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# Revisiting Functional Connectivity for Infraslow Scale-Free Brain Dynamics using Complex Wavelets

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## 2 ABSTRACT

3 The analysis of human brain functional networks is achieved by computing  
4 functional connectivity indices reflecting phase coupling and interactions between  
5 remote brain regions. In magneto- and electroencephalography, the most often used  
6 functional connectivity indices are constructed on Fourier-based cross spectral  
7 estimation applied to specific fast and band limited oscillatory regimes. Recently,  
8 infraslow arrhythmic fluctuations (below the 1Hz) were recognized as playing a  
9 leading role in spontaneous brain activity. The present work aims to propose  
10 to assess functional connectivity, from fractal dynamics, thus extending the  
11 assessment of functional connectivity to the infraslow arrhythmic or scale-free  
12 temporal dynamics of M/EEG-quantified brain activity. Instead of being based on  
13 Fourier analysis, new Imaginary Coherence and weighted Phase Lag indices are  
14 constructed from complex-wavelet representations. Their performance are, first,  
15 assessed on synthetic data, by means of Monte-Carlo simulations, and compared  
16 favorably against the classical Fourier-based indices. These new assessment of  
17 functional connectivity indices are, second, applied to MEG data collected on 36  
18 individuals, both at rest and during the learning of a visual motion discrimination

19 task. They demonstrate a higher statistical sensitivity, compared to their Fourier  
20 counterparts, in capturing significant and relevant functional interactions in the  
21 infraslow regime, and modulations from rest to task. Notably, the consistent overall  
22 increase in functional connectivity assessed from fractal dynamics from rest to  
23 task, correlated with a change in temporal dynamics, as well as with improved  
24 performance in task completion, suggests that complex-wavelet weighted Phase  
25 Lag index is the sole index able to capture brain plasticity in the infraslow scale-free  
26 regime.

27 **Keywords:** Human brain temporal dynamics, functional connectivity, infraslow, arrhythmic, scale-free, phase  
28 coupling, functional connectivity assessed from fractal dynamics, complex-wavelet, MEG data.

## 1 INTRODUCTION

29 **Human brain univariate temporal dynamics.** The dynamics of Human brain activity  
30 can be studied non-invasively using electro- and magnetoencephalography (EEG and  
31 MEG, respectively). Interpreted as resulting from the synchronous activation of neuronal  
32 populations in specific frequency bands, these fluctuations are often analyzed as fast (10Hz  
33 and above) oscillatory rhythms, now well associated with cognitive functions, such as  
34 perception, attention or decision making (cf. e.g., (Freeman, 2000; Jensen and Colgin,  
35 2007)), well-described by band-limited models and well-analyzed by classical Fourier  
36 transform-based spectral analysis.

37 At the turn of the 21st century, the large-band infraslow activity of the brain (typically  
38 below 1 Hz), that for long had been considered as either instrumental or head-movement  
39 noises, received growing interest and has been documented as a prominent part of recorded  
40 electromagnetic brain signals and a critical component of brain activity (Gong et al., 2003;  
41 Vanhatalo et al., 2004; Stam and De Bruin, 2004; Miller et al., 2009; Werner, 2010). This  
42 large-band infraslow activity in the brain differs significantly from band-limited oscillations  
43 in the sense that it is not characterized by specific frequencies or scales of times, but  
44 rather corresponds to arrhythmic, or scale-free, temporal dynamics. [While exact scale-free  
45 dynamics remains debatable \(Dehghani et al., 2010; Ignaccolo et al., 2010\), it has been  
46 proposed by an abundant literature \(cf. eg., \(Vanhatalo et al., 2004; He et al., 2010; Van de  
47 Ville et al., 2010; Dehghani et al., 2010; He, 2011, 2014; Buzsáki and Mizuseki, 2014; Zilber  
48 et al., 2012; Gadhomi et al., 2015; La Rocca et al., 2018b\)\) that infraslow macroscopic  
49 brain activity is better described by a scaling exponent \(historically the power-law exponent  
50 of the Fourier spectrum, and more recently and relevantly the selfsimilarity exponent  \$H\$ \) that  
51 relates together dynamics across a large continuum of slow time scales \(or low frequencies\).](#)  
52 While most oscillatory regimes are only observed in evoked activity, elicited by stimuli,

53 infraslow scale-free brain temporal dynamics are persistent, observed both at rest and during  
54 task performance, or even in unconscious states (e.g., sleep stages). It was also shown that  
55 infraslow scale-free brain temporal dynamics are modulated when contrasting rest and  
56 task-related brain activity, with task inducing systematically a decrease in  $H$  and *faster*  
57 infraslow dynamics (Bhattacharya and Petsche, 2001; Linkenkaer-Hansen et al., 2004;  
58 Vanhatalo et al., 2004; Popivanov et al., 2006; Bianco et al., 2007; Buiatti et al., 2007; He  
59 et al., 2010; Zilber et al., 2013; La Rocca et al., 2018b). Infraslow scale-free brain activity  
60 has thus been hypothesized to be functionally associated with neural excitability (He, 2014).  
61 Altered scale-free brain dynamics has also been reported in specific condition such as  
62 Alzheimer's disease for which larger selfsimilarity exponents were reported in multiple  
63 brain areas (e.g. lateral temporal lobes, insula, etc) early involved in the neurodegenerative  
64 process (Maxim et al., 2005).

65 Infraslow arrhythmic brain activity can be efficiently described with large-band scale-free  
66 models, such as selfsimilarprocesses (fractional Brownian motion and fractional Gaussian  
67 noise) (Mandelbrot and van Ness, 1968). It is also now well established and documented  
68 that, while Fourier analysis can be used to assess  $1/f$  power law spectra at low frequencies,  
69 accurate and robust assessments of scale-free dynamics requires replacing Fourier-based  
70 spectral estimation with multiscale wavelet analysis. Interested readers are referred to  
71 (Flandrin, 1992; Muzy et al., 1993; Veitch and Abry, 1999; Kantelhardt, 2008; Abry et al.,  
72 2019b) for methodological developments, and to (Ciuciu et al., 2008, 2012, 2014; La Rocca  
73 et al., 2018b) for applications to neuroimaging data. Further, it has recently been shown that  
74 the dself-similar escription of scale-free temporal dynamics could be enriched by combining  
75 the concept of multifractality with that of selfsimilarity (Wendt et al., 2007; Abry et al.,  
76 2019b), requiring the use of wavelet-leaders, consisting of nonlinear nonlocal transforms of  
77 wavelet coefficients, for practical analysis. The potential interest of multifractality for the  
78 analysis of fMRI and M/EEG signals has been investigated in e.g., (Shimizu et al., 2004;  
79 Popivanov et al., 2005, 2006; Shimizu et al., 2007; Ciuciu et al., 2008, 2012; Proekt et al.,  
80 2012; La Rocca et al., 2018b).

81 **Human brain multivariate temporal dynamics: Functional connectivity.** Remote  
82 brain regions are known to interact within large scale functional networks (e.g., the default  
83 Mode Network at rest) which mediate the information flow inside the brain integrating the  
84 activity of functionally segregated modules that are activated in particular mental states, task  
85 execution or health condition (Power et al., 2011). These interactions (correlations, delays,  
86 phase synchronization,...) between different brain regions are quantified by indices of  
87 similarity computed from signals collected in each region, and are referred to as *functional*  
88 *connectivity*. Assessing functional connectivity thus entails performing a multivariate  
89 analysis of the temporal recordings, thus complementing univariate analysis of each signal

90 separately. Classically, functional connectivity is assessed mostly from band-limited signals  
91 reflecting the oscillatory activity of the brain, by measures of cross (bivariate) second  
92 order statistics (correlation coefficient, cross-correlation function, . . .). However, M/EEG  
93 measurements suffer from the so-called *volume conduction effects*: Linearity in Maxwell  
94 equations and electromagnetic quasi-static approximation (for the forward model below 100  
95 Hz) induce a linear mixing of electromagnetic sources on M/EEG sensors with negligible  
96 temporal delays. Close-by EEG electrodes or SQUID MEG sensors thus redundantly capture  
97 brain activity from a given current cortical dipole hence inducing spurious correlations  
98 amongst recordings, thus precluding a relevant assessment of functional connectivity (Nolte  
99 et al., 2004; Stam et al., 2007; Vinck et al., 2011). Source-space reconstructed signals  
100 are documented to still suffer from residual volume conduction effects because of the  
101 approximate and imperfect nature of inverse problem resolutions (Siebenhühner et al., 2016;  
102 Palva et al., 2018). The design of indices robust to such spurious correlations has been based  
103 on measuring average phase delays, such as in the Phase Locking Value (Stam et al., 2007),  
104 and also naturally calls for the use of Fourier-based cross spectral estimation. Indeed, the  
105 Fourier transform, being by definition based on complex numbers, permits to incorporate  
106 automatically phases and thus delays in the assessment of functional connectivity: zero  
107 delay between correlated signals corresponds to zero phase and imaginary part but non-  
108 zero real part for the cross-Fourier spectrum (on average). Therefore, the moduli of the  
109 cross-Fourier spectrum and of the coherence function (F-COH) are affected by volume  
110 conduction effects, but their imaginary parts and phases are robust to such spurious effects  
111 and in theory depart from zero only for dependent sources with actual delays, a crucial  
112 property for assessing functional connectivity. This observation has led to the design,  
113 study and use of the Imaginary Coherence function (F-ICOH) (Nolte et al., 2004) and the  
114 (weighted-)Phase Lag Index (F-wPLI) (Vinck et al., 2011) as relevant indices to assess  
115 functional connectivity for the band-limited oscillatory brain activity measured by M/EEG  
116 measurements. Interested readers are referred to e.g., (Varela et al., 2001; Engel et al.,  
117 2001; Nolte et al., 2004; Stam et al., 2007; Vinck et al., 2011; Siegel et al., 2012) for  
118 thorough reviews and further details (see also Section 2.1 for definitions). Beyond second  
119 order statistics and linear correlation, higher order (nonlinear) dependencies have also been  
120 investigated using directed partial correlations; moreover, the Granger causality approach  
121 has been used to infer causal links, see (Sakkalis, 2011) for a review.

122 Functional connectivity was so far mainly measured via the band-limited oscillatory  
123 activity of the brain, and has hardly been applied to characterize the infraslow arrhythmic  
124 brain activity. Preliminary attempts in that direction (Achard et al., 2008; Ciuciu et al., 2014),  
125 though based on wavelet representation, remained tied to the coherence function, hence  
126 essentially to direct correlation, and thus severely impaired by volume conduction effect in

127 functional connectivity assessment in M/EEG. This lack of functional connectivity tools  
128 dedicated to the infraslow regime is partly due to the role infraslow arrhythmic temporal  
129 dynamics to brain activity remaining controversial, but also, and prominently, because  
130 conceptual and practical tools reconciling the modeling and analysis of both multivariate  
131 and scale-free dynamics were lacking. This situation changed recently with the theoretical  
132 definition and formal study of multivariate selfsimilarity (Didier and Pipiras, 2011) as well  
133 as with the design and assessment of multivariate wavelet transform based practical tools  
134 (Wendt et al., 2017; Abry and Didier, 2018a,b; Abry et al., 2019a,b), thus permitting the  
135 investigation of functional connectivity within the infraslow arrhythmic brain activity, at  
136 the core of the present work.

137 **Goals, contributions and outline.** The present work aims to revisit the analysis of  
138 functional connectivity in human brain activity in two ways:

139 First, functional connectivity assessment will be based on the on-going (or spontaneous)  
140 infraslow arrhythmic (or scale-free) activity of the human brain, rather than on stimulus-  
141 induced band-limited oscillatory faster rhythms. This will be referred to as *functional*  
142 *connectivity assessed from fractal dynamics* (see (La Rocca et al., 2018a) for a preliminary  
143 attempt).

144 Second, indices quantifying functional connectivity from fractal dynamics will be  
145 constructed from multivariate complex wavelet transforms, rather than from Fourier-based  
146 cross-spectral analysis. The key intuitions underlying the design of these indices are  
147 double: Based on wavelet transforms, these tools will inherit from their well-documented  
148 performance and robustness for the analysis of scale-free dynamics (Flandrin, 1992; Abry  
149 and Veitch, 1998; Veitch and Abry, 1999; Abry et al., 2000; Veitch and Abry, 2001; Abry  
150 et al., 2019b); Complex wavelets allow to incorporate phase information in the analysis of  
151 multivariate cross-temporal dynamics.

152 To that end, after a brief recall of Fourier-based spectral estimation and of the classical  
153 Fourier-based functional connectivity indices (F-ICOH and F-wPLI) in Section 2.1,  
154 Complex wavelet transforms and the corresponding Complex Wavelet-based functional  
155 connectivity indices (W-ICOH and W-wPLI) are defined in Section 2.2. The performance  
156 of several Complex Wavelet-based functional connectivity indices proposed here are  
157 compared ones against the others, and against their corresponding Fourier counterparts, by  
158 means of Monte Carlo numerical simulations, involving a large number of independent  
159 drawings of synthetic signals, sampled from stochastic processes commonly used to model  
160 scale-free temporal dynamics, multivariate fractional Brownian motions and multivariate  
161 fractional Gaussian noises (cf. Section 2.3). Several scenarii (different temporal dynamics,  
162 connectivity networks, additive trends) are investigated to assess the interest and relevance

163 of the proposed Complex Wavelet indices (W-ICOH and W-wPLI) compared to Fourier-  
164 based ones, in terms of estimation performance and robustness to trends.

165 The proposed Complex Wavelet indices assessing functional connectivity from fractal  
166 dynamics are extensively tested on MEG data, collected on 36 individuals, both at rest  
167 and during a visual discrimination learning task. The experimental data is described in  
168 Section 3 (see also (Zilber et al., 2014)).

169 Analyses of functional connectivity assessed from fractal dynamics within infraslow  
170 arrhythmic cross temporal dynamics regime, ranging from 0.1 to 1.5Hz for this data  
171 set (La Rocca et al., 2018b), are reported in Section 4 and discussed in Section 5.  
172 The proposed Complex Wavelet indices are demonstrated to have a high sensitivity in  
173 capturing significant and meaningful group-level functional connectivity assessed from  
174 fractal dynamics networks both at rest and during task performance, that present long-  
175 range spatial interactions between fronto-occipital and temporo-parietal brain regions.  
176 Further, a significant increase in functional connectivity assessed from fractal dynamics  
177 is shown to be positively correlated with behavioral performance in the task and to be  
178 further reinforced by the training stage and thus by learning. Finally, our results suggest  
179 an interplay between temporal and spatial dynamics: Arrhythmic infraslow brain activity  
180 evolves from strongly and globally structured slow temporal dynamics for each region  
181 individually at rest, related across the brain by a clear functional network, to faster and less  
182 globally structured temporal dynamics per region, yet with significantly stronger spatial  
183 couplings across the brain, during task.

184 The proposed Complex Wavelet tools constitute, to the best of our knowledge, the  
185 first operational tools for a relevant assessment of functional connectivity from fractal  
186 dynamics, i.e., functional connectivity in scale-free cross-temporal dynamics for the large-  
187 band infraslow arrhythmic brain activity recorded in M/EEG. MATLAB codes, designed and  
188 implemented by ourselves, for the synthesis of multivariate scale-free synthetic data and  
189 for the computation of Complex Wavelet-based indices to assess functional connectivity  
190 from fractal dynamics, will be made publicly available at the time of publication.

## 2 METHODOLOGY: FUNCTIONAL CONNECTIVITY ASSESSMENT

### 191 2.1 Frequency domain functional connectivity assessment

192 The  $M$ -variate data  $(X_m(t))_{m=1,\dots,M}, t \in \mathbb{R}$  available for analysis are assumed to be  
193 real-valued finite power realizations of stochastic processes, with well-defined power  
194 cross-spectral density  $S_{m,m'}(f)$ . *Welch periodogram* constitutes one of the classical  
195 nonparametric spectral estimation procedures (Papoulis, 1977), grounded on the use of a  
196 windowed Fourier transform. This Fourier-based estimate  $S^{(F)}$  of the cross-spectrum  $S$  is

197 indeed defined as a time average of the squared-moduli of the windowed (or short-time)  
 198 Fourier transform coefficients  $g_X(\ell, k) = \int X(t)\phi_{\ell,k}(t)dt$ :

$$S_{m,m'}^{(F)}(f = \ell\nu_0) = \sum_k g_{X_m}(\ell, k)g_{X_{m'}}^*(\ell, k), \quad (1)$$

199 where  $\phi_{\ell,k}(t) = \phi(t - kT_0)\exp(-2i\ell\nu_0 t)$  denotes the collection of translated and  
 200 frequency-shifted templates of a reference pattern  $\phi(t)$ , and  $T_0$  and  $\nu_0$  positive constants  
 201 that can be arbitrarily chosen, provided that they satisfy  $T_0\nu_0 \leq 1/(4\pi)$ .

202 Straightforward calculations yield

$$\mathbb{E}S_{m,m'}^{(F)}(\ell\nu_0) = \int S_{m,m'}(\ell\nu_0 - f)|\tilde{\phi}(f)|^2 df, \quad (2)$$

203 with  $\tilde{\phi}$  denoting the Fourier transform of  $\phi$  and  $\mathbb{E}$  the ensemble average. This is thus showing  
 204 that  $S_{m,m'}^{(F)}$  provides a biased estimate of  $S_{m,m'}(f)$ . The time and frequency resolutions of  
 205 the functions  $\phi_{\ell,k}$  being uniformly controlled by the choice of the function  $\phi$ ,  $S^{(F)}$  achieves  
 206 a fixed *absolute-frequency resolution* multivariate spectral analysis.

207 From  $S_{m,m'}^{(F)}(f)$ , three functions are classically involved in functional connectivity  
 208 assessment, the modulus (F-COH), the Imaginary (F-ICOH) part of the coherence  
 209 function (Nolte et al., 2004), and the weighted Phase Lag Index (F-wPLI) (Vinck et al.,  
 210 2011) (with  $\Im$  the imaginary part of a complex number):

$$\text{F-COH}_{m,m'}(f) \triangleq \frac{S_{m,m'}^F(f)}{\sqrt{S_{m,m}^F(f)S_{m',m'}^F(f)}}, \quad (3)$$

$$\text{F-ICOH}_{m,m'}(f) \triangleq \frac{\Im\{S_{m,m'}^F(f)\}}{\sqrt{S_{m,m}^F(f)S_{m',m'}^F(f)}}, \quad (4)$$

$$\text{F-wPLI}_{m,m'}(f = \ell\nu_0) \triangleq \frac{\sum_{k=1}^{n_j} \Im\{g_{X_m}(\ell,k)g_{X_{m'}}^*(\ell,k)\}}{\sum_{k=1}^{n_j} |g_{X_m}(\ell,k)g_{X_{m'}}^*(\ell,k)|}. \quad (5)$$

211 To quantify functional connectivity on MEG signals, the corresponding indices are  
 212 practically computed as sums of the absolute values of these functions over the range of  
 213 frequencies defining the targeted band-limited oscillations. Large values (above predefined  
 214 thresholds) are used as markers of functional connectivity at the individual level, usually  
 215 followed by statistical testing for assessing group-level significance.

216



## 2.2 Wavelet domain functional connectivity assessment

**Complex wavelet transform.** The classical discrete wavelet transform relies on the use of a real-valued mother-wavelet (cf. e.g., (Mallat, 1998)). To assess phases and delays amongst signals, it is proposed here to use a complex wavelet transform, defined as follows. Let  $\psi^{(r)}$  denote a real-valued oscillating and sufficiently smooth reference pattern, referred to as the *mother wavelet*, and constructed such that the collection of dilated and translated templates  $\{\psi_{j,k}(t) = 2^{-j/2}\psi(2^{-j}t - k)\}_{(j,k)\in\mathbb{Z}^2}$  of  $\psi$  form an orthonormal basis of  $L^2(\mathbb{R})$  (cf. e.g., (Mallat, 1998)). From  $\psi^{(r)}$ , an analytic complex mother-wavelet can be defined as  $\psi = \psi^{(r)} + i\psi^{(i)}$ , where  $\psi^{(i)}$  consists of the Hilbert transform of  $\psi^{(r)}$ . The design of a complex, invertible and analytic mother wavelet is not straightforward. In the present work, we build on the excellent approximate solution proposed in (Kingsbury, 2001; Selesnick et al., 2005), referred to as the dual-tree complex wavelet transform.

For a signal  $X$ , the coefficients of the dual-tree complex wavelet transform are defined as  $d_X(j, k) \triangleq d_X^{(r)}(j, k) + id_X^{(i)}(j, k)$ , with  $d_X^{(r)}(j, k) \triangleq \int \psi_{j,k}^{(r)}(t)X(t)dt$  and  $d_X^{(i)}(j, k) \triangleq \int \psi_{j,k}^{(i)}(t)X(t)dt$ . Computing a dual-tree complex wavelet transform thus amounts to computing two standard Discrete Wavelet Transforms, with the two real mother-wavelets  $\psi^{(r)}$  and  $\psi^{(i)}$ , respectively, independently.

**Wavelet cross spectrum and functional connectivity.** It has been well-documented that the study of univariate scale-free temporal dynamics should be performed using a wavelet-based spectral estimation rather than a Fourier-based one (cf. e.g., (Flandrin, 1992; Abry and Veitch, 1998; Veitch and Abry, 1999, 2001)). This has recently been extended to multivariate scale-free temporal dynamics analysis and wavelet cross-spectrum estimation (cf. e.g., (Wendt et al., 2017; La Rocca et al., 2018a; Abry et al., 2019b; Abry and Didier, 2018b)). Given a pair of signals  $X_m, X_{m'}$ , the multivariate wavelet (cross-)spectrum can be defined as

$$S_{m,m'}^W(j) \triangleq \frac{1}{n_j} \sum_{k=1}^{n_j} d_{X_m}(j, k) d_{X_{m'}}^*(j, k) \quad (6)$$

where  $n_j \approx \frac{N}{2^j}$  are the number of coefficients available at scale  $j$ , and  $*$  stands for complex conjugate.

It has been shown (Abry et al., 2019b) that

$$\mathbb{E}S_{m,m'}^{(W)}(j = \nu_\psi/2^j) = \int S_{m,m'}(f) |\tilde{\psi}(f/2^j)|^2 df, \quad (7)$$

245 with  $\tilde{\psi}$  denoting the Fourier transform of  $\psi$ . This indicates that  $S_{m,m'}^{(W)}(j)$  estimates  
 246  $S_{m,m'}(f = \nu_\psi/a_0^j)$  around frequency  $f = \nu_\psi/a_0^j$  and achieves a *fixed relative-frequency*  
 247 resolution multivariate spectral analysis (Abry and Veitch, 1998; Abry et al., 2019b).

248 Eqs. (2) and (7) combined together show that Fourier-based  $S_{m,m'}^{(F)}$  and (Complex)  
 249 Wavelet-based  $S_{m,m'}^{(F)}$  constitute two biased estimates of the power spectral density  $S_{m,m'}$ ,  
 250 that can be compared theoretically and practically, as illustrated in Fig. 1. Interested readers  
 251 are referred to (Abry and Veitch, 1998; Abry et al., 2019b) for further discussions. As  
 252 an illustration, the wavelet spectra and cross-spectrum of the two MEG signals displayed  
 253 in Fig. 1 (a)-(b) are shown in Fig. 1(c)-(f) and compared to Fourier spectra and cross  
 254 spectrum (cf. Fig. 1(g)-(j)), using Eqs. (2) and (7) and converting scales  $a = 2^j$  into  
 255 frequencies as  $f = f_0 \times f_s/2^j$  where  $f_s$  is the data sampling frequency and  $f_0$  a constant  
 256 that depends on the specific choice of the mother wavelet. Readers interested by further  
 257 theoretical and practical discussions on comparing Fourier and wavelet-based spectral  
 258 estimations, are referred to e.g., (Abry and Veitch, 1998; Veitch and Abry, 1999, 2001;  
 259 Abry et al., 2000; Ciuciu et al., 2012; Abry et al., 2019b).

260 **Wavelet-based functional connectivity indices.** From the wavelet-based estimate of the  
 261 power spectrum, wavelet-based indices can be constructed to assess functional connectivity,  
 262 as was the case with Fourier spectrum, *mutatis mutandis*:

$$\text{W-COH}_{m,m'}(j) \triangleq \frac{S_{m,m'}^W(j)}{\sqrt{S_{m,m}^W(j)S_{m',m'}^W(j)}}, \quad (8)$$

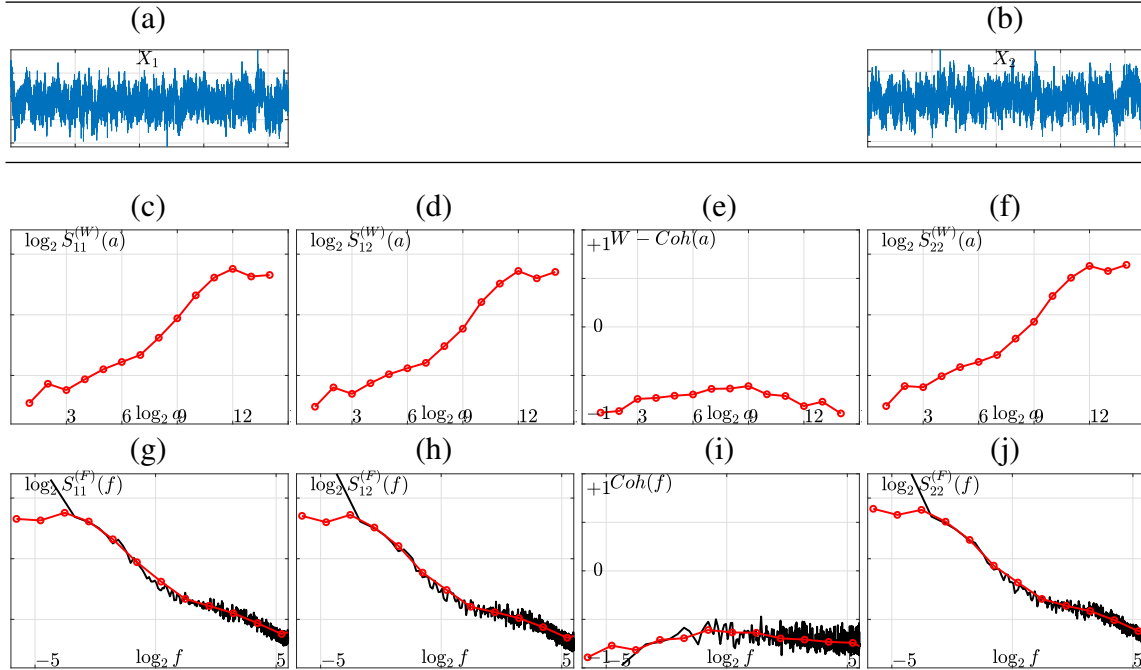
$$\text{W-ICOH}_{m,m'}(j) \triangleq \frac{\Im\{S_{m,m'}^W(j)\}}{\sqrt{S_{m,m}^W(j)S_{m',m'}^W(j)}}, \quad (9)$$

$$\text{W-wPLI}_{m,m'}(j) \triangleq \frac{\sum_{k=1}^{n_j} \Im\{d_{X_m}(j,k)d_{X_{m'}}^*(j,k)\}}{\sum_{k=1}^{n_j} |\Im\{d_{X_m}(j,k)d_{X_{m'}}^*(j,k)\}|}. \quad (10)$$

263 Unlike the standard discrete wavelet transform coherence function used in, e.g., (Whitcher  
 264 et al., 2000; Wendt et al., 2017),  $\text{W-COH}_{m,m'}(j)$  is *complex-valued*.

265

**Functional connectivity assessed from fractal dynamics.** Functional connectivity for  
 scale-free infraslow temporal dynamics, consists in averaging the absolute values of these  
 functions over the corresponding range of octaves  $j_1 \leq j \leq j_2$  (equivalently over the range



**Figure 1. Fourier versus wavelet spectral estimation on actual source-reconstructed MEG time series.** **Top:** Two source-reconstructed MEG time series  $X_1$  (a) and  $X_2$  (b). **Middle:** Wavelet spectra ((c), (f)), cross spectrum (d) and coherence function (e) as functions of the (log of the) scales (top row, red lines). **Bottom:** Comparison to Fourier spectra ((g), (j)), cross-spectrum (h) and coherence function (i) (solid black lines) after remapping scales into frequencies (bottom row). The scale-free (or arrhythmic) regime is marked by linear behaviors of the power spectra across coarse scales,  $8 \leq j \leq 12$  corresponding to low frequencies,  $0.1 \leq f \leq 1.5$  Hz, in these log-log plots.

of scales  $a = 2^j$  or frequencies  $f = f_0/2^j$ ) where scale-free dynamics are observed:

$$\frac{1}{j_2 - j_1 + 1} \sum_{j=j_1}^{j_2} \text{W-wPLI}_{m,m'}(j) \quad \text{or} \quad \frac{1}{j_2 - j_1 + 1} \sum_{j=j_1}^{j_2} \text{W-ICOH}_{m,m'}(j)$$

266 Remapping scales into frequencies, calculations inspired from those leading to Eqs. (2)  
 267 and (7) permit to compare theoretically and practically W-COH, W-ICOH and W-wPLI to  
 268 F-COH, F-ICOH and F-wPLI, as illustrated in Figs. 2, 3 and 5 on synthetic data.

269 This is here critical to emphasize that *functional connectivity assessed from fractal*  
 270 *dynamics* as defined and used in the present work is associated with (the statistics of)  
 271 *cross-temporal dynamics*. It should not be confused with the so-called *fractal networks*, as  
 272 studied in e.g., in (Bassett et al., 2006; Varley et al., 2020), which are related to topological

273 (thus static) properties of a spatial graph.

274

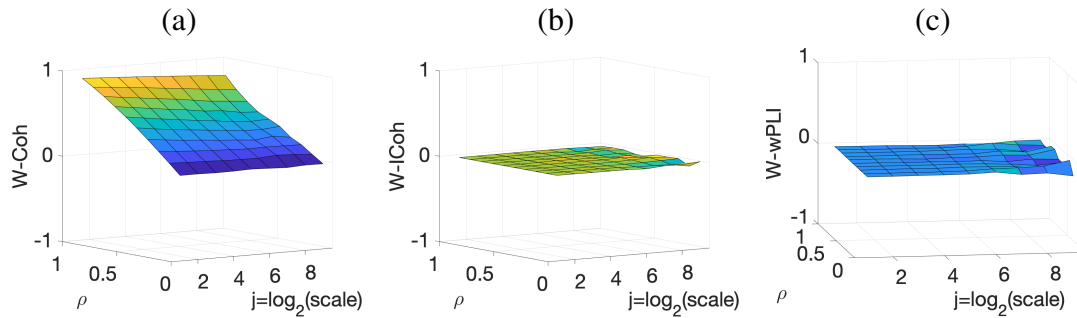
### 275 **2.3 Functional connectivity from fractal dynamics performance** 276 **assessment**

277 **Monte Carlo numerical simulations.** To assess the performance of the proposed indices  
278 aiming to quantify functional connectivity from fractal dynamics, Monte Carlo numerical  
279 simulations were conducted. They make use of synthetic bivariate fractional Brownian  
280 motion, a specific instance of the multivariate selfsimilar model recently introduced  
281 in (Didier and Pipiras, 2011) and studied in (Abry and Didier, 2018a,b). Bivariate  
282 fractional Brownian motion consists of a pair of fractional Brownian motions  $B_{H_1}$   
283 and  $B_{H_2}$ , with possibly different selfsimilarity parameters  $H_1$  and  $H_2$ , with pointwise  
284 correlation  $\rho$ . In addition, one component is delayed by  $\Delta$ . Correlation coefficient  $\rho$  is  
285 set to range within  $\rho \in \{0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9\}$  and delays range in  
286  $\Delta = \{0, 1, 2, 4, 8, 16, 32, 64\}$  samples. Sample size is  $n = 2^{14}$ , chosen to match the size of  
287 the infraslow regime of the MEG data (cf. Sections 3 and 4).

288 To model MEG data as those analyzed in Section 4 and as commonly indicated in the  
289 literature (He et al., 2010), one needs to use both fractional Gaussian noise (fGn), the  
290 increments of fractional Brownian motion (fBm), with parameter  $H$  ranging from say 0.6 to  
291 1 and fractional Brownian motion itself with parameters ranging from 0 to 1. Therefore, the  
292 numerical simulations conducted here were based on bivariate processes, each component  
293 being either fGn or fBm, with  $0 < H < 1$ . For the Fourier-based spectral estimation,  
294 the classical averaged windowed periodogram estimate of the power spectral density was  
295 computed, with Hanning windows of width corresponding with the frequency bands of  
296 the complex wavelet filters, to enable relevant comparisons of the tools. For the Complex-  
297 Wavelet based estimation, q-shift complex wavelets were used, as described in (Selesnick  
298 et al., 2005) and references therein, (see, e.g., (Lina and Mayrand, 1995) for an alternative  
299 choice).

300 Indices assessing functional connectivity from fractal dynamics (both Fourier and wavelet-  
301 based) were computed as average over a range of frequencies and scales that match those of  
302 the infraslow scale-free range observed on the MEG data described and analyzed hereafter.  
303 Performance are reported as means (and confidence intervals) computed from  $N = 1000$   
304 independent realizations of bivariate fractional Gaussian noise.

305 **Spurious connectivity.** To start with, we analyzed scenarii where the two components  
306 of bivariate fractional Gaussian noise were correlated but not delayed:  $\Delta \equiv 0$ . Fig 2 reports  
307 the averaged (over realizations) values of W-COH, W-ICOH and W-wPLI as functions of

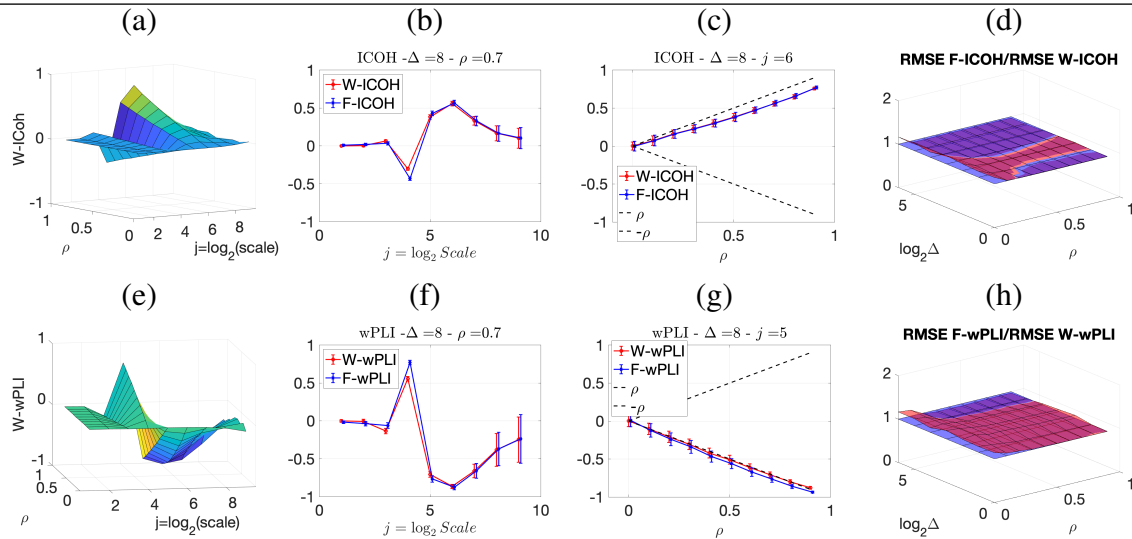


**Figure 2. Complex Wavelet-based connectivity on synthetic bivariate fractional Gaussian noise with correlation but no delay.** W-COH (a), W-ICOH (b) and W-wPLI (c) as function of octaves  $j$  and correlation coefficient  $\rho$ . As it should, W-COH correctly assesses correlations with no delays and thus departs from 0 at all scales. W-COH would hence lead to incorrectly assessing functional connectivity. In contrast, W-ICOH and W-wPLI show averages values of 0 at all scales, and across all correlation levels, thus leading to assess no connectivity, as expected for non delayed components.

308 octaves  $j$  and correlation coefficients  $\rho$ . Fig 2(a) shows that W-COH correctly assesses  
 309 correlations between components as predicted by theory when they are not delayed. W-  
 310 COH thus leads to an incorrect assessment of functional connectivity as it is sensitive to  
 311 0-delay correlation and thus to the volume conduction effect. This spurious connectivity  
 312 consists of a well-documented fact for the classical (Fourier-based) coherence function  
 313 index F-COH, which is, as theoretically expected, not corrected by the use of W-COH.  
 314 Fig 2(b)-(c) also shows that W-ICOH and W-wPLI average to 0 at all scales, and across all  
 315 correlation levels, thus correctly leading to the assessment of no functional connectivity, as  
 316 expected for non delayed components. Again, this is consistent with observations made  
 317 when using the Fourier-based F-ICOH and F-wPLI. This rules out the use of W-COH (and  
 318 F-COH) to assess functional connectivity.

319 **Functional connectivity assessed from fractal dynamics.** We then analyzed signals  
 320 with delays amongst components. Fig 3 and Fig 4 report, for different sets of synthetic data,  
 321 for given delays  $\Delta$ , the averaged values (over realizations) of W-ICOH and W-wPLI as  
 322 functions of octaves  $j$  and correlation coefficients  $\rho$  (left column, see panels (a) and (e)),  
 323 complemented with slices for fixed  $\rho$  as functions of  $j$  (second column, see panels (b) and  
 324 (f)), slices for fixed  $j$  as functions of  $\rho$  (third column, see panels (c) and (g)) and functional  
 325 connectivity indices averaged across scales  $3 \leq j \leq 7$  (right column, see panels (d) and (h)).  
 326 Fig 3 and Fig 4 show that:

- 327 i) Both W-ICOH and W-wPLI do depart from 0 across  $j$  and  $\rho$  when  $\Delta \neq 0$  (left column).
- 328 ii) As functions of  $j$ , W-ICOH and W-wPLI display different patterns that depend on  $\Delta$ .
- 329 However, these patterns both show independently maximum absolute deviations from 0 at

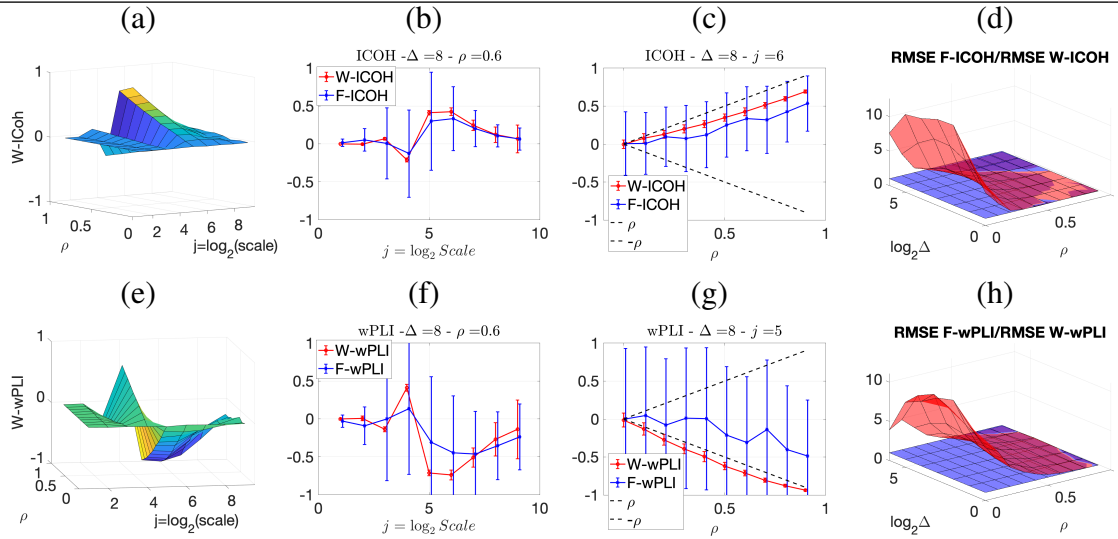


**Figure 3. Complex Wavelet-based connectivity on synthetic bivariate fractional Gaussian noise with correlation and delay  $\Delta = 8$ . Top row: W-ICOH results. Bottom row: W-wPLI results. From left to right: W-ICOH (a) and W-wPLI (e) as functions of octaves  $j$  and correlation coefficient  $\rho$ ; W-ICOH (b) and W-wPLI (f) as functions of octaves  $j$ , for a given  $\rho$ ; W-ICOH (c) and W-wPLI (g) as functions of  $\rho$  for given octaves  $j$ ; Ratio of the RMSE of F-ICOH to W-ICOH (d) and ratio of RMSE of F-wPLI to W-wPLI (h), averaged across scales  $3 \leq j \leq 7$ , and color-coded in red as functions of delay  $\Delta$  and correlation coefficient  $\rho$ . A ratio larger than the value of 1 (made explicit to ease comparisons by horizontal blue plans) indicates poorer performance for Fourier-based estimates compared to wavelet-based ones. Synthetic data consists of bivariate fGn with  $H_1 = 0.7$  and  $H_2 = 0.8$ .**

330 scales that vary with  $\Delta$  (second column). This was quantified for W-ICOH and used as a  
 331 delay estimation procedure (Didier et al., 2019).

332 iii) When a scale  $2^j$  in relation to  $\Delta$  is chosen, both (the absolute values of) W-ICOH and  
 333 W-wPLI are proportional to (the absolute value of)  $\rho$  (third column). This shows not only  
 334 that W-ICOH and W-wPLI depart from 0 when delays amongst components exist, but also  
 335 that the amplitude of the departure is proportional to the correlation  $\rho$  between components,  
 336 a crucial property to assess quantitatively functional connectivity, clearly and originally  
 337 quantified in these numerical simulations.

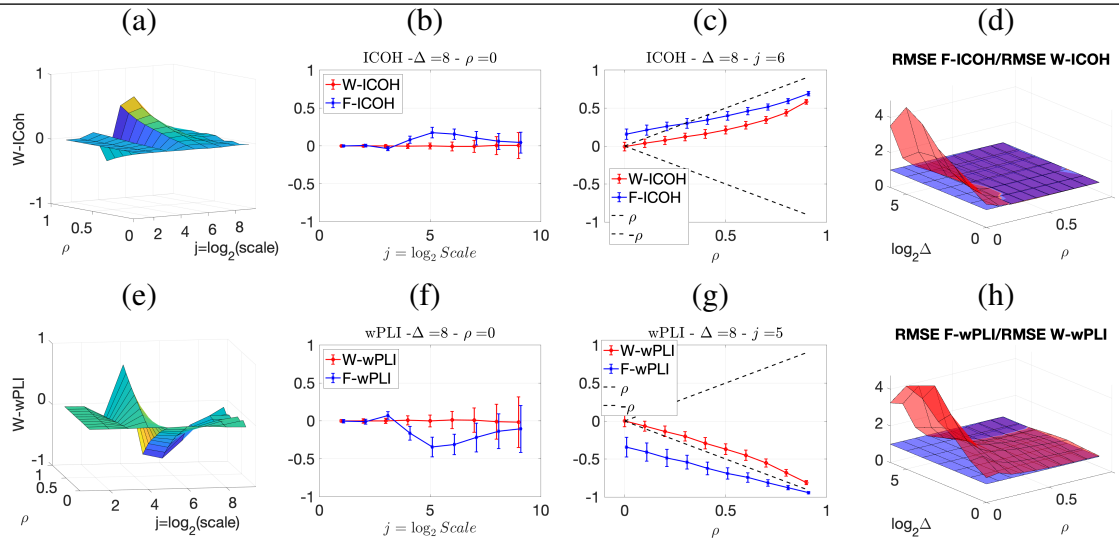
338 iv) The conclusions stemming from comparing the performance of Fourier-based F-ICOH  
 339 and F-wPLI to Complex Wavelet-based W-ICOH and W-wPLI depend on the parameters  
 340 used for simulating bivariate synthetic time series. When the latter consist of bivariate fGn  
 341 with  $H_1 = 0.7$  and  $H_2 = 0.8$  (Fig 3), F-ICOH vs. W-ICOH and F-wPLI vs. W-wPLI, show  
 342 comparable performance, either in bias (second and third columns) or in terms of root



**Figure 4. Complex Wavelet-based connectivity on synthetic bivariate fractional Brownian motion with correlation and delay  $\Delta = 8$ . Top row: W-ICOH results. Bottom row: W-wPLI results. From left to right: W-ICOH (a) and W-wPLI (e) as functions of octaves  $j$  and correlation coefficient  $\rho$ ; W-ICOH (b) and W-wPLI (f) as functions of octaves  $j$ , for a given  $\rho$ ; W-ICOH (c) and W-wPLI (g) as functions of  $\rho$  for given octaves  $j$ ; Ratio of the RMSE of F-ICOH to the RMSE of W-ICOH (d) and ratio of the RMSE of F-wPLI to the RMSE of W-wPLI (h), averaged across scales  $3 \leq j \leq 7$ , and color-coded in red as functions of delay  $\Delta$  and correlation coefficient  $\rho$ . A ratio larger than the value of 1 (made explicit to ease comparisons by horizontal blue plans) indicates poorer performance for Fourier-based estimates compared to wavelet-based ones. Synthetic data consists of bivariate fBm with  $H_1 = 0.7$  and  $H_2 = 0.8$ .**

343 mean square error (RMSE) (right column). When synthetic data consists of bivariate fBm  
 344 with  $H_1 = 0.7$  and  $H_2 = 0.8$  (Fig 4), F-ICOH and F-wPLI show significantly degraded  
 345 performance compared to W-ICOH and W-wPLI, both in bias and variance (second and  
 346 third columns) and in terms of RMSE (right column). Notably, RMSE of F-ICOH and  
 347 F-wPLI can be ten times larger than RMSE of W-ICOH and W-wPLI for small values of  $\rho$ .  
 348 Therefore, Complex Wavelet-based indices outperform Fourier-based ones for data with  
 349 large scaling exponents, i.e., large powers at very low frequencies or, in other words, very  
 350 slow dynamics. Similar conclusions can be drawn from other values of delays  $\Delta \neq 0$  tested  
 351 here but not shown (available upon request).

352 **Functional connectivity assessed from fractal dynamics in the presence of additive**  
 353 **trends.** We finally analyzed more complicated scenarios with correlation and delays  
 354 amongst components, but also additive smooth slow trends, superimposed as noise to the  
 355 actual scale-free components. Fig 5 reports, for a given delay  $\Delta = 8$ , the averaged (over



**Figure 5. Complex Wavelet-based connectivity on synthetic bivariate fractional Gaussian noise with correlation and delay, and additive trends. Top row: W-ICOH results. Bottom row: W-wPLI results. From left to right: W-ICOH (a) and W-wPLI (e) as functions of octaves  $j$  and correlation coefficient  $\rho$ , W-ICOH (b) and W-wPLI (f) as functions of octaves  $j$ , for a given  $\rho$ , W-ICOH (c) and W-wPLI (g) as functions of  $\rho$  for given octaves  $j$ , Ratio of the RMSE of F-ICOH to the RMSE of W-ICOH (d) and ratio of the RMSE of F-wPLI to the RMSE of W-wPLI (h), averaged across scales  $3 \leq j \leq 7$  and color-coded in red as functions of delay  $\Delta$  and correlation coefficient  $\rho$ . A ratio larger than the value of 1 (made explicit to ease comparisons by horizontal blue planes) indicates poorer performance for Fourier-based estimates compared to wavelet-based ones. Synthetic data consists of bivariate fGn with  $H = 0.8$  and fBm with  $H = 0.2$ .**

356 realizations) values of W-ICOH and W-wPLI as functions of octaves  $j$  and correlation  
 357 coefficient  $\rho$  (left column, panels (a) and (e)), complemented with slices for fixed  $\rho$  as  
 358 functions of  $j$  (second column, panels (b) and (f)) and slices for fixed  $j$  as functions of  $\rho$   
 359 (third column, panels (c) and (g)). Focusing the analysis of Fig 5 on  $\rho = 0$  or on the small  
 360 values of  $\rho$  shows that:

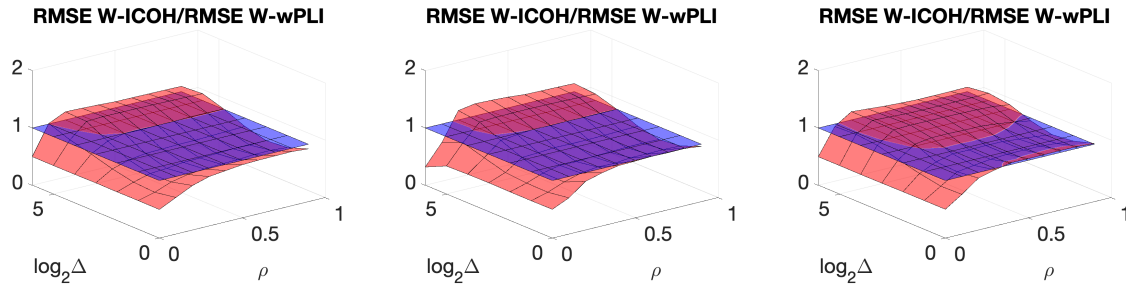
361 i) F-ICOH and F-wPLI depart from 0 across scales when there is no correlation while the  
 362 Complex Wavelet-based W-COH and W-wPLI do not (second column) ;

363 ii) F-ICOH and F-wPLI significantly overestimate correlations at small  $\rho$  while W-COH  
 364 and W-wPLI do not (third column) ;

365 iii) The RMSE of F-ICOH and F-wPLI becomes up to ten times larger than RMSE of  
 366 W-ICOH and W-wPLI for small values of  $\rho$  (fourth column).

367 **Functional connectivity from fractal dynamics assessment performance.** In  
 368 addition, Fig. 6 compares the ratio of the RMSE of W-ICOH to the RMSE of W-wPLI





**Figure 6.** Ratio of the RMSE of W-ICOH to the RMSE of W-wPLI, averaged across scales  $3 \leq j \leq 7$ , as functions of delay  $\Delta$  and correlation coefficient  $\rho$ , for the synthetic data in Figs. 3, 4 and 5. Horizontal blue plans indicate the constant level 1 to ease reading.

369 over several synthetic data sets and shows that both indices perform comparably. However,  
 370 W-ICOH shows a slightly smaller RMSE for small values of  $\rho$  and conversely, a slightly  
 371 larger RMSE for large values of  $\rho$  and for the largest delays  $\Delta$  tested here. This (slight)  
 372 superiority of W-wPLI is much more visible when additive smooth trends are present  
 373 (right plot). In sum, these numerical simulations yield the following conclusions for the  
 374 assessment of functional connectivity from fractal dynamics.

375 i) They indicate that W-COH cannot be used to assess functional connectivity as it is  
 376 fooled by zero-delay (volume conduction effect) correlations, thus confirming an already  
 377 documented observation for F-COH in the literature (Nolte et al., 2004; Stam et al., 2007).  
 378 To the converse, W-ICOH and W-wPLI (and F-ICOH and F-wPLI) are much less affected  
 379 by these spurious correlations.

380 ii) The Complex Wavelet W-ICOH and W-wPLI can be used to assess functional  
 381 connectivity for scale-free temporal dynamics.

382 iii) The Complex Wavelet W-ICOH and W-wPLI perform significantly better than the  
 383 Fourier-based F-COH and F-wPLI, first, when the signals show very large scaling exponents  
 384  $\beta$  in their  $f^{-\beta}$  power spectral density behavior, as is the case with fBm-like time series, or,  
 385 second, when additive noise in the form of smooth and slow trends are superimposed to  
 386 data with scale-free dynamics, a situation commonly observed in recordings collected from  
 387 neuroimaging techniques.

388 iv) W-ICOH and W-wPLI perform comparably with (slightly) better performance of  
 389 W-wPLI when  $\rho$  or  $\Delta$  increases, or when smooth trends are superimposed to scale-free  
 390 dynamics, as often the case on MEG data. This will be further discussed in Section 4.

391

### 3 EXPERIMENTAL MEG DATA

392 The proposed complex wavelet based assessment of functional connectivity in infraslow  
393 arrhythmic brain activity was tested on MEG measurements, consisting of non-invasive  
394 recordings of simultaneous time-series reflecting the whole brain activity, both at rest and  
395 during the completion of a task. All details about the experimental paradigm and the task  
396 can be found in (Zilber et al., 2014).

397 In short, the task was designed from a short-term learning paradigm and consisted of a  
398 visual coherence discrimination. Two sets of colored (green and red) dots were mixed and  
399 shown on a screen, each dot with random and independent movement. After a variable  
400 duration interval (0.3 to 0.6 s) of incoherent motion, a fraction of randomly chosen dots  
401 belonging to either of the two sets (also randomly chosen at each trial) followed a coherent  
402 motion during one second. Participants were asked to tell which of the red or green clouds  
403 had a coherent motion by pressing a button of the same color. Task difficulty was increased  
404 by decreasing the rate of dots in coherent motion.

405 The experiment was organized as interleaved MEG blocks alternating rest and task  
406 measurements: It started with a 5-minute rest recording ( $REST_i$ ), followed by a 12-minute  
407 pre-training block ( $TASK_i$ ); this was followed by 4 successive 5-minute long individualized  
408 training blocks. Another 5-min resting-state block ( $REST_f$ ) was recorded prior to a  
409 final 12-minute post-training block ( $REST_f$ ), consisting of the same visual coherence  
410 discrimination task as in  $TASK_i$ . During  $TASK_i$  and  $TASK_f$ , the motion coherence  
411 discrimination accuracy of each participant was assessed. Pre-training and post-training  
412 behavioral thresholds were computed for each participant as the visual coherence level  
413 associated with 75 % of correct responses (hit rate). During REST blocks, participants were  
414 instructed to keep eyes opened, and were not following any other explicit instruction, thus  
415 permitting the analysis of spontaneous fluctuations of brain activity from MEG recordings.

416 For the experiment, 36 healthy participants (mean age: 22.1 +/- 2.2) were recruited. All  
417 participants were right-handed, had normal hearing and normal or corrected-to-normal  
418 vision. Before the experiment, all participants provided a written informed consent in  
419 accordance with the Declaration of Helsinki (2008) and the local Ethics Committee on  
420 Human Research at NeuroSpin (Gif-sur-Yvette, France).

421 Brain activity was recorded via MEG modality, in a magnetically shielded room using  
422 a 306 MEG system (Neuromag Elekta LTD, Helsinki). MEG signals originally sampled  
423 at 2 kHz were downsampled at 448 Hz, and preprocessed to remove external and internal  
424 interferences, in accordance with accepted guidelines for MEG research (Gross et al.,  
425 2013). Signal Space Separation (SSS) was applied with `MaxFilter` to remove exogenous  
426 artifacts and noisy sensors (Taulu and Simola, 2006). Ocular and cardiac artifacts (eye

427 blinks and heart beats) were removed using Independent Component Analysis (ICA) on  
428 raw signals. ICA were fitted to raw MEG signals, and sources matching the ECG and  
429 EOG were automatically found and removed before signals reconstruction, following the  
430 procedure described in (Jas et al., 2017). Source localization from MEG signals was used  
431 to reconstruct source cortical activity using the `mne_analyze` tools within MNE (Gramfort  
432 et al., 2013). Details regarding the source localization technique are reported in (Zilber et al.,  
433 2014). Finally, following analyses reported in (Zilber et al., 2014; La Rocca et al., 2020),  
434 28 cortical regions-of-interest (ROIs), recruited in task performance (including frontal,  
435 somato-sensory, temporal, parietal and occipital areas) were retained for the analysis of  
436 functional connectivity in infraslow temporal dynamics.

## 4 FUNCTIONAL CONNECTIVITY ASSESSED FROM FRACTAL DYNAMICS IN INFRASLOW ARRHYTHMIC MEG-RECORDED BRAIN ACTIVITY

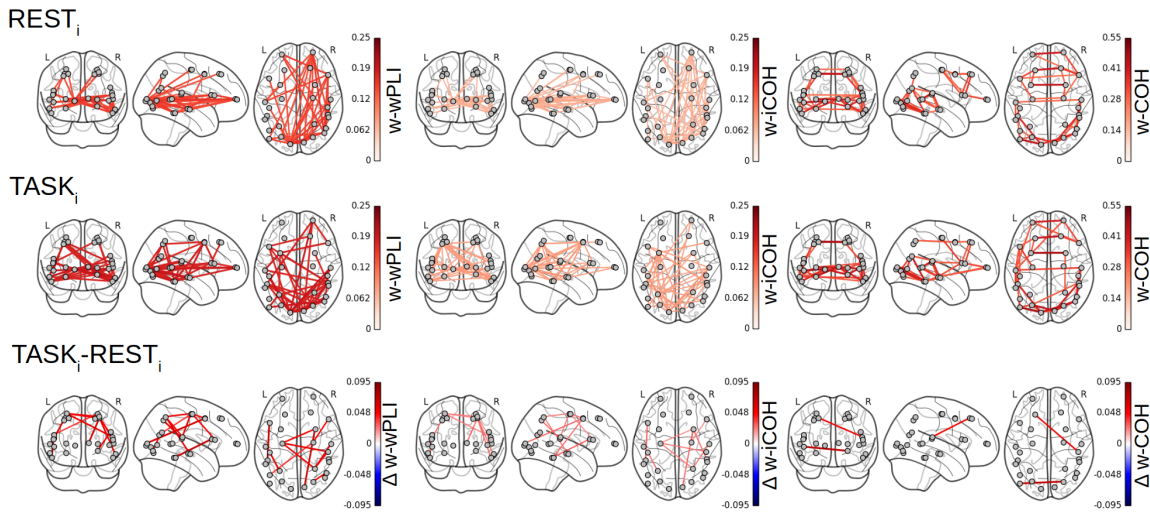
### 4.1 Infraslow scale/frequency range and functional connectivity from fractal dynamics assessment methodology

439 **Infraslow scale/frequency range.** Following the systematic inspections of the wavelet  
440 spectra and cross-spectra reported in (La Rocca et al., 2018b) for the same MEG data,  
441 the scale-free range of scales is set uniformly for the 28 times series and across the 36  
442 participants, for the analysis of arrhythmic functional connectivity to  $8 \leq j \leq 12$ , thus  
443 corresponding to frequencies in  $0.1 \leq f \leq 1.5\text{Hz}$  or equivalently to time scales ranging  
444 roughly from 1 to 10s. This scale-free regime is illustrated in Fig. 1 for arbitrarily chosen  
445 MEG signals shown in Fig. 1(a)-(b).

446 **Experimental conditions.** Infraslow functional connectivity was assessed for several  
447 experimental conditions: resting-state ( $\text{REST}_i$ ), pre-training ( $\text{TASK}_i$ ) and post-training  
448 ( $\text{TASK}_f$ ) tasks, thus enabling us to assess changes in functional interactions from rest to  
449 task and modulations related to learning.

450 **Functional connectivity from fractal dynamics indices.** Three proposed complex  
451 wavelet based indices were then computed to assess infraslow functional connectivity  
452 by averaging across octaves corresponding to the scale-free regime,  $8 \leq j \leq 12$ , the  
453 functions  $\text{W-COH}(j)$ ,  $\text{W-ICOH}(j)$  and  $\text{W-wPLI}(j)$ , resulting in 3 sets of  $28 \times 28 \times 36$   
454 indices.

455 **Tests.** These indices were filtered at the group-level ( $N = 36$ ), using  
456 a recently introduced network density threshold method, the Efficiency Cost  
457 Optimization (De Vico Fallani et al., 2017), thus yielding group-level  $28 \times 28$  fractal



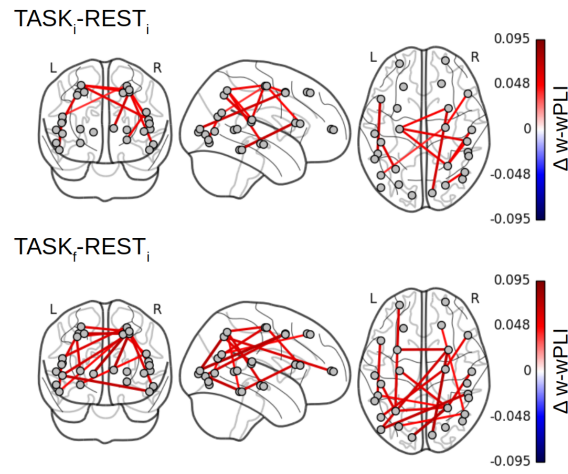
**Figure 7. Functional connectivity assessment from fractal dynamics: Group-level functional connectivity in infraslow MEG-source reconstructed brain dynamics.** Filtered  $28 \times 28$  connectivity networks measured from Complex Wavelet based W-wPLI (left), W-ICOH (middle) and W-COH (right), for  $REST_i$  (top row) and pre-training  $TASK_i$  (center row). The red color intensity codes for the values of the connectivity indices (ranging from 0 to 1 by construction). Functional connectivity differences between conditions  $TASK_i$  and  $REST_i$  when assessed significant by a group level FDR corrected t-test are displayed in bottom row. Color codes for the  $TASK_i - REST_i$  differences in the values of indices from blue (negative) to red (positive), thus indicating that only increases in functional connectivity are observed from  $REST_i$  to  $TASK_i$ .

458 dynamics-based functional connectivity matrices across the brain for each experimental  
 459 condition independently. See also (La Rocca et al., 2020) for further details on the use of  
 460 such technique.

461 To investigate significant differences in infraslow functional connectivity between two  
 462 different experimental conditions (e.g.,  $TASK_i - REST_i$ ), independently for each chosen  
 463 index, a group-level paired t-test was performed, with a demanding preset significance  
 464 level:  $p < 0.01$ . The false discovery rate (FDR) procedure was used to correct p-values for  
 465 multiple comparisons across the  $28 \times 27/2$  possible connections.

466 **Comparisons against Fourier-based indices.** To compare Fourier-based F-ICOH and  
 467 F-wPLI to Complex Wavelet-based W-ICOH to W-wPLI, Fourier-based spectral estimation  
 468 was conducted using Welch Periodogram procedures (as described in Section 2.1), using a  
 469 windowed Fourier transform with a Hanning-type window of duration 80s.

470



**Figure 8. Fractal dynamics-based functional connectivity assessment (W-wPPLI) differences between  $REST_i$  and  $TASK_i$  and between  $REST_i$  and  $TASK_f$ .** The increase in functional connectivity assessed from fractal dynamics from rest to task is strengthened with training, i.e. from  $TASK_i$  to  $TASK_f$ , and emerged between several intra- or inter-hemispheric pairs of regions (Frontal polar/IPS, ITC/MT, FEF/pSTS) involved in task performance.

## 471 4.2 Fractal dynamics-based functional connectivity networks

472 Fig. 7 reports the  $28 \times 28$  thresholded connectivity networks yielded by the Complex  
 473 Wavelet based indices defined in Section 2, W-wPPLI (left), W-ICOH (middle) and W-  
 474 COH (right), for two different experimental conditions  $REST_i$  (top row) and pre-training  
 475  $TASK_i$  (center row). Further, Fig. 7(bottom row) reports the FDR corrected statistically  
 476 significant differences between indices measured during  $TASK_i$  and  $REST_i$ . Fig. 7 leads to  
 477 the following observations:

478 i) The connectivity networks yielded by W-COH predominantly display short-range  
 479 and inter-hemispheric interactions throughout the cortex and most notably amongst frontal  
 480 regions on one hand and temporo-occipital regions on other hand, both for  $REST_i$  and  
 481  $TASK_i$ .

482 ii) The connectivity networks yielded by W-ICOH and W-wPPLI display similar structures,  
 483 dominated by long-range spatial interactions, that differ significantly from those of the  
 484 networks produced by W-COH, dominated by shorter-range spatial interactions. [These](#)  
 485 [differences in network structures can be quantified using the Average Degree, i.e., the](#)  
 486 [average number of connections per node, as a network structure metrics. For  \$REST\_i\$ , the](#)  
 487 [Average Degrees for the graphs obtained by W-COH, W-ICOH and W-wPPLI are respectively](#)  
 488 [of  \$0.95\(\pm 0.37\)\$ ,  \$0.21\(\pm 0.24\)\$  and  \$0.44\(\pm 0.52\)\$ . Medians in distributions of number of links](#)

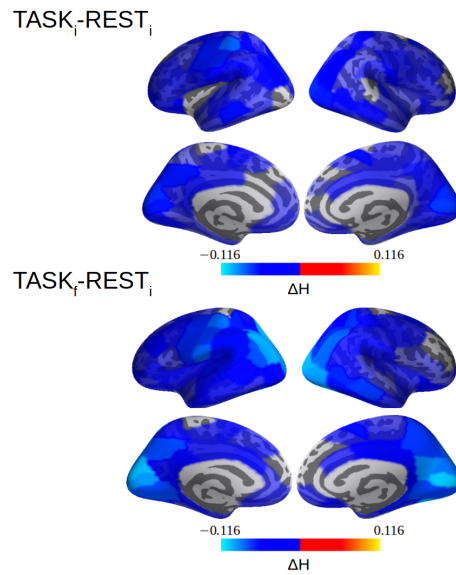
489 per node differ significantly between W-COH and W-ICOH ( $p < 10^{-11}$ ) or between  
490 W-COH and W-wPLI ( $p < 10^{-6}$ ). The same holds for  $TASK_i$ , with average degrees of  
491 respectively  $1.0(\pm 0.49)$ ,  $0.25(\pm 0.24)$  and  $0.52(\pm 0.50)$ , and significance of respectively  
492  $p < 10^{-8}$  and  $p < 10^{-3}$ .

493 iii) While yielding comparable networks, W-wPLI and W-ICOH differ insofar as the  
494 former yields larger connectivity indices than the latter. In addition, connectivity networks  
495 using W-wPLI or W-ICOH differ in structure, however much less than when comparing  
496 W-wPLI vs. W-COH or W-ICOH vs. W-COH. Indeed, for  $REST_i$  the Average Degrees  
497 of W-wPLI and W-ICOH are respectively of  $0.44(\pm 0.52)$  and  $0.21(\pm 0.24)$ , yielding a  
498 quantifiable difference ( $p = 0.04$ ), and for  $TASK_i$  the Average Degrees of W-wPLI and  
499 W-ICOH are respectively of  $0.52(\pm 0.50)$  and  $0.25(\pm 0.24)$ , yielding a clearer difference  
500 ( $p = 0.01$ ).

501 iv) When comparing  $TASK_i$  versus  $REST_i$ , W-wPLI and W-ICOH both indicate an  
502 increase in functional connectivity during task performance. This increase in functional  
503 connectivity assessed from fractal dynamics highlights interactions between regions  
504 recruited in the achievement of the task, notably fronto-temporal couplings (between  
505 the right ventro-lateral prefrontal cortex (vlPFC) and inferior temporal cortex (ITC)),  
506 interactions linking temporal regions (anterior superior temporal sulcus (aSTS) and auditory  
507 cortex) with the intra-parietal sulcus (IPS), motor-occipital couplings between the left  
508 frontal BA6 (including premotor and supplementary motor regions) and primary visual  
509 areas (V1/V2). Interaction between the key region hMT+, sensitive to visual motion, and  
510 the associative area, pSTS, is also significant in the left hemisphere.

511 Focusing on the W-wPLI index only, Fig. 8 shows the additional comparisons of the  
512 post-training task  $TASK_f$  to the initial rest  $REST_i$ , which, compared to the contrast  
513  $TASK_i - REST_i$  (cf. Fig. 7 bottom left plot), indicates first that functional interactions  
514 in infraslow temporal dynamics are globally strengthened by the training and second that  
515 new intra- and inter-hemispheric couplings emerged with training involving much more  
516 the parieto-occipito-temporal network (IPS, primary visual cortex and anterior STS). We  
517 also noticed new interactions between the left fronto-polar region and the left IPS, between  
518 the right frontal eye fields (FEF) and the pSTS and finally between the BA6 complex and  
519 hMT+ region.

520

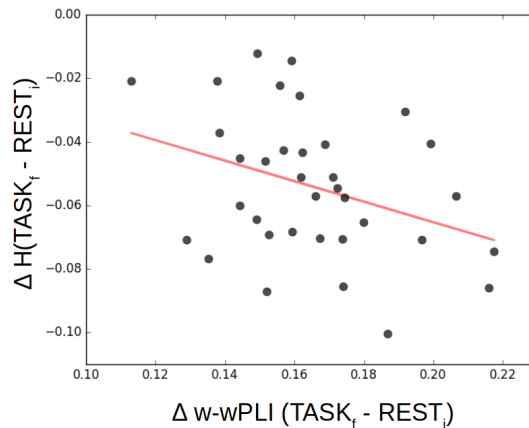


**Figure 9. selfsimilarity ( $H$ ) differences between  $REST_i$  and  $TASK_i$  and between  $REST_i$  and  $TASK_f$ .** The decrease in selfsimilarity from rest to task is strengthened with training, i.e. from  $TASK_i$  to  $TASK_f$ , and more heavily in the parieto-occipital (hMT+, visual cortices, V1/V2/V4) regions involved in task performance. Note that a value of  $H$  was computed per cortical label here. See (La Rocca et al., 2018b) for methodological details.

### 521 4.3 Functional connectivity assessed from fractal dynamics and 522 selfsimilarity

523 In (La Rocca et al., 2018b), selfsimilarity was systematically quantified by wavelet-  
524 based measurements of the selfsimilarity exponent  $H$  and a global decrease from rest to  
525 task was observed over the whole brain (see Fig. 4E in (La Rocca et al., 2018b)). This  
526 result, obtained from 24 participants, is here strengthened by using 36 subjects. Fig. 9  
527 reports a decrease in  $H$  not only between  $REST_i$  and  $TASK_i$  but also between  $REST_i$   
528 and  $TASK_f$ . Further, Fig. 9 shows a strengthening of the decrease in  $H$  from  $TASK_i$  to  
529  $TASK_f$  in the parieto-occipital regions involved in task performance, notably the bilateral  
530 hMT+ regions, the visual cortices including V1/V1 and V4 for the visual color detection.  
531 Interestingly, after training these regions are also more strongly coupled with others during  
532 task performance ( $TASK_f$  vs  $REST_i$ ).

533 To investigate a potential training-induced relation between the decrease in selfsimilarity  
534 and the increase in W-wPLI,  $\Delta H = H_{TASF_f} - H_{REST_i}$  and  $\Delta W\text{-wPLI} = W\text{-wPLI}_{TASF_f} - W\text{-wPLI}_{REST_i}$   
535 were averaged across the whole brain for each subject. Corresponding averages  
536 are shown in Fig. 10 which interestingly suggests a significant ( $p = 0.05$ ) anticorrelation



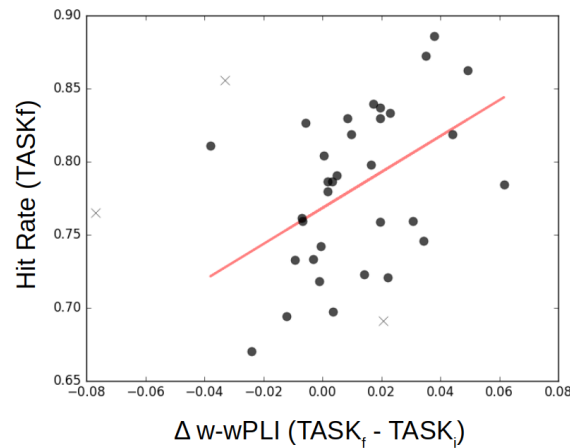
**Figure 10. Decrease of selfsimilarity vs. increase in functional connectivity assessed from fractal dynamics from rest to task.**  $\Delta H = H_{TASK_f} - H_{REST_i}$  as a function of  $\Delta W\text{-wPLI} = W\text{-wPLI}_{TASK_f} - W\text{-wPLI}_{REST_i}$ , averaged across the whole brain for each of the 36 participants (each marked as a dot), shows that the decrease of selfsimilarity correlates negatively ( $r = -0.33$ ,  $p = 0.05$ ) with the increase of functional connectivity assessed from fractal dynamics.

537 of  $r = -0.33$ . When averages are restricted to the part of the brain where statistically  
 538 significant changes in W-wPLI between  $REST_i$  and  $TASK_f$  can be assessed (after false  
 539 discovery rate-based corrections for multiple hypothesis testing), the relation between  $\Delta H$   
 540 and  $\Delta W\text{-wPLI}$  is strengthened,  $r = -0.35$  and  $p = 0.04$ .  
 541

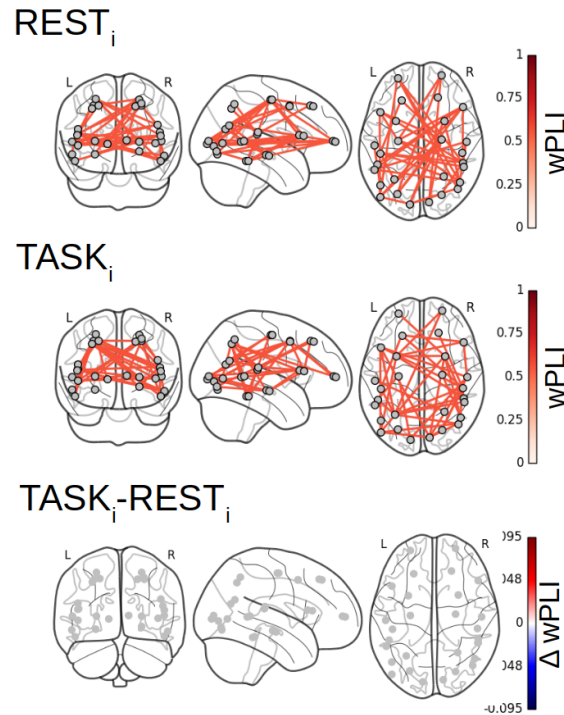
#### 542 4.4 Functional connectivity assessed from fractal dynamics and task 543 performance

544 Finally, functional connectivity in the infraslow range of temporal dynamics can be related  
 545 to task performance, notably after training. Fig. 11 reports, for each participant, post-training  
 546 performance in achieving the task quantified by percentage of correct responses (detection  
 547 of the color associated with the coherent visual motion), referred to as hit rate, as function  
 548 of the variation in the W-wPLI indices measured in  $TASK_i$  and  $TASK_f$ . It shows that  
 549 participants with the larger increase in functional connectivity assessed from fractal  
 550 dynamics induced by training, i.e., the larger increase of  $W\text{-wPLI}_{TASK_f} - W\text{-wPLI}_{TASK_i}$ ,  
 551 are also those achieving the better performance in post-training task.  
 552





**Figure 11. Functional connectivity assessment from fractal dynamics vs. Task Performance.** Individual performance in post-training task shows significant ( $p = 0.01$ ) positive correlation ( $r = 0.45$ ) with the difference in functional connectivity assessed from fractal dynamics from pre- to post-training, i.e.,  $W\text{-wPLI}_{\text{TASK}_f} - W\text{-wPLI}_{\text{TASK}_i}$ . Each participant is represented as a dot, outliers are marked with a  $\times$ .



**Figure 12. Fourier-based wPLI estimator in the scale-free regime.** No significant difference between  $F\text{-wPLI}_{\text{TASK}_i}$  and  $F\text{-wPLI}_{\text{REST}_i}$  in arrhythmic regime can be found.

#### 553 **4.5 Functional connectivity from fractal dynamics: Fourier-based vs.** 554 **Complex-Wavelet assessment**

555 Averaging (the absolute values) of F-wPLI across a range of frequencies that match the  
556 range of scales associated with the infraslow scale-free scaling range, permits to compare  
557 Fourier-assessed functional connectivity from fractal dynamics. Fig. 12 reports the density  
558 networks obtained from F-wPLI for REST<sub>i</sub> and TASK<sub>i</sub>, showing significant differences  
559 with those obtained using W-wPLI. The network topography associated with the F-wPLI  
560 index are denser compared to W-wPLI. Indeed, using the Average Degree, used as a  
561 graph structure metrics, it was found that for REST<sub>i</sub>, the Average Degrees of W-wPLI  
562 and F-wPLI are respectively of 0.44(±0.52) and 1.62(±1.11), yielding a very significant  
563 difference, assessed by a p-value below  $6 \times 10^{-6}$ , and for TASK<sub>i</sub>, the Average Degrees  
564 of W-wPLI and F-wPLI are respectively of 0.52(±0.50) and 1.65(±1.21), yielding also a  
565 significant difference, assessed by a p-value of  $5 \times 10^{-5}$ . Further, the number of significant  
566 interactions with F-wPLI is more balanced between the two hemispheres during REST<sub>i</sub> in  
567 contrast to W-wPLI, which captures more couplings in the right one. Also, the resting-state  
568 W-wPLI-based network configuration is more dominated by fronto-occipital couplings  
569 whereas the F-wPLI-based shows a larger number of inter-hemispheric interactions. During  
570 the pre-training task TASK<sub>i</sub>, W-wPLI and F-wPLI network topographies both show similar  
571 connections but also strong differences: the former is more dominated by fronto-parieto-  
572 occipital couplings with a hub role played by the visual cortices, while the latter does not  
573 strongly differ from the F-wPLI network found during REST<sub>i</sub>. Finally and more importantly,  
574 no statistically significant difference in F-wPLI<sub>TASK<sub>i</sub></sub>-F-wPLI<sub>REST<sub>i</sub></sub> can be evidenced (see  
575 Fig. 12-bottom), while a significant increase in W-wPLI was found from REST<sub>i</sub> to TASK<sub>i</sub>  
576 between fronto-parieto-occipital regions that are involved in task performance (see Fig. 9-  
577 top). The coupling between V4 and MT in the right hemisphere reflects the color-motion  
578 binding, while the significant interactions involving the anterior STS, IPS and vlPFC are  
579 likely due to their role in multisensory processing. Hence, the W-wPLI index provides  
580 much more meaningful information when contrasting rest to task brain activity.

## 5 DISCUSSION

581 **Functional connectivity from fractal dynamics assessment.** At the methodological  
582 level, the results presented in Section 4 clearly showed that W-COH fails to characterized  
583 correctly functional connectivity, in clear agreement with the numerical simulations reported  
584 in Section 2.3 on synthetic data fGn/fBm and with results reported in the literature (cf. (Stam  
585 et al., 2007; Vinck et al., 2011)).

586 More interestingly, compared to W-ICOH, W-wPLI was observed to more accurately

587 quantify functional connectivity assessment from fractal dynamics, both at rest and during  
588 task in MEG data, as well as to better highlight relevant changes in functional connectivity  
589 assessed from fractal dynamics between rest and task. This is in agreement with previously  
590 reported results, showing that for band-limited oscillatory activities, F-wPLI was a better  
591 index to assess functional connectivity than F-ICOH. This was attributed to the denominator  
592 of F-wPLI being different from that of F-ICOH and less sensitive to (residual) volume  
593 conduction effects (Stam et al., 2007; Vinck et al., 2011). These arguments straightforwardly  
594 extend to W-wPLI and W-ICOH thus likely explaining the enhanced ability of W-wPLI to  
595 assess functional connectivity from fractal dynamics compared to W-ICOH. Interestingly,  
596 the numerical simulations conducted in Section 2.3 on synthetic fGn/fBm data showed  
597 only a moderate superiority of W-wPLI over W-ICOH to quantify functional connectivity  
598 from fractal dynamics, except for slightly improved estimation (RMSE) performance. This  
599 suggests that fGn/fBm, even with delays, correlations and possible additive trends, are not  
600 rich enough models to account for all the difficulties encountered in modeling real MEG  
601 data. This is calling for richer modeling, potentially involving multifractality. This will be  
602 further explored.

603 The benefits of using wavelet-based (multiscale) tools to analyze scale-free temporal  
604 dynamics and estimate the corresponding scaling exponent compared to classical Fourier-  
605 based spectral estimation have been abundantly documented elsewhere (cf. e.g., (Abry  
606 and Veitch, 1998; Veitch and Abry, 1999, 2001; Ciuciu et al., 2008, 2012; Abry et al.,  
607 2019b)). First, they provide better (unbiased and controlled variance) estimates of  $H$ ;  
608 Second, by tuning the so-called number of vanishing moments of the mother wavelet  
609 (Mallat, 1998), wavelet-based spectral estimation is robust to additive smooth slow trends in  
610 data which are, to the converse, strongly altering Fourier-based spectral estimation. These  
611 benefits are straightforwardly inherited by the wavelet-based indices for assessing functional  
612 connectivity from fractal dynamics. This was clearly evidenced by the numerical simulations  
613 reported in Section 2.3 showing the robustness to trends and the better performance for  
614 large scaling exponents of Complex Wavelet-based indices over Fourier-based ones.

615 **Functional connectivity assessed from fractal dynamics in time relates to long-range**  
616 **spatial interactions.** On MEG data, functional connectivity in the infraslow arrhythmic  
617 regime assessed by W-COH, i.e., based on direct correlation, was observed to yield mostly  
618 spatial short-range connectivity networks across the brain, notably with spurious short-  
619 range functional intra- and inter-hemispheric interactions, visible between frontal regions  
620 both at rest and during task. This is likely a consequence of residual common source  
621 effects, strongly biasing the real part of the coherence function, and thus yielding spurious  
622 connectivity measures, in agreement with results reported in (Stam et al., 2007). In contrast,  
623 functional connectivity assessed by W-ICOH and W-wPLI indices, i.e., based on phase

624 coupling, did not show such short-range links, but rather functional connectivity patterns  
625 dominated by long-range spatial interactions. This yields the first major result of the  
626 present work: Functional connectivity pertaining to the large-band infraslow arrhythmic  
627 temporal dynamics, (from 1 to 10s, or equivalently from 0.1 to 1Hz), reveals long-range  
628 spatial interactions, evidencing notably couplings between frontal, parietal and occipital  
629 brain regions. Functional connectivity assessed from fractal dynamics thus permits to  
630 quantify phase couplings and interactions associated with large lags. This departs from  
631 functional connectivity networks produced by the analysis of band-limited oscillatory  
632 temporal dynamics, that pertains to the fast (high frequency) brain activity and thus focuses  
633 on short time delays.

634 **Functional connectivity assessed from fractal dynamics increases during task**  
635 **performance and with training.** Compared to F-wPLI, W-wPLI showed an enhanced  
636 statistical sensitivity as it revealed a positively engaged parieto-temporo-occipital network in  
637 infraslow temporal dynamics when contrasting rest to pre-training activities. This network  
638 comprises previously identified key brain regions (e.g. hMT+, ITC, vIPFC, pSTS) during  
639 task performance. Interestingly, such regions also consistently identified as recruited by task  
640 when using standard temporal or spectral data analysis (Zilber et al., 2014; La Rocca et al.,  
641 2020). However, W-wPLI was the only index further showing that functional connectivity  
642 assessed from fractal dynamics actually increased during task performance in these regions.  
643 A second key result consists of the observation of the strengthening of this functional  
644 connectivity from fractal dynamics based functional network with training, i.e. when  
645 contrasting rest to post-training activity. It shows the rising of new key couplings between  
646 frontal and parieto-temporal cortices that suggest that some cortical representations of the  
647 visual detection and decision making process may emerge even at slow time scales (1 s to  
648 10 s) and may be used as a substrate for facilitating faster dynamics in oscillatory regimes.  
649 Such increased functional connectivity assessed from fractal dynamics is a hallmark of  
650 brain plasticity induced by the training stage.

651 The third finding of this study is the positive correlation between the increase in functional  
652 connectivity assessed from fractal dynamics and task performance when contrasting pre-  
653 to post-training brain activity. This suggests that the consolidated network eases task  
654 completion for each individual, experiencing averaged increase in functional couplings  
655 within the infraslow regime.

656 **Functional connectivity from fractal dynamics and selfsimilarity quantifying an**  
657 **interplay between temporal and spatial dynamics.** Finally, the increase in functional  
658 connectivity assessed from fractal dynamics was shown to be correlated with a decrease in  
659 selfsimilarity from rest to task. These results on functional connectivity assessment from  
660 fractal dynamics, combined with the univariate (regionwise) analysis of scale-free temporal

661 dynamics of the same data (La Rocca et al., 2018b), lead to the following global picture for  
662 the large-band arrhythmic infraslow temporal dynamics of brain activity.

663 At rest, each region displays a globally very structured and slow activity in time  
664 (large selfsimilarity exponent  $H$ , hence strong temporal autocorrelation) with no transient  
665 structures (no burstiness, no multifractality, (La Rocca et al., 2018b)). The regions are  
666 connected across the brain by a clear spatial structure, that of functional connectivity  
667 assessed from fractal dynamics, constructed on measures of infraslow arrhythmic  
668 interactions.

669 During task performance, temporal dynamics in each region independently become  
670 less globally structured and faster (decrease in  $H$  hence globally less correlated) with  
671 transient dynamical structures for regions involved in the task (burstiness and multifractality  
672 (La Rocca et al., 2018b)). These changes in regionwise temporal dynamics are accompanied  
673 by stronger functional connectivity assessed from fractal dynamics, i.e., by stronger spatial  
674 structures connecting regions.

675 This permits to conjecture an interplay between temporal and spatial dynamics for the  
676 large-band infraslow arrhythmic brain activity: A decrease in global temporal structures  
677 induces faster and transient temporal dynamics and is associated with an increase in spatial  
678 structures and interactions between remote brain regions. Interestingly, these modulations  
679 are further strengthened with training, i.e. when contrasting the post-training to the resting-  
680 state activity in comparison with the pre-training vs. rest contrast. Overall, such modulations  
681 of brain spatio-temporal dynamics can be conjectured as a hallmark of brain plasticity.

682

## 6 CONCLUSIONS

683 In this work, we have introduced the notion of *functional connectivity assessment from*  
684 *fractal dynamics* for MEG data, defined as functional connectivity associated with the  
685 large-band infraslow (typically below the Hz) arrhythmics (scale-free) cross temporal  
686 dynamics, in contradistinction with the classical functional connectivities associated with  
687 the band-limited rapid oscillatory rhythms ( $\alpha$ -,  $\beta$ -,  $\gamma$ - bands).

688 It has been argued and demonstrated that complex wavelet (multiscale) based analyses  
689 permit to construct indices to assess functional connectivity from fractal dynamics that  
690 inherit from the theoretical and practical benefits of wavelet representations for scale-free  
691 (cross-temporal) dynamics analysis, notably in terms of robustness to trends and large  
692 selfsimilarity parameters  $H$ . It was confirmed that wPLI outperforms ICOH, as commonly  
693 observed and that COH is not suited for functional connectivity assessment.

694 While Fourier-based tools are natural to use to assess functional connectivity in band-limited

695 rapid oscillatory rhythms, it was shown, using simulated synthetic data and mostly on  
696 MEG data, that the assessment of functional connectivity for large-band slow scale-free  
697 cross-temporal dynamics is better achieved by complex wavelet based indices. Therefore,  
698 Fourier and complex wavelet based spectral estimation must be regarded as complementary,  
699 rather than as mutually exclusive, tools.

700 Complex wavelet based analyses of functional connectivity assessment from fractal  
701 dynamics conducted on MEG data recorded on 36 participants at rest and during a visual  
702 discrimination task with individualized training, yielded several key conclusions. First,  
703 large-band infraslow arrhythmic cross temporal dynamics can be associated with long-range  
704 (fronto-temporo-occipital) spatial interactions. Second, functional connectivity from fractal  
705 dynamics increases during task performance (in a set of brain regions consistent with  
706 those evidenced by other analyses performed on the same data with different tools) and is  
707 strengthened with training. Interestingly, a larger overall fractal dynamics-based functional  
708 connectivity increase correlates with a better task performance (larger hit rate). Third, the  
709 increase in spatial structure (quantified by the increase in functional connectivity assessed  
710 from fractal dynamics) is accompanied by changes in temporal structures, combining a  
711 decrease in the global temporal correlations (quantified by a decrease in the selfsimilarity  
712 index) and the increased occurrence of local transient structures (quantified by an increase  
713 in multifractality). These spatiotemporal modulations are reinforced with intensive and  
714 individualized training to the task.

715 Routines (in MATLAB) to synthesize (correlated and delayed) bivariate fractional Gaussian  
716 noise, to perform Fourier and complex-wavelet based analysis and to compute indices  
717 quantifying functional connectivity from fractal dynamics, on synthetic or MEG data, have  
718 been developed by ourselves and will be made publicly available at the time of publication.

719 [Such tools could further be used to examine the relevance of functional connectivity](#)  
720 [assessed from fractal dynamics in the context of network physiology, and of networks of](#)  
721 [networks, relating brain activity to other physiological functions \(heart rate, respiration,](#)  
722 [sleep, ocular and motor systems,...\), cf. e.g., \(Bartsch and Ivanov, 2014; Bartsch et al.,](#)  
723 [2015; Liu et al., 2015; Catrambone et al., 2020\).](#)

## CONFLICT OF INTEREST STATEMENT

724 The authors declare that the research was conducted in the absence of any commercial or  
725 financial relationships that could be construed as a potential conflict of interest.

## AUTHOR CONTRIBUTIONS

726 [The original experimental design and access to MEG data was provided by Virginie van](#)  
727 [Wassenhove.](#)

728 The methodological question studied here was framed and conceptualized by Patrice Abry  
729 and Philippe Ciuciu.

730 The data analysis tool design, implementation and performance assessment and  
731 interpretation were performed by Herwig Wendt and Patrice Abry.

732 MEG data analysis, results production and interpretation were performed by Daria La  
733 Rocca and Philippe Ciuciu.

734 The article was written by Patrice Abry and Philippe Ciuciu.

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