Patients' consciousness analysis using Dynamic Approximate Entropy and MEMD method

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***Abstract*—Electroencephalography (EEG) based preliminary examination has been proposed in the clinical brain death determination. Multivariate empirical mode decomposition(MEMD) and approximate entropy(ApEn) are often used in the EEG signal analysis process. MEMD is an extended approach of empirical mode decomposition(EMD), in which it overcomes the problem of the decomposed number and frequency, and enables to extract brain activity features from multi-channel EEG simultaneously. ApEn as a complexity based method appears to have potential for the application to physiological and clinical time series data. In our previous studies, MEMD method and ApEn measure were always used severally, if MEMD and ApEn are used to analysis the same EEG signal simultaneously, the result of experiment will be more accurate. In this paper, we present MEMD method and ApEn measure based blind test without knowing about the clinical symptoms of patients beforehand. Features obtained from two typical cases indicate one patient being in coma and another in quasi- brain-death state.**

Keywords - Electroencephalography (EEG); Multivariate empiri-calmode decomposition (MEMD); Approximate entropy (ApEn)

I. Introduction

For supporting the diagnosis of brain death, we have proposed an EEG preliminary examination method as a reliable yet safety and rapid way for the determination of brain death [1]. That is, after three items have been verified, and an EEG preliminary examination along with real-time recorded data analysis method is applied to detect the brain wave activity at the bedside of patient. To extract informative features from noisy EEG signals and evaluate their significance, ApEn measure and MEMD were proposed for the EEG analysis in our previous study. ApEn is to extract informative features from noisy EEG signals and evaluate their statistical significance, several complexity measures are developed for the quantitative EEG analysis [3]. A robust principal factor analysis (PFA) associated with independent component analysis (ICA) approach is developed to reduce the power of additive noise and separate the brain activities and interference sources [2]. In the determination of brain death, EEG energy analysis is used to evaluate the brain activity. Several methods of EEG energy analysis such as empirical mode decomposition (EMD) [1] and multivariate empirical mode decomposition (MEMD) [2] have been proposed to evaluate the brain activity [3]. The MEMD is a fully data-driven time- frequency technique which adaptively decomposes a set of signals into a finite set of amplitude-frequency modulated components, namely intrinsic mode functions (IMFs). In this paper, we present ApEn measure and MEMD based blind experiment to analysis the real-life recorded EEG signal without knowing any clinical symptoms of patients. Feature differences between 2 cases indicate one patient being in coma state and the other in quasibrain- death state.

II. Method of Data Analysis

A. Approximate Entropy

Approximate entropy (ApEn) is a regularity statistic quantifying the unpredictability of fluctuations in a time series that appears to have potential application to a wide variety of physiological and clinical time-series data [12], [13]. Intuitively, one may reason that the presence of repetitive patterns of fluctuation in a time series renders it more predictable than a time series in which such patterns are absent.

Given a time series $\{x(n)\}$, $(n = 1, \cdots, N)$, to compute the ApEn$(\mathbf{x}(n), m, r)$ (m: length of the series of vectors, r: tolerance parameter) of the sequence, the series of vectors of length m, $\mathbf{v}(k) = [x(k), x(k+1), \cdots, x(k+m-1)]$ is firstly constructed from the signal samples $\{x(n)\}$. Let $D(i,j)$ denote the distance between two vectors $\mathbf{v}(i)$ and $\mathbf{v}(j)$ $(i, j \leq N-m+1)$, which is defined as the maximum difference in the scalar components of $\mathbf{v}(i)$ and $\mathbf{v}(j)$, or

$$D(i,j) = \max_{l=1,\cdots,m} |v_l(i) - v_l(j)| \ . \tag{1}$$

Then, we further compute the $N^{m,r}(i)$, which represents the total number of vectors $\mathbf{v}(j)$ whose distance with respect to the generic vector $\mathbf{v}(i)$ is less than r, or $D(i,j) \leq r$. Now define $C^{m,r}(i)$, the probability to find a vector that differs from $\mathbf{v}(i)$ less than the distance r. And $\phi^{m,r}$, the natural logarithmic average over all the vectors of the $C^{m,r}(i)$ probability as

$$C^{m,r}(i) = \frac{N^{m,r}(i)}{N-m+1} \ , \tag{2}$$

$$\phi^{m,r} = \frac{\sum_{i=1}^{N-m+1} \log C^{m,r}(i)}{N-m+1} \ . \tag{3}$$

For $m+1$, repeat above steps and compute $\phi^{m+1,r}$. ApEn statistic is given by

$$ApEn(\mathbf{x}(n), m, r) = \phi^{m,r} - \phi^{m+1,r} \ . \tag{4}$$

The typical values $m = 2$ and r between 10% and 25% of the standard deviation of the time series $\{x(n)\}$ are often used in practice[12].

Furthermore, base on the algorithm for computing ApEn of one sequence, we extend it in the temporal domain along timecoordinate of EEG signal. Supposing an EEG data series $\mathbf{S}_N$ consists of N sequence intervals $\{x_i(n)\}$, the ApEn measure is carried out through each interval. We define the dynamic ApEn measure of given EEG signal as

$$\mathbf{ApEn}(\mathbf{S}_N, m, r) = [ApEn(\mathbf{x}_1(n), m, r), ..., ApEn(\mathbf{x}_N(n), m, r)] \quad (5)$$

Consequently, in our experiment, the **ApEn**($\mathbf{S}_N$, m, r) statistic measures the variation the of complexity of a EEG data series $\mathbf{S}_N$. The occurrence of irregular pattern of one interval is excepted to be followed by the next in brain-death EEG.

B. Existing EMD Algorithm

EMD decomposes the original signal into a finite set of amplitude- and/or frequency-modulated components, termed IMFs, which represent its inherent oscillatory modes [11]. More specifically, for a real-valued signal $x(k)$, the standard EMD finds a set of N IMFs $\{c_i(k)\}_{i=1}^N$, and a monotonic residue signal $r(k)$, so that

$$x(k) = \sum_{i=1}^{n} c_i(k) + r(k). \quad (6)$$

IMFs $c_i(k)$ are defined so as to have symmetric upper and lower envelopes, with the number of zero crossings and the number of extrema differing at most by one. The process to obtain the IMFs is called sifting algorithm.

The first complex extension of EMD was proposed in [3]. An extension of EMD to analyze complex/bivariate data which operates fully in the complex domain was first proposed in [4], termed rotation-invariant EMD (RI-EMD). An algorithm which gives more accurate values of the local mean is the bivariate EMD (BEMD) [10], where the envelopes corresponding to multiple directions in the complex plane are generated, and then averaged to obtain the local mean. An extension of EMD to trivariate signals has been recently proposed in [8]; the estimation of the local mean and envelopes of a trivariate signal is performed by taking projections along multiple directions in three-dimensional spaces.

C. The n-Variate EMD Algorithm[5]

For multivariate signals, the local maxima and minima may not be defined directly because the fields of complex numbers and quaternions are not ordered [8]. Moreover, the notion of 'oscillatory modes' defining an IMF is rather confusing for multivariate signals. To deal with these problems, the multiple real-valued projections of the signal is proposed in [5]. The extrema of such projected signals are then interpolated componentwise to yield the desired multidimensional envelopes of the signal. In MEMD, we choose a suitable set of direction vectors in n-dimensional spaces by using: (i) uniform angular coordinates and (ii) low-discrepancy pointsets.

The problem of finding a suitable set of direction vectors that the calculation of the local mean in an n-dimensional space depends on can be treated as that of finding a uniform sampling scheme on an n sphere. For the generation of a pointset on an $(n-1)$ sphere, consider the n sphere with centre point C and radius R, given by

$$R = \sum_{j=1}^{n+1} (x_j - C_j)^2. \quad (7)$$

A coordinate system in an n-dimensional Euclidean space can then be defined to serve as a pointset on an $(n-1)$ sphere. Let $\{\theta_1, \theta_2, \cdots, \theta_{n-1}\}$ be the $(n-1)$ angular coordinates, then an n-dimensional coordinate system having $\{x_i\}_{i=1}^n$ as the n coordinates on a unit $(n-1)$ sphere is given by

$$x_n = sin(\theta_1) \times \cdots \times sin(\theta_{n-2}) \times sin(\theta_{n-1}). \quad (8)$$

Discrepancy can be regarded as a quantitative measure for the irregularity (non-uniformity) of a distribution, and may be used for the generation of the so-called 'low discrepancy pointset', leading to a more uniform distribution on the n sphere. A convenient method for generating multidimensional 'low-discrepancy' sequences involves the family of Halton and Hammersley sequences. Let $x_1, x_2, \cdots, x_n$ be the first n prime numbers, then the ith sample of a one-dimensional Halton sequence, denoted by r_i^x is given by

$$r_i^x = \frac{a_0}{x} + \frac{a_1}{x}^2 + \frac{a_2}{x}^3 + \cdots + \frac{a_s}{x}^{s+1}, \quad (9)$$

where base-x representation of i is given by

$$i = a_0 + a_1 \times x + a_2 \times x^2 + \cdots + a_s \times x^s. \quad (10)$$

Starting from $i = 0$, the ith sample of the Halton sequence then becomes

$$(r_i^{x_1}, r_i^{x_2}, r_i^{x_3}, \cdots, r_i^{x_n}). \quad (11)$$

Consider a sequence of n-dimensional vectors $\{\mathbf{v}(t)\}_{t=1}^T = \{v_1(t), v_2(t), \cdots, v_n(t)\}$ which represents a multivariate signal with n-components, and $\mathbf{x}^{\theta_k} = \{x_1^k, x_2^k, \cdots, x_n^k\}$ denoting a set of direction vectors along the directions given by angles $\theta_k = \{\theta_1^k, \theta_2^k, \cdots, \theta_{n-1}^k\}$ on an $(n-1)$ sphere. Then, the proposed multivariate extension of EMD suitable for operating on general nonlinear and non-stationary n-variate time series is summarized in the following.

1) Choose a suitable pointset for sampling on an $(n-1)$ sphere.
2) Calculate a projection, denoted by $p^{\theta_k}(t)\}_{t=1}^T$, of the input signal $\{\mathbf{v}(t)\}_{t=1}^T$ along the direction vector $\mathbf{x}^{\theta_k}$, for all k (the whole set of direction vectors), giving $p^{\theta_k}(t)\}_{k=1}^K$ as the set of projections.
3) Find the time instants $\{t_i^{\theta_k}\}$ corresponding to the maxima of the set of projected signals $p^{\theta_k}(t)\}_{k=1}^K$.
4) Interpolate $[t_i^{\theta_k}, \mathbf{v}(t_i^{\theta_k})]$ to obtain multivariate envelope curves $\mathbf{e}^{\theta_k}(t)\}_{k=1}^K$.

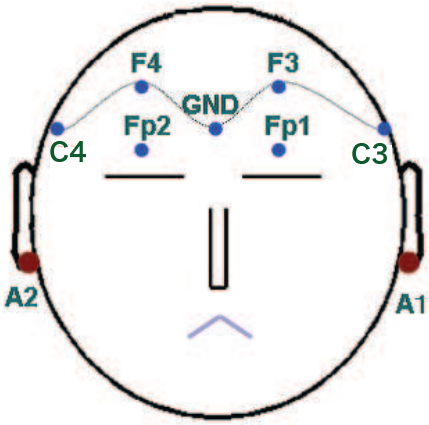

Fig. 1. The layout of six exploring electrodes.

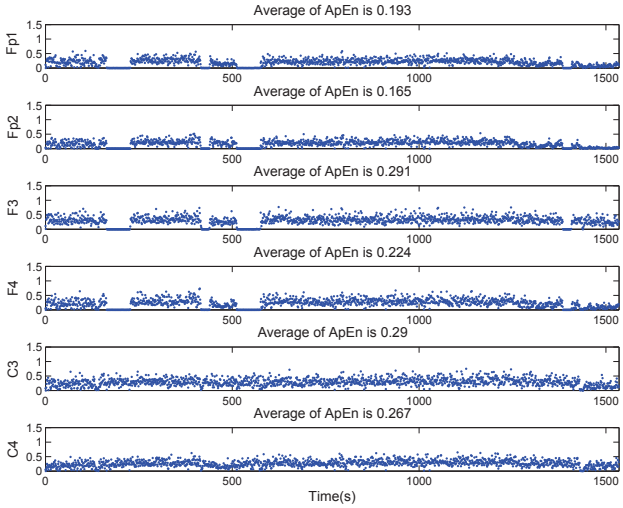

Fig. 2. Approximate Entropy measure's distribution and average value of the first Patient.

5) For a set of K direction vectors, the mean $\mathbf{m}(t)$ of the envelope curves is calculated as

$$\mathbf{m}(t) = \frac{1}{K}\sum_{k=1}^{K}\mathbf{e}^{\theta_k}(t). \tag{12}$$

6) Extract the 'detail' $d(t)$ using $d(t) = x(t) - m(t)$. If the 'detail' $d(t)$ fulfills the stoppage criterion for a multivariate IMF, apply the above procedure to $x(t) - d(t)$, otherwise apply it to $d(t)$.

The stoppage criterion for multivariate IMFs is similar to the standard one in EMD, which requires IMFs to be designed in such a way that the number of extrema and the zero crossings differ at most by one for S consecutive iterations of the sifting algorithm. The optimal empirical value of S has been observed to be in the range of 2–3 [9]. In the MEMD, we apply this criterion to all projections of the input signal and stop the sifting process once the stopping condition is met for all projections.

III. Experiments and Results

A. EEG Experiment

The patients' EEG signal was collected by a portable EEG system (NEUROSCAN ESI) in a hospital in Shanghai. In the EEG recording, only nine electrodes are chosen to apply to patients. Among these electrodes, six exploring electrodes (Fp1, Fp2, F3, F4, C3 and C4) as well as GND were placed on the forehead, and two electrodes (A1, A2) as the reference were placed on the earlobes based on the standardized 10-20 system (Fig. 1). The sampling rate of EEG was 1000 Hz and the resistances of the electrodes were set to less than 10 kΩ.

B. A Patient with a Coma State

First, we use ApEn to analysis the patients' EEG signal. In our previous study, when the patients in Quasi-Brain-Death state, ApEn value will be approximate to 1, or greater than 1. Another case of brain-death state is the value of ApEn close to 0. However the patients' brain activity in the coma state produces ApEn of a low number but not approximate to 0. We first demonstrate our result by an example of a patient who presented a similar symptom to a brain-death case. The EEG examination was carried out one day in April 2010 and lasted 1535 seconds. From the previous research, we have demonstrated regular and predictable brain activities such as a wave exists in the EEG of coma. As ApEn is suggested as a complexity- based statistics to measure the regularity or predictability of time series signal, and we calculate every 1 second data of each channel by ApEn measure(r=0.25) from 1 second to 1535 second. It can be seen for example, ApEn measures distribution of channel Fp1 is mostly lower than 0.5, and the average results of each channel are from 0.165 to 0.291(Fig. 2). According to the definition of the ApEn and the similar ApEn distributions of near the range of 0.2 are obtained from each channel, the result indicates the patient still having spontaneous brain activity. Furthermore, clinical diagnosis from the doctor says the patient is under treatment up till now.

And then, we use MEMD to analysis the patients'EEG signal. Through the MEMD method described in Section II, we obtained 9 IMF components (C1 to C9) with different frequency from high to low. Each IMF carries a single frequency mode, illustrating the alignment of common scales within different channels. Therefore, generally in our experiment, the IMF components from C1 to C3 with the same high frequency scales refer to electrical interference or other noise from environment that contains in the recorded EEG. The residual component (r) is not the typical useful components considered, either. The desired components from C4 to C9 are combined to form the denoised EEG signal, and changed into frequency domain by fast Fourier transform (FFT). As showed in Fig. 3, the upper line gives each channels denoised EEG signal in time domain, and the lower line display the denoised EEG signal of each channel in their frequency domain. With y-coordinate in the scope from 0 to 7000 in the frequency domain, we

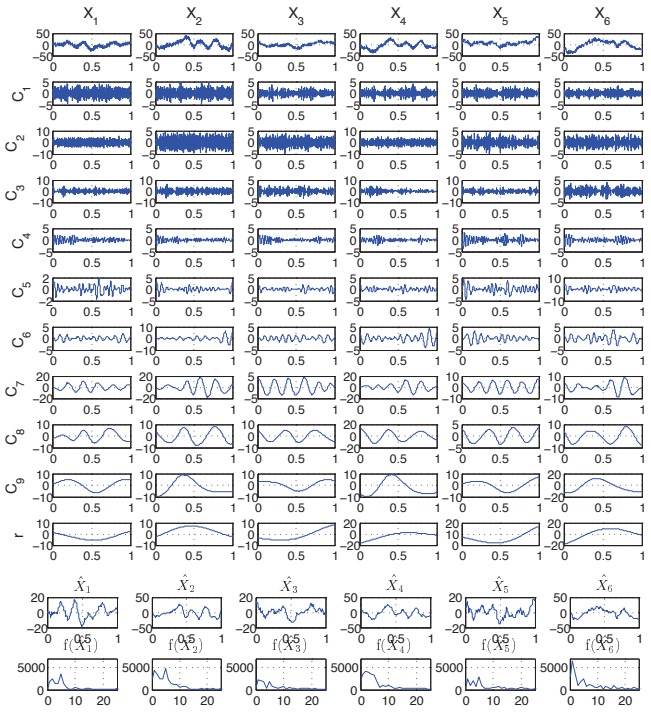

Fig. 3. The first Patient for comatose patient used MEMD.

find the value of power spectra at 2-10 Hz is very high. The average energy of each channel is 2.14×10^4. The analysis result indicated the patient still had strong physiological brain activity, and in fact, the patient was in a comatose state. Furthermore, clinical diagnosis from the doctor confirm the patient is in a coma state at recorded time.

C. A Patient in the Quasi-Brain-Death State

The second patient's EEG examination was carried out one day in June 2010, and was lasted 1030 seconds. Being similar analysis to the previous, we calculate every 1 second data of each channel by ApEn measure(r=0.25) from 0 second to 1030 second. It can be seen from the Fig. 4, comparing with the first patient, ApEn measure distribution of each channel is mostly over 0.9, and the average results of each channel are from 0.972 to 1.22, and gives us a much higher ApEn value of approximate to 1. According to the definition of the ApEn, random sequence produces a higher ApEn value of approximate to 1, we consider this patient's EEG data is without spontaneous brain activity. From this result above, we suspect the patient was in the quasi-brain-death state. Then we use the MEMD to analysis the patient's EEG. As showed in Fig. 5, with the same analysis of the first patient, contrary to the first patient power spectrum, the value is in a low range. The average energy of each channel is 0.229×10^4. The analysis result indicate that this patient physiological brain activity is extremely low and we suspect the patient was in the quasi-brain- death state. Later, the clinical doctor confirm this result is correct.

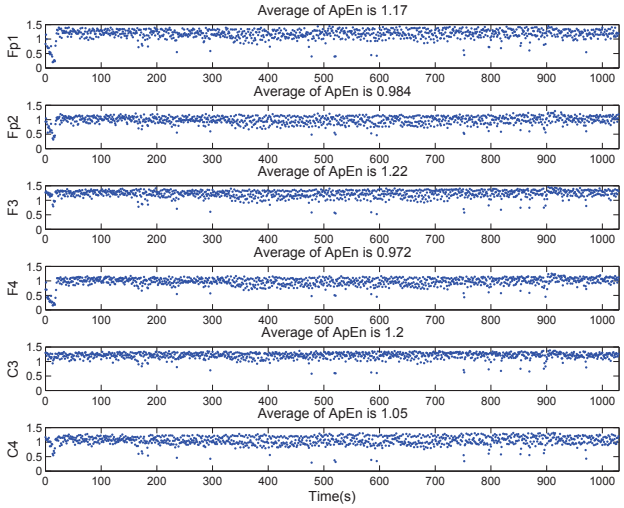

Fig. 4. Approximate Entropy measure's distribution and average value of the second Patient.

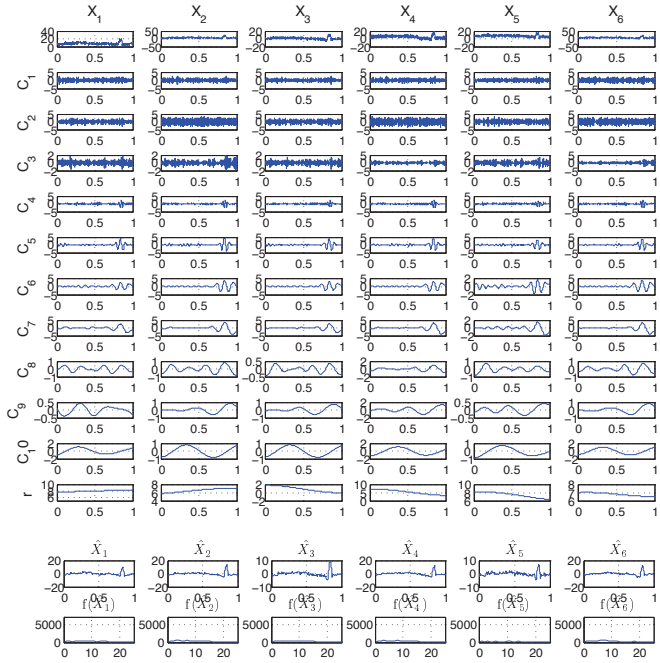

Fig. 5. The second Patient for quasi-brain-death state used MEMD.

D. The EEG Energy of all patients

EEG energy analysis is supplied to evaluate the brain activity. EEG energy of healthy human is higher than comatose patient and brain death. However, Fig. 6 show the EEG energy of all patients. In Fig. 6, healthy human's maximum EEG energy of each channel is 7.42×10^4, and the minimum is 0.806×10^4. Contrary to this, brain deaths reflected no EEG energy over 0.48×10^4. However, comatose patients' EEG energy of each channel is between 8.00×10^4 and 0.8×10^4. This illustrate that the brain activity of comatose patients whose EEG energy is close to the brain deaths' are not high. We speculate that they are brain damage. But another part of comatose patients' EEG energy is close to, even more than the

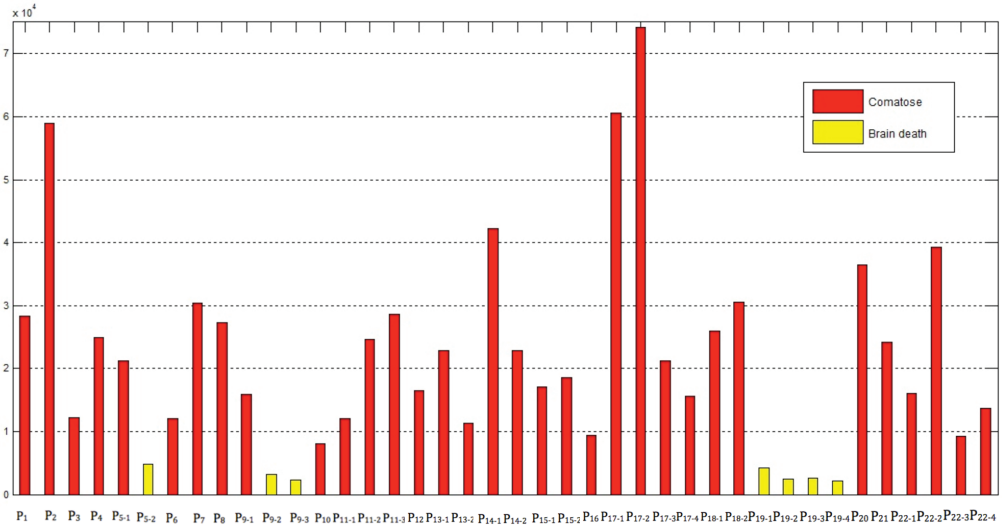

Fig. 6. The EEG energy of all the patients

healthy human's. These patients still have high brain activity.

IV. Conclusions

In our previous studies,we use the MEMD and ApEn severally to analysis the state of patients. In this paper, we use both of two methods to analysis the same EEG data.The experiment is proposed and the analysis was carried out without any clinical diagnosis of the patient, after our experiment, the data analysis results have be compared to the diagnosis results achieved by the clinical doctors. All the cases are completely identical.

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