Technical Note

Synchronization likelihood with explicit time-frequency priors

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Cognitive processing requires integration of information processed simultaneously in spatially distinct areas of the brain. The influence that two brain areas exert on each others activity is usually governed by an unknown function, which is likely to have nonlinear terms. If the functional relationship between activities in different areas is dominated by the nonlinear terms, linear measures of correlation may not detect the statistical interdependency satisfactorily. Therefore, algorithms for detecting nonlinear dependencies may prove invaluable for characterizing the functional coupling in certain neuronal systems, conditions or pathologies. Synchronization likelihood (SL) is a method based on the concept of generalized synchronization and detects nonlinear and linear dependencies between two signals (Stam, C.J., van Dijk, B.W., 2002. Synchronization likelihood: An unbiased measure of generalized synchronization in multivariate data sets. Physica D, 163: 236–241.). SL relies on the detection of simultaneously occurring patterns, which can be complex and widely different in the two signals. Clinical studies applying SL to electro- or magnetoencephalography (EEG/MEG) signals have shown promising results. In previous implementations of the algorithm, however, a number of parameters have lacked a rigorous definition with respect to the time-frequency characteristics of the underlying physiological processes. Here we introduce a rationale for choosing these parameters as a function of the time-frequency content of the patterns of interest. The number of parameters that can be arbitrarily chosen by the user of the SL algorithm is thereby decreased from six to two. Empirical evidence for the advantages of our proposal is given by an application to EEG data of an epileptic seizure and simulations of two unidirectionally coupled Hénon systems.
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Introduction

Cognition depends on coordinated neuronal activity in spatially distinct areas of the brain (Varela et al., 2001). Two central issues in cognitive neuroscience are to detect the brain areas that interact during various tasks and to reveal the nature of their interaction. It is natural to assume that the coordination of activity or exchange of information between brain areas gives rise to a statistical interdependence between the activities in these areas. In other words, we may reveal the spatial functional connectivity underlying cognitive processing by mapping the statistical interdependencies between time series of neuronal data recorded from different anatomical locations (Lee et al., 2003). The evidence suggests that functional interactions are mediated by synchronization of oscillations and that the frequency content of these oscillations has some specificity to the function that they serve (Sarnthein et al., 1998; von Stein and Sarnthein, 2000; Varela et al., 2001). Nevertheless, neuronal activity patterns may be related through nonlinear functions including strongly transient or cross-frequency phase locking (Friston, 2000; Stam et al., 2003; Palva et al., 2005a). To detect statistical interdependencies that are not governed by simple linear functions, so-called "nonlinear methods" are required.

Many coupling measures for detecting linear and nonlinear interdependencies have been proposed (for a review, see Stam, 2005). Currently, there is no consensus on how to best detect nonlinear interdependencies in neurophysiological data (Quiroga et al., 2002; David et al., 2004). In fact, different algorithms have been shown to detect nonlinear interactions between brain regions (Stam et al., 2003). The most general form of interaction between two dynamical systems is generalized synchronization, where the state of a response system Y is a function of the state of the driver system X: $Y = F(X)$ (Rulkov et al., 1995). For neural systems, this implies that if a given area generates a specific pattern of activity (X) at different times, the functionally connected brain areas are likely to generate specific patterns of activity $F(X)$ at those same points in time. Note that the patterns in the different areas may be widely different because of the potentially nonlinear coupling that governs the functional relationships (in other words, F may be a nonlinear

function). Moreover, one may be interested in the coupling between organs that produce qualitatively different signals, e.g., heart-rate variability and sleep EEG (Dumont et al., 2004).

A natural way to investigate generalized synchronization is to represent the state of dynamic systems in a given time window by vectors in the so-called state space formed by time-delay embedding (Takens, 1981; Ott, 1993). The problem of detecting similar dynamic states then translates into finding embedding vectors that are close in state space. This approach was used in the interdependency measure of generalized synchronization between two time series (Arnhold et al., 1999). However, as pointed out previously, the interdependency measure is sensitive to signals having different amplitudes or different degrees of freedom (Arnhold et al., 1999; Pereda et al., 2001). To solve this problem, Stam and van Dijk (2002) introduced a measure of generalized synchronization termed synchronization likelihood. In synchronization likelihood, the critical distances determining whether state vectors are close or not are defined separately for the two systems. The interdependency measure (S) and the synchronization likelihood (SL) share the problem, however, of having six parameters to be chosen by the user of the algorithms and little is known about their influence on the estimation of interdependency between coupled systems.

Here we argue that when choosing the values of the time-delay parameters, the SL algorithm is implicitly biased towards detecting patterns in certain frequency bands. Thus, we introduce lower or upper bounds for the values of SL parameters on the basis of the frequency range of interest and the sampling frequency of the signals. Moreover, we show for the first time examples of recurrent patterns detected by the SL algorithm and how these patterns are distributed in the time series. Finally, we explain the importance of having a lower bound for the number of recurrences and in what sense the temporal resolution of the SL algorithm is surprisingly good.

Methods

Time-frequency synchronization likelihood

Here we describe the synchronization likelihood method with explicit time-frequency priors. The differences between the present and the previous version of SL are addressed in the discussion.

The basic assumption of the method is that the state of the system at any given moment may be represented by an embedding vector, and thus that recurrent states are represented by similar embedding vectors (Takens, 1981). The computation of SL between two time series can be divided into the following five steps: (1) definition of the frequency band of interest and band-pass filtering; (2) construction of time-delay embedding vectors that represent dynamical states of the neural systems; (3) localization of the times of recurrent dynamical states in both systems; (4) computation of the likelihood (SL) that the recurrence of a state in one system is accompanied also by a recurrent state in the other system; and (5) repetition of steps 2–4 at different times in order to obtain a time series of SL values.

Definition of the frequency band of interest and band-pass filtering

Before applying the SL algorithm, one has to decide for the frequency band of interest, i.e., the lower and upper bounds of the frequency content of the patterns. Note that this does not imply that the patterns cannot have complex shapes, although this would

usually require a broad range of frequencies. The signals are then filtered with a suitable band-pass filter.

Representation of the dynamical state of the neural systems with time-delay embedding vectors

Following the decision on the frequency range of interest, we use time-delay embedding to form a state-space representation of the system dynamics. The rationale in the present study is that the state vector must sample the signal at sufficiently short intervals to pick up the fastest oscillation and also to be long enough to sample the slowest oscillation. From the time series $x_{k,i}$ of channel k, the state vector $X_{k,i}$ representing the state of the system at time i is given by:

$$X_{k,i} = (x_{k,i}; x_{k,i+L}; x_{k,i+2*L}; \dots; x_{k,i+(m-1)*L}) \tag{1}$$

Here, L is the lag and m is the dimension of the embedding vector in state space. Note that $X_{k,i}$ represents the state of the system in a time interval of length $L*(m-1)$, but for convenience we will refer to this interval as the state at time i, i.e., the beginning of the interval.

The SL method assumes that in a given period of time a pattern of activity will closely repeat itself a number of times in one signal and in the case of generalized synchronization between two signals another pattern tends to repeat itself in the other signal at those same times. The likelihood of repetition in the second signal may depend, e.g., on the strength of coupling between the two systems or on the signal-to-noise ratio of the data. The highest frequency in the patterns was defined above (step 1) and the embedding lag is chosen so as to sample the fastest oscillations. According to the Nyquist sampling theorem, a dynamical process must be sampled at minimum twice the highest frequency (HF) of its fluctuations in order for the discrete signal to adequately represent the dynamics of the underlying system. In practice, however, a factor of three is commonly used (Smith, 1999):

$$L = \frac{fs}{3*\text{HF}} \tag{2}$$

where fs is the sampling frequency in Hz.

The lowest frequency (LF) has the longest period and thus determines the length of the state vector:

$$L*(m-1) = \frac{fs}{\text{LF}} \Leftrightarrow m = \frac{3*\text{HF}}{\text{LF}} + 1 \tag{3}$$

Detection of recurrences of states in two potentially coupled systems

Having the dynamical states of a system A represented in state space, a criterion for when to consider states at different times similar or "recurrent" is needed. We construct a reference vector in channel A at time i, $X_{A,i}$, and vectors $X_{A,j}$ at times j, ranging from $i - W_2/2$ to $i - W_1/2$ and from $i + W_1/2$ to $i + W_2/2$ in steps of $1/fs$ (Fig. 1a). The time windows W_1 and W_2 are defined later in this section. The Euclidean distance between the state vectors $X_{A,j}$ and the reference vector is computed (other distance measures such as the maximum norm may also be used). The p_{ref} is now introduced to denote the percentage of vectors $X_{A,j}$ that are considered close enough to $X_{A,i}$ to represent the same state of the system (Fig. 2), which leads to the definition of a critical Euclidean distance, r_A, for which: $|X_{A,i} - X_{A,j}| < r_A$. A $p_{\text{ref}} = 0.05$ means that five percent of the vectors $X_{A,j}$ will be considered recurrences of $X_{A,i}$. The same procedure is applied to channel B at the same time point. The p_{ref} is generally associated with different critical distances (r_A and r_B)