MULTIFRACTAL ANALYSIS OF RESTING STATE NETWORKS IN FUNCTIONAL MRI
Philippe Ciuciu, Gaël Varoquaux, Patrice Abry, Moty Almog

To cite this version:
Philippe Ciuciu, Gaël Varoquaux, Patrice Abry, Moty Almog. MULTIFRACTAL ANALYSIS OF RESTING STATE NETWORKS IN FUNCTIONAL MRI. IEEE International Symposium on Biomedical Imaging, Mar 2011, Chicago, United States. paper ID 1544. cea-00558870

HAL Id: cea-00558870
https://hal-cea.archives-ouvertes.fr/cea-00558870
Submitted on 24 Jan 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
MULTIFRACTAL ANALYSIS OF RESTING STATE NETWORKS IN FUNCTIONAL MRI

Philippe Ciuciu(1)*, Gaël Varoquaux(2), Patrice Abry(3) and Moty Almog(1)

(1) LNAO/NeuroSpin, CEA Saclay, Bat. 145, 91191 Gif-sur-Yvette, cedex France
(2) INSERM U992 and INRIA Saclay Parietal project, NeuroSpin, 91191 Gif-sur-Yvette, cedex France
(3) CNRS, UMR 5672, Laboratoire de Physique. ENS Lyon, France.

1 firstname.lastname@cea.fr, 2 gael.varoquaux@normalesup.org, 3 patrice.abry@ens-lyon.fr

ABSTRACT

It has been know for at least one decade [1] that functional MRI time series display long-memory properties, such as power-law scaling in the frequency spectrum. Concomitantly, multivariate model-free analysis of spatial patterns, such as spatial Independent Component Analysis (sICA) [2], has been successfully used to segment from spontaneous activity Resting-State Networks (RSN) that correspond to known brain function. As recent neuroscientific studies suggest a link between spectral properties of brain activity and cognitive processes [3], a burning question emerges: can temporal scaling properties offer new markers of brain states encoded in these large scale networks? In this paper, we combine two recent methodologies: group-level canonical ICA for multi-subject segmentation of brain network, and wavelet leader-based multifractal formalism for the analysis of RSN scaling properties. We identify the brain networks that elicit self-similarity or multifractality and explore which spectral properties correspond specifically to known functionally-relevant processes in spontaneous activity.

Index Terms— spatial ICA, multifractality, scaling, resting state, fMRI

1. INTRODUCTION

The presence of scale invariance in functional MRI (fMRI) data has been considered as confound or noise for a long time. Preliminary evidence that fMRI time series display long-memory properties, such as power-law scaling in the frequency spectrum, has been demonstrated on “resting state” motion-corrected datasets [1]. Physiological factors such as cardiac beat or breathing cycle may also contribute to this scaling phenomenon since they contaminate the Blood Oxygenated Level Dependent (BOLD) signal with properties depending on the sampling period of data (i.e. short/long time of repetition (TR)) [4]. Early investigations therefore considered these space-varying low frequency components as noise, responsible for potential non stationarities.

Other authors pointed out that the BOLD signal itself contains power at virtually all frequencies, notably in randomized event-related designs [5]. Interestingly, recent studies have reported that low-frequency spatial fluctuations in cortical BOLD signals may be indicative of synchronized long memory neuronal oscillations rather than merely noise [6, 7]. Concomitantly, greater persistence during brain activation has been found in normal subjects in [6]. Also, higher predictability summarized in terms of scaling exponent (controlling the power law decrease of 1/f spectra) has been reported in patients with Alzheimer disease or with major depressive disorder, especially in brain regions implicated in the early stages of the degeneracy process [7, 8]. More recently, scale invariance has been demonstrated to be an intrinsic property of ongoing brain activity. It may thus provide a new insight on how the brain works provided that quantitative parameters can be mapped with good specificity to cognitive states (resting or awake states), task performance, or neurological disorder (epilepsy) [3]. These last works relied on tools such as window-averaged periodograms which are grounded on assumptions self-similarity. However, the empirical results in [3] (Hurst parameter larger than 1) show that the data cannot be considered as realizations of fractional Brownian motion noise, for which scaling properties are controlled by the sole self-similarity (or Hurst) parameter lying in the range [0, 1]. A richer description is thus needed to reflect the signal properties.

Inspired by the connection between 1/f and long range dependence, several groups have argued that the analysis of fMRI time series should be performed in the wavelet domain [9–11]. A first attempt to identify stimulus-induced signal changes from scaling parameters was proposed in [6, 12]. These authors developed a voxel-based fluctuation analysis (FA) and applied it to high temporal resolution fMRI data. Interestingly, they showed that fractal features of voxel time series can discriminate active from inactive brain regions [6, 12]. Also, to decide whether scaling analysis can help to distinguish motion artifacts from true BOLD responses, complementary analyses were conducted in [13]. They are based on detrended fluctuation analysis (DFA) and conclude that DFA succeeds in distinguishing amongst three types of voxels, noise, motion artifacts, and true BOLD responses when the classical FA fails to robustly recognize which active regions in the brain are truly involved in certain tasks. However, it has been argued in [14] that wavelet tools perform better than DFA. Moreover, while scale invariance was first modeled with 1/f processes and long range dependence, these classes of models have fruitfully been embodied into the larger description of self-similar processes. More recently, multifractal (MF) processes were proposed has another versatile class of models for scale invariance. Therefore, akin to [11, 15], in the present contribution, the analysis of scale invariance is based on the recently introduced wavelet Leaders [16], a tool which, compared to those listed above, brings in two major benefits: i) it shows by far the best estimation performance, and ii) it enables to discriminate efficiently multifractality from self-similarity or long memory.

However, in [11, 15], due to voxelwise analysis and between-voxel variability, the MF spectra suffered from a lack of robustness in certain brain regions. To overcome these drawbacks, here we make use of a multivariate approach, i.e. spatial Independent Component Analysis (sICA), which has been popularized in the last decade as an exploratory or model-free approach for analyzing fMRI...
data [2,17]. Hence, it appears as the method of choice for studying resting-state datasets. At the group-level however, classical sICA schemes (group ICA, tensor ICA,...) lack of reproducibility due to between-subject variability. Also, statistical decision rules may appear too conservative. This has motivated the development of the canonical ICA (canICA) methodology, which relies on a generalized canonical analysis to find out reproducible components across subjects [18]. In this paper, canICA is used to segment salient features from multi-subject resting-state datasets, thus decomposing the multivariate datasets in a product of K spatial components and associated time series. The wavelet leader based multifractal analysis is applied to these time-series, to differentiate functional processes encoded in RSNs from other brain regions in terms of scaling exponents.

The remainder of the paper is organized as follows. Section 2 summarizes the canICA framework we rely on. Then, Section 3 introduces the key notions underlying multifractal analysis as well as the wavelet Leader-based multifractal formalism that permits to analyze precisely the scaling properties in empirical data. Section 4 is devoted to experimental results and group-level statistical analysis on the multifractal parameters. Conclusion are drawn in Section 6.

2. FROM SPONTANEOUS-ACTIVITY RECORDINGS TO BRAIN-NETWORK TIME SERIES

In this section, we describe how the time-series used to perform multifractal analysis are extracted from multi-subject fMRI resting-state datasets. Let us denote \( \{ Y^s \in R^{T \times P}, s = 1 : S \} \) datasets composed of T images with P voxels. We apply an ICA-based analysis [19] to decompose the original voxelwise signals into K subject-specific time series \( X^s \in R^{T \times K} \) and group-level spatial components \( A \in R^{K \times P} \), with residuals \( N^s \):

\[
\forall s = 1 : S, \quad Y^s = X^s A + N^s. \tag{1}
\]

The spatial maps A segment salient and reproducible features of resting-state fluctuations such as brain functional networks or structured noise (eg physiological or movement artifacts). Note however that noICA ever guarantees any independence (or gives a p-value). The corresponding subject-specific time series \( X^s \) will be used in subsequent scaling analysis.In the following, we summarize how A is derived.

2.1. Generative model for the spatial patterns

The spatial features of interest A are observed mixed together and confounded by unstructured background noise, inter-subject resting-state variability, and observation noise. More specifically, following [18, 19], the observed signal can be written as a generative model made of hierarchical decompositions with different noise terms at each level. First, we model group-level patterns, \( C \in R^{K \times N} \), as generated by the set of sources \( A \in R^{K \times N} \), confounded by additive unstructured noise \( E \in R^{K \times N} \), and observed as a random linear mixture in the group-level signal sub-space spanned by \( C \):

\[
C = MA + E,
\]

where \( M \) is an orthogonal mixing matrix. Each subject s is described by patterns \( P^s \), generated from linear combinations of the group-level patterns C and additional within-subject variability \( R^s \):

\[
\forall s = 1 : S, \quad P^s = \Lambda^s C + R^s,
\]

where \( \Lambda^s \) is a subject-specific loading matrix. Finally, each image in the observed data is a combination of different subject-specific patterns \( P^s \) confounded by observation noise:

\[
\forall s = 1 : S, \quad Y^s = W^s P^s + T^s.
\]

To summarize, Eq. (1) holds provided that \( X^s = W^s A^s M \) and \( N^s = W^s A^s E + W^s R^s + T^s \).

2.2. CanICA estimation procedure

Starting from the available datasets \( \{ Y^s, s = 1 : S \} \), we first select \( P^s \) using Principal Component Analysis (PCA) to maximize subject-level explained variance. Second, group-level components \( C \) are computed using generalized canonical correlation to select only components reproducible across subjects [19]. Finally, sparse and non-overlapping spatial sources \( A \) are extracted using ICA on \( C \) followed by thresholding to control for unstructured noise \( E \) [18]. The number of components \( K \) and the threshold are set with a p-value of 5\( \times 10^{-2} \) according to [18, 19].

Note that spatial ICA procedures favor high kurtosis, and thus components that are either super-Gaussian or sub-Gaussian. Super Gaussian components can be seen as sparse components confounded with Gaussian noise. In this regards, CanICA is not special, and the importance of sparsity in ICA analysis of fMRI data has been outlined elsewhere [20].

3. SCALING AND MULTIFRACTAL ANALYSIS

3.1. Scale invariance (or scaling)

In numerous modern applications, real-world data are well-described by the scale invariance (or scaling) paradigm. Conventional modeling of time series relies on the identification of a single, or a few, characteristic time scales or frequency bands, that play a central role. Conversely, in the scale invariance paradigm, the modeling stems from a mechanism that gives a relationship between all the scales in the data, that hence are all of equal importance. The intuition beyond scale invariance is often quantified through wavelet coefficients. In this section we give the mathematical formalism underlying the scaling properties we wish to investigate, but also and most importantly, we outline state-of-the-art analysis tools to estimate the corresponding parameters on short time series, such as those encountered in fMRI.

3.2. Scaling, wavelet coefficients and multifractal analysis

In what follows, we drop the subject superscript \( s \). Let \( dx(j,n) \) denote the (\( L^1 \)-normalized) discrete wavelet transform coefficients of a componentwise subject-specific time series \( X \) (eg column \( x_c \) in \( X \) in Eq. (1)), where \( j \) refers to the analysis scale (\( a = 2^j \)) and \( n \) to the time position (\( t = 2^j n \)), computed from a mother-wavelet \( \psi_0(t) \). Scale invariance often refers to the fact that \( S_\psi(j,q) \), the time averages of the \( q \)-th power of the wavelet coefficients \( dx(j,n) \), behave as power-laws with respect to the analysis scales \( a = 2^j \), over a large range of scales (cf. e.g., [16]):

\[
S_\psi(j,q) \overset{\Delta}{=} \frac{1}{N_j} \sum_{n=1}^{N_j} |dx(j,n)|^q \sim c_q 2^{j \zeta_\psi(q)}. \tag{2}
\]

The function \( \zeta_\psi(q) \), usually termed the scaling exponents, is then commonly used into data classification tasks. Its popularity stems from its deep relationship to the multifractal properties of the time
series $X$. Indeed, another important quantity often used to characterize the complexity of empirical data is the multifractal spectrum $D(h)$. It consists of the Hausdorff dimension of the set of time positions, $t_k$, on the real line, where the local regularity of $X$ is well described by the same regularity (or Hölder) exponent $h$.

Therefore, $D(h)$ measures globally and statistically how wide are the fluctuations in time of the local regularity $h(t)$ of $X$ [21]. A Legendre transform of $\zeta(q)$ yields a concave upper bound of $D(h)$: $\min_{q \neq 0} (1 + qh - \zeta(q)) \geq D(h)$ [21]. It is here crucial to note that a correct estimation of $D(h)$ requires the use of both positive and negative values of $q$. For further introduction to multifractal analysis, the reader is referred to e.g. [16, 21]. It is however well-known that this upper bound is poor, especially for negative values of $q$.

Recently, it has been shown [16] that this can be significantly improved, both theoretically and practically, by replacing the wavelet coefficients $d_X(j, n)$ by wavelet Leaders $L_X(j, n)$.

### 3.4. Log-cumulants and estimation

The wavelet Leader based scaling exponents, $\zeta(q)$, have been shown to offer, compared to the wavelet coefficient based ones [16]: i.) a better mathematically grounded analysis of the multifractal and scaling properties of the data; ii.) a much tighter bound for $D(h)$, notably by allowing the efficient use of negative $q$; iii.) a significantly improved estimation of the scaling exponents, in terms of statistical performance. In practice, this permits to address efficiently important issues such as: a.) are the data short-range dependent (SRD) or long-range dependent (LRD)? b.) are the data monofractal (or self-similar) or truly multifractal? This latter question can be recast practically into that of testing whether $\zeta(q)$ (or $\zeta(q)$) consists of a linear or concave function of $q$ or not [16, 21].

#### 3.4.1. Description of the datasets

Twelve healthy volunteers were scanned twice at rest ($TR = 1.5$s), eyes closed, for a period of 20 minutes during each session. Each individual dataset consists of two sessions, each being made of $n = 820$ volumes (time points) with a 3mm isotropic resolution, corresponding to approximately 50,000 voxels within the brain. Standard neuroimaging preprocessing was applied using the SPM software-1: after motion correction, cerebral volumes were realigned to an inter-subject template and smoothed with a 6mm isotropic Gaussian kernel. Next, as explained in Section 2, CanICA was applied to the whole dataset to exhibit the group-level spatial components (or sources) $A$ and the subject- and source-specific time series $X_s$. As indicated in Section 2, our tresholding procedure generated $K = 42$ components for $A$. Finally, the multifractal spectrum $D(h)$ associated with each component-specific time series in matrix $X_s$, $s \in \{1 : 5\}$ was computed. To this end, we only focused on the leader-based scaling exponents $\zeta(q)$ for a range of statistical orders $q \in [-10, 10]$. Scale invariance was observed within a 3-ocative range of scales corresponding to $[12, 192]$ seconds. In practice, we restricted the polynomial expansions of $\zeta(q)$ to the estimation of $(c_1^L, c_2^L)$ from each time series. In what follows, we drop the superscript $L$ for conciseness and derive group-level statistical tests to assess the scaling properties of the spatial components and to localize which of them exhibit multifractal behaviour or not.

#### 4.2. Group-level Statistical analysis

The goal now consists in assessing the statistical significance at the group level of the two first multifractal coefficients $(c_1^L, c_2^L)$ computed for every spatial component $k$ and subject $s$. More precisely, we perform the following one-sided tests, $\forall k = 1 : K$:

where H-sssi stands for $H$ self-similar process with stationary increments (or monofractal). On the one hand, rejecting $H_0^{(1)}$ clearly amounts to localizing brain areas or components eliciting temporal long range dependencies. On the other hand, rejecting $H_0^{(2, k)}$ enables to discriminate multifractality from self-similarity.

Since there is no evidence in the data that the scaling parameters are normally distributed across subjects, we use nonparametric tests and different statistics (Student $t$, Wilcoxon’s signed rank (WSR) statistic, Empirical Likelihood Ratio), the $t$-score statistics being only optimal in terms of sensitivity/specificity trade-off for Gaussian

1Wellcome Department of Cognitive Neurology; www.fil.ion.ucl.ac.uk/spm
MFX statistical analysis on statistics. In what follows, we only report MFX results. To account for the multiple comparison problem, a large value of |c2|, respectively. As expected empirically from the previous results, the MF spectra for components 2) and 5) are shifted to the right part of the x-axis because of larger c1. These curves also emphasize a large Full-Width at Half Maximum (FWHM), which corroborates the high level of multifractality (large $|c_2|$). Note that component 1) also exhibits a large value of $|c_2|$ but at the expense of a lower c1, hence of a weaker long memory. The narrow spectra of components 3) and 4) and the location of their maximum confirm that they would not survive to more conservative hypothesis testing on $c_2$ and $c_1$, respectively.

5. ACKNOWLEDGEMENTS

The authors are grateful to Dr. Andreas Kleinschmidt and Dr Sepideh Sadaghiani for providing the data, insightful discussions and constructive comments. The authors thank the ANR for its financial support to the SCHUBERT young researcher project in 2009.
Fig. 2. Statistical confidence on multifractality for each component studied. The outlines of the salient features of each component are drawn with a color reflecting the component-wise corrected p-value of $C_2$ being non-zero. Non-significantly multifractal components are drawn with thin lines.

The white-on-black numbered labels give the location of specific components, the spectrum of which is reported on Fig. 3:

1.) Artifacts in the transverse sinus
2.) Dorsal fronto-parietal functional network
3.) White-matter artifact
4.) Ventricles
5.) Primary visual areas

Fig. 3. Group-averaged multifractal spectra and between-subject variability (i.e., standard deviation) for the outlined spatial components in Fig. 2: 1.) Cerebellum; 2.) Dorsal fronto-parietal network; 3.) White matter artifact; 4.) Ventricles; 5.) Primary visual areas and 6.) all the previous MF spectra are superimposed for visualization purpose with the following color-coding: 1.) $h$; 2.) $h$; 3.) $h$; 4.) $h$; 5.) $h$. 
In this contribution, we have proposed to combine a group-level spatial ICA approach [19] with a recent multifractal analysis method based on wavelet leaders [16] to derive a multivariate scaling analysis approach of resting-state fMRI networks. Because the study takes place on a cohort of 12 subjects, group-level inference on multifractal parameters allows us to segregate brain regions that only generated strong long range dependence from those that exhibit multifractality as well. Among the latter, well-known functional resting-state networks were found as well as artifactual regions. A more generated strong long range dependence from those that exhibit multiscalar properties brings into light that the mechanism of the BOLD signal and related vascular effects might also influence the mono vs multifractal behaviour, future work will also be devoted to the use of sparser spatial decompositions in order to better disentangle vascular and neural effects and to the analysis of activation datasets to investigate the impact of the hemodynamic variability [23] on MF attributes.

7. REFERENCES