Fuzzy-entropy threshold based on a complex wavelet denoising technique to diagnose Alzheimer disease

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The presence of irregularities in electroencephalographic (EEG) signals entails complexities during the Alzheimer's disease (AD) diagnosis. In addition, the uncertainty presented on EEG raises major issues in the improvement of the classification rate. The multi-resolution analysis through an optimum threshold will likely achieve better results in distinguishing AD and normal EEG signals. Hence, a fuzzy-entropy concept defined in a complex multi-resolution wavelet has been proposed to obtain the most appropriate threshold. First, the complex coefficients are fuzzified using a Gaussian membership function. Afterwards, the ability of the proposed fuzzy-entropy threshold has been compared with traditional thresholds in complex wavelet domain. Experimental results show that the authors' methodology produces a higher signal-to-noise ratio and a lower root-mean-square error than traditional approaches. Moreover, a neural network scheme is performed along several features to classify AD from normal EEG signals obtaining a specificity of 87.5%.

1. Introduction: Alzheimer disease (AD) is a brain disorder that degrades the neurons leading to patient death [1, 2]. In 2015, the World Alzheimer Organization estimated over 9.9 million of new dementia patients each year in the world, implying one case every 3.2 s. Specifically, the distribution of new dementia patients is the following: 2.5 million in Europe, 4.9 million in Asia, 1.7 million

in America and 0.8 million in Africa [3]. The annual number of total cases has increased approximately by 30% since 2010.

Electroencephalographic (EEG) is a potential and efficient tool for screening AD [4, 5], especially at early stages. In addition, it is an available technology in a high number of hospitals due to its low cost. However, EEG needs to improve its overall specificity

Fig. 1 General block diagram of the proposed methodology

Fig. 2 SNR and RMSE plots for AD and normal EEG

in order to be used as the main method in clinical practice. Besides, in some cases these signals are tedious to distinguish AD due to the presence of noise [2, 6, 7]. Since ocular artefacts occur in frequency bands lower than 5 Hz [6], time-frequency complex wavelet transform (CWT) analysis [8, 9] are expected to give better results over the filtering [10, 11] and Fourier transform analysis [9, 12–17].

The presence of fuzziness and disorders in the wavelet coefficients can be separated using both fuzzy [18, 19] and entropy [20–23] concepts. A novel fuzzy-entropy threshold has been therefore proposed and the obtained results are compared with the traditional Visu, normal [13, 14, 24] and Bayes thresholds [25]. The main objectives of our work are:

- (i) The assessment of the fuzziness impact in the EEG.
- (ii) The development of a new fuzzy-entropy method to select an optimal threshold value.

- (iii) The recovery of the noise signal using the proposed thresholding technique.
- (iv) The classification of AD and normal EEG using a feed-forward neural network.

The proposed methodology to meet the aforementioned goals is shown in Fig. 1.

This Letter contents are organised as follows. Section 2 provides a brief summary of the closest related works. In Section 3, we explain the proposed fuzzy-entropy thresholding technique. Section 4 shows the feature extraction stage and the supervised classification. In Section 5, results and discussion are presented. The summary of the work and some conclusions are pointed out in Section 6.

2. State-of-the-art: Thanks to the Hans Berger [26] pathological remarks in the EEG sequences, a high percentage of Alzheimer patients were discovered. Since then, the scientific community has devised and developed novel approaches to improve EEG diagnosis.

EEG technique currently allows to determine whether a patient suffers from AD, thus it has become a powerful diagnosis tool. First, Sankari and Adeli [27] realised that an unusual pattern emerged when studying the interhemispheric, intrahemispheric and distal brain coherence. Afterwards, Absolo *et al.* [28] utilised entropy, sample entropy and multiscale entropy to obtain a precision of 77.27%. On the contrary, Sankari and Adeli [27] presented a neural network based on probabilities, which was focused on the use of wavelet coherence features. An impressive 100% of accuracy was attained. Moreover, Polikar *et al.* [29] selected Daubechies (Db) wavelets to perform an event-related potential test. They obtained a classification average of 78.2% in comparison with other kinds of wavelets. Torrents-Barrena *et al.* [30] evaluated the effectiveness of Tsallis entropy instead of Shannon to calculate an optimal threshold in CWT. As a result, the accuracy was improved from 90 to 95% using Tsallis entropy.

Graph theory, in which the representation of the objects is made thanks to the weights, vertices, nodes and the relationship between edges, can also be applied. Generally, this theory allows to implement three kinds of neural networks: the first uses clusters of nodes and short paths between them (Han *et al.* [31]); the second utilises ordered networks in which both large clusters and path lengths are used; the third one takes advantage of small clusters and path distances. Ahmadlou *et al.* [32] obtained a high accuracy of 97.7% by applying two classifiers with a radial kernel in a chaos-wavelet approach. Next, McBride *et al.* [33] computed pairs of EEG electrodes in an inter channel and performed a visual schema via network features. Furthermore, a support vector machine (SVM) classifier with leave-one-out cross-validation was utilised to divide AD from normal patients.

The last novel method is based on a deep learning architecture, which analyse EEG signals of AD through an unsupervised feature approach in order to take advantage of its main pros [34]. Specifically, they first trained a network with 25 data units per electrode in a separate way. Next, 15 data unit tests were selected to get the final accuracy for each electrode. Finally, a SVM was trained by merging the data from 16 electrodes. A 92% of accuracy was obtained.

Although the aforementioned methodologies provide striking results on how to analyse the signals, several issues must be circumvented to increase the precision. For instance, the noise of the whole EEG data should be drastically reduced.

3. Fuzzy-entropy threshold based on complex coefficients: The unpredictable behaviour of the wavelet coefficients due to the signal shift can be overrun by the CWT through its insensitivity and redundancy property [15, 16]. Let $y(t)$ be the observed EEG

Fig. 3 Mean values for

a Alzheimer's disease

b Normal EEG signals (25). Both bar plots include the mean values before (with noise) and after applying the following threshold methods: DWT, Bayes shrink, Visu shrink, Normal shrink and CWT-fuzzy

that comprises the signal $x(t)$ and the noise $n(t)$ (see (1):

$$y(t) = x(t) + n(t) \quad (1)$$

The complex coefficients of (1) have been obtained after applying a translation and scaling process of the CWT. Note that EEG signals are orthogonal. Therefore, the selected mother wavelet should also be orthogonal with a finite impulse response filter, providing compact support that suits transient non-stationary signal analysis. There are several wavelet functions that satisfy the properties above. Of these, the popular Haar wavelet function works well in time domain with the use of two coefficients, but fails in frequency domain. On the contrary, Db wavelets have more vanishing points providing higher support than Haar function. Furthermore, through its non-overlapping windows, Db wavelets pick out all variations in adjacent samples. Hence, db4: $\psi_c(t) = \psi_r(t) + j\psi_i(t)$ is used because of its smoothing characteristic and maximum flatness [13] to detect changes in EEG, as it is expressed in (2). The imaginary part is obtained by taking the

Hilbert transform (HT) of the real part as (3) shows.

$$\text{CWT}_y^\psi(a, b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} y(t) \cdot \psi_c^* \left(\frac{t-b}{a} \right) dt, \quad (2)$$

$$\psi_i(t) = \text{HT} \{ \psi_r(t) \} = \frac{1}{\pi} \int_{-\infty}^{\infty} \frac{\psi_r(t)}{t - \tau} d\tau, \quad (3)$$

Next, the convolution with the high pass (h_p) and low pass (l_p) filters is performed. As a result, the approximation of the complex coefficients are detailed in (4) and (5), respectively.

$$\psi_{r/i}(t) = \sqrt{2} \sum_n h_{r/i}(n) \varphi_{r/i}(2t - n) \quad (4)$$

$$\varphi_{r/i}(t) = \sqrt{2} \sum_n l_{r/i}(n) \varphi_{r/i}(2t - n) \quad (5)$$

The complex wavelet coefficients $C_y(w)$ are partitioned into two separate classes: $c_{y1}(u)$ and $c_{y2}(v)$ as follows

$$c_{y1}(u) \cup c_{y2}(v) \in C_y(w) \quad (6)$$

Fig. 4 Standard deviation values for
a Alzheimer's disease
b Normal EEG signals (25). Both bar plots include the standard deviation values before (with noise) and after applying the following threshold methods: DWT, Bayes shrink, Visu shrink, Normal shrink and CWT-fuzzy

Taking into account that $u, v = 1, 2, \dots, w$, where w represents the length of the coefficients, both sets are classified based on a threshold parameter T , which is expressed in the following equations

$$c_{y1}(u) = \{w: w_{\min} < w < T\} \quad (7)$$

$$c_{y2}(v) = \{w: T < w < w_{\max}\} \quad (8)$$

Finally, the fuzzification is done to enhance the complex wavelet coefficients. In order to select the optimum threshold, the next process is performed to fuzzify the partitioned coefficients. Afterwards, the fuzzy set of both classes can be given as

$$F_1 = \{(\mu_{c_{y1}}(u), u), \forall u \in w\} \quad (9)$$

$$F_2 = \{(\mu_{c_{y2}}(v), v), \forall v \in w\} \quad (10)$$

where $\mu_{c_{y1}}(u)$ and $\mu_{c_{y2}}(u)$ are the Gaussian membership functions of

centre c and variance σ . They can be expressed as

$$\mu_{c_{y1}}(u) = \exp\left[-\frac{|u - c|}{2\sigma}\right]^m \quad (11)$$

$$\mu_{c_{y2}}(v) = \exp\left[-\frac{|v - c|}{2\sigma}\right]^m \quad (12)$$

Thus, the information of the fuzzified classes has been evaluated by means of the entropy term as follows

$$E_{yi} = - \sum P(\mu_{c_{yi}}) \log_2(P(\mu_{c_{yi}})), \text{ where } i = 1, 2. \quad (13)$$

Then, the optimal threshold T is chosen as the position of maximum mutual information (MI) value of the fuzzy entropy partitioned classes as follows

$$T = \text{argmax}(\text{MI}_y) \quad (14)$$

Fig. 5 PSD values for
a Alzheimer's disease
b Normal EEG signals (25). Both bar plots include the PSD before (with noise) and after applying the following threshold methods: DWT, Bayes shrink, Visu shrink, Normal shrink and CWT-fuzzy

where mutual information MI_y is

$$MI_y = E_{y1} + E_{y2} - JE_y \quad (15)$$

E_{y1} and E_{y2} are the entropies of both classes and JE_y represents the joint entropy, as it is shown through the following equation

$$JE_y = - \sum_w P(\mu_{c_{y1}} \cap \mu_{c_{y2}}) \log_2(P(\mu_{c_{y1}} \cap \mu_{c_{y2}})) \quad (16)$$

Therefore, the recovered coefficients are analysed and classified to correctly diagnose AD.

4. Feature extraction and supervised classification: The mean, standard deviation, power spectral density (PSD), entropy and sample entropy features have been extracted from the fuzzy-entropy threshold applied to the previous recovered signals. Moreover, the supervised classification between AD and normal EEG has been carried out by means of a feed forward neural network (FNN) [35]. Regarding the configuration of the FNN, several architectures have been tested. The most accurate one

was: five input, two hidden and one output neurons, using the gradient descent training function and the adaptive learning rate back propagation algorithm. In addition, the initial weights and bias are assigned randomly and the log sigmoid is used as activation function. Note that the learning length depends on the input data, error, learning rate and bias values. After the learning phase, the prediction starts with another different set of data. The error difference between the generated and the desired outputs are measured. Based on this value, which is propagated back towards the inputs, the weights are changed. Hence, depending on the training process, the neurons are classified as: AD or normal EEG.

5. Results and discussion: AD EEG and normal EEG of four patients at different time scales are taken to perform the experimental part. The data are arranged in standard neuro-scan ASCII format, i.e. a .txt file with a list of numbers, where the columns indicate electrodes and rows the consecutive time samples. Specifically, the order of the electrodes in the ASCII file is as follows: F3, F4, T3, T4, C3, C4, P3, P4, FZ, CZ, PZ, Fp1, Fp2, F7, F8, T5, T6, O1, O2. Moreover, two different cases of data are stored in the database. On the one hand, the first case consists of 24 Alzheimer's EEG signals. Of these, the first 12

Fig. 6 Entropy values for
a Alzheimer's disease
b Normal EEG signals (25). Both bar plots include the entropy before (with noise) and after applying the following threshold methods: DWT, Bayes shrink, Visu shrink, Normal shrink and CWT-fuzzy

signals are Alzheimer's EEG from the dataset and the next 12 signals are synthetic Alzheimer's EEG. The synthetic is generated with a sample frequency rate of 128 Hz on a white Gaussian signal peak referred to the original model. Note that all tests are simulated using MATLAB software. On the other hand, the second case consists of 12 normal EEG signals from the dataset and 12 synthetic EEG signals created from the normal EEG models. Furthermore, we apply three levels of decomposition, hard thresholding and a fuzzification factor: $m = 1.5$. The parameters c and σ that belong to the membership function are assigned by measuring the centre and variance of the data. Therefore, the performance of the proposed method has been verified using signal to noise ratio (SNR) and root mean square error (RMSE).

The SNR and RMSE plots for AD and normal EEG patients are shown in Fig. 2. The CWT with fuzzy-entropy based threshold is compared with Bayes, Visu, normal and discrete wavelet transform (DWT) with fuzzy-entropy thresholds. It can be seen that AD EEG has higher SNR values compared with the SNR obtained from the normal EEG signals. Similarly, the error rate RMSE is also lower in the case of AD EEG. This is due to the lower complexity of AD EEG [36]. On the contrary, CWT with fuzzy-entropy threshold shows a higher SNR about 32.0346 and a lower RMSE of 0.1617.

Features extracted from the denoised signals, namely the PSD, sample entropy, entropy, mean and standard deviation, are shown in Figs. 3–7. In particular, the mean of AD and normal denoised EEG signals, using CWT with fuzzy entropy, as well as DWT with fuzzy, Bayes shrink, normal shrink and Visu shrink, are compared in Fig. 3. Note that higher mean values were obtained through the proposed CWT with fuzzy entropy-based threshold. This is made clear when results are confronted with other thresholds. Below, the chart shows higher mean values for normal EEG.

A comparison of the standard deviation for each method at different denoised signals is depicted in Fig. 4. Note that smaller values presented in AD EEG are due to its low complexity. Hence, higher numbers are observed for normal EEG, especially for the following methods: DWT and CWT-fuzzy. In the AD EEG case, intermediate signals (from 8 to 11) achieve higher standard deviation values. On the contrary, first signals (from 1 to 5), which belong to normal EEG, have larger numbers than the others.

PSD is a measure of signal's power intensity in the frequency domain, thus the highest PSD value (about 148.5) was obtained for AD EEG. Fig. 5 shows the PSD result of the denoised signals using the proposed method and the other thresholds. Signal 16 (approximately 140) yields the largest PSD in the CWT-fuzzy

Fig. 7 Sample entropy values for
a Alzheimer's disease
b Normal EEG signals (25). Both bar plots include the sample entropies before (with noise) and after applying the following threshold methods: DWT, Bayes shrink, Visu shrink, Normal shrink and CWT-fuzzy

approach of normal EEG. The remaining signals, except numbers 1, 19 and 20, have reached values lower than the average.

EEG complexity is measured through the entropy feature vector. A comparison of this vector and the other thresholds is shown in Fig. 6. Better values have been obtained in the case of the proposed method compared with DWT-based approaches. As a consequence, relevant information is gathered from the former.

Sample entropy evaluate data unpredictability and also to what extent a given data point depends on previous data points. Sample entropy measurements are shown in Fig. 7. The obtained values for AD EEG are slightly lower than the normal EEG, especially when the following methods are applied: DWT, normal shrink and CWT-fuzzy.

It should be noted that entropy varies according to noise levels. After applying our fuzzy-entropy threshold, the entropy was found to decrease. Concurrently, it is seen that AD patients have lower PSD values than healthy people.

The classification process in both AD and normal EEG was performed by a traditional neural network. The selected features were: the mean, standard deviation, PSD, entropy and sample entropy. In addition, its architecture was modified with 40 neurons (20 normal and 20 AD) in order to feed the classifier for the training phase.

During the testing stage, another 40 neurons were chosen and the efficiency of the whole classification was found out. Therefore, the confusion matrix is used to measure our performance rate (see Fig. 8). Specifically, the first column of the first row gives the correctly classified class AD ('0') and the second column shows the misclassified class normal ('1'). In the same way, the first column of the second row shows the misclassified class AD and the second column provides the correctly classified class as normal EEG.

As a result, 17 out of 20 AD EEG signals were correctly classified and three were misclassified as normal cases using fuzzy-entropy threshold. Similarly, 18 out of 20 normal EEG were perfectly classified and two were misclassified. Thus, a specificity rate of 87.5% was obtained after applying our methodology. Compared with the DWT method that achieves 75% of specificity, our approach greatly improves the final classification. Unlike, normal shrink provides a classification rate about 72.5% due to its remarkable ability to detect normal EEG cases. On the contrary, a total of 11 AD EEG signals were misclassified. Moreover, there is a huge step in accuracy regarding the Bayes shrink approach, since only 55.0% was achieved because its low prediction rate in both AD and normal EEG signals. The worst performance corresponds to the

Fig. 8 Confusion matrices

Table 1 Classification rate using a feed-forward neural network

Method	Classification rate, %
denoised signal using DWT (fuzzy)	75.0
proposed approach (CWT with fuzzy)	87.5
denoised signal with normal shrink	72.5
denoised signal with Bayes shrink	55.0
denoised signal with Visu shrink	35.5

Visu shrink denoising method, as the obtained classification rate was about 35.5%. It can be seen that only five out of 20 AD EEG signals were correctly classified, while 15 were incorrectly predicted. Even worse, only two normal signals were perfectly classified. The specificity rates of all methods are presented in Table 1.

Our work presents several advantages. First, an analysis of the EEG through fuzzy entropy and CWT has been performed, showing an improvement in the diagnosis rate of AD. Furthermore, a traditional and non-complex classification process has been used in order to increase the specificity rate without compromising the computational time. Finally, noise reduction has been achieved via an optimal threshold based on a Gaussian membership fuzzification. Even though the presented method renders competitive results, computing CWT on EEG is a complex process. Therefore, alternative optimisation algorithms should be investigated to tackle such complexity.

6. Conclusion: The randomness of EEG poses additional difficulties in the analysis of AD signals. Nevertheless, their fuzzification through a Gaussian membership and a CWT solves these issues. The optimal threshold is chosen thanks to the fuzzy entropy over the time-frequency domain. According to the output data, our approach shows the best denoising capabilities compared with the other methods. The extracted feature vectors are used to fit a FNN classifier in order to distinguish between AD and normal EEG signals. In conclusion, our method provides a specificity as high as 87.5%. Thus, it is expected that our diagnosis tool would make it possible to detect AD at early stages and, in turn, reduce the death rate of AD patients considerably.

Several open aspects can be highlighted as future lines of research. First, the denoising process could be improved by varying the threshold value. Therefore, an optimisation method will be designed to make this search as much efficient as possible. Regarding the feature extraction and the classification phases, the accuracy rate can be improved by adding more features and increasing the dimensionality of the resulting vector. In order to improve the extracted features and the classification rate, we plan to use a deep convolutional neural network. Moreover, higher performance could be achieved if CWT is replaced by the empirical mode decomposition (EMD). In addition, the complexity mentioned as a disadvantage can be reduced by means of the aforementioned adaptive data driven method (EMD). Such implementation is under progress.

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