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Causality estimates among brain cortical areas by Partial Directed Coherence: simulations and application to real data

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Abstract—**The problem of the definition and evaluation of brain connectivity has become a central one in neuroscience during the latest years, as a way to understand the organization and interaction of cortical areas during the execution of cognitive or motor tasks. Among various methods established during the years, the Partial Directed Coherence (PDC) is a frequency-domain approach to this problem, based on a multivariate autoregressive modeling of time series and on the concept of Granger causality. In this paper we propose the use of the PDC method on cortical signals estimated from high resolution EEG recordings, a non invasive method which exhibits a higher spatial resolution than conventional cerebral electromagnetic measures. The principle contributions of this work are the results of a simulation study, testing the performances of PDC, and a statistical analysis (via the ANOVA, analysis of variance) of the influence of different levels of Signal to Noise Ratio and temporal length, as they have been systematically imposed on simulated signals. An application to high resolution EEG recordings during a foot movement is also presented.**

Keywords—**Partial Directed Coherence, High resolution EEG, foot movement**

I. INTRODUCTION

The necessity to describe how different brain areas communicate with each other is gaining more and more importance in the neuroscience field. The increase of non-invasive brain imaging methods (like functional Magnetic Resonance Imaging, fMRI; high resolution electroencephalography, EEG, or magnetoencephalography, MEG) that return information about the different cerebral areas activation during a motor or cognitive task makes the concept of brain connectivity a central one.

Many approaches to this problem have been object of study during the years. Baccalà and Sameshima [1] proposed a multivariate spectral measure called the Partial Directed Coherence (PDC), which is used to determine the directional influences between any given pair of channels in a multivariate data set. This is an estimator characterizing at the same time direction and spectral properties of the interaction between brain signals, and requires only one multivariate autoregressive (MVAR) model to be estimated from all the time series. The advantages of MVAR modelling of multichannel EEG signals in order to compute efficient connectivity estimates has been stressed recently [2]. In such study the superiority of multichannel approach with respect to the pairwise approach has been demonstrated. In this paper we propose the use of the PDC method to estimate the cortical connectivity between cortical areas during a task by using non invasive EEG recordings. Despite the use of surface EEG signals, we will be able to assess cortical connectivity by applying the PDC on cortical signals estimated in different Regions Of Interest (ROIs) of a realistic human cortical model. To achieve this, we used high resolution EEG recordings, realistic head models and a cortical reconstruction with 5,000 dipoles, uniformly disposed along the cortical surface. The efficacy of the PDC to retrieve effective cortical connectivity was first tested by a simulation study in which we take into account the different conditions that afflicts the EEG recordings, mainly the signal to noise ratio (factor SNR) and the length of the recordings (factor LENGTH).

In particular, the present experimental design is based on some specific questions about the use of PDC as an estimator of the cortical connectivity:

1) What is the influence of a variable SNR level imposed on the high resolution EEG data on the accuracy of the connectivity estimation?
2) What is the amount of data necessary to get a good accuracy of the estimation of connectivity between cortical areas?
3) What are PDC performances in discriminating direct or indirect causality patterns?

In order to answer these questions, a simulation study has been performed, on the basis of a predefined connectivity scheme linking four cortical areas. Cortical connections between the areas were retrieved by the estimation process under different experimental conditions. The influence of different factors on PDC performances was evaluated by a statistical analysis. Finally, we applied the PDC technique to high resolution EEG recordings during the foot movement in humans.

II. METHODS

The Partial Directed Coherence [1] is a full multivariate spectral measure, used to determine the directed influences between any given pair of signals in a multivariate data set. It is computed on a Multivariate Autoregressive model (MVAR) that simultaneously models the whole set of signals. It has been demonstrated [1] to be based on the concept of Granger causality, according to which an observed time series x(n) can be said to cause another series y(n) if the prediction error for y(n) at the present time is reduced by the knowledge of x(n)'s past measurements. This kind of relation is not reciprocal, thus allowing to determine the direction of information flow between signals.

The Simulation study: The experimental design aimed at analyzing the recovery of the connectivity pattern by PDC, under different levels of SNR and signal temporal length, as they have been imposed during the generation of test signals simulating cortical average activations. The simulated signals were obtained starting from a neural mass model of a region of interest (ROI).

Signal generation: different sets of test signals have been generated in order to fit an imposed coupling scheme, involving four different cortical areas, as well as to respect imposed levels of Signal to Noise Ratio (factor SNR) and duration in seconds (factor LENGTH). Signal x_1 was a waveform generated by a model of three neural populations, arranged in parallel. Each population simulates neural activity in a specific frequency band: 4-12 Hz, 12-30 Hz and 30-50 Hz, approximately. The model of each population is based on equations proposed by Wendling et al. [3]. The basic idea behind this model is that oscillations derive from the interactions of pyramidal neurons with three other local neural subsets, i.e., excitatory interneurons, slow inhibitory interneurons, and fast inhibitory interneurons. Parameters of the three populations (time constants and synaptic gains) have been given by using an automatic best-fitting procedure, to mimic the entire power spectrum density of cortical activity in a ROI. The other signals were generated as shown in the following:

$$x_j(t) = \sum_{i=1}^{N} a_{ji} \cdot x_i(t - \tau_{ji}) + n_j(t) \qquad (1)$$

for j = 2, …, N

where:

- N is the number of ROIs
- τ_{ij} is the delay in the propagation from the i^th^ to the j^th^ area;
- a_{ij} is the amplitude of the connection between the i^th^ and the j^th^ area
- n_j is the residual representing the part of the j^th^ area activation not depending from other areas, here playing the role of noise.

All procedures of signal generation were repeated under the following conditions:

SNR factor levels = [1, 5, 10];

LENGTH factor levels = [12, 20 40, 80] seconds, divided in 3 trials, at a sampling frequency of 250 Hz.

The levels chosen for both SNR and LENGTH factors cover the typical range for the cortical activity estimated with high resolution EEG techniques.

Evaluation of performances: a statistical evaluation of PDC performances required a precise definition of an error function, describing the goodness of the pattern recognition performed. This was achieved by focusing on MVAR model structure:

$$\underline{\mathrm{X}} = -\sum_{k=1}^{p} \underline{\underline{A}}(k)\underline{\mathrm{X}}(t-k) + \underline{E}(t) \qquad (2)$$

and comparing it to the signals generation scheme:

$$x_j(t) = \sum_{i=1}^{N} a_{ji} \cdot x_i(t - \tau_{ji}) + n_j(t) \qquad (3)$$

for j= 1, …, N.

It is possible to associate each parameter in the MVAR model to parameters used in signal generation, as follows:

$$A_{ij}(k) \leftrightarrow -a_{ij}(\tau_{ij}) \qquad \text{for } k = \tau_{ij} \qquad (4)$$

In this way, reference PDC functions have been computed, on the basis of the signal generation parameters. The error function was then evaluated as the difference between these reference functions and the estimated ones (both averaged in the frequency band of interest).

To evaluate the performances in retrieving the connections between areas, we computed the error on each single connectivity arc:

$$E_{ij} = \left\| \gamma_{ij}(f)\Big|_{band} - \hat{\gamma}_{ij}(f)\Big|_{band} \right\| \qquad (5)$$

In this formula $\gamma_{ij}(f)|_{band}$ represents the average value of PDC function from j to i, in the frequency band of interest. Simulations were performed by repeating for 50 times each generation-estimation procedure, in order to increase the robustness of the successive statistical analysis.

High resolution EEG recordings: The estimation of connectivity patterns by using PDC on high resolution EEG recordings has been applied to the analysis of a simple movement task. In particular, we considered a self-paced right foot movement. We used the PDC approach on the cortical signals estimated from high resolution EEG recordings, by using realistic head models and a cortical reconstruction with on average of 5,000 dipoles uniformly disposed along such cortical surface. The estimation of the cortical activity was obtained by the application of the linear inverse procedure [4]. Cortical activity were then estimated in ROIs generated by the segmentation of the Brodmann areas on the accurate cortical model used. The average cortical signals obtained in each ROI will be then subjected to the MVAR modelling in order to compute the PDC

III. RESULTS

A. *Simulation study*

Several sets of signals have been generated as described in the previous section by eq. 1, in order to fit a predefined connectivity pattern involving four cortical areas (shown in fig.1). A multivariate autoregressive model of order 10 has been fitted to each set of simulated data. Then, the normalized PDC functions have been computed from each autoregressive model. The index of performances used in this study, i.e. the error on each connectivity arc (eq. 5) has been computed for each generation-estimation procedure performed, and then subjected to Analysis of Variance (ANOVA). ANOVA revealed a strong statistical influence of all the main factors (SNR, LENGTH and ARC).

Results indicate a clear decrease of the error in the connectivity estimation with an increase of the length of the available data and of the Signal to Noise Ratio. The influence of factor SNR on the error on different arcs of the connectivity pattern (Fig.1) was statistically significant. Post hoc tests (Duncan at 5%) have shown statistically significant differences between levels 1 and 5, while no significant differences were revealed for higher levels of SNR. Where there were not any causality relation imposed, the error was evaluated as difference from the estimated value and zero. It is interesting to note that the error on arc 1->4 was significantly higher than on all the other arcs were the connection lacks (2->1, 3->1, 3->2, 4->2, 4->3). This is due to the existence of some indirect causality interactions among ROI 1 and 4, as will be discussed in the following section.

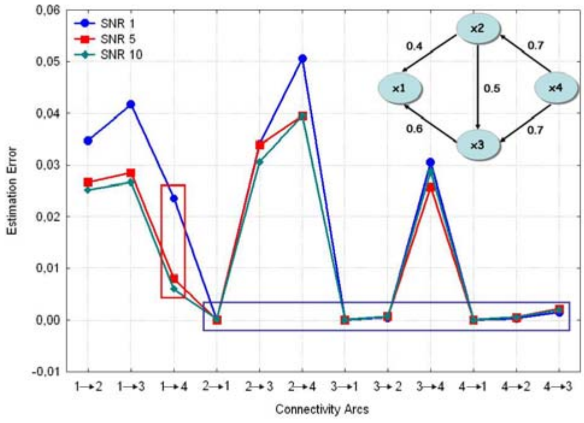

Fig. 1. Results of ANOVA performed on the estimation error on each connectivity arc, for different SNR. The values were considered in the THETA band (4-7 Hz). ANOVA showed a high statistical significance (F=6.88, p<0.0001). On the top right: diagram depicting the connectivity pattern imposed between different ROIs. In the circle, the different error levels obtained for arc 1->4, which is lacking from the generation scheme but is characterized by an indirect signal pathway.

The same effect can be seen in Fig. 2, showing the influence of factor LENGTH on the error on each connectivity arc.

B. *An application to high resolution event related potential recordings*

After the solution of the linear inverse procedure, the estimation of the current density waveforms in the employed ROIs were obtained as described in the Methods Section. Connectivity estimations were performed by PDC after the computation of the statistical threshold via the shuffling procedure described previously. Fig.3 shows the cortical connectivity patterns obtained for the period preceding the movement onset in all the subjects examined. Here, we present the results obtained for the connectivity pattern in the gamma band. The presence of a functional connection is represented with an arrow, moving from a cortical area toward another one. The arrow colors and sizes code the level of strength of the connection. The labels indicate the names of the ROIs employed. Only the cortical connections statistically significant at $p < 0.01$ are represented, after the computation of the shuffling procedure described above.

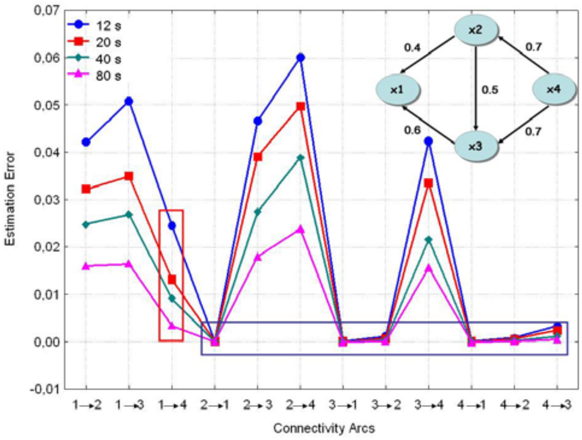

Fig. 2. Results of ANOVA performed on the error on each connectivity arc, for different numbers of data points considered in the estimation. Same model used before. The figure shows the error values obtained for indirect influence (red circle) and for the other arcs lacking from the generation scheme (blue circle).

Note that the connectivity patterns during the period preceding the movement in the gamma band involves mainly the supplementary and the primary motor ROIs for the right foot movement The stronger functional connections are relative to the link between the premotor and primary motor areas of both cerebral hemispheres.

IV. DISCUSSION

A.Methodological considerations

In this paper we propose a study on the application of the PDC technique, already used for the assessment of information flows between scalp or implanted electrodes [2,5], to the cortical activity estimated by using realistic models of head as volume conductor and high resolution EEG recordings. In the first phase of this study we performed a series of simulations studying the use of PDC technique on test signals, generated in order to simulate the average electrical activity of regions of the cerebral cortex, as it can be estimated from high resolution EEG recordings gathered under different conditions of noise and length of the registrations. The ANOVA results (integrated with the Duncan post-hoc tests performed at p< 0,05) indicated a clear influence of different levels of the main factors SNR, LENGTH and ARC on the efficacy of the estimation of cortical connectivity via PDC. This allowed to give an answer to the questions raised in the Introduction section:

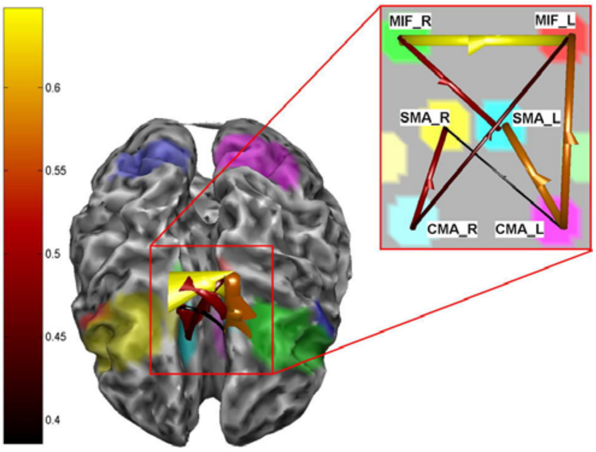

Fig. 3. Cortical connectivity patterns obtained for the period preceding the movement onset in a representative subject, in the gamma frequency band. Cortical functional connections are represented with arrows, that moves from the source cortical area toward the target one. The arrows' colors and sizes code the level of strengths of the connections. Left: connectivity patterns obtained from EP data represented on the realistic cortical reconstruction, obtained from sequential MRIs, seen from above. Inset: Detail of the connectivity patterns for the central areas. Only the cortical connections statistically significant at p < 0.01 are represented.

1) there is a statistical influence of a variable SNR level imposed on the high resolution EEG data on the accuracy of the connectivity pattern estimation obtained by PDC. However, post-hoc tests revealed that a SNR equals to 5 is sufficient to obtain a good accuracy, since higher values do not show a significant improvement in the performances;

2) the length of the high resolution EEG recordings has a statistically significant influence on the accuracy of PDC connectivity pattern estimation. Multiple trials can be considered without loosing in accuracy with respect to consecutive recordings;

3) While the PDC method has the capability to distinguish between direct and indirect pathways better than other methods, the level of the error on arcs related just to indirect connectivity is strongly influenced by the conditions under which the estimation is performed. For low values of SNR and length of the signal recordings, the value on this arc becomes comparable with that obtained for directed arcs. Particular attention should be put on this point, since the level of this error is critical to discriminate between direct and indirect causality pathways. In fact, a high value would lead to erroneous conclusions about the existence of a direct connectivity interaction among cortical areas. In the second phase of this study, the information obtained by the previous simulations were used to evaluate the applicability of PDC to actual Event Related recordings. The gathered ERP signals related to the foot movement data analyzed showed an SNR between 3 and 5. Furthermore, the total recording length was of 180 trials of 1.5 s length, at 200 Hz of sampling rate. So, according to the simulation results, we applied the PDC method on the estimated cortical current density data, expecting a limited amount of errors in the estimation of cortical connectivity patterns.

B. Application to real EEG data

Although here presented in order to highlight the technology possibilities, the physiological results obtained are consistent and integrate those already present in literature on the foot movements obtained with both neuroelectric and hemodynamic measurements. The activity noted in the supplementary and primary motor areas in the present study is consistent with the role that such cortical areas have in the organization and in the performance of simple foot movements.

V. CONCLUSION

In this paper a simulation study on the efficacy of the PDC as a tool for retrieve cortical connectivity from non invasive EEG measurements has been presented. Simulations suggest that PDC is adequate to estimate cortical connectivity under a large range of SNR and LENGTH factors. The presented technology can be applied to retrieve patterns of cortical connectivity during more complex cognitive tasks in human, by using non invasive EEG recordings.

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