ELSEVIER

Neurocomputing 44–46 (2002) 1149–1153

NEUROCOMPUTING

www.elsevier.com/locate/neucom

A spike train analysis for quantifying inhibitory near synchrony in spike firings

David C. Tam*

Department of Biological Sciences, University of North Texas, Denton, TX 76203, USA

Abstract

We introduce a multiple single-unit spike train analysis method to detect the inhibitory synchrony in spike firings. This paper focuses on inhibitory synchrony among neural firings, while excitatory synchronized firings are often considered in recent years. The present analysis provides a phase-plane analysis that is used to determine the inhibitory phase-locking characteristics of spike firings in a set of three simultaneously recorded neurons. The absence of points in the three-neuron phase plane provides a signature of the inhibitory synchrony phase-locked characteristics in these neurons.

Keywords: Spike train analysis; Near synchrony; Inhibitory interactions

1. Introduction

One of the frequently observed characteristics in neural firing is synchronized spike firing in the central nervous system (CNS). There have been numerous reports characterizing the significance of synchronized firing in the CNS. Excitatory synchronized firings had been implicated in the processing of neural signals in biological networks that correlate with sleep and wakefulness brain states. Yet, these analyses often focused on excitatory synchronization rather than inhibitory synchronization.

Since inhibitory synchronizing may play an important role in the processing of signals in the CNS, this paper focuses on establishing a spike train analysis technique that detects the inhibitory synchrony of spike firings. We extend the spike train analysis method introduced earlier [9] to include inhibitory near synchrony in this present paper. We apply a two-dimensional phase-plane analysis to quantify the phase relationships among three simultaneously recorded neurons.

* Tel.: +1-940-565-3261; fax: +1-940-565-4136.
E-mail address: dtam@unt.edu (D.C. Tam).

0925-2312/02/$ - see front matter
PII: S0925-2312(02)00441-1

We introduced a three-wise cross-correlation method to detect three-way correlation among three neurons since classical cross-correlation method only performs primarily pair-wise correlation. Normally, a three-dimensional (3D) correlogram is required to detect a three-way correlation, we introduced a method that will collapse the 3D space into 2D space without loss of generality. Although there is degeneracy in reducing the plotting dimension of the correlation graph, the reduction in random variable actually allows us to provide a time-scale invariant measure to quantify the near synchrony. In other words, the current method can detect near synchrony in microsecond-scale, millisecond-scale, or even second-scale, using the same algorithm.

This analytical method is an extension of a number of novel spike train analyses introduced to detect the spike firing patterns from single neuron analysis [2] to two-neuron analysis [7,8], and to three-neuron analysis in the present paper.

2. Three-way correlation spike train analysis

This three-neuron spike train analysis is a graphical quantitative measure based on the phase differences of spike firings among these three neurons. Let us select three neurons from a network of neurons for analysis, and then iterate this same analysis for all neurons within the network.

Let these neurons be denoted as A, B and C, and the time of occurrence of each spike is recorded as the spike train for each neuron. The lead time is defined as the time difference between the firing of a spike in the reference neuron and a previous spike in another neuron. The lag time is similarly defined as the time difference between the firing of a spike in the reference neuron and a succeeding spike in another neuron. These lead and lag times can be considered as the phase difference between two neurons, although conventionally phase difference is defined with respect to the firing frequencies rather than firing times.

Using this alternate definition, the phase difference in spike firings of neurons A and B can be quantified as the depending on sign of the time difference between neuron A and neuron B's firings. This phase difference (actually time difference) is plotted on the x-axis to produce a phase plot for phase-plane analysis. Similarly, the lead and lag times between the spike firings of neurons A and C can be quantified as phase differences (time differences), which are plotted on the y-axis of the phase plot.

Using this method, the lead and lag times between three neurons (i.e., the spike firings of neurons B and C with respect to neuron A) can be graphically represented as phase differences (time differences) in a (2D) plot rather than a (3D) plot.

Although there existed spike train analysis for three-neuron correlation, such as the "snow-flake diagram" of Perkel et al. [3], the snow-flake analysis requires a non-orthogonal three-axis snow-flake representation rather than the two-axis orthogonal Cartesian representation. The current analysis is also different from the joint peri-stimulus time histogram (JPSTH) of Aertsen et al. [1] because external stimulus is required to produce the JPSTH, and the origin of the plot represents the onset of the stimulus in the JPSTH. No external stimuli are required for our analysis. It is also different from the joint-interspike (JISI) analysis of Rodieck et al. [4] which is a two-neuron corre-

lation. Similarly, it is different from the non-linear analysis return map [5,6] because JISI and return maps describe the timing relationship of a single neuron rather than a three-neuron analysis.

3. Theoretical methods

To investigate the inhibitory effects, we will define the excitatory interaction first. The inhibition can be deduced from the absence of spikes below the baseline firing level. That is, when the neuron is "expected" to fire probabilistically from the statistical analysis but did not, then it is likely that the spikes were suppressed. (The baseline uncorrelated firing is used as the *null hypothesis* in our test.)

Using the same notation as in the previous paper [9], let us define the excitatory interactions first, then the inhibitory interactions. Let the three spike trains of neurons A, B and C be represented by $a(t)$, $b(t)$, and $c(t)$, respectively. Let us select $a(t)$ as the reference spike train with a total of N spikes, which is represented by

$$a(t) = \sum_{n=1}^{n=N} \delta(t - t_n) \tag{1}$$

and the compared spike trains to be cross correlated be denoted by $b(t)$ and $c(t)$, with a total of L and M spikes, respectively:

$$b(t) = \sum_{l=1}^{l=L} \delta(t' - t_l),$$

$$c(t) = \sum_{m=1}^{m=M} \delta(t - t_m), \tag{2}$$

where t_n, t_l and t_m are the occurrence times of nth, lth and mth spikes in spike trains $a(t)$, $b(t)$, and $c(t)$, respectively, and $\delta(t)$ is a delta function denoting the occurrence of a spike at time t.

Let us define the cross-interval, CI, between two neurons as the time interval between adjacent spikes in two spike trains. Let us also define the "pre-cross-interval" (pre-CI) as the CI before the reference spike, and the "post-cross-interval" (post-CI) as the CI after the reference spike.

The kth order pre-CI relative to the nth reference spike in the reference spike train, $a(t)$, with respect to spike trains $b(t)$ and $c(t)$ are defined as

$$\begin{aligned} \tau'_{n,-k} &= |t'_{l-k+1} - t_n| = t_n - t'_{l-k+1}, \\ \tau'_{n,-k} &= |t'_{m-k+1} - t_n| = t_n - t'_{m-k+1}, \end{aligned} \tag{3}$$

respectively, as described previously [9]. The joint number pairs of Eq. (3) are plotted as the coordinates in the 2D phase plot. The kth order post-CIs can analogously be defined as above for the pre-CIs.

With the pre-CIs and post-CIs plotted for all spikes in the reference neuron, a distribution of points can be obtained in the phase plot. Normalizing the distribution will produce a probability density function (pdf), of the kth order pre-CI between the compared train, $b(t)$, and the nth spike in the reference train $a(t)$. With this probability density function established, the inhibitory interactions among three neurons can be revealed as a decrease in firing probability relative to the control uncorrelated distribution (in the null hypothesis). The uncorrelated probability distribution is simply the joint product of the pre-CIs and post-CIs using standard probability theory.

4. Theoretical interpretations

The phase relationship (time difference) in the compared neurons B and C with respect to neuron A can be characterized by the distribution of points in the 2D phase plot. Near-synchronous firings are identified as a band of points lying along the diagonal line of the phase plot. Synchrony that is excitatory in nature can be identified as bands of points phase-locked together parallel the diagonal line. Synchrony is inhibitory in nature can be identified as absence of points along the diagonal band, i.e., below the baseline level.

In order to clearly show the level of inhibition (or excitation) beyond the control level (null hypothesis), a difference phase plot can be used. The difference phase plot is constructed by obtaining the difference between the pdfs of the above phase plot and the joint product phase plot (for the uncorrelated case as the control). The difference phase plot will revealed that a negative pdf profile indicates an inhibitory interaction, a positive pdf profile indicates an excitatory interaction, and a flat-zero pdf profile indicates no interactions among these three neurons.

5. Results

The result of the phase-plot analysis is that three-neuron spike firing interactions can be quantified by the distribution profile of a 2D plot without resorting to a 3D representation. The phase-plane analysis can be used to represent the probability of spike firing relative to one another based on the relative time differences (phase differences). The pdf of uncorrelated firings (without synchrony) can be obtained using the joint product of pre-CIs and post-CIs. Synchronized correlated firing can be revealed by the diagonal bands of the phase plot. Excitatory synchrony is revealed by the positive probability density profile in the difference phase plot. Inhibitory synchrony is revealed by the negative probability density profile in the difference phase plot.

Using this analysis, synchrony which is inhibitory in nature can be detected. Since inhibitory synchrony is often exhibited as non-firing of spikes, inhibitory synchrony are often missed in conventional spike train analysis observations since no spikes are present. The present analysis recovers the inhibitory interactions resulted in synchrony even though spikes were suppressed in the synchrony.

6. Summary

Inhibitory synchrony among the spike firing in three neurons can be revealed by a difference phase-plot analysis as introduced. This difference phase-plane analysis provides a graphical representation of the correlated spike firings among three neurons. Inhibitory interactions, are characterized by the negative probability profile in the difference phase plot. Inhibitory synchrony among three neurons can be detected by the diagonal band of negative probability profile in the difference phase plot.

References

[1] A.M.H.J. Aertsen, G.L. Gerstein, M.K. Habib, G. Palm, Dynamics of neuronal firing correlation: modulation of effective connectivity, J. Neurophysiol. 61 (1989) 900–917.
[2] M.A. Fitzurka, D.C. Tam, A joint interspike interval difference stochastic spike train analysis: detecting sequential changes in the firing trends of single neurons, Biol. Cybernet. 80 (1999) 309–326.
[3] D.H. Perkel, G.L. Gerstein, M.S. Smith, W.G. Tatton, Nerve-impulse patterns: a quantitative display technique for three neurons, Brain Res. 100 (1975) 271–296.
[4] R.W. Rodieck, N.Y.-S. Kiang, G.L. Gerstein, Some quantitative methods for the study of spontaneous activity of single neurons, Biophys. J. 2 (1962) 351–368.
[5] K.A. Selz, A.J. Mandell, Critical coherence and characteristic times in brain stem neuronal discharge patterns, in: T. McKenna, J. Davis, S. Zornetzer (Eds.), Single Neuron Computation, Academic Press, San Diego, CA, 1992, pp. 525–560.
[6] C.E. Smith, A heuristic approach to stochastic models of single neurons, in: T. McKenna, J. Davis, S. Zornetzer (Eds.), Single Neuron Computation, Academic Press, San Diego, CA, 1992, pp. 561–588.
[7] D.C. Tam, A cross-interval spike train analysis: the correlation between spike generation and temporal integration of doublets, Biol. Cybernet. 78 (1998) 95–106.
[8] D.C. Tam, A spike train analysis for detecting temporal integration in neurons, Neurocomputing 26–27 (1999) 1055–1060.
[9] D.C. Tam, A multi-unit spike train analysis for quantifying phase relationships of near-synchrony firings, Neurocomputing 38–40 (2001) 945–949.

David C. Tam is an associate professor at the University of North Texas. He holds a Ph.D. in physiology, and three B.S. degrees in computer science, physics and astrophysics, all from the University of Minnesota. His current research interest is developing statistical multiple spike trains analysis techniques and applying these analytical methods to both simulated and experimental neurophysiological data to understand the signal processing functions of the central nervous system (CNS) as well as extracting the encoding schemes used by the CNS.