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Recent Trends in Nonlinear Methods of HRV Analysis: A Review

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***Abstract*—**The linear methods of heart rate variability analysis such as non-parametric (e.g. fast Fourier transform analysis) and parametric methods (e.g. autoregressive modeling) has become an established non-invasive tool for marking the cardiac health, but their sensitivity and specificity were found to be lower than expected with positive predictive value <30%. This may be due to considering the RR-interval series as stationary and re-sampling them prior to their use for analysis, whereas actually it is not. This paper reviews the non-linear methods of HRV analysis such as correlation dimension, largest Lyupnov exponent, power law slope, fractal analysis, detrended fluctuation analysis, complexity measure etc. which are currently becoming popular as these uses the actual RR-interval series. These methods are expected to highly accurate cardiac health prognosis.

***Keywords*—**chaos, nonlinear dynamics, sample entropy, approximate entropy, detrended fluctuation analysis.

I. Introduction

THE linear methods of HRV analysis (such as time and spectral domain measures) asumes that analysed segments of RR-interval series are stationary or variations are harmonic or sinusoidal in nature. However, the heart rate is continuously modulated nonlinear fluctuations. These nonlinear fluctuations can be due to postural or physical activities, multip le interactions with other physiological systems and it may also be affected by small perturbations (e.g. premature ventricular contraction, atrioventricular block). So, linear methods of HRV analysis are prone to give inaccurate heart health prognosis. The sensitivity and specificity of these measures were found to be lower than expected with positive predictive value of <30%. Moreover, the prediction capability has been found to be unexpectedly similar with both time and spectral domain measures. The spectral analyses were able to quantify the principal rhythmic components of autonomic control in the HRV signal. The high frequency (HF) and low frequency (LF) components of power spectral density of HRV signal signified para-sympathetic (vagal) and sympathetic tone respectively. The predominant LF and smaller HF in MI patients were found to be due to reduced vagal tone but markedly reduced LF power in high risk patients was unexplanable. These unanswered queries have led to the interest in analysing original RR-interval time series with comprehensive account of peripheral mechanisms influencing the cardiac rhythm [1],[2],[20].

The non-linear fluctuations are not completely random in nature, but these follows chaotic nature and exhibit short range correlations which can be determined by deterministic laws. The non-linear methods for HRV analysis are proposed to give better insight of autonomic control based upon nonlinear mathmatics and chaos theory. These are broadly classified based upon system trajectory in its phase space, computing fractal dimensions, determinig self- similarirty properties or by determining short and long-range correlations. These methods can describe complexity or fractal dynamics of RR-interval series and their predictive value for risk stratification is expected to be higher than the linear methods of time and frequency domain methods. It is to be noted that amount of information can not be extracted with single approach because specific patterns of fluctuations present in the variability signal and duration of recording may require different modalities for their study. This paper presents the comprehensive review of various non-linear methods currently being used for investigating the heart rate variability dynamics [4],[6],[18],[19],[32].

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II. Methods

The nonlinear methods of HRV analysis are based on theory of chaos. For a dynamical system to be classified as chaotic it must be sensitive to initial conditions which means that each point in phase space of such a system is closely approximated by other points with significantly different future trajectories. Their phase space must be topologically mixing means that the system will evolve over time so that any given region or open set of its phase space will eventually overlap with any other given region. This gives the impression that the system is behaving randomly, but these systems are deterministic in nature as their future dynamics can be fully determined by their initial conditions with no random elements involved. This type of behavior is known as deterministic chaos or simply chaos. Linear systems are never chaotic and for a dynamical system to display chaotic behaviour it has to be nonlinear in nature. The various nonlinear methods courrently being used for HRV analysis are described in next sections [7], [8],[15], [21].

A. Correlation Dimension Analysis

Phase space indicates all possible states of a system with each possible state indicated by one unique point in the phase space. Some dynamical systems are chaotic everywhere but in many cases chaotic behaviour is found only in a subset of phase space. The interesting case arises when chaotic behaviour takes place on an attractor. The chaotic motion gives rise to what are known as strange attractors, attractors that can have great detail and complexity. Correlation dimension is one of the most widely used measures of fractal dimension and is a useful indicator for various pathologies

such as ventricular tachycardia, congestive heart failure. For a RR-interval series having N data points, the phase space plot is constructed with heart rate X[n] on the x-axis and heart rate after a delay on the y-axis i.e. X [n+1]. The embedding dimension of 10 and delay of 1 is chosen for heart rate signals. The spread of phase space plot differs as per the cardiac health or kind of disease. The idea in correlation dimension (CD) is to construct a probability function C(r) such that two arbitrary points on the orbit are closer together than r. This is done by calculating separation between every two points in the set of N number of data points and sorting them into bins of dr proportionate to r. The CD can be calculated using distance between each pair of points in the set of N number of points

$$s(i, j) = \left| X_i - X_j \right| \tag{1}$$

A correlation is then calculated using:

$$C(r) = \frac{1}{N^2} \times \text{(Number of pairs of } (i, j) \text{ with } s(i, j) < r \text{)}$$

$$C(r) = kr^D \tag{2}$$

So, CD is estimated by:

$$CD = \lim_{r \to 0} \frac{\log(C(r))}{\log(r)} \tag{3}$$

The CD is high for chaotic data and it decreases with decrease in variation of RR-interval series [22].

B. Largest Lyupnov Exponent

The phase space determined by ploting RR-interval seies consists of different trajectories. The exponential divergence of neighboring trajectories is indicative of sensitivity of system on its initial conditions. These trajectories folds up to ensure that solutions are finite and these are general mechanism for generating deterministic randomness. The Lyupnov exponent (λ) is measure of this sensitive dependence of neighboring trajectories on initial conditions or the rate at which these trajectories separate from each other. The positive Lyupnov exponent for all bounded dynamical systems is used and are said to be on chaotic attractor. Negative Lyupnov exponent indicate that trajectories approaches a common fixed point. To determine Lyupnov exponent, two nearby points x_0 and $x_{0+} \Delta x_0$ will generate orbits of its own and separation Δx_0 wil be function of time $\Delta x_0(x_0, t)$. For chaotic data the mean exponential rate of divergence of two initially close orbits is characterised by:

$$\lambda = \lim_{t \to \infty} \frac{1}{t} \ln \frac{\left| \Delta x(x_{0,t}) \right|}{\left| \Delta x \right|} \tag{4}$$

Maximum positive λ is chosen as it quantify sensitivity of the system to initial consditions and gives a measure of predictability This value decreases for slowly varying signals such as in ischemic or dilated cardiomyopathy and will be higher in normal cases [26],[27].

C. Power law slope

The power law slope measures the long term fractal scaling of heart rate variability signal based upon spectral power in HRV signal in 24 hours of data recording. When HRV signal is analysed in frequency domain, the variance is determined in various spectral ranges of ULF, VLF, LF and HF. The power spectrum is plotted on log-log scale and it has been observed that amount of power is increased as the frequency decreases. This relationship is termed as 1/f relationship and region between 0.1 to 0.0001 Hz is used to determine power law slope. The power law slope in healthy and normal subjects has been observed to be around ≈-1 and it becomes steeper in case of diseased subjects, such as in patients with heart transplant or in patients after myocardial infarction. The power law regression parameters have proved to be stronge predictors' death from any cause or arrhythmic death [21],[24].

D. Detrended Fluctuation Analysis

The highly complex heart rate signals are non-linear, non-stationary and non-equilibrium in nature.These highly complex heart rate series may contain important hidden information not extractable using conventional methods. Fractal analysis is an important approach to extract such hidden information in such complex dynamics.

1) Fractals and heart rate dynamics

The concept of fractals is generally associated with geometrical objects, satisying two criterias: self-similarity and fractional dimensionality. Self similarity means that the object is composed of sub-units and sub-sub units on multiple scale levels that statistically resemble the whole object structure. There are upper and lower limits of scale over which this self-similar behaviour applies. The second criterion is that fractal objects should have a fractional dimension which distinguishes it from Euclidean objects. The concept fractal structures, which do not have characteristic length scale can be extended for analysis of complex temporal proceses such as heart rate time series. But there is challenge in detecting self similar process in heart rate time series as it involves two independent physical units (minutes on x-axis and beats/minute on y-axis), so we need two magnification factors [12],[13].

A time series is self-similar if the statistical properties of a time series and its rescaled subunits are identical. Although self-smilarity may not be attained with higher order of moments, so it is usually approximated with a weaker criterion of mean and variance. Mathematically, if:

$y(t)$ - is heart rate time series with y (heart rate on y-axis) and time in minutes on x-axis. Then rescaled process: $a^{\alpha} y(t/a)$: Re-scaled on x-axis by factor of 'a'(i.e. $t \to t/a$) and on y-axis by a factor of a^{α} (i.e. $y \to a^{\alpha} y$). Where 'α' is self-similarity parameter. The self-similarity parameter can be evaluated with appropriate choice of scaling

factors on x and y-axis. If m_x and m_y are scaling factors on x and y-axis respectively, then self-similarity parameter is given by:

$$\alpha = \frac{\ln(m_x)}{\ln(m_y)} \tag{5}$$

Where scaling factors m_x and m_y are evaluated as:

$m_x = n_2 / n_1$ and $m_y = s_2 / s_1$ for given observation windows n_2 and n_1 on x-axis and corresponding standard deviation (s_2 and s_1) probability distributions histograms for these two observation windows. The actual analysis of time series for determination of 'α' is performed by deviding time series in equal window size and then averaging the standard deviation over all windows. This calculation is performed over window sizes. The 'α' is estimated by fitting log-log plot of s versus n [3].

2) Mapping of heart rate time series to self-similar process

In self-similar process with $\alpha > 0$, the fluctuations grow in a power law fashion with increase in window size. So, the fluctuations become exponentially larger in large sized windows, thereby the time series becomes unbounded. However, physiological time series such as heart rate time series are bounded for any size of data set. This practical fact causes still further complications for analysis. Moreover, the self-similarity parameter may result in same values for a heart rate time series and a randomized data although they are different in nature. To counter this problem, it is suggested that fractal properties of accumulated (integrated) time series is to be studied rather than that of original signals as it will be able to distinguish the time series. So, mapping original bounded time series to an integrated time series is crucial step in fractal time series analysis. The physiological time-series are often highly non-stationary and integration process makes its non-stationarity even more apparent. So, to overcome this, a modified root mean square analysis of biological data is proposed, which is termed as detrended fluctuation analysis (DFA). It permits detection of intrinsic self-similarity in a seemingly nonstationary time series and avoids spurious detection of apparent sel-similarity which may be due to artifact of extrinsic trends. DFA works well with time-series whos trends vary slowly.

Detrended fluctuation analysis provides a quantitative method for determining the degree to which a time series is random at the one extreme and correlated at the other. DFA ranges in value from 0.5 (random) to 1.5 (correlated), with normal values of just over 1.0. Decreased DFA (also called alpha 1) has been associated with adverse outcomes in cardiac patient populations.The details of this method have been described below. Only N-N intervals were used for this calculation. DFA can be considered a short-term nonlinear measure [11].

The DFA algorithm is applied to interbeat time series containing 'N' number of intervals. This interbeat time-series is integrated as:

$$y(k) = \sum_{i=1}^{k} \left[B(i) - B_{ave} \right] \tag{6}$$

Where $B(i)$ is the i-th interbeat interval and B_{ave} is average interbeat interval. This integration step maps the original time series for self-similarity process.For self-similarity process, the integrated time-series is devided into boxes of equal length 'n'. A least square line is fit to data in each box. The y-coordinate of this least square line in each box is denoted by $y_n(k)$. The time series $y(k)$ is detrended by subtracting the local trend $y_n(k)$ in each box from integrated time series $y(k)$. The characteristic size of fluctuation is given by $F(n)$:

$$F(n) = \sqrt{\frac{1}{N} \sum_{K=1}^{N} \left[y(k) - y_n(k) \right]^2} \tag{7}$$

$F(n)$ is computed over all box sizes or time scales. To give relationship between '$F(n)$' and 'n'. A linear graph between '$\log F(n)$' and 'log n' indicates presence of self-similarity. The slope of line relating '$F(n)$' and 'n' determines the scaling exponent (self-similarity parameter) α. The scaling parameter is characterized by as follows:

- In white noise, where value at a given instant is completely uncorrelated with any previous value, the value of self-similarity parameter α approaches 0.5.
- The initial slope of $\log F(n)$ Vs log n may be different from 0.5, but will approach 0.5 for large window sizes.
- The value of α greater than 0.5 and less than or equal to 1.0 indcates persistent long range power-law correlations.
- When $0 < \alpha < 0.5$, power law anticorrelations are present such that large values are more likely to be followed by small values.
- When $\alpha > 1$, correlations exists but cease to be of power law form.
- The spectrum of original non-integrated signal is of power law form

  $S(f) \sim 1/f^{\beta}$, where $\beta = 2\alpha - 1$, and for $\alpha = 1$,

$$S(f) \sim 1/f \tag{8}$$

So, $1/f$ noise is interpreted as compromise between complete unpredictability of white noise and much smoother Brownian noise [14],[16],[19],[28].

E. Complexity Measures

Entropy is defined as rate of information producted and it requires a very long data set of time series. The cardiovascular time series is usually short and noisy as there are inherent difficulties in recording long data sets. Pincus introduced set

of complexity measure called approximate entropy (ApEn) but it gives inconsistent results. Richman and Moorman developed new and related complexity measure called sample entropy (SampEn). The SampEn when applied to time series, it agreed with theory closely than ApEn. The cross-ApEn & cross-SampEn measures the similarity of two time series [27],[29],[31],[33].

1) Approximate Entropy

The ApEn is a measure of system complexity, which quantifies the unpredictability of fluctuations in a time series such as heart rate time series. The method examines the time series for similar epochs (period marked by distinctive character). The more frequent and more similar epoch lead to lower value of ApEn. Informally, given *N* points, the family of statistics ApEn (*m*, *r*, *N*) is approximately equal to the negative average natural logarithm of the conditional probability that two sequences that are similar for *m* points remain similar within a tolerance *r*, at the next point. The ApEn algorithm counts each sequence as matching itself to avoid the occurrence of ln(0) in the calculations. This leads to bias of ApEn which causes two important expected properties. First, ApEn is heavily dependent on the record length and is uniformly lower than expected for short records. Second, it lacks relative consistency. That is, if ApEn of one data set is higher than that of another, it should, but does not, remain higher for all conditions teste.If 'N' is length of time series and 'm' is length of sequence to be compared and 'r' is tolerance for accepting matches. It is convenient to set tolerance = r*SD. The standard deviation (SD) of data has been set at SD =1.

Define vector $u(j)$ for time series of N data points:

$$u(j): 1 \le j \le N \tag{9}$$

This series forms $N-m+1$ number of $x_m(i)$ vectors where, $x_m(i): 1 \le i \le N-m+1$ and $x_m(i)$ has data length of m points defined as $\left[\ u(i+k): 0 \le k \le m-1\ \right]$ from $u(i)$ to $u(i+m-1)$.

If B_i is number of vectors $x_m(j)$ within 'r' of $x_m(i)$, ($x_m(i)$ - template and $x_m(j)$ -template match) and A_i is number of vectors $x_{m+1}(j)$ within 'r' of $x_{m+1}(i)$. Then $C_i^m(r)$ - probability that $x_m(j)$ is within 'r' of $x_m(i)$

$$C_i^m(r), = (B_i)/(N-m+1)$$

The average of the natural logarithm of $C_i^m(r)$, is

$$\phi^m(r) = \frac{1}{(N-m+1)} \sum_{i=1}^{N-m+1} \ln\left[C_i^m(r)\right] \tag{10}$$

The ApEn for fixed parameters of N, m & r is:

$$ApEn(m,r,N) = \phi^m(r) - \phi^{m+1}(r) \tag{11}$$

After algebraic manipulation:

$$ApEn(m,r,N) = \frac{1}{(N-m+1)} \sum_{i=1}^{N-m+1} \ln\left[C_i^m(r)\right] - \frac{1}{(N-m)} \sum_{i=1}^{N-m} \ln\left[C_i^{m+1}(r)\right] \tag{12}$$

When N is large:

$$ApEn(m,r,N) \cong \frac{1}{(N-m)} \sum_{i=1}^{N-m} \left[\ -\ln\left(\frac{A_i}{B_i}\right)\ \right] \tag{13}$$

The quantity $C_{N-m+1}^m(r)$ is defined but $C_{N-m+1}^{m+1}(r)$ is not, because the vector $u_{m+1}(N-m+1)$ does not exist. So, ApEn can be thought as the negative natural logarithm of the probability that sequences that are close for *m* points remain close for an additional point. Because conditional probabilities lie between 0 and 1, the parameter ApEn (*m*, *r*) is a positive number of infinite ranges. ApEn (m, r, N) is biased and suggests more similarity than is present.

The bias caused by self matches is evident only when data set N is of finite length. So, ApEn (m, r, N) is biased towards lower values of ApEn and returns values below those predicted by theory. Moreover, the difference between biased and unbiased CP makes it sensitive to recording length. Removing self matches from ApEn would make it highly sensitive to outliers and there is likelihood of occurrence of 'ln (0)'. Thus for these many practical reasons self- matches can be excluded from ApEn and there is no family of estimators which minimizes bias caused by self- matches [5].

2) Sample Entropy

Joshua S. Richman and J. Randall Moorman developed new and related complexity measures called sample entropy and have compared ApEn and SampEn by using them to analyze sets of random numbers with known probabilistic character. The SampEn agreed with theory much more closely than ApEn over a broad range conditions. The improved accuracy makes it useful for studying experimental clinical cardiovascular and other biological time series [30]. The SampEn statistics has been made to be free of bias because of self matching. So, two major differences between SampEn and ApEn are:

i. SampEn does not count self matches.
ii. SampEn does not use template wise approach when estimating conditional probability. SampEn requires only that one template find a match of length m+1.

The work began from Grassberger and Procaccia, who approximated Kolmogrov entropy when self matches are counted. Richmann and Randall made two alterations to this: Calculating correlation integrals using

I. $C^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} C_i^m(r)$ (14)

II. Consider only first N-m vectors of length m ensuring that, for $1 \le i \le N-m$, $x_m(i)$ and $x_{m+1}(i)$ are defined.

For calculating $B^m(r)$:

$B_i^m(r) = \frac{1}{N-m+1} \times$ (No of vectors $x_m(j)$ within r of $x_m(i)$, where j ranges from 1 to N-m and $j \ne i$)

Define $B^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} B_i^m(r)$ (15)

For calculating $A^m(r)$:

$A_i^m(r) = \frac{1}{N-m+1} \times$ (No of vectors $x_{m+1}(j)$ within r of $x_{m+1}(i)$, where j ranges from 1 to N-m and $j \ne i$)

And set $A^m(r) = \frac{1}{N-m} \sum_{i=1}^{N-m} A_i^m(r)$ (16)

So, $B^m(r)$ is the probability that the two sequences will match for m points, and $A^m(r)$ is the probability that the two sequences will match for m+1 points. We then define

statistic SampEn (m, r, N) = $-\ln\left[\frac{A^m(r)}{B^m(r)}\right]$ (17)

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

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

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

So, $\frac{A}{B} = \left[\frac{A^m(r)}{B^m(r)}\right]$

and SampEn (m, r, N) = $-\ln\left[\frac{A}{B}\right]$ (18)

The quantity $\frac{A}{B}$ is precisely the conditional probability that two sequences within a tolerance 'r' for 'm' points remain within r of each other at the next point.It is to be noted that ApEn (m, r, N) calculates probability in a template wise fashion, where as SampEn (m,r,N) calculates the negative logarithm of a probability associated with time series as a whole. SampEn (m, r, N) is defined except at A=0 or B=0.

III. Conclusions

The interest in nonlinear methods has enhanced significantly in recent times due to their dependence on actual RR-interval series. However, most of these methods require long term ECG data recording for dependable heart health prognosis e.g. correlation dimension, largest Lyupnov exponent, power law slope (1/f) and detrended fluctuation analysis (DFA) which becomes hindrance for their applicability. The complexity measure of sample entropy method has evolved from approximate entropy with the requirement of manageable data length requirement. Efforts are on for enhancing the specificity and reduction of data length requirement for these nonlinear methods of HRV analysis.

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