Quantification of Neural Functional Connectivity during an Active Avoidance Task

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Abstract—Many behavioral and cognitive processes are associated with spatiotemporal dynamic communication between brain areas. Thus, the quantification of functional connectivity with high temporal resolution is highly desirable for capturing in vivo brain function. However, brain functional network quantification from EEG recordings has been commonly used in a qualitative manner. In this paper, we consider pairwise dependence measures as random variables and estimate the pdf for each electrode of the arrangement. A metric imposed by the quadratic Cauchy-Schwartz Mutual Information quantifies these pdfs. We present the results by brain regions simplifying the analysis and visualization drastically. The proposed metric of functional connectivity quantification is addressed for temporal dependencies of the brain network that can be related to the task.

I. INTRODUCTION

The principle of brain organization in humans has been widely studied in terms of imaging neuroscience. The integration of segregated areas has proven more difficult to access [1]. One approach to characterize integration is in terms of functional connectivity, which is usually inferred as correlations among measurements of neuronal activity. However, correlation is a weak measure of similarity since it only quantifies the second order statistics of the underlying data.

Functional connectivity is an observable phenomenon that can be best quantified with better measures of statistical dependence. Examples include mutual information [2], [3] and Granger causality [4], [5]. Recently, the pairwise generalized measure of association or GMA [6], [7] and its modification Time Series GMA or TGMA [8], [9], [10], [11] have been applied on EEG time series to extract relational information between different recordings.

Typically, electroencephalographic (EEG) time series are recorded from an array of electrodes with a given spatial configuration. Quantification of these brain functional dependence measure networks from EEG recordings is both useful and needed when studying a particular cognitive paradigm. However, quantification on brain functional data is still a big challenge.

Several tools are currently available such as Brain Vision Analyzer, eeglab, fieldtrip, spm8, nutmeg, ELAN, BrainStorm, and others [13]. In 2011, Fadlallah et al. [14] proposed to use a time-variant dependence graph — a 2D circle where the circumference contains electrode nodes and uses lines to connect pairs of electrodes with high functional connectivity in terms of a dependence measure. This is simply a qualitative illustration, not providing a quantitative measure of functional connectivity. More recently, in 2015, Shamas et al. [15] proposed EEGNET that includes 2D and 3D visualizations of brain networks. Yet, again, the displays proposed by these authors are qualitative “line-oriented” and not particularly easy to interpret.

The rest of the paper is organized as follows. In Section II, we present the methodology for analyzing the spatiotemporal dynamics of brain networks and in Section III we present the experimental task and EEG recording procedure. Section IV presents the quantification of functional connectivity and Section V offers discussion and concluding remarks.

II. METHODS

The primary goal of this study is to address the issue of brain functional network quantification from dependence structures of EEG recordings, providing a visual information as well. The pairwise dependence measures are going to be captured by the Time Series Generalized Measure of Association (TGMA). We propose to model the TGMA values referenced to an electrode as a random variable. Since TGMA for each referenced electrode has as many values as electrodes in the montage (minus one), we consider all these values as realizations of the same random variable (RV). Furthermore, we will estimate the pdf of TGMA for each referenced electrode using Parzen windows using a Gaussian kernel [16]. So the spatial variability of the TGMA over the head will be captured by this pdf, which is just a first order quantifier of the spatial structure, but simplifies the analysis and visualization drastically.

In fact, if we are interested in temporal dependency of the brain networks within the task, we can use divergence measures over RVs between consecutive windows. Alternatively, if the goal is to study the spatial dependencies of the brain networks for the same data window, we can utilize divergence measures between the TGMA pdfs of two different referenced electrodes.

There are many possible ways to estimate divergence between pdfs [17], the most common being the Kulback-Leibler (KL) divergence. Here, we avoid the difficult estimation of the KL divergence by using quadratic Cauchy-Schwartz...
Mutual Information [17]. This is an estimator for continuous RVs that can be evaluated in a Reproducing Kernel Hilbert Space (RKHS) using the kernel trick if we use a positive definite function (such as the Gaussian) in Parzen estimation.

Let $X_1$ and $X_2$ be two random variables. The Cauchy-Schwartz quadratic mutual information ($I_{CS}$) between the two variables $X_1$ and $X_2$ is defined as the Cauchy-Schwartz divergence between the joint distribution of $X_1$ and $X_2$ and the product of the marginal distribution of $X_1$ with the marginal distribution of $X_2$ [17], that is

$$I_{CS}(X_1, X_2) = D_{CS}(f_X(x_1, x_2), f_{X_1}(x_1)f_{X_2}(x_2))$$  \hspace{1cm} (1)

where $D_{CS}$ is the Cauchy-Schwartz divergence for two pdfs defined as [17]

$$D_{CS}(f, g) = - \log \left( \frac{\int f(x)g(x)dx}{\int f(x)dx \int g(x)dx} \right)^2$$

$$= \log \int f^2(x)dx + \log \int g^2(x)dx - 2 \log \int f(x)g(x)dx$$  \hspace{1cm} (2)

Let $X = f(x)$, $Y = g(x)$ and $Z = f(x)g(x)$, hence equation 2 can be written in terms of Renyi’s quadratic entropy [17], as follows:

$$D_{CS}(f, g) = 2\hat{H}_2(fg) - \hat{H}_2(f) - \hat{H}_2(g).$$  \hspace{1cm} (3)

where $\hat{H}_2(f)$ is the Renyi’s quadratic entropy estimator of the pdf $f$. Using a Gaussian kernel (Parzen) estimator [16], for samples $x_i$ drawn from pdf $f$, $\hat{H}_2(f)$ can be written as [17]

$$\hat{H}_2(f) = - \log \int_{-\infty}^{+\infty} \left( \frac{1}{N} \sum_{i=1}^{N} G_{\sigma}(x - x_i) \right)^2 dx$$

$$= - \log \left( \frac{1}{N^2} \sum_{i=1}^{N} \sum_{j=1}^{N} G_{\sigma}(x_j - x_i) \right)$$  \hspace{1cm} (4)

A. TGMA Estimation

The Generalized Measure of Association (GMA) is a parameter-free measure of spatial dependency measure of association. The rank-based GMA has the advantage that it can be easily estimated from realizations of a given random variable, unlike statistical dependence [19]. Since the EEG can be modeled as a stochastic time series, GMA was modified to Time Series GMA or TGMA, which includes a pre-optimization step to minimize the time correlation properties of stochastic processes [9]. The values it assumes range between 0.5 and 1. For TGMA the parameters needed to estimate are the embedding dimension $m$ and the lag value $L$. For this study the authors considered $m = 5$ and $L = 7$. These values can be computed directly from data as described in [9].

III. EXPERIMENTAL SETUP

The experimental data presented here has been previously used by Miskovic et al. [10] and Hazrati et al. [11] with different study goals.

A. Participants

A total of 18 participants were recruited from a pool of undergraduate students participating for course credit. Of these 18 participants, three were excluded because of noncompliance with the instructions ($n = 3$) and lack of significant driving, tested by means of the circular T-square statistic [11]. The remaining sample comprised 15 participants (8 females, 7 males, mean age = 18.47 years, standard deviation [SD] = 0.74 years).

B. Procedure

All visual stimuli were generated using the Psychophysics Toolbox [18] for MATLAB. They consisted of gray and white Gabor gratings shown on a black background and subtending horizontal and vertical visual angles of 7°. The CS+ and CS– gratings had the same spatial frequency (1.4 cycles per degree) and differed from each other only in orientation: 45° clockwise tilt (CS+) or 45° anticlockwise tilt (CS–). A loud white noise burst (1.2 s duration, 92 dB sound pressure level) was used as the unconditioned stimulus (UCS) and was played through free-field speakers placed next to the participant.

![Fig. 1. Experimental paradigm consists of four different conditions, which were presented to the subjects in a pseudorandom order – Avoidance conditioning: CS+ trials were always paired with the unconditioned stimulus (UCS). A loud white noise burst was used as UCS. The CS– trials were never paired. The avoidable versus unavoidable context was signaled by geometric shapes. This figure was adapted from [10] and [11].](image)

Participants were given instructions to fixate, avoid eye movements and blinks, and to expect occasional loud noises. Stimuli were displayed on a 23-inch LED monitor (Samsung S23A750D) with a 120 Hz refresh rate positioned at a distance of 1 m.

Stimulus presentation (CS+ vs CS– and active vs passive) was pseudo-randomized in each phase such that no more than two identical trial types were ever presented in succession. Trials were 6 s in length and the inter-trial interval varied randomly between 4 and 5 s.

C. EEG data recording

EEG was continuously recorded from 129 sensors using an Electrical GeodesicsTM HydroCel Geodesic Sensor Net [12], digitized at a rate of 250 Hz with the online band-pass filter set at 50 Hz (low-pass). Sensor impedances were kept below 50 kΩ.
IV. QUANTIFICATION OF FUNCTIONAL CONNECTIVITY

A. Parameters

Each window used for analysis has a duration of 1 s, sliding by 0.2 s (50 sample points) forward to generate a time series of TGMA values. Therefore, the minimum time resolution is 200 ms. With this we are able to compute pairwise association measures between pairs of all 129 electrodes for each time window (total of 26). We have 26 symmetric matrices of $129 \times 129$ dimension, where each column corresponds to TGMA values referenced to the correspondent electrode.

We then use quadratic Cauchy-Schwartz mutual information (Equation 1) to address only the temporal dynamics between pairs of columns of TGMA matrix values. To estimate the pdf of each random variable we use Parzen window estimator using a Gaussian kernel (Equation 4). The authors used $\sigma = 0.05$ as the kernel width.

B. Results

We considered five brain regions (frontal, left temporal, parietal, right temporal and occipital regions) as seen in Figure 2. This arrangement is an intermediary step that provides some anatomical organization, and it is preferred to the simple channel number that is commonly utilized. It also opens the door for some spatial smoothing if the goal is to quantify inter cortical communication.

Across time windows the estimated pdfs using $\sigma = 0.05$ have a distinct shape for each brain region. Figure 2 depicted some of those pdfs for time window 10 which corresponds to 1.8 s – 2 s of the task, for participant #8 and condition CS+Active and condition CS-Active. The considered electrodes for frontal (Fr) area are 10, 17 and 23; for the right temporal (RT) region 102, 114 and 122; for the left temporal (LT) region are 44, 51 and 128; for the parietal (Pa) region 6, 37 and 79; and for the occipital (Oc) region are 66, 75 and 84.

The temporal dependency of the brain networks evaluated with the Cauchy-Schwartz divergence, $I_{CS}$, within the task can be seen in Figure 3 for CS+ (Active and Passive) conditions and in Figure 4 for CS- (Active and Passive) conditions. Only results for four participants (# : 6, 8, 11, 13) are shown here but they are prototypical.

As metric distance, Quadratic Cauchy-Schwartz mutual information returns small values if the two pdfs are similar and higher values otherwise. The averaged $I_{CS}$ values for the occipital area are mostly low along the trial for all participants and all conditions as seen in both Figures 3 and 4. This means that the shape of the pdf for all electrodes belonging to the occipital area are maintained similar across the task, while the other brain areas are interacting differently. This feature is reasonable since the occipital cortex is being stimulated always during the task, so its dynamics do not change much.

In the Active trials the participant is required to press the button to prevent a loud noise at the end of the task (CS+, left column of Figure 3) or not hearing the loud noise but still having to press the button (CS–, left column of Figure 4) between the 2 s–3 s (window 10–15). On both these Active trials, we observe that the pdfs on the left temporal region are different during the time the participant is asked to press the
Different random variable (RV) is promising. The visualization of these quantifications can be done as the user finds useful, either at cortical or electrode level.

In future work, this method can be extended also to quantify the differences in space across cortical networks for each window of data. If the goal is to quantify and visualize both time and space quantification, a video of the spatial organization can be composed to combine both information.

### V. CONCLUSION AND REMARKS

Qualitative measures of functional connectivity are widely used. This paper proposed a metric to quantify functional connectivity providing visual information. Furthermore, we addressed the temporal dependency of the brain network for an active avoidance task.

We used the Time Series Generalized Measure of Association (TGMA) to capture the pairwise dependence of EEG recordings and estimated the pdf of TGMA for each electrode using Parzen windows using a Gaussian kernel. Here the quadratic Cauchy-Schwartz Mutual Information was applied to quantify only the temporal dependency of the brain networks within the task.

Quantification of statistical changes over time using the proposed modeling approach are simple and easy to interpret. The results using the hypotheses of modeling TGMA values referenced to a channel/electrode as a realization of the

### REFERENCES