# Graph-theoretic analysis of scalp EEG brain networks in epilepsy – the influence of montage and volume conduction

Manolis Christodoulakis, Avgis Hadjipapas, Eleftherios S. Papathanasiou, Maria Anastasiadou, Savvas S. Papacostas and Georgios D. Mitsis

*Abstract*— **It is well established that both the choice of recording reference (montage) and volume conduction affect the connectivity measures obtained from scalp EEG. Our purpose in this work is to establish the extent to which they influence the graph theoretic measures of brain networks in epilepsy obtained from scalp EEG. We evaluate and compare two commonly used linear connectivity measures —cross-correlation and coherence— with measures that account for volume conduction, namely corrected cross-correlation, imaginary coherence, phase lag index and weighted phase lag index. We show that the graphs constructed with cross-correlation and coherence are the most affected by volume conduction and montage; however, they demonstrate the same trend — decreasing connectivity at seizure onset, which continues decreasing in the ictal and early post-ictal period, increasing again several minutes after the seizure has ended— with all other measures except imaginary coherence. In particular, networks constructed using cross-correlation yield better discrimination between the pre-ictal and ictal periods than the measures less sensitive to volume conduction. Thus, somewhat paradoxically, although removing effects of volume conduction allows for a more accurate reconstruction of the true underlying networks this may come at the cost of discrimination ability with respect to brain state.**

## I. INTRODUCTION

Epilepsy is one of the most common neurological disorders of the brain, characterized by sudden and unpredictable seizures. It is essential for a patient to have a warning that a seizure is about to occur in order to avoid potentially endangering situations. To this end, the scientific community has continuously performed research for the development of automated seizure detection and prediction algorithms based on electroencephalographic (EEG) measurements, in order to characterize the transition from the inter-ictal to the ictal state (pre-ictal phase) in quantitative terms.

In the last decade or so, many researchers have used complex network analysis —a methodology based on graph theory— to investigate the brain. Different network types, such as random or small-world networks, are associated with different underlying brain properties. Previous studies have provided evidence that epileptic seizures are characterized by changes in functional network features [1], [2].

The effect of volume conduction on connectivity measures obtained from scalp EEG is well-established; it has been shown that it may influence measures of correlation in the time and frequency domains considerably [3]. Therefore, alternative and/or modified measures have been proposed in order to obtain correlation estimates between different scalp EEG channels that take into account volume conduction and reference effects (see e.g. [3], [4], [5]). Moreover, methods that aim to reconstruct a suitable source space and then apply measures to determine functional interactions have been proposed (see e.g. [6], [7]). However, the quality of source reconstruction strongly depends on the number of available recording electrodes, which in the clinical setting is typically low.

Since the correlation measures that are used for the construction of the brain networks are known to be affected by the montage and by volume conduction, it is very likely that the estimated graph-theoretic measures may be influenced as well. This influence has been considered on a limited basis until now to our knowledge, using simulated data in a recent study [5]. In this work, we compare several correlation metrics —namely, cross-correlation, the odd part of correlation, coherence, imaginary coherence, phase lag index (PLI) and weighted PLI— and concluded that graph-theoretic measures obtained from cross-correlation and coherence were the ones mostly affected by the choice of reference and volume conduction.

## II. METHODS

### A. EEG recordings

Long-term video-EEG recordings were collected from patients with epilepsy in the Neurology Ward of the Cyprus Institute of Neurology and Genetics. Twenty-one electrodes were placed according to the 10-20 international system with two additional anterotemporal electrodes. The data were recorded at a sampling rate of 200Hz. A 50Hz Notch filter was applied to remove line noise and subsequently the signals were band-pass filtered between 1 and 45Hz. Eye artifacts were removed by applying Independent Component Analysis (ICA) from the EEGLAB toolbox of Matlab. In order to assess the possible effects of muscle artifacts, we band-pass filtered the data between 1 and 20 Hz; the results

This work was partially supported by the European Regional Development Fund and the Republic of Cyprus through the Research Promotion Foundation (Project ΥΓΕΙΑ/ΔΓΕΙΑ/0609(BE)/11).

M. Christodoulakis, M. Anastasiadou and G. D. Mitsis are with the Department of Electrical and Computer Engineering, University of Cyprus, P.O. Box 20537, 1678 Nicosia, Cyprus {christodoulakis.manolis, anastasiadou.maria, mitsis.georgios}@ucy.ac.cy

A. Hadjipapas is with St George's University of London Medical School at the University of Nicosia, 93 Agios Nicolaos Street, 2408 Engomi, Nicosia, Cyprus hadjipapas.a@unic.ac.cy

E. S. Papathanasiou and S. S. Papacostas are with The Cyprus Institute for Neurology and Genetics, P.O.Box 23462, 1683 Nicosia, Cyprus {neurophy,savvas}@cing.ac.cy

M. Christodoulakis and A. Hadjipapas contributed equally to this work.

978-1-4799-3163-7/13/$31.00 

were similar overall, therefore we present results when the data were pre-processed as mentioned above.

Of the 5 patients we analyzed, here we focus on one patient only, in order to rigorously examine the effects of montage and volume conduction on the results. For this specific patient, the seizure started focally on the EEG at P4-O2 and generalized afterwards. The duration of the seizure was 154 seconds and in this work we examined a section of 15 minutes before and 15 minutes after the seizure onset.

### B. Recording Montages

Scalp EEG recording devices use differential amplifiers to compute the voltage of each EEG channel, which take as input the measurements of two electrodes and produce the corresponding EEG channel as the difference between the two inputs, after it has been amplified. The choice of input electrodes to each amplifier is known as *montage*.

In the original recordings of our system, each amplifier takes as input one of the 10-20 electrodes and one cephalic reference electrode. This is an example of a *common reference* montage, since the reference electrode is common to all amplifiers. Additionally, we have mathematically re-referenced the data to Cz, which is often the reference electrode of choice. The *average reference* montage subtracts the average signal over all channels from the signal at each channel. Finally, for the *bipolar* montage, pairs of electrodes placed in near-by locations of the scalp are used to obtain the time-series by subtracting the corresponding measurements.

### C. Functional Network Construction

We calculated pairwise correlations between all pairs of time series using the connectivity measures described next. Edges were added between node pairs if the corresponding connectivity measure exceeded a pre-specified threshold, the value of which was dependent on the employed measure.

*1) Cross-correlation:* Given two time series $x(t)$ and $y(t)$, with $t \in 1..n$, the normalized cross-correlation function between $x$ and $y$ as a function of the lag, $\tau$, is given by:

$$C_{xy}(\tau) = \frac{1}{n-\tau} \sum_{t=1}^{n-\tau} \left(\frac{x(t)}{\sigma_x}\right) \left(\frac{y(t+\tau)}{\sigma_x}\right)$$

where $\sigma_x$, $\sigma_y$ are the standard deviations of $x$ and $y$ respectively. Then, the correlation between the two signals is computed as $max_\tau |C_{xy}|$, over $\tau \in -100..100ms$.

*2) Corrected cross-correlation:* Cross-correlation often takes its maximum at zero lag in the case of scalp EEG measurements. Consistent zero-lag correlations could be due to volume conduction effects: currents from underlying sources are conducted instantaneously through the head volume to the EEG sensors. In order to measure true interactions not occurring at zero lag, the odd-part of cross-correlation is calculated as [8]:

$$\widetilde{C}_{xy}(\tau) = C_{xy}(\tau) - C_{xy}(-\tau) \qquad \text{for } \tau > 0$$

*3) Coherence:* *Coherency* is the equivalent of cross-correlation in the frequency domain; it measures the linear correlation between two signals $x$ and $y$ as a function of the frequency $f$. It is defined as the cross-spectral density between $x$ and $y$ normalized by the auto-spectral densities of $x$ and $y$. Coherency is a complex number, and for this reason in many cases *coherence* is employed, which is defined as the magnitude of coherency:

$$\kappa_{xy}(f) = \frac{|\langle S_{xy}(f)\rangle|}{\sqrt{|\langle S_{xx}(f)\rangle||\langle S_{yy}(f)\rangle|}}$$

where $S_{xy}$ is the cross-spectral density and $S_{xx}$, $S_{yy}$ are the auto-spectral densities of $x$ and $y$ respectively.

*4) Imaginary coherence:* Nolte et al. [9] defined imaginary coherence as the imaginary part of coherency, after observing that the imaginary part of coherency is insensitive to volume conduction, while the real part is strongly affected.

*5) Phase lag index (PLI):* It is an index of asymmetry for the distribution of instantaneous phase differences between two time-series [10]. The instantaneous phases are obtained by first band-pass filtering the signals in the frequency bands of interest and then using the Hilbert transform to obtain the phase of the analytic signal.

$$PLI_{xy} = |\langle sgn(\Delta\phi(\tau))\rangle|$$

where $\Delta\phi$ is the phase difference between $x$ and $y$.

*6) Weighted phase lag index (WPLI):* Vinck et al. [11] argued that PLI's sensitivity to noise and volume conduction is hindered by the discontinuity of the measure, which is caused by small perturbations turning phase lags into leads and vice versa. To overcome this problem, they defined the weighted phase lag index (WPLI), as follows:

$$WPLI = \frac{|\langle Imag(S_{xy}(f))\rangle|}{\langle|Imag(S_{xy}(f))|\rangle}$$

### D. Network Properties

*1) Average degree:* It is the average number of connections of a node in the graph

$$K = \frac{1}{n} \sum_{i \in N} k_i$$

where $k_i$ is the degree (number of connections) of node $i$.

*2) Global efficiency:* The *shortest path length*, $d_{i,j}$, between a pair of nodes, $i$ and $j$, is the minimum number of edges that have to be traversed to get from node $i$ to $j$. The *efficiency* between $i$ and $j$ is defined as $1/d_{i,j}$. Global efficiency [12] is the average efficiency over all pairs of nodes.

$$E = \frac{1}{n(n-1)} \sum_{i,j \in N, i \neq j} \frac{1}{d_{i,j}}$$

*3) Clustering coefficient:* The *clustering coefficient*, $C_i$, of a node $i$ is the fraction of existing edges between neighbours of $i$ over the maximal number of such possible connections [13]. The *global clustering coefficient*, $C$, of the network is the mean clustering coefficient among all nodes.

$$C = \frac{1}{n} \sum_{i \in N} C_i$$

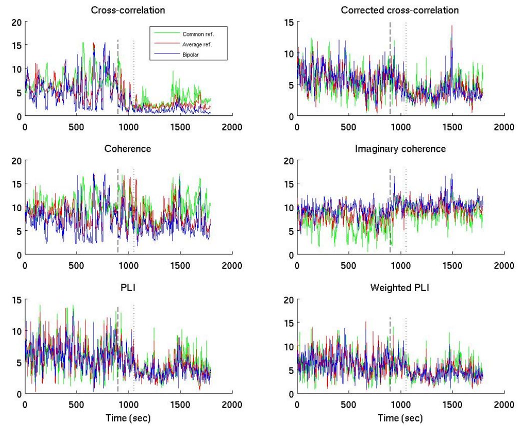


Fig. 1. The average degree of the functional brain networks as a function of time (seconds); comparison of montages for all connectivity measures.

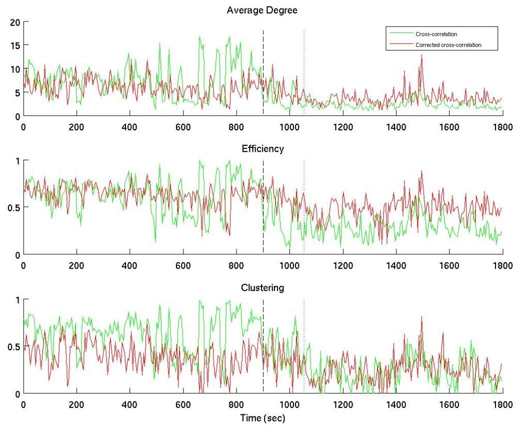


Fig. 2. Network properties of the functional brain networks constructed using cross-correlation (green line) and corrected cross-correlation (red line).

## III. RESULTS

### A. The effect of montage on connectivity measures

Fig. 1 illustrates the average degree of the network as a function of time (in seconds). The vertical dashed line shows the beginning of the seizure, while the dotted line indicates its end, as marked by the expert neurophysiologists. It is evident that all measures, except imaginary coherence, indicate a gradual decrease in the network average degree after the seizure onset, which persists for approximately six minutes, followed by a gradual increase, albeit to lower levels than the pre-seizure period. The aforementioned decrease is more pronounced when the network was constructed by standard cross-correlation.

Corrected cross-correlation, imaginary coherence, PLI and WPLI are less affected by the choice of reference than cross-correlation and coherence. In the graphs corresponding to cross-correlation and coherence we also observe that the average degree is largest for the common reference derivation (green line), followed by the average reference (red line) and bipolar derivation (blue line). This again is consistent with the notion of more pronounced instantaneous spurious correlations at zero lag in the two former montages. Interestingly, imaginary coherence is reversely affected by the montage of choice, with bipolar montage yielding higher connectivity, followed by common reference and then by average reference.

We should note that the average degree obtained when using measures sensitive to zero-lag correlations is not only affected by the reference problem but also by volume conduction. The bipolar montage yields better estimates of the local gradient of the potential along the scalp surface than a fixed reference at a far distance [14, p. 289].

In the following sections, functional brain networks have been constructed using bipolar montage. However we note that despite the differences, the overall changes of the connectivity measures as a function of brain state (inter-ictal, ictal, post-ictal) remained the same regardless of montage.

### B. Time-domain connectivity measures

Fig. 2 illustrates the network properties defined in Section II-D as a function of time, for the standard (green line) and corrected (red line) cross-correlation functional brain networks. Whereas the results from both measures exhibit similar trends as before, during and after the seizure, the seizure-related changes are more pronounced for standard cross-correlation —the drops in average degree, efficiency and clustering coefficient during the ictal and post-ictal period are overall steeper. For corrected cross-correlation, the clustering coefficient is the measure that exhibits the clearest seizure-related changes; whereas the average degree remains relatively constant, clustering drops in the post-ictal period, suggesting a different topology (less clusters) even though the average network connectivity does not change much. As mentioned earlier, we assessed the possible effects of muscle artifacts by repeating the analysis when the data where band-pass filtered between 1–20Hz; the results were qualitatively the same and hence we do not show these separately.

### C. Coherence and Imaginary Coherence (IC)

We constructed networks with coherence and imaginary coherence for all the frequency bands of interest —delta $(1-4\text{Hz})$, theta $(4-8\text{Hz})$, alpha $(8-13\text{Hz})$, beta $(13-30\text{Hz})$ and gamma $(30-45\text{Hz})$. We observed that, for the networks constructed with the standard coherence, the clearer drop in all three measures occurred in the theta and alpha bands and to a lesser degree in the beta band. On the other hand, IC exhibits a different behaviour overall: the larger values were obtained in the higher frequency bands (beta, gamma), while a slight increase was observed in the theta and alpha bands, suggesting that the two measures reflect different aspects of the underlying functional interactions. Similar to the results shown for cross-correlation, their values obtained by coherence drop markedly in the ictal and post-ictal period, whereas no clear patterns emerge when their values were obtained by imaginary coherence. Fig. 3 illustrates coherence and IC for the theta and alpha bands, where the largest changes were observed.

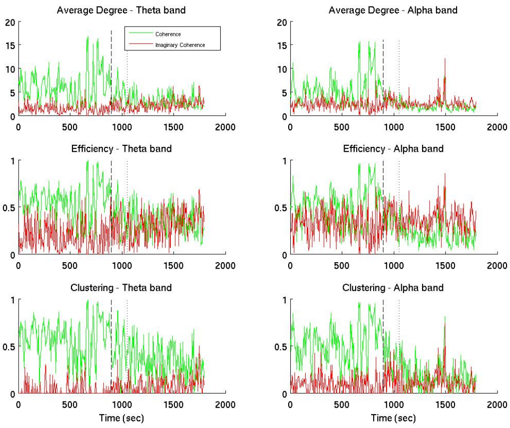


Fig. 3. Network properties of the functional brain networks constructed using coherence (green line) and imaginary coherence (red line) in the theta ($4-8$Hz) and alpha ($8-13$Hz) bands.

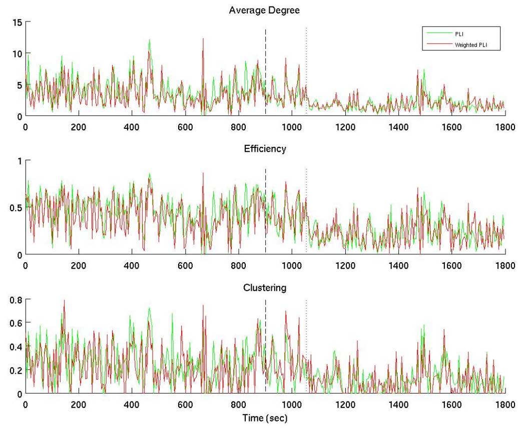


Fig. 4. Network properties of the functional brain networks constructed using PLI (green line) and weighted PLI (red line) in the broadband ($1-45$Hz) signal.

### D. PLI and WPLI

Both PLI and WPLI were designed to mitigate effects of volume conduction [10], [11]. As shown in Section II-C both the PLI and WPLI were mostly unaffected by the choice of montage. Fig. 4 depicts the network properties of PLI and weighted PLI as a function of time. The same trend is observed as with correlation-based measures and coherence (Figs. 2, 3). We constructed the networks again at the different frequency bands with PLI and weighted PLI and noticed that the decrease in the network connectivity that is observed for the broadband signal at seizure onset is mainly due to the beta band. In the remaining bands the PLI and WPLI-based network showed very little modulation with brain state, similar to what is observed with imaginary coherence.

## IV. CONCLUSIONS

In this work, we investigated the effects of choice of reference (montage) and volume conduction on six bivariate signal correlation measures. The measures mostly affected by the montage and volume conduction were the standard cross-correlation and, to a lesser degree, coherence, where the average reference and the common reference montages resulted in higher connectivity than the bipolar montage. Corrected cross-correlation, PLI and WPLI were the least affected measures, whereby all three montages yielded similar connectivity patterns. Imaginary coherence, contrary to all other measures, was reversely affected by the montage, with bipolar resulting in higher connectivity.

Interestingly, our data also suggest that in some cases, measures that are more prone to the effects of volume conduction (e.g. standard cross-correlation) may yield results that are more sensitive in detecting seizure-related changes in brain state (inter-ictal, ictal, post-ictal, see Fig. 2). That said, clustering and average degree measures of corrected-cross-correlation and PLI/ WPLI also show changes when moving from the inter-ictal to the ictal and post-ictal periods.

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