Epileptic brain network from scalp EEG

Identifying the epileptic driver by connectivity analysis on brain waveforms

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Abstract— **Epilepsy is a neurological disorder characterized by seizures, i.e. abnormal synchronous activity of neurons in the brain. During a focal seizure the epileptic activity spreads rapidly from the ictal onset region to neighboring brain areas. ElectroEncephaloGraphy (EEG) is a commonly used technique to diagnose epilepsy. EEG has a high temporal resolution which allows us to investigate the dynamics of the underlying brain activity. Due to the rapid propagation of a seizure, the seizure can originate from a network of brain regions which are simultaneously active before being noticeable on the EEG. In this paper we investigate two state of the art source localization techniques, the Recursive Applied and Projected (RAP) and the pre-correlated and orthogonally projected (POP) multiple signal classification (MUSIC) algorithm, to identify the location of the driver behind the simulated epileptic brain network. Furthermore we investigate the applicability of connectivity analysis to identify the source driving the underlying brain network. We showed that the POP-MUSIC algorithm outperforms the RAP-MUSIC algorithm to identify the locations of the simultaneous brain activity. Furthermore, we showed the feasibility of identifying the driver behind a brain network by POP-MUSIC algorithm followed by connectivity analysis.**

Keywords- Electroencephalography; epilepsy; source localization; connectivity analysis

I. INTRODUCTION

A commonly used tool to investigate brain activity is the ElectroEncephaloGram (EEG). This technique has a temporal resolution of milliseconds, which allows us to investigate the rapidly changing information flows between brain areas. Due to volume conduction effects the EEG can be seen as a mixture of the activity of cerebral electrical sources. Each cerebral source will contribute to the recorded EEG of each channel. The EEG is a widely used to investigate brain functions and to diagnose neurological disorders, such as epilepsy

Epilepsy is a common neurological disorder characterized by recurrent epileptic seizure, i.e. abnormal synchronous activity of neurons in the brain. During a focal seizure the epileptic activity spreads from the ictal onset zone to other brain areas. Due to the rapid spreading and the involvement of deep brain regions, the onset of the spreading of epileptic activity in the brain is not always noticeable on the scalp EEG. This means that at the time the seizure is seen on the scalp EEG, the epileptic activity can already originate from a network of different brain areas instead from a single brain area. The underlying epileptic network can be simplified as a network which exists out of synchronous sources and in which one source, i.e. the ictal onset zone, drives the other sources.

EEG source localization [1] is a technique to estimate brain activity from the EEG. Source analysis estimates 1 or several cerebral sources out of the scalp EEG. The algorithms used to solve the inverse problem can be divided into the spatial and the spatio-temporal approaches. The spatial approaches allow a sample based analysis of the EEG. For each time point a source distribution is calculated. An examples of this is the Weighted Minimum Norm (WMN) approach [2]. On the other hand spatio-temporal techniques calculate source distributions based on the temporal characteristic of the EEG epoch. The multiple signal classification (MUSIC) algorithm [3] belongs to this category. Unfortunately, most techniques have difficulties in separating highly correlated sources and can, thus, produce large localization errors when such sources are present [4].

Brain connectivity describes the structural and functional relation between brain areas, how the brain regions cooperate and how information is spread between them. Structural connectivity refers to the direct anatomical connections in the brain and can be imaged in vivo by Diffusion Tensor Imaging [5]. Functional connectivity is defined as the temporal correlations between spatially remote neurophysiological events [6]. It reveals the statistical dependency between neural activities of different brain regions regardless of any underlying anatomical connection.

This paper investigate the feasibility of detecting the driver of the brain network during an epileptic seizure from scalp EEG. First the source locations and corresponding time series are estimated by using EEG source localization methods. Afterwards the functional connectivity pattern between the intensities of the time series is estimated to identify the driver of the brain network.

II. METHODS

A. *EEG source localization*

EEG source localization estimates the brain activity from the scalp EEG. It calculates the source distribution in the brain most suitable to generate the measured EEG. The EEG source localization consists of two problems: a forward problem and an inverse problem. The forward problem calculates the electrode potentials at the scalp given the source distribution in

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the brain. A realistic head model is used to model the conduction effects of the different tissue types of the head. The inverse problem calculates the source distribution out of the measured scalp EEG based on the forward solution.

In this paper the Finite Difference Method with Reciprocity (FDM-R) was used to calculate the forward problem given a realistic head model [7].

We compare two state of the art inverse problem solving techniques based on the well known MUSIC algorithm, namely: Recursive Applied and Projected (RAP) MUSIC and pre-correlated and orthogonally projected (POP) MUSIC.

B. RAP-MUSIC vs. POP-MUSIC

The RAP-MUSIC algorithm [8] uses a recursive procedure in which each source is found as the global maximizer of a different cost function. This is done by recursively scanning through the source space. In essence, the method works by applying a MUSIC search to a modified problem in which we first project both the estimated signal subspace and the array manifold vector away from the subspace spanned by the sources that have already been found.

The POP-MUSIC algorithm [4] is designed to improve the reconstruction of synchronous sources based on the integration of the spatio-temporal (RAP-MUSIC) and spatial-only approaches (WMN) in a way to preserve both of their advantages.

In this paper we only use the first 4 steps of the traditional POP-MUSIC algorithm:

1. Iteratively search for k single-source independent topographies (IT) using RAP-MUSIC, where k is the rank of the measurements. Find the neighbors of those k source locations.
2. Reduce the source space to the source set found by step 1, including the neighbors. Estimate the source waveform for each source in this space by applying WMN at each time sample.
3. For each source, find the *N* largest correlated companions, thus forming a collection of "correlated groups," excluding nearest neighbors.
4. Perform RAP-MUSIC to find *r* ITs from these correlated groups.

Both algorithms result in several locations of possible sources. At each of these locations the brain waveform is estimated by using the WMN approach. This leads to time-variant source waveforms at each of the estimated locations by either the RAP-MUSIC or the POP-MUSIC algorithm. The estimated brain waveforms are depicted as:

$$s_i(n) \text{ with } i = 1..K \tag{1}$$

where *K* is either the number of locations found by the RAP-MUSIC algorithm or the number of locations found by the POP-MUSIC algorithm.

C. Source selection out of estimated brain waveforms

To select which of the previously derived source locations is considered to be the driver behind the brain network we will investigate two techniques.

A first simple approach is based on the energy contained in the estimated brain waveforms. We select the source location corresponding to the maximum variance of the intensity of the estimated brain waveform:

$$\max_{i=1..K} \operatorname{var}(s_i(n)) \tag{2}$$

where *K* is the number of brain waveforms and $s_i(n)$ is the intensity of brain waveform *i* at time point *n*. The idea behind it is that the source which has the highest energy is the most important in the brain network.

Another more sophisticated technique looks at the functional connectivity between the brain waveforms of the estimated sources. Functional connectivity reveals the statistical dependency between the intensities of the brain waveforms.

The full-frequency Adaptive Directed Transfer Function (ffADTF) [9] is a measure which reveals the functional connectivity between the signals over time. The ffADTF is defined as:

$$\varphi_{ij}(n) = \frac{\sum_{f=f_1}^{f_2} \left|H_{ij}(f,n)\right|^2}{\sum_{k=1}^{K} \sum_{f=f_1}^{f} \left|H_{ij}(f,n)\right|^2} \tag{3}$$

where *K* is the number of waveforms, *[f1, f2]* represents the frequency interval of interest and $H_{ij}(f,n)$ is an element of the time-variant system matrix which reveals the causal information flow from signal *j* to signal *i* at frequency *f* at time point *n*. The ffADTF-values lie in the interval [0, 1] and represent the time-variant strengths of the connections between all pairwise combinations of the signals. The closer a value lies to 1 the stronger the connection.

Out of these ffADTF-values we calculate the mean out-degree of signal j over time, $deg^+(j)$, as:

$$\deg^+(j) = \frac{1}{N} \sum_{n=1}^{N} \sum_{k=1, k\neq j}^{K} \varphi_{kj}(n) \tag{4}$$

where *K* represents the number of brain waveforms, *N* is the number of time points and $\varphi_{kj}(n)$ is the ffADTF-value representing the connection strength from brain waveform *j* to brain waveform *k* at time point *n*. The mean out-degree of a signals explains how much information flow is sent from the signal to all the other signals during the considered time interval. The signal with the highest mean out-degree value will be pinpointed as being the driver behind the brain network.

D. *Simulation Setup*

1) *From simulated brain network to EEG*

The epileptic seizure is simulated by two sources (dipoles) placed in different brain regions which are simultaneously active. Source 1 mimics the ictal onset zone, it drives the other source. A realistic head model is build out of MR images. The source space consists of 4847 locations sampled from the gray matter at a resolution of 5 x 5 x 5 mm. Source 1 is placed in each of these locations and the location of source 2 is randomly chosen. The minimum distance between both sources is set to 1cm. The head model is depicted in Fig. 1A.

The brain waveform mimicking the epileptic seizure is a 10Hz sinusoid of 1s with sampling frequency equal to 512Hz. A delayed version of this waveform (5 samples delay) is chosen as the brain waveform of source 2. The dipole orientation of both waveforms is randomly chosen. The placement and relation between the dipoles in the brain is shown in Fig. 1B.

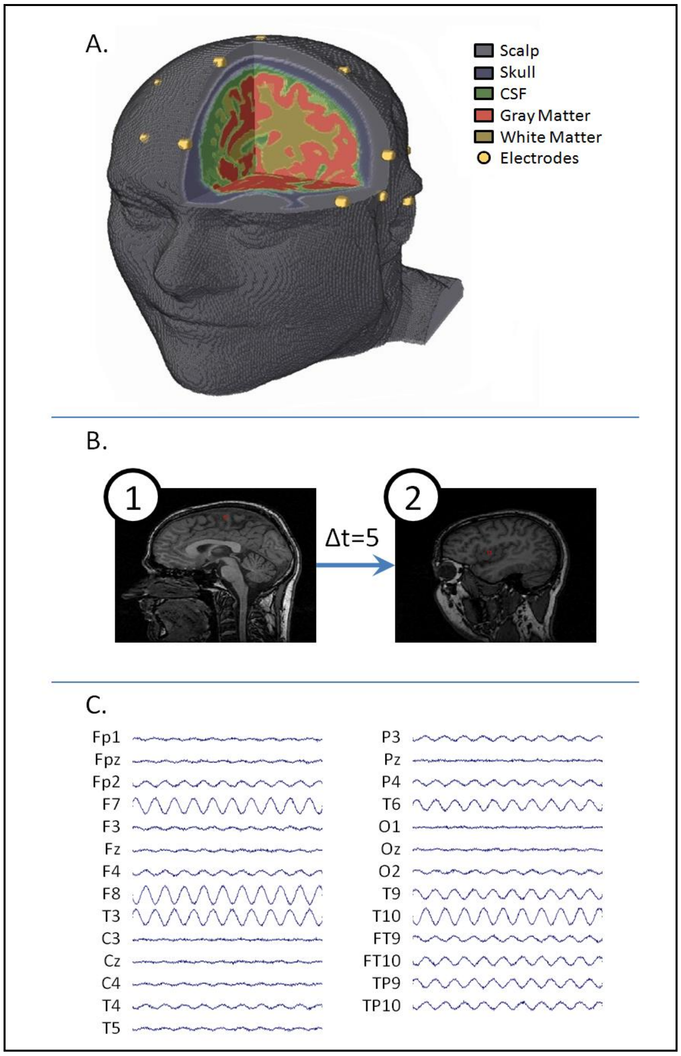

Figure 1. From the simulated brain network to the EEG. Panel A: the realistic head model, Panel B: the placement of the 2 sources in the gray matter and the underlying network and Panel C: the resulting EEG with a SNR equal to 15dB.

The forward problem is solved using the FDM-R with a realistic head model. Twenty-seven EEG channels are simulated. The head model has 5 tissue types: gray matter, white matter, cerebrospinal fluid, skull and scalp. The conductivity of the soft tissue types (scalp, CSF, gray matter and white matter) is set to 0.33 S/m and the conductivity of the skull is set to 0.0206 S/m. All tissue types are considered isotropic.

Additional noise is added to the EEG channel with a Signal-to-Noise Ratio (SNR) ranging from 5dB to 30dB in 5dB increments. The resulting EEG for a SNR of 15dB is depicted in Fig.1C.

2) *From EEG to source locations*

The RAP-MUSIC and POP-MUSIC algorithms are applied to the simulated EEG. For the RAP-MUSIC algorithm the number of estimated dipoles is set to 5. For the POP-MUSIC algorithm the rank of the measurements is set to the full rank of the simulated EEG, in this case 27. The number of largest correlated companions is set to 5 and the number of ITs to find in Step 4 is set to 2.

Both MUSIC algorithms find multiple source locations. The minimum distance from the group of sources found by RAP-MUSIC and that found by POP-MUSIC to the original location of the driver of the brain network, here source1, is called the localization error. This gives an idea whether it is possible to use the algorithm to identify the driver of the underlying network.

3) *Source location selection*

The brain waveforms are estimated for each of these locations using the WMN approach. To select the source which drives the underlying brain network we use the energy and connectivity approach as explained in previous paragraph.

For the energy based selection approach we compare the variance of the different brain waveforms. The location of the brain waveform with the highest variance is identified as the location of driver behind the simulated epileptic network.

For the connectivity based approach we apply the ffADTF to the magnitude of the brain waveforms in the frequency interval [16Hz, 24Hz], because the magnitude of the brain waveform modeled as a sinusoid of 10Hz has a peak in the frequency spectrum at 20Hz.

III. RESULTS

A. *RAP-MUSIC vs. POP-MUSIC*

The localization error (symbol: e) of the set of sources found by the RAP-MUSIC algorithm and the set found by the POP-MUSIC algorithm are investigated. The percentage of simulations in which this localization error was less or equal to 10mm is depicted in Fig. 2 for the SNR ranging from 30dB to 5dB with decrement steps of 5dB. The percentage of simulations in which the localization error was 0mm is also shown in Fig. 2.

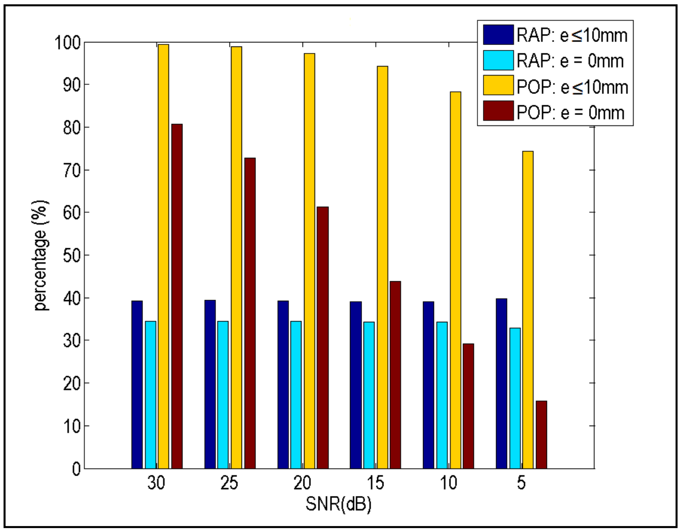

Figure 2. Comparison of the Source localization error (symbol: e) of the RAP-MUSIC and POP-MUSIC algorithm at different SNRs. The percentage of simulations in which the localization error is smaller than or equal to 10mm ($e \leq 10$mm) and those where the localization error is equal to 0mm ($e = 0$mm) are depicted for the RAP-MUSIC algorithm and the POP-MUSIC algorithm.

The POP-MUSIC algorithm is clearly better in identifying the location of the driver of the epileptic network within the source set. We see that the percentage of the localization error smaller than 10mm ($e \leq 10$mm) is larger than 90% for a SNR ranging from 30 to 15dB. This means that in over 90% of the cases, a location closer than 1cm to the simulated location is pinpointed by the POP-MUSIC algorithm out of 4847 possible locations.

The RAP-MUSIC algorithm finds approximately 40% of the simulated origins of the epileptic network within a distance of 1cm. The RAP-MUSIC has a constant performance over the considered SNR range. At a SNR equal to 5dB and 10dB a higher percentage of the localization error equal to zero ($e = 0$) of the RAP-MUSIC algorithm is found compared to the POP-MUSIC algorithm. However, in this cases there is still a difference of over 35% if we look at sources located within 1cm of the simulated source in favor of the POP-MUSIC algorithm.

B. Source selection

Because POP-MUSIC clearly outperforms RAP-MUSIC for the localization of the driver of the simulated epileptic network, we will only consider the set of locations resulting from the POP-MUSIC algorithm.

Out of this set of locations we selected a single location either based on the energy of the signals or based on the connectivity analysis between the signals. The percentage correctly identified sources from the given set of locations is shown in Fig. 3A. The percentage is over 80% for the connectivity based selection for a SNR ranging from 20 to 30dB. The connectivity based selection is more sensitive to the SNR compared to the energy based selection, a larger decrease can be noticed between the 30dB and the 5dB percentages.

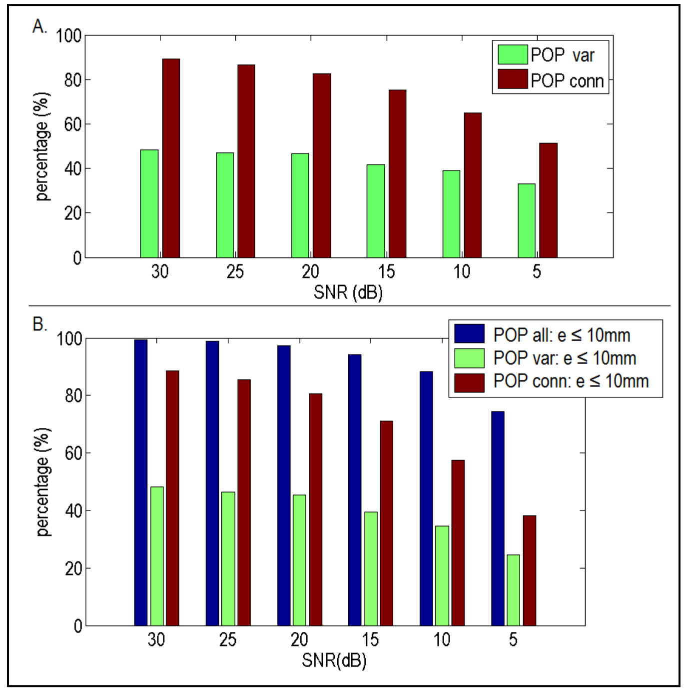

Figure 3. Comparison of source selection method: energy based approach (*POP var*) versus connectivity based approach (*POP conn).* Panel A: percentage of correctly identified sources given the source location set. Panel B: percentage of simulations in which the localization error was less or equal to 10mm ($e \leqslant 10$mm). POP all shows the maximum, which is the percentage of simulations in which a source with $e \leqslant 10$mm is present in the set of estimated locations by the POP-MUSIC algorithm.

The overall percentage of simulations in which the localization error is smaller or equal to 10mm are shown in Fig. 3B. The results based on the connectivity analysis outperform those based on the energy of the brain waveforms. They are approximately 35% higher for high SNRs: 15 to 30dB.

IV. Discussion

In this paper the simple epileptic network only consists of two sources. During an epileptic seizure the number of brain regions which are active are patient and even seizure dependent. We only used two sources to show the feasibility of finding the driver of simple networks by applying source localization algorithms followed by connectivity analysis.

For the source localization we used two state-of-the-art spatio-temporal techniques, RAP-MUSIC and POP-MUSIC. The source distribution is based on the temporal characteristics of the EEG epoch. The algorithms to calculate the distributed linear inverse solution (f.i. WMN, LORETA [10], sLORETA [11] or FOCUSS [12]) use a spatial-only approach. By processing the data on a single time sample basis, such methods have higher localization errors on correlated sources due to the presence of noise in the data.

The POP-MUSIC algorithm clearly outperforms the RAP-MUSIC algorithm of finding a set of locations with a small localization error. This is because POP-MUSIC is designed to find correlated sources, which is the case in the simulated network. The small sample delay between both simulated sources is a disadvantage for the RAP-MUSIC algorithm. The algorithm cannot distinguish both sources and treats the EEG as being generated by one single source.

The RAP-MUSIC algorithm performs the same for different SNRs. This is because in the RAP-MUSIC algorithm we considered the covariance matrix of the noise as given. This way we make an equally good estimation of the noise subspace for each different SNR.

The POP-MUSIC algorithm was designed to find correlated sources. By using this algorithm we were able to reduce the source localization space to on average 6 locations. Reducing the size of the set of possible locations from 4847 to only 6 allows us to perform connectivity analysis on the reconstructed brain waveforms.

Overall we have showed that source localization followed by connectivity analysis can identify the driver of a simple simulated epileptic network. The connectivity analysis is the best selection approach if multiple brain areas are involved. The measure used to investigate the functional connectivity between the signals has the intrinsic capacity to model the indirect flows. This means that if the EEG recorded during a seizure originates from a network consisting of multiple sources generated from one driver that the ffADTF has the intrinsic capabilities to identify that driver.

V. CONCLUSION

In this paper we showed the feasibility of identifying the driver behind a brain network by applying source localization followed by connectivity analysis. POP-MUSIC combined with connectivity analysis can find the location of the source that drives the network in 80% and 60% of the cases at a SNR of 30dB and 10dB, respectively.

VI. FUTURE WORK

Further simulations will be conducted to investigate the effect of the location of the source driving the epileptic network, to see whether deep sources are more difficult to identify. The network will also be extended to more sources. In a later stage we will investigate how the method can cope with time-variant networks or even separate networks.

The method will also be applied to the retrospective data of epileptic patients to investigate the correlations between the identified location and the ictal onset zone marked by the neurologist.

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