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A hybrid unsupervised approach toward EEG epileptic spikes detection

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Abstract:	Epileptic spikes are complementary sources of information in EEG to diagnose and localize the origin of epilepsy. However, not only is visual inspection of EEG labor intensive, time consuming and prone to human error, but it also needs long-term training to acquire the level of skill required for identifying epileptic discharges. Therefore, computer-aided approaches were employed for the purpose of saving time and increasing the detection and source localization accuracy. One of the most important artifacts that may be confused as an epileptic spike, due to morphological resemblance, is eye blink. Only a few studies consider removal of this artifact prior to detection, and most of them used either visual inspection or computer-aided approaches, which need expert supervision. Consequently, in this paper, an unsupervised and EEG-based system with embedded eye blink artifact remover is developed to detect epileptic spikes. The proposed system includes three stages: eye blink artifact removal, feature extraction, and classification. Wavelet Transform was employed for both artifact removal and feature extraction steps, and Adaptive Neuro Fuzzy Inference System for classification purpose. The proposed method is verified using a publicly available EEG dataset. The results show the efficiency of this algorithm in detecting epileptic spikes using low-resolution EEG with least computational complexity, highest sensitivity and lesser human interaction compared to similar studies. Moreover, since epileptic spike detection is a vital component of epilepsy source localization, therefore this algorithm can be utilized for EEG-based pre-surgical evaluation of epilepsy.
Response to Reviewers:	Response to Reviewers' Comments Pegah Khosropanah, Abdul Rahman Ramli, Mohammad Reza Abbasi, Mohammad Hamiruce Marhaban, Ravshan Ashurov, Anvarjon Ahmedov This statement concerns our revision of the manuscript number NCAA-D-17-01380R2,

entitled “A hybrid unsupervised approach toward EEG epileptic spikes detection”, based on the referees' report.

The authors would like to thank the editor-in-chief and the reviewers for their precious time and invaluable comments. We tried to carefully address all the comments point-by-point. We hope the revisions have improved the paper to a level of their satisfaction. The corresponding changes and refinements made in the revised paper are summarized in our response below. The changes in the manuscript have red colored font.

Comments by Reviewer #1

Comment
Need to show clearly where all the corrections are made in the paper.

Response
We have already marked changes in the previous revised manuscript in red colored font, the whole manuscript has been checked and all modified parts are marked in red font again.

Comment
Need to show latest references on this subject and AI applications.

Response
Recent publications related to application of AI in this field have been reviewed and included in the current study as follows:
“Xuyen LT, Thanh LT, Viet D Van, et al (2018) Deep Learning for Epileptic Spike Detection. VNU J Sci Comput Sci Commun Eng 33:1–13. doi: 10.25073/2588-1086/vnucsce.156
Saini J, Dutta M (2017) An extensive review on development of EEG-based computer-aided diagnosis systems for epilepsy detection. Netw Comput Neural Syst 28:1–27. doi: 10.1080/0954898X.2017.1325527
Guo L, Rivero D, Dorado J, et al (2011) Automatic feature extraction using genetic programming: An application to epileptic EEG classification. Expert Syst Appl 38:10425–10436. doi: 10.1016/j.eswa.2011.02.118
Johansen AR, Jin J, Maszczyk T, et al (2016) Epileptiform spike detection via convolutional neural networks. In: 2016 IEEE Int. Conf. Acoust. Speech Signal Process. IEEE, pp 754–758
Carey HJ, Manic M, Arsenovic P (2016) Epileptic Spike Detection with EEG using Artificial Neural Networks. Proc 2016 9th Int Conf Hum Syst Interact 89–95. doi: 10.1109/HSI.2016.7529614
Fergus P, Hignett D, Hussain A, et al (2015) Automatic Epileptic Seizure Detection Using Scalp EEG and Advanced Artificial Intelligence Techniques. Biomed Res Int 2015:1–17. doi: 10.1155/2015/986736”.

Comments by Reviewer #2

Comment
The paper strongly improved!
But the corrections were not done with the needed rigor; please visit (i) my previous comments, (ii) the paper, again and completely do them.
There are sooo many "," and "." IN and BEHIND formula contexts missing.
Unfortunately, by now, a number formulas appear not structured / not as one expects them to be, for aforementioned reasons.
There are mistakes with the use or non-use of blanks, etc.
Please make it now become "perfect".
I strong recommend you to gain again from an experienced scientists help - experienced with use of mathematical formalism.
In fact, some parts are mathematically / formally not yet fully clear to the reader - or slightly incorrect:
--- When you have 2-3 indexes in an equation, say: k and l, in one formula, but one of them appears at one side only, it could become a bit clear how to understand this situation, at each place of the paper, what are "independent" and what are "dependent"

	variables/indexes, etc. But: I recognize your great efforts! --- When you use in an equation one index name, say: i, as an independent variable and as an dependent (say: summation), then this is wrong and you have to correct and clarify. For , ... , please do not use dots at middle height (like multiplication dots) but lower dots (at the height of full stops). Use small blanks in formula contexts for better reading and understanding (as has to be in math-based work). With great care - and advise by an experienced mathematicians - these and other issues should become resolved. Response We have checked the formulas for punctuation, and style. All formulas have been rewritten using MathType to avoid mis-usage of blanks. The size of blanks were corrected but the size of blanks are normally not decided by the authors but by the journal production office during the typesetting stage based on the journal guidelines. The commas and full stops were added to the formulas as needed. Indexes were checked and corrected. The last author is a mathematician as has checked and approved the corrected formulas. Furthermore, to improve the language and take care of all the impurities, the paper has been edited and proofread by native English language editors who are familiar with the subject. Comments by Reviewer #6 ____ Comment Has merit but needs work. Response The works requested by the reviewers has been done and are marked in red font in the manuscript.

A hybrid unsupervised approach toward EEG epileptic spikes detection

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Abstract

Epileptic spikes are complementary sources of information in EEG to diagnose and localize the origin of epilepsy. However, not only is visual inspection of EEG labor intensive, time consuming and prone to human error, but it also needs long-term training to acquire the level of skill required for identifying epileptic discharges. Therefore, computer-aided approaches were employed for the purpose of saving time and increasing the detection and source localization accuracy. One of the most important artifacts that may be confused as an epileptic spike, due to morphological resemblance, is eye blink. Only a few studies consider removal of this artifact prior to detection, and most of them used either visual inspection or computer-aided approaches, which need expert supervision. Consequently, in this paper, an unsupervised and EEG-based system with embedded eye blink artifact remover is developed to detect epileptic spikes. The proposed system includes three stages: eye blink artifact removal, feature extraction, and classification. Wavelet Transform was employed for both artifact removal and feature extraction steps, and Adaptive Neuro Fuzzy Inference System for classification purpose. The proposed method is verified using a publicly available EEG dataset. The results show the efficiency of this algorithm in detecting epileptic spikes using low-resolution EEG with least computational complexity, highest sensitivity and lesser human interaction compared to similar studies. Moreover, since epileptic spike detection is a vital component of epilepsy source localization, therefore this algorithm can be utilized for EEG-based pre-surgical evaluation of epilepsy.

Keywords: *DWT, ANFIS, epileptic spike detection, eye blink remover.*

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1 Introduction

Epilepsy is identified by unexpected, temporary and extreme discharge of a group of neurons in the brain. Approximately one percent of the world's population suffers from epilepsy [1, 2]. Unfortunately, predicting the time of epileptic seizure is tough, and its process is a long way off from being fully understood [3]. Normally, epilepsy is controlled, but cannot be treated with medications. There are different modalities that are used for epilepsy diagnosis, but the most common tool in clinics to evaluate the brain activities is Electroencephalograph (EEG), due to its cost-effective, direct measurement and high temporal resolution characteristics.

EEG records brain electrical activity generated by cortex neurons from the scalp [3]. There are various morphologies of epileptic waves in EEG, including main ingredients such as: slow waves, spikes and sharp waves. Usually, sharp-and-slow waves (SWW) or spike-and-sharp waves (SSW) emerge at the same time. Although spikes are the most important epileptic waves for diagnosis and epilepsy source localization [4], they are also the morphology most difficult of identification. Moreover, spikes can be confused with eye blink artifacts due to their morphological resemblance, which makes the visual assessment more challenging. Another hurdle to epileptic spike recognition is their transient and subtle nature, which makes them hard to distinguish in the time domain. Consequently, visual inspection of EEGs is labor intensive, time consuming and prone to human error. Moreover, long-term training is necessary to obtain the required level of EEG recognition skill. Therefore, recent studies tend to employ computer-based methods for EEG analysis to reduce the assessment period, increase precision in analysis and minimize human error. Diagnosis of changes in EEG using automated systems has been under scrutiny over the past several decades [5–9].

Detection of abnormal activities in EEG is difficult using conventional methods, due to their slight amplitude in the time domain. Moreover, using mimic-based methods to convert the qualitative diagnosis features into more quantitative signals creates problems in classification, besides requiring a neurological background. Although time-domain analyses such as time-averaging method are widely used in signal processing to detect epileptic spikes with similar morphology to averaged template, they struggle to figure out which frequencies are involved in those events. On the other hand, although frequency-domain analyses such as Fourier transform separate the frequencies that exist in a signal, they cannot find the time of their manifestation. Time-Frequency (T-F) analysis techniques have, therefore, been developed to overcome these limitations [10]. T-F methods can be categorized into two main types: fixed-basis and data-driven methods. Even though Empirical Mode Decomposition (EMD) and its multivariate extension are data-driven and do not have the limitations of fixed-basis methods such as wavelet and Machine Matching Pursuit (MMP), the results have demonstrated that wavelet-based algorithms show better performance in the context of epilepsy detection [11, 12]. Many researchers implemented Singular Value Decomposition (SVD) to feature epileptic discharges [13–15]. However, since the final results are evaluated visually, the efficiency of this method is still unclear. Guarnizo and Delgado [16] used the EMD method as a feature extractor, and the extracted features were instantaneous frequency (IF), amplitude, skewness, kurtosis, and Shannon's entropy. They implemented Linear Bayes classifier and the reported accuracy was 98%. Later, Bajaj and Pachori [17] also used EMD method with Intrinsic Mode Function (IMF) to classify epileptic and non-epileptic EEG. Classification accuracy of 90% was obtained, in the latter study. Tafreshi et al. [18] examined the efficiency of EMD method using Multilayer Perceptron Neural Network (MPNN) and Self-Organizing Map (SOM). They reported that a combination of IMF features and mean feature of wavelet coefficients resulted in classification accuracy of 95.42% and 92.14% for MPNN and SOM, respectively. Although using EMD to feature epileptic spikes may result in high classification accuracy, not only does the EMD method suffer from the mode mixing issue, but also it can only analyze one channel at a time. Zahra et al. [19] reported 87.2% of total classification accuracy using Multivariate Empirical Mode Decomposition (MEMD) feature extraction method and Artificial Neural Network (ANN), which shows the relative inefficiency of MEMD in detecting epileptic spikes as compared to other methods. Moreover, according to the results from literature, WT method has proved to have the highest capability to retrieve important hidden information in the time-domain of non-stationary signals such as EEG, with less computational complexity [3, 6, 20–29]. Therefore, in the current study WT was employed to remove eye blink artifact and extract epileptic spike feature from noise-free EEG. However, choosing the proper mother wavelet which features the signal of interest plays a critical role. For instance, a mother wavelet which can differentiate eye blink artifact from epileptic spike with less distortion is desirable.

Furthermore, since artificial neural networks (ANNs) have superior predictive powers compared to signal processing methods, they have been used as computational applications to recognize and classify disease patterns [30–35]. In addition, while dealing with uncertainty in making decisions, fuzzy systems play a key role in medical applications. As a result, fuzzy systems have received ongoing attention from researchers in production techniques, modern information technology, decision making, diagnostics, pattern recognition, data analysis and other related fields [36–40].

To utilize the capabilities of ANN and fuzzy systems, the adaptive neuro-fuzzy inference system (ANFIS) was developed and has demonstrated remarkable success in modeling nonlinear functions in its applications. In ANFIS, the membership function factors are taken out from a data set that defines the system performance. The ANFIS acquires specifications in the dataset and fine-tunes the system factors based on the known error criterion [41, 42]. ANFIS has been effectively employed in biomedical engineering for classification and data analysis [26, 43–45]. Thus, ANFIS was utilized in this study for classification purpose.

Since EEG has small amplitude, different internal and external artifacts may affect its analysis and need to be removed. Some of these artifacts like cardiac or muscular activities or main power frequency are easily differentiable from epileptic spikes, whereas eye blink artifacts can easily be confused with epileptic spikes due to their morphological resemblance. Although many studies have been conducted to remove eye blink artifact from normal EEG, eye blink artifact removal from epileptic EEG is more complex due to the morphological resemblance of epileptic spikes and eye blink artifacts [46]. In most of the previous studies, this artifact was visually detected from epileptic EEG by experts. This approach is time consuming and needs professionally trained specialists to recognize this artifact. Due to inevitable human error, even the most expert and experienced specialists may confuse these artifacts as epileptic spikes, rendering their results and diagnosis less accurate [10]. Although there are some studies that utilized computer-aided methods such as wavelet Transform (WT), Independent component analysis (ICA), Principal Component Analysis (PCA) and regression methods to remove eye blink artifact, these methods have their own limitations. To utilize regression method for the purpose of eye blink removal, a neat record of Electrooculogram (EOG) reference is required. However, since EOG electrodes are placed near the eyes, EOG recordings comprise EEG signal as well. Therefore, regression methods suffer from a lack of EOG and EEG independency [47]. Since PCA method extracts spatially orthogonal components, it is not an appropriate method to remove eye blink artifacts, due to the fact that EEG and eye blink artifacts sources are not necessarily spatially orthogonal to each other. Moreover, using ICA method to remove eye blink artifact also needs expertise to identify the artifact components to be excluded from the signal. Nevertheless, all the above-mentioned methods were reported as successful in removing eye blink artifact without investigating distortion of the signal. Wavelet method, on the other hand, shows that if a proper mother wavelet is chosen, higher signal to noise ratio with less distortion would be achieved to remove artifacts.

To overcome these problems, in the present study a fully automated, hybrid Artificial Intelligence (AI) based system with embedded eye blink artifact remover is developed. Bior 3.3 mother wavelet is used to remove eye blink artifact effectively with less distortion and expert supervision. Since epileptic spikes lie in the delta frequency band [48], in this methodology Duabechies 4 mother wavelet is used for 3 levels of decomposition to extract the signal of interest's features. Since the quantum of change in frequency distribution in delta frequency band is much higher in epileptic segments than normal, only standard deviation of delta band WT coefficients (two features) were fed to the classifier. The first order Sugeno type ANFIS, trained by the combination of gradient descent and least square error is applied to classify the feature vectors of the training dataset. The proposed system achieved the highest possible classification accuracy with less computational effort (features dimension) and supervision. Moreover, it has the potential to be used for unsupervised epileptic seizure detection in clinics in order to save time and cost, and to enhance accuracy of the epileptic spike detection process.

2 Datasets and methods

In the current study, the datasets were taken from an Epilepsy center in Bonn, Germany by Ralph Andrzejak [49]. Wavelet method was used for both eye blink removal and epileptic spike feature extraction. Moreover, first order Sugeno type ANFIS trained by hybrid method was applied to classify epileptic and normal EEG segments. The following sections describe the methods employed and datasets used in this study.

2.1 Datasets

Two out of the five freely accessible EEG datasets (B and E) [49] were used in this study. Different percentages of each dataset were devoted to training the ANFIS, and the remaining data were used to evaluate the ANFIS. Each set includes 100 single-channel EEG data with a duration of 23.6 seconds (4097 sample). Set B holds scalp EEG recordings of five healthy subjects with closed eyes. Set E consists of seizure activity, which was selected from all recording spots presenting ictal activity. Set E was recorded intra-cranially.

The frequency range for all EEGs was $0 - 85\ Hz$, so that band-pass filter to select the desired frequency band may be applied. Set B was chosen because alpha rhythm ($8 - 13\ Hz$ frequency range), which is the predominant physiological rhythm, could be identified during the relaxed situation of healthy subjects with eyes closed [49]. Useful information of EEG lies below $30\ Hz$ frequency. Since Butterworth is a maximally flat magnitude filter wherein the roll offs are sharper by increasing its order, therefore, in this study Butterworth filter has been applied. To cut out desired frequency range, a Butterworth band-pass order 8 filter was applied. Moreover, to remove electrical interface of $50\ Hz$ frequency, a Butterworth band-stop filter order 8 was used. Each signal was broken down into 16 segments by a rectangular window, and each segment contained 256 samples. No segment has overlapping slides with the next segment. All the segments were scored by a specialist to 0 and 1 for healthy and epileptic subjects respectively, to have a gold standard (target) both for training and testing the ANFIS. To remove the segments which contain irrelevant information, the standardized normal Probability Density Function (PDF) of wavelet coefficients' statistical features was computed for each group. For each dataset (normal and epileptic), the statistical features with $\mathrm{P-value} < 0.005$ have been discarded.

2.2 Methods

The following subsections explain the method applied in the current study. Moreover, the quantitative evaluation of eye blink artifact removal is included.

2.2.1 Wavelet theory, denoising and feature extraction

Wavelet transform (WT) is a developed version of Fourier transform (FT), which allows analyzing the signal in time-frequency domain with the advantage of providing multi-resolution signal schemes. Wavelets are like high-pass and low-pass filters which break down signal into distinct frequency details. Then each detail with resolution related to its scale is investigated. Each scale represents a certain coarseness of the signal under study. In Fig.1, wavelet decomposition is illustrated schematically.

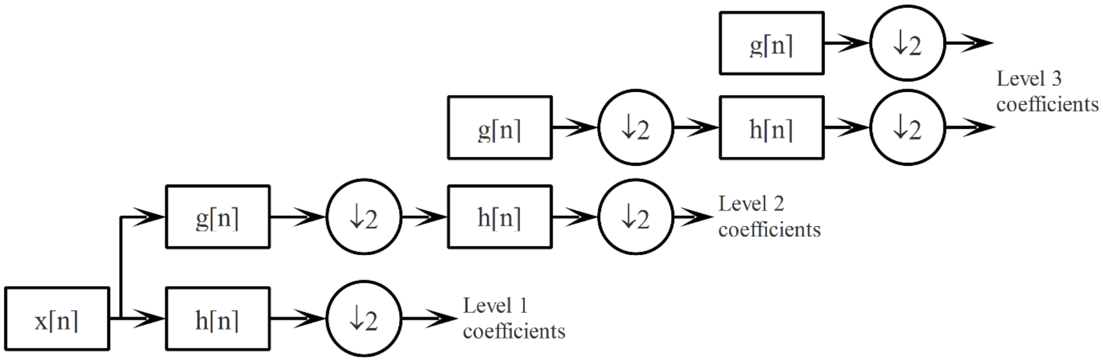

Fig.1 Schematic of Wavelet decomposition to 3rd level [50]

A wavelet low-pass filter *h* needs to satisfy the standard quadrature mirror filter term:

$$H\left(z\right)H\left(z^{-1}\right)+H\left(-z\right)H\left(-z^{-1}\right)=1 \ ,$$

where *H(z)* specifies the z-transform of the filter *h*. Its equivalent high-pass filter is determined as:

$$G(z) = z\,H\left(-z^{-1}\right).$$

Since Continuous Wavelet Transform (CWT) produces many coefficients, Discrete Wavelet Transform (DWT) can be employed in order to reduce unnecessary information.

A sequence of filters with growing size (indexed by *i*) can be reached by:

$$H_{i+1}(z) = H\left(z^{2^i}\right)H_i(z),$$

$$G_{i+1}(z) = G\left(z^{2^i}\right)H_i(z)\ , \quad i = 0,\ldots,I-1,$$

with the initial condition $H_0(z) = 1$. Relation of two sequence scales in time is determined as:

$$h_{i+1}(k) = [h]_{\uparrow 2^i}\, h_i(k),$$

$$g_{i+1}(k) = [g]_{\uparrow 2^i}\, h_i(k),$$

where the subscript $[\ ]_{\uparrow m}$ writes down the up-sampling by a factor of *m* and *k* is the equally sampled discrete time.

The standardized wavelet and scale base functions of $\varphi_{i,l}(k)$, $\psi_{i,l}(k)$ can be defined as:

$$\varphi_{i,l}(k) = 2^{\frac{i}{2}} h_i\left(k - 2^i l\right),$$

$$\psi_{i,l}(k) = 2^{\frac{i}{2}} g_i\left(k - 2^i l\right),$$

where the factor $2^{\frac{i}{2}}$ is an inner product standardization, *i* and *l* are the scale and the translation factor, respectively.

The DWT can be determined as:

$$a_{(i)}(l) = x(k)^* \varphi_{i,l}(k),$$

$$d_{(i)}(l) = x(k)^* \psi_{i,l}(k),$$

where $a_{(i)}(l)$ and $d_{(i)}(l)$ are respectively the approximation coefficients and the detail coefficients at resolution i [44].

Signal break down process can be continued till those parts of the signal that correlate well with the frequencies required for classification of the signal are retained in the wavelet coefficients. When analyzing a signal, normally a proper number of level for decomposition is considered based on the dominant frequency of the signal under study.

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EEG signal can be contaminated by different artifacts that mask our signal of interest. The most important internal artifact in the process of epileptic spike detection and epilepsy source localization is the eye blink artifact, due to the morphological resemblance between the two. Most of the artifacts due to eye blinking, head and eyeball moving usually lie at low frequencies [51]. Since the aim of this study is to develop a fully automated algorithm with less human interaction, therefore in the present work Bior 3.3 is applied as the mother wavelet due to its morphological resemblance to the eye blink artifact and yet differentiable characteristics from epileptic spikes [52]. The signal decomposition by DWT was carried out at 6 levels. Then, the sixth approximation signal which included the lowest frequency band and did not have the epileptic spike information was removed, and EEG signal was finally reconstructed without this approximation.

2.2.2 Performance measurement for eye blink artifact removal method

The common approach to evaluating the performance of the eye blink removal method is using simulated data. In this process, artifact-free EEG is artificially combined with an artifact, then the mixed signal is processed using the eye blink removal method. To evaluate the method, some feature of the processed signal (e.g. signal-to-noise ratio (SNR)) is computed and compared to the artifact-free EEG. However, since the artifact-free ("true") EEG is unknown while using real EEG, the performance of the algorithm is subject to visual inspection of the resulting signals. Puthusserypady and Ratnarajah [53] evaluated the eye blink removal method's performance as the ratio of the power of the removed artifact to the remaining EEG:

$$R = \frac{\sum_{1}^{C}\sum_{1}^{N}\left(E_e - Y\right)^2}{\sum_{1}^{C}\sum_{1}^{N} Y^2},$$

where N is the number of samples and C the number of channels recorded. E_e is the signal measured at EEG electrode sites, and Y is processed EEG after eye blink removal.

This metric proposed that the higher the ratio is, the better the performance of the algorithm. They simply considered that the algorithm is only being applied to data with significant eye blink. However, for data without eye blink artifact, a higher ratio does not necessarily indicate better performance. Therefore, an evaluation metric which calculates the performance of an eye blink removal algorithm constantly on EEG that has periods both with and without eye blink is desired.

Borna Nuredine et al. [54] proposed a new metric that shows how much an eye blink removal algorithm may distort the underlying EEG. This metric is as follow:

$$R' = \frac{\sum_{1}^{C} \left(E_e - Y\right)^2}{\sum_{1}^{C} E_e^{\,2}}.$$

Whenever $R' > 1$, the power of the processed signal is higher than the original EEG, representing that the algorithm has distorted signal or introduced new artifacts. Therefore, the higher the percentage of samples ε in which $R' > 1$ (how often it removes too much signal), the worse is the performance of the eye blink removal method.

When combined with the power ratio of Puthusserypady and Ratnarajah [53], these metrics can be used to effectively evaluate eye blink removal algorithms on real EEG data [54]. Therefore, in the current study removal of eye blink artifact has been evaluated both visually by a specialist and quantitatively. Visual assessment of EEG segments by a specialist confirms the efficiency of this method for eye blink removal. Average values for R and ε over all segments were 17% and 15%, respectively. These metrics demonstrate that the proposed eye blink removal method effectively removed eye blink artifact from healthy and epileptic segments with minimum distortion.

After removing the eye blink artifact, EEG signal can be prepared for the classification step. Since preprocessed EEG signals contain $0.5 - 30\ Hz$ frequency component, and epileptic spike information exists in the delta frequency band ($1 - 4\ Hz$), in this study 3 levels of decomposition were chosen for the epileptic feature extraction step using different mother wavelets (Coif4, Sym10, Db1, Db4 and Db2).

A large number of features were obtained through wavelet decomposition for each segment, which reduced the classification speed. To reduce the dimension of features' vector, some statistical features were employed to characterize time-frequency distribution of EEG segments, which are as follows:

1. Maximum (Max) of wavelet coefficients in each sub-band frequency for each segment.
2. Mean of wavelet coefficients in each sub-band frequency for each segment.
3. Standard deviation (STD) of wavelet coefficients in each sub-band frequency for each segment.

These features were calculated over Coefficient Detail 1 (CD1), Coefficient Detail 2 (CD2), Coefficient Detail 3 (CD3) and Coefficient Approximation 3 (CA3) wavelet coefficients.

2.2.3 Adaptive Neuro-Fuzzy Inference System (ANFIS)

ANFIS is a combination of artificial neural network and Fuzzy Sugeno inference system, first proposed by Jang [42]. In this system, if-then rules and membership functions are built up in accordance with the input data and exploit the adaptive basis to fine-tune the system parameters automatically. Fig.2 shows the simple structural design of ANFIS with two inputs (x and y) and one output (f). ANFIS contains many non-recursive layers, where each node performs a certain role on the obtained inputs. Then, by altering node parameters, each node is adjusted and trained.

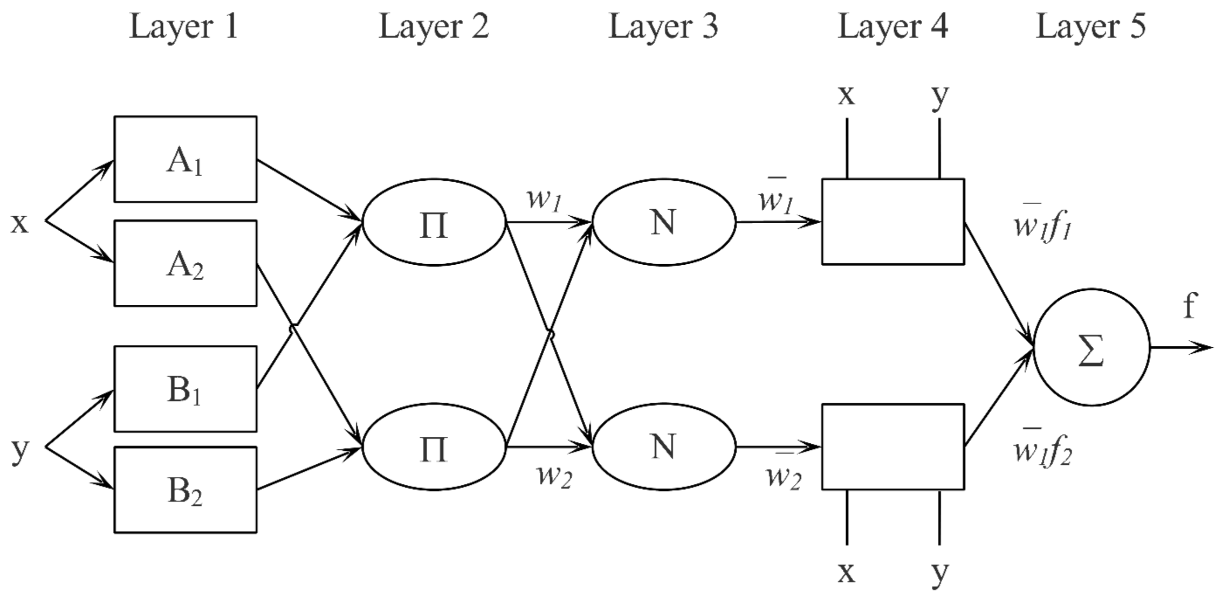

Fig.2 ANFIS architecture [44]

Here, two fuzzy if-then rules, based on a first order Sugeno model are considered:

Rule 1: If x is A_1 and y is B_1 then z is $f_1(x, y; p_1, q_1, r_1) = xp_1 + yq_1 + r_1$,

Rule 2: If x is A_2 and y is B_2 then z is $f_2(x, y; p_2, q_2, r_2) = xp_2 + yq_2 + r_2$,

where x and y stand for the inputs, A_i and B_i stand for the fuzzy sets, f_i is the outcome in the fuzzy domain imposed via the fuzzy rule, p_i, q_i and r_i are the intended parameters obtained within the training process. A circle illustrates a fixed node, while a square point toward an adaptive node.

Jang [42] proposed 5 different layers to explain the performance of the nodes:

Layer 1: An initial assumption for membership functions is considered. For instance, generalized bell:

$$\mu_A(x;a,b,c) = \frac{1}{1+\left[\frac{x-c}{a}\right]^{2b}}.$$

In the current study, the fuzzy rule architecture of the ANFIS classifier was designed by using a generalized bell-shaped membership function. For medical applications including the current study, generalized bell membership function has better performance of classification in comparison with others due to the fact that it deals with imprecision, and provides smoothness and concise notation, along with the freedom to adjust steepness. By changing the values, the membership function profile also alters accordingly. The parameters involved in this layer are called the premise factors. The outputs of layer 1 are the fuzzy membership grade of the inputs, which are given by:

$$Q_{1,i} = \mu_{A_i}(x), \quad i = 1,2,$$

$$Q_{1,i} = \mu_{B_i}(y), \quad i = 3,4,$$

where, any membership function can be accepted by $\mu A_i(x)$, and $\mu B_{i-2}(x)$.

Layer 2: The so-called firing strength of the rules are obtained from output of this layer in the fuzzy inference system. The output of this layer can be denoted as:

$$Q_{2,i} = w_i = \mu_{A_i}(x)\mu_{B_i}(y), \quad i = 1,2.$$

Layer 3: In this layer, the fraction of the i^{th} rule's firing strength is computed. Normalized firing strengths (output of this layer), can be computed as:

$$Q_{3,i} = \bar{w}_i = \frac{w_i}{w_1 + w_2}, \quad i = 1,2.$$

Layer 4: The so-called consequent parameters are involved parameters in this layer. The outputs of this step are calculated by:

$$Q_{4,i} = \bar{w}_i f_i = \bar{w}_i (xp_i + yq_i + r_i), \quad i = 1,2.$$

Layer 5: Here, all the nodes are fixed, and all received signals from previous steps are added up. The ultimate output can be calculated by:

$$Q_{5,i} = f_{out} = \sum_{i=1}^{2} \bar{w}_i f_i = \frac{\sum_{i=1}^{2} w_i f_i}{\sum_{i=1}^{2} w_i} = overal\ output\ .$$

Two approaches are used to update the ANFIS factors. Gradient descent method can be used in the backward pass to adjust premise parameters which describe membership functions. Least squares approach also can be employed in the forward pass to find consequent parameters. Consequent parameters figure out the coefficients of each equation. Using a combination of gradient descent in backward pass and least squares method in forward pass while the other pass is fixed is called the hybrid learning method. In the current work, a hybrid learning approach is the chosen method, since this approach converges faster [26].

3 Results and discussions

The results obtained using the proposed hybrid method with embedded unsupervised eye blink artifact removal and the related discussions are given in the following subsections.

3.1 Results

In the proposed approach, firstly eye blink artifacts are removed using DWT as explained in section 2.1 and validated using visual assessment by a specialist and quantitative metrics. Then, to find the most suitable mother wavelet that best features epileptic spikes, different types of mother wavelets (Coif4, Sym10, Db1, Db4 and Db2) are applied. Results show the superiority of the Duabechies family in extracting the epileptic spike features. Fig.3 shows the classification accuracy using ANFIS for these wavelets. As can be seen, the highest possible classification accuracy is obtained by using Duabechies 4 mother wavelet as feature extractor.

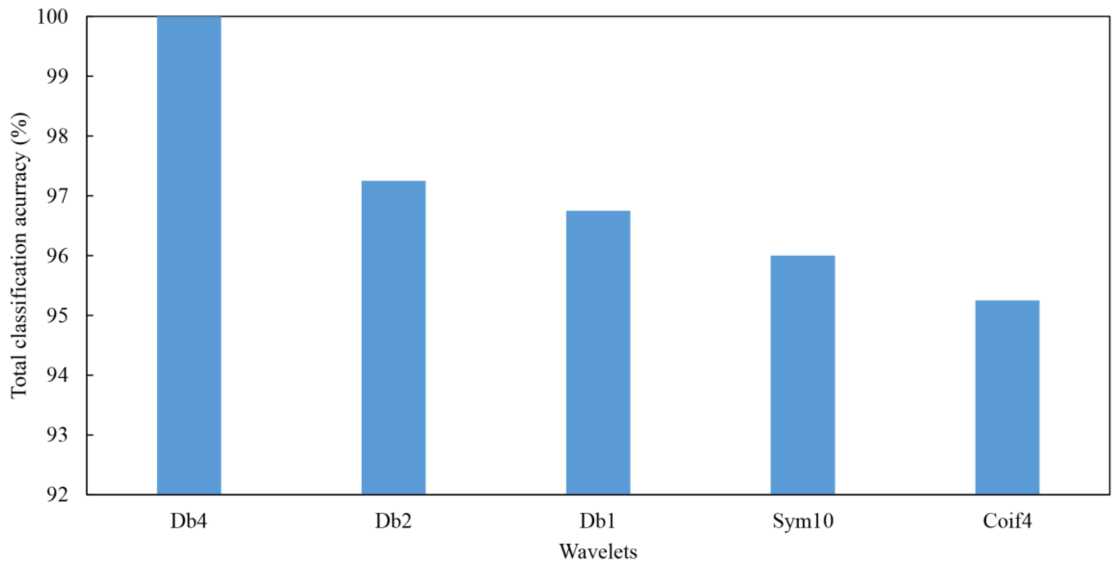

Fig.3 Total classification accuracy of different mother wavelets

The dataset is divided into two groups; training and testing. The ultimate membership function deviations (after training) in comparison to the input parameters' original membership functions (before training) were studied. Five regions described as: very small (VS), small (S), medium (M), large (L) and very large (VL), were considered for each input parameter's membership function. 3 and 4 input parameter membership functions resulted in lesser classification accuracy, as compared to 5 membership functions, based on their confusion matrix and least square error. The result of analysis of original and ultimate membership functions shows significant variations in the final membership function. These significant changes display the saliency of the selected features for the classification stage.

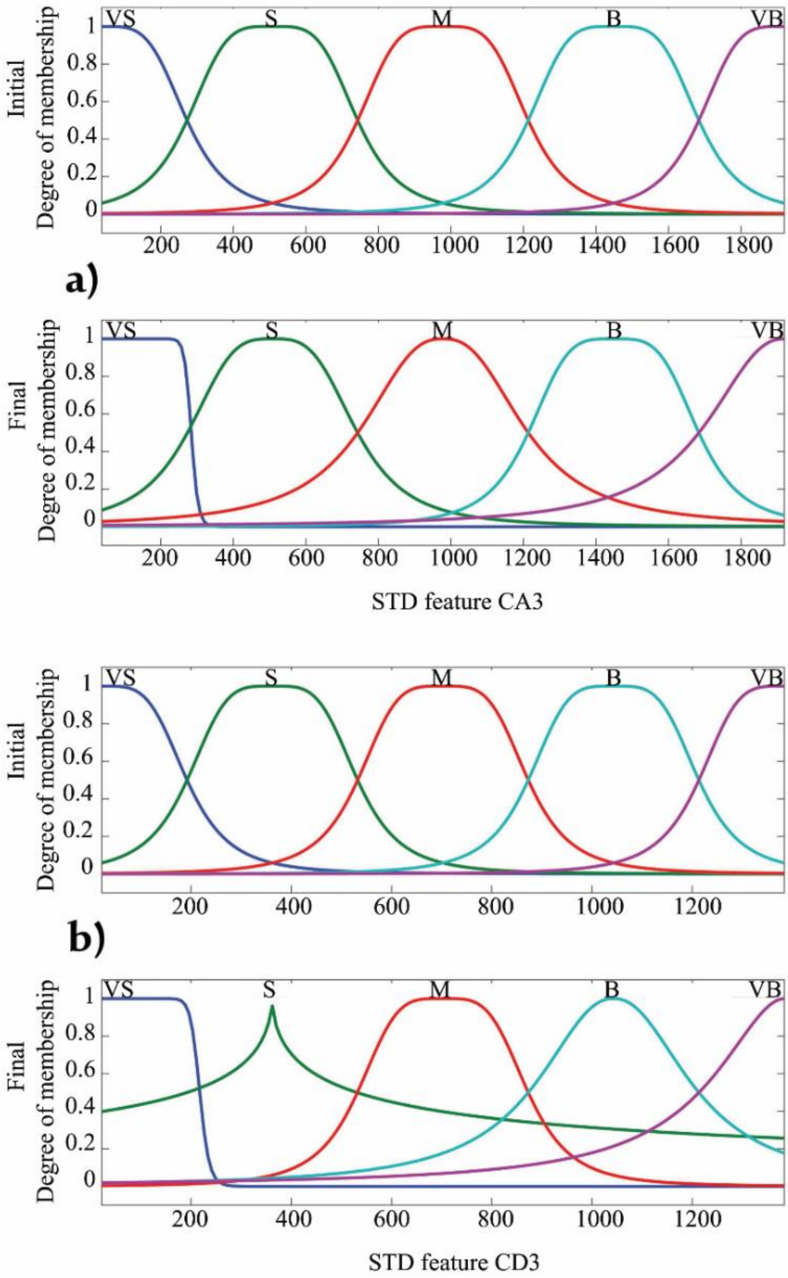

Fig.4 a) Initial membership function and final membership function for STD feature CA3, **b)** Initial membership function and final membership function for STD feature CD3

Fig.4 illustrates the original membership functions and ultimate membership functions of ANFIS. This figure shows that ANFIS fed by STD extracted from CA3 (input 1) and CD3 (input 2) using Db4 results in a considerable change in the final membership function of the wavelet coefficients. Moreover, network error convergence which shows the difference between estimated values by ANFIS in comparison with actual value (target) is derived to evaluate network performance. Fig.5 displays network error convergence. To choose the number of epochs, a few points were considered. The linguistic meaning of final membership function was maintained while minimizing training errors and avoiding data overfitting. Final error convergence of trained ANFIS is about 0.005 for 800 epochs. Although zero error is desirable for a network, but it is also important to avoid overfitting. Therefore, training of the ANFIS network was stopped at 800 epochs with network error convergence of 0.005 after examining 500, 700 and 1000 epochs.

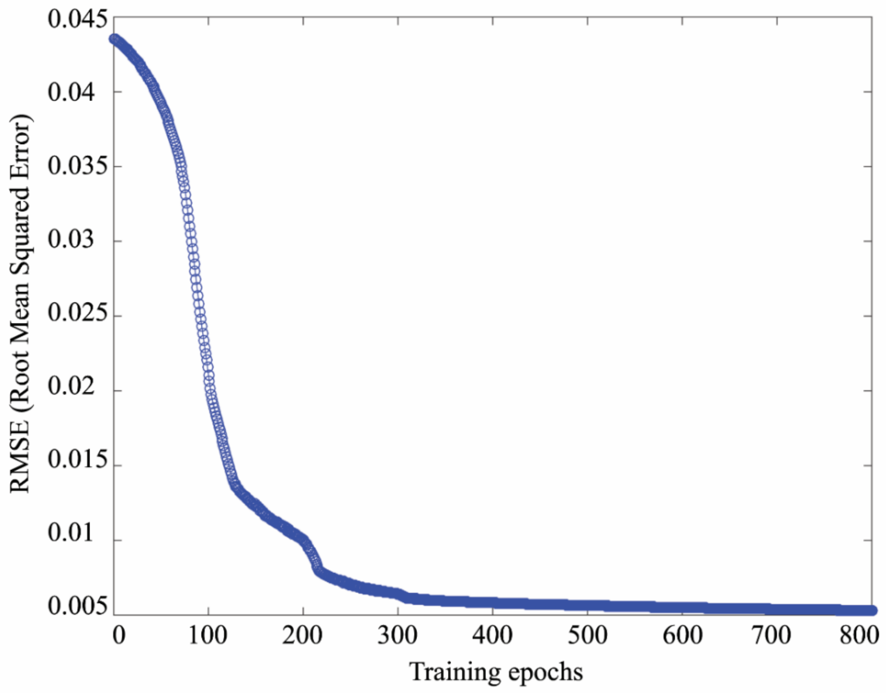

Fig.5 Network error convergence of ANFIS for STD feature CA3 and CD3

To verify the accuracy of the proposed algorithm and to classify epileptic spikes after training, the remaining data were used for testing. The intention of classification is to label input forms to one of the classes (healthy or epileptic), displayed with outputs limited in the range of 0 to 1 which show the probability of class membership. Generally, a form is labeled as a class based on its selection criteria to classify data.

There are some definitions before reporting the results:

True Positive (TP): The number of epileptic segments that are correctly classified as epileptic.

False Positive (FP): The number of normal segments that are incorrectly classified as epileptic.

True Negative (TN): The number of normal segments that are correctly classified as normal.

False Negative (FN): The number of epileptic segments that are incorrectly classified as normal.

The outcome of classification using the ANFIS model is usually represented by a confusion matrix defined by labelling the desired classification on the columns and the actual network outputs on the rows. This matrix is used to evaluate the robustness and accuracy of the classifier. The comparisons were based on two scalar performance measures derived from the confusion matrices; namely specificity and sensitivity.

Specificity: number of normal subjects identified correctly/number of normal subjects in total. It can be calculated as follows:

$$Specificity = \frac{TN}{TN + FP}.$$

Sensitivity: number of classified epileptic patients recognized correctly/number of epileptic patients in total. It can be calculated as follows:

$$Sesitivity = \frac{TP}{TP + FN}.$$

Total classification accuracy: number of classified subjects classified correctly/number of total subjects.

$$Total\ classification\ accuracy = \frac{TP + TN}{TP + FN + FP + TN}.$$

There are two classes in the current study: epileptic and normal. As mentioned before, epileptic spike information consists of delta range (less than $4\ Hz$). Thus, the sub-bands that contain epileptic information are CA3 and CD3. To start the classification, ANFIS was fed with statistical features which were extracted from CA3 using Db4. Then, the combination of statistical features was examined to train ANFIS. Table 1 shows the results of ANFIS fed with each statistical feature extracted from CA3. As can be seen in this table, the highest sensitivity with fair specificity belongs to the ANFIS fed with STD extracted from CA3.

Table 1 Result comparison for one-dimension ANFIS (Db4)

	Maximum	Mean	STD
Sensitivity (%)	97	67.625	98.5
Specificity (%)	92.25	94.5	94.875

Since CD3 also contains epileptic spike information (delta range), it can be used to further improve the results. In this study, this was achieved by combining the statistical features extracted from CA3 and CD3. ANFIS fed with this combination demonstrates a significant improvement in its results. The confusion matrix of the ANFIS fed by STD of CA3 and CD3 is represented in Table 2. The desired result for a classifier is to have the least rate of misclassification for the classes being analyzed. As is evident from this table, from 638 epileptic features fed to the ANFIS, all have been correctly identified as epileptic class, which represents 100% sensitivity for the ANFIS classifier and 0% misclassification rate. Moreover, of 380 healthy features fed to the ANFIS, all have been correctly classified as normal class, which indicates 100% specificity of the ANFIS classifier. Since the total accuracy is the average of sensitivity and specificity, therefore, the accuracy of the ANFIS which is fed with the STD features of CA3 and CD3 is 100%.

Table 2 Confusion matrix STD feature CA3 and CD3

		Desired	
		Epileptic	Normal
Actual output	Epileptic	638	0
	Normal	0	380

3.2 Discussions

Table 3 shows the total accuracy, sensitivity and specificity for different classifiers used in earlier studies, including the current algorithm's results. As can be seen, apart from the current study, only two more studies achieved 100% accuracy: Subasi and Gursoy [28] and Polat & Güneş [55]. Polat & Güneş [55] applied Fast Fourier Transform (FFT) method for feature extraction, PCA for dimension reduction and AIRS with fuzzy resource allocation classifier. Although they achieved 100% accuracy, since EEG is a non-stationary signal, using FFT which treats a signal as a stationary one is not suitable to extract epileptic EEG features. Subasi & Gursoy [28] computed linear discriminant analysis (LDA) weight for features extracted from wavelet coefficients of each sub-band. They employed Support Vector Machine (SVM) as classifier. Although Subasi & Gursoy [28] also obtained 100% accuracy, applying LDA to reduce the classifier's input dimensions is not necessary, when the same accuracy can be obtained without this computation effort. As is evident, normal subjects and epileptic patients were classified with 100% accuracy via the proposed algorithm by only using the quantum of changes in frequency distribution in delta frequency band (two features). Not only has the current study achieved the highest accuracy using two features of delta frequency band (less computation efforts), it also has an unsupervised embedded eye blink remover. Eye blink artifact removal is an important part of epilepsy diagnosis and source localization because such artifacts can easily be confused with epileptic spikes (the signal of interest). Usually, this artifact is discarded either by visual inspection or by computer-aided method, which needs supervision and expertise. However, the current study proposes an epileptic classification algorithm using WT features and ANFIS classifier with embedded unsupervised eye blink removal. Based on these results, the proposed ANFIS model shows high potential for use in unsupervised epileptic seizure detection from long-term EEG in clinics. Moreover, since epileptic spike detection is a pre-stage toward epilepsy source localization, the proposed method can be used to design an integrated algorithm of pre-surgical evaluation toward epilepsy source localization. High accuracy, time saving, precision improvement and less computational effort with reduced expert supervision are among the advantages of the current work.

Table 3 Comparison of different methods for EEG classification

Method	Reference	Total accuracy (%)	Specificity (%)	Sensitivity (%)
MLPNN- LBDWT- LR	[56]	92.5	92.3	92.8
RNN-Lyapunov exponents	[57]	96.79	97.38	96.13
ANFIS-WT	[44]	98.68	99.67	98.678
ME-WT	[58]	94.5	94	95
ANFIS-WT	[59]	94	93.7	94.3
FFT-Decision tree classifier	[60]	98.72	99.31	99.40
AIRS(Fuzzy)-FFT-PCA	[55]	100	100	100
SVM-WT-LDA	[28]	100	100	100
k.NN-WT	[22]	99.5	-	-
WT-ANFIS with embedded eye blink remover	Current study	100	100	100

4 Conclusions

Visual inspection of EEG signals toward epileptic spike recognition is labor intensive, time consuming and prone to human error. Moreover, due to morphological similarity of epileptic spikes and eye blink artifacts, they may be confused in the process of epileptic spike detection, and hence the need for an automated approach. Unfortunately, few studies considered removing eye blink artifact prior to epileptic spike detection, which may lead to faulty classification and wrong source localization. Therefore, in the current study a fully automated algorithm with less human interaction was developed. This approach comprises an unsupervised algorithm to remove eye blink artifacts via DWT by using Bior 3.3. Two hundred EEG signals, each with a duration of 23.6 seconds and 4097 sample points, were used (100 signals from healthy subjects and 100 from epileptic subjects). Each signal was windowed into 16 segments and the noisy ones were discarded. DWT coefficients via Db4 mother wavelet were extracted for 3 levels, and statistical features of all 4 sub-bands were calculated. The statistical features that present the changes in frequency distribution of delta frequency band improved the ANFIS classifier performance. This approach showed significant improvements, both in total accuracy and sensitivity, compared to other similar works from the literature. The proposed system has the potential to be used in diagnosis and warning systems in clinics to save time and increase the accuracy of epilepsy diagnosis. Additionally, this system can be employed to detect epileptic spikes as an early stage of pre-surgical evaluation toward epilepsy source localization.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Table 1 Result comparison for one dimension ANFIS (Db4)

	Maximum	Mean	STD
Sensitivity (%)	97	67.625	98.5
Specificity (%)	92.25	94.5	94.875

Table 2 Confusion matrix STD feature CA3 and CD3

		Desired	
		Epileptic	Normal
Output	Epileptic	638	0
	Normal	0	380

Table 3 Comparison of different methods for EEG classification

Method	Reference	Total accuracy (%)	Specificity (%)	Sensitivity (%)
MLPNN- LBDWT-LR	[38]	92.5	92.3	92.8
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ANFIS-WT	[41]	94	93.7	94.3
FFT-Decision tree classifier	[42]	98.72	99.31	99.40
AIRS(Fuzzy)-FFT-PCA	[37]	100	100	100
SVM-WT-LDA	[17]	100	100	100
k.NN-WT	[11]	99.5	-	-
WT-ANFIS with embedded eye blink remover	Current study	100	100	100

Fig.1

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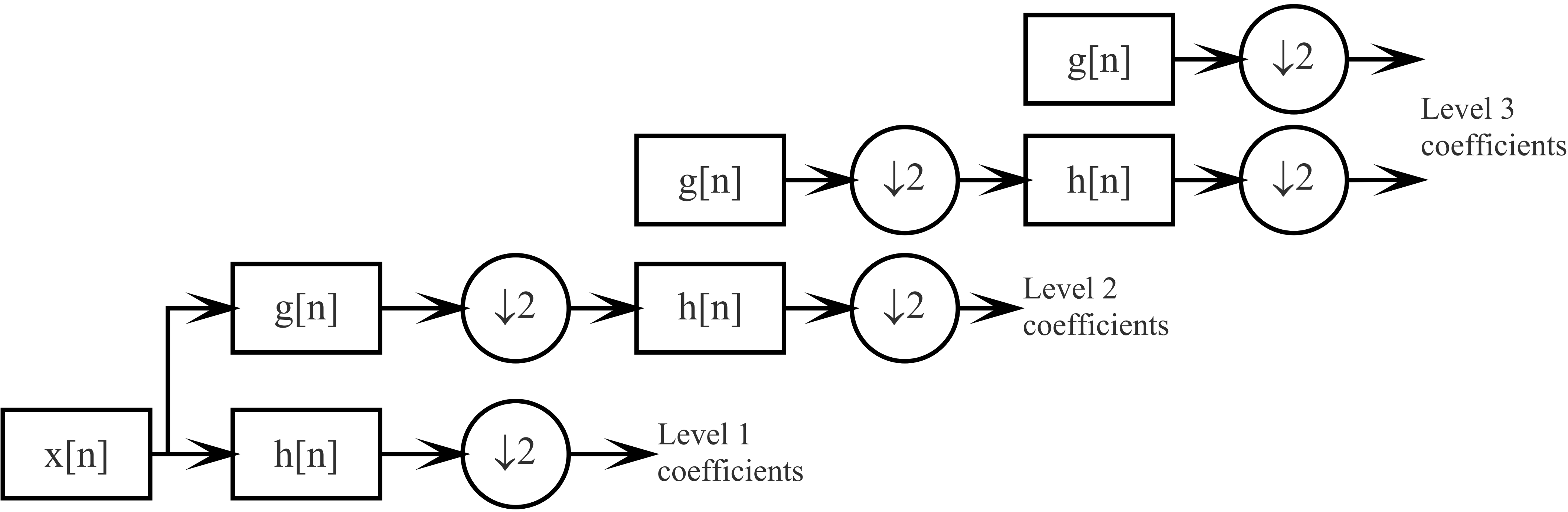

Fig.2

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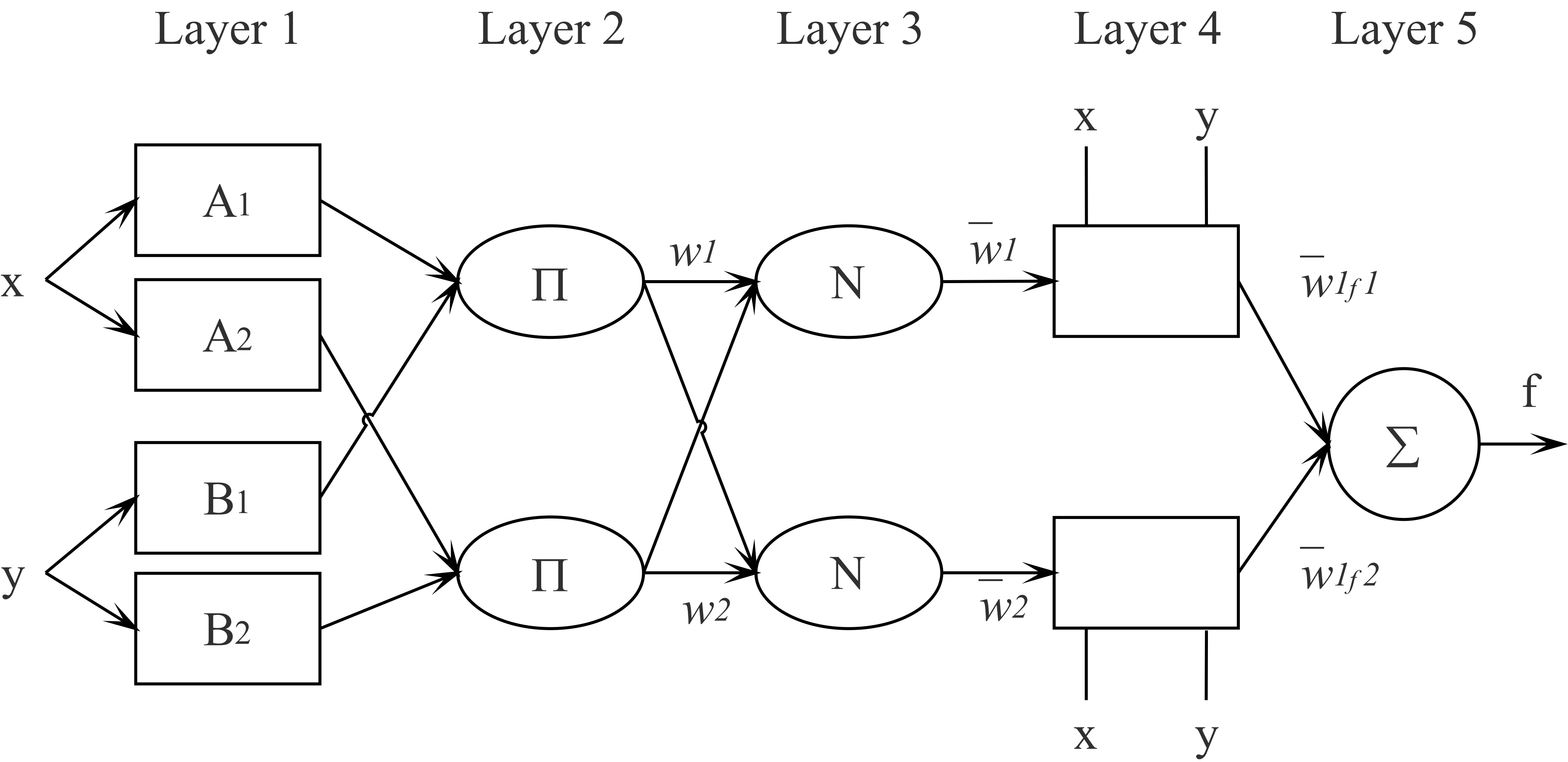

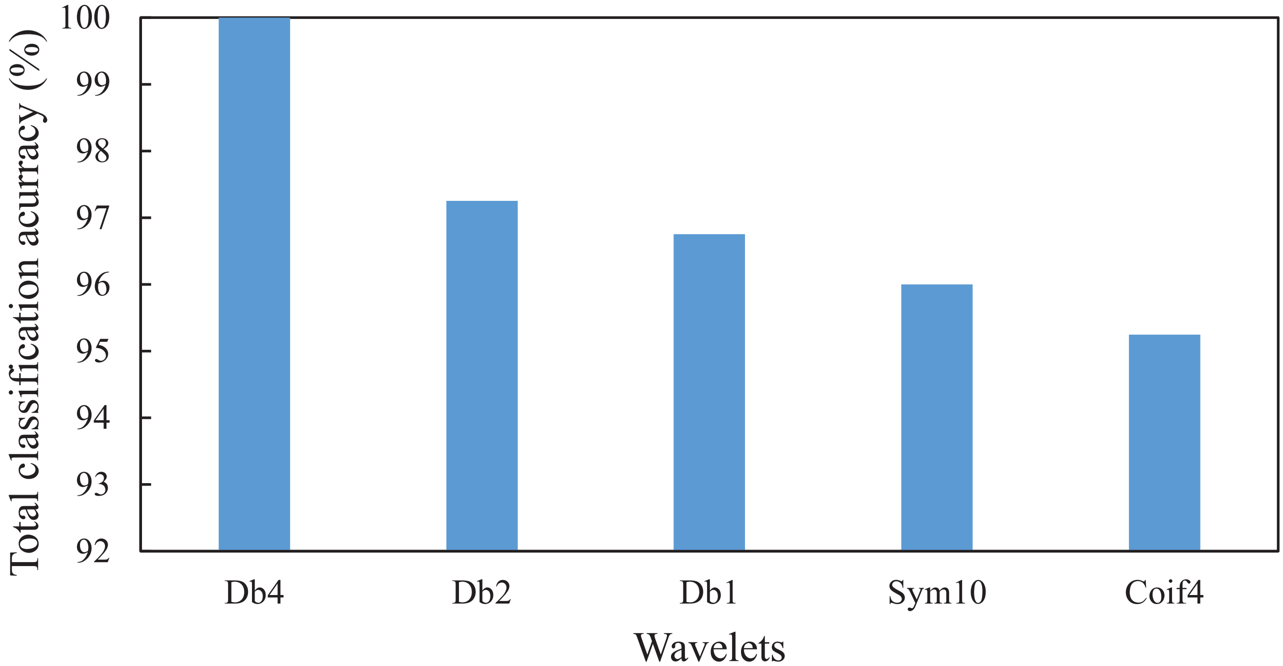
Total classification acurracy (%)
100
99
98
97
96
95
94
93
92
Db4
Db2
Db1
Sym10
Coif4
Wavelets

Fig.4

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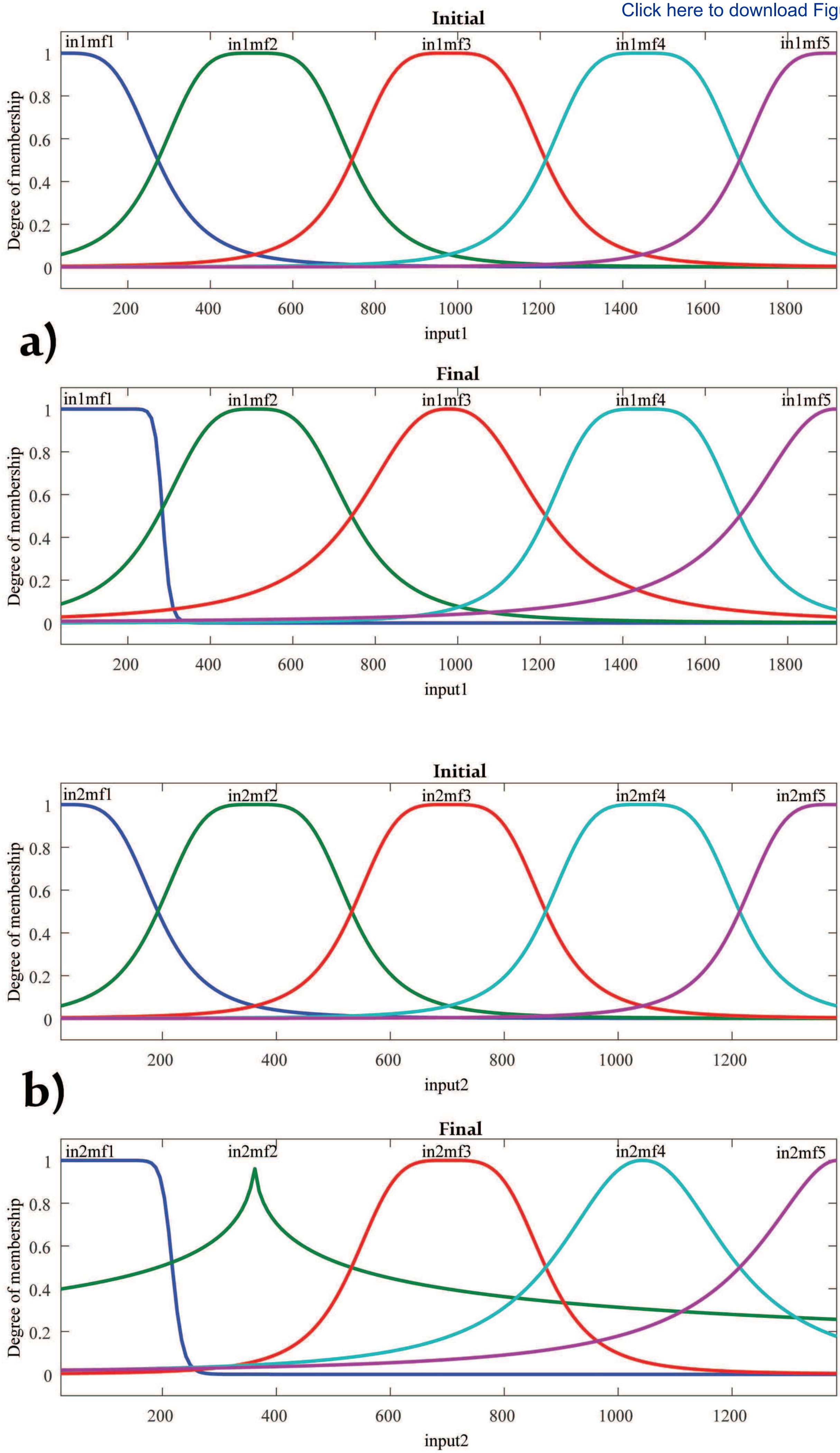

Fig.5

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