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Detection of directed information flow in biosignals

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Abstract

Several analysis techniques have been developed for time series to detect interactions in multidimensional dynamic systems. When analyzing biosignals generated by unknown dynamic systems, awareness of the different concepts upon which these analysis techniques are based, as well as the particular aspects the methods focus on, is a basic requirement for drawing reliable conclusions. For this purpose, we compare four different techniques for linear time series analysis. In general, these techniques detect the presence of interactions, as well as the directions of information flow, in a multidimensional system. We review the different conceptual properties of partial coherence, a Granger causality index, directed transfer function, and partial directed coherence. The performance of these tools is demonstrated by application to linear dynamic systems.

Keywords: directed transfer function; Granger causality; multivariate time series analysis; partial coherence; partial directed coherence.

Introduction

Different analysis techniques for time series have been introduced to process possible multidimensional biomedical signals. These techniques were developed primarily within the theoretical framework of linear stochastic processes and non-linear dynamics. An important application is the detection of interactions between electromagnetic signals representing information flow in the brain [10]; for example, synchronization phenomena between different brain structures have been analyzed by means of electroencephalography (EEG) recordings [8, 13]. Besides interactions among brain signals themselves, the interdependence between brain signals and other physiological signals is of particular interest. For instance, in tremor research, the interaction between EEG and electromyography (EMG) has been studied in patients suffering from Parkinson's disease or essential tremor [4, 9, 11].

The analysis techniques applied are characterized by different assumptions and capture distinct dynamic phenomena. When applying these analysis techniques to biomedical signals such as electrocorticogram, electrothalamogram, EEG or EMG recordings, the underlying dynamic system generating these signals is essentially unknown. For appropriate interpretation of analysis results, researchers should be aware of the different concepts these methods are based on and of the aspects that these analysis techniques focus on.

In this paper, we compare four analysis techniques for time series based on the theory of linear stochastic processes, which were introduced to allow detection of directed information flow in multidimensional dynamic systems based on measured time series. First, a nonparametric spectral approach, partial coherence, in combination with the partial phase spectrum (PC), is investigated. Second, three analysis tools are examined that utilize linear vector autoregressive processes to model the multivariate dynamic system under investigation: a Granger causality index (GCI) in the time domain, the frequency-domain directed transfer function (DTF), and partial directed coherence (PDC). We briefly introduce the theoretical background for each analysis technique, and illustrate the different aspects in applications to simulated model systems. Here, we have restricted the analysis to linear model systems to illustrate the basic properties of each analysis technique and to reveal the intrinsic differences between them. Further aspects concerning their applicability to biomedical signals are also discussed.

Simulated dynamical system

To illustrate the performances of the four multivariate time series analysis techniques described in this paper, the following four-dimensional vector autoregressive process of model order $p=5$ (VAR [5]) was chosen to reveal the intrinsic properties of the analysis techniques such that their differences become evident:

$$\begin{aligned}
X_1(t) &= 1.1X_1(t\text{-}1)\text{-}0.6X_1(t\text{-}2)+0.5X_2(t\text{-}3)+\eta_1(t)\\
X_2(t) &= 0.6X_2(t\text{-}1)\text{-}0.4X_1(t\text{-}5)+\eta_2(t)\\
X_3(t) &= 0.5X_3(t\text{-}3)+0.4X_2(t\text{-}4)+\eta_3(t)\\
X_4(t) &= 1.2X_4(t\text{-}1)\text{-}0.7X_4(t\text{-}2)\text{-}0.5X_1(t\text{-}2)+\eta_4(t).
\end{aligned} \tag{1}$$

This model system is characterized by direct and indirect interactions between the process components. The model coefficients and time lags reflect absent, unidirectional and bidirectional information flows.

We simulated $N=200{,}000$ data points for each process. The covariance matrix of the noise terms $\eta_i(t)$ was

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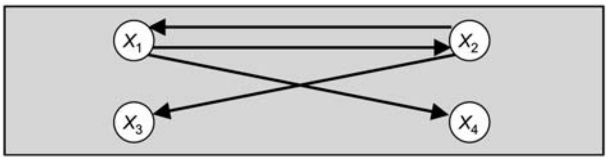

Figure 1 Diagram summarizing the interdependence structure in the simulated VAR system.

set to the identity matrix. The interrelations indicated by non-zero coefficients between the four processes are summarized in the graph in Figure 1. Processes X_1 and X_2 mutually influence each other, while there is a unidirectional influence from process X_1 on process X_4, as well as from process X_2 on process X_3.

Non-parametric spectral method to detect directions of information flow

Partial coherence in combination with the partial phase spectrum is a non-parametric spectral approach used to detect direct interrelations in multivariate dynamic systems. To differentiate direct and indirect interactions between processes, the bivariate cross-spectrum between process X_i and process X_j is modified. All linear information contained in the remaining Z processes is subtracted, leading to the notion of the partial cross-spectrum:

$$S_{X_iX_j|Z}(\omega)=S_{X_iX_j}(\omega)-S_{X_iZ}(\omega)\ S_{ZZ}^{-1}(\omega)\ S_{ZX_j}(\omega). \tag{2}$$

The normalized absolute value of the partial cross-spectrum is partial coherence

$$\mathrm{Coh}_{X_iX_j|Z}(\omega)=\frac{|S_{X_iX_j|Z}(\omega)|}{\sqrt{S_{X_iX_i|Z}(\omega)\ S_{X_jX_j|Z}(\omega)}}\in[0,1] \tag{3}$$

and its argument is the partial phase spectrum [2]:

$$\Phi_{X_iX_j|Z}(\omega)=\arg\{S_{X_iX_j|Z}(\omega)\}. \tag{4}$$

To validate the statistical significance of partial coherence values, critical values for a significance level α are utilized [12].

Partial coherence is a symmetric measure of the linear influence between two processes conditioned on all other processes under consideration. The direction of interrelations can be inferred if and only if there is a strict linear phase relation. The slope quantifies the time delay between the processes. As the asymptotic variance of the phase is approximately inversely proportional to the squared coherence value at the corresponding frequency, a reliable assessment of the phase spectrum is only possible if coherence values are highly significant over a broad range of frequencies. For narrow band signals, a linear phase relationship must be assumed rather than detected, leading to possible false conclusions.

Partial coherences and partial phase spectra estimated for the four-dimensional VAR-(5) system are shown in Figure 2A. Spectra of the four single processes are drawn on the diagonal, partial phase spectra above the diagonal, partial coherence spectra and below the diagonal. The horizontal gray lines indicate critical values for a 1% significance level for the absence of partial coherence. Significant partial coherence values are observed between processes X_1 and X_2, between X_1 and X_4, and between X_2 and X_3.

Since processes X_1 and X_2 mutually influence each other, the direction of the influences cannot be estimated on the basis of the phase spectra. This is due to the absence of a linear phase relation between the processes. The phase relations between processes X_1 and X_4 and between X_2 and X_3 could be approximated by a linear function in a certain frequency range.

The resulting graph based on partial coherence and partial phase spectral analysis is shown in Figure 2B. The interdependences are correctly revealed, since direct and indirect influences are distinguishable by this analysis technique. However, tracing of the directions of the information flow in this dynamic system is limited. This property is indicated in the graph, as no direction is shown between processes X_1 and X_2; the dashed arrows specify that the approximation by linear relationships may become difficult, for instance, when narrow-band signals are to be analyzed.

Parametric methods to detect directions of information flow

The parametric analysis techniques discussed here are based on modeling the system under investigation by linear n-dimensional vector autoregressive processes:

$$\begin{pmatrix} X_1(t) \\ \vdots \\ X_n(t) \end{pmatrix}=\sum_{r=1}^{p} a_r \begin{pmatrix} X_1(t-r) \\ \vdots \\ X_n(t-r) \end{pmatrix}+\begin{pmatrix} \varepsilon_1(t) \\ \vdots \\ \varepsilon_n(t) \end{pmatrix}. \tag{5}$$

A reliable estimation of the elements $\hat{a}_{kl,r}$ ($k,l=1, \ldots, n$; $r=1, \ldots, p$) of the coefficient matrices and a reliable estimation of the covariance matrix $\hat{\Sigma}$ of the Gaussian distributed noise $\varepsilon(t)=(\varepsilon_1(t),\ldots,\varepsilon_n(t))'$ are essential for application of the three parametric approaches.

Estimated covariance matrices, estimated VAR-matrix coefficients themselves or their frequency domain representations

$$\hat{A}_{kl}(\omega)=\delta_{kl}-\sum_{r=1}^{p}\ \hat{a}_{kl,r}\ e^{-i\omega r} \tag{6}$$

are utilized by the GCI, the DTF, and the PDC to detect the direction of the information flow in the dynamic system.

Granger causality index

Granger introduced a causality term based on the consensus that a cause must precede its effect [3]. To introduce a GCI index in the time domain that allows detection of a directed influence from process X_j to process X_i in an n-dimensional system, n- and (n-1)-dimen-

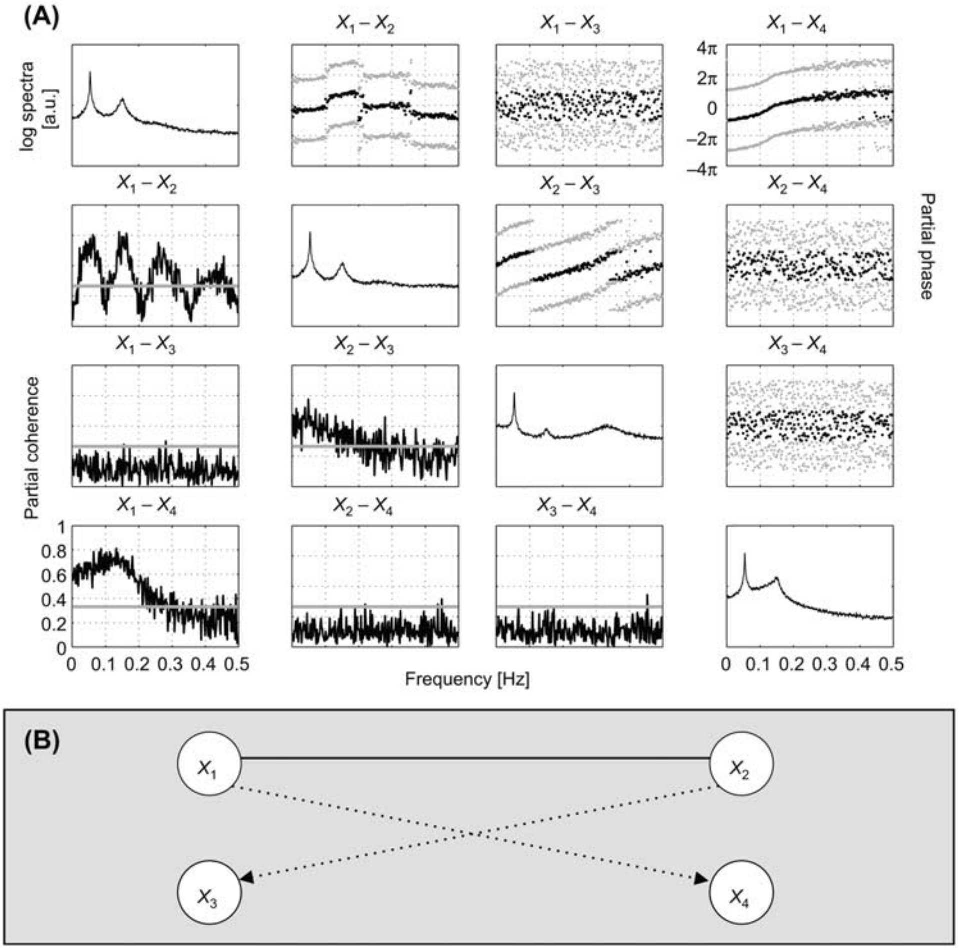

Figure 2 (A) Partial coherence and corresponding phase spectra. Auto-spectra are shown on the diagonal, with partial coherence spectra below the diagonal and partial phase spectra above the diagonal. Differentiation between direct and indirect influences is possible. However, the bidirectional interaction between X_1 and X_2 is not traceable by evaluating the phase spectra. (B) Graph summarizing the results.

sional VAR models are considered. An n-dimensional VAR model is fitted to the system investigated, leading to residual variance $\hat{\Sigma}_{i,n}(t)=\text{var}(\varepsilon_{i,n}(t))$ for X_i. In a second step, an (n-1)-dimensional VAR model is fitted to the subsystem $\{X_k,\ k=1,\ldots,n|k\neq j\}$, which leads to the residual variance $\hat{\Sigma}_{i,n-1}(t)=var(\varepsilon_{i,n-1}(t))$. A GCI quantifying a linear influence from process X_j to process X_i is defined by [5]:

$$\gamma_{i\leftarrow j}(t)=\ln\left(\frac{\hat{\Sigma}_{i,n-1}(t)}{\hat{\Sigma}_{i,n}(t)}\right). \tag{7}$$

For the detection of time-resolved transitions in the interdependence structure, a time-variant VAR parameter estimation, the recursive least square algorithm (RLS), is utilized [7]. In summary, the GCI allows time-resolved detection of directed interactions between two processes X_j and X_i in the time domain.

Time-resolved values of the GCI applied to the model system are given in Figure 3A. Using the GCI, the correct interrelation structure and the corresponding directions are detected. For example, for the influence from process X_1 to X_4, the corresponding values of the GCI are non-zero. In contrast, the values of the GCI fluctuate around zero for the opposite direction. The graph based on GCI analysis is shown in Figure 3B and is identical to the simulated interaction structure (cf. Figure 1).

Directed transfer function

The DTF is an analysis technique for the frequency domain based on Fourier transformation of the coefficient matrices [cf. Eq. (6)]. The transfer function $H_{ij}(\omega)=A_{ij}^{-1}(\omega)$ leads to a definition of the DTF [6]:

$$\delta_{i\leftarrow j}(\omega)=\frac{|H_{ij}(\omega)|^2}{\sum_l |H_{il}(\omega)|^2}. \tag{8}$$

Normalized to the unit interval, an interaction from process X_j onto process X_i is identified for non-zero values of the DTF. In the following investigation, parameter matrices were estimated using multivariate Yule-Walker equations.

Applying DTF analysis to the model system under investigation [cf. Eq. (1)] leads to the results illustrated in Figure 4A. The auto-DTFs are shown on the diagonal and the DTF spectra on the off-diagonal. Using DTF analysis,

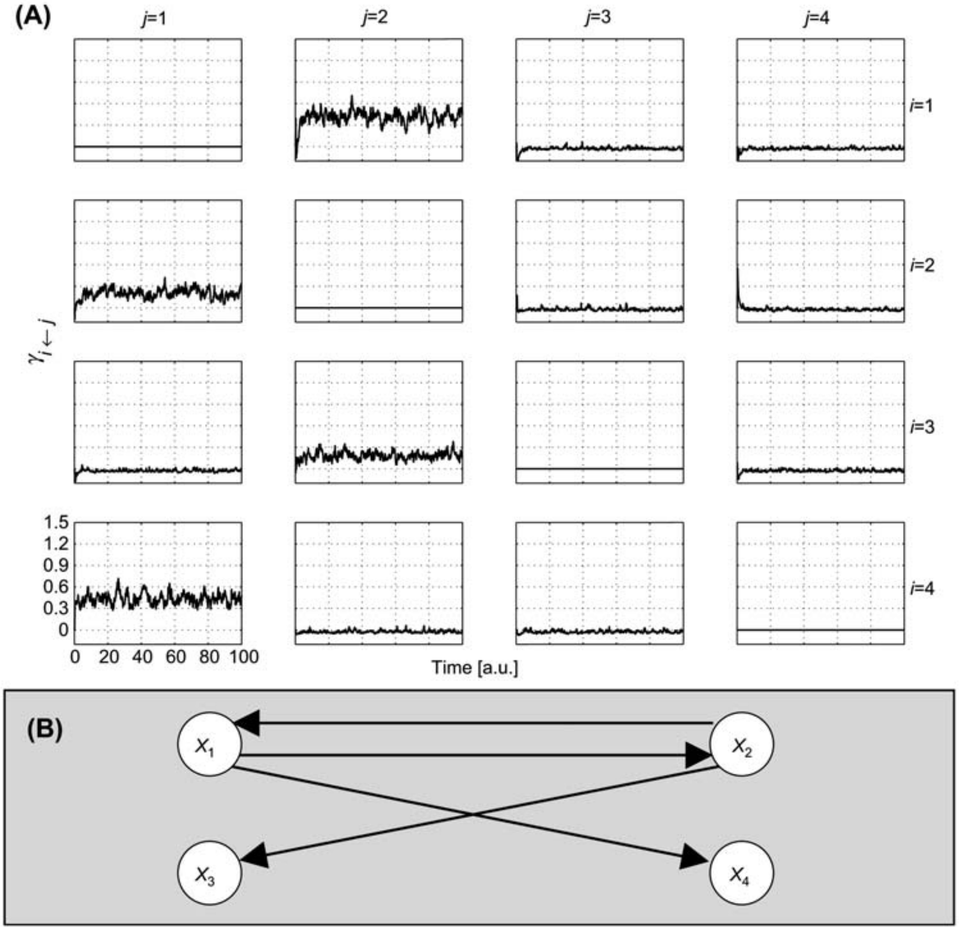

Figure 3 (A) Granger causality index for the VAR model and (B) the resulting directed graph.
The simulated interrelation structure is reproduced correctly by non-zero values of the Granger causality index. a.u., arbitrary unit.

all simulated directed interactions are detected correctly. However, differentiation between direct and indirect interactions is not possible, thereby leading to a greater number of interactions than are actually present. For instance, the influence from process X_1 to process X_3 is indirect, since it is mediated by process X_2. Similarly, the influence from process X_2 to process X_4 is mediated by process X_1. The corresponding DTF spectra are non-zero and DTF analysis cannot distinguish between direct and indirect interactions. This is indicated by the dashed arrows in the graph in Figure 4B.

Partial directed coherence

PDC has been introduced in the frequency domain as an analysis tool to detect Granger-causal interactions in multidimensional systems. Based on Fourier transformation of the coefficient matrices [cf. Eq. (6)], PDC is defined by [1]:

$$\pi_{i \leftarrow j}(\omega) = \frac{|A_{ij}(\omega)|}{\sqrt{\sum_k |A_{kj}(\omega)|^2}} \quad . \tag{9}$$

Normalized to the unit interval, a direct influence from process X_j to process X_i is detected by a non-zero PDC spectrum. In the following investigation, parameter matrices were estimated utilizing multivariate Yule-Walker equations.

The results of PDC analysis for system (1) are presented in Figure 5A. Auto-spectra of the four processes are shown on the diagonal. The PDC spectra are shown above and below the diagonal. Only the PDCs from process X_1 onto process X_2, from process X_1 onto process X_4, from process X_2 onto process X_1, and from process X_2 onto process X_3 are non-zero. The results are summarized in the graph in Figure 5B. Using PDC analysis, the correct interaction structure is detected (cf. Figure 1). PDC accounts for the entire multivariate system and allows differentiation between direct and indirect influences.

Detecting information flow in non-stationary systems

When analyzing biomedical signals, transitions in the interaction structure may contain the most important information. Therefore, time-resolved analysis tools are required. The GCI has been introduced in the time domain as a time-resolved analysis technique, applying the recursive least-square algorithm. Alternatively, time-varying state space modeling offers an estimate for time-

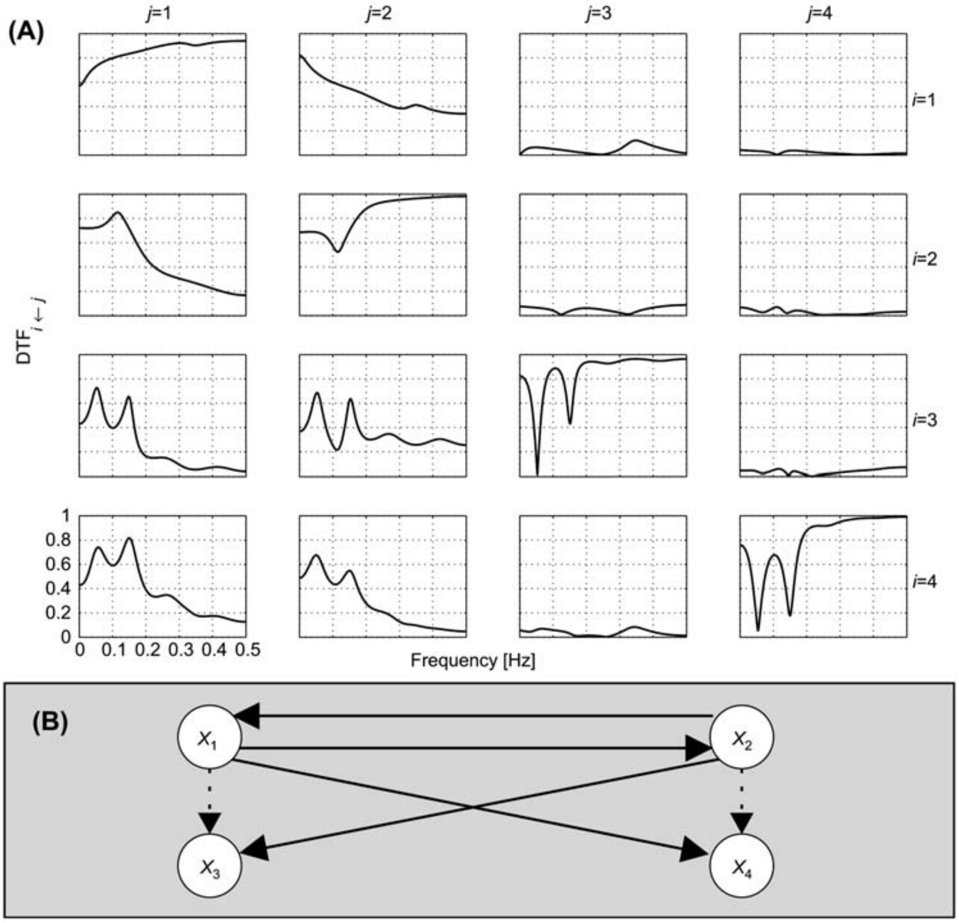

Figure 4 (A) Directed transfer function for the VAR model considered. The auto-directed transfer functions $\delta_{i \leftarrow i}$ are shown on the diagonal. The directions of the simulated interactions are revealed correctly by directed transfer function analysis. Nevertheless, two indirect interactions are inferred from process X_1 to X_3 and process X_2 to X_4. This is indicated by the dashed arrows in the graph in (B).

resolved parameters in VAR models. In combination with the concept of PDC, detection of directed information flow dependent on frequency *and* time is possible [14].

To illustrate the performance of this procedure, a two-dimensional VAR-(2) process

$$X_1(t) = 0.5X_1(t\text{-}1)\text{-}0.7X_1(t\text{-}2) + c_{12}(t)X_2(t\text{-}1) + \eta_1(t)$$
$$X_2(t) = 0.8X_2(t\text{-}1)\text{-}0.5X_2(t\text{-}2) + c_{21}(t)X_1(t\text{-}1) + \eta_2(t)$$
$$\eta_i \sim N(0,1), \quad i = 1,2 \qquad (10)$$

is examined. A transition in the interaction was modeled by setting $c_{12} = 0.6$ and $c_{21} = 0$ for the first half of the simulation period and $c_{12} = 0$ and $c_{21} = 0.6$ for the second half of the simulation period.

Figure 6 shows results for a time-resolved application of PDC to the simulated two-dimensional system. High PDC values in the frequency range between 0.1 and 0.2 Hz are observed for the first half of the simulation period (Figure 6A), correctly indicating the influence from process X_2 to process X_1. The transition in the direction of information flow in the middle of the simulation period is also correctly detected, as high PDC values were observed in the PDC spectrum representing the influence from process X_1 to process X_2.

Discussion

We have presented a comparison of four analysis techniques for time series that allow detection of information flow in multivariate dynamic systems. As the sole representative of the class of non-parametric spectral analysis techniques, we examined partial coherence in combination with the partial phase spectrum. Three parametric approaches, GCI, DTF and PDC, were studied, which are based on modeling the system under investigation by linear vector autoregressive processes. When analyzing biosignals to increase understanding of diseases or physiological implications, knowledge of both the possibilities and limitations of the analysis techniques applied is essential.

All four multivariate analysis techniques are capable of detecting the direction of information flow in the system investigated. When applying GCI, DTF, or PDC, it is generally possible to determine whether two signals interact mutually, whether there is an influence in only one direction, or whether no interaction exists. All four analysis techniques are based on measured signals. If the signals measured do not well represent the underlying dynamic processes, the analysis is restricted to statements about measured signals. In particular, no conclusions about

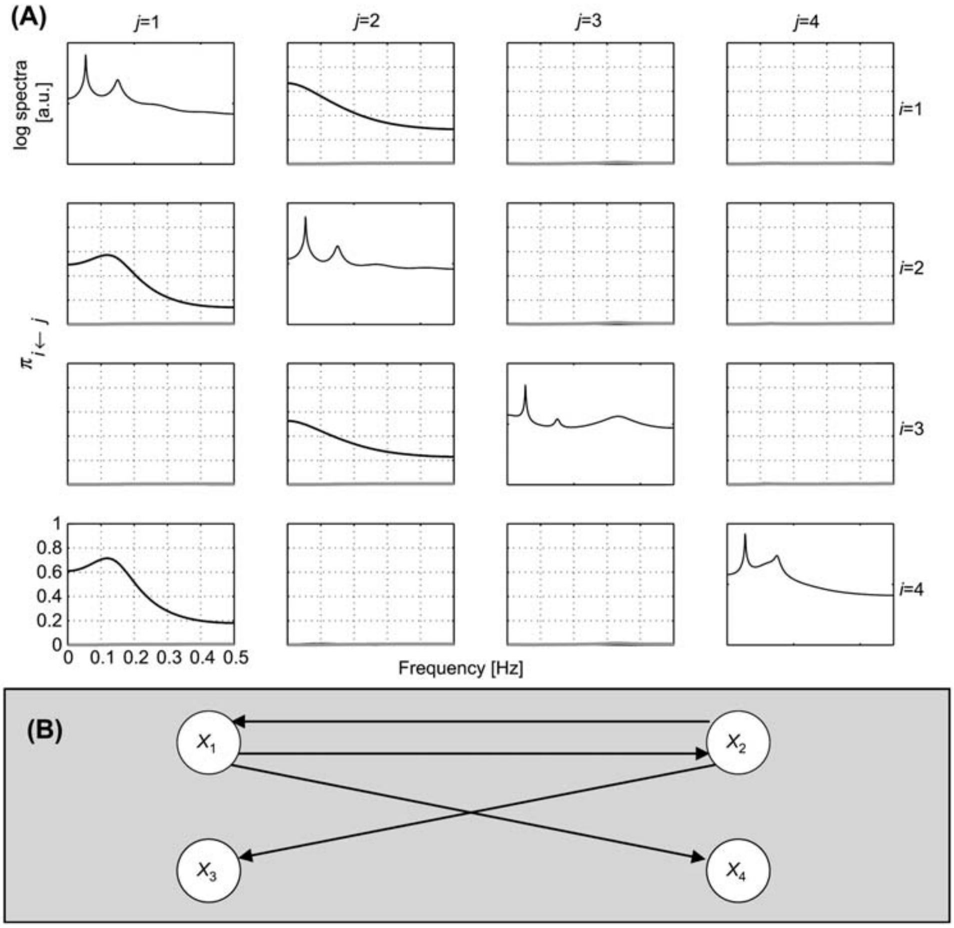

Figure 5 (A) Partial directed coherence for the VAR model considered. Auto-spectra are shown on the diagonal and partial directed coherence spectra on the off-diagonal. All simulated directed influences are detected correctly by partial directed coherence analysis. Furthermore, in contrast to the directed transfer function, differentiation between a directed and indirect information flow is possible. (B) Graph summarizing the results of PDC analysis, which is identical to the simulated interdependence structure (cf. Figure 1).

unobserved processes are possible. However, multivariate analysis tools are still superior to bivariate techniques, which are also hampered by their inability to differentiate direct and indirect interactions, even when observing all important signals.

The interpretation of partial coherences in combination with partial phase spectra is limited by the asymptotic variance and a possible non-linear phase relation. Furthermore, only unidirectional interactions can be reliably assessed by partial phase spectra.

In multidimensional systems, differentiation between direct and indirect information flows is often desirable. Using DTF, it is not possible to determine whether or not two signals interact directly. The remaining three analysis techniques investigated are capable of distinguishing direct and indirect interactions.

In summary, a favorable technique used for analysis of empirical signals should always be based on the problem in hand. There is no general superior technique that allows solution of all problems.

We investigated an example of a linear multivariate system, but in applications to biomedical dynamic systems, non-linearities and non-stationarities may play an important role. The results for a more detailed comparison are reported elsewhere [14].

Applying time-resolved techniques to estimate the VAR coefficients, non-stationary data can be processed and detection of interactions dependent on time and frequency is feasible. This has been demonstrated in an application of PDC in combination with a time-resolved parameter estimation technique. The transition in the direction of the information flow in the two-dimensional dynamic system investigated could be detected correctly by applying the proposed procedure.

For non-linear systems, a higher model order allows better description of the second-order properties. This approximation has been verified for at least some non-linear model systems [14]. By increasing the model order, the variability in DTF and PDC spectra is also increased. Therefore, tests are required to validate non-zero values in the corresponding spectra. Recently, an analytical significance level was introduced for PDC [9]. The application of PDC in combination with this significance level ensures reliable detection of directed information flow.

The time-series analysis techniques discussed here are powerful tools for detecting information flow in multi-

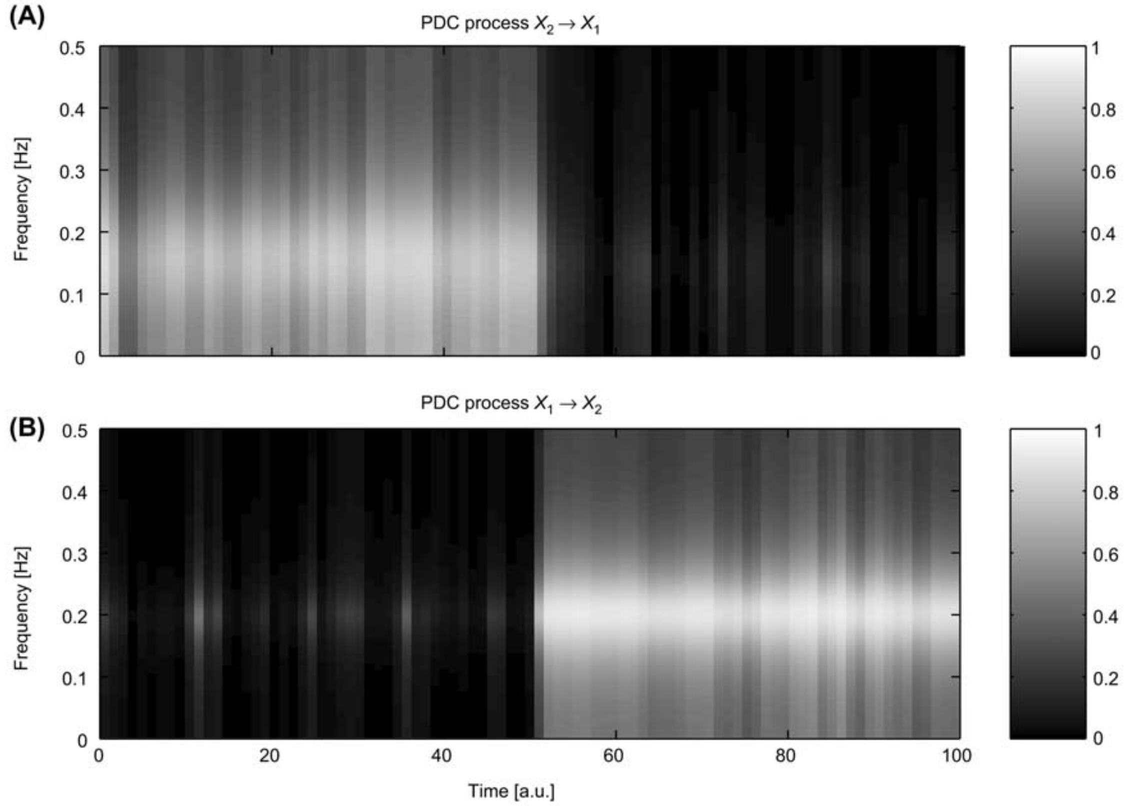

Figure 6 Application of time-resolved partial directed coherence.
The transition in the interaction structure between processes X_1 and X_2 is detected correctly. a.u., arbitrary unit.

dimensional dynamical systems. With expanded knowledge of their particular capabilities and limitations, wider application of these analysis tools in biomedical research is possible.

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