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# Towards the Time Varying Estimation of Complex Brain Connectivity Networks by means of a General Linear Kalman Filter Approach

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*Abstract*— **One of the main limitations of the brain functional connectivity estimation methods based on Autoregressive Modeling, like the Granger Causality family of estimators, is the hypothesis that only stationary signals can be included in the estimation process. This hypothesis precludes the analysis of transients which often contain important information about the neural processes of interest. On the other hand, previous techniques developed for overcoming this limitation are affected by problems linked to the dimension of the multivariate autoregressive model (MVAR), which prevents from analysing complex networks like those at the basis of most cognitive functions in the brain. The General Linear Kalman Filter (GLKF) approach to the estimation of adaptive MVARs was recently introduced to deal with a high number of time series (up to 60) in a full multivariate analysis. In this work we evaluated the performances of this new method in terms of estimation quality and adaptation speed, by means of a simulation study in which specific factors of interest were systematically varied in the signal generation to investigate their effect on the method performances. The method was then applied to high density EEG data related to an imaginative task. The results confirmed the possibility to use this approach to study complex connectivity networks in a full multivariate and adaptive fashion, thus opening the way to an effective estimation of complex brain connectivity networks.**

## I. Introduction

In the last decades, the concept of Granger causality [1] has gained more and more importance in the field of brain connectivity estimation due to many reasons, among which the fact that it can describe separately the functional influences between two neural assemblies in the two directions (i→j and j→i) and that it has been extended from a pairwise to a multivariate analysis [2, 3]. In fact, as pointed out from the very beginning by its Author [1] this analysis is able to depict an accurate connectivity pattern given that all relevant sources of the problem are included in the model (the "hidden source-dilemma") because hidden sources, i.e. not-measured brain activity, can cause misleading interaction results. According to these considerations, not only a multivariate approach is preferable, in terms of accuracy of the pattern reconstruction, to a bivariate one, as demonstrated in [4], but it is also crucial to insert all relevant sources in the multivariate modelling. The issue of the model dimension becomes then crucial to reach a full description of brain networks.

All the MVAR based methodologies for the functional connectivity estimation require the hypothesis of stationary signals. Thus, the temporal dynamics of the influences between cerebral areas are completely loss. To overcome this limitation, different algorithms for the estimation of MVAR with time dependent coefficients were recently developed. In particular, these methodologies are based on short-time window approaches, assuming the signals are stationary in short time intervals [5] or on an adaptive estimation of the MVAR model by a recursive algorithm involving a weighted influence of the past of the signal, as in the multi-trial Recursive Least Square (RLS) method with Forgetting Factor [6, 7]. However, even if the RLS overcomes the problem of non-stationary data, it presents a limitation on the number of signals to be considered contemporary in the estimation, due to computational complexity [7]. The problem of the model dimension can be solved by reducing the number of electrodes time series to be included in the model [7] or by using cortical waveforms derived for some regions of interest from high resolution EEG data [8]. However, the need to reduce the model dimension introduces a significant source of error, since each time a relevant source of information of the problem is removed from the autoregressive modelling, this introduces spurious connectivity links and degrades the reconstruction of the connectivity network. In 2010, a new method based on a General Linear Kalman Filter (GLKF), was provided as a solution to the limitation in the number of signals [9]. This work aims at testing the performances of the GLKF method

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on large networks (number of brain areas >= 60) in terms of estimation accuracy and adaptation speed, by means of a simulation study. Results will provide an estimation of these indices of the performances under specific conditions of the signals and a statistical analysis (Analysis Of Variance, ANOVA) of the dependency of the performances from the SNR and the amount of trials used for the estimation. The new method testing will be completed with an application of the GLKF to high density EEG data acquired during the imagery of hands grasping.

## II. METHODS

### *A. Multivariate Methods for the Estimation of Connectivity*

Supposing that the following multivariate autoregressive (MVAR) model is an adequate description of the dataset Y:

$$\sum_{k=0}^{p} \Lambda(k) Y(t-k) = E(t) \tag{1}$$

where **Y(t)** is the data vector in time, **E(t)** is a vector of multivariate zero-mean uncorrelated white noise processes, **Λ(k)** is the matrix of model coefficients at lag **k** and **p** is the model order, that can be chosen by means of the Akaike Information Criteria (AIC) for MVAR processes [9], to investigate the spectral properties of the examined process, (1) is transformed to the frequency domain:

$$\Lambda(f) Y(f) = E(f), \; \Lambda(f) = \sum_{k=0}^{p} \Lambda(k) e^{-j 2\pi f \Delta t k} \tag{2}$$

where **Δt** is the temporal interval between two samples.

### *B. Partial Directed Coherence*

The PDC [3] is a full multivariate spectral measure, used to determine the directed influences between any given pair of signals in a multivariate data set. This estimator was demonstrated to be a frequency version of the concept of Granger causality [1].

It is possible to define PDC as:

$$\pi_{ij}(f) = \frac{\Lambda_{ij}(f)}{\sqrt{\sum_{k=1}^{N} \Lambda_{ki}(f) \Lambda_{ki}(f)}}, \; \sum_{n=1}^{N} \left|\pi_{ni}(f)\right|^2 = 1 \tag{3}$$

Different estimators generalizing PDC were developed during the years [11]-[12]-[13]. Among them, squared values of PDC were shown to provide higher accuracy and stability [13]. The performances of a time varying adaptation of this estimator based on a Recursive Least Square with forgetting factor were analyzed by a simulation study in [8].

### *C. The General Linear Kalman Filter*

In the GLKF an adaptation of the Kalman Filter to the case of multi-trial time series is provided. In particular:

$$\begin{aligned} Q_n &= G_{n-1} Q_{n-1} + V_n \\ O_n &= H_n Q_n + W_n \end{aligned} \tag{4}$$

where $O_n$ represents the observation, $Q_n$ is the state process, $H_n$ and $G_n$ are the transition matrices and $V_n$ and $W_n$ are the additive noises. To obtain the connection with the time-varying MVAR it is necessary to make the following associations:

$$Q_n = \begin{bmatrix} \Lambda_1(n)^T \\ \vdots \\ \Lambda_p(n)^T \end{bmatrix}, \; O_n = \begin{pmatrix} x_1^{(1)}(n) & \cdots & x_d^{(1)}(n) \\ \vdots & \ddots & \vdots \\ x_1^{(K)}(n) & \cdots & x_d^{(K)}(n) \end{pmatrix} = Y_n \tag{5}$$

$$G_{n-1} = I_{dp}, \qquad H_n = \left(O_{n-1}, \; \cdots, \; O_{n-p}\right) \tag{6}$$

where $K$ denotes the number of trials, whereas $d$ is the dimension of the measured process. The details of the algorithm are provided in [9].

### *D. The Simulation Study*

The simulation study involved the following steps:

1) Generation of different simulated datasets fitting a predefined model composed by 60 nodes and achieved imposing different levels of trials number (factor TRIAL: 10, 20, 30, 50, 100) and Signal to Noise Ratio (factor SNR: 0.1, 1, 3, 5).
2) Evaluation, for each dataset, of time varying MVAR coefficients by means of GLKF method and estimation of time varying PDC.
3) Evaluation of performance indexes such as the relative error and the samples at settling, defined as in [8].
4) Analysis Of Variance (ANOVA) for repeated measures of the performance indexes, in order to evaluate the effects of the factors TRIAL and SNR on the performances of the analyzed method.

### *E. The High Density EEG Study*

Ten healthy volunteers took part in the experiment. They were asked to perform an imagery task (i.e. prolonged hands grasping) or simply relax (baseline condition) according to the position of a red target on a screen. The experiment was divided into 6 sessions of 12 trials each (6 for each task), with events randomly ordered within each session. We set a task length of 15s and an inter-trial interval of 2s. The recordings were performed by means of a cap equipped with 61 channels disposed according to an extension of 10-20 system. Data were band pass filtered (1-45 Hz + 50Hz Notch) and segmented in the interval [- 500 ; +500] ms in respect to the task execution onset. After the application of a semi-automatic procedure for artifacts rejection, based on threshold criteria, data were subjected to time varying functional connectivity estimation process by means of GLKF method. Then, a statistical comparison between connectivity patterns related to task and baseline conditions was performed to highlight the functional links related to the task execution.

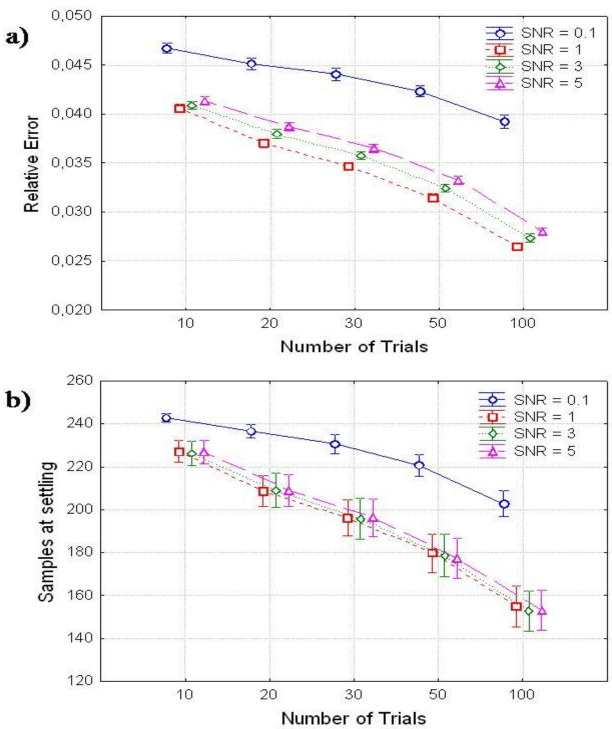


Fig. 1. Results of ANOVA performed on the Relative Error (a) and Samples at settling (b) obtained on a 60 nodes model: plot of means with respect to the factors TRIAL and SNR. ANOVA shows a high statistical significance (F=603.79, p<0.0001) for the case a) and (F=102.13, p<0.0001) for the case b) respectively.

## III. RESULTS

### A. Results of Simulation Study

A time varying MVAR model of order 16 was fitted to each set of 60 channels simulated data. The procedure of signal generation and time varying PDC estimation was repeated 50 times for each level of factors TRIAL and SNR in order to increase the robustness of the statistical analysis. The performance indexes were computed for each iteration and then subjected to the ANOVA for repeated measures.

Results of one way ANOVA computed by setting as dependent variable the relative error revealed a strong statistical influence of the main factors TRIAL and SNR (F=603.79, p<0.0001). Results of one way ANOVA computed by setting as dependent variable the samples at settling revealed a strong statistical influence of the main factors TRIAL and SNR (F=102.13, p<0.0001).

Fig.1 shows the influence of the different levels of the main factors TRIAL and SNR on the relative error (panel a) and samples at settling (panel b). The bar on each point represents the 95% confidence interval of the mean errors computed across the simulations. The plot in panel a) indicates that the relative error remains under 1% for all the considered values of number of trials and SNR and decreases with the increase of the number of trials for each value of SNR. The highest error values were achieved for SNR equal to 0.1, the lowest for SNR equal to 1. An increase of SNR between 1 and 5 improved the relative error. The plot in panel b) shows a decrease of the samples at settling with the increase of the number of trials for each value of SNR. The highest values for samples at settling were achieved for SNR equal to 0.1. For values of SNR higher than 1 no effects on the adaptation speed were showed, as confirmed by the Tukey's post hoc analysis.

### B. Results of High Density EEG Study

In order to apply the Kalman Filtering algorithm to real data and to test its capacity to accurately infer functional connectivity patterns on high dimensional models, time varying PDC was estimated for each condition (task and baseline) from the high density EEG data collected during the imaginative task. To highlight only the information flows related to the task execution, a statistical comparison between task and baseline conditions was performed with a significance level of 5%, corrected with False Discovery Rate criterion for multiple comparisons. The significant connectivity patterns were averaged within four frequency bands defined according to the Individual Alpha Frequency (IAF) [14] and within four time intervals, two before and two after the beginning of task execution.

Functional connectivity patterns elicited during the prolonged hands grasping imagery in Beta band were reported in Fig.2 for a representative subject. In the figure, each network is related to a specific time interval defined according to the onset of the task execution: (-500 ; -250) ms (a), (-250 ; 0) ms (b), (0 ; 250) ms (c), (250; 500) ms (d). Connectivity patterns are represented on a scalp model seen from above, with the nose pointing to the upper part of the page. The colors and sizes of the arrows code the strength of the connections. Few connections (less than 5%) survived to the statistical comparison between task and baseline conditions in the two time intervals before the task execution (a and b). c and d showed the temporal evolution of connectivity patterns during hands grasping imagery. The major involvement of the frontal regions and of the centro-parietal regions, mainly in the dominant hemisphere (left part of the head) related to motor imagery tasks was evident since the first 250 ms of imagination (c). Such involvement was confirmed and reinforced in the following 250 ms (d).

## IV. DISCUSSION

The results provided by the simulation study suggest that the GLKF based estimation of time varying PDC is a able to follow the temporal evolution of high dimensional connectivity networks. In fact, for values of SNR and TRIAL levels largely met, for instance, in usual EEG recordings (SNR>1, TRIAL>=30), the method is able to follow the transitions of the connectivity flows with good accuracy (relative error below 1%) and speed (samples at settling below 200 samples). Low values of SNR and insufficient number of trials led to inaccurate estimations.

These results are confirmed by the application of GLKF to high density EEG data. In fact, the method allowed to describe the temporal evolution of connectivity patterns related to hands grasping imagery. No significant connectivity, with respect to the baseline condition, was shown before the imagery task onset, while a high involvement of frontal and left centro-parietal areas was described during the task execution. Such results are in agreement with the literature associated to this type of task [15]. The transition between baseline and motor imagery was accurately described in the first 250 ms of task execution, thus showing the good adaptation speed of the method.

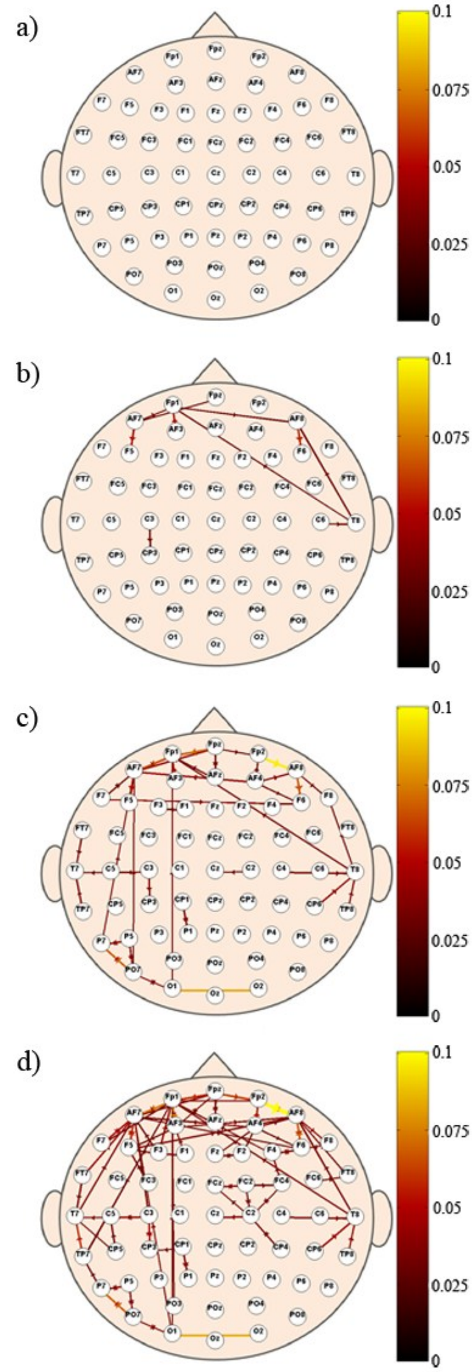


Fig. 2. Functional connectivity patterns elicited during the prolonged hands grasping imagery in Beta band, in a representative subject. Each network is related to a specific time interval, defined according to the imagery onset: [-500 ; -250] ms (a), [-250 ; 0] ms (b), [0 ; 250] ms (c), [250 ; 500] ms (d). Head seen from above, the nose pointing to the upper part of the page. The color and size of the arrows code the connection strength.

## V. Conclusion

The results achieved by the simulation study and the application on high density EEG showed how GLKF based time varying functional connectivity overcomes the limits of previously used RLS, by providing an accurate estimation of functional connectivity patterns and allowing to analyze high dimensional models, thus opening the way to an effective estimation of complex brain connectivity networks.

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