Cross-Modulated Amplitudes and Frequencies of Epileptic EEG

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Abstract. Epilepsy is a neural disorder with the hallmark of recurrent seizures. To characterize the epileptic brain electrical activities, we employed the cross modulation of instantaneous amplitudes and frequencies to separate synchronous and anti-synchronous modulation. Amplitude-amplitude, amplitude-frequency and frequency-frequency cross modulation were adopted to analyse the difference between EEG signal of epileptic patients and that of normal people. By comparing the observed patterns with two groups of EEG signals we demonstrate that the cross-modulation exponentials at the temporal region and the occipital region of right hemisphere are significant different.

1. Introduction
The brain is the commander of all human activities. The neuron cells send electrical signals and produce a small electric field. Brain cells with electric allow electrodes to pick up electrical signals generated during brain activity by placing them in a standard position on the surface of the brain. The potential difference in different positions of the skull can be measured, and the weak electrical activity in the brain can be recorded regularly by using the potential difference.

Epilepsy is a kind of chronic disease of the brain, the seizure of epilepsy is usually due to excessive discharge of brain cells. Electroencephalogram (EEG) signals has played an important role in the activity of the brain, especially in diagnosis of epilepsy.

1.1. Previous Work
Some success have been achieved in study of EEG signals of the epileptic patients. Serval were based on an artificial neural network (ANN) to detect the seizure, but the direct comparison of seizure detectors would be very difficult if the detectors are not tested on the same data set [1]. There are also some research based on wavelet transform and approximate entropy. This method used discrete wavelet transform (DWT) to get approximation and detail coefficients and calculate the approximate entropy (ApEn) [2] values, and then find the difference by comparing the ApEn values. In the past few years, some wearable devices have appeared, such as an e-glass based on four EEG electrodes [3]. There are also some devices based on a self-learning methodology for epileptic seizure detection.
without medical supervision [4]. These methods and devices are expensive and complicated. We hope to use some new methods to make the diagnosis and detection of epilepsy easier.

1.2. Introduction to This Paper
In this paper, quantifying non-linear interactions between oscillatory in the human brain is the key. We employed amplitude and frequency cross-modulation analysis technique to EEG signals of the epileptic and the normal. Then this article compare the difference between them. This method is an effective way to analyse the simultaneously recorded time series for non-linear interactions. Especially, the approach let us observe how amplitude or frequency of EEG signal in a specific position or in a particular frequency band affects another signal’s amplitude or frequency. What deserves to be mentioned is that the epileptic patients in this paper are patients with symptomatic epilepsy.

2. The Basic Principle of Cross Modulation
The whole process of cross modulation is shown in the flowchart (figure 1).

![Flowchart of the method](image)

Figure 1. Flowchart of the method

In general, EEG signals are often divided into different positions and different frequency bands. According to the international standard rules, the international electroencephalogram society has stipulated the standard electrode mounting method. According to the International 10-20 electrode placement system, the electrodes were placed on the surface of the skull to get the EEG signals [5]. In this paper, 16-channel (Figure 2) EEG signals of epileptic patients and their control group were obtained by using 16-channel EEG acquisition system. The 16 channels are Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, and T6 respectively.

There are 16 leads EEG signals corresponding to 16 electrodes. Next steps, six sequences of six frequency bands are extracted from each raw EEG signal. FFT band-pass filter in Hamming window is
used to complete the extraction operation [6], keeping the Fourier coefficients in a particular range, as shown in Table 1.

In this paper, we define $M = 96$ because each subject has 16 leads EEG signals and each EEG signal would be decomposed into six frequency bands. Then the time series $x_k = 1, 2, ..., M$ is obtained.

Table 1. Six frequency bands for eeg signals.

| Band | Frequency (Hz) | Band | Frequency (Hz) | Band | Frequency (Hz) |
|------|----------------|------|----------------|------|----------------|
| $\delta_1$ | 0.5-1.99 | $\theta$ | 4-6.99 | $\sigma$ | 11.5-11.99 |
| $\delta_2$ | 2-3.99 | $\alpha$ | 7-11.49 | $\beta$ | 16-22 |

Hilbert transform was employed to the 96 EEG signals. Firstly, complete the sequence $x_k$ with an imaginary part $ix_k$.

$$ix(t) = \frac{i}{\pi} P.V. \int_{-\infty}^{\infty} \frac{x(t)}{t-t'} dt',$$

where P.V. stands for Cauchy Principal Value [7].

Then the amplitude sequence $A_k$ and the frequency sequence $f_k$ can be obtained by (2), (3) and (4),

![Figure 3](image-url). Example of the raw signals, the imaginary part, the amplitudes and frequencies
Figure 3 is an example of the extraction of $\delta_1$-band signals. Figure 3(a) is the raw EEG signal. Blue in Figure 3(b) is the extraction of $\delta_1$-band from the raw EEG signal and the red is the imaginary part. Figure 3(c) and Figure 3(d) are $\mathcal{X}_{\omega}$ sequence and $\mathcal{S}_{\omega}$ sequence respectively.

In order to study the long-term correlation and prove the amplitude time series and frequency time series are independent respectively, then calculate the Hurst exponent of $\mathcal{X}_{\omega}$ and $\mathcal{S}_{\omega}$. This paper use the centred moving average (CMA) technique [8] instead of the detrended fluctuation analysis (DFA). When Hurst exponent is about 0.5, it means the time series has no long-term correlation, while the Hurst exponent is greater than 0.55, the sequence is long-term correlation data [9]. Moreover, the result of the calculation indicates that the Hurst exponents of $\mathcal{X}_{\omega}$ and $\mathcal{S}_{\omega}$ are both more than 0.7.

To quantify the interactions between the amplitude sequence and frequency sequence, the next is to study the cross correlation between them. As mentioned above, the data of each subject would be decomposed to 96 amplitudes $A_k$ and 96 frequencies $f_k$. So there are a total of $(96 \times 2) \times (96 \times 2) = 36864$ pairs. For each of the 36864 pairs, we apply a second Hilbert transform to the amplitudes $A_k$ and frequencies $f_k$ respectively instead of $x_k$ to get the instantaneous phases $\varphi_{k1}$ and $\varphi_{k2}$, the formulas are shown as (2), (3) and (4). Obtain the coefficient exponentials according to (5), and then average their exponentials over segments $v$ of 0.1s:

$$\mu_v = \exp \left[ i \left( \varphi_{k1} - \varphi_{k2} \right) \right].$$

The last step is averaging all $|\mu_v|$ belonging to segments of the same type of person (the epileptic and the normal) [10] and the data include 22 epileptics and 22 normal people. Figure 4(a) shows the phase of the amplitudes (see Figure 3(c)) and the frequencies (see Figure 3(d)), and Figure 4(b) shows $\mu_v$.

Most phase differences $\varphi_{k1} - \varphi_{k2}$ is about 0 or about $\pm \pi$. Then consider that when the phase differences are about 0 the modulation is synchronous and when the phase differences are about $\pm \pi$ the modulation is anti-synchronous. To distinguish these two cases, sum the $|\mu_v|$ with phases of $\mu_v$ in the interval $\left(-\frac{\pi}{2}, \frac{\pi}{2}\right)$ and the other. Then average their exponentials over segments $v$ of 0.1s to eliminate the effects of random events.
After the process above, two complex coefficients are obtained from each pair, $\mu^+$ and $\mu^-$. The 36864 coefficients for synchronous modulation and 36864 coefficients for anti-synchronous modulation are shown in Figure 5 and Figure 6. This paper use a color-coded matrix to describe the modulation coefficients of the same type of person. In both cases, the Figure 5(a) and Figure 6(a) shows the analysis of instantaneous amplitudes and the Figure 5(d) and Figure 6(d) shows the analysis of instantaneous frequencies. The upper triangle shows the exponentials of synchronous modulation while the lower triangle shows the exponentials of anti-synchronous modulation. The Figure 5(b) and Figure 6(b) and Figure 5(c) and Figure 6(c) shows the result of amplitude-frequency cross-modulation and (b) represents for synchronous modulation, (c) represents for anti-synchronous modulation. The different colours means different modulation exponentials and the exponentials increase from dark blue to red. The first 16 rows and 16 columns refer to different frequency bands, they are respectively Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6. Others are in the same.

![Figure 5](image1.png)

**Figure 5.** Color-coded matrix of the cross-modulation of the epileptic

![Figure 6](image2.png)

**Figure 6.** Color-coded matrix of the cross-modulation of the normal

### 3. Data and Analysis

22 healthy volunteers (aged 15 to 49, mean 26.95 ± 8.91 years) and 22 epileptic patients (aged 4 to 51, mean 30.0 ± 13.1 years) are recruited from Nanjing General Hospital of Nanjing Military Command [11, 12]. EEG recordings are in duration of around 1 min and sampled with 512 Hz. Epileptic patients are all in their non-seizure intervals during brain activities collection and all of the subjects are in idle states. The time intervals between the data recording and nearest seizures of the epileptic patients are about 20 to 30 days. The data has done artifact rejection.
The results of applying cross-modulation to these EEG signals are shown in the Figure 5 and Figure 6, describing the size of modulation exponentials of the epileptic and the normal respective.

The Figure 5(a) and Figure 6(a) show strong anti-synchronous inter-band amplitude modulation while the synchronous exponentials of amplitude modulation is small in both two pictures. Each 16×16 matrix in the anti-synchronous part is close to the diagonal obviously. This is because the interaction at the same location is strong. In the synchronous part, the values of the matrices near the diagonal are also bigger than those in the upper right triangle. This shows that the interactions between the amplitudes in the same frequency band are enhanced.

The Figure 5(d) and Figure 6(d) show similar characteristics to part (a), but the value is bigger than the value of part (a).

The Figure 5(b) and Figure 6(b) show the synchronous amplitude-frequency cross-modulation exponentials. The coefficients have little fluctuation. After the process of averaging, stabilized around one. The synchronous amplitude-frequency cross modulation of both groups is not obvious.

The Figure 5(c) and Figure 6(c) reveal positive amplitude-frequency cross modulation of $A_k$ in high frequency with $f_k$ in all frequency bands, especially $\delta_2$, $\theta$ and $\alpha$ band. Traces of modulation of $f_k$ in $\delta_2$, $\theta$ and $\alpha$ bands with $A_k$ in $\alpha$, $\sigma$ and $\beta$ bands are observed in both two pictures, especially in O2 and T6 leads. The relations can be explained that the change of $f_k$ in $\delta_2$, $\theta$ and $\alpha$ band can affect the amplitudes in $\alpha$, $\sigma$ and $\beta$ bands.

This enhanced relationship can be observed more clearly in the color-coded matrix of the normal than in the matrix of the epileptic when $f_k$ is in $\delta_2$, $\theta$ and $\alpha$ bands and $A_k$ is in $\alpha$ band at two EEG leads (O2 and T6). The two EEG leads, O2 and T6, are at the temporal region and the occipital region of right hemisphere. It shows that the abnormal movement of epileptic is, in essence, a reduction in $\alpha$ activity near the occipital of right at the temporal region and the occipital region of right hemisphere and an increase in the $f_k$ in $\delta_2$, $\theta$, $\alpha$ and $\sigma$ bands. If it is interpreted as a loss of complexity in brain electrical activity, these changes could reflect the hypothesized continuous increase of synchronization between pathologically discharging neurons and allow one to study seizure-generating mechanisms in humans. Temporal lobe epilepsy and occipital lobe epilepsy are both common types. Lesions in the temporal lobe cause hearing and balance problems, mostly manifested as symptoms of seizures.

Another prominent features present in the matrix of the normal but not in the matrix of the epileptic is a negative modulation of $f_k$ in $\alpha$ band with $f_k$ in $\beta$ band which is related with phase synchronization between $\alpha$ and $\beta$ brain waves.

4. Discussion

Previous research has shown that the anti-synchronous amplitude-frequency cross modulation exponentials of the epileptic are different to the exponentials of the normal at O2 and T6, especially when the frequencies are at $\delta_2$, $\theta$ and $\alpha$ bands and the amplitudes are at $\alpha$ bands. To study whether there are significant differences between the exponentials of the epileptic and the normal, we used the independent sample t-test to two sequences, one of them is the 22 cross-modulation exponentials at O2 or T6 leads of the epileptic at a particular band and the other is the exponentials of the normal.

We discover that the probability are about 0.01 and 0.05 respectively when the frequencies are at $\delta_2$ band and the amplitudes are at $\alpha$ band at O2 or T6 leads. We can conclude that the anti-synchronous amplitude-frequency cross modulation exponentials at O2 and T6 leads when the amplitudes are at $\alpha$ band and the frequencies are at $\delta_2$ band are significant different between the epileptic and the normal.

Mentioned in some related publication, the attractor of the $\alpha$ band has high complexity in epileptic patients during seizure-free intervals in the study of wavelet-chaos methodology [13]. This is similar to the result of this paper.

5. Conclusion

The cross modulation technique was used to calculate the modulation exponentials and the matrices were drawn. The comparison of the two groups of data shows some commonalities, and also shows that the EEG signals of the epileptic at the temporal region and the occipital region (O2 and T6 leads)
are different from the normal. Change of EEG signal’s amplitude at O2 and T6 leads would cause an abnormal deviation of the frequency.

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