MULTISCALE SAMPLE ENTROPY FOR TIME RESOLVED EPILEPTIC SEIZURE DETECTION AND FINGERPRINTING

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ABSTRACT

Early detection of epileptic seizures is still a challenge in the state-of-the-art. The proposed method exploits multi-resolution sample entropy for both seizure detection and fingerprinting. First, a SVM classifier is used to detect the seizures' onset with high temporal accuracy, then the seizures fingerprints across the subband structure are derived exploiting sample entropy non stationarity. Over 8 hours of EEG data recordings from patients suffering from temporal lobe epilepsy were used for training and testing the system, and validation was performed based on annotation by one expert neurophysiologist. All the seizures were successfully detected and provides an effective time-scale fingerprinting of their evolution. A prominent impact in high (γ) frequency band was observed whose neurophysiological ground is currently under investigation.

Index Terms— Biomedical Signal Processing, Entropy, Electroencephalography, Epilepsy, Wavelet transform

1. INTRODUCTION

Epilepsy is a common chronic neurological disorder characterized by recurrent, unprovoked seizures [1, 2]. The statistical properties of the EEG depend on both time and space. Characteristics of the EEG, such as the existence of limit cycles (alpha activity, ictal activity), instances of bursting behavior (during light sleep), jump phenomena (hysteresis), amplitude-dependent frequency behavior (the smaller the amplitude the higher the EEG frequency) and existence of frequency harmonics (e.g., under photic driving conditions), are among the main properties of nonlinear systems [3]. The presence of nonlinearities in EEGs recorded from an epileptogenic brain supports the concept that the epileptogenic brain is a nonlinear system. Therefore, non-linear analysis methods would be more suitable to its processing. As a measure of complexity, entropy and its variations have been considerably exploited in the last years. Recently, sample entropy (SampEn) was introduced as an improvement of approximate entropy (ApEn) [4] and used as a feature for detecting epileptic seizures. A further refinement was then proposed in [5] where an optimized sample entropy algorithm combined with extreme learning machines (ELMs) was employed for detecting ictal segments within the EEG recordings. In [6] a support vector machine (SVM) was used for classifying segments of normal and epileptic EEGs reaching high accuracy. In [7] the Neyman-Pearson criteria and SVMs were applied for detecting ictal segments after computing the discrete wavelet transform (DWT) and extracting the approximate entropy. Results demonstrated that the wavelet coefficients and the ApEn are features that represent the EEG signals well. By comparison with Neyman-Pearson criteria the SVM applied on these features achieved higher detection accuracies. Overall, results of epileptic EEG signal detection using SVM show that nonlinear methods can improve the performance of the detector reaching an accuracy of 98%.

However, none of these methods target the early detection of the epileptic seizures with high temporal accuracy. Though, this is a very important issue since the accurate temporal detection of the onset of the seizures would allow not only the prompt intervention of the clinical personnel but also the investigation of the transient from rest to ictal conditions that could be revealing of the underlying neurophysiological process. This is also highlighted in [8], were they applied wavelet decomposition and feature extraction to intracranial EEG including high frequency (80-500 Hz) activity in order to detect the seizures with a low delay after onset. Their results show a sensitivity of 72%, a false detection rate of 0.7/h and a median delay of 5.7 s. Our work targets such issues with the additional aim of preserving the spatial information. This enables the investigation of the transient from rest to seizure and supports source reconstruction and the analysis of the signal propagation across the epileptic network for connectivity analysis.

2. METHODS

2.1. Dataset

Clinical data were acquired at the Verona University hospital from 5 subjects using a headset with 19 electrodes (Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, Pz) positioned according to the international 10-20 system of electrode placement. The equipment was a GEM

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100 digital mobile system (ATES MEDICAL devices). EEG signals were sampled at 250 Hz. A notch filter was used to eliminate the interference of the power supply. The cut-off frequency was set to 50 ± 2 Hz. A neurologist reviewed the EEG to identify the seizures onset in each patients. A total of 10 seizures onset were registered during over 8 hours of recording.

2.2. Multiscale sample entropy based analysis

A five levels stationary wavelet transform (SWT) was applied to the 250 Hz sampled EEG signal to recover the delta δ ($0.5-4$ Hz), theta θ ($4-8$ Hz), alpha α ($8-13$ Hz), beta β ($13-30$ Hz) and gamma γ (> 30 Hz) frequency bands as in Table 1. The (db4) wavelet was used.

Decomposed signal	Frequency band (Hz)
D1	$\approx$ 62-125 Gamma
D2	$\approx$ 31-62 Gamma
D3	$\approx$ 16-31 Beta
D4	$\approx$ 8-16 Alpha
D5	$\approx$ 4-8 Theta
A5	$\approx$ 0-4 Delta

Table 1. Frequency mapping of the decomposition sub bands. D1, D2, D3, D4, D5 represent the detail coefficients of each decomposition level and A5 is approximation subband.

Sample entropy was defined according to [4]

$$\text{SampEn}(m, r) = \lim_{N \to \infty} \ln \frac{B^m(r)}{A^m(r)} \quad (1)$$

Since the time series length is finite, SampEn is estimated using the N available samples:

$$\text{SampEn}(m, r, N) = \ln \frac{B^m(r)}{A^m(r)} \quad (2)$$

$B^m(r)$ represents the probability that two sequences will match in m point, whereas $A^m(r)$ represents the probability that two sequences will match in $m + 1$ points. Therefore the quantity$B^m(r)/A^m(r)$ is the conditional probability that two sequences $X_m(i)$ and $X_m(j)$ remain within r of each other in m points with a *tolerance* r, where $X_m(i) = [x(i), x(i+1), ..., x(i+m-1)]$, for $1 \leq i \leq N - m + 1$.

Previous studies have proved that SampEn has a good statistical validity for $m = 1$ or $m = 2$ and $0.1 < r < 0.25$ times the standard deviation (σ) of the time series [9, 10]. According to [5], best discrimination performance between ictal and interictal segments was obtained with $m = 2$ and $r = 0.2 \times \sigma$, so such indications were followed in the present work. Starting from the values suggested in the literature, a generalization of the approach proposed in [5] was taken to meet the best trade-off condition. The m, r space was spanned in a multiresolution manner in order to identify the pair of values leading to maximum temporal accuracy and detection performance. A wide spectrum of conditions was considered. Different values of m were tested jointly with the estimation of r either signal-wise or subband-wise. In this case, each subband was analyzed independently and different modulations of the standard deviation in resting conditions were considered ($r = k \times \sigma$). Overall, results showed that the best trade-off for the SVM performance could be reached by setting $m = 2$ and $r = 0.2 \times \sigma$, σ being the standard deviation of the signal. Furthermore, $N = 250$ samples allowed to bound the duration of the temporal analysis window to 1 sec, which permits high temporal accuracy.

2.3. Seizure detection and fingerprinting

Seizure detection was performed at the signal level by extracting the sample entropy values across the subbands and adding to the resulting vector of features the power spectral density (PSD) of the signal in the same analysis window. An one class support vector machine (SVM) with a radial basis function (RBF) kernel was then applied to segregate the seizure from the resting condition. The ground truth for the performance in the seizures onset detection was obtained by visual inspection of the joint EEG and video recordings of the patients by an expert neurophysiologist.

Parametric statistics based detection was performed for characterizing the SampEn behavior through the analysis of the multi-scale fingerprints. A z-test was performed separately in the different subbands to locate the deviations of the SampEn from resting conditions. This would allow to identify the fingerprint of the seizures onset over the subband structure that could help disambiguating the underlying pathological mechanism. The mean and standard deviation of SampEn during ten minutes of rest were estimated in order to characterize the reference distribution. The value of α to be used in the test was obtained by inspection based on the trade-off between the number of false detections and the delay in identifying the seizure.

3. RESULTS AND DISCUSSION

The 1C-SVM classifier was trained on the samples obtained by a ten minutes observation in resting conditions. The SampEn values in the frequency bands and the signal PSD within the analysis window were gathered in feature vectors that were used to feed the classifier. The detection performance of the SVM was determined by classical indexes based on the counting of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN) against the manually defined ground truth. Accordingly, sensitivity, specificity and accuracy were calculated.

The detection delay, or latency, was defined as the time course between the onset of the seizure and the first event

labelled as seizure

$$\Delta t = T_m - T_r \quad (3)$$

where T_m is the marked EEG seizure onset time as determined by the expert neurophysiologist and T_r is the time at which the seizure onset was detected by the 1C-SCV system. The latency was defined as the minimum delay in the onset detection across all the channels, and in all cases it resulted to be associated to one of the focal channels. Five patients were considered, out of which two went through two seizures (P3 and P4), one through four seizures (P5) while the other two only experienced one single seizure (P1 and P2) during the observation period. In all cases except for P1 the automatic 1C-SVM system was able to detect the onset with high temporal accuracy in the focal channels that were previously identified by the neurophysiologist. Table 2 provides the performance of 1C-SVM. The sensitivity (Se), number of false negatives (FN), specificity (Sp) and accuracy(Ac) were averaged over the focal channels. The majority of FN was located either before the detection or after the end of the seizure. In the first case this increases the detection delay, as it was the case for P1, while in the second it could suggest that the end of the seizure would take place in advance with respect to what can be established by visual inspection. In any case, FNs reduce sensitivity that is lowered by missing detections.

For P5 many outliers were detected within the fourth seizure duration, decreasing the sensitivity. However, P5 can be considered as a worst case because of his pathology making the EEG very noisy. Nevertheless, he was included in the analysis because despite the relatively large number of FN at the end of the seizure, it could always be detected with very high temporal accuracy. Overall, the seizures were detected for all the patients reaching the 100% of seizures detected. Moreover, our results show a median and mean latency of zero and 3.1 sec, respectively.

P (sz)	Latency (sec)	Se	Sp	Ac	FN
P1 (1)	21	0.38	0.99	0.97	21
P2 (1)	5	0.91	0.98	0.98	5
P3 (1)	0	1	0.99	0.99	0
P3 (2)	0	0.88	0.99	0.99	1
P4 (1)	3	0.63	0.99	0.99	3
P4 (2)	2	0.81	0.99	0.98	4
P5 (1)	0	1	0.97	0.97	0
P5 (2)	0	0.63	0.97	0.94	36
P5 (3)	0	0.49	0.97	0.89	86
P5 (4)	0	0.25	0.98	0.94	90

Table 2. Average results of 1C-SVM classification. First column: patient (P) and number of seizure events (sz); last column: focal channels.

3.1. Frequency band signatures

A second level of performance evaluation consisted in the assessment of the percentage of samples labeled as seizures against the total number of samples within the ictal segments as manually identified by the physician in the EEG signal, jointly with the delay in seizure detection within the different frequency bands. This is a critical point because the ground truth only holds at the signal level, while the impact of the seizure on the structural properties of the signal in the different subbands is still unknown and its characterization is one of the objectives of this study.

The underlying hypothesis is that a seizure could selectively alter the signal structure in the different frequency bands in a manner related to the pathology and other clinical factors.

The frequency-dependent detection delay (D) was defined as the time course between the beginning of the seizure as indicated in the ground truth and the first event labeled as seizure across the subbands

$$D = T_m - T_{r,j}$$

where T_m is the marked EEG seizure onset time as determined by expert neurophysiologist and $T_{r,j}$ is the time at which the first outlier is detected in the subband j. The positive seizure detection rate (PSDR) was defined as the percentage of samples labeled as seizures between the first detected seizure and the end of the seizure in any subband. This provides an indication of the estimate of the conditional probability of detecting a seizure in a certain frequency band given the fact that a seizure was detected. It could be useful to remark here that the assessment of the absolute probability of seizure detection by the classifier in a given subband would require prior knowledge on the subbands affected by the seizure, namely of the ground truth. Though, this information can not be derived by visual inspection of the EEG signal and it is currently unavailable. Results suggest that the major changes take place in high frequency bands, namely γ (D1 and D2) and β (D3) for all the patients. Noteworthy, seizures were detected in the high frequency bands (D1 and D2) of focal channels in all cases.

The analysis of sample entropy variations across subbands in the different channels show that the SampEn increments in the eloquent frequency bands clearly identify the cortical involvement of the seizure. Figure 1 provides an examples highlighting the increase of activity in the γ and δ bands in the temporal channels at two different time instants. The detection latency and PSRD showed a large inter-subject variability while it was relative stable across the seizures. As mentioned before, the main changes in sample entropy were recorded at high frequencies (γ and β). Figure 2 provides an example of SampEn increment with respect to inter-ictal conditions in the γ band.

4. RELATION TO PRIOR WORK

The early detection of the seizure onset with high temporal resolution is a hot topic in the state-of-the-art. Though, most

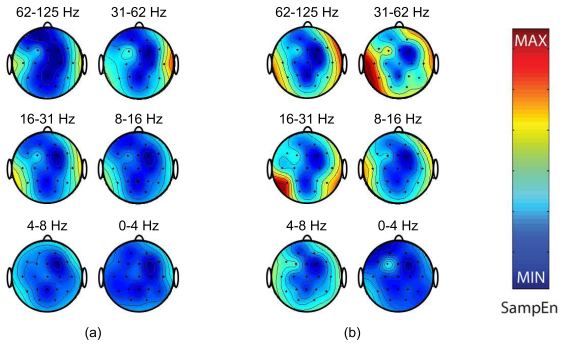

Fig. 1. Cortical involvement as detected by SampEn increments at two different time points. Plots (a) are taken 3 seconds after the seizure onset, instead (b) are taken after 42 seconds in the middle of the seizure.

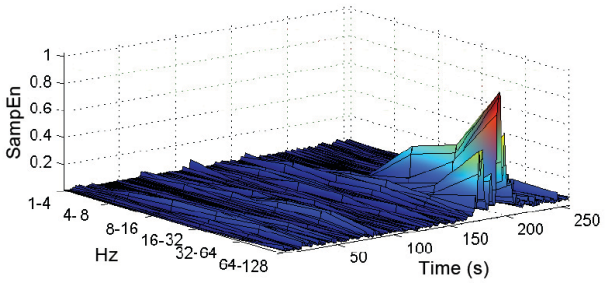

Fig. 2. Time-frequency sample entropy fingerprint. Increase of SampEn in high frequency bands.

of the studies focus on signals acquired through stereo EEG depth intracerebal recordings. Few data do exist on surface EEG despite the relevance of the identification and characterization of the seizure onset in the focal paroxymal activity from the clinical perspective. The proposed approach allows reaching high temporal accuracy (1 sec) with the result of zero sec of median latency and high seizure detection efficiency while preserving the spatial information about cortical activation. Accordingly, using an higher number of electrodes might improve spatial resolution about the cortical involvement. Furthermore, our work enables the analysis of the impact of the seizure at different frequency bands and thus the definition of time-frequency fingerprints that support neurophysiological modeling.

In general, works reaching high sensitivity and specificity use epochs of long durations (e.g. 23.6 seconds in [4] where the sensitivity and specificity reached the of 99% and 96%, respectively). This prevents the detection of short term seizures such those considered in this work.

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