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Modified multiscale Renyi distribution entropy for short-term heart rate variability analysis

Manhong Shi[1*†], Yinuo Shi[2†], Yuxin Lin[3,4*] and Xue Qi[1]

Abstract

Background Multiscale sample entropy (MSE) is a prevalent complexity metric to characterize a time series and has been extensively applied to the physiological signal analysis. However, for a short-term time series, the likelihood of identifying comparable subsequences decreases, leading to higher variability in the Sample Entropy (SampEn) calculation. Additionally, as the scale factor increases in the MSE calculation, the coarse-graining process further shortens the time series. Consequently, each newly generated time series at a larger scale consists of fewer data points, potentially resulting in unreliable or undefined entropy values, particularly at higher scales. To overcome the shortcoming, a modified multiscale Renyi distribution entropy (MMRDis) was proposed in our present work.

Methods The MMRDis method uses a moving-averaging procedure to acquire a family of time series, each of which quantify the dynamic behaviors of the short-term time series over the multiple temporal scales. Then, MMRDis is constructed for the original and the coarse-grained time series.

Results The MMRDis method demonstrated superior computational stability on simulated Gaussian white and 1/f noise time series, effectively avoiding undefined measurements in short-term time series. Analysis of short-term heart rate variability (HRV) signals from healthy elderly individuals, healthy young people, and subjects with congestive heart failure and atrial fibrillation revealed that MMRDis complexity measurement values decreased with aging and disease. Additionally, MMRDis exhibited better distinction capability for short-term HRV physiological/pathological signals compared to several recently proposed complexity metrics.

Conclusions MMRDis was a promising measurement for screening cardiovascular condition within a short time.

Keywords Modified multiscale Renyi distribution entropy, Renyi distribution entropy, Multiscale sample entropy, Heart rate variability

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Introduction

Quantifying the dynamic characteristics of a one-dimensional time series, obtained from the complex systems to monitor the status of such systems, is becoming more and more important, especially with the fast development of smart sensors for physiological signal monitoring [1]. For the characterization of the one-dimensional complex signals, various measures such as, irreversibility [2], similarity analysis [3], Lyapunov exponent [4], entropy estimation [5], etc. have been proposed. Entropy, first proposed by T.Clausius in 1865 and extended to channel communication for assessing the irregularity of information by Shannon in 1948, is an appealing approach and has been widely applied to the physiological signal analysis. Extensively used irregularity estimations for time series are approximation entropy [6], sample entropy (SampEn) [5], permutation entropy [7], etc.. the Values of these conventional entropy-based measures increase with growth of orderliness and is minimum for a periodic sequence. According to the theory of the physiologic complexity, the physiological signals obtained from the healthy system exhibit the long-range correlations due to the better adaptive ability of the individual and are more complex compared to the diseased and aging systems [8]. However, the orderliness measured by these conventional entropy approaches have no direct relationship with the complexity underlying in time series, for example, White Gaussian noise (WGn) is assigned a higher SampEn value compared to 1/f noise having the long-range correlations, which is against study proposed by Fogedby, suggesting that the SampEn method fails to characterize the complexity including in time series [9]. To address this shortcoming, Costa introduced the multiscale entropy (MSE) method to evaluate the complexity of a time series through the SampEn calculation over multiple temporal scales, instead of the single-scale analysis employed by these conventional entropy approaches. their experimental results demonstrated the complexity of heart rate variability (HRV) signals in disease and aging conditions was lower than that in healthy young condition, which is consistent with a universally cognitive that the complexity reduces with aging and disease [10]. Since then, MSE has been widely used in various research fields, e.g., rainfall time series [11], financial time series [12], postural control [13], heart rate variability [14], vibration of rotary machine [15], etc.. However, the reliable MSE analysis needs very large data sets [16], it yields an inaccurate measurement or induces undefined entropy assessments, for short-term time series [17]. For time series with length of N, the length of the coarse graining time series shorten to N/s as scale factor is set to s, suggesting that the coarse graining time series significantly become short as the scale factor is large. Therefore, the modified multiscale entropy methods have been proposed by many scholars with the goal of overcoming the above limitation. For instance, Wu et al. proposed composite multiscale entropy (CMSE) aiming at improving the stability of the entropy values on large scales, and the CMSE-based feature derived from fault bearing vibration signals improves the linear distinguish ability, compared to the MSE-based feature [18]. Modified multiscale entropy (MMSE) was put forward on the basis of performing a moving-average process on the original time series in order to avoid the imprecise entropy assessments [17]. Liu et al. in 2018 developed the refined generalized multiscale entropy (RGME), which considered the higher moments in coarse-graining process instead of first moment (mean values), their results showed that RGME provided the more precise entropy measurements of the complexity for the short-term signals and present the better separation between the pathological and healthy signals in comparison with MSE [8].

However, the reliable MSE analysis requires a large dataset for reliable estimation due to the involvement of coarse-grained sequences at multiple scales and high scales reducing the length of the sequence. A large dataset makes sure there are enough data points at each scale for stable statistical estimates of entropy. Larger datasets also serve to capture the underlying complexity and variability within a time series while simultaneously reducing the noise impact and ensuring entropy measures are responsive to the ordering of samples, thus providing more accurate assessments of signal complexity [5, 19, 20], it yields an inaccurate measurement or induces undefined entropy assessments, for short-term time series [17]. For time series with length of N, the length of the coarse graining time series shorten to N/s as scale factor is set to s, suggesting that the coarse graining time series significantly become short as the scale factor is large. The assessment of the complexity of the downsampled signal is biased by the including artificial components in the MSE algorithm. Additionally, the suboptimal process for the elimination of the fast temporal scales result in the appearance of spurious MSE [21]. Therefore, the modified multiscale entropy methods have been proposed by many scholars with the goal of overcoming the above limitation. Valencia et al. proposed refined multiscale entropy to deal with the bias of MSE in the elimination of the fast temporal scales associated with the use of averaging procedure [21]. Wu et al. proposed composite multiscale entropy (CMSE) aiming at improving the stability of the entropy values on large scales, and the CMSE-based feature derived from fault bearing vibration signals improves the linear distinguish ability, compared to the MSE-based feature [18]. Modified multiscale entropy (MMSE) was put forward on

the basis of performing a moving-average process on the original time series in order to avoid the imprecise entropy assessments [17]. Liu et al. in 2018 developed the refined generalized multiscale entropy (RGMSE), which considered the higher moments in coarse-graining process instead of first moment (mean values), their results showed that RGMSE provided the more precise entropy measurements of the complexity for the short-term signals and present the better separation between the pathological and healthy signals in comparison with MSE [8].

Measuring the complexity of short-term time series is very central across a range of scientific fields such as neuroscience [22], cardiovascular science [23], environmental sciences [24],and finance [12]. Timely seizure onset detection can aid in achieving early intervention in patient care and enhance subsequent patient outcomes when it comes to neuroscience. In addition, in the area of cardiovascular health evaluation, there is increasing attention paid to the use of personal health monitoring and point-of-care diagnostic tests in brief screening windows, such as 5 min [25]. This trend thus emphasizes the need to develop highly efficient and reliable tools for quick assessment of cardiovascular parameters during short examination periods, but the traditional entropy algorithms such as approximate entropy(ApEn), SampEn, have been reported that they are very unstable in the short-term time series [26]. Therefore, Porta et al. proposed a local version of SampEn to acquire a reliable assessment of complexity and identification of nonlinearities [27]. They also employed several strategies to artificially increase the number of matches in the SampEn algorithm, but the simulation results demonstrated these strategies were of no practical use, as they had the inherent risk to destroy specific features of the dynamic in the physiological series [28]. Additionally, SampEn is considered as highly parameter-dependent. Specifically, data length N, reconstructed dimension m (Parameter "m" specifically refers to the length of the sequences compared to each other during the computation. In the SampEn algorithm, the process computes the conditional probability to measure the resemblance between two sequences with varying lengths, designated as "m" and "m + 1", where "m" signifies the dimensionality of the reconstructed phase space used in the analysis [29]), tolerance r (similarity criterion) have direct influence on their assessments and an inappropriate option of the three parameters may cause inconsistent measures, a tiny change in the selection of parameter r among these parameters results in a large variation of the estimations of complexity [30]. Unstable and inconsistent measurement results inevitably occur as multiscale entropies mentioned above such as MSE, CMSE, MMSE, RGMSE were used to evaluate the complexity of time series due to the fact that these multiscale entropies were constructed based on SampEn.

Recently, Li et al. proposed a novel entropy algorithm-distribution entropy (DisEn) aiming at precluding the usage of r in the traditional entropy computations [23]. DistEn makes the best of information hidden in a time series by quantifying the distribution of vector-to-vector distances. Parameter B as the number of bins is introduced in the DistEn measure and the choice of B is independent of data analyzed, unlike parameter r used in ApEn and SamEn, their results demonstrated that the changes of the input parameters, e.g. data length N, reconstructed dimension m, bin number B, had little influence on the DistEn estimations and DistEn was proved to be the best quantifier of short-term HRV signals compared to the ApEn and SampEn measures [31]. However, DistEn quantifies the complexity of time series over only signal scale and may ignore the critical information hidden in multiple temporal scale. Subsequently, Lee et al. in 2018 proposed multiscale distribution entropy (MDE) by computing the DistEn values of the coarse-grained time series obtained via a moving-averaged process [32]. In our recent work, we developed Renyi distribution entropy (RdisEn) based on distribution entropy and Renyi entropy, and numerical experimental results showed that RdisEn possesses the superior ability to differentiate the short-term HRV signals belonging to different groups. Additionally, we proposed a coronary artery disease (CAD) detection scheme combining RdisEn and wavelet packet decomposition, the proposed scheme had achieved 97.5% accuracy, 95% specificity, and 100% sensitivity respectively in identifying the CAD, outperforming most of the existing scheme on CAD detection [1]. Xu et al. in 2019 put forward multiscale Renyi distribution entropy (MRDis) by calculating the RdisEn values of the coarse-graining time series achieved from the conventional coarse-graining algorithm, to analyze the complexity of signals across multiple temporal scales. Simulation results on the financial time series demonstrated that MRDis provided more information by selecting an optimal value of order parameter q [33]. However, the MRDis maybe not applicable to extremely short-term time series due to the limitation of conventional coarse-graining algorithm.

We present in this paper the modified multiscale Renyi distribution entropy (MMRDis) to characterize the complexity of short-term time series. The MMRDis works through a moving-average technique to compute Renyi distribution entropy for the coarse-grained time series. This approach overcomes some limitations of the classical coarse-graining algorithms, especially shortening the length of time series with increasing scale factors.

MMRDis inherits some robustness from RdisEn and gives consistent separation between physiological and pathological signals of short-term HRV. We investigated its performance on synthetic signals with known degrees of complexity to see whether it could glean long-range correlations in short-term data. We also looked at short-term HRV signals of varying lengths from healthy elderly, young individuals, and congestive heart failure and atrial fibrillation patients. Our results confirm MMRDis performing stable and consistent characterization of physiological and pathological states.

Materials and methods

Entropy methods

In this section, we start with a brief overview of the RDisEn, SampEn, MSE, CMSE, RGMSE, and MMSE algorithms, followed by an introduction to the proposed MRDis method in this study.

Renyi distribution entropy

Given a time series with length N,, The RDisEn algorithm constructed by our previous work is described as follows [1]:

(1) Multidimensional vector reconstruction: (N-m+1) vectors are formed by

$$U_i^m = \{u(i+k) : 0 \le k \le m-1\}, 1 \le i \le N-m+1$$

where m denotes embedding dimension.

(2) Distance matrix definition: $D = \{d_{i,j}\}$ between template vectors U_i^m and U_j^m is computed by

$$d_{i,j} = \max\{|u(i+k) - u(j+k)|\}$$

(3) Probability density measurement: the probability is obtained by applying the histogram method to the distance matrix D, where B is a fixed number of bins. The components of the distance matrix D at i=j are excluded in order to reduce bias.

(4) The RDisEn calculation:

$$RDisEn(B,m,q) = \frac{1}{(1-q)\log_2^B}\log_2(\sum_{t=1}^{B} p_t^q)$$

Sample entropy

For a time series $U = (u_1, u_2, \cdots, u_N)$ with length N, the SampEn algorithm is calculated as follows [5]:

(1) Form m-dimensional vectors as

$$U_i^m = \{u(i+k) : 0 \le k \le m-1\}, 1 \le i \le N-m+1$$

(2) Define the distance $d_{i,j} = \max\{|u(i+k) - u(j+k)|\}$ and U_j^m, then a match exists as $d_{i,j} < r$, and then let denotes the total number of matched template vectors.

(3) Repeat the procedures (1) and (2) for m+1-dimensional vectors andis acquired to denote the total number of matched template vectors for m+1-dimensional vectors.

(4) The SampEn calculation:

$$SamEn(m,r) = -\ln\frac{n(m+1,r)}{n(m,r)}$$

Multiscale entropy

Multiscale sample entropy

Costa et al. proposed the concept of classical coarse-grained algorithm of time series and computed the sample entropy value of coarse-grained time series, namely multiscale sample entropy [12]. The MSE methodology is implemented via the following two steps:

(1) Construct coarse-grained time series Z_1^s for a time series $U = (u_1, u_2, \cdots, u_N)$ with length N:

$$v_j^s = \frac{1}{s}\sum_{i=(j-1)s+1}^{js} u_i, \quad 1 \le j \le \lfloor N/s \rfloor$$

Where s is the scale factor,$\lfloor a \rfloor$ represents the largest integer and smaller than a, Fig. 1a shows the procedure of coarse-grained algorithm for scale 3

(2) Calculate SampEn demonstrated in Sect. " Sample entropy", of each coarse-grained time series to obtain the MSE value.

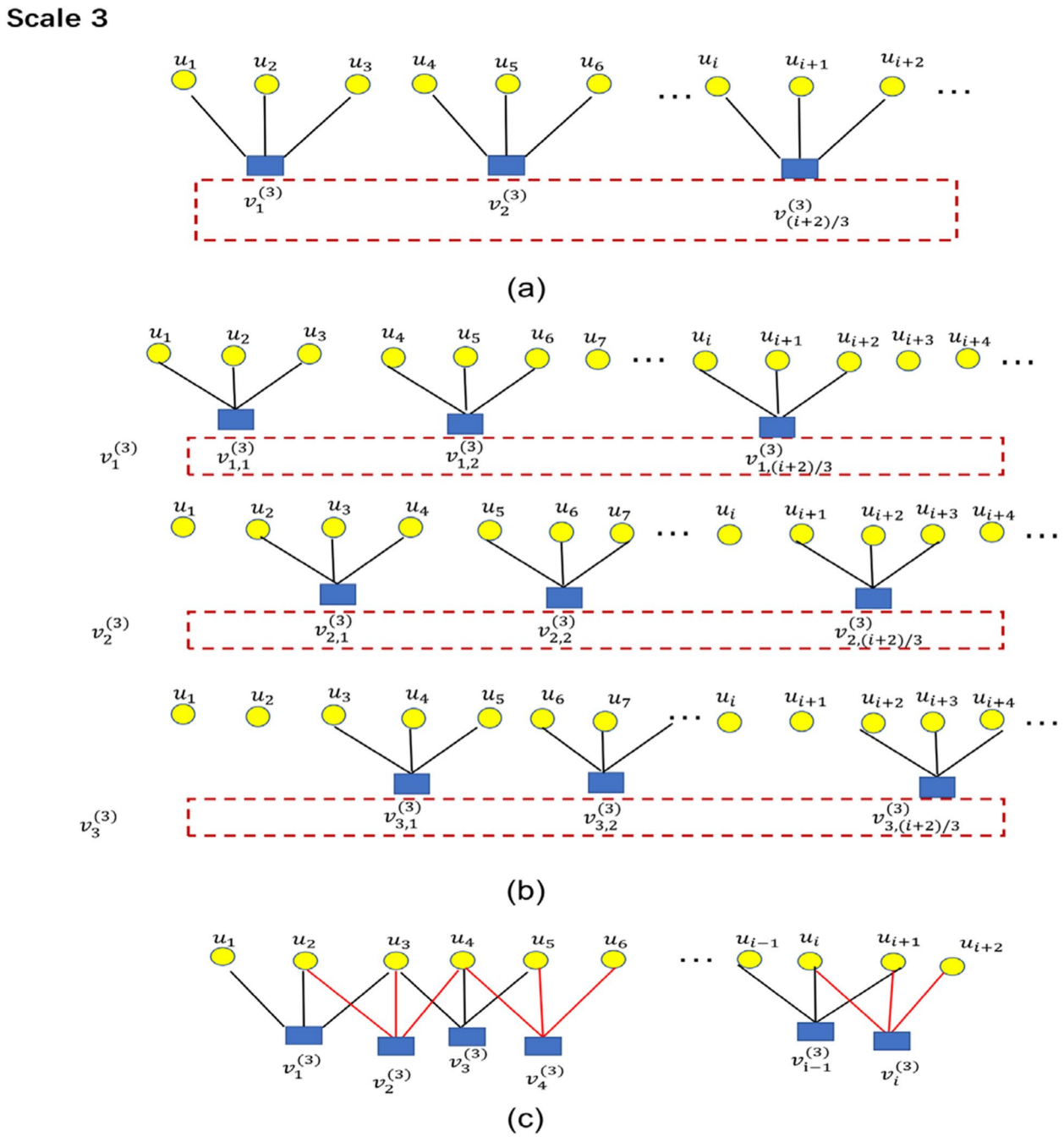

Fig. 1 Schematic drawing of (**a**) coarse-grained algorithm, (**b**) refined generalized coarse-grained algorithm and (**c**) moving-averaging algorithm for scale 3

$$MSE(U,m,r) = SamEn(Z_1^s,m,r) = -\ln\frac{n(m+1,r)}{n(m,r)}$$

Composite multiscale entropy

The CMSE methodology is performed via the following two steps [18]:

(1) s coarse-grained time series Z_2^s are constructed by refined generalized coarse-grained algorithm for each scale factor s, the pth coarse-grained time series $v_p^s = \left\{v_{p,1}^s, v_{p,2}^s, \cdots, v_{p,k}^s\right\}$ is computed by.

(2) Calculate SampEn demonstrated in Sect. " Sample entropy", of each composite coarse-grained time series to obtain the CMSE value.

Where $n(p, m+1, r)$ represents the total number of the matched template for m+1 dimension vectors, Fig. 1b shows the procedure of the composite coarse-grained algorithm for scale 3.

Refined generalized multiscale entropy

The RGMSE methodology is performed via the following three steps [8]:

(1) s coarse-grained time series Z_2^s are constructed by refined generalized coarse-grained algorithm for each scale factor s, the pth coarse-grained time series $v_p^s = \left\{v_{p,1}^s, v_{p,2}^s, \cdots, v_{p,k}^s\right\}$ is computed by.

$$v_{p,j}^s = \frac{1}{s-1} \sum_{j(s-1)+1}^{js+p-1} (u_1 - \overline{u}),\ 1 \le j \le \left\lfloor \frac{N}{S} \right\rfloor, 1 \le p \le s$$

Where $\overline{u} = \frac{1}{s} \sum_{j(s-1)+p}^{js+p-1} u_i$, the procedure of refined generalized coarse-grained algorithm for scale 3 is shown in Fig. 1b

(2) Calculate the total number $n(p, m+1, r)$ and $n(p, m, r)$ of matched template vectors for a scale factors, where $1 \le p \le s$.
(3) Let $\overline{n(m+1, r)}$ and $\overline{n(m, r)}$ represent the average values of $n(p, m+1, r)$ and $n(p, m, r)$
(4) RGMSE is calculated for a scale factor s by.

$$RGMSE\left(Z_2^s, m, r\right) = -1n\frac{\overline{n(m+1, r)}}{n(m, r)}$$

Modified multiscale entropy

The MMSE methodology is performed via the following two steps [17]:

(1) Construct the coarse-grained time series Z_3^s shown in Fig. 1c for a time series$U = (u_1, u_2, \cdots, u_N)$ with length N by using the moving-averaging process of a time series.
(2) Calculate SampEn demonstrated in Sect. " Renyi distribution entropy" of each coarse-grained time series to obtain the MMSE values.

Multiscale Renyi distribution entropy

The MRDis algorithm incorporates the following two procedures [34]:

(1) Construct coarse-grained time series Z_1^s described in Fig. 1a for a time series $U = (u_1, u_2, \cdots, u_N)$ with length N:
(2) Calculate RDisEn demonstrated in Sect. " Renyi distribution entropy" of each coarse-grained time series to obtain the MRDis values.

Modified multiscale Renyi distribution entropy

In this work, we proposed MMRDis is based on the moving-averaging process of a time series, the MMRdis algorithm is composed of two procedures:

(1) Construct coarse-grained time series Z_3^s,described in Sect. " Modified multiscale entropy".
(2) Calculate RDisEn demonstrated in Sect. " Renyi distribution entropy" of each coarse-grained time series to obtain the MMRDis values.

The recently proposed three coarse-grained algorithms of time series are shown in Fig. 1, the classical coarse-grained process (Fig. 1a) is applied to the original time series to divide into non-overlapping sequences with length of s, so that the length of the divided time series reduces from N to N/s, the variability of the entropy assessment grows as the length gets shorter. To alleviate this obstacle, the other two improved coarse-grained algorithms were introduced, there were s coarse-grained time series acquired from the composite coarse-grained algorithm (Fig. 1b), rather than only one obtained from the classical coarse-grained process, avoiding the significant reduction of the length. Different from the non-overlapping sequences acquired from the two above-mentioned coarse-grained algorithms, the moving-averaging proce**ss** proposed by Wu et al. separate the time series into some smaller overlapped sequences (Fig. 1c) [17]. In their work, they developed modified multiscale entropy (MMSE) based on SampEn and the moving-averaging process and the simulation results showed that MMSE outperformed MSE on measuring the complexity of short-term time series. In our work, we adopted the moving-averaging proce**ss** so that the original time series were separated into several overlapping sequences with s data points of each sequence, the length with no dramatic reduction changed into N-$s+1$, shown in Fig. 1c. The probability of generating undefined value was reduced and the accuracy of entropy measurement was improved.

Evaluation signals

Synthetic signals

In this work, 20 white Gaussian noises (WGn) and 1/f noises with 1000 data points of each noise respectively, were used in order to explore the ability of MMRDis to correctly differentiate various signals with different complexity levels. Another set of the synthetic signals composed of 20 chaotic signals, MIX(0.2) process, and periodic

signals were employed to inspect the performance of MMRDis on quantifying the irregularity degree of diverse signals. 20 signals of chaotic, periodic and deterministic chaos with 1000 samples of each signal were generated by the logistic attractor $x_{n+1} = wx_n(1 - x_n)$ where $w = 3.8$,$w = 3.5$ and $w = 3.7$ respectively. 20 The MIX(p) process is a sinusoidal signal in nature with length N, in which $N \times p$ randomly selected data points are taken place of independent identically distributed signal, and its definition is presented as $MIX = (1 - x)z + xy$,where x represents a random variable, the probability is p when x = 1,and the probability is 1-p when x = 0, z describes a periodic signal in terms of $z_k = \sqrt{2}\sin(2\pi k/12)$, and y is a variable with uniform distribution on $[-\sqrt{3}, \sqrt{3}]$. Additionally, in order to test detection of nonlinear dynamics of the proposed multiscale entropy in this paper, we built surrogate series for each above-mentioned deterministic chaos signal, by via iterated amplitude-adjusted Fourier [28].

Real ECG signals

The Fantasia, BIDMC CHF and MIT-BIH AF module of the PhysioNet database were employed to acquire the ECG signals of normal, CHF and AF respectively. The ECG signals of the Fantasia module were obtained from 20 healthy young people (age: 21–34) and 20 elderly people (age: 68–85), the measured time of each ECG signal was approximately 2 h and the sampling rate was 250 Hz. The ECG signals of the BIDMC CHF module were acquired from CHF subjects including 11 men (age: 22–77) and 4 women (age: 54–63), the measured time of each ECG signal was approximately 20 h and the sampling rate was 250 Hz. The MIT-BIH AF module includes 23 AF ECG signals and the sampling rate of each AF ECG signal was 250 Hz. A total of 78 HRV recordings were extracted from 40 normal, 15 CHF and 23 AF ECG signals by using a Pan-Tompkins methodology to determine the R peaks of ECG signals [26]. The HRV segments used in this study, having various length of 100, 200, 500 and 1000 respectively, were extracted from each HRV recording. Firstly, 20 healthy young and elderly HRV signals were analyzed for inspecting capability of MMRDis to classify different physiological (young and elderly) conditions. Subsequently, we further analyzed the normal, CHF and AF HRV segments to assess the performance of MMRDis on distinguishing the normal from CHF and AF condition. To verify the improved stability and consistency of the MMRDis metric, we compared the performance of the MMRDis metric to those of other entropy metrics such as MSE, CMSE, RGMSE, MMSE and MRDis. m = 2 and $r = 0.15\sigma$ frequently used in previous study, were set in the MSE, CMSE, RGMSE and MMSE metrics, m = 2, B = 512, and $q = 0.5$ were set in the MMRDis and MRDis metrics in the following study.

Statistical analysis

To explore the capability of the multiscale entropy algorithms mentioned above, to differentiate the HRV signals with various lengths from different groups. Statistical analysis is performed, we firstly verify whether the results of the six entropies (MSE, CMSE, RGMSE, MMSE MRDis and MMRDis) obey normal distribution by employing the Kolmogorov–Smirnov test, the t-test methodology is performed to evaluate the statistical difference between CHF patients and normal subjects as the results obey normal distribution, otherwise, the Mann–Whitney test methodology is conducted. A p-value less than 0.05 obtained from the statistical analysis, is considered statistically significant in general.

Model assumptions

The selected HRV data samples were assumed to accurately represent the heart rate characteristics of both healthy individuals and patients, effectively capturing the typical variability and patterns of these groups.

Results

Performance of MMRDis on synthetic signals

Figure 2 shows the measurement results of applying MSE, RGME, MMDis, MRDis and MMRDis to the analysis of 1/f noises and WGn, which are widely used to test utility of the multiscale entropy methodologies, with length of 1000 of each noise. As can be illustrated in Fig. 2a, the MSE values of 1/f noises remain constant, whereas the MSE indicator induces undefined values for WGn as the scale factor increases. Additionally, when the scale factor is 3, the error bars for 1/f noises and WGn overlap, indicating no significant statistical difference between their MSE values at this scale. We observe from Fig. 2b that WGn have the higher RGME entropy values than those of 1/f noises across all scales, indicating WGn are more complex, which is deviated with previous finding [9]. Figure 2d-g shows the performances of MRDis and MMRDis on measuring the complexity of 1/f noises and WGn for various parameters q ($q = 0.1$, 0.5, 0.9, 1.1, 1.5, 2). In Fig. 2d-e, the curves of the MRDis values of 1/f and WGn present the similar tendency, that is firstly monotonic increase and then monotonic decrease with the growth of scale factor for all parameters q, except $q = 0.1$, where the values of the MRDis metric monotonously decrease. And we can find that the distinction between 1/f and WGn seems to be negligible, Fig. 2f-g shows the MMRDis values are defined on all scales and presents monotonously increase with the scale factor growing. Moreover, there is no difference between the two types of noises as scale = 1, in this case MMRDis degenerates into RdisEn, suggesting that RdisEn has no ability to distinguish 1/f noises from WGn. the curves of MMRDis of 1/f

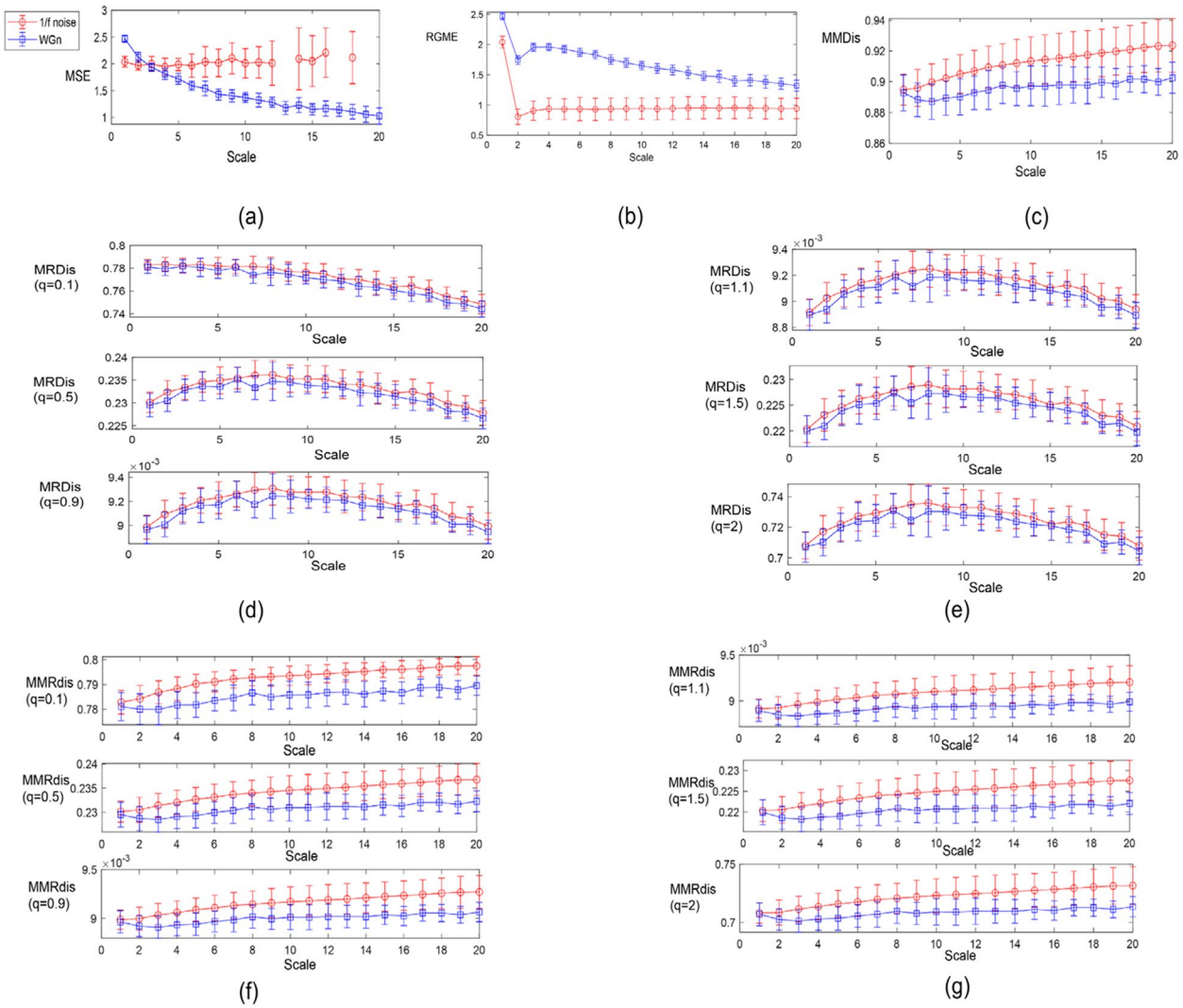

Fig. 2 Error bars of (**a**) MSE values; (**b**) RMGE values; (**c**) MMDis values; (**d**) MRDis with various parameters q (0.1, 0.5 and 0.9) values; (**e**) MRDis with various parameters q (1.1, 1.5 and 2) values; (**f**) MMRDis with various parameters q (0.1, 0.5 and 0.9) values; (**g**) MMRDis with various parameters q (1.1, 1.5 and 2) values computed from 1/f noises and WGn. Scales from 1 to 20 are employed for each multiscale entropy mentioned above

noises are higher than those of WGn for all parameters q after scale 1, illustrating the superiority of MMRDis over RdisEn in terms of quantifying signals of different complexity by using improved coarse-grained algorithm of the time series. Beyond that, we also apply the MMRDis entropy with parameter $q=1$(MMRDis $\rightarrow$ MMDis inferred by Sect. " Modified multiscale entropy") to the analysis of the two types of noises illustrated in Fig. 2c, the distinction between the two types of noises is available and the entropy values of 1/f noises are higher than those of WGn for all scale factors. Considering the MSE, MMDis and MMRDis algorithms have an ability to discriminate the two classes of noises, We utilize coefficient of variation (CV), referred to the standardized standard deviation (SD) and computed by the SD divided by the mean, to evaluate the computational stability of MSE, MMDis and MMRDis ($q=0.5$) [27], tabulated in Table 1. Table 1 demonstrates that the CV values of MMRDis are smaller than those of MSE and MMDis, indicating that the superior performance of MMRDis on the computational stability for all scale factors. In addition, we explore the impact of the combined parameters on the MMRDis measurement ($N=200$, 400, 600, 800, 1000, $B=200$, 400, 600, 800, 1000, $s=20$, $q=0.5$, $m=2$) for quantifying the complexity of 1/f and WGn noises, in comparison to the performance of the MSE measurement (($N=200$, 400, 600, 800, 1000; $r=0.1$, 0.3, 0.5, 0.7, 0.9; $s=20$, $m=2$), shown in Fig. 3. Different to the MSE evaluation, the

Table 1 CV values for WGN and 1/f noise by using MSE, MMDis, MMRDis methods at scales from 1 to 20

Signal	Entropy	S = 1	S = 2	S = 3	S = 4	S = 5	S = 6	S = 7	S = 8	S = 9	S = 10
1/f noise	MSE	0.05	0.05	0.07	0.08	0.06	0.11	0.14	0.13	0.14	0.14
	MMDis	0.011	0.013	0.013	0.014	0.014	0.015	0.015	0.015	0.017	0.017
	MMRDis	0.009	0.011	0.011	0.011	0.011	0.011	0.012	0.011	0.013	0.013
WGn	MSE	0.03	0.04	0.04	0.06	0.06	0.05	0.09	0.07	0.08	0.07
	MMDis	0.013	0.012	0.013	0.013	0.013	0.012	0.014	0.013	0.012	0.014
	MMRDis	0.011	0.011	0.011	0.011	0.011	0.010	0.011	0.011	0.011	0.012
Signal	**Entropy**	**S = 11**	**S = 12**	**S = 13**	**S = 14**	**S = 15**	**S = 16**	**S = 17**	**S = 18**	**S = 19**	**S = 20**
1/f noise	MSE	0.14	0.21	NA	0.28	0.23	0.21	NA	0.23	NA	NA
	MMDis	0.017	0.018	0.018	0.017	0.017	0.017	0.017	0.018	0.018	0.019
WGn	MMRDis	0.013	0.013	0.013	0.013	0.012	0.013	0.013	0.013	0.014	0.014
	MSE	0.10	0.08	0.10	0.11	0.09	0.12	0.11	0.12	0.14	0.15
	MMDis	0.014	0.015	0.013	0.013	0.011	0.011	0.009	0.009	0.009	0.011
	MMRDis	0.012	0.012	0.011	0.011	0.009	0.009	0.007	0.008	0.008	0.009

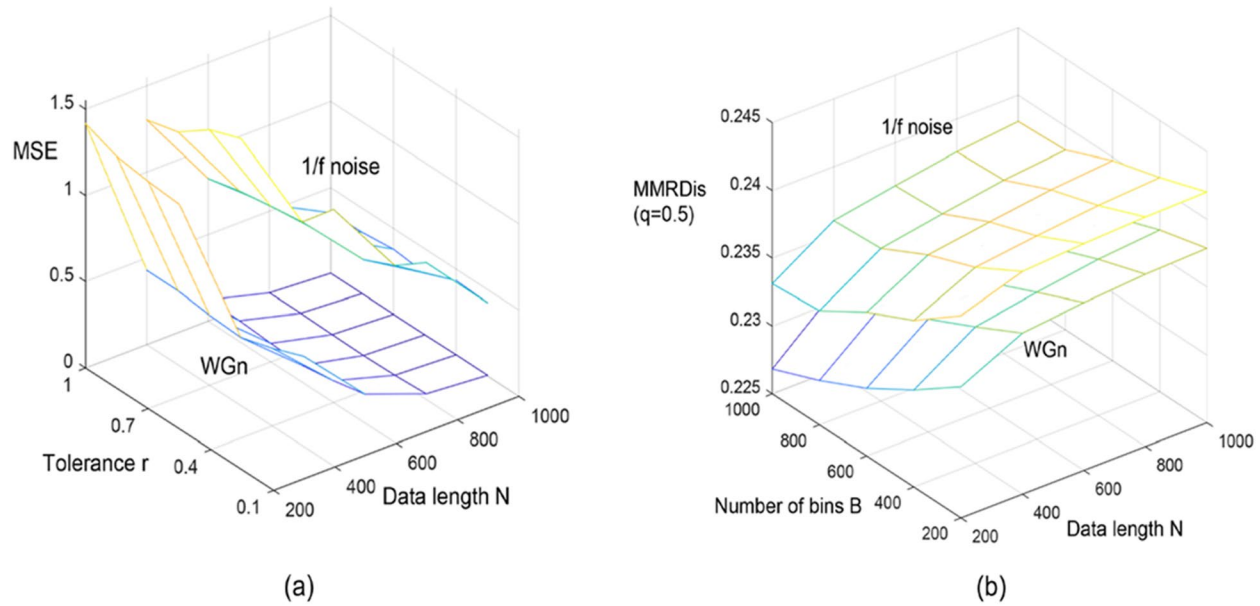

Fig. 3 Mean variation of MSE and MMRDis with changing parameters (r and N for MSE and B and N for MMRDis) for 1/f noises and WGn

MMRDis evaluation is minimally affected by varying combined parameters and remains bring about reasonable values instead of undefined or extreme values for the short-term time series, implying MMRDis inherits computation superiority of RDisEn [1].

Figure 4 displays the evaluation results of four entropy algorithms (MSE, RGME, MRDis, and MMRDis) for chaotic, periodic and MIX(0.2) signals with length 1000 of each signal respectively. Noticeable differences among the three types of signals for both MMRdis and MRDis evaluations are observed, exhibited in Fig. 4c-d, whereas there is no obvious distinction between MIX(0.2) and periodic signals for the MSE and RGME evaluations on most scale factors, suggesting that they fail to classify various signals with different randomness (Fig. 4a-b). The MMRDis curve of MIX (0.2) signals shows a more stable trend compared to the MRDis curve. In addition, we can find that smallest values of MMRDis and MRDis entropies are repeated when quantifying the periodic signals on 4 multiscale scales, the reason behind the fact is the period of the signals used in this work is 4.

Performance of MMRDis on short-term HRV signals

To further investigate the performance of the proposed entropy on measuring the dynamic behaviors existing in the short-term physiologic and pathological HRV signals,

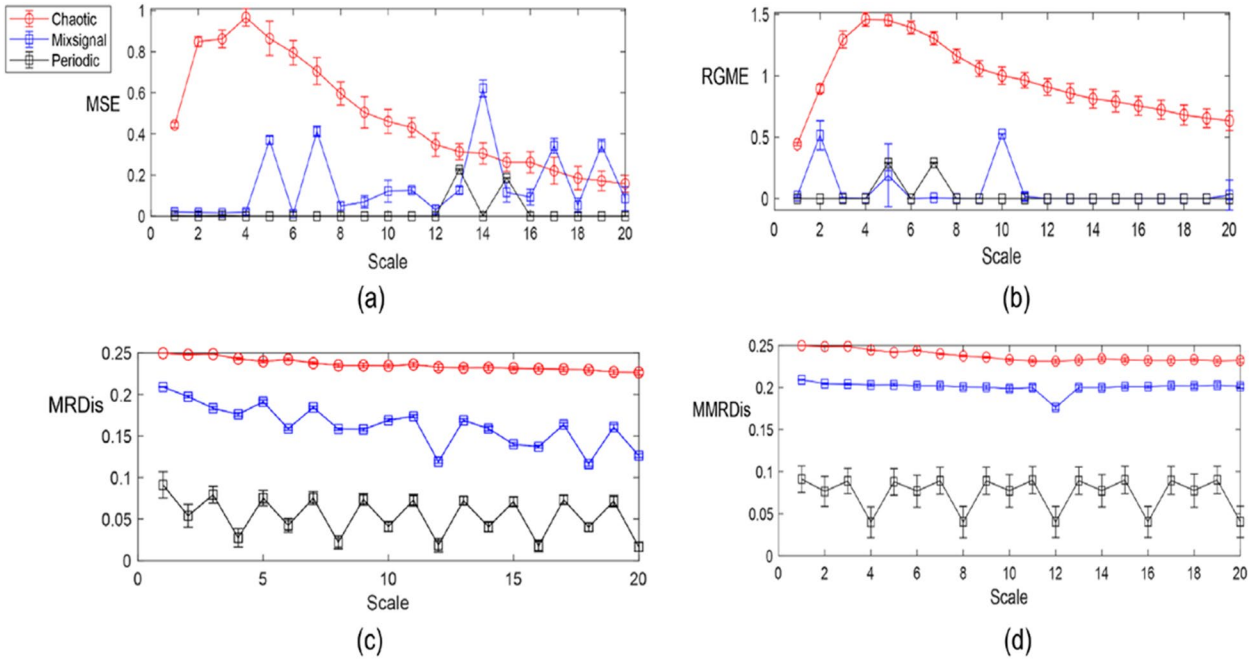

Fig.4 Error bars of (**a**) MSE values; (**b**) RGME values; (**c**) MRDis values; (**e**) MMRDis values computed from chaotic, mixsignal and periodic noises. Scales from 1 to 20 are employed for each multiscale entropy mentioned above

we apply the MMRDis algorithm to the analysis of these signals with varying length (100, 200, 500 and 1000) and compare the results of the proposed entropy to those of the MSE, RGME and MRDis metrics.

To maintain the readability and conciseness of the manuscript, the detailed *p*-values obtained from statistical analysis using MSE, CMSE, RGME, MMSE, MRDis, and MMRDis metrics for HRV segments of different lengths ($N=100$, 200, 500, and 1000) are provided in the supplementary materials (Tables S1, S2, S3 and S4).

Performance of MMRDis on short-term physiologic HRV signals

Firstly, to illustrate the non-stationarity of HRV signals, we plotted the time series and autocorrelation functions of HRV signals from both young and elderly subjects, as shown in Fig. 5. These plots clearly demonstrate the inherent non-stationarity and variability in HRV data across different age groups.The time series plots reveal significant variations in both the mean and variance over time, indicating the non-stationary nature of the signals. the The corresponding autocorrelation function (ACF) plots exhibit slow decay and irregular patterns, with significant autocorrelations persisting over long lags. This lack of rapid decay and the presence of long-term correlations are characteristic of non-stationary signals. Additionally, the ACF plots display erratic and unpredictable fluctuations, further confirming that the statistical properties of HRV signals change over time.

Then, we explored the impact of the combined parameters on the MMRDis measurement ($N=200$, 400, 600, 800, 1000; $B=200$, 400, 600, 800, 1000; $s=5$; $q=0.5$; $m=2$) for quantifying the complexity of young and elderly HRVs, in comparison to the performance of the MSE measurement ($N=200$, 400, 600, 800, 1000; $r=0.1$, 0.3, 0.5, 0.7, 0.9; $s=5$; $m=2$), as shown in Fig. 6. The results indicate that the MMRDis provides stable and consistent entropy estimates across different parameter settings, demonstrating its robustness against the non-stationary nature of HRV signals.This stability is attributed to the inherent design of the MMRDis method, which relies on the global distribution characteristics of distances among vectors in the state space. Unlike traditional methods, which may be affected by variations in standard deviation, the MMRDis focuses on the probability density estimated by a fixed bin number, making it less sensitive to changes in variance.

Figures 7, 8 and 9 illustrate the analysis results of the MSE, CMSE, RGMSE, MMSE, MRDis and MMRDis metrics by using 60 HRV segments acquired from the healthy young (Y) and old (O) subjects, with length $N=100$, 200, 500 and 1000 respectively. Tables S1-S4 tabulate the *p*-values obtained by using the t-test or Mann–Whitney methodology for different lengths of the HRV segments. The MSE, CMSE and RCMSE measurements

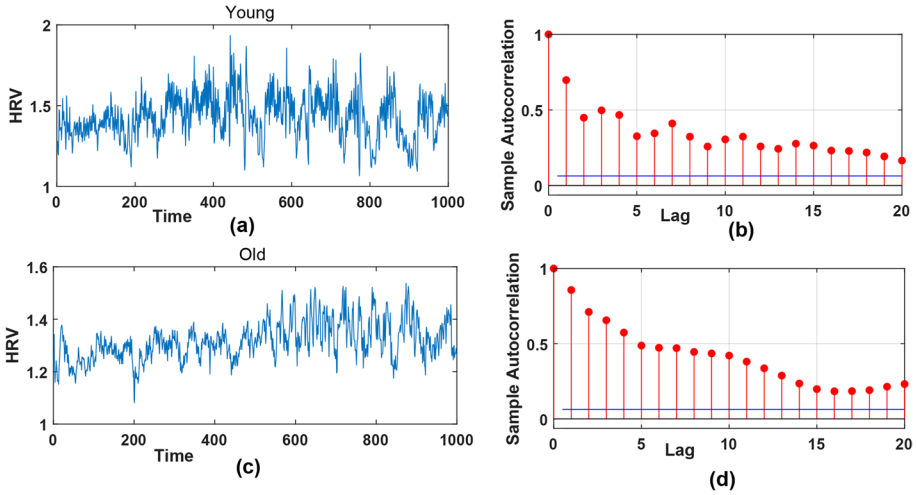

Fig. 5 **a** HRV signals of young subjects (**b**) Autocorrelation functions of young subjects' HRV signals (**c**) HRV signals of elderly subjects (**d**) Autocorrelation functions of elderly subjects' HRV signals

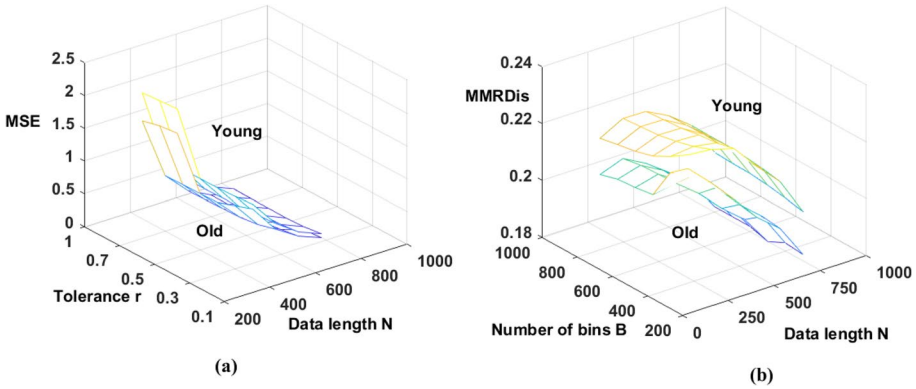

Fig. 6 Mean variation of MSE and MMRDis with changing parameters (r and N for MSE and B and N for MMRDis) for the healthy young and old HRV segments

are not defined on most of scales, indicating their inability to analyze very short-term HRV signals (Fig. 7a-c; see Table S1 for details in footnotes). It is worth mentioning that the MMSE value is defined on all scales by using the moving-averaging process for various length (Fig. 7d), but the distinction between the two classes is difficulty on the scales less than 15 (Table S1).We can observe in Fig. 7e that the MRDis values firstly increase and then gradually decrease, the difference between the two groups of HRV signals is unavailable on the scales more than 10 (Table S1). Notably, the analysis results of the MMRDis estimation shown in Fig. 7f indicates that the entropy has a capability to discriminate between the healthy young and elderly subjects.

Next, we apply the six entropy algorithms to analyze the three types of the HRV segments with length 200, 500 and 1000 illustrated in Figs. 8, 9 and 10, we can find that as the length of signals grows, the range of the MSE, CMSE and RCMSE values defined on scale factors are extended. The RCMSE and MMSE values are defined on all scales for the HRV segments with length 500, the distinction appears to be apparent between the two types of short-term HRV signals (Figs. 9c-d and 10c-d and Table S3-S4). The MRDis behaviors depicted in Figs. 8e, 9 and 10e are similar to Fig. 9e that the mean values of MRDis monotonously decrease, the difference between the two types of signals is minor as scales are greater than 15 (Fig. 9e). Similar to Fig. 7f, the variation tendency of the MMRDis curves is to increase and then keep constant. Additionally, the mean values of MMRDis for HRV signals in healthy young condition are significantly higher than those in healthy aging condition (Figs. 8f, 9 and 10f).

The comprehensive assessment provided by Figs. 7, 8, 9 and 10 and Tables S1-S4 shows that (1) compared with

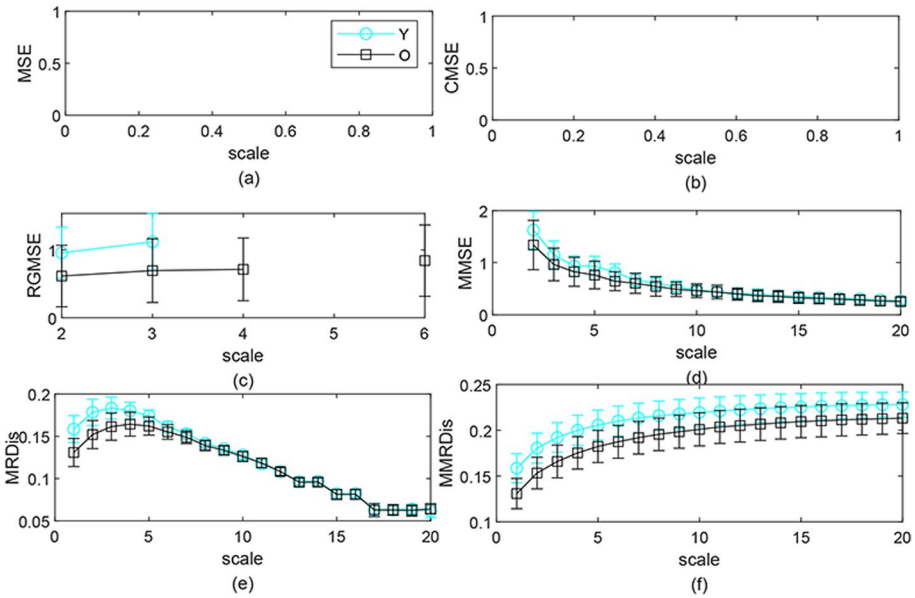

Fig. 7 Error bars of the (**a**) MSE values; (**b**) CMSE values; (**c**)RGME values;(**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from healthy old and young HRV signals with each length $N = 100$

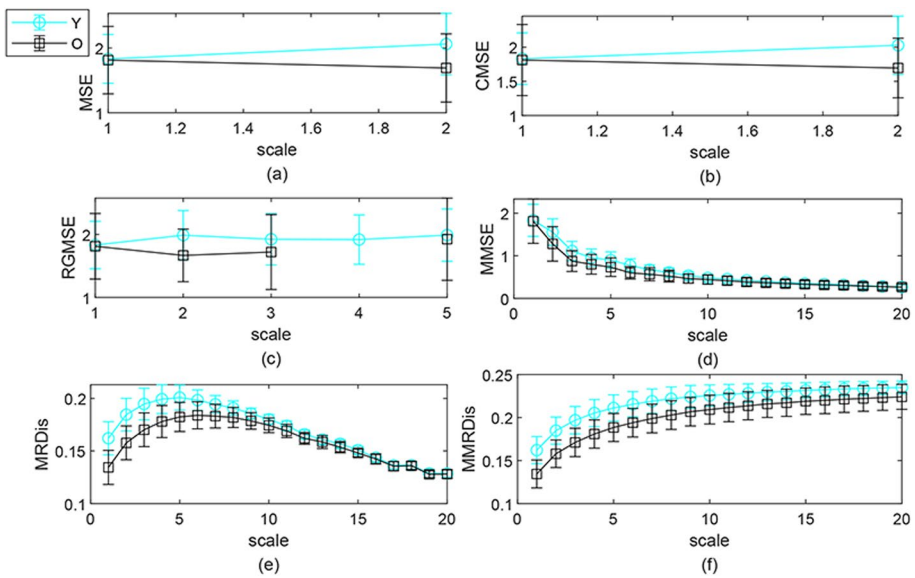

Fig.8 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**)RGME values;(**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values values with varying scales from 1 to 20, computed from healthy old and young HRV signals with each length $N = 500$

the other five entropy algorithms, the MMRDis values proposed in this paper are defined for various length of the HRV segments on all scales, (2) There exists significant difference between the healthy young and elderly groups for all scales, (3) The HRV segments of the healthy young subjects include more complexity of healthy elderly compared with those of the healthy ole subjects, manifesting that the complexity decreases with aging, which is consistent with the previous studies on the reduced complexity with advancing age.

Performance of MMRDis on short-term pathological HRV signals

To further investigate the performance of the proposed entropy on measuring the dynamic behaviors existing in the pathological HRV signals, we apply the MMRDis

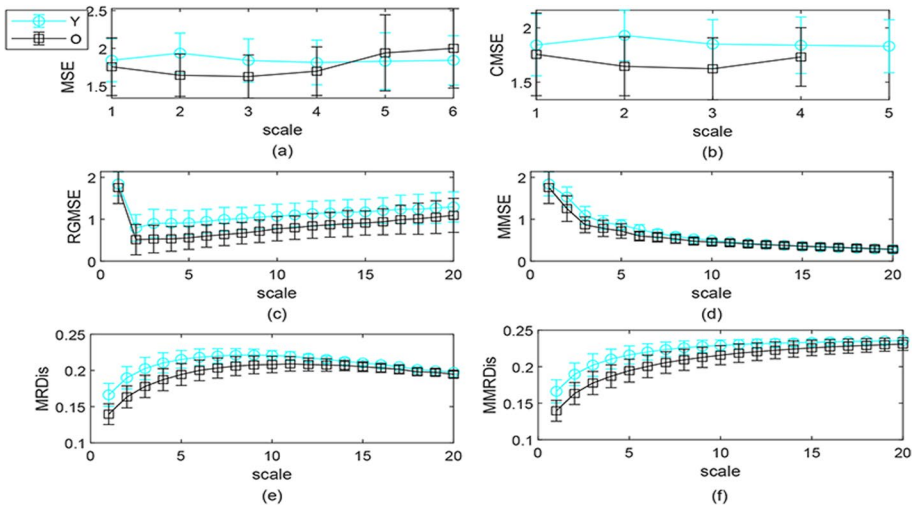

Fig. 9 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**) RGME values; (**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from healthy old and young HRV signals with each length $N = 200$

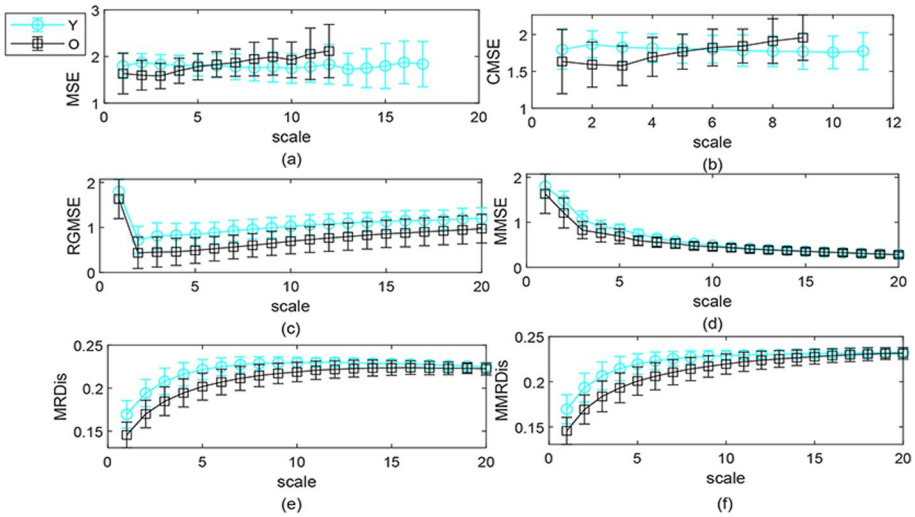

Fig. 10 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**)RGME values;(**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values values with varying scales from 1 to 20, computed from healthy old and young HRV signals with each length $N = 1000$

algorithm to the analysis of the healthy (H), CHF and AF(A) HRV segments with varying length (100, 200, 500, 1000) and compare the results of the proposed entropy to those of the MSE, CMSE, RGMSE, MMSE and MRDis metrics.

Figures 11, 12, 13 and 14 illustrate the simulation results of the six entropy algorithms for the HRV segments with length $N = 100$, 200, 500 and 1000. For the very short HRV segments such as 100, the MSE, CMSE metrics are not defined on all scales (Fig. 11a-b) due to the following reasons: Firstly, short time series typically lack sufficient data points, which can lead to unreliable estimates and variable entropy values. Moreover, with a limited number of data points, the probability of finding matching similar subsequences is lower, resulting in greater variability in the SampEn computation [35]. At last, as the scale factor increases, the coarse-graining process further reduces the length of the time series. Each new time series generated at a larger scale contains fewer data points, which can lead to unreliable or undefined entropy values, especially at higher scales. This reduction in data points affects the statistical robustness of the entropy calculations, making it impractical to define MSE and CMSE across all scales [8, 36].The defined range of the MSE, CMSE, RCMSE values extend with increasing length of the HRV

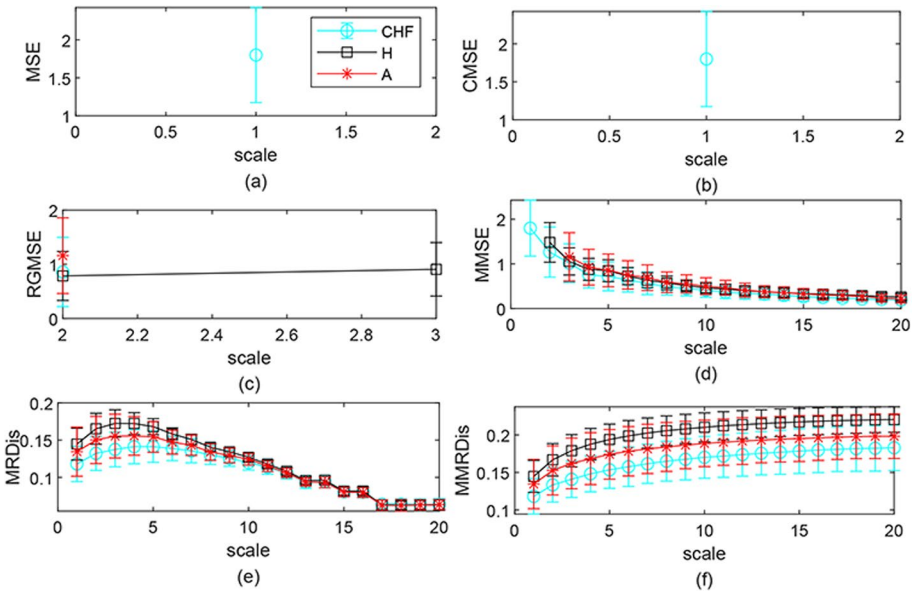

Fig. 11 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**) RGME values; (**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from normal, CHF and AF HRV signals with each length $N = 100$

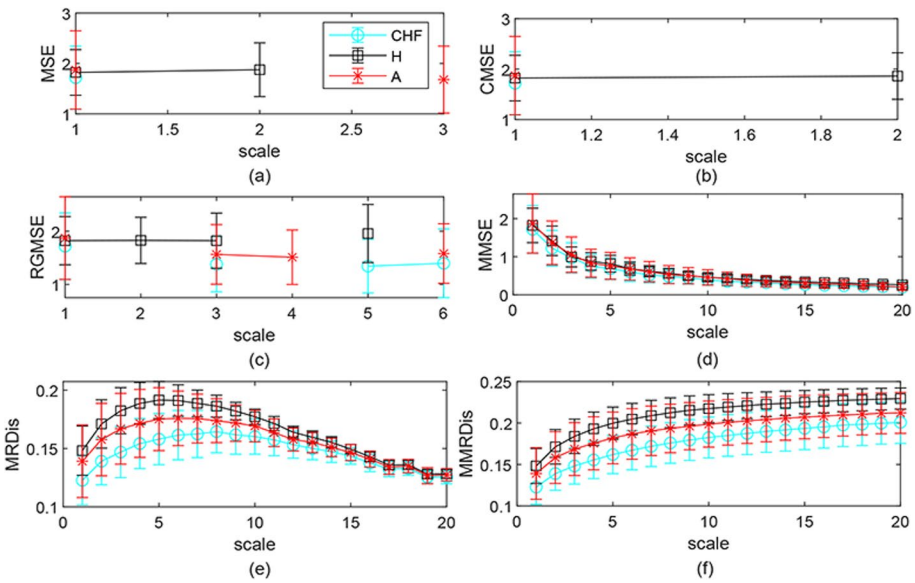

Fig. 12 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**) RGME values;(**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from normal, CHF and AF HRV signals with each length $N = 200$

segments (Figs. 12a-c, 13 and 14a-c), and the RCMSE curves of the subjects with AF and CHF are lower than that of the healthy subjects. MMSE value is defined on all scales, and the difference between the three groups is unapparent (Figs. 11, 12, 13 and 14).The MRDis values present a dramatic decrease as the scale factor is more than 5, suggesting weak stability of MRDis on the very short-term HRV signals (Fig. 14e). Compared to the other five entropies mentioned above, there is a significant separation among the MMRDis values of CHF, AF and normal HRV segments. Additionally, the MMRDis values stay constant with growth of the scale factor, indicating insensitivity to the length of signals studied, the curves of healthy people is on the top, indicating that the complexity of the HRV segments under health status is higher than those of the HRV

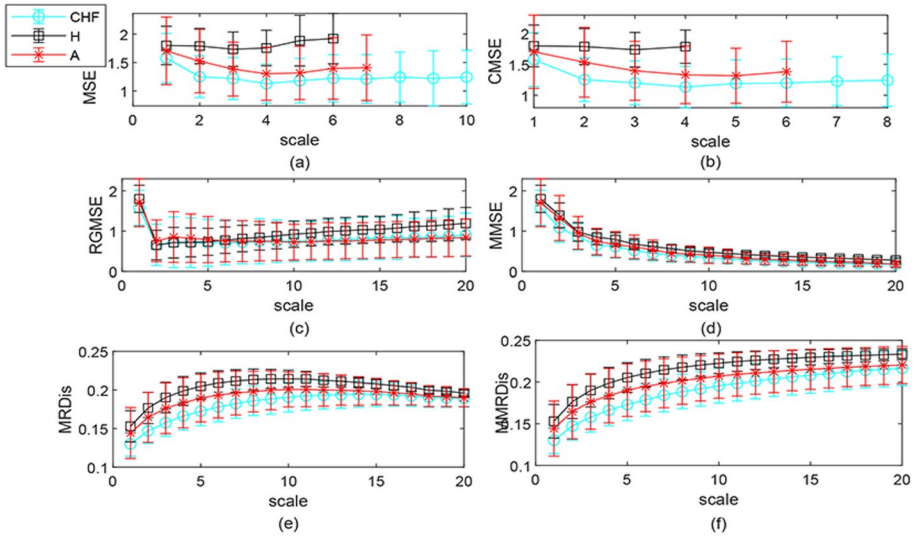

Fig. 13 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**)RGME values;(**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from normal, CHF and AF HRV signals with each length $N = 500$

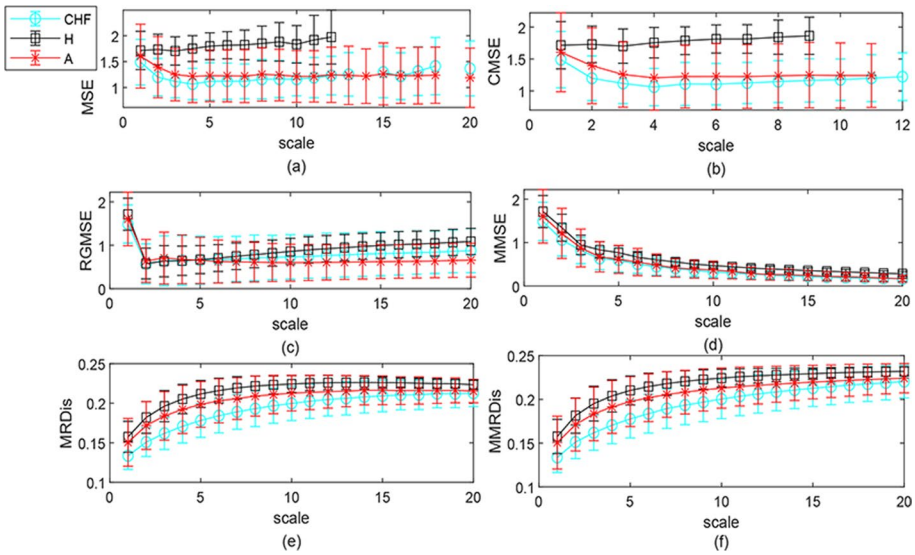

Fig. 14 Error bars of (**a**) MSE values; (**b**) CMSE values; (**c**) RGME values; (**d**) MSE values; (**e**) MRDis values; (**f**) MMRDis values with varying scales from 1 to 20, computed from normal, CHF and AF HRV signals with each length $N = 1000$

segments under pathological status, shown in Figs. 11f, 12, 13 and 14f.

To further confirm the capability of the six entropies to differentiate the HRV segments obtained from the three groups (H,CHF and A) with various lengths (100, 200, 500 and 1000), statistical analysis is performed to evaluate the statistical difference among the three groups (Tables S1-S4). Table S1 demonstrates the comparison results of the six entropy algorithms for separating CHF from normal, and AF from H HRV segments with each length 100. For the MSE, CMSE, RGMSE, MMSE evaluations, it is unavailable for p-value over most scale factors. The distinction between the two groups is unclear over scales from 12 to 20 by using the MRDis evaluation as the p-values are more than 0.05. Compared to the other five entropy algorithms, the p-values are all less than 0.05 by using the MMRDis evaluation, suggesting that MMRDis performs best on differentiating normal subjects from CHF patients. In Table S2, the range of available p-values for the RGME measurement expands when the length of

HRV signals increases to 200, but it fails to distinguish between the three groups for p-value more than 0.05 over most scales. Both the MRDis and MMRDis measurements have the capability to discriminate normal subjects from CHF patients (p-value < 0.05), and MMRDis performs better than MRDis on discriminating normal subjects from AF patients over scales from 18 to 20. Similar to the comparison result shown in Table S2, Tables S3-S4 exhibit that for lengths 500 and 1000 of HRV signal, the MMRDis algorithm is superior to perform better on classifying the pathological HRV signals compared with the other five algorithms.

The synthetic analysis results summarized by Figs. 11, 12, 13 and 14 and Tables S1-S4 demonstrate that (1) MMRDis proposed in this work outperforms the other five entropies (MSE, CMSE, RGMSE, MMSE and MRDis) for short-term HRV signals (100, 200, 500 and 1000) on categorization of CHF, AF patients and normal subjects; (2) Results of computations are stable with increases in scale factors, implying that MMRDis measurement is less sensitive to the length of HRV signal. (3) HRV series of pathological conditions such as CHF and AF have lower complexity than those from healthy subjects.

We found inconsistencies in the MSE estimation for short-term heart rate variability (HRV) time series. Some sources of error can be attributed to the explanatory factors such as sample size, data distribution, and selection of parameters. Some showed evidence that MSE measures are sensitive to these factors, especially in short time series. Costa and colleagues introduced MSE and drew attention to its dependence on the length of the time series [19]. Richman and Moorman discussed the statistical instability of entropy estimation in small samples and this is similarly true for MSE [5]. Pincus described how data distribution affects approximate entropy calculations, contributing to the compound effect on MSE, as well [37]. Riedl et al. pointed out the importance of noise impact on entropy measures including MSE [38]. Lake et al. examined the influence of parameter selection on entropy measures [38]. Bandt and Pompe also discussed boundary effects and their impact on entropy estimation in short time series [7]. Since we took into consideration these aspects, we tried to optimize the robustness of MSE estimation in HRV time series.

To address these inconsistencies, we propose the MMRDis method for entropy estimation; the new approach amalgamates Renyi distribution entropy and moving average in its multiscale algorithm. The Renyi distribution entropy takes into account the global distribution characteristics of distances between vectors in the state space, concentrating its efforts on the specific probability density estimated by a fixed number of bins. In comparison with the usual methods, this approach exhibits greater robustness against variance variations. The moving-averaging process also assures time series length consistency for all entropy calculations, eliminating significant reductions. In addition, the results indicated that the MMRDis provided stable and consistent entropy estimates under all parameter settings, indicating robustness with respect to the non-stationary characteristics of short-term HRV signals.

Conclusions

Complexity of time series has served as an indispensable characteristic for comprehending the dynamic mechanism of complex systems. Considering the limitation of traditional MSE approach suffering from the unreliable or undefined estimations for a short-term series. In this paper, we proposed a new complexity metric namely MMRDis, which outperformed MSE and recently proposed improved multiscale entropy algorithms, such as RGMSE and MRDis for a short-term time series. Analysis of these multiscale entropy algorithms on 1/f noises and WGn show that MMRDis provide a more accurate and robust measurements and reduces variance of the entropy assessments than other multiscale entropy algorithms mentioned. Moreover, we apply MMRDis to analysis of the short-term physiology/pathological HRV signals, derived from frequently used databases, the experimental results demonstrate that compared to other multiscale entropy algorithms, MMRDis gives the more precise estimations and enhance the discriminate ability of the short-term HRV signals with different complexity degree extracted from groups of the physiology and pathological states.

Through our work, MMRDis proposed here presents the potential to evaluate the complexity of a short-term time series and can be used as a promising index for monitoring cardiovascular function in rapid clinical examinations. One major limitation is the reliance on a single-source dataset, which may not fully encompass the diversity of patient data from various regions and backgrounds. To address this, future research efforts will focus on expanding the dataset to include HRV data from a wider range of populations and locations, thereby further validating the effectiveness of the proposed MMRDis method. Additionally, our study did not extensively investigate the influence of boundary effects and noise on entropy estimation. Future work should aim to explore these factors more comprehensively to better understand their impact and enhance the overall robustness of the MMRDis measure in HRV analysis. These steps aim to ensure that MMRDis, as proposed here, is robust and applicable across different scenarios, providing a more comprehensive and accurate analysis of heart rate variability.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12911-024-02763-1.

Supplementary Material 1.

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Authors' contributions
M.S. and Y.S.contributed the majority of the writing and conducted major parts of the experiments, they contributed equally to this work. Y.L. conducted some experiments and contributed to the methodology, X.Q. supervised the work and revised the manuscript. All authors have read and agreed to the published version of the manuscript.

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Data availability
Publicly available datasets were analyzed in this study. This data can be found here: https://www.physionet.org/content/fantasia/1.0.0/; https://www.physionet.org/content/chfdb/1.0.0/; https://www.physionet.org/content/afdb/1.0.0/.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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