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Average Entropy: Measurement of disorder for cardiac RR interval signals

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HIGHLIGHTS

- AE reflects the disorder of both probability distribution & randomness of a series.
- AE analysis is able to differentiate the CHF, the healthy, and the AF subjects.
- EoE (complexity) vs. AE (disorder) exhibits a distinct inverted U curve.

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ABSTRACT

We introduce average entropy (AE) as a disorder measure of heart rate time series. The AE measurement reflects both the probability distribution of all discrete values in a time series and the randomness of the series. The AE analysis is able to differentiate the congestive heart failure (CHF), the healthy, and the atrial fibrillation (AF) subjects for both short and long heart rate time series. The differentiation accuracy of AE is higher than 90%. In addition, since the meaning of "disorder" is easily confused with "complexity", we explore the relation between them by analyzing heart rate time series. Specifically, we demonstrate that the complexity measured by entropy of entropy (EoE) versus the disorder measured by AE plot of heart rate time series exhibits a distinct inverted U relation.

1. Introduction

Quantifying the disorder and the complexity of physiologic signals in health and disease as well as their relation have been explored in many studies [1–14].

Disorder of a time series is the uncertainty of the next value in a series when the preceding values are known [15]. Among the various disorder measures, Shannon entropy (ShannonEn) and sample entropy (SampEn) are widely used [14–16]. ShannonEn measures the average uncertainty of the probability distribution of all discrete values in a time series [15,16]. ShannonEn of a series is maximal when all values in the series are uniformly distributed within a fixed range. However, ShannonEn does not take into account the sequential irregularity of the series.

On the contrary, SampEn measures the disorder of a series in terms of the sequential irregularity (randomness) of the series [14]. This results in a maximal SampEn value for a completely random series. However, the overall amplitude of a time series is subject to change since the standard deviation of the series is always normalized to 1 in SampEn measurement [14]. In other words, SampEn does not reflect the original discrete probability distribution of the series.

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Both ShannonEn and SampEn have been applied to the analysis of physiologic signals in health and disease for a long time. For example, they have been used to differentiate the RR interval series extracted from the congestive heart failure (CHF) subjects, the healthy subjects, and the atrial fibrillation (AF) subjects [1,2,10]. However, it was found that ShannonEn is not effective in differentiating the healthy from the AF groups [10] while the SampEn leaves the healthy and the CHF groups indistinguishable [1].

Multiscale entropy (MSE) is SampEn of a time series calculated under multiple time scale. MSE is able to differentiate the three groups of subjects, namely CHF, healthy, and AF for the scales between 2 and 5. Under this range, the MSE values for CHF, healthy, and AF subjects are small, medium, and large, respectively. It is worth noting that MSE was proposed as a measure of the complexity of a physiologic time series. It reflects the degree of healthiness of a biological system through its output physiologic signals. For a large scale factor ($\sim$20), the MSE value of a RR interval series from the healthy group is higher than both those from CHF and AF subjects [1,2].

We introduce a new measure of disorder, called Average Entropy (AE), which reflects both the probability distribution of all discrete values in a series and the randomness of the series. We first test the AE method on a set of simulated series whose probability distribution and randomness are independently tunable. The results evaluated by using AE are compared with those obtained using ShannonEn and SampEn. Then, we test the AE method on simulated white and 1/f noises.

Next, we apply AE to differentiate CHF, healthy, and AF subjects for both short (500 data points) and long (10,000 data points) cardiac RR interval series from the online databases on PhysioNet [17]. The results evaluated by using AE are then compared with those obtained by using ShannonEn, SampEn, MSE (at scale 2 to 5), and distribution entropy (DistEn). The DistEn can also be applied to differentiate the three groups [12,13]. In addition, we also explore the relation between the complexity measured by entropy of entropy (EoE) [10] and the disorder measured by AE for both of the simulated series and the RR interval series.

2. Method and materials

2.1. Average entropy (AE) method

The algorithm of AE method consists of three steps in analyzing a time series $\{x_i\} = \{x_1, \ldots, x_N\}$ of length N. First, we equally divide the series $\{x_i\}$ into consecutive and non-overlapping subseries $w_j^{(\tau)} = \left\{x_{(j-1)\tau+1}, \ldots, x_{(j-1)\tau+\tau}\right\}$, where τ is the length of each subseries $w_j^{(\tau)}$ and j is the subseries index ranging from 1 to N/τ. Note that τ corresponds to the scale factor.

Next, we calculate the ShannonEn value for each subseries $w_j^{(\tau)}$. Suppose that x_{max} and x_{min} are the maximum and minimum of all series in this study. We divide the range from x_{max} to x_{min} into s_1 slices of equal width, $\Delta s_1 = (x_{max} - x_{min})/s_1$, such that each slice represents an independent state. Subsequently, the ShannonEn value $y_j^{(\tau)}$ of subseries $w_j^{(\tau)}$ is

$$y_j^{(\tau)} = -\sum_{k=1}^{s_1} p_{jk} \ln p_{jk}, \tag{1}$$

where p_{jk} is the probability of slice index k to occur in subseries $w_j^{(\tau)}$, where k ranges from 1 to s_1. Repeating the same process for every subseries, we construct a local Shannon entropy sequence $\left\{y_j^{(\tau)}\right\}$ of length N/τ.

Finally, the AE is defined simply as the average of the local Shannon entropy sequence $\left\{y_j^{(\tau)}\right\}$ in the form of

$$AE = \frac{\sum_{j=1}^{N/\tau} y_j^{(\tau)}}{N/\tau}. \tag{2}$$

Note that AE is a function of time scale τ.

In this study, the AE method will be applied to 218 cardiac RR interval time series. The data size N of each time series is either 500 or 10,000. Among them, the maximum and the minimum RR interval values of the 218 series are found to be $x_{max} = 1.6$ and $x_{min} = 0.3$, respectively. The analysis is robust with respect to the parameter s_1 within 30 to 70, thus we set s_1 at 55 in this study, as suggested in our previous study on EoE [10].

Fig. 1 demonstrates the application of the AE method to a RR interval time series. For simplicity, the series is analyzed under conditions $N = 100$ and $\tau = 5$.

2.2. Data description

The 218 cardiac RR interval time series used in this study are extracted from the following three groups of databases in the online database on Physionet [17]. Namely, they are (i) the BIDMC (Beth Israel Deaconess Medical Center) Congestive Heart Failure Database, (ii) the MIT (Massachusetts Institute of Technology)-BIH (Beth Israel Hospital) Normal Sinus

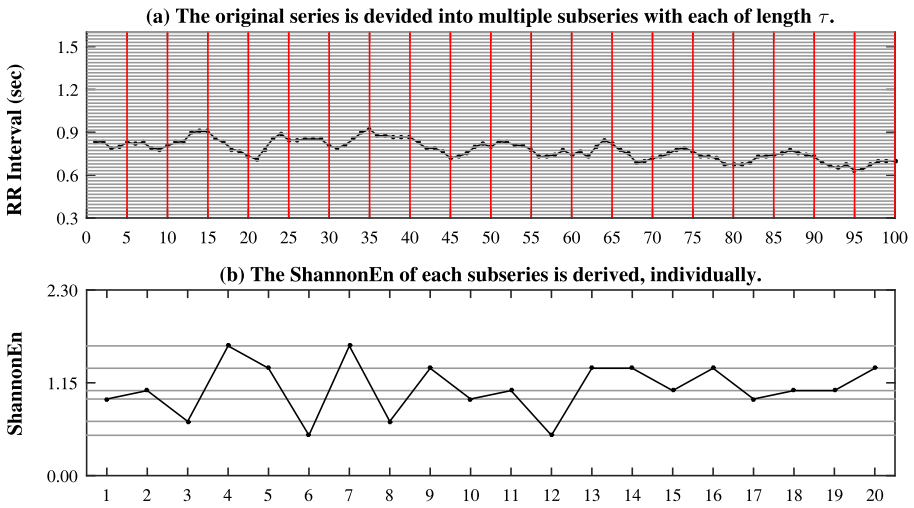

Fig. 1. Illustration of the AE method. (a) shows the original RR series with $N = 100$ data points, and the series is equally divided into $N/\tau = 20$ subseries with each of $\tau = 5$ data points in the red frames. The range of the RR intervals from $x_{min} = 0.3$ to $x_{max} = 1.6$, derived from the three databases on PhysioNet, is equally divided into $s1 = 55$ slices. Then, the ShannonEn for each subseries is calculated, and this results in a sequence of 20 ShannonEn values as shown in (b). Finally, the AE value of the original series is the average of the ShannonEn sequence. For reference, EoE value is the ShannonEn of the ShannonEn sequence [10].

Rhythm Database, which is a database of healthy subjects, and (iii) the Long Term AF Database. For convenience, they are abbreviated as CHFDB, NSRDB, and LTAFDB in the following context. Note that CHFDB, NSRDB, and LTAFDB consist of 15, 18, and 83 24-hour-long Electrocardiography (ECG) raw records, respectively. And the RR interval series extracted from each of the long-term ECG raw records is more than 50,000 data points.

To remove the outlier data points in RR interval series, which may be the noise or detection error, the following two-step process is applied to each of the 116 long-term RR interval series. First, for each individual data point in a RR interval series, we calculate the mean (MEAN) of the 10 data points before and after the data point itself. The data point under test will be removed under the condition that it is out of the range MEAN $\pm$ 0.5 MEAN. Second, for each of the remaining data points which pass the test in step one, we repeat step one for the mean (MEAN′) and the standard deviation (SD′). The data point under test will be removed under the condition that it is out of the range MEAN′ $\pm$ 2.5 SD′.

Then, for each of the 15 and 18 long-term ECG signals from the CHFDB and the NSRDB, we extract the first 50,000 data points and truncate it into 5 sets of 10,000 data points for analysis. The purpose of analyzing 5 single time series for every subject is to dilute the influence of any sampling error such as abnormal series or detection errors in any single series. As for each of the 83 long-term ECG signals from the LTAFDB, we first extract all the data segments during AF episodes, according to the annotation in PhysioNet. Among them, we adopt 53 segments whose lengths all exceed 10,000 data points, individually. As a result, there are 218 long-term time series, in which 75, 90, and 53 sets are from CHFDB, NSRDB, and LTAFDB, respectively. From each of the 218 sets of time series, we further extract the first 500 or 10,000 data points as a short or long time series for the following analysis

2.3. The overall accuracy in differentiating subjects into AF, healthy, and CHF groups

We will compare the proposed AE with Shannon entropy (ShannonEn), multiscale entropy (MSE), and distribution entropy (DistEn) in terms of the overall accuracy in differentiating all subjects into AF, healthy, and CHF groups. The evaluation of overall accuracy for the four kinds of entropy is as following.

Consider a group of cardiac RR interval time series consisting of N_{CHF} CHF, N_H healthy, and N_{AF} AF sets so that there are N_{Total} $(= N_{CHF} + N_H + N_{AF})$ sets in total. For each entropy, we first compute the entropy value of each of the N_{Total} sets. Since the CHF, healthy, and AF heart rate time series exhibit low, medium, and high disorder, respectively, we assign two thresholds of values th_1 and th_2 for the separation of the N_{Total} sets into the three groups according to their entropy values.

Suppose that, among the N_{CHF} CHF, N_H healthy, and N_{AF} AF sets of RR interval time series, there are N_{TC}, N_{TH}, and N_{TA} sets whose values of the entropy are below th_1, between th_1 and th_2, and above th_2, respectively. In another words, these N_{TC}, N_{TH}, and N_{TA} sets are identified and classified under CHF, healthy, and AF groups. Thus, we define the overall accuracy of the entropy in differentiating the three groups as a function of th_1 and th_2 as given by:

$$\text{overall accuracy } (th_1, th_2) = \frac{N_{TC} + N_{TH} + N_{TA}}{\#\text{ of all set } (= N_{Total})}, \tag{3}$$

Consequently, the optimal values of th_1 and th_2 are determined when the maximal overall accuracy $A_{overall}$ is reached. Under this condition, the corresponding three optimal accuracies of the entropy in identifying each of the three groups are:

$$\text{CHF accuracy} : A_{CHF} = \frac{N_{TC}}{N_{CHF}}, \tag{4}$$

$$\text{Healthy accuracy} : A_H = \frac{N_{TH}}{N_H}, \tag{5}$$

$$\text{AF accuracy} : A_{AF} = \frac{N_{TA}}{N_{AF}}, \tag{6}$$

This method is valid for ShannonEn and DistEn to evaluate their maximal overall accuracies but not sufficient for the multiscale-based MSE and AE. This is because the optimal time scales τ of MSE and AE in separating the three groups have to be determined, correspondingly. Thus, according to Eq. (3), we first evaluate the maximal overall accuracy of MSE or AE at every τ, separately. Then, the optimal τ, $th_1(\tau)$, and $th_2(\tau)$ are determined when the maximum $A_{overall}$ among the various maximal overall accuracies of MSE or AE is reached.

3. Results

A set of series is synthesized for the numerical validation of the AE method. It will be demonstrated that the two parameters of each of the series, the probability distribution of all discrete values and the randomness, are tunable, independently. Then, the dependence of the AE method on the two parameters of the simulated series is examined. In addition, the AE method on simulated white and 1/f noises series are also examined.

As a practice of analysis, the AE method is applied to a set of RR interval time series from the online databases on PhysioNet [17]. The results evaluated by using AE are compared with those obtained by using ShannonEn, SampEn, MSE (at scale 2 to 5), and DistEn. Finally, an inverted U relation between the complexity and the disorder of the RR interval series is illustrated for further exploration.

3.1. Numerical validations

3.1.1. Randomly shuffled series from ordered to disordered

Consider an oblique straight line of 10,000 data points which are equally distributed from 0 to R, where R represents the range of the time series and is tunable between 0.0 and 1.0. Fig. 2(a) shows an original series whose $R = 0.8$. Under an extreme condition of $R = 0.0$, the probability distribution of the values in the series looks like a delta function peaking at 0.0. The ShannonEn of the series is 0.0. On the contrary, under the extreme condition of $R = 1.0$, the probability distribution is constant within the range from 0 to 1. The ShannonEn of the series is maximal. It is worthy of noting that the ShannonEn of any series reaches maximal only under the condition that the probability distribution of the values in the series is uniform within an assigned range.

Fig. 2(b), (c), and (d) illustrate the results of the three different series derived from the original one, in which 500, 2000, and 10,000 data points are randomly selected and shuffled, respectively. Obviously, the degree of randomness of the three shuffled series increases along with the number M of the data points shuffled. By comparison, the original series in Fig. 2(a) and the shuffled one in Fig. 2(d) are considered extremely ordered and disordered under the fixed distribution range of R.

Figs. 3(a) and 3(b) shows the ShannonEn and SampEn values as a function of the number M of data points randomly shuffled for the five different original series whose distribution range R are 1.0, 0.5, 0.25, 0.13, and 0.06, separately. Here, the number of slices s_1 for ShannonEn is set at 55, as suggested in our previous study on EoE [10]. The parameters (m, r) for the vector length and the similarity criterion in SampEn are set at (2, 0.15 $\times$ SD) where SD is the standard deviation of the original time series as suggested [1,2]. It can be seen that the ShannonEn value is independent of the randomness in terms of M, but increases along with the distribution range R of the shuffled series. On the contrary, the SampEn value is independent of R but increases along with M.

For comparison, Fig. 4 illustrates the AE value as a function of the distribution range R and the randomness in terms of M for the shuffled series like those in Fig. 2. The analysis is performed under the condition at $x_{max} = 1$, $x_{min} = 0$, $s_1 = 55$, and $\tau = 5$. Each AE value in Fig. 3 is averaged from ten randomly shuffled series of the same R and M. Obviously, the AE value increases with increasing R and M.

In Fig. 5, we explore the relation between the disorder and the complexity of the shuffled series. Here, the disorder is measured by AE, and the complexity is measured by entropy of entropy (EoE) [10]. Both methods are evaluated at $x_{max} = 1$, $x_{min} = 0$, $s_1 = 55$, and $\tau = 5$. We compute the EoE and the AE values for series of $R = 1$ and M ranging from 0 to 10,000 at an interval of $\Delta M = 100$. For each M, 10 simulations are computed, from which a pair of averaged EoE and AE values is obtained. The dots are the results of all the 1010 (=101 $\times$ 10) simulations. The curve indicates the 101 pairs of the M-associated averages.

It can be seen in Fig. 5 that the complexity *vs*. disorder plot exhibits a distinct inverted U relation, where the maximal complexity value appears in the middle of extreme order and disorder. The result is consistent with the hypothesis in many studies [1–7]. This confirms that the complexity and the disorder are different.

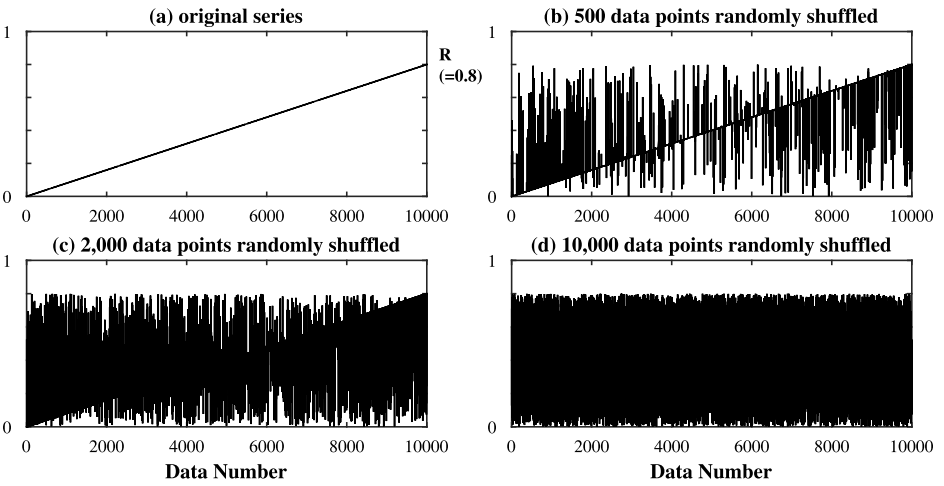

Fig. 2. (a) shows the original series which is an oblique straight line of 10,000 data points ranging from 0 to $R = 0.8$. (b), (c), and (d) show the series, in which $M = 500$, 2000, and 10,000 data points are randomly shuffled, respectively. Note that (a) is considered extremely ordered while (d) is extremely disordered under the fixed distribution range of R.

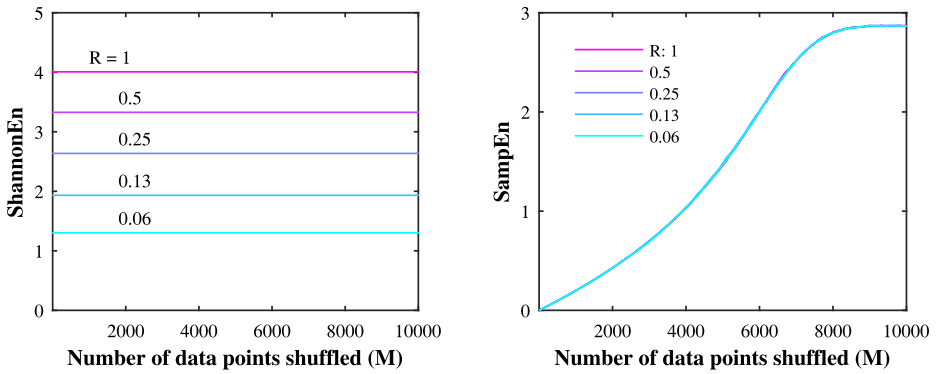

Fig. 3. (a) ShannonEn and (b) SampEn values of the randomly shuffled series as a function of the number M of data points randomly shuffled at the distribution range $R = 1$, 0.5, 0.25, 0.13, and 0.06, separately.

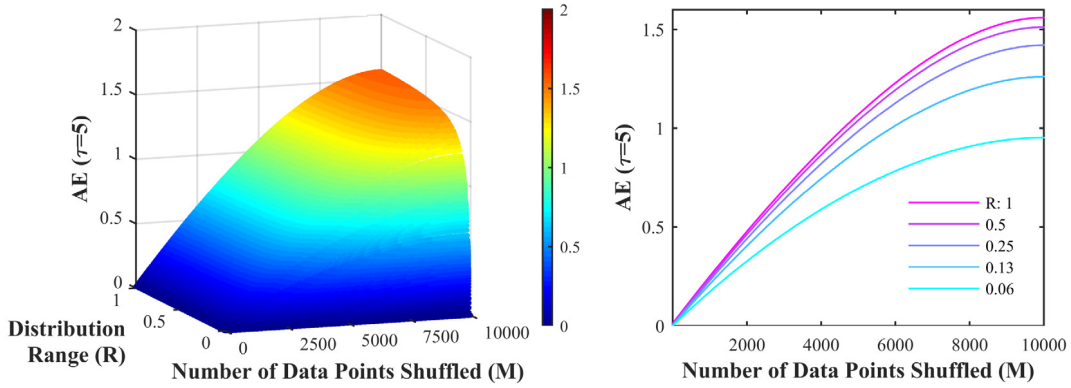

Fig. 4. Left: AE values of the randomly shuffled series as a function of the distribution range R and the number M of data points randomly shuffled. The analysis is performed under the condition at $\tau = 5$, $x_{max} = 55$, $x_{min} = 1$, and $s_1 = 55$. Right: Five typical AE curves as a function of M at $R = 1$, 0.5, 0.25, 0.13, and 0.06, separately.

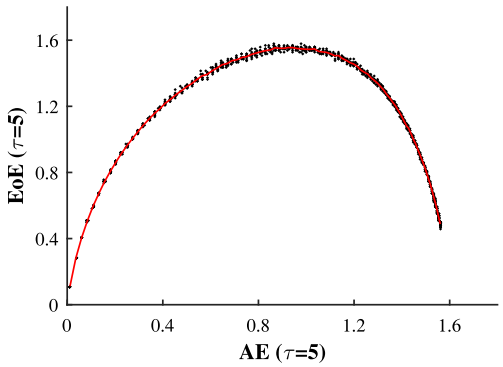

Fig. 5. EoE *vs.* AE for series with $R = 1$ and M ranging from 0 to 10,000 at an interval of $\Delta M = 100$. For each M, 10 simulations are computed, from which a pair of averaged EoE and AE values is obtained. The dots are the results of all the 1010 (=101 × 10) simulations. The curve indicates the 101 pairs of the M-associated averages.

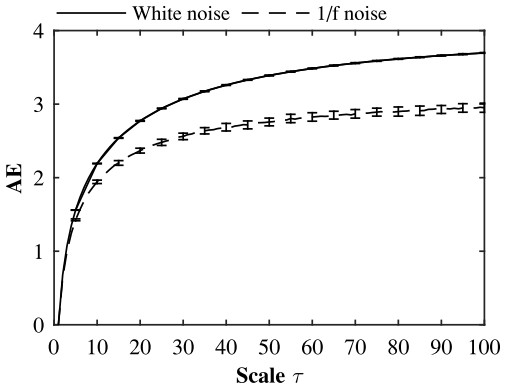

Fig. 6. AE analysis of 100 simulated 1/f noise and uniform distributed white noise time series, with each of 10,000 data points. Symbols represent the mean values and error bars the standard deviation. The AE value of the white noise is higher than the 1/f noise for scale factor larger than 1.

3.1.2. Simulated 1/f noises and uniformly distributed white noises

We apply the AE method to two kinds of synthetic noises that are commonly used for test. Specifically, 100 simulated time series of 1/f noise and uniformly distributed white noise are separately generated with each series consisting of 10,000 data points. And the maximum and the minimum of every noise are normalized so that $x_{max} = 1$ and $x_{min} = 0$, respectively. The range is then equally divided into $s_1(= 55)$ slices, as suggested in the study of EoE [10].

Fig. 6 shows the average AE values of the 100 1/f noise time series and those of the 100 uniformly distributed white noise series, separately. It can be seen that the average AE values of the 1/f noises are lower than those of the white noises for the scale factors τ larger than 1, which is as expected.

3.2. Short (500 points) and long (10,000 points) RR interval series

Then, we apply the AE analysis to the RR interval series. Among the 218 short (500 points) and the 218 long (10,000 points) data sets of 75 ($= N_{CHF}$) CHF, 90 ($= N_H$) healthy, and 53 ($= N_{AF}$) AF, we differentiate the CHF, the healthy, and the AF subjects with ShannonEn, MSE, DistEn, and AE. Figs. 7(a) and 7(b) exhibit the three average AE values of the three groups of the short and the long series as a function of time scale τ, respectively. It can be seen that the three average AE curves in Fig. 7 are well separated apart from each other, highlighted by the two auxiliary threshold curves $th_1(\tau)$ and $th_2(\tau)$, functions of time scale τ, in dots. As a result, the maximums of the various maximal overall accuracies of AE in separating the three groups of the short and the long series are 91% and 94%, respectively. It happens that both cases occur at $\tau = 14$.

Similarly, Fig. 8 exhibits the three average MSE values of the three groups of long series (10,000 points) as a function of time scale τ, separately. It is found that the three average MSE curves can be separated apart from each other within $2 \leq \tau \leq 5$, highlighted by the two sets of auxiliary threshold with each of four dots. As a result, the maximum of the various maximal overall accuracies of separation for MSE is 79% at $\tau = 3$. Note that MSE is equal to SampEn at scale 1, where the healthy and the CHF groups are indistinguishable though.

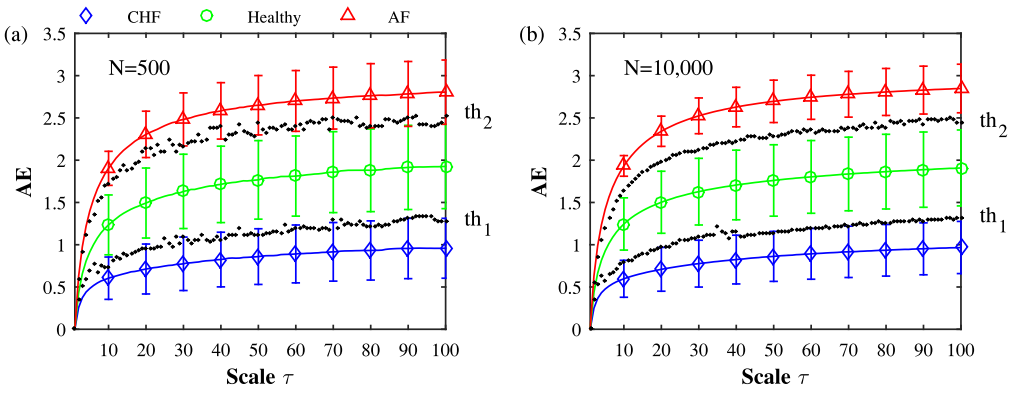

Fig. 7. AE value *vs.* time scale τ at $s_1 = 55$ for the 75, 90, and 53 sets of RR interval time series with each of (a) 500 and (b) 10,000 data points from the CHFDB, the NSRDB, and the LTAFDB. Symbols represent the mean values of AE for each group and bars represent the standard deviations. The three average AE curves are well separated apart from each other, highlighted by the two auxiliary threshold curves $th_1(\tau)$ and $th_2(\tau)$, functions of time scale τ, in dots.

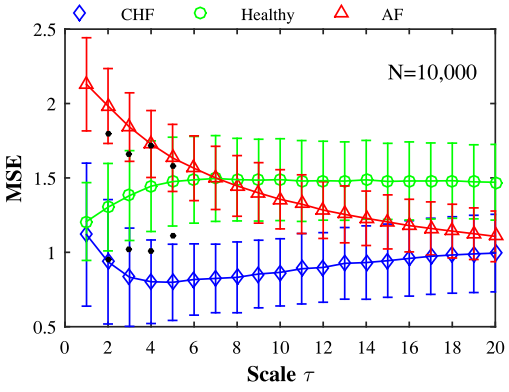

Fig. 8. MSE value *vs.* time scale τ for the 75, 90, and 53 sets of RR interval time series with each of 10,000 data points from the CHFDB, the NSRDB, and the LTAFDB. Symbols represent the mean values of AE for each group and bars represent the standard deviations. The three average MSE curves can be separated apart from each other at $2 \leq \tau \leq 5$, highlighted by the two sets of auxiliary threshold with each of four dots.

Table 1
$A_{overall}$, A_{CHF}, A_H, and A_{AF} of AE, ShannonEn, and DistEn in differentiating the 218 short RR interval time series (500 data points) into CHF, healthy, and AF groups, separately.

Accuracies (N = 500)	A_{CHF}	A_H	A_{AF}	$A_{overall}$
AE ($\tau = 14$)	0.88	0.96	0.89	0.91
ShannonEn	0.77	0.89	0.85	0.84
DistEn	0.73	0.91	0.64	0.78

Figs. 9(a) and 9(b) show the averages and the standard deviations of the four different entropy values of the three groups of the short (500 points) and the long (10,000 points) series, respectively. Here, the number of slices s_1 in ShannonEn is set at 55. The parameters (m, r) for the vector length and the similarity criterion in MSE are (2, 0.15 × SD) where SD is the standard deviation of the original time series as suggested [1,2]. The optimal τ is 3 in MSE. The parameters (m, M) for the vector length and the number of bins in DistEn are (2, 512) as suggested [12,13]. The optimal τ is 14 in AE.

In Table 1, according to Eqs. (3)–(6), we list the maximal overall accuracy $A_{overall}$ and the three corresponding optimal accuracies A_{CHF}, A_H, and A_{AF} of AE, ShannonEn, and DistEn to differentiate the 218 short RR interval time series into CHF, healthy, and AF groups, separately.

Similarly, in Table 2, we list the maximal overall accuracies of AE, ShannonEn, MSE, and DistEn to differentiate the 218 long RR interval time series into CHF, healthy, and AF groups, separately. By comparison, AE exhibits the best performance for both short and long series, according to Eqs. (3)–(6).

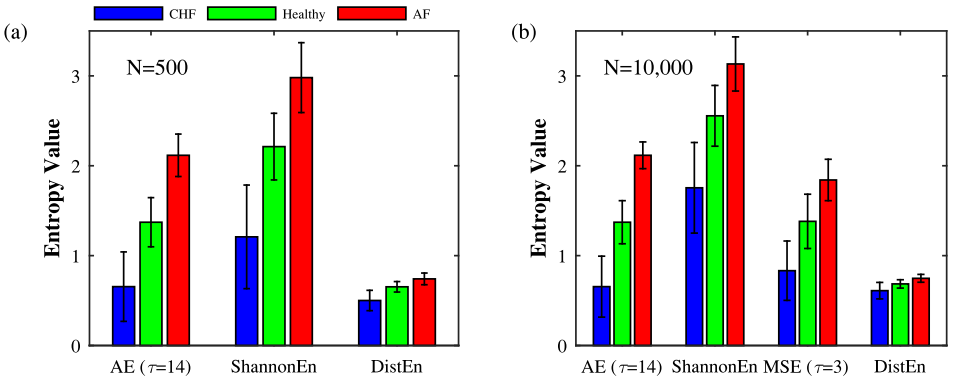

Fig. 9. (a): Comparison of the three entropy measures for short (500 points) time series: AE ($\tau = 14$), ShannonEn, and DistEn in terms of the averages and standard deviations of the entropy values for the CHF, the healthy, and the AF subjects. Bars represent the standard deviations. (b): Comparison of the four entropy measures for long (10,000 points) time series: AE ($\tau = 14$), ShannonEn, MSE ($\tau = 3$), and DistEn.

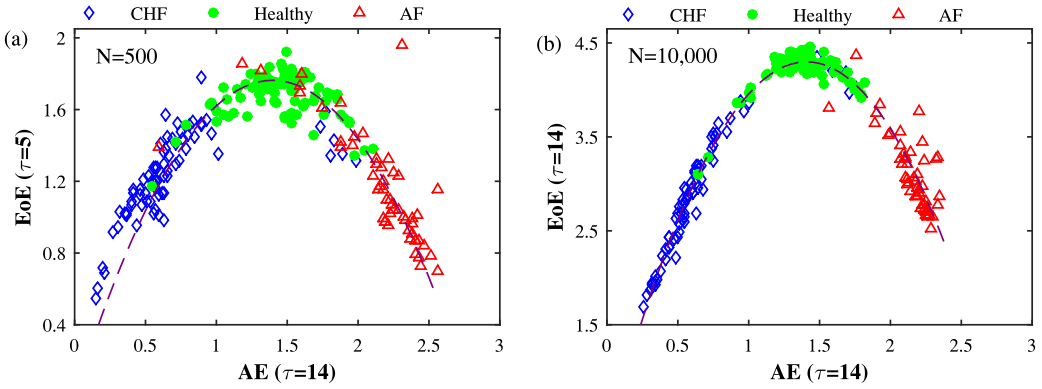

Fig. 10. EoE *vs.* AE for the same 218 sets of time series with each of (a) 500 and (b) 10,000 data points. The 75 diamond, 90 circle, and the 53 triangle symbols are from the 15 CHF, the 18 healthy, and the 53 AF subjects. The dashed line is a quadratic fitting in each plot.

Table 2
$A_{overall}$, A_{CHF}, A_H, and A_{AF} of AE, ShannonEn, MSE, and DistEn in differentiating the 218 long RR interval time series (10,000 data points) into CHF, healthy, and AF groups, separately.

Accuracies (N = 10,000)	A_{CHF}	A_H	A_{AF}	$A_{overall}$
AE ($\tau = 14$)	0.88	0.97	0.96	0.94
ShannonEn	0.83	0.77	0.85	0.81
MSE ($\tau = 3$)	0.73	0.77	0.93	0.80
DistEn	0.60	0.81	0.60	0.69

3.3. Inverted U relation between complexity and disorder for RR interval series

Finally, we explore the relation between the disorder and the complexity of both the 218 short and the 218 long RR interval series. Again, the disorder is measured by AE, and the complexity is measured by entropy of entropy (EoE) [2]. Both methods are evaluated at $x_{max} = 1.6$, $x_{min} = 0.3$, and $s_1 = 55$. The AE is computed at the optimal $\tau = 14$, as in Section 3.2. The EoE is computed at the optimal $\tau = 5$ for the short series [2] and the optimal $\tau = 14$ for the long time series to best separate the healthy subjects from the pathologic subjects.

As a result, Fig. 10(a) illustrates the EoE ($\tau = 5$) vs. AE ($\tau = 14$) of the 75 CHF, the 90 healthy, and the 53 AF sets of short RR interval series (500 data points). Fig. 10(b) illustrates the EoE ($\tau = 14$) vs. AE ($\tau = 14$) of the same 218 long series (10,000 data points). It can be seen that both the EoE *vs.* AE plots exhibit a very sharp inverted U shape.

4. Discussion

In the introduction section, we have mentioned the drawback of quantifying the disorder of a time series by ShannonEn and SampEn. ShannonEn quantifies the disorder of a time series by taking into account the probability distribution of the discrete values of the series, while neglecting the sequential irregularity of the series. On the contrary, SampEn measures

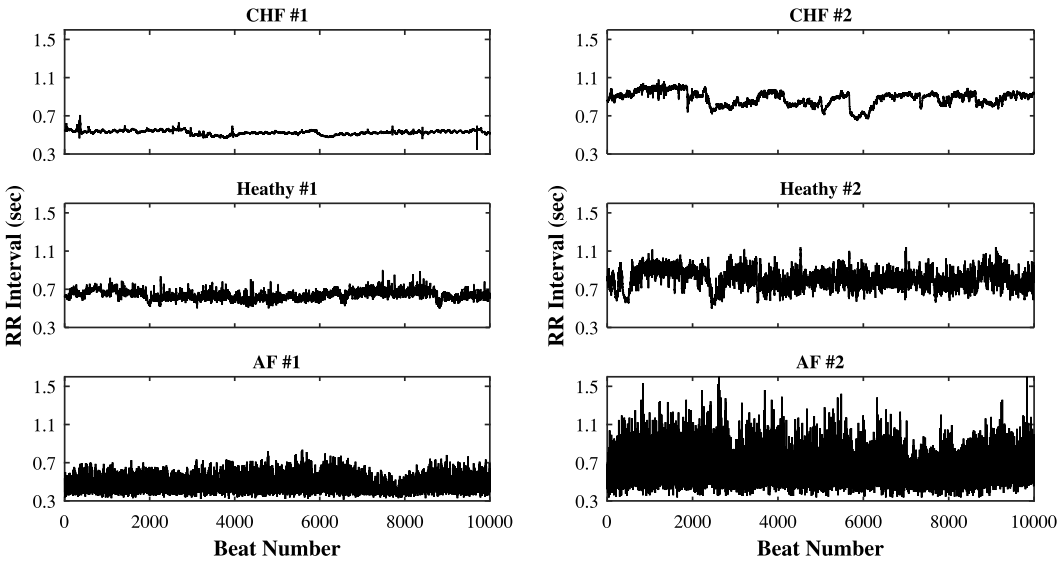

Fig. 11. Six RR intervals time series from two CHF, two healthy, and two AF subjects with each of 10,000 data points.

Table 3
The ShannonEn, SampEn, and AE values for the six RR interval time series illustrated in Fig. 11.

	ShannonEn	SampEn	AE ($\tau = 14$)
CHF #1	1.40	1.82	0.42
CHF #2	2.49	0.81	0.73
Healthy #1	2.10	1.48	1.19
Healthy #2	2.81	1.58	1.73
AF #1	2.53	2.10	1.93
AF #2	3.23	1.91	2.20

the disorder of a series in terms of the sequential irregularity (randomness) of the series, while it does not reflect the original discrete probability distribution of the series.

In this section, we illustrate some misjudgments while applying ShannonEn and SampEn to differentiate the RR interval time series from the CHF, the healthy, and the AF subjects. Fig. 11 illustrates RR interval time series from two CHF, two healthy, and two AF subjects. Each series consists of 10,000 data points. And the ShannonEn, SampEn, and AE values of each series are listed in Table 3.

Since AE values of the series reflects both the probability distribution of all discrete values in a time series and the randomness of the series, AE values of RR interval series from CHF, healthy, and AF subjects are relatively small, medium, and large, respectively. And thus each group is well separated from the others.

For comparison, the ShannonEn of CHF #2 series is higher than Healthy #1, and that of Healthy #2 is higher than AF #1. Thus, the ShannonEn values of the three groups in this example are not well separated. This is because the ShannonEn of a series is not able to reflect the randomness of the series.

On the other hand, the SampEn of CHF #1 series is higher than both Healthy #1 and Healthy #2 even though the distribution of the CHF #1 is quite concentrated. That is because the algorithm of SampEn is to normalize the series to have its standard deviation equals to 1 [14]. Therefore, SampEn does not reflect the original discrete probability distribution of the series.

5. Conclusion

We have introduced AE to measure the disorder for both simulated and physiologic RR interval series. In the analysis of the simulated series, we have shown that the AE measurement reflects both the probability distribution of all discrete values in a time series and the randomness of the series.

In the analysis of the 218 short (500 data points) and the 218 long (10,000 data points) RR interval time series, we have demonstrated that the disorder of the AF group measured by AE is higher than that of the healthy group, while the disorder of the CHF group is lower than that of the healthy group. The overall accuracy of AE in differentiating the three groups is 91% for the short series and 94% for the long series. Both are higher than those measured by ShannonEn, MSE (scale 2 to 5), and DistEn.

Finally, we explore the relation between the complexity measured by EoE and the disorder measured by AE. We have confirmed that the two measures are different as they exhibit inverted U relation for both the simulated and the physiologic series, which is consistent with the hypothesis in many studies [1–7].

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Author contributions

Conceptualization, Chang Francis Hsu, Sien Chi, and Ping-Yen Lin; Formal analysis, Chang Francis Hsu and Hsuan-Hao Chao; Methodology, Chang Francis Hsu, Sien Chi, and Ping-Yen Lin; Supervision, Sien Chi; Writing — original draft, Chang Francis Hsu and Long Hsu; Writing — review & editing, Long Hsu and Sien Chi.

Declaration of competing interest

The authors declare no conflict of interest.

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