PROPOSAL OF SYNCHRONIZATION INDEXES OF SINGLE NEURON ACTIVITY ON PERIODIC STIMULUS

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ABSTRACT

Synchronization of a neuronal response to a given periodic stimulus is usually measured by Goldberg and Brown's vector strength metric (1969). The limitations of this index are discussed and two alternative indexes are proposed: the corrected vector strength index and the phase variance index. Using a standard data set, the three metrics are compared and the results indicate that the vector strength index should be interpreted with great care. The proposed new indexes are both more relevant to 'synchronization'. Moreover, these two indexes can be tuned to show a large variation of behavior depending on the user's idea of synchronization.

Index Terms - *Phase synchronization, nervous system, amplitude modulation.*

1. INTRODUCTION

To find or define a temporal relation between a stimulus and a neuronal response, one can use synchronization indexes. Synchronization is a large concept. In Newtonian physics, two coupled systems are considered to be synchronized when they produce a periodic response with the same frequency and a constant phase difference. This characterization is extended to noisy and chaotic oscillators [1]. So we talk about 'generalized synchronization' when the variation of signals phases difference is below a given value. In the Fourier sense, phase is related to frequency and delay. This implies two kinds of synchronization measurement. Firstly, when all the phase information is considered, the phase synchronization index is used. Secondly, when delay information is not considered, the frequency synchronization index is used. In this paper, we only deal with the second one since, in neuronal response studies, propagation delay could be measured using other methods.

We consider that a neuronal response and a periodic stimulus are synchronized when the neuron fires one time per stimulus period and spikes are spaced apart by a stimulus period. That is to say that spikes arrive at the same time of each stimulus' period. Synchronization falls when the irregularity increases. What about neuronal responses consisting in spikes emitted at the same time in periods but not regularly (*i.e.* not in every period)? We assume that each missed period is a desynchronization factor. We consider that a supplementary spike emitted in a period (more than one spike per period) participates to desynchronization.

Since this work only concerns discrete signals, a sampling frequency f_s is defined. The stimulus has a periodic component whose period is T_m. The total length of the neuronal response as well as the length of the stimulus are assumed to be a multiple of T_m ($N.T_m$). From the neuronal response, we create a signal $x(k)$, with k a count of time steps $T_s = 1/f_s$. This signal is equal to one when an action potential (AP) is present and zero otherwise. To this end, a threshold is applied to the neuronal response to decide the presence of an AP. As we want a single one per AP, a binwidth is defined. Let k_0 be the first sample above threshold, $x(k) = 1$ for k in $[k_0 \,;\, k_0 + \text{binwidth} - 1]$, $x(k) = 0$ after, until the signal reaches the threshold again.

Synchronization measurements are based upon the stimulus reduced period and $x(k)$. Indexes are described in section 2. First, the standard 'vector strength index' [2] is presented as well as its drawbacks. Then, two new indexes, the 'corrected vector strength index' and the 'phase variance index', are proposed. A dataset is established to allow parallel evaluation of the three indexes and results are presented in section 3 before drawing some conclusions.

2. METHODS AND MATERIALS

2.1. The Vector Strength Index

Goldberg and Brown's [2] vector strength index (1969) is frequently used in neuroscience by physiologists (e.g., [3], [4]) and by those who want to evaluate their computer model capacity to reproduce physiologists' measurements (e.g., [5]). When assessing periodic data, a 'period histogram' is used. The period histogram of $x(k)$, R_k, is defined by: $R_k = \sum_{i=0}^{N-1} x(k+iQ),\ k \in [0, Q-1]$

where N is the number of entire periods in $x(k)$ recording. Q is the number of samples per period of the stimulus periodic component. In order to not introduce additional error due to sampling effects and to make the following definitions clearer, Q is the same on each period such as $T_m = Q.T_s$.

The vector strength index (VSI) of the period histogram is defined by:

$$\text{VSI} = \frac{\sqrt{\left[\sum_{k=0}^{Q-1} R_k \cos(2\pi \frac{k}{Q})\right]^2 + \left[\sum_{k=0}^{Q-1} R_k \sin(2\pi \frac{k}{Q})\right]^2}}{\sum_{k=0}^{Q-1} R_k}.$$

VSI is an index varying between 0 and 1. The value 1 is commonly interpreted to represent perfect synchronization. It can be shown that this is equivalent to the neuronal response Fourier coefficient at the periodic component frequency. From a geometrical point of view, we consider the period histogram's projection on the unit circle. The VSI index is properly related to the normalized vectorial sum of this projection. When the neuronal response is not synchronized, the period histogram is widely distributed and the resulting vector norm is small. On the other hand, when the neuronal response is synchronized, the period histogram is narrow. This involves a resulting vector norm which is close to the number of spikes. Synchronization is assessed as being proportional to the resulting vector strength.

Let us consider synchronization performance as a period detection problem. We assume that a perfectly synchronized neuronal response consists of one spike per period and that each spike occurs at the same time in the period. If there is no spike in a stimulus period, we say that there is an omitted spike. If there are two (or more) spikes in a period, there are additional spikes. From this point of view, the vector strength index fails in some cases. Consider a perfectly synchronized response, VSI = 1. If some spikes of the response are removed, VSI = 1 and that until there is one spike left on the length of the neuronal response.

2.2. The Corrected Vector Strength Index

Given the limitations of the previous index, a corrected vector strength index is proposed. It is based on the same principle but a normalization factor takes into consideration omitted and/or additional spikes. The denominator of the new index is defined as follows:

$$Den(n, N) = p.|N - n| + n$$

where N is the total number of periods in $x(k)$ recording and n is the number of spikes in the recording. Note that N is also the number of spikes in the perfect response (one per period of the periodic component). From the period histogram definition, we have $\sum_{k=0}^{Q-1} R_k = n$. Parameter p is a penalty factor for omitted and additional spikes. First, we note that $Den(N,N) = N$ which does not depend on p. Secondly, when $p = 0$, $Den(n,N) = n$. Since this denominator has to be more drastic than the old one, p must be chosen so that $Den(n, N) > \sum_{k=0}^{Q-1} R_k$, for $n \neq N$. It implies $p > 0$.

Following this, the corrected vector strength index (CVSI) is defined by:

$$\text{CVSI} = \frac{\sqrt{\left[\sum_{k=0}^{Q-1} R_k \cos(2\pi \frac{k}{Q})\right]^2 + \left[\sum_{k=0}^{Q-1} R_k \sin(2\pi \frac{k}{Q})\right]^2}}{p.\left|N - \sum_{k=0}^{Q-1} R_k\right| + \sum_{k=0}^{Q-1} R_k}.$$

2.3. The Phase Variance Index

The greater the synchronization, the smaller the variance of the period histogram. At the opposite, a uniformly distributed period histogram results in the greatest variance and reveals the lack of synchronization between signals. This leads to the proposal of a second index. Firstly, the period histogram is unwrapped setting the minimum of the period histogram as the first sample. Secondly, the period histogram variance $\sigma^2_{period-histogram}$ is computed over the periodic component period (T_m). Then, it is normalized by the largest possible variance: the variance of a uniformly distribution over the same interval $\sigma^2_{uniform}$.

The following index (α) is synchronization relevant:

$$\alpha = 1 - \frac{\sigma^2_{period-histogram}}{\sigma^2_{uniform}}.$$

α is zero when the period histogram is uniform (desynchronized response). For perfectly synchronized responses, the period histogram consists of one non-zero value, then $\sigma^2_{period-histogram}$ is zero and α equals one.

In a second step, we add some non-detection (omitted spikes) and false alarm (additional spikes) penalties using the denominator $Den(n,N)$ introduced in § 2.2. Since $0 \leq \alpha \leq 1$, the penalty must be lower than (or equal to) one to obtain a final index lower than or equal to one. The minimum value of $Den(n,N)$ is n, obtained when $p = 0$ or $n = N$. We write the penalty factor in the following way:

$$\beta = \frac{n}{Den(n, N)}$$

where N and n are those defined in section 2.2.

The Phase Variance Index (PVI) is now defined by:

$$\text{PVI} = \alpha.\beta = \frac{\left(1 - \frac{\sigma^2_{period-histogram}}{\sigma^2_{uniform}}\right).n}{p.\left|N - \sum_{k=0}^{Q-1} R_k\right| + \sum_{k=0}^{Q-1} R_k}.$$

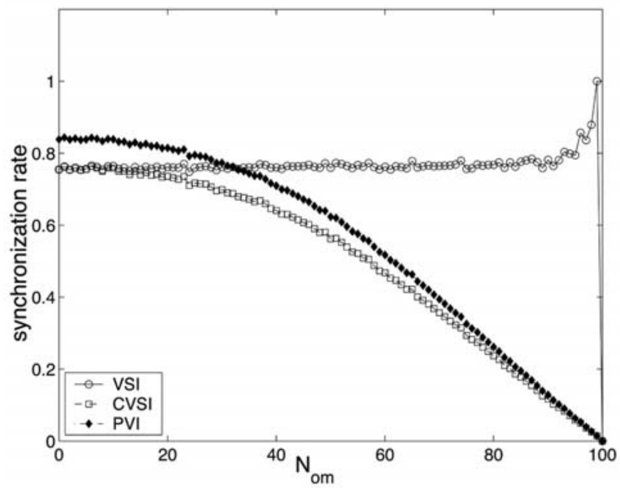

Fig. 1 – Impact of non-detection on the synchronization index (N_{ad} = 0, v = 0.2). New indexes CVSI and PVI decrease with the averaged number of spikes. VSI does not decrease and rises to one when there is one spike left.

3. RESULTS

After considering neuronal responses to a stimulus that contains a periodic component, a set of possible responses is created.

Three neuronal response characteristics influencing synchronization have been studied:

- Irregularity in periodic firing
- Non-detection of a period
- Emission of supplementary spikes not related to the periodic component.

The reference response, which is the perfect one, consists of spikes regularly spaced with a reduced period Q. The signal is built with a binwidth equal to 1. Irregularity in firing is introduced. Around each perfect spike instant, another spiking time is defined with a Gaussian law whose mean is the perfect spiking time and $v.Q$ the standard deviation. v is the uncertainty parameter, given in percent of T_m. Taking this criterion into account, a new response is built by gaussianly distributing spikes on each uncertainty interval. The greater the value of v, the less synchronized the simulated neuronal response.

Non-detection is introduced by randomly removing N_{om} spikes in the response described before. N_{om} is the omitted period parameter and must be less than (or equal to) N, the number of periods in the recorded response.

Emission of supplementary spikes is performed by adding N_{ad} spikes randomly during the whole simulated response duration.

For all tests presented in this paper, f_s=1000 Hz, and f_m=10 Hz, which gives $Q = 100$. Signals last 5 seconds.

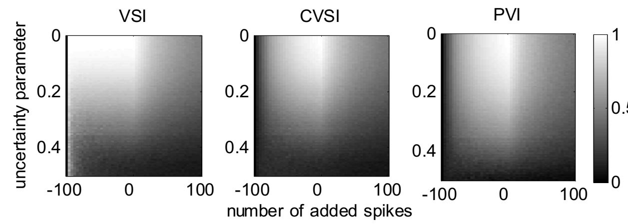

Fig. 2 – Values of the three indexes by varying three parameters of simulated neuronal response: number of omitted spikes (added spikes in [-100 ; 0]), number of added spikes (added spikes in [0 ; 100]), and uncertainty parameter. All indexes are sensitive to the increase of uncertainty in the spiking time and in the number of spikes. Contrary to VSI, CVSI and PVI are both sensitive to removed spikes.

Figure 1 illustrates indexes' evolution for removed spikes. Simulated responses take into account an uncertainty factor ($v = 0.2$) to provide more realistic signals. The introduction of this random factor does not affect global results. Of course, it induces a slight variance in synchronization depending on distribution realizations. This figure shows VSI drawback because omitted spikes are not considered as a loss in synchronization. When there is only one spike left, this index rises to one as it is for a perfectly synchronized response. The new denominator is introduced to compensate this drawback. Consequently, CVSI and PVI behave better than VSI.

Figure 2 is a plot of indexes' evolution versus desynchronization parameters of the simulated neuronal response (N_{om}, N_{ad}, v). In the right part, for added spikes in [0 ; 100], VSI, CVSI and PVI decrease with the number of added spikes and the uncertainty parameter. In the left part, for omitted spikes, added spikes in the range [-100 ; 0], VSI is affected by the uncertainty parameter but as the number of spikes decreases, VSI increases. This is considered as a VSI drawback. Of course, when there is no spike left, VSI = 0. CVSI and PVI behave as VSI except that the lack of spikes is considered as a desynchronization factor.

The penalty parameter (p) value can be tuned to correspond to different ideas about synchronization. What kind of neuronal response could be a temporal code for a periodic component? Figure 3 gives an example of two different types of behavior of the CVSI compared to the VSI. PVI's behavior is globally comparable to CVSI and is not represented. Figures 3-a and 3-b show clearly that, for a penalty parameter close to zero, CVSI is similar to VSI, except that the VSI low firing rate problem is avoided. In this case, non-detection and uncertainty in the spiking time are important to consider in synchronization. If, for another response evaluation, the spiking time is less important than non-detection or added spikes, the value of p used in figure 3-c has to be chosen.

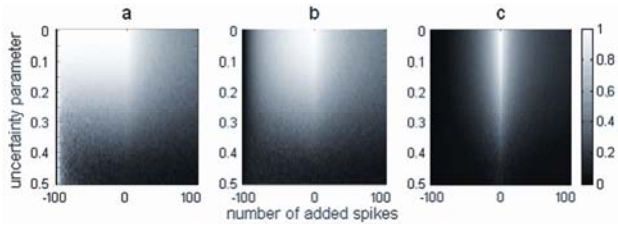

Fig. 3 – Impact of the penalty parameter by varying three parameters: number of omitted spikes (added spikes in [-100 ; 0]), number of added spikes (added spikes in [0 ; 100]), and uncertainty rate. (a) VSI is represented as a reference, (b) CVSI with $p = 0.2$, (c) CVSI with $p = 3$.

4. DISCUSSION

Firstly, by considering only the uncertainty impact on synchronization, all indexes react in the same manner. Secondly, they are also sensitive to the supplementary spikes impact on synchronization. Thirdly, it is clear that VSI is not relevant for omitted spikes. CVSI and PVI correct this drawback and have a similar behavior. Moreover, the new denominator is tunable changing p.

In the literature [2], [3], [4], VSI is often presented with the neuron firing rate (FR). The FR is the average number of spikes emitted by a neuron in a second. It could be shown that a combination of FR and VSI leads to a unique value of CVSI, for a given p. This means that a combination of CVSI and FR presents the same amount of information as a combination of VSI and FR. That is why the impact of the VSI drawback is not important if known. To avoid misinterpretation, two solutions are proposed: use of a combination of CVSI and FR or drawing the ideal FR curve with the neuron FR measurement. The first one is a better decomposition of the information because all the synchronization information is contained in CVSI. The second one is a curve for which FR equals the frequency of the stimulus periodic component.

Equivalence between (VSI, FR) and (CVSI, FR) is interesting because all previous measures may be quickly recomputed. We should note that the testing set proposed before is intellectually satisfying but its nature differs from the physiological data. Nevertheless, the equivalence ensures some matching with physiological data.

The combination of VSI and FR may also be expressed by their product. This corrects VSI non detection problem, but it is insensitive to additional spikes.

The phase variance index has corrected vector strength index like features and presents a specific quality: accurate frequency selectivity. This is shown by the following experiment. Let f_a be the frequency of the periodic component in the stimulus. Consider a neuronal response which does not depend on this stimulus but which is periodic at f_b frequency. Each index takes a value that leads us to consider those signals as desynchronized until $|f_b - f_a|$ falls below a set value. It appears that the PVI is the most selective index because its threshold value is lower than the value of the other indexes. As there is no equivalence between VSI and PVI, PVI must be tested on physiological data to confirm that it behaves correctly.

Other attempts have been made to update the VSI. Some are based on entropy [6] or autocorrelogram [7]. As their normalization is proportional to the number of spikes in the response, they do not avoid non detection problem. Of course the concept of time dispersion [8] is more appropriate to interpret results but this measure has the same drawback, in terms of synchronization, as it is VSI based.

5. CONCLUSION

Synchronization is important to characterize or highlight relations between signals. This is useful in neuroscience exploration as there are two kinds of coding: rate and synchronization coding. In this contribution, we proposed two indexes: one improves VSI behavior and the other one is based on the phase of the period histogram. The main idea relies on the normalization that penalizes missing spikes. Variation of all criteria gives us the following results:

- Uncertainty impact: all indexes behave similarly.
- Non-detection impact: the VSI problem is corrected in the two new indexes CVSI and PVI. Different sensitivities to this factor could be defined by tuning the penalty factor p.
- False detection impact: all indexes behave similarly. The two indexes proposed here could be tuned by changing the penalty factor p.

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