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Optimal ECG Sampling Frequency for Multiscale Entropy-Based HRV

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Abstract**—**Multiscale entropy (MSE) is an extensively used index to provide a general understanding of multiple complexity of physiologic mechanism of heart rate variability (HRV) that operates on a wide range of time scales. Accurate selection of electrocardiogram (ECG) sampling frequency is an essential concern for clinically significant HRV quantification; high ECG sampling rate increase memory requirements and processing time, whereas low sampling rate degrade signal quality and results in clinically misinterpreted HRV. In this work, the impact of ECG sampling frequency on MSE based HRV have been quantified. MSE measures are found to be sensitive to ECG sampling frequency and effect of sampling frequency will be a function of time scale.

Keywords**—**ECG, heart rate variability, HRV, multiscale entropy, sampling frequency.

I. Introduction

HRV is a reflector of the sympatho-vagal balance between sympathetic and parasympathetic mediators acting on the sino-atrial and atrio-ventricular nodes [1], [2]. HRV measures the variation between RR intervals and the oscillations between consecutive heart rates. The clinical consequence of HRV was appreciated by Hon and Lee in 1965 [3]. HRV is the result of interaction among complex feedback mechanisms in the cardiovascular system. Therefore, as the feedback mechanisms are degraded by diseases, the HRV diminishes. Nowadays, HRV has become a central topic in physiological signal analysis, serving as a vital non-invasive indicator of cardiovascular and autonomic system function, with direct connections to respiratory, central nervous and metabolic dynamics [4]-[6]. Variation in heart rate, HRV may be evaluated by time-domain, frequency-domain and non-linear analysis [7], [8].

Analysis of complex variations in heart rate has become an important non-invasive technique to study the cardiovascular control mechanism, sympathovagal interactions in physiological and pathological conditions [8], [9]. Cardiovascular control is governed by several regulatory mechanisms interacting across multiple temporal scales. Therefore, concomitant effect of these regulatory mechanisms, referred to as HRV, occurs over a large set of temporal scales [8]. MSE proposed by Costa et al. [9]-[11], is a widely used method to provide a general understanding of complexity of multiple physiologic control mechanisms occurs over a wide range of time scales. Although classical entropy and physiologic concepts like approximate entropy (ApEn) and sample entropy (SampEn) have been capable in discriminating healthy and cardiac states [12]-[14], but these traditional methods are single scale-based approaches and could not measure the complexity of physiological systems at multiple time-scales. Whereas computation of MSE is essentially consists, elimination of fast temporal scales to focus slower time scales, coarse graining procedure to assess entropy and calculation of entropy rates [15].

Along with various technical and biological difficulties, data acquisition, memory considerations, and signal pre-processing; the selection of optimal sampling rate is also a technical blockade in ECG signal processing [2]. The fast sampling rate may cause increase in processing time and storage memory requirements. On the other side, with low sampling rate there may be degradation in the ECG Signal quality and misinterpretation of HRV measures. The erroneous marking and detection of the R peak, alters the spectrum and produce clinically misinterpreted HRV results due to jitter generation at low sampling rate. This misinterpreted and inaccurate HRV quantification of RR tachograms may obscure critical issues and may impede rather than foster the advancement of medical applications. Sampling frequency of more than 250 Hz was recommended by the task force of the European Society of Cardiology and North American society of Pacing and Electrophysiology [2]. The resampling induced significant error in time domain HRV indices [16]. Hejjel et al. recommended that 1000 Hz ECG sampling frequency was required for accurate time domain HRV quantification even in low variability samples16. But, for high variability samples, a lower sampling rate may be adequate [16]. Ziemssen et al. have studied the influence of different ECG sampling frequencies on spectral and baroreflex parameters of EUROBAVAR data set [17]. When we analysis HRV by trigonometric regressive spectral parameters, ECG sampling frequencies induced significant effect on pathological subject's HRV [17]. ECG sampling frequency of 100 Hz in comparison to 500 Hz was required for spectral and baroreflex analysis [17]. According to Abboud and Barnea [18], 128 Hz is the adequate ECG sampling rate to give a sufficient enough signal to noise ratio of the RR interval time series. However, for cardiac subjects with lower HRV, at least 1000 Hz ECG sampling frequency is required [18]. Errors in the computation of the ApEn and SampEn based complexity measures of HRV by ECG sampling frequency was investigated [19], [20]. The errors induced were clinically significant for low ECG sampling frequencies.

Despite the Task Force recommendations [2] for accurate ECG sampling frequency for linear HRV parameters, a

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systematic study to quantify the effect of sampling rate on MSE based HRV is the need of day for the widespread applications of complexity based non-linear HRV in clinical situation. In an effort to provide a contribution to clarify these issues, this study assessed and investigated:

i) The influence of ECG sampling frequency on MSE based HRV; and,
ii) The optimal sampling frequency for MSE measures of HRV.

II. Subject & Methods

Bio-signals obtained from physiological systems are mostly non-stationary, non-linear and complex signals. They may contain caveats of current and impending abnormalities. The reflectors may be occurring at all times or may present at random time scale. However, to study anomalies in voluminous data collected over several hours is strenuous and time consuming. ECG and HRV are the signals acquired from cardiovascular system to analyze the complex physiological interaction that occur in heart and vessels. Hence, many methods have been developed to analyze these signals and extract information about the complex cardiovascular system.

A. Experimental Condition

ECG signal have been acquired from ten young healthy subjects (age 31±7 years) having no history of any cardiac disorder. All the subjects were kept quiet in a natural environment and data were acquired in the supine condition. No subject was addicted to smoking, alcohol or drugs. The subjects were made to rest in supine condition for 10 minutes prior to data acquisition, to stabilize them to the laboratory environment. The subjects were allowed to normal breathing during the whole acquisition.

ECG data was acquired in Lead-II configuration on Biopac® MP150 system. For each subject, ectopic-free normal RR intervals with data length N = 1000 were derived with 125 Hz, 250 Hz, 500 Hz, 1000 Hz, 1500 Hz and 2000 Hz sampling frequencies. Thus in total, 60 ectopic-free RR interval time series were obtained. Prior to analysis, the ECG signals were processed to filter power line interference, muscle tremors, spikes and respiration noises. Many QRS detection algorithms [21], [22] have been proposed in literature and in the present work the RR interval time series were estimated by the Tompkins method proposed in [23] for its simple implementation and high detection accuracy (Fig. 1).

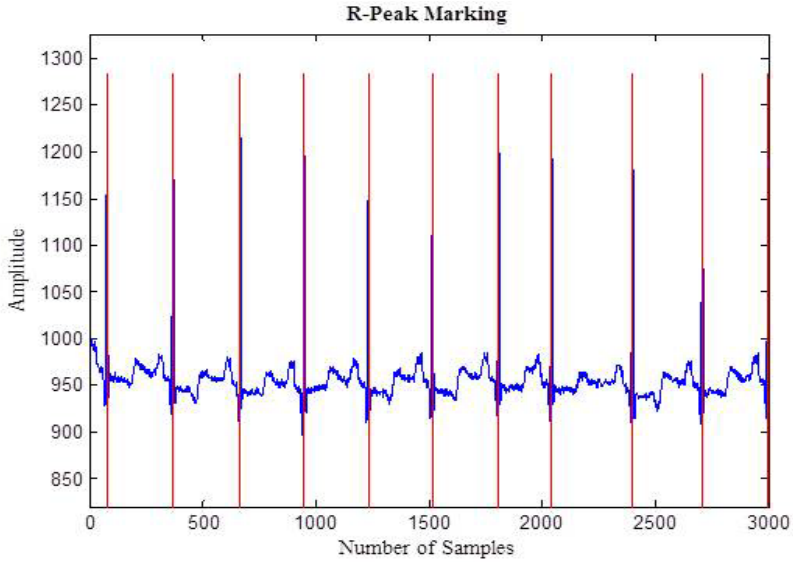

Fig. 1 QRS complex marking and R peak detection by Tompkins method

B. Multiscale Complex Dynamics Properties and Estimator

Since continuous interaction of cardiovascular system with other physiological systems results highly nonlinear HRV signal, a complex, chaotic and non stationary behavior is always expected. Entropy is an invariant quantity measuring the rate of generation of information in the context of nonlinear and complex time series analysis [14], [15]. Although conventional ApEn and SampEn based entropies are classical complexity measures but these measures are unable to detect the subtle but important complexity at higher temporal scales.

1. Multiscale Entropy

Costa et al. developed MSE for the multiscale analysis of physiologic time series [9], [10]. The computation of MSE essentially consists of elimination of fast temporal scales to focus on slower time scales, coarse graining procedure to assess entropy rates and calculation of entropy. For multiscale analysis, SampEn have been preferred to estimate entropy since SampEn is a refinement of the ApEn family of statistics [8]-[11]. The MSE method incorporates two procedures:

1. For a physiological time series with *N* points data length, multiple coarse-grained time series are created by averaging a successively increasing number of data

samples within non-overlapping windows of increasing length, τ. Each element of the coarse-grained time series is calculated as:

$$y_j^{\tau} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \qquad 1 \le j \le N/\tau.$$

where τ represents the scale factor and length of each coarse-grained time series is N/τ.

For scale 1: the coarse-grained time series will simply be the original signal $x_1, x_2 \ldots x_N$

For scale 2:

$$\frac{x_1 + x_2}{2}, \frac{x_3 + x_4}{2}, \ldots \frac{x_{N-1} + x_N}{2}$$

For Scale 3:

$$\frac{x_1 + x_2 + x_3}{3}, \frac{x_4 + x_5 + x_6}{3}, \ldots \frac{x_{N-2} + x_{N-1} + x_N}{3}$$

2. For each coarse-grained time series, SampEn is calculated with predefined parameters *m,* the embedding dimension and *r*, a threshold, which is in effect a noise filter. The parameter *m* specifies the length of patterns and *r* is the tolerance threshold for accepting similarity between these patterns. SampEn is a "regularity statistic". It "looks for patterns" in a time series and quantifies its degree of predictability or regularity.

For each coarse grained time series *u(i*) the SampEn is calculated by forming m vectors *X (1) to X (N-m+1)* defined by

$$X(i) = [u(i), u(i+1), \ldots u(i+m+1)], \; 1 \le i \le N-m+1,$$

where the distance *d[X(i),X(j)]* between the vectors *X(i) and X(j)* as the maximum absolute difference between respective scalar components is calculated as:

$$d[X(i), X(j)] = \max_{1,2,\ldots m} (u(i+k) - u(j+k))$$

Then define,

$$B_i^m(r) = \frac{1}{N-m+1} v^m(i)$$

i=1,2,...N-m and,

$$v^m(i) = \text{Number of } d[X(i), X(j)] \le r \text{ and } i \ne j \text{ .}$$

For each *i=1, 2...N-m* define:

$$B_i^m(r) = \frac{1}{N-m+1} v^m(i)$$

where $v^{m+1}(i) = \text{no of } d_{m+1}[X(i), X(j)] \le r$ and $i \ne j$

Finally,

$$SampEn(m, r, N) = -\ln\left(\frac{A^m(r)}{B^m(r)}\right)$$

where,

$$B^m(r) = \frac{1}{N-m} \sum_{1}^{N-m} B_i^m(r) \quad A^m(r) = \frac{1}{N-m} \sum_{1}^{N-m} A_i^m(r)$$

In this study, *m i*s fixed to 2 and *r* is considered as the 20% of the standard deviation of the datasets.

III. Results and Discussion

Linear mathematical model does not match physiological system exclusively. Furthermore, the influences of undefined stimuli on physiological processes should be taken into consideration for HRV analysis. Therefore, appropriate approach for physiological heart rate time series analysis is fractal, chaotic and complexity based non-linear analysis. In cardiovascular system analysis, wide consensus has been reached that a decrease in the complexity is in most instances bounded to a pathological condition.

This study aimed on non-linear method based on MSE analysis, capable of identifying complexity at temporal scales. We considered estimator applicable on data sets of about 1000 RR intervals as they are suitable for the experimental protocols of HRV routinely used by medical practitioners. To investigate the influence of ECG sampling frequency and the scaling factor τ, MSE of 60 ectopic-free RR interval series having data length of N=1000 samples was computed. Table I demonstrates the effect of ECG sampling frequency variation on MSE at different scale.

TABLE I
Effect of ECG Sampling Frequency on Average MSE of Ten Healthy Subjects

Sampling frequency (Hz)	Multiscale Entropy									
	scale 1	scale 2	scale 3	scale 4	scale 5	scale 6	scale 7	scale 8	scale 9	scale 10
125 Hz	1.5757	1.5692	1.5128	1.4486	1.4127	1.3309	1.3011	1.2889	1.2388	1.2263
250 Hz	1.5869	1.5751	1.5209	1.4472	1.4124	1.3369	1.2975	1.2991	1.236	1.222
500 Hz	1.6427	1.5929	1.5086	1.4402	1.4132	1.3214	1.2887	1.2895	1.2243	1.2206
1000 Hz	1.6412	1.5969	1.5134	1.4426	1.4026	1.3239	1.2896	1.2808	1.2161	1.2172
1500 Hz	1.6419	1.5912	1.5102	1.4389	1.4157	1.3211	1.2941	1.2879	1.2201	1.2155
2000 Hz	1.6422	1.5919	1.5123	1.4359	1.4152	1.32	1.2943	1.2869	1.2189	1.2147

The impact of variation in ECG sampling rate on the MSE was evaluated by relative errors (*REs*) calculated by comparing MSE calculated from the RR interval time series derived from ECG with sampling frequency 2000 Hz. For MSE parameters *{X1, X2, . . . Xn}* obtained with a sampling frequency of 125 Hz, 250 Hz, 500 Hz, 1000 Hz and 1500 Hz and *Xorigin* obtained with ECG sampling frequency of 2000 Hz, the relative errors, RE_k were calculated *as* $|Xorigin - Xk|/Xorigin \times 100$ (%). For MSE measure at each sampling frequency, 50 error values were computed (Table II) and used for the statistical analysis. The correlation coefficients values for the increase in sampling frequency with decrease in *REs* of MSE at different scales are shown in Table III.

TABLE II
THE RELATIVE ERRORS IN MSES AT SAMPLING FREQUENCIES OF 125, 250, 500 1000 AND 1500 HZ WITH RESPECT TO MSE AT SAMPLING FREQUENCY OF 2000 HZ

Sampling frequency (Hz)	Relative Error									
	scale 1	**scale 2**	**scale 3**	**scale 4**	**scale 5**	**scale 6**	**scale 7**	**scale 8**	**scale 9**	**scale 10**
125 Hz	4.0494	1.4260	0.0331	0.8845	0.1767	0.8258	0.5254	0.1554	1.6326	0.9550
250 Hz	3.3674	1.0553	0.5687	0.7870	0.1979	1.2803	0.2472	0.9480	1.4029	0.6010
500 Hz	0.0304	0.0628	0.2447	0.2995	0.1413	0.1061	0.4327	0.2020	0.4430	0.4857
1000 Hz	0.0609	0.3141	0.0727	0.4666	0.8903	0.2955	0.3631	0.4740	0.2297	0.2058
1500 Hz	0.0183	0.0440	0.1389	0.2089	0.0353	0.0833	0.0155	0.0777	0.0984	0.0659
2000 Hz	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

TABLE III
CORRELATION COEFFICIENTS BETWEEN INCREASE IN SAMPLING FREQUENCY AND DECREASE IN *REs* OF MSE BASED HRV

Correlation coefficients									
scale 1	**scale 2**	**scale 3**	**scale 4**	**scale 5**	**scale 6**	**scale 7**	**scale 8**	**scale 9**	**scale 10**
0.7440	0.7728	0.5080	0.8915	0.1689	0.7493	0.8487	0.5470	0.8625	0.9269

For very low ECG sampling frequency of 125 Hz, the *REs* in MSE with reference to values at sampling frequency 2000 Hz were approximately 4 and 0.95% for low time scale-1 and large time scale-10, respectively. At a medium ECG sampling frequency of 500 Hz, *REs* were 0.03 and 0.48%, whereas at high sampling frequency of 1500 Hz REs were 0.001% and 0.06% for low time scale-1 and large time scale-10, respectively. Therefore, entropy measures of HRV at different time scales are found to be sensitive to ECG sampling frequency and time scales.

IV. CONCLUSIONS

Variation in MSE based HRV due to the ECG sampling frequency was quantified at different time scales. The significance change is found in MSE with variation in sampling frequency and scaling factor. The errors in entropy measures depend upon data length of RR interval time series. This erroneous quantification results a bias in entropy measure and clinically misinterpretation of HRV indices. The findings of the present work can be partly used as a reference for selection of optimal sampling frequency and the acceptable amount of error for the MSE based HRV analysis at different time scales.

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