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Multivariate Analysis of Dynamical Processes with Applications to the Neurosciences

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Abstract— **Nowadays, data are recorded with increasing spatial and temporal resolution. Commonly these data are analyzed using univariate or bivariate approaches. Most of the analysis techniques assume stationarity of the underlying dynamical processes. Here, we present an approach that is capable of analyzing multivariate data, the so-called renormalized partial directed coherence. It utilizes the concept of Granger causality and is applicable to non-stationary data. We discuss its abilities and limitations, and demonstrate its usefulness in an application to murine electroencephalography (EEG) data during sleep transitions.**

I. INTRODUCTION

In many fields of research data can be recorded with high spatial as well as temporal resolution. This has elicited studies applying network theory to such data sets, see e.g. [1]. Researchers approach these networks from two different angles:

- The direct approach refers to the inference of network topologies based on prior knowledge about their nodes and interactions. This is for instance a standard approach for modeling traffic networks where the network topology is known in advance.
- The inverse approach refers to the strategy of using measured signals to infer the network structure.

The latter of the two is investigated here. Several approaches have been discussed. Usually bivariate analysis techniques are thresholded to deduce the interaction structure. Whenever the threshold is crossed, an edge is assigned between the corresponding nodes [1]. Different concepts on the optimal selection of these thresholds are possible such as keeping the number of edges in a network constant for different recording conditions. Alternatively, thresholds based on significance levels are conceivable.

Although these significance tests provide some insights, they are potentially leading to false positive conclusions about the true interaction structure which can be seen in a three dimensional example when applying bivariate analysis techniques such as correlation or coherence analysis. Consider the network as illustrated in Fig. 1. Suppose that the interaction is quantified by a bivariate correlation between the nodes of the network. If the true correlation between

$$\xi_1(t) \longleftrightarrow \xi_2(t) \longleftrightarrow \xi_3(t)$$

Fig. 1. Networks of coupled oscillators. Dashed arrows indicate indirect interactions.

nodes one and two and between two and three was 0.4 (solid lines in Fig. 1), than the true correlation between nodes one and three would be 0.16 (dashed line in Fig. 1). This correlation of 0.16 would, however, correspond to an indirect interaction. In principle a sensible significance test should indicate the presence of a significant correlation between all nodes, which would be a false positive conclusion in the sense that the correlation between nodes one and three would indicate a spurious interaction. In a realistic scenario with finite sample size, a statistical test might eventually result in a nonsignificant value for the weakest connection. In the above examples the connection between nodes one and three of strength 0.16 would likely not be statistically significant; thus a false positive conclusion would be prevented but only because of a small sample size. In all scenarios there is no direct connection between nodes one and three. In other words, for finite sample sizes indirect interactions might correctly be identified, i.e. assessed as non-significant but only if they are rather weak. This decision about the presence or absence of interactions that is just due to the sample size is, of course, not desirable.

To overcome this limitation of bivariate approaches, multivariate analysis techniques with valid statistics that are able to distinguish direct and indirect interactions are necessary. There is indeed a variety of techniques available for this purpose [2], [3], [4], [5].

Another important question is concerned with the direction of information transfer between the constituents of a network. To this end, the concept of Granger-causality [6] is often applied. Ganger based his concept of causality on the idea of predictability. In other words, if including knowledge of one process add to the prediction of the future of a given process this one process is Granger causal for the given process. Granger formulated his approach to causal inference for multivariate systems. In other words, the predictability needs to be improved but with respect to the condition that this holds true in the presence of third processes.

Granger causality usually bases on vector-autoregressive processes. Analysis techniques derived from this are for instance directed transfer function [5], direct directed transfer

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function, partial directed coherence [7], Geweke's measure for Granger causality [8] as well as the recently introdcued renormalized partial directed coherence [9]. We emphasize here that [10] has shown that neither directed transfer function nor direct directed transfer function are measures for Granger-causality.

Renormalized partial directed coherence as introduced in [9] assumes stationarity of the processes. Especially in applications this is often not a valid assumption. Particularly in the neurosciences when for instance investigating brain dynamics one is indeed interested in the changes of the dynamics as well as the temporal evolution of interactions. A technique that is capable of inferring network structure in a time-resolved manner is needed here. In this manuscript we suggest an extension of renormalized partial directed coherence that enables a time-resolved estimation of multivariate Granger causal interactions between the constituents of a network.

II. AUTOREGRESSIVE PROCESSES AND RENORMALIZED PARTIAL DIRECTED COHERENCE

In the following, the concepts of Granger causality and partial directed coherence (PDC) are briefly introduced and the extension to renormalized PDC and its estimates are discussed.

A. AUTOREGRESSIVE PROCESSES AND PARTIAL DIRECTED COHERENCE

A vector autoregressive model of order p, abbreviated VAR[p], is given by

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

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 with covariance matrix $\boldsymbol{\Sigma}$.

In this model, the coefficients $\mathbf{a}_{ij}(r)$ describe how the present values of x_i depend linearly on the past values of the components x_j. Thus, $\mathbf{a}_{ij}(r)$ quantifies the Granger causal influence from process x_j onto x_i [6].

In order to provide a frequency domain measure for Granger causality, Baccala and Sameshima introduced the concept of partial directed coherence [7] based on the Fourier transform of the coefficient series

$$\mathbf{A}(\omega) = I - \sum_{r=1}^{p} \mathbf{a}(r)\,e^{-\mathrm{i}\omega r}\,. \tag{2}$$

Partial directed coherence from x_j to x_i is defined as

$$|\pi_{i\leftarrow j}(\omega)| = \frac{|\mathbf{A}_{ij}(\omega)|}{\sqrt{\sum_k |\mathbf{A}_{kj}(\omega)|^2}}. \tag{3}$$

If the autoregressive process is stationary, partial directed coherence is well defined. Furthermore, PDC $|\pi_{i\leftarrow j}(\omega)|$ takes values between 0 and 1 and vanishes for all frequencies ω if and only if the coefficients $\mathbf{a}_{ij}(r)$ are zero for all $r = 1, \ldots, p$. Thus, PDC $|\pi_{i\leftarrow j}(\omega)|$ provides a measure for the direct linear influence of x_j on x_i at frequency ω. More precisely, it compares the linear influence of process x_j on process x_i at frequency ω with the influence of x_j on other variables, that is, partial directed coherence ranks the interaction strengths with respect to a given signal source.

Partial directed coherence $|\pi_{i\leftarrow j}(\omega)|$ is estimated by fitting an n-dimensional VAR[p] model to the data and using Eqn. (2) and (3) with the parameter estimates $\hat{\mathbf{a}}_{ij}(k)$ substituted for the true coefficients $\mathbf{a}_{ij}(k)$. The statistical properties of the estimates of partial directed coherence $|\hat{\pi}_{i\leftarrow j}(\omega)|$ can be derived from those of the parameter estimates $\mathbf{a}_{ij}(k)$ [9]. In particular, it has been shown that, if $|\mathbf{A}_{ij}(\omega)|^2 = 0$, the asymptotic distribution for N data points of

$$\frac{N}{C_{ij}(\omega)}\,|\hat{\mathbf{A}}_{ij}(\omega)|^2 \tag{4}$$

is that of a weighted average of two independent χ^2–distributed random variables each with one degree of freedom for $p \geq 2$ and $\omega = 0 \bmod \pi$ [9].

The denominator of Eq. (4) is given by

$$C_{ij}(\omega) = \boldsymbol{\Sigma}_{ii}\Big[\sum_{k,l=1}^{p} \mathbf{H}_{jj}(k,l)\big(\cos(k\omega)\cos(l\omega) + \sin(k\omega)\sin(l\omega)\big)\Big], \tag{5}$$

with $\mathbf{H}_{jj}(k,l)$ being the entries of the inverse $\mathbf{H} = \mathbf{R}^{-1}$ of the covariance matrix $\mathbf{R}$ of the VAR process $\mathbf{x}$.

B. RENORMALIZED PARTIAL DIRECTED COHERENCE

For the derivation of renormalized partial directed coherence, consider the two-dimensional vector

$$\mathbf{X}_{ij}(\omega) = \begin{pmatrix} \mathrm{Re}\,\mathbf{A}_{ij}(\omega) \\ \mathrm{Im}\,\mathbf{A}_{ij}(\omega) \end{pmatrix}, \tag{6}$$

with $\mathbf{X}_{ij}(\omega)'\mathbf{X}_{ij}(\omega) = |\mathbf{A}_{ij}(\omega)|^2$. The corresponding estimator $\hat{\mathbf{X}}_{ij}(\omega)$ with $\hat{\mathbf{A}}_{ij}(\omega)$ substituted for $\mathbf{A}_{ij}(\omega)$ is asymptotically normally distributed with mean $\mathbf{X}_{ij}(\omega)$ and covariance matrix $\mathbf{V}_{ij}(\omega)/N$, where

$$\mathbf{V}_{ij}(\omega) = \sum_{k,l=1}^{p} \mathbf{H}_{jj}(k,l)\,\boldsymbol{\Sigma}_{ii} \begin{pmatrix} \cos(k\omega)\cos(l\omega) & \cos(k\omega)\sin(l\omega) \\ \sin(k\omega)\cos(l\omega) & \sin(k\omega)\sin(l\omega) \end{pmatrix}. \tag{7}$$

For $p \geq 2$ and $\omega \neq 0 \bmod \pi$, the matrix $\mathbf{V}_{ij}(\omega)$ is positive definite [9], and it follows that, for large N, the estimated renormalized partial directed coherence

$$\hat{\boldsymbol{\lambda}}_{ij}(\omega) = \hat{\mathbf{X}}_{ij}(\omega)'\hat{\mathbf{V}}_{ij}(\omega)^{-1}\hat{\mathbf{X}}_{ij}(\omega).$$

under the null hypothesis of $\boldsymbol{\lambda}_{ij}(\omega) = 0$ is χ^2–distributed with two degrees of freedom [9].

III. STATE SPACE MODELING AND AUTOREGRESSIVE PROCESSES

To enable a time-resolved estimation of renormalized partial directed coherence, a time-resolved estimation of the autoregressive parameter matrices is necessary. To this end the framework of state-space modeling [11], [12] can be utilized. State space models are characterized by two equations.

One of these equations models the hidden dynamic process, in our case the autoregressive model

$$\mathbf{x}(t) = \sum_{r=1}^{p} \mathbf{a}_r\, \mathbf{x}(t-r) + \boldsymbol{\varepsilon}(t). \tag{8}$$

To fit in the framework of state-space modeling, this autoregressive model of order p has to be rewritten as a VAR[1], which is always possible by increasing the dimension

$$\tilde{\mathbf{x}}(t) = \begin{pmatrix} x_1(t) \\ \vdots \\ x_n(t) \\ \vdots \\ x_1(t-p+1) \\ \vdots \\ x_n(t-p+1) \end{pmatrix} \tag{9}$$

resulting in the following VAR[1]-process

$$\tilde{\mathbf{x}}(t) = \begin{pmatrix} \mathbf{a}_1 & \dots & \mathbf{a}_p \\ \mathrm{id}_n & 0_n & 0_n \\ 0_n & \ddots & 0_n \end{pmatrix} \tilde{\mathbf{x}}(t-1) + \begin{pmatrix} \boldsymbol{\varepsilon}(t) \\ 0 \\ \vdots \\ 0 \end{pmatrix}. \tag{10}$$

Thereby, id_n denotes the n-dimensional identity matrix and 0_n the n by n matrix containing only zeros.

The second equation in the state-space modeling framework is the observation equations, which reads

$$\mathbf{y}(t) = \begin{pmatrix} \mathrm{id}_n & 0_n & \dots & 0_n \end{pmatrix} \tilde{\mathbf{x}}(t) + \eta(t). \tag{11}$$

The noise term $\eta(t)$ is Gaussian distributed white observational noise. The state-space model consisting of Eqns. (10) and (11) does not account for time-dependent parameters that would be needed for a time-resolved estimation of renormalized partial directed coherence. To achieve this, the hidden dynamic process needs to be extended by one equation such that the whole state-space model results in

$$\begin{aligned} \mathbf{a}_1(t) &= \mathbf{a}_1(t-1) + \xi_1 && (12)\\ \vdots \quad & \vdots \quad \vdots \\ \mathbf{a}_p(t) &= \mathbf{a}_p(t-1) + \xi_p && (13)\\ \tilde{\mathbf{x}}(t) &= \begin{pmatrix} \mathbf{a}_1(t) & \dots & \mathbf{a}_p(t) \\ \mathrm{id}_n & 0_n & 0_n \\ 0_n & \ddots & 0_n \end{pmatrix} \tilde{\mathbf{x}}(t-1) + \tilde{\boldsymbol{\varepsilon}}(t) && (14)\\ \mathbf{y}(t) &= \begin{pmatrix} \mathrm{id}_n & 0_n & \dots & 0_n \end{pmatrix} \tilde{\mathbf{x}}(t) + \eta(t). && (15) \end{aligned}$$

Equations (12)-(13) account for the dynamic changes in the parameter matrices of the VAR process. The whole state-space model can be fitted to measurements of an n-dimensional system using the Expectation-Maximization algorithm applying the extended [13], unscented [14], [15] or dual Kalman filter [16]. In the application below we used the Expectation-Maximization algorithm with dual Kalman filter, which turned out to be a robust estimator with reasonable numerical performance.

IV. APPLICATION

To demonstrate the applicability of the proposed approach to data, we used electroencephalography (EEG) recordings of a mouse during a transition from slow-wave-sleep to rapid-eye-movement (REM) sleep [17]. Data were recorded with a sampling rate of 199 Hz simultaneously from left (lHC) and right hippocampus (rHC) and prefrontal cortex (PFx).

The result of time-resolved renormalized partial directed coherence is shown in Fig. 2 for a representative example of a transition in one mouse. The transition takes place after 17 seconds marked by the vertical line. Especially in frequencies close to 10 Hz, there is a strong interaction between all brain regions that sets in with the transition point from slow-wave to REM sleep. In particular the directed interaction from the right hippocampus to left hippocampus seems to be stronger and rather stationary in this example as compared to the other interactions. Noteworthy there is also a strong interaction from the prefrontal cortex onto the hippocampi which sets in later than that from left hippocampus to prefrontal cortex.

In a forthcoming manuscript we will evaluate to which extent those features are unique or to which extent they present a common pattern in such transitions across animals.

V. CONCLUSIONS

Challenges often faced when analyzing real-world data manifest themselves in the fact that recorded data are, first, multivariate, second, nonstationary, and third, contaminated with observational noise. Tackling these problems with a bivariate analysis techniques without proper statistical evaluations inevitably leads to a result that is at best presenting a coarse view of the actual network structure. The results will in most cases be characterized by false positive or false negative conclusions about the network structure.

Here, we presented a technique that is capable of dealing with all these issues. It is based on state-space modeling and renormalized partial directed coherence, and enables estimation of the true network structure when analyzing multivariate, non-stationary, noisy data.

State-space modeling presents a rather flexible framework which could even be extended beyond what we have shown here by for instance allowing for correlated observational noise.

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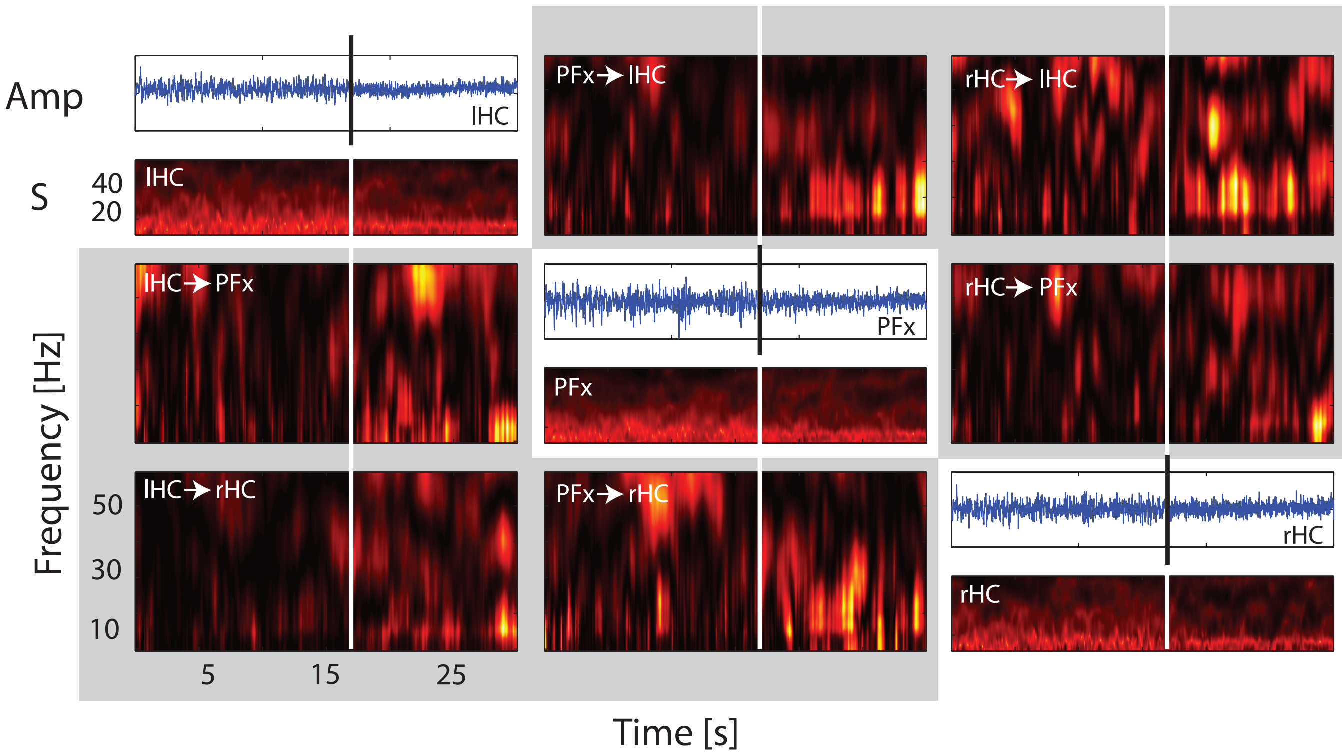

Fig. 2. Results of renormalized partial directed coherence analysis using state space modeling for estimation of the time-resolved multivariate interaction structure. lHC: left hippocampus, PFx: prefrontal cortex, rHC: Right hippocampus. On the diagonal the raw data, amplitude A in arbitrary unit over time in seconds, are presented together with the autospectra – logarithm of the spectra color coded with respect to frequency in Hz (y-axis) and time in seconds (x-axis). The gray shaded plots denote the time-resolved rPDC analysis – direction of information flow is from column to row indicated by the arrows.

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