An Analysis of Subdural EEG Parameters for Epileptic Seizure Evaluation

Maria Tito[1], Mercedes Cabrerizo[1], Melvin Ayala[1], Malek Adjouadi[1], Prasanna Jayakar[2], Armando Barreto[1]

[1]*Department of Electrical and Computer Engineering, Florida International University*

[2]*Brain Institute, Miami Children's Hospital*

cabreriz@fiu.edu, adjouadi@fiu.edu, ayalam@fiu.edu

Abstract

This study evaluates intracranial electroencephalographic (EEG) recordings with the intent to detect epileptic seizures. It provides a complete evaluation (inter and intra patient) of several parameters in order to perform a retrospective analysis of the attributes of such parameters in their accuracy to detect seizures. As a corollary of this retrospective, is the appreciation of the complexity of their general behavior, and in understanding the difficulties engendered in the attempts of researchers to generalize their use for seizure detection, and for seizure prediction. The analysis conducted involves both intra and inter patient studies and provides a performance evaluation of the most relevant parameters in both frequency and time domains, which are deemed extremely useful in determining those patterns that signify the existence of an epileptic seizure.

1. Introduction

In this study a variety of parameters were initially investigated, so that reliable measurements could be used to detect a seizure. The merits of the algorithm are: (a) in providing an analysis of the parameters in terms of their significance to detect a seizure based on Receiver Operating Characteristics (ROC) standards and using the time and frequency domain; (b) in providing a similar analysis of the relevance of the same parameters based on an intra and inter patient analysis.

Given several important studies in the past decade, on epilepsy, a definite consensus was reached about the chaotic nature of EEG signals and how limited is the collective knowledge we have gathered over the years [1, 2, 3]. Correlation integral is currently the most common basis on which the claim of chaotic dynamics has been made in biological systems [4, 5, and 6]. Correlation dimension oriented analysis applied to raw EEG and some variations including autocorrelation and entropy [7] are being directed with encouraging results, especially in the elusive problem of seizure detection and prediction, where promising results are claimed to be obtained [8]. Based on our experience, we have denoted that each patient has a different behavior of its EEG signal. Having a method that adapts to every patient would be very helpful for the precise location of an epileptic focus. The detection process is designed such as to allow physicians to make evaluative assessments of epileptic seizures, which in turn will enable targeted treatment. Methods for the automated detection of seizures can be very useful, especially during long-term EEG monitoring sessions, and may serve as a support mechanism to the decisions made by EEG experts.

2. Methods

2.1. Data collection

Subdural EEG recordings of eight epileptic children were considered. A total of twenty six different seizures were studied. Recordings were performed during pre-surgical monitoring at the Miami's Children Hospital (MCH) using XLTEK Neuroworks Ver.3.0.5, equipment manufactured by Excel Tech Ltd. Ontario, Canada. This data was collected at 500 Hz sampling frequency and filtered to remove DC and high frequency components using a 0.1-70 Hz band-pass filter.

The patients involved were about to undergo surgery interventions in response to intractable seizures. The number of electrodes implanted differed from patient to patient. Up to 88 subdural electrodes were implanted on the surface of the cerebral cortex of each patient to record seizure activity. Intracranial recordings of eight patients were performed by using subdural strips or grid electrodes. In some cases, 4 contact depth electrodes were implanted.

2.2. Data analysis

2.2.1. Data preprocessing. The objective was to analyze the entire array of electrodes, and depending on the size of the file, up to sixty minutes preceding a seizure and two minutes after seizure onset was analyzed. Data sets used are obtained from 8 patients (six males, two females with the age range of 3–17 years). Each patient had a different number of EEG files. The time interval for the other 4 patients was much longer with 60 minutes prior to seizure onset and 2 minutes after.

2.2.2. Parameter extraction. Due to the high volume of information contained in the pre-filtered EEG data files, size reduction was necessary. Data files were segmented in one second time windows and parameters were extracted for all windows and for each electrode. The size of the set was thus reduced to a small number of parameters that are representative of the EEG. This set of parameters was then used for the study. A comparison of all of them was conducted in order to analyze and determine among all these parameters which ones were the most suitable to use in seizure detection. Confusion matrices were generated with the purpose of eliciting a better understanding of the performance attributes of each of the following 12 parameters:

F1: activity
F2: mobility
F3: complexity
F4: mean of auto correlation (AC)
F5: standard deviation (STD) of (AC)
F6: correlation integral (CI)
F7: spectral power (SP) in delta band (< 4 Hz)
F8: spectral power (SP) in theta band (4-8 Hz)
F9: spectral power (SP) in alpha band (8-13 Hz)
F10: spectral power (SP) in beta I band (13- 20 Hz)
F11: spectral power (SP) in beta II band (20-36 Hz)
F12: spectral power (SP) in gamma band (36-44 Hz)

Please note that parameters F1 through F6 were extracted from the signal's time domain, whereas the rest of the parameters were computed from the frequency spectrum of the signal.

Other interesting parameters are used in EEG processing in seizure studies, such as the Lyapunov exponent which is a complex mathematical quantity in which the amount of chaos in the brain is measured [10]. This exponent is somehow computationally intensive, however, it contains in its formula a quantity called correlation integral, which also deals with the signal chaos. This quantity was included in the parameter's list.

Some of the most studied parameters such as mobility and complexity are known as Hjorth parameters [11]. The activity (A_x) is defined as the variance σ_x of the signal. The mobility *(Mx)* is computed as the square root of the ratio of the activity of the first derivative of the signal A'_x to the activity of the original signal A_x:

$$M_x = \sqrt{\frac{A_{x'}}{A_x}} = \frac{\sigma_{x'}}{\sigma_x} \quad (1)$$

where x' represents the first derivative of the input EEG signal x.

Mobility gives a measure of deviation of the voltage changes with respect to deviation of the EEG voltage amplitude. Complexity *(C)* is defined as the ratio of the mobility of the first derivative of the signal to the mobility of the signal itself:

$$C = \frac{M_{x'}}{M_x} = \frac{\sigma_{x''} / \sigma_{x'}}{\sigma_{x'} / \sigma_x} \quad (2)$$

where x'' stands for the second derivative of the input EEG signal.

The complexity of a sinusoidal wave is unity; other waveforms have complexity values increasing with the extent of variations present in them. Complexity represents the deviation from the sine shape of the EEG signal.

Correlation integral was also computed and it is mostly used to detect randomness in data. It is given by:

$$C_{m,r} = C_r = \frac{1}{N}\sum_{k=1}^{N}\left[\frac{1}{N}\sum_{i=1}^{N}\theta(r - |x_i - x_k|)\right] \quad (3)$$

where N is the total number of samples in the EEG data segment inside the sliding window, *θ(.)* is the step function, and $| x_i - x_k |$ is the distance between x_i and x_k. The vector x_i used in the correlation integral is a point in the embedded phase constructed from the input EEG signal as a single time series according to the following:

$$X_i = (x_i, x_i + \tau, x_i + 2\tau, \ldots. x_i + (m-1)\tau) \quad (4)$$

where m is the embedding dimension and τ is a delay. The correlation integral can be interpreted as the number of point pairs inside a hyper-ball of radius *r*.

Initially, only different groups of electrodes were employed for the pattern extraction analysis. The behavior of the parameters for the group of electrodes leading to seizure and not leading to seizure has been previously studied [12, 13]. However, for the detection purpose, it was more suitable to use all electrodes because at the time of the seizure all of them synchronize with each other and the behavior of every parameter at the seizure time was similar.

After extracting the parameters for each electrode and patient, further data reduction was necessary for the following reasons: (1) there were too many electrodes per patient; (2) not all patients had the same amount of electrodes, and (3) not all electrodes were placed at the same position from patient to patient. This situation lead to a large database that would also make impossible to create a model for seizure detection that would work regardless of the number of electrodes and their position. A solution to contend with both the large data base and the different number and locations of electrodes was to compute the average of all parameters across all electrodes for each time window.

2.3. Construction of the seizure detectors

The procedure implemented for creating seizure detectors was based on establishing 4 thresholds for each parameter that could be used to automatically detect a seizure. These 4 thresholds consist of the mean, standard deviation, minimum, and maximum of the parameter that is applied to the EEG data. Since, we are implementing 12 parameters, and each parameter is subdivided into 4 statistical features, we ended up with 48 (4*12) parameters to be analyzed. In this study, the procedure was performed inter and intra patient, and therefore, 50% of the patient files were used as reference files or baseline to extract the thresholds. The remaining files were kept for testing.

A procedure was applied to the reference files in order to obtain thresholds that would maximize classification accuracy. These thresholds were used to test the remaining files. The classification results obtained were then compiled in order to perform an ROC-based analysis.

Throughout this paper, classifier names will be simplified by numbers according to the parameter that they are based on. For example, the classifier based on parameter 1 will be named "classifier 1", and so on.

2.4. Seizure classification results

2.4.1. Evaluation criteria. Performance evaluation of the classifiers was conducted based on the (ROC) terminology [14]. An ROC analysis is initiated with a confusion matrix [15] which contains information about actual and predicted classifications done by a classification system. Table 1 shows the entries of the confusion matrix for a two class classifier.

- TP (true positives) is the number of correct predictions that an instance is positive
- FN (false negatives) is the number of incorrect predictions that an instance is negative
- FP (false positives) is the number of incorrect predictions that an instance is positive, and
- TN (true negatives) is the number of correct predictions that an instance is negative.

Table 1. Entries of a confusion matrix

		Detected as	
		Positive	Negative
Actual	Positive	TP	FN
	Negative	FP	TN

Positive and negative refers to the outcome given by the classifier, whereas true and false refers to the correctness of this outcome (i.e. right or wrong with respect to the actual state of the patient).

Important quantities can be extracted from the confusion matrixes, namely the TP rate (also known as sensitivity, hit rate or recall), the FP rate (also known as false alarm rate, or 1 - specificity), the precision and the accuracy, among others. The use of such measures is widely used in pattern recognition for test evaluation purposes.

The TP rate is the proportion of the number of TP to the total number of positive instances. It is expressed as:

$$TP_r = \frac{TP}{TP + FN} \tag{5}$$

The PF rate is the proportion of the number of TN to the total number of negative instances and it is computed as:

$$FP_r = \frac{FP}{FP + TN} \tag{6}$$

The precision is the proportion of the number of TP to the total number of positive detections as given below:

$$Precision = \frac{TP}{TP + FP} \tag{7}$$

Accuracy is the proportion of the number of correct detections to the total number of detections, and it is computed as follows:

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{8}$$

At inter-patient level, an analysis was performed in order to show the relationship of the accuracy values of all parameters for across all patients. As opposed to this type of analysis, many types of medical studies are often performed intra-patient, to avoid comparing results from patients that are naturally supposed to be different. This is why inter-patient analysis can be regarded as a challenging task depending on the specific situation. Varying a classifier threshold can have contradictory effects. Increasing the TP rate can also increase the FP rate, which is an undesired collateral effect. Therefore, an answer is found in the so-called ROC curves. These are parametric curves that are constructed based on the values of the TP rate and the FP rate.

Two major reasons hindered us from using ROC curves: Firstly, the classifiers were tested on different patients; and secondly, the test thresholds were not varied within each patient. Due to the inability to rely on ROC curves, classifiers were ranked according to a simple criterion: the highest level of accuracy. The TP and FP rate values allowed us to calculate the accuracy of each parameter implemented. The best parameter is said to be the one that produces the highest accuracy value.

In this study, all classifiers were tested for all patients, thus 96 (12 parameters * 8 patients) different confusion matrixes were obtained and the corresponding accuracy values were calculated.

At an intra-patient level, 12 classifiers (one for each parameter) were created and tested for each patient.

2.4.2. Parameter analysis. A grey scale map illustrating the accuracy of the parameters is depicted in Figure 1, this way the parameters across all patients with the highest accuracy values will be located. Note that the highest accuracy levels are observed to belong to classifier 6 and patient number 5.

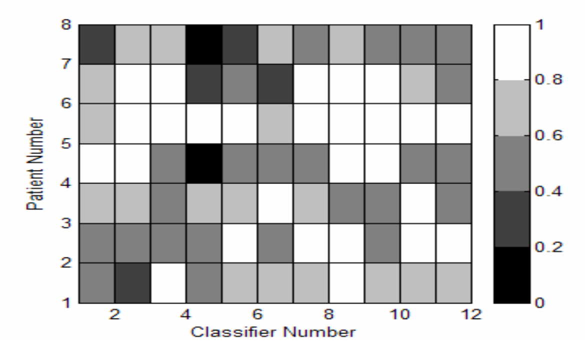

Figure 1. Grey scale map displaying the accuracies of all classifiers

As illustrated in Table 2, patient 1, the classifiers 3 and 8 had a performance higher than 0.5, whereas for patient 2, the best performing classifiers were numbers 5, 7, 8, 10, and 11. All of them were higher than 0.5 (e.g. 50%). By comparing the results across all patients, no consistency was observed.

The detection algorithm was able to be performed for each patient with a high accuracy within the same patient; nevertheless, when a good classifier (based on one patient) was applied to any other patient, results were not as good as expected. An example of the results of the best parameter (CI) is illustrated for visual analysis in Figure 2.

Table 2. List of classifiers with more than 80% accuracy

Patient #	Classifiers over 80% accuracy (in descending order)
1	3, 9
2	5, 8, 9, 11, 12
3	6, 7, 11
4	1, 2, 6, 9, 10
5	10, 11, 2, 3, 4, 5, 6, 8, 9, 12
6	3, 2, 8, 6, 9, 10
7	6
8	6, 2, 3

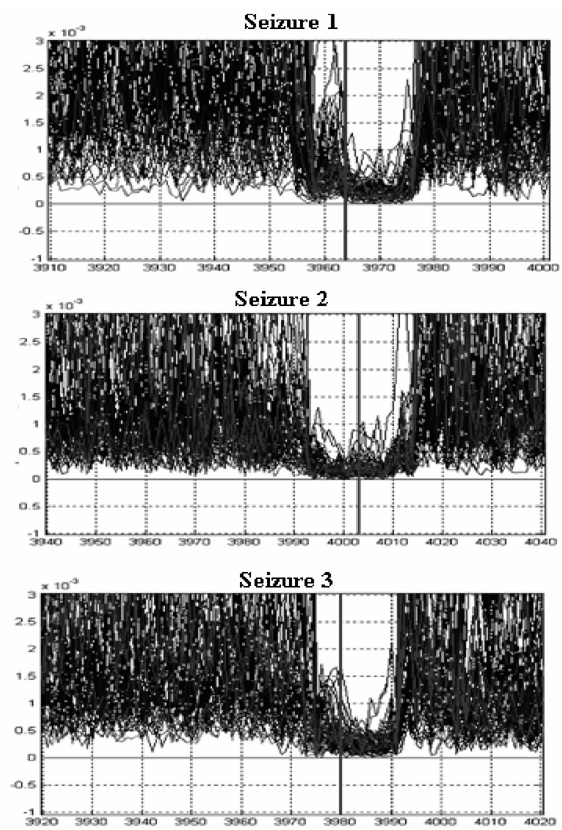

Figure 2. Correlation integral (CI) versus time for seizure 1, 2 and 3 for patient 1

Figure 2 illustrates the behavior of the correlation integral over time for three different seizures within the same patient. As it can be observed, the magnitude of the correlation integral abruptly changes at the time of the seizure for all electrodes with an evident decrease of the standard deviation. The vertical line represents the seizure onset, previously labeled at the observation room by the EEG technician. The shrinking of the CI plot around the three seizures is highly noticeable.

Each individual has a peculiar and different EEG behavior. If the results were to be represented in a graph, a chaotic behavior would be observed. This is best expressed with a plot of the detection statistics for each patient (see Figure 3). Observe that the plot circles (representing individual patients) are scattered in a relative big area of the chart range. Another fact is that there is no a clear relationship between average and STD. The scattering in the plot results from including all features in the statistics. However, for more valuable information one would need a feature-based representation.

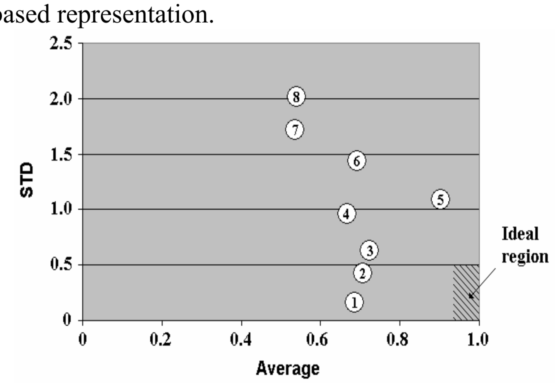

Figure 3. Average vs. STD plot for the accuracy values of all patients

Once the intra-patient analysis was finished, the analysis was continued by parameters across all patients. To assign a performance value to each classifier across all patients, we looked at the average and standard deviation of the accuracy values obtained.

Table 3. Average and STD of the classifier accuracy sorted by average in descending order.

Classifier #	Average	STD
6	0.86	0.19
9	0.82	0.18
2	0.76	0.24
3	0.74	0.22
11	0.72	0.26
8	0.71	0.26
10	0.67	0.27
5	0.66	0.25
12	0.65	0.22
7	0.59	0.27
1	0.58	0.25
4	0.45	0.31

As previously mentioned, the highest average value would be used as criterion to select the best candidate parameters for seizure detection across all patients. A sorting in descending order reveals that the classifier that performed best across all patients was the correlation integral (0.7071) and the worst the AC (-0.0941). Table 3 shows a compilation of the results.

The results obtained in this section served to prove that no parameter consistently predominated across all patients.

If we assign a range based on the average classifier accuracy, it can be concluded that, from the list of 12 parameters and based on 8 different subdural EEG data files, the correlation integral is the most appropriate to be used for seizure detection purposes. However, one may also look at low STD values to pick also a classifier whose accuracy does not change much, provided that it has a high average accuracy. An optimum classifier would be one whose average accuracy is high and whose STD is low. In Figure 4 the numbers in circles denote the classifier. The figure shows that the best classifiers are #6 and #9. They perform with the highest accuracy and the smallest variation among all classifiers.

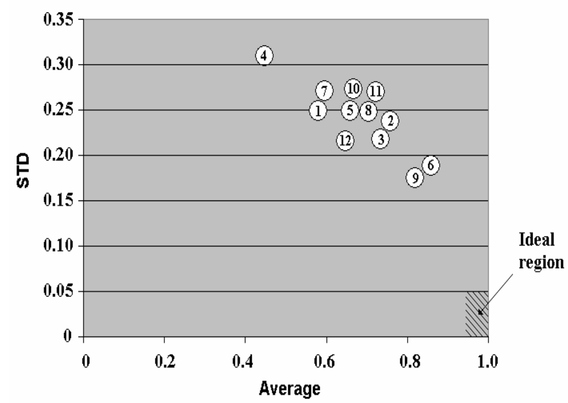

Figure 4. Average vs. STD plot for the accuracy values of all classifiers

Notice that classifiers #6 (CI) and #9 (SP in the alpha band) perform very similar and distinct from the rest. This served to conclude that these classifiers had the best performance when compared to the rest of the group. It is also interesting to note that these two classifiers operate not only in time (#6) but also in frequency domain (#9). Combinations of these two classifiers should be further analyzed to create better seizure detectors [16].

A closer look at the plot of Figure 3 also reveals an interesting trend: STD decreases with higher average. This tendency is very helpful, since it points to an ideal case: performance with high average and low STD. It is expected that better seizure detectors based on other EEG parameters might produce better results that continue the tendency illustrated in Figure 3. This serves to conclude that in this study, it is the proper parameter selection (and not the patient) what generates better accuracies in seizure detection.

3. Conclusions

In this study, a total of 26 EEG files recorded at least ten minutes before a seizure were scrutinized in order to extract information through the application of different parameters. The uniqueness of this algorithm is in the establishment of a mathematical foundation capable of detecting an epileptic seizure from different EEG datasets. In order to accentuate the influence of the different parameters, an inter-patient analysis was conducted by applying each classifier-type to all different patients with their own thresholds. As a result, it has been found that the correlation integral and the spectral power in the alpha band are the best parameters to detect a seizure, once the specific thresholds have been set. In terms of the accuracy value, the correlation integral has the highest accuracy percentage (86%) value.

The clinical success of this study consists in detecting seizures from long duration subdural EEG data. This achievement makes the method suitable for real-time detection applications. It is the hope of the authors that this research advances the extensive knowledge about the seizure detection endeavor and helps to disguise the seizure prediction problem.

As this research will involve a higher number of epileptic patients as they become available, additional results will provide more weight to our findings.

Acknowledgments

The authors appreciate the support provided by the National Science Foundation under grants HRD-0317692, CNS-0426125, CNS-0520811, CNS-0540592 and IIS-0308155. The authors are also thankful for the clinical support provided through the Ware Foundation and the joint Neuro-Engineering Program with Miami Children's Hospital.

References

[1] Adjouadi, M., Cabrerizo, M., Ayala M., Jayakar, P., Yaylali I., & Barreto, A., "Interictal spike detection using the Walsh transform", IEEE Transactions on Biomedical Engineering, Vol.51, No.5, May 2004, pp.868-873.

[2] Adjouadi, M., Cabrerizo, M., Ayala, M., "Seizing lesions in 3-D", IEEE Potentials, Vol. 24, No.5, 2006, pp. 11-17.

[3] Cabrerizo, M., Adjouadi, M., Ayala, M., Sesin, A., "3D Epileptic Foci Detection Using an Integrated Neuro-Imaging Approach", WSEAS Transactions on Information Science and Applications, Vol.2, No.7, 2005, pp.987-995.

[4] G.W. Frank, T. Lookman, M.A.H. Nerenberg, C. Essex, J. Lemieux and W. Blume, "Chaotic time series analyses of epileptic seizures", Physica D, Vol.46, 1990, pp.427-438.

[5] M.R. Guevara, "Chaos in electrophysiology, concepts and techniques in bioelectric measurements: Is the medium carrying the Message?", edited by LeBlanc, A-R, Billette, J., Editions de l'Ecole Polytechnique de Montreal, Montreal, 1997, pp.67-87,

[6] Iasemidis, L. D., Barreto, A., Gilmore, R. L., Uthman B. M., Roper S. A., & Sackellares J.C., "Spatiotemporal evolution of dynamical measures precedes onset of mesial temporal lobe seizures", Epilepsia, Vol. 35, 1994, pp.133-134.

[7] A. Bezerianos, S. Tong and N. Thakor, "Time-dependent Entropy Estimation of EEG rhythm changes following brain ischemia", Annals of Biomedical Engineering, Vol.31, 2003, pp.221-232.

[8] J. Martinerie, C. Adam and M. Le Van Ouyen, "Epileptic seizures can be anticipated by non-linear analysis", Nat. Med, Vol.4, 1998, pp.1173-1176.

[9] Software development at Center for Advanced Technology and Education. Available at: http://www.cate.fiu.edu/Software/index.htm

[10] J.C. Sackellares, P.M. Pardalos, L.D. Iasemidis, W. Chaovalitwongse, and D.S. Shiau, "Optimization of spatio-temporal pattern processing for seizure warning and prediction", U.S. Patent application filed August 2004 (Attorney Docket No. 028724-150).

[11] B. Hjorth,(1970), "EEG analysis based on time series properties", Electroencephalography and Clinical Neurophysiology. Vol.29, 1970, pp.306-310.

[12] M. Cabrerizo, M. Adjouadi, M. Ayala, M. Tito, "Pattern extraction in interictal EEG recordings towards detection of electrodes leading to seizures", Biomedical Sciences Instrumentation, 42 (ISA Vol. 464) 2006, pp.243-248.

[13] Adjouadi, M., Cabrerizo, M., Ayala, M., Sanchez, D., Jayakar, P., Yaylali, I., & Barreto, A., "A new approach to the analysis of epileptogenic data using statistically independent operators", Journal of Clinical Neurophysiology, Vol.22, No.1, 2005, pp.53-64.

[14] L. Fausett, "Fundamentals of Neural Networks. Architectures, Algorithms, and Applications" Prentice-Hall Inc., 1994.

[15] Kohavi, R. and Provost, F., "Glossary of terms", Machine Learning, 30, 1998, 271–274.

[16] M. Cabrerizo, M. Adjouadi, M. Ayala, Kirenia Nunez, Jayakar and I. Yaylali "Integrated Analysis of EEG Functional Brain Mapping Based on an Auditory-Comprehension Process Augmented Through Topographical Maps and a New Eigensystem Study", Brain Topography, Vol. 17 (3), pp. 151-163, March 2005.