Dynamic Concerted Activities among Retinal Ganglion Cells

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Abstract — **Concerted firing is one of the important ways for neurons to encode sensory stimuli. In the present study, we investigated dynamic concerted activities among retinal ganglion cells (RGCs) in response to natural movie and pseudo-random checkerboard flicking stimuli. The results showed that concerted activity patterns among RGCs changed dynamically during both stimuli, which were represented by the number of synchronously activated neurons and synchronous groups formed among the activated neurons. During natural movie stimulation, concerted activities were varying with time. On the contrary, the number of synchronized neurons and synchronous groups during pseudo-random checkerboard stimulation had a decreasing tendency.**

Keywords - concerted activities; dynamic; information-theoretic algorithm; retinal ganglion cell.

I. INTRODUCTION

Visual information is transmitted from the retina to the brain in the form of spike trains [1]. Retinal ganglion cells (RGCs) are the origin of action potentials in the visual pathway. As the optic nerve is the narrowest part in the visual system [2, 3], it is impossible to convey information effectively if each neuron acts as an independent communication channel [4]. Previous works indicate that concerted activities are widely existed among RGCs and have impact on efficient transmission of visual information [4-5].

Over the years, concerted activities elicited by artificial laboratory stimulus patterns, such as uniform illumination, checker-board flicking, etc., have been studied between pair-wise spike trains [4, 6]. But the primary function of the visual system is to process visual information in natural environment, and natural stimuli are more complex than artificial stimuli. Besides, the dynamic grouping of concerted activities among three or more spike trains may contain more useful information, as compared to single cell's activity and pair-wise correlated activities, in response to external stimulation [7-8].

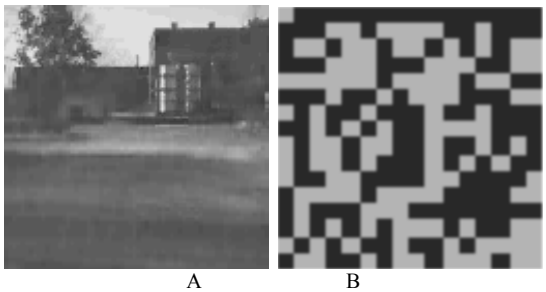
In the present study, information-theoretic algorithm [9] was adopted to study the dynamically concerted activities among RGCs when retinal activities were evoked by natural movie and pseudo-random checker-board flicking, respectively. It was found that the number of synchronously activated neurons and synchronous groups among RGCs changed dynamically during both stimuli. During natural movie stimulation, the number of synchronized neurons and synchronous groups were both varying along time. On the contrary, the number of synchronized neurons and synchronous groups during pseudo-random checkerboard stimulation both had a decreasing tendency.

II. MATERIALS AND METHODS

A. Electrophysiology Recording

Detailed extracellular-recording procedure can be found in our previous report [10]. Spikes from RGCs were recorded from retinas of newly-hatched chicks (about 1-3 weeks post-hatching) using multi-electrode array (MEA, 8×8) (MEA60, MCS GmbH, Germany) via a commercial multiplexed data acquisition system with a sampling rate of 20 kHz. Recorded data were stored in PC for off-line analyses.

The following stimulation protocols were applied: (1) Full-field white light flashes with light-ON duration of 1 sec and light-OFF intervals of 9 sec were applied (lasted for 30 sec) to test the functional condition of the neurons being recorded; (2) Digitized grayscale video recording of natural movies (downloaded from the website of van Hateren's lab, http://hlab.phys.rug.nl/vidlib/index.html [11]) were presented with a refresh rate of 10 Hz and lasted for 192 sec; (3) Pseudo-random binary checker-board flickering (16×16 grid) were applied at a refresh rate of 9.05 Hz and lasted for 221 sec [12]. Example frames of natural movie and checker-board flickering are shown in Fig. 1. These images were of the same size when being presented on the screen and projected onto the retinal piece via an optical lens system.



A B

Figure 1. Example frames. (A) Natural movie; (B) Checker-board flickering

B. Information-theoretic algorithm

In order to test whether the interactions among ganglion cells are limited to pair-wise neurons or extended to neuron groups containing more cells, information-theoretic algorithm

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based on entropy analysis was adopted [9]. Detailed procedures are as follows:

Firstly, the spike trains are symbolized into "0" and "1" with time bin of 2 ms, where "1" represents that there is a spike in the time bin and "0" represents that there is no spike in the time bin. Given two neurons A and B, a new symbolic neuron AB can be defined such that:

$$r_j^{(AB)} = r_j^{(A)} r_j^B = \begin{cases} 1, \text{ if the neuron } A \text{ and neuron } B \text{ fired in time bin } j \\ 0, \text{ otherwise} \end{cases} \quad (1)$$

Secondly, to see whether the neurons A and B are concertedly activated, the entropy is computed:

$$H_i = -(P_i \log_2 P_i + (1-P_i)\log_2(1-P_i)) \quad (2)$$

where P_i is the probability that symbolic neuron i has a spike in the time bin ($P_i = \frac{1}{N}\sum_{i=1}^{N} r_j^{(i)}$, N is the number of time bins in the data set). As usually only a small fraction of each neuron's spikes fire in synchrony with others, the net reduction in entropy can be calculated as [9]:

$$\Delta H_{AB} = H_A + H_B - H_{AB} \approx P_{AB} \log_2 (P_{AB} / P_A P_B) \quad (3)$$

The identification of concerted neuron groups starts with computing ΔH for all the cell pairs. If the largest ΔH value is greater than a predetermined threshold (see below), we regard these two cells as a concerted group. We then further search for other synchronous neuron pairs or synchronous groups containing more cells. The process is repeated until the largest ΔH falls below the predetermined threshold. To define the threshold, all the spike trains are shifted by a randomly chosen time delay, and the largest ΔH in the shuffled data set is defined as the threshold.

C. Correlation Index

Correlation index is the ratio between the observed frequency of synchronous activities and that expected by chance [4], which is used to estimate the significance of the synchronous firings. The correlation index is measured as follows:

The frequency of synchronous firings among M cells is

$$P_{1\ldots M} = \frac{1}{N}\sum_{j=1}^{N}\prod_{i=1}^{M} r_j^{(i)} \quad (4)$$

The frequency of synchronous firings expected by chance can be calculated as:

$$P_1 \ldots P_M = \prod_{i=1}^{M}\frac{1}{N}\sum_{j=1}^{N} r_j^{(i)} \quad (5)$$

Then we can compute the correlation index as:

$$C_{1\ldots M} = P_{1\ldots M} / \prod_{i=1}^{M} P_i \quad (6)$$

III. RESULTS

It was previously reported that the strength of pair-wise correlations decreased with distance between two neurons [4]; we therefore focused on the concerted activities among RGCs recorded by adjacent electrodes in the present work. Most RGCs recorded in our experiments are of On-Off subtype [14]. In the present work, all the analyses were performed on this type of cells.

Fig. 2 illustrates the geometric position of eight electrodes by which a group of On-Off RGCs were recorded from one retina. Fig. 3 gives the raster plots for the relevant neurons' activities elicited by natural movie (Fig. 3A) and pseudo-random checker-board flickering (Fig. 3B). It is clearly shown that the firing rate elicited by the checker-board flickering is higher.

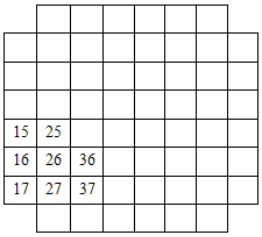

Figure 2. Geometric position of eight adjacent electrodes by which a group of RGCs were recorded from one example retina

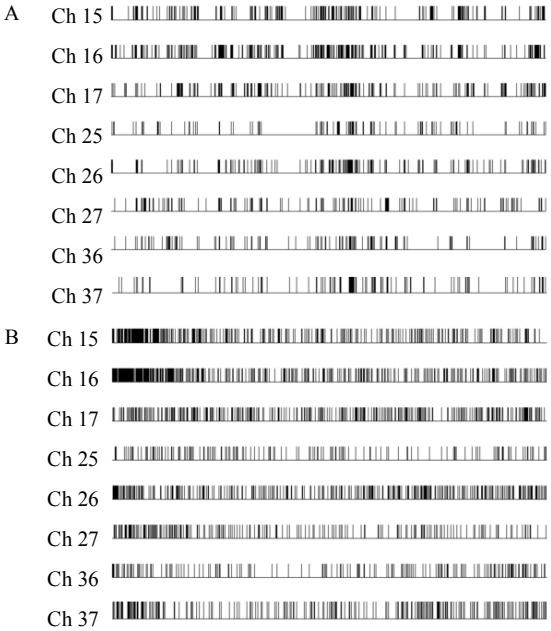

Figure 3. Raster plots of firing activities of 8 RGCs, recorded by the electrodes in Fig. 2, in response to natural movie (A) and pseudo-random checker-board flicking (B) respectively (bin = 2 ms, 10-130 s after the stimulus on-set).

A. Total Firing Rate

In order to investigate the population response elicited by both stimuli, the group neurons' ensemble activities during the 120-s period in response to natural movie and checker-board

flickering are plotted in Fig. 4 (bin = 2 ms, time window w = 500 ms). The ensemble firing rate varies with time in response to natural movie (Fig. 4A), but has a decreasing tendency during checker-board flicking (Fig. 4B). Similar results were observed from other neuron groups from the same retina and other retinas (data not shown).

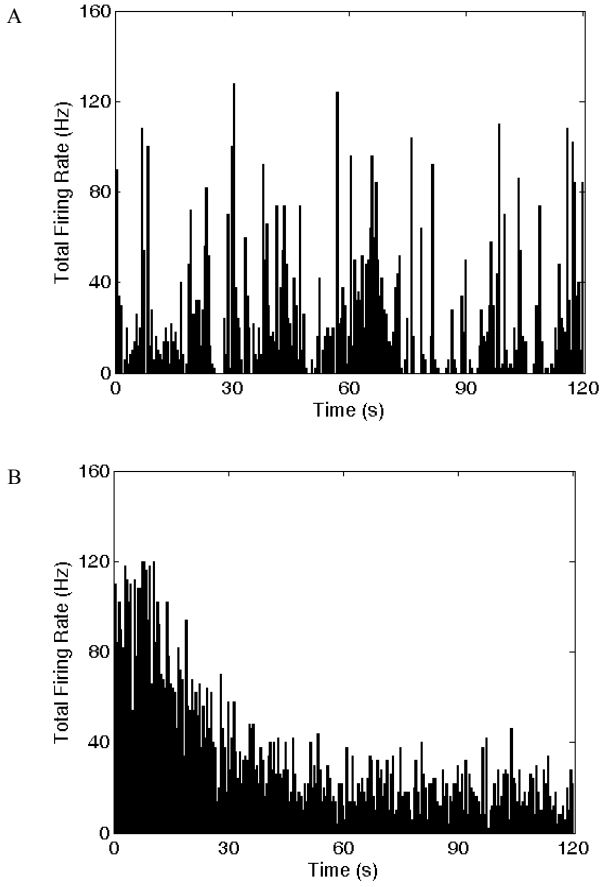

Figure 4. The ensemble firing rates in response to natural movie (A) and checker-board flicking (B) respectively.

B. Concerted Activities

The information-theoretic algorithm was further applied to analyze the dynamically concerted activities among the RGCs in response to natural movie and pseudo-random checker-board stimuli respectively. The analyses were performed on the 120-s data sets, using time window of 500 ms. Statistics of synchronously firing neurons and synchronous groups in one retina, in response to natural movie and checker-board flickering, are shown in Fig. 5, A and B respectively. It is shown that during natural movie stimuli, concerted activities existed among the RGCs in the whole course, with the numbers of neurons and groups varying greatly (Fig. 5A). However, the numbers of synchronized neurons and synchronous groups tended to decrease during the checker-board flicking (Fig. 5B). During both stimuli, the change of concerted groups was coincident with concerted neurons.

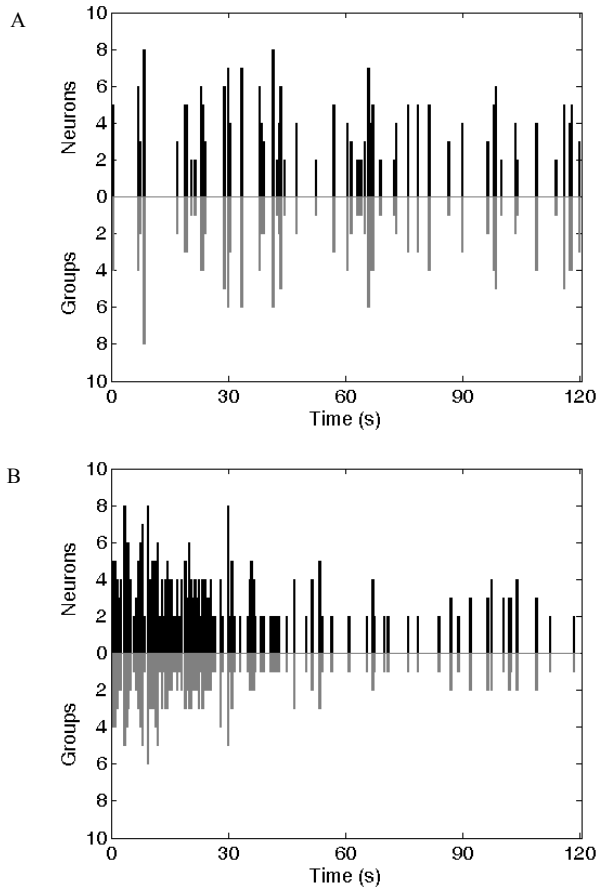

Figure 5. Statistics of synchronously firing neurons (black bars) and synchronous neuronal groups (gray bars) in the chick retina in response to natural movie (A) and pseudo-random checker-board flicking (B), respectively.

Some synchronous groups included three or more neurons and quite a portion of neurons participated in more than one synchronous group at one time. Groupings of the eight neurons being investigated during some particular time periods, in response to both stimuli are displayed in Fig. 6. For natural movie stimuli, synchronization patterns were dynamically changing during different periods (Fig. 6, A-C). On the contrary, during pseudo-random checker-board flicking, concerted patterns were getting simpler, during the neuronal adaptation to the stimuli (Fig. 6, D-F). To estimate the significance for the concerted activities, we calculated the correlation index [4, 11] of all the synchronous groups. The frequency of synchronous firing in neuronal groups was, on average, about 39.7 times more than expected during natural movie stimuli. However, during pseudo-random checker-board flicking, synchronous firing occurred, on average, about 67.9 times more frequently than expected.

IV. DISCUSSION

In the present study, information-theoretic algorithm [9] was adopted to investigate the concerted activities of neurons recorded by adjacent electrodes in response to natural movie and pseudo-random checker-board stimuli respectively. The results revealed that the RGCs presented dynamic concerted

activities in response to external stimulation. During movie response, the number of synchronized neurons and synchronous groups were both varying with time. On the contrary, the number of synchronized neurons and synchronous groups during checker-board response were both decreasing.

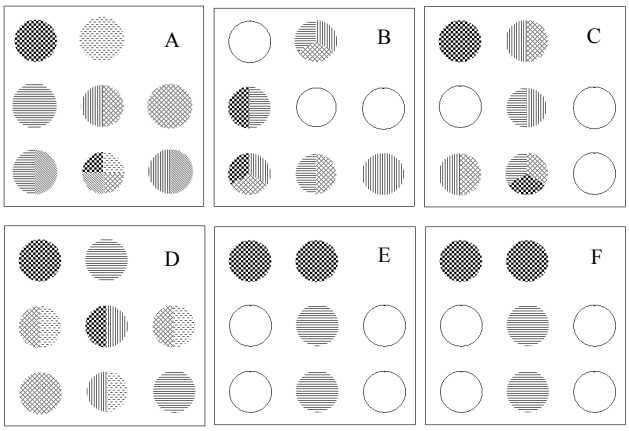

Figure 6. Grouping of the eight neurons (represented by circles) recorded at different moments during both stimuli. For movie responses, the groupings during 41 ~ 41.5 s (A), 66.5 ~ 67 s (B) and 115.5 ~ 116 s (C) are plotted; for checker-board responses, the groupings during 29.5 ~ 30 s (D), 67 ~ 67.5 s (E) and 97.5 ~ 98 s (F) are shown. Neurons with the same sign participated in the same group. Some neurons filled with more than one sign participated in different groups at one time. Open circles indicate the neurons that didn't participate in any groups.

The information-theoretic algorithm is an effective method for investigating the dynamic concerted activities of a large group of cells. Although the algorithm only provides a conservative estimate [4, 9], the strength of correlation detected in our experiments were quite high during both stimuli. Since natural stimuli are more complex than pseudo-random checker-board flickering, the activities of neurons elicited by these two stimuli were different. As neurons didn't adapt to the natural movie stimuli, the firing rate, the number of synchronized neurons and synchronous groups were all varying along time. On the contrary, neurons adapted to the pseudo-random checker-board stimuli quickly, so both of firing rate and concerted activities decreased with time (Figs. 4 and 5).

Neurons generally encode the local differences in temporal and spatial domains [14] and they communicate with each other via synapses. There are two ways for postsynaptic neuron to convey input from its presynaptic neurons: temporal summation and spatial summation. Spatial summation is more efficient as the threshold for postsynaptic will be lower [15]. When presynaptic neurons fire in synchrony, spatial summation contributes to efficient information transmission. So the relationship between dynamic concerted activities and information transmission is worth for further study.

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