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Design and Development of Prediction Model to Detect Seizure Activity Utilizing Higher Order Statistical Features of EEG signals.

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ABSTRACT

Clinical data is complex, context-dependent, and multi-dimensional, and such data generates an amalgamation of computing research challenges. To extract and interpret the useful information from raw data is a challenging job. This study aims at developing an automated predictive model to diagnose the state of an epileptic patient using EEG signals. The segmented EEG signals are utilized to extract various statistical features which are used for prediction. Strategically, we have designed a fully automated neural network model, capable of classifying the seizure activity into ictal, interictal and normal state with an accuracy as high as 99.3%, maximum sensitivity of 100% and specificity as high as 98.3% for all the classes. For the different set of parameters and optimum number of neurons in hidden layer, ANN model revealed a superior model for validating the classification.

Keywords: Epilepsy; Electroencephalogram (EEG); Prediction Model; Variance Inflation Factor (VIF); Artificial neural network (ANN); Computer Aided Classification (CAC).

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INTRODUCTION

Epilepsy affects about 1 % of world population, out of which 85 % is prevalent in the developing countries [1]. Epilepsy is a chronic neurological brain disorder characterized by abnormal brain electrical activity which may alter consciousness, behavior, perception, sensation, and body movement. Abnormal brain activity is primarily due to hyper synchronous neuronal firing in the cerebral cortex and is manifested as epileptic seizures. The seizures are sudden, brief and recurrent, depending on the location and extent of the affected brain tissue [2]. According to the International League Against Epilepsy (ILAE-1981), seizures are classified into two categories (1) Generalized seizures that involve almost the entire brain, (2) Partial (or focal) seizures that originate from a specific portion of the brain and remain restricted to that area [3]. Diagnosis of epilepsy is a complicated problem due to overlapping symptomatology with other neurological disorders, not-so-clear knowledge of exact mechanism responsible for epilepsy, and lack of knowledge about the seizure progression [4]. However, detection of the disorder and recognition of the affected brain area is essential for the clinical diagnosis and treatment of epileptic patients. Electroencephalogram (EEG) is a non-invasive method and is an effective tool for understanding the complex dynamical behavior of the brain and studying physiological states of the brain. Electroencephalogram has become a golden standard in epilepsy recognition and diagnosis. However, it generates massive volume of data which often requires the subjective judgment and analysis by an expert. Their complete visual analysis is not routinely possible. Usually, confirmation of the diagnosis involves a combination of the medical history of the patient and the EEG interpretation by an expert neurologist [5]. Development of accurate and reliable EEG-based automated tools are still in its infancy. Many automated system for accurate and timely diagnosis of epilepsy have emerged [6-8]. Nevertheless, with the advent of new signal processing techniques, there has been an increased interest in the analysis of the EEG for prediction of epileptic seizures. These algorithms can detect abnormal disorder and malfunctioning of the brain not only during the seizure but also before the onset of seizure up to some extent.

In recent years, attempts have been reported on seizure detection and prediction from EEG analysis. Srinivasan et al. [9], employed time domain and frequency domain features to Elman recurrent neural network for classifying EEG signals. H. Ocak, et al [10] investigated entropy and approximate entropy for discriminating EEG signals. S Liang et al [11] used time frequency analysis and approximate entropy to detect epilepsy using linear least square method and linear discriminant analysis. H. Adeli et al. [12] have reported seizure prediction using artificial neural networks with wavelet pre-processing. Subasi et al. [13] have used neuro-fuzzy system for seizure detection. Varun Bajaj [14] has classified the EEG signals using intrinsic mode functions generated by empirical mode decomposition using SVM classifiers. In this study attempts are made to detect the seizure activity as a three group classification problem: (1) healthy subjects (normal EEG), (2) epileptic subjects during a seizure-free interval or just beginning of seizure (interictal EEG), and (3) epileptic subjects during a seizure (ictal EEG). Since the medical interest is different for each one of these conditions, many different classification problems exist in the literature, [15-16], we have examined and selected few of them for the evaluation of our prediction model.

The study includes statistical methods including linear and some higher order cumulants features. They are quiet informative and efficient to analyze EEG signals and helpful for detection of epileptic seizure. Features used are derivable directly from the raw EEG having a very low computational complexity, which is an advantage when designing an on-line algorithm. The authors have used this technique to check the feasibility and effectiveness of developing a seizure detection paradigm that can easily be implemented on any embedded system device. The proposed method has potential in designing EEG based diagnostic system for detection of electroencephalographic changes.

MATERIAL AND METHODOLOGY

Data Acquisition

For the present study, EEGs from five patients for each condition were selected and data comprising recordings taken by standardized International 10-20 system, containing 100 single-channel EEG signals of 23.6 s duration available in public domain (University of Bonn, Germany) [17]. Signals were recorded extra-cranially and intra-cranially with 128-channel amplifier system using an average common reference, omitting electrodes containing pathological activity (C, D and E) or strong eye movement artifacts (A and B), digitized using 12-bit resolution and sampled at a rate of 173.61 Hz. Band-pass filter settings used were 0.53–40 Hz (12 dB/octave). The total number of EEG signals was 300 (100 ictal signals, 100 normal signals and 100 interictal signals). In the present study, all EEG signal segments were selected and cut out from continuous multichannel EEG recordings after visual inspection for artifacts, (e.g., due to muscle activity or eye movements). Since discontinuities between the end and beginning of a time series are known to cause spurious spectral frequency components, segments of 4396 samples were at first cut out of the recordings. The final segments of N = 4096 samples were then chosen in such a way that the amplitude difference of the last and first data points was within the range of amplitude differences of consecutive data points, and the slopes at the end and beginning of the time series had the same sign [17]. The epochs were chosen such that they pass a weak stationary criterion, which makes the data suitable to be used as en masse. The data set comprises five different sets (F, Z, N, S, E) with different conditions, out of which the signals of set Z (as normal condition), set F (as interictal condition) and signals in set S (exhibiting ictal activity) are chosen for our work. One of the signals with amplitude in microvolts (μV) from each respective category is depicted in Fig 1.

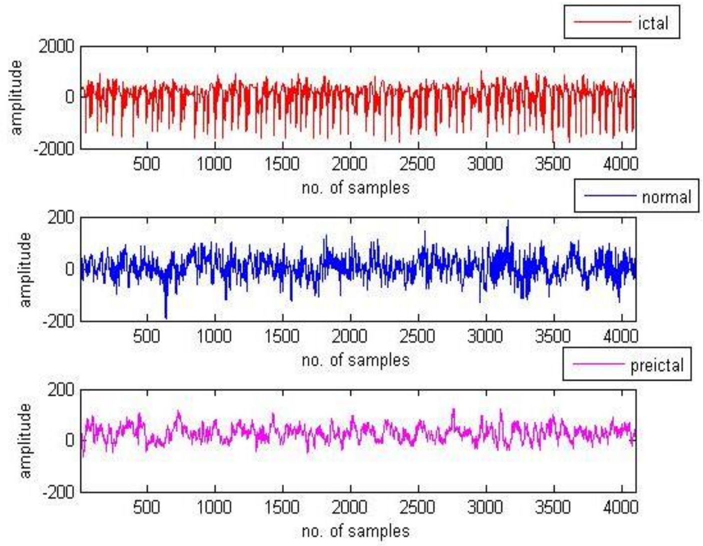


Fig.1 Amplitude of the signals (in µV) a) ictal state b) normal state c) pre-ictal state

Features Extraction

Two primary considerations for developing any prediction model for detection and classification are the type of features to be extracted from the EEG input signal and the type of analysis techniques to be applied on these extracted features [18]. Extracted features are meant to minimize the loss of important information embedded in the signal and to simplify the amount of resources needed to describe a huge set of data accurately [19].

In the present study, in order to investigate the adequacy for the discrimination of three stages of an epileptic patient, a set of quantitative features was extracted from EEG signals tabulated in Table 1. Features are extracted using different techniques summarizing the original signal and have been widely used in predicting different classes of epileptic EEG. It is very difficult to evaluate the nonlinear dynamic property of the bio-signals using first and second order statistics [20]. Hence, third and higher order cumulant which highlights the nonlinear behavior can be used for EEG signals. Taking this into consideration, the features selected for this study (set of thirteen features which include variance, skew, kurotosis, energy, entropy, median, mode) result from thorough review of literature, research efforts and understanding of EEG signals. The general idea of feature extraction is to convert features into mathematical descriptors. These features are then analyzed to find out the most relevant and effective features while discarding the nonperforming features. The chosen features are simple but robust for the morphology of EEG data for the classification problem.

Table 1: Statistical Features extracted from the raw data

Feature ID	Feature Name	Feature
1	*Mean*	$M = \sum_{i=1}^{n} \frac{x_i}{N}$
2	*Median*	$Median = l + \frac{h}{f}\left(\frac{n}{2} - c\right)$
3	*Mode*	$\text{Mode} = L + \left(\frac{f_1 - f_0}{2f_1 - f_0 - f_2}\right) \times h$
4	*Max Amplitude*	$\text{Max}(x_i)$
5	*Min Amplitude*	$\text{Min}(x_i)$
6	*Entropy*	$En(n) = -\sum_{k=n}^{n+N} p(k) \log_2 p(k)$
7	*Energy*	$E(n) = \frac{1}{N} \sum_{n=1}^{N} x(n)^2$
8	*Variance*	$\sigma^2 = \sum_{i=1}^{n} \frac{(x_i - \mu)^2}{N}$
9	*Skew*	$skew = E\left[\frac{(x-\mu)^3}{\sigma^3}\right]$
10	*Kurtosis*	$kurt = \sum \frac{(x-\mu)^4}{\sigma^4} - 3$
11	*Signal to Noise Ratio*	$SNR = \frac{\mu}{\sigma}$
12	*Non linear energy*	$NE(n) = \sum_{k=n}^{n+N} x^2(k) - x(k-1)x(k+1)$
13	*coefficient of variation*	$c_v = \frac{\sigma}{\mu}$

Relevance of Features Selected

Designing a prediction model with optimum number of features is always desired as it leads to better performance of the classifier in terms of time complexity. Prediction importance of each feature, in terms of rank and importance parameter in this study is extracted. All these features are distinct and uncorrelated to each other. The inter correlation between these features used in the prediction model was calculated based on variance inflation factor (VIF) indicating multi-collinear analysis. The VIF value for each feature was calculated using

$$VIF = \frac{1}{\left(1 - R_j^2\right)} \quad Tolerance = \left(1 - Rj^2\right) \quad (1)$$

,

Where Rj2 is the multiple correlation coefficient of one feature's effect regressed onto the remaining features. Tolerance value obtained is less than 1 for these features indicating that the variable under consideration is almost a perfect linear combination of the independent variables. The R square and VIF value for each parameter is calculated and represented in Fig 2. The R square value obtained for the model as 0.869 leading to VIF equal to 4. If the VIF value is larger than 10 for a feature, its information could be hidden by other descriptors. [21-22]. Authors have performed the statistical analysis for the features extracted using Kruskal Wallis Test, a non-parametric method for testing whether samples are independent, or not related. Table 2 provides chi-square value and significance ($p < 0.05$) of each feature.

Table 2: Statistical results obtained by Kruskal Wallis

		Kruskal Wallis Test	
Feature ID	**Feature Name**	**Chi-square**	**Significance**
1	*Mean*	3.632	0.163
2	*Median*	79.306	0.000
3	*Mode*	252.220	0.000
4	*Max Amplitude*	132.922	0.000
5	*Min Amplitude*	97.964	0.000
6	*Entropy*	14.382	0.001
7	*Energy*	134.661	0.000
8	*Variance*	94.818	0.000
9	*Skew*	54.907	0.000
10	*Kurtosis*	83.632	0.000
11	*Signal to Noise Ratio*	16.340	0.012
12	*Non linear energy*	4.149	0.126
13	*coefficient of variation*	205.202	0.000

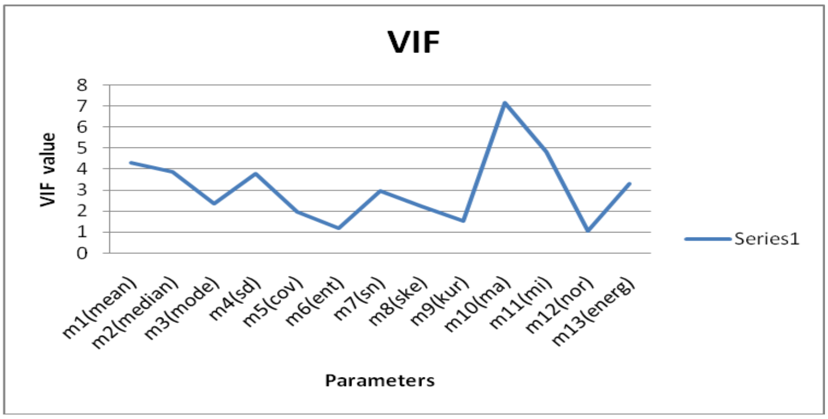
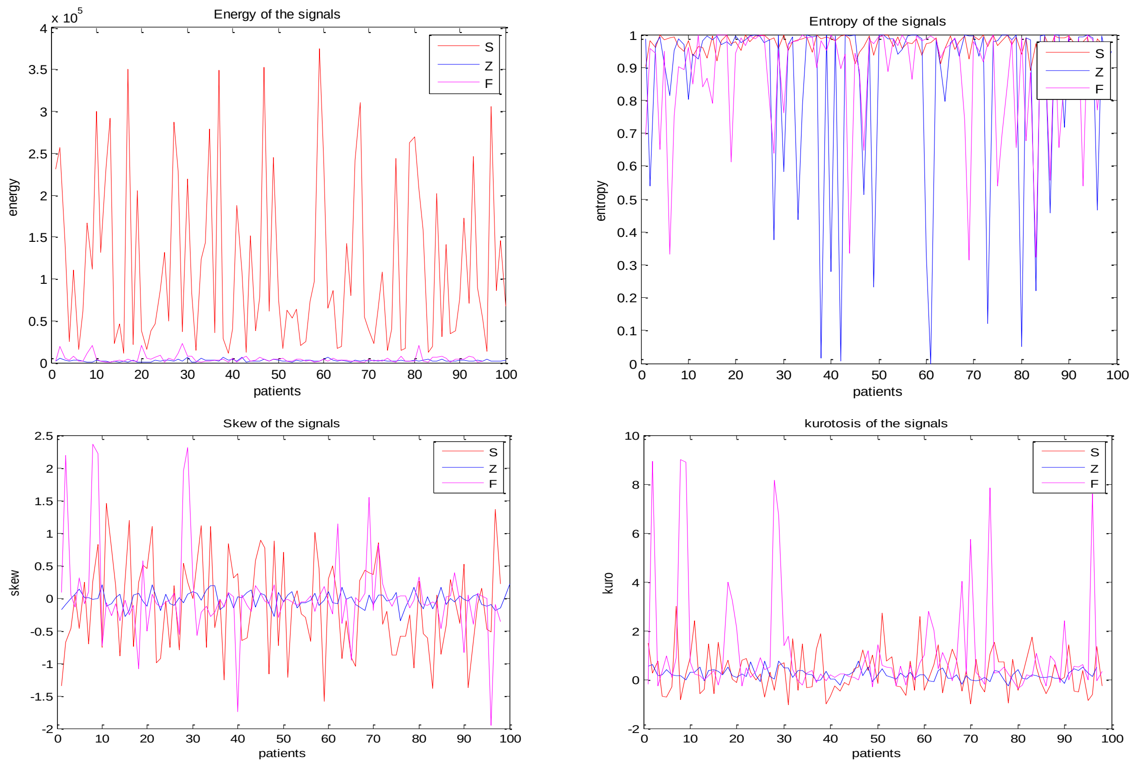


Fig 2. Variation of VIF for different features

Model	**R**	**R Square**	**Std. Error of the Estimate**
1	**0.932**	**0.869**	**0.30287**

The various features extracted from the signals are informative and apt to analyze the EEG signals and few of them are reported. The energy signifies the strength of the signal, entropy quantifies how randomly the seizure signals are distributed as compared to non-seizure signals whereas variance indicates the distribution of the data with respect to mean [23]. Third order cumulants highlight the nonlinear behavior of EEG signals [18]. Fig 3 represents some of the features chosen for the study for three different classes of signals. It has been observed that the signal having high energy of the order of (2 -3.5) x 105 mW lies in the ictal range [24], whereas the energy in range of (0.3 - 1) x105 mW depicts interictal signal, and the energy less than 0.3 x 105 mW represents the normal signal (Fig 3(a)). A decrease in entropy (as in normal state) indicates reduced stochastic behavior [25] as shown in Fig 3 (b), and high entropy indicates more disorder representing ictal state. The kurtosis range levels for S class is (1 - 3) and for Z class is (0 - 1) as shown in Fig 3 (c). It is clear from Fig 3 (d) that seizure state is more skewed [26] with the values in the range (-1 to 1) as compared to the normal state lying in the range of (0 to 0.7). The F state has the extreme values for skew and kurtosis depicting involvement of large number of dominating process.



S- ictal state
Z- Normal state
F- pre-ictal state

Fig 3(a) Energy (b) Entropy (c) Skew (d) Kurtosis of normal, ictal and pre-ictal states

Methodology

EEG is an indicator which provides insight into brain's activity. Many abnormalities of brain related to improper functioning of brain can be analyzed by studying the EEG signals. Human knowledge of functioning of the brain is still insufficient to understand the sudden occurrence of epileptic seizures. But the detection of the disorder and recognition of the affected brain area is essential for the clinical diagnosis and treatment of epileptic patients. The purpose of the work is to develop a robust and efficient predictive model to analyze human EEG signal for epilepsy. The strength of this study is its rigorous feature selection procedure which when applied to the prediction model gives high sensitivity and high specificity, allowing a high generalization and accurate classification.

Work Flow

The block diagram for the proposed computer aided classification (CAC) of EEG signals is shown in Fig 4 comprising feature extraction, feature selection and classification module. In feature extraction module, statistical texture features based on first-order, second-order, and higher-order statistics are computed from all 300 signals using MATLAB. For the design of proposed CAC system a database of thirteen non-overlapping features are chosen from all clinically acquired EEG signals. The parameter values were normalized to fit in the range of (0-1) by min-max approach (Eqn 2.)

$$\text{Feature}_{\text{norm}} = \frac{\text{Feature}_{\text{value}} - \text{Min}_{\text{value}}}{\text{Max}_{\text{value}} - \text{Min}_{\text{value}}} \tag{2}$$

Where Feature norm is the normalized value of the feature, Featurevalue , Maxvalue, and Minvalue represents actual value, maximum and minimum value of the parameter respectively under consideration. The brief description of the experiments carried out in the present work is depicted in Table 3.

Table 3 Brief description of the experiments

Experiment 1	In this experiment, the efficacy of feature vectors is analyzed and the prominent features which are significant are selected, discussed in 2.1.3.
Experiment 2	In this experiment, exhaustive experiments are carried out to develop the architecture of prediction model by varying the number of neurons in the hidden layer thus deciding the best network topology.
Experiment 3	I In this experiment, the network having the best efficiency as obtained in Experiment 2 was ascertained further for classification purpose. The classification was performed with varying feature length and performance was analyzed.

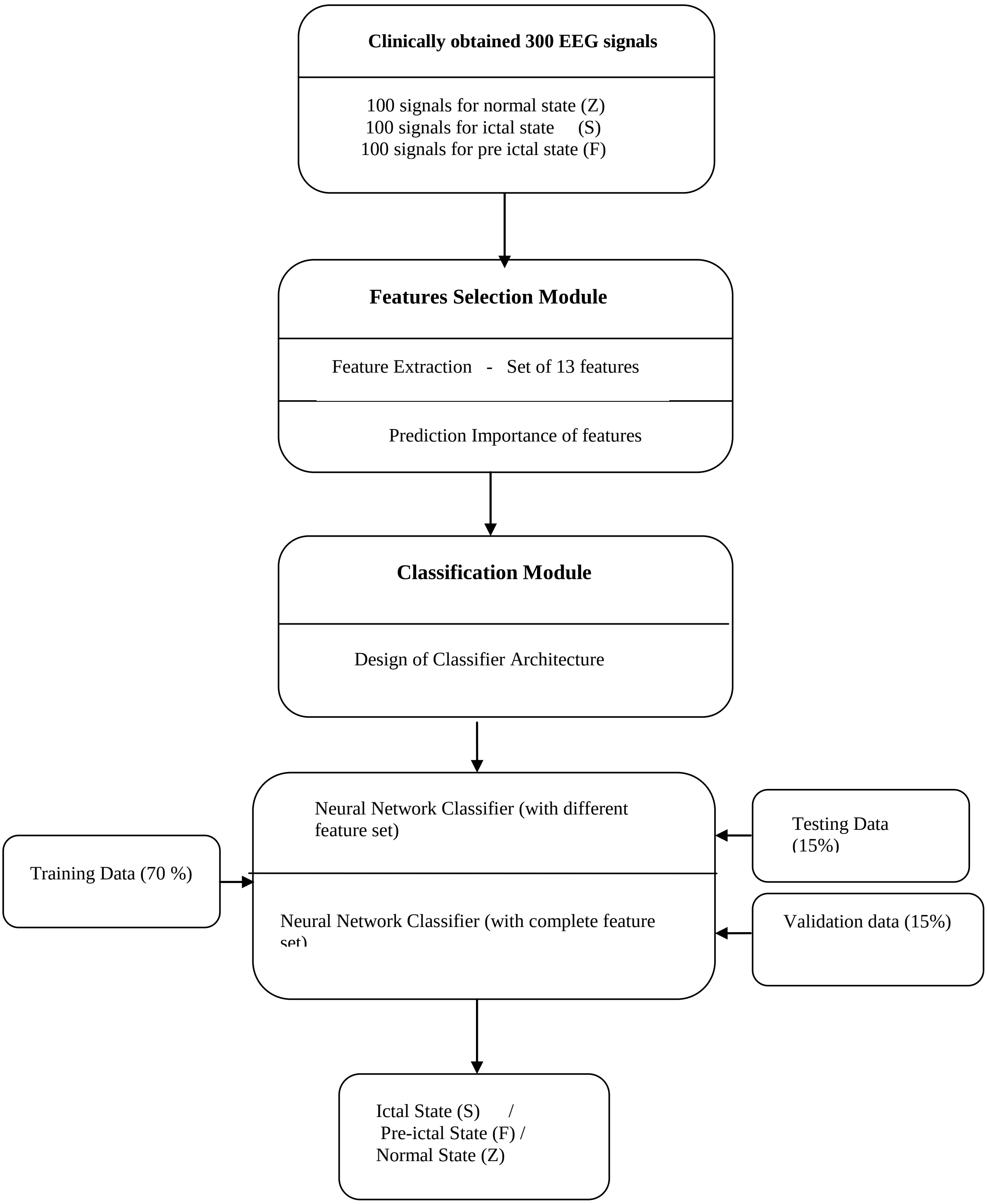


Fig. 4 Proposed CAC system

System Architecture

To analyze the EEG signals with enhanced accuracy and precision, various computational techniques such as neural networks, support vector machines, Bayes classifiers could be useful. However, neural networks have been successfully employed to process EEG signals because of its quality of generalization and great predictive power [27]. With large number of training samples and relatively larger number of synaptic weights, there is always a possibility of the network's free parameters adapting to special features of the training data. In our experiments, feed-forward multi-layered Neural Network technique is employed to obtain a predictive model as this classifier is less prone to over fitting and obtain good generalization performance to a certain extent even without feature space dimensionality reduction. [28]. The overall classification system consist of three layers of artificial NN with tan-hyperbolic and softmax function as the activation function for hidden and output layers respectively with Cross Entropy as error function and BFGS (Broyden-Fletcher-Goldfarb-Shanno) as the technique used for training neural network. To reduce the bias of training and testing data set, bootstrapping technique and 5-fold and 10-fold cross-validation technique are preferred. These techniques provide the information how well the classification model will operate on unseen data [29]. For effective training of the network (primarily to avoid over fitting), to evaluate the average predictive ability of the method and for enhancing the prediction accuracy, we have used 70 % data set for training, 15% data set for testing and 15% for validation using bootstrapping method with 1000 seed points. The bootstrap data set is a fair representative of a generic training set extracted from input space.

RESULTS AND DISCUSSION

EEG captures the blueprint of the brain functionality and physiology of brain. The underlying physiology is the hyper synchronous activity of neurons resulting in abrupt surge of energy causing epileptic seizures [18]. Our study aims at developing a seizure detection technique which can be developed as a simple software application that can be easily installed in labs for aiding the neurophysiologists in the diagnosis and decision-making process of seizure detection. The chosen set of features is simple but robust for the morphology of EEG data needed for the classification problem. In our design, the selected features in Experiment 1 represent thirteen neurons in the input layer. As this is a three classification problem, three neurons are taken in the output layer to classify ictal (S), interictal (F) and normal (Z) categories. To find the neurons in the hidden layer, exhaustive hit and trial was conducted in Experiment 2. The topology of the network was decided by varying the number of hidden nodes in neuron layer. Starting with five neurons in the hidden layer, the number of neurons was incremented till optimum classification accuracy of the network was achieved. Each of the architecture with varying hidden neurons is trained, tested and validated; and the performance accuracies of the best ten models achieved are depicted in Fig 5.

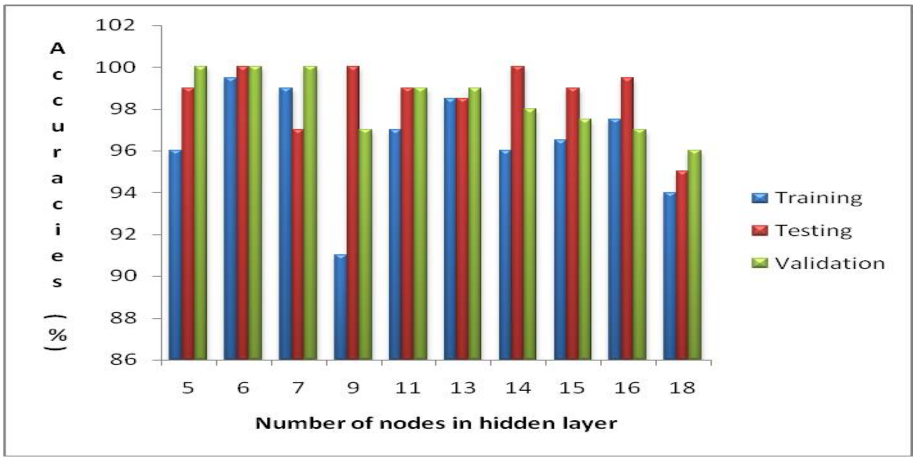


Fig 5. Performance accuracies of different models in terms of training, testing and validating; with varying number of neurons in hidden layer.

It was observed that the best classification accuracy was obtained with six neurons in hidden layer. It gives 100 % testing and validation accuracy and 99.5 % training accuracy. This network performs significantly better and requires a smaller number of iterations to train a neural network. As the number of nodes are increased the training efficiency decreases. In Experiment 3 the classification of the three stages was done by varying the size of FL. In this procedure, subsets of features were used to train the network and classify the signals, and NN performance was evaluated. This process was continued till all the available 13 features were used. The performance was evaluated in terms of training, testing and classification efficiencies of the network with different FL as shown in Table 4.

Table 4. Performance accuracy and validation results of NN with varying number of features

Efficiencies (in %)

Features	No of features	FL	Training Sensitivity	Testing		Validation
Mean-std	2	26	61.428	71.111	68.888	61.42
Mean-std-eng	3	39	84.28	82.22	86.66	76.65
Me-std-eng-ent	4	52	88.151	88.636	88.636	88.29
Me-std-eng-ent-Sk-ku	6	78	88.625	86.363	90.909	88.68
Me-std-eng-ent-Sk-ku-sn 91.63	7	91	93.364	88.636		86.363
Me-std-eng-ent-Sk-ku-sn-cov	8	104	93.838	95.454	95.454	94.31
Me-std-eng-ent-Sk-ku-sn-cov med-mod	10	130	96.208	100	100	97.32
Me-std-eng-ent-Sk-ku-sn-cov med-moamax	11	143	98.578	100	100	98.99
All	13	169	99.8	100	100	99.3

It was observed that high classification ability in epileptic seizure detection was obtained by NN classifier by feature vector of length 13 in comparison with feature vectors of lengths 2, 3, 4 and so on as clearly depicted in Fig 6. Thus, 13 features computed from EEG signal are considered for further analysis with 6 nodes in hidden layer and 3 nodes in the output layer of NN (Fig 7)

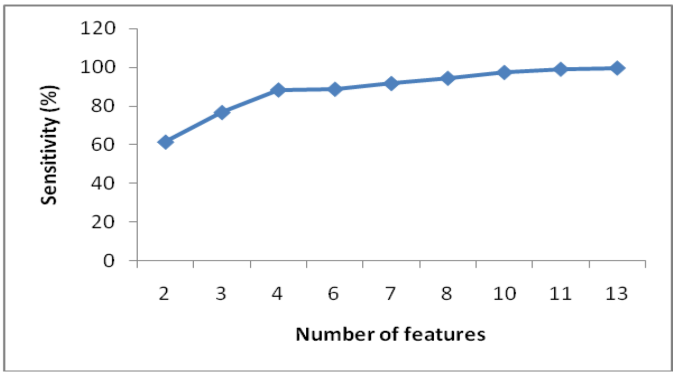


Fig 6 Sensitivity analysis with respect to varying FL.

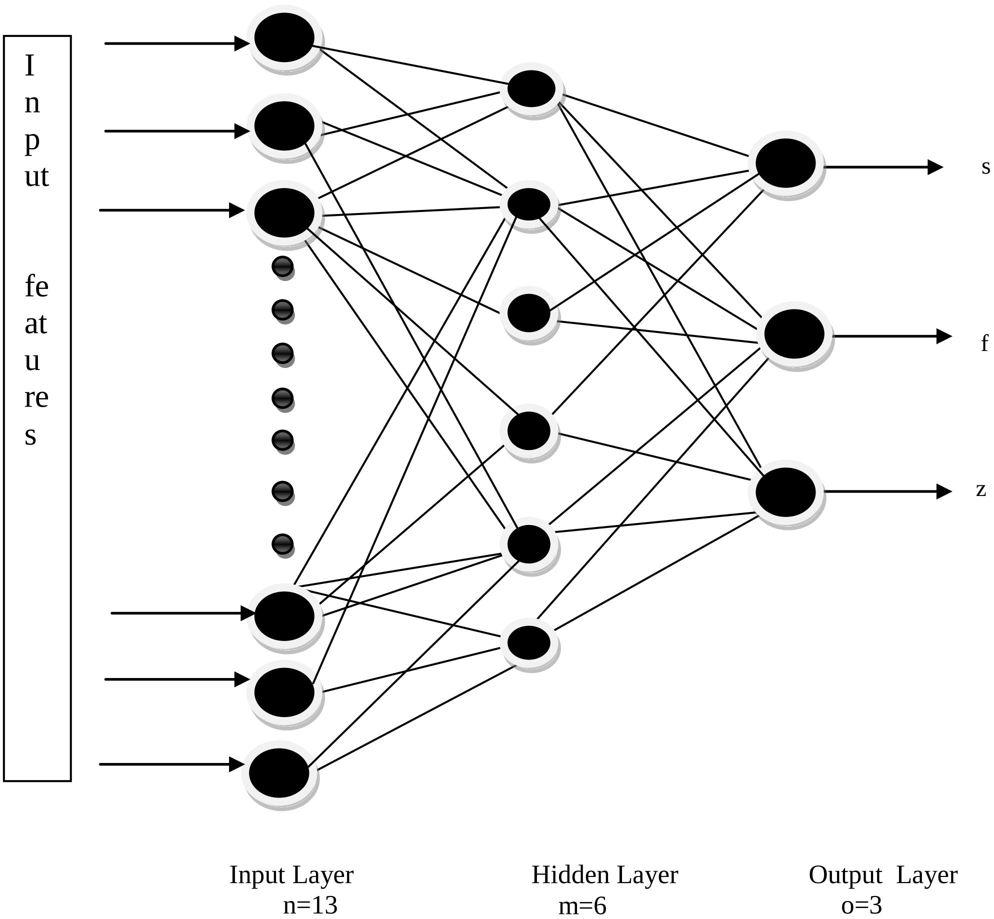


Fig 7. Configuration of artificial neural network (ANN) used to develop predictive model

Performance Metrics

The most important aspect of a prediction method is its ability to make correct predictions. For correct classification and validity of the proposed method, sensitivity, specificity, accuracy and gain charts are the key parameters. The confusion matrix and classification summary are useful tools in evaluating the effectiveness of a classification network. Table 5 depicts the confusion matrix for the three stage classification with varying size of feature length. The results clearly indicate that accuracies and sensitivity obtained when only two features are used is low (85 %, 47 %, 52 % and 61.4 %, respectively). The performance becomes better as FL increases and for whole set of feature vector the sensitivities for all the three classes is maximum (98.8 % as Sens F, 99 % as Sen S and 100 % as Sen Z) with accuracy as high as 99.3 %. It can be stated that that the proposed approach yields good results with use of comprehensive and represented data for design of classifier.

Table 5 : Confusion Matrix for classification of EEG signals into three classes for varying feature length.

Confusion matrix							
	f	**s**	**z**	**Sen F (%)**	**Sen S(%)**	**Sen Z(%)**	**Acc(%)**
FL=2							
f	61	18	15	85			61.4
s	4	34	16		47		
z	7	21	34			52.3	
FL=3							
f	94	13	0	94			91.6
s	3	85	4		85		
z	3	2	96			96	
FL=4							
f	95	20	4	95.9			88.29
s	1	79	6		79		
z	3	1	90			90	
FL=6							
f	87	11	0	87.8			88.6
s	10	85	7		85		
z	2	4	93			93	
FL=8							
f	97	1	3	97.9			94.3
s	1	92	4		92		
z	1	7	93			93	
FL=10							
f	97	4	1	97.9			97.32
s	1	96	1		96		
z	1	0	98			98	
FL=11							
f	96	0	0	96.9			98.9
s	3	100	0		100		
z	0	0	100			100	
FL=13							
f	98	0	0	98.98			
s	0	99	0		99		99.3
z	1	1	100			100	

TABLE 6 (a) Confusion Matrix for the selected prediction model.

category		Predicted	
	Pre-ictal	Ictal	Normal
Pre-ictal	98	0	0
Ictal	0	99	0
Normal	1	1	100

(b) Performance Measure

	POSITIVE(Seizure)	NEGATIVE(Normal)
POSITIVE (Correctly detected)	197 (*TruePositive*)	0(*False Negative*)
NEGATIVE(Not detected)	2(*False Positive*)	100(*True Negative*)

(c) Classification Summary for three classes using 13-6-3 network architecture with FL = 13.

	Classification summary				
		category-f	**category-s**	**category-z**	**category-All**
	Total	99	100	100	299
	Correct	98	99	100	297
	Incorrect	1	1	0	2
	Correct (%)	98.98	99	100	99.33
	Incorrect (%)	1.01	1	0	0.67

After all the three experiments, the prediction model was evaluated for classification with the proposed architecture. The confusion matrix and classification summary for the model is depicted in Table 6, (a) Confusion matrix, (b) Performance Measure, (c) Classification Summary . For clinical applications, diagnosis system should not only give high sensitivity and high specificity but also should give almost zero false positive and false negative events [31]

The performance measures [30]for the prediction model are:

$$Sensitivity = \frac{TruePositive}{TruePositive + FalseNegative} = 100\%$$

$$Specificity = \frac{TrueNegative}{TrueNegative + FalsePositive} = 98\%$$

$$Accuracy = \frac{TrueNegative + TruePositive}{All} = 99.3\%$$

The correct classification accuracy is 99.3 % and misclassification accuracy is 0.67 %. With our methodology, a normal EEG is misclassified only 0.67 % and gives 99.3 % correct categorization. The inter-ictal EEG is misclassified as ictal EEG for 1 % of the time and ictal EEG is misclassified as inter-ictal for 1 % of the time.

CONCLUSION

This paper presents the designing of predictive neural network model for classification of EEG signals with high accuracy. The experimental results show that proposed classifier promises high classification accuracy (99.3 %), maximum sensitivity (100 %), specificity (98.3 %) and high gains for classifying different stages of epileptic patient. The proposed model can assist clinicians for diagnosing different epileptic stages. The promising performances observed are demonstrative of the efficiency and efficacy of systems developed for classification and prediction of normal, ictal and interictal conditions of epileptic patients. The method and technique adopted are simple, less complex, quick and easily realizable on the DSP processors. In the present study authors have primarily used linear features and some of higher order cumulants. However, the system performance can be further improved by using nonlinear features as LLE, CD, Hurst Exponent, App Entropy, HOS for seizure detection.

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