

# FUNCTIONAL BRAIN CONNECTIVITY AS REVEALED BY SINGULAR SPECTRUM ANALYSIS

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**Abstract**—Correlation based measures have widely been used to characterize brain connectivity. In this paper, a new approach based on singular spectrum analysis is proposed to characterize brain connectivity. It is obtained by deriving the common basis vector of two or more trajectory matrices associated with functional brain responses. This approach has the advantage illustrating the existence of joint variations of the functional brain responses and to characterize the correlation structure. The performance of the method are illustrated on both simulated autoregressive data and real fMRI data.

**Index Terms**—Brain networks, functional connectivity, fMRI, singular spectrum analysis, correlation.

## I. INTRODUCTION

With the widespread acceptance of the network description onto brain processing functions, identification and quantification of interactions between brain structures that support the processing of specific brain functions (perceptual, cognitive or motor functions) is a fundamental issue in neuroscience. For example, information about the functioning or dysfunctioning of the brain can be inferred from the network structure. The current theories of schizophrenia emphasize that the core aspects of the pathophysiology is due to the disconnection hypothesis [1] rather than deficits in specific brain areas. The availability of neuroimaging techniques, such as electroencephalography (EEG), magnetoencephalography (MEG), functional near infrared imaging (fNIR) and functional magnetic resonance imaging (fMRI), offers ways to address questions of functional connectivity that is fundamental for the description of these brain networks. This is done through the statistical analysis of the time series they produce. Functional connectivity is defined in [2] as temporal correlation between spatially remote neurophysiological events, is one method to characterize such interactions. Correlation measures the simultaneous coupling between two time series. Various other correlation methods have been proposed in brain imaging data analysis to extract information of interaction from data sets; among them partial correlation [4] and coherence [5]. The idea behind functional connectivity is to characterize the resemblance between two or more brain regions on

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the basis of similarities in their functional time series. For example, if two or more brain regions show similar fMRI density spectrum, then we could deduce that they are functionally connected even though there may be no direct anatomical connection between these regions. Other measure of resemblance that are not correlation based could be used to characterize functional connectivity.

The purpose of this paper is to introduce a novel method to study or characterize functional connectivity between two or more brain regions. The method is based on singular spectrum analysis that was introduced in [6] to study the structure of time series. The aim of singular spectrum analysis is to decompose an observed time series of interest into a number of additive time series components that can be interpreted as trend components (smooth and slowly varying parts of the times series), various oscillatory components and unstructured noise. It is a model-free technique and the principle consists in unfolding an observed time series into the columns of a Hankel matrix known as the trajectory matrix [7]. A characteristic time series which can be used for characterizing the structure of the observed time series or for forecasting can be obtained from the SVD of a trajectory matrix. Singular spectrum analysis is used in this paper to extract similarities between two or more functional brain responses to characterize functional brain connectivity. This is done by deriving the common basis vector time of the two or more trajectory matrices obtained from the functional brain responses of interest.

Basic singular spectrum analysis of a time series is described in the following section. The method used to extract similarities to characterize the connectivity between two or more time series is presented in Section 3. The performance results of the proposed measure on both simulated autoregressive and real fMRI data are presented in Section 4. Concluding remarks are given in Section 5.

## II. SINGULAR SPECTRUM ANALYSIS

Singular spectrum analysis consists of two complementary tasks: decomposition and reconstruction [7]. Each task is composed of two steps.

Let  $y_i$ ,  $i = 1, \dots, N$  be an observed fMRI or fNIR time series,  $k$  be an integer value and define  $l = N - k + 1$ . At the first step, the corrected mean observed time series  $\tilde{y}_i$ ,  $i = 1, \dots, N$  is mapped into a sequence of multidimensional lagged vectors that form the columns of of a  $k \times l$  Hankel

matrix

$$\mathbf{Y} = [\tilde{\mathbf{Y}}_1, \tilde{\mathbf{Y}}_2, \dots, \tilde{\mathbf{Y}}_l] = \begin{bmatrix} \tilde{y}_1 & \tilde{y}_2 & \dots & \tilde{y}_l \\ \tilde{y}_2 & \tilde{y}_3 & \dots & \tilde{y}_{l+1} \\ \vdots & \vdots & \vdots & \vdots \\ \tilde{y}_k & \tilde{y}_{k+1} & \dots & \tilde{y}_N \end{bmatrix}. \quad (1)$$

The matrix  $\mathbf{Y}$  is called the trajectory matrix and the number  $k$  of rows of  $\mathbf{Y}$  is referred to as the embedded dimension or window length. Its choice is restricted to  $2 \leq k \leq \lfloor \frac{N+1}{2} \rfloor$  and is the sole parameter of this step.

The second step consists in generating the singular value decomposition of the trajectory matrix. This allows the trajectory matrix to be written as the sum of rank one bi-orthogonal matrices. Let  $S = \mathbf{Y}\mathbf{Y}^\top$ , denote  $\lambda_1 \geq \dots \geq \lambda_k$  the eigenvalues and  $u_1, \dots, u_k$  the corresponding eigenvectors of  $S$ . Using  $v_i = \mathbf{Y}^\top u_i / \sqrt{\lambda_i}$ , the following trajectory matrix decomposition is generated

$$\mathbf{Y} = \mathbf{Y}_1 + \mathbf{Y}_2 + \dots + \mathbf{Y}_d, \quad (2)$$

where  $\mathbf{Y}_i = \sqrt{\lambda_i} u_i v_i^\top$  have rank one and  $d = \max\{i, \text{ such that } \lambda_i > 0\}$ . The elements  $(\sqrt{\lambda_i}, u_i, v_i)$  are called the eigentriples of (2). These two steps constitutes the decomposition task.

The reconstruction task starts with the grouping step. In this step, the indices  $\{1, \dots, d\}$  are partitioned into  $m$  groups and the matrices are summed within each group creating the decomposition

$$\mathbf{Y} = \tilde{\mathbf{Y}}_1 + \tilde{\mathbf{Y}}_2 + \dots + \tilde{\mathbf{Y}}_m. \quad (3)$$

This step results in a representation of the trajectory matrix as a sum of several resultant matrices.

The last step of the reconstruction task maps each resultant matrix into a time series of length  $N$ , which is an additive component of the observed time series. A time series of length  $N$  is generated from a matrix  $\tilde{\mathbf{Y}}$  by diagonal averaging

$$\tilde{y}_i = \begin{cases} \frac{1}{s} \sum_{i=1}^s \tilde{y}_{i, s-i+1} & 1 \leq s \leq k \\ \frac{1}{k} \sum_{i=1}^k \tilde{y}_{i, s-i+1} & k \leq l \leq n \\ \frac{1}{N-s+1} \sum_{i=1}^{N-s+1} \tilde{y}_{i+s-n, n-i+1} & n \leq s \leq N \end{cases} \quad (4)$$

Therefore, the initial time series  $\mathbf{y} = y_i, i = 1, \dots, N$  is decomposed into the sum of  $m$  component time series

$$\mathbf{y} = \sum_{i=1}^m \tilde{\mathbf{y}}_i. \quad (5)$$

The separability aspect is an important part of the singular spectrum analysis method. The periodic component in the data will be reflected as a pair of almost equal eigenvalues [7].

<sup>1</sup>[.] denote the integer part.

### III. USING SINGULAR SPECTRUM ANALYSIS FOR BRAIN CONNECTIVITY

A standard approach for whole brain analysis is to derive a single time series for each region-of-interest (ROI) either by averaging or by extracting a principal component; alternatively repeated pairwise analysis can be performed on pairs of voxels. Assume  $y_i$  and  $z_i, i = 1, \dots, N$  correspond to the measurement of two fMRI time series representing two regions between which the connectivity is to be characterized. Rather than using a correlation based measure to characterize the connectivity, the proposed method looks at extracting variations the functional brain responses of interest have in common. The rationale of the method is that if there is connectivity between two brain regions of interest, then some time series components that characterize the same variations may be present in each functional brain response but with different importance.

One way to extract these common time series components is to use a common basis to decompose both trajectory matrices  $\mathbf{Y}$  and  $\mathbf{Z}$  obtained from  $y_i$  and  $z_i, i = 1, \dots, N$ . The matrix of normalized eigenvectors  $U = [u_1, \dots, u_d]$  of the column space of  $\mathbf{Y}$  and  $\mathbf{Z}$  corresponds to this basis if it simultaneously diagonalize or makes them as diagonal as possible in a sense to be defined [8]

$$U^\top S_i U = \Lambda_i \quad i = 1, 2 \quad (6)$$

where  $S_1 = \mathbf{Y}\mathbf{Y}^\top, S_2 = \mathbf{Z}\mathbf{Z}^\top$  and  $\Lambda_{i=1,2}$  are diagonal. The vector  $u_i$  gives the coefficients of the  $i^{\text{th}}$  common basis vector and the diagonal elements of  $\Lambda_{i=1,2}$  characterize the contribution proportion of the  $i^{\text{th}}$  time series to the observed time series.

However, since the time series  $y_i$  and  $z_i, i = 1, \dots, N$  share only some information it is only possible to find two matrices of normalized eigenvectors  $U_1$  and  $U_2$  with common  $r < d$  eigenvectors  $[u_1, \dots, u_r]$ , the rest describes the difference in information. The matrices  $U_1$  and  $U_2$  are of the forms  $[u_1, \dots, u_r, u_{1(r+1)}, \dots, u_{1d}]$  and  $[u_1, \dots, u_r, u_{2(r+1)}, \dots, u_{2d}]$

$$U_i^\top S_i U_i = \Lambda_i \quad i = 1, 2. \quad (7)$$

As described in [8], algorithms for simultaneous diagonalization can be used to estimate  $[u_1, \dots, u_d]$ . The common signal for  $y_i$  and  $z_i, i = 1, \dots, N$  that can be used to characterize brain connectivity is then obtained by reconstructing the trajectory matrices using (2),

$$\begin{aligned} \mathbf{Y}_c &= \mathbf{Y}_1 + \mathbf{Y}_2 + \dots + \mathbf{Y}_r, \\ \mathbf{Z}_c &= \mathbf{Z}_1 + \mathbf{Z}_2 + \dots + \mathbf{Z}_r, \end{aligned}$$

where  $\mathbf{Y}_i = \sqrt{\lambda_i} u_i v_i^\top$  with  $v_i = \mathbf{Y}^\top u_i / \sqrt{\lambda_i}$  and  $\mathbf{Z}_i = \sqrt{\lambda_i} u_i w_i^\top$  with  $w_i = \mathbf{Z}^\top u_i / \sqrt{\lambda_i}$ . The common signals are obtained using (4) and (5). A normalized measure of the energy  $\sum_i y_{c_i}^2 / \sum_i y_i^2$  of this time series can then be used as a measure of connectivity. The number  $r$  of common eigenvectors in  $S_1$  and  $S_2$  needed to characterize the shared information can be selected using a model selection criterion [9] as follows

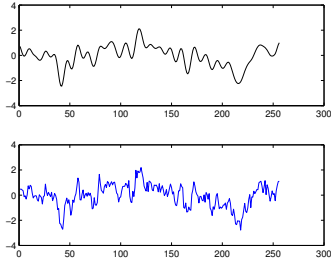


Fig. 1. Original time series  $x$  bottom and its singular spectrum top.

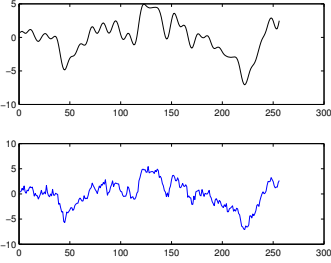


Fig. 2. Original time series  $y$  bottom and its singular spectrum top.

$$\begin{aligned}
 & ICPPCA(r) \\
 &= \sum_{l=1}^2 \ln \left( \left( \prod_{i=1}^r \lambda_{li} \right) \cdot \left( \frac{1}{d-r} \sum_{i=r+1}^d \lambda_{li} \right)^{(d-r)} \right) \\
 & \quad + \frac{r}{N} \ln(N) \quad (8)
 \end{aligned}$$

Other forms of model selection criteria could be used such as  $AIC_c$  [13], [14] or  $KIC_c$  [15]

#### IV. SIMULATION EXAMPLE

In order to test and validate the proposed method in identifying brain connectivity, two autoregressive processes consisting of 256 samples with the second being driven by the first according to the following model

$$\begin{cases} x_k = -0.84x_{k-1} + u_k \\ y_k = -0.5x_{k-1} + -0.84y_{k-1} + v_k \end{cases} \quad (9)$$

where  $v_i$  and  $u_i$  are independent and (i.i.d)  $N(0, 0.28)$  were generated.

The top figure of figure 1 display the singular spectrum obtained by the method described in Section 2 with the number of retained eigenvalues estimated with (8). The bottom figure represents the original time series  $x$ . In a similar way top figure of figure 2 display the singular spectrum obtained by the method described in Section 2 with the number of retained eigenvalues estimated with (8). The bottom figure represents the original time series  $y$ . The connectivity between the two time series is extracted by using a common basis for the two trajectory matrices  $\mathbf{X}$  and  $\mathbf{Y}$  as described in Section 3. If such basis exists, then the time series  $x$  and  $y$  share some information and this basis can be used to obtain singular spectrum of both  $x$  and  $y$  as illustrated in figure 3. We can observe from this figure that both singular spectrums approximate the associated time

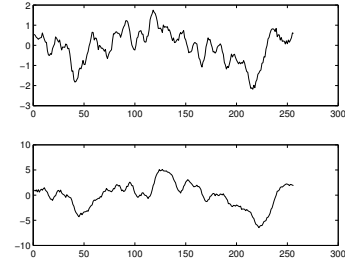


Fig. 3. singular spectrum of  $x$ , top and  $y$  bottom.

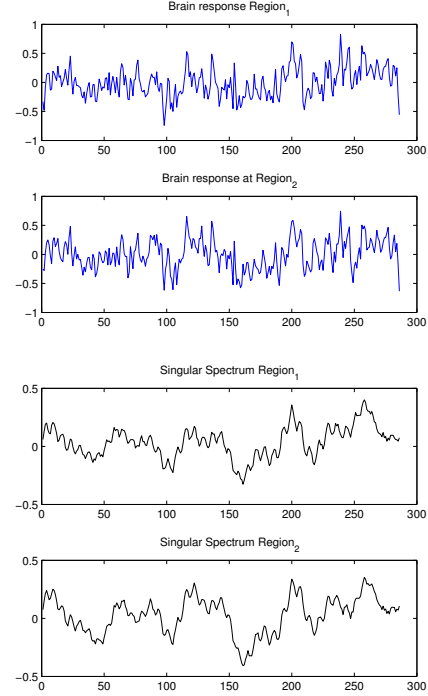


Fig. 4. Real fMRI data - functionally connected regions: region response (top), and shared structure (bottom) as revealed by the proposed method.

series. In case such basis doesn't exist the reconstruction with this basis of  $x$  or  $y$  will not be possible and therefore the singular spectrum will not approximate the original time series  $x$  and  $y$ . By considering single representative time-series for ROIs under investigation, the proposed method can perform the whole brain analysis fairly fast with modern day computers. It took an average time of 1.2 s to compute the shared structure with the proposed method, averaged over 100 realizations of model (9), with a 3 GHz Intel Core-2 Quad CPU and RAM 3.25 GB. For quantifying the similarity, 100 realizations based on model (9) for both functionally connected (first driving the second series) and functionally unconnected (zero influence from the first on the second series with other parameters remaining the same) regions were simulated and an average correlation measure is derived that is reported in Table-1 along with the real fMRI data (next section). The measure clearly indicates that the proposed method is asserting functional connectivity better than simply based on correlation of the original ROIs response.

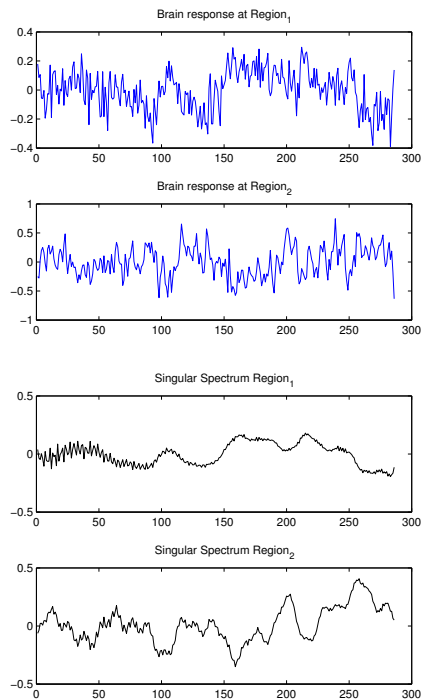


Fig. 5. Real fMRI data - functionally unconnected regions: region response (top), and shared structure (bottom) as revealed by the proposed method.

## V. fMRI APPLICATION

### *Discriminating Visual Targets - Event-related Design:*

After obtaining informed consent approved by the ethics committee, the experiment was performed on six subjects with no psychiatric or neurological disorders. In this fMRI study, a spatial cue was followed by a sequence of bilateral visual stimulus arrays, and the subject had to discriminate a target item from surrounding distractor items at the attended location. fMRI images were acquired using a General Electric 1.5T Signal LX neuro-optimized scanner. After structural scanning, functional images were acquired in nine runs lasting 8.5 min each (TR: 2 sec, TE: 40 msec, flip angle: 90°, matrix: 64 x 64 voxels, 2.8125 x 2.8125 x 3 mm, 14 slices oriented vertical to the calcarine fissure). Subjects were asked to covertly shift their attention to the side (right, left or neutral) indicated by a symbolic cue. Then, a sequence of 10 bilateral stimuli ('item') appeared in the upper visual field. Stimuli on both sides consisted of 3 x 3 arrays of crosses superimposed on a background checkerboard that was locally and globally smoothed. The subjects had to discriminate whether a target T in the middle of the attended stimulus was upright or inverted (50/50 %) and to press one of the two buttons. Details of this experiment can be found in [11]. Image processing and statistical analysis were carried out using SPM8 [12] and Matlab. For analyzing the condition: symbolic cue followed by discriminating the target item 'T' under low contrast, the 286 acquisitions had the visual stimulus activating the part of the brain responsible for interpreting cues and discriminating specific target behavior, with the corresponding HRF estimated in [3].

We take the principal component as a representative time-series for each ROI (22-voxels) in a pair of activated regions,

Correlation	Real data SS / OBR*	Synthetic data SS / OBR
Connected ROIs	0.9227 / 0.9084	0.7121 / 0.5518
Unconnected ROIs	-0.49 / -0.3448	-0.0194 / -0.0155

TABLE I

FUNCTIONAL CONNECTIVITY (\* : SHARED STRUCTURE / ORIGINAL BRAIN RESPONSE)

the hidden shared structure has been easily extracted by the proposed method revealing the strong functional connectivity among them as shown in Fig. 4. Similarly, a pair of activated and non-activated regions was selected and their principal components are tried for common structure in them. Fig. 5 shows clearly the absence of any common structure revealing that the brain regions are functionally not connected. Same observations can easily be made from Table-1.

## VI. CONCLUSION

In this paper a new approach based on singular spectrum analysis has been proposed to characterize brain connectivity. The approach has the advantage of allowing to investigate the existence of common structure among several brain responses. The common structure is explained by the number of retained eigenvalues and the common basis vector shared by the trajectory matrices associated to the brain responses. The performance of the method were illustrated on both simulated autoregressive data and real fMRI data.

## REFERENCES

- [1] K. J. Friston, The disconnection hypothesis, *Schizophrenia Research*, vol. 30, pp. 115 - 125, 1998.
- [2] K. J. Friston, C. D. Frith, P. F. Liddle, and R. S. Frackowiak, Functional connectivity: the principal component analysis of large PET data sets, *Journal of Cerebral Blood Flow and Metabolism*, vol. 1, pp. 5 - 14, 1993.
- [3] A. K. Seghouane and A. Shah, HRF Estimation in fMRI Data With an Unknown Drift Matrix by Iterative Minimization of the Kullback-Leibler Divergence, *IEEE Trans. on Medical Imaging*, vol. 2, pp. 192 - 206, 2012
- [4] G. Marrelec, A. Krainik, H. Duffau, M. Pelegrini-Issac, S. Lehericy, J. Doyon, and H. Benali, Partial correlation for functional brain interactivity investigation in functional MRI, *Neuroimage*, vol. 32, pp. 228 - 237, 2006.
- [5] F. T. Sun, L. M. Miller, and M. DeSposito, Measuring interregional functional connectivity using coherence and partial coherence analyses of fMRI data, *Neuroimage*, vol. 21, pp. 647 - 658, 2004.
- [6] D. S. Broomhead, Extracting qualitative dynamics from experimental data, *Physica D*, vol. 20, pp. 217 - 236, 1986.
- [7] N. Golyandina, V. Nekrutkin, and A. Zhigljavsky, *Analysis of Time Series Structure: SSA and Related Techniques*, Chapman and Hall, 2001.
- [8] I. T. Jolliffe, *Principal Component Analysis*, Springer, 2nd ed., 2004
- [9] A. K. Seghouane, Bayesian estimation of the number of principal components, *Signal Processing*, vol. 87, pp. 562 - 568, 2007.
- [10] K. J. Friston, A. P. Holmes, and J. Ashburner and J. B. Poline, SPM8, <http://www.fil.ion.ucl.ac.uk/spm/>
- [11] H. Hinrichs et al., Deconvolution of event-related fMRI responses in fast-rate experimental designs: Tracking amplitude variations, *J. Cogn. Neurosci.*, vol. 12, pp. 76 - 89, 2000
- [12] K. J. Friston, A. P. Holmes, and J. Ashburner and J. B. Poline, SPM8, <http://www.fil.ion.ucl.ac.uk/spm/>
- [13] A. K. Seghouane and S. I. Amari, The AIC criterion and symmetrizing the Kullback-Leibler divergence, *IEEE Transactions on Neural Networks*, vol. 18, pp. 97 - 106, 2007.
- [14] A. K. Seghouane, Asymptotic bootstrap corrections of AIC for linear regression models, *Signal Processing*, vol. 90, pp. 217 - 224, 2010.
- [15] A. K. Seghouane and M. Bekara, A small sample model selection criterion based on Kullbacks symmetric divergence, *IEEE Transactions on Signal Processing*, vol. 52, pp. 3314 - 3323, 2004.