MEMD-enhanced Multivariate Fuzzy Entropy for the Evaluation of Complexity in Biomedical Signals

MEMD-enhanced Multivariate Fuzzy Entropy for the Evaluation of Complexity in Biomedical Signals

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***Abstract*— Multivariate multiscale entropy (mvMSE) has been proposed as a combination of the coarse-graining process and multivariate sample entropy (mvSE) to quantify the irregularity of multivariate signals. However, both the coarse-graining process and mvSE may not be reliable for short signals. Although the coarse-graining process can be replaced with multivariate empirical mode decomposition (MEMD), the relative instability of mvSE for short signals remains a problem. Here, we address this issue by proposing the multivariate fuzzy entropy (mvFE) with a new fuzzy membership function. The results using white Gaussian noise show that the mvFE leads to more reliable and stable results, especially for short signals, in comparison with mvSE. Accordingly, we propose MEMD-enhanced mvFE to quantify the complexity of signals. The characteristics of brain regions influenced by partial epilepsy are investigated by focal and non-focal electroencephalogram (EEG) time series. In this sense, the proposed MEMD-enhanced mvFE and mvSE are employed to discriminate focal EEG signals from non-focal ones. The results demonstrate the MEMD-enhanced mvFE values have a smaller coefficient of variation in comparison with those obtained by the MEMD-enhanced mvSE, even for long signals. The results also show that the MEMD-enhanced mvFE has better performance to quantify focal and non-focal signals compared with multivariate multiscale permutation entropy.**

I. Introduction

Entropy methods quantify the degree of regularity of a univariate signal by evaluating the appearance of repetitive patterns [1]. One of the most popular and powerful entropy approaches is sample entropy (SampEn) [2]. SampEn is relatively robust to noise and data length [2]. Moreover, in comparison with permutation entropy (PerEn), SampEn takes into account the presence of equal values and the differences between neighboring samples in embedded vectors [2, 3]. These characteristics make the SampEn an appealing tool for a large number of real world signal processing applications [4, 5]. Nevertheless, SampEn is not reliable when the signal is short.

Conventional methods to measure the complexity of physiological time series fail to account for the multiple time scales inherent in such signals [6, 7]. To tackle this deficiency, multiscale entropy (MSE) was proposed by Costa *et al.* [8]. In the MSE algorithm, the original signal is initially divided into non-overlapping segments of length β, termed scale factor. Then, the average of each segment is estimated to obtain the coarse-grained signals (called coarse-graining process). Finally, the SampEn value is calculated for each coarse-grained series.

The MSE-based methods, though powerful and widespread, are not able to reveal the dynamics across channels of a multivariate recording. For such time series, evaluation of cross-statistical properties between multiple channels is necessary for a complete understanding of the underlying dynamics of a system [9, 10]. Accordingly, multivariate SampEn (mvSE) was proposed [10] and, consequently, the combination of MSE and mvSE lead to the multivariate MSE (mvMSE) [10].

In spite of the abovementioned mvSE benefit, when mvSE is applied to short signals, the results may be undefined or unreliable. To alleviate this shortcoming, the multivariate FuzEn (mvFE) method has been recently proposed [11]. However, this method, though powerful, is slow.

Since the coarse-graining step of mvMSE decreases the signal length proportionally to the scale factor, the results achieved by mvMSE might not be reliable and stable for high scale factors, especially for short signals. To address this problem, the combination of multivariate empirical mode decomposition (MEMD) and mvSE was proposed [9]. MEMD is a fully data-driven multiscale algorithm decomposing the original multivariate signal into a number of intrinsic mode functions (IMFs) [12]. Unlike MSE, MEMD can tackle the non-stationarity and nonlinearity of signals [12]. Unlike the coarse-graining process of the MSE, the length of each decomposed signal is equal to the original signal.

In this paper we propose a new fuzzy membership function to decrease the computation time of existing mvFE and consequently introduce a new complexity indicator, termed MEMD-enhanced mvFE. The performance of this technique is illustrated with publicly-available focal and non-focal signals as this kind of biomedical data is a popular candidate to evaluate entropy metrics [13-15]. Sharma and colleagues showed that the focal EEG time series are more regular in comparison with non-focal ones. They also demonstrated that all entropy measures of focal EEG signals are smaller than non-focal ones [13, 14].

II. Materials

A. White Gaussian (discrete-time) noise

White Gaussian noise (WGN) is a random time series having equal energy at all frequencies. The name white has its origin from the fact that this kind of signal has a constant power spectral density $S(f)$ as $S(f) = C_w$, where C_w is a

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constant number [16]. A WGN signal is defined as a sequence of consecutively uncorrelated random variables with zero mean and finite variance [17].

B. Real EEG Recordings

The intracranial EEG signals were recorded from five patients suffering from pharmacoresistant focal-onset epilepsy leading to two main separate sets of signals. The first one was recorded from brain regions where the primarily ictal EEG recordings changes were detected as judged by expert visual inspection ("focal signals"). The second set of signals was recorded from brain regions not involved at seizure onset ("non-focal signals"). Each of 5 patients includes 750 focal and 750 non-focal time series. The length of each signal was 10240 sample points: 20 seconds at a sampling frequency of 512 Hz. Each of focal and non-focal signals includes two EEG time series recorded from adjacent channels. For more information about the dataset, please, refer to [15]. Before computing the existing and proposed approaches, all signals were digitally filtered employing an FIR band-pass filter with cut-off frequencies at 0.5 Hz and 40 Hz.

III. Methods

The proposed MEMD-enhanced mvFE includes two steps:

A. Multivariate Empirical Mode Decomposition

First, the original multivariate signal $\mathbf{Y}$ is decomposed to a number of IMFs. In each step of the MEMD algorithm, the mode with the highest frequency is removed from a signal [12]. In fact, the characteristics frequency decreases with the IMF number. Thus, the first IMF, IMF_1, shows the highest frequency component in a time series. In contrast, the last IMF, IMF_{jmax}, depicts the trend of the signal usually containing the signal power and little signal detail [9].

One of the most important characteristics of EMD-based methods is that the IMFs show a quasi- dyadic filterbank structure for WGN. MEMD is able to align the frequency sub-bands from different channels both for single and averaged noise realizations. For more information about the MEMD please refer to [12]. Using MEMD, unlike the coarse-graining process, the signal length does not decrease leading to more reliable results [12]. After calculating all IMFs, the cumulative sums of IMFs, $\mathbf{C}^k(\mathbf{Y})$, for each scale factor k are defined as follows:

$$\mathbf{C}^k(\mathbf{Y}) = \sum_{j=1}^{k} IMF_j \tag{1}$$

Starting from the first scale to the last one leads to a multilevel filtering of the original time series. It is worth noting that the last cumulative sum is equal to the original signal, i.e., $\mathbf{C}^{k_{\max}}(\mathbf{Y}) = \mathbf{Y}$ [9, 18]. The second step of the proposed method is to use mvFE for each $\mathbf{C}^k(\mathbf{Y})$.

B. Multivariate Fuzzy Entropy

One of the biggest deficiencies of the mvSE is that it ignores every distance (d) between two composite delay vectors that is larger than a defined threshold r [11]. To alleviate this problem, a fuzzy membership function $\theta(d,r)$ [11] was proposed as follows:

$$\theta(d,r) = \begin{cases} 1, & d \le r \\ e^{-\left(\frac{d-r}{r}\right)^2 \ln(2)}, & d > r \end{cases} \tag{2}$$

Although the above-mentioned problem is solved by using that function [11], this method is noticeably slower than the mvSE, especially when the number of channels or sample points of every channel, or the value of embedding dimension is high. To tackle this deficiency, we propose to use another well-known fuzzy membership function as:

$$\theta(d,r) = \exp\left(-(d)^n / r\right) \tag{3}$$

where n shows the fuzzy power and is usually equal to 2.

To calculate mvFE, multivariate embedded vectors are initially generated based on the Takens embedding theorem [10, 11, 19]. The multivariate embedded reconstruction is defined as:

$$X_m(i) = [x_{1,i}, x_{1,i+\tau_1}, ..., x_{1,i+(m_1-1)\tau_1}, x_{2,i}, x_{2,i+\tau_2}, ..., x_{2,i+(m_2-1)\tau_2}, \\ ...x_{P,i}, x_{P,i+\tau_P}, ..., x_{P,i+(m_P-1)\tau_P}] \tag{4}$$

where $M = [m_1, m_2, ..., m_p]$ and $\boldsymbol{\tau} = [\tau_1, \tau_2, ..., \tau_p]$ are the embedding and the time lag vectors, respectively [20].

For p-variate time series $\{\mathbf{X}_{k,b}\}_{k=1,b=1}^{k=p,b=N}$, where N is the length of each channel, the mvFE algorithm, as a natural extension of the standard univariate FuzEn [21], includes the following steps:

1. Form multivariate embedded vectors $X_m(i) \in R^m$ where i=1,2,...,N-n and n=max$\{M\}$1×max$\{\boldsymbol{\tau}\}$.
2. Calculate the distance between any two composite delay vectors $X_m(i)$ and $X_m(j)$ as the maximum norm.
3. For a given threshold r and fuzzy power n, define a global quantity $\phi^m(r)$, as the average membership grade as:

$$\phi^m(r) = \frac{1}{(N-n)} \sum_{i=1}^{N-m} \frac{\sum_{j=1, i\neq j}^{N-m-1} \exp\left(\frac{-\left(d[X_m(i), X_m(j)]\right)^n}{r}\right)}{N-n-1} \tag{5}$$

4. Extend the dimensionality of the multivariate delay vector in (5) from m to (m+1). This can be done in p different ways, as from $[m_1, m_2, ..., m_h, ..., m_p]$ to $[m_1, m_2, ..., m_{h+1}, ..., m_p]$ $(h = 1, ..., p)$. In this process, the dimension of the other variables are unchanged.
5. Calculate $\phi^{(m+1)}(r)$ which denotes the average over all $\phi^{(m_h+1)}(r)$ values in an (m+1)-dimensional space.
6. Finally, mvFE is defined as:

$$\text{mvFE}(\mathbf{X}, \boldsymbol{\tau}, r, n) = -\ln\left(\frac{\phi^{(m+1)}(r)}{\phi^m(r)}\right) \tag{6}$$

Since multi-channel signals may have different amplitude ranges, the distances calculated on embedded vectors may be biased toward the largest amplitude ranges variates. Accordingly, we scale all the data channels to the same amplitude range [0,1], which is the preferred choice [10].

IV. Results

A. White Gaussian noise

To understand the ability of mvFE and mvSE to quantify the regularity of short and long signals, we use uncorrelated 3-channel WGN signals as functions of sample points of size N.

Fig. 1 depicts the mvSE and mvFE values for signal lengths equal to 30, 100, 300, 1000, 3000, and 10000, computed from 40 different multichannel WGN time series. The results demonstrate that the greater the value of N, the more robust both the mvSE and mvFE estimates, as seen from the error bars. τ_k, m_k, and r for mvSE and mvFE were 1, 2, and 0.15 multiplied by the standard deviation (SD) of the original time series according to [2, 10].

It has been recommended that the number of sample points is at least 10^m, or preferably at least 30^m, to robustly estimate mvSE [10]. In mvSE, we count the number of instances where $d = [X_m(i), X_m(j)] \le r,\ j \ne i$. In case the time series length is too small, this number may be 0, leading to an undefined entropy value. Accordingly, the results obtained by mvSE for N=30 and 100 are not defined in Fig. 1.

In contrast, the fuzzy entropy-based methods consider any two composite delay vectors $X_m(i)$ and $X_m(j)$, leading to more reliable results for short time series. For example, the mvFE values, unlike mvSE ones, are defined for N=30 and N=100. We also calculate the coefficient of variation (CV) of existing and proposed mvFE- and mvSE-based results, shown in Table I. As expected, for each number of sample points, the CV value for mvFE was noticeably lower than that for mvSE. It shows the advantage of mvFE for short and long multivariate signals. We also compare the running time of the existing and proposed mvFE and mvSE methods for different number of sample points (i.e., 1000, 3000, and 30,000) using WGN signals in Table II. Generally, the longer the signals, the more noticeable differences between the computation time of these methods. As can be seen in Table II, the proposed mvFE is about 3 to 7 times faster than the existing mvFE [11], although their CV values are similar (Table I).

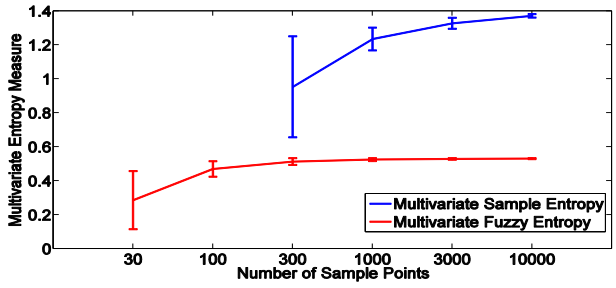


Fig. 1. Error bars illustrating the mean ± SD of the mvSE (blue) and mvFE (red) values as functions of the length of the 3-channel WGN signals computed from 40 different multichannel WGN time series.

TABLE I: THE CV VALUES OF THE PROPOSED AND EXISTING MVFE AND MVSE RESULTS FOR 3-CHANNEL WGN SIGNALS.

Methods	30 samples	100 samples	300 samples	1000 samples	3000 samples	10000 samples
proposed mvFE	0.601	0.097	0.039	0.016	0.008	0.005
mvFE [11]	0.593	0.098	0.040	0.016	0.008	0.005
mvSE	undefined	undefined	0.311	0.054	0.024	0.008

TABLE II: THE COMPUTATION TIME OF THE EXISTING MVFE [11] AND PROPOSED MVFE AND MVSE USING 3-CHANNEL WGN SIGNALS.

Methods	1000 samples	3000 samples	10000 samples
proposed mvFE	0.231 s	1.013 s	7.141 s
mvFE [11]	0.684 s	3.842 s	46.42 s
mvSE	0.247 s	1.019 s	7.214 s

B. *Real EEG Focal and Non-focal Signals*

To locate the area of the brain affected by focal epilepsy as a pre-surgical diagnosis of seizure, EEG signals are widely used [13-15]. The error bars demonstrate the mean ± standard deviation (SD) of the MEMD-enhanced mvSE (Fig. 2) and MEMD-enhanced mvFE values (Fig. 3), computed from focal and non-focal EEGs. The error bars in Fig. 2 and 3 show that the non-focal signals are more irregular than focal time series and it is in agreement with [13-15].

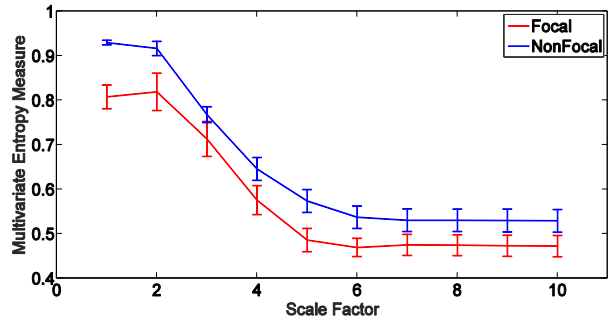
The CV values obtained by the proposed MEMD-enhanced mvFE are lower than those done by MEMD-enhanced mvSE. These facts show that the proposed method leads to more stable results in comparison with MEMD-enhanced by mvSE for not only short signals but also long ones.

Multivariate multiscale PerEn (mvMPE) has been recently proposed [22] to quantify the irregularity of multivariate signals. Since mvMPE is conceptually simple and structurally robust to noise, it has been widely used in many biomedical signal processing applications [22-24]. Here, we also use mvMPE to compare with our proposed method. The results obtained by mvMPE are shown in Fig. 3. The average of entropy values for focal signals are higher than that for non-focal ones at scale 1 to 3 showing to contradict previous findings in short scales. In contrast, the average of entropy values for non-focal signals are larger than those for focal ones at time scales 4 to 10. It is in agreement with [13-15]. Nevertheless, mvMPE seems to be less sensitive to differences between focal and non-focal EEGs. As demonstrated before, the MEMD-enhanced mvFE leads to higher irregularity for non-focal signals at all scale factors. It shows the proposed method outperforms mvMPE to characterize focal and non-focal signals. Note that the time delay and embedding dimension for mvMPE were 1 and 5 according to [22, 23].

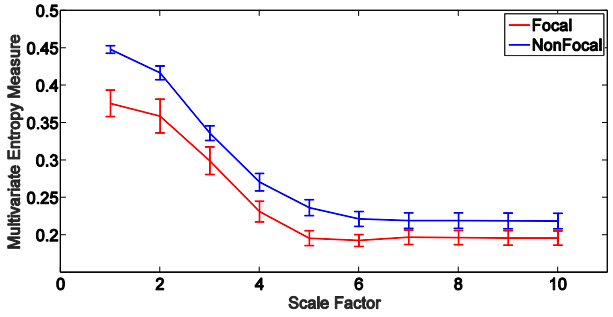
A paired t-test was also run for AD patients vs. controls. We adjusted the false discovery rate independently for each multivariate entropy measure. The results show that the mvMPE achieves significant differences at scales 4-10, although MEMD-enhanced mvSE and mvFE lead to significant difference at all scales. Note that the significance level of p-value tests was 0.01 for the EEG time series.

V. CONCLUSION

We first proposed the mvFE with a new fuzzy membership function to reduce its computation time. The proposed mvFE was significantly faster than the existing mvFE. Moreover, we showed mvFE leads to more stable results for short and long time series, in comparison with mvSE. Based on the new mvFE, we introduced the MEMD-enhanced mvFE to quantify the complexity of multivariate signals. Using the focal and non-focal signals, the MEMD-enhanced mvFE-based results, in comparison with those obtained by MEMD-enhanced mvSE and mvMPE, as two powerful multivariate approaches, demonstrated the power of the proposed method. Our results show that MEMD-enhanced mvFE is a powerful tool to quantify multivariate signals.



(a) MEMD-enhanced mvSE



(b) MEMD-enhanced mvFE

Fig. 2. Error bars illustrating the mean ± SD of the (a) MEMD-enhanced mvSE and (b) MEMD-enhanced mvFE values computed from focal and non-focal EEG signals. Red and blue indicate focal and non-focal signals, respectively.

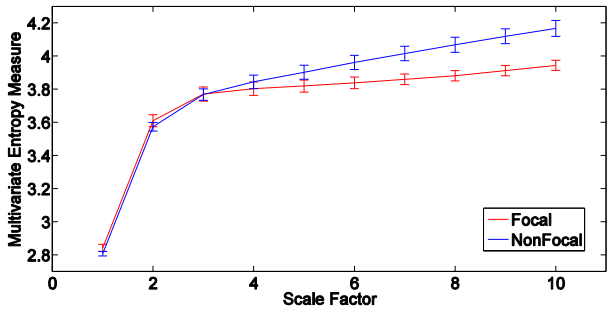


Fig. 3. Error bars illustrating the mean ± SD of the mvMPE values computed from focal and non-focal EEG signals. Red and blue indicate focal and non-focal signals, respectively.

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