INTERACTION OF NEURONAL ACTIVITY WITH AN EM PERTURBATION IN A NOISY ENVIRONMENT: MODELING FIRING AND BURSTING NEURONS.

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INTRODUCTION

The process of neuronal encoding is rather complex: embedded in a noisy environment, neurons operate a spatial and temporal integration of the input stimuli, encoding them into firing or bursting patterns which carry information on the inputs in both spike rate or timing [1]. Therefore accurate models of neurons able to reproduce realistic behaviors such as bursting activity are required. Here a double compartment neuron model, which accounts for both axo-somatic and dendritic areas related to various neuronal morphologies is realized and characterized in order to simulate a variety of firing and bursting responses. Noise arising from stochastic gating of ionic channels is accurately modeled, thus allowing the system to capture the basic features of neuronal activity observed with experimental recordings [2]. An exogenous electromagnetic (EM) field can be thought of as inducing a perturbation on membrane potential, thus acting as an input of the neuronal encoding process. A field-related signal is therefore introduced in the model, and numerical simulations are performed to investigate possible effects in both bursting and firing statistical features and temporal responses.

MODELS AND METHODS

The neuron model is realized through the electrical coupling of two compartments, described as Hodgkin-Huxley like oscillators. Various neuronal morphologies can be represented simply adjusting model parameters like coupling conductance and the area ratio between compartments [3].
Sodium and Potassium channels with fast dynamics are introduced in the compartment representing the axo-somatic excitable membrane, while slow dynamics ionic channels are placed in the compartment accounting for dendritic tree (1).
V_f and V_s being membrane voltage of fast and slow compartment, I_{Na}, I_K, I_{NaP} and I_{KS} the ionic currents, C_m the membrane capacity, g_c the coupling conductance and p the area ratio between dendritic and axo-somatic compartments.

$$\begin{aligned} C_m \frac{dV_f}{dt} &= -I_{Na} - I_K - I_{leak_f} - \frac{g_c}{p}(V_f - V_s) + I_f \\ C_m \frac{dV_s}{dt} &= -I_{NaP} - I_{KS} - I_{leak_s} - \frac{g_c}{1-p}(V_s - V_f) + I_s \\ \frac{dy}{dt} &= \phi_y\left(\alpha_y(V)(1-y) - \beta_y(V)y\right) \end{aligned} \tag{1}$$

Channel noise has been shown to play 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 [4]. Here ionic channel stochastic gating is described by the introduction of an additive random term in the equation of the gating particles. This process is assumed to be Gaussian with zero mean and standard deviation depending nonlinearly on the fraction of open channels and membrane potential, and inversely on total number of channels. Applying an input constant current with increasing values, the system displays a variety of output regimes, ranging from a strongly periodic bursting to a chaotic one, and finally to a multiple tone and a regular firing. Channel noise effects on neuronal activity are studied in comparison with data from experimental recordings [5].
An exogenous EM field in the ELF range is introduced as an additive perturbation over membrane potential, with amplitude dependent on frequency and intensity of the internal E field, as well as on the geometrical features and the time constant of the modeled structure, according to [6] and reported in (2).

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

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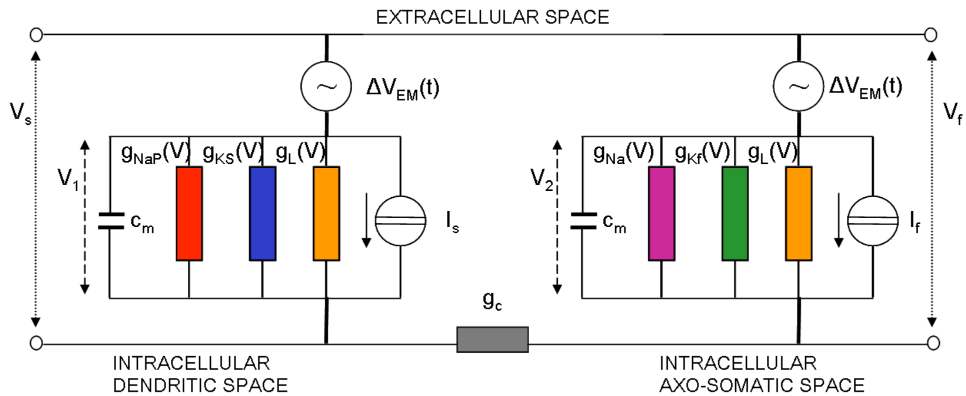


Fig. 1. Electric circuit representing the neuronal model. The fast and slow compartments are coupled through an electrical conductance and the field-induced EM signal is introduced with voltage generators in series with ionic channels conductances.

R being cell radius, τ the circuit time constant, and θ the angle between membrane normal and the direction of the exogenous field, whose intensity and frequency are indicated with E and ω respectively

The complete circuital scheme adopted for this study can be summarized as in Fig. 1, where it is possible to identify the two compartments (slow and fast dynamics) the coupling conductance g_c and the two *in series* generators accounting for the induced EM-ELF field. Field-induced effects are evaluated in the presence of biological noise on both temporal output regimes and statistics of bursting and firing.

RESULTS

Simulations performed in the presence of biological noise of different intensities resulted into significant variations of the output temporal regimes displayed by the system. Some behaviors exhibited by the noise-free model such as weakly periodic bursting and 4-tones firing were replaced by chaotic bursting, whose stimulation range resulted broadened. An analysis of system stable states was also conducted in the phase space, explaining the mechanisms at the basis of such noise-induced output changing. Such variations, exhibited even for low noise levels, well capture the output temporal regimes observed in [5] for the experimental registrations of an isolated crustacean stomatogastric ganglion (Fig. 2 for a 3% noise level).

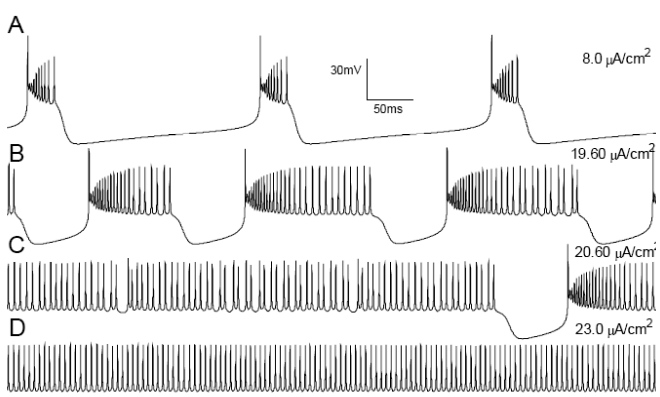


Fig. 2.a Simulated output regimes in the presence of 3% noise in the ionic channel activating gating variable. Traces are obtained for different values of the stimulation current I_f.

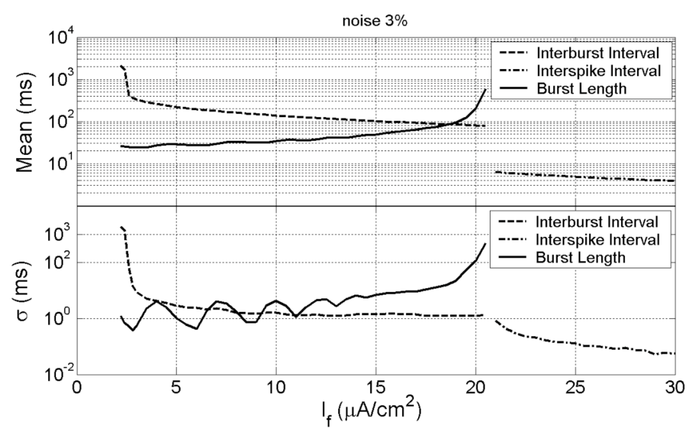
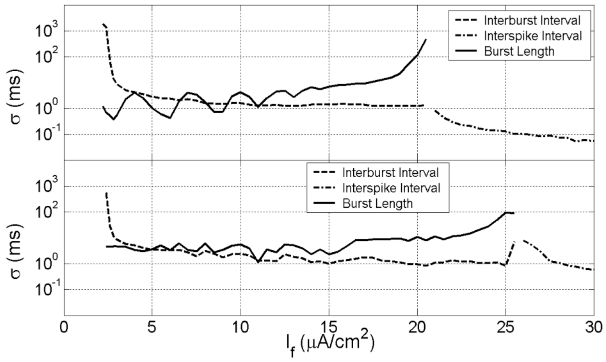


Fig. 2.b Course of IBI, BL and ISI mean versus stimulation current, in the case of 3% noise in both fast and slow compartment. A good agreement is shown with the experimental data reported in [5].



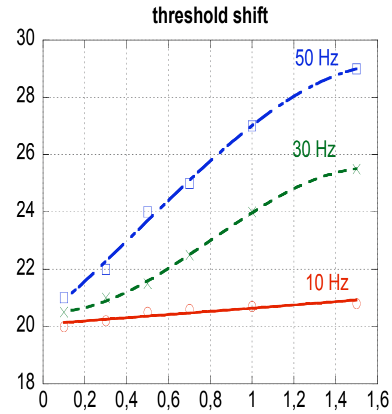


Fig. 3.a Same as Fig.2.b in the presence of a 50 Hz field-induced sinusoidal signal with amplitude 500 μV. A clear right-shift in the transition threshold between bursting and firing is shown.

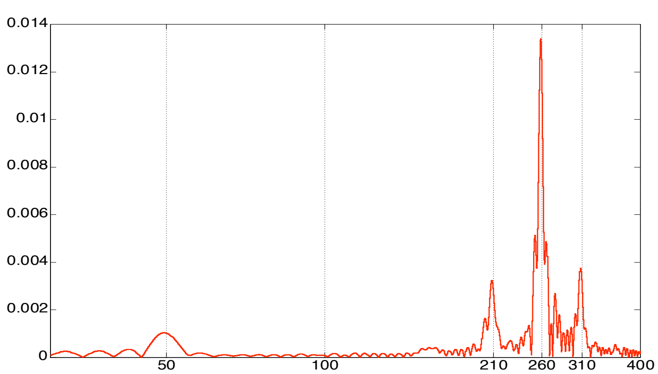
Fig. 3.b Transition threshold between bursting and firing is amplitude and frequency dependent.

As for the firing and bursting statistics, a good qualitative agreement with experimental data is shown for the course of both mean and standard deviation versus stimulation current (Fig. 2.b). Due to its realistic behavior, the model is assumed suitable for bioelectromagnetic studies.

Simulations in the presence of a field-induced sinusoidal additive signal with frequency 50 Hz and amplitude from 10 to 1000 μV have been performed, showing a significant shift in the transition threshold between bursting and firing regimes (Fig. 3.a). This means that bursting can occur when firing was exhibited in unexposed conditions. Such an effect increases with field amplitude, and frequency sensitivity is also shown (Fig. 3.b)

The analysis of the power spectrum reveals the presence of a component at the frequency of the input EM signal, which accounts for the neuronal encoding of the exogenous EM field. Moreover, two peaks around the firing frequency are visible (Fig. 4.a).

Moreover, looking at the neuron behavior for what concerns its ability of information encoding by means of spike time occurrence, it is possible to observe that during firing, the presence of a sinusoidal ELF signal can induce periodic oscillations, coherent with the EM signal, visible (for 50 Hz) with a 2-D tracking of the ISI vector, which circles around the mean value. This effect is dependent on signal amplitude (fig. 4.b).



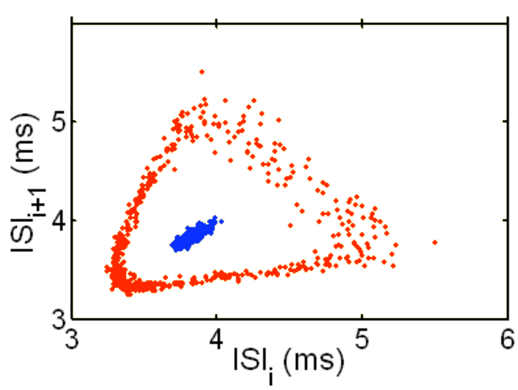


Fig. 4.a Power spectrum reveals the presence of a component at 50 Hz (EM signal), and two peaks around the firing frequency.

Fig 4.b Spike jitter representation performs a 2-D tracking of the ISI vector, which circles around the mean value.

DISCUSSION AND CONCLUSIONS

The proposed neuron model exhibits a variety of output regimes, related to different neuronal morphologies. Channel noise modeling allows the system to reproduce a realistic behavior on both temporal and statistic features of firing and bursting, making it suitable for investigations concerning interaction with EM fields.

The introduction of an EM field induces periodic oscillations in spike occurrences, thus modulating neuronal encoding process. Moreover, a clear shift of the transition threshold between bursting and firing is shown, dependent on field amplitude and frequency. This kind of realistic modeling may help the understanding of EM coupling with the Nervous System, leading to the comprehension of possible effects on neuronal encoding and memory processes.

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