

# A Matlab<sup>®</sup> software for detection & counting of epileptic seizures in 72 hours Holter-EEG

G. Filligoi, M. Padalino, S. Pioli

**Abstract**—The computer analysis of EEG signals as a useful diagnostic aid dates several years ago. With modern SW/HW techniques, it is possible to overcome the problems of epileptic seizure identification. This can be performed in a reasonable time. In this paper, we describe a software tool for the analysis of long-term (up to 72 hours) Holter-EEG recordings. The template-matching algorithm uses a statistical approach to compare the EEG signal with a data-base of known epileptic spikes. The cross-correlation coefficient can be used simply for discerning different types of epileptic spike and excluding many of the artifacts involved in the EEG recordings, and particularly in those data obtained by means of the Holter technique. To simplify the use of the software by the clinician, we have developed a Graphic User Interface (GUI), that allows to view the whole 8-channel Holter recording together with the spikes, founded by the computer program during the search, suitably highlighted.

**Index Terms**—EEG, Epileptic seizures, Pearson correlation coefficient, Matlab<sup>®</sup> processing script

## I. INTRODUCTION

THE signal electroencephalographic (EEG) is defined as a representation of post-synaptic potentials that are generated at cortical level by synchronous activity of about  $10^5$  neurons.

Most of the EEG recordings can be considered as random signal, being almost 90% of the signal to be interpreted as background activity (namely noise). This entirely spontaneous background EEG activity is of the order of  $\mu\text{V}$  and represents an index of integrity of the structure and brain function, during different mental states of sleep/wake or, alternatively in certain diseases [1]. These different EEGs are typically represented by their spectral content which is characterized by different sub-bands, namely  $\delta$  delta (0.4-4 Hz) representing a state of deep sleep or coma;  $\theta$  theta (4-8 Hz) are recorded in sleep;  $\alpha$  alpha (8-12 Hz) detected in a state of relaxed wakefulness (eyes closed);  $\beta$  beta (12-30 Hz) and  $\gamma$  gamma ( $> 30$  Hz) waves, indicative of a bark activated (i.e., waking state with open eyes).

Manuscript received January 10, 2011.

Giancarlo Filligoi is with the DIET Department at “Sapienza” University of Rome, via Eudossiana 18, 00184 Rome, Italy. (corresponding author e-mail: giancarlo.filligoi@uniroma1.it).

Matteo Padalino e Stefano Pioli are students of Biomedical & Clinical Engineering at “Sapienza” University of Rome, via Eudossiana 18, 00184 Rome, Italy.

It is well known that EEG analysis is of fundamental importance for neurologic diagnosis of severe pathologies such as: a) Alzheimer, which is the most common form of dementia [2, 3]; b) Parkinson, a degenerative disorder of the central nervous system that impairs motor skills, cognitive processes, and other functions [4]; c) multiple sclerosis, an inflammatory disease in which the fatty myelin sheaths around the axons of the brain and spinal cord are damaged, leading to demyelination and scarring as well as broad spectrum of signs and symptoms [5]; d) trauma [6, 7]; e) epilepsy, a common chronic neurological disorder characterized by recurrent seizures which are transient signs and symptoms of abnormal, excessive or synchronous neuronal activity in the brain [8÷11].

## II. EPILEPTIC DETECTION SEIZURES IN THE RECENT LITERATURE

In the last years, the EEG analysis was mostly focused on epilepsy and seizure detection diagnosis [12÷17]. The methodology is based on three different adroit integration of computing technologies and problem solving paradigms (e.g., neural networks, wavelets, and chaos theory).

Particularly wavelet transform is effective in representing various aspects of non-stationary signals such as trends, discontinuities, and repeated patterns, where other signal processing procedures fail or are not so effective [18÷26]. The power of this mathematical instrument to analyze different scales of neural rhythms is particularly suitable to investigate small-scale oscillations of the EEG.

In the last decade, also chaos-theory has been applied to EEG analysis for detection of epilepsy and seizure diagnosis. The non-linear dynamics of the original EEGs are quantified in the form of correlation dimension (CD, representing system complexity) and largest Lyapunov exponent (LLE, representing system chaoticity) [27÷29].

Recently, a novel wavelet-chaos-neural network approach [30] has been applied to EEG analysis for epileptic spikes classification. Relative implementation is based on three parameters: standard deviation (that quantifies the signal variance), correlation dimension, and Lyapunov exponent. This methodology has shown to be able to correctly classify epileptic spikes with high accuracy (96.6%).

In this paper we address the problem of providing relevant informations about seizures (epileptic spikes) from the analysis of EEG. The idea was to develop a software that can recognize and count template EEG signals, with special attention to epileptic spikes [31].

A program has been developed to discriminate between several different signal configurations, among them: a) electrode movement artifacts; b) interference due to eyes blinking; c) 50Hz interference; d) sleep K-complex; e) EMG interference and f) epileptic spikes.

Moreover, the intent was to discern differences between pathological and physiological intervals within a long-term EEG continuous recording (Holter-EEG).

### III. OUR APPROACH

Our template-matching approach searches for similarities among Holter-EEG long-term records (up to 72 hours of EEG channels recordings) and a local data-base of various signal configurations in order to facilitate the task of the physicians in diagnosing presence, type and depth of epileptic episodes.

For this propose, two different methodologies has been suggested in the literature: linear method which uses the linear cross-correlation or the coherence function [32, 33]; non-linear regression analysis, a bivariate method that measures the degree of association between two variables (the so called non-linear correlation coefficient) [34÷36].

In particular, we implemented in Matlab<sup>®</sup> language a software able to match epileptic spikes with EEG-Holters recordings by means of cross-correlation linear method.

As is well known, EEG electrodes must be placed accurately on the skin, following some standard able to guarantee a correspondence between cortical areas and site of their apposition. The most common standard displacement is the "10/20 International System" (19 scalp's electrodes). For our proposes, in order to record EEG data the "Jasper" configuration, encoded by the physician Herbert Jasper [37], has been used. Such method is commonly utilized in Holters EEG for brief exploration of electrical activity with only 8 electrodes referred to G2 (i.e., a reference Ground taken on the frontal branch).

EEG data are sampled at 128 samples/sec and the relative stored file consists of eight columns of ASCII coded data.

### IV. CROSS-CORRELATION AND PEARSON'S CORRELATION COEFFICIENT

In order to analyze the relationship between EEG and templates, the cross correlation technique [38] assessed the degree of linear association, i.e. a measure of similarity between two signals as a function of time shift (*lag*) applied to one of them. If we call the sampled EEG as  $x(i)$  and the discrete vector representing the template as  $y(i)$ , then the discrete cross-correlation is given by:

$$R_{xy}(m) = \begin{cases} \sum_{n=0}^{N-m-1} x_{n+m} y_n^* \leftarrow m \geq 0 \\ R_{yx}(-m) \leftarrow m < 0 \end{cases} \quad (1)$$

It is important to note that a high correlation between two variables does not always imply a cause-effect relationship.

When  $R_{xy}(m)$  reaches a local maximum greater then a certain threshold, this means that, for the corresponding lag, there is a high-similarity between  $x(i)$  and  $y(i)$ . Obviously this threshold will depend on the power of both signals that are going to be cross-correlated.

In order to apply a unique criterion for choosing a threshold valid for all data, independent of the signal power, the cross correlation, as in Eq. (1), is normalized with respect to the standard deviations  $\sigma_x$  and  $\sigma_y$ . In this way, we follow an approach analogous to that used to get the Pearson-correlation coefficient  $\rho_{xy}$  (or Bravais-Pearson) [38] between two random variables. This coefficient expresses the relationship between their covariance and the product of their standard deviations:

$$\rho_{xy} = \frac{\sigma_{xy}}{\sigma_x \sigma_y} = \frac{\sum_{i=1}^n (X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum_{i=1}^n (X_i - \bar{X})^2} \sqrt{\sum_{i=1}^n (Y_i - \bar{Y})^2}} \quad (2)$$

The correlation coefficient, as shown in (2), is an adimensional number that varies between [-1,1]. In general: a)  $\rho_{xy} < 0$  means that the variables  $x$  and  $y$  are inversely (or negatively) related; in other words, Pearson's coefficient is negative when the values of a variable grows with decreasing values of the other; b)  $\rho_{xy} = 0$  the variables are uncorrelated; c)  $\rho_{xy} > 0$  when the values of variables  $x$  and  $y$  grow together. In substance: there is no correlation when  $\rho_{xy} = 0$ ; low degree of correlation is expected when  $\rho_{xy}$  ranges between [0,0.25]; middle degree of correlation when  $\rho_{xy}$  is in [0.25,0.75]; high degree of correlation when  $\rho_{xy}$  is in [0.75,1]; there is a perfect correlation when  $\rho_{xy} = 1$ .

### V. MATLAB<sup>®</sup> PROCESSING SCRIPT

Our software loads the signal generated by the Holter, and accesses to an artifact & epileptic spikes local database. The Holter data, recorded according to Jasper configuration, are stored in one array with a column for each of the eight electrodes. Epileptic spikes are mainly detected from two signals (i.e., Fp1 and Fp2) recorded in the patient's forehead and further distinguished from artifacts by observing the other 6 channels.

The epileptic spike database is continuously updated by the new encountered templates observed during the computer analysis, in accord with the clinician approval. Due to the enormous dimension of whole data to be analyzed, particular attention has been paid to CPU execution time & RAM/disk memory management and to the consequent optimization of relative computer-code algorithms (Fig. 1).

#### *Cross-Correlation in Matlab<sup>®</sup>*

Within Matlab<sup>®</sup> "Signal Processing Toolbox", the cross-correlation can be obtained by means of the 'XCORR' function. The 'XCORR' command uses two vectors, X and Y as shown in Eq. (1), of length N, where X is maintained fixed and Y is delayed by m lags in the interval [-(N-1), +(N-1)]. Then, the result of such operation will be a matrix formed by 2N-1 elements, where the N-th value of the correlation

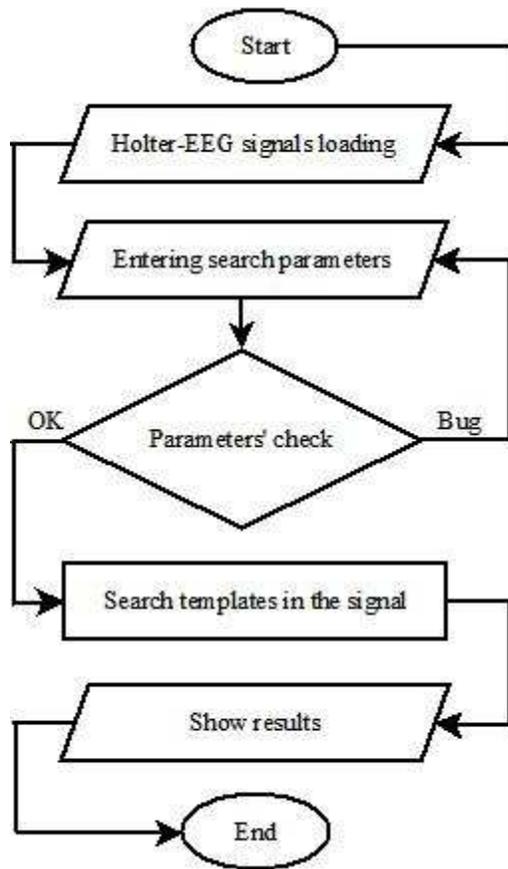


Fig. 1. Software flow diagram. The Holter-EEG file was loaded from the file selected by the user. Then, the user can open the control panel and choose which templates to search for. On next step, the software checks and prepares the template list and begins the analysis. At the end, the results are shown superimposed on the EEG signal with different color highlights for each template.

corresponds to "zero lag". We used the attribute 'coeff' to normalize the correlation (as for Pearson's coefficient).

For these types of calculation, Matlab<sup>®</sup> package requires to execute the inter-correlation function on two arrays X and Y of equal length. Therefore, the EEG recordings were divided into segments of the same length as the template to be searched for. Despite the fact the Pearson's coefficient can assume values between [-1, +1], only its absolute value was used since our interests lied in detecting those values of lags m for which the cross-correlation function took a local maximum greater than a prefixed threshold. The value of this threshold was determined in two ways: a) an average value based on previously analyzed EEG recordings; b) the suggestion of the clinicians.

#### User Interface

The program has a GUI (Graphic User Interface) that allows users to simultaneously display eight channels of Jasper configuration acquired by the Holter.

Firstly, this GUI presents a control panel to set-up the display preferences (e.g., signal sampling and how much signal has to be displayed) (Fig. 2).

Then, next panel shows all loaded templates and specifies which are active for the next search, and which are grouped

according to Jasper branch. Moreover, the Pearson's coefficient value for each template can be selected.

At the end of template search, segments of signals that showed correspondence with the templates are uploaded on the track and highlighted with different colors. On the sidebar, a bar diagram shows the count of individual templates found during the scan.

#### Load the Holter-EEG File

The loading script asks the user for the directory where the file of the patient's dynamic EEG is. In case of 32-bit operating systems with little RAM (Random Access Memory), the unrecoverable error for "stack overflow" will easily happen. This error is called by Matlab<sup>®</sup> "out of memory" and evokes more clearly the nature of the problem. In 32-bit systems, it is not possible to install more than 4GB of RAM, while in 64-bit systems (according to current Windows<sup>®</sup> version restrictions) only up to 32GB are available. Moreover, another large RAM section is automatically devoted to the "virtual memory", which the OS uses when the RAM is full. Whenever this "virtual memory" is wholly filled up, system crash will happen.

As a matter of fact, one day EEG-Holter recording means at least one GByte file. Loading this file takes almost 15 minutes, while the software is idle and the operating system dramatically slows down.

In order to reduce as much as possible the time for the whole EEG data storage, instead of a unique enormous block of data, data were divided into blocks of minor dimensions (14000 lines of EEG ASCII utf-8 data). Then, a particular efficient procedure using a 'while' loop has been implemented and iterated block by block until it reaches the end of the file. During the iteration, only 14000 lines are read and stored as strings in an array, by the 'TextSCAN' command. This command reads each new cycle starting with the last line taken in the previous cycle. The 14000 lines read at each cycle are added to the array. Using this load function, it was possible to stabilize the process by finding a good balance between CPU's workload and RAM's space.

#### How to find a template

The local database stores several templates to be found within the EEG derivations. These signals have been provided by clinicians as epileptic spikes or artifacts and then uploaded to the database. The template search is hierarchically organized so that the shortest are analyzed first. In the Appendix section, some of the templates stored in our local database are also shown.

The user can choose which template to search for and to select the relevant Pearson correlation coefficient which, accordingly, makes the scanning more or less sensitive to certain types of signal (the higher  $\rho_{xy}$ , the lower the possibility to find a template which matches the Holter-EEG at that level). We verified that the script is able to recognize the template with an accuracy of 98% (with respect to the gold standard represented by the clinician diagnosis), with the condition that the correlation coefficient is between 0,6 and 0,8.

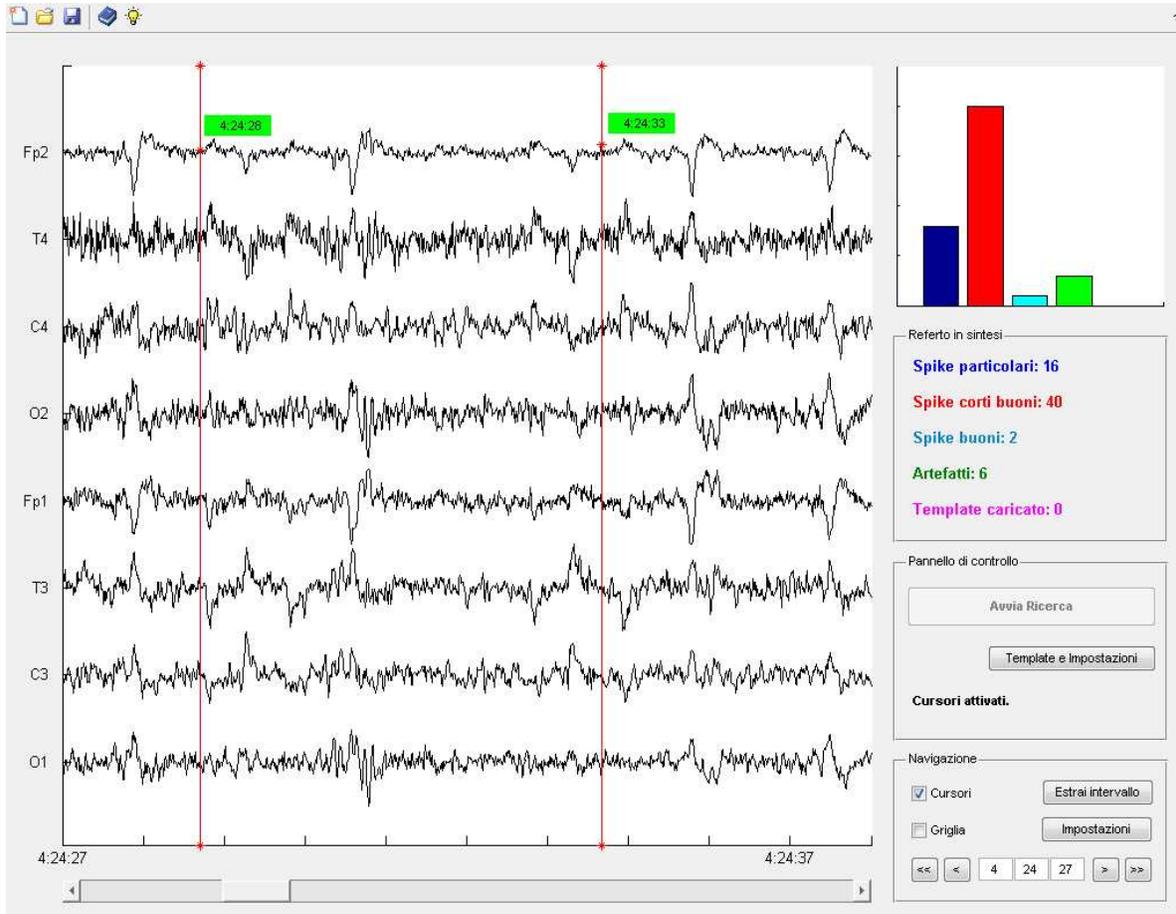


Fig. 2. The software GUI. The user can time-scroll along the tracks and view the eight channels simultaneously. On the left: histogram and templates count, research and navigation control panel.

As already stated, the EEG signal is divided into segments with time width equal to the length of the chosen template. The program processes the first EEG segment by calculating the maximum cross-correlation between Holter-EEG and all the templates. Whenever more than one template is recognized within an EEG-segment (i.e., the correlation coefficient is higher than the prefixed threshold), the template with highest Pearson's coefficient will be assumed as the most alike to that windowed EEG-signal.

As an example of our results, possible successful recognitions within the EEG frontal scalp electrodes of eye-blinking and 50Hz artifacts are reported in Fig. 3, epileptic sleep spikes in Fig. 4, and physiological K-complex in Fig. 5.

Whenever the program correctly recognizes (within the limits of the chosen Pearson's coefficient) a specific template, the corresponding EEG-segment is highlighted by means of a color bar which specifies position and length of that template within the EEG signal. After the scan, the number of times we encountered a template will be counted along all the EEG signal course. Since we are able to observe at what time of the day an epileptic spike was present, and how often, this will provide the clinician with important information for the diagnosis of the disease.

An iterative technique has been implemented which automatically evaluates the best value of Pearson's coefficients to be adopted for an optimal recognition of K-complex (physiological spikes) other than epileptic spike.

## VI. RESULTS

As a first check, pure random signals were generated and different length segments were extracted from them. In these tests, such segments were assumed as templates. Afterwards, some epileptic spikes have been superimposed to some segments of noisy-signal (with a prefixed signal-to-noise ratio, SNR, within those specific segments) and some pre-estimate of the correct Pearson's coefficient as a function of SNR was evaluated.

Therefore, Holter-EEG recording has been firstly analyzed by the clinician for a manual identification of epileptic spikes and artifacts. Then, on the basis of the templates selected by the clinician, the automatic recognition program has been executed and its accuracy evaluated (98% correct responses). Then, all templates were put in the local database for further recognition within other Holter-EEG recorded signals. Periodically, the database is verified and up-dated by the clinician in order to increase the EEG-analysis accuracy.

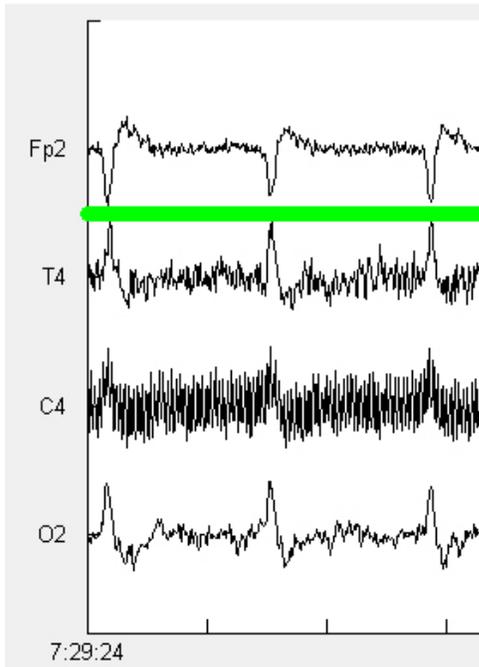


Fig. 3. Eye-blinking and 50Hz artifacts found. When the software recognize this artifact, it highlights its position and dimension with a specific color bar over the EEG signal.

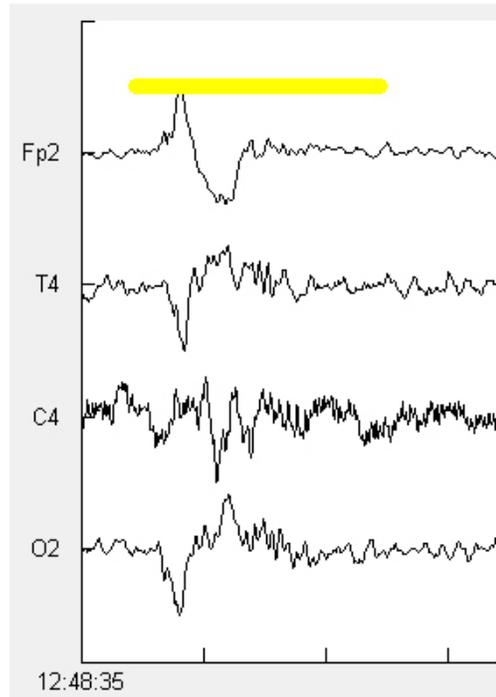


Fig. 5. Physiological K-complex found.

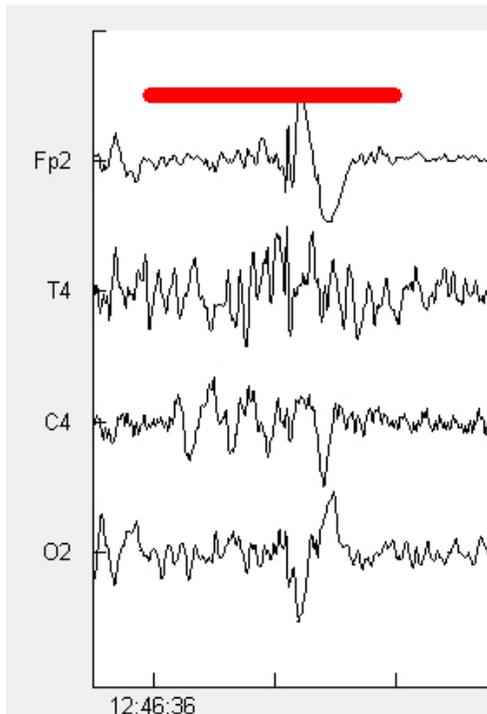


Fig. 4. Correct recognition of an epileptic sleep spike.

## VII. CONCLUSION

The analysis of EEG signals anyway requires the supervision of a clinician who identifies the epileptic spike manually. Usually, in the daily routine the physician has to observe (and count) each epileptic spike, and often this method could be very time consuming.

With the code developed and herewith described, an Holter-EEG can be analyzed in about 10 minutes.

The software stores and upgrades a database of epileptic events and artifacts which are progressively used, thus improving the quality of the analysis.

Preliminary tests on this software have been carried out on simulated signals & template as well as on real EEG recordings. At this stage of the research, the golden-standard is represented by the manual count carried out by the medical doctors.

## APPENDIX: EPILEPTIC SIGNALS AND ARTIFACTS IN DATABASE

In figg. A1÷A12, some of the templates stored in the local database for search are represented.

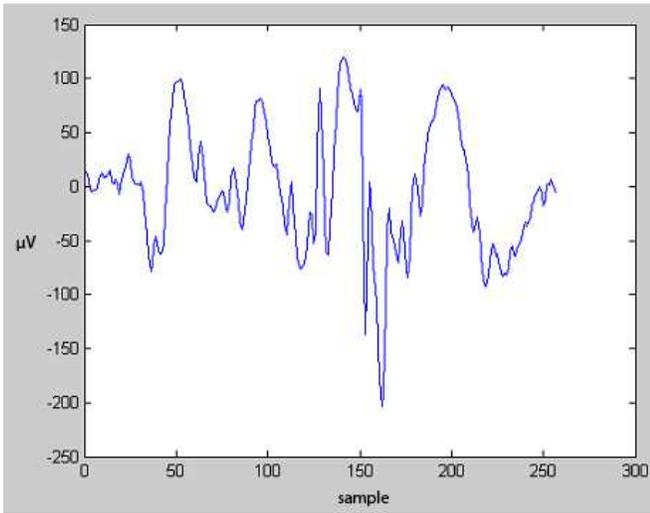


Fig. A1. Epileptic spike of 2 seconds.

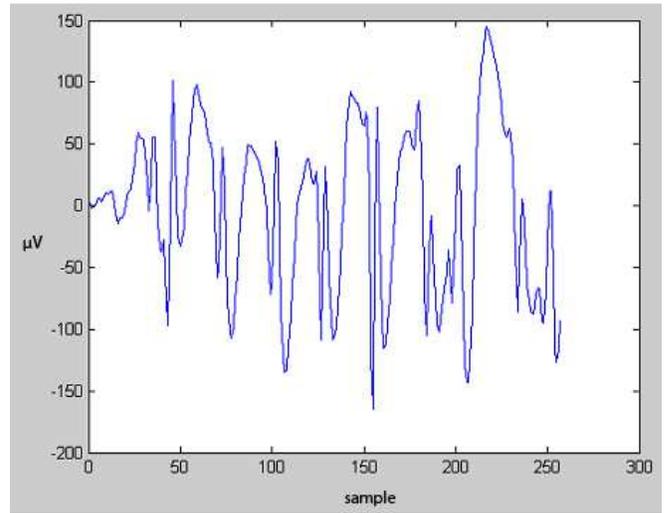


Fig. A4. Epileptic spike of 2 seconds.

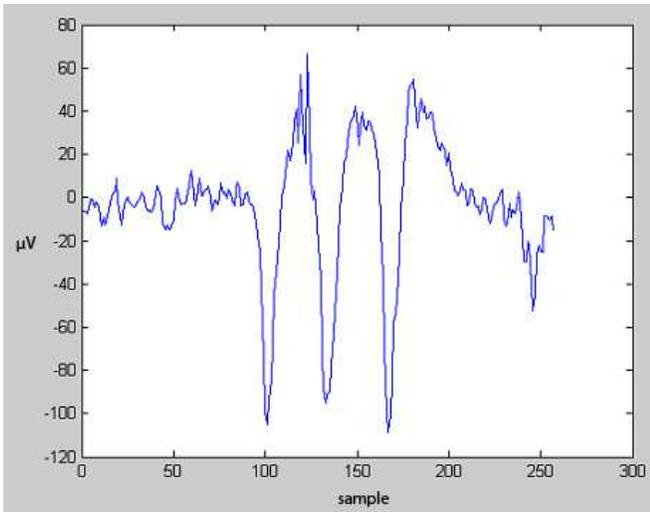


Fig. A2. Epileptic spike of 2 seconds.

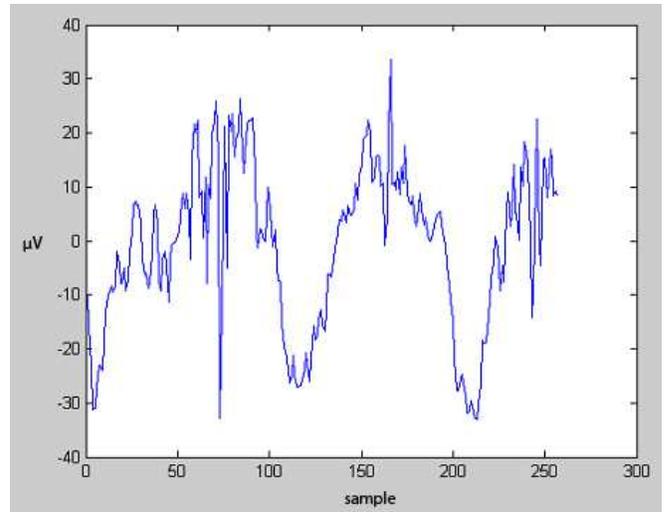


Fig. A5. Miographic artifact of 2 seconds.

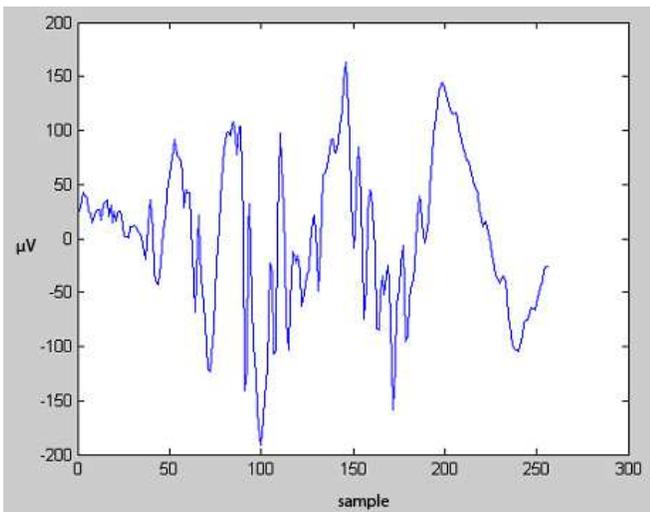


Fig. A3. Epileptic spike of 2 seconds.

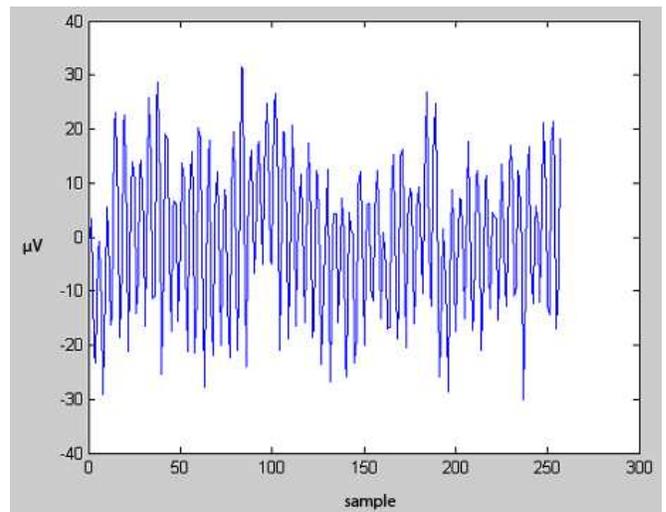


Fig. A6. 50Hz Artifact of 2 seconds.

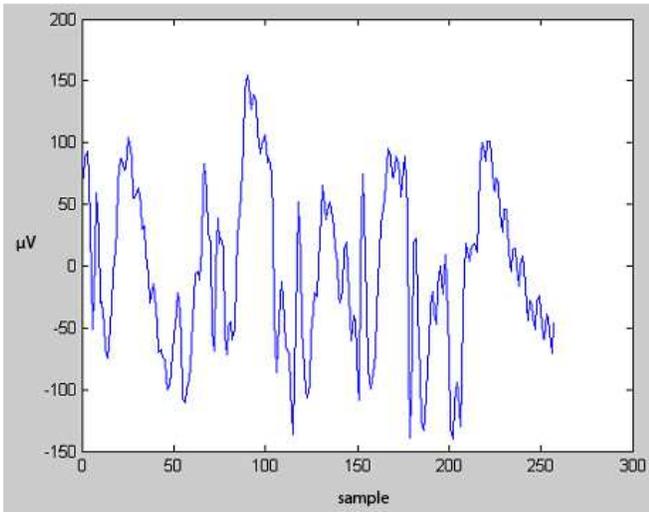


Fig. A7. Epileptic spike with 50Hz artifact of 2 seconds.

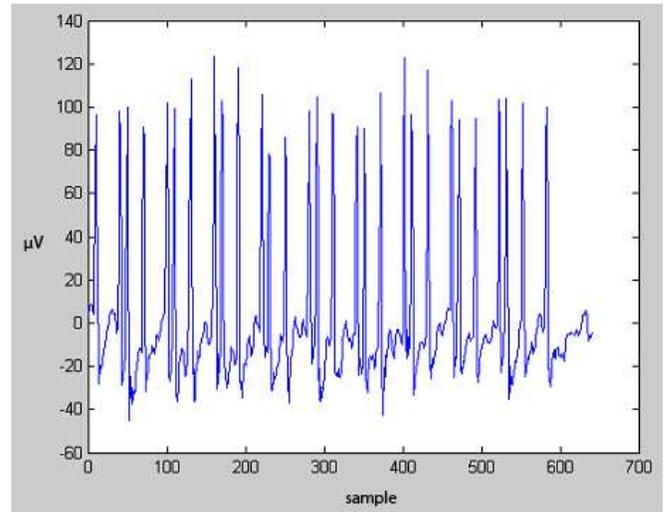


Fig. A10. Mobile phone artifact of 5 seconds.

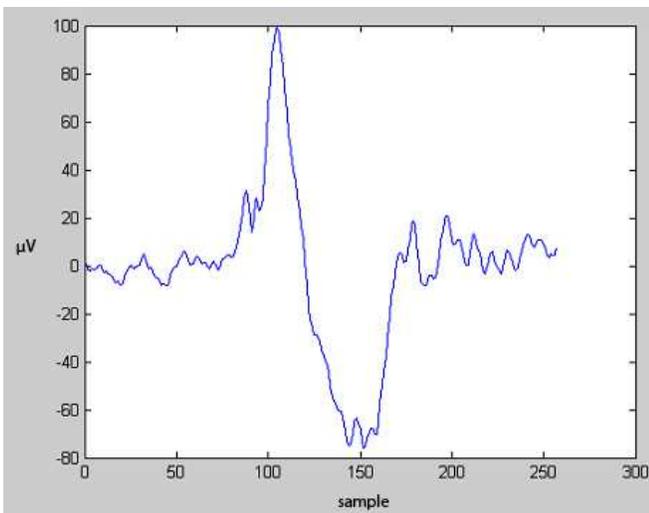


Fig. A8. Physiological K-complex of 2 seconds.

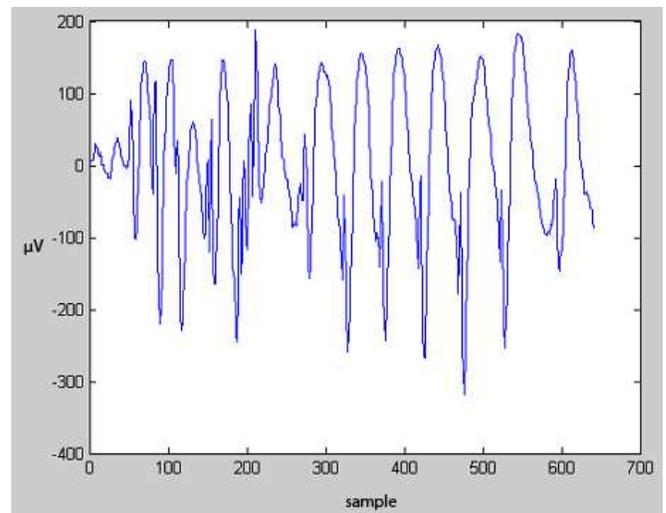


Fig. A11. Epileptic spike of 5 seconds.

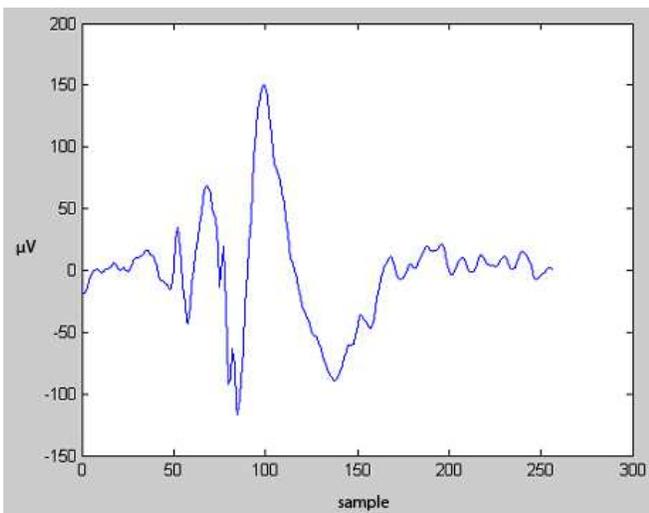


Fig. A9. Epileptic spike during sleep of 2 seconds.

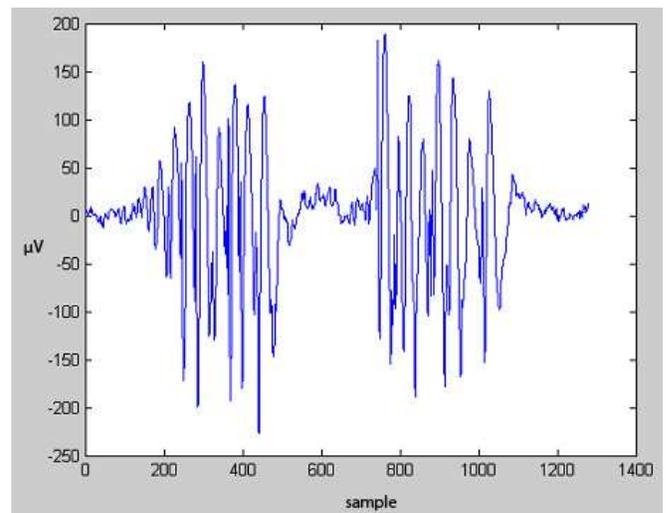


Fig. A12. Epileptic double spike of 10 seconds.

## ACKNOWLEDGMENT

The authors would like to thank Dr. O. Mecarelli, Full Professor, Neurological Sciences Department at “Sapienza” University of Rome, for encouragement during the development of this technical work. The authors extend their thanks to generous support of Dr. L. Davi, Neurological Sciences Department, in the collection of the relative research material, and to Dr. Beatrice Cocciolillo for her precious English revision.

## REFERENCES

- [1] Hauser, W. A. & Lee, J. R. 2002 Do seizures beget seizures? *Prog Brain Res* 135, 215-9.
- [2] Adeli, H., Ghosh-Dastidar, S, and Dadmehr, N. (2005a) “Alzheimer’s Disease and Models of Computation: Imaging, Classification, and Neural Models”, *Journal of Alzheimer’s Disease*, Vol. 7:3, pp. 187-199.
- [3] Adeli, H., Ghosh-Dastidar, S., Dadmehr, N. (2008), “A Spatio-temporal Wavelet-Chaos Methodology for EEG-based Diagnosis of Alzheimer’s Disease, *Neuroscience Letters*, 444:2, pp. 190-194.
- [4] Steven E. Newman, MD; Richard P. Tucker, MD; Kenneth A. Kooi, MD “Lack of Levodopa Effect on Preexisting Temporal Lobe Focus”, *Arch Neurol.*, vol. 29, no.2, 1973;29(2):122-123.
- [5] Koch M, Uyttenboogaart M, Polman S and De Keyser J. “Seizures in multiple sclerosis”. *Epilepsia* 2008; 49: 948–953.
- [6] K. Alper, “Nonepileptic seizures,” *Neurologic Clinics*, vol. 12, no. 1, pp. 153–173, 1994.
- [7] A. Krumholz, “Non-epileptic seizures: diagnosis and management,” *Neurology*, vol. 53, supplement 2, pp. S76–S83, 1999.
- [8] Blume WT, Luders HO, Mizrahi E, et al. Glossary of descriptive terminology for ictal semiology: report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 2001;42:1212–8.
- [9] Alarcon G, Binnie C, Elwes R, Polkey C. Power spectrum and intracranial EEG patterns at seizure onset in partial epilepsy. *Electroencephalogr Clin Neurophysiol*, 1994;94:326–337.
- [10] Esteller, R. Detection of Seizure onset in Epileptic Patients from Intracranial EEG Signals. PhD thesis, School of Electrical and Computer Engineering; 1999.
- [11] Hopfenga rtrner R, Kerling F, Bauer V, Stefan H. An efficient, robust and fast method for the offline detection of epileptic seizures in long-term scalp EEG recordings. *Clin Neurophysiol* 2007;118:2332–2343.
- [12] Deacon C, Wiebe S, Blume WT et al. Seizure identification by clinical description in temporal lobe epilepsy: how accurate are we? *Neurology* 2003; 61:1686-9.
- [13] L. Diambra, J.C. Bastos, C.P. Malta, “Epileptic activity cognition in EEG recording”, *Physica A* 273 (1999) 495–505.
- [14] J. Gotman, “Automatic recognition of epileptic seizures in the EEG,” *Electroencephalogr. Clin. Neurophysiol.*, vol. 54, pp. 530–540, 1982.
- [15] Layne SP, Mayer-Kress G, & Holzfuss J: “Problems associated with the analysis of EEG data, in *Dimensions and Entropies in Chaotic Systems*”, Springer NY. 1986.
- [16] Klaus Lehnertz, Florian Mormann, Thomas Kreuz, Ralph G. Andrzejak, Christoph Rieke, Peter David, And Christian E. Elger, “Seizure Prediction By Nonlinear EEG Analysis” in proceeding of IEEE engineering in medicine and biology magazine, vol.22, no. 1, January/February 2003, pp: 57-63.
- [17] L.D. Iasemidis, D.S. Shiau, W. Chaovalitwongse, J.C. Sackellares, P.M. Pardalos, and J.C. Principe, "Adaptive epileptic seizure prediction system," *IEEE Transactions on Biomedical Engineering*, vol. 50, no.5,2003, pp. 616–627.
- [18] Pakrashi, V., O’Connor, A., and Basu, B. (2007), “A Study on the Effects of Damage Models and Wavelet Bases for Damage Identification and Calibration in Beams,” *Computer-Aided Civil and Infrastructure Engineering*, Vol. 22, No. 8, pp. 555-569.
- [19] Su, H.Z., Wu, Z.R., and Wen, Z.P. (2007), “Identification Model for Dam Behavior Based on Wavelet Network,” *Computer-Aided Civil and Infrastructure Engineering*, Vol. 22, No. 6, pp. 438-448.
- [20] Xie, Y., Zhang, Y., and Ye, Z. (2007), “Short-term Traffic Volume Forecasting Using Kalman Filter with Discrete Wavelet Decomposition,” *Computer-Aided Civil and Infrastructure Engineering*, 22:5, pp. 326-334.
- [21] Spanos, P.D., Giaralis, A., Politis, N.P., and Roesset, J. (2007), “Numerical Treatment of Seismic Accelerograms and of Inelastic Seismic Structural Responses Using Harmonic Wavelets,” *Computer-Aided Civil and Infrastructure Engineering*, 22:4, pp. 254-264.
- [22] Montejo, L.A. and Kowalsky, M.J. (2008), Estimation of Frequency Dependent Strong Motion Duration via Wavelets and its Influence on Nonlinear Seismic Response, *Computer-Aided Civil and Infrastructure Engineering*, Vol., 23, No. 4, pp. 253-264.
- [23] Umesha, P.K., Ravichandran, R., Sivasubramanian K. (2009), “Crack detection and quantification in beams using wavelets,” *Computer-Aided Civil and Infrastructure Engineering*, 24:8, pp. 593-607.
- [24] Yazdani, A. and Takada, T. (2009), “Wavelet-Based Generation of Energy and Spectrum Compatible Earthquake Time-Histories,” *Computer-Aided Civil and Infrastructure Engineering*, 24:8, pp. 623-630.
- [25] Rizzi, M. D’Aloia, M. and Castagnolo, B. (2009), “Computer Aided Detection of Microcalcifications in Digital Mammograms Adopting a Wavelet Decomposition,” *Integrated Computer-Aided Engineering*, 16:2, pp. 91-103.
- [26] Adeli, H., Zhou, Z., and Dadmehr, N. (2003), "Analysis of EEG Records in an Epileptic Patient Using Wavelet Transform", *Journal of Neuroscience Methods*, Vol. 123:1, pp. 69-87.
- [27] Hornero, R. Espino, P. Alonso, A. Lopez, M., “Estimating complexity from EEG background activity of epileptic patients”, *Engineering in Medicine and Biology Magazine, IEEE*, vol 18 no.6, pp. 73-79, Nov/Dec 1999.
- [28] E. M. Tamil, H. M. Radzi, M. Y. I. Idris and A. M. Tamil,” A Review on Feature Extraction & Classification Techniques for Biosignal Processing (Part II: Electroencephalography) “, 4th Kuala Lumpur International Conference on Biomedical Engineering 2008, IFMBE Proceedings, , Volume 21( Part 3, Part 4),pp. 113-116,2008.
- [29] V. Srinivasan,C. Eswaran, N. Sriraam, “Approximate Entropy-Based Epileptic EEG Detection Using Artificial Neural Networks, *IEEE Transactions on information technology in biomedicine*,vol. 11, no.3, may 2007.
- [30] Adeli, H., Ghosh-Dastidar, S., and Dadmehr, N. (2007), “A Wavelet-Chaos Methodology for Analysis of EEGs and EEG Sub-bands to detect Seizure and Epilepsy”, *IEEE Transactions on Biomedical Engineering*, 54:2, pp. 205-211.
- [31] Prilipko, L., M de Boer, H., Dua, T. & Bertolote, J. 2006 *Epilepsy Care –The WHO/ILAE/IBE Global Campaign Against Epilepsy*. US Neurological Disease, 39-40.
- [32] Brazier, M. A. 1972 Spread of seizure discharges in epilepsy: anatomical and electrophysiological considerations. *Exp Neurol* 36, 263-72.
- [33] Franaszczuk, P. J. & Bergey, G. K. 1999 An autoregressive method for the measurement of synchronization of interictal and ictal EEG signals. *Biol Cybern* 81, 3-9.
- [34] Pijn, J., Veli, s., DN & Lopes da Silva, F. 1992 Measurement of interhemispheric time differences in generalised spike-and-wave. *Electroencephalogr Clin Neurophysiol* 83, 169-71.
- [35] Wendling, F., Bartolomei, F., Bellanger, J. J., Bourien, J. & Chauvel, P. 2003 Epileptic fast intracerebral EEG activity: evidence for spatial decorrelation at seizure onset. *Brain* 126, 1449-59.
- [36] Nikolaev, A. R., Ivanitsky, G. A., Ivanitsky, A. M., Posner, M. I. & Abdullaev, Y. G. 2001 Correlation of brain rhythms between frontal and left temporal (Wernicke’s) cortical areas during verbal thinking. *Neurosci Lett* 298, 107-10.
- [37] Antonio V. Delgado-Escueta, Herbert H. Jasper, Roger J. Porter 1999 *Jasper’s Basic Mechanisms of the Epilepsies*, Lippincott Williams & Wilkins, vol.79.
- [38] L. G. Portney, M. P. Watkins, “Foundations of Clinical Research: applications to practice”, 2<sup>nd</sup> ed., *Prentice-Hall, New Jersey (USA)* 2000.