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A Comparative Analysis of Alternative Approaches for Quantifying Nonlinear Dynamics in Cardiovascular System

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***Abstract*—Heart rate variability (HRV) analysis has emerged as an important research topic to evaluate autonomic cardiac function. However, traditional time and frequency-domain analysis characterizes and quantify only linear and stationary phenomena. In the present investigation, we made a comparative analysis of three alternative approaches (i.e., wavelet multifractal analysis, Lyapunov exponents and multiscale entropy analysis) for quantifying nonlinear dynamics in heart rate time series. Note that these extracted nonlinear features provide information about nonlinear scaling behaviors and the complexity of cardiac systems. To evaluate the performance, we used 24-hour HRV recordings from 54 healthy subjects and 29 heart failure patients, available in PhysioNet. Three nonlinear methods are evaluated not only individually but also in combination using three classification algorithms, i.e., linear discriminate analysis, quadratic discriminate analysis and k-nearest neighbors. Experimental results show that three nonlinear methods capture nonlinear dynamics from different perspectives and the combined feature set achieves the best performance, i.e., sensitivity 97.7% and specificity 91.5%. Collectively, nonlinear HRV features are shown to have the promise to identify the disorders in autonomic cardiovascular function.**

I. Introduction

Heart rate variability (HRV) refers to the fluctuations in the sequential heart-beat intervals, also called RR intervals. Heart-beat dynamics are highly pertinent to the function of autonomic nervous system. Thus, HRV analysis plays an important role in assessing the disorders in autonomic cardiovascular function. Since the 1980s, linear and frequency-domain approaches are widely used in the HRV analysis, and are shown to have a certain degree of descriptive and predictive power. However, conventional frequency-domain analysis and linear statistical approaches tend to have limitations to capture nonlinear and nonstationary behaviors in the long-term HRV time series. For example, Fast Fourier transformation (FFT) is efficient to transform data from time domain to frequency domain. However, Fourier analysis does not provide the temporal localization of frequency components, and assumes that spectral components exist at all times (i.e., stationarity). Also, linear statistical methods, e.g., analysis of variance (ANOVA), have certain difficulties to capture the nonlinearity, nonstationarity and high-order variations. Therefore, linear methods tend to bring less realistic characterization and quantification of nonlinear time series.

In the present paper, we aim to make a comparative analysis of three different approaches for quantifying nonlinear dynamics in cardiac systems, and evaluate their classification performances. For that purpose, we have used three well-known classification algorithms, namely linear discriminant analysis, quadratic discriminant analysis and k-nearest neighbor. Three nonlinear methods are multifractal analysis, Lyapunov exponents and multiscale entropy analysis. It may be noted that we build three classification models for features extracted from three nonlinear methods individually so as to establish the benchmark performance of each method. Furthermore, features from three nonlinear methods are combined to exploit more useful information from different perspectives, thereby establishing a better model for detecting disorders in autonomic function.

This paper is organized as follows: Section II will introduce the methodology of three nonlinear approaches, feature selection and classification models. Materials and experimental design will be discussed in Section III. Section IV shows the experimental results of HRV analysis with three alternative nonlinear methods. Section V discusses and concludes the studies in this paper.

II. Research Methodology

A. Wavelet Multifractal Analysis

The method of wavelet transform modulus maxima (WTMM) is widely used to quantify the multifractal spectrum in a nonlinear time series. This wavelet-based multifractal analysis evaluates the local Hurst exponent h through the continuous wavelet transform [1]. Note that this method uses wavelets in different scales as the box functions to quantify the self-similarity in the time series. The partition function $Z(q,a)$ is defined as

$$Z(q,a) = \sum_{l \in \mathcal{L}(a)} (\sup_{a' \le a} |\Psi_x^{\psi}(b_l(a'), a')|)^q$$

Where $\Psi_x^{\psi}(b_l(a'), a')$ are wavelet transform coefficients at location $b_l(a')$ and scale a', $\sup_{a' \le a}|\ \ |$ is the local maxima of modulus for all scales $a' \le a$, $l \in \mathcal{L}(a)$ denotes the maxima line at the scale a. Hence, $Z(q,a)$ is the sum of q-th powers of maxima's in wavelet modulus. If $a \to 0^+$, $Z(q,a) \cong a^{\tau(q)}$. It was shown that monofractal signals yield a linear scaling-exponent function: $\tau(q) = qH - 1$, where H is the global Hurst exponent. For multifractal signals, there will be a nonlinear scaling-exponent function: $\tau(q) =$

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$qh(q) - D(h)$, where local Hurst exponent is not constant and calculate as $h(q) = d\tau(q)/dq$. To this end, the multifractal spectrum $D(h)$ can be derived from $\tau(q)$ through a Legendre transform, $D(h) = qh - \tau(q)$.

Recent research shows that a major life-threatening condition, i.e., congestive heart failure, leads to a loss of multifractality [2]. In this present investigation, we extracted the scaling exponents function and multifractal spectrum from HRV time series. As shown in Figure 1a, scaling exponents $\tau(q)$ of the healthy subject (blue dots) are more linear than those of heart failures (red crosses). Multifractal spectrum $D(h)$ in Figure 1b is obtained through a Legendre transform from the $\tau(q)$ in Figure 1a. Noted that multifractal spectrum $D(h)$ for the heart failure group is narrower than healthy controls, indicating the loss of multifractality.

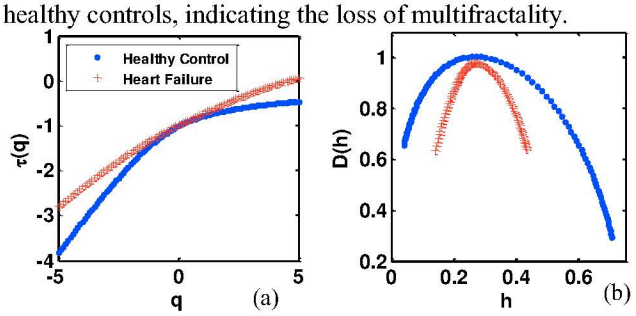

Figure 1. Multifractal analysis of heart rate variability for healthy control and heart failure group. (a) $\tau(q)$ versus q. (b) $D(h)$ versus h.

B. Lyapunov Exponents

Lyapunov exponents measure the exponential divergence or convergence of nearby trajectories in nonlinear systems, which are one of the fundamental indicators of deterministic chaos [3]. Given a time series, the n-dimensional phase space can be reconstructed (i.e., through Takens' embedding theorem) to monitor the long-term evolution of an infinitesimal n-sphere of initial conditions. The ith Lyapunov exponent is then defined in terms of the length of the ellipsoidal principal axis $p_i(t)$:

$$\lambda_i = \lim_{t\to\infty} \frac{1}{t} \ln \frac{p_i(t)}{p_i(0)}$$

where λ_i's are ordered from the largest to the smallest. Further, Lyapunov spectrum can be used to estimate the rate of entropy production and the Kaplan-Yorke dimension of nonlinear dynamical system as follows:

$$D_{KY} = k + \frac{\sum_{i=1}^{k} \lambda_i}{|\lambda_{i+1}|}$$

where k is the maximum integer such that the sum of the k largest exponents is still non-negative. Moreover, the sum of all the positive Lyapunov exponents gives an estimate of the Kolmogorov-Sinai entropy:

$$E_{KS} = \sum_{i=1}^{n} \Theta(\lambda_i) \cdot \lambda_i$$

where $\Theta(\cdot)$ is the Heaviside function.

C. Multiscale Entropy Analysis

Multiscale entropy (MSE) analysis was first proposed by Costa et al. [4]. The MSE approach calculates sample entropy at multiple scales of the time series. The two steps in MSE are as follows: (i) For a given time series $\{x_1, \cdots, x_N\}$, multiscale coarse-grained time series are built by taking local averages as follows:

$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i$$

where τ represents the scale factor and $1 \le j \le N/\tau$. For scale 1, $y_j^{(1)}$ is simply the original time series. (ii) Then, the sample entropy is calculated for each of the multiscale coarse-grained time series $y_j^{(\tau)}$. The MSE spectrum plots the variations of sample entropy vs. the scale factor τ.

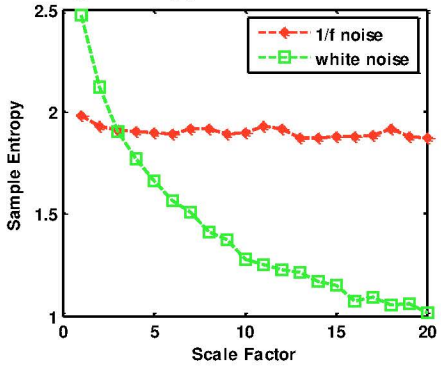

Figure 2. Sample entropy as a function of the scale factor for multiscale coarse-grained time series of white and 1/f noises.

Figure 2 shows that white noises yield a higher value of sample entropy than 1/f noises in the scale 1. However, the sample entropy for 1/f noises does not show big variations as the scale increases, while the value of sample entropy for white noises monotonically decreases from scale 1 to 20. It may be noted that the sample entropy for white noises becomes smaller than the corresponding values for 1/f noises in the scale 3 and above. The results of MSE analysis are consistent with the fact that, unlike white noises, 1/f noises contain correlations across multiple time scales and is, therefore, more complex than white noises. However, this information cannot be extracted, and is usually buried in the single-scale entropy analysis.

D. Feature Selection and Classification

Note that a large amount of features are extracted from three nonlinear approaches. As a result, this may bring the "curse of dimensionality" issues for classification models, e.g., increased model parameters and overfitting problems [5]. Hence, we use the strategy of sequential forward feature selection to optimally choose a subset of features that are strongly correlated with process variations. Starting from an empty feature subset, an additional feature $\mathcal{s}^+$ is selected when it maximizes the objective function $\Gamma(\mathcal{S}_\ell + \mathcal{s}^+)$, which wraps the classification model. This process is repeated until it reaches the desired subset size. Feature selection not only surmounts the aforementioned classification complexity and overfitting problems, but also provides faster and more cost-effective models with the optimal feature subset.

Classification models associate the input feature pattern $\mathcal{s}$ to one of the $\mathcal{K}$ classes of process conditions, $\mathcal{C}_1, \ldots, \mathcal{C}_\mathcal{K}$. We partitioned the whole dataset $\mathcal{D}$ into the training dataset $\mathcal{D}_1 = \{\langle y(i), \mathcal{s}(i)\rangle | i = 1, \cdots, N_1\}$ and testing dataset $\mathcal{D}_2 = \{\langle y(i), \mathcal{s}(i)\rangle | i = N_1 + 1, \cdots, N_1 + N_2\}$, where N_1 and N_2 are

the size of training and testing datasets, $y(i)$ takes values in the output sets $\mathcal{C}_1, \ldots, \mathcal{C}_{\mathcal{K}}$, $\boldsymbol{s}(i) = \{s_{i1}, s_{i2}, \ldots, s_{i\ell}\}$ is the set of ℓ selected features for the ith record in $\mathcal{D}$. Two parametric classification models (i.e., linear and quadratic discriminant analysis) and one non-parametric k-nearest-neighbor (KNN) are considered in this investigation.

In parametric methods, we assumed a multivariate Gaussian distribution for each class density as:

$$f_c(\boldsymbol{s}) = \frac{1}{(2\pi)^{\ell/2}|\Sigma_c|^{1/2}} e^{-\frac{1}{2}(\boldsymbol{s}-\mu_c)^T \Sigma_c^{-1}(\boldsymbol{s}-\mu_c)}$$

If π_c is the prior probability of class c, and $\sum_{c=1}^{\mathcal{K}} \pi_c = 1$, linear discriminant analysis (LDA) assumes that all classes have a common covariance matrix $\Sigma_c = \Sigma, \forall c$. Therefore, linear discriminant functions are expressed as

$$\delta_c(\boldsymbol{s}) = \boldsymbol{s}^T \Sigma^{-1} \mu_c - \frac{1}{2} \mu_c^T \Sigma^{-1} \mu_c + log\pi_c$$

Similarly, quadratic discriminant analysis (QDA) assumes different covariance matrix Σ_c for each class and the quadratic discriminant functions are defined as

$$\delta_c(\boldsymbol{s}) = -\frac{1}{2} log|\Sigma_c| - \frac{1}{2}(\boldsymbol{s}-\mu_c)^T \Sigma_c^{-1}(\boldsymbol{s}-\mu_c) + log\pi_c$$

These two discriminant functions yield linear and quadratic decision boundaries between each pair of classes c and m, i.e., $\{\text{boundary } \boldsymbol{s}: \delta_c(\boldsymbol{s}) = \delta_m(\boldsymbol{s})\}$ [6].

The KNN rule is an intuitive method that classifies unlabeled examples based on nearest training samples in the feature space. For a given feature point $\boldsymbol{s}$ from the testing dataset $\mathcal{D}_2$, find the k "closest" feature samples $\boldsymbol{s}_{(r)}, r = 1, \cdots, k$ in the training dataset $\mathcal{D}_1$ and assign $\boldsymbol{s}$ to the class that appears most frequently within the k-subset.

III. Materials and Experimental Design

In this investigation, we analyzed the 24-hour heart rate time series using three aforementioned nonlinear approaches. The fundamental hypothesis here is that nonlinear properties underlying HRV time series are different between healthy control and heart failure subjects. In total, we have 54 recordings of normal sinus rhythm (NSR) and 29 recordings of congestive heart failure (CHF), available in the PhysioNet [7]. The HRV time series is preprocessed to eliminate erroneously large intervals and outliers due to missed beat detections following the same procedures as in [2]. The preprocessing procedures include (a) a moving-window average filter, and (b) increment smoothing. For the 5 consecutive points in a moving window, the central point is removed if it is greater than twice the local mean calculated from the other four points. There is no interpolation in this moving-window average filter. The second step calculates differences between adjacent elements in the time series. If successive increments has opposite sign with amplitudes > 3×standard deviation of increment series, both increments will be replaced by the interpolated value in between. This present investigation uses the new HRV time series that is reconstructed from post-processed series of increments.

A. Experimental Design

As shown in figure 3, we designed a computer experiment to evaluate the comparative performance of three nonlinear approaches. Features extracted in the wavelet multifractal analysis include multifractal spectrum $\tau(q)$ and fractal dimension $D(h)$. Further, we extracted the spectrum of Lyapunov exponents along with Kaplan-Yorke dimension D_{KY} and the Kolmogorov-Sinai entropy E_{KS}. Finally, multiscale entropy analysis provides sample entropies in multiple temporal scales of HRV time series. To this end, the performances of classification models are not only evaluated for each group of features but also the combined feature set from all three nonlinear approaches.

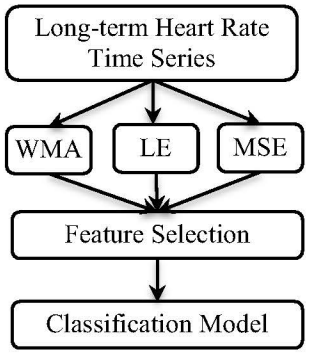

Figure 3. Flow Chart of research methodology used.

B. Cross-Validation and Performance Evaluation

To reduce the bias in classification performance evaluation, we have utilized both K-fold cross-validation and random subsampling in this investigation. K-fold cross-validation partitions the whole dataset $\mathcal{D}$ into K folds, in which K-1 folds are used for the training purpose and the rest one fold for testing. The 1-fold of testing samples is shifted without overlaps in the dataset $\mathcal{D}$ for K times. The estimate of true performance is obtained as the average of those K error rates on testing samples. In addition, random subsampling method will randomly replicate such K-fold cross-validation experiments for 100 times by randomly creating the K-fold partitions to obtain the probability distribution of performance statistics. This integration of K-fold cross-validation and random subsampling methods can prevent the biases from the inequitable selection of training dataset [6].

Two performance metrics used in this investigation are sensitivity and specificity. Both metrics are computed from testing dataset $\mathcal{D}_2$. Sensitivity measures the proportion of actual positives, i.e., heart failure conditions, are correctly identified as such. Specificity measures the proportion of true negatives that represents the healthy controls are correctly identified. It may be noted that there are two classes for response variable y_i, i.e., +1 for heart failure and -1 for healthy control in this present investigation. The performance statistics, sensitivity and specificity, are defined as

$$\text{Sensitivity} = \frac{\sum_{i=N_1+1}^{N_1+N_2} [I(\tilde{y}_i=+1 | y_i=+1)]}{\sum_{i=N_1+1}^{N_1+N_2} I(y_i=+1)},$$

$$\text{Specificity} = \frac{\sum_{i=N_1+1}^{N_1+N_2} [I(\tilde{y}_i=-1 | y_i=-1)]}{\sum_{i=N_1+1}^{N_1+N_2} I(y_i=-1)}$$

where $I(\cdot)$ is the indicator function, y_i, $\tilde{y}_i$ are the actual and predicted class labels.

TABLE I. 1-DIMENSIONAL UNPAIRED *t*-TEST AND KS TEST FOR SELECTED FEATURES

Statistic Tests	Analysis Methods*	Test Statistics									
		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
Unpaired *t*-test (*p*-value)	WMA	6.2e-04	3.5e-03	0.012	8.9e-04	3.1e-03	0.030	8.5e-03	0.037	0.020	3.5e-03
	LE	2.1e-04	6.2e-04	8.9e-04	0.440	0.021	0.180	0.025	0.904	0.417	1.1e-04
	MSE	1.2e-05	4.6e-04	0.054	2.1e-03	3.5e-03	0.071	1.8e-03	1.6e-03	1.2e-03	4.0e-03
Two-sample KS test (KS statistic)	WMA	0.613	0.372	0.324	0.467	0.425	0.343	0.430	0.343	0.375	0.433
	LE	0.565	0.613	0.467	0.250	0.322	0.326	0.462	0.096	0.241	0.462
	MSE	0.671	0.393	0.305	0.377	0.303	0.348	0.374	0.374	0.383	0.327

*WMA – Wavelet Multifractal Analysis; LE – Lyapunov Exponents; MSE – Multiscale Entropy Analysis

IV. RESULTS

As shown in Table I, we evaluated the individual feature separately using two statistical tests, namely unpaired *t*-test and Kolmogorov-Smirnov (KS) test. There are a total of 30 features, 10 in each nonlinear dynamic method, that are optimally chosen by the feature selection algorithms. In unpaired *t*-test, the smaller *p*-value indicates that we have more evidences to reject the null hypothesis, i.e., this feature has the same distribution between NSR and CHF groups. A larger KS statistic shows that this feature has more distinct cumulative distribution functions between NSR and CHF groups. Table I shows that two statistic tests agree on the fact that most of the features are significant, because the majority of *p*-values are <0.05 and KS statistic >0.3. However, 1-dimensional statistical test does not account for the feature dependence in the high-dimensional space.

Therefore, we carried out classification experiments with three groups of features and three different classification models. It may be noted that wavelet multifractal analysis and multiscale entropy analysis have previously yields important results pertinent to the nonlinear behaviors in the heart rate time series [8, 9]. Table II shows the mean and standard deviation of performance metrics for all three classification models. The average performances of LDA (i.e., sensitivity and specificity) are shown in Table II to be as follows: 91.1% and 57.3% for wavelet multifractal analysis, 92.6% and 74.7% for Lyapunov exponents and 93.2% and 64.2% for multiscale entropy analysis. In addition, if we combine the features from all three nonlinear analysis methods, LDA classification achieves a sensitivity of 97.7% and a specificity of 91.5%, and yields the better overall accuracy 92.6% (i.e., calculated in terms of $(29 \times 0.977 + 54 \times 0.915)/(29 + 54)$) than QDA and KNN models.

TABLE II. PERFORMANCES OF CLASSIFICATION MODELS FOR THREE NONLINEAR DYNAMIC ANALYSIS METHODS

Classification models	Nonlinear Methods	Performances			
		Sensitivity (%)		*Specificity* (%)	
		mean	s.d.	mean	s.d.
LDA	WMA	91.1	0.28	57.3	0.50
	LE	92.6	0.04	74.7	0.10
	MSE	93.2	0.03	64.2	0.01
	COMBINED	97.7	0.01	91.5	0.04
QDA	WMA	91.4	0.47	69.3	0.48
	LE	93.8	0.04	74.0	0.05
	MSE	91.1	0.08	78.3	0.18
	COMBINED	98.8	0.02	89.1	0.10
KNN	WMA	92.0	0.01	68.2	0.07
	LE	95.3	0.02	62.9	0.07
	MSE	95.6	0.02	64.7	0.09
	COMBINED	94.0	0.05	80.4	0.06

V. CONCLUSION AND DISCUSSION

In this present study, we conducted a comparative analysis of three nonlinear approaches and their capabilities to identify congestive heart failure subjects using the 24-hour heart rate time series. The results of computer experiments demonstrated that three nonlinear approaches yield a comparable performance. The MSE approach is slightly better by delineating nonlinear and nonstationary behaviors in multiple scales of time series. For the combination feature sets, the LDA classification models achieve a sensitivity around 97.7% and with small deviations (<0.02%) and an average specificity of 91.5% with 0.05% deviations. The QDA models yields a sensitivity around 98.8% with small deviations (<0.03%) and a specificity of 89.1% with the combined features, but the KNN model provides a relatively low sensitivity (≈94%) with a specificity of 80.4%.

In a nutshell, three nonlinear approaches are shown to effectively capture nonlinear dynamic behaviors in the 24-hour heart rate time series. The outstanding performances of the combinational feature set show that three nonlinear methods capture nonlinear characteristics in HRV time series from different perspectives. Collectively, they provide a more complete picture of nonlinear dynamics in HRV datasets.

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