

# Application of Steady-state Visual Evoked Potentials and Magnetoencephalographic Signals in Schizophrenia

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**Jiang *et al.*: Application of Steady-state Visual Evoked Potentials and MEG Signals**

In order to understand the basic mechanism of brain diseases, autoregressive model coefficients, frequency band energy, approximate entropy, and Lempel-Ziv complexity of magnetoencephalographic signals of schizophrenia were extracted as features. Distance criterion and Plus-L Minus-R algorithm were used to screen channels, back propagation neural network and support vector machine were applied to distinguish magnetoencephalographic signals of schizophrenic and normal people, and genetic algorithm was adopted to select features with significant differences. Finally, electroencephalography experiments were designed based on steady-state visual evoked potentials, and electroencephalographic signals of multiple subjects were collected. The collected signals were analysed using discrete Fourier transform, canonical correlation analysis and multivariable synchronization index analysis methods. The results showed that the correct classification rates of schizophrenic and normal people were 96.25 and 98.75 %, respectively. The correct classification rates of back propagation neural network and support vector machine were 98.5 and 99.75 %, respectively. Signal energy, correlation coefficient and synchronization index were the highest at the target stimulus frequency. The in-depth study of brain signals in patients with schizophrenia provided a reference for clinical diagnosis.

**Key words:** Brain signal, schizophrenia, steady state visual evoked potential

Electroencephalography (EEG) is the discharge activity of brain neurons recorded by scalp electrodes. EEG signals indicate the change of voltage difference between two different locations of the brain over time. EEG is often used in the diagnosis and monitoring of epilepsy, and can also be used to analyse other diseases, such as Alzheimer's disease, schizophrenia and so on<sup>[1]</sup>. Magnetoencephalography (MEG) is a non-invasive technique for detecting brain function. It can detect the magnetic field produced by nerve current in the brain. It is another study of brain function and clinical application developed after EEG<sup>[2]</sup>. Schizophrenia is a serious and persistent mental illness, which affects 0.4-0.6 % of the world's population. Most of the patients are in post-adolescence or early adulthood<sup>[3]</sup>.

In recent years, more and more scholars have devoted themselves to the study of schizophrenia. Huang *et al.* have designed a simple choice task. The subjects need to predict 500 random left-or right-facing stimuli. By analysing the mutual information and crossover mutual information of the binary response signals of the subjects, it was found that the response sequences

produced by the patients with schizophrenia show stronger interdependence<sup>[4]</sup>. Schizophrenic patients lack synchronous alternation ability in completing memory tasks. There are differences in brain activity between patients and normal people in frontal and temporal lobes<sup>[5]</sup>. Akar *et al.* used approximate entropy (AE), Shannon entropy, Kolmogorov complexity (KC) and Lempel-Ziv complexity (LZC) to analyse EEG complexity. Compared to normal people, the complexity of schizophrenic patients was lower, and there were significant differences in the left frontal lobe (F3) and parietal lobe (P3) regions of the brain. Compared with other eigenvalues, KC could detect EEG complexity more sensitively in patients with schizophrenia. In addition, there were significant hemispheric complexity differences in the frontal and parietal regions of the brain<sup>[6]</sup>. Nugent *et al.* analysed the brain source connectivity in resting state and task state of schizophrenia patients. It was found that the average connectivity of schizophrenia patients and normal people was significantly different in  $\theta$  band, and the scalp oscillation power of schizophrenia patients was higher than that of normal people<sup>[7]</sup>.

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Schizophrenia is a very common mental disorder, and it seriously endangers human health. The in-depth study of brain signals of schizophrenic patients can provide reference for clinical diagnosis and bring hope for the rehabilitation of schizophrenic patients.

## MATERIALS AND METHODS

### Magnetoencephalographic data of schizophrenia:

The MEG data used are from the NIH (National Institute mental Health) Research Center. The magnetoencephalographic data were collected by a 275-channel CTF-275 magnetoencephalograph. The subjects include 10 healthy subjects and 10 schizophrenics. In the experiment, the subjects were in a closed-eye resting state. The acquisition time of magnetoencephalographic signals was 4 min and the sampling frequency was 600 Hz. Before extracting features, the signal was pre-processed as follows: firstly, the signal was filtered by 0.1-50 Hz band-pass filter, then principal component analysis combined with independent component analysis was used to remove artifacts such as eye and electrocardiograph (ECG), and the sampling frequency was 150 Hz. The 40 s data of beginning and end were removed, and the actual analysis time was 160 s, so that the data of each participant was a group of  $273 \times 24000$  data array.

### Extraction of characteristic parameters of magnetoencephalographic signals in schizophrenia:

Before feature extraction, MEG signals were windowed and segmented into stationary signals with 200 sample points per segment. Firstly, feature parameters such as model coefficients, bandwidth energy, AE and LZC were extracted, and 12 feature parameters were obtained from each segment of data. In order to visually represent the extracted features, the average and standard deviation of frequency band energy characteristics, AE and LZC were calculated, respectively. 20 subjects were divided into 10 groups, each consisting of one normal person and one schizophrenic patient. According to Eqn. 1, the separability measure  $J$  was calculated for 273 channel data of each group, and all channels were arranged in descending order according to  $J$  value, and the first 80 channels were selected. Of the 80 channels in 10 groups, channels with more than 6 occurrences were selected. Eqn. 1,  $J = trS_b / tsS_w$ .

### Back propagation (BP) neural network and support vector machine (SVM) network selection channel:

Channel selection for BP neural network and SVM

classifier was done on the basis of distance criterion, LRS (Plus-L Minus-R selection) algorithm was used to further select the 21 selected channels. In LRS algorithm, each time a one-dimensional feature of 12-dimensional features was used as the data sample of the classifier, and the classification accuracy of the classifier was used as the evaluation function. The algorithm stops when the number of channels was 15. Genetic algorithm combined with BP neural network selection: genetic algorithm was used to select features. Table 1 is the parameter setting of genetic algorithm, the maximum evolutionary algebra was 100, and the fitness function is defined as the classification accuracy of classifier.

### Design of experimental system:

The experimental system mainly included four stages, signal acquisition, pre-processing, feature extraction and pattern classification. Pre-processing is mainly used to eliminate the interference signals in the steady state visually evoked potentials (SSVEP) signal. In feature extraction part, DFT, CCA and MSI were used to extract the features of SSVEP signal. Considering the real-time performance of brain-computer interface (BCI) system, a simple and efficient value comparison method was used for classification. Feature extraction and classification methods were used to identify the subjects' gaze targets. These algorithms are very important to the performance of the whole BCI system. Design and implementation of visual stimulation interface: during the experiment, all stimuli were presented to the subjects simultaneously. The subjects focus on one stimulus, and the oscillating component of the EEG signal was the evoked SSVEP signal. When designing stimulator, the effects of stimulator equipment, stimulus frequency and stimulus colour on SSVEP signal should be considered.

NeuroScan EEG acquisition system was used to collect EEG signals. The system included Synamps2/RT amplifier, 64-conductive electrode cap and Curry7 analysis software. Synamps2/RT amplifier included

**TABLE 1: GENETIC ALGORITHM PARAMETERS**

Items	Parameters
Population size	20
Stopping criteria	Maximum evolutionary algebra
Initialization	Uniform distribution in [0,...,1]
Selection	Roulette selection
Crossover	Single point crossover
Mutation	Boundary mutation

two parts, a control box (system) and an amplifier (head box). The position of 64-conductive electrode cap electrode meets the international 10-20 system standard. The parameters of the amplifier such as sampling frequency and available electrodes, were set by Curry7 analysis software, and the impedance of each electrode is displayed online. In addition, the software can also pre-process the collected EEG signals, including baseline correction, removal of direct current (DC) drift, removal of eye, and filtering subsection.

### EEG experimental process:

The subjects were made to sit 60 cm away from the display. The four stimulation frequencies were 7.5, 8.57, 10 and 12 Hz, respectively. There were three healthy male subjects aged 20-25. Participants were required to complete two sessions, each session consisting of 10 trials. Each trial participant continued to watch the flicker of a block on the interface for 16 s. The target stimulation frequency of session 1 was 8.57, 12, 7.5, 12, 10, 8.57, 10, 10, 12, and 12 Hz; the target stimulation frequency of session 2 was 12, 8.57, 7.5, 10, 12, 12, 7.5, 10, 8.57 and 10 Hz. When the subjects looked at the target stimulus at a certain frequency, they could detect the same frequency of SSVEP signal and harmonic signal, which were mainly distributed in the occipital lobe of the brain. The data of O1, O2, Oz and VEO were recorded. VEO is a vertical eye signal. The electrode impedance was less than 5000 Euros and the sampling frequency of SSVEP was 500 Hz.

### EEG frequency recognition:

Signal pre-processing was using Curry7 software to pretreat the collected SSVEP signal. Covariance method was used to remove the eye artifacts and segment the data in different time windows. SSVEP frequency recognition based on DFT, Fourier transform is generally used to process linear steady-state signals. The segmented SSVEP signals can be approximately regarded as linear steady-state signals. The collected data were divided into two overlapping segments for 2 s, and the DFT was carried out on the segmented data that are the spectrum of the SVEP signals of 7.5, 8.57, 10 and 12 Hz, respectively. Segmentation with overlapping multi-time windows for the data of three subjects was conducted, and the data after segmentation were performed with DFT. The energy at all four stimulation frequencies was calculated and the frequency corresponding to the maximum energy was used as the target frequency recognized.

## RESULTS AND DISCUSSION

Six AR model coefficients, four frequency band energies, one AE feature and one LZC feature obtained by extracting the characteristic parameters of the signal. Finally, 12 characteristic parameters were obtained from each segment of the data. In order to visually represent the extracted features, the average and standard deviation of band energy characteristics, AE and LZC were calculated, respectively. Fig. 1 shows the energy of four bands,  $\delta$ ,  $\theta$ ,  $\alpha$ , and  $\beta$ . Fig. 2 shows the AE and LZC.

Because there were redundant channels in 273 channels of MEG signal, the distance criterion was used to pre-select 273 original channels. Separability measure J was calculated for 273 channel data of each group,

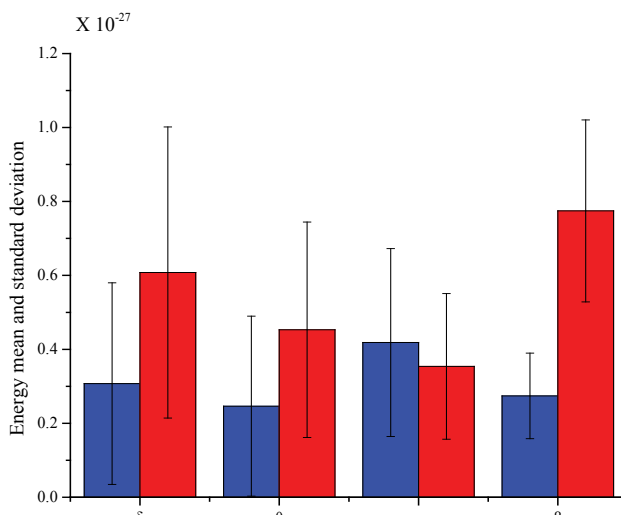


Fig. 1: Average and standard deviation of band energy characteristics

■ Normal person, ■ patient

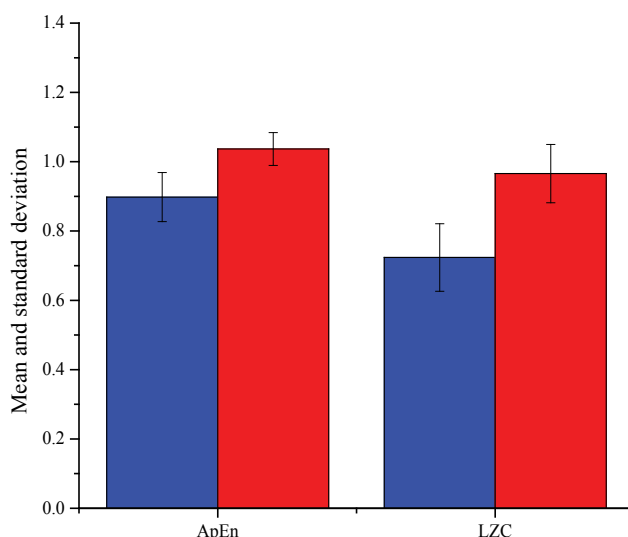


Fig. 2: Mean and standard deviation of ApEn and LZC features

■ Normal person, ■ patient

and all channels were arranged in descending order according to J value. Separability measure of the first 80 channels was selected as shown in fig. 3. The results of channel selection based on BP neural network and SVM classifier are shown in Table 2. The shadows in the table represent the channels in the temporal lobe.

As can be seen from Table 2, most of the selected channels are located in the temporal lobe region, which indicates that the channels in the temporal lobe region may carry more differential information. In addition, the evaluation function values of the 6<sup>th</sup> order AR coefficients were relatively high, and the highest classification accuracy could reach 98.75 %. Twelve channels, MRF25, MRC15, MRF65, MLO42, MRF44, MRT31, MRF14, MRT11, MLO41, MRT2 2, MRT53 and MRF35, which appear at least nine times in the 12 columns screened by BP, are selected as the final result of LRS algorithm based on SVM classifier. Similarly, 13 channels, MLO41, MRT 24, MLC 42, MRF 14, MRT 11, MRF 65, MRT 31, MRT 44, MRF 44, MRT 51, MRT 32, MRT 21 and MRF 25, which appear at least nine times in 12 columns of SVM screening channels, were selected as the final results of the BP neural network-based LRS algorithm. After using LRS method to select channels based on BP neural network classifier, there were 144-dimensional (12-channel $\times$ 12 features) features, and 156-dimensional (13 channels $\times$ 12 features) features based on SVM classifier selected. Proper feature selection can effectively remove irrelevant and redundant features and improve the learning efficiency of classifiers.

The 80-dimensional features were obtained by combining genetic algorithm with BP neural network. After using genetic algorithm and SVM to select features, the number of features was 75 dimensions, which is nearly half of the number of features reduced compared with 144 dimensions and 156 dimensions before feature selection. The features selected by genetic algorithm were used as training and testing data of classifier. The classification results of MEG signals are shown in Table 3. The final classification accuracy of BP neural network and SVM was 98.5 and 99.75 %, respectively. Comparing the classification results before and after feature selection, it was found that the true positive rate, the true negative rate and the classification accuracy rate were improved after feature selection by genetic algorithm, and the true negative rate of SVM was 100 %. In addition, the modelling time of BP neural network and SVM was

greatly reduced after feature selection, and the running speed of classifier was significantly improved. By comparing BP neural network with SVM classifier, it was found that the classification result of SVM is better than that of BP neural network, and the modelling time was shorter, so in general, the performance of SVM was better than that of BP neural network.

SSVEP signals were generated by periodic visual stimuli of a certain frequency. In addition to the main fundamental component, they usually contain harmonic components. In DFT analysis, the results are shown in fig. 4A-D. It is obvious that the peak energy of the signal appears at the target stimulus frequency.

The data of three subjects were divided into overlapping segments with multiple time windows. The data after segmentation were carried out with DFT and the energy at all four stimulation frequencies was calculated. The frequency corresponding to the maximum energy was used as the target frequency recognized. The results of SSVEP frequency recognition based on DFT method are shown in fig. 5. With the increase of data length, the recognition accuracy was improved.

A multi-dimensional complexity-based method for the analysis of magnetoencephalographic signals in schizophrenia was proposed. The method of genetic algorithm combined with BP neural network and SVM was used and the classification accuracy of magnetoencephalographic signals in schizophrenia and normal people was 98.5 and 99.75 %, respectively. At the same time, EEG experiments based on SSVEP were designed and EEG data of many subjects were successfully collected. Spectrum analysis of SSVEP signals was carried out by DFT method. It was found that the energy of signals was the largest at the target stimulus frequency, and the recognition accuracy was increased with the increase of data length. It is helpful to further understand the basic pathogenesis of brain

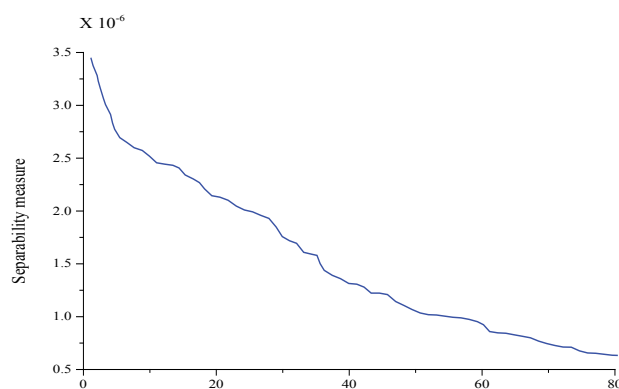


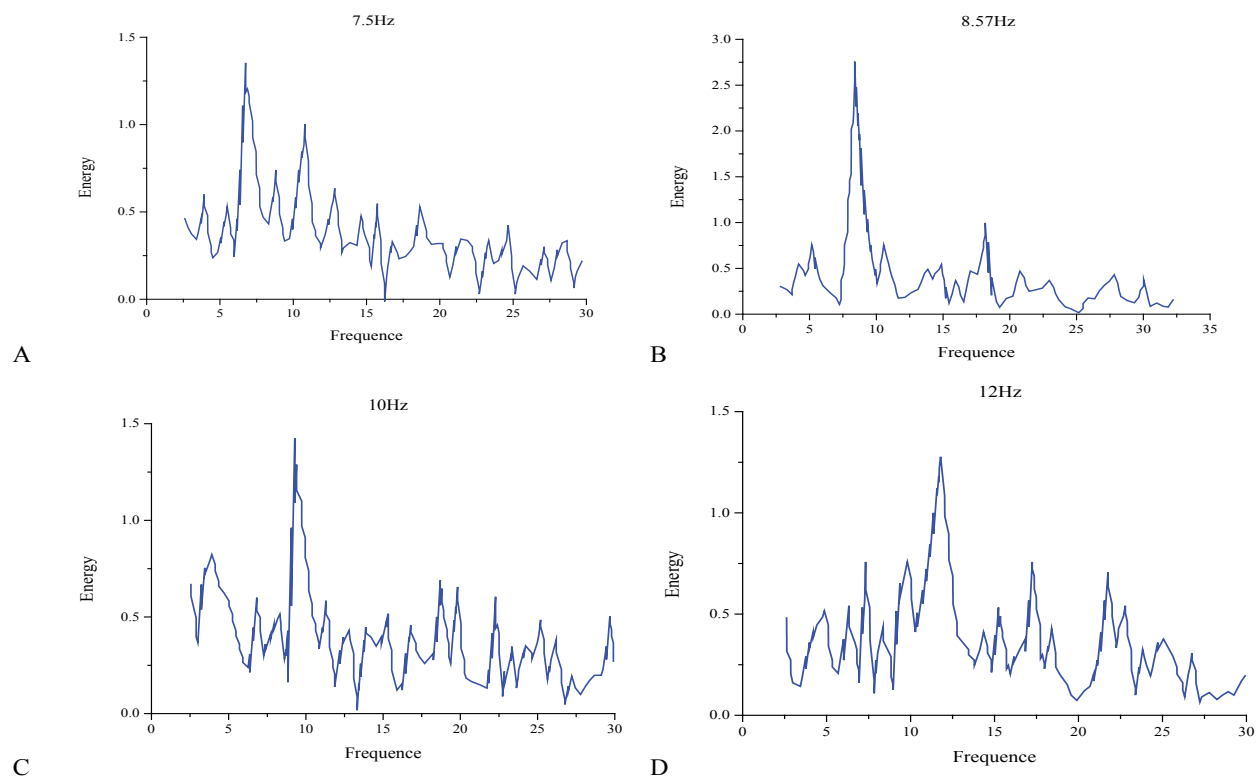
Fig. 3: Separability metrics for the first 80 channels

**TABLE 2: LRS CHANNEL SELECTION (BP) AND (SVM)**

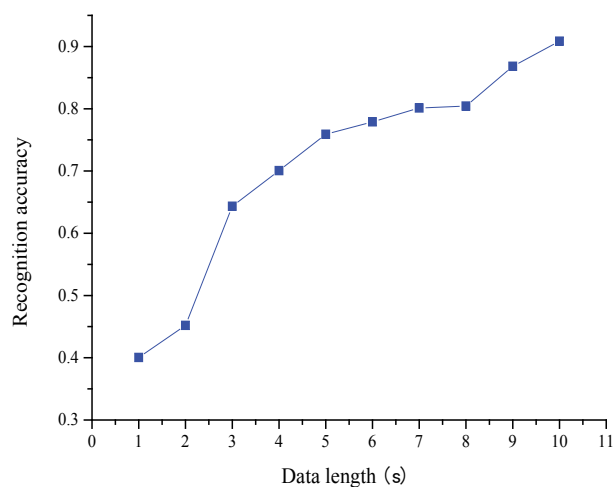
Classification characteristics	AR <sub>1</sub>	AR <sub>2</sub>	AR <sub>3</sub>	AR <sub>4</sub>	AR <sub>5</sub>	AR <sub>6</sub>	$\alpha$	$\beta$	$\delta$	$\theta$	ApEn	LZC
LRS channel selection (BP) screening channel	MRT24	MLO41	MRT24	MLC42	MRT24	MRT53	MRT52	MLO42	MLO41	MLO41	MLO41	MRT44
	MRT44	MRT24	MLC42	MRF65	MRF65	MLO42	MRF35	MRC15	MRT22	MRC15	MRF65	MLC42
	MLC42	MRF65	MRC15	MRC15	MRC15	MRC15	MLO42	MRF65	MRF65	MRF44	MLC42	MLO42
	MRT41	MLC42	MRF65	MRT24	MLC42	MRF65	MRT11	MRF14	MRT31	MRF14	MRT11	MRT31
	MRT42	MRT44	MLO42	MRT32	MRF44	MRT52	MRC15	MRF35	MRF35	MRF35	MRF25	MLO41
	MRF25	MRC15	MRT42	MLO42	MRT11	MRF25	MRT31	MRT44	MRC15	MRT11	MRT22	MRF44
	MRC15	MRT31	MRT52	MRT41	MRT51	MRF44	MRT51	MRF25	MRT32	MRT51	MRT31	MRT52
	MRF65	MRF14	MRT53	MRF14	MRT52	MRT32	MRF65	MRT31	MRF44	MRT31	MRT44	MRT53
	MRT32	MRT41	MRT21	MRF35	MRF25	MRT42	MRT53	MRT22	MRT11	MRT22	MRT52	MRT51
	MLO42	MRT22	MRT44	MRF44	MRT53	MRT22	MRF14	MRT42	MRT24	MRT53	MRT41	MRF35
	MRF44	MRT32	MLO41	MRT22	MLO42	MRT21	MLC42	MRT21	MRF25	MRF25	MRF44	MRF25
	MRT31	MRF44	MRT11	MRT51	MRF14	MLO41	MRT42	MRT51	MRT53	MRT52	MRT53	MRT22
	MRT21	MRT53	MRF44	MRF25	MLO41	MRF35	MRT22	MRT11	MRT44	MRT21	MRF35	MRC15
	MRF14	MRT51	MRT31	MLO41	MRT31	MRT31	MRT32	MRT52	MLO42	MRT44	MRT24	MRT11
MRT11	MRT42	MRF14	MRT21	MRF35	MRF14	MRT21	MRT41	MRT41	MRF65	MRF14	MRF14	
Evaluation function	95.25	96.25	96.75	96.25	93.5	85.75	70.75	75.25	77	76.25	72.5	65.75
LRS Channel selection (SVM) screening channel	MLO41	MLO41	MRF65	MRT24	MLO42	MRF65	MRF44	MRF44	MRT44	MLO41	MLO42	MLO41
	MRT52	MRT24	MRC15	MLO41	MRF65	MRT32	MRT31	MRT11	MLC42	MLC42	MRT44	MRT42
	MRT24	MRF65	MLO42	MLC42	MRC15	MLC42	MLO42	MRT21	MRT52	MRT41	MRF65	MLO42
	MLC42	MRC15	MRT24	MRT51	MRT24	MRT22	MRC15	MLC42	MRF65	MRT52	MRT41	MRT41
	MRF14	MRF35	MRT44	MRF44	MLC42	MRT53	MLC42	MRT24	MRC15	MRT53	MRT32	MRF44
	MRT11	MRF44	MRF44	MRC15	MRF44	MRT41	MRT11	MRF25	MLO41	MRF35	MRT51	MRT51
	MRC15	MRF14	MRF14	MRF14	MRT21	MRT42	MRF35	MRT32	MRT53	MRT21	MRF44	MRF14
	MRF65	MRT21	MRT21	MRT44	MRF25	MRT52	MRT44	MRF14	MRT24	MRT22	MRF14	MRF65
	MRT31	MRT51	MRT51	MRT31	MRF14	MRT51	MRT21	MLO41	MRT51	MRT32	MRT21	MRT24
	MRT44	MRT53	MLO41	MRT11	MRF35	MRT21	MRT24	MRT41	MRT22	MRF65	MRT53	MRT32
	MRF44	MRT42	MRF25	MRF25	MLO41	MRT44	MRT32	MLO42	MRF25	MRT51	MLC42	MRT52
	MRT22	MRT32	MRT53	MRT42	MRT31	MRT11	MRT52	MRT22	MRF35	MRT11	MRF35	MRT31
	MRT51	MRT31	MRT11	MRT21	MRT11	MRF44	MRF25	MRT31	MRT11	MRF44	MRT42	MRC15
	MRT32	MRT52	MRF35	MRT41	MRT44	MRF35	MRF65	MRT51	MRF14	MRT24	MRT31	MRT44
MRT42	MRF25	MRT31	MRT53	MRT22	MRF25	MRT51	MRT42	MRT32	MLO42	MRT22	MRF25	
Evaluation function	96	98.25	98.75	98.75	97.5	88	74	77.25	77.25	86.25	77.5	67.2

**TABLE 3: CLASSIFICATION RESULTS**

Items	Before feature selection		After feature selection	
	BP	SVM	BP	SVM
Feature dimension	144	156	80	75
True positive rate (%)	97.5	99	98.5	99.5
True negative rate (%)	95.5	98.5	98.5	100
Classification accuracy (%)	96.25	98.75	98.5	99.75
Modeling time (s)	2.64	2.34	0.7	0.44



**Fig. 4: DFT (A) 7.5 Hz, (B) 8.57 Hz, (C) 10 Hz, (D) 12 Hz spectrum**



**Fig. 5: DFT-based SSVEP frequency recognition results**

diseases and provide reference for clinical diagnosis of brain diseases.

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