Seizure Onset Zone Detection and Localization in iEEG Using DTF

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Abstract— **This paper presents the possibility of early detection and localization of epileptogenic focus in the iEEG (intracranial Electroencephalography) signal using a method based on multidimensional autoregressive models. The work provides the first results of the method in the iEEG signal, and discusses technical aspects in terms of the suitability of the sampling frequency, AR model order and segmentation step.**

Keywords-component; iEEG, DTF, SOZ, AR model order

I. INTRODUCTION

At present, evaluation of iEEG signals is performed subjectively by neurologists. A set of linear filters is initially applied to the signal, after which the neurologist visually seeks out typical patterns that indicate the epileptogenic bearings, where the genesis of impulses causes the onset of seizures. The filters sometimes use complex frequency characteristics for highlighting areas with the typical patterns (ictal discharges). The occurrence, location and extent of the patterns are determined solely through individual evaluation by the specialist, implying a highly complex procedure that strongly depends on the experience of the individual evaluator in most cases. In the final assessment of a case, independent evaluations from different specialists are used for reducing the level of subjectivity.

Surgical treatment is often the only hope for improving the quality of life of patients with pharmaco-resistant epilepsy. The aim of our workgroup is to create algorithms for automatic and semiautomatic iEEG evaluation in which the uncertainties of the standard evaluation procedures are improved or at least maintained.

II. SEIZURE ONSET ZONE DETECTION METHODS

Various methods of Seizure Onset Zone (SOZ) detection have been described in publications. The main approaches can be divided into a few groups. Techniques using Time-Frequency analysis, Correlation analysis and techniques based on Auto Regressive Models. A special group can be the Neural Network approach.

It must, however, be said that the current trend in this area makes use of the correspondence between High Frequency Oscillations (HFO) phenomena and the SOZ. Current efforts in EEG signal processing research focus on the HFO clinical correlates. The main approaches are listed below.

A. Time-frequency analysis

T. Tzallase and M.G. Tsipourase present a review of basic functions in time-frequency distributions for the power spectral density computation (PSD) [1]. The symptoms are extracted from the PSD and then are classified by forward neural networks (NN). The authors also introduce other Bayesian classifiers (e.g. k-Nearest neighbor and decision trees) for comparison. The input data are divided by the classifier into two classes: the first consisting of symptoms corresponding to the seizure, the second corresponding to symptoms where no seizure is present. The present authors are primarily interested in the issue of classification of accuracy in the presence of a seizure, but also the possibility of determining the time of the seizure's onset.

The method of Chan et al. also seeks to find the time of the seizure onset [2]. The signal is segmented by a window sliding along the record. In each segment, the power spectral density (PSD) is estimated. The feature vector is calculated from the PSD by integrating the frequency bands corresponding to the standard EEG bands i.e. alpha, beta, theta, delta and gamma. The vectors are classified by the Support Vector Machine (SVM) classifier, which is trained by data containing the onset of a seizure or data without seizures. Classification using regression analysis is used to detect the exact time of SOZ values.

The detector warning system for hospital staff described in [3] is composed of a two-stage filter. The first bandpass filter in the range 5 - 45 Hz is an FIR filter set up on the third level of wavelet coefficients of the wavelet DAUB4 family. The resulting coefficients are squared and filtered by a window median filter to cancel statistically biased samples. The different arrangement for the median filter produces a "background" and "foreground" signal from the first filter. Using a suitable threshold ratio "foreground" and "background" triggers a warning signal.

The research of Shoebat et al. was motivated by dosing radiopharmaceuticals for single photon emission tomography

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(SPECT) procedures. The detection algorithm needs to react as fast as possible when the seizure starts. The feature vector is formed by the energy signal of four different time scales after passing through the filter bank of wavelet transformation in the range 0.5 - 25 Hz [4]. Each channel is segmented a by window with a length of two seconds and counted for 4 values. For each given time window, a feature vector consisting of contributions four values of each channel is set up. The feature vector is classified using the SVM to class "seizure / no seizure". If three consecutive feature vectors are classified in the class "seizure", the radiopharmaceuticals are applied.

Gotman et al. used a modified classifier to the nearest neighbor [5]. A parameterized signal with segments of length 2.5 s is used as a feature vector. The feature vector parameters are six elements: the average amplitude of the wave, the average duration of waves, wave duration variance, significant frequency, average power and flag of the position.

B. Neural Networks

The work of R. Bates et al. [6] uses a neural network, in this case a three-layer recurrent net with architecture 5-10-5. The iEEG signals input in the network and the network is trained on a target of zero or one in dependence on seizure presence in the signal.

C. Correlation Analysis

Use of correlation analysis currently suggests a promising direction for seizure detection. For instance K. Schindler et al. filtered multi-channel signals in the range 80 - 200 Hz [7] and computed the Total Correlation Strength. A coefficient increase in the correlation matrix can be observed in the time of the seizure onset, but the method has not been verified with a sufficient number of patients.

D. Methods based on autoregressive (AR) models

B. Swiderski et al. analyzed EEG signals using Directed Transfer Function (DTF) [8]. The described parametric method is based on multidimensional AR models estimating the direction of power flow and brain electrical activity. Channel signals are segmented in 2-second windows with a 50% overlap. The DTF forms a feature vector for each segment, calculated in the same time of corresponding segments from different channels. The feature vector is classified using One-Class SVM into classes "seizure / no seizure". Not all segments, however, are classified into the correct classes: what is needed is an estimate of the a priori probability of seizure (p-estimate) of several consecutive segments classified counts.

Most of the publications deal with scalp EEG records. Our interdisciplinary workgroup works with the data of several dozen patients with intracerebral (intracranial) EEG implantation. The preliminary results presented in this abstract focus on signal processing methods based on AR models. In particular, the algorithm presented in [8] is modified and applied to the iEEG records. The full paper intends to discuss technical aspects in terms of suitability of sampling frequency, AR model order and segmentation step. All measurements and comparisons in the abstract are related to one patient and one seizure.

III. IMPLEMENTATION OF THE DTF METHOD

The method described in [8] is modified for applicability for the iEEG records instead of scalp EEG. The signal, generally with *m*-channels, is split into segments with defined overlap. A multivariate autoregressive model (MAR) is estimated for each *m*-channel segment *X*. The MAR with m variables is defined by equations (1-3) [9].

$$\begin{aligned} X_1(n) &= \sum_{j=1}^{m}\left[\sum_{i=1}^{N} A'_{1j}(i)X_j(n-i)\right] + e_1(n) \\ &\vdots \\ X_m(n) &= \sum_{j=1}^{m}\left[\sum_{i=1}^{N} A'_{mj}(i)X_j(n-i)\right] + e_m(n) \end{aligned} \quad (1)$$

where N is model order, $X_1(n)..X_m(n)$ are the current value of each time series of the iEEG signal segment, $A'_{11}...A'_{mm}$ are model coefficient et delay i and $e_1(n)...e_m(n)$ are predictor errors. The equations (1) can be re-written to equations (2) in matrix form.

$$X(n) = \sum_{i=1}^{N}\begin{bmatrix} A'_{11}(i) & \cdots & A'_{1m}(i) \\ \vdots & \ddots & \vdots \\ A'_{m1}(i) & \cdots & A'_{mm}(i) \end{bmatrix}\begin{bmatrix} X_1(n-i) \\ \vdots \\ X_m(n-i) \end{bmatrix} + \begin{bmatrix} e_1(n) \\ \vdots \\ e_m(n) \end{bmatrix} \quad (2)$$

The predictor error filter is expressed as equations (3).

$$\sum_{i=0}^{N} \mathbf{A}_i \mathbf{X}_{n-i} = \mathbf{E}_n . \quad (3)$$

in which $\mathbf{A}_i$ is the coefficient matrix of the model, $\mathbf{X}$ is a matrix of m vectors iEEG in discrete time n-i and $\mathbf{E}_n$ is a matrix of uncorrelated white noise, where $\mathbf{A}_0=\mathbf{I}$ and $\mathbf{X}_i=-\mathbf{X}'_i$. The function *mvar* from the biosig4octmat toolbox [10] is used, which makes use of the Partial Correlation Method computational method. The AR model order N is estimated using the Akaike criterion [11], and is estimated individually for each patient and each EEG frequency range. The length of the segments i.e. the duration is set as short as possible due to better time accuracy. The limit factor is 10 x N samples. Experiments with shorter segments show relatively increased errors. The matrix of transfer function $\mathbf{H}(f)$ has been defined using the Fourier transform.

$$\mathbf{H}(f) = \left(\sum_{i=0}^{N} \mathbf{A}_i \exp(-\mathrm{j}2\pi i \frac{f}{f_s})\right)^{-1} \quad (4)$$

in which f is frequency, f_s is sampling frequency.

It is possible to define an “electric activity flux” from channel j to channel i using the normalized directed transfer function DTF.

$$\gamma_{ij}^2(f) = \frac{\left|H_{ij}(f)\right|^2}{\sum_{k=1}^{m}\left|H_{ik}(f)\right|^2} \tag{5}$$

in which $H_{ij}(f)$ is an element of the transfer matrix $\mathbf{H}(f)$ in i-th column and j-th row.

The source signal is filtered by band pass filters bank using FIR filters of $3f_s$ order. See the table 1.

TABLE I. EEG SIGNAL SUB-BANDS

Symbol	δ	θ	α_1	α_2	β_1	β_2	γ_1	γ_2	γ_3	γ_4	γ_5
Band [Hz]	2-4	4-8	8-10	10-12	12-18	18-25	25-48	52-85	85-150	150-250	250-350

A mean "flux" is defined for each sub-band from channel j to channel i. $\gamma_{ij}(band) = mean\left(\gamma_{ij}(f_k)\right)$ in which f_k is the discrete frequency of each sub-band. The "flux" of the channel j to all other channels is given by (6).

$$DF_j = \frac{1}{m-1}\sum_{\substack{i=1 \\ j\neq i}}^{m}\gamma_{ij}(band) \tag{6}$$

The vector of the partial DFs represents a parametric segment of channel j. See the vector

$$\mathbf{y}_j = \left[DF_j(\delta),\ \ldots, DF_j(\gamma_5)\right]. \tag{7}$$

The vectors $\mathbf{y}_j$ are classified using one class support vector machine (OC-SVM). There are two output classes – baseline/seizure (+1/−1 represented by numbers). The classifier is trained on the set of parametric segments corresponding to times, when the patient is classified as in the interictal state. There is no significant energy change in spectral domain during this state [12]. The principal component analysis (PCA) algorithm is used to decrease the $\mathbf{y}_j$ dimensions for the classifier.

The OC-SVM finds the decision vector with 10% error to classify the baseline, which implies decreasing the sensitivity for the baseline state classification but not directly increasing the sensitivity for the seizure class. However, some parameterized segments from the baseline are classified into the seizure class. Therefore, the seizure is determined by a prior probability P (P-estimation) which is calculated by equation (8).

$$P = \frac{M^-}{M} \tag{8}$$

in which M is the number of following segments and M^- is the number of seizure classes.

The P-estimate increase in partial channels indicates the seizure onset.

IV. RESULTS

A. Detection and localization of SOZ

Figure 1 shows examples of intracranial EEG with epileptic seizures. This signal was processed by the method described above.

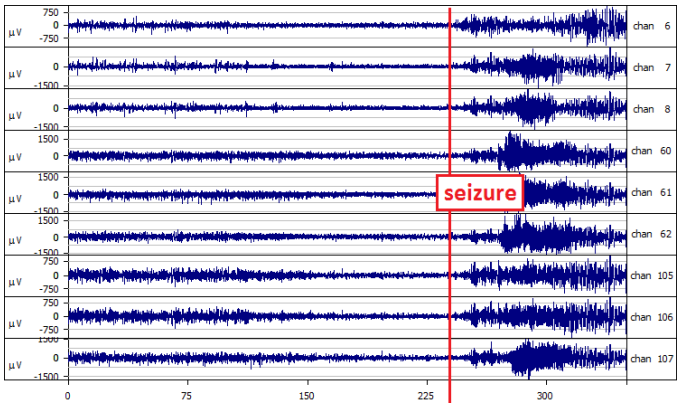

Figure 1. Example of intracranial EEG with epileptic seizure

The seizure onset is indicated by a steep increase in the P-estimate. The P-estimate is observable earlier in channels corresponding to electrodes placed over the zones with epileptoform activity than in electrodes with secondary propagated activity. Figure 2 shows the cortical map of placing the electrodes. The P-estimate is colored in respect to the rule on top. The figure of zero equals the probability of no seizure at all, and the opposite one, the maximal probability that the particular channel detects epileptoform activity. Figure 3 shows an example of three P-estimate transients of three representative channels.

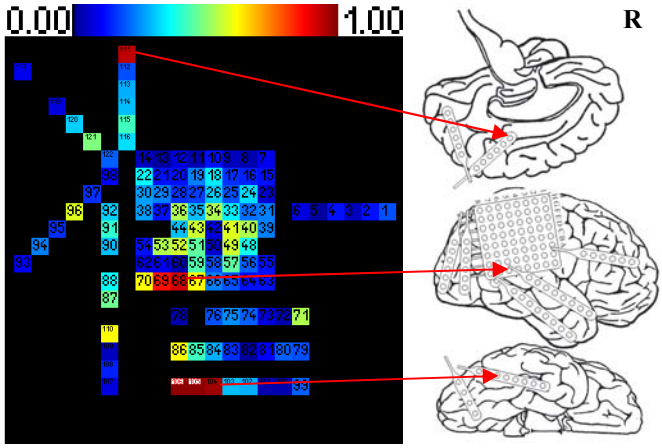

Figure 2. Example of visualization of the P-estimate in the cortical map

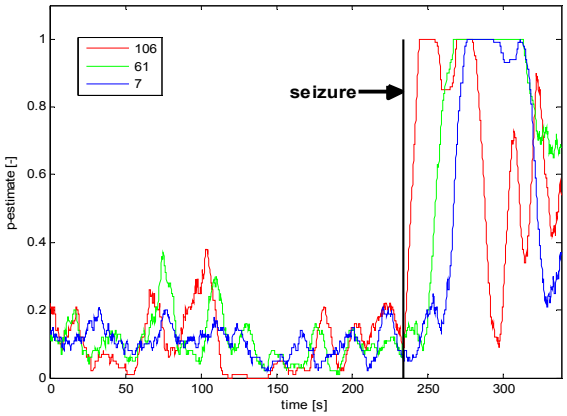

Figure 3. An example of the difference between *P*-estimates for the three channels at the time of SOZ

Channel number 106 is the first electrode that shows a *P*-estimate increase. The time of the increase equals the time given by neurologists. The electrode is placed very close to a lesion area. The electrode 61 is a member of a set of electrodes close to the lesion, but there is a delay in the beginning of epileptic activity. The electrode number 7 is situated over the cortex without any pathological changes. The epileptic activity is propagated relatively late.

The *P*-estimate fluctuations before the seizure are caused by artefacts, pathologic interictal patterns, low amplitude fast activities and noise. The sensitivity to those fluctuations is influenced by the choice of training data.

B. Effect of sampling frequency

The sampling frequency f_s has a direct influence on the visibility of the details in the signals, and also the parametric description of the segments in the sub-bands. The data acquisition system used allows for the use of the sampling frequencies 200 Hz and 1 kHz. Hence it is also possible to analyze the sub-bands γ_3 - γ_5. The higher frequency also allows for shorter segments and consequently more accurate time resolution. Figure 2 shows the cortical map of the seizure onset with f_s = 1 kHz. The *P*-estimate is computed for a 10-sec window. Figure 4 shows the situation for a decimated signal to f_s = 200 Hz. There are no significant maximums in comparison to the higher sampling frequency. In any event, it is clear that the "hot" zones correspond to the lesion. Figure 5 shows the difference between the *P*-estimate transients of both sampling frequencies for electrodes 106 and 61 at different f_s and the same parameters as described in paragraph 4.C. Both signals can be located by the time when the *P*-estimate begins to grow, but the change-point appears worse for lower sampling frequency f_s.

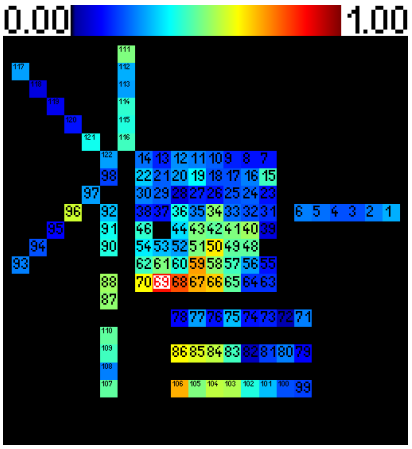

Figure 4. Example of visualization of the *P*-estimate in the cortical map with lower sampling frequency

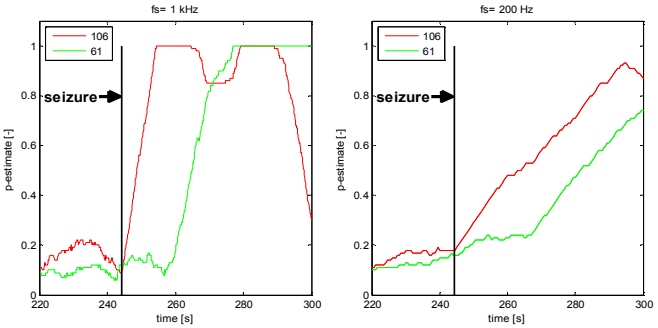

Figure 5. An example of *P*-estimates for different sampling frequencies

C. Effect of window length

The length of the segmentation window is chosen as a compromise between good time resolution, stability calculation of the AR model and a signal stationarity presumption. With respect to model orders used as < 20, the condition of stability has already been met by the window length of 200 samples. The signal stationarity depends on the sampling frequency f_s assumed for 0.2 or 1 second. However, it appears that the use of a window length of 400 samples gives better results in the calculation of the AR model. A stationarity signal with a lower sampling rate is assumed for 2 seconds; in particular, the γ sub-band may not be valid. The overlap 90% of window segmentation is applied to improve the time resolution. The size of the overlap seems high because the adjacent segments will result in only minor changes. However, this high overlap gives a consistent training set for OC-SVM classifier. A greater number of parameterized segments and calculation of the *P*-estimate (6) makes it possible to obtain the result using a larger overlap in short signals. The number of *M* parameterized segments used for the estimation of *P*-estimation defines the number of quantization levels of a priori probability of an attack. The trend of the seizure cannot be determined with a low value of *M* , making the result imprecise with large deviations. Conversely, a high value blurs the details. The value M= 50 - 100 was chosen subjectively. Using the appropriate choice of parameters, we can obtain the seizure

probability in a 2.5-second segment signal at f_s = 1 kHz and 10-second segment at f_s = 200 Hz.

D. *Effect of AR model order selection*

AR model order selection affects the ability for the relevant parameterizing of the signal. Using a low order, the important details in individual sub-bands may be missed, while high orders bring sizeable errors and greatly increase the computational costs. The Akaike criterion (AIC) was used to determine the optimal order, which must be determined for each patient and each sub-band individually, see Figure 6. The appropriate model order corresponds with the minimum or slight decrease of the waveform AIC. For δ - γ_1 sub-band it is N=7, for γ_2, N=8, for γ_3, N=10 and for γ_4 - γ_5, N=18.

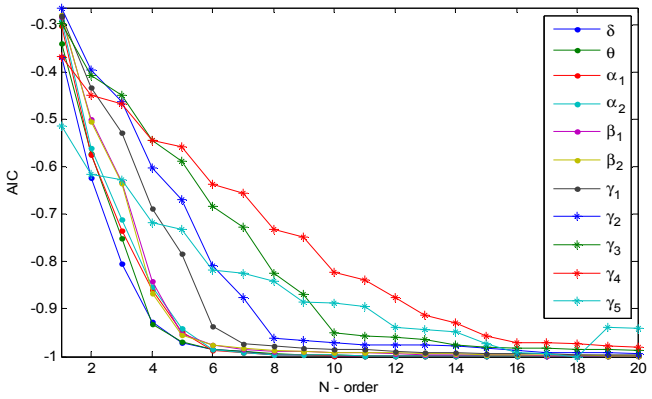

Figure 6. Akaike criterions sub-bands

V. CONCLUSION

Using the algorithm described above, the exact time of the seizure onset was determined and the source contacts were located. The seizure extent and change propagation were also marked (see screenshot in Fig.1). The present case report, involving a child patient showed an unusual method of localization of the seizure onset zone that was followed by visualization of the spreading of the seizure. Using appropriate methods of intracranial EEG analysis, we can achieve a greater distinctiveness perspective of events and the links between them. We are also able to create a more objective view of the evaluator diagnostic symptoms. Nonetheless, interpretation remains uncertain with respect to seizures during the phases of sleep and aura.

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