Introducing weighted approaches to study network brain dynamics from EEG epilepsy measurements: the *EigenBrain* algorithm.

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***Abstract* — It is fairly established that dynamic recordings of functional activity maps can naturally and efficiently be represented by functional connectivity networks. In this article we study weighted and fully-connected brain networks, created from electroencephalographic (EEG) measurements that concern patients with focal and generalized epilepsy. We introduce a totally new methodology that has never been utilized before and that investigates weighted and fully-connected networks, which includes eigen-decomposition analysis, feature extraction and quantitative comparisons among entire graph datasets. Our goal is to establish epileptic seizure detection/prediction rules, by identifying repetitive EEG activity in patients before and after each seizure onset.**

In the present paper we treat each brain network as a weighted and full adjacency matrix, without cutting, binarizing or ignoring any values. In this way, it is the first time that the full structure of the connectivity weighing profile is exploited. Also apart from graph theory approaches, mathematical models such as eigen-decomposition analysis are used in our research, in order to study and analyze brain networks. Finally, we present and discuss the results and conclusions of our new method, which are in line with earlier EEG epilepsy findings and demonstrate a standard EEG behavior in both the postictal and preictal period.

I. Introduction

Epilepsy is characterized by sudden and unpredictable seizures and constitutes one of the most common neurological disorders of the human brain [1]. It is a condition that affects many people at any age, regardless of gender or ethnic group, given that approximately 1 in 26 people develop epilepsy at some point during their lifetime [2]. Also, since almost one in four patients with epilepsy cannot be controlled by any anti-epileptic drugs or surgery [3,4], anyone can understand that it is highly essential for a patient to have some kind of warning that a seizure is about to occur in order to avoid potentially endangering situations.

Over the last few decades, several methods have been developed to detect seizures and perform predictions based on electroencephalographic (EEG) measurements, in order to characterize the transition from pre-ictal or inter-ictal to ictal state in quantitative terms [5,6]. This happens because measurements of brain electrical activity with EEG have long been one of the most valuable sources of information for epilepsy research and diagnosis [7], since it carries a large amount of rich information that is valuable in detecting ongoing seizures.

The vast majority of the proposed methods include feature computation directly from the initial EEG time series in order to detect changes immediately prior or after the onset of seizures [6]. All these studies strongly suggest that the information contained in EEG data relevant to seizure detection has not yet been fully exploited and thus, continued research and new approaches are needed. Also, individual patient-based detector training could be necessary to increase sensitivity and specificity [6].

For these reasons, during the last few years there has been a focus on studying EEG signals as graphs using complex network analysis – a methodology based on graph theory – in order to investigate the human brain. The graphs that have been derived from EEG signals are weighted, undirected and fully-connected. Some studies [8,9] have already provided evidence that epileptic seizures are characterized by changes in functional network features, but they came to these conclusions by truncating and binarizing the graphs and studying differences only between some parts of these (truncated) networks' topology before and after the seizure onset.

In this paper we treat the fully-connected brain graphs that derive from the initial EEG signals as weighted adjacency matrices and we perform feature extraction by applying mathematical models from linear algebra, such as eigen-decomposition analysis, to the entire graph. In this way, we take advantage of the full structure of connectivity weights without truncating, binarizing or ignoring any edges of the graphs.

Afterwards, the following approach is pursued: each

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weighted and fully connected graph is represented by the unique vector of its eigenvalues. For every patient, datasets of the recorded data 15 minutes before and after each seizure onset were examined. Next, the datasets are processed in rounds defining each graph before the seizure onset as the reference graph and then calculate the similarities between the reference graph and all its subsequent graphs. The measures of correlation, dot product and cosine are used for calculating similarity between graphs. This procedure is repeated for each patient separately, in order to study the behavior of the recorded data concerning the periods before and after the seizure onset. As will be shown in the Results section, a standard EEG behavior is observed both in the postictal and the preictal period.

The rest of the paper is organized as follows: After a short description of the data that we use in this study, section II presents our novel algorithm that is called *EigenBrain* and describes the adopted experimental procedure. Section III demonstrates the obtained results, while conclusions and future work are cited in section IV.

II. METHODOLOGY

A. Functional Connectivity Data

The data that are used in this study come from the Neurology Ward of the Cyprus Institute of Neurology and Genetics, where long-term EEG recordings were collected from 5 patients with epilepsy. Brain activity was recorded using twenty-one electrodes which were placed according to the 10-20 international system with two additional anterotemporal electrodes. Also, another four electrodes were used to record the electrooculogram (EOG) and electrocardiographic signals (ECG) respectively. The data were recorded at a sampling rate of 200Hz and subsequently converted to the bipolar montage.

The aforementioned data as well as the functional connectivity graph datasets were created as an intermediate result in previous studies [10,11] and hence a more detailed description can be found therein.

The nodes in each functional network correspond to the areas of the scalp around the electrodes that monitor the brain activity of each patient. Every edge, that connects two particular nodes in each graph, represents the correlation between these brain areas. Numbers close to 1 denote high correlation, while numbers close to 0 denote low correlation. All the graphs are weighted, undirected and fully connected. The data were processed in consecutive non-overlapping windows of length 5 seconds and one functional network for each such window was constructed. In this study, all networks are represented by square, weighted and symmetric adjacency matrices.

For every patient, recorded data 15 minutes before and 15 minutes after each seizure onset are provided. One epileptic seizure was recorded from patients 1, 4 and 5, while two epileptic seizures were recorded from patients 2 and 3.

B. Feature Extraction

1) The Eigen-Decomposition method:

Eigenvectors and ***eigenvalues*** are numbers and vectors associated to square matrices and together they provide the eigen-decomposition of a matrix which analyzes the structure of this matrix. Eigenvectors and eigenvalues are also referred to as characteristic vectors and latent roots or characteristic equation. The set of eigenvalues of a matrix is also called its spectrum [12].

There are several ways to define eigenvectors and eigenvalues. The most common approach defines an eigenvector of a matrix A as a vector u that satisfies the following equation:

$$\mathrm{Au} = \lambda \mathrm{u} \tag{1}$$

when rewritten, the equation becomes:

$$(\mathrm{A} - \lambda \mathrm{I})\mathrm{u} = 0 \tag{2}$$

where λ is a scalar called the eigenvalue associated to the eigenvector and I is the identity matrix.

2) Similarity Measures:

a) Dot (inner) product similarity measure.

The simplest similarity measure of two vectors is the dot product which finds the square of Euclidean Distance between these vectors. The dot product of two *d*-dimensional vectors *x* and *y* is defined as [13]:

$$dot(x, y) = x \cdot y = \sum_{i=1}^{d} x_i y_i \tag{3}$$

b) Cosine similarity measure.

It is computed as the dot product of the vectors *x* and *y* divided by their magnitudes. The cosine similarity gives the cosine of the angle between the vectors for which the similarity is computed [14].

$$\cos(x, y) = \frac{x \cdot y}{\|x\| \cdot \|y\|} \tag{4}$$

c) Correlation similarity measure.

The only difference between inner and correlation similarity measure is that the mean of the sample vector is subtracted from itself. Let *x* and *y* be *d*-dimensional vectors. The mean of their components and the correlation similarity between these two vectors is computed as follows [13]:

$$\bar{x} = \frac{1}{d}\sum_{i=1}^{d} x_i, \quad \bar{y} = \frac{1}{d}\sum_{i=1}^{d} y_i \tag{5}$$

$$corr(x, y) = \sum_{i=1}^{d} (x_i - \bar{x})(y_i - \bar{y}) \tag{6}$$

C. The EigenBrain Algorithm

Each person's seizures are unique, with a unique origin and a unique seizure network that the abnormal brain waves traverse, causing a unique seizure behavior for each patient [15]. For this reason, in the present paper we study each

patient separately. As already mentioned above, each weighted, undirected and fully connected graph is treated as a weighted, square and full adjacency matrix. So after the application of the eigen-decomposition analysis to all matrices, every brain network is finally represented by its unique vector of ascending eigenvalues as shown in Figure 1.

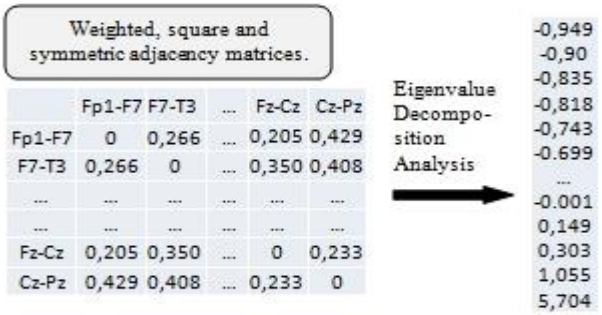

Fig. 1. In our study, each graph (weighted adjacency matrix) is represented by its unique vector of eigenvalues.

Also as mentioned before, each graph corresponds to a consecutive non-overlapping 5 seconds length window. Taking this information into account, we proceed to the next step. We process the data in 144 rounds and in each round we consider every graph in succession, as a reference pre-ictal graph, for the time period 15 minutes until 3 minutes before the seizure onset. Then we compare the eigenvalue vector of each reference graph with all the subsequent graphs until the end of the dataset. This practically means that the first reference graph corresponds to 15 minutes before seizure onset, the second reference graph corresponds to 14 minutes and 55 seconds before seizure onset, the third reference graph corresponds to 14 minutes and 50 seconds before seizure onset and so on. Consequently, we create and test a total of 144 rounds in each dataset, using each time a different reference graph. The reason for this is that we want to ensure the robustness of our results. In this way, we compare different reference graphs (that correspond to different times) with all the graphs that come after it and as will be shown in the next section we arrive every time to equal results. A schematic representation of the aforementioned procedure is depicted in Figure 2.

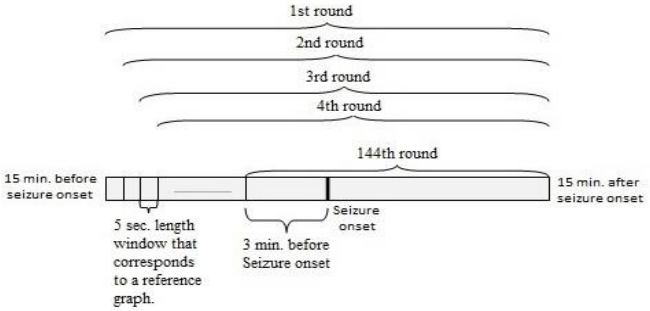

Fig. 2. Schematic representation of how the datasets are processed, for each patient separately.

In fact, we compare the eigenvalue vector of the reference graph with all the other eigenvalue vectors of the dataset's graphs in each round. The three aforementioned similarity measures were used for this purpose: correlation, dot product (Euclidean Distance) and cosine similarity. Network evolution was monitored by observing the similarity values of each examined dataset. As will be shown in the Results section, during epileptic seizures a great similarity divergence is noted between the seizure graphs and the initial pre-seizure graphs of each examined round and this fact could be the key to the accurate prediction or detection of a possible emerging epileptic episode.

III. RESULTS

Seven epileptic seizures have been recorded in total. Three of them come from patients 1, 4 and 5, while two seizures were recorded from patients 2 and 3. For each dataset, a total of 144 different rounds were studied according to the procedure that was described in the previous section. Due to lack of space we only demonstrate results from the second patient and specifically from the second recorded seizure, using the Euclidean Distance similarity measure and three arbitrary rounds from the 144 that were studied in total. It is important to mention here that analogous results were obtained from the study of the other patients and similarity measures as well.

Figure 3 illustrates the Euclidean Distance similarity measure of the three different rounds that correspond to the second seizure of patient 2. For the Euclidean Distance measure, it is known that values near zero indicate high similarity, while the opposite stands for higher values. In Figure 3, "S" denotes the Seizure onset and the word "End" denotes the end of the epileptic episode. Directly from the course of the similarity measure of those three rounds, a clear pattern is visible: observe, for instance, the increase of values after the seizure onset and the characteristic patterns that are formed before and after the end of the epileptic episode. Note that the same patterns were witnessed in all the other examined rounds of the second patient, in both seizures 1 and 2.

The results of each of the observed rounds were further quantified by computing the average values of the similarity measure before and after the seizure onset. It is obvious in Figure 3 that during and after epileptic seizures a large similarity divergence is observed between the initial recorded graphs and those that follow after seizure onset. This similarity divergence can be either upward (as shown in Figure 3) or downward, but the pattern in all cases retains the same shape. The results that are obtained from our newly suggested methodology generally agree with previous EEG epilepsy findings, that use graph theoretic approaches as well, such as those presented in [10,11].

IV. CONCLUSIONS AND FUTURE WORK

We studied the functional connectivity networks of seven seizures from five patients with epilepsy. Since, it is well established that seizure characteristics in each epilepsy patient are unique, it is expected that each patient also has a

unique seizure network and a unique seizure behavior. Thus, we examined each patient separately, by applying eigen-decomposition analysis in all networks and introducing a totally new methodology for studying weighted and fully-connected networks, by taking advantage of the full exploitation of connectivity weights without truncating, binarizing or ignoring any edges of the graphs. We also presented an implementation of our proposed scheme in one of the patients (Patient 2) with quite promising results. Our methodology also explored the provided data in multiple rounds (Figure 2), in order to ensure that the patterns that are formed before and after the seizure onset are the same regardless of the start time of the examined graphs.

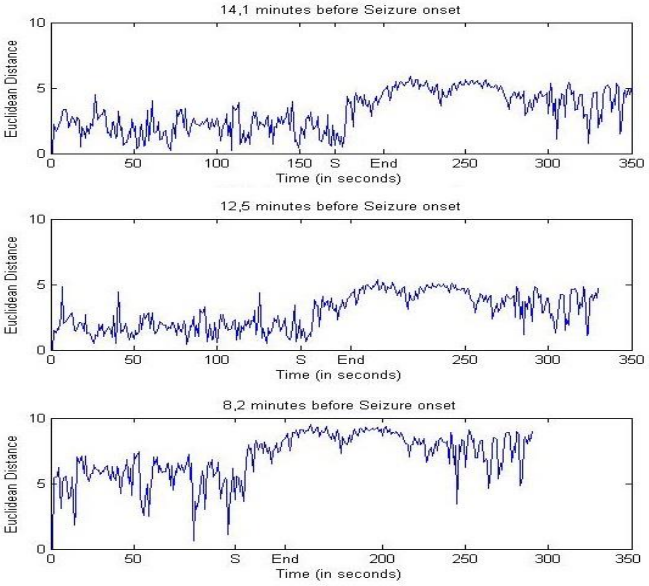

Fig. 3. Similarity comparisons between eigenvalue vectors in which the reference graph corresponds to: 14.1 minutes before Seizure onset (top panel), 12.5 minutes before Seizure onset (middle panel) and 8.2 minutes before Seizure onset (bottom panel). The letter "S" denotes the seizure onset, while the word "End" denotes the end of the epileptic episode.

Several parameters play an important role in the investigation of epilepsy network data using the proposed methodology, such as the duration of the epileptic episode. For example, suppose that a seizure lasts less than five or ten seconds, given that each graph corresponds to a consecutive non-overlapping 5 seconds length window. In this case the impact of such an epileptic seizure may miss or fail to be imprinted to the network data and consequently the data will not form any characteristic pattern before or after the seizure onset.

The computation of average values of the similarity measures before and after the seizure onset, can constitute a powerful weapon for the prediction of an upcoming epileptic seizure. In the very near future, we are planning to perform statistical validation procedures in order to set a threshold that will detect and predict any seizure before it occurs.

As a future work, we are also planning to study extensive datasets that include longer recording periods of time (for example 24-hours recordings) and larger networks that will provide information from more electrodes placed on each patient's scalp. We would also like to enrich our methodology by adding more and different similarity criteria.

Our primary goal in this paper was to ascertain that the introduced technique can provide promising and interesting results. In the future, we are aiming at applying the suggested methodology to a sufficient number of patients in order to reaffirm and validate our results and conclusions.

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