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Model-free detection of synchrony in neuronal spike trains, with an application to primate somatosensory cortex

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Abstract

Synchronized neuronal firing has been reported in many neural systems and may play a role in the representation of sensory stimuli and the modification of sensory representations by both experience and attention. In this report we describe a bootstrap procedure for computing the statistical significance of changes in the degree of synchrony and apply it to recordings from the second somatosensory (SII) cortex of Macaques performing tactile and visual discrimination tasks. A majority (68%) of neuron pairs in SII fire synchronously in response to a tactile stimulus. In a fraction of those pairs (17.5%), the degree of synchrony covaries with the focus of attention. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

Synchronous firing of action potentials amongst multiple neurons is a phenomenon that has been observed in a wide range of neural systems. Temporal structures of similar nature have been proposed to play a functional role in representing sensory information, as possible representations of internal behavioral states, and in motor planning [1–4,7,11,10]. One of the challenges in the field is the development of statistical methods suitable for characterizing the significance of synchronous firing. In the present report, we are concerned with the question whether the degree of synchrony observed changes significantly with the behavioral state of the animal. To this purpose, we develop a model-free analysis of the cross-correlogram [6].

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Significance was tested by bootstrap procedures at two levels using appropriate null hypothesis.

2. Experimental methods

The activity of a total of 553 pairs of neurons in SII from two awake behaving monkeys was recorded using seven extracellular electrodes driven individually [9]. Physiological methods were similar to those described by Hsiao et al. [8]. The experimental protocol required both monkeys to alternate between performing a tactile discrimination task (considered the “attentive” task for recordings in somatosensory cortex) and a visual (“nonattentive”) task.

3. Statistical methods

3.1. Test for significance of the degree of synchrony

The spike trains of two neurons α and β recorded simultaneously are denoted as $S_{\alpha sm}^n(t)$ and $S_{\beta sm}^n(t)$. Here, $n = 1 \dots N_{sm}$ indexes the trial number, for a particular behavioral state m and stimulus s , and $t = 1 \dots T/b$ the bin number where T is the length of the spike trains and b the bin width. The raw cross-correlogram $C_{\alpha\beta sm}^n(\tau)$ averaged over N_{sm} trials is

$$C_{\alpha\beta sm}(\tau) = \frac{1}{N_{sm}} \sum_t \sum_n S_{\alpha sm}^n(t + \tau) S_{\beta sm}^n(t). \quad (1)$$

In order to subtract the contribution of stimulus locked mean rate effects from the raw cross-correlogram, the shift predictor (or shuffle predictor) is subtracted, yielding the covariogram $\zeta_{\alpha\beta sm}(\tau)$

$$\zeta_{\alpha\beta sm}(\tau) = C_{\alpha\beta sm}(\tau) - \frac{1}{N_{sm}(N_{sm} - 1)} \sum_{i \neq j} \sum_t S_{\alpha sm}^i(t + \tau) S_{\beta sm}^j(t). \quad (2)$$

The stimulus-averaged covariogram $\zeta_{\alpha\beta m}(\tau)$ for a particular behavioral state m is computed as the average of Eq. (2) over all S_m stimuli in this state.

Our first objective is to test whether the covariogram for small time shifts (around $\tau = 0$) for a specific neuron pair is significantly above noise. We define the deviation of the covariogram from zero (i.e. the degree of synchrony) as the sum-squared area under the covariogram in a 50 ms time window around $\tau = 0$ and refer to it as to our statistic S . In particular, let us denote the observed statistic $S[\zeta_{\alpha\beta m}(\tau)]$ as $Z_{\alpha\beta m}$. The significance of the number of excess coincidences was tested using a bootstrap² method [5]. We use the null hypothesis H_0 that the two neurons α and β are

² More precisely, a Fisher permutation test; results are similar with bootstrapping.

independent. Let $\Pi_{N_{sm}}$ denote a permutation of N_{sm} trials for stimulus s and behavioral state m . We generate for each iteration S_m such permutations and use them to compute a bootstrapped covariogram $\zeta_{\alpha\beta sm}^{\Pi_{N_{sm}}}(\tau)$ for each stimulus. The covariogram $\zeta_{\alpha\beta m}^{\Pi}(\tau)$ for a particular iteration under H_0 is computed by averaging over all S_m such covariograms. The significance level of the observed statistic $Z_{\alpha\beta m}$ is then tested against the distribution of $\tilde{Z}_{\alpha\beta m}(S[\zeta_{\alpha\beta m}^{\Pi}(\tau)])$ computed from all S_m iterations to determine the probability that the data could have arisen assuming H_0 is true. No a priori assumptions are required about the underlying nature of the random process generating the spike trains, particularly the independence of firing in neighboring bins of the binned spike trains or the distribution of the test statistics, contrary to what is assumed in many statistical models.

3.2. Significance of attentional effect

Our second objective is to determine whether attention has a significant effect on synchronous firing. Only pairs of neurons which possess a significant degree of synchrony according to the test in Section 3.1 were included.

Single trial covariograms for each stimulus and behavioral type were computed as in Section 3.1. An appropriate null hypothesis for this test is that the degree of synchrony is independent of behavioral state or presented stimulus. Again, our measure of the degree of change in synchrony, our statistic D , was the sum-squared deviations between the averaged covariograms in a 50 ms time window centered around zero time shift. In order to test the difference in synchrony as a function of one of the behavioral states (attended vs. unattended), indexed as $m = 1$ or 2 , we compute the observed statistic as

$$Z_{\alpha\beta} = D[C_{\alpha\beta 1}(\tau) - C_{\alpha\beta 2}(\tau)]. \quad (3)$$

If the null hypothesis is true, covariograms obtained by averaging over trials during the tactile task should not be different, except for random variations, from those obtained in the baseline condition, the visual task. Let Π_n denote a set of n trials drawn with replacement from the set of visual trials and $C_{\alpha\beta}^{\Pi_n}(\tau)$, the averaged covariogram over this set. We use a Monte-Carlo simulation to estimate the distribution of the bootstrapped test statistic, defined as

$$\tilde{Z}_{\alpha\beta}(N_t, N_v) = D[C_{\alpha\beta}^{\Pi_{N_t}}(\tau) - C_{\alpha\beta}^{\Pi_{N_v}}(\tau)] \quad (4)$$

with $N_t = \sum_{s=1}^{S_m} N_{s1}$ and $N_v = \sum_{s=1}^{S_m} N_{s2}$. The significance level of $Z_{\alpha\beta}$ is then tested against the distribution of $\tilde{Z}_{\alpha\beta}(N_t, N_v)$.

4. Results

We applied the above statistical procedures to spike data recorded from macaque area SII while the animals were performing attentional tasks. Table 1, Column 2 shows the number of neuron pairs that showed a significant peak in the covariogram (all significances reported at $p < 0.05$). Overall, 68% of neuron pairs in SII showed

Table 1

The second column indicates the fraction of cell pairs which showed significant synchrony ($p > 0.05$) for each monkey. The third column shows the fraction of those which showed a significant change in the synchrony ($p < 0.5$) with the attentional state. Finally, the fourth column indicates the percentage in which synchrony in SII increased with attention directed on the tactile task

Monkey	Synchrony	Change	Increase
Monkey 1	113/145 (80%)	41/113 (36%)	37/41 (90%)
Monkey 2	264/408 (65%)	25/264 (9%)	17/25 (68%)
Total	377/553 (68%)	66/377 (17.5%)	54/66 (82%)

a significant degree of synchronous firing. Column 3 shows the number of pairs that had a significant change in the degree of synchronous firing between the attended and unattended tasks. Overall, 17% of the pairs selected in the first test show a significant change in the degree of synchrony with the amount of attention focused on the tactile stimulus. Furthermore, we found that of all pairs with a significant change, 82% had a greater degree of synchronous firing during performance of the attended tactile detection task than during the visual task (Column 4).

5. Discussion

In complex nervous systems, behavior is not only influenced by the immediate sensory input but also by the internal cognitive or perceptive state of the animal. It has been suggested on theoretical grounds that the temporal structure of spike trains plays a role in the coding of such states and that the correlational structure of spike trains varies with the attentional state of the animal [10]. We test this prediction by analyzing spike trains recorded from the cortex of an awake behaving monkey working in a task under attentional control. We show that statistically significant increases in the synchrony of neurons in somatosensory are positively correlated with the level of attention devoted to tactile stimuli. These changes in synchronization are evidence for a functional role of synchronous firing in processing sensory information [12].

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