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Automated Diagnosis of Encephalopathy Based on Empirical Mode EEG Decomposition

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In this study, an empirical mode decomposition (EMD) technique has been applied for EEG signals to identify a neurological disease state qualified as encephalopathy. The EMD technique is an efficient method for decomposing nonstationary and nonlinear signals, which makes it suitable for biosignal processing. This technique generates various components of the signal called intrinsic mode functions (IMFs) whose features are examined for the diagnosis of the disease. We found significant differences between the healthy and patient groups for both statistical and nonlinear parameters of IMFs of the recorded EEGs, which makes those suitable for the diagnosis of encephalopathy. Statistical values, namely minimum, maximum, mean, and standard deviation, and nonlinear parameters, namely approximate entropy and sample entropy of the IMFs, were calculated. Both these features were fed to a Support Vector Machine (SVM) classifier, and their performance parameters were evaluated. It is concluded that statistical parameters, as well as nonlinear parameters of the EEG IMFs, are prospective potential features for automated diagnosis of encephalopathy.

Keywords: electroencephalography, empirical mode decomposition, intrinsic mode functions, statistical and nonlinear parameters, support vector machine (SVM), encephalopathy.

INTRODUCTION

Electroencephalograms are highly complex signals detailing the functioning of the brain. Highly useful information for the diagnosis of neurological disorders is contained in those signals, but they are not currently utilized to their full potential in clinical scenarios. Various signal processing techniques have been tested to find if they give better results for analyzing EEGs. Signal processing engineers apply various frequency-domain and time-frequency-domain techniques for studying various biomedical signals. Though these methods could extract much greater volumes of information than those obtained by visual inspection, EEGs could not be studied completely using these techniques. So, another stream of analysis emerged in EEG signal processing, namely, nonlinear analysis. This approach to a greater extent considers the complex nature of the brain and the nonlinear and chaotic nature of EEGs. Much more hidden information could be revealed from EEG signals using nonlinear techniques.

Empirical mode decomposition (EMD) is a nonlinear decomposition technique [1]. It is an adaptive and data-dependent method that does not require assumptions of linearity and stationarity [2]. Such a situation makes this approach more adequate for EEG analysis. The local properties of the signal are extracted very well using this technique [1].

EMD is a signal decomposition technique utilized in nonstationary and nonlinear signals to generate a set of symmetric, amplitude- and frequency-modulated (AM-FM) components called intrinsic mode functions (IMFs) [3,4].

EMD has been reported as an efficient method for analyzing EEG signals considering their nonlinear and nonstationary nature. Pachori [5] utilized the EMD technique to classify seizure and seizure-free EEG signals by comparing the mean frequency of each intrinsic mode functions (IMF) and using the area measure of each calculated IMF to discriminate epilepsy cases from normal healthy controls [6].

Various features of the IMFs were utilized for the diagnosis of various neurological disorders. Our study aimed at exploring the potential of the EMD

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technique for the diagnosis of encephalopathy; the latter is a disease state/disorder of the brain due to metabolic problems, infections, or malfunctioning of some other parts of the body. Hepatic encephalopathy occurs due to liver diseases, and uremic encephalopathy accompanies renal diseases. Thus, encephalopathy can be considered as a secondary neurological disease, as it occurs due to some other primary disorders or diseases.

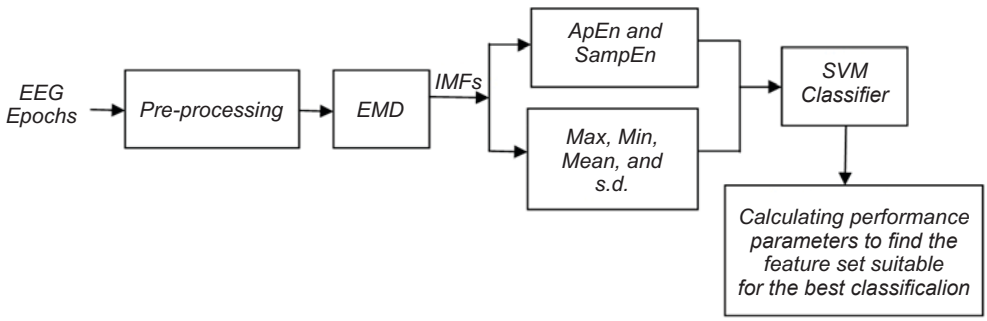
The objective of our study was to apply EMD for EEGs of encephalopathy cases and normal EEGs via generation of the IMFs. Statistical parameters, namely minimum, maximum, mean, and standard deviation (s.d.), were calculated for the IMFs of each EEG epoch. Entropies (approximate entropy and sample entropy) were also calculated for each IMF. Both these feature sets were utilized to classify between the EEGs of the normal and patient groups using a support vector machine (SVM) classifier, and their performance parameters were compared.

METHODS

In our study, we have analyzed 150 EEG epochs of 20 patients with diagnosed metabolic encephalopathy and 125 EEG epochs of 15 normal healthy subjects. The data were collected in the EEG lab of the Neurology Department, Government Medical College, Thiruvananthapuram, Kerala, India. Patients with brain structural pathology, infections of the CNS, cerebral vascular insult (confirmed by neuroimaging or other investigations), with a clinical picture suggestive of metabolic encephalopathy but without obvious metabolic disturbances detected in the necessary biochemical investigations, and metabolic encephalopathy occurring against the background of some other neurological illness causing cognitive dysfunction or a degenerative condition were excluded from the patient sampling. Patients who came with a single episode of syncopes, but were clinically normal and having normal brain imaging, where seizures and structural lesions were ruled out, have been enrolled as normal healthy controls.

Recording of EEGs was performed using a widely applied average reference montage in the Nicolet EEG machine (USA) using NicVue v.3.0 software. The 10–20 electrode system was adopted for the EEG tracing. The sampling rate was set to 500 sec^{-1}. Twelve-sec-long EEG epochs were saved in text files (ASCII format).The noise-free segments free from the effects of eye movements or other muscle contraction artifacts were selected.

EEG Analysis. The outline of the work is depicted in Fig. 1. The EEG signals saved as 12-sec-long epochs were first preprocessed using low-pass filtering and a total variation denoising technique. The details will be described below. After preprocessing, the clean EEG epochs were empirical mode decomposed to get the IMFs. The first four IMFs of EEG epochs were processed in this study for the sake of convenience, as we are exploring the possibility to utilizing those features for the diagnosis of encephalopathy. The statistical parameters, namely minimum, maximum, means, and s.d. of four IMFs were computed, i.e., 16 statistical features were obtained. Entropies, i.e., sample entropy and approximate entropy of the first four IMFs, were also calculated; thus, eight features were obtained. An SVM classifier was implemented to differentiate EEGs of encephalopathy patients from normal EEGs of healthy subjects. Two feature sets were utilized in our study for classification: (i) statistical parameters, i.e., minimum, maximum, mean, and s.d. of each IMF, and (ii) approximate entropy and sample entropy of each IMF.



F i g. 1. Block diagram of the proposed work.

The performance parameters of the classifier in both cases were analyzed and compared.

Pre-processing. This study used simultaneous low-pass filtering and total variation denoising filtering (LPF-TVD) for preprocessing our EEG signals [7]. Linear-time invariant low-pass filtering was combined with the total variation denoising technique utilized for sparse signals in this method. While low-pass filtering allows signal components to be filtered up to a maximum frequency component, say *fm*, the total variation denoising technique is based on addressing the TVD as an optimization problem and minimizing a predefined cost function. The cost function can be minimized using the majorization-minimization algorithm given by Figuiredo et al. [8].

Empirical-Mode Decomposition (EMD). The concept was developed by Huang et al. [1] for analyzing nonstationary and nonlinear signals. As biomedical signals have these characteristics, this technique was utilized in this study for the EEG analysis. This technique decomposes an input signal into a finite number of subparts called, as was mentioned above, intrinsic mode functions (IMFs). Different features of these IMFs can then be analyzed instead of analyzing the signal as a whole.

The EMD technique decomposes the signal into various IMFs, in which those decomposed components obey the two conditions [9]: (i) the number of zero crossings and extremas must be the same or differ by almost 1; (ii) at all points, the mean value of an envelope formed by local maxima and that of local minima should be zero.

The major steps in EMD are the following [6,10]: (i) Find the number of extreme points (both maxima and minima) in the signal $s(t)$; (ii) generate the upper envelope $e_{up}(t)$ and lower envelope $e_{low}(t)$ by connecting maxima and minima separately using a cubic spline method; (iii). then the mean is calculated as $\mu(t) = (e_{up}(t) + e_{low}(t))/2$; (iv) IMF should have this mean value as zero. Define $s'(t) = s(t) - \mu(t)$ to get the detail of the signal; (v) check if $s'(t)$ is an IMF by checking the two conditions described earlier, and (vi) repeat the above steps till an IMF is generated.

When an IMF is obtained, $\text{IMF}_1 = i_1(t) = h_1(t)$.

A residue $r_1(t)$ is taken as the signal after subtracting the first IMF, i.e., $r_1(t) = s(t) - i_1(t)$.

After this, the residue $r_1(t)$ is taken as the next signal, and the above steps are repeated to get the rest of the IMFs. This is continued till the final residue is a constant. Figure 2 shows the IMFs generated by the empirical mode decomposition of normal EEG and EEG of patients with encephalopathy.

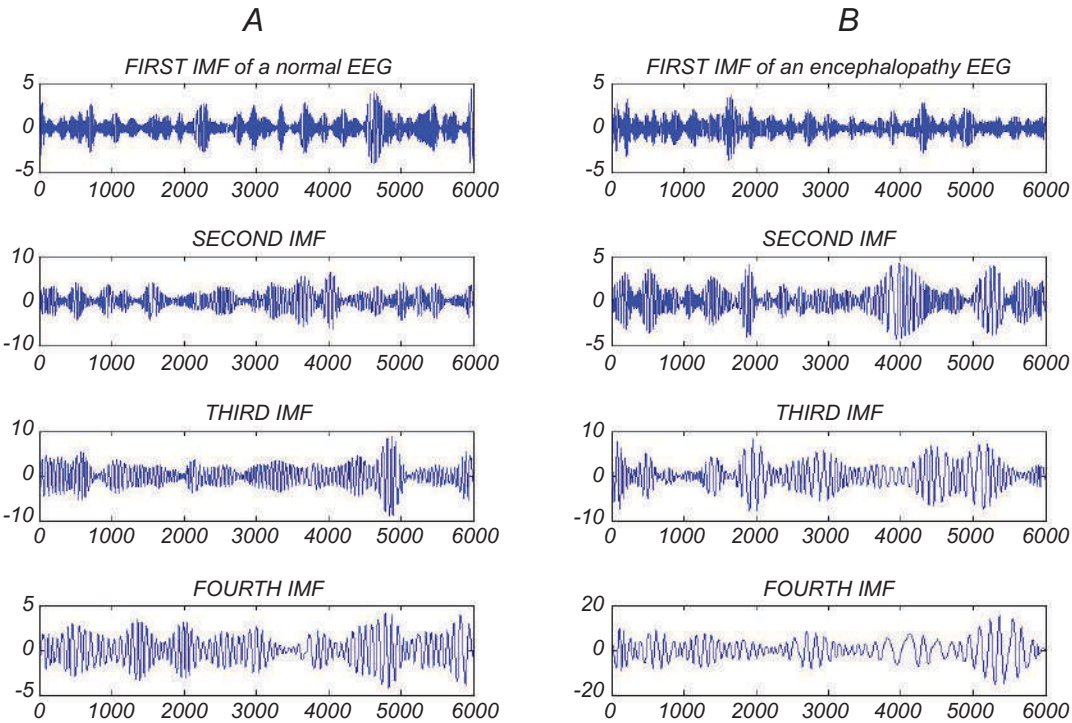


Fig. 2. IMFs generated by empirical mode decomposition of EEGs of a normal person (A) and a patient suffering from encephalopathy (B).

Feature Extraction. Andrade et al. [11] and Lima et al. [12] described the early works of applying the EMD technique to brain signals. Various features of the EEG IMFs were extracted for classifying between the disease and normal groups [3, 5, 6, 13–16]. Orosco et al. [17] calculated the energy of IMFs of EEG in epileptic patients and concluded that these indices can be utilized for the classification of epilepsy, though the sensitivity value for classifying was lower in the respective group. Djemili et al. [4] utilized statistical parameters, namely minimum value, maximum value, mean, and s.d., of each of the four IMFs extracted from the EEG signal for the diagnosis of epilepsy. The weighted frequency of each IMF was studied by Oweis et al. [18], and this index was also identified as a good feature for classifying the ictal state with seizures from normal cases. Bajaj et al. [19] utilized another feature called an instantaneous area of the IMFs to detect focal temporal lobe epilepsy. Other features, namely the coefficient of variation and fluctuation index of IMFs, were utilized by Li et al. [14] for the diagnosis of this disease.

In our study, we have calculated the above-mentioned statistical parameters (min, max, mean, and s.d.) for the first four IMFs, as was done in seizure classification by Djemili et al. [4], but we also estimated the entropies for the IMFs. Sharma et al. [20] have applied the entropy on the IMFs of focal EEGs and reported significant results for classifying focal EEG signals from nonfocal ones. Both these feature sets were given to the classifier for distinguishing the normal and disease groups, and their performance was compared.

Feature Extraction. In thermodynamics, the term entropy is defined as the measure of disorder or randomness in a system. The entropy can also be considered as the extent of complexity of the system.

Approximate Entropy. The approximate entropy gives the measure of randomness and complexity of the system. This nonlinear feature was proposed by Pincus [21]. It is calculated as the logarithmic likelihood that two close sequences will remain close to each other after the next increment. A higher value of the approximate entropy indicates higher random behavior and more unpredictability [22]. The approximate entropy gives a non-negative number to a time series based on which its complexity can be measured. It can be applied to relatively short and noisy data. The $C_i^m(r)$ is the correlation integral, and N is the total number of data points. The approximate entropy can be calculated from the equation

$$\mathrm{ApEn}(m,r,N)=\frac{1}{N-m+1}\sum_{i=1}^{N-m+1}\log C_i^m(r)-\frac{1}{N-m}\sum_{i=1}^{N-m}\log C_i^{m+1}(r) \quad (1)$$

where the correlation integral is:

$$C_i^m(r)=\frac{1}{N-m+1}\sum_{j=1}^{N-m+1}(r-\|X_i-X_j\|) \quad (2)$$

Sample Entropy. The sample entropy is defined as the negative natural logarithm of the conditional probability that two sequences, which are similar for m points, remain similar to each other at the next point, where m is the embedding dimension [23]. Compared to the approximate entropy, the sample entropy is more robust to noise and is largely independent of the data series length. A lower value of the sample entropy indicates a higher self-similarity in the time series. The sample entropy can be calculated from the equation

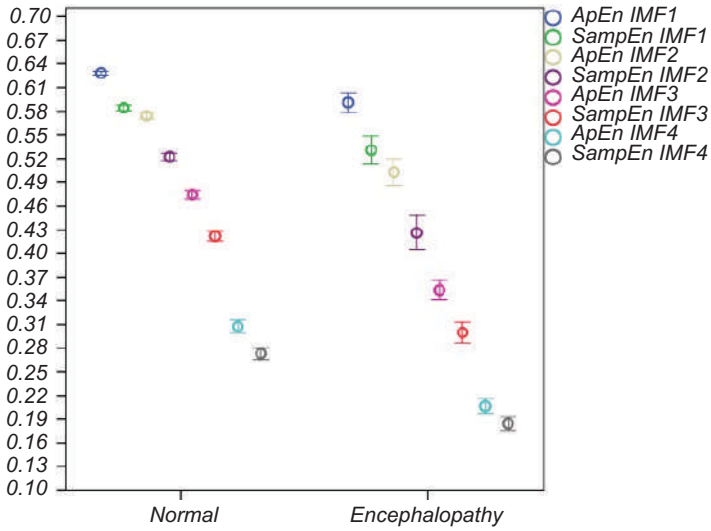
$$\mathrm{SampEn}(m,r,N)=-\ln[C^{m+1}(r)/C^{m(r)}], \quad (3)$$

where $C^{m(r)}$ is the probability that two sequences will match for m points, and $C^{m+1}(r)$ is the probability that two sequences will match for $m + 1$ points.

The selfsimilarity of the time series can be measured using approximate entropies and sample entropies. Sharma et al. [20] have reported that entropies of the EEG IMFs can be utilized for discriminating between focal and nonfocal EEGs. Martis et al. [2].also reported the application of the spectral entropy of the EEG IMFs to the diagnosis of epilepsy.

RESULTS AND DISCUSSION

The EEG signals of both groups, i.e., encephalopathy patients and normal healthy controls, were decomposed using EMD to generate the IMFs. The first four IMFs have been taken in the study for convenience (see Fig. 2). It is clearly seen that the frequency decreases after each level of decomposition. Figure 3 shows the distribution of entropy values for 30 EEG epochs of each of the patients with encephalopathy and of normal healthy



F i g. 3. Comparison of the mean entropy values (ApEn and SampEn) of the first four EEG IMFs.

T a b l e 1. Comparison of the Statistical Parameters of the First Four IMFs of EEG Epochs in the Two Groups

Group	IMF1	IMF2	IMF3	IMF4
Control (normal)	-9.79, 9.73, 0.00, 2.28	-9.67, 9.68, -0.01, 2.78	-8.23, 8.24, 0.00, 2.55	-7.12, 6.99, 0.00, 2.09
Patient (encephalopathy)	-6.41, 6.34, 0.01, 1.19	-11.16, 10.97, 0.00, 2.59	-13.42, 13.36, 0.01, 3.93	-16.66, 16.69, 0.04, 5.31

Footnote: In each IMF column, minimum, maximum, mean, and s.d. values are indicated

T a b l e 2. Comparison of the Entropy Values of the First Four IMFs of EEG Epochs in the Two Groups

Group	IMF1	IMF2	IMF3	IMF4
Control (normal)	0.63, 0.58	0.57, 0.52	0.47, 0.42	0.31, 0.27
Patient (encephalopathy)	0.59, 0.53	0.51, 0.43	0.35, 0.30	0.21, 0.19

Footnote: In each IMF column, approximate entropy and sample entropy values are indicated.

T a b l e 3. Number of EEG Epochs Taken for Training and Testing

	Encephalopathy	Normal	Total
Training	110	65	175
Testing	40	60	100

T a b l e 4. Performance Parameters of the SVM Classifier (%) for Different Feature Vectors Based on the Sub-Band Energies of EEG

Feature set taken for classification	Sensitivity	Specificity	Accuracy
Statistical parameters of the IMFs	93.33	97.5	95
Entropies of the IMFs	98.33	85	93

subjects. All the eight parameters, i.e., approximate entropies and sample entropies of the first four IMFs, were found to be significantly lower in the encephalopathy group ($P < 0.01$; independent t-test; Fig. 3). Similar results were reported in the analysis of EEGs of patients with Alzheimer's disease using the same EMD method [24]. This can be due to the lower complexity of neuronal activity and the less complex neuron-to-neuron interactions under conditions of the disease state. Another important point noted in the entropy values of the IMFs is that these values decrease with increase in the levels of decomposition. The IMF_1 has a higher value of both entropies when compared to that of the IMF_2, and so on.

T a b l e 5. Performance Parameters of the SVM Classifier (%) Based on Features of the EEG IMFs

	IMF_1	IMF_2	IMF_3	IMF_4	IMF_1 and IMF_2	IMF_1 and IMF_3	IMF_1 and IMF_4	IMF_2 and IMF_3	IMF_3 and IMF_4	IMF_2 and IMF_4
Accuracy	86	73	90	91	80	95	97	91	95	93
Sensitivity	76.67	75	100	91.67	70	100	96.67	96.67	96.67	91.67
Specificity	100	70	75	90	95	87.5	97.5	82.5	92.5	95

Based on the results obtained, we can understand that entropies of IMFs serve better than statistical parameters for classifying the two groups. Differences between all the eight features, namely ApEn and SampEn of four IMFs, were found significant in statistical comparisons (independent *t*-test). So, the clear ability of various features to distinguish between two examined groups has been found by this test. This test estimates the probability of the zero hypothesis, known as the *P* value, for each feature using the Student's *t*-test [25]. The features were said to be significant if $P < 0.001$. All 16 statistical parameters were, however, insignificantly different in this test. We have implemented a Support Vector Machine (SVM) classifier for the diagnosis of encephalopathy based on the statistical parameters and entropies of the IMFs of EEG epochs. The SVM classifier has been employed in many studies related to EEG analysis for differentiation of EEGs of the disease cases from those of normal healthy subjects [26–29]. Both parameters can be utilized as a feature set for classifying EEGs of encephalopathy cases from that of normal healthy subjects. The details of the dataset utilized for classification are given in Table 3.

The performance parameters of the classifier given in Table 4 clearly show that both features, namely statistical parameters and entropies of the IMFs, are potential prospective parameters for classifying between the two groups. The accuracies of classification using both feature sets were found to be comparable. In the case of classification using statistical parameters, the feature set consisted of 16 features (minimum, maximum, mean, and s.d. for each of the four IMFs). In entropy-based classification, eight features were utilized, the approximate entropy and sample entropy, for four IMFs.

We also analyzed the performance of the classifier based on features of each IMF and combinations of two IMFs. Table 5 gives the performance for the respective cases. We can say that the accuracy, sensitivity, and specificity have been found the highest for a combination of the features of IMF_1 and IMF_4 together. This result is similar to that reported by Djemili et al. [4] in their comparable study, but with respect to epilepsy.

Thus, a method based on empirical mode decomposition (EMD) has been reinvestigated in our study for interpreting EEGs with respect to diagnosis of encephalopathy. This study was conducted on a set of EEGs of encephalopathy patients and normal healthy subjects (controls). After filtering, EEGs were decomposed into intrinsic-mode functions using empirical mode decomposition. The entropies of these IMFs were then calculated and used as features for the SVM classifier. The statistical parameters of IMFs were also used by the classifier for distinguishing between the two groups. This work may be extended for the diagnosis of other neurological diseases. The results showed that both statistical parameters and entropies of the IMFs of EEG epochs are potential prospective parameters for diagnosing encephalopathy cases based on EEG analysis. On comparing the features of various IMFs, it can be understood that the IMF_1 and IMF_4 features together can yield the best performance parameters for classifying encephalopathy cases from normal healthy cases based on EEG.

To the best of our knowledge, results of applying the EMD technique for EEG in the diagnosis of encephalopathy have not been reported so far. These results clearly show that the EMD technique can be an adequate and successful signal processing tool for evaluating encephalopathy, and both statistical parameters, as well as entropies, can be employed as features for the same. Authors have earlier reported the results of applying chaotic analysis technique[30] and also based on energies of EEG sub-bands for the diagnosis of encephalopathy [31].

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All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki Declaration and later amendments or comparable ethical standards. All participants gave their written informed consent.

The authors, J. E. Jacob, K. Gopakumar, T. Iype, and A. Cherian, declare the absence of any conflict in commercial or financial relations, relationships with organitations or persons that in any way could be related to the study, and also in interrelations of the co-authors.

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