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Gender Based Variability Time Series Complexity Analysis

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Abstract**—**Non linear methods of heart rate variability (HRV) analysis are becoming more popular. It has been observed that complexity measures quantify the regularity and uncertainty of cardiovascular RR-interval time series. In the present work, SampEn has been evaluated in healthy normal sinus rhythm (NSR) male and female subjects for different data lengths and tolerance level r. It is demonstrated that SampEn is small for higher values of tolerance r. Also SampEn value of healthy female group is higher than that of healthy male group for short data length and with increase in data length both groups overlap each other and it is difficult to distinguish them. The SampEn gives inaccurate results by assigning higher value to female group, because male subject have more complex HRV pattern than that of female subjects. Therefore, this traditional algorithm exhibits higher complexity for healthy female subjects than for healthy male subjects, which is misleading observation. This may be due to the fact that SampEn do not account for multiple time scales inherent in the physiologic time series and the hidden spatial and temporal fluctuations remains unexplored.

Keywords**—**Heart rate variability, normal sinus rhythm group, RR interval time series, sample entropy.

I. Introduction

IN recent years, HRV has emerged as a powerful non-invasive diagnostic tool used to investigate the autonomic control on the cardiac activity. HRV is the variation in beat-to-beat intervals and is one of the most important markers for evaluating overall cardiac health. It is a proven fact that HRV is usually high in normal and healthy subjects, whereas reduced HRV has been observed in certain pathologies such as myocardial infarction, ischemic heart disease, congestive heart failure and others [1]-[5].

Time and frequency domains are the linear methods, used to access the autonomic nervous system control over cardiac rhythm. These Linear methods of HRV analysis assume that R-R interval series to be stationary or any variations in it are harmonic or sinusoidal in nature. But cardiac rhythm has multiple interactions with other physiological systems such as respiration and it may also be affected by small disturbances such as premature ventricular contraction, atrioventricular block etc. so resulting signal is nonlinear, non-stationary and chaotic in nature, exhibiting some short range and long range correlations [6]. Linear approach is more prone to give inaccurate analysis. Also the sensitivity and specificity of these methods was less than expected positive predictive value of < 30% [7]-[9]. The highly complex heart rate signals are nonlinear and non- stationary, usually chaotic in nature and exhibits some short range and long range correlations. Analysis of HRV signal using non linear approach is proposed to give better results, because here original RR time series is analyzed. With the help of these nonlinear methods one can analyze the hidden complexity of RR interval series. Also the predictive value is expected to be higher than the linear methods [10]. Some of the nonlinear dynamics used are the poincare plot, correlation dimension, power law slope, largest lyupnov exponent, and approximate entropy (ApEn), sample entropy (SampEn) and detrended fluctuation analysis.

Entropy based measures are used to quantify the regularity and uncertainty of cardiovascular RR interval time series. Pincus [11]-[13] introduced ApEn for measuring complexity of a time series. But ApEn statistics gives inconsistent results and is biased suggesting less complexity than actually present in the signal. Richman and Mooran [14] developed new refined complexity measure SampEn, which agree with the theory much more closely than ApEn. Tuzcu and Selman [15] observed significant decrease in SampEn in children who undergone heart transplant, thereby indicating loss of system complexity. Al-Angari and Sahakian [16] reported significant loss of complexity in patients suffering from obstructive sleep apnea syndrome. Loss of complexity has been proposed with age [17] and in certain pathological conditions [18]. Goya-Esteban et al. [18] applied SampEn to distinguish healthy subjects from patients with congestive heart failure at fixed tolerance level r. Also it has been observed that HRV of male subjects is higher in comparison to female subjects [22]-[25].

In this paper we evaluated SampEn technique on NSR male and female subjects to observe the effect of the variation in data length N and tolerance level r on the SampEn.

II. Materials and Method

The entire dataset is retrieved from the physionet site (http://www.physionet.org/) [19], consists of RR time series recorded from 10 healthy subjects, 5 male and 5 female subjects, each sampled at 128 samples per second (from MIT-BIH NSR Database) All the database of RR interval time series is filtered to remove outliers [20]. Table I presents the record numbers of these subjects.

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TABLE I
RECORD NUMBERS OF SUBJECTS OF NSR MALE AND FEMALE SUBJECTS

Group	Record Number
NSR male	16265,16773, 16483,19090,19093
NSR female	16272, 16420, 16786, 17453, 19140

NSR-normal sinus rhythm

In the present work SampEn technique is used, which is the negative natural logarithm of the conditional probability that two sequences similar for *m* points remain similar i.e. within the tolerance level r for one more point. Here self-matches are excluded while calculating probabilities. Lesser the SampEn more regular is the time series. The differences between SampEn and ApEn are: firstly SampEn exclude self-matches; secondly SampEn does not use template-wise approach when estimating conditional probabilities. Following is the algorithm used to calculate SampEn [14]:

For a time series of N data points, define a vector u(j):

$$u(j):1\le j\le N \tag{1}$$

Fix the value of m and r. Here m is the length of sequences to be compared and r is the filtering level or tolerance for accepting matches. Tolerance is set at r = r*SD. The SD (standard deviation) of data set has been set at SD = 1, by standardizing the time series. This series form (N-M+1) number of $x_m(i)$ vectors within vector. Where $x_m(i):1\le i\le N-m+1$, having data length of m points defined as $[u(i+k):0\le k\le m-1]$ from u(i) to u(i+m-1). The distance between two such vectors is calculated as:

$$d[x(i),x(j)]=\max\{|u(i+k)-u(j+k)|:0\le k\le m-1\} \tag{2}$$

This is maximum distance between scalar components of these vectors. Now calculate $B^m(r)$, which is the probability that the two sequences will match for m points, using the formula

$$B_i^m(r)=\frac{1}{(N-m+1)} * (\text{Number of vectors } x_m(j) \text{ within r of } x_m(i), \text{ where j ranges from 1 to N-m and } j\neq i) \tag{3}$$

Then define

$$B^m(r)=\frac{1}{(N-m)}\sum_{i=1}^{N-m}[B_i^m(r)] \tag{4}$$

Similarly calculate $A^m(r)$, which is the probability that the two sequences are similar for m+1 points, using the formula

$$A_i^m(r)=\frac{1}{(N-m+1)} * (\text{Numbers of vectors } x_{m+1}(j) \text{ within r of } x_{m+1}(i), \text{ here j ranges from 1 to N-m and } j\neq i) \tag{5}$$

Then define

$$A_i^m(r)=\frac{1}{(N-m)}\sum_{i=1}^{N-m}[A_i^m(r)] \tag{6}$$

Calculate SampEn as

$$\text{SampEn (m,r,N)} = -In\left[\frac{A^m(r)}{B^m(r)}\right] \tag{7}$$

Find

$$B=\left\{\frac{[(N-m-1)(N-m)]}{2}\right\}B^m(r) \tag{8}$$

and

$$A=\left\{\frac{[(N-m-1)(N-m)]}{2}\right\}A^m(r) \tag{9}$$

Here B is the total number of template matches of length m and A is the total number of forward matches of length m+1.

$$\text{So, } \frac{A}{B}=\left[\frac{A^m(r)}{B^m(r)}\right] \text{ and SampEn (m,r,N)} = -In\left[\frac{A}{B}\right] \tag{10}$$

Here A/B is the conditional probability that two sequences similar for m points remain similar for one more next point, i.e. both within tolerance limit r.

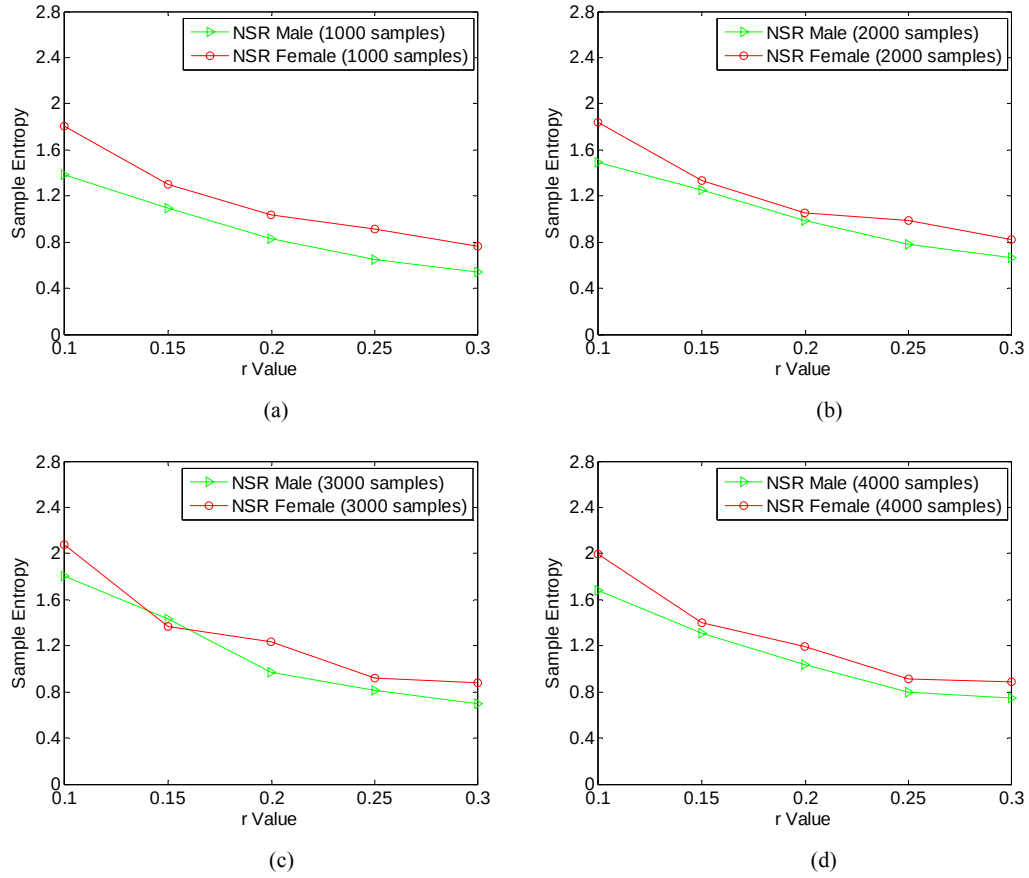
III. RESULTS & DISCUSSION

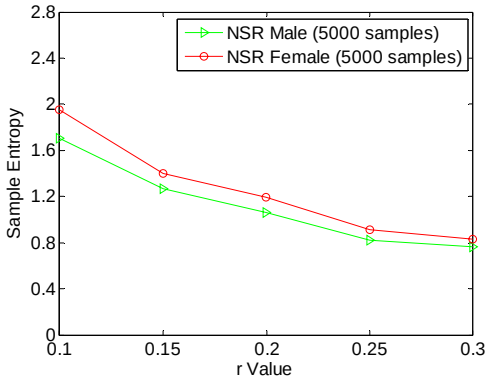
SampEn is applied on RR interval time series derived from NSR male and female subjects. Before applying the SampEn technique it is necessary to remove all the outlier points. The filtered RR-interval series is standardized to give SD of 1. This standardized series is used for determining SampEn for template lengths of m = 2, template matching tolerance r = 0.10, 0.15, 0.20, 0.25, 0.3 of SD of data series and data length N = 1000 to 20000. Table II and Fig. 1 present SampEn analysis of the NSR male and female subjects. Here we can observe that SampEn value of NSR female subjects is higher than that of NSR male subjects for the data length varying from 1000 to 5000. Afterwards with increase in data length, N = 10000 and 20000, both groups overlap each other and it is difficult to distinguish them. Hence it is concluded that SampEn sometimes gives inaccurate results by assigning higher value to female subjects, because RR time series of healthy male subject have more complex pattern than that of female subjects i.e. HRV of healthy male subject is more than that of female subjects. Also as we go on increasing data length both groups overlap, so difficult to distinguish between both groups, which is in agreement with M. Costa [21] results that traditional entropy measures sometimes gives misleading results as entropy is measured on single scale, hence ignoring the complex spatio-temporal fluctuations inherent in HRV signal.

TABLE II
SAMPEN (MEAN ± STD) OF NORMAL SINUS RHYTHM (NSR) MALE AND FEMALE SUBJECTS

r value		r = 0.1	r = 0.15	r = 0.2	r = 0.25	r = 0.3
Groups	Samples	mean ± std	mean ± std	mean ± std	mean ± std	mean ± std
NSR Male	1000	1.380±0.379	1.097±0.379	0.830±0.281	0.648±0.228	0.541±0.161
NSR Male	2000	1.488±0.486	1.250±0.266	0.990±0.309	0.779±0.150	0.667±0.217
NSR Male	3000	1.806±0.249	1.436±0.366	0.973±0.179	0.810±0.128	0.697±0.120
NSR Male	4000	1.679±0.185	1.310±0.290	1.039±0.124	0.798±0.095	0.744±0.066
NSR Male	5000	1.701±0.191	1.268±0.179	1.063±0.110	0.818±0.086	0.764±0.077
NSR Male	10000	1.797±0.331	1.377±0.169	1.048±0.124	0.792±0.099	0.793±0.099
NSR Male	20000	1.766±0.256	1.411±0.172	1.077±0.129	0.847±0.078	0.821±0.114
NSR Female	1000	1.802±0.468	1.303±0.228	1.035±0.259	0.909±0.355	0.768±0.186
NSR Female	2000	1.841±0.472	1.336±0.247	1.056±0.263	0.991±0.302	0.818±0.207
NSR Female	3000	2.075±0.403	1.365±0.224	1.233±0.242	0.919±0.115	0.883±0.187
NSR Female	4000	1.996±1.997	1.402±1.402	1.192±1.192	0.913±0.913	0.889±0.889
NSR Female	5000	1.954±0.284	1.402±0.172	1.193±0.240	0.913±0.116	0.830±0.173
NSR Female	10000	1.744±0.482	1.267±0.213	1.114±0.336	0.839±0.189	0.800±0.218
NSR Female	20000	1.663±0.326	1.208±0.119	0.984±0.118	0.755±0.101	0.677±0.094

r-tolerance level; NSR - normal sinus rhythm ; std- standard deviation





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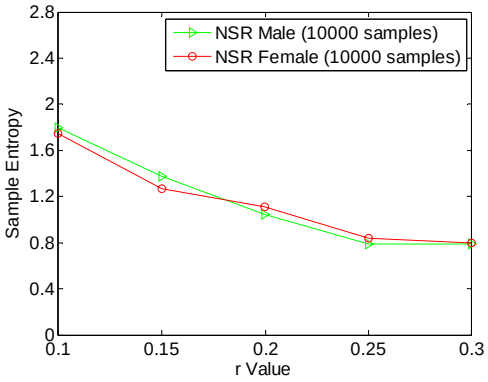

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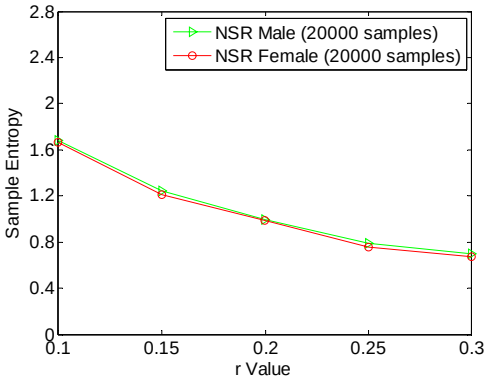

(g)

Fig. 1 (a)-(g) SampEn analysis of RR interval time series derived from healthy normal sinus rhythm (NSR) male and female subjects for different data lengths N and tolerance level r. SampEn parameter are template lengths of m=2, tolerance level r = 0.1, 0.15, 0.2, 0.25, 0.3 and data lengths N = 1000, 2000, 3000, 4000, 5000, 10000 and 20000

IV. Conclusion

In this present study, SampEn was evaluated for NSR male and female groups. The SampEn for female subjects was observed higher than NSR male subjects for the data length varying from 1000-to-5000. For higher data lengths of N = 10,000 and 20000, both groups overlap each other and it is difficult to distinguish them. Thus the SampEn sometimes gives misleading results by assigning higher value to female subjects, because heart rate variability of male subject is considered more than female subjects [22]-[25]. The recently proposed method of multiscale entropy has the potential to overcome these shortcomings.

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