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Estimation of the time-varying cortical connectivity patterns by the adaptive multivariate estimators in high resolution EEG studies

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Abstract—**The Directed Transfer Function (DTF) and the Partial Directed Coherence (PDC) are frequency-domain estimators, based on the multivariate autoregressive modelling (MVAR) of time series, that are able to describe interactions between cortical areas in terms of the concept of Granger causality. However, the classical estimation of these methods requires the stationary of the signals. In this way, transient pathways of information transfer remains hidden.**

The objective of this study is to test a time-varying multivariate method for the estimation of rapidly changing connectivity relationships between cortical areas of the human brain, based on DTF/PDC and on the use of adaptive MVAR modelling (AMVAR). This approach will allow the observation of transient influences between the cortical areas during the execution of a task.

Time-varying DTF and PDC were obtained by the adaptive recursive fit of an MVAR model with time-dependent parameters, by means of a generalized recursive least-square (RLS) algorithm, taking into consideration a set of EEG epochs. Simulations were performed under different levels of Signal to Noise Ratio (SNR), number of trials (TRIALS) and frequency bands (BAND), and of different values of the RLS adaptation factor adopted (factor C).

The results indicated that time-varying DTF and PDC are able to estimate correctly the imposed connectivity patterns under reasonable operative conditions of SNR ad number of trials. Moreover, the capability of follow the rapid changes in connectivity is highly increased by the number of trials at disposal, and by the right choice of the value adopted for the adaptation factor C.

The results of the simulation study indicate that DTF and PDC computed on adaptive MVAR can be effectively used to estimate time-varying patterns of functional connectivity between cortical activations, under general conditions met in practical EEG recordings.

Keywords— **Cortical connectivity, EEG, PDC, DTF, RLS**

INTRODUCTION

Today in the neuroscience field it is well accepted that one of the major issues still open is to describe how different brain areas communicate with each other. To this purpose are contributing, on one side, the increase of non-invasive brain imaging methods (like functional Magnetic Resonance Imaging, fMRI; high resolution electroencephalography, EEG, or magnetoencephalography, MEG) that return information more and more detailed, in terms of time and space resolution, about the activation of different cerebral areas during a motor or cognitive task. On the other side, the algorithms for the estimation of the communication between different areas of the human cortex are constantly improving.

The limits of conventional pairwise methods with respect to the multivariate spectral measures based on the autoregressive modeling of multichannel EEG, in order to compute efficient connectivity estimates, has been recently stressed [1]. Among the multivariate methods, the Directed Transfer Function (DTF) [2] and the Partial Directed Coherence [3] are estimators characterizing at the same time direction and spectral properties of the interaction between brain signals, and require only one MVAR model to be estimated from all the time series. However, the classical estimation of these methods requires the stationary of the signals; moreover, with the estimation of a unique MVAR model on an entire time interval, transient pathways of information transfer remains hidden.

Recently, different algorithms for the estimation of adaptive MVAR, with time dependent coefficients, were developed. Among them, an application to MVAR estimation of the extension of the recursive least squares (RLS) algorithm with forgetting factor was proposed in [4]. The estimation procedure allows the simultaneous fit of one mean MVAR model to a set of single trials, each one representing a measurement of the same task.

In this paper we propose the use of the adaptive multivariate approach to define time-varying multivariate estimators based on DTF and PDC, able to follow rapid changes in the connectivity between cortical areas during an experimental task.

Such methods were tested by means of a simulation study based on the following questions:

1) What are the performances of the proposed time-varying estimators in retrieving the rapid changes in time of the cortical connectivity pattern?

2) What is the effect of different factors affecting the recordings, like the signal to noise ratio and the amount of trials at disposal?

3) What is the influence of the adaptation constant c on the performances, and which can be a criterion for the choice of its optimum value?

4) Which of the two methods is the most effective in reconstructing a connectivity model under the conditions usually met in linear inverse estimations?

In this study, the performances of time-varying DTF and PDC were studied by means of simulations, performed on the basis of a predefined connectivity scheme linking three cortical areas. Cortical connections between the areas were retrieved by the estimation process under different experimental conditions. The results obtained for the different methods were evaluated by a statistical analysis, with particular attention to the adaptation speed and precision of the pattern retrieved.

METHODS

Time-varying multivariate connectivity estimation

The Directed Transfer Function (DTF) [2] is a method used to determine the directed influences between any given pair of signals in a multivariate data set. The approach is based on a multivariate autoregressive model (MVAR) simultaneously modeling the whole set of signals. In order to distinguish between direct and cascade flows, another estimator describing the direct causal relations between signals, the Partial Directed Coherence (PDC), was proposed in 2001 [3]. Like DTF, it is defined in terms of MVAR coefficients transformed to the frequency domain. Both methods are 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.

In this study, an adaptive formulation of DTF and PDC is proposed and tested, based on an adaptive MVAR (AMVAR) model.

The time dependent parameter matrices were estimated by means of the recursive least squares (RLS) algorithm with forgetting factor, as described in [4]. A mean MVAR model was fit to a set of trials, each one representing the measurement of the same task.

The Simulation study

The simulation was designed in order to test the capability of the two methods to follow rapid changes in the cortical connectivity as well as the precision of the estimation performed. Test signals simulating cortical average activations in different regions of the cortex were generated in order to fit an imposed coupling scheme, involving three cortical areas (shown in fig. 1a). Different levels of Signal to Noise Ratio (SNR) and different number of trials have been systematically imposed during the signal generation, in order to evaluate the influence of these factors on the estimates produced by the two methods.

Signal x_1 was the average activity of a cortical region of interest, obtained by a linear inverse estimation procedure from a real EEG recording. The other signals were generated as shown in the following:

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

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;
- $a_{ij}(t)$ is the time dependent amplitude of the connection between the i^{th} and the j^{th} area
- $n_j(t)$ is the residual representing the part of the j^{th} area activation not depending from other areas, here playing the role of noise.

The connectivity model used is shown in fig.1a.

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

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

TRIALS factor levels = [1, 2, 3, 5, 10, 20, 40, 80] each of 1000 samples, at a sampling frequency of 256 Hz.

Adaptation constant C factor levels = [0.01, 0.02, 0.03, 0.04, 0.05, 0.06, 0.07, 0.08, 0.09, 0.10]

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

The results obtained by the two estimators were evaluated in four frequency bands, Theta (4:7 Hz), Alpha (8:12 Hz), Beta1 (13:22 Hz) and Beta2 (23:30 Hz).

To evaluate both the adaptation speed and the precision of the connectivity patterns estimated by the two methods, two different indices of the performances were defined.

The first index was the times at settling, or t_s, defined as the first instant following the transition after which the error is below the ε% of the transition amplitude (in our case, ε=10), corresponding to the following condition:

$$\left|\hat{\sigma}_{ij}(t,b) - \sigma_{ij}(t,b)\right| \le \varepsilon \Delta_{ij}^{k}(b)/100 \quad , \quad \forall\, t \in k \,, \quad t > t_s \tag{2}$$

where $\sigma_{ij}(t,b)$ is the theoretical time-frequency function of the estimator (DTF or PDC), $\hat{\sigma}_{ij}(t,b)$ the estimated function, Δ^{k}_{ij} is the average value in the transition interval and ε the percentage of the transition amplitude desired. The second index, used to evaluate the precision of the estimation performed, is the average error in each time interval during which the values of connection strengths are kept constant after the transition, and is defined as follows:

$$\overline{E_{ij}^{k}(b)}^{t} = \overline{\left|\hat{\sigma}_{ij}(t,b) - \sigma_{ij}(t,b)\right|}^{t} \tag{3}$$

Results of the simulations underwent a statistical analysis (ANOVA, Analysis of Variance), with the method used, the SNR, the number of trials and the adaptation constant as main factors, and the two indices previously defined as dependent variables.

RESULTS

Simulated data representing the activations in 3 cortical areas were generated as described by eq. 1, in order to fit a time-varying connectivity pattern, shown in fig.1a. The procedure was repeated under all the different conditions of adaptation constant c, number of trials and SNR. An adaptive MVAR of order p=3 was fitted to each set of simulated data. The model order p was chosen by means of a method proposed in [5]. The multivariate Akaike Criterion was applied on each time interval and the maximum order obtained was then adopted for all the recursive estimation.

After the estimation of time-varying DTF and PDC, an Analysis of Variance (ANOVA) was performed on the indices of performances described in eq. 2 and 3, in order to evaluate in a statistically rigorous manner the capability of the method to retrieve the correct connectivity pattern (an example of the values obtained for time-varying DTF, in comparison to the theoretical ones, is shown in fig. 1b and 1c). The statistical factors analyzed were the SNR, the number of trials, the frequency band and the adaptation factor c.

The first ANOVA (dependent variable: time at settling) revealed a strong statistical influence of the factors SNR, TRIALS and C ($p<0,0001$). In particular, the plots of means for different values of C, TRIALS, and for the two-ways interaction between the two factors are shown in fig. 2. It can be noted from fig. 2a that, for both DTF and PDC, there is a minimum in the time at settling for a certain value of c. This can be explained with a trade-off between the adaptation speed (which decreases for low values of c) and the variance of the estimation (which decreases with high values of c). Moreover, the adaptation speed of DTF is higher than PDC. From fig. 2b it can be also noted that an high number of trials makes the time at settling decrease. This leads to fig. 2c, where it can be seen that an increase of the number of trials makes the minimum of the time at settling shift to higher values of the forgetting factor c. This means that, in practical applications, a higher value of c, and consequently a higher adaptation speed, can be reached if the number of trials at disposal increases.

The second index of performance analyzed was the average error in each time interval during which the values of connection strengths are kept constant after the transition. The ANOVA performed revealed a strong influence of the factors SNR, TRIALS, C in all the frequency bands analyzed. In fig. 3 the effect of different levels of SNR and TRIALS is shown. It can be noted that there is a decrease for higher values of SNR, as well as for higher number of trials, for both time-varying DTF and PDC. Moreover, such error is higher for DTF than for PDC in all conditions.

DISCUSSION

In this paper we propose an evaluation of the performances of two adaptive, multivariate estimators of the cortical connectivity, based on methods usually applied to stationary signals, and to the estimation of an AMVAR with a RLS method. The performances were evaluated with particular attention to two aspects: the capability to follow rapid changes in the connectivity patterns (adaptation speed) and the precision in the estimation of connectivity strengths. The effects of different factors affecting the EEG recordings were statistically evaluated, together with the influence of different choices of the forgetting factor. The results of the simulation study showed that:

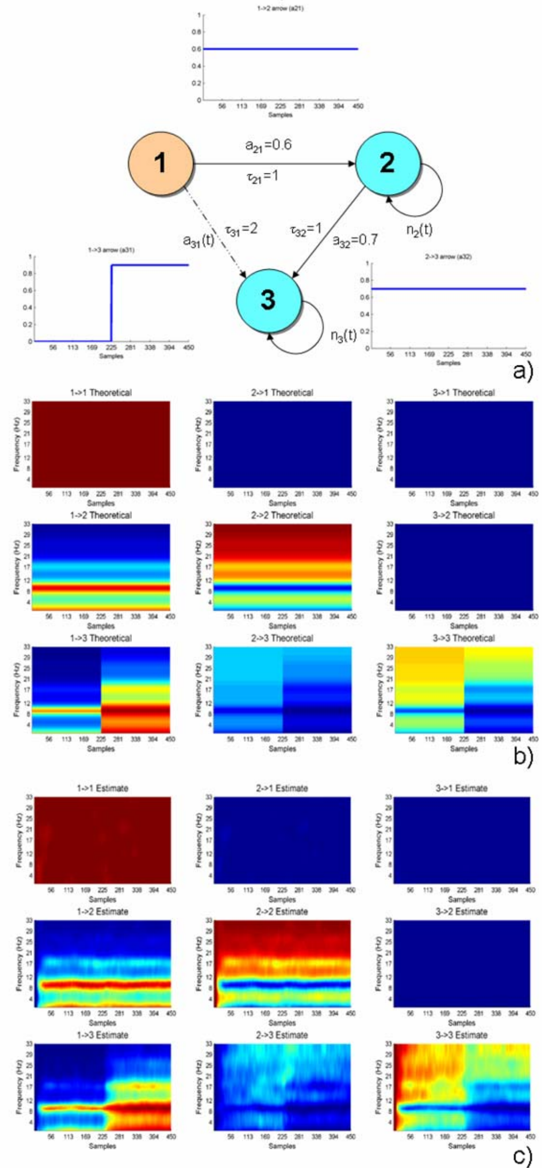

Fig.1: a) Connectivity pattern imposed between different regions of the cortex during simulation. The values of the connection strengths a_{ij} are time dependent, and are represented by the blue plots near each connectivity arrow. b) the time-frequency distribution of the theoretical values for the time varying DTF related to the model. Changes in the link 1-3 affect also links between the other areas, because DTF is normalized in entrance to each area. c) the time-frequency distribution of the estimated DTF.

1) The proposed time-varying estimators are effective in

retrieving the rapid changes in time of the cortical connectivity pattern.

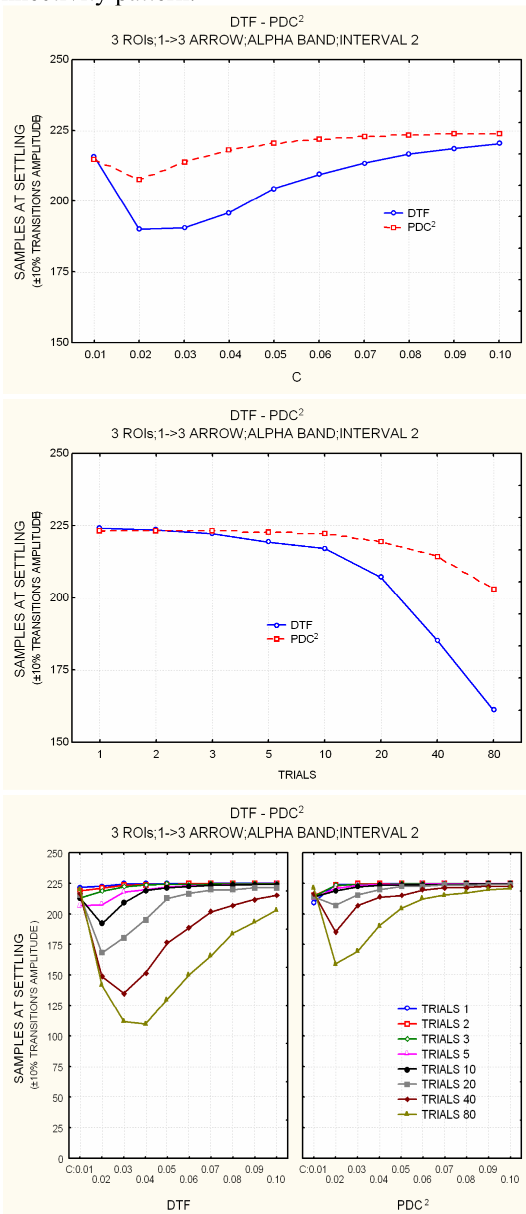

Fig. 2. Results of ANOVA performed on the time at settling (10% of the transition amplitude) for different values of the factors C and TRIALS. a) plot of means in function of the adaptation factor c used in the estimation of the AMVAR. A minimum can be noted for values of 0.02 for DTF and 0.02-0.03 for PDC. b) effect of different number of trials used for the recursive estimation. A better adaptation speed is shown for higher number of trials. c) two-ways interaction between factors C and TRIALS. It can be noted that for higher number of trials the minimum shifts to values of c comprised between 0.01 and 0.04. Results in the ALPHA band (8-12 Hz).

2) The signal to noise ratio and the amount of trials at disposal have a statistically significant effect on the performances both on the side of the adaptation speed and on the side of the accuracy of the estimation.

3) There is an optimum value for the choice of the adaptation constant c, which varies with the experimental conditions. In particular, a large amount of trials at disposal can increase the value of the optimum choice, thus allowing to have a higher adaptation speed without loosing the estimation accuracy.

4) The DTF method showed better performances with respect to the PDC on the side of the adaptation speed, while the PDC provided better results on the side of the estimation accuracy.

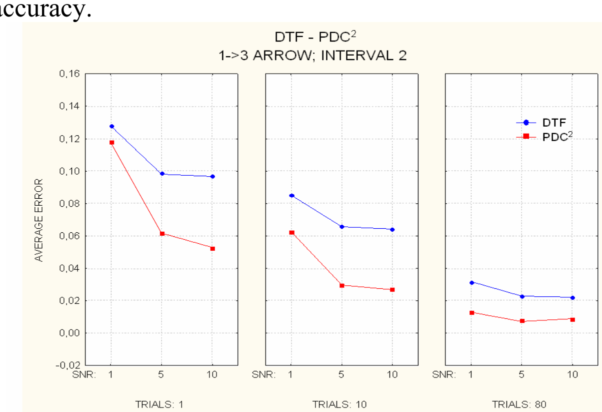

Fig. 3. Results of ANOVA performed on the average error on the arrow 1->3 of the model of fig. 1a, in the second time interval (values of connection strengths constant after the transition) on each connectivity arc of the model. $F(4, 196)=836.44$, $p<0.00001$.

CONCLUSION

In this paper we presented a simulation study testing the efficacy of two multivariate causality estimators to retrieve rapidly changing cortical connectivity. Simulations suggest that the methods were adequate to estimate cortical connectivity under a large range of SNR and TRIALS factors, normally encountered in the standard practice of the high resolution EEG recordings. It has been highlighted that the DTF estimator can assure a higher adaptation speed than PDC, but on the other hand PDC ensures a better accuracy in the estimation of connectivity strengths. Possible values for the optimum choice of the adaptation factor *c* have been proposed, according to the different operative conditions. In conclusion, this study opens the way to the application to real cortical estimations, in order to study detailed time-frequency patterns describing the evolution of cortical connectivity.

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