Detection of Direct Causal Effects among Parts of the Brain of Epileptic Patients

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An extension of transfer entropy, called partial transfer entropy, is proposed here to detect causal effects among observed interacting systems, and particularly distinguish among direct and indirect causal effects. The measure is presented for time series from three interacting systems, but can be extended for more time series. Partial transfer entropy is evaluated on simulated and real data and is compared with partial directed coherence, a linear causality measure defined in the frequency domain. The simulation study showed that both measures can identify linear and nonlinear causal effects for the correct parameters. Both measures are then tested on electroencephalograms of epileptic patients for the detection of the direction of the interaction among brain areas during the preictal, ictal and postictal states.

Keywords: causality, information flow, partial transfer entropy, directed coherence

1. Introduction

The identification of the information structure and the hidden dependencies among the components of complex dynamical systems, observed from respective time series, is a difficult and challenging problem. A even more difficult task is to distinguish between direct and indirect information flow. Identification of effective connectivity among the variables of multivariate systems is an open issue in many disciplines, as neurophysiology. Mapping the brain connectivity could be a major step in understanding the functions of the brain and the of mechanism of diseases such as epilepsy.

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Common measures inferring dependence are non directional, e.g. cross-correlation, coherence and mutual information, whereas nonlinear directional measures mainly rely on bivariate analysis [Baccala & Sameshima, 2001; Frenzel & Pompe, 2001], such as transfer entropy (TE) [Schreiber, 2000], which is found to be very effective in detecting the direction of information flow [Papana & Kugiumtzis, 2008]. Here, the extension of TE, partial transfer entropy (PTE), in an attempt to detect direct information flow. PTE is compared to the partial directed coherence (PDC) [Baccala & Sameshima, 2001], which is a linear measure of direct causal effects commonly used in applications, including information flow and connectivity analysis of the brain system.

The two directed causality measures, PTE and PDC, are evaluated on simulated data from coupled systems with three variables, where the strength and the direction of the information flow are known. Results from the simulation study are indicative of the effectiveness of the measures and are used in order to interpret the results of the measures from real applications. Thus, measures are used to study the brain activity of epileptic patients based on the recordings of their electroencephalogram (EEG). EEG are considered as a set of univariate time series carrying information about the electric potential at different brain areas. The EEG records cover the preictal period (up to 3 hours prior to seizure onset), as well as the ictal (seizure) and postictal periods (minutes after the seizure).

The paper is organized as follows. First, we introduce the two measures of direct causal effects, partial directed coherence and partial transfer entropy in Sec 2. The two measures are evaluated on simulated and real data in Sec 3. Finally, the of this evaluation are discussed in Sec 4.

2. Methods

2.1. Partial Transfer Entropy

Transfer entropy (TE) is a nonlinear measure defined in the time domain, which quantifies the amount of information explained in $Y$ at $h$ time steps ahead from the state of $X$ accounting for the concurrent state of $Y$. For its definition, let us consider the reconstructed vectors of the state space of each system $x_t = (x_t, x_{t-\tau}, \ldots, x_{t-(m-1)\tau})'$ and $y_t = (y_t, y_{t-\tau}, \ldots, y_{t-(m-1)\tau})'$, where $\tau$ is the delay time and $m$ is the embedding dimension. TE from $X$ to $Y$ is defined as

$$TE_{X\rightarrow Y} = H(x_t, y_t) - H(x_{t+h}, x_t, y_t) + H(x_{t+h}, y_t) - H(y_t)$$  \hspace{1cm} (1)

where $H(x)$ is the Shannon entropy of the variable $X$. Partial transfer entropy (PTE) is the extension of TE accounting for the direct causal effect of $X$ to $Y$ conditioning on the rest interacting systems, here represented by $Z$. Considering a similar reconstruction for $Z$, PTE is defined as

$$PTE_{X\rightarrow Y|Z} = H(y_{t+h}|y_t, z_t) - H(y_{t+h}|x_t, y_t, z_t)$$  \hspace{1cm} (2)

PTE is estimated here using the $k$-nearest neighbors method [Kraskov et al, 2004].

2.2. Partial Directed Coherence

Partial directed coherence (PDC) is a linear measure of causality defined in the frequency domain. Let $x(t) = (x_1(t), ..., x_n(t))$ be a stationary $n$-dimensional time series with zero mean. A vector autoregressive model VAR[$P$] of order $P$, for $x$ is given by

$$x(t) = \sum_{r=1}^{P} a(r)x(t-r) + \epsilon(t)$$  \hspace{1cm} (3)

where $a(r)$ are the $n\times n$ coefficient matrices of the model and $\epsilon(t)$ is a multivariate Gaussian white noise process. Let us denote the covariance matrix of the noise process $\Sigma$ and the $n$-dimensional identity matrix by $I$. The Fourier transform of the coefficients is
\[ A(f) = I - \sum_{r=1}^{P} a(r)e^{-i2\pi f r}. \] (4)

PDC for the direct effect of component process \( j \) to \( i \) is defined as

\[ PDC_{j\rightarrow i}(f) = \frac{|A_{ij}(f)|}{\sqrt{\sum_k |A_{ij}(f)|^2}}. \] (5)

PDC provides a measure for the directed linear influence of \( x_j \) on \( x_i \) at frequency \( f \), conditioned on the rest of the signal variables.

3. Application

3.1. Simulated Data

The two causality measures are first evaluated on simulated data from different types of three coupled systems \( X, Y \) and \( Z \). At all cases, \( X \) drives \( Y \) \((X \rightarrow Y)\) and \( Y \) drives \( Z \) \((Y \rightarrow Z)\). Measures are estimated from 100 realizations of interacting systems for different coupling strengths \( c \), as given below for each system, and time series lengths \( n = 512, 1024, 2048, 4096, 8192 \). PTE is estimated for different number of neighbors \( k \) and embedding dimensions \( m \), whereas PDC is estimated for different VAR orders \( P \). PDC is computed as the average of \( PDC_{j\rightarrow i}(f) \) for a range of frequencies in \([0,0.5]\). Three types of interacting systems are used here, linear and nonlinear maps nonlinear flows. Specifically:

(a) 3 Coupled autoregressive AR(1) models

\[
\begin{align*}
x_t &= \theta_t \\
y_t &= x_{t-1} + \eta_t \\
z_t &= 0.5z_{t-1} + y_{t-1} + \epsilon_t
\end{align*}
\]

where \( \theta_t, \eta_t, \epsilon_t \) are Gaussian white noise with zero mean and standard deviations 1, 0.2 and 0.3, respectively.

(b) 3 Coupled Henon maps

\[
\begin{align*}
x_{t+1} &= 1.4 - x_t^2 + 0.3x_{t-1} \\
y_{t+1} &= 1.4 - cx_ty_t + (1-c)y_t^2 + 0.3y_{t-1} \\
z_{t+1} &= 1.4 - cy_tz_t(1-c)z_t^2 + 0.3z_{t-1}
\end{align*}
\]

with coupling strengths \( c = 0,0.05,0.1,0.2,0.3,0.4,0.5 \).

(c) 3 Coupled Lorenz systems

\[
\begin{align*}
\dot{x}_1 &= 10(y_1 - x_1) \\
\dot{y}_1 &= 28x_1 - y_1 - x_1z_1 \\
\dot{z}_1 &= x_1y_1 - 8/3z_1 \\
\dot{x}_2 &= 10(y_2 - x_2) + c(x_1 - y_1) \\
\dot{y}_2 &= 28x_2 - y_2 - x_2z_2 \\
\dot{z}_2 &= x_2y_2 - 8/3z_2 \\
\dot{x}_3 &= 10(y_3 - x_3) + c(x_2 - y_2) \\
\dot{y}_3 &= 28x_3 - y_3 - x_3z_3
\end{align*}
\]
\[ \dot{z}_2 = x_3 y_3 - 8/3 z_3, \]

with coupling strengths \( c = 0, 1, 2, 3, 4, 5 \).

Both measures correctly detect the direction of causal effects, but only for the correct selection of their parameters. PTE seems to be sensitive on the embedding dimension \( m \), while PDC on the model order \( P \). PTE presents less bias than PDC in case of no causal effects giving values in the limit of zero. Increase of the time series length reduces the variance of the estimated values of the measures; its selection seems to be significant in case of flows. Finally, PDC poorly performed in the case of the nonlinear flows.

In case of linear interacting systems, e.g. for the 3 coupled autoregressive AR(1) models, one would expect that PDC would outperform PTE. However, both measures correctly detected the direction of causal effects for small values of \( m \) and \( P \), respectively (see Fig. 1). For larger parameter values, both measures failed in correctly detecting the causal effects.

![Fig. 1. (a) Mean estimated values of PTE vs log of time series length \( n \) from 100 realizations of the 3 coupled autoregressive AR(1) models, for \( m = 1 \) and \( k = 2 \). In (b) and (c), as is (a) but for \( m = 1, k = 10 \), and \( m = 2, k = 2 \), respectively. In (d) and (e), as in (a) but for PDC for \( P = 1 \) and \( P = 2 \), respectively.](image)

In case of the nonlinear interacting systems, PTE outperformed PDC, as expected. PTE for the 'correct' selection of the embedding dimension \( m \) and number of neighbors \( k \), correctly detected the causal effects even for small time series lengths. On the other hand, PDC failed in this case even for large time series lengths. Both measures indicated sensitivity in the selection of their parameters. Indicative results for PTE and PDC vs the coupling strength \( c \), for the 3 coupled Henon maps, are presented in Fig. 2.

Simulations on the coupled nonlinear flows confirmed the superiority of PTE over PDC in case of nonlinear interacting systems. PDC failed to detect the causal effects for all the selected parameters, while PTE proved to be effective, however only for large time series lengths (see Fig. 3).

### 3.2. Physiological Data

The two causal measures, PTE and PDC are tested on EEG recordings from 6 epileptic patients in order to examine their ability to detect the direction and strength of the interaction among different brain...
areas during the propagation of the epileptic activity. Thus, it is investigated whether measures can detect changes in the directionality of the information flow among the different brain areas at the preictal, ictal and postictal states. The EEG recordings are extracranial. A high-pass filter at 0.3 Hz and a low-pass filter at 40 Hz have been used and data are down-sampled to 100 Hz. No other pre-processing or artifact rejection is performed. To attain better source derivation at small cortical regions, for each EEG channel, the mean EEG of the four neighboring channels is subtracted. The 5 EEG records are from generalized tonic clonic seizures (denoted as A to E) and one EEG record is from left back temporal lobe seizure (F). Both measures are estimated on the following pairs of channels: central left (C3) and right (C4), temporal left (T7) and right (T8), based on the standard 10-10 system. Each EEG record covers at least 3h prior to seizure onset and extends into the postictal period.

The two causality measures are calculated at all directions on non-overlapping consecutive EEG segments of 30s for the aforementioned channel pairs from each of the 6 records. The embedding dimension $m$ for the estimation of PTE is set to be 3 and 5. The other parameters of TE are $\tau = 5$ and $h = 5$. For the estimation of PDC, three orders for the VAR models are tested, $P = 6$ and 20, and PDC is averaged over frequencies from 1 to 30 Hz with step 1 Hz.

PTE indicates the increase of information flow during the ictal and postictal states; this discrimination was observed at all episodes. However, PTE and PDC do not indicate the same causal effects; e.g. for record A, PDC indicates driving of T7 and T8 on F3 and F4, and bidirectional interaction among all pairs of channels while PTE indicates weak bidirectional causal effect among F3 vs F4, F3 vs T7 and T7 vs T8 (see Fig.4a and c). Both measures vary much across the episodes, the channels and the states and give positive values (in larger or smaller scale) suggesting the existence of bidirectional causal effects among the different brain areas. Both measures seem to be insufficient in detecting a precursor of the seizure onset, as no changes in the information flow are detected.
4. Discussion

In this study, the identification of the interdependencies of coupled systems represented by observed time series was addressed. A nonlinear causality measure, partial transfer entropy, has been presented and was compared to a standard linear one, partial directed coherence. On applying the two causality measures on simulated data from coupled systems, the usefulness of PTE was indicated. The parameters of both measures have to be carefully selected, as both measures are sensitive to the selection of them.

A recent work has also indicated the use of partial transfer entropy for the identification of the directionality of the coupling between the nodes of a network [Vakorin et al., 2009], however another estimator of PTE is proposed here. A problem of PTE discussed there is the model mis-specification, i.e. the fact that one might not include all the involved variables of a coupled system. There are also limitations imposed in the complexity of a model, i.e. the large dimensionality of the vectors in the estimation of PTE in case of large number of variables. The correct trade of between the complexity of the models and the reliability of the results is an open issue for investigation.

In the application on EEG, results are not conclusive as there is no consistency in the measure profiles. Therefore, there should be further investigation for the effectiveness of the measures in such applications, and also optimization of the parameters of the measures. The fact that measures were ineffective in this application might be also due to the model mis-specification, as only certain channels have been used. Therefore, the consideration of all the variables of the system, i.e. all the channels should be included in the estimation of the causal effects. The potentials of PTE in terms of the system’s complexity concerning the number of it’s variables will be thoroughly investigated in the future.

References

