A complex network-based approach to detecting and characterizing ictal states in patients with Childhood Absence Epilepsy

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Abstract—This paper proposes a network analysis-based approach to detecting and characterizing ictal states in patients with Childhood Absence Epilepsy. Our approach defines and uses some suitable data structures, consisting of ad-hoc complex networks and subnetworks, and a new network analysis-based parameter, called connection coefficient. The examination of the values of this parameter on the adopted data structures allows our approach to reach its objectives. Obtained results are extremely encouraging and stimulate the extension of our approach in several directions.

Keywords—Childhood Absence Epilepsy, Electroencephalogram, Complex Networks, Network Analysis, Connection Coefficient, Subnetworks

I. INTRODUCTION

Nearly 1% of the world population is affected by epilepsy, a neurological disorder characterized by recurrent seizures. Epileptic seizures are still considered unpredictable, despite the huge efforts spent in recent years by scientific community to develop predictive algorithms. These are mainly based on electroencephalography, which consists in recording the scalp potentials produced by cortical electrical activity. Nearly 66% of patients can be successfully treated with anti-epileptic drugs, which have remarkable side effects, whereas nearly 8% of the drug-untractable patients are treated with surgery, which is high-invasive and high-risk. There is no way to treat the remaining 26% of patients.

In this paper, the attention is focused on Childhood Absence Epilepsy (CAE), an idiopathic generalized epileptic disorder [1], [2] characterized by recurrent “absence seizures” that cause disruption of awareness and are often associated with staring. Subjects experiencing absence seizures must undergo electroencephalography, which is a totally non-invasive and comfortable examination, consisting in recording the cortical electrical activity by means of scalp electrodes that are wired to an acquisition system, connected to a computer.

The electroencephalography acquisition can last from minutes to hours, depending on the number of recorded seizures and of the specific goal of the examination. In order to evaluate electroencephalograms (EEGs), a neurologist manually scrolls them, for detecting and inspecting every possible ictal state (seizure) or abnormality in the inter-ictal (seizure-free) activity. However, manual review is a time-consuming, inefficient and subjective procedure.

To expedite it and to facilitate the diagnosis, worldwide researchers are working to automatically mark the critical events occurring in an EEG, as well as to extract meaningful features from EEG signals, which can help a neurologist to make a diagnosis, to understand the pathology and, therefore, to optimize the treatment.

So far, many methodologies were proposed in the literature for the analysis of EEGs registering absence seizures. Permutation Entropy (PE), a symbolic complexity measure, was introduced in [3] and applied in [4] to analyze epileptic EEGs. Authors of [4] used PE to discriminate the different phases of epileptic activity in intracranial EEG time series, recorded from three intractable patients. In [5], PE was tested as a possible predictor of absence seizures in Genetic Absence Epilepsy Rats from Strasbourg (GAERS). PE outperformed Sample Entropy (SE) and detected the pre-ictal state in 169 out of 314 seizures from 28 rats, and the average anticipation time was 4.9 s. In [6], the authors exploited complexity analysis to detect vigilance changes in epileptic patients. In [7], Multiscale Permutation Entropy (MPE) was proposed to analyze human EEG signals at different absence seizure states. MPE, used in conjunction with Linear Discriminant Analysis (LDA), achieved a 90.6% sensitivity and exhibited a reduction of MPE levels from the inter-ictal state to the ictal one. In [8], the authors proposed Multi-Scale K-means (MSK-means) unsupervised learning to classify epileptic EEG signals and detect epileptic areas. In order to analyze the dynamics of EEG time series, while taking their mutual spatial dependence into account, a spatial-temporal analysis of epileptic EEGs was proposed in [9], [10], [11]. Due to the ability of PE in capturing the dynamics of EEGs registering absence seizures, a PE-based spatial-temporal analysis was proposed in [12], [13], [14]. Here, the authors showed that the frontal temporal lobes exhibited relatively high PE levels, whereas the parieto-occipital areas appeared associated with relatively low PE values. However, being PE univariate, it is only able to quantify the randomness of single EEG channels independently; instead, it is not able to quantify the interaction between channels. To investigate this
last issue, the necessity arises of bivariate descriptors, which can provide an estimation of the interaction between channels.

Among this last kind of descriptors, coherence is one of the most promising [15]. As a matter of fact, in [16], Partial Directed Coherence (PDC) was employed to quantify the strength and the direction of the interactions between the electrodes during the inter-ictal (i.e., seizure free) EEG segments in CAE patients. PDC revealed an abnormal cortical network activity during the inter-ictal state, in particular in the alpha band. In [17], the authors proposed a method consisting of a three level wavelet decomposition, a coherence estimation and a phase synchrony feature extraction to classify ictal vs inter-ictal EEG segments.

Since absence ictal states appear associated with an increased EEG synchronization, coherence revealed a powerful descriptor of absence seizure EEG signals [16], [15]. In [15], the authors constructed EEG networks, based on the estimation of coherence and Synchronization Likelihood (SL), to investigate the network changes associated with seizure onset. Ictal EEG segments were characterized by an increased synchronization and a more ordered network topology. In [18], the authors applied PDC-based weighted directed graph analysis to EEGs of patients with absence seizures to perform a classification of nodes (electrodes) according to their source/sink nature.

This paper aims at providing a contribution in this setting. In fact, it studies the temporal variation of the synchronization between EEG signals to automatically discriminate ictal vs inter-ictal states, while keeping the global view of how these temporal variations involve the different areas of the cortex. For this purpose, an EEG-based complex network model was developed, where nodes represent electrodes (i.e., cortical areas) and the weight of edges represents the complementary of the coherence value between the EEG signals, recorded at the electrodes associated with the corresponding nodes. A complex network-analysis was carried out to find possible changes in the network features driven by the onset of epileptiform activity. By studying the behavior of the network and its subnetworks over time, a global evaluation of the behavior of the cortex is possible, and the presence of seizures can be automatically detected.

The proposed approach differs significantly from previous studies related to EEGs with absence seizure. To our best knowledge, this is the first time that social network analysis is applied to the EEG of patients with absence seizures. Furthermore, in previous studies, based on the use of complex networks for the detection of absence ictal states, for every patient, only one seizure was manually selected [15], whereas, in the present work, all the recorded seizures are considered, and an overall accuracy is achieved for every patient. In our approach, the whole EEG recording is segmented into overlapping windows and, then, it is processed window by window, so that an overall and smooth analysis of it is achieved. Moreover, no artifact rejection preprocessing was carried out in order to introduce no discontinuity in the dataset and to track the dynamics of the EEG time series continuously. Furthermore, a novel complex network parameter, called connection coefficient, is introduced. It proved particularly adequate to quantify the connection level of a network. The present paper is mainly methodological as it introduces a novel approach for the analysis of EEGs with absence seizures. However, since preliminary results, achieved on a dataset of 9 CAE patients, are very encouraging, the proposed method will be tested on a larger dataset in the near future.

This paper is organized as follows: in Section II, we describe available data and define coherence. In Section III, we introduce some support data structures employed by our approach. Section IV represents the core of this paper, because it illustrates our approach. Finally, in Section V, we draw our conclusions and give a look at some future developments of this research.

II. AVAILABLE DATA

A. EEG recording and preprocessing

A dataset including 9 EEG recordings from patients diagnosed with CAE was studied. The children mean age was 7.44 years, with a standard deviation of 1.67 years. The average duration of EEG recordings was 25.68 mins.

The dataset was provided by UnEEG™ medical A/S (Lyng, Denmark) within a research cooperation agreement. The EEG montage was set according to the international 10/20 system. EEGs were recorded by means of Stellate Harmonie (Stellate Systems, Inc., Montreal, Quebec, Canada) and Cadwell Easy II (Cadwell Laboratories, Inc., Kennewick, WA) systems. EEG traces were reviewed by a board-certified epileptologist, who marked all the paroxysms.

The method flowchart can be described as follows: 1) the n-channels EEG is recorded, band-pass filtered between 0.5 and 32 Hz (because absence seizure activity mainly lies in this range [19]), digitized with a sampling rate of 200 Hz and stored on a computer; 2) the EEG is segmented into M overlapping windows (with 2s width and 1s overlap) and analyzed window by window; 3) given the kth window EEG(k) (where k = 1, . . . , M), the complementary 1 − Cvi,vj of the coherence between every pair of electrodes (vi, vj) is estimated, and used as the weight of the edge between the nodes corresponding to vi and vj.

The width of the overlapping windows was set at 2s because the paroxysms longer than 2s are those considered to be clinically relevant. The 1s overlap ensures that the EEG is processed smoothly and that there is no abrupt variation in estimated descriptors. EEG processing was implemented and carried out in MATLAB R2016b (The MathWorks, Inc., Natick, MA, USA).

B. Coherence estimation

The magnitude squared coherence between two signals vi and vj depends on the frequency f and is defined as:

\[ C_{v_i,v_j}(f) = \frac{|P_{v_i,v_j}(f)|^2}{P_{v_i,v_i}(f)P_{v_j,v_j}(f)} \]

where \( P_{v_i,v_i}(f) \) and \( P_{v_j,v_j}(f) \) are the Power Spectral Densities (PSD) of vi and vj, respectively, whereas \( P_{v_i,v_j}(f) \) represents the cross power spectral density between vi and vj. Coherence \( C_{v_i,v_j} \) is a measure of synchronization between vi and vj and is bounded between 0 and 1. In this work, it was estimated using the method of Welch’s averaged, modified periodogram [20].
The $k^{th}$ EEG window under analysis, and the estimated values of coherence $C_{v_i,v_j}(f)$ for every frequency $f$, were averaged over the frequencies of the range under consideration ($f_L=0.5$ Hz - $f_U=32$ Hz):

$$\overline{C}_{v_i,v_j}^k = \frac{1}{f_U-f_L} \int_{f_L}^{f_U} C_{v_i,v_j}(f) df$$

Therefore, for every analyzed window EEG($k$), and for every pair of electrodes $(v_i, v_j)$, an average value of coherence $\overline{C}_{v_i,v_j}^k$ is computed.

III. SUPPORT DATA STRUCTURES

Let $eeg$ be a generic EEG. Starting from it, a network (that we call brain network) $N = \langle V, E \rangle$ can be defined.

Here, $V$ is the set of nodes of $N$. Each node $v_i \in V$ corresponds to an electrode. In our EEGs, electrodes were applied by following the 10-20 system and it can be represented as $v_i = (u_i, v_{ij}, w_{ij})$. Here, $w_{ij}$ is a measure of “distance” between $v_i$ and $v_j$. It is an indicator of the disconnection level of $v_i$ and $v_j$. Indeed, each measure representing this feature could be adopted in our model. In the experiments presented in this paper, we employed the complementary of the coherence value between $v_i$ and $v_j$ (i.e., we set $w_{ij} = 1 - C_{v_i,v_j}$).

A preliminary investigation performed in our research consisted of determining the edge weight distribution (averaged on all available patients) in ictal, pre-ictal, post-ictal and inter-ictal states, even if, in this paper, our focus is on ictal and inter-ictal states. In carrying out this task, we separated the range of edge weights (which, we recall, is $[0, 1]$) in ten intervals of the same length. The obtained distribution for inter-ictal and ictal states is reported in Figures 1 and 2. From a deeper evaluation of these distributions, we can observe that there are some intervals more relevant than others for distinguishing the two states. As a consequence, to better detect and characterize ictal states, it is reasonable to consider some ad-hoc subnetworks, each taking only the edges belonging to specific intervals into account.

In particular, we defined the following subnetworks: $N_b = \langle V, E^b \rangle$, $N_m = \langle V, E^m \rangle$, $N_g = \langle V, E^g \rangle$, $N_y = \langle V, E^y \rangle$, $N_br = \langle V, E^br \rangle$. We used a color name to provide a more mnemonic way of distinguishing sub-networks.

Thus, the superscripts $b, m, r, g, y, br$ stand for blue, magenta, red, green, yellow and brown, respectively.

Given that the set of nodes is the same for all subnetworks, we focus on defining only the set of edges of each of them:

$$E_b = \{ e_{ij} \mid e_{ij} \in E, 0.9 < w_{ij} \leq 1 \},$$
$$E_m = \{ e_{ij} \mid e_{ij} \in E, 0.8 < w_{ij} \leq 0.9 \},$$
$$E_g = \{ e_{ij} \mid e_{ij} \in E, 0.7 < w_{ij} \leq 0.8 \},$$
$$E_y = \{ e_{ij} \mid e_{ij} \in E, 0.6 < w_{ij} \leq 0.7 \},$$
$$E_y = \{ e_{ij} \mid e_{ij} \in E, 0.5 < w_{ij} \leq 0.6 \},$$
$$E_{br} = \{ e_{ij} \mid e_{ij} \in E, 0.3 < w_{ij} \leq 0.4 \}.$$

Finally, we constructed two further subnetworks. The former was obtained by merging blue, magenta, red, green and yellow subnetworks (we called “rainbow” this network). The latter was constructed by considering all the edges of the original network not belonging to the rainbow one (we called “black” this network). Formally speaking, the two networks are defined as: $N_{br} = \langle V, E_{br} \rangle$, $N_{bk} = \langle V, E_{bk} \rangle$, where:

$$E_{br} = \{ e_{ij} \mid e_{ij} \in E, 0.5 < w_{ij} \leq 1 \},$$
$$E_{bk} = \{ e_{ij} \mid e_{ij} \in E, 0 \leq w_{ij} \leq 0.5 \}.$$

Since each EEG is in the form of a time series, it could be useful to introduce the concept of mean network. Thus, given $q$ networks $N_1 = \langle V, E_1 \rangle$, $N_2 = \langle V, E_2 \rangle$, ..., $N_q = \langle V, E_q \rangle$, we define the mean network $\overline{N}$, corresponding to them, as: $\overline{N} = \langle V, E \rangle$, where:

$$E = \{ (v_i, v_j, \overline{w}_{ij}) \mid e_{ij} = (v_i, v_j, w_{ij}) \in E_k, 1 \leq k \leq q, \overline{w}_{ij} = \frac{\sum_{k=1}^{q} w_{ij}}{q} \}.$$

Observe that $0 \leq \overline{w}_{ij} \leq 1$.

IV. DETECTION AND CHARACTERIZATION OF ICTAL STATES

A. Connection coefficient

As pointed out before, one of the main features to investigate for the detection of ictal states is the connection level of the brain areas. In network analysis, one of the most powerful tools for investigating the connection level of a network is the concept of clique [21]. Starting from cliques, it is possible to define a quantitative coefficient, which we call connection coefficient, capable of measuring the connectivity level of a network associated with an EEG. This coefficient takes the following considerations into account: (i) both the dimension...
and the number of cliques are important as connectivity indicators; (ii) the concept of clique is intrinsically exponential; in other words, a clique of dimension $n + 1$ is exponentially more complex than a clique of dimension $n$. We are now able to define the connection coefficient $c_{cN}$ of a network $N$. In particular, let $C$ be the set of the cliques of $N$; let $C_k$ be the set of cliques of dimension $k$ of $N$; finally, let $|C_k|$ be the cardinality (i.e., the number of cliques) of $C_k$. Then, $c_{cN}$ is defined as:

$$c_{cN} = \sum_{|k|=1}^{V} |C_k| \cdot 2^k$$

### B. Detecting ictal states

Detecting ictal states is a very delicate and time consuming task for a neurologist, who have to analyze a whole EEG. Our effort, in this case, was to compute, on a time-slot base, the value of the connection coefficient for an EEG. And so, for each patient and each time-slot, we computed the value of the connection coefficient of the brain network associated with the EEG at that time-slot.

Indeed, in order to better evidence this phenomenon, we considered the brain subnetworks $N^{rbw}$ and $N^{blk}$, defined in Section IV. We recall that $N^{rbw}$ considers the five intervals of edge distribution characterized by the heaviest weights, whereas $N^{blk}$ encompasses the other ones. As a consequence, since edge weights represent distances, on the basis of the results of [15], we can expect that, in presence of an ictal state, the connection coefficient associated with $N^{rbw}$ presents a minimum, whereas the one corresponding to $N^{blk}$ shows a maximum. This is explained by the fact that, during the ictal states, the weights of the edges tend to decrease and, therefore, several edges disappear from $N^{rbw}$ and appear in $N^{blk}$. For the sake of brevity, we will only look at the results obtained for Patient 18 as an example, but we obtained very similar results for all of the other patients.

In Table I, we report data about figures specified by an expert neurologist when she examined the whole EEG of Patient 18. The physician identified 8 seizures, which took place into the time-slots specified in this table.

<table>
<thead>
<tr>
<th>Seizure id</th>
<th>Start time-slot</th>
<th>End time-slot</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>120</td>
<td>122</td>
</tr>
<tr>
<td>3</td>
<td>165</td>
<td>205</td>
</tr>
<tr>
<td>4</td>
<td>306</td>
<td>332</td>
</tr>
<tr>
<td>5</td>
<td>449</td>
<td>451</td>
</tr>
<tr>
<td>6</td>
<td>470</td>
<td>496</td>
</tr>
<tr>
<td>7</td>
<td>642</td>
<td>659</td>
</tr>
<tr>
<td>8</td>
<td>891</td>
<td>913</td>
</tr>
</tbody>
</table>

We use this table as a starting point and a benchmark of accuracy for the detection of ictal states performed by our approach.

In Figure 3, we plotted the values of the connection coefficient ($y$ axis) for each time-slots ($x$ axis) for Patient 18 and for $N^{rbw}$, whereas, in Figure 4, we represented the values of the same coefficient for the same patient, but for $N^{blk}$.

Clearly, in Figure 3 it is straightforward to observe that there are some time-slots in which connection coefficient is several orders of magnitude less than others. The important result is that those time-slots are exactly the ones that the neurologist spotted as ictal states. For instance, in Figures 5 and 6, we show more closely the part of the plot of Figure 3 corresponding to the first and the eighth seizures, in such a way as to allow the reader to more appreciate the differences, in terms of magnitude, of the value of connection coefficient in the involved states.

Thus, without having to manually analyze the whole EEG for a patient, thanks to this coefficient, we can easily distinguish ictal states from the others.

In order to provide a quantitative evaluation of the performance of our approach, we computed its sensitivity, specificity and precision for each patient and, then, for the set of seizures of all patients, taken as a whole. Obtained results are reported in Table II. Taking into account that, in this application
context, sensitivity is more important than specificity, we have considered the union of the seizures detected by using $\mathcal{N}^{rbw}$ and $\mathcal{N}^{blk}$.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>0.9032</td>
<td>0.8400</td>
<td>0.7272</td>
</tr>
<tr>
<td>18</td>
<td>1.0000</td>
<td>0.9291</td>
<td>0.9661</td>
</tr>
<tr>
<td>23</td>
<td>0.9629</td>
<td>0.9882</td>
<td>0.9167</td>
</tr>
<tr>
<td>29</td>
<td>1.0000</td>
<td>0.9483</td>
<td>0.9473</td>
</tr>
<tr>
<td>31</td>
<td>1.0000</td>
<td>0.9287</td>
<td>0.9438</td>
</tr>
<tr>
<td>32</td>
<td>1.0000</td>
<td>0.9156</td>
<td>0.8644</td>
</tr>
<tr>
<td>39</td>
<td>1.0000</td>
<td>0.8642</td>
<td>0.7400</td>
</tr>
<tr>
<td>47</td>
<td>1.0000</td>
<td>0.9610</td>
<td>0.9917</td>
</tr>
<tr>
<td>57</td>
<td>1.0000</td>
<td>0.9012</td>
<td>0.4375</td>
</tr>
<tr>
<td>Overall</td>
<td>0.9704</td>
<td>0.9169</td>
<td>0.6482</td>
</tr>
</tbody>
</table>

From the analysis of this table, we can see that our approach provides excellent results, especially if we look at sensitivity. However, also specificity and precision are very good. Clearly, we are conscious that the number of examined patients is small. However, as previously pointed out, due to the encouraging results obtained, and due the methodological nature of our paper, we believe the present research can contribute to motivate clinical centers to engage an experimentation of our approach with a much higher number of patients.

C. Characterizing ictal states

In order to understand and characterize what happens during ictal states, we analyzed the subnetworks defined in Section III. For this purpose, we computed a mean network for each inter-ictal time-slot, up to 40 time slots before the seizures, and we mediated those networks among all patients. We did the same task for ictal time-slots, up to 8 time-slots after the start of a seizure, until the center-ictal time-slot.

The subnetworks we used were the blue one $\mathcal{N}^{b}$, the magenta one $\mathcal{N}^{m}$, the red one $\mathcal{N}^{r}$, the green one $\mathcal{N}^{g}$, the yellow one $\mathcal{N}^{y}$ and the brown one $\mathcal{N}^{brw}$. We computed the values of connection coefficient for each colored subnetwork of the mean networks previously derived. Obtained results are plotted in Figure 7. Here, we show the average connection coefficient of some colored networks for 40 time-slots of inter-ictal state and 8 time-slots of ictal state.

As we can see from this figure, during the inter-ictal state, the values of connection coefficient do not deeply change until the first time-slot before ictal. At this time, we can see that the values of connection coefficient increase for yellow and green subnetworks and become higher than the corresponding ones of magenta and blue subnetworks. An increase of the values of connection coefficient for yellow and green subnetworks, coupled with a strong decrease of the values of this coefficient for blue and magenta subnetworks, implies that, during ictal states, both the number and the dimension of the cliques in yellow and green subnetworks increase, whereas the corresponding ones in blue and magenta subnetworks decrease. In turn, this implies that a certain number of edges migrate from magenta and blue subnetworks to green and yellow ones. Now, recall that yellow and green edges have a weight between 0.5 and 0.7, whereas magenta and blue edges have a weight between 0.8 and 1. As a consequence, the edge migration described above implies that a hyper-synchronization of brain areas happens during ictal states.

This characterization result for ictal state is particularly interesting because we were able to confirm, through a network analysis-based approach, what several authors had found in the past, through completely different approaches (see, for instance, [15]), namely that ictal states are characterized by hyper-synchronization, which can be automatically detected. With reference to this feature, it is worth emphasizing that we evaluated the sensitivity and the specificity of the proposed approach over the whole EEG recording, and not over selected epochs, which makes our approach suitable for possible real-time applications. Interestingly, in our tests, no artificial epoch was discarded, in order to track the behavior of the EEG continuously and to evaluate the sensitivity, specificity and precision of our approach in real conditions, when noise and artifacts may be present. Furthermore, the usage of complex networks allows the investigation of the interactions between the different areas of the brain in absence and in presence of a seizure, which we aim at deepening in the future. Finally, we point out that, at the moment, the system can be used off-line to mark the seizures automatically and allow the neurologist to skip the manual EEG review, which is extremely time consuming. However, we plan to optimize it in the future in such a way as to allow for a continuous, real time, long-term monitoring.

V. Conclusion

In this paper, we have presented a network analysis-based approach to detecting and characterizing ictal states in patients with CAE. Our approach associates one or more complex networks and subnetworks with each EEG at disposal. To reach its objective, it introduces a new parameter, called connection coefficient, and evaluates this parameter on each available network and some ad-hoc subnetworks, defined in such a way as to maximally evidence the differences between inter-ictal and ictal states. Obtained results are extremely encouraging, as shown in Sections IV-B and IV-C.

In the future, we plan to extend our approach in several directions. First, we would like to make it capable of detecting and characterizing pre-ictal states, which is a much more complex but, at the same time, extremely useful task. Then, we plan to extend our approach to investigate the mechanisms of area recruitment that occur in the inter-ictal and pre-ictal states. Furthermore, we plan to construct a dashboard of parameters...
(instead of the only connection coefficient) to adopt for the detection and the characterization of ictal and pre-ictal states. Last, but not the least, we plan to make our approach able to handle other forms of epilepsy.

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