

Sample Entropy based HRV: Effect of ECG Sampling Frequency

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Abstract Biomedical signals carry important information about the behaviour of the living systems under study. A proper processing of these signals in principle enhances their physiological and clinical information. Analysis of variations in the instantaneous heart rate time series using the beat to-beat RR intervals (the RR tachogram) is known as heart rate variability (HRV) analysis. Sample entropy (SampEn), refined version of approximate entropy (ApEn), is a nonlinear complexity measure used to quantify the irregularity of a RR interval time series without biasing. An increase in SampEn is an indicator of increases in complexity. Linear HRV parameters are very sensitive to ECG sampling frequency and low sampling frequency may result in clinically misinterpretation of HRV. In this study consequences of errors in SampEn based HRV induced by ECG sampling frequency have been investigated. The error induced in SampEn based HRV was found to be a function of ECG sampling frequency and RR interval data length. The relative error in SampEn was approximately 3.5% for medium and long term data (N=500, 1000 respectively) and less than 2% for short term data (N=200) at low ECG sampling frequency of 125 Hz with respect to reference values at 2000 Hz. Therefore the SampEn based HRV indices computed from RR interval time series with low ECG sampling should be regarded with caution. The finding of this study can be partly used as a reference for the optimal ECG sampling frequency for the SampEn-based HRV assessment.

Keywords: ECG, HRV, sample entropy, sampling frequency

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1. Introduction

The Electrocardiogram (ECG), as shown in Figure 1, is the record of variation of bio-electric potential with respect to time as the human heart beats. Interpretation of ECG patterns is needed for diagnosing malfunctions of the human heart. A single normal cycle of the ECG represents the successive atrial depolarization/repolarization and ventricular depolarization/repolarization which occurs with every heartbeat. These can be approximately associated with the peaks and troughs of the ECG waveform labelled P, Q, R, S, and T.

The instantaneous variation in time intervals between RR peaks of ECG is known as heart rate variability (HRV) [1]. HRV is a non-invasive indicator reflecting the sympathetic and parasympathetic activity of the autonomic nervous system (ANS) on the sinoatrial node of the heart. It expresses the total amount of variations of both instantaneous heart rate (HR) and RR intervals (intervals between QRS complexes of normal sinus depolarisations) [2,3,4]. HRV is important because it provides a window to observe the heart's ability to respond to normal regulatory

impulses that affect its rhythm. A primary focus of clinical work and research is in observing or modifying the balance in regulatory impulses from the parasympathetic and sympathetic nervous system. Prospective studies have shown that HRV independently predicts mortality within the initial two years following a heart attack. Different physiological factors may influence HRV such as gender, age, circadian rhythm, respiration and body position. In 1996 a Task Force of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology (NASPE) defined and established standards of measurement, physiological interpretation and clinical use of HRV. Time domain indices, geometric measures frequency domain indices and non-linear indices constitute nowadays the standard clinically used HRV parameters [5].

Analysis of HR dynamics by methods based on chaos theory and nonlinear system theory has gained recent interest. This interest is based on observations suggesting that the mechanisms involved in cardiovascular regulation likely interact with each other in a nonlinear way. The cardiovascular system is composed of multiple subsystems and sub-subsystem units that exhibit nonlinear deterministic and stochastic characteristics, which are

subject to hierarchical regulations. Interactions among these units may induce irregular time courses in the processes, but the underlying sub-processes include well-determined behavior. Therefore, it is presumed that these irregular time courses can be characterized more adequately by dynamic nonlinear analyses rather than by linear time series analyses [6]. There are strong evidences to consider the complex behavior of HRV as a non-linear dynamic and chaotic process controlled by the ANS [7]. Analysis of HRV by non-linear dynamics can significantly improve the identification of an increase in sudden cardiac death, in comparison with the conventional analysis in the time or frequency domain [3]. Recent studies demonstrated that HRV present a non-linear behavior that may contain hidden information, which may not extractable with conventional methods of analysis [8,9]. Such information promises to be of clinical values as well as to relate to basic mechanism of healthy and pathologic functions.

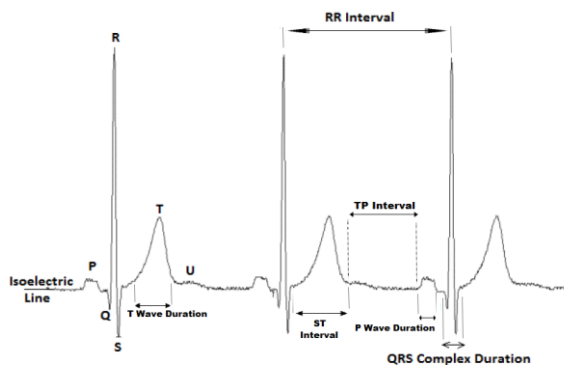


Figure 1. ECG intervals

Non-linear HRV quantification techniques can be classified in three categories i) chaotic analysis ii) graphical representation and iii) complexity analysis. Fractal Dimension (FD), largest Lyapunov exponent and detrended fluctuation analysis (DFA) are the chaotic analysis; Poincaré plot and recurrence plot are graphical representation and entropy measures are the complexity analysis techniques for HRV quantification respectively. Non-linear dynamics analysis may be a powerful tool to reveal the characteristics and mechanism of HRV signal. But a very long data sequence is needed to estimate accurately chaotic analysis and graphical representation measures. The popularity of complexity analysis stems from its capability to provide quantitative information about the complexity of the experimental data that are short in data length [13].

Complexity analysis can be performed through the evaluation of entropy and entropy rate. Entropy calculates the degree of complexity of the distribution of the samples of a signal. Approximate entropy (ApEn) and Sampling entropy (SampEn) are the efficient nonlinear techniques to quantify the complexity or irregularity of time series data like RR intervals [10]. The aptness of entropy based HRV stems from its potential to provide quantitative information about the complexity of the short length experimental data [11]. SampEn has the advantage of being less dependent on the time-series length and shows consistency over broad ranges of possible data sequence length to be compared (m), tolerance (r) and total RR

interval data length (N). When these parameters are adjusted appropriately, the SampEn method appears to yield more consistent results than does the ApEn method and it appears to be affected to a lesser degree by the choice of m and the data length [12]. Furthermore the values of SampEn agree with the theoretical values expected for a uniform random noise time-series much more than the ApEn values, even for very short time-series [13].

Although HRV patterns hold considerable promise for clarifying issues in clinical applications, the inaccurate quantification and interpretation of these patterns may obscure critical issues or relationships and may impede rather than foster the development of clinical applications. Besides technical and biological difficulties, data acquisition, data storage, signal pre-processing, representation and optimal sampling rate are numerous technical barrier in ECG signal processing [14,15]. The task force of the European Society of Cardiology and North American society of Pacing and Electrophysiology recommended the use of 250-500 Hz or high sampling frequency for the measurement of HRV without any interpolation [5]. Unnecessarily fast sampling rate results in high processing time, extreme memory requirement for data storage and access. Beside this Low sampling rate degrades the quality of ECG Signal results in misinterpretation of HRV measures. A low sampling rate may produce a jitter in the estimation of the R wave fiducial point, which alters the spectrum considerably and produce inaccurate results. Abboud and Barnea investigated the effect of ECG sampling frequency for healthy and cardiac subjects and concluded that a sampling frequency of 128 Hz is sufficient, in patients with normal HRV levels, to give a large enough signal to noise ratio in the RR tachogram. However, for patients such as heart transplant patients, a sampling rate of at least 1000 Hz is required [16]. The optimal range is 250 to 500 Hz or perhaps even higher, while a lower sampling rate (100 Hz) may behave satisfactorily only if an algorithm of interpolation is used to improve the R wave fiducial point. Hejjel *et al.*, investigate the consequences of errors induced by resampling on the time domain parameters of HRV [14]. They recommended an ECG sampling frequency of 1000 Hz for adequate time domain based HRV analysis without interpolation even in seriously reduced-variability samples. However, a lower sampling rate was found to be acceptable for higher variability samples [14]. No matter whether short-or long-term data are analyzed, the analysis of HRV depends on the integrity of the input data. Most systems obtain computer-digitized ECG signals. The RR intervals are derived either online or offline. The rate of digitization varies from system to system. Ziemssen *et al.*, evaluate the effect of different ECG sampling frequencies on parameters of spectral and baroreflex analysis of EUROBAVAR data set [15]. They found that pathologically decreased variability of RR time series was highly affected by variation in ECG sampling frequencies. ECG sampling frequency of 100 Hz in comparison to 500 Hz was recommended for spectral and baroreflex analysis by trigonometric regressive spectral [16].

ECG sampling rate analysis on entropy measure of HRV is the need of attention for widespread use of HRV in clinical situation. Although the Task Force

recommended ECG sampling frequency ranges for time and frequency domain HRV, but no systematic study has not yet been performed to evaluate the influence of sampling rate on SampEn based HRV. In this study, an effort has been made to explore the influence of ECG sampling frequency on SampEn based HRV and to assess the optimal sampling frequency for entropy measure of HRV based on computer simulation.

2. Subjects and ECG Acquisition

The ECG is the most appropriate signal to study HRV because it offers the most accurate representation of the cardiac activities. In this study, ECG signal have been recorded from ten healthy subjects having no history of any cardiac disorder. All subjects were refrained from alcohol, coffee and smoking for 12 hour prior to data recording. No participant was addicted to drugs, taking any medication or involved in endurance training. The data acquisition was performed at rest in the supine position and the subjects were kept quiet in a natural environment at comfortable light and temperature levels. The subject were made to rest in supine position for 10 minutes prior to recording, so that the they may stabilize to the laboratory environment after that the subjects were laid on a bed in a well air-conditioned room. The ectopic-free normal RR intervals time series with data length $N = 1000$ (long-term data), 500 (medium-term data) and 200 (short-term data) were derived for each subject by Lead-II ECG recordings on Biopac® MP150 system having sampling frequencies of 125, 250, 500, 1000, 1500 and 2000 Hz resulting in a total of 180 ectopic-free RR interval time series. The subjects were allowed to normal breathing during the whole recording.

3. Complexity Analysis of HRV by Entropy Measures

Heart is a complex biological system and every complex system has emergent properties which define its very nature. Complexity has proved to be an elusive concept. Different researchers in different fields are bringing new philosophical and theoretical tools to deal with complex phenomena in complex systems. Complexity analysis can also be performed through the evaluation of entropy and entropy rate. Entropy calculates the degree of complexity of the distribution of the samples of a signal. The largest entropy is obtained when the distribution is flat (the samples are identically distributed). On the contrary, if some values are more likely (e.g., the sample distribution is Gaussian), the entropy decreases. The historical development of mathematics to quantify complexity or regularity has centred on various types of entropy measures. Kolmogorov–Sinai (K-S) entropy, developed by Kolmogorov and expanded upon by Sinai, allows classification of deterministic dynamical systems by rate of information generation [17]. Unfortunately, K-S entropy was not developed for statistical applications, and its blind application to practical time series will only evaluate system noise, not underlying system properties, as it generally requires a vast amount of input data to achieve convergence. Usually, in the analysis of HRV,

entropy is not calculated directly over the samples of the series but over patterns of length m . In this case, entropy measures the complexity of the pattern distribution as a function of m .

3.1. Sample Entropy (SampEn)

In ApEn each sequence matches itself, So ApEn is a biased estimator and it is lower than expected for short records. This also implies that it lacks relative consistency, making it difficult to interpret the comparison of different datasets. The SampEn is a modification of ApEn, in which the self- comparison between vectors is avoided. The differences with respect to ApEn are: (1) self-matches are not counted and (2) only the first $N - m$ vectors of length m are considered [12]. Entropy is a measure of the rate of information production and in this context comparing data with themselves is meaningless. Self-matching is explicitly dismissed with SampEn. Furthermore, SampEn does not use a template-wise approach [13]. SampEn algorithm can be summarized as follows:

1. Form m vectors $X(1)$ to $X(N-m+1)$ defined by $X(i) = [u(i), u(i+1), \dots, u(i+m-1)]$, $1 \leq i \leq N-m+1$

2. Define the distance $d[X(i), X(j)]$ between the vectors $X(i)$ and $X(j)$ as the maximum absolute difference their respectively scalar components $d[X(i), X(j)] = \max_{1,2,\dots,m} (u(i+k) - u(j+k))$

3. Define $v^m(i) =$ no of such that $d[X(i), X(j)] \leq r$ and $i \neq j$ from which we define $B_i^m(r) = \frac{1}{N-m+1} v^m(i)$ Here $i=1, 2 \dots N-m$.

4. For each $i=1, 2 \dots N-m$ define $B_i^m(r) = \frac{1}{N-m+1} v^m(i)$ Where $v^{m+1}(i) =$ no of $X(j)$ and $d_{m+1}[X(i), X(j)] \leq r$ $i \neq j$

5. Now Define $B^m(r) = \frac{1}{N-m} \sum_1^{N-m} B_i^m(r)$ and

$$A^m(r) = \frac{1}{N-m} \sum_1^{N-m} A_i^m(r)$$

6. Finally SampEn for a finite length of N can be taken as $SampEn(m, r, N) = -\ln\left(\frac{A^m(r)}{B^m(r)}\right)$.

4. Statistical Analysis

The effects of the ECG sampling frequency on the SampEn based HRV parameter was evaluated based on the relative errors (REs) compared with the parameters calculated from the RR interval data derived from ECG at sampling frequency 2000 Hz. When $\{X_1, X_2, \dots, X_n\}$ is obtained for SampEn based HRV parameter of the data set with a sampling frequency 125, 250, 500 1000 and 1500 Hz and X_{origin} is the corresponding parameter value at ECG sampling frequency of 2000 Hz, the relative errors RE_k are computed as $|X_{origin} - X_k|/X_{origin} \times 100$ (%). For HRV parameter at each sampling frequency and data

length of ECG signal, 150 error values were derived and used for the statistical calculations

5. Results

To investigate the influence of ECG sampling frequency on, SampEn, HRV complexity measure, the SampEn, based entropy of RR interval series of RR interval long term, medium and short term data lengths *N* 1000, 500 and 200 respectively was computed and compared with reference values. The reference values were the entropies of RR interval time series derived from ECG sampled at sampling frequency 2000 Hz. The REs in entropies of RR intervals time series derived from ECG at sampling frequency 125, 250, 500, 1000 and 1500 Hz were computed and compared with reference values to assess the effect of ECG sampling frequency. Table 1 demonstrates the effect of ECG sampling frequency on variation in (average±Standard deviation) SampEn, of RR interval time series of ten healthy subjects. Entropy measures of HRV for long term data and medium term data at data length *N*=1000, 500 found to be more sensitive to ECG sampling frequency. When ECG Signal was sampled at very low sampling frequency of 125 Hz, the RE in SampEn of RR interval time series with respect to reference values at 2000 Hz was approximately 3.5%.for long term data, medium data and less than 2% for short term data. The REs was decrease up to 0.2 % and 0.02% for long term and short term data respectively at medium ECG sampling frequency of 1000 Hz. Figure 2 and Figure 3 show the pattern of entropy measures and REs in SampEn, based HRV for short term, medium and long term RR interval data. These reductions in REs have been found to be dependent on level of sampling frequency and data length. Results show that errors due to the ECG sampling frequency in SampEn, can be very high at low sampling frequency. The correlation coefficients between increase in sampling frequency and decrease in REs in.

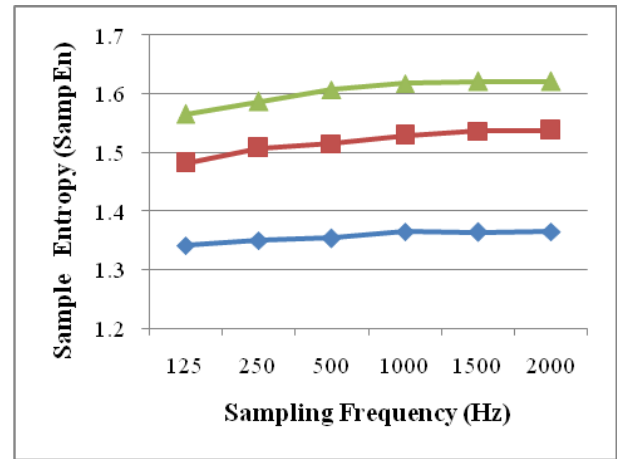


Figure 2. Average of Sampling Entropy (SampEn) based HRV of ten healthy subjects at various ECG sampling frequencies

▲.. Short Term Data (N=200), .. Medium Term Data (N=500), .. ▲.. Long Term Data (N=1000)

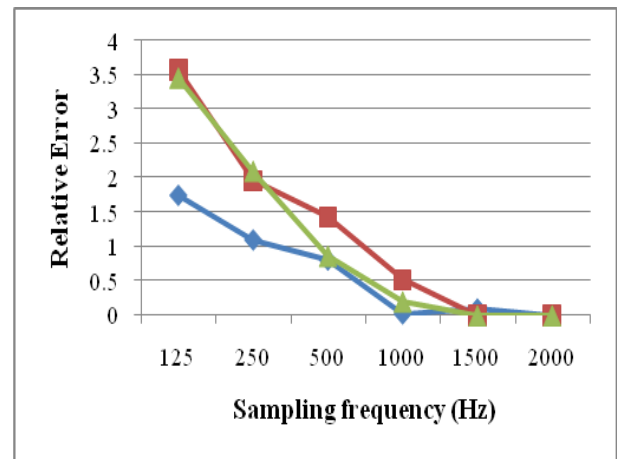


Figure 3. Relative error in SampEn based HRV of ten healthy subjects with respect to the reference value

◆.. Short Term Data (N=200), .. Medium Term Data (N=500), .. ▲.. Long Term Data (N=1000)

Table 1. Effect of ECG Sampling Frequency on Average SampEn of Ten Healthy Subjects

S. No.	Sampling Frequency (Hz)	Mean±SD of SampEn			Relative Error (RE)		
		Data Length			200	500	1000
		200	500	1000			
1	125	1.34109±0.044	1.48214±0.121	1.56521±0.152	1.74373	3.58121	3.459569
2	250	1.3499±0.044	1.50699±0.116	1.58721±0.154	1.098257	1.964624	2.102634
3	500	1.35389±0.021	1.51513±0.082	1.60724±0.053	0.805926	1.435086	0.867205
4	1000	1.36527±0.034	1.52921±0.075	1.61801±0.050	0.027841	0.519129	0.202924
5	1500	1.36353±0.018	1.53657±0.054	1.62104±0.044	0.099642	0.000403	0.00016
6	2000	1.36489±0.018	1.53719±0.050	1.62130±0.013	0	0	0

SampEn with respect to reference values were found to be 0.8732, 0.8803 and 0.8332 for short term, medium and long term data respectively.

6. Conclusion

The errors in the estimation of the SampEn based HRV due to the ECG sampling frequency is quantified. The errors in SampEn based HRV is clinically significant when ECG is sampled at low sampling frequency of 125 or 250 Hz. The errors in entropy measures depend upon

data length of RR interval time series. Thus we have shown that the absolute entropy based HRV estimated by the SampEn algorithm is sensitive to ECG sampling frequency and data length. This erroneous quantification results a bias in entropy measure and clinically misinterpretation of HRV indices

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