold stochastic neuron model.

The number of these action potentials is strictly related to noise intensity: the lower is the number of channels (higher noise), the more spikes will be generated. As a result, the output power will increase with noise, as can be evaluated considering the power spectrum of the output membrane voltage for several patch areas (result not shown).

Such a behavior is related to the HH equations describing an intrinsic bistable system, which can be studied in the phase space (Fig. 2). When the input stimulation is suprathreshold, the system describes periodic stable oscillations (limit cycle), related to firing activity. When the state trajectory is close to the resting state conditions, noisy fluctuations may take the system into the attracting influence of the resting state, thus leading to missing spikes. On the other hand, in the case of subthreshold stimulations, the system moves around the resting state, and noise may occasionally bridge the small distance with the limit cycle. The system will then exhibit a spontaneous action potential and then relax again to the resting state (Fig. 2).

2.3 Electromagnetic signal detectability

An exogenous EM field has been assumed to induce an additive perturbation over the membrane potential, according to the relation (5) [7]:

$$\Delta V_{EM}(\theta) = \frac{1.5ER\cos(\theta)}{\left[1+(\omega\tau)^2\right]^{\frac{1}{2}}} \tag{5}$$

being E, ω and θ, respectively, the amplitude, the frequency and the direction of the exogenous EM field, R the radius of the cell, and τ the time constant of the cell membrane.

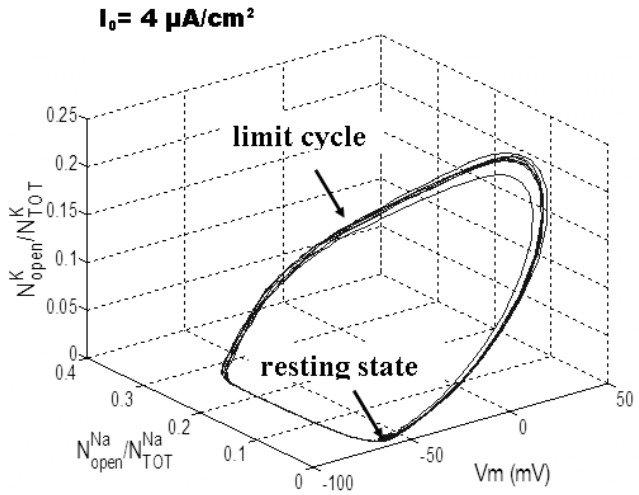

Fig. 2: Phase space diagram of the stochastic neuronal model for a membrane patch area of 200 μm^2 in subthreshold stimulation condition.

In such a hypothesis, the exogenous EM field can be considered, in a circuital representation, as a voltage generator in series with the components describing the neuron model (Fig. 3).
The additive EM voltage term over membrane potential perturbs the activity of the voltage-dependent ion channels, whose gating is modulated by the membrane voltage.
In order to evaluate the detectability of such a kind of exogenous signal, it should be remembered that neurons encode information in the output spike rate and timing. This is related to a nonlinear encoding process, where every crossing of a voltage threshold corresponds to an action potential generation. The presence of a periodic oscillation, like a weak sinusoidal EM signal, may therefore modulate firing activity, which will exhibit a coherent component with the input signal, as confirmed by the power spectrum (Fig. 4) of the system output. In our simulations the time course of membrane voltage is converted in a time series *U(t)* of standard pulses, each one correspondent to an action potential. This procedure has been adopted to remove the noisy oscillations on the output biosignal (V_m), as well as the superimposed EM signal. This implies isolating the information related to spike time occurences (known to be the most significant in neuronal encoding) and allows therefore a more robust analysis in the frequency domain. The spectrum, calculated averaging over 200 realizations in order to reduce standard error, reveals a clear component at the same frequency of the applied EM field (f=50 Hz). Therefore, the EM signal detectability could be evaluated calculating the signal to noise ratio (SNR) from the power spectra in the presence and in the absence of the EM perturbation; however, for big membrane areas (low noise), the additive energy introduced by the EM signal is no more neglectable, making the power density values of the spectrum always higher than those evaluated in the absence of the EM signal.

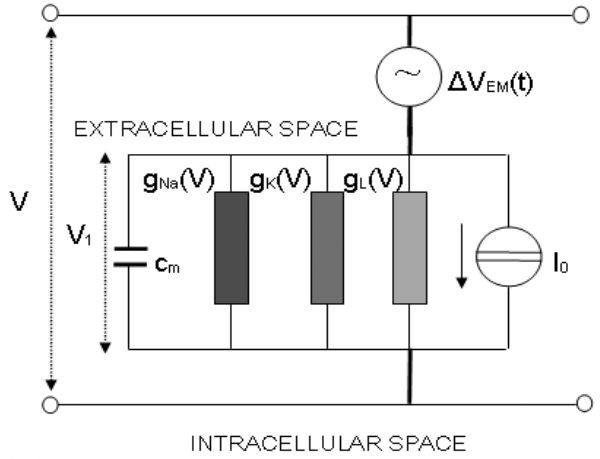

Fig. 3: Circuital representation of the neuron model and the equivalent electromagnetic signal.

Therefore, a more reliable observable is the Cross Power Spectrum [8], described in the block diagram of Fig. 5, which directly links the system output *U(t)* with the input EM signal, allowing a robust estimation of signal detectability.

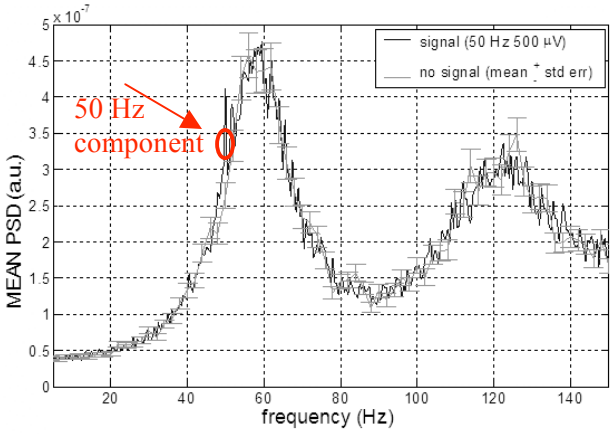

Fig. 4: Comparison between the power spectral densities of the spikes train in the presence and in the absence of the EM sinusoidal signal (amplitude ΔV_{EM}=500 μV; frequency f=50 Hz) in subthreshold condition (I_0=4 μA/cm^2) and for a well-defined noise level (patch area A=64 μm^2).

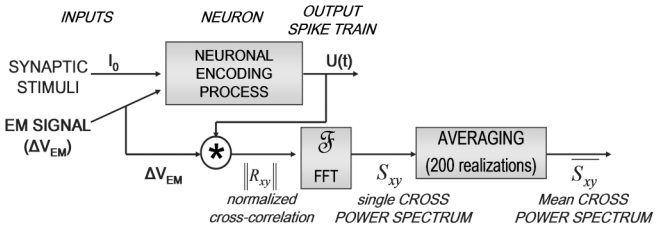

Fig. 5: Block diagram representing the procedure used for the cross power spectrum calculation.

3 Results

To investigate the role of biological noise in neuronal capability of detecting an exogenous EM signal, the aforementioned cross power spectrum of the neuron pulses train *U(t)* has been evaluated for various patch areas, corresponding to different noise levels. The neuron model has been stimulated with a subthreshold current (I_0=4 μA/cm^2), so that for internal noise level close to zero, i.e. for bigger patch areas, no spikes are present. In addition, a weak sinusoidal EM signal (ΔV_{EM}=300 μV; f=50 Hz) has been applied.
The mean cross pover spectrum, calculated over 200 realizations (Fig. 6), shows a typical bell shaped curve, with a maximum in correspondence of a well-defined internal noise level. This phenomenon, already evidenced in a neuron when an external Gaussian noise is applied [9,10], is known as stochastic

resonance, and consists in the optimization of the response of a system to a weak external stimulus, in correspondence of a particular amount of noise [11].

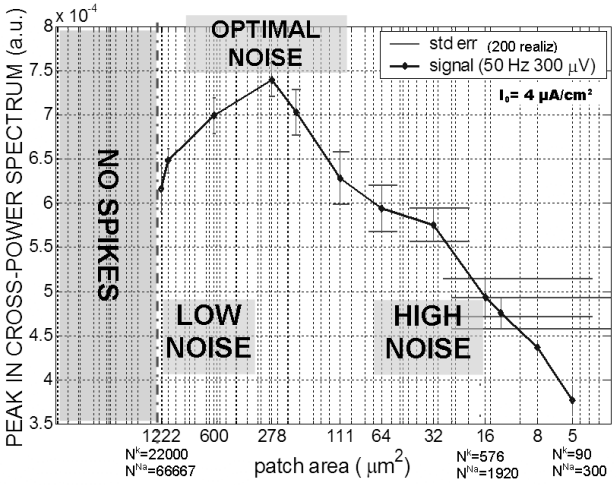

Fig. 6: Mean cross power spectrum of the neuron pulses train *U(t)* versus channel noise, quantified with the patch areas and the related number of *Na* and *K* channels, for a subthreshold stimulating current (I_0=4 μA/cm^2) and a sinusoidal EM signal (ΔV_{EM}=300 μV; f=50 Hz).

Since such a noise is strongly dependent on typology and density of channels embedded in the membrane patch, different kinds of neuronal cells (with various channel numbers) may detect EM signals in a very different way. Therefore possible induced EM effects will vary according to the considered specific neuron.

4 Conclusions

In this work neuronal capability to detect EM signals has been investigated in the presence of biological noise. For this purpose stochastic models representing ion channels activity have been introduced into the HH neuron. This allows the model to capture the basic features of neuronal stochastic excitability and to reproduce some important aspects of neuronal signal transduction [12]. In these conditions signal detectability has been evaluated calculating the cross power spectrum, which indicates a stochastic resonant behavior.

This implies that neurons with different channels number and typology may detect EM signals differently, and the induced effects may also vary. Such a phenomenon is likely to depend on the mean synaptic current and on the EM frequency and amplitude, which will be the subject of future investigations.

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