Optimizing Multiscale Entropy Analysis for the Detection of Cardiac Pathology

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Abstract

The study investigates the use of the Rényi entropy algorithm with variable threshold and a signal temporal multiscaling approach for analyzing RR interval signals. The study involved 8-minute ECG recordings of 90 participants from the PhysioNet database and grouped into three groups: normal sinus rhythm, cardiac arrhythmia, and congestive heart failure. A time coarse-graining algorithm was used to obtain different temporal scales of the original signal. Rényi entropy probabilities of each scale-factored signal were calculated using a method of density based on sequences of the RR interval time series. ANOVA and post-hoc t-test were used to determine significant differences between the multiscaled Rényi entropy measures of the different groups of RR interval signals. The novel multiscaled Rényi entropy analysis provided enhanced significant discrimination between healthy and pathological (NSR vs. ARR and NSR vs. CHF) signals at post hoc t-test probability values of $p < 5\text{x}10^{-6}$ *and within pathological signals (ARR vs. CHF) at* $p < 5\text{x}10^{-3}$*. The study concludes that applying a joint approach of cardiac signal temporal multiscaling and calculating its modified Rényi entropy with variable thresholding provides an optimized approach to identifying and separating healthy and pathological cardiac signals, and further supports the complex nature of the heart dynamics.*

1. Introductory Background

Interest in nonlinear dynamics has increased in recent years, particularly in cardiology, where the normal cardiac rhythm is linked to complex nonlinear dynamics and chaos. This has opened new avenues for using nonlinear dynamics as diagnostic tools for analyzing physiological data and gaining a better understanding of cardiac rhythm dynamics in health and disease [1].

Entropy-based algorithms, which quantify the regularity of a time series, have been applied for some time and are constantly being developed to improve the analysis and understanding of the dynamics of physiological data and optimize diagnostic and treatment outcomes [2]. However, changes in entropy may not always be associated with an increase in dynamic complexity [1]. This inconsistency may be due to the fact that widely used entropy measures are based on single-scale analysis and do not take into account the complex temporal fluctuations inherent in healthy physiologic control systems as a function of scales [1, 3]. Numerous entropy-based and multiscale entropy algorithms have been proposed for analysis of EEG or heart rate signals [4-8]. One of these is Rényi entropy, which has been shown as a robust metric to detect congestive heart failure (CHF) [9] and differentiate between healthy and cardiac autonomic neuropathy (CAN) subjects and CAN progression [10,11].

The purpose of this study was to investigate the effect of extending the Rényi entropy density method to its temporal mutliscaling version using a second moment-based formula. This was performed by applying the proposed method on RR interval signals from PhysioNet ECG datasets of two pathologies and normal sinus rhythm, to study whether there is an improvement in the discriminatory ability of the new method as opposed to using the Rényi entropy approach on its own.

Entropy is a measure that is used in various biomedical applications, such as detecting cardiac autonomic neuropathy (CAN) in diabetes patients [10], distinguishing healthy subjects from congestive heart failure patients [9], and improving the accuracy of epileptic seizure detection [12]. Different types of entropy measures and multiscale entropy analysis have been applied to physiological time series, such as EEG, ECG, EMG, and EHG [2]. Multiscale entropy (MSE) measures have been proposed since the 2000s to evaluate the complexity of time series by considering multiple time scales in physiological systems [3,6].

The efficacy of applying multiscale Rényi entropy on heart rate variability (HRV) was investigated, finding statistically significant differences between disease classes [10]. In another relevant study, Rényi entropy was used to detect cardiac autonomic neuropathy and its progression in diabetes patients, finding significant differences between controls and early CAN. The innovation introduced was to determine probabilities of RR intervals calculated using a density method based on sequences of RR intervals compared to the common histogram method with fixed thresholds [11]. Consequently, this variable threshold served as a considerable improvement on the originally existing multiscale entropy method [6].

A multiscale distribution entropy based on a moving

average multiscale process and distribution entropy to study short-term heart rate variability (HRV) was proposed [13], and a method based on multimodal multiscale dispersion entropy for the biometric characterization of heart sounds was developed [14]. The multivariate multiscale dispersion entropy (mvMDE) to quantify the complexity of multivariate time series was introduced in [15]. El- Dynamics, consistency, and robustness of MSE, multiscale time irreversibility (MTI), and multifractal spectrum in HRV characterization in long-term scenarios were also investigated [16].

All these studies either proposed new developments on entropy-based measures and improvements in the understanding of existing ones or developed new applications of existing entropy-based measures; however, many of these studies are case-specific and may not be generalizable to other types of physiological and pathologies applications. Moreover, despite the numerous studies and modeling of heart signal dynamics, a deeper understanding of the complexity dynamics and fluctuations of the heart is yet to be gained, and their complete characteristics are constantly yet to be learned [17].

Hence, this study proposes a multiscaled Rényi entropy method providing a means of varying the entropy probability thresholding when computing Rényi entropy of RR interval signals as in [11], but at different temporal scaling factors, to improve its discriminatory performance tested on RR intervals extracted from normal and pathological ECG data from PhysioNet.

2. Methodology

A total of 90 subjects from the open-access PhysioNet database were included in this study. ECG recordings, each lasting 8 minutes, were obtained from these participants. The recordings were categorized into normal sinus rhythm (NSR) [18], cardiac arrhythmia (ARR) [19], and congestive heart failure (CHF) [20]. ECGs were recorded with a sampling rate of 128 Hz, encompassing a total of 60,000 sample points, resulting in a duration of 469 seconds. The ECGs were filtered using the Kaiser window approach [21]. Next, RR intervals (RRI) were extracted from the ECG using wavelet decomposition [22] to detect the QRS complex. All analyses were implemented using MATLAB R2022b software.

A time coarse-graining approach that relied on a second-moment method to derive nineteen temporal scales of the original RRI signal [7]. The Rényi entropy probabilities for each scale-factored signal were computed using the recommended parametrization of the density-based method that relied on sequences of the RR interval time series, as opposed to individual values [11]. Finally, an analysis of variance test (ANOVA) and *post-hoc* t-test were employed to assess and compare the statistical significance of the disparities observed in the multiscaled Rényi entropy measurements between healthy, ARR, and CHF recordings.

3. Results and Discussion

Table 1. Rényi entropies averaged over 90 subjects of healthy (NSR) and pathologic (CHF and ARR) RRI signals across the first 15 temporal scale factors (SF) versus Rényi entropies compared to results from the first temporal scale (original signal). Values are shown for 45 subjects, the first 15 from each group.

SF	$\overline{\text{NSR}}$	$\overline{\text{ARR}}$	$\overline{\text{CHF}}$	Sub	NSR	ARR	CHF
1	60	35	16	1	91	75	8.6
2	43	29	13	2	60	15	0.4
3	30	23	9.2	3	21	19	9.0
4	55	33	11	4	96	29	1.6
5	46	42	7.5	5	25	2.5	2.5
6	32	20	10	6	12	2.4	2.0
7	44	27	8.6	7	26	25	7.9
8	51	31	8.3	8	88	3.0	0.1
9	22	16	10	9	88	0.9	1.0
10	52	25	8.1	10	130	22	3.4
11	35	14	11	11	12	11	3.7
12	22	10	7.1	12	93	4.2	0.3
13	11	10	9.4	13	91	75	8.6
14	13	10	7	14	60	15	0.4
15	11	8	7.1	15	21	19	9.0
Anova p-value	**$2.3\text{x}10^{-5}$**				$1.1\text{x}10^{-3}$		

Rényi entropies were averaged for the 90 subjects of the RRI signals of the three groups (NSR, ARR and CHF) across 20 temporal scale factors. Table 1 shows the results for the first 15 scale factors (SF) for the first 45 subjects (15 from each group to fit the number of rows in the table). The higher SF till 20 showed insignificant differences and thus were not included in the table.

Across SF 1 to 15 in Table 1, Rényi entropy values for the NSR group tend to be higher than those for the ARR and CHF groups. The same overall trend can be observed across the first 15 subjects (Sub 1 to 15 in Table 1) when looking at the first temporal scale. This indicates that NSR subjects generally have higher signal complexity across various temporal scales. For the ARR group, Rényi entropy values tend to be lower than NSR but higher than CHF in many cases, suggesting that ARR subjects have intermediate signal complexity. The CHF group consistently exhibits the lowest Rényi entropy values across all SF, indicating lower signal complexity compared to NSR and ARR. The lower complexity observed in the CHF group is consistent with the known reduced HRV complexity often seen in individuals with congestive heart failure [23].

The ANOVA p-values at the bottom of the table indicate the statistical significance of the differences in

Rényi entropy values between the three groups (NSR, ARR, CHF) across the various SFs. The p-values are very small (e.g., 2.3x10^-5 and 1.1x10^-3), suggesting that there are significant differences in Rényi entropy values between the groups across different temporal scales. The Multiscaled groups show a lower p-value than the first scale group (original RRI signal) indicating higher confidence in the distinction between the groups. Thus, the evidence against the null hypothesis is stronger in the case of multiscaling, meaning that at least one group mean is significantly different from others. Hence, a post hoc t-test was conducted to determine which specific groups are different from each other and if true, how strongly they differ from each other.

Table 2. Post hoc t-test p values showing the extent of the significance of the Rényi entropies in discriminating healthy and pathological groups from each other. The multiscaled data is compared to the data from the first temporal scale (original RRI signal).

T-test groups	Multiscaled	Scale 1
NSR vs. ARR	**$2.3x10^{-6}$**	$4.5x10^{-5}$
NSR vs. CHF	**$2.1x10^{-6}$**	$2.7x10^{-3}$
ARR vs. CHF	**$1.1x10^{-3}$**	0.02

Table 2 presents the p-values obtained from *post-hoc* t-tests conducted to compare Rényi entropies between NSR and those with pathological conditions, specifically ARR and CHF. The comparisons were made using both multiscaled data and data just from the first temporal scale (Scale 1).

In each of the three comparisons (NSR vs. ARR, NSR vs. CHF, ARR vs. CHF), the p-values obtained from the analysis of multiscaled had a higher significance than those obtained from the analysis of data from Scale 1. This means that the group differences in the multiscaled data are stronger and more statistically significant due to the smaller p-values. The utilization of the multiscaled approach with the Rényi entropy calculations tends to yield more pronounced statistical significance, indicating its potential as a more resilient approach for distinguishing between these groups. This supports the hypothesis that the traditional MSE and modified Rényi entropy calculations are optimized by embedding them together as temporal multiscaling modified Rényi entropy analysis.

The results relate to the multifractality of the heart signals demonstrated in [17], where multifractal complexity is higher for healthy signals than pathological ones. Additionally, a scale-free temporal structure was observed in long-term heart rate recordings for healthy subjects, which invites more research into longer-term signal analysis in comparison to shorter-term physiological signals [24,25].

4. Conclusion

The utilization of a combined methodology using temporal cardiac signal multiscaling and the computation of Rényi entropy yields an enhanced strategy for the discrimination and differentiation of healthy and abnormal cardiac signals, surpassing the efficacy of employing each technique in isolation. the utilization of Rényi entropies, particularly when examining multiscaled data, exhibits significant promise in differentiating between healthy and diseased cohorts based on the complexity of their RRI signals.

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