

Research Article

Comparison of Synchronization Indices: Behavioral Study

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The synchronization of a neuronal response to a given periodic stimulus is usually measured by Goldberg and Brown's vector strength metric. This index does not take omitted spikes into account. This particular limitation has motivated the development of two new indices: the corrected vector strength index and the corrected phase variance index, both including a penalty factor linked to the firing rate. In this paper, a theoretical study on the normalization of the corrected phase variance index is conducted. Both indices are compared to four existing ones using a simulated dataset which considers three desynchronizing disturbances: irregularity in firing, added spikes, and omitted spikes. In the case of unimodal responses, the two new indices are satisfying and appear the more promising in the case of real signals. In the multimodal case, the entropy-based index is better than the others even if this index is not drawback-free.

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1. Introduction

Three criteria are generally used to analyze neuronal responses to periodic stimuli: post stimulus time histogram (or period histogram in this context), average firing rate, and synchronization indices. The poststimulus time histogram evaluates a typical neuronal response. This leads to the following classification. A period histogram with one maximum characterizes a unimodal response whereas a period histogram that consists of more than one maximum is multimodal. The average firing rate quantifies the neuronal activity. This may be of relevance when evaluating the neuron sensitivity to the stimulus. It is very useful to characterize rate coding.

Defined by Goldberg and Brown [1], the Vector Strength Index (VSI) is often used in neuroscience by physiologists [2, 3] to quantify synchronization. A VSI equal to one is commonly interpreted as a representation of a perfect synchronization between the stimulus and the neuronal response whereas a VSI equal to zero indicates a totally unsynchronized response. The VSI and, more generally, synchronization indices are affected by the firing rate and the firing pattern. A perfectly synchronized unimodal response is characterized by one spike arriving at the same time in

each period. A perfectly synchronized multimodal response consists of several spikes, each one arriving at the same time in each period. Synchronization falls when irregularity increases. How neuronal responses consisting of spikes emitted at the same time in some periods but not in every period should be considered? It is important for neurophysiologists to have an index which would really reveal synchronization. For example, in the auditory pathway, temporal processing is of great importance, and synchronization indices are extensively used [2, 4] and appear as a tool in models' validation [5].

In a previous paper [6], we assumed that each omitted or additional spike participates in desynchronization, and we proposed two new indices which take into account this aspect contrary to the VSI. These indices are the Corrected Vector Strength Index (CVSI) and the Corrected Phase Variance Index (CPVI). As the definition and the measurement of synchronization are not trivial, other indices have already been proposed [7–10].

This study expands the previous one [6]. Firstly, the phase variance index will be completely justified in Section 2.2. To this end, we will compute the maximal variance of spikes distribution in order to derive pertinent normalization in the phase variance index. Secondly, the

CPVI and the CVSI will be compared to a panel of four existing indices: the magnitude function of the modulation frequency, the entropy based index, the central peak height of the normalized shuffled autocorrelogram, and the time dispersion index. Moreover, to conclude this work, indices behaviors will be characterized in the unimodal case and in the multimodal case.

2. Method and Material

2.1. Notation. This work concerns discrete signals. f_s is the sampling frequency, and T_s the associated period. The stimulus is T_m -periodic. T_m is chosen to be a multiple of the sampling frequency: $T_m = QT_s$. Q is an integer and corresponds to the reduced period. The fact that T_m is a multiple of T_s makes the following definitions clearer and avoids additional errors due to sampling effects. A binary signal $x(k)$, with k the amount of time steps, has a value equal to one when an action potential (AP) is present and zero otherwise. Here, indices ability to quantify the synchronization of the response $x(k)$ with the periodic component of the stimulus T_m is evaluated. When assessing periodic data, a period histogram is used. The period histogram of $x(k)$, $R(k)$, is defined by

$$R(k) = \sum_{i=0}^{N-1} x(k+iQ), \quad k \in [0; Q-1], \quad (1)$$

with N the number of entire periods in the stimulus. The average firing rate (FR) is the number of action potentials in one second. According to the previous definitions: $FR = n/(NT_m)$, n being the number of spikes emitted in the response.

2.2. The Phase Variance Index. In this study, we focus on synchronization of a periodic stimulation with a neuronal response. The neuronal response latency is unknown. That is why the Phase Variance Index (PVI) is, as the VSI, a metric based on the circular representation of the period histogram. Whereas the VSI reflects the strength of the mean direction [11], the PVI addresses the question of the dispersion around this mean direction.

The angle $\bar{\theta}$ associated to the mean direction is given by

$$\bar{\theta} = \begin{cases} \arctan(\bar{S}/\bar{C}), & \text{if } \bar{C} \geq 0 \\ \arctan(\bar{S}/\bar{C}) + \pi, & \text{if } \bar{C} < 0, \end{cases} \quad (2)$$

with

$$\begin{aligned} \bar{C} &= \sum_{i=0}^{Q-1} R(i) \int_{i(T_m/Q)}^{(i+1)(T_m/Q)} \cos\left(2\pi \frac{t}{T_m}\right) dt, \\ \bar{S} &= \sum_{i=0}^{Q-1} R(i) \int_{i(T_m/Q)}^{(i+1)(T_m/Q)} \sin\left(2\pi \frac{t}{T_m}\right) dt. \end{aligned} \quad (3)$$

The time step of the period histogram associated to this angle is: $k_\mu = \text{round}((\bar{\theta}/2\pi)Q)$, with $\text{round}(X)$ the function that

rounds the value of X to the nearest integer. A centered period histogram is then defined to avoid error in the evaluation of synchronization due to the latency of the response. This centered period histogram $R_\mu^c(k)$ is based on the cyclic period histogram $R^c(k)$:

$$R^c(k+nQ) = R(k), \quad \forall k \in [0; Q-1], \forall n \in \mathbb{Z} \quad (4)$$

and is defined as: $R_\mu^c(k) = R^c(k - k_\mu)$, $\forall k \in [0; Q-1]$.

Then, the phase variance index is computed as: $PVI = 1 - (\sigma_{c,\mu}^2/\sigma_{\max}^2)$, with

$$\sigma_{c,\mu}^2 = \begin{cases} \sum_{k=-Q/2}^{(Q/2)-1} k^2 R_\mu^c(k), & \text{if } Q \text{ even,} \\ \sum_{k=-(Q-1)/2}^{((Q-1)/2)-1} k^2 R_\mu^c(k), & \text{if } Q \text{ odd,} \end{cases} \quad (5)$$

and σ_{\max}^2 the maximal variance so that $0 < PVI < 1$. In the unimodal case, the period histogram has one maximum which is local and global. In this case, the period histogram leading to σ_{\max}^2 is given by the resolution of the following optimization problem: $\max_{R(k)}(\sigma_{c,\mu}^2)$ under the three constraints.

- (1) $R(k)$ is a distribution estimate: $\sum_{k=0}^{Q-1} R(k) = 1$.
- (2) $R(k)$ is centered: $\bar{\theta} = 0$.
- (3) For a value k_0 of k , $R(k)$ has one maximum $R(k_0)$ which is local and global such as: $\forall k \in [0; Q-1]$, $R(k) \leq R(k_0)$ and we have,

$$R(k) \geq R(k-1), \quad \text{if } 1 \leq k \leq k_0, \quad (6)$$

$$R(k) \geq R(k+1), \quad \text{if } k_0 \leq k < Q-1.$$

Under these constraints, the uniform distribution ($R(k) = 1/Q$) leads to the maximal variance $\sigma_{\max}^2 = \sigma_{\text{uniform}}^2$ with $\sigma_{\text{uniform}}^2 = Q^2/12$. This intuitively corresponds to the spike distribution of the more desynchronized response.

In some cases, the 2nd and 3rd constraints leading to $\sigma_{\max}^2 = \sigma_{\text{uniform}}^2$ are not verified, and PVI may be negative. For example, the distribution that maximizes $\sigma_{c,\mu}^2$ without any monotony constraint is

$$R(k) = \begin{cases} 0.5, & \text{if } k = \frac{Q}{2}, \\ 0.25, & \text{if } k = 0 \text{ or } k = Q-1, \\ 0, & \text{otherwise.} \end{cases} \quad (7)$$

This distribution leads to $\sigma_{\max}^2 = Q^2/8$. In order to keep a good dynamic in synchronization coding, we use $\sigma_{\text{uniform}}^2$ as the maximum variance, and, to avoid negative values, a threshold is applied so that

$$PVI = \begin{cases} 1 - \left(\frac{\sigma_{c,\mu}^2}{\sigma_{\text{uniform}}^2}\right) & \text{if } \sigma_{c,\mu}^2 \leq \sigma_{\text{uniform}}^2 \\ 0, & \text{otherwise.} \end{cases} \quad (8)$$

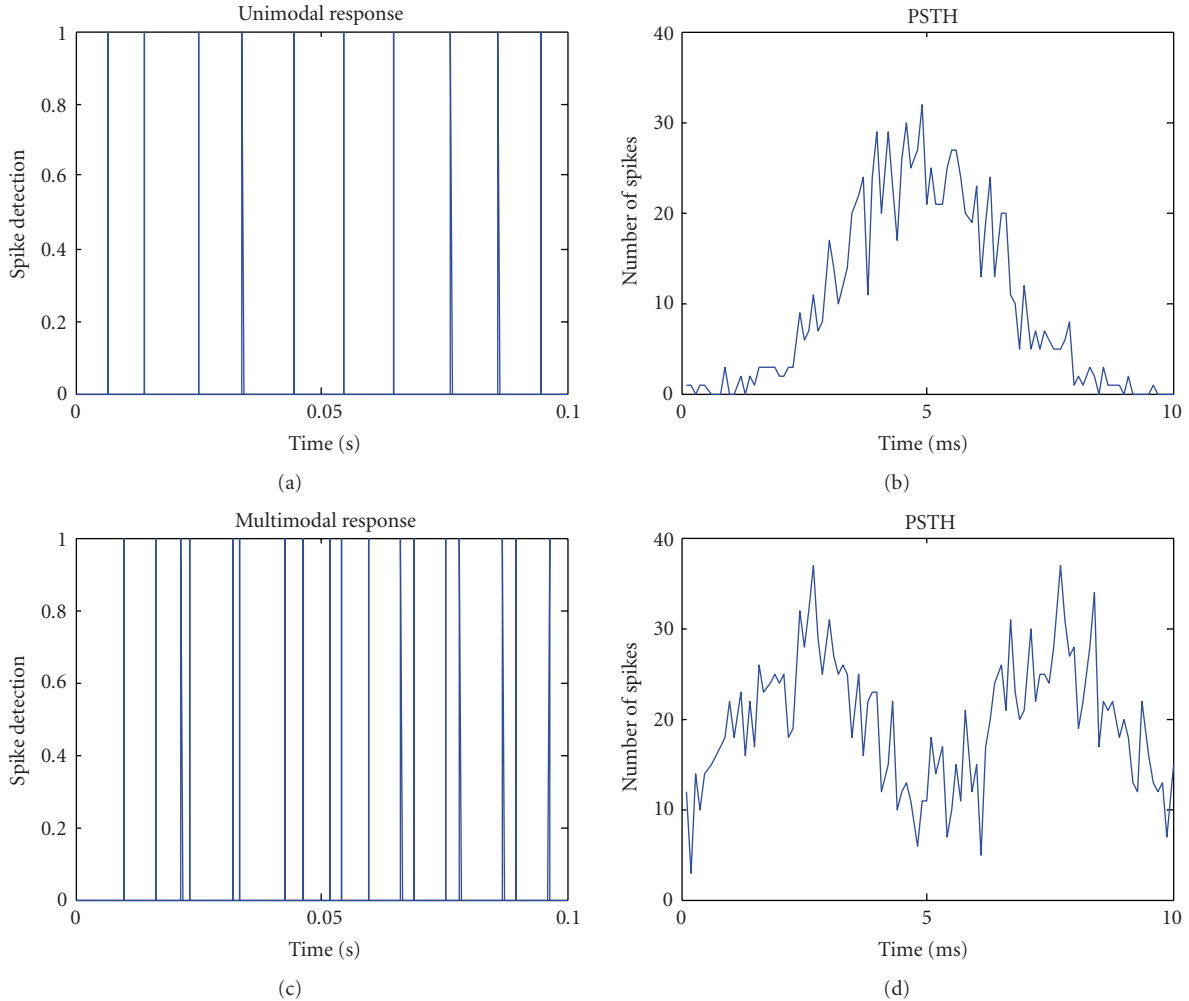


FIGURE 1: Example of the simulated dataset for $\nu = 0.15$, $N_{\text{dif}} = 0$, $N = 100$. On the left: spike detection in the unimodal and bimodal cases represented only on a sequence of 0.1 s. On the right: Post-Stimulus Time Histograms (PSTH) in unimodal and bimodal cases.

2.3. Corrected Indices. In [6], we introduced a penalty factor PF that takes into consideration omitted and/or additional spikes:

$$\text{PF} = \frac{n}{p|N - n| + n}. \quad (9)$$

The parameter of the penalty factor, p , must be positive. PF is then equal to one when the number of spikes (n) matches the number of recorded periods (N), which is the number of spikes in the perfect unimodal response (one per period of the periodic component). Otherwise, PF decreases in the presence of omitted and added spikes. The penalty factor is used to correct the VSI as well as the PVI and leads, respectively, to the definition of the corrected vector strength index (CVSI) and the corrected phase variance index (CPVI):

$$\text{CVSI} = \text{VSI} \times \text{PF}, \quad \text{CPVI} = \text{PVI} \times \text{PF}. \quad (10)$$

2.4. Other indices

2.4.1. The Magnitude Function of the Modulation Frequency. The Magnitude Function of the Modulation Frequency

(MFMF) used in [7] is defined as the product of the VSI and the average firing rate. It takes into account the neuron firing rate and reflects many aspects of the neuronal response. It mixes two neuronal characteristics, which implies a loss of information.

2.4.2. The Entropy-Based Index. Kajikawa and Hackett [8] proposed an Entropy-Based Index (EBI). Commonly used in information theory, entropy is even greater that responses are unexpected. The EBI characterizes the synchronization of different kinds of neuronal responses whereas other indices are designed only for unimodal responses.

2.4.3. Indices Extracted From the Normalized Shuffled Autocorrelogram. Louage et al. [9] extracted two indices from the normalized Shuffled Autocorrelogram (SAC). According to Joris procedure [12], the SAC is an histogram in which interspike intervals between several responses to a given stimulus are tailed. This method does not require any information on the stimulus such as the frequency of the

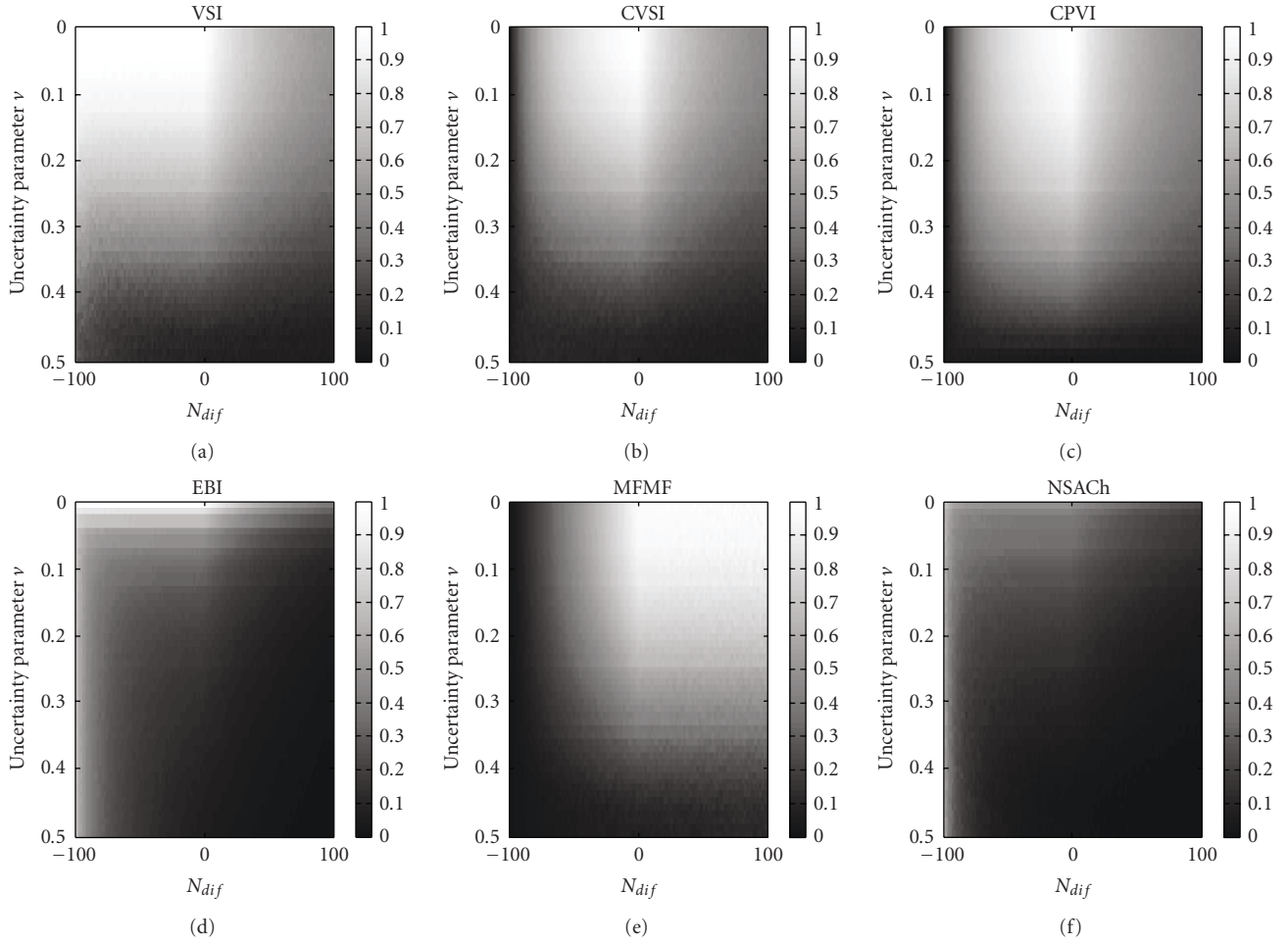


FIGURE 2: Values of synchronization indices for unimodal neuronal responses when varying the uncertainty rate and the number of added or omitted spikes N_{dif} ($N_{\text{dif}} = N_{\text{ad}}$ if $N_{\text{om}} = 0$ or $N_{\text{dif}} = -N_{\text{om}}$ if $N_{\text{ad}} = 0$). For CVSI and CPVI, $p = 0.2$. The perfectly synchronized simulated response is obtained with $\nu = 0$ and $N_{\text{dif}} = 0$. The synchronization is all the strongest as the index under study is close to one. The VSI, the NSACH and the EBI overestimate synchronization as the number of missing spikes becomes close to 100 (low firing rate) whereas the MFMF overestimates it at high firing rates (N_{dif} close to 100). Moreover, EBI and NSACH are very selective indices.

periodic component. The normalized SAC has a central lobe from which two indices are extracted. The central peak height (NSACH) quantifies the capacity of the neuron to fire in the same temporal positions on each stimulus presentation, and the peak width (NSACw) depends on the temporal accuracy of these responses.

2.4.4. The Time Dispersion Index. Paolini et al. developed the concept of time dispersion [10]. They considered irregularity in the spiking time as a jitter on the perfectly synchronized spike train. The jitter distribution is assumed to be Gaussian. The Time Dispersion Index (TDI) is the standard deviation of the jitter distribution. The TDI is derived from the VSI and presents similar drawbacks in spite of a more accurate description of unsynchronized responses. As a consequence, numerical results on this index are not presented hereafter.

2.5. Simulated Dataset. In this work, CVSI and CPVI are compared to existing indices using a simulated dataset.

Three characteristics that influence the synchronization of neuronal responses have been studied.

- (i) Irregularity in periodic firing.
- (ii) Nondetection or false detection in a period.
- (iii) Emission of additional spikes not related to the periodic component.

The reference response, which is a perfectly synchronized one, depends on the kind of neuronal response considered. For the unimodal response, it consists of spikes regularly spaced with a reduced period Q . For the multimodal response, a firing pattern is defined and repeated in each period. 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 uniform distribution whose mean is the perfect spiking time and $[-\nu Q; \nu Q]$ its value range. ν is the uncertainty parameter, given as a percentage of T_m . Taking this criterion into account, a new response is built by uniformly distributing

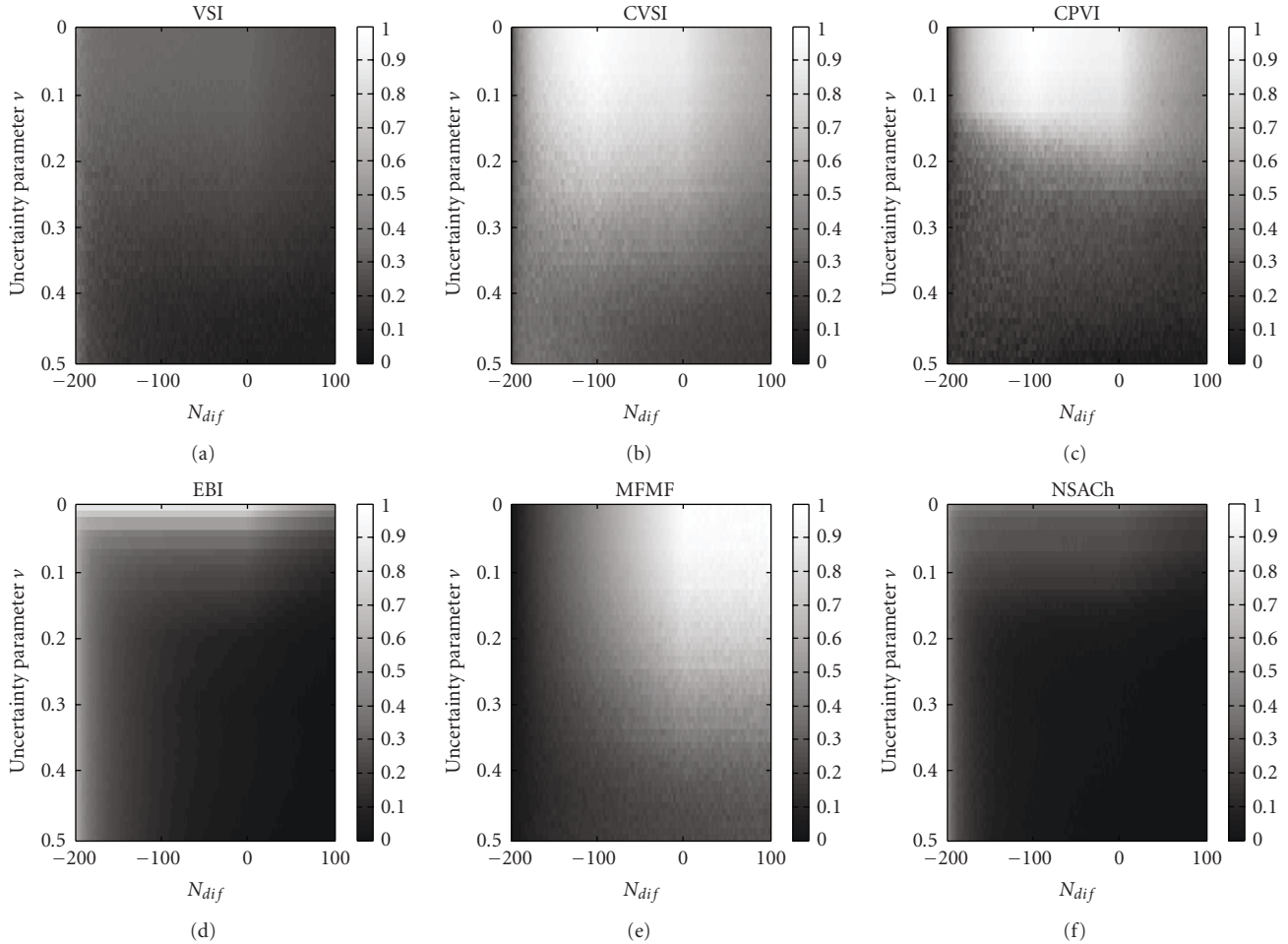


FIGURE 3: Values of synchronization indices for multimodal neuronal responses when varying the uncertainty rate and the number of added or omitted spikes N_{dif} ($N_{dif} = N_{ad}$ if $N_{om} = 0$ or $N_{dif} = -N_{om}$ if $N_{ad} = 0$). For CVSI and CPVI, $p = 0.2$. The perfectly synchronized simulated response is obtained with $\nu = 0$ and $N_{dif} = 0$. The synchronization is all the strongest as the index under study is close to one. The VSI, the NSACH, the EBI and the MFMF overestimate synchronization as observed in the unimodal case. The CVSI and CPVI have two maxima due to their normalization. The CPVI is more sensitive to the uncertainty rate.

spikes on each uncertainty interval. The greater the value of ν , the less synchronized the simulated neuronal response. Nondetection is introduced by randomly removing N_{om} spikes in the response described before. N_{om} is the omitted period parameter. Emission of additional spikes is performed by randomly adding N_{ad} spikes in the simulated response. To facilitate the results reading, a variable is introduced: $N_{dif} = N_{ad} - N_{om}$. As nondetection and false alarm are not simultaneously considered, we have $N_{dif} = N_{ad}$ if $N_{om} = 0$ or $N_{dif} = -N_{om}$ if $N_{ad} = 0$. For all tests presented in this paper, $f_s = 10$ kHz and $f_m = 100$ Hz, which gives $Q = 100$, and signals last 1 second, so that, in the unimodal case, $N = 100$. Figure 1 gives an example of this dataset, for $\nu = 0.15$, $N_{dif} = 0$, in the case of unimodal and multimodal (more specifically bimodal) responses. For these cases, spike detection and poststimulus time histogram are represented.

Under the previous conditions, experiments do not reveal a great difference between the NSACH and the NSACw. That is the reason why only the NSACH is represented. In

Figures 2 and 3, the MFMF and the NSACH are arbitrarily normalized to be comparable to other indices. To this end, they are divided by their maximal experimental value. So, all presented indices vary between 0 and 1, and the synchronization is all the strongest as the index under study is close to one.

3. Results

The parameter (p) of the penalty factor depends on the idea that one has about synchronization and has been discussed in [6]. In the present study, its value is set 0.2. A too important value of the parameter p makes the penalty factor decrease quickly when there are missing or additional spikes, and so the corrected indices fall too, which could lead to a misinterpretation of the synchronization of the detected spikes. To fix this parameter, a set of values has been tested. For a number of spikes corresponding to a half-period

TABLE 1: Indices advantages (+) and drawbacks (-).

	Nondetection sensitivity	false alarm sensitivity	uncertainty rate sensitivity	Normalized index	comments
VSI	-	+	+	yes	+ very used index
MFMF	+	-	+	no	- mixing of two neuronal characteristics
NSACH	-	+	-*	no	+ no a priori information needed
EBI	-	+	-*	yes	+ designed for multimodal responses
CVSI	+	+	+	yes	+ variable selectivity
CPVI	+	+	+	yes	+ variable selectivity

*Indicates that high sensitivity to the uncertainty rate may be considered as a drawback.

($n/N = 0.5$), $p = 0.2$ leads to $PF = 83\%$ while $p = 0.5$ leads to $PF = 67\%$. So, $p = 0.2$ appears to be a correct value. When the number of spikes is twice the number of periods, $p = 0.2$ leads to $PF = 91\%$ and $p = 0.5$ leads to $PF = 80\%$. Even if the increase in p is less influential when the number of spikes is higher than the number of periods, the value $p = 0.2$ seems to be a sufficiently high value. As a matter of fact, given this value of $p = 0.2$, the CVSI is comparable to the VSI, except that the low firing rate problem of the VSI is avoided.

3.1. Unimodal Responses. Figure 2 is a plot of the indices evolution versus the parameters of the simulated neuronal response (N_{dif}, ν). All the indices except the MFMF decrease with the number of added spikes. When the number of omitted spikes increases, the MFMF, CVSI and CPVI decrease. The VSI, EBI, and NSACH have the same drawback: they tend to move toward their maximum value when the number of omitted spikes increases. All the indices are affected by the uncertainty parameter. The EBI and NSACH are more sensitive than the other indices. One can suppose that the NSACH sensitivity to desynchronization is due to the binwidth of the histogram used to compute the shuffled autocorrelogram. Nevertheless, different binwidths have been tested and do not confirm this assumption.

3.2. Multimodal Responses. Figure 3 illustrates the behavior of synchronization indices in the multimodal case. The multimodal response pattern is composed of two spikes spaced apart by half a period. This is the worst situation to evaluate the VSI-based indices. Considering the circular representation of the period histogram of a perfectly synchronized response, the two vectors are opposed, and the resulting vector strength is close to zero except when there are few spikes left. Values of omitted spikes are chosen in the range $[0; 200]$ since there are 100 periods of stimulation. The maximum number of additional spikes remains equal to 100 in order to get a correct compromise between the region of interest and the legibility of the figure. Global behaviors of the MFMF, NSACH, and EBI are comparable to those observed in Section 3.1. The CVSI and CPVI have their maximum for half of the omitted spikes because it corresponds to the perfect firing rate of the unimodal case. Multimodal responses induce a bias in all indices except in the EBI. This bias is particularly important for the VSI and

NSACH because they increase continuously until there is only one spike left. This explains the lack of contrast in the VSI.

4. Discussion

The previous results lead us to some warning about indices. According to its definition, the VSI detects synchronization between stimuli and neuronal responses even if there are omitted spikes. The EBI and NSACH present the same drawback due to their normalization. The MFMF behaves well with omitted spikes but fails with added ones. Due to the denominator of the penalty factor, the CVSI and the CPVI are sensitive to the three factors that affect synchronization. For multimodal responses, the EBI is the best index tested here. However, it is also very sensitive to uncertainty in the spiking time, and it has the VSI trouble when the number of omitted spikes increases. Each of the following indices—VSI, MFMF, NSACH—has globally the same behavior for unimodal and multimodal responses, but each one has a weaker contrast in the second case which is explained by their common drawback. The CVSI and CPVI have weaker values but they still penalize a great number of omitted and additional spikes.

These results have to be extended to real neuronal signals. The CVSI tends to be the best index when answering the question of synchronization with clearly unimodal responses. It corrects the VSI drawback while keeping its relevant features. In the case of multimodal responses, the choice is more difficult. The EBI design is well suited for this kind of signal, but its drawbacks may be too important. That is why we promote the use of the CVSI. Even if it is tested here in the worst case (bimodal signal with spikes separated by half a period), it shows satisfying results. The CPVI may be considered as an alternative to the CVSI due to its similar behavior. In the case of real signals, the differentiation between these two modes will be obtained thanks to poststimulus time histogram.

Synchronization is one aspect of the neuronal response. Other approaches exist to get more information on neuron temporal properties to characterize synchronization but do not provide indices. Kvale and Schreiner [13] use high order statistical analysis to study temporal adaptation to the stimulus envelope. Recio-Spinoso et al. [14] show that Wiener-kernel analysis can reveal temporal features of neuronal responses.

5. Conclusion

In this study, a comparison of six synchronization indices is presented. For unimodal responses, the two novel indices behave better than the previous ones (see Table 1). For multimodal responses, there is no adequate index even if the EBI is well designed for this kind of response. Correct behavior of the CVSI and CPVI is due to their penalty factor, which can be easily adapted to any index. Synchronization evaluation of real neuronal responses with these indices should be combined with physiologists' opinions in order to complete this study.

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