

An Integration Model for Detection and Quantification of Synchronous Firing Within Cell Groups

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Purpose

The idea that neurons may form functional assemblies to encode structure was proposed by Hebb in 1949. To test this hypothesis, researchers used single electrodes to simultaneously record from pairs of neurons. Perkel et al. (1967) introduced the cross-correlogram method to quantify these synchronous relationships. Currently, we have the technology to simultaneously record from dozens of neurons using multielectrode arrays. However, the cross-correlogram method and other cross-correlation techniques (Aertsen et al., 1989) cannot be applied to large groups of cells. Other methods such as gravitational clustering (Gerstein et al., 1985) and information-theoretic distances (Johnson et al., 2001) still rely on pair-wise calculations. We derive a new measure for detecting and quantifying cooperative firing within cell groups of any size based on modeling EPSP integration. We use this measure to describe how synchrony that is independent of firing rate depends on orientation. We also examine the characteristics of group membership.

Methods

We recorded from 28 neurons in the visual cortex of cats anesthetized with Propofol and N₂O and paralyzed with Pancuronium Bromide. A 10 x 10 multielectrode array (Cyberkinetics, Foxborough, MA) was pneumatically inserted to a depth of 0.6 mm in areas 17 and 18. Drifting sinusoidal gratings were presented on a for 2 seconds each, preceded by a 1 second period with only the mean luminance background. The null condition was mean luminance and orientation was varied from 10-180 degrees in 10 degree increments. The method described below in Figure 1 was derived to describe significant cooperative firing among different cell groups. Inherent synchrony was calculated based on firing rates and Poisson statistics. Significance was determined using a Student's 1-tailed t-test ($\alpha = 0.01$).

Integration Model for Computing a Synchrony Score

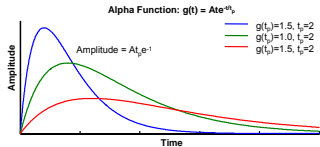
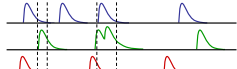


Figure 1 (Above): (A) An alpha function is used to represent the EPSP wave-form. By adjusting the amplitude and time constant, various efficacy and temporal properties can be modeled. For all subsequent calculations, an amplitude of 1.0 mV and time constant of 2.0 ms were used.

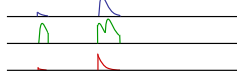
Step 1: For a group of cells, preprocess all data so that the time of spike initiation is retained (i.e. spike train).



Step 2: Place an alpha waveform at each spike initiation time (i.e. create an EPSP train) and sum overlapping waveforms contributed by burst firing.



Step 3: Filter each EPSP train to remove parts of waveforms that are not coincident with ALL other EPSP trains in the group.



Results

Synchrony that is Independent of Firing Rate Depends on Stimulus Orientation for Individual Cells

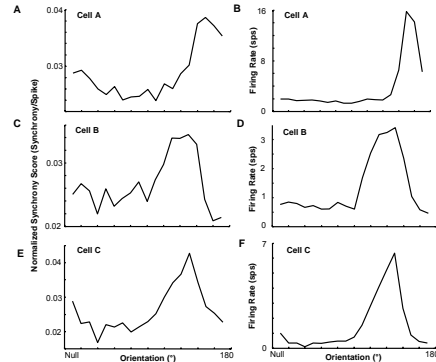


Figure 2: (A) The Normalized Synchrony Scores from all pair groups ($n=27$) containing Cell A were averaged and multiplied by the average contribution from Cell A to produce an **Individual Normalized Synchrony Score**. This Individual Normalized Synchrony Score was plotted vs. stimulus orientation. (B) Average firing rate is plotted vs. stimulus orientation to produce an orientation tuning curve. Note that the amount of synchrony, which is independent of firing rate, increases for the optimal orientation as predicted by firing rate (comparing A and B). (C)-(F) Two more examples of how synchrony increases for optimal stimuli.

Step 4: Inherent Synchrony Score: The number of spikes expected to contribute to inherent synchrony (i.e., due simply to firing rate and chance). We calculate the number of spikes by using the probability based on firing rate and normalize by dividing by the total number of spikes in the group (range between 0 and 1).

Step 5: Group Score: Sum the filtered EPSP trains and normalize by the area of one waveform and the total number of spikes in the group. This ranges between 0 and 1 and represents the percentage of total spikes that are coincident in a group.

Step 6: Compare the Group Score to the Inherent Synchrony Score to determine significance.

Step 7: Synchrony Score: The percentage of waveforms in the group that are coincident, but not due to inherent synchrony. We subtract the Inherent Synchrony Score from the Group Score. The Synchrony Score can be renormalized (so the range is between 0 and 1) to produce a **Normalized Synchrony Score** (mathematically convenient, but no longer has the same physical meaning as a Synchrony Score).

Our method was derived to quantify cooperative firing among groups of cells. It equates the firing of action potentials to the integration of resultant EPSPs generated in a post-synaptic cell. The area of coincident waveforms can be calculated to provide a measure of synchrony. The benefits of this method are summarized as follows: (1) An alpha function has adjustable parameters to model different EPSP waveforms. (2) This EPSP model is biologically representative of integration because spikes that arrive closely within the integration time period are emphasized more than those that arrive further apart. (3) This measure can quantify synchrony among any number of cells (not just pairs). (4) A simple Student's t-test can be used to determine the significance of group synchrony vs. inherent synchrony due to probability based on firing rate. (5) The Synchrony Score is normalized to remove inherent synchrony and allow the analysis of effects that are independent of firing rate. (6) The members of larger groups can be predicted based on scores from smaller groups, thus reducing the number of scores from different cell combinations that need to be computed.

Examining Characteristics of Membership for a Significant Group of Cells

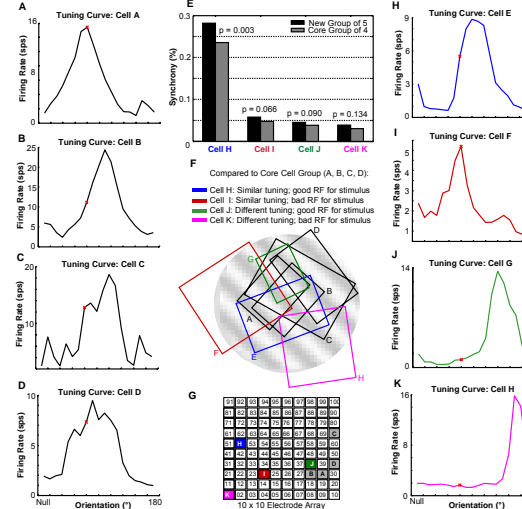


Figure 3: (A)-(D) Orientation tuning curves for a core group of 4 cells that have significant synchrony as a group of 4 during stimulation with a 70-degree oriented grating, marked with an 'X'. (E) Bar graph of the amount of synchrony maintained when each cell described by tuning curves (H)-(K) are added as a 5th group member. The gray bar indicates the amount of synchrony maintained within the core group only, but integration time is restricted by the lower co-activation time of the fifth cell. (F) Plot of each cell's receptive field compared to stimulus location. Note that Cell H with the core group produced the only significant group of 5. The tuning for Cell H was similar to the core group and the stimulus was placed well for its receptive field. (G) 10 x 10 electrode array showing the spatial configuration of each cell. Note that although the core group is clustered spatially, it synchronizes with Cell H, which is approximately 2.8 mm away.

Results Summarized

- On average, Individual Normalized Synchrony Scores (described in Figure 2) increased 93.5% from the least optimal stimulus to the most optimal stimulus.
- (Refer to Figure 3E) When added to the core group, Cell H maintained 28.2% of the synchrony in the original group ($p = 0.0027$), which was much greater than the maximum of 5.8% maintained by either Cell I, Cell J, or Cell K.
- (Refer to Figure 3E) When Cell H was added to the core group, the core cells maintained 23.6% of their original synchrony, whereas with Cells I, J, or K this figure fell to a maximum of only 3.0%.
- (Refer to Figure 3G) Cell H is approximately 2.8 mm from the central area of the core cells, while Cell J is approximately 0.4 mm away.
- (Refer to Figure 4) Cells W, X, and Y form a significant group (max score = 0.0279 , $p = 1.22 \times 10^{-6}$) during 6 stimuli (20-70 degrees). Cells X and Z form a significant group (max score = 0.0712 , $p = 3.36 \times 10^{-6}$) during 9 stimuli (100-180 degrees).

Conclusions

- The results from Figure 2 suggest that an individual neuron synchronizes (independently from firing rate) with other cells maximally when presented with its preferred stimulus orientation.
- The results from Figure 3E suggest that synchrony depends on an optimal stimulus for the group as well as suitable placement of the stimulus across all receptive fields in the group.
- The results from Figure 3E also suggest that additional group members alter the synchrony of the group. Therefore, synchrony does not superpose in a simple way.
- Figure 3G shows synchrony between cells with a large physical separation, suggesting that it is not likely to be generated only by a common input to the group of cells.
- The results from Figure 4B,C suggest that group membership is dynamic, depending on the spatial configuration of the stimuli. Also, group synchrony is highest for the stimulus that is most optimal for the group.

References

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