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Detecting neuronal activity changes using an interspike interval algorithm compared with using visual inspection

Yu Liu, John M. Denton, Brett P. Frykberg, Randall J. Nelson *

Department of Anatomy and Neurobiology, University of Tennessee Health Science Center, 855 Monroe Avenue, Memphis, TN 38163, USA

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Abstract

A universally accepted method for efficiently detecting neuronal activity changes (NACs) in neurophysiological studies has not been established. Visual inspection is still considered to be one of the most reliable methods, although it is limited when it is used for analyzing large quantities of data. In this study, an algorithm that considers interspike intervals (ISIs) was developed to define the onset of NACs. Two criteria, involving the mean and the standard deviation (S.D.) of the ISIs during a control period, were used in the ISI algorithm to evaluate the NACs that occurred during a detection period. The first, an ISI decrease of more than 1 S.D. from the mean ISI of the control period, proved to be an effective criterion for qualifying the increased NACs (firing rate increases). The second, an ISI increase greater than 3 S.D.s, efficiently demarcated periods of decreased NACs (firing rate decreases). Statistically significant correlations between the detection of NAC onset times by the ISI algorithm and the detection of those times by visual inspections were observed after offline analyses of recorded neuronal activity. The present results suggest that this ISI algorithm is a reliable and efficient way of defining the onset of NACs.

Keywords: Interspike interval; Neuronal activity; Visual inspection

1. Introduction

Techniques for analyzing neuronal spike trains exist and have been reviewed recently (Kass et al., 2005). These, however, may be difficult to implement under certain conditions, such as for online determinations, and may not yield results that differ greatly from simpler techniques, particularly when specifying the onset of neuronal activity changes (NACs). Determining NACs may be crucial when selecting individual neurons for further study either online or offline. Moreover, detecting the onset of NACs on a trial-by-trial basis is frequently needed in neurophysiological studies (DiCarlo and Maunsell, 2005; Liu et al., 2005; Ventura et al., 2005). Techniques available, however, are not always satisfactory for this purpose. Even the most commonly used cumulative sum (CUSUM) technique has some disadvantages (Ellaway, 1978; Davey et al., 1986). Churchward et al. (1997) suggested that CUSUM techniques may fail to detect NACs for single trial data when there are larger variations in interspike intervals (ISIs). CUSUM techniques also may introduce timing delays between actual and detected onsets. Human visual inspection is still considered to be one of the most reliable methods available for NAC onset detection (see Churchward et al., 1997, for details), but it also has certain limitations. For example, it is cumbersome for analyzing large quantities of data.

The limitations of these techniques caused us to seek a new method that is as reliable as visual inspection and also more efficient in processing large databases. Understanding that NACs stem from significant changes in ISIs, we focused our attention on establishing analytical criteria that may mirror the detection of changes in spike records achievable by visual inspection. Toward this end, an ISI algorithm was developed with plausible ISI variation limits to define the onset of NACs. A preliminary report using our application of ISI algorithm for analyzing cortical neuronal activity in behaving monkeys has been published (Liu et al., 2005). The present study systematically examined the algorithm to investigate more fully its reliability and utility in neurophysiological studies.

2. Methods

We use two terms to describe neuronal activity changes. “Increased NACs” occur when the ISIs in an examined period

* Corresponding author. Tel.: +1 901 448 5979; fax: +1 901 448 7193.
E-mail address: rnelson@utmem.edu (R.J. Nelson).

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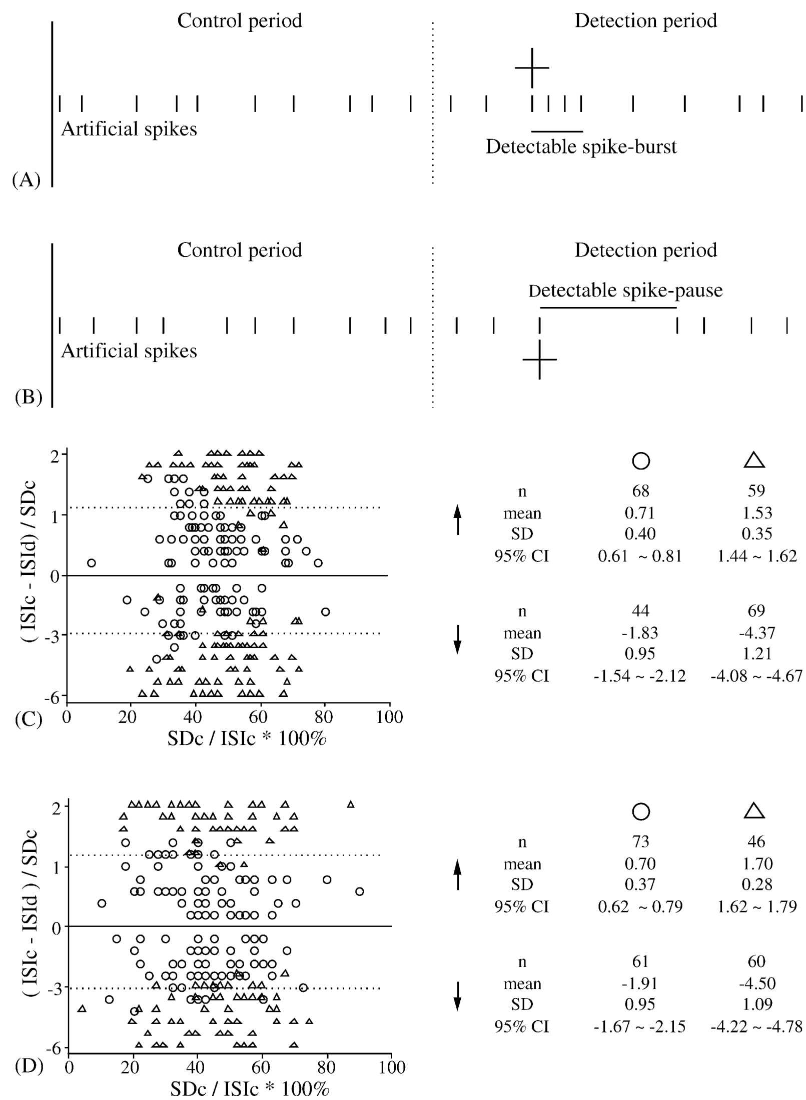
are shorter than during a reference period. “Decreased NACs” occur when ISIs are longer than during the reference period. Four steps were taken to evaluate the ISI algorithm when determining the onset of NACs. First, we used visual inspection to establish criteria for defining the onset of longer or shorter ISIs in artificial neuronal activity records generated by computer. Second, we used an offline application implementing our ISI algorithm to examine neuronal activity records sampled from primary motor cortical neurons. Third, the same sample of records was inspected by three examiners. Finally, correlations between analyses using the ISI algorithm and visual inspection were examined.

2.1. Visual detection of pattern changes of artificial spikes

Two examiners with experience in electrophysiological techniques participated in the visual inspection of computer-generated neuronal activity records. These examiners were naive about how these records were constructed. The artificial spike trains were generated by a Matlab 7^{TM} program and displayed on a computer display. In each visual inspection trial, artificial spikes were displayed over two periods—a control period and a detection period, each representing a 1-s period. No time scale, however, was displayed to avoid possible referential or distractive influence on the examiners (Fig. 1). Two types of control



(C)

		○	△
↑	n	68	59
	mean	0.71	1.53
	SD	0.40	0.35
	95% CI	0.61 ~ 0.81	1.44 ~ 1.62
↓	n	44	69
	mean	-1.83	-4.37
	SD	0.95	1.21
	95% CI	-1.54 ~ -2.12	-4.08 ~ -4.67

(D)

		○	△
↑	n	73	46
	mean	0.70	1.70
	SD	0.37	0.28
	95% CI	0.62 ~ 0.79	1.62 ~ 1.79
↓	n	61	60
	mean	-1.91	-4.50
	SD	0.95	1.09
	95% CI	-1.67 ~ -2.15	-4.22 ~ -4.78

Fig. 1. Results of visual inspection of artificial spike trains. (A and B) Trials with a detectable spike burst and a detectable spike pause, respectively. Crosses indicated movable cursors for marking the onsets of spike burst or spike pause highlighted by horizontal solid lines. No time scale was displayed during visual inspection to avoid possible referential or distractive influence on the examiners. (C and D) Scattergrams showing the effect of interspike interval (ISI) variation during control and detection periods on the outcome of visual inspection. The spike rates during the control periods are 10 and 20 spikes/s (in C and D, respectively). Positive ordinal values represent spike bursts (upward arrows: panels related to increases in firing rates) with ISIs that were shorter than the mean ISIs during control period imbedded in the detection period. Negative ordinal values represent spike pauses (downward arrows: panels related to decreases in firing rates) with ISIs that were longer than mean ISIs during the control period imbedded in the detection period. Triangles: the onsets of spike bursts or spike pauses were correctly defined. Circles: instances where visual inspection failed to define the onsets. Dashed lines represented the diagnostic criterion (DC) of ISI changes for correctly determining the onsets. The value of DC depends on the means (m_1 and m_2; $m_1 < m_2$) and standard deviations (S.D.$_1$ and S.D.$_2$) of the two groups compared, represented by circles and triangles, respectively. The DC was given by an equation: (DC $- m_1$)/S.D.$_1$ = ($m_2 -$ DC)/S.D.$_2$. Tables are related to scattergrams to their left. CI: confidence interval; ISIc: ISI during control period; ISId: ISI of the spike burst or spike pause for visual detection; S.D.c: standard deviation of the ISI during control period.