Feedback Effects in Simulated Stein's Coupled Neurons[⋆]

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Abstract. A network consisting of two Stein-type neuronal units is analyzed under the assumption of a complete interaction between the neurons. The firing of each neuron causes a jump of constant amplitude of the membrane potential of the other neuron. The jump is positive or negative according to whether the firing neuron is excitatory or inhibitory.

Making use of a simulation procedure designed by ourselves, we study the interspike intervals of the two neurons by means of their histograms, of some descriptive statistics and of empirical distribution functions. Furthermore, via the crosscorrelation function, we investigate the synchronization between the neurons firing activity in the special case when one neuron is excitatory and the other is inhibitory.

1 Introduction

The dynamics of a pair of Stein's neuronal units serially connected has been recently analyzed under the hypothesis that they are subject to excitatory and inhibitory stimuli with constant or alternating rates ([6], [7]). Making use of an ad hoc simulation procedure designed by ourselves, various quantitative results have been already obtained. In particular, the existence has been disclosed of an "optimal" value for the amplitude γ of the jumps of the membrane potential of the second unit (the "receiving neuron") attained as effect of the firing of the first unit (the "sending neuron"). We also studied the reaction time, defined as the random time elapsing between a firing of the sending neuron and the subsequent firing of the receiving neuron. The reaction times have been analyzed in [7], under the assumption of constant inhibitory rate, for both constant and alternating excitatory rates, with emphasis on the effects of various choices of γ and of the amplitude of the refractory period.

The model described in [6] and [7] is re-considered here under the novel assumption that a complete interaction between the two neurons exists. The

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effect of the firing of each neuron is a sudden constant magnitude jump of the membrane potential of the other neuron.

By means of our simulations, we obtain the neurons interspike intervals (ISIs) histograms and their empirical distribution functions. The synchronization of the firing activity of the neurons is studied in the special case in which one neuron is excitatory and the other is inhibitory.

We point out that the analysis of firing activity of coupled neurons under various mutual interactive paradigms is particularly relevant in various respects: for instance, it is known that the cerebellar cortex includes pairs of coupled neurons, which has motivated some previous studies (see, for instance, [4] and [5]). Synchronization will be studied via the firing times crosscorrelation function (see [2]). Furthermore, by means of the autocorrelation function, we have been able to disclose particular patterns of spikes elicited by each single neuron.

2 The Method

In previous papers we analyzed the behavior of two coupled neuronal units that interact according to a sending-receiving model, assuming that an unidirectional connection from the first to the second neuron exists. We now present a statistical analysis of the firing activity of the two neurons under the hypothesis of complete interaction. For each neuronal unit, changes in the membrane potential between two consecutive spikes are described by the Stein's differential equation; however, the further hypothesis is now added that whenever a neuron fires, the membrane potential of the other neuron undergoes a jump of constant magnitude. Let $\{[X_1(t), X_2(t)];\ t \geq 0\}$ be the stochastic process describing the time-evolution of the membrane potential of the pair of neurons between consecutive firings. We consider the following stochastic differential equations:

$$\mathrm{d}X_1(t) = -\frac{1}{\tau}\, X_1(t)\,\mathrm{d}t + \alpha\,\mathrm{d}N_1^+(t) - \beta\,\mathrm{d}N_1^-(t) + \gamma_1\,\mathrm{d}M_2(t) \qquad (1)$$

$$\mathrm{d}X_2(t) = -\frac{1}{\tau}\, X_2(t)\,\mathrm{d}t + \alpha\,\mathrm{d}N_2^+(t) - \beta\,\mathrm{d}N_2^-(t) + \gamma_2\,\mathrm{d}M_1(t), \qquad (2)$$

where τ is the positive time constant according to which, in absence of stimuli, the membrane potential exponentially decays to the resting level. The effects of excitatory and inhibitory stimuli, that are assumed to occur according to independent Poisson processes, consist of instantaneous jumps of the membrane potential of magnitudes α and $-\beta$, respectively, where α and β are positive constants. The stochastic processes $N_i^+(t)$ and $N_i^-(t)$ $(i = 1, 2)$ in the above equations are assumed to be independent time-homogeneous Poisson processes describing the arrival of excitatory and inhibitory stimuli on the i-th neuronal unit originating from the environment. Processes $M_1(t)$ and $M_2(t)$ count the number of firings produced in [0,t] by the first and second neuron, respectively. The amplitude of the jump of the first (second) neuron membrane potential caused by the spike of the second (first) neuron is γ_1 (γ_2). Its value is positive or negative according to the excitatory or inhibitory nature of the firing neuron.

As implied by Eqs. (1) and (2), in absence of stimuli the neuronal membrane potential exponentially decays with time constant τ to the resting level that, without loss of generality, is set to be 0. A firing occurs when the membrane potential of a neuronal unit crosses the constant firing threshold S. We also assume that after each firing a refractory period of fixed duration takes place, at the end of which the membrane potential is reset in the neighborhood of the resting level according to some probability density. Here we shall assume that the reset occurs according to some probability density. Here we shall assume that the reset occurs according to the truncated Gaussian probability density $f(x) = C\, e^{-x^2/2}$, $-3 < x < 3$.

Since an analytical solution of the membrane potential dynamics for the model described by Eqs. (1) and (2) is not available, a Monte-Carlo simulation method has been devised and implemented by us. This procedure, described in [6], is very suitable for the statistical description of coupled neurons firing activity.

3 Statistical Results on ISIs

In this Section we study the dependence of interspike intervals of both neurons on parameters γ_1 and γ_2. Hereafter we shall focus our attention on three related matters: (i) to discuss the shape exhibited by ISIs histograms, (ii) to calculate the relevant statistical indices of ISIs, and (iii) to perform some comparisons between ISIs empirical distribution functions.

3.1 ISI Histograms

A measure of the variability in the timing of the sequence of spikes generated by the neurons is provided by the histograms interspike intervals. We consider the case in which the first neuron is excitatory whereas the second may possess excitatory or inhibitory nature. Computational results based on extensive simulations show that when the second neuron sends large inhibitory inputs, the probability mass of first neuron's ISI spreads over the temporal axis. The opposite occurs for large positive values of γ_1, i.e. when the second neuron is highly excitatory (see, for instance, Figure 1).

Feedback effects appear in the firing activity of the two coupled neurons. For instance, if the first neuron is excitatory and causes a jump of amplitude γ_2 of the membrane potential of the second neuron, then the interspike intervals of the latter exhibit a dependence on the behavior of γ_1. This is shown in Figure 2, where the second neuron ISI histograms are more spread when $\gamma_1 < 0$.

3.2 Some Statistical Indices of ISIs

Some relevant descriptive statistics of both neurons' ISIs are analyzed in this Section. The intrinsic symmetry property of the model, evident from Eqs. (1) and (2), is reflected in the ISIs statistical indices. The mean of the first neuron's

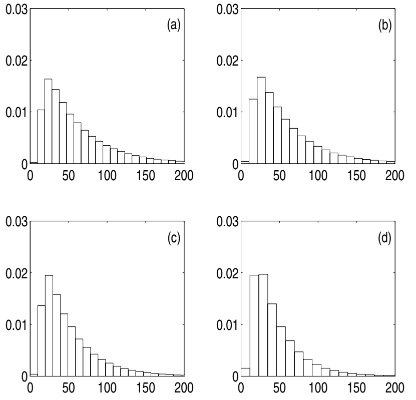

Fig. 1. First neuron's ISI histograms for $\gamma_2 = 2$ and (a) $\gamma_1 = -2$, (b) $\gamma_1 = -1$, (c) $\gamma_1 = 1$, (d) $\gamma_1 = 2$

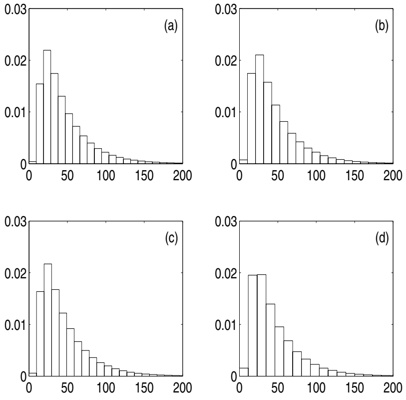

Fig. 2. Second neuron's ISI histograms for $\gamma_2 = 2$ and (a) $\gamma_1 = -2$, (b) $\gamma_1 = -1$, (c) $\gamma_1 = 1$, (d) $\gamma_1 = 2$

ISI evaluated for the couple of parameters (γ_1, γ_2) equals the mean of second neuron's ISI for (γ_2, γ_1). A similar behavior is exhibited also by the standard deviation and by the coefficient of variation of the interspike intervals.

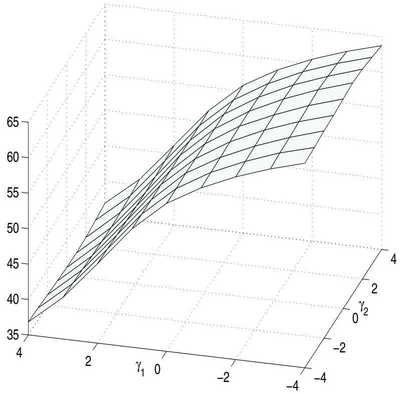

Fig. 3. Mean of first neuron's ISI

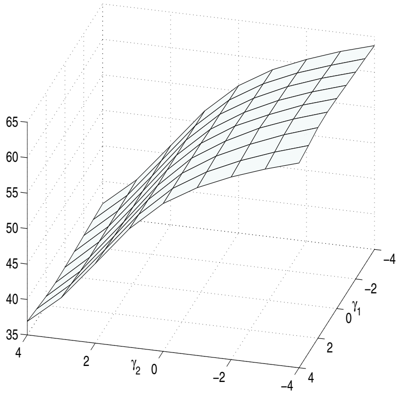

Fig. 4. Mean of second neuron's ISI

The mean of the first neuron's ISI decreases when γ_2 is fixed and γ_1 increases. Similarly, the mean of second neuron's ISI decreases for fixed γ_1 when γ_2 increases (see Figures 3 and 4). Moreover, mean of first neuron's ISI is larger (smaller) than the mean of the second neuron's ISI when γ_2 is larger (smaller) than γ_1. The means of the two neurons' ISIs are closer when γ_1 approaches γ_2, and viceversa. These remarks suggest that firing activity properties of the couple of neurons are globally dependent on the difference between γ_1 and γ_2.

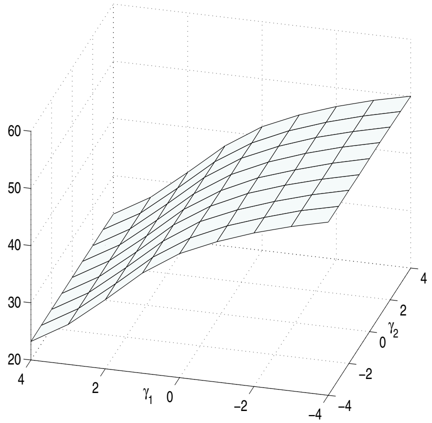

Fig. 5. Standard deviation of first neuron's ISI

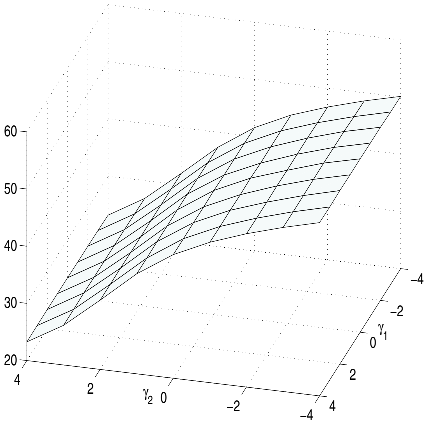

Fig. 6. Standard deviation of second neuron's ISI

Similar remarks about symmetry hold for the standard deviation (see Figures 5 and 6) and for the coefficient of variation (see Figures 7 and 8). Both statistical indices for the ISI of the first neuron decrease when γ_1 increases and γ_2 is fixed. By symmetry, the standard deviation and the coefficient of variation of the second neuron's ISI decrease when γ_1 is fixed and γ_2 increases. Moreover, if γ_1 is larger (smaller) than γ_2, the standard deviation and the coefficient of variation of second neuron's ISI are larger (smaller) than those of first neuron's ISI.

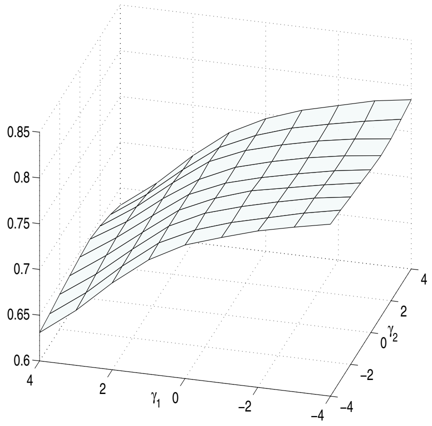

Fig. 7. Coefficient of variation of first neuron's ISI

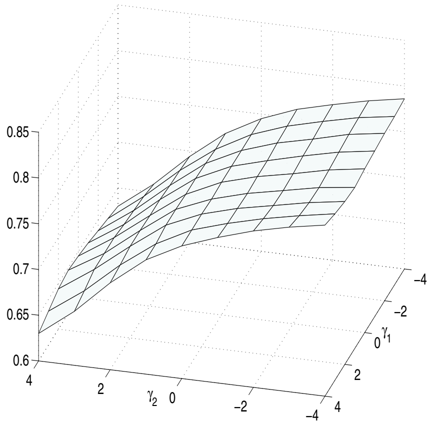

Fig. 8. Coefficient of variation of second neuron's ISI

3.3 ISIs Distribution Functions

Due to the symmetry of the model, first neuron's ISI distribution function is identical to that of the second neuron when the values of parameters γ_1 and γ_2 are exchanged. An example of this property is shown in Figures 9 and 10, where the ISIs cumulative distribution functions of first and second neuron are plotted for some choices of γ_1 and γ_2, respectively.

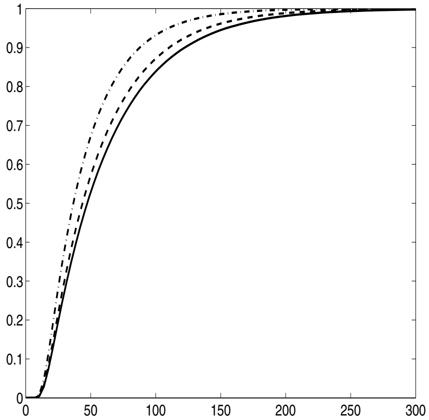

Fig. 9. First neuron's ISIs distribution functions for $\gamma_2 = 2$, and $\gamma_1 = -2$ (solid line), $\gamma_1 = 0$ (dashed line), $\gamma_1 = 2$ (dashed-dotted line)

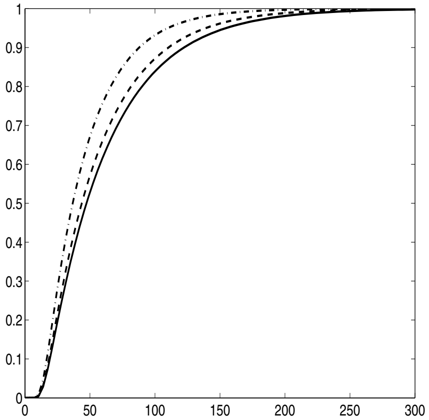

Fig. 10. Second neuron's ISIs distribution functions for $\gamma_1 = 2$, and $\gamma_2 = -2$ (solid line), $\gamma_2 = 0$ (dashed line), $\gamma_2 = 2$ (dashed-dotted line)

Comparing first neuron's ISIs distribution functions for different values of γ_1 we notice that the cumulative distribution function becomes larger when γ_1 increases (see Figure 9). The same property holds for the second neuron's ISI distribution function when γ_2 increases (see Figure 10). This suggests the existence of some kind of stochastic ordering. Indeed, denoting by $Y_i^{(\gamma_1,\gamma_2)}$ the random variable describing the i-th neuron interspike intervals and by $H_i^{(\gamma_1,\gamma_2)}(t)$ its distribution function ($i = 1, 2$), for $\delta > 0$ we have:

$$H_1^{(\gamma_1,\gamma_2)}(t) \leq H_1^{(\gamma_1+\delta,\gamma_2)}(t) \quad \text{and} \quad H_2^{(\gamma_1,\gamma_2)}(t) \leq H_2^{(\gamma_1,\gamma_2+\delta)}(t), \quad \text{for all } t \geq 0. \tag{3}$$

Eq. (3) shows that

$$Y_1^{(\gamma_1,\gamma_2)} \geq_{st} Y_1^{(\gamma_1+\delta,\gamma_2)} \quad \text{and} \quad Y_2^{(\gamma_1,\gamma_2)} \geq_{st} Y_2^{(\gamma_1,\gamma_2+\delta)},$$

where $\geq_{st}$ denotes the usual stochastic order. (For the definition of usual stochastic order see, for instance, [9]).

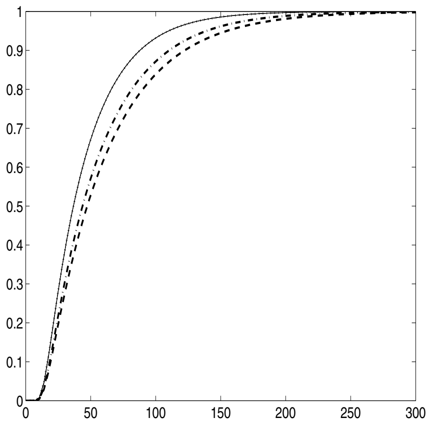

Fig. 11. ISIs distribution functions for the first neuron, with $\gamma_1 = 2$ (solid line), and for the second neuron, with $\gamma_2 = -2$ (dashed line), $\gamma_2 = 0$ (dashed-dotted line), $\gamma_2 = 2$ (dotted line)

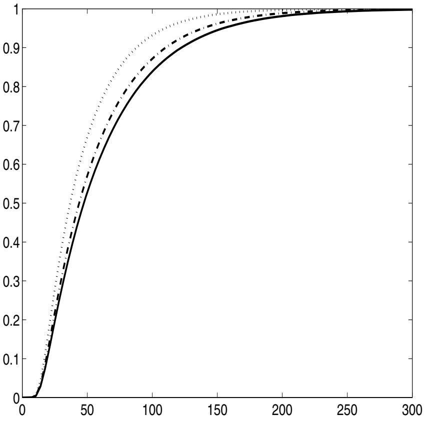

Fig. 12. ISIs distribution functions for the first neuron, with $\gamma_1 = -2$ (solid line), and for the second neuron, with $\gamma_2 = -2$ (dashed line), $\gamma_2 = 0$ (dashed-dotted line), $\gamma_2 = 2$ (dotted line)

Let us now compare the ISIs distribution functions of the two neurons. We note that when γ_1 is larger (smaller) than γ_2, the first neuron's ISI distribution function is larger (smaller) than that of second neuron. The distribution functions are equal when $\gamma_1 = \gamma_2$. Hence, since

$$\begin{aligned} H_1^{(\gamma_1,\gamma_2)}(t) &\geq H_2^{(\gamma_1,\gamma_2)}(t), \quad \text{for all } t \geq 0, \text{ with } \gamma_1 \geq \gamma_2, \\ H_1^{(\gamma_1,\gamma_2)}(t) &\leq H_2^{(\gamma_1,\gamma_2)}(t), \quad \text{for all } t \geq 0, \text{ with } \gamma_1 \leq \gamma_2, \end{aligned}$$

we conclude that

$$Y_1^{(\gamma_1,\gamma_2)} \leq_{st} Y_2^{(\gamma_1,\gamma_2)} \quad \text{for} \quad \gamma_1 \geq \gamma_2 \quad \text{and} \quad Y_1^{(\gamma_1,\gamma_2)} \geq_{st} Y_2^{(\gamma_1,\gamma_2)} \quad \text{for} \quad \gamma_1 \leq \gamma_2.$$

Figures 11 and 12 show the distribution functions of the two neurons' ISIs for different values of (γ_1, γ_2).

4 Entropies and Correlation Functions

Information theory is widely used in neuronal coding to quantify the information on the received stimuli conveyed by the neural response [3]. Aiming to obtain a measure of information on the coupled neuronal activity, hereafter we consider the following discrepancy measure between the distributions of $Y_1^{(\gamma_1,\gamma_2)}$ and $Y_2^{(\gamma_1,\gamma_2)}$:

$$I_{(Y_1,Y_2)}^{(\gamma_1,\gamma_2)} = \int_0^{+\infty} h_1^{(\gamma_1,\gamma_2)}(u) \log \frac{h_1^{(\gamma_1,\gamma_2)}(u)}{h_2^{(\gamma_1,\gamma_2)}(u)} \, \mathrm{d}u, \tag{4}$$

$$I_{(Y_2,Y_1)}^{(\gamma_1,\gamma_2)} = \int_0^{+\infty} h_2^{(\gamma_1,\gamma_2)}(u) \log \frac{h_2^{(\gamma_1,\gamma_2)}(u)}{h_1^{(\gamma_1,\gamma_2)}(u)} \, du. \tag{5}$$

Here, $h_i^{(\gamma_1,\gamma_2)}(t)$ denotes the probability density function (pdf) of $Y_i^{(\gamma_1,\gamma_2)}$ $(i = 1, 2)$. Functions $I_{(Y_i,Y_j)}^{(\gamma_1,\gamma_2)}$ $(i, j \in \{1, 2\}, i \neq j)$ are called relative entropies, or discrimination measures. They provide a measure of the inefficiency of assuming that the probability density function of interspike intervals is $h_j^{(\gamma_1,\gamma_2)}(u)$ when the true p.d.f. is $h_i^{(\gamma_1,\gamma_2)}(u)$.

According to the nature of our simulation scheme, $I_{(Y_1,Y_2)}^{(\gamma_1,\gamma_2)}$ and $I_{(Y_2,Y_1)}^{(\gamma_1,\gamma_2)}$ are evaluated by means of a discretization of the right-hand sides of Eqs. (4) and (5). Figures 13 and 14 show the ISIs relative entropies as γ_1 and γ_2 vary. The symmetry is again evident by comparing these entropies. We point out that, as expected, the minimum of such functions is attained for $\gamma_1 = \gamma_2$.

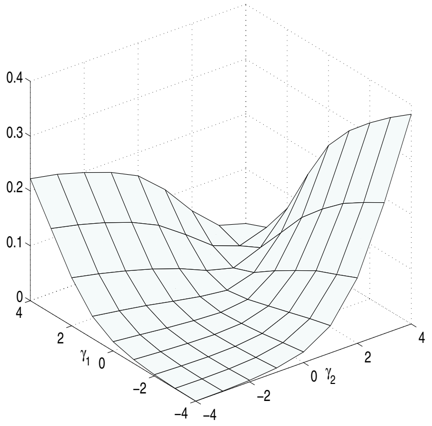

Fig. 13. Relative entropy of first neuron's ISI for some choices of γ_1 and γ_2

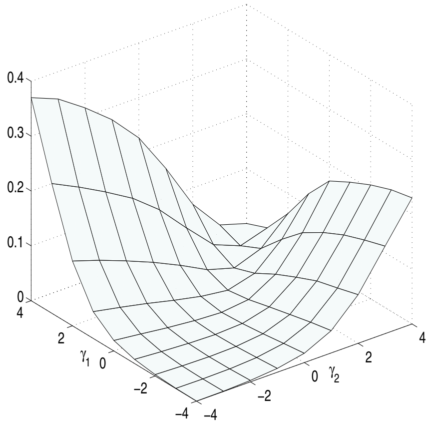

Fig. 14. Relative entropy of second neuron's ISI for some choices of γ_1 and γ_2

Let us denote by $\{T_n^i, n \in \mathbb{N}\}$ the stochastic process describing i-th neuron firing time $(i = 1, 2)$, where T_n^i denotes the random time in which the i-th neuron $(i = 1, 2)$ fires for the n-th time $(n \in \mathbb{N})$. We adopt the following definition of autocorrelation function (see [1] for a more general definition):

$$AC^i(\tau) = \frac{\sum_k (T_{k+j}^i - \overline{T}^i)(T_k^i - \overline{T}^i)}{\sum_k (T_k^i - \overline{T}^i)^2} \quad (i = 1, 2), \tag{6}$$

where $\overline{T}^i = \dfrac{1}{n_{tot}} \sum\limits_n T_n^i$ is the mean firing time of the i-th neuron, with n_{tot} denoting the total number of spikes released by the i-th neuron. The index j appearing in the right-hand-side of (6) is larger than k, and it is such that $T_{k+j}^i - T_k^i = \tau$.

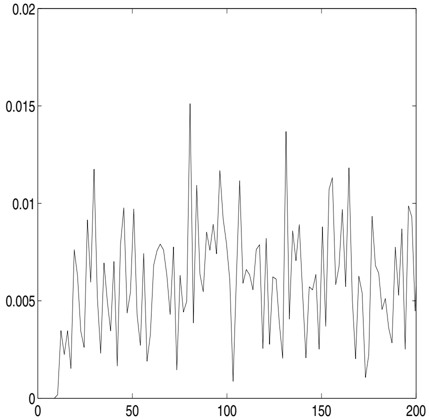

Fig. 15. First neuron's autocorrelation function for $\gamma_1 = -1$ and $\gamma_2 = 2$

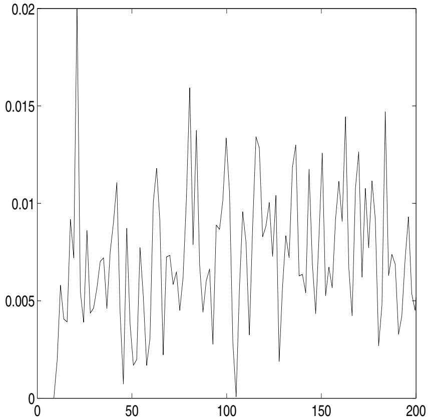

Fig. 16. Second neuron's autocorrelation function for $\gamma_1 = -1$ and $\gamma_2 = 2$

As Eq. (6) shows, the autocorrelation function is an even function of τ that may take both positive and negative values. When τ is small, the firing times T^i_{k+j} and T^i_k involved in $T^i_{k+j} - T^i_k = \tau$ are very close, and the autocorrelation function takes positive values. On the contrary, for large values of τ we have observed negative values for the function $AC^i(\tau)$. A plot of the autocorrelation function when the first neuron is excitatory and the second inhibitory is shown in Figures 15 and 16. Second neuron's autocorrelation function is larger than that of the first neuron and shows numerous peaks. Hence, for the second neuron's firing times, some lags are more likely than others: in particular, for the case described in Figure 16, the firing times show a very frequent lag of about 30 ms.

Aiming to analyze the synchronization between the two neurons firing activity we consider the crosscorrelation function defined as:

$$CC^1(\tau) = \frac{\sum_k (T^1_{k+j} - \overline{T}^1)\,(T^2_k - \overline{T}^2)}{\sqrt{\sum_k (T^1_k - \overline{T}^1)^2}\,\sqrt{\sum_k (T^2_k - \overline{T}^2)^2}}, \tag{7}$$

$$CC^2(\tau) = \frac{\sum_k (T^2_{k+m} - \overline{T}^2)\,(T^1_k - \overline{T}^1)}{\sqrt{\sum_k (T^1_k - \overline{T}^1)^2}\,\sqrt{\sum_k (T^2_k - \overline{T}^2)^2}}, \tag{8}$$

where $\overline{T}^i$ is the mean firing time of the i-th neuron ($i = 1, 2$), and $j \geq 1$ ($m \geq 1$) is such that $T^1_{k+j} - T^2_k = \tau$ ($T^2_{k+m} - T^1_k = \tau$). Due to Eqs. (7) and (8) it is

$$CC^1(\tau) = CC^2(-\tau), \qquad \tau > 0.$$

Figure 17 shows $CC^1(\tau)$ when $\gamma_1 = -1$ and $\gamma_2 = 2$. The peak exhibited by this function at the lag -1.75 ms suggests that the second neuron is very likely to fire about 1.75 ms after a spike of the first neuron. The crosscorrelation function $CC^1(\tau)$ for $\gamma_1 = 1$ and $\gamma_2 = -1$ is plotted in Figure 18. In this case the crosscorrelation function does not show significant peaks.

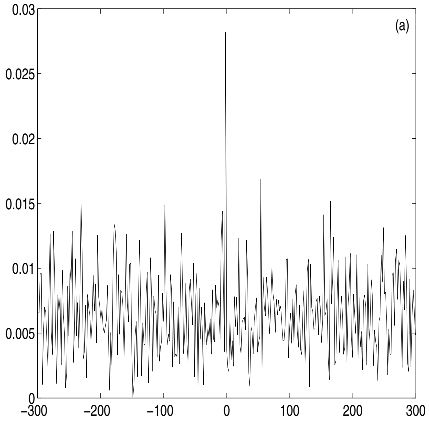

Fig. 17. Crosscorrelation function in the case $\gamma_1 = -1$ and $\gamma_2 = 2$

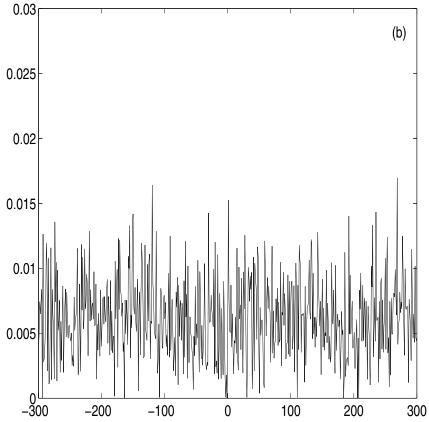

Fig. 18. Crosscorrelation function in the case $\gamma_1 = 1$ and $\gamma_2 = -1$

5 Concluding Remarks

Under the assumption of complete interaction between the neurons, the firing activity of the coupled Stein-type neuronal units is characterized by the presence of evident feedback effects. These effects can be observed looking at the shape of histograms of neurons interspike intervals when both γ_1 and γ_2 are different from 0 (see Section 3.1).

The comparison between the means of the ISIs of the two neurons suggests that the firing activity properties of the pair of neurons are globally dependent on the difference between γ_1 and γ_2. Indeed, in Section 3.2 it is emphasized that the mean of the first neuron's ISI is larger (smaller) than that of the second neuron's when γ_2 is larger (smaller) than γ_1, and is equal to the mean of the second neuron's ISI when $\gamma_1 = \gamma_2$. The standard deviation and the coefficient of variation show a similar behavior. Moreover, in Section 3.3 the analysis of ISIs distribution functions proves the existence of a stochastic ordering between the random variables describing the two neurons interspike intervals.

Finally, the crosscorrelation function studied in Section 4 when the coupled neurons have different nature, reveals the phase-locked connection between the neurons firing activity existing when γ_1 and γ_2 take very distant opposite values.

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