Characteristics analysis of acupuncture electroencephalograph based on mutual information Lempel–Ziv complexity*

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As a convenient approach to the characterization of cerebral cortex electrical information, electroencephalograph (EEG) has potential clinical application in monitoring the acupuncture effects. In this paper, a method composed of the mutual information method and Lempel–Ziv complexity method (MILZC) is proposed to investigate the effects of acupuncture on the complexity of information exchanges between different brain regions based on EEGs. In the experiments, eight subjects are manually acupunctured at 'Zusanli' acupuncture point (ST-36) with different frequencies (i.e., 50, 100, 150, and 200 times/min) and the EEGs are recorded simultaneously. First, MILZC values are compared in general. Then average brain connections are used to quantify the effectiveness of acupuncture under the above four frequencies. Finally, significance index P values are used to study the spatiality of the acupuncture effect on the brain. Three main findings are obtained: (i) MILZC values increase during the acupuncture; (ii) manual acupunctures (MAs) with 100 times/min and 150 times/min are more effective than with 50 times/min and 200 times/min; (iii) contralateral hemisphere activation is more prominent than ipsilateral hemisphere's. All these findings suggest that acupuncture contributes to the increase of brain information exchange complexity and the MILZC method can successfully describe these changes.

Keywords: electroencephalograph, acupuncture, mutual information Lempel–Ziv complexity method

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1. Introduction

As an important part of Chinese medicine, the effectiveness of acupuncture has been fully demonstrated during long-term clinical experiments. In recent years, in order to reveal the underlying mechanism of acupuncture, position emission tomography (PET), functional magnetic resonance imaging (fMRI) and other advanced technologies have been used to monitor the response of the whole brain to acupuncture and many great achievements have been obtained. The achievements have demonstrated that acupuncturing on some meridians that are related to analgesia, vision and stomach activities has significant modulatory effects on brain functional networks and brain activities.[1−4]

Information transmission is the foundation that guarantees the normal activities of organism. Clinical and experimental data indicate that the acupuncture takes effect by affecting information transmission and generation.[5] For example, the acupuncture-induced analgesia has been achieved by the generation of chemical substances 5-hydroxytryptamine and orphanin FQ.[6] Besides the chemical information, the electrical information is also one of the essential elements in information transmission. However, acupuncture effects have seldom been studied based on electrical information. The cerebral cortex electroencephalograph (EEG) signals directly characterize cerebral cortex electrical information, which reflects not only brain functions, but also states of the whole body. For example, there are obvious differences in the complexity of EEG characteristics between shallow phase and sleep phase, before and after seizures, before and after

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visual stimulation, dementia and normal state.[7−13] Acupuncture can be considered as a kind of external stimulation to the nervous system. Acupuncture information is transmitted mainly through the peripheral nervous system to the central nervous system in the form of nervous impulse. Central nervous system integrates signals to modulate nerve, endocrine, humor network and then influences target organs.[14]

As a consequence of the scale free network organization of neurons, EEG signals which are believed to derive from pyramidal cells aligned in parallel in the cerebral cortex and the hippocampus, carry complex nonlinear system information reflecting the underlying brain characteristics. A great deal of information about brain characteristics remains undiscovered because currently the linear analysis techniques fail even to detect them. That is why nonlinear methods of contemporary physics are much more appropriate to analyse living systems and bio-signals than linear methods traditionally used in medicine.

Many nonlinear and linear methods have been proposed for analysing EEG, such as mutual information, phase synchronization, linear correlation degree, Granger causality, directional coherence, nonlinear causality, correlation dimension, generalized synchronization and phase space reconstruction.[15−18] However, these methods are confined only to the studies of the quantity, direction, synchronization and relevance of the information and the information exchange, but have never been used to investigate the complexity of the information exchange as yet. In this study, the complexity degree of information exchange between different EEG time sequences of electrodes is analysed with Lempel–Ziv complexity (LZC) approach based on mutual information method, named MILZC. As the results show, the complexity degree of information exchange between different regions of brain can be effectively found with this method.

Considering the fact that the acupuncture influences target organs through the central nervous system and EEG signals can reflect body functional states, we study the effects of acupuncture on brain function through analysing EEG signals. These results are believed to be useful to lay a foundation for revealing acupuncture mechanism.

The remaining parts of the paper are organized as follows. In Section 2, the experimental process and data pretreatment are explained. In Section 3, the method MILZC is introduced and certified. In Section 4, the corresponding data analysis and results are presented. Finally, in Section 5 conclusions are given.

2. Experiment description

This experiment was performed on 8 healthy volunteers (at ages 23–27), including 5 male and 3 female persons who had not taken any drug that could affect cognition or EEG activity before. All volunteers had been explicitly informed of the purposes of this experiment. Subjects, who were students majoring in acupuncture and had no fears of this which eliminated the influence on EEG signals recording induced by psychological fear, were explicitly informed of the purposes of this experiment. Since ST-36 is an important meridian on Stomach Meridians (mainly for handling gastrointestinal diseases, dizziness insomnia) and has calm and sedative effects, we manually performed acupuncture by using steel needles at the acupuncture point ST-36 on the right leg. This meridian works effectively and has been widely applied in traditional Chinese medicine (TCM) acupuncture experiments.[19] In this experiment EEG signals (as shown in Fig. 1) of 20-channel (channels Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, OZ, and O2) were recorded.

Four conditions under different-frequency stimulus are discussed in this paper. In order to avoid the influence induced by the acupuncture order of the four-frequency acupuncture method, the order is chosen randomly. The experiment process is shown in Fig. 2. Data 1–6 are six segments we chose: before acupuncture (BA), acupuncture with 50 times/min, 100 times/min, 150 times/min, 200 times/min and after acupuncture (AA). During the recording process, the subjects were instructed to lie still and keep their eyes closed during the whole process in order to obtain as many artifacts-free EEG data as possible.

Data were first processed by a band-pass hardware filter with cut-off frequencies at 0.5 Hz–100 Hz and were sampled at 256 Hz. Figure 1 shows the EEG signals that were recorded from one subject. Only EEG data free from movement artifacts were selected by an acupuncturist visually from recordings. Afterwards, EEGs were organized into 80-s artifacts-free segment for each state (BA, 50 times/min, 100 times/min, 150 times/min, 200 times/min, AA) of each subject. All selected segments were digitally filtered with cut-off frequencies at 0.5 Hz–48 Hz prior to analysis in order to remove residual electromyographic (EMG) activity and the noise due to the electrical mains.

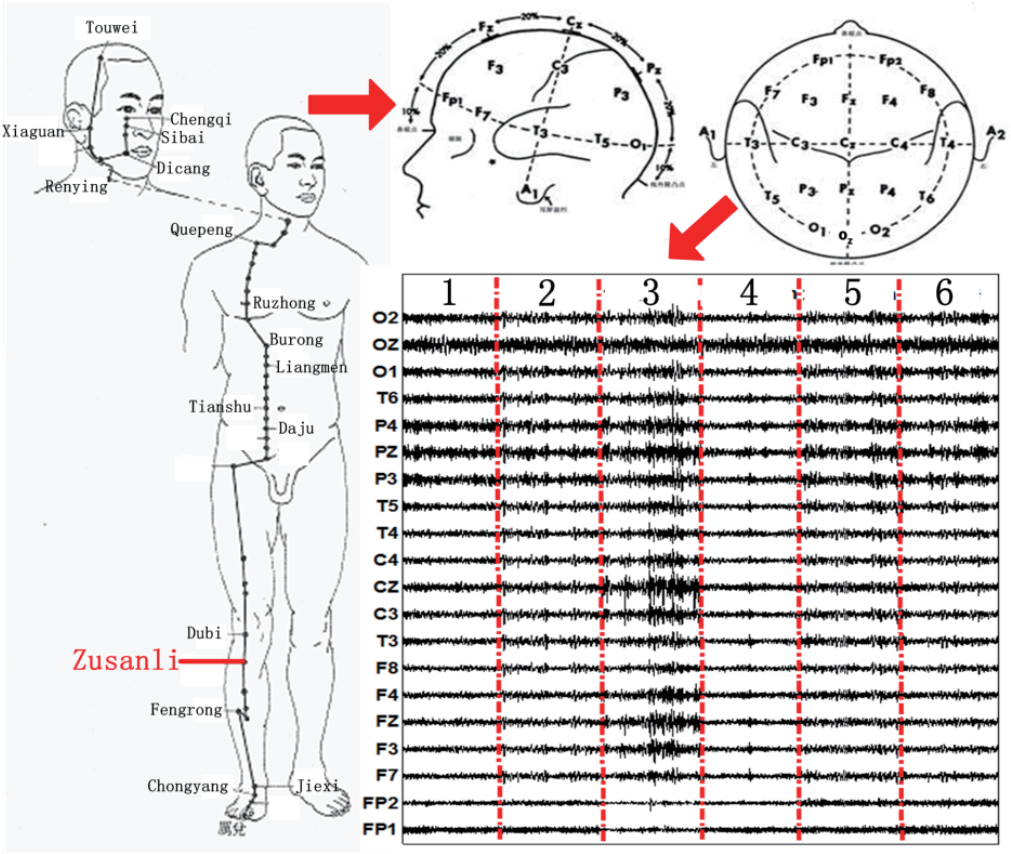


Fig. 1. (colour online) Stomach Meridians, the electrode positions on brain and the corresponding EEG signals of one subject. Numbers 1–6 respectively represent six states: before acupuncture, acupuncture at 50 times/min, acupuncture at 100 times/min, acupuncture at 150 times/min, acupuncture at 200 times/min and after acupuncture.

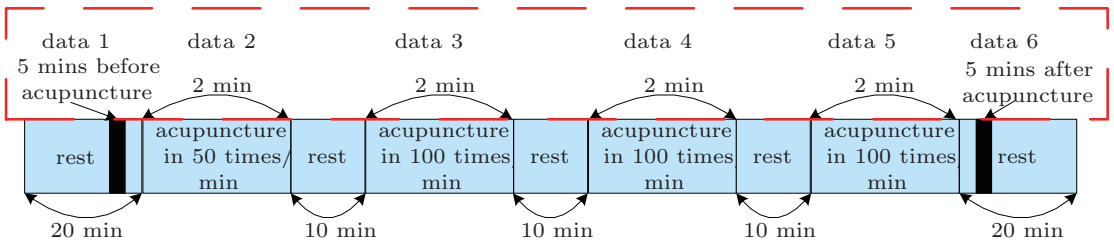


Fig. 2. (colour online) Experiment process.

3. Method

As a measure of correlating two time sequences,[20] mutual information (MI) method is especially effective when the dependence structure is non-linear.[21] This measure essentially shows how much extra information one can obtain from one signal by knowing the outcomes of the others. Thus, if there is no relationship between them, MI is zero. Given two random variables x and y, the MI between them is defined in terms of their probabilistic density functions $p(x)$, $p(y)$ and $p(x,y)$ as

$$I(x;y) = \iint p(x,y) \log \left[p(x,y)/p(x)p(y) \right] \mathrm{d}x \mathrm{d}y. \quad (1)$$

Here, we use the density estimator introduced in Ref. [22] to calculate the MI.

LZC evaluates the complexity degree of time sequence from one-dimensional perspective which is evaluated by the number of distinct substrings and the rate of their recurrence along the given sequence.[23] As a nonlinear complexity measure, since LZC is well suited for characterizing the development of spatiotemporal activity patterns in high-dimensional

nonlinear systems,[24,25] it can effectively reveal the regularity and the randomness in a time varying EEG of the brain system and gain the information regarding the dynamics of the specific regional brain subsystem. So LZC method is widely used in the studies of brain functions, such as predicting seizures of epilepsy[23] and quantizing depth of anesthesia.[26,27]

LZC analysis which is based on a coarse graining of the measurements first transforms the signal into a digital sequence composed of zeros and ones. Then it evaluates the complexity of a finite sequence from the point of view of a simple self-delimiting learning machine which, as it scans a given n digit sequence $S = s_1 s_2 \cdots s_m$, from left to right, adds a new word to its memory every time it discovers a substring of consecutive digits not previously encountered.[28] Complexity counter $c(n)$ is increased by one unit every time a new substring is encountered in the scanning process. $c(n)$ tends to the same value:

$$\lim_{n\to\infty} c(n) = b(n) = n/\log_2 n, \tag{2}$$

where $b(n)$ gives the asymptotic behaviour of $c(n)$ for a random string. $c(n)$ can be normalized by $b(n)$ with the following equation:

$$C(n) = c(n)/b(n). \tag{3}$$

After normalization the complexity measure reflects the rate of new pattern occurring with time. Higher LZC value corresponds to higher complexity of sequence. Obviously $C(n) \to 1$ means that the complexity of the signal reaches a maximum. Moreover, the concept of $C(n)$ is simpler to understand and its computation is easier to implement. Further detailed description of the algorithm can be found in Ref. [29].

The MI method and LZC method are both widely used in EEG signal analysis. However, at present no one has ever combined these two methods together to analyse acupuncture EEG data. MILZC method is proposed by combining LZC method and MI method, which contains the functions and the advantages of the two methods mentioned above. The method is described as follows.

Given two random series x and y (x and y have the same length); denote window length as W_1 and sliding window length as S_1; separate x and y as $\{x_1, \ldots, x_N\}$ and $\{y_1, \ldots, y_N\}$ where N is an integer and $N = (\text{length}(x) - W_1)/S_1$. $x_i = x\{[(i-1)S_1+1] : [(i-1)S_1 + 1 + W_1]\}$ where $1 \le i \le N$, so is the variable y_i. A mutual information sequence $\{i_1, \ldots, i_N\}$ is estimated based on the method mentioned above:

$$i_i = I(x_i, y_i). \tag{4}$$

Given window length W_2 and sliding window length S_2, mutual information sequence $\{i_1, \ldots, i_N\}$ is partitioned into $\{I_1, \ldots, I_M\}$, where integer $M = (\text{length}(i) - W_2)/S_2$. Then the LZC c_i of I_i ($1 \le i \le M$) is calculated by the method mentioned in Subsection 3.2. Finally, the sequence $\{c_1, \ldots, c_M\}$ is averaged to obtain the final MILZC values of x and y.

In order to verify whether this method can reflect the complexity of information exchange between two time sequences, we use coupling chaotic Lorenz sequence and sine sequence to verify the effectiveness of the method. Generally speaking, the information exchange of chaotic system is more complex than that of periodic system. If we can prove this with MILZC method, it can be proved that our method can successfully reflect the complexity of information exchange between two coupling sequences.

The results are shown in Fig. 3. Abscissa axis represents the coupling strength and ordinate axis refers to MILZC value. Comparing Lorenz sequence and sine sequence, MILZC value of Lorenz sequences is significantly higher than the sine sequences' under various coupling strength. This result proves that the MILZC method can successfully reflect the complexity of information exchange between two coupling sequences.

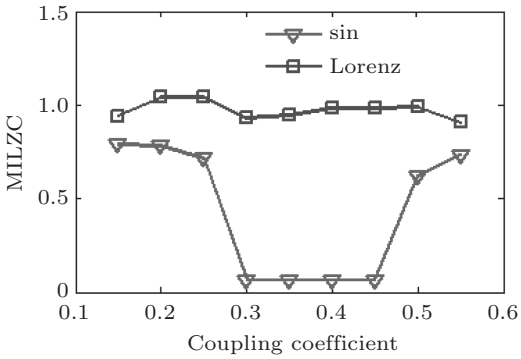


Fig. 3. MILZC values of coupled Lorenz sequence and sine sequence under different coupling strengths.

4. Data analysis

4.1. Mutual information and complexity analysis

We select a time series with 80 s from data between every two channels for each subject under each state and each series is calculated by MILZC method

with parameters $W_1 = 4$ s, $S_1 = 0.16$ s, $W_2 = 0.4$ s, $S_2 = 0.02$ s (sampling frequency: 256 Hz). The data of every subject are transformed into a $20 \times 20 \times 6$ matrix (20 channels $\times$20 channels $\times$6 states).

The results are normalized for the purpose of eliminating the influence of individual differences between different volunteers. The normalization method is as follows: $V_{\max}$, $V_{\min}$, and V_{mean} respectively represent the maximum, minimum and mean element of $20 \times 20 \times 6$ matrix. $V(i,j,k)$ is the element in the matrix, with $1 \leq i \leq 20$, $1 \leq j \leq 20$, $1 \leq k \leq 6$, where i and j represent channels, k represents the state. $V'(i,j,k)$ is the value in the normalized matrix and calculated as follows:

$$V'(i,j,k) = [V(i,j,k) - V_{\min}]/(V_{\max} - V_{\min}). \quad (5)$$

For every subject, a normalized matrix with values between 0 and 1 is obtained. On this basis, the values of same channels in the same states obtained from 8 volunteers are averaged for analysis. Finally a $20 \times 20 \times 6 \times 8$ matrix is turned into a $20 \times 20 \times 6$ matrix.

Figure 4 shows the MILZC values of every two channels in six different states. In this figure, a lighter colour corresponds to a higher MILZC value between the two channels.

As figure 4 shows, the MILZC value increases in the whole process of acupuncture. Comparing the states of 8 volunteers, they all show similar trends in general, but still possess differences in the most effective frequency. Figure 5 shows 6 states of two volunteers, indicating that although MILZC values of different subjects increase during the acupuncture, their most effective frequencies are different from each other. The most effective frequency of subject 1 is 150 times/min while that of subject 2 is about 50 times/min or 100 times/min. It turns out that the difference of body reaction can be successfully reflected by analysing the acupuncture EEG signals with MILZC method, which lay a foundation for EEG real-time monitoring of acupuncture effect.

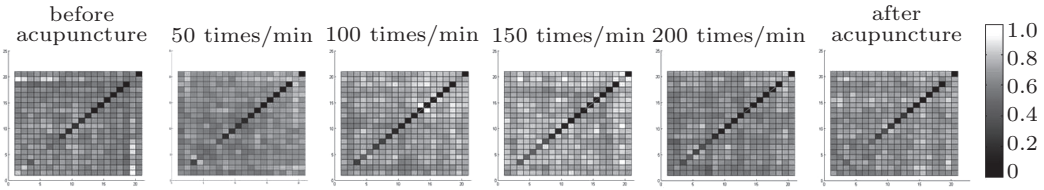


Fig. 4. MILZC values of all volunteers after normalization and average.

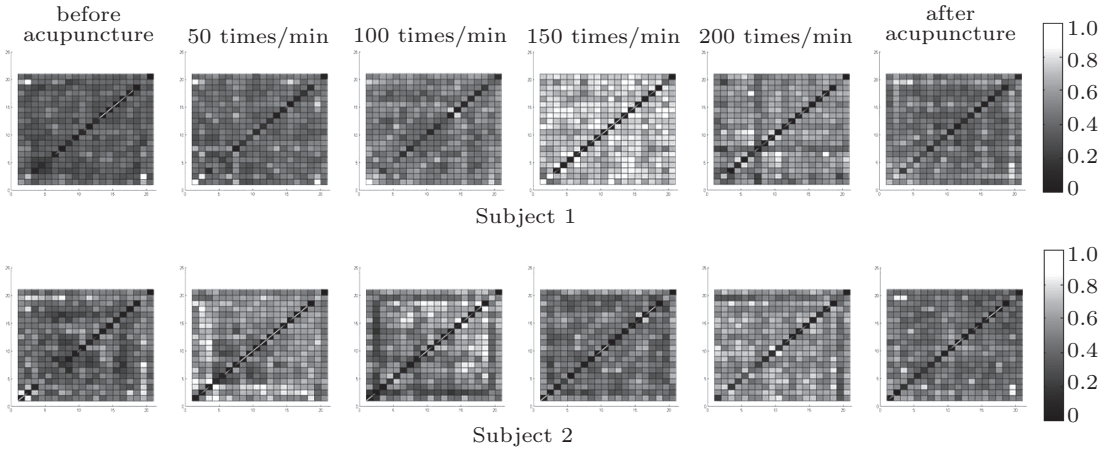


Fig. 5. MILZC values of two subjects.

4.2. Brain region connection analysis

Based on the general analysis mentioned above, the spatial characteristics are analysed by brain region connections. Define a threshold value which presents the average situation of all volunteers' information exchange complexity between different brain regions as the mean MILZC value of all volunteers. When the values of two channels are above the threshold, the information exchange between them is considered as complexity which is represented by a straight line connection. Figure 6 shows brain connections. Connec-

tions between different channels of different brain regions are expressed by different line types as shown in Fig. 6, where LL represent connections within the left brain, LM denotes the connections between left brain and the midbrain, LR refers to the connections between left and right brain, RR to the connections within right brain, RM to the connections between right brain and midbrain and MM to the connections with midbrain. It is shown that the number of connections increases during the acupuncture.

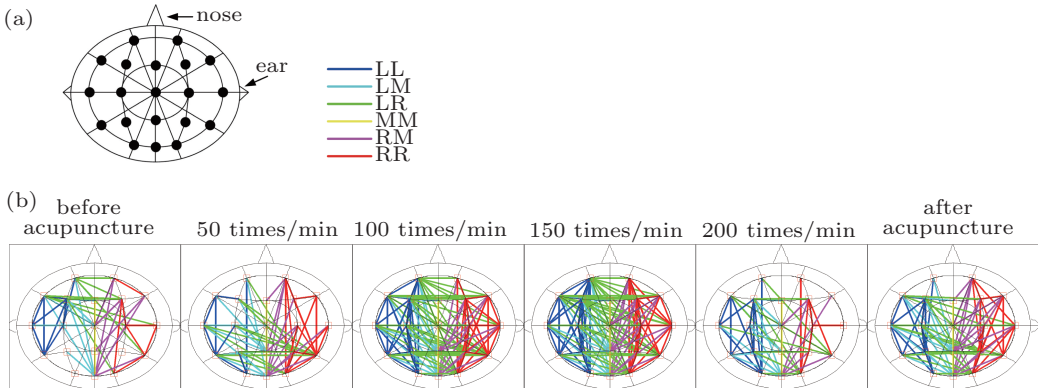


Fig. 6. (colour online) Electrode distributions on the brain and the brain connections. Panel (a) shows the electrode distribution, where the elipse presents brain and every black point refers to the position of electrode. Panel (b) exhibits the brain connections of all subjects after normalization and average.

Figure 7 shows the quantitative comparison between brain connections in different states and different brain regions. In this figure, brain connection number reaches the maximum during the acupuncture under the frequencies of 100 times/min and 150 times/min. This phenomenon means that the information exchange reaches the most complex at these two frequencies, which is the same as the result of acupuncture thesis[31] where effective frequencies of acupuncture are 90 times/min–150 times/min. Furthermore the connection numbers of LL and LM areas in the process of acupuncture are larger than those of RR and RM areas. For the case of acupuncturing the right leg, this phenomenon is consistent with the conclusion: contralateral hemisphere activation is prominent, which was mentioned in Ref. [30] and proved by fMRI.

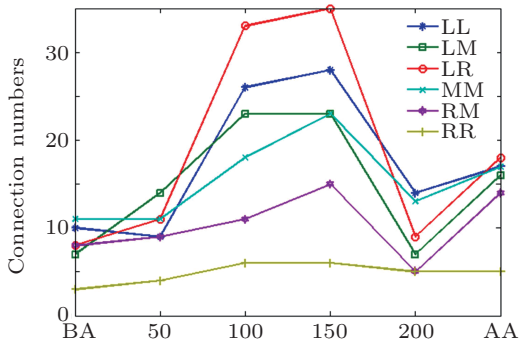


Fig. 7. (colour online) Brain connections of volunteer's different states and different brain regions.

4.3. Reaction of different brain functional areas

The corresponding significance index P values of every-two-channel MILZC value before acupuncture and acupuncture with 150 times/min, are calculated with ANOVA1 method. The ANOVA1 is one-way analysis of variance. The significant index P value resulting from an ANOVA1 test will indicate the probability of outcome under the null hypothesis. If P is near zero, it casts doubt on the null hypothesis and suggests that at least one sample mean is significantly different from the other sample mean. Here we choose

Table 1. P values of channels that is less than 0.05 between the states of before acupuncture and acupuncture at 150 times/min.

Channels		P
P3	O1	0.0333
O1	O2	0.0314
OZ	O2	0.0269
T4	O1	0.039
T5	O1	0.0404
T5	O2	0.0499
T3	O1	0.0141
C3	O1	0.0377
F8	O1	0.0394
F3	O1	0.0114
F7	O1	0.0067
F7	O2	0.0468

significance level to be 0.05. The electrodes and corresponding significance index P values where $P < 0.05$ are listed in Table 1. These results suggest that EEG information transformation in the process of acupuncture is more complicated in certain regions. As shown in Fig. 8, the most obviously influenced area is left brain, which is corresponding to the results mentioned above.

Then three-group channels (P3 & O1, T3 & O1, T5 & O1) are randomly selected from Table 1 for further analysis. These time series of three channels of one subject in two states (BA and MA with 150 times/min) are shown in Fig. 9(a). Two states of three time series are respectively plotted into three-dimensional space picture as shown in Fig. 9(c). The coordinates represent the elements of P3 & O1, T3 & O1, T5 & O1. It is clear that the differences between these two states are significant. The other 7 subjects' cases are similar to this subject.

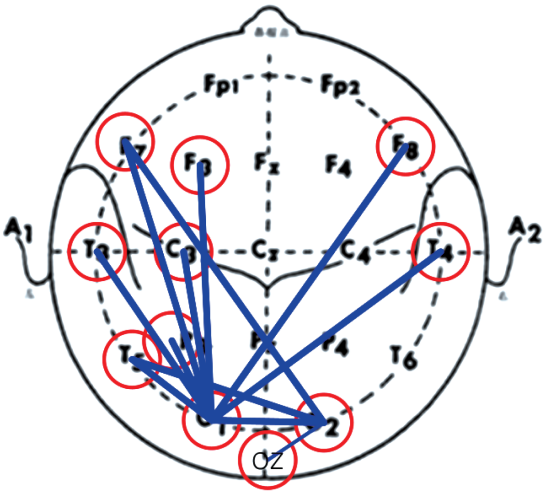


Fig. 8. (colour online) Electrodes with $P < 0.05$ are coloured by red and connected by blue line.

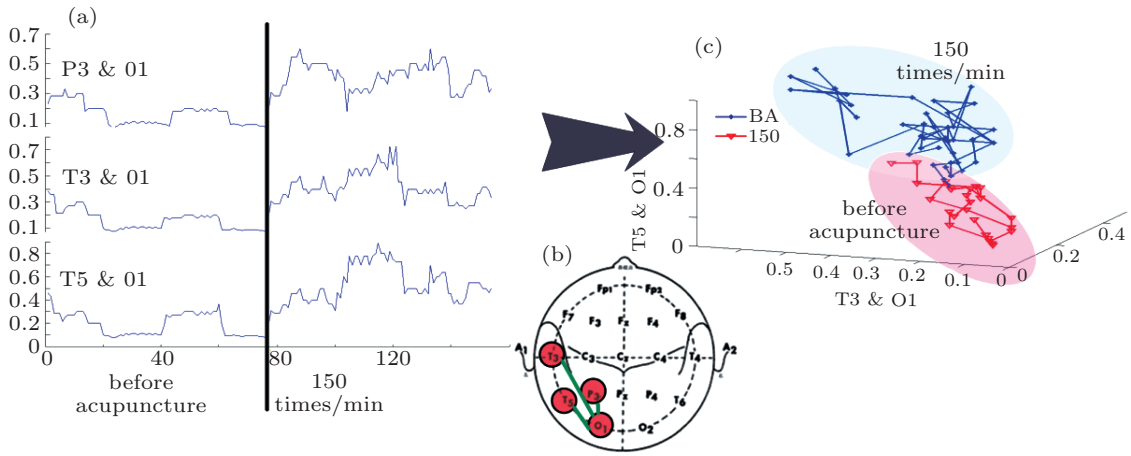


Fig. 9. (colour online) Time series of channels P3 & O1, T3 & O1, T5 & O1 and the corresponding three-dimensional plots. Panel (a) shows the time series of channels P3 & O1, T3 & O1, T5 & O1, where abscissa axis represents MILZC values and ordinate axis represents time; the solid line in the middle shows the delimitation between the states before acupuncture and those of acupuncture at 150 times/min. Panel (b) displays the positions of channels P3 & O1, T3 & O1, T5 & O1. Panel (c) indicates the corresponding three-dimensional plots of channels P3 & O1, T3 & O1, T5 & O1 in two states: before acupuncture and acupuncture at 150 times/min.

5. Conclusion

In this paper, we studied the complexity of information exchange characteristics among cerebral cortexes extracted by analysing EEG signals recorded in the process of acupuncturing at ST-36 acupuncture point of right leg with MILZC method. The results indicate that the acupuncture can make information exchange between brain regions much more complex. Acupuncture at right leg meridians obviously affects complexity of information exchange on contralateral hemisphere corresponding to the contralateral theory of body and the conclusion of (Xiao Y Y *et al.*, 2006) proved by fMRI. The results also demonstrate that MAs with 100 times/min and 150 times/min produce the most obvious effect which is consistent with the result from the theory of TCM acupuncture. The difference in MILZC value between BA and MA with 150 times/min is tested by significance index P, proving that the difference is significant. All these results show that the acupuncture at ST-36 acupuncture point can increase the complexity of information ex-

change and MILZC method can well quantify these changes.

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