Conditional Correlation as a Measure of Mediated Interactivity in fMRI and MEG/EEG

Guillaume Marrelec, Jean Daunizeau, Mélanie Pélégrini-Issac, Julien Doyon, and Habib Benali, *Member, IEEE*

***Abstract*—Many measures have been proposed so far to extract brain functional interactivity from functional magnetic resonance imaging (fMRI) and magnetoencephalography/electroencephalography (MEG/EEG) data sets. Unfortunately, none has been able to provide a relevant, self-contained, and common definition of brain interaction. In this paper, we propose a first step in this direction. We first introduce a common terminology together with a cross-modal definition of interaction. In this setting, we investigate the commonalities shared by some measures of interaction proposed in the literature. We show that temporal correlation, nonlinear correlation, mutual information, generalized synchronization, phase synchronization, coherence, and phase locking value (PLV) actually measure the same quantity (namely correlation) when one is investigating linear interactions between independently and identically distributed Gaussian variables. We also demonstrate that these data-driven measures can only partly account for the interaction patterns that can be expressed by the effective connectivity of structural equation modeling (SEM) . To bridge this gap, we suggest the use of conditional correlation, which is shown to be related to mediated interaction.**

***Index Terms*—Coherence, conditional correlation, effective connectivity, functional brain imaging, functional brain interactivity, functional connectivity, functional MRI, generalized synchronization, mediated interaction, MEG/EEG, mutual information, nonlinear correlation, phase locking value, phase synchronization, temporal correlation.**

I. Introduction

NEUROIMAGING includes different imaging methods that enable to dynamically and noninvasively follow various markers of brain activity, such as functional magnetic resonance imaging (fMRI), electroencephalography (EEG), and magnetoencephalography (MEG): three modalities on which this paper will focus. The signals measured by fMRI, MEG, or EEG originate from different consequences of brain activity, even though the exact underlying process is still under investigation [1]–[5]. Most fMRI acquisitions rely on the so-called blood oxygen level dependent (BOLD) contrast, which measures metabolic and hemodynamic consequences of brain activity [6], [7]. On the other hand, the signals obtained in MEG/EEG are more closely related to the neuronal currents [8], [9]. It is furthermore believed that fMRI and MEG/EEG are sensitive to different characteristics of a local neuronal and synaptic event: MEG/EEG is rather sensitive to post-synaptic activity, while fMRI is also influenced by neuronal firing rates [2], [3], [10].

Combined use of different modalities to investigate a given behavioral or cognitive task will bring information of different nature and is hence highly desired. Due to the intrinsic complementarity of fMRI and MEG/EEG data sets, combined and/or simultaneous recordings are increasingly more often included in experimental protocols [11], [12]. It is therefore highly relevant to be able to perform combined analysis or at least be able to compare results from separate analyses [13], [14].

To this end, connections must be found between MEG/EEG and fMRI data sets and analyses. These connections can either originate from a precise understanding of the physiological causes that generated the signals measured by both modalities or emerge at a more formal level. In the recent literature, some studies have suggested that there exists a direct relationship between neuronal activity and BOLD contrast [2], [15], even though no quantitative relationship between BOLD measurements and neural events was proposed. Nonetheless, despite this lack of physiological connection, formal relationships have successfully been developed between fMRI and MEG/EEG in order to take advantage of both modalities and, eventually, allow for data fusion.

A dynamic vision of brain processes has recently been brought to neuroimaging data analysis. In this approach, it is not only a collection of brain areas but, rather, a network of distributed and interacting regions that is hypothesized to process the functional task under investigation. While the former emphasizes the functional specialization of brain areas, the latter, rather, focuses on the massively parallel nature of brain networks: Function also emerges from the flow of information between brain areas [16]–[18]. It is increasingly believed that brain interactions can be captured by neuroimaging, resulting in a new investigation field: functional brain connectivity. Its objective is to capture the dynamic, context-dependent processes leading to preferential recruitment of some networks over others [16]–[19].

However, as stressed by [20], functional brain connectivity has about as many meanings as there are authors in the literature. Indeed, different neuroimaging disciplines have focused on

Manuscript received September 30, 2004; revised March 25, 2005. G. Marrelec was supported by the Fondation Fyssen. J. Daunizeau was supported by the Association pour la Recherche contre le Cancer. The associate editor coordinating the review of this paper and approving it for publication was Guest Editor Guido Nolte.

G. Marrelec is with INSERM UMR-S 678/UPMC, CHU Pitié-Salpêtrière, 75634 Paris Cedex 13, France, and also with the Functional Neuroimaging Unit, Université de Montréal, Montréal, QC, H3W 1W5 Canada (e-mail: Guillaume.Marrelec@umontreal.ca).

J. Daunizeau, M. Pélégrini-Issac, and H. Benali are with INSERM UMR-S 678/UPMC, CHU Pitié-Salpêtrière, 75634 Paris Cedex 13, France (e-mail: Jean.Daunizeau@imed.jussieu.fr; Melanie.Pelegrini@imed.jussieu.fr; Habib.Benali@imed.jussieu.fr).

J. Doyon is with the Département de Psychologie, Université de Montréal, Montréal, QC, H3C 3J7, Canada (e-mail: julien.doyon@umontreal.ca).

Digital Object Identifier 10.1109/TSP.2005.853211

distinct metrics to assess interactivity, without providing a relevant self-contained cross-modal definition of brain interactivity.

Precursors working on invasive neurophysiological animal studies have provided convincing evidence that *neural synchronization* represents an important code for brain information processing [21]–[23]. *Synchrony* and *asynchrony* between two spatially remote neuronal spike trains are interpreted with regard to the so-called "binding problem" [24], which is still in debate, as the necessary brain mechanisms, providing a coherent sensorial/emotional experience integration [16]. Working at the spatial scale of neuronal populations ($\sim 10^4$ cells), similar studies were conducted with MEG/EEG data. Suffering from the lack of reliable inverse approaches allowing us to infer the neural activity sources, MEG/EEG *phase synchrony* analyses were mostly considered as they appeared at sensors [25], [26]. Still, a few works have been achieved in measuring *temporal coherence* between two dipoles or recording sites in a specific frequency band and in a given time window [27]–[29]. *Phase locking value (PLV)* has been introduced as a way to avoid spurious variability induced by signal nonstationarity [30], [31] and the *nonlinear correlation coefficient* h^2 to account for nonlinear interactions [32], [33]. *Mutual information* has recently been applied in an attempt to extract nonlinear interactions between non-Gaussian variables [34]–[37]. Tools originating from the study of dynamic systems have also been introduced into the MEG/EEG community, such as *generalized synchronization* [38], [39] (for a comprehensive review of this notion, see [40]) or *mutual dimension* [41], [42]. Last, measures have been applied in an attempt to infer causality, such as Granger causality [43], [44].

Proposed by [45] and [46] for fMRI and positron emission tomography (PET) data analysis, *effective connectivity* considers the influence that regions exert on each other. Its implementation heavily relies on structural equation modeling (SEM) [47], [48]. Starting from a set of D regions, a model is set *a priori* that expresses the time course $y_d(t)$ of each region as a linear function of other region time courses, $y_d(t) = \sum_{e \neq d} \lambda_{d,e} y_e(t)$, some coefficients $\lambda_{d,e}$ being constrained to 0, and the others being estimated to best fit the data. $\lambda_{d,e}$ quantifies the strength that region e exerts on region d, hence the name of effective connectivity. By estimating these coefficients for two different experimental settings, it is possible to analyze the influence of the protocol modification on $\lambda_{d,e}$ and, therefore, on the actions exerted by region e on region d. Dynamical causal modeling (DCM) is a more recent model for effective connectivity that aims at taking nonlinearities and temporal correlation into account through a neuronal model of interaction and a hemodynamic model [49],[50].

Functional connectivity was proposed by [51] for fMRI. Functional connectivity between two voxels or regions is defined as the temporal correlation between their time courses. It has proven to be a useful tool to explore the spatial extent of a functional network, given one of its regions when no obvious *a priori* interactivity model is available [52]–[54]. Mutual information has also been applied to fMRI [55]–[57].

In spite of the wide variety of quantities just mentioned, the issues faced in fMRI and MEG/EEG functional interactivity data analyses boil down to the same question, namely, to extract relevant information from the data relative to the interactions between brain areas. Consequently, it is logical to expect that the various tools developed so far to answer this question, which have been declined according to different imaging modalities, share conceptual commonalities. Unfortunately, very little literature exists on the topic [37], [58], and common definitions and metrics to assess interactivity in neuroimaging data analysis remain to be proposed.

On the one hand, if the interaction strengths can be determined through effective connectivity, the presence or absence of an interaction cannot be assessed; working with effective connectivity requires the setting of an *a priori* model that will—and can—hardly be challenged. Despite active ongoing research to allow for model comparison [48], [59], these methods remain not well adapted for complex and/or exploratory analysis. This constraint renders effective connectivity practically inefficient in many cases since the structural network underlying a given task is usually unknown, and its investigation is the goal of the experiment.

On the other hand, although correlational connectivity is computationally convenient and capable of revealing certain aspects of connectivity, it embraces neither the generality of functional interactivity nor the wide variety of interaction patterns that could be expected. Indeed, if a zero correlation can be interpreted as an absence of interaction, nothing can be said about a nonzero correlation, which could either be implied by direct interactions between the corresponding regions or by influence of a common input. This theoretical fact has already been noticed from a more practical point of view in fMRI data analysis [54]. As to mutual information, increasing it sensibility is achieved at the cost of an exponential increase of the number of bins used to classify the data and, hence, by a concomitant dramatic decrease of the estimation accuracy.

Finally, even though there exist many differences between fMRI and MEG/EEG, reviews of functional brain interactivity investigation by neuroimaging should include both MEG/EEG and fMRI studies. By contrast, most reviews concentrate on fMRI (e.g., [20], [60], [61]). This discrimination can partly be explained by the apparent dissemblance of interactivity measures in MEG/EEG and fMRI.

Proving that a proposed cross-modal system could account for all the measures detailed earlier would provide a compelling argument toward its recognition in neuroimaging data analysis. Conversely, if such a common framework exists, it seems sound to expect that it should heavily rely on features shared by quantities already proposed. Hence, it is hoped that examination of the relationships between interactivity measures defined so far will provide a first step toward a common setting for functional brain interactivity investigation and, hence, benefit both separate fMRI and MEG/EEG data analysis, as well as supply new tools for common analyses.

In this paper, we demonstrate that under very simple assumptions, the most commonly used measures of functional connectivity (temporal correlation, nonlinear correlation, mutual information, generalized synchronization, phase synchrony, coherence, and PLV) are all functions of correlation. Correlation is a measure of functional connectivity when linear relationships are sought between temporally independent and identically distributed (i.i.d.) Gaussian variables; the above-mentioned mea-

sures generalize it when one or more of these hypotheses do not hold.

Using this result, we then examine what the gap between functional and effective connectivity consists of through SEM and a very simple structural model. SEM only models the linear relationships that exist between i.i.d. Gaussian variables. Since all measures of functional connectivity boil down to correlation in this setting, we investigate to what extent correlation fails to account for SEM's effective connectivity. Other measures of functional connectivity, however complex they might be, will essentially behave in the same manner as correlation and will, hence, not perform any better in representing SEM's effective connectivity.

The outline of this paper is the following. In Section II, we propose a short terminology that allows for cross-modal investigation of functional brain interactivity and provides an example on which the analogies will be demonstrated. In Section III, we derive the theoretical relationships that exist between the most commonly used data-driven measures of functional interactivity and correlation. Section IV shows how certain connectivity patterns of effective connectivity can be translated in terms of correlation, whereas some patterns cannot be discriminated. To remedy this defect, we introduce conditional correlation and show that it is strongly related to mediated interaction. We then detail how most interaction patterns can be discriminated in this setting. Further issues are tackled in the discussion.

II. General Background and Terminology

We hereby propose a general terminology that makes it possible to describe fMRI and MEG/EEG analyses from a more theoretical, yet common framework.

A. Brain Units and Functional Processes

As a consequence of the intrinsic difference between MEG, EEG, and fMRI, the spatial and temporal resolution vary greatly between these modalities.

In fMRI, typical regions are composed of voxels or regions selected according to anatomical and/or functional criteria. Due to the rather important size of the voxels and the limited precision of the detector, brain localization of functional regions cannot usually go under a few millimeters. In EEG or MEG, the signal measured is much more local, originating from neuron columns. However, due to complexity of the inverse problem, many analyses remain at the level of recording sites in EEG/MEG. To account for all these cases, the functional extents considered (regions, neuron columns, or recording sites) will henceforth be known as *brain units*. A brain unit can be thought of as the amount of brain tissue giving rise to the activity recorded in a single time series. It is the information-theoretical pendant of "elemental tissue volume" put forward by [10].

Each unit is then associated with a *functional process*, or phenomenon, that characterizes it. In fMRI, it can be thought of as the BOLD contrast measured at a particular time sample. In MEG/EEG, it could be the intensity of the electromagnetic field related to the brain unit considered, recorded on the scalp, or reconstructed on the cortex. In a dynamical system approach, it could also be taken as vectors reconstructed from the measured signals into the embedding phase space.

Definition and selection of brain units and related functional processes are a crucial step in functional interactivity analysis, and the literature is very rich on this topic. The effects of these choices on the framework proposed here are further examined in the discussion.

B. Defining Functional Brain Interactivity

Analysis of functional brain connectivity can now be tackled. Transposing what has previously been proposed in an other area [62] in terms of information theory, we propose that functional brain interactivity be defined as *all potential or real information exchanges between brain units*.

In a given context, information exchanges that are observed within a distributed network are real. On the other hand, if one considers all possible contexts and, hence, all potential interactions that could take place, potential information exchanges then become relevant. For instance, a simple hand movement performed by a healthy subject is processed by the standard motor network (real exchanges). Considering brain plasticity, as potentially induced on this same subject by, e.g., motor skill learning, stroke, or surgery, implies various possible network reorganizations; assessing how a simple hand movement would be processed in such conditions necessitates the handling of potential exchanges.

Of course, this definition varies greatly, depending on the spatial and temporal scales at which we examine brain activity and what we consider as functional units and as information exchange. For instance, transient synchronies between neuron populations, which are observable in MEG/EEG and interpreted as an evidence of functional interactivity, do not necessarily imply a change of functional interactivity as measured from fMRI time courses. On the contrary, a strong correlational connectivity between two brain regions in fMRI may appear much less coherent at a neuronal scale. However, this approach possesses two interesting features: generality and flexibility. Because it is general, it releases us from any constraint related to a particular imaging method—that would otherwise influence us toward the choice of a quantity that is operational, yet not necessarily general or really relevant. On the other hand, this definition can be equally well applied to fMRI and MEG/EEG. The difference lies in the definition of information exchange. Further investigation will cast some light on this issue, which will be recalled in the discussion.

C. Common Example and Objective

Our objective is an attempt to understand how information exchange can be expressed in neuroimaging or, rather, to find the necessary conditions that make information exchange a well-defined concept. To exemplify our approach, we consider the three following brain units in the visual pathway: 1) V1, 2) V2, and 3) V5. We add a fourth unit (HG), which is the primary auditory region on Heschl's gyrus, for a model composed of a total of $N = 4$ regions. We also assume that we are given four processes $Y_n(t)$, $n = 1, \ldots, 4$, each process corresponding to a brain unit.

We restrict our attention to the wide variety of problems that can be considered in a probabilistic framework. Probability

theory is a consistent, general, and very convenient framework that allows to take uncertainty into account. Whether in the form of probability density functions or statistics, most problems of functional neuroimaging data analysis are embedded in a probabilistic framework. For this reason, we can assume, without much restriction, that it is possible to associate each state of $\boldsymbol{Y}(t) = (Y_n(t))$ with a probability distribution $\Pr(\boldsymbol{Y}(t))$.

Given the increasing literature on functional interactivity in both fMRI and MEG/EEG, there are clear indicators that the concepts proposed so far can indeed extract a certain part of interactivity. Information exchange must, therefore, at least partly be expressible in such terms. Therefore, our first objective is to find what these definitions have in common. Note that the actual existence of similarities have already been hinted upon in [37] for MEG/EEG. Using simulations performed with a neural mass model [63], striking resemblances were found between various measures of connectivity.

A first obvious way to classify and relate the tools for interactivity analysis is by their mathematical content. For instance, correlation between two functional units in fMRI and MEG/EEG is defined by the same mathematical notion, namely, the correlation between the two unit time courses. Effective connectivity, whether in fMRI or MEG/EEG, strongly relies on the *a priori* definition of directed graphical models and linear relationships.

A further, more subtle classification can be performed by considering the relative weight of the prior model and the data for each method. On the one hand, effective connectivity provides an *a priori model* relating the time course of the different regions. The model is defined based on previous knowledge of the anatomical and functional circuitry underlying the functional task under investigation. On the other hand, correlation, mutual information, and coherence all clearly define interaction between two regions from the data. For instance, almost no prior knowledge relative to structural interactions in the motor network is required to calculate correlation maps with a seed region in M1. This distinction will structure our exploration: We will first relate all data-driven measures introduced to correlation and then inspect the connections between model-based and data-driven concepts under very simple hypotheses.

III. Relating Data-Driven Measures to Each Other

In this section, we show that, despite very distinctive definitions, temporal correlation, nonlinear correlation, mutual information, generalized synchronization, phase synchrony, coherence, and PLV indeed essentially measure the same quantity as correlation. In order to do so, we model $(\boldsymbol{Y}(t))_{t=1,\ldots,T}$ as being T (T large) i.i.d. realizations of a multivariate Gaussian variable $\boldsymbol{Z}$ with mean $\boldsymbol{\mu} = (\mu_n)$ and covariance matrix $\boldsymbol{\Sigma} = (\Sigma_{ij})$. For convenience, we set $\Sigma_{nn} = \sigma_n^2$ and $\Sigma_{ij} = \rho_{ij}\sigma_i\sigma_j$. Our objective is then to relate all measures mentioned to ρ_{ij} and ρ_{ij} only.

A. Temporal Correlation

The sample mean and variance of $Y_n(t)$ are defined by

$$m_n = \frac{1}{T}\sum_t Y_n(t)$$

and

$$v_n = \frac{1}{T}\sum_t (Y_n(t) - m_n)^2$$

respectively. As to the sample covariance between $Y_i(t)$ and $Y_j(t)$, it reads

$$v_{ij} = \frac{1}{T}\sum_t (Y_i(t) - m_i)(Y_j(t) - m_j).$$

Last, the temporal correlation between $Y_i(t)$ and $Y_j(t)$ is given by

$$c_{ij} = \frac{v_{ij}}{\sqrt{v_i v_j}}.$$

It can be shown that this quantity converges to ρ_{ij} for large sample size T [64], i.e.,

$$c_{ij} = \rho_{ij}.$$

B. Nonlinear Correlation Coefficient

The nonlinear correlation h_{ij}^{2*} is a function of the minimum residual variance after parametric regression (e.g., [32], [33]). Given a function $h_{\boldsymbol{\theta}}(y)$ of parameter $\boldsymbol{\theta}$ and a time shift τ, one first determines the parameter $\widehat{\boldsymbol{\theta}}$ so that the regression model

$$Y_j(t+\tau) = h_{\boldsymbol{\theta}}(Y_i(t))$$

best fits the data by calculation of

$$\widehat{\boldsymbol{\theta}}_{ij}(\tau) = \arg\min_{\boldsymbol{\theta}} E[(Y_j(t+\tau) - h_{\boldsymbol{\theta}}(Y_i(t)))^2]. \quad (1)$$

One then derives the following quantity:

$$h_{ij}^2(\tau) = 1 - \frac{\mathrm{Var}[Y_j(t+\tau) - h_{\widehat{\boldsymbol{\theta}}_{ij}(\tau)}(Y_i(t))]}{\mathrm{Var}[Y_j(t+\tau)]}. \quad (2)$$

The nonlinear correlation coefficient is then given by

$$h_{ij}^{2*} = \max_{\tau} h_{ij}^2(\tau). \quad (3)$$

Assuming linearity of the regression function in mean-shifted coordinates, i.e.,

$$\boldsymbol{\theta} = (a, b) \text{ and } h_{\boldsymbol{\theta}}(y) = \mu_j + a + b(y - \mu_i) \quad (4)$$

we obtain (see Appendix A for details)

$$h_{ij}^{2*} = \rho_{ij}^2. \quad (5)$$

In this case, the nonlinear correlation coefficient is nothing but the squared correlation coefficient; it is represented in Fig. 1(a).

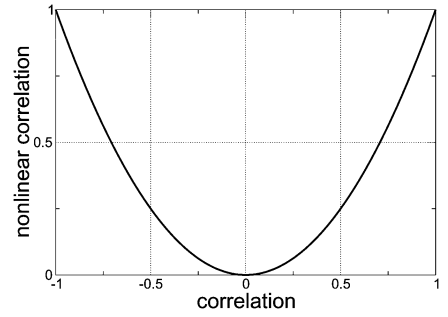
C. Mutual Information

The mutual information between two regions i and j is defined as [65]

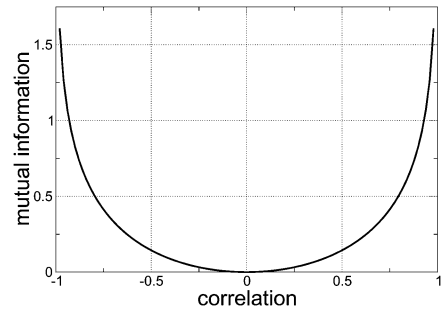
$$\mathrm{MI}_{ij} = H(Y_i(t)) + H(Y_j(t)) - H(Y_i(t), Y_j(t)) \quad (6)$$

where $H(X)$ is the entropy associated to $\Pr(X)$, i.e.,

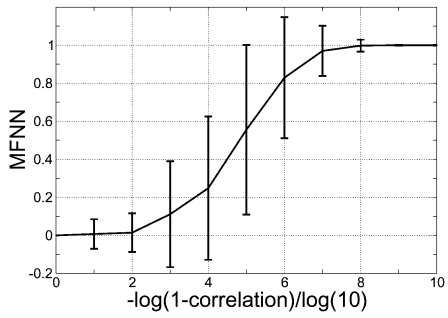
$$H(X) = -\int \Pr(X) \cdot \ln \Pr(X) dX. \quad (7)$$



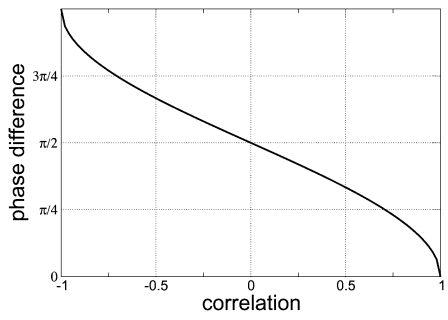
(a)



(b)



(c)



(c)

Fig. 1. Functional relationship between correlation ρ_{ij} and (a) nonlinear correlation h_{ij}^{2*}, (b) mutual information MI_{ij}, (c) generalized synchronization MFNN_{ij}, and (d) phase difference ψ_{ij} when investigating linear relationships between i.i.d. multidimensional Gaussian variables.

Under our hypotheses, the expression for the mutual information between two regions is simplified as

$$\mathrm{MI}_{ij} = -\frac{1}{2}\ln(1-\rho_{ij}^2) \tag{8}$$

(see Appendix B for a sketch of proof), and mutual information is a function of correlation, as represented in Fig. 1(b).

D. Generalized Synchronization

Generalized synchronization between two signals $Y_i(t)$ and $Y_j(t)$ emerges when the notions of neighboring, distance, and ordering are similar (or, at least, comparable) for $Y_i(t)$ and $Y_j(t)$ [38], [40]. To test for generalized synchronization, we use the mutual false neighbors (MFNN) parameter [38], although other measures could be applied to the same goal [39], [40]. For each $Y_n(t)$, we denote by $Y_n(\tau_{n,t})$ its nearest neighbor, i.e.,

$$\tau_{n,t} = \arg\min_u |Y_n(t) - Y_n(u)|.$$

The MFNN parameter between $Y_i(t)$ and $Y_j(t)$ is then defined as

$$\mathrm{MFNN}_{ij} = \frac{|Y_i(t) - Y_i(\tau_{i,t})|}{|Y_j(t) - Y_j(\tau_{i,t})|} \cdot \frac{|Y_j(t) - Y_j(\tau_{j,t})|}{|Y_i(t) - Y_i(\tau_{j,t})|}.$$

Although the closed-form distribution of MFNN is not obvious, it is possible to use numerical simulations instead. More precisely, we draw samples $\boldsymbol{Y}(t) = (Y_i(t), Y_j(t))$ according to $\mathcal{N}(\mathbf{0}, \boldsymbol{\Sigma})$, with

$$\boldsymbol{\Sigma} = \begin{pmatrix} 1 & \rho \\ \rho & 1 \end{pmatrix} \tag{9}$$

calculate the corresponding MFNN_{ij} for each t, and then average across t to obtain a sample mean $\pm$ standard error of the MFNN. This procedure was then repeated with increasing values of ρ. The results are summarized in Fig. 1(c).

In this case, generalized synchronization is, hence, an increasing function of the correlation. Note that since we had i.i.d. samples, the values taken by ρ had to be very close to 1 to show this effect.

E. Phase Synchronization

There exist many ways to define phase synchronization [40]. For the sake of simplicity, we will model each brain unit n as undergoing a perfect oscillation at frequency ν_n and phase ϕ_n [58]:

$$Y_n(t) = a_n \cos(2\pi\nu_n t + \phi_n). \tag{10}$$

In this model, the phase difference between two regions is then, by definition, equal to

$$\psi_{ij} = \phi_i - \phi_j. \tag{11}$$

Calculating the covariance matrix related to the temporal model defined in (10) and equating it to that of $\boldsymbol{Z}$ leads to a matrix $\boldsymbol{\Sigma}$ with variances

$$\sigma_n^2 = \frac{a_n^2}{2} \tag{12}$$

and covariances[1]

$$\Sigma_{ij} = \begin{cases} \frac{a_i a_j \cos(\psi_{ij})}{2}, & \text{if } \nu_i = \nu_j \\ 0, & \text{otherwise} \end{cases} \tag{13}$$

or, equivalently, correlations of

$$\rho_{ij} = \begin{cases} \cos(\psi_{ij}), & \text{if } \nu_i = \nu_j \\ 0, & \text{otherwise} \end{cases} \tag{14}$$

[1]This result differs from [58] by a factor 1/2.

(see Appendix C for a proof of this assertion). In words, correlation is equal to the cosine of the phase difference; for two signals of identical frequency, a zero correlation is equivalent to a zero phase difference, i.e., a phase quadrature. For $\nu_i = \nu_j$, this relationship also reads

$$\psi_{ij} = \arccos(\rho_{ij}) \tag{15}$$

and is illustrated in Fig. 1(d).

If the phase difference has probability distribution $f(\psi_{ij})$, the correlation between two signals of the same frequency will vary from epoch to epoch, according to distribution $g(\rho_{ij})$ so that

$$f(\psi_{ij})d\psi_{ij} = g(\rho_{ij})d\rho_{ij}. \tag{16}$$

The mean phase difference will, hence, be given by

$$\begin{aligned} E[\psi_{ij}] &= \int \psi_{ij} \cdot f(\psi_{ij})d\psi_{ij} \\ &= \int \arccos(\rho_{ij}) \cdot g(\rho_{ij})d\rho_{ij} \end{aligned} \tag{17}$$

which is, again, a function of ρ_{ij} only.

F. Coherence and PLV

Our goal is now to estimate the consistency of the phase lock over E epochs. Coherence is usually used to answer this question [27]. To this end, we switch from time to frequency representation of the processes and assume that the signals have the following spectral representations:

$$S_{n,e}(\nu) = \beta_{n,e} \cdot e^{i\phi_{n,e}}, \quad e = 1, \ldots, E \tag{18}$$

e.g., obtained by the Fourier transform. The coherence is then given by [27]

$$\gamma_{ij}^2(\nu) = \frac{\left| \frac{1}{E} \sum_{e=1}^{E} S_{i,e}(\nu) S_{j,e}(\nu)^* \right|^2}{\left[\frac{1}{E} \sum_{e=1}^{E} S_{i,e}(\nu) S_{i,e}(\nu)^* \right] \left[\frac{1}{E} \sum_{e=1}^{E} S_{j,e}(\nu) S_{j,e}(\nu)^* \right]}. \tag{19}$$

Assuming that $\beta_{n,e} = \beta_n$ (i.e., that $\beta_{n,e}$ does not depend on e), this expression simplifies into

$$\gamma_{ij}^2(\nu) = \left| \frac{1}{E} \sum_{e=1}^{E} e^{i\psi_{ij,e}} \right|^2 \tag{20}$$

where we set $\psi_{ij,e} = \phi_{i,e} - \phi_{j,e}$; in this particular case, the coherence boils down to the PLV [30], [31]. If all $\psi_{ij,e}$ are i.i.d distributed according to $f(\psi_{ij})$, then when the number of epochs E is large

$$\begin{aligned} \gamma_{ij}^2(\nu) &= f(\rho_{ij}) \\ &= \left[\int \cos(\psi_{ij}) \cdot f(\psi_{ij})d\psi_{ij} \right]^2 \\ &\quad + \left[\int \sin(\psi_{ij}) \cdot f(\psi_{ij})d\psi_{ij} \right]^2 \end{aligned} \tag{21}$$

cf. Appendix D. This is again a function of ψ_{ij} only and, hence, of ρ_{ij}, according to (15).

TABLE I
SUMMARY OF RELATIONSHIPS BETWEEN VARIOUS MEASURES OF FUNCTIONAL CONNECTIVITY AND CORRELATION

measure of interaction	expression	no interaction	maximum interaction
temporal correlation	$c_{ij} = \rho_{ij}$	0	± 1
nonlinear correlation	$h_{ij}^{2*} = \rho_{ij}^2$	0	1
mutual information	$\mathrm{MI}_{ij} = -\frac{1}{2}\ln\left(1-\rho_{ij}^2\right)$	0	$+\infty$
generalized synchronization	not in close form	0 or $+\infty$	1
coherence	$\gamma_{ij}^2(\nu) = f(\rho_{ij})$	0	1

G. Summary

Through the previous examples, we showed that temporal correlation, nonlinear correlation, mutual information, generalized synchronization, and phase synchrony are all expressions of correlation; their expressions have been gathered in qTable I. Coherence and PLV are, rather, measures of the uncertainty on the correlation but are still functions of ρ_{ij}.

These quantities have been introduced to account for nonlinearities, non-Gaussian distributions, and temporal dependence; however, in the case of linear interactions in i.i.d. multivariate Gaussian variables, they all measure the same quantity or function thereof.

IV. Relating Model-Based to Data-Driven Definitions

To complete the investigation, we now try to relate effective to correlational connectivity.

A. Identifying the Gap Between Effective and Correlational Connectivity

The term "effective connectivity" has so far only been given to model-based methods for connectivity investigations, such as SEM or DCM. In this section, we delve into the potential interaction structures that can be generated by such models. Our purpose is to pinpoint what patterns cannot be rendered by functional connectivity; knowing this, what can be done to palliate this lack?

To this end, we consider SEM, which is the simplest way to model effective connectivity; it can be used when one is seeking linear relationships between i.i.d. Gaussian variables. In this setting, we demonstrated earlier that the information carried by all measures of functional connectivity introduced in this paper boil down to correlation; without loss of generality, we can, hence, concentrate our attention on comparing SEM with correlation.

1) Structural Modeling: We propose the following, fictitious, structural model on the four brain units and processes defined earlier:

$$\begin{aligned} Y_1(t) &= E_1(t) \quad \text{a)} \\ Y_2(t) &= \lambda \cdot Y_1(t) + E_2(t) \quad \text{b)} \\ Y_3(t) &= \mu \cdot Y_2(t) + E_3(t) \quad \text{c)} \\ Y_4(t) &= E_4(t) \quad \text{d).} \end{aligned}$$

For instance, this could possibly be a structural model for movement-related information transfer in the visual pathway, from

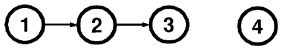


Fig. 2. Structural model.

V1 to V2 to V5, during purely visual stimuli. The resulting model is represented in Fig. 2.

Different patterns of connectivity emerge from this model. For instance, it seems obvious that regions 1 and 4 do not interact. On the other hand, regions 1 and 2 do interact, as do regions 1 and 3. On a closer look, the last two examples can be further differentiated as follows: While regions 1 and 2 directly interact (since there exists a direct relationship between these two regions, represented by an arrow), regions 1 and 3 only indirectly interact, as indicated by the absence of arrows between the two regions.

2) Probabilistic Modeling: The noise $(\boldsymbol{E}(t))$, with

$$\boldsymbol{E}(t) = (E_1(t), E_2(t), E_3(t), E_4(t)), \quad t = 1, \ldots, T \tag{22}$$

is now assumed to be composed of T i.i.d. realizations of a multivariate Gaussian variable $\boldsymbol{F}$. For the sake of simplicity, and without loss of generality, we assume that $\boldsymbol{F}$ has a unit covariance matrix. In matrix form, the relationships (a)–(d) read

$$\boldsymbol{Y}(t) = \boldsymbol{M}\boldsymbol{Y}(t) + \boldsymbol{E}(t) \tag{23}$$

where $\boldsymbol{M}$ is a function of (λ, μ). A usual resolution scheme to solve for (λ, μ) is to represent the structural equations in matrix form as

$$[\boldsymbol{I} - \boldsymbol{M}]\boldsymbol{Y}(t) = \boldsymbol{E}(t) \tag{24}$$

where $\boldsymbol{I}$ is the identity matrix. (λ, μ) can then be estimated as the vector maximizing a log-likelihood function. However, since our objective is not estimation, our approach varies from there on. Rather, we try to calculate what distribution $\boldsymbol{Y}(t)$ follows. Since we know the probability distribution of $\boldsymbol{E}(t)$, this can be achieved by expressing $\boldsymbol{Y}(t)$ as a linear function of $\boldsymbol{E}(t)$ according to the structural model, leading to

$$\boldsymbol{Y}(t) = \boldsymbol{T}\boldsymbol{E}(t). \tag{25}$$

The expression of $\boldsymbol{T} = (\boldsymbol{I} - \boldsymbol{M})^{-1}$ is detailed in Appendix E. From a property of Gaussian distributions [64], and since $\boldsymbol{E}(t)$ is Gaussian distributed, it follows that $(\boldsymbol{Y}(t))_{t=1,\ldots,T}$ is also composed of T i.i.d. realizations of a multivariate Gaussian variable $\boldsymbol{Z}$ with mean $\boldsymbol{0}$ and covariance matrix $\boldsymbol{\Sigma} = \boldsymbol{T}\boldsymbol{T}^t$ (see Appendix E for its exact expression).

3) Correlation: The structural model being set, we propose to calculate the correlation between regions 1 and 4, as well as between regions 1 and 2 and regions 1 and 3. Correlation can easily be obtained by normalization of the covariance matrix $\boldsymbol{\Sigma}$:

$$\mathrm{Corr}[Z_1, Z_4] = 0 \tag{26}$$

$$\mathrm{Corr}[Z_1, Z_2] = \frac{\lambda}{\sqrt{\lambda^2 + 1}} \neq 0 \tag{27}$$

$$\mathrm{Corr}[Z_1, Z_3] = \frac{\lambda\mu}{\sqrt{(\lambda^2 + 1)\mu^2 + 1}} \neq 0. \tag{28}$$

In words, a lack of interaction for the structural model between regions 1 and 4 can be characterized by a zero correlation between these two regions. On the other hand, an interaction for the structural model between regions 1 and 2 and regions 1 and 3 implies a nonzero correlation between these two regions. Yet, correlation is not able to discriminate between the intrinsic difference of interaction between both region pairs.

B. Conditional Correlation and Mediated Interaction

Functional connectivity can translate certain patterns of effective connectivity but fail to discriminate between others. So far, we have, hence, been able to interpret a lack of interaction, i.e., a zero correlation coefficient. If this coefficient is not equal to zero, we obtain a correlation whose interpretation remains problematic, but can we go further? We can consider two cases: Either both regions directly interact—as regions 1 and 2 do—, or this interaction is indirect, i.e., it is *mediated* by other regions—as interactivity between regions 1 and 3 is mediated by region 2. Correlation, however, cannot differentiate between these two cases, as we saw earlier.

As (marginal) correlation was defined, it is possible to define conditional covariance and correlation [64]. For instance, $\mathrm{Cov}[Z_1, Z_2|Z_3]$ is the conditional covariance of regions 1 and 2, given region 3. Normalizing this conditional covariance leads to the conditional correlation $\mathrm{Corr}[Z_1, Z_2|Z_3]$. Going back to our example, we obtain the following conditional correlations (see Appendix F for detailed calculations):

$$\mathrm{Corr}[Z_1, Z_2|Z_3] = \frac{\lambda}{\sqrt{(\lambda^2 + 1)(\mu^2 + 1)}} \neq 0 \tag{29}$$

$$\mathrm{Corr}[Z_1, Z_3|Z_2] = 0. \tag{30}$$

Conditional correlation is hence able to tell the direct 1–2 interaction apart from the indirect 1–3 interaction. In the first case, it assigns a nonzero correlation between regions 1 and 2 when conditioned on region 3; in the second case, the correlation between regions 1 and 3 is zero when conditioned on region 2, hinting that, given region 2, regions 1 and 3 behave independently and, hence, presumably do not exchange information.

C. Summary

In this section, we showed that some patterns of interaction present in the model of effective connectivity could be discriminated by a zero/nonzero marginal correlation. Yet, the complexity of connectivity could not be apprehended by marginal correlation. To remedy this flaw, we resorted to conditional correlation and mediated interaction. All calculations of correlation performed have been summarized in Table II.

$\mathrm{Corr}[Z_1, Z_4]$ is zero, and regions 1 and 4 indeed do not interact. Correlation can therefore be interpreted as a quantity that is representative of how much (global) interactivity there exists between two regions. Similarly

$$\mathrm{Corr}[Z_1, Z_3|Z_2] = 0 \tag{31}$$

the conditional correlation of regions 1 and 3 given region 2, is zero if all interactions between regions 1 and 3 are mediated by region 2. Consequently, $\mathrm{Corr}[Z_1, Z_3|Z_2]$ comes up as a natural

TABLE II
SUMMARY OF THE INTERACTION PATTERNS EXAMINED AND CORRESPONDING VALUES OF INTERACTION MEASURES

regions	interaction?	correlation	conditional correlation
1 and 4	no	$\mathrm{Corr}[Z_1, Z_4] = 0$	
1 and 2	yes, direct	$\mathrm{Corr}[Z_1, Z_2] \neq 0$	$\mathrm{Corr}[Z_1, Z_2 \vert Z_3] \neq 0$
1 and 3	yes, indirect (mediated by 2)	$\mathrm{Corr}[Z_1, Z_3] \neq 0$	$\mathrm{Corr}[Z_1, Z_3 \vert Z_2] = 0$

measure of how much interaction between regions 1 and 3 is *not* mediated by region 2.

We, hence, demonstrated that if all interactions between two regions i and j are mediated by a third region or set of regions $\mathcal{R}$, then we have

$$\mathrm{Corr}[Z_i, Z_j | \boldsymbol{Z}_{\mathcal{R}}] = 0 \tag{32}$$

where $\boldsymbol{Z}_{\mathcal{R}}$ stands for $(Z_n)_{n \in \mathcal{R}}$. If some interaction between regions i and j is not mediated by regions in $\mathcal{R}$, then a natural measure of how much interaction is not mediated by this set of regions is given by $\mathrm{Corr}[Z_i, Z_j | \boldsymbol{Z}_{\mathcal{R}}]$. This quantity can easily be derived from $\boldsymbol{\Sigma}$ by first calculating the conditional covariance matrix

$$\mathrm{Var}[\boldsymbol{Z}_{\{i,j\}} | \boldsymbol{Z}_{\mathcal{R}}] = \boldsymbol{\Sigma}_{\{i,j\}} - \boldsymbol{\Sigma}_{\{i,j\},\mathcal{R}} \boldsymbol{\Sigma}_{\mathcal{R}\mathcal{R}}^{-1} \boldsymbol{\Sigma}_{\{i,j\},\mathcal{R}}^{t}. \tag{33}$$

Normalizing this 2-by-2 conditional covariance matrix then directly yields the desired conditional correlation coefficient.

V. DISCUSSION

Despite their distinctive characteristics and the lack of established model linking both modalities, there exist formal connections between MEG/EEG and fMRI data analysis since both share common models and tools. For instance, the General Linear Model (GLM) is ubiquitous in both fMRI activation detection procedures [66], [67] and MEG/EEG resolution of the inverse problem [9], [68], [69], in spite of the fact that the GLM does not have the same role in fMRI and EEG inverse problems. It is hoped that the analysis led in the present paper for functional interactivity will help build another strong formal link between fMRI and MEG/EEG.

The lack of an established physiological model linking MEG/EEG and fMRI prevents them from providing a common definition of information exchange. Nonetheless, if one accepts that such a concept exists, the connection can be made at a formal level once again. We first provided a theoretical framework, defining brain units and brain processes. We also defined functional brain interactivity as all real or potential information exchanges between brain units. We then showed that, under the assumption of linear relationships between i.i.d. multivariate Gaussian variables, all measures of functional connectivity introduced in this paper—temporal correlation, nonlinear correlation, mutual information, generalized synchronization, phase synchrony, coherence, and PLV—indeed extract the same information from the data, namely correlation, or a function thereof. These measures are generalizations of correlation that have been introduced in order to compensate for the lack of one or several of the above-mentioned assumptions. Indeed, being able to precisely state the assumptions underlying each measure of connectivity is of importance for functional brain interactivity investigation and should be examined thoroughly.

To investigate further the gap that remains between models of effective connectivity and measures of functional connectivity, we considered a very simple structural model in the framework of SEM. SEM specifically requires the above-mentioned assumptions to be valid; all measures of functional connectivity, hence, boil down to correlation. Starting from there, we showed that some patterns of effective connectivity could be characterized by correlation, whereas others could not. A close inspection showed that correlation was not able to differentiate *direct* from *mediated* interactions. To remedy this flaw, we introduced conditional correlation that proved capable of making such a difference.

Indeed, the necessity of conditioning is omnipresent in Bayesian inference theory [70], [71], where only conditional probabilities have a meaning. An assertion can be true or false, depending on the context; two statements can be correlated or not conditional on the background assumptions. Introduction of mediated interaction and conditional correlation is the acknowledgment of this reality.

This takes us back to the definition of functional brain interactivity that we set in Section II-B and the measures of functional connectivity between two units i and j examined in this paper. Note that all of them are only defined in terms of Y_i and Y_j, i.e., they all share the abstract functional form

$$\kappa(Y_i, Y_j). \tag{34}$$

Consequently, they calculate the connectivity between units i and j independently of the remaining units, which could be associated to other processes or even modified or changed without changing $\kappa(Y_i, Y_j)$. On the contrary, modifying a structural model anywhere has an influence on the strength of all links and, hence, on effective connectivity. We, hence, strongly suspect that all functions that have the form of (34) can only partially account for effective connectivity, however complex and able of handling nonlinearities, non-Gaussianity, or temporal correlation they might be. On the other hand, connectivity measures of the form

$$\epsilon(Z_1, \ldots, Z_N) \tag{35}$$

are more likely to give a fair representation of effective connectivity. From this perspective, it would be of interest to investigate further what measures are of the form of (35). Temporally conditioned correlation has already been defined, both in fMRI [56] and in MEG/EEG [72]; conditioning on the stimulus has already been examined in fMRI [73]. To our knowledge, very few measures of interactivity between two regions try to condition on a third region or set of regions. Only partial coherence [73], [74] and directed transfer functions [43] were applied to this goal. In addition, phase synchronization was utilized in a multidimensional context [75]. How they could relate to our framework remains a topic to be further examined.

A major issue is to be able to infer the true marginal or conditional correlation structure from neuroimaging data.

Working with theoretical measures and models exempted us from coping with this question; yet it should be addressed to be able to analyze real data. There already exists methods to estimate correlation coefficients, through mappings and asymptotic results (e.g., Fisher test) or bootstrap methods; how such methods should be generalized to conditional correlation remains an open issue. The interdependence between estimates should also be considered, i.e., how the inferences made on qualitatively different conditional correlations (e.g., $\mathrm{Corr}[Z_1, Z_4]$ and $\mathrm{Corr}[Z_1, Z_2|Z_3]$) influence each other.

This being said, it is crucial to stress that the given definition of functional brain interactivity is only meaningful in a given context, i.e., with well-defined brain units. This seems like a perfunctory remark, but it implies that there is no such thing as absolute direct or mediated interaction; both notions, again, only make sense in a given context, with given brain units. Mutual information, for instance, measures information exchanges when only two units are considered; for three or more units, conditional measures should be introduced.

Oddly enough, it is actually a lack of information that always seems easier to translate. A zero marginal correlation translates a lack of interaction, but nothing can be said relative to a nonzero correlation. A zero conditional correlation indicates a mediated interaction, whereas a nonzero coefficient only requires more investigation. We believe that this originates from our inability to precisely and uniquely define what is meant by information exchange. Note that there also remain other aspects that should be considered when dealing with zero correlation in MEG/EEG, such as the influence of volume conduction and the influence of active reference electrodes.

As we pointed out in Section II-A, the choice of the basic entities whose relationships are examined is of importance, and changes of what is thought to be a legitimate brain region may, in some cases, have dramatic influence on the functional analysis. [10] provides a discussion of the potential influence of this factor on MEG/EEG or a BOLD fMRI signal.

The analysis also strongly depends on the choice of the quantity that is associated with each region and how it should be estimated. This debate is still vivid in fMRI data analysis. Regions are mostly selected from the activation map, but correlation maps tend to gain increasingly more influence [76]. Another question is what the signal that "represents" the region should be: the time course of the most significantly activated voxel in the region or the spatial mean of time courses over the whole region [77]? Once this has been addressed, we must still decide on which part connectivity analysis should be performed: the raw signal or the filtered signal? If filtered, what components should be kept? It is not yet obvious which part of the signal carries the connectivity information [78]–[80]. Generative models, that have recently been applied to the field of neuroimaging [81], [82], might prove to be an elegant way to solve this issue in both MEG/EEG and fMRI. Nonetheless, regardless of the final decision as to what should be analyzed, the proposed framework remains valid.

A last point that we did not mention in this paper is the research of causal relationships. This is a challenging issue, and it would be of interest to see if and how it would fit in this framework. Note, however, that, as there were direct and indirect interactions between variables, there might be direct and indirect causal influences. For instance, Granger causality, as applied in [44], is of the form of (34) and is, hence, unlikely to translate to a direct causal effect.

VI. Conclusion

The first step of our investigation consisted of setting a common terminology for functional brain connectivity, and we proposed to consider *brain units* and *brain processes*. Functional brain interactivity was then defined as *all potential or real information exchanges between brain units*. We distinguished model-based effective connectivity from data-driven measures of functional connectivity. We then showed that temporal correlation, nonlinear correlation, mutual information, generalized synchronization, phase difference, coherence, and PLV all measure the same quantity, namely, correlation, under the premise that we are seeking linear relationships between i.i.d. multivariate Gaussian variables. Using SEM under such assumptions, we demonstrated that these quantities are insufficient to account for the variety of interaction patterns that can appear in models of effective connectivity and compensated for this weakness by introducing conditional correlation, which was shown to be strongly related to mediated interaction. Within this setting, most patterns of connectivity can be expressed.

Further investigation includes a closer consideration of the hypotheses required for each measure of interactivity to be valid. Finding a framework that can account for the totality of them should provide a good direction for another step toward a common framework for joint fMRI and MEG/EEG functional brain connectivity exploration. Generalizing the measure of conditional correlation to cases where the assumptions of linearity, Gaussianity, and independence do not hold would provide powerful tools to perform exploratory analysis of effective connectivity.

Appendix A
Nonlinear Correlation Coefficient

We first perform the regression, through minimization of the mean square error

$$\mu(a,b) = E\left[[Y_j(t+\tau) - (\mu_j + a + b(Y_i(t) - \mu_i))]^2\right].$$

This expression can be decomposed into

$$E\left[(Y_j(t+\tau) - \mu_j)^2\right] + E\left[(a + b(Y_i(t) - \mu_i))^2\right] - 2E[(Y_j(t+\tau) - \mu_j)(a + b(Y_i(t) - \mu_i))].$$

The second and third expectations can be further expanded as

$$a^2 + 2abE[Y_i(t) - \mu_i] + b^2 E\left[(Y_i(t) - \mu_i)^2\right]$$

and

$$aE[Y_j(t+\tau) - \mu_j] + bE[(Y_j(t+\tau) - \mu_j)(Y_i(t) - \mu_i)]$$

respectively. By definition, we then have

$$\begin{aligned} E[Y_i - \mu_i] &= 0 \\ E[Y_j(t+\tau) - \mu_j] &= 0 \\ E\left[(Y_i(t) - \mu_i)^2\right] &= \sigma_i^2 \\ E\left[(Y_j(t+\tau) - \mu_j)^2\right] &= \sigma_j^2. \end{aligned}$$

As far as $E\left[(Y_j(t+\tau)-\mu_j)(Y_i(t)-\mu_i)\right]$ is concerned, it is equal to

$$\begin{cases}\Sigma_{ij}=\rho_{ij}\sigma_i\sigma_j, & \text{if } \tau=0\\ 0, & \text{otherwise.}\end{cases}$$

Bringing all results together yields

$$\mu(a,b)=\begin{cases}a^2\sigma_i^2-2a\rho_{ij}\sigma_i\sigma_j+b^2+\sigma_j^2, & \text{if } \tau=0\\ a^2\sigma_i^2+b^2+\sigma_j^2, & \text{otherwise.}\end{cases}$$

When $\tau\neq 0$, the minimum is attained for $(a,b)=(0,0)$, and the expected square mean is

$$\mu(a,b)=\sigma_j^2.$$

For $\tau=0$, we set $\widehat{a}=\rho_{ij}\sigma_j/\sigma_i$ and complete the quadratic form in a, leading to

$$\mu(a,b)=\sigma_i^2(a-\widehat{a})+b^2+\sigma_j^2-\sigma_i^2\widehat{a}^2.$$

This loss function is minimum for $a=\widehat{a}$ and $b=0$. In this case, we have

$$\mu(a,b)=\sigma_j^2\left(1-\rho_{ij}^2\right).$$

Since $\mathrm{Var}[Y_j(t+\tau)]=\sigma_j^2$, we finally obtain that

$$h_{ij}^2=\begin{cases}\rho_{ij}^2, & \text{if } \tau=0\\ 0, & \text{otherwise}\end{cases}$$

for a nonlinear correlation coefficient of

$$h_{ij}^{2*}=\rho_{ij}^2.$$

Appendix B
Mutual Information

The entropy of a Gaussian variable is equal to [83]

$$H(Z_n)=\frac{1}{2}\ln\left(2\pi\sigma_n^2\right).$$

As far as the mutual information is concerned, it yields

$$\mathrm{MI}_{ij}=\frac{1}{2}\ln\left(\frac{\sigma_i^2\sigma_j^2}{\det(\mathrm{Cov}[\boldsymbol{Z}_{\{i,j\}}])}\right)$$

where $\mathrm{Cov}\left[\boldsymbol{Z}_{\{i,j\}}\right]$ is the 2-by-2 covariance matrix of (Z_i,Z_j). Since $\det\left(\mathrm{Cov}\left[\boldsymbol{Z}_{\{i,j\}}\right]\right)$ is equal to

$$\Sigma_{ii}\Sigma_{jj}-\Sigma_{ij}^2=\sigma_i^2\sigma_j^2\left(1-\rho_{ij}^2\right)$$

the expression for mutual information can be simplified to yield

$$\mathrm{MI}_{ij}=-\frac{1}{2}\ln\left(1-\rho_{ij}^2\right).$$

Appendix C
Correlation Between Two Shifted Cosines

As in many problems of Bayesian analysis where the probability density function does not belong to any known density function, we can resort to numerical sampling to approximate its various moments. For instance, assuming that we have drawn L samples $\left(Z_n^{[l]}\right)_{l=1,\ldots,L}$, approximation of the mean can be performed by the sample mean, i.e.,

$$\mu_n=E[Z_n]\approx\frac{1}{L}\sum_{l=1}^{L}Z_n^{[l]}.$$

It now remains to sample according to the right probability distribution. However, this is straightforward, since we equate the moments of $\boldsymbol{Z}$ with that of $\boldsymbol{Y}(t)$; calculation of $Y_n(t)$ for $t=l\cdot\Delta t, l=1,\ldots,L$ hence provides us with such a sample. With Δt small enough, we can approximate the sum by an integral, leading to

$$\begin{aligned}\mu_n&\approx\frac{1}{L\Delta t}\int_0^{L\Delta t}Y_n(t)dt\\ &=\frac{1}{L\Delta t}\int_0^{L\Delta t}a_n\cos(2\pi\nu_n t+\phi_n)dt\\ &=\frac{a_n\sin(2\pi\nu_n L\Delta t+\phi_n)}{2\pi\nu_n L\Delta t}.\end{aligned}$$

This integral tends toward 0 as the number of samples L increases, regardless of Δt. Hence

$$\mu_n=0$$

and the mean of the process is zero. As to the variance, it can be expanded as

$$\sigma_n^2=\mathrm{Var}[Z_n]=E\left[Z_n^2\right]$$

since the mean of Z_n is zero. The right-hand side can again be approximated by its sample counterpart, which reads, when Δt is small enough

$$\begin{aligned}\sigma_n^2&\approx\frac{1}{L\Delta t}\int_0^{L\Delta t}Y_n(t)^2dt\\ &=\frac{1}{L\Delta t}\int_0^{L\Delta t}a_n^2\cos^2(2\pi\nu_n t+\phi_n)dt.\end{aligned}$$

Expanding $\cos^2(u)$ as $(1+\cos(2u))/2$, we are led to

$$\sigma_n^2\approx\frac{a_n^2}{2}\left[1+\frac{\sin(4\pi\nu_n L\Delta t+2\phi_n)}{4\pi\nu_n L\Delta t}\right]$$

that tends to $a_n^2/2$ when L increases, yielding that

$$\sigma_n^2=\frac{a_n^2}{2}.$$

Expanding the covariance as we did for the variance yields

$$\Sigma_{ij}=\mathrm{Cov}[Z_i,Z_j]=E[Z_i\cdot Z_j].$$

Here again, the right-hand side can be approximated by its sample counterpart and, hence, by an integral

$$\begin{aligned}\Sigma_{ij}&\approx\frac{1}{L\Delta t}\int_0^{L\Delta t}Y_i(t)\cdot Y_j(t)dt\\ &=\frac{1}{L\Delta t}\int_0^{L\Delta t}a_i\cos(2\pi\nu_i t+\phi_i)\\ &\quad\times a_j\cos(2\pi\nu_j t+\phi_j)dt.\end{aligned}$$

Applying the formula

$$\cos(u)\cdot\cos(v)=\frac{1}{2}[\cos(u+v)+\cos(u-v)]$$

we obtain for Σ_{ij}

$$\frac{a_ia_j}{2L\Delta t}\int_0^{L\Delta t}\cos[2\pi(\nu_i+\nu_j)t+(\phi_i+\phi_j)]dt + \frac{a_ia_j}{2L\Delta t}\int_0^{L\Delta t}\cos[2\pi(\nu_i-\nu_j)t+(\phi_i-\phi_j)]dt.$$

The first integral can readily be calculated as

$$\frac{a_ia_j}{2}\left[\frac{\sin(2\pi(\nu_i+\nu_j)t+(\phi_i+\phi_j))}{2\pi(\nu_i+\nu_j)L\Delta t}\right].$$

As far as the second integral is concerned, two cases have to be considered. If $\nu_i\neq\nu_j$, it is equal to

$$\frac{a_ia_j}{2}\left[\frac{\sin(2\pi(\nu_i-\nu_j)t+(\phi_i-\phi_j))}{2\pi(\nu_i-\nu_j)L\Delta t}\right]$$

that tends to 0 when $L\Delta t\to\infty$. If $\nu_i=\nu_j$, then it is equal to

$$\frac{a_ia_j}{2}\cos(\phi_i-\phi_j)$$

which is independent of the sampling quality. Bringing both integrals together yields

$$\begin{aligned}\Sigma_{ij}&=\frac{a_ia_j}{2}\cos(\phi_i-\phi_j)\\&=\frac{a_ia_j}{2}\cos(\psi_{ij})\end{aligned}$$

when $L\to\infty$. Dividing the covariance by the square root of the product of the variances, the correlation finally yields

$$\rho_{ij}=\mathrm{Corr}[Z_i,Z_j]=\begin{cases}0, & \text{if } \nu_i\neq\nu_j\\ \cos(\psi_{ij}), & \text{if } \nu_i=\nu_j.\end{cases}$$

Appendix D
Coherence and PLV

Define δ_{ij} as

$$\delta_{ij}=\frac{1}{E}\sum_{e=1}^{E}e^{i\psi_{ij,e}}.$$

According to the law of large numbers, δ_{ij} converges toward $E\left[e^{i\psi_{ij}}\right]$ when the number of epochs E is large, with

$$\begin{aligned}E[e^{i\psi_{ij}}]&=\int e^{i\psi_{ij}}\cdot f(\psi_{ij})d\psi_{ij}\\&=\left[\int\cos(\psi)\cdot f(\psi)d\psi\right]+i\left[\int\sin(\psi)\cdot f(\psi)d\psi\right].\end{aligned}$$

Consequently, $\gamma_{ij}^2(\nu)$ tends toward $|E\left[\delta_{ij}\right]|^2$, which is equal to

$$\left[\int\cos(\psi_{ij})\cdot f(\psi_{ij})d\psi_{ij}\right]^2+\left[\int\sin(\psi_{ij})\cdot f(\psi_{ij})d\psi_{ij}\right]^2$$

when E is large.

Appendix E
Expression of Matrices $\boldsymbol{T}$ and $\boldsymbol{\Sigma}$

Matrix $\boldsymbol{U}=\boldsymbol{I}-\boldsymbol{M}$ is equal to

$$\boldsymbol{U}=\begin{pmatrix}1&0&0&0\\-\lambda&1&0&0\\0&-\mu&1&0\\0&0&0&1\end{pmatrix}.$$

Inverting this matrix yields

$$\boldsymbol{T}=\boldsymbol{U}^{-1}=\begin{pmatrix}1&0&0&0\\\lambda&1&0&0\\\lambda\mu&\mu&1&0\\0&0&0&1\end{pmatrix}.$$

Setting $\boldsymbol{\Sigma}=\boldsymbol{T}\boldsymbol{T}^t$, direct calculation shows that

$$\boldsymbol{\Sigma}=\begin{pmatrix}1&\lambda&\lambda\mu&0\\\lambda&\lambda^2+1&(\lambda^2+1)\mu&0\\\lambda\mu&(\lambda^2+1)\mu&(\lambda^2+1)\mu^2+1&0\\0&0&0&1\end{pmatrix}.$$

Appendix F
Expression of the Conditional Correlation Coefficients

Appropriate use of (33) leads to

$$\begin{aligned}\mathrm{Var}[\boldsymbol{Y}_{\{1,2\}}|Y_3]&=\begin{pmatrix}1&\lambda\\\lambda&\lambda^2+1\end{pmatrix}-\begin{pmatrix}\lambda\mu\\(\lambda^2+1)\mu\end{pmatrix}\\&\quad\times((\lambda^2+1)\mu^2+1)^{-1}\begin{pmatrix}\lambda\mu\\(\lambda^2+1)\mu\end{pmatrix}^t\\&=\frac{1}{(\lambda^2+1)\mu^2+1}\begin{pmatrix}\mu^2+1&\lambda\\\lambda&\lambda^2+1\end{pmatrix},\end{aligned}$$

and

$$\begin{aligned}\mathrm{Var}[\boldsymbol{Y}_{\{1,3\}}|Y_2]&=\begin{pmatrix}1&\lambda\mu\\\lambda\mu&(\lambda^2+1)\mu^2+1\end{pmatrix}-\begin{pmatrix}\lambda\\(\lambda^2+1)\mu\end{pmatrix}\\&\quad\times(\lambda^2+1)^{-1}\begin{pmatrix}\lambda\\(\lambda^2+1)\mu\end{pmatrix}^t\\&=\frac{1}{\lambda^2+1}\begin{pmatrix}1&0\\0&\lambda^2+1\end{pmatrix}.\end{aligned}$$

By normalization, we directly obtain

$$\begin{aligned}\mathrm{Corr}[Y_1,Y_2|Y_3]&=\frac{\lambda}{\sqrt{(\lambda^2+1)(\mu^2+1)}}\\\mathrm{Corr}[Y_1,Y_3|Y_2]&=0.\end{aligned}$$

Acknowledgment

The authors are in debt to the two anonymous referees for significantly improving the scope and quality of this paper. They are also thankful to P. Bellec, S. Jbabdi, O. Jolivet, and V. Perlbarg for fruitful discussions and to J. Foucher for pointing out to us the existence of the PLV. This paper is dedicated to the memory of V. Stuart.

REFERENCES

[1] T.-Q. Li, T. N. Haefelin, B. Chan, A. Kastrup, T. Jonsson, G. H. Glover, and M. E. Moseley, "Assessment of hemodynamic response during focal neural activity in human using bolus tracking, arterial spin labeling and BOLD techniques," *Neuroimag.*, vol. 12, pp. 442–451, 2000.

[2] N. K. Logothetis, J. Pauls, M. Augath, T. Trinath, and A. Oeltermann, "Neurophysiological investigation of the basis of the fMRI signal," *Nature*, vol. 412, pp. 150–157, 2001.

[3] D. Attwell and C. Iadecola, "The neural basis of functional brain imaging signals," *Trends Neurosci.*, vol. 25, pp. 621–625, 2002.

[4] A. Aubert and R. Costalat, "A model of the coupling between brain electrical activity, metabolism, and hemodynamics: Application to the interpretation of functional neuroimaging," *Neuroimag.*, vol. 17, pp. 1162–1181, 2002.

[5] R. G. Shulman, D. L. Rothman, K. L. Behar, and F. Hyder, "Energetic basis of brain activity: Implication for neuroimaging," *Trends Neurosci.*, vol. 27, pp. 8–8, 2004.

[6] W. Chen and S. Ogawa, "Principles of BOLD functional MRI," in *Functional MRI*, C. Moonen and P. Bandettini, Eds. Berlin, Germany: Springer, 1999, pp. 103–113.

[7] S. A. Huettel, A. W. Song, and G. McCarthy, *Functional Magnetic Resonance Imaging*. Sunderland, U.K.: Sinauer, 2004.

[8] J. Malmivuo and R. Plonsey, *Bioeletromagnetism*. Oxford, U.K.: Oxford Univ. Press, 1981.

[9] M. Hämäläinen, R. Hari, R. Ilmoniemi, J. Knuutila, and O. V. Lounasmaa, "Magnetoencephalography—Theory, instrumentation, and application to noninvasive studies of the working human brain," *Rev. Modern Phys.*, vol. 65, pp. 413–497, 1993.

[10] P. L. Nunez and R. B. Silberstein, "On the relationship of synaptic activity to macroscopic measurements: Does co-registration of EEG with fMRI make sense?," *Brain Topogr.*, vol. 13, pp. 79–96, 2000.

[11] F. Babiloni, C. Babiloni, F. Carducci, P. M. Rossini, A. Basilisco, L. Astolfi, F. Cincotti, L. Ding, Y. Ni, J. Cheng, K. Christine, J. Sweeney, and B. He, "Estimation of the cortical connectivity during a finger-tapping movement with multimodal integration of EEG and fMRI recordings," in *Int. Congr. Ser.*, vol. 1270, 2004, pp. 126–129.

[12] M. J. Mäkiranta, J. Ruohonen, K. Suominen, E. Sonkajärvi, T. Salomäki, V. Kiviniemi, T. Seppänen, S. Alahuhta, V. Jäntti, and O. Tervonen, "BOLD-contrast functional MRI signal changes related to intermittent rhythmic delta activity in EEG during voluntary hyperventilation—Simultaneous EEG and fMRI study," *Neuroimag.*, vol. 22, pp. 222–231, 2004.

[13] N. J. Trujillo-Barreto, E. Martínez-Montes, L. Melie-García, and P. A. Valdés-Sosa, "A symmetrical Bayesian model for fMRI and EEG/MEG neuroimage fusion," *Int. J. Bioelectromag.*, vol. 3, 2001.

[14] E. Martínez-Montes, P. A. Valdés-Sosa, F. Miwakeichi, R. I. Goldman, and M. S. Cohen, "Concurrent EEG/fMRI analysis by multiway partial least squares," *Neuroimag.*, vol. 22, pp. 1023–1034, 2004.

[15] M. Jones, N. H.-S. J. Martindale, P. Redgrave, and J. Mayhew, "Nonlinear coupling of neural activity and CBF in rodent barrel cortex," *Neuroimag.*, vol. 22, pp. 956–965, 2004.

[16] F. J. Varela, J.-P. Lachaux, E. Rodriguez, and J. Martinerie, "The brainweb: Phase synchronization and large-scale intergration," *Nat. Rev. Neurosci.*, vol. 2, pp. 229–239, 2001.

[17] R. S. J. Frackowiak, K. J. Friston, C. D. Frith, R. J. Dolan, C. Price, J. Ashburner, and W. Penny, Eds., *Human Brain Function*, Second ed. New York: Academic, 2003.

[18] N. Ramnani, T. E. J. Behrens, W. Penny, and P. M. Matthews, "New approaches for exploring anatomical and functional connectivity in the human brain," *Biol. Psych.*, vol. 56, pp. 613–619, 2004.

[19] O. Sporns, D. R. Chialvo, M. Kaiser, and C. C. Hilgetag, "Organization, development and function of complex brain networks," *Trends Cogn. Sci.*, vol. 8, pp. 418–425, 2004.

[20] B. Horwitz, "The elusive concept of brain connectivity," *Neuroimag.*, vol. 19, pp. 466–470, 2003.

[21] E. D. Lumer, G. M. Edelman, and G. Tononi, "Neural dynamics in a model of the thalamocortical system. I. Layers, loops and the emergence of fast synchronous rhythms," *Cereb. Cortex*, vol. 7, pp. 207–227, 1997.

[22] A. Riehle, S. Grun, M. Diesmann, and A. Aertsen, "Spike synchronization and rate modulation differentially involved in motor cortical function," *Science*, 1997.

[23] R. Kötter and F. T. Sommer, "Global relationship between anatomical connectivity and activity propagation in the cerebral cortex," *Phil. Trans. R. Soc. Lond. B*, vol. 355, pp. 127–134, 2000.

[24] A. Treisman, "The binding problem," *Curr. Opin. Neurobiol.*, vol. 6, pp. 171–178, 1996.

[25] C. Tallon-Baudry, O. Bertrand, F. Peronnet, and J. Pernier, "Induced gamma-band activity during the delay of a visual short-term memory task in humans," *J. Neurosci.*, vol. 18, pp. 4244–4254, 1998.

[26] R. Srinivasan, D. P. Russel, G. M. Edelman, and G. Tononi, "Increased synchronization of neuromagnetic responses during conscious perception," *J. Neurosci.*, vol. 19, pp. 5435–5448, 1999.

[27] P. L. Nunez, R. Srinivasan, A. F. Westdorp, R. S. Wijesinghe, D. M. Tucker, R. B. Silberstein, and P. J. Cadusch, "EEG coherency I: Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales," *Electroenceph. Clin. Neurophysiol.*, vol. 103, pp. 499–515, 1997.

[28] J. Gross, J. Kujala, M. Hämäläinen, L. Timmermann, A. Schnitzler, and R. Salmelin, "Dynamic imaging of coherent sources: Studying neural interactions in the human brain," *Proc. Nat. Acad. Sci.*, vol. 98, pp. 694–699, 2001.

[29] O. David and L. Garnero, "Time-coherent expansion of MEG/EEG cortical sources," *Neuroimag.*, vol. 17, pp. 1277–1289, 2002.

[30] J.-P. Lachaux, E. Rodriguez, J. Martinerie, and F. J. Varela, "Measuring phase synchrony in brain signals," *Hum. Brain Mapp.*, vol. 8, pp. 194–208, 1999.

[31] F. Mormann, K. Lehnertz, P. David, and C. E. Elger, "Mean phase coherence as a measure for phase synchronization and its application to the EEG of epilepsy patients," *Phys. D*, vol. 144, pp. 358–369, 2000.

[32] F. Bartolomei, F. Wendling, J.-J. Bellanger, J. Régis, and P. Chauvel, "Neural networks involving the medial temporal structures in temporal lobe epilepsy," *Clin. Neurophysiol.*, vol. 112, pp. 1746–1760, 2001.

[33] F. Wendling, F. Bartolomei, J. J. Bellanger, J. Bourien, and P. Chauvel, "Epileptic fast intracerebral EEG activity: Evidence for spatial decorrelation at seizure onset," *Brain*, vol. 126, pp. 1449–1459, 2003.

[34] J. Xu, Z. Liu, R. Liu, and Q. Yang, "Information transmission in human cerebral cortex," *Phys. D*, vol. 106, pp. 363–374, 1997.

[35] J. Jeong, J. C. Gore, and B. S. Peterson, "Mutual information analysis of the EEG in patients with Alzheimer's disease," *Clin. Neurophysiol.*, vol. 112, pp. 827–835, 2001.

[36] S. H. Na, S.-H. Jin, S. Y. Kim, and B.-J. Ham, "EEG in schizophrenic patients: Mutual information analysis," *Clin. Neurophysiol.*, vol. 113, pp. 1954–1960, 2002.

[37] O. David, D. Cosmelli, and K. J. Friston, "Evaluation of different measures of functional connectivity using neural mass model," *Neuroimag.*, vol. 21, pp. 659–673, 2004.

[38] N. F. Rulkov, M. M. Sushchik, L. S. Tsimring, and H. D. I. Abarbanel, "Generalized synchronization of chaos in directionally coupled chaotic systems," *Phys. Rev. E*, vol. 51, pp. 980–994, 1995.

[39] J. Arnhold, P. Grassberger, K. Lehnertz, and C. E. Elger, "A robust method for detecting interdependences: Application to intracranially recorded EEG," *Phys. D*, vol. 134, pp. 419–430, 1999.

[40] S. Boccaletti, J. Kurths, G. Osipov, D. L. Valladares, and C. S. Zhou, "The synchronization of chaotic systems," *Phys. Rep.*, vol. 366, pp. 1–101, 2002.

[41] T. Buzug, K. Pawelzik, J. von Stamm, and G. Pfister, "Mutual information and global strange attractors in Taylor–Couette flow," *Phys. D*, vol. 72, pp. 343–350, 1994.

[42] C. J. Stam, T. C. A. M. van Woerkom, and W. S. Pritchard, "Use of nonlinear EEG measures to characterize EEG changes during mental activity," *Electroenceph. Clin. Neurophysiol.*, vol. 99, pp. 214–224, 1996.

[43] M. Kamiński, M. Ding, W. A. Truccolo, and S. L. Bressler, "Evaluating causal relations in neural systems: Granger causality, directed transfer function and statistical assessment of significance," *Biol. Cybern.*, vol. 85, pp. 145–157, 2001.

[44] M. Chávez, J. Martinerie, and M. Le Van Quyen, "Statistical assessment of nonlinear causality: Application to epileptic EEG signals," *J. Neurosci. Methods*, vol. 124, pp. 113–128, 2003.

[45] K. J. Friston, C. D. Frith, and R. S. J. Frackowiak, "Time-dependent changes in effective connectivity measured with PET," *Hum. Brain Mapp.*, vol. 1, pp. 69–79, 1993.

[46] A. R. McIntosh, F. L. Bookstein, J. V. Haxby, and C. L. Grady, "Spatial pattern analysis of functional brain images using partial least squares," *Neuroimag.*, vol. 3, pp. 143–157, 1996.

[47] F. Gonzalez-Lima and A. R. McIntosh, "Analysis of neural interactions related to associative learning using structural equation modeling," *Math. Comput. Simulation*, vol. 40, pp. 115–140, 1995.

[48] E. Bullmore, B. Horwitz, G. Honey, M. Brammer, S. Williams, and T. Sharma, "How good is good enough in path analysis of fMRI data?," *Neuroimag.*, vol. 11, pp. 289–301, 2000.

[49] K. J. Friston, L. Harrison, and W. Penny, "Dynamic causal modeling," *Neuroimag.*, vol. 19, pp. 1273–1302, 2003.
[50] W. D. Penny, K. E. Stephan, A. Mechelli, and K. J. Friston, "Modeling functional integration: A comparison of structural equation and dynamic causal models," *Neuroimag.*, vol. 23, no. S1, pp. S264–S274, 2004.
[51] K. J. Friston, C. D. Frith, P. F. Liddle, and R. S. J. Frackowiak, "Functional connectivity: The principal component analysis of large (PET) data sets," *J. Cerebr. Blood Flow Metab.*, vol. 13, pp. 5–14, 1993.
[52] B. Biswal, F. Z. Yetkin, V. M. Haughton, and J. S. Hyde, "Functional connectivity in the motor cortex of resting human brain using echoplanar MRI," *Magn. Reson. Med.*, vol. 34, pp. 537–541, 1995.
[53] B. B. Biswal, J. V. Kylen, and J. S. Hyde, "Simultaneous assessment of flow and BOLD signals in resting-state functional connectivity maps," *NMR Biomed.*, vol. 10, pp. 165–170, 1997.
[54] J. Xiong, L. M. Parsons, J.-H. Gao, and P. T. Fox, "Interregional connectivity to primary motor cortex revealed using MRI resting state images," *Hum. Brain Mapp.*, vol. 8, pp. 151–156, 1999.
[55] K. Niki, J. Hatou, J. Luo, and I. Tahara, "Functional connectivity analysis for fMRI data using mutual information as interaction," *Neuroimag.*, vol. 11, p. S484, 2000.
[56] P.-J. Lahaye, J.-B. Poline, G. Flandin, S. Dodel, and L. Garnero, "Functional connectivity: Studying nonlinear, delayed interactions between BOLD signals," *Neuroimag.*, vol. 20, pp. 962–974, 2003.
[57] W. Tedeschi, H.-P. Müller, D. B. de Araujo, A. C. Santos, U. P. C. Neves, S. N. Ernè, and O. Baffa, "Generalized mutual information fMRI analysis: A study of the Tsallis q parameter," *Phys. A*, vol. 344, pp. 705–711, 2004.
[58] K. J. Friston, K. M. Stephan, and R. S. J. Frackowiak, "Transient phase-locking and dynamic correlations: Are they the same thing?," *Hum. Brain Mapp.*, vol. 5, pp. 48–57, 1997.
[59] W. D. Penny, K. E. Stephan, A. Mechelli, and K. J. Friston, "Comparing dynamic causal models," *Neuroimag.*, vol. 22, pp. 1157–1172, 2004.
[60] J. V. Stone and R. Kötter, "Making connections about brain connectivity," *Trends Cogn. Sci.*, vol. 6, pp. 327–328, 2002.
[61] L. Lee, L. M. Harrison, and A. Mechelli, "A report of the functional connectivity workshop, Düsseldorf 2002," *Neuroimag.*, vol. 19, pp. 457–465, 2003.
[62] H. Humbert-Droz, "Évaluation du rôle de la connectivité comme facteur de la régulation de la biodiversité des petits plans d'eau," *Mémoire de Diplôme D'études Supérieures en Sciences Naturelles de L'environnement*, no. 70, 2001.
[63] O. David and K. J. Friston, "A neural mass model for MEG/EEG: Coupling and neuronal dynamics," *Neuroimag.*, vol. 20, pp. 1743–1755, 2003.
[64] T. W. Anderson, *An Introduction to Multivariate Statistical Analysis*, ser. Wiley Publications in Statistics. New York: Wiley, 1958.
[65] D. J. C. MacKay, *Information Theory, Inference, and Learning Algorithms*. Cambridge, U.K.: Cambridge Univ. Press, 2003.
[66] K. J. Friston, P. Jezzard, and R. Turner, "Analysis of functional MRI time-series," *Hum. Brain Mapp.*, vol. 1, pp. 153–171, 1994.
[67] K. J. Friston, A. P. Holmes, J.-B. Poline, P. J. Grasby, S. C. R. Williams, R. S. J. Frackowiak, and R. Turner, "Analysis of fMRI time-series revisited," *Neuroimag.*, vol. 2, pp. 45–53, 1995.
[68] P. L. Nunez, *Electric Fields of the Brain*. New York: Oxford Univ. Press, 1981.
[69] J. Sarvas, "Basic mathematical and electromagentic concepts of the biomagnetic inverse problem," *Phys. Med. Biol.*, vol. 32, pp. 11–22, 1987.
[70] H. Jeffreys, *Theory of Probability*. Oxford, U.K.: Oxford Univ. Press, 1939.
[71] E. T. Jaynes, *Probability Theory: The Logic of Science*. Cambridge, U.K.: Cambridge Univ. Press, 2003, vol. I, Principles and Elementary Applications.
[72] M. Le Van Quyen, J. Martinerie, C. Adam, and F. J. Varela, "Nonlinear analyzes of interictal EEG map the brain interdependences in human focal epilepsy," *Physica D*, vol. 127, pp. 250–266, 1999.
[73] F. T. Sun, L. M. Miller, and M. D'Esposito, "Measuring interregional functional connectivity using coherence and partial coherence analyzes of fMRI data," *Neuroimag.*, vol. 21, pp. 647–658, 2004.
[74] F. H. L. da Silva, J. E. Vos, J. Mooibroek, and A. V. Rotterdam, "Relative contributions of intracortical and thalamo-cortical processes in the generation of alpha rhythms, revealed by partial coherence analysis," *Electroenceph. Clin. Neurophysiol.*, vol. 50, pp. 449–456, 1980.
[75] C. Allefeld and J. Kurths, "An approach to multivariate phase synchronization analysis and its application to event-related potentials," *Int. J. Bifurcat. Chaos*, vol. 14, pp. 417–426, 2004.
[76] P. Bellec, G. Marrelec, V. Perlbarg, S. Jbabdi, O. Jolivet, M. Pélégrini-Issac, J. Doyon, and H. Benali, "Identification of a large-scale functional network in functional magnetic resonance imaging," in *Proc. IEEE ISBI*, 2004, pp. 848–851.
[77] M. Gavrilescu, G. W. Stuart, A. Waites, G. Jackson, I. D. Svalbe, and G. F. Egan, "Changes in effective connectivity models in the presence of task-correlated motion: An fMRI study," *Hum. Brain Mapp.*, vol. 21, pp. 49–63, 2004.
[78] K. Arfanakis, D. Cordes, V. M. Haughton, C. H. Moritz, M. A. Quigley, and M. E. Meyerand, "Combining independent component analysis and correlation analysis to probe interregional connectivity in fMRI task activation datasets," *Magn. Reson. Imaging*, vol. 18, pp. 921–930, 2000.
[79] D. Cordes, V. M. Haughton, K. Arfanakis, G. J. Wendt, P. A. Turski, C. H. Moritz, M. A. Quigley, and M. E. Meyerand, "Mapping functionally related regions of brain with functional connectivity MR imaging," *Amer. J. Neuroradiol.*, vol. 21, pp. 1636–1644, 2000.
[80] V. Perlbarg, P. Bellec, G. Marrelec, S. Jbabdi, and H. Benali, "Selection of spatially independent components to explain functional connectivity in fMRI," in *Proc. IEEE ISBI*, 2004, pp. 852–855.
[81] K. J. Friston and C. J. Price, "Dynamic representations and generative models of brain function," *Brain. Res. Bull.*, vol. 54, pp. 275–285, 2001.
[82] ——, "Generative models, brain function and neuroimaging," *Scand. J. Psychol.*, vol. 42, pp. 167–177, 2001.
[83] R. M. Gray, *Entropy and Information Theory*. New York: Springer-Verlag, 1990.

Guillaume Marrelec received the M.S. in engineering and applied mathematics jointly from the École Centrale Paris, Paris, France, and the Universität Stuttgart, Stuttgart, Germany, in 1999. He then joined brain functional imaging research within the U494 INSERM, Paris, France, where he specialized in Bayesian analysis, from which he received the Ph.D. degree in 2003.

He is currently involved in post-doctoral research at the Université de Montréal, Montréal, QC, Canada. His research interests include investigation of functional brain interactivity through neuroimaging and brain plasticity induced by learning or surgery.

Jean Daunizeau was born in Boulogne France, in 1977. In 2002, he received the M.Sc. degree in physics from Université Paris-Sud, Orsay, France, with a specialization in medical imaging. Since 2002, he has been working toward the Ph.D. degree with the Unité 678 Laboratoire d'imagerie fonctionnelle, INSERM, Paris, France, and with the Centre de Recherches Mathématiques, Université de Montréal, Montréal, QC, Canada.

His research interests include statistical modeling, inverse problems, and information fusion with applications mainly in EEG/MEG/fMRI activation/connectivity data analysis.

Mélanie Pélégrini-Issac received the Ph.D. degree in physics from the Universiíté Paris 11, Orsay, France, in 1997.

In 2000, she became a Research Engineer with the French National Institute of Health and Medical Research (INSERM), Paris, France. From 2000 to 2004, she was with the Unité 483 INSERM, Paris, where she was mainly concerned with the processing of fMRI data in the context of multimodality (fMRI/EEG/MEG) experiments. Since 2005, she has been with the Functional Imaging Laboratory, Unité 678, INSERM. Her research interests include statistical image and signal processing for the detection of cerebral activation in fMRI and MEG and the analysis of brain functional connectivity in fMRI.

Julien Doyon received the Ph.D. degree in 1988 from the Montreal Neurological Institute, McGill University, Montréal, QC, Canada, under the supervision of Dr. B. Milner.

He accepted an academic position as assistant professor with the Department of Psychology, Laval University, Laval, QC, Canada. He then became a Professor with the Department of Psychology and the Research Center at the Geriatric Institute, University of Montréal, in July 2000, where, at present, he is the Scientific Director of the Functional Neuroimaging Unit.

Habib Benali (M'03) received the Ph.D. degree in signal processing and statistics in 1984 from Rennes University, Rennes, France, and the "Habilitation à Diriger des Recherches" (diploma to lead research project) degree in 1995 from Paris Dauphine University Paris, France.

From 1984 to 1987, he was an Assistant Professor with the Department of Computer Science and Statistics, IUT Vannes, Vannes, France. He joined the French National of Health and Medical Research (INSERM), Paris, in 1987. He is currently a researcher director with the Unit 678 "Laboratory of Functional Imaging," INSERM, where he leads the group "Parametric Imaging of the Cerebral Activity and Metabolism." Since 1999, he has been affiliated with the Mathematical Research Center, University of Montréal, Montréal, QC, Canada, as a regular researcher. He has published more than 70 papers including original publications in peer-reviewed journals, didactic publications, and books. His current research interests are in human brain mapping and functional connectivity analysis using fMRI/EEG/MEG data and statistical modeling of the neural networks involved in motor skill learning in humans.

Dr. Benali is a member of the OHBM, ASU, SFdS, and SFGBM.