Unitary Event Analysis of Synchronous Activities in Cat LGN

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Introduction

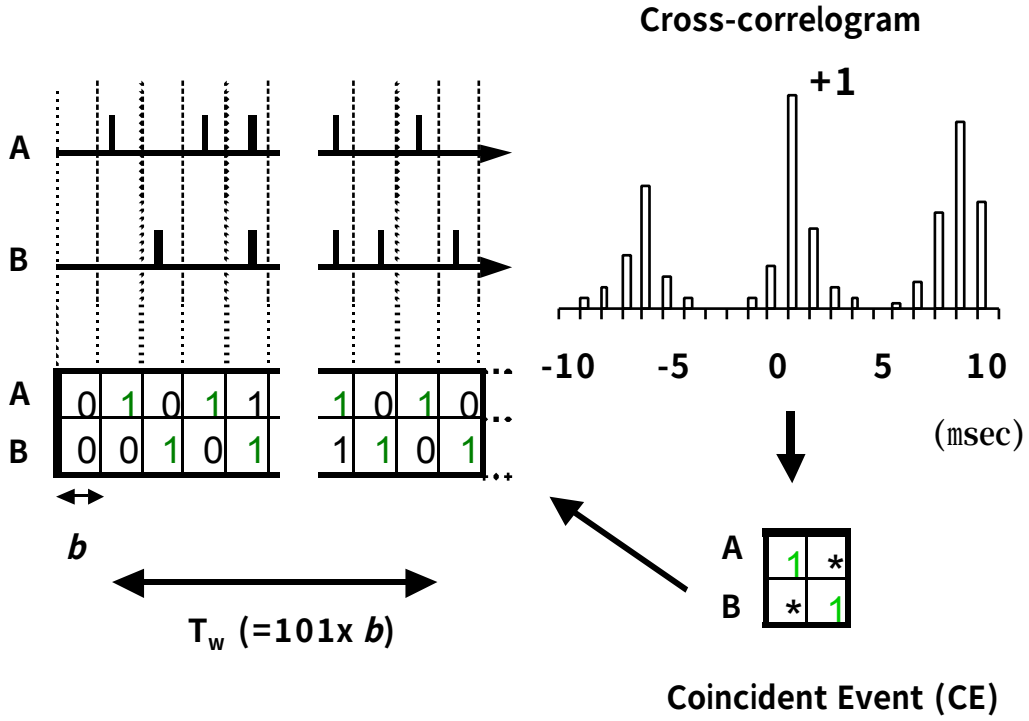
Several studies have shown that cells in the visual cortex (A17) of the cat display stimulus-evoked oscillatory firings (30 - 60Hz) and synchronization among multiple cells [Gray et al., 1989]. It was reported that the cells in the lateral geniculate nucleus (LGN) also showed stimulus evoked synchronous oscillatory firings of higher frequency range (60 - 100Hz) [Ito et al., 1994; Neuenschwander et al., 1996]. The difference in their frequency ranges suggested that the oscillatory activity in the cortex was not likely to derive from that in the LGN. On the other hand, Gray et al. [1992] reported a transient nature of the synchronization of the oscillatory local field potentials in the cortex, that is, the transition between asynchronous and synchronous states could occur within a trial duration. For further comparison of the synchronization between the two areas, we investigated whether such non-stationarity exists also in the synchronization in the LGN. Since the traditional method of the cross-correlogram loses any information on the non-stationarity by the temporal averaging over the trial duration, we adopted the novel method, the unitary event (UE) analysis, which was originally applied to the higher area (motor cortex) [Riehle et al., 1997]. We found that also in the LGN, a large portion of synchronous oscillatory activities was non-stationary. The modulation of the number of the UEs had apparently different time scale (less than a few hundred milliseconds) from the rate modulations of the two cells.

Materials and Methods

Electrophysiological recordings were performed on 9 adult cats using previously published techniques [Gray and Viana di Prisco, 1997]. The subjects were maintained under general anesthesia using halothane or isoflurane in a mixture of N_2O and O_2 (2:1) throughout surgery and during the recordings. Stationary light spots were presented (0.5-3 sec) at the receptive fields on the monitor with a refresh rate of 80 Hz placed at a distance of 57cm. Activities of the neuron were simultaneously recorded by two tetrodes (separated by 500 micrometer) in all layers of the LGN. Units were spike-sorted from the multi units by the cluster cutting algorithm.

The previous analysis of the cross-correlogram showed that 84 pairs out of 847 pairs were judged as significantly synchronized (see [Maldonado et al., 2000] for statistical criteria). The UE analysis was applied to those 84 sets of pairs for further examination of non-stationarity (see [Gruen, 1996] for the method of the UE analysis). However, 20 sets of those were excluded from the final analysis, because the statistical test of the UEs was difficult for such data of a low firing rate. First, we divide the trial duration into multiple bins with a small interval b (1~4 msec) as shown in the left panel in Fig.1. In each bin of each unit (units A and B), we place a variable, which takes 0 when there is no spike event within the bin, and 1 otherwise. That is, the occurrence of the multiple spike events within a bin leads to the same configuration as a single spike event (clipping). Next, the peak of the cross-correlogram is detected in a

precision of 1 msec (right panel in Fig.1). In the pair of spike trains in each trial, the spike pairs of the two units having the corresponding time delay are picked up throughout the trial duration (Coincident Events, CEs). The number of the raw CEs within a small moving window (size, T_w=101 × b) is averaged over all the trials. The number of the accidental CEs in the null hypothesis of independent firings obeys the binomial distribution computed by the firing rates of the two units. The mean of the distribution gives the predicted number of the CEs in the null hypothesis. The number of the raw CEs is judged as significant, that is, leading to a unitary event (UE), when it exceeds the 95% confidence limit of the binomial distribution. We repeat such statistical test by sliding the window by the bin size b basis over the trial duration. The bin width b (1, 2, 3 or 4 msec) is selected as the minimum number so that the mean of the number of the raw CEs over the response duration (stimulus duration etc.) is greater than 1.



Fig,1

Unitary event analysis of the spike trains of the two units A and B. The trial duration is divided into multiple bins with a small interval b (1 msec, in this example) in the left panel. In each bin of each unit, we place a variable, which takes 0 when there is no spike event and 1 otherwise. Next, the peak of the cross-correlogram is detected in a precision of 1 msec (right panel). In the pair of spike trains in each trial, the spike pairs of the two units having the corresponding time delay are picked up throughout the trial duration (Coincident Events, CEs). In this example, unit B fires 1 msec after the firing of unit A, so we look for the corresponding CE shown below the cross-correlogram (asterisk represents a wild card which can be either 0 or 1). The number of the raw CEs within a small moving window (size, T_w=101 × b) is averaged over all the trials.

Non-stationarity of the number of the CEs is quantified by computing the modulation index (MI). First, subtract the number of predicted CEs from the number of raw CEs. Due to the nonlinearity in binomial distribution, the modulation of (raw-predicted) CE number still has the influence of the modulation of the firing rates. In this analysis, we normalize the (raw-predicted) CE number by ((95% confidence limit) – predicted) CE number at each bin. Then,

within a response duration, compute the maximum and the minimum of the above-normalized modulation. Finally, let the difference between the two values be the modulation index of the test data, MI^{test}. Similarly, we compute the MI^{shift} for all possible trial shifted combinations. The test data is judged as having a significant temporal modulation when the MI^{test} is larger than the maximum of the MI^{shift}s.

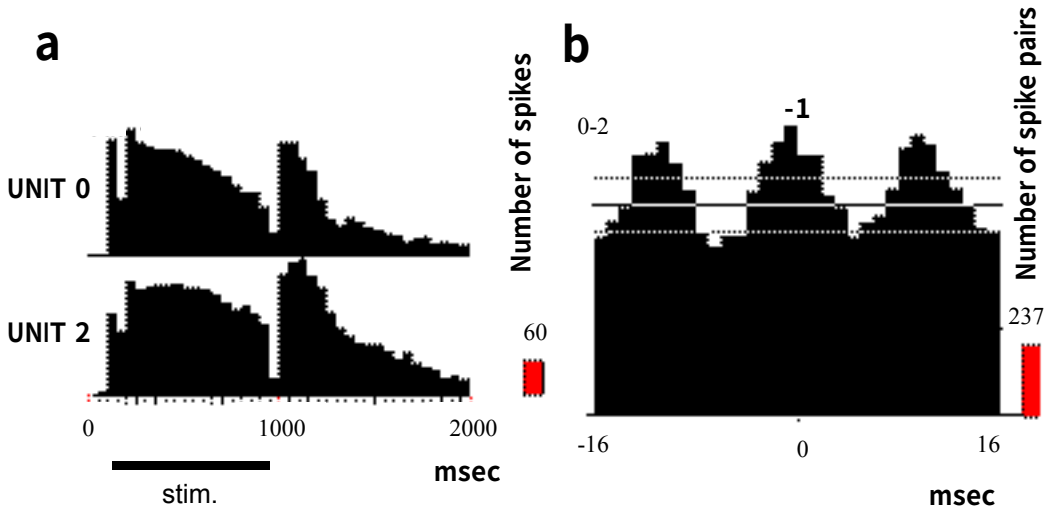
Results

A typical example showing a significant temporal modulation of the number of the CEs is shown in Fig. 2. Two well isolated single units were recorded simultaneously at the two different receptive fields [Unit 0: Y cell in C lamina; Unit 2: Y cell in A lamina]. Relatively large spots were presented at the two receptive fields simultaneously and evoked both ON and OFF responses of the two cells (PSTHs in Fig. 2a). The auto-correlograms of the both units show vigorous oscillatory spike activities with 96Hz only during the ON responses (figure not show). The cross-correlogram in Fig. 2b shows the synchronization between the two oscillatory activities at the distant sites. The unit 2 tended to fire 1 msec prior to the firing of the unit 0. The result of the unitary event analysis is summarized in Fig. 2c (b=1msec) . The red line, the green line, and the blue line in the bottom panel represents the number of the raw CEs, the number of predicted CEs, and the 95% confidence limit of the binomial distribution, respectively. The raster plots of the two cells are shown in the top panel. The number of the raw CEs transiently exceeds the 95% confidence limit and then leads to the UEs only in the limited interval of the ON response. All the CEs within this limited interval are high lightened by red circles in the raster plots. The number of the CEs starts to decrease to the predicted value even the rates of the two units remain still high. In the off-response, the two units fire almost independently. Those correlation structures are completely eliminated by the trial shuffling (figure not shown).

The results of the global statistics are summarized in Table I. Out of 64 unit pairs showing the significant synchronous oscillations in their cross-correlograms, the UEs appear only in 24 cases (38%). Samples were classified also by the significance of the modulation index. Out of 24 unit pairs showing the UEs, nearly 80% (19cases) show a significant temporal modulation of the CEs having a different time scale from the modulation of the firing rates.

		Non-stationarity in CE number		
		Significant	Not significant	
Significance of CEs	Significant	19	5	24 (38%)
	Not significant	7	33	40 (62%)
				total 64

Table 1. The classification of the coincident events (CEs) of the unit pairs



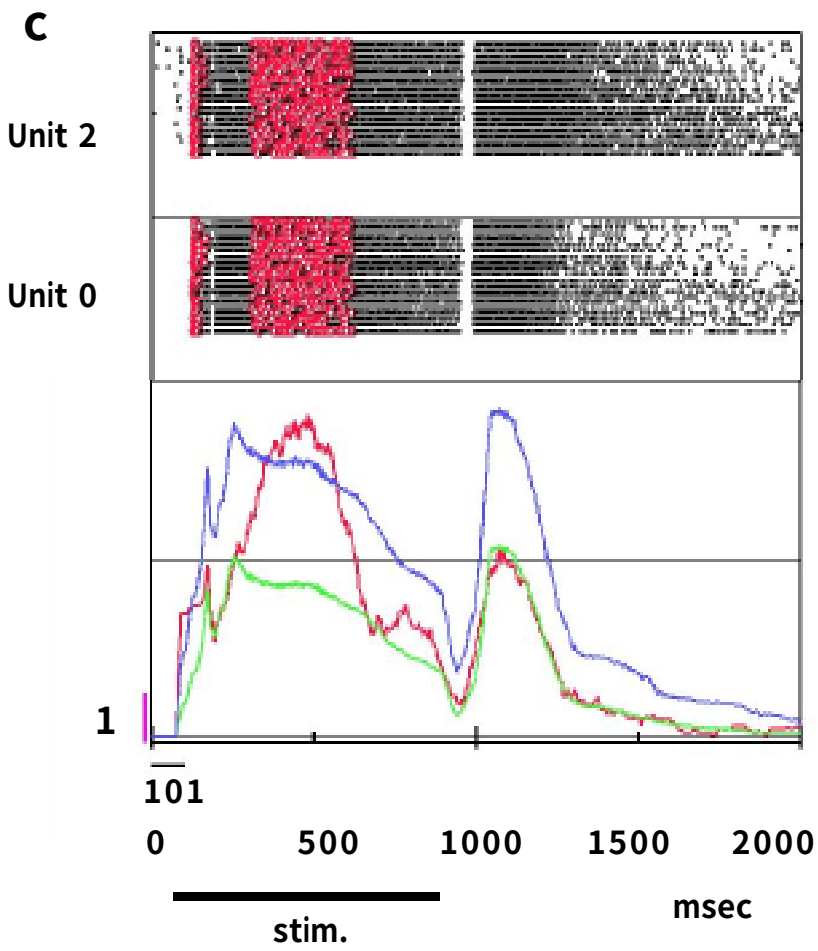


Fig.2

Typical example of a significant temporal modulation of the number of the coincident events (CEs). **a** post-stimulus time histogram of the two single units recorded by the different tetrodes. The off-response was also observed as well as the on-response. **b** The cross-correlogram between the two units during the on-responses showing synchronization. Both units showed vigorous oscillatory firings (auto-correlogram not shown). The peak at -1 msec suggests that unit 2 tended to fire 1 msec prior to unit 0. **c** Raster plot of each unit and the unitary events (UEs). Red line: the number of the raw CEs, Green line: the predicted CE number, Blue line: 95%

confidence limit computed by the binomial distribution of the null hypothesis. The open circles in the raster plot represent the CE judged to be significant (UE). The UEs near the onset are an artifact of the on-response transient.

Discussion

A large portion of the unit pairs having the UEs showed non-stationary modulations of the number of the CEs. There is a definite period in which the UEs occur more frequently. And it is loosely time locked to the stimulus onset. In each trial, however, the detailed timing in which the UEs occur is not locked to the stimulus onset, so that the occurrence of the UEs is completely eliminated by the trial shuffling. In this initial investigation on the non-stationarity in the correlation structure, we focused our attention mainly on the activities evoked by the stationary light spots. Since the stationary spots themselves did not have any temporal structure, we isolated the intrinsic non-stationarity in spike correlation.

There are two possible cases leading to the non-stationarity in synchrony. The first one is the case when the synchrony appears transiently, because the oscillatory nature of the spike firings appears only transiently at the two units. In the other case, although the oscillatory firing of each unit is stable, their synchronization (phase locking) occurs only transiently. Our preliminary analysis of the non-stationarity in the auto-correlograms shows that the first possibility is likely to be the case [Hirata, et al., 2002]. It is probable that the synchronous oscillation derives from the retinal inputs [Castelo-Branco et al., 1998]. What is the origin of the non-stationarity in the synchronization? It is known that there is little lateral connection within the LGN. One possibility is that non-stationary exists already in the input from the retina. The other possibility is that the feedback from the cortex modulates the synchronization. In addition to the afferent inputs from the retina, the LGN receives massive feedback inputs from the cortex. What is the functional role of the non-stationarity of the UEs? For further examination, we need to analyze the change of the properties of the UEs under the different stimulus context (spot, two short bars, single long bar). There we found a few cases in which the firings of the two units change their temporal relationship leading to the UEs of a different temporal offset under the presentation of different stimulus contexts [Hirata, et al., 2002].

We found that there are some problems in applying the unitary event analysis to the actual neuronal spike data. In the analysis of cross-correlogram, we take a temporal averaging over all the spikes within the entire trial duration. On the other hand, the temporal averaging is taken over a short interval in the UE analysis. Therefore, the small number of spikes in the data of low firing could not bear a reliable statistical analysis. This is a trade-off for the visualization of the fast temporal modulation of the correlation structure within the trial duration. Also this is a possible reason why not so many unit pairs show the UEs even if their cross-correlogram does show a significant correlation structure.

Conclusion

Unitary event analysis suggested that the synchronization between the cells in the LGN showed a non-stationary modulation within the trial duration even under the presentation of the stationary spot stimulus. The modulation of the number of the coincident events showed an apparently distinct temporal profile from that of the firing rates. This result may suggest that the synchrony plays a different functional role from the firing rate in the visual information processing.

References

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