Rate synchronization as a deterministic signal in neural spike trains

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We introduce a simple method to analyze recorded spike trains in sensory neurons that allows to reveal deterministic aspects of spiking dynamics. In particular, events with an associated firing rate f_r, are defined whenever two successive spikes on a given cell α occur at times t_i^α and t_{i-1}^α such that $(f_r + \Delta f_r)^{-1} < |t_i^\alpha - t_{i-1}^\alpha| < (f_r - \Delta f_r)^{-1}$, for a given Δf_r. We then look for synchronization of those events on different cells. Our results show that synchronized events are sharply correlated with stimuli. The method is used to analyze experimental time series obtained on retinal ganglion cells and synthetic time series.

INTRODUCTION

Synchronous activity at several time scales in general, and in the visual system in particular, has received much attention [3, 7, 8]. The main conclusion of these studies is that it seems very plausible that much of the information transmitted in the visual system has a great degree of synchronicity.

In this paper, we have developed a simple method to detect synchrony of events in retinal ganglion cells, whose activity was simultaneously recorded by using multi-electrode arrays. The events we shall consider are conditioned spike times, where the condition we impose is the presence of other spike in its temporal vicinity. In this way, we are taking into account the instantaneous firing rate (IFR) of the cells. In looking for synchrony of these events, we are in fact evaluating synchronization of firing rates. The last step of our method consists of evaluating the degree of causality in the relation between these synchronized events (SE) and the stimuli presented to the cells. The results show that there effectively is a dynamical relation between stimuli and synchronization of firing rates.

METHODS

Extracellular recordings were obtained from ganglion cells in the isolated superfused albino rabbit (Oryctolagus cuniculus) retina using an array of 100, 1.5 mm long electrodes, as reported previously [4] For visual stimulation a NEC high-resolution RGB monitor was used. The retinas were then stimulated with random flicker stimulation.

Besides experimental data we have also simulated a synthetic data file using a Multivariate Non-Homogeneous Poisson Processes (MNHPP). Given a time discretization Δt, the probability that a single spike (SiS) occurs at time t in the interval Δt is [5]

$$Pr[SiS] = \mu \Delta t e^{\mu \Delta t} \tag{1}$$

for a Poisson process with mean rate μ. In a multivariate case, for an array of 100 synthetic cells, 100 random numbers between 0 and 1, $r(i)$, $i = 1, 100$, with uniform distribution are generated in each time step t. If $r(i) \leq Pr[SiS]$, a spike is presumed to have occurred between t and $t + \Delta t$ for cell i. In the case of MNHPP, the procedure is the same as described above but doing $\mu = \mu(t)$. In particular, we have simulated stimuli responses by changing abruptly μ from μ_0 to a maximum value, μ_{max}, when a stimulus happens, and then, let it decay exponentially to the original value until the next simulated stimulus appear. In this way, for a MNHPP(μ_0, μ_{max}), $\mu(t)$ is given by

$$\mu(t) = \mu_0 + (\mu_{max} - \mu_0) e^{-\lambda t'} \tag{2}$$

where t' is reset to zero every time a stimulus appears (every 2 seconds in our simulations). We have used a time discretization of 0.1 ms, while λ was fixed at 50 s^{-1}. This value gives a 36 % decay of the maximum firing rate 20 ms after the stimulus. In our simulations we have set $\mu_0 = 1$ s^{-1} and $\mu_{max} = 50$ s^{-1}, that is, MNHPP(1,50). The preocedure described above is repeated for up to 99 simulated cells.

Given an experimental record from a single neuron, we call t_i the time of the i-th spike. In the case of multi-electrodes registers, from N_c different cells, we call t_i^α the time of the spike i from neuron α. In this way we have

a multivariate, discrete, time series with the information about the spiking dynamics of neurons. Using the above information we define events with associated times τ_k^α given by,

$$\tau_k^\alpha = t_i^\alpha \iff (f_r + \Delta f_r)^{-1} < t_i^\alpha - t_{i-1}^\alpha < (f_r - \Delta f_r)^{-1} \tag{3}$$

where $k = 1, n_\alpha$, $i = 2, m_\alpha$ and n_α is the number of events in cell α and m_α is the number of spikes cell α has fired. Note that index k is incremented every time a new event show up. The above procedure selects discrete events with IFR f_r. For the sake of clarity we shall call SiS (Single Spike) events to single spike times, and 1-CoS (Conditioned Spike) to the case defined by Equation 3. We now use the concept of synchronization of events recently defined by Quian Quiroga et al. [6]. We look for events in different cells, that show up at the same time, allowing a time lag t_{SE} between two synchronized events. Let us define "event synchronization" J_l^2, between *at least 2 events*, τ_i^α, at time i, in neuron α, and event τ_j^β at time j in neuron β, as

$$J_l^2 = \begin{cases} 1 \iff \exists\ \tau_i^\alpha, \tau_j^\beta\ (\alpha \neq \beta), \text{ such that } |\tau_i^\alpha - \tau_j^\beta| < t_{SE} \\ 0 \text{ otherwise} \end{cases} \tag{4}$$

with i and j (as defined before) $1 \leq i \leq n_\alpha$, $1 \leq \alpha \leq N_c - 1$, $1 \leq j \leq n_\beta$, $\alpha < \beta \leq N_c$, and l running $1 \leq l \leq N_E = \sum_{\alpha=1}^{N_c-1} n_\alpha$, total number of events, and we use as the instant of this event synchronization, $t_{J_l^2}$, the time of the first event considered, $t_{J_l^2} = \tau_i^\alpha$ (note that indexes however run over different ranges).

We shall now look for the existence of causal relations between synchronized events and stimuli, increase and decrease in the light intensity. We are interested in quantifying the degree of connection between SE and stimuli times, but in such a way that information about the actual existence of SE give us some clues upon the existence of stimulation. This will be done by means of conditional probabilities. If we know that SE occurred at time t', what we want to know is the probability that this SE was elicited by a stimulus s at time t (where $t' > t$). This conditional probability, named hereafter as $P[s(t)/SE(t')]$, is in fact an inference about the stimuli. In order to estimate this conditional probability, we simply count the number of SE which are actually correlated with any of the stimuli times and divide it by the total number of SE. Because we are looking for a *causal* relation between SE and stimuli, we use a temporal window at the "left" of the coincidence of events. In other words, if any coincidence of events was triggered by the stimuli, the time of this coincidence must be after the stimulus. In order to fix the value of this temporal window, we must take into account the latency time for the various kind of cells, ON, OFF, fastON, fastOFF, etc., for physiological data. Average latencies range from 50 to 110 ms in the mammalian visual system [1] and in particular for the rabbit ganglion cells the fastest latencies correspond to 57 ms for the fastOFF cells and the slower to the ON cells with 107 ms [10]. Accordingly, we fixed the correlation time between stimuli and events in 100 ms. In addition, the correlation time must be shifted in 50 ms from the instant at which a given stimulus occurs, because usually no ganglion cell responds in less than this time. In the case of synthetic data, however, no latency has been included. Thus, we look for coincidences in the range 50-150 ms for physiological data, and 0-100 ms for synthetic data, after each stimulus time. We use as the time of this event synchronization, $t_{J_k^2}$, the "center" of the temporal window t_{SE}, the time of the first event, namely, $t_{J_k^2} = \tau_i$

$$\phi_{il} = \begin{cases} 1 \iff 50\ ms \leq t_{J_i^2} - s_l \leq 150\ ms \\ 0 \text{ otherwise} \end{cases} \tag{5}$$

for physiological data, and

$$\phi_{il} = \begin{cases} 1 \iff 0\ ms \leq t_{J_i^2} - s_l \leq 100\ ms \\ 0 \text{ otherwise} \end{cases} \tag{6}$$

for synthetic realizations. where s_l is the time of stimulus l and ϕ_{il} its indicator function. N_s is the total number of stimuli in our calculations, and therefore we can estimate the probability as:

$$P[s(t)/SE(t')] = \frac{\sum_{l=1}^{N_s} \sum_{i=1}^{N_{SE}} \phi_{il}}{N_{SE}} \tag{7}$$

where N_{SE} is the total number of SE.

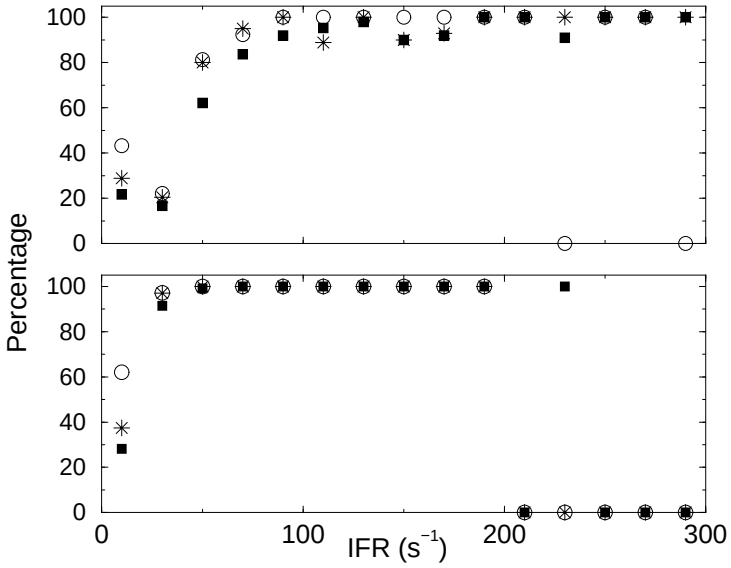

FIG. 1: Percentage of synchronized events which are correlated with the stimuli. Three synchronization windows has been used, 2 ms (empty circles), 10 ms (stars) and 50 ms (solid squares).
Upper panel: Experimental data file. Lower panel: Synthetic data file.

RESULTS

Our main results are presented in Figure 1, where we have plotted the percentage of SE that are correlated with any of the stimuli, as a function of IFR.

At low firing rates the number of coincidences is not related with the stimuli. That is, different cells do not fire in synchrony or, if they do, it occurs independently of the stimuli timing. However, at firing rates above a certain IFR, events in synchrony begin to follow the stimuli timing very closely. In fact, for a t_{SE}= 2 ms and a firing rate of 90 $\pm$ 10 s^{-1}, the correlation of synchronized events with the stimuli is 100 % in the case of the flicker experiment (upper panel of Figure 1). Thus every time there are two "close" spikes on the same cell (where close is defined in terms of IFR), and, they are close in time to another pair of spikes on different cells (now the time scale is the synchronization time t_{SE}), we certainly are in the presence of a stimulus. It seems that above a given firing rate threshold, our approach identifies a deterministic behavior of the spiking dynamics. For the MNHPP(1,50), the percentage of SE correlated with stimuli is very high, even for $t_{SE} = 50$. It is worth noting that, although 100 % correlation between SE and stimuli begin at IFR = 50 s^{-1} and it is sustained until IFR = 210 s^{-1} is reached, the number of correlated SE decreases steadily from 28 events at IFR = 50 s^{-1} to just 1 event at IFR = 210 s^{-1} (data not shown).

We now look for synchrony of spikes for a given correlation window t_{SE}, and calculate the percentage of synchronized spikes correlated with stimuli. Figure 2, upper panel, shows results for the experimental series. We have made calculations for t_{SE} up to 50 ms. For small t_{SE} the percentage of synchronized spikes correlated with stimuli begins around 55%. At t_{SE} larger than 20 ms it stabilize at around 30 %. This is due to the fact that cells fire randomly in the absence of stimulation, and the chance that two cells fire at the same time is low, but different from zero. In this way it is possible to get two spikes synchronized outside the stimuli correlation windows. When this Figure is compared with Figure 1, upeer panel, it is concluded that correlation of synchronized spikes with stimuli needs a very narrow temporal window. Instead, SE are highly correlated with stimuli times even at large t_{SE}. For example in Figure 1, for a $t_{SE} = 50$ ms, and starting at firing rate of 120 s^{-1}, the correlation of synchronized events with the stimuli is always greater that 90 %. The results of Figure 2 for the same t_{SE} gives a correlation around 30 %.

For the case of MNHPP(1,50) identical conclusions could be extacted by comparing Figure 2, lower panel, against Figure 1, lower panel. In this case, MNHPP(1,50), percentage of synchronized spikes is higher than the same quantity in the case of the flicker experiment, mainly due to the sharp simulated response. However, SE have much better correlation with stimuli than synchronized spikes.

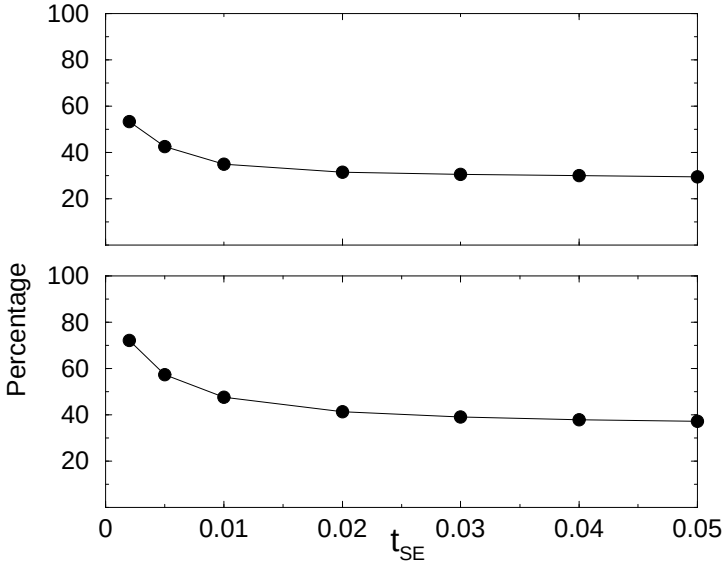

FIG. 2: Percentage of synchronized spikes which are correlated with the stimuli, in relation to the total number of synchronized spikes. Upper panel: Experimental data file. Lower panel: Synthetic data file.

CONCLUSIONS

In this paper we have presented a new approach to analyze simultaneous activity of recorded ganglion cells. We have introduced two new concepts. The first one is related with event's definition. Our choice of event's definition rest mainly on physiological grounds, because it is well known the fact that sensory neurons modify its firing rate with stimulation. We have tried to cope with this fact by classifying spikes accordingly to the IFR in which they are embedded. In that way, each spike belongs to a determined event.

The definition of synchronization, borrowed from a recent publication [6], however, is stated in a way that allows more flexibility. In this way, we are coping with the fact that neurons responses are somewhat unreliable. The conjunction of these two new definitions, spikes as IFR events and a "fussy" synchronization, yields the basic elements of our approach, that is, firing rate synchronization. We have tried to quantify our working hypothesis, i.e., event synchronization is caused by stimulation. Throughout the paper we have numerically demonstrated that this conditional probability is very high in the presence of stimulation and low in other cases.

Our results are in accordance with recent findings in theoretical [2] and experimental [9] neurobiology, in the sense that two close spikes, named "paired-spike interaction", seem to be one of the fundamental symbols in neural information transmission.

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[1] W. Bair, Spike timing in the mammalian visual system, Curr. Op. Neurobiol. 9 (1999) 447-453.
[2] N. Brenner, R. Strong, S.P. Koberle, W. Bialek, R.R. de Ruyter van Steveninck, Synergy in a neural code, Neural. Comput. 12(7) (2000) 1531-1552.
[3] M. Castelo-Branco, S. Neuenschwander, W. Singer, Synchronization of visual responses between the cortex, lateral geniculate nucleus, and retina in the anesthetized cat, J. Neurosc. 18(16) (1998) 6395-6410.
[4] E. Fernández, J.-M. Ferrandez, J. Ammermüller, R.A. Normann, Population Coding in spike trains of simultaneously recorded retinal ganglion cells, Brain Res. 887 (2000) 222-229.
[5] C. Koch, Biophysics of Computation: Information processing in single neurons, New York, Oxford, Oxford University Press 1999.
[6] R. Quian Quiroga, T. Kreuz, P. Grassberger, Event Synchronization: A simple and fast method to measure synchronicity and time delay patterns, Phys. Rev. E 66 (2002) 041904.
[7] F. Rieke, D. Warland, R. de Ruyter van Steveninck, W. Bialek, Spikes: Exploring the neural code, MIT Press, Cambridge 1997.
[8] M.W. Usrey, R.C. Reid, Synchronous activity in the visual system, Ann. Rev. Physiol. 61 (1999) 435-456.
[9] M.W. Usrey, J.B. Reppas, C.R. Reid, Paired-spike interactions and synaptic efficacy of retinal input to the thalamus. Nature 395 (1998) 384-387.
[10] D. Warland, P. Reinagel, M. Meister, Decoding visual information from a population of retinal ganglion on cells, J. Neurophysiol. 78 (1997) 2336-2350.