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Measuring synchronization in coupled simulation and coupled cardiovascular time series: A comparison of different cross entropy measures

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ABSTRACT

Synchronization provides an insight into underlying the interaction mechanisms among the bivariate time series and has recently become an increasing focus of interest. In this study, we proposed a new cross entropy measure, named cross fuzzy measure entropy (C-FuzzyMEn), to detect the synchronization of the bivariate time series. The performances of C-FuzzyMEn, as well as two existing cross entropy measures, i.e., cross sample entropy (C-SampEn) and cross fuzzy entropy (C-FuzzyEn), were first tested and compared using three coupled simulation models (i.e., coupled Gaussian noise, coupled MIX(p) and coupled Henon model) by changing the time series length, the threshold value for entropy and the coupling degree. The results from the simulation models showed that compared with C-SampEn, C-FuzzyEn and C-FuzzyMEn had better statistical stability and compared with C-FuzzyEn, C-FuzzyMEn had better discrimination ability. These three measures were then applied to a cardiovascular coupling problem, synchronization analysis for RR and pulse transit time (PTT) series in both the normal subjects and heart failure patients. The results showed that the heart failure group had lower cross entropy values than the normal group for all three cross entropy measures, indicating that the synchronization between RR and PTT time series increases in the heart failure group. Further analysis showed that there was no significant difference between the normal and heart failure groups for C-SampEn (normal 2.13 ± 0.37 vs. heart failure 2.07 ± 0.16, $P = 0.36$). However, C-FuzzyEn had significant difference between two groups (normal 1.42 ± 0.25 vs. heart failure 1.31 ± 0.12, $P < 0.05$). The statistical difference was larger for two groups when performing C-FuzzyMEn analysis (normal 2.40 ± 0.26 vs. heart failure 2.15 ± 0.13, $P < 0.01$).

1. Introduction

Measuring the coupling relationship between two cardiovascular time series, as well as named synchronization measurement, has been an increasing focus of interest in clinical research [1–3]. It is a prerequisite for the understanding of the complexity of underlying signal generating mechanisms and thus for the detection of cardiovascular disorders and ongoing perturbations to the circulation system [4]. Traditionally, the cross-correlation in the time domain as well as the cross-spectrum or coherency in the frequency domain has been used for synchronization measurement [5]. These techniques are able to give the linear relationship between two systems. However, they are not suitable for characterizing the real cardiovascular signals, which are non-stationary and inherently nonlinear [6].

In recent years, entropy-based measures, such as the typical approximate entropy (ApEn) and sample entropy (SampEn), have been widely used for the physiological time series analysis to explore their inherent complexity. And their generalized forms, cross-approximate entropy (C-ApEn) [7] and cross-sample entropy (C-SampEn) [8], were used for the synchronization test [9–12]. For fixed bivariate time series $x(i)$ and $y(i)(1 \le i \le N)$, C-ApEn measures the conditional regularity or frequency of y-patterns similar to a

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given x-pattern of embedding dimension m within the threshold value r. When coupling in two time series is tight, patterns in one time series cause predictable patterns in the other one, inducing the low C-ApEn value [8,10]. In the calculating process of C-ApEn, each vector must match at least one vector when embedding dimension comes from m to $m+1$ [6,13]. However, there is no self-matching in C-ApEn, and thus there is no assurance that the probability will be defined. Moreover, C-ApEn is not direction independent, i.e., C-ApEn(m, r, N)($y|x$) does not equal to C-ApEn(m, r, N)($x|y$), which brings difficulties to the practical application. In order to handle these potential difficulties, Richman and Moorman [14] proposed the SampEn method instead of counting the self-matching of the vectors and generalized it to C-SampEn for bivariate time series. Compared with the fact that C-ApEn was a biased evaluation and was sensitive to noisy, C-SampEn could reduce the bias and showed better relative consistency than C-ApEn. Meanwhile, C-SampEn is direction independent, i.e., C-SampEn(m, r, N)($y|x$) equals to C-SampEn(m, r, N)($x|y$). Thus it has been used as an alternative nonlinear statistic to analyze physiological time series [8,10].

Similar to ApEn and SampEn, in both C-ApEn and C-SampEn, the similarity of two vectors is judged using the Heaviside function, i.e., binary classification, which makes the boundary very rigid. Only the vectors within the threshold r are treated equally, whereas the vectors outside of this threshold r are ignored. This rigid boundary may induce to the abrupt changes of entropy values when the threshold r changes slightly, and it may even fail to define the entropy if no vector-matching could be found for this very small threshold r [14]. To enhance the statistical stability, a new entropy measure, named fuzzy entropy (FuzzyEn), has been proposed for univariate time series analysis by emerging the notion of entropy with the fuzzy theory [15,16]. FuzzyEn employed a fuzzy function to replace the Heaviside function to make a gradually varied entropy value when the threshold r monotonously changes. Its generalized form, cross fuzzy entropy (C-FuzzyEn), has also been developed for the bivariate time series analysis [6,10].

However, no matter for FuzzyEn or C-FuzzyEn, the local vector similarity is overemphasized. Thus both of them might give inaccurate results for some slow signals since they both neglected the signal global characteristics. In our previous work, we developed a novel fuzzy measure entropy (i.e., FuzzyMEn) that combined both the local and global similarity, and FuzzyMEn has shown better algorithm discrimination ability than FuzzyEn [17,18]. In this study, we generalized the FuzzyMEn method for the bivariate time series analysis and compared its performance with C-SampEn and C-FuzzyEn for quantifying the synchronization in both coupled simulation and coupled cardiovascular time series. We defined this new synchronization measure as cross fuzzy measure entropy (i.e., C-FuzzyMEn).

The rest of the paper is organized as follows: Section 2 gives the definition of C-SampEn, C-FuzzyEn and C-FuzzyMEn to allow the detailed comparison and inspection of these three cross entropy measures to be observed. Section 3 discusses the experimental design where three coupled simulation models (i.e., coupled Gaussian noise, coupled MIX(p) and coupled Henon signals) and two cardiovascular time series (RR interval and pulse transit time (PTT) time series) from both the normal and heart failure subjects were constructed for the cross entropy analysis. In Section 4, the results of cross entropy measures from both coupled simulation and coupled cardiovascular time series are provided. Finally, Section 5 draws the discussions and identifies the future work.

2. Cross entropy measures

In this section, we first give a brief introduction for C-SampEn and C-FuzzyEn, and then describe the definition of C-FuzzyMEn.

2.1. Cross sample entropy (C-SampEn)

The calculation process of C-SampEn was summarized as follows [8,14]:

The time series $x(i)$ and $y(i)(1 \le i \le N)$ were first normalized to have a mean value of 0 and standard deviation of 1. Then given the input parameters m and r, the vector sequences X_i^m and Y_j^m were formed as follows:

$$\begin{aligned} X_i^m &= \{x(i), x(i+1), \ldots, x(i+m-1)\} \\ Y_j^m &= \{y(j), y(j+1), \ldots, y(j+m-1)\} \end{aligned} \quad 1 \le i, \quad j \le N-m \tag{1}$$

These vectors represent m consecutive x and y values, respectively. Then the distance between X_i^m and Y_j^m based on the maximum absolute difference is defined as:

$$d_{i,j}^m = d\left[X_i^m, Y_j^m\right] = \max_{k=0}^{m-1} \left|x(i+k) - y(j+k)\right| \tag{2}$$

For each X_i^m, denote $B_i^m(r)$ as $(N-m)^{-1}$ times the number of Y_j^m $(1 \le j \le N-m)$ that meets $d_{i,j}^m \le r$. Similarly, set $A_i^m(r)$ is $(N-m)^{-1}$ times the number of Y_j^{m+1} that meets $d_{i,j}^{m+1} \le r$ for all $1 \le j \le N-m$.

Finally C-SampEn is defined as

$$\mathrm{C-}SampEn(m, r, N) = -\ln\left(\frac{\sum_{i=1}^{N-m} A_i^m(r)}{\sum_{i=1}^{N-m} B_i^m(r)}\right) \tag{3}$$

2.2. Cross fuzzy entropy (C-FuzzyEn)

In both C-ApEn and C-SampEn, the decision rule for vector similarity is very rigid because X_i^m and Y_j^m are considered as similar vectors only when $\max_{k=0}^{m-1} \left|x(i+k) - y(j+k)\right| \le r$. In the definition of C-FuzzyEn, the vectors X_i^m and Y_j^m are formed as follows:

$$\begin{aligned} X_i^m &= \{x(i), x(i+1), \ldots, x(i+m-1)\} - \bar{x}(i) \\ Y_j^m &= \{y(j), y(j+1), \ldots, y(j+m-1)\} - \bar{y}(j) \end{aligned} \quad 1 \le i, \quad j \le N-m \tag{4}$$

These vectors X_i^m and Y_j^m also represent m consecutive x and y values respectively but removing the local baseline $\bar{x}(i)$ and $\bar{y}(j)$, which are defined as:

$$\begin{aligned} \bar{x}(i) &= \frac{1}{m}\sum_{k=0}^{m-1} x(i+k) \\ \bar{y}(j) &= \frac{1}{m}\sum_{k=0}^{m-1} y(j+k) \end{aligned} \quad 1 \le i, \quad j \le N-m \tag{5}$$

Calculate the distance between X_i^m and Y_j^m also using the maximum absolute difference:

$$d_{i,j}^m = d\left[X_i^m, Y_j^m\right] = \max_{k=0}^{m-1} \left|(x(i+k) - \bar{x}(i)) - (y(j+k) - \bar{y}(j))\right| \tag{6}$$

Given vector similarity weight n and threshold r, calculate the similarity degree $D_{i,j}^m(n, r)$ between X_i^m and Y_j^m by a fuzzy function $\mu(d_{i,j}^m, n, r)$:

$$D_{i,j}^m(n, r) = \mu(d_{i,j}^m, n, r) = \exp\left(-\frac{(d_{i,j}^m)^n}{r}\right) \tag{7}$$