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

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Abstract

An extension of transfer entropy, called Partial Transfer Entropy (PTE), 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. PTE is evaluated on simulated and real data and is compared with partial directed coherence (PDC), 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. PTE and PDC are then tested on electroencephalograms (EEG) of epileptic patients for the detection of the direction of the interaction among brain areas during the preictal, ictal and postictal states.

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. Even more difficult is to distinguish direct from indirect information flow. Common measures inferring dependence are non-directional, e.g. cross-correlation, coherence and mutual information, whereas nonlinear directional measures mainly rely on bivariate analysis [1,2], such as Transfer Entropy (TE) [3], which is found to be very effective in detecting the direction of information flow [4]. Here, we extend TE to Partial Transfer Entropy (PTE), in an attempt to detect direct information flow. Further, we compare PTE to the Partial Directed Coherence (PDC) [1], which is a linear measure of direct causal effects commonly used in applications, including information flow and connectivity analysis of the brain system.

Partial Transfer Entropy (PTE)

TE is a nonlinear measure defined in the time domain, and 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 $\mathbf{x}_t=(x_t, x_{t-\tau}, \ldots, x_{t-(m-1)\tau})'$ and $\mathbf{y}_t=(y_t, y_{t-\tau}, \ldots, y_{t-(m-1)\tau})'$, where τ is the delay time and m the embedding dimension. TE from X to Y is defined as

$$TE_{X\to Y} = H(\mathbf{x}_t, \mathbf{y}_t) - H(x_{t+h}, \mathbf{x}_t, \mathbf{y}_t) + H(x_{t+h}, \mathbf{y}_t) - H(\mathbf{y}_t)$$

where $H(x)$ is the Shannon entropy of the variable X. 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

$$PTE_{X\to Y|Z} = H(y_{t+h} | \mathbf{y}_t, \mathbf{z}_t) - H(y_{t+h} | \mathbf{x}_t, \mathbf{y}_t, \mathbf{z}_t)$$

PTE is estimated using the k-nearest neighbors method [5].

Partial Directed Coherence (PDC)

Let $\mathbf{x}(t) = (x_1(t), \ldots, x_n(t))'$ be a stationary n-dimensional time series with zero mean. A vector autoregressive model VAR[P] of order P, for $\mathbf{x}$ is given by

$$\mathbf{x}(t) = \sum_{r=1}^{P} \mathbf{a}(r)\, \mathbf{x}(t-r) + \varepsilon(t)$$

where $\mathbf{a}(r)$ are the $n \times n$ coefficient matrices of the model and $\boldsymbol{\varepsilon}(t)$ is a multivariate Gaussian white noise process. Let us denote the covariance matrix of the noise process $\boldsymbol{\Sigma}$ and the n-dimensional identity matrix by $\boldsymbol{I}$. The Fourier transform of the coefficients is

$$\mathbf{A}(f) = I - \sum_{r=1}^{P} \mathbf{a}(r) e^{-i2\pi fr}$$

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

$$\pi_{j\to i}(f) = \frac{|A_{ij}(f)|}{\sqrt{\sum_k |A_{kj}(f)|^2}}$$

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

Evaluation of PTE and PDC

The two causality measures are first evaluated on simulated data from different types of 3 coupled systems X, Y and Z, where X drives Y **($X \to Y$)** and Y drives Z **($Y \to Z$)**. Measures are estimated from 100 realizations of interacting systems for different coupling strengths c and time series lengths n. 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 $\pi_{j\to i}(f)$ for a range of frequencies in [0,0.5].

(1) 3 Coupled autoregressive AR(1) models

ξ_t, η_t, ε_t are Gaussian white noise with mean 0 and standard deviations σ_1=1, σ_2=0.2, σ_3=0.3, respectively.

$$\begin{aligned} x_t &= \xi_t \\ y_t &= x_{t-1} + \eta_t \\ z_t &= 0.5 z_{t-1} + y_{t-1} + \varepsilon_t \end{aligned}$$

(2) 3 Coupled Henon maps

coupling strengths c = 0, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5

$$\begin{aligned} x_{t+1} &= 1.4 - x_t^2 + 0.3 x_{t-1} \\ y_{t+1} &= 1.4 - c x_t y_t + (1-c) y_t^2 + 0.3 y_{t-1} \\ z_{t+1} &= 1.4 - c y_t z_t + (1-c) z_t^2 + 0.3 z_{t-1} \end{aligned}$$

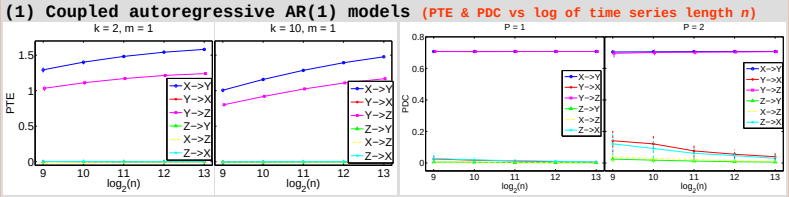
(3) 3 Coupled Lorenz systems coupling strengths c = 0, 1, 2, 3, 4, 5

$$\begin{aligned} \dot{x}_1 &= 10(y_1 - x_1) & \dot{x}_2 &= 10(y_2 - x_2) + c(x_1 - y_1) & \dot{x}_3 &= 10(y_3 - x_3) + c(x_2 - y_2) \\ \dot{y}_1 &= 28x_1 - y_1 - x_1 z_1 & \dot{y}_2 &= 28x_2 - y_2 - x_2 z_2 & \dot{y}_3 &= 28x_3 - y_3 - x_3 z_3 \\ \dot{z}_1 &= x_1 y_1 - \frac{8}{3} z_1 & \dot{z}_2 &= x_2 y_2 - \frac{8}{3} z_2 & \dot{z}_3 &= x_3 y_3 - \frac{8}{3} z_3 \end{aligned}$$

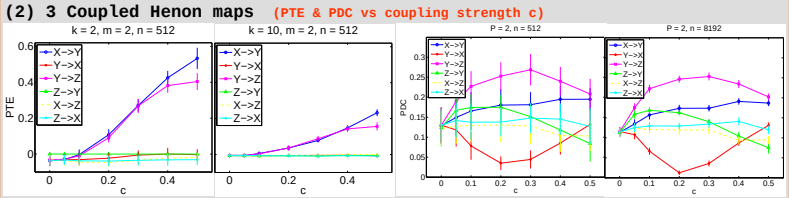
Results from the simulation study

Correct detection of the direction of causal effects for the 'correct' selection of parameters for both measures. Sensitivity of PTE on the embedding dimension m and of PDC on P. PTE presents less bias in case of no causal effects giving values in the limit of zero. Increase of time series length reduces the variance of the estimated values of measures; its selection seems to be significant in case of flows. Poor performance of PDC in nonlinear flows.

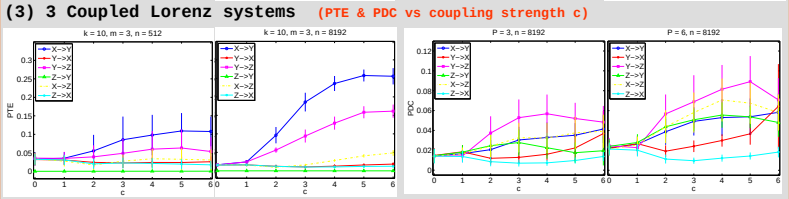
(1) Coupled autoregressive AR(1) models (PTE & PDC vs log of time series length n)



(2) 3 Coupled Henon maps (PTE & PDC vs coupling strength c)



(3) 3 Coupled Lorenz systems (PTE & PDC vs coupling strength c)

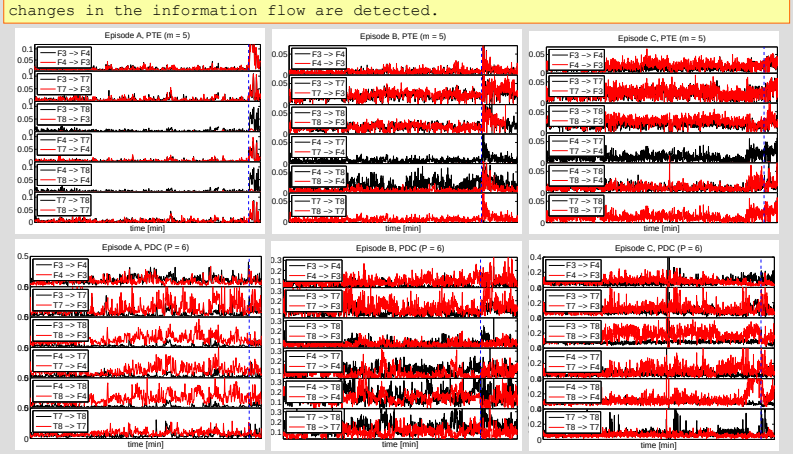


Application on EEG

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 interaction of brain areas during the propagation of the epileptic activity. Data are extracranial; 5 records are from generalized tonic clonic seizures (denoted as A to E) and one is from left back temporal lobe seizure (F). 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. Both measures are estimated on the following pairs of channels: central left (C3) and right (C4), temporal left (T7) and right (T8). Each EEG record covers at least 3h prior to seizure onset and extends into the postictal period.

Results from the application to EEG

PTE indicates the increase of information flow during the ictal and postictal states; this discrimination was observed at all episodes. PTE and PDC do not indicate the same causal effects; e.g. for record A PDC indicates driving of T7 and T8 on F3, 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. 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.



Conclusions

The simulation study indicated the usefulness of PTE for all types of data, while PDC performs well only on linear systems. The parameters of both measures have to be carefully selected. For the application to EEG, results are not conclusive (no consistency in the measure profiles). There should be further investigation for the selection of the parameters.

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