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A combination of statistical parameters for epileptic seizure detection and classification using VMD and NLTWSVM



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ABSTRACT

The epileptic seizure detection and classification is of great significance for clinical diagnosis and treatment. To realize the detection and classification of epileptic seizure, this paper proposes a method based on the combination of signal decomposition and statistical methods. First, the algorithm of variational mode decomposition (VMD) is applied to extract the components of intrinsic mode functions (IMFs) by decomposing the EEG signals. Then the statistical method is utilized to calculate the eight features of maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index for each extracted IMF component. Finally, the best combinations of extracted features are fed into the non-linear twin support vector machine (NLTWSVM) to classify the epileptic signals. The EEG database from University of Bonn is used to confirm the effectiveness of the proposed method for epileptic seizure detection. The final experimental results demonstrate that the classification accuracy can reach 98.86%, 98.37%, 99.02%, 99.41% and 99.57% for the database of C-E, D-E, CD-E, ABCD-E and AB-CD-E, respectively. The TUSZ corpus in the TUH EEG corpus is also used to classify epileptic seizure types using the method in this article. The result is expressed by the confusion matrix and the weighted F_1 score is 0.923, which shows this method has potential to help experienced neurophysiologists classify epileptic seizure types in the clinic.

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1. Introduction

Epilepsy is a recurring neurological brain disease and can lead to transient brain dysfunction, which is generally generated from a sudden, severe and hypersynchronous discharge by the abnormal brain neurons [1,2]. According to the World Health Organization (WHO), more than 50 million people suffer from epilepsy all over the world, of which about 80%

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epileptic patients live in low- and middle-income countries [3]. Epilepsy not only has serious impacts on the patients' life, study, work and spirit, but also endangers the safety of the patients [2,4], especially among children [4] and older people [5]. Electroencephalography (EEG) is a technique to record the brain electrical activity [1]. EEG signals are recorded through invasive electrodes positioned on certain specific locations of the cerebral cortex or non-invasive surface electrodes on the scalp. At present, the experienced neurophysiologists analyze EEG signals for detecting and classifying epileptic seizure by visual examination [6-9]. However, the currently adopted visual examination by trained neurophysiologists is a time-consuming and labor-intensive procedure, and there may be diagnostic errors due to human subjective factors during the examination process [7,10]. Therefore, the epileptic seizure detection and classification is of great significance to the field of clinical diagnosis and treatment.

The EEG signal is a typical non-linear and non-stationary weak biological signal [11]. Thus, the feature extraction and feature classification of EEG signals are currently a research on hot issue of scholars worldwide. The analysis methods of EEG signals can be divided into four categories, including time domain, frequency domain, time-frequency domain and nonlinear dynamics [12,13]. The analysis approaches in time-frequency domain and non-linear dynamics are the current mainstream methods. Time-frequency methods such as discrete short-time Fourier transform (DSTFT), discrete wavelet transformation (DWT), wavelet packet transform, Stockwell transform (ST), dual-tree complex wavelet transform (DT-CWT), empirical mode decomposition (EMD), local mean decomposition (LMD) and smoothed pseudo Wigner-Ville distribution (SPWVD) are widely utilized in the field of diagnosis and treatment of epilepsy [9,14-24]. The methods of nonlinear dynamics such as entropy, correlation dimension, higher-order moments and fractal dimension are commonly employed in the field of epileptic signal analysis [20,25-27]. In recent years, the combination of time-frequency domain and statistical methods for realizing the feature extraction of epileptic signals has been recognized and valued by scholars [14,20,28-35].

T. Zhang et al. used frequency slice wavelet transform to extract different rhythm signals, and the vectors of features were formed by approximate entropy and fluctuation index, then the support vector machine optimized by genetic algorithms was utilized to classify epileptic signals, and the classification accuracy reached 98.3% [36]. J.-L. Song et al. presented an approach of detection of epileptic seizures based on lagged Poincaré plots and extreme learning machine, and the classification accuracy, sensitivity and specificity attained 96.16%, 96.00% and 96.37%, respectively [37]. M. Sharma et al. described an approach for detecting the epileptic seizures by analytic time-frequency flexible wavelet transform (ATFFWT) and least-squares support vector machine (LS-SVM), and the accuracy, sensitivity and specificity reached 98.67%, 100.00% and 96.00% [20]. J. Jia et al. constructed the growth curve and extracted statistical features using complete ensemble empirical mode decomposition with adaptive noise (CEEMDAN), and the method realized 98.00% accuracy, 100.00% sensitivity and 99.00% specificity by the random forest classifier [38]. Y. Li et al. employed a multiscale radial basis function with a modified particle swarm optimization (MRBF-MPSO) and reported 98.73% accuracy, 98.00% sensitivity and 99.10% specificity for the dataset of S-NF [39].

In 1998, N.E. Huang et al. proposed the approach of EMD, which is appropriate to analyze weak biological signals [40]. EMD can decompose the epileptic signals into the intrinsic mode functions (IMFs) by time scale adaptively. However, this method has some problems such as end effect and mode mixing, which are generated because the error of envelope estimation is gradually amplified when multiple recursive decompositions are performed through the envelope of the extreme point [41]. These problems result in the inability to correctly separate the similar frequency components, and the signal will lose part of the detailed information, which affects the signal integrity and detection accuracy. Moreover, the decomposition error of this method is relatively large when the signal is polluted by noise. Due to the drawback of mode mixing in EMD, Z. Wu and N.E. Huang proposed the method of ensemble empirical mode decomposition (EEMD) by mixing the analysis signal with white noise [42]. The method eliminates the phenomenon of mode mixing and improves noise immunity using the uniform distribution of the power spectrum density of white noise to change the characteristics of extreme points in the frequency domain [43]. However, this method increases the amount of calculation and decomposes the signal into multiple components that exceed the true composition of the original signal.

Due to the above approaches' limitations, K. Dragomiretskiy and D. Zosso proposed a new multi-scale and time-frequency signal analysis decomposition method named variational mode decomposition (VMD) in 2014 [44]. The method introduces the variational model to search for the optimal solutions by iteration to make the sum of the estimated bandwidth of each mode minimized. In the frequency domain, each mode and the corresponding center frequencies are constantly updated so that the algorithm can adaptively extract the narrow-band components, and the decomposed components are also defined as intrinsic mode functions (IMFs), where each component is a stationary amplitude modulation and frequency modulation signal with limited bandwidth [32,45]. This algorithm can effectively avoid the drawback of mode mixing generated by gradual amplification of the estimation error in the recursive process and has certain advantages in calculation speed, decomposition accuracy of complex signals and anti-noise interference.

Considering the characteristics of weak biological signals, this paper uses VMD to extract the decomposed components of epileptic EEG signals. Since statistics can objectively describe the overall quantitative characteristics and quantitative relationships of signals, this article applies statistical methods to extract IMF components' eight features of maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index. Then the best combinations of extracted features are fed into the non-linear twin support vector machine (NLTWSVM) for training

to realize the detection and classification of epileptic seizure.

This proposed method realizes the combination of signal decomposition and statistical analysis for epileptic EEG signals, and it is tested on the public datasets and compared with other similar methods.

2. Materials and methods

2.1. Database-A

Database-A uses a publicly available online database from Department of Epileptology, University of Bonn, Germany [46]. The EEG database has been widely used in the epileptic seizure detection. The details of this database are shown in Table 1. The database is composed of five groups of EEG datasets, and each dataset includes 100 segments of EEG signals with a sampling frequency of 173.6 Hz and a duration of 23.6 s.

2.2. Database-B

Database-B uses the Temple University Hospital EEG Seizure Corpus (TUSZ, v1.5.2), which contains annotations of occurrence time and epileptic seizure types and includes the patient information such as ID, age, gender, seizure event number and seizure duration in the database [47]. Eight types of epileptic seizures annotated from the database are Focal Non-Specific Seizure (FNSZ), Generalized Non-Specific Seizure (GNSZ), Complex Partial Seizure (CPSZ), Tonic Clonic Seizure (TCSZ), Absence Seizure (ABSZ), Simple Partial Seizure (SPSZ), Tonic Seizure (TNSZ) and Myoclonic Seizure (MYSZ). The database statistics description is shown in Table 2. This database contains two sets, called training set and development set. The training set is used to train the algorithm model, and the development set is used to test the performance of the model.

2.3. Variational mode decomposition

Assuming that the input signal x(t) contains k number of IMF components $u_k(t)$ [44]. The method consists of the construction and solution of variational model.

2.3.1. Construction of variational model

Essentially, the IMF is defined as a bandwidth-limited amplitude modulation and frequency modulation function [48]. The specific methods of construction are below:

- 1. Perform Hilbert transform on each IMF component $u_k(t)$ to construct an analytic signal for obtaining its unilateral frequency spectrum;
- 2. Mix the analytic signal of each IMF component with the index $e^{-j\omega_k t}$ to shift spectrums of IMF components to basebands;
- 3. Calculate the squared L²-norm of the gradient of the demodulated signal, estimate corresponding bandwidths of IMF components, and construct a constrained variational model:

$$\begin{cases} \min_{\{u_k\},\{\omega_k\}} \left\{ \sum_k \left\| \partial_t \left[\left(\delta(t) + \frac{j}{\pi t} \right) * u_k(t) \right] e^{-j\omega_k t} \right\|_2^2 \right\} \\ \text{s.t.} \qquad \sum_k u_k(t) = x(t) \end{cases}$$
 (1)

where δ is the Dirac function, $\{u_k\} = \{u_1, u_2, \cdots, u_K\}$ is the set of all IMF components, $\{\omega_k\} = \{\omega_1, \omega_2, \cdots, \omega_K\}$ is the set of center frequencies, K is the number of IMF components. Equally, $\sum_k = \sum_{k=1}^K$ is explained as the summation of all IMF components.

2.3.2. Solution of variational model

1. In order to resolve the constrained variational problem, the constructed augmented Lagrangian function expression is proposed based on quadratic penalty term and Lagrangian multiplier:

$$\begin{split} \mathscr{L}(\{u_k\},\{\omega_k\},\lambda) &= \alpha \sum_{k} \left| \left| \partial_t \left[\left(\delta(t) + \frac{j}{\pi t} \right) * u_k(t) \right] e^{-j\omega_k t} \right| \right|_2^2 \\ &+ \left| \left| x(t) - \sum_{k} u_k(t) \right| \right|_2^2 \\ &+ \left\langle \lambda(t), x(t) - \sum_{k} u_k(t) \right\rangle \end{split} \tag{2}$$

Among them, the quadratic penalty term α is the limitation index of data-fidelity and the Lagrangian multiplier λ can ensure strict enforcement [49].

2. The alternate direction method of multipliers (ADMM) is applied to search for the saddle point of the augmented Lagrangian found by an alternate update of $u_k^{n+1}(t)$, $\omega_k^{n+1}(t)$ and $\lambda^{n+1}(t)$. This saddle point is the optimal solution of the variational model. The iteration formulas are below:

$$u_k^{n+1} \leftarrow \mathop{\text{arg\,min}}_{u_k} \mathscr{L}(\{u_{i < k}^{n+1}\}, \{u_{i \geqslant k}^n\}, \{\omega_i^n\}, \lambda^n) \tag{3}$$

$$\omega_{\mathbf{k}}^{n+1} \leftarrow \mathop{\arg\min}_{\omega_{\mathbf{k}}} \mathscr{L}(\{\mathbf{u}_{\mathbf{i}}^{n+1}\}, \{\omega_{\mathbf{i} < \mathbf{k}}^{n+1}\}, \{\omega_{\mathbf{i} > \mathbf{k}}^{n}\}, \lambda^{n}) \tag{4}$$

| Table 1 – T | Table 1 – The details of the Bonn database. | | | | | | |
|-------------|---|--------------|--------------------------|-------------------|----------------------------|--|--|
| Dataset | Testing object | Record type | Status of testing object | Number of samples | Electrode position | | |
| Α | Healthy volunteers | Surface | Awake, open eyes | 100 | 10–20 electrode system | | |
| В | Healthy volunteers | Surface | Awake, close eyes | 100 | 10–20 electrode system | | |
| C | Epileptic patients | Intracranial | Interictal | 100 | Outside epileptogenic zone | | |
| D | Epileptic patients | Intracranial | Interictal | 100 | Inside epileptogenic zone | | |
| E | Epileptic patients | Intracranial | Ictal | 100 | Inside epileptogenic zone | | |

| Table 2 – The statistics description of the TUSZ database. | | | | | |
|--|----------------|----------------------|------------------------|--|--|
| Seizure type | Patient number | Seizure event number | Seizure duration (sec) | | |
| FNSZ | 150 | 1836 | 121,139 | | |
| GNSZ | 81 | 583 | 59,717 | | |
| CPSZ | 41 | 367 | 36,321 | | |
| TCSZ | 14 | 48 | 5548 | | |
| ABSZ | 12 | 99 | 852 | | |
| SPSZ | 3 | 52 | 2146 | | |
| TNSZ | 3 | 62 | 1204 | | |
| MYSZ | 2 | 3 | 1312 | | |
| Total | 306 | 3050 | 228,239 | | |

$$\lambda^{n+1} \leftarrow \lambda^n + \tau \left(x(t) - \sum_k u_k^{n+1} \right) \tag{5}$$

The convergence criterion is defined by:

$$\sum_{k} \| u_{k}^{n+1} - u_{k}^{n} \|_{2}^{2} / \| u_{k}^{n} \|_{2}^{2} < \varepsilon$$
 (6)

where τ denotes the Lagrangian multiplier update parameter and ε represents the convergence tolerance.

3. Mode u_k update and solution

Rewrite Eq. (3) as the following equivalent expression:

$$u_k^{n+1} = \underset{u_k \in X}{\operatorname{argmin}} \left\{ \alpha \left| \left| \partial_t \left[\left(\delta(t) + \frac{j}{\pi t} \right) * u_k(t) \right] e^{-j\omega_k t} \right| \right|_2^2 + \left| \left| x(t) - \sum_i u_i(t) + \frac{\lambda(t)}{2} \right| \right|_2^2 \right\}$$
(7

where ω_k is equal to ω_k^{n+1} , $\sum_i u_i(t)$ is equal to $\sum_{i\neq k} u_i(t)^{n+1}$.

Due to the Parseval/Plancherel Fourier isometry, Eq. (7) is converted into the spectral domain as below:

$$\begin{split} \hat{u}_{k}^{n+1} &= \underset{\hat{u}_{k}, u_{k} \in X}{\text{argmin}} \left\{ \alpha \left| \left| j\omega[(1 + \text{sgn}(\omega + \omega_{k})) \hat{u}_{k}(\omega + \omega_{k})] \right| \right|_{2}^{2} \right. \\ &\left. \text{left} + \left| \left| \hat{x}(\omega) - \sum_{i} \hat{u}_{i}(\omega) + \frac{\hat{\lambda}(\omega)}{2} \right| \right|_{2}^{2} \right\} \end{split} \tag{8}$$

Replace ω in Eq. (8) of penalty term with $\omega-\omega_k$, the expression is replaced as follows:

$$\begin{split} \hat{\mathbf{u}}_{k}^{n+1} &= \underset{\hat{\mathbf{u}}_{k}, \mathbf{u}_{k} \in \mathbf{X}}{\text{argmin}} \left\{ \alpha \left| \left| \dot{j}(\omega - \omega_{k}) \left[(1 + sgn(\omega)) \hat{\mathbf{u}}_{k}(\omega) \right] \right| \right|_{2}^{2} \right. \\ &\left. + \left| \left| \hat{\mathbf{x}}(\omega) - \sum_{i} \hat{\mathbf{u}}_{i}(\omega) + \frac{\hat{\lambda}(\omega)}{2} \right| \right|_{2}^{2} \right\} \end{split} \tag{9}$$

Since the real signals have the characteristic of Hermitian symmetry, Eq. (9) can be changed to half-space integrals over the non-negative frequencies as below:

$$\hat{\boldsymbol{u}}_{k}^{n+1} = \underset{\hat{\boldsymbol{u}}_{k}, \boldsymbol{u}_{k} \in X}{\text{argmin}} \left\{ \int_{0}^{\infty} 4\alpha (\omega - \omega_{k})^{2} |\hat{\boldsymbol{u}}_{k}(\omega)|^{2} + 2 \left| \hat{\boldsymbol{x}}(\omega) - \sum_{i} \hat{\boldsymbol{u}}_{i}(\omega) + \frac{\hat{\lambda}(\omega)}{2} \right|^{2} d\omega \right\}$$

$$\tag{10}$$

Solving Eq. (10) as a quadratic optimization problem, the above expression can be further described as:

$$\hat{\mathbf{u}}_{k}^{n+1}(\omega) = \frac{\hat{\mathbf{x}}(\omega) - \sum_{i \neq k} \hat{\mathbf{u}}_{i}(\omega) + \frac{\hat{\lambda}(\omega)}{2}}{1 + 2\alpha(\omega - \omega_{k})^{2}}$$
(11)

4. Center frequency ω_k update and solution Rewrite Eq. (4) as the following equivalent expression:

$$\omega_{k}^{n+1} = \underset{\omega_{k}}{\operatorname{argmin}} \left\{ \left| \left| \partial_{t} \left[\left(\delta(t) + \frac{j}{\pi t} \right) * u_{k}(t) \right] e^{-j\omega_{k}t} \right| \right|_{2}^{2} \right\}$$
 (12)

According to the same process, Eq. (12) is transformed as below:

$$\omega_{k}^{n+1} = \underset{\omega_{k}}{\operatorname{argmin}} \left\{ \int_{0}^{\infty} (\omega - \omega_{k})^{2} |\hat{\mathbf{u}}_{k}(\omega)|^{2} d\omega \right\} \tag{13}$$

Solving Eq. (13) as a quadratic optimization problem, the above expression can be further represented as:

$$\omega_{\mathbf{k}}^{n+1} = \frac{\int_0^\infty \omega |\hat{\mathbf{u}}_{\mathbf{k}}(\omega)|^2 d\omega}{\int_0^\infty |\hat{\mathbf{u}}_{\mathbf{k}}(\omega)|^2 d\omega} \tag{14}$$

2.4. EEG feature extraction

In the paper, the original EEG signals are decomposed by the VMD algorithm to obtain the IMF components, and feature extraction is performed to acquire eight features of maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index.

Assuming that the signal $u_k(t)$ obtained by decomposing the EEG signal x(t) through VMD is a time series of length L, the extracted features are shown in Table 3.

2.5. Twin support vector machine

In recent years, Twin support vector machine (TWSVM), as an extension of support vector machine (SVM), has received extensive attention. The difference from the traditional SVM algorithm is that TWSVM constructs a corresponding supporting hyperplane for each category, and each hyperplane is as close as possible to the data points of the corresponding class and far away from the data points of other classes [50]. TWSVM is not limited to whether the hyperplane is parallel and the size of the interval. Compared with SVM, TWSVM has more advantages in the effect of classification and speed calculation.

For the classifier of linear twin support vector machine (LTWSVM), consider the problem of binary classification with training samples, including p positive samples and q negative samples, the expression is as follows:

$$T = \{(x_1, +1), (x_2, +1), \cdots (x_p, +1), (x_{p+1}, -1), (x_{p+2}, -1), \cdots (x_{p+q}, -1)\} \quad (15)$$

where $x_i \in \mathbb{R}^n, i = 1, 2, \dots, p + q$. LTWSVM seeks a pair of non-parallel hyperplanes as follows:

$$(\omega_{+} \cdot \mathbf{x}) + b_{+} = 0$$

 $(\omega_{-} \cdot \mathbf{x}) + b_{-} = 0$ (16)

where $\omega_+, \omega_- \in \mathbb{R}^n$, $b_+, b_- \in \mathbb{R}$. In order to acquire the pair of hyperplanes, two primal quadratic programming problems (QPPs) are described below:

| Table 3 – Extracted features used in this | Table 3 – Extracted features used in this work. | | | | | |
|---|--|--|--|--|--|--|
| Feature name | Mathematical formulation | | | | | |
| Maximum (Max) Minimum (Min) Average (Ave) | $\begin{aligned} & \textit{Max} = \max(u_k(t)) \\ & \textit{Min} = \min(u_k(t)) \\ & \textit{Ave} = \frac{1}{L} \sum_{i=1}^{L} u_{k,i}(t) \end{aligned}$ | | | | | |
| Variance (Var) | $Var = \frac{1}{L-1} \sum_{i=1}^{L} (u_{k,i}(t) - Ave)^2$ | | | | | |
| Skewness (Skew) | Skew $= \frac{1}{L} \sum_{i=1}^{L} \left(\frac{u_{k,i}(t) - Ave}{Var^{1/2}} \right)^3$ | | | | | |
| Kurtosis (Kurt) | $\text{Kurt} = \tfrac{1}{L-1} \textstyle \sum_{i=1}^L (u_{k,i}(t) - A \nu e)^4 / V \alpha r^2 - 3$ | | | | | |
| Coefficient of variation (CV) | $CV = \frac{Var}{Ave^2}$ | | | | | |
| Volatility index (VI) | $VI = \frac{1}{L} \sum_{i=1}^{L-1} \left u_{k,i+1}(t) - u_{k,i}(t) \right $ | | | | | |

$$\min_{\substack{\omega_{+}, b_{+}, \xi_{-} \\ \omega_{+}, b_{+}, \xi_{-}}} \frac{1}{2} (A\omega_{+} + e_{+}b_{+})^{T} (A\omega_{+} + e_{+}b_{+}) + c_{1}e_{-}^{T}\xi_{-}
s.t. - (B\omega_{+} + e_{-}b_{+}) + \xi_{-} \geqslant e_{-}, \xi_{-} \geqslant 0$$
(17)

And

$$\min_{\substack{\omega_{-}, b_{-}, \xi_{+} \\ \omega_{-}, b_{-}, \xi_{+}}} \frac{1}{2} (B\omega_{-} + e_{-}b_{-})^{T} (B\omega_{-} + e_{-}b_{-}) + c_{2}e_{+}^{T}\xi_{+}
s.t. (A\omega_{-} + e_{+}b_{-}) + \xi_{+} \ge e_{+}, \xi_{+} \ge 0$$
(18)

where $A = (x_1, x_2, \cdots, x_p)^T \in R^{p \times n}$, $B = (x_{p+1}, x_{p+2}, \cdots, x_{p+q})^T \in R^{q \times n}$, and l = p + q. e_+ and e_- are the column vectors of ones of appropriate dimensions. ξ_+ and ξ_- are slack vectors. c_1 and c_2 are penalty parameters, which are used to penalize a few linearly inseparable samples to maximize the separability of samples. The dual problems are as follows:

$$\max_{\alpha} e_{-}^{T} \alpha - \frac{1}{2} \alpha^{T} G(H^{T} H)^{-1} G^{T} \alpha$$
s.t. $0 \le \alpha \le c_{1} e_{-}$ (19)

And

$$\max_{\gamma} e_{+}^{T} \gamma - \frac{1}{2} \gamma^{T} H(G^{T}G)^{-1} H^{T} \gamma$$
s.t. $0 \leq \gamma \leq c_{2} e_{+}$ (20)

where $H = \begin{bmatrix} A & e_+ \end{bmatrix} \in \mathbb{R}^{p \times (n+1)}$, $G = \begin{bmatrix} B & e_- \end{bmatrix} \in \mathbb{R}^{q \times (n+1)}$.

The non-parallel hyperplanes can be acquired by the solutions to the QPPs of Eq. (17) and Eq. (18), as the following formulations:

$$(\omega_{+}^{T}, b_{+})^{T} = -(H^{T}H)^{-1}G^{T}\alpha$$

$$(\omega_{+}^{T}, b_{-})^{T} = -(G^{T}G)^{-1}H^{T}\gamma$$
(21)

For a new input $x \in \mathbb{R}^n$, its discrimination function of the category is described as:

$$Class = \arg\min_{k} |(\omega_k \cdot x) + b_k|$$
 (22)

where $|\cdot|$ denotes the perpendicular distance of the sample x from the hyperplane.

For the classifier of non-linear twin support vector machine (NLTWSVM), the kernel functions are applied to convert linear inseparable problems of original space to linear separable problems of high-dimensional space [51]. NLTWSVM still searches for a pair of non-parallel hyperplanes below:

$$K(x^{T}, C^{T})u_{+} + b_{+} = 0$$

 $K(x^{T}, C^{T})u_{-} + b_{-} = 0$ (23)

where $C^T = [A;B]^T \in R^{n \times l}$, $K(\cdot, \cdot)$ stands for an appropriate kernel function, and the QPPs can be described below:

$$\min_{\substack{u_+,b_+,\xi_-\\ v_+,b_-}} \frac{1}{2} \| K(A,C^T)u_+ + e_+b_+ \|^2 + c_1e_-^T\xi_-
\text{s.t.} - (K(B,C^T)u_+ + e_-b_+) + \xi_- \geqslant e_-, \xi_- \geqslant 0$$
(24)

And

$$\begin{split} \min_{u_-,b_-,\xi_+} & \frac{1}{2} \| \ K(B,C^T) u_- + e_- b_- \ \|^2 + c_2 e_+^T \xi_+ \\ \text{s.t.} & \ (K(A,C^T) u_- + e_+ b_-) + \xi_+ \geqslant e_+, \xi_+ \geqslant 0 \end{split} \tag{25}$$

The dual formulations of the corresponding dual problems are below:

$$\max_{\alpha} e_{-}^{T} \alpha - \frac{1}{2} \alpha^{T} R (S^{T} S)^{-1} R^{T} \alpha$$
s.t. $0 \le \alpha \le c_{1} e_{-}$ (26)

And

$$\max_{\gamma} e_{+}^{T} \gamma - \frac{1}{2} \gamma^{T} S(R^{T} R)^{-1} S^{T} \gamma$$

$$s.t. \quad 0 \leqslant \gamma \leqslant c_{2} e_{+}$$
(27)

where $S = [K(A, C^{T})e_{+}], R = [K(B, C^{T})e_{-}].$

The non-parallel hyperplanes can be acquired by the solutions to the QPPs of Eq. (24) and Eq. (25), as the following formulations:

$$(u_{+}^{T}, b_{+})^{T} = -(S^{T}S)^{-1}R^{T}\alpha$$

$$(u_{-}^{T}, b_{-})^{T} = -(R^{T}R)^{-1}S^{T}\gamma$$
(28)

For a new input $x \in \mathbb{R}^n$, its discrimination function of the category is described as:

$$Class = \arg\min_{k=-,+} \left| K(x^{T}, C^{T}) u_{k} + b_{k} \right|$$
 (29)

3. Experiments and results

3.1. Experimental design

For database-A, the experiment selects all segments of EEG signals from the selected datasets and divides the first 23 s EEG data of each segment into 23 data fragment samples with one second as a unit. And each extracted data fragment sample is decomposed by VMD algorithm to acquire the corresponding IMF components, then the eight features of each

IMF component are extracted to obtain the maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index. The datasets generate five combination cases to test the classification effect and analyze the combinations' impact of different datasets, and the combination cases are shown in Table 4.

For database-B, since the seizure event number of seizure type of MYSZ is too small, we eliminate this seizure type and use the remaining seven seizure types to build a model for the 7-class classification. Perform a 60 Hz notch and a band-pass filter from 0.1 Hz to 80 Hz on the EEG data of the remaining 7 seizure types within the seizure event time, and then extract the FP1-FP2 electrode channel EEG data from the processed data. The EEG data fragments are extracted by dividing the processed data with a time interval of 1 s. The data fragments extracted in the training set are used as the model training set, and the data fragments extracted in the development set are used for model testing. The algorithm performs 4layer VMD decomposition to acquire IMF components and extracts eight types of features from IMF components, and then inputs features to the NLTWSVM for multi-class training and testing.

The proposed approach for the epileptic seizure detection and classification is described in Fig. 1. All the experiments implement on the same PC with Intel-core i3-9100F CPU@3.60 GHz processor-based machine with 8 GB RAM using Python 3.6. The representative original EEG signals in the datasets corresponding to the three statuses of normal, interictal and ictal periods are presented in Fig. 2.

The IMF components k and quadratic penalty term α are important parameters that affect the results of classification. If the number of k in the algorithm is less than theoretical components, the signals will not be completely decomposed, resulting in under-decomposition; if the number of k is greater than theoretical components, unreasonable false will components be produced, leading decomposition. When k is constant and α is small, the spectra of two adjacent mode functions will be partially overlapped; as α increases, the passband becomes narrower and narrower, which will result in a larger error for reconstructing signals [52]. Therefore, it is important to acquire a reasonable number of IMF components k and quadratic penalty term α for signal decomposition. In this paper, the different numbers of k and α are analyzed, and the experiments determine that the number of k is 4 and α is 2000.

In the paper, the classifier of NLTWSVM is selected to classify the samples, and the radial basis function is selected as kernel function as follows:

$$K(x, x_i) = exp\left(\frac{-\parallel x - x_i \parallel^2}{2\sigma^2}\right)$$
 (30)

| Table 4 – Combination cases from the database-A. | | | | | |
|---|---|--|--|--|--|
| Combination case Classes type | | | | | |
| C vs. E D vs. E CD vs. E ABCD vs. E AB vs. CD vs. E | Interictal vs. ictal Interictal vs. ictal Interictal vs. ictal Non-ictal vs. ictal Healthy vs. interictal vs. ictal | | | | |

where σ represents the width of function. In this paper, different parameters are tested to observe the classification effect, and the parameters which obtain the best classification accuracy are chosen as the used classifiers' parameters for each combination case.

3.2. Results

In this paper, four-layer VMD decomposition is applied to data fragment samples to acquire IMF components. The representative EEG data fragment samples and the corresponding IMF components of three statuses of normal, interictal and ictal periods are shown in Fig. 3. It illustrates that the IMF components of each order obtained from the VMD decomposition represent different characteristic compositions in the original EEG signal, and the EEG amplitude of the ictal period is higher than that of normal and interictal periods.

After VMD decomposition is applied to acquire IMF components of the EEG data fragment samples, the corresponding eight features of maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index are calculated for each IMF component. Fig. 4 shows the eight features' box plots of IMF1, IMF2, IMF3 and IMF4 obtained from VMD decomposition in five datasets of normal, interictal and ictal periods. Among them, the black, red, blue and green colors represent the corresponding features' box plots of IMF1, IMF2, IMF3 and IMF4, respectively. It can be seen the IMF components of each order during the ictal period have significant differences compared with the IMF components of the normal and interictal periods for each extracted feature. These differences establish a good foundation for detecting epileptic seizure accurately.

The performance of the classifier is evaluated by the evaluation parameters named sensitivity (SEN), specificity (SPEC) and accuracy (ACC) [53,54]. To ensure the effectiveness of the classification results, the 10-fold cross-validation method is applied to the experiments described in this article. The evaluation parameters are calculated below:

$$\begin{split} \text{SEN} &= \frac{TP}{TP_{T}+FN} \\ \text{SPEC} &= \frac{TN}{TN_{T}+FP} \\ \text{ACC} &= \frac{TP_{T}+TN_{T}}{TP_{T}+FN_{T}+TN_{T}+FN} \end{split} \tag{31}$$

For the 7-class classification problem proposed in this paper, the weighted F_1 score is used to evaluate the performance of the classifier. The formula is as follows:

$$\begin{split} & \text{Precision} = \frac{\text{TP}}{\text{TP+FP}} \\ & \text{Weighted } F_1 = \sum_{i=1}^{7} \frac{2 \cdot \text{Precision}_i \cdot \text{Sensitivit} y_i}{\text{Precision}_i + \text{Sensitivit} y_i} * \omega_i \end{split} \tag{32}$$

where ω_i is the weight of positive samples in the i-th class.

In order to test the impact and classification effect for the selected features, the different feature numbers and types of the eight extracted features are selected to train each combination case in turn, and the best feature combinations and the corresponding evaluation parameters of each combination case are shown in Table 5.

It can be seen from Table 5 that the classification accuracy can reach 98.86%, 98.37%, 99.02%, 99.41% and 99.57% for the database of C-E, D-E, CD-E, ABCD-E and AB-CD-E under the

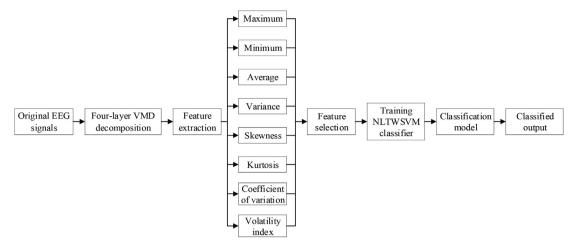


Fig. 1 - Block diagram of the proposed method for the epileptic seizure detection and classification.

best feature combination, respectively. The best feature combinations of each combination case are fed into the used classifiers for training, which can better describe the characteristics of epileptic signals and improve the classification effect.

For multi-classification problems, this article uses the confusion matrix representation method to illustrate the classification effect. The result of the confusion matrix of 7-class classification is shown in Fig. 5. It illustrates that the correct classification of seizure types FNSZ, GNSZ, SPSZ, CPSZ, ABSZ, TNSZ and TCSZ reaches 0.93, 0.93, 0.89, 0.90, 0.97, 0.98 and 0.86 respectively. For the 7-class classification problem, the weighted F_1 score is 0.923. Judging from the classification results, this method can assist experienced neurophysiologists to help identify the seizure type clinically.

4. Discussion

In the article, the classification methods of SVM, LTWSVM and NLTWSVM are applied to compare classification effects. Table 6 illustrates the best evaluation parameters obtained from the different feature numbers and types using the classifiers of SVM, LTWSVM and NLTWSVM for each combination case. It can be seen the proposed classifier of NLTWSVM has the best classification accuracy, sensitivity and specificity than those of other classifiers. The significant improvements in classification accuracy, sensitivity and specificity indicate that the proposed method is conducive to the realization of epileptic seizure detection.

Tables 7–11 present the classification results of the proposed method and the existing methods for the database of C-E, D-E, CD-E, ABCD-E and AB-CD-E. The above tables indicate that the overall classification results of the five combination cases have better results than other algorithms. Therefore, the proposed method is suitable for epileptic seizure detection.

D. Ahmedt-Aristizabal proposed the method based on neural memory networks (NMNs) and external memory model to classify the TUSZ corpus for 7-class classification, and the result of seizure types classification was described by the confusion matrix [67]. The probability of correct classi-

fication of the 7 types differed greatly from the confusion matrix, with the lowest being 0.33 and the highest being 1.00. The seizure durations of the SPSZ, TNSZ and TCSZ types in the TUSZ corpus are less than other types, which is challenging for the classifier to classify correctly. The NMNs model had a low correct classification on the above three types, up to 0.50. The number of correct classifications of the above three types of data by the classification method proposed in our article has been reduced, but the minimum correct classification is 0.86, which proves that the method in this paper has a good classification effect on such data types with small seizure durations and has the potential for clinical use.

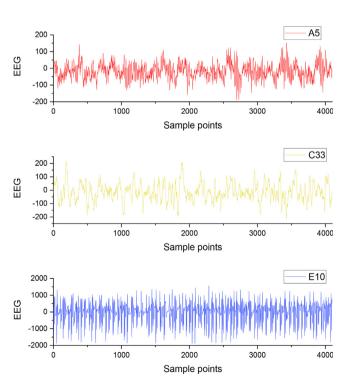


Fig. 2 – The representative original data of normal (A5), interictal (C33) and ictal (E10) EEG signals.

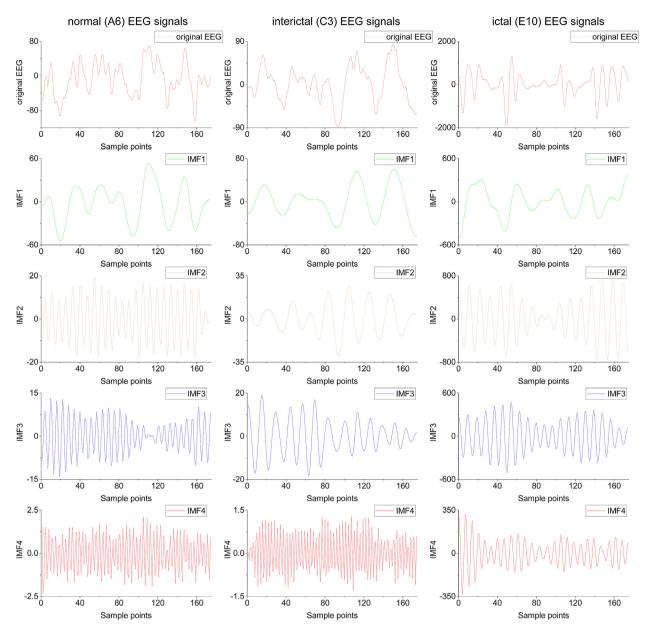


Fig. 3 – The representative EEG data fragment samples and the corresponding IMF components of normal (A6), interictal (C3) and ictal (E10) EEG signals.

N. McCallan used a bagged tree classifier to classify the TUSZ corpus [68]. The first classification objects are FNSZ, GNSZ and NNSZ. From the confusion matrix, the correct classifications of FNSZ, GNSZ and NNSZ can be obtained up to 0.85, 0.74 and 0.64, respectively. The correct classification of FNSZ and GNSZ can both reach 0.93 by the method proposed in our article, which has a better classification effect for these types. The second classification objects are ABSZ, CPSZ, MYSZ, NNSZ, SPSZ, TCSZ and TNSZ. The correct classifications are 0.80, 0.84, 0.34, 0.66, 0.10, 0.47 and 0.53 for the above types, which shows the classification results of ABSZ, CPSZ and NNSZ are better. Compared with the results, our article has higher correct classification results for each type, which

can form an effective identification of epileptic seizure types and is helpful for clinical application.

U. Asif used the TUSZ corpus to automatically classify the seizure types [69]. The deep learning framework SeizureNet with multi-spectral feature learning method was utilized to classify 7-class classification problems, and the correct classification of seizure types FNSZ, CPSZ, GNSZ, ABSZ, SPSZ, TNSZ and TCSZ reached 0.93, 0.94, 0.93, 1.00, 0.88, 1.00 and 0.70 respectively. It can be seen from the confusion matrix that the correct classification of TCSZ type is low. Compared with our article, the correct classification of TCSZ type can reach 0.86, which describes that our method can stably classify each type.

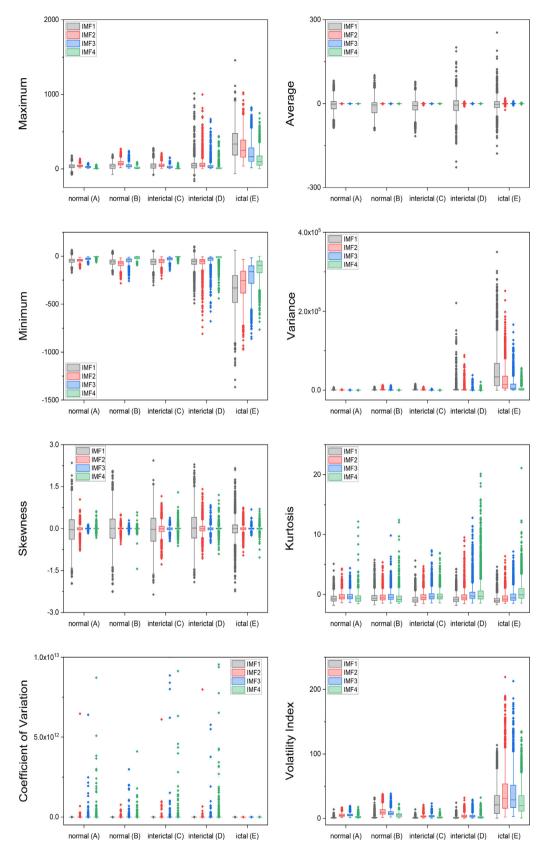


Fig. 4 – The features' box plots of IMF1, IMF2, IMF3 and IMF4 in five datasets of normal, interictal and ictal periods.

| Table 5 – The best feature combinations and evaluation parameters results for each combination case. | | | | | | |
|--|-----------------------------------|---------|----------|---------|--|--|
| Combination case | Best feature combination | SEN (%) | SPEC (%) | ACC (%) | | |
| C vs. E | Max + Min + Ave + CV + VI | 99.02 | 98.70 | 98.86 | | |
| D vs. E | Ave + Var + Skew + Kurt + CV + VI | 98.64 | 98.10 | 98.37 | | |
| CD vs. E | Max + Ave + Skew + Kurt + CV + VI | 99.13 | 98.97 | 99.02 | | |
| ABCD vs. E | Min + Ave + Var + Skew + CV + VI | 99.24 | 99.46 | 99.41 | | |
| AB vs. CD vs. E | Max + Min + Skew + Kurt + CV + VI | 99.28 | 99.66 | 99.57 | | |

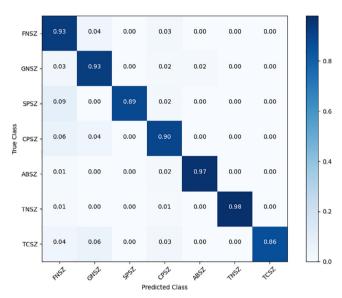


Fig. 5 – The result of the confusion matrix of 7-class classification.

There are many epileptic researches directions that can be used as future research priorities. The detection of epileptic spikes is one direction. K. Fukumori proposed a model called recurrent neural network with self-attention that can detect epileptic spikes without using spike candidates. The average accuracy and F1 value of the classifier reached 90.2% and 88.7% [70]. Detecting and classifying epileptiform discharges

is another research direction. C. Lourenco used deep learning method of VGG to detect interictal epileptiform discharges and reported 79% sensitivity and 99% specificity [71]. J.H. Seo used the dynamic mode decomposition to catch the frequency phase transition and realized the identification of ictal and interictal patterns [24]. M.O. Baud found that epileptiform activities display fluctuating dynamics with patient-specific circadian and multidien periodicities, which make signal acquisition and analysis difficult [72].

Epileptic seizure prediction is part of future work. Predicting epileptic seizures can warn epilepsy patients and experienced neurophysiologists of seizure risk, which can help physicians refer to prescribing drugs to epileptic patients to control epileptic seizures and remind epileptic patients to pay attention to their own safety. T. Proix analyzed the recorded RNS intracerebral EEG signals and realized the prediction of epileptic seizures days in advance by the method based on multiday cycles [73]. F. Turco indicated that the maximum length and the mean duration of generalized epileptiform discharges from prolonged ambulatory EEG can predict seizure recurrences [74].

5. Conclusion

In this paper, a new method based on VMD and NLTWSVM is proposed for epileptic seizure detection and classification. This study introduces variational mode decomposition into the analysis of epileptic EEG signals and calculates the IMF components obtained from VMD to extract eight features of maximum, minimum, average, variance, skewness, kurtosis, coefficient of variation and volatility index, then the best

| Classifier | Index | Combination case | | | | |
|------------|-------|------------------|---------|----------|------------|-----------------|
| | | C vs. E | D vs. E | CD vs. E | ABCD vs. E | AB vs. CD vs. E |
| SVM | SEN | 94.56 | 92.39 | 91.30 | 92.50 | 90.58 |
| | SPEC | 96.41 | 94.02 | 95.49 | 92.91 | 94.99 |
| | ACC | 95.49 | 93.21 | 94.09 | 92.83 | 93.33 |
| LTWSVM | SEN | 97.32 | 97.09 | 98.01 | 98.29 | 95.60 |
| | SPEC | 96.79 | 96.52 | 97.77 | 97.95 | 97.54 |
| | ACC | 97.05 | 96.80 | 97.85 | 98.02 | 96.88 |
| NLTWSVM | SEN | 99.02 | 98.64 | 99.13 | 99.24 | 99.28 |
| | SPEC | 98.70 | 98.10 | 98.97 | 99.46 | 99.66 |
| | ACC | 98.86 | 98.37 | 99.02 | 99.41 | 99.57 |

| Table 7 – The classification results of different methods for database C vs. E. | | | | | |
|---|--|---------|----------|---------|--|
| Authors | Methods | SEN (%) | SPEC (%) | ACC (%) | |
| M. Sameer et al. [34] | Short-time Fourier transform + Adaboost | - | _ | 98.00 | |
| S. Siuly et al. [35] | Hermite Transform + LS-SVM | 98.18 | 99.09 | 98.50 | |
| S. Raghu et al. [55] | Multi-features + MLP | - | - | 97.68 | |
| A. Gupta et al. [56] | Discrete cosine transform + SVM | 98.00 | 97.00 | 97.50 | |
| P. Swami et al. [9] | DT-CWT + General regression neural network | 97.55 | 99.00 | 98.28 | |
| S. Raghu et al. [57] | Matrix determinant + MLP | 95.75 | 99.45 | 97.60 | |
| P. Mathur et al. [58] | Ramanujan periodic subspace + SVM | 97.00 | 99.00 | 98.00 | |
| Proposed method | VMD + NLTWSVM | 99.02 | 98.70 | 98.86 | |

| Authors | Methods | SEN (%) | SPEC (%) | ACC (%) |
|-------------------------|--|---------|----------|---------|
| JL. Song et al. [37] | Lagged Poincaré plots + ELM | 96.00 | 96.37 | 96.16 |
| M. Sameer et al. [34] | Short-time Fourier transform + Adaboost | _ | _ | 95.50 |
| S. Siuly et al. [35] | Hermite Transform + LS-SVM | 98.09 | 97.18 | 97.50 |
| S. Raghu et al. [55] | Multi-features + MLP | _ | _ | 94.56 |
| Y. Li et al. [39] | MRBF-MPSO + SVM | 96.80 | 97.20 | 97.60 |
| T. Zhang et al. [19] | LMD + SVM optimized by genetic algorithm | 98.80 | 97.40 | 98.10 |
| A. Gupta et al. [56] | Discrete cosine transform + SVM | 96.50 | 96.20 | 96.35 |
| S. Raghu et al. [57] | Matrix determinant + MLP | 95.80 | 99.40 | 97.60 |
| A.R. Hassan et al. [59] | CEEMDAN + Linear programming boosting | 97.40 | 98.25 | 97.00 |
| P. Mathur et al. [58] | Ramanujan periodic subspace + SVM | 95.00 | 100.00 | 97.50 |
| Proposed method | VMD + NLTWSVM | 98.64 | 98.10 | 98.37 |

combination of extracted features is fed into the non-linear twin support vector machine for training and testing to complete epileptic seizure detection and classification. Since the clinical diagnosis and treatment for epileptic patients are mainly carried out by trained neurophysiologists using EEG through visual examination, the visual examination is still a time-consuming, labor-intensive and inefficient procedure. The proposed method for epileptic seizure detection and classification can clinically reduce neurophysiologists' workload and improve work efficiency. In the experimental results,

the classification accuracy can reach 98.86%, 98.37%, 99.02%, 99.41% and 99.57% for the database of C-E, D-E, CD-E, ABCD-E and AB-CD-E. The three indicators of accuracy, sensitivity and specificity of our proposed method have achieved good performance results compared to other existing methods, which proves that the method in this article is effective in detecting epileptic seizures. Moreover, compared with the classifiers of LTWSVM and SVM, the three indicators of the NLTWSVM classifier used in this article have significantly improved in all the combination cases, which further proves

| Authors | Methods | SEN (%) | SPEC (%) | ACC (%) |
|--------------------------|--|---------|----------|---------|
| M. Sameer et al. [34] | Short-time Fourier transform + Adaboost | _ | _ | 96.33 |
| S. Raghu et al. [55] | Multi-features + MLP | - | _ | 84.58 |
| M. Sharma et al. [60] | Orthogonal wavelet filter banks + SVM | 98.00 | 99.00 | 99.00 |
| Y. Li et al. [39] | MRBF-MPSO + SVM | 98.00 | 99.10 | 98.73 |
| S. Siuly et al. [35] | Hermite Transform + LS-SVM | 97.18 | 98.54 | 98.00 |
| P. Swami et al. [9] | DT-CWT + General regression neural network | 91.74 | 96.64 | 95.00 |
| A. Gupta et al. [56] | Discrete cosine transform + SVM | 96.85 | 97.00 | 96.92 |
| A.K. Jaiswal et al. [61] | One-dimensional Local Gradient Pattern + ANN | 97.20 | 99.57 | 98.78 |
| S. Raghu et al. [57] | Matrix determinant + MLP | 97.60 | 94.30 | 96.95 |
| M. Mursalin et al. [14] | DWT + RF | 98.70 | 98.70 | 98.67 |
| S. Patidar et al. [62] | Tunable-Q wavelet transform + LS-SVM | 97.00 | 99.00 | 97.75 |
| M. Sharma et al. [20] | ATFFWT + LS-SVM | 100.00 | 96.00 | 98.67 |
| B. Mandhouj et al. [63] | STFT + CNN | 100.00 | 98.33 | 98.88 |
| S.M. Beeraka et al. [29] | STFT + CNN | 98.99 | 93.51 | 98.17 |
| Proposed method | VMD + NLTWSVM | 99.13 | 98.97 | 99.02 |

| Authors | Methods | SEN (%) | SPEC (%) | ACC (%) |
|------------------------------|--|---------|----------|---------|
| M. Sameer et al. [34] | Short-time Fourier transform + Adaboost | _ | - | 97.40 |
| W. Zhao et al. [64] | Convolutional neural network | 97.00 | 100.00 | 99.40 |
| M. Sharma et al. [60] | Orthogonal wavelet filter banks + SVM | 98.00 | 99.75 | 99.20 |
| P. Swami et al. [9] | DT-CWT + General regression neural network | _ | _ | 96.87 |
| S. Siuly et al. [35] | Hermite Transform + LS-SVM | 96.31 | 98.06 | 97.60 |
| V. Bajaj et al. [23] | SPWVD + LS-SVM | 97.87 | 98.03 | 98.00 |
| M.Y. Li et al. [33] | Maximal overlap DWT + RF | 98.20 | 99.33 | 99.10 |
| A.S.M. Murugavel et al. [65] | Wavelet transform + Hierarchical multi-class SVM | - | - | 99.00 |
| T. Zhang et al. [19] | LMD + SVM optimized by genetic algorithm | 99.25 | 97.33 | 98.87 |
| A. Gupta et al. [56] | Discrete cosine transform + SVM | 97.97 | 97.60 | 97.79 |
| A.K. Jaiswal et al. [61] | Local neighbor descriptive pattern + ANN | 98.30 | 98.82 | 98.72 |
| S. Raghu et al. [57] | Matrix determinant + MLP | 97.90 | 96.50 | 97.20 |
| A.R. Hassan et al. [59] | CEEMDAN + Linear programming boosting | 99.17 | 99.04 | 99.20 |
| M. Mursalin et al. [14] | DWT + RF | 97.40 | 97.50 | 97.40 |
| M. Sharma et al. [20] | ATFFWT + LS-SVM | 100.00 | 96.00 | 99.20 |
| A.R. Hassan et al. [43] | CEEMDAN + Adaptive Boosting | 98.75 | 98.75 | 99.20 |
| Sukriti et al. [52] | VMD + RF | 99.10 | 100.00 | 99.30 |
| Y. Kumar et al. [18] | DWT + SVM | 98.10 | 94.40 | 97.38 |
| K. Samiee et al. [17] | DSTFT + MLP | 99.20 | 93.80 | 98.10 |
| B. Mandhouj et al. [63] | STFT + CNN | 93.33 | 100.00 | 98.66 |
| Proposed method | VMD + NLTWSVM | 99.24 | 99.46 | 99.41 |

| Table 11 – The classification results of different methods for database AB vs. CD vs. E. | | | | | | |
|--|--|---------|----------|---------|--|--|
| Authors | Methods | SEN (%) | SPEC (%) | ACC (%) | | |
| Sukriti et al. [52] | VMD + RF | 98.20 | 99.70 | 98.70 | | |
| W. Zhao et al. [64] | Convolutional neural network | 95.40 | 97.70 | 97.07 | | |
| B. Mandhouj et al. [63] | STFT + CNN | 97.78 | 98.61 | 98.22 | | |
| Y. Jiang et al. [66] | Synchroextracting chirplet transform + SVM | - | - | 99.33 | | |
| S. Raghu et al. [57] | Matrix determinant + MLP | 96.88 | 95.50 | 96.19 | | |
| A.R. Hassan et al. [43] | CEEMDAN + Adaptive Boosting | 97.67 | 97.35 | 97.60 | | |
| T. Zhang et al. [19] | LMD + SVM optimized by genetic algorithm | 98.44 | - | 98.40 | | |
| A.R. Hassan et al. [59] | CEEMDAN + Linear programming boosting | 98.11 | 96.93 | 97.60 | | |
| Proposed method | VMD + NLTWSVM | 99.28 | 99.66 | 99.57 | | |

the effectiveness of the method in this article. For the 7-class classification problem, the article uses the confusion matrix representation method and the weighted F_1 score to illustrate the effectiveness of classifying seizure types. For the 7 seizure types, the correct classification rate for this method can reach up to 0.98 and the weighted F_1 score is 0.923. This method is valuable for clinical assistant experienced neurophysiologists to identify seizure types in patients with epilepsy.

CRediT authorship contribution statement

Shang Zhang: Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. Guangda Liu: Conceptualization, Supervision. Ruolan Xiao: Software. Wenjie Cui: Investigation. Jing Cai: Writing – review & editing. Xinlei Hu: Writing – review & editing. Yubing Sun: Validation. Jiqing Qiu: Resources. Yuan Qi: Resources.

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Conflicts of Interest

The authors declare no conflict of interest.

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