Signal Processing for Heart Rate Variability: Part-II

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Abstract: *The study of heart rate variability (HRV) provides a mean for observing the heart's ability to respond to normal regulatory signals that affect its rhythm. The HRV analysis has proven useful in diagnosis, treatment and monitoring of various pathologies. The modern field of HRV processing is extremely diverse, involving many areas like spectral estimation, system modeling, nonlinear dynamics and chaotic analysis, etc. Thus, there is an urgent need to keep a track of recent advancements and activities taking place in this emerging field. Moreover, the development of chaos theory in the last decades supplied the framework to study the complex dynamics, of heart rate, through a new approach. Many efforts were made to explain the complex behavior of deterministic systems with the presence of nonlinear features instead of the usual stochastic models. In the second of two articles on signal processing for HRV, we explore the HRV using time-frequency and non-linear analysis approaches.*

Keywords: *HRV, Wavelet, Non-linear dynamics*

1. INTRODUCTION

In our first paper (Part-I), we presented a detailed survey and general backgrounds of research and development of time-domain and frequency-domain analysis ttechniques of HRV, which could be applied to variability signals in order to estimate their basic properties. Recent advances, such as time-scale and time-frequency transforms have been able to provide sufficiently robust solutions in several biomedical signal processing applications like noise reduction, restoration, detection, spatiotemporal dynamics esimation, source localizatiton, and pattern recognition. However, the classical assumptions (stationarity, linearity, etc.) usually do not apply in real situations. Further, part of the answers to the challenges raised in Part-I comes from the advancements in signal processing tools and changing our way of thinking organizing and working on biomedical data. These technological advancements and changes are depicted in Fig. 1. This figure presents a detailed summary of various linear and nonlinear measures of HRV.

HRV is a widely investigated signal and it is an important maker of autonomic nervous sysem (ANS) dysfunction[1]. Heart rate (HR) is controlled by several central nervous system oscillators and different control loops. 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. There are strong evidences to consider the complex behavior of HRV as a nonlinear dynamic and chaotic process controlled by the ANS[2-4]. It has been shown that analysis of HRV by nonlinear dynamics can significantly improve the identification of an increase in sudden cardiac death, in comparison with the conventional linear analysis in the time or frequency domain[5]. Significant nonlinear dynamics of heart-rate fluctuations and respiratory movements were found in rabbits and piglets[6,7]. The rationale in the emergence of nonlinear measures of HRV is that the heart is not a periodic oscillator under normal physiological conditions[8] and complicated feedback control of the heart may give rise to nonlinear dynamics that are not well reflected by conventional linear measures of HRV. The complex characteristics of HRV signals in terms of their (sometimes multiple) generating systems, as well as the statistics of the superimposed noises which most often are not known, make the solutions of the more though problems in HRV extremely difficult which the traditional approaches. The development of the time-frequency domain and nonlinear dynamical sysem analsyis has led to the introduction of a large amount of signal analysis techniques aimed at the extraction of HRV parameters from RR interval time series. The original objective was the evaluation of the generating system characteristics in order to better understand its nature.

Lee *et al.*[9] used a Wigner-Ville distribution[10] as a time-frequency analsys tool to analyze nonstationary HRV signals in patients with vasovagal

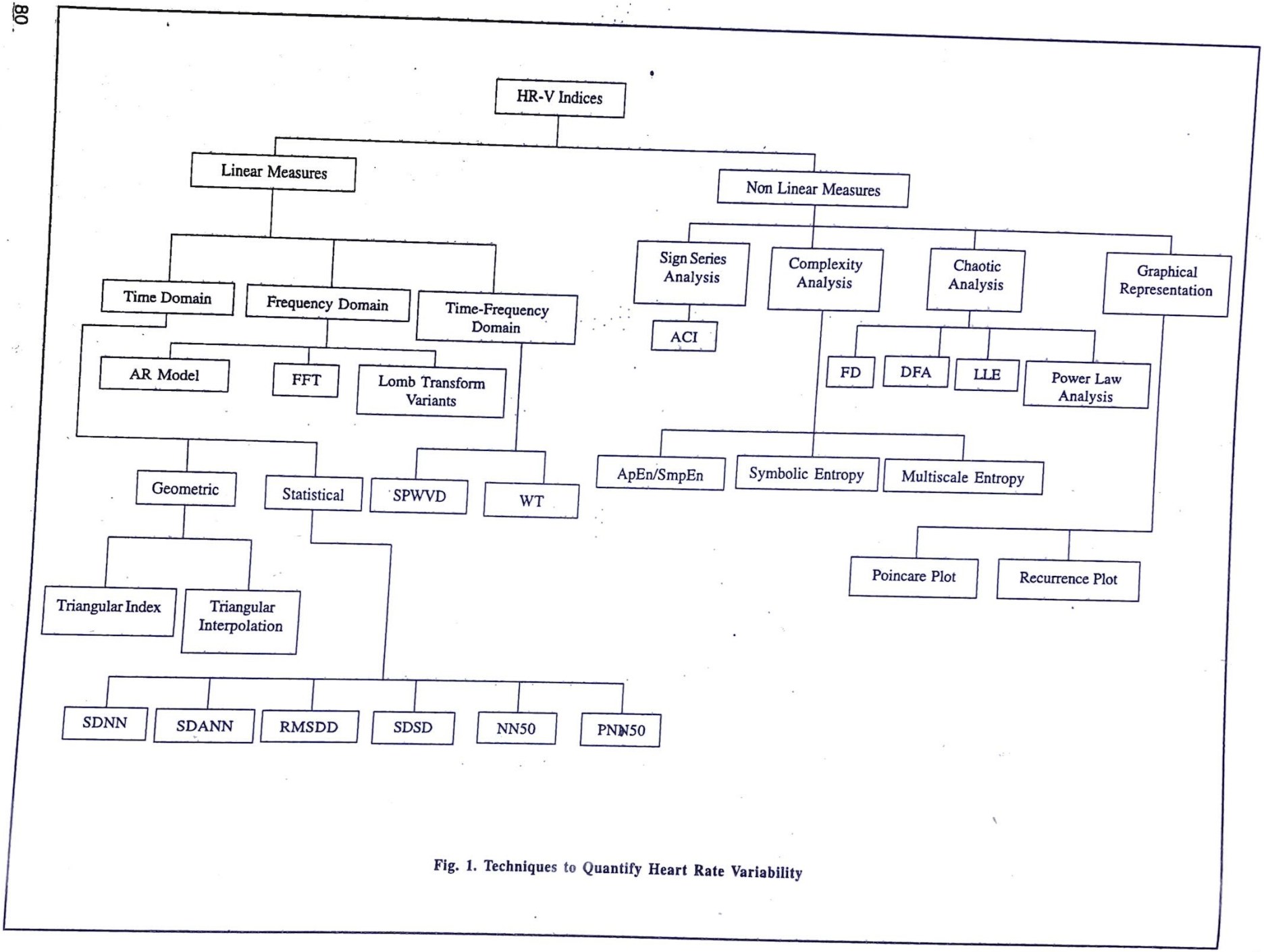

Fig. 1. Techniques to Quantify Heart Rate Variability

syncope. Charvallho *et al.*[11] used an auto-regressive method for time-frequency analysis of HRV. Chan and Zhang[12,13] proposed the Lomb periodogram with variable window for the time-frequency analysis of HRV signals. Bail on *et al.*[14] analyze the HRV signals using time-varying frequency bands based on respiratory frequency. Seong *et al.*[15] and Ebden *et al.*[16] analyze the HRV signal using an SPWVD algorithm. Mendez *et al.*[17] performs a comparative analysis of different time-frequency analysis methods for a condition during arousal from sleep. Wiklund *et al.*[18], Yang and Liao[19] characterized the HRV signal using wavelet transform as a time-frequency analysis method to characterize HRV. Unser[20] and Akay[21] presents a detailed summary on the applications of wavelet transform in biomedical signal processing. Pichot *et al.*[22] used wavelet transform to quantify HRV and to access its instantaneous changes. Spaargaren and English[23] used continuous wavelet transfom for detecting ventricular late potentials. Wiklund and colleagues[24] quantified the HRV signal in the time domain by using wavelets. There are few other researchers who have investigated wavelets for HRV analysis and quantification[24-31]. Ramchurn and Murray[32] used multifractal analysis of the day and night characteristics of HRV. Newandee and Reisman[31] analyze the HRV signal using three different wavelets: Morelet, Daubechies-4, and Haar and Martinez *et al.*[33] used an, undecimated wavelet transform[34-36], for the analysis of HRV signals and Yamamoto *et al.*[37] used the fractal properties of HR to analyze long-term HRV. Saini *et al.*[38] designed statistically matched wavelets[39-47] for deciphering the true changes in HRV signals and used these wavelets for quantifying the HRV in survived heart attack patients. Togo and others[48] analyze the unique very low-frequency HRV during deep sleep in humans using wavelets analysis for classifying HR during lying and sitting and Singh *et al.*[50] used a time-scale analysis to study cardiovascular variability during various autonomic function tests in humans. Further, Goren *et al.*[51] used continuous wavelet transform in time-frequency analysis of HRV. Cnockaert *et al.*[52] used continuous wavelet transform for the analysis of respiratory sinus arrhythmia.

Recent advancements in the theory of nonlinear dynamics have increased the interest for analyzing signals generated from nonlinear physiological systems[53-64]. Pincus *et al.*[65] developed approximate entropy (ApEn), a nonlinear complexity index, to quantify the randomness of physiological time series. With other means of characterizing physiological signals, ApEn has been most extensively studied in the evaluation of HR dynamics. Acharya *et al.*[66] found that ApEn have smaller value for middle and old aged subjects, indicating smaller variability in the beat to beat. Schuckers *et al.*[67] have used ApEn to classify sinus rhythm, ventricular techycardia and ventricular fibrillation. Makikallio *et al.*[68] concluded that ApEn analysis of R-R interval time series provide useful information on abnormalities in HR behavior that are not easily detected by linear parameters. Signorini *et al.*[69] concluded that ApEn can also be used to classify the normal and Myocardial infracted patients. In[70], Marati *et al.* studied the effect of postural related changes on ApEn. Signorini *et al.*[71] characterize the heart rate variability (HRV) of patients affected by congesive heart failure and concluded that these patients reflect a higher value ApEn than healthy subjects. Richman *et al.*[72] have developed and characterized sample entropy (SampEn), a new family of statistics, measuring complexity and regularity of clinical and experimental time-series data and compared it with ApEn. Chen *et al.*[73] compared ApEn and SampEn for neural respiratory signals. Lake *et al.*[74] optimized the SampEn parameters and found that SampEn falls early in the course of neonatal sepsis and sepsis like illnes. Costa *et al.*[75-77] suggested a technique, multiscale entropy (MSE), to measure complexity at multiple scales and applied MSE to cardiac interbeat interval time series of healthy and diseased subjects and observed that the dynamics of healthy subjects are more complex than diseased subjects. The multiscale approach gave more details about the time scales at which irregularities occur and it allows extracting the information about the signal strucure[77]. Gonzalez[78] proposed acceleration change index (ACI) to characterize HRV. ACI is the modification to echnique suggested by Ashkenazy *et al.*[79] that uses the differences of the RR-interval time series as the intermediate time series for the scaling analysis of time series. Liang *et al.*[80] studied the changes of fractal dimension of the cardiovascular system during head down tilt (HDT) and observed that fractal dimension increased during HDT. Fractal dimension of elderly subjects was smaller than that of young subjects[81]. The long-term variability of HRV (SDI) derived from Poincare plots was considered as the marker of parasympathetic activity as SDI was also found to be decreased with upright posture and further decreased during exercise in healthy subjects[82]. The short-term variability (SD2) decreased during atropine administration, and further decreased during exercise after complete parasympathetic bockade[83], which indicated that the SD2 was influenced by both parasympathetic as well as sympathetic activity. Largest Lyapunov exponent (LLE) quantifies sensitivity of the

system to initial conditions and gives a measure of predictability. LLE decreases for slowly varying signals from congestive heart failure and ischemic/dilated cardiomyopathy subjects and will be higher for the other cases in which the variation of RR intervals is more[66]. Kobayashi *et al.*[84] demonstrated that power law behavior describes fluctuations in the HR. Decreased or steeper slope of HR power behavior was observed in healthy elderly subjects and patients suffering from coronary artery disease[85]. Huikuri *et al.*[86] studied a random sample of 347 healthy subjects (aged 65 years or older) and found that the steeper power law was the best predictor of all cause mortality[86].

This paper will focus on advanced and innovative methods of HRV signal processing. The study envisaged time-frequency and non-linear measures to better described various physiological and clinical behaviors using HRV. Emphasis is given on the concept of a bridge between HRV signal processing and physiologic modeling to open up aspects of the complex and non-linear dynamics, thus providing new avenues for innovative interpretations and explorations.

2. TIME-FREQUENCY DOMAIN

The HRV metric which were discussed earlier are based on frequency domain methods. The main difficulty in frequency-domain processing of RR-intervals series is non-stationary behaviour of heart beats. The heart beats of even a normal healthy person tend to be time variant. This non-stationarity becomes more severe in abnormal cardiac rhythms. Thus the conventional PSD estimation techniques are not suitable for analyzing heart beat signal whose frequency components change rapidly with time. The problem concerning the estimation of such time varying signal has become now a days a source of an active research.

2.1 Smooth Pseudo Wigner-Ville Distribution

The accuracy in the measurements of the spectral parameters of HR signal depends on a number of processing variables, such as the resolution and bias of the algorithm used, the length of the observation window, and the interaction between different harmonic components. In this regard the Wigner-Ville distribution (WVD) is a powerful time-frequency distribution that gives excellent time-and frequency-resolution and other properties, so that it is extensively used in many areas of signal processing, such as speech, seismic, and biomedical signals[87]. This method provides localized time and frequency descriptions of HRV to characterize the changing autonomic regulation.

The WVD of a real signal [88], *x(n)*, is defined using equation (1)

$$WVD_X(n,\omega) = \int_{-\infty}^{\infty} z\left(n+\frac{\tau}{2}\right) Z^*\left(n-\frac{\tau}{2}\right) \exp(-jwr)\, dr \quad \ldots (1)$$

where, z(n) is the analytic signal associated with x(n) The equation (1) is very rarely used in its pure form, and the Smooth pseudo Wigner-Ville distribution SPWVD is employed instead[9]. The discrete form of the SPWVD is given using equation (2)[88], [89].

$$SPWVD(n,m) = 2 \sum_{n=M+1}^{M+N} |h(k)|^2 \sum_{m=1}^{M} f_n(m) \exp(-j2\omega m) \quad \ldots (2)$$

where, h(k) is the frequency smoothing Hann window; m is the frequency index; N is the total number of data points; M is the total number of frequency points; $f_n(m)$ is a discrete kernel function given by equation (3)[176]

$$f_n(m) = z(n+m)\, z^*(n-m)\, w(m)\, w^*(m) \quad \ldots (3)$$

where, w(m) is the time smoothing Gaussian window

2.2 Continuous Wavelet Transform

The continuous wavelet transform[90] is defined as follows using equation (4) :

$$CWT_x^{\psi}(b,a) = \psi_s^{\psi}(b,a) = \frac{1}{\sqrt{|a|}} f_x(t)\, \psi^*\left(\frac{t-b}{a}\right) dt \quad \ldots (4)$$

where $\psi(t)$ is the transforming function called as mother wavelet, *b* and *a* are the translation and scale parameters. The term mother wavelet gets its name due to two important properties of wavelet analysis as explained below:

The term wavelet means a "small wave". The smallness refers to a condition that this function is of finite length. The wave refers to a condition that this function is oscillatory. The term mother implies that the functions with different regions of support that are used in the transformation process are derived from one main function or mother wavelet. In other words the mother wavelet is a prototype for generating the other window functions.

2.3 decimated (Discrete) Wavelet Transform in HRV

The decomposition of the signal with the decimated (discrete) wavelet transform (DWT) is based on a partition in the frequency plane using a guadrature mirror filter (QMF) bank[92]-[94]. This filter bank consists of pairs of digital high-pass and low-pass filters organized in a tree structure. The signal is decomposed at each scale into its detail (high-pass component) and

approximation (low-pass component) signals and down sampled. The detail signal is then stored and the decomposition continues by filtering the approximate signal as the input signal for the next scale. At each scale, j, the frequency axis is recursively divided into halves at the ideal cutoff frequencies given by equation (6)[95].

$$f_j = 2^{-j} \frac{1}{2T} \quad \ldots (6)$$

The DWT based decomposition algorithm is shown in Fig. 2 where the cardiovascular signals were decomposed into eight wavelet scales (J=7) with sampling interval T=1/2.4 sec [171]. This resulted in the following set of bank limits for the filter bank: 0.01875, 0.0375, 0.075, 0.15, 0.30, 0.60, and 1.2 Hz. The decomposed LF and HF signals were obtained by merging the detail signals at scales 5 and 6 (0.0375-0.15 Hz) and at scales 3 and 4 (0.15-0.60 Hz), respectively. The VLF component corresponded to the detail signal at scale 7. However, the critical down sampling which has been performed in this algorithm makes this transform shift variant. This justifies the use of an undecimated wavelet transform (UWT) for HRV studies. In UWT firstly the filter is stretched to take into account the rescaling and then the convolution is performed without any sub-sampling[34]. This procedure makes the transform bulky and is said to be redundant or over complete, in the sense that superfluous coefficients are retained in the transform and successive coefficient metrics are of the same size as the input data, that makes the transform shift-invariant[33], [35]. In addition to shift-invariance the UWT gives increased amount of information about the transformed signal as compared to the DWT.

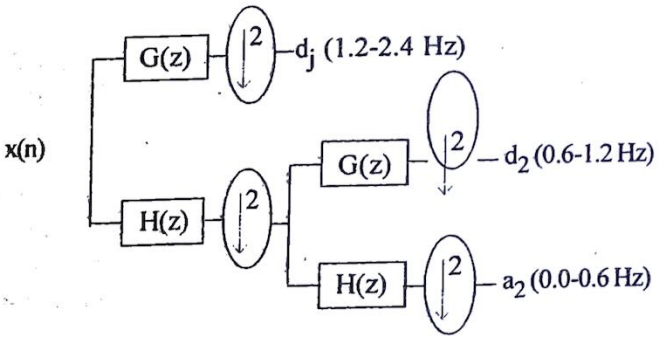

Fig. 2. Two filter bank implementation of Mallat algorithm for frequency bands of HRV signals. G(Z) and H(Z) are high and low pass filters. d's and a's are detail and approximation coefficients.

The DWT and UWT algorithms are both special cases of the same filter bank structure. Therefore, in principle it is possible to combine both algorithms in the same decomposition structure to gain the benefits of both these approaches[36]. That is, the computational efficiency and sparse representation are the inherent advantages of DWT, while shift-invariance and aliased free spectrum are the advantages of a fully sampled UWT. Thus based upon these merits, the DWT and UWT algorithms are blended together to propose a new algorithm called over-complete decimated (discrete) wavelet transform (OCDWT) for the accurate assessment of HRV signals. The OCDWT algorithm is critically sub-sampled to a given level of decomposition, below which it is then fully sampled. Saini *et al.* proposed this OCDWT for deciphering the true changes in HRV of healthy subjects in lying and standing postures in comparison to DWT algorithm.

3. NON-LINEAR TECHNIQUES

Much of what is known about physiological systems has been learned using linear system theory. However, many biomedical signals are apparently random or aperiodic in time[96]. The most direct link between chaos theory and the real world is the analysis of time series from real systems in terms of nonlinear dynamics.

3.1 Complexity Analysis

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. Recent studies demonstrated that HRV present a complex behavior that may contain hidden information, which may not be extractable with conventional methods of analysis[96]. Such information promises to be of clinical values as well as to relate to basic mechanism of healthy and pathologic functions[97].

3.1.1 Approximate entropy

Approximate entropy (ApEn) is a statistic that can be used as a measure to quantify the complexity of a signal. It was first proposed by Pincus in 1991[65]. It has been widely adopted by many researchers especially in the field of HRV[66],[98]. Nonlinear dynamics analysis may be a powerful tool to reveal the characteristics and mechanism of biosignals. But a very long data sequence is needed to estimate accurately many of nonlinear parameters[99]. The popularity of approximate entropy stems from its capability to provide quantitative information about the complexity of the experimental data that are short in data length[98]. ApEn measures that (logarithmic) likelihood that runs of

patterns that are close for m observations remain close on next incremental comparison. Greater likelihood of remaining close, *i.e.*, high regularity, produces smaller ApEn values. ApEn is closely related to the Kolmogrov entropy, which is a measure of rate of generation of new information[72]. To compute ApEn, the time series is evaluated for patterns to recur. This is performed by evaluating the data sequences of length m and determining that other sequences fall within tolerance r. Thus two parameters m and r must be fixed to calculate ApEn, referring to both theoretical and clinical applications. There are two ways to look at ApEn. From one point of view, it is a statistical characteristic (average of the logarithm of a conditional probability), which makes it applicable to both deterministic and stochastic processes. From the other point of view, it reflects the rate of new pattern generation and is thus related to the concept of entropy.

3.1.2 Sample entropy

Richman *et al.*[72] have developed and characterized sample entropy (SampEn), a new family of statistics measuring complexity and regularity of clinical and experimental time-series data and compared it with ApEn, a similar family. The sample entropy (SampEn) is a modification of ApEn. The differences with respect to ApEn are: (i) self-matches are not counted (ii) only the first $N = m$ vectors of length m are considered[71,72]. SampEn has the advantage of being less dependent on the time series length and shows consistency over broad ranges of possible m, r and 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[73]. 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[74].

3.1.3 Symbolic entropy

Symbolic time series analysis involves the transformation of the original time series into a series of discrete symbols that are processed to extract useful information about the state of system. Symbolic time series analysis closely related to symbolic dynamics, introduced by Hadmard *et al.*[96]. There have been various approaches for symbolization of time series. The type and number of symbols depends upon length of time series. Long time series allow higher number of symbols than short time series. The most common approach is to assign value '1' and '0' according to its occurrence. Kurth et al.[5] used two different kinds of procedures to transform the HRV into symbol sequences. The first transformation refers to four symbols using mean RR interval. The second transformation considered the first difference of RR intervals, which reflects fluctuation properties inherent in HRV. Kurth *et al.*[5] analyzed the RR intervals and first difference of the intervals, using both the Shanon and Renyi entropies as measures of signal complexity. The generalized Renyi entropy was found to be more useful than Shanon entropy. Park *et al.*[98] observed that corrected symbolic entropies consistently separate the normal and physiological symbolic sequences.

3.1.4 Multiscale entropy

Cardiovascular control is carried out by several regulatory mechanisms interacting across multiple temporal scales. Short-term neural regulation, carried out by the ANS via sympathetic and parasympathetic branches, is relatively fast (with periods ranging from 3 to 15 seconds), while vasomotor control, chemoreflex regulation and thermoregulation are slower and hormonal control ever more sluggish. As a result of the concomitant action of all these regulatory mechanisms, heart period changes on a beat-to-beat basis and its variations, usually referred to as HRV, occur over a large set of temporal scales. Due to this multiscale behavior, HRV cannot be completely characterized on a single time scale[100] and as a result, cardiac interbeat (RR) time series under healthy conditions have a complex temporal structure with multiscale correlations[75-77]. Although entropy-based algorithms for measuring the complexity of physiologic time series have been widely used and proved to be useful in discriminating between healthy and disease states, but due to multiple scales mechanism of HR some results may lead to misleading conclusions. Multiscale entropy (MSE) is a measure of complexity at multiple scales. To calculate MSE[75-76], the original time series is converted into coarse-grained time series corresponding to scale factor τ. The sample entropy of coarse grained time series is calculated and plotted as a function of scale factor[75,76]. MSE requires adequate length of time series to provide reliable entropy measure on each scale. Costa *et al.*[77] used time series with 2000 data points for analysis extending up to scale 20. Costa *et al.*[76] had tested the MSE method on simulated white and l/f noises. They have shown that for the scale one, the value of entropy is higher for the white noise time series in comparison to the l/f noise. This may apparently lead to the conclusion that the inherent complexity is more in the white noise in comparison to the l/f noise. This may apparently lead to the conclusion that the inherent complexity is more in the white noise

in comparison to the 1/f noise. However, the application of the MSE method shows that the value of the entropy for the 1/f noise remains almost invariant for all the scales while the value of entropy for the white noise time series monotonically decreases and for scales greater than 5, it becomes smaller than the corresponding values for the 1/f noise.

3.2 Sign Series Analysis

Sign series analysis involves the transformation of the original RR interval time series into a series of differences of RR intervals[96].

3.2.1 Acceleration change index

Acceleration change index (ACI) as presented by Garcia Gonzalez to characterize HRV[78], is a modification of technique suggested by Ashkenazy *et al.*[79] that uses the differences of the RR interval time series as the intermediate time series for the scaling analysis of time series. Ashkenazy *et. al.*[79] decomposed the original time series into two groups (a) magnitude series $m_i = |\Delta RRi|$ (b) sign series $Si = sign(\Delta RRi)$. The detrended fluctuation analysis (DFA) was applied on sign series to obtain the scaling exponent. Sign series is robust in handling complex signals that include spikes. ACI increases only when a local minimum is followed by local maximum or vice-versa. It detects the presence of very high frequency contents in the HRV time series. This index is robust in the presence of artifacts because of its insensitivity to fast changes due to sign operation.

3.3 Graphical Representation

3.3.1 Poincaré plot

Poincaré plot is a visual tool in which each RR interval is plotted as a function of previous RR interval. Poincaré plot provides summary information as well as detailed beat-to-beat information on the behavior of heart. Beat-to-beat variation can be easily displayed for visual assessment by graphing of each RR interval against the subsequent RR interval. The problem regarding Poincaré plot use has been lack of obvious quantitative measures that characterize the salient features of Poincaré plots. To quantitatively characterize the plot, a number of techniques like converting the two-dimensional plot into various one-dimensional views; the fitting of an ellipse to the plot shape; and measuring the correlation coefficient of the plot have been suggested[101,102]. The width of the Poincaré plot corresponds to the level of short-term HRV, while the length of the plot corresponds to the level of long-term variability[83],[101],[102].

3.3.2 Recurrence plot

The dynamic properties of the time series are relevant and valid only for stationary data. Recurrence plots are used to reveal nonstationarity of the series. Eckmann *et al.*[103] has proposed this graphical tool for the diagnosis of drift and hidden periodicities in the time evolution, which are unnoticeable otherwise. The recurrence plot of normal HR has diagonal line and less squares indicating more variation indicating high variation in the HR. Abnormalities like CHB and in Ischemic/ dilated cardiomyopathy cases, show more squares in the plot indicating the inherent periodicity and the lower HR variation[104].

3.4 Chaotic Analysis

The word 'chaos' means undesired randomness or disorder. In mathematics, chaos theory (also known as dynamical instability) began as the study of the evolution in time of systems that are extremely sensitive to initial conditions[105-107]. Chaos theory has evolved into the study of the behavior of physical systems that at first seem entirely random but in fact are not entirely so.

3.4.1 Fractal dimension

A fractal is a set of points that when looked at smaller scales, resembles the whole set. The concept of fractal dimension (FD) that refers to a noninteger or fractional dimension originates from fractal geometry. The FD emerges to provide a measure of how much space an object occupies between Euclidean dimensions. The FD of a waveform represents a powerful tool for transient detection. This feature has been used in the analysis of ECG and EEG to identify and distinguish specific states of physiologic function. Fractal dimension can be quantified n meaningful way by a number of techniques[107-109].

3.4.2 Detrended fluctuation analysis

The detrended fluctuation analysis (DFA) is used to quantify the fractal scaling properties of short interval RR interval signals. DFA is scaling analysis technique proposed by Peng *et al.*[110] in 1995 to detect long-range correlations in the time series having nonstationaries. DFA was developed specifically to distinguish between intrinsic fluctuations generated by the complex systems and those caused by the external or environmental stimuli[110]. The principal advantage of DFA is that it is able to detect long-range correlation in time series having non-stationarieities. However, data requirements are greater than as compared with other techniques and at least 8000 data points have been

suggested to be included[110]. DFA was found to carry additional information that was not provided by the traditional time and frequency HRV measures. In a retrospective comparison of 24 hour HRV analysis using several HRV measures in MI patients with or without inducible ventricular tachyarrhythmia[111], a decrease in scaling exponent α_1 was strong predictor fo risk tachyarrhythmia.

3.4.3 Largest Lyapunov exponent

Lyapunov exponent (λ) quantify the average exponential separation between nearby phase trajectories. It is a quantitative measure of the sensitive dependence on the initial conditions. It defines the average rate of divergence of two neighboring trajectories[66],[107]. To discriminate between chaotic dynamics and periodic signals Lyapunov exponent are often used. It is a measure of the rate at which the trajectories separate one from other. The trajectories of chaotic signals in phase space follow typical patterns. Closely spaced trajectories converge and diverge exponentially, relative to each other. For dynamical systems, sensitivity to initial conditions is quantified by the Lyapunov exponent. They characterize the average rate of divergence of these neighboring trajectories. A negative exponent implies that the orbits approach a common fixed point. A zero exponent means the orbits maintain their relative positions; they are on a stable attractor. Finally, a positive exponent implies the orbits are on a chaotic attractor[66],[99]. The algorithm proposed by Wolf *et al.*[99] is used to determine the Largest Lyapunov Exponent (LLE). LLE quantify sensitivity of the system to initial conditions and gives a measure of predictability. Lyapunov exponent provides significant information about the ANS and observed that there is a well organized behavior of HRC[112]. LLE decreases with aging indicating that the HRV becomes less chaotic as healthy subject grows old[66].

3.4.4 Power law analysis

Power law analysis can measure the long range correlation, enabling the clinicians and scientists to classify physiological and pathological signals[84]. This analysis was performed by calculating the power spectrum and then plotting the log of spectral power against the log of frequency. A straight line with slope of approximately '-1' is obtained. Frequency domain analysis and power law analysis assess different characteristics of the underlying signal. Frequency domain analysis measures the contributions of specific frequencies to the underlying signal, whereas, the power analysis determines the correlations across the frequency spectrum. Power law analysis has been applied in numerous clinical studies and a change in the intercept and slope has been present and is of prognostic information in disease.

4. FUTURE CHALLENGES

A major challenge in this area of biomedical signal processing is to demonstrate the utility and clinical implications of specific measures of HRV in diagnosis and monitoring so that such measures become part of routine patient care. The current clinical applications of HRV are limited in use and the task of finding simple but effective parameters is yet to be accomplished. Furthermore, no consensus or clear definitions for the analysis methods have been found and guidelines of the Task Froce of ESC & NASPE[1] is just a step in this direction. Perhaps it is even time to consider another task force initiative on HRV with appropriate updating, critical review and suggestions for new directions, taking into account the important results obtained in the last 10 years.

An important innovative aspect in this direction is considering the integration between HRV signal processing and physiological modeling of the cardiovascular system. In this way, it is possible to directly attribute patho-physiological meaning to the parameters obtained from the processing, or vice versa, the physiological modeling fitting could certainly be improved by taking into account the results from the signal processing procedure. Generally, scientists who do signal processing do not do modeling: biomedical engineering must integrate these two aspects in order to properly train young scientists in the area and to provide a cultural vision for the implementation of important tools for newer investigations. Further, a modern and very promosing approach of HRV signal processing, which is capable also to combine the outputs from physiological modeling, is the so-called MMM-paradigm (i.e., multivariate, multiorgan, and multiscale). Such an approach makes the system genesis explicit, where complexity is potentially allocated and how it is possible to detect information from it. No doubt that processing signals from multileads of the same system (multivariate), from the interaction of different physiological systems (multiorgan) and integrating all this information across multiple scales (from genes, to proteins, molecules, cells, up to the whole organ) could really provide a more complete look at the overall phenomenon of physiological system complexity, in respect to the one which is obtainable from its single constituent parts.

5. CONCLUSIONS

This study anticipates an increase in interest to understanding cardiovascular functions by using HRV as a noninvasive tool and its coupling with advanced signal processing methods. The variety of HRV estimation methods and contradictory reports in this field indicate that there is a need for a more rigorous investigations of these methods as aids to clinical evaluation. Furthermore, much effort remains to be done for elucidating the mechanism underlying complex HR dynamics and cardiovascular control. A diverse application of signal processing and modeling efforts in this context has yielded substantial enhancement in understanding. A stronger integration between physiological modeling and HRV signal processing should help to construct fundamental links between more speculative research and real world clinical impact.

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