Comparative Analysis of Heart Rate Variability Signals

A dissertation submitted in partial fulfillment of the requirements for the award of degree of

Master of Engineering

In

Electronic Instrumentation and Control

Submitted by:

Kamlesh Pathak

Roll No: 801651004

Under the Guidance of:

Dr. Mandeep Singh

Associate Professor

EIED

Department of Electrical and Instrumentation Engineering

Thapar Institute of Engineering & Technology

(Deemed to be University)

Post Box No. 32, Patiala – 147004, Punjab (India)

June 2018

DECLARATION

I hereby declare that the work which is presented in dissertation entitled **"Comparative Analysis of Heart Rate Variability Signals"** in partial fulfillment of the requirements for the award of the degree of **Master of Engineering in Electronics Instrumentation and Control**, submitted to Electrical & Instrumentation Engineering Department of Thapar Institute of Engineering & Technology, Patiala is an is an authentic record of my own work carried under the supervision of **Dr. Mandeep Singh, Associate Professor**. It refers other researcher's works which are duly listed in the reference section. The matter contained in this dissertation has not been submitted neither in part nor in full to any other degree to any other university or institute except as reported in text and references.

Kamlesh Pathak

Place: Patiala

Date: June 28, 2018

Kamlesh Pathak

RollNo.801651004

It is certified that the above statement made by the student is correct to the best of my knowledge and belief.

Date: 02/07/18

Dr. Mandeep Singh

Associate Professor

EIED

ACKNOWLEDGEMENT

I am very thankful to **Dr. Prakash Gopalan**, Director of Thapar Institute of Engineering & Technology, Patiala for providing the facilities for the completion of **Master of Engineering**. I express my deep sense of gratitude towards **Dr. R.S. Kaler**, Head of the Department of Electrical & Instrumentation Engineering, Thapar Institute of Engineering & Technology, Patiala who has been a constant source of inspiration for me throughout this work.

I would like to express my gratitude and sincere thanks to my esteemed and worthy supervisor **Dr. Mandeep Singh**, Associate Professor (EIED) and **Mr. Puneet Arya** (PHD Student, EIED), Thapar Institute of Engineering &Technology, Patiala for his valuable guidance in carrying out this work under his effective supervision, encouragement, enlightenment and cooperation. Most of the novel ideas and solutions found in this dissertation are the result of our numerous stimulating discussions. His feedback and editorial comments were also invaluable for writing this report.

I am also very thankful to **Dr. Nirbhowjap Singh**, Assistant Professor and PG coordinator and entire Faculty and staff members of Department of Electrical and Instrumentation Engineering for their direct-indirect help and cooperation.

Finally, I would like to express my sincere gratitude and thanks to my Parent and Friends for their strong support in all situations

Kamlesh Pathak

KAMLESH PATHAK

ABSTRACT

Heart Rate Variability Analysis is the method of evaluating the state of mechanisms for regulating the physiological functions in the human beings and animals. It is a measure of neuro-cardiac function reflecting the autonomic nervous system and heart-brain interactions. The study and investigation of HRV mainly have centre of interest on the process of analysis of fluctuations in inter-beat intervals in the heart rate and the ability of diagnosis provided by the fluctuations. The information obtained from the records of HRV has eminent importance for the clinicians and researchers for the identification of the nature of any illness or symptoms. The main focus of this dissertation work is the implementation of the visibility graph method and calculation of network measures which can be obtained from the network graph constructed from RR interval segments over long term Electrocardiogram (ECG) recordings. Time domain, frequency domain and nonlinear methodologies for HRV analysis has been studied and reviewed. We evaluated mainly three network measures such as characteristic path length (CPL), average clustering coefficient (ACC), and standard deviation of the shortest path length (CPL-STD) of the network graph obtained from the RR interval segment on scale of different data points for Congestive Heart Failure (CHF) and Normal Sinus Rhythm (NSR) signals. Time domain, frequency domain and Poincare plot measures for HRV was analyzed using Kubios HRV analysis software. All the network measures estimated from RR interval segment showed statistically significant result between Normal Sinus Rhythm and Congestive Heart Failure subjects on different scale of data points except the Characteristic Path Length (CPL) on scale of 1500 data points and CPL, and standard deviation of shortest path length (CPL-STD) on 2000 data points. Characteristic Path Length (CPL) was found to be more in Normal Sinus Rhythm subjects and decreased in Congestive Heart Failure subjects while Average Clustering Coefficient has increased value in case of Congestive Heart Failure patients. Statistically significant time domain measures were found to be lower in CHF as compared to NSR. Frequency domain measure LF/HF ratio was lower in CHF. For nonlinear analysis using Poincare plot showed lower values of SD1 and SD2 in CHF and higher value of SD1 and SD2 in NSR while SD2/SD1 ratio was found to be higher in NSR. Time domain analysis results have shown an increase of HR and reduction of HRV in CHF as compared to NSR and hence, a higher heart rate in combination of lower Heart Rate Variability is a well known indicator of (acute) stress.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ANS-Autonomic Nervous System

ACC-Average Clustering Coefficient

BP-Blood Pressure

CPL-Characteristic Path Length

CPL STD-Standard Deviation of Shortest Path Length in Graph

CNS-Central Nervous System

CHF- Congestive Heart Failure

CWT-Continuous Wavelet Transform

ECG- Electrocardiogram

EDA-Electrodermal Activity

HF -High Frequency

HR -Heart Rate

HRV- Heart Rate Variability

LF-Low Frequency

NSR-Normal Sinus Rhythm

NYHA- New York Heart Association Classification

PNS-Parasympathetic Nervous System

PSD-Power Spectrum Density

RSA- Respiratory Sinus Arrhythmia

SNS- Sympathetic Nervous System

SD-Standard Deviation

ULF-Ultra Low Frequency

VLF-Very Low Frequency

CHAPTER 1

INTRODUCTION

1.1 HEART RATE VARIABILITY: A BRIEF HISTORY

The study and investigation of HRV mainly have centre of interest on the process of analysis of fluctuations in inter beat intervals in the HR (heart rate) and the ability of diagnosis provided by the fluctuations. The information obtained from the records of HRV has eminent importance for the clinicians and researchers for the identification of the nature of any illness or symptoms, treatment and investigation of several a disease or period of sickness which have relation with cardiovascular system and autonomic systems such as myocardial infarction, sudden cardiac death, risk stratification, psychological disorders, diabetic neuropathy and high blood pressure. Emotional arousals in mental and social aspects are also related to HRV[1].

Even for a body being at rest, it has been well acknowledged since ancient times that the considerable variability exists in HR (heart rate). Steven Hales in 1733 reported that respiration was synchronous with beat-to-beat HRV. It took much long time for this fact to make the clinical relevance even if the cause and effect relationship was established[2]. The advent of digital computer allowed the collection and analysis of long term heart rate records.

The development of HRV Analysis has come into being about the 1960s. The success of space medicinal research was one of the most vibrant reasons for the development of HRV analysis. In 1965 heart rate variability became clinically relevant when it was noted by Hon and Lee that before any large or important enough to be noticed change taken place in heart rate itself , the fetal distress precedes by change in characters in the inter beat intervals. The first conference or meeting to discuss HRV analysis based on analyzing the rhythm of heart mathematically took place in 1966 in Moscow. The beginning 70s-80s noticed the maximum activity of HRV based research[3].

In the late1980s, the clinical importance of heart rate variability became readily perceived or understood following the confirmation that HRV can be considered as a strong and independent mortality predictor as a result of an acute myocardial infarction[1].

Over the last two decades there has been widespread growth in the investigation and research of HRV analysis and analysis methods and notably large amount of tools and various methodologies to explore HRV has been developed and published by different companies and researchers.

However, there is requirement for a more exhaustive and accurate investigation and research of these methodologies for clinical significance due to the variety of estimation methods and contradictory reports in these fields.

1.1.1 PHISIOLOGICAL ORIGIN OF HEART RATE VARIABILITY

The periodic and spontaneous activation of the pacemaker cells occurring inside the SA (sinoatrial) node in the absence of any outside influences and effects determines the heart rate. Once initiated the action potential propagates along the cell membrane until the depolarization of entire cells. Next at the AV (atrioventrical) node there is a propagation delay which allows the complete atrial depolarization before the propagation of action potentials through the bundle of His, Purkinjie fibers and throughout ventricles ultimately. Next septal depolarization occurs. The wall between the ventricles is known as septum. It tends to propagate left to right when the action potential enters to the septal myocardium. In ventricular depolarization, the electrical activities are also in the right ventricle but activity dominates in the left ventricle since it is much more massive. After the depolarization of various portions of myocardium, they contract by the excitation-contraction coupling process.

Finally the repolarization of individual cells begins and through the heart another wave of charges passes. After the ventricle repolarization the heart then returns to their resting states and hence a new cycle is started by another electrical stimulus. The cardiac electrical activity has been shown in the Fig.1.1 as below.

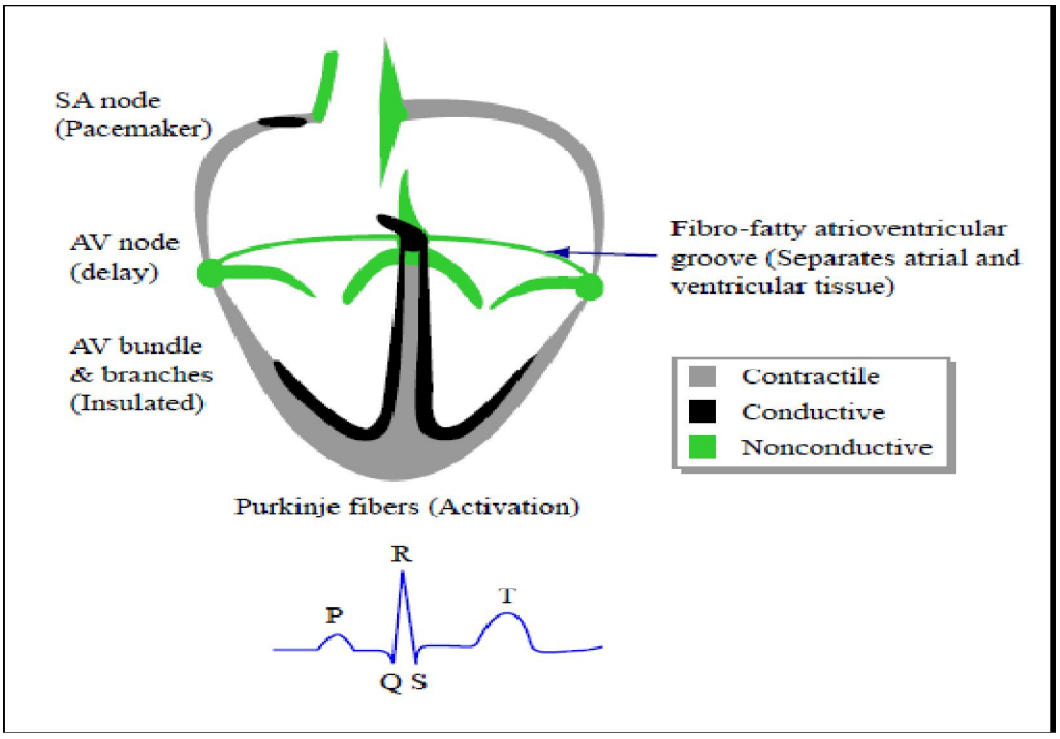


Fig.1.1 Cardiac electrical activity (Figure by MIT open course ware [4])

1.1.2 ECG COMPONENTS

The electrocardiogram (ECG) provides the view of activities of the heart through the generated electrical signals during the cardiac cycle. The location of the different waves on the

electrocardiogram are named alphabetically as P, Q, R, S, T and occasionally U ,this wave is hard to identify as having low amplitude or may be absent or may be masked by following beats. The standard ECG waveform showing R-R interval and most of the important ECG wave features in a cardiac cycle are labeled along with physiological cause of the feature is shown in Fig.1.2.The normal ECG parameters are given in Table 1.1.

- P wave-It represents the electrical signal caused by SA node in the right atrium and impulse propagation to AV (atrioventricular) node and to the atrial myocardium. It is caused by the atrial depolarization.
- Q wave-It occurs due to the septal region activation of ventricular myocardium.
- R wave-It occurs because of ventricular depolarization.
- S wave-It is due to the posterior basal portion activation of the ventricles.
- T wave-It is caused by the ventricle repolarization.
- PR interval-It represents flat part of the interval during which Atrial contraction occurs.
- ST interval-It represents contraction of ventricles.
- QRS-It represents ventricles depolarization.
- QT-It represents time taken for depolarization and repolarization of ventricles.

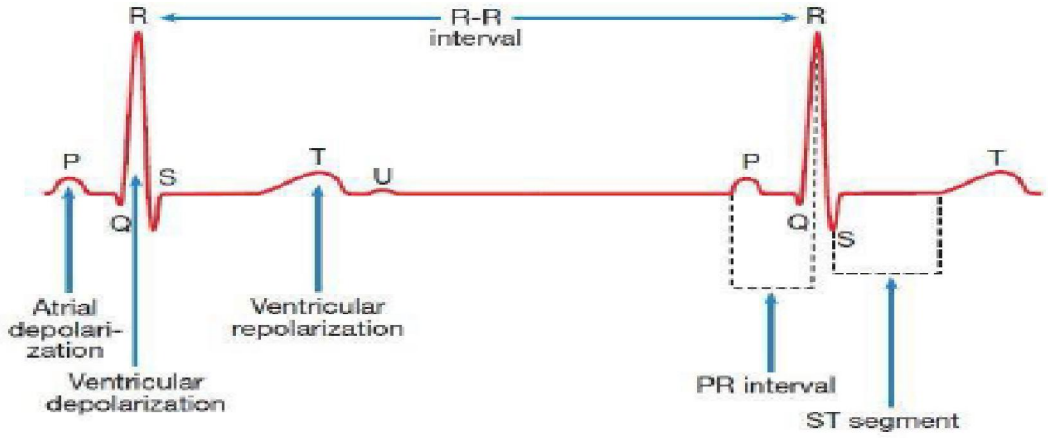


Fig.1.2 The standard ECG waveform [6]

Table 1.1 The normal ECG Parameters

Wave phase	Duration (in sec.)	Amplitude (in mV)
P wave	0.06 to 0.11	< 0.25
PR interval	0.12 to 0.20	
PR segment	0.08	
QRS complex	< 0.12	0.8 to 1.2
ST segment	0.12	

QT interval	0.36 to 0.44	
T wave	0.16	< 0.5

The calculation of HR_{60} (the heart rate averaged over time) is done by determining the total number of heart-beats in sixty seconds period of time while the heart rate on particular instant is calculated as dividing 60 by the time between the successive R-peaks i.e. RR interval.

1.2 THE AUTONOMIC NERVOUS SYSTEM (ANS) AND THE SYMPATHOVAGAL BALANCE

Human nervous system comprises mainly two parts viz. Central Nervous System (CNS) and the Peripheral Nervous System (PNS). CNS mainly includes brain and spinal cords while PNS includes mainly nerves and groups of neurons outside the brain and the spinal cord. The brain regulates two motor systems named as voluntary motor system which comprises mainly muscular control of the limbs, head and the body and another one is ANS or the involuntary motor system[4].

The internal organs mainly heart, lungs, blood vessels, digestive tracts and bladder is controlled by the ANS. The ANS is subdivided into two branches which exert the opposing effects on most of the organs and named as the sympathetic and parasympathetic nervous system. Cardiovascular control system in a simplified model presenting the regulation of heart rate through the feedback loops of parasympathetic and sympathetic actions is shown in Fig.1.3.

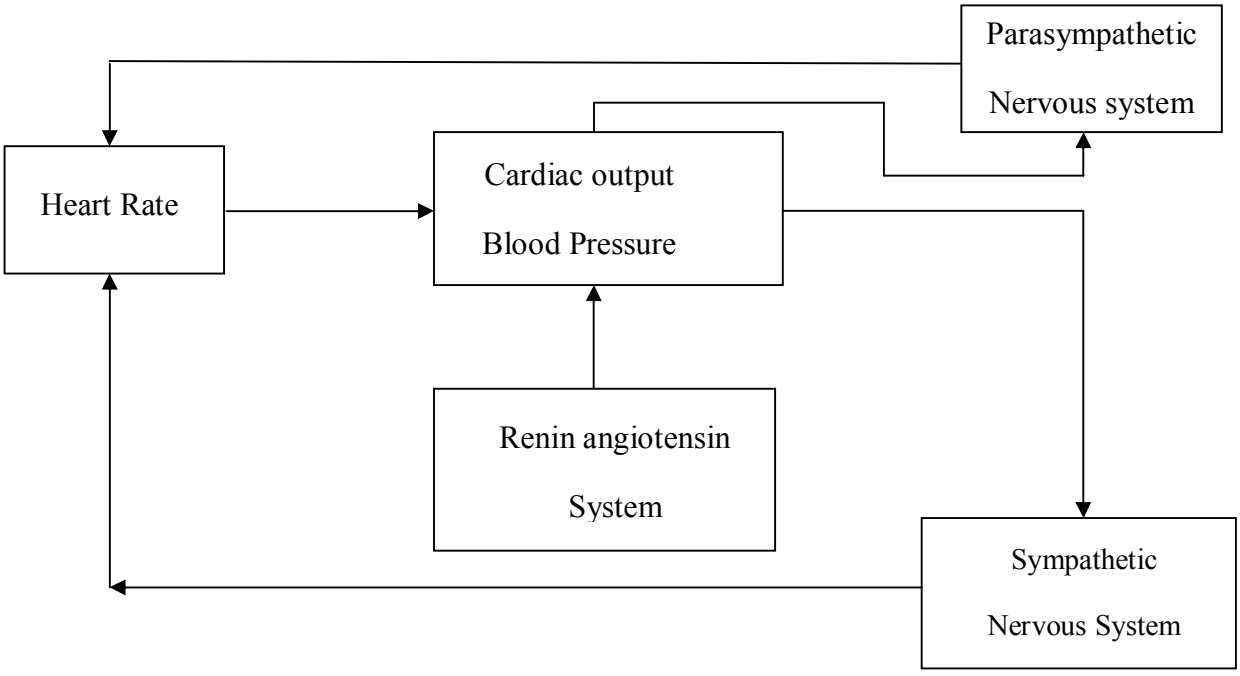


Fig.1.3 Model of Cardiovascular Autonomic Control in simplified form

1.2.1 THE PARASYMPATHETIC NERVOUS SYSTEM

The Parasympathetic Nervous System (PNS) could be considered as the mechanism of 'rest and digest' which makes drop in HR and BP and increase in digestive system activities and also cause pupils to constrict. In PNS, brain's motor neurons innervate the ganglia which innervate organs in which they are located. The dominant path for parasympathetic stimulation is those nerves that spread out over an extensive part of the lining of inner wall and hence, parasympathetic action is called as vagal nerve activity. Acetylcholine at the terminal is released by the neurons of the parasympathetic ganglia.

1.2.2 THE SYMPATHETIC NERVOUS SYSTEM

In the situation of physical or mental stress, the Sympathetic Nervous System is rapidly activated and hence, called as the 'fight or flight' response occasionally. Increase in heart rate, dilation of pupil, and digestive system activity decrement and also increase the blood flow of muscles and cardiac output. The spinal cord neurons through nerves supply an adjacent series of the ganglia in the sympathetic system and then internal organs are innervated by the neurons from these ganglia. Norepinephrine (or noradrenalin) at the terminal is released from the sympathetic ganglia[4].

The overall effect on the cardiovascular system and the autonomic tone auto regulation due to the complicated interaction between the branches of ANS (sympathetic and parasympathetic) is referred to as Symphatovagal balance.

The summary of the differences between parasympathetic and sympathetic nervous system have been shown in Table 1.2.

Table1.2 Parasympathetic versus Sympathetic

Parasympathetic	Sympathetic
It is referred to as 'Rest and Digest'	It is referred as 'Fight or Flight'
It causes decrease in heart rate	It causes increase in heart rate
It decreases the blood pressure	It increases the blood pressure
Miosis (Pupil constriction) occurs	Mydriasis (pupil dilation) occurs
Bronchoconstriction	Bronchodilation
Increase secretions	Decrease secretions
Vasoconstriction occurs	Vasodilatation occurs
No innovation of sweat glands	It increases the sweating

1.3 BASIC WORKING DEFINITIONS

HRV Analysis is defined as the method of evaluating the state of mechanisms for regulating the physiological functions in the human beings and animals. It is a measure of neuro-cardiac function reflecting the autonomic nervous system and heart-brain interactions.

The method is based on detection and measuring the time intervals in the period separating the successive R peaks of the ECG (RR intervals) and making the dynamic series of the cardio-intervals. The dynamic series of cardio-intervals are known as cardiointervalogramm (CIG).

Analysis of HRV signals mainly consists of the three stages:

1. Measuring the RR intervals and presenting the dynamic series of cardio-intervals.
2. Analyzing the dynamic series of cardio-intervals.
3. Evaluating the results of HRV analysis.

The analysis methods of dynamic series of cardio-intervals can be classified into visual (developed by D.Zhemajtite (1965, 1972) and mathematical. The mathematical analysis methods could be grouped into the following three classes:

1. Statistical methods or analysis in time domain.
2. Frequency domain analysis.
3. Research of internal organization of a dynamic sequence of cardio intervals. (Autocorrelated analysis, correlation dimension, methods of non-linear dynamics).

As a result of HRV analysis various parameters of HRV are obtained and depending upon the scientific-theoretical concepts estimated in different ways by various explorers and researchers[3]. HRV analysis approach is mainly based on the suggestion as to a possible course of action of mechanisms of neurohormonal regulation.

The primary objective for the analysis of HRV is estimating the function of the nervous systems. Analysis of the ECG assesses the problems regarding the formation of beat of heart but analysis of HRV make assumption that every individual heart beat with a normal ECG signature is a normal heart beat i.e. the records of RR interval should contain those heart beats having generation in accordance of sinus origin. This is considered as existing in the sinus rhythm.

The sinus nodes rate of firing is directly controlled by the ANS. How the heart actually goes to make up a beat is not assessed by the HRV but HRV estimate the nature of heat rhythm. Non-invasive and unobtrusive facts or knowledge regarding the regulation of heart rate in a variety of circumstances by the ANS is provided by the variability in the heart rate (HRV).

Heart Rate Variability decreases with higher level of psychological or work related stress. Hence, there is need of training in subjects so that Heart Rate Variability (HRV) should be incremented [28].

1.4 OBJECTIVES OF THE DISSERTATION

- To study and explore HRV analysis techniques for better classification of HRV signals.
- To implement the visibility graph approach for HRV analysis.
- Comparative study of HRV features in Normal Sinus Rhythm (NSR) and Congestive Heart Failure (CHF) signals.
- Selection of features with better statistical significance in Congestive Heart Failure and Normal Sinus Rhythm signals.

1.5 DISSERTATION ORGANIZATION

CHAPTER 1 provides introduction about HRV analysis including a brief history of HRV analysis, physiological origin of HRV signals, ECG components, and basic idea about autonomic nervous system and its effects on heart rate variability and heart rate.

CHAPTER 2 contains literature review including important research works which is already explored and investigated in this field. It provides a brief idea about methodologies used and results of that particular research work.

CHAPTER 3 describes the methods of HRV analysis. Time domain, frequency domain and nonlinear methods for analyzing the HRV have been explained for estimation of HRV measures.

CHAPTER 4 contains a brief idea about Kubios software for HRV analysis.

CHAPTER 5 provides a brief idea about visibility graph algorithm and its network measures for estimation of HRV analysis and its implementation using Matlab.

CHAPTER 6 contains the Results and Discussion part of the dissertation work

CHAPTER 7 contains the conclusion of the work done and Future scope.

CHAPTER 2

LITERATURE REVIEW

The literature includes number of papers reporting HRV analysis methods, its clinical relevance with disease, physiology and psychological behavior. Some of them are as follows:

Task Force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology presented that the role of ANS shows fluctuation in normal or healthy subjects and in those diseased person having cardiovascular or non-cardiovascular disorders can be assessed with considerable potential by heart rate variability. Also, stated that HRV studies enhance the understanding and knowledge about physiological phenomenon, mechanisms of disease and action of medications. Therefore deep and broader prospective study and research for identifying individuals which are on the verge of a situation involving exposure to diseases or death are needed for determination of sensitivity, specificity, and predictive estimate of HRV[1].

R.K. Dishman et al. examined the relationships between the parasympathetic nervous system and the emotional stress or the self rating of anxiety in a clinical setting existing to a standardized exercise test. Spectral analysis methods were used for decomposing the HRV datasets into LF (0.05-0.15 Hz) and HF (0.15-0.5 Hz.) components using methodology of spectral analysis. The inverse relationship was found between the perceived emotional stress and the normalized HF components of HRV (p value=0.038) indicating that a smaller cardiac vagal components of HRV exits among the men and women having regarded stress[2].

The Committee for Clinic Diagnostic Apparatus and the Committee of New Medical Techniques of Ministry of Health of Russia in their methodical recommendations concluded the enduring experiences of the research in this area. These recommendations have relevance for short records of the heart rhythm. Theoretical foundations for HRV analysis methodologies, areas of applications of methods and reasons for using it were presented. Clinical and physiological interpretation along with functional states evaluation including some basic methods for evaluation of the results of HRV analysis were also investigated[3].

G. D. Clifford studied and explored the techniques for signal processing of HRV in an attempt for the development of robust methods for the analysis of HRV. This study includes extraction of signals, the estimation of cardiovascular explanation of metrics and methodologies to minimize the number of free quantifiable characteristics of the system for clinical circumstances. The ratio of LF to HF presents to be a sensitive index of ANS response for the sudden change in cardiovascular system. The analysis of RR intervals for sinus beats, non sinus beats and artefacts on 24 hour datasets of RR tachograms of healthy subjects were also presented[4].

J. P. Niskanen et al. presented a computer program using Matlab for analyzing the advanced heart rate variability (HRV) in which most of the frequently used measures of time domain, frequency domain along with Poincare plot of nonlinear methods were estimated. Parametric and the non-parametric estimates were estimated in frequency domain analysis[5].

Jennifer A. Healey et al. presented the methods for analyzing and collecting the physiological data for determining the stress level of a driver during the tasks of real world driving. Drivers were directed to follow a set route through the open roads and the ECG, electromyogram, respiration and skin conductance were continuously recorded. 50 minutes duration of data from 24 drivers were collected for analysis. Analysis included two ways in which first way include 5 minutes of data during the highways, rest and conditions of city driving for distinguishing the three levels of drivers stress and in second way comparison includes continuous features which were calculated at 1-second interval during the whole drive with a metric of observable stressor. The result showed that conductivity of skin and the HR metrics were most correlated closely with the level of stress of most of the drivers[6].

M. Kumar et al. suggested a new proposal for the assessment of stress by the interpretation of the parameters of ANS using the Fuzzy models method. Quantification of the idea of mental stress and establishing a function based relationship between the mental stress and activities of ANS was the main achievement of this paper. Approach of the fuzzy evaluation applied for the assessment of mental stress have motivated for the beginning of new interesting investigation and research for the separation of mental and physical stress[7].

R. Schneider et al. analyzed the correlation between the standard measures of the HRV and the descriptors of RR interval of Poincare plot. There are four descriptors such as SD1, SD2, S, and SD2/SD1 of the Poincare plot. All these descriptors, time and frequency domain HRV indices were estimated for 5-minutes recordings of database. Short term HRV have been characterized by the value of SD1 while long term HRV is described by the value of SD2 and S measures total HRV was correlated significantly with time and the frequency domain measures. SD2 and SD2/SD1 correlated significantly with the LF/HF showing the balance between the short term and long term HRV. None of the descriptors of the Poincare plots were correlated with the mean RR interval[8].

L. Salahuddin et al. investigated and explored the relationship between the HRV features and physiological measures on stress factors and ages. Comparison includes HRV features and physiological measures in high and low stress group with age as covariate. It was reconfirmed that age was the one of the significant factor having influence on the physiological measures and most of the features of HRV. Body temperature, LF/HF and LF in normalized unit were found significantly higher in the group having higher stress while normalized HF, aggression level and systolic blood pressure were lower. Hence, ages , HRV features and physiological measures were associated as shown by the results[9].

L. Lacasa et al. investigated and presented the algorithm of visibility graph for converting the time series in to a network graph as a simple and fast estimation method. Various properties of the time series in its structure are inherited by the constructed graph. Thereby, regular graphs are obtained as conversion of periodic series and random graphs as by random series. Some analytical tools and remarkable examples are outlined for testing the reliability of this method[10].

J. Taelman et al. explored the indices of HR and HRV accompanied by a situation of stress imposed. In a group of 28 persons which were at rest and with mental stressors they recorded the change in heart rate (HR) and HRV. The results suggested that there were significant changes in HR and HRV with mental tasks. They have shown that the mean RR with mental task is lower than in rest condition. pNN50 remains higher in rest conditions while LF/HF ratio increases with mental task[11].

J. Choi et al. described the approach for detection of mental stress by using a wearable unobtrusive sensor. The idea completely relied on the estimation of state of the ANS from the heart rate variability analysis. They used principal dynamic modes (PDM), a nonlinear system identification technique for predicting the activation level of SNS and PNS of the automatic nervous system. The results indicated that features of the PDM were having greater stability and having less dependency on subjects than spectral features[12].

C. Schubert et al. examined about the short term and chronic stress effects on HRV by the comparison between time and frequency domain and complexity (phase domain) indices in adults which were healthy. For measuring chronic stress the subscale of hassles frequency of the combined hassles and uplifts scale were taken. Under short-term stress there is no action of changing in RSA and LF/HF ratios. The differential bring-about of chronic and small duration stress were observable on various indices of HRV[13].

J. F. Thayer et al. reviewed the evidence which links heart rate variability to establish and emerging CVD risk factors being modifiable and non-modifiable such as obesity, work stress, hypertension and family history. Substantial evidences are available which support that decrease in HRV precedes developing number of risk factors. They suggested that the autonomic imbalance model might provide a uniform framework within which investigation can be made for the influence of risk factors, work stress and psychological factors on cardiovascular diseases. Work stress is in association with the decrement in HRV and work stress is one important and significant risk factor for cardiovascular situations [14].

R. Bail et al. proposed an approach for the analysis of heart rate variability for stress testing during exercise which was based solely on the model of integral pulse frequency modulation (IPFM) in which time threshold varying over time was selected for accounting the mean HR. The ANS modulation on an exercise testing database estimated by this approach were closer to physiology than that obtained by the classical IPFM model with constant threshold[15].

S. Boonnithi et al. investigated the various measures of HRV for identifying the presence of mental stress by the use of ultra short term HRV analysis. Mainly mean heart rates (mHR), mean RR intervals (mRR), power spectrum in various frequency ranges, index of symphatovagal balance, etc are the measures which were investigated. HRV measures such as mRR, mHR, normalized LF, difference between LF and HF in normalized unit, and SVI were seen effective indices for the classification of the mental stress state and normal as revealed by the results[16].

K. Yoshino et al. investigated and explored the correlation between the mood and the indices of HRV. The heart rate, RMSSD of RR-interval series, the HF power in normalized unit for RR interval variability and the average frequency in the high-frequency band of HRV are the main indices of HRV which were calculated and demonstrated that vigor during daily life has the most statistical significant correlations with the measures of HRV of eight mentioned moods[17].

J. Choi et al. addressed the sensitivity to respiratory influence as a major disadvantage of subsequently followed analysis of HRV for the stress monitoring determination. By the use of commercial HR monitors and respiratory sensors, a model for identifying linear system of the cardio respiratory system was constructed for addressing this issue. Their results suggested that, the residual HRV having comparatively more discriminative power than traditional analysis of HRV by separating respiration influences for the purpose of monitoring mental stress and workloads[18].

L. Lacasa et al. investigated a procedure to measure the real valued irreversibility of time series that includes two tools the horizontal visibility graph algorithm and Kullback-Leibler divergence. This method according to the geometric criterion represents a time series into a directed network graph. The Kullback-Leibler divergence (i.e. the distinguish-ability) between the in and out degree share-out of the associated graph is then used for the estimation of degree of irreversibility of the series. This method point out differences correctly between the reversible and irreversible stationary time series[19].

H. Costin et al. have investigated the objective characteristics for detecting stress such as various short-term HRV measures along with morphologic changes of the ECG signals. HRV indices in time and frequency domain were mainly investigated. By analyzing using morphologic variability procedure and a decision support module based on both methodologies HRV and MV, better results were obtained[20].

Che Hao Hsu et al. validated that Poincare method estimates the Symphatovagal irregularities in subjects during process of inducting anesthesia with sevoflurane qualitatively and quantitatively. It was concluded that Poincare plot analyzing procedure is easier and greater sensitive at assessing the Symphatovagal balance and noticing the beat to beat HRV. The HF shows parasympathetic activities, the LF shows the sympathetic regulation, and LF/HF ratio point out

symphatovagal balance. A better correlation between the spectral and Poincare analysis was found[21].

J. Choi et al. described the development of a wearable sensors platform for monitoring various physiological connections of mental stress. Particularly they proposed a new spectral feature which estimates the even distribution ensuring stability (balance) of the ANS by the combination of information from the PSD of respiration and HRV and prove the validity of the effectiveness of methodology on the binary distinguish problem for subjects when subjects are being allocated under mental stress and relaxation conditions[22].

H. Chu Duc et al. clarified the basic relationship between HRV measurements and congestive heart failure and investigated for the identification of individual level factor which are related to work and time of leisure for prediction of recovery of ANS during congestion measured by long time (24-hr) heart rate variability[23].

P. Karthikeyan et al. introduced a method to resolve the problem for detecting the stresses in human by means of short term ECG and HRV (5 minutes). The methodology explored helps for improving the detection of stress and reliability via numerous evidences initiated in the same sensors. For removing the high frequency, baseline wandering and noise due to power line the wavelet denoising algorithm was applied. The results obtained experimentally indicated that this method for short term ECG and HRV signals can bring about higher mean classification accuracy of in the subject independent mode[24].

David Liu et al. presented a model for predicting stress level from the ECG data that can be measured by wearable consumers grade heart rate (HR) monitors. Time and frequency domain indices of HRV and the components of spectral power of the ECG were incorporated in their model. The prediction was made on a sliding window of electrocardiogram signal and for prediction of stress a linear model was applied and prediction was correlated with actual GSR[25].

M.G. Poddar et al. analyzed and compared the heart rate variability of healthy and subjects having hypertension and used the time and frequency domain, and nonlinear methods. Time domain features such as variance, SDSD, RMSSD and pNN50 in case of normal have higher values over the subjects of hypertension. In Poincare plot SD1 and SD2 have greater values in normal cases and in case of hypertension it is lower[26].

G. D'addio et al. concluded that because of high signal nonstationary, linear indices of HRV during the stress testing have been widely questioned and that limitations can be succeed in dealing with indices of nonlinear methods of HRV based on the typical properties of deterministic fractal and system showing chaotic behavior. It can be an effective index for exploring relevant facts or knowledge about recovering underlying physiological process as suggested on the performance of fractal analysis of HRV during and after high intensive exercises[27].

Mandeep Singh presented and suggested that HRV is variation in beat to beat interval of heart beat and greater HRV shows more adaptability of heart and can be considered as the healthy symptom. HRV decreases with higher stress level[28].

D.H. Patil et al. investigated that HRV serves as a substitute for the vertical integration of the brain and it provides beneficial information for understanding the problems related to stress and health as "vertical integration" of the brain mechanism guides flexible control over behavior with peripheral physiology. Their expectation was to maintain accurate stress using Artificial Neural Network (ANN) and analyzing the records provided by the hardware machine and hence depending on that reading to determine stress level[29].

Lijuan Zhang et al. developed an autonomic classification system in which from four kinds of cardiac arrhythmias, five geometrical patterns of the Poincare plot can be distinguished. The results obtained experimentally demonstrated the intended result of the extracted indices along with better outcomes of the classifier. Study showed that the geometrical patterns of the Poincare plots having corresponding relationship with numerous cardiac arrhythmias[30].

M. Bernat et al. presented the software tool along with graphical user interface for evaluating the appropriate steps of processing of ECG signals which includes filtering, transformations, and decision making logics until the analysis of RR intervals. The assumption of the project was to develop the software tools for the ECG signal preparation process, selection and analysis of R waves optimization[31].

K. Patil et al. reviewed and analyzed the various methods available for the assessment of mental stress. Mainly analysis results in time and frequency were explored to understand the significance of HRV. Analyses were carried out to measure the effectiveness of several developed instruments. Results of the two case studies carried out in two distinct environments to establish the relation between HRV and mental stress perceived have been reported[32].

Mario Salai et al. presented the concepts and results of two studies focused for stress detection using a low cost sensor and a chest belt. They compared heart rate data and other features from the belt to those measured by a gold standard device for assessing the reliability of the sensor in course of validation study of the device[33].

D. Bassett et al. addressed whether the mood disorder that is associated with impaired PNS functions persists in to the temporary diminution in the unipolar and bipolar disorder. Results showed that HRV was found lower in depression and bipolar group and additionally the having depression showed a difference statistically significant from the control group predominantly in high frequency HRV. It was concluded that ANS functioning for bipolar and subjects in depression subjects was impaired significantly [34].

F.Z. Hou et al. in their study based solely on the method of visibility graph, constructed the complex network graph from very short termed HRV at a particular point in the course of

distinct sleeping period. Estimation of network measures changed progressively for various sleeping periods mentioned which exhibits great potential abilities for estimating the nature of sleep [35].

A. Bhaduri et al. studied and investigated that the dynamics related to the heart throughout the course of meditation can be quantitatively investigated with non-linear techniques based on chaotic behavior such as multi fractal detrended fluctuation analysis and visibility graph methods. The results obtained by both the analysis techniques showed the congruous differences between the quantitative characters indicating the intricacy of the cardiac dynamics during meditation become different[36].

M.K. Moridani et al. presented a new method to predict in hospital mortality by using HRV collected from the time of stay of patent in ICU. A novel method named as return map developed revealing information from the HRV time series. Several features that can be extracted from the return map include the angle between two vectors, the area of triangles formed by successive points, shortest distance to 45° line and their various combinations. It is capable for predicting the state of being mortal based on these features relying on the variations of the HRV dynamic characteristics as per results [37].

R. Castaldo et al. study aimed for detection of mental stress by the use of nonlinear features of the HRV extracted from 3 minutes of ECG recordings during oral examination which was meant to be stress. The classifier which was presented can bring about satisfactory results by validating the through procedure and enables for detecting stress with a better rate of sensitivity and specificity. Subjects which were stressed showed lower HRV and a reduction in the nonlinear dynamics of heartbeat [38].

Tamas Madal et al. used the Horizontal visibility graph (HVG) to distinguish the dynamical systems from the stochastic systems to convert the time series of HRV into networks having scale freeness. They introduced and evaluated a general class of predictors that could be used for augmenting the already used features used in the analysis of HRV and that showed the high predictive power for various kind of heart disease solely based on the horizontal visibility graph[39].

B. Hwang et al. research demonstrates that spectral features of the ECG within duration of ultra short term (10 sec) can be utilized for monitoring the emotional state of human. The results obtained experimentally exhibited feasible classification results of spectral indices and features of the ECG compared to parameters of HRV and also response of stress in mental arithmetic tasks has greater ability to be separated from those having in rest state as compared to the stress in other situations[40].

Nan Bu et al. explored and developed a novel index for estimating and evaluating the stress based on the Poincare plot of pulse rate (PR) data and the explored index was based solely on measurement of distance between corresponding data points. Analysis of HRV with the

referenced RR intervals data was also accomplished for checking subject's stress level. Short term PR data (one min.) was used for evaluating the dynamic changes of level of stress [41].

S. Sannino et al. investigated and studied that visibility graph algorithm which maps time series into network graphs for the characterization of time series. The differences in the similarities of temporal networks and hence, in correlated dynamics across resting-state networks as revealed on applications to a large open datasets gives indications that some differences in brain activity connected to psychiatric disorders could be picked up by this approach[42].

S. A. Priya et al. compared the HRV indices of the frequency domain before and during the mental arithmetic test for stress between obese and non-obese adults. LFnu and LF/HF ratio exhibited statistically significant increment in obese group before the stress test while LFnu, HFnu and LF/ HF ratio was reduced in obese subjects with LFnu reduction being statistically significant ($p<0.01$) during the mental arithmetic stress test. Whereas, there was statistically increase in LFnu ($p<0.001$) with reduction in HFnu ($p>0.05$) which was statistically not significant in non-obese subjects[43].

M. Saidi et al. proposed a real time stress monitoring system showing the user a new signal for feedback level of stress. This signal was considered as the combination of weighted measures of photoplethysmography signals and galvanic skin response. Mainly linear regression and correlation feature selection methods was used for the combination and selection of features[44].

F. Uysal et al. explored the effects of stressors on the activities of autonomic nervous system using time and frequency domain HRV. A statistically significant reduction was noticed in the mean RR interval in stressor based test while time domain indices (HR, SDRR) become greater during the tests. Also, there was an increment in LF power reflecting sympathetic activities under stress situation and a decrement in HF band which reflects parasympathetic activities[45].

D. P. Tobon et al. presented a methodology based on the spectro-temporal depiction of the ECG signals, very often termed as "modulation spectral" representation for estimation of heart rate and heart rate variability. Using both synthetic and recorded ECG signals with noises, the HR and MD-HRV (modulation domain HRV) metrics were extensively examined and hence as per these findings suggested that for ambulant cardiac observation applications, particularly those including intense movements (e.g., elite athletic training), presented HR indices and obtained MD-HRV metric are well suited[46].

CHAPTER 3

METHODS OF HRV ANALYSIS

3.1 INTRODUCTION TO ANALYSIS METHODS

The methods for analyzing Heart Rate Variability (HRV) have been mainly categorized in time domain, time-frequency domain, frequency-domain, and nonlinear methods. The time domain measures had been explored very earlier and even now these are widely admired measures. The measures of frequency domains permit the separating variability into distinct regular repeated patterns solely based on frequencies. The methodology in nonlinear category are based on an underlying assumption of HRV being chaotic time series, since the cardiovascular system being related to heart and blood vessels can be considered very complicated . They are very active field presently for being the latest development. The inter beat intervals are frequently described as NN intervals for emphasizing that RR intervals to be analyzed have been corrected or edited. The normal to normal intervals which results from abnormal beats correction and noise removal from the RR intervals are termed as the NN intervals.

3.2 TIME DOMAIN METHODS

Time domain measures are perhaps the easily understood methodology to be performed for evaluating the variations in heart rate. The heart rates at any instances of time or the following normal complexes intervals are estimated by these methods. The mean of RR interval, heart rate mean value, the difference of maximum and minimum NN interval and the difference between night time and day time heart rate, etc. are the simple time domain variable which could be calculated[1]. The statistical or geometric properties of RR intervals are measured by the time domain indices of HRV.

Time domain methods of HRV analyses are frequently classified as statistical or geometric methods.

3.2.1 STATISTCAL METHODS

Statistical indices for time domain are based upon the several moments of the RR intervals and statistical based measures calculated directly from the Inter-beat interval (IBI) series. Statistical characteristics of dynamic row of cardio-intervals include: SDNN, RMSSD, PNN50, NN50, etc. Statistical indices of time series are broadly categorized in two groups.

1. Variables which are derived from IBI viz. the mean of heart rate (mHR) and the SD for the whole records of data.

2. Variables which are based on the difference between the adjoining or adjoining cycles viz. the proportional differences between an adjoining cycles exceeding an unspecified value limit.

The Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology has recommended the below mentioned measures or indices.

- SDNN (ms): Standard deviation of NN interval also stated as SDRR and estimated as the square root of variances. SDNN reflects all the cyclic components which are credited for the recording period variability since mathematically variance equals to the spectral analysis total power. It is worthy notable that as the length of analyzed recordings increase, the total variances for heart rate variability increases. The recording for short term (5-minutes) and nominal (24 hours) recordings for long term seem to be proper options for the duration of recording for determining SDNN. Mathematically SDNN of RR interval is stated as

$$SDNN = \sqrt{\frac{1}{N-1}\sum_{j=1}^{N}(RR_j - \overline{RR})^2} \tag{3.1}$$

  Here RR_j indicates the j^{th} RR interval value; N is the total number of RR intervals.
- SDANN (ms): The standard deviation of average of NN intervals estimated from segments of period of total observation time usually for short duration period (5-minute). It is the estimation of changes in heart rates because of cycles being greater than 5 minutes.
- SDNN index (ms): The mean of standard deviation of all NN intervals for the segment of 5 minutes over 24 hour recording. It estimates the variability in heart rate because of cycle shorter than 5 minutes.
- SDSD (ms): The standard deviation of difference between adjoining or successive RR-intervals.
- RMSSD (ms): The square root of the average of the sum of the squared differences of consecutive NN intervals. RMSSD having better immunity to ectopic beats and hence this measure is better preferred for short term HRV.

$$RMSSD = \sqrt{\frac{1}{N-1}\sum_{j=1}^{N-1}(RR_{j+1} - RR_j)^2} \tag{3.2}$$

- NN50: It is the number of pairs of adjoining NN intervals having difference of greater than 50 milliseconds for whole recording. This is highly correlated with RMSSD and a measure for heart rate variability (HRV) over short time.

- pNN50 (%): It is the percentage of successive NN which differs by more than 50 ms over an entire long time (24 h) recording.

$$pNN50 = \frac{NN50}{N-1} \times 100\% \tag{3.3}$$

All these measuring for short term variations are highly correlated and estimates (HF) high frequency variability in heart rate[1].

3.2.2 GEOMETRICAL METHODS

The geometric methods cause to change the RR intervals data in form of geometrical pattern and HRV indices are formed on the basis of various qualities of shapes and patterns measured[4]. Generally the performance of geometric methods is better on poorly edited datasets. There are three basic approaches which are used commonly in geometric methods.

1. Measuring some fundamental geometrical patterns of distribution histograms (the width of baseline, height of sample density) and converting it into the HRV measures.
2. Approximation of geometric patterns of distribution histogram by means of mathematically stated shape (triangle, exponential curve) and from shape parameters HRV measures are derived.
3. Classifying the geometric shape in various pattern based categories representing various sets of HRV.

The Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology has recommended the below mentioned indices:

- HRV triangular index: It is obtained as the integral of the density spread-out histogram i.e. dividing the number of all NN intervals by the maximal of density distributions. On a discrete scale, the approximation of the index is done by the value: (total numbers of all NN intervals)/(the number of NN interval in the modal bins). A bin width of 1/128 sec. is recommended for obtaining comparable results.
- TINN (ms): The triangular interpolation of distribution histogram of the NN intervals is the width of the baseline of distribution which is measured as base of the triangle by approximation of NN intervals distribution.

Some of the others geometrical methodologies still are in phase of explanation and explorations. The relative insensitivity to the qualitative analysis for the NN interval series is considered as

advantage of geometrical methods while the requirement of reasonable numbers of NN intervals for construction of the geometric pattern is considered major disadvantage of this method. Preferably long term (24 h) but at least 20 minutes of recordings should be used in practice for ensuring the better performance of geometrical methods[1].

3.3 FREQUENCY DOMAIN METHODS

Heart rate fluctuations are considered to be periodic oscillations and found to occur on a considerable range of the time scaling. Quantification of these fluctuations occurring inside the inter-beat-interval time series can be performed by power spectral density (PSD). Spectral power density as a function of frequency of a time series is presented by the power spectral density (PSD). Hence, the information regarding the amount of power referring certain frequencies contribute to a time series can be obtained by PSD estimation. In 1981, Akselrod et al. presented the power spectral analysis into analysis of HRV[4]. Generally the methods for calculating the PSD are classified as parametric and non-parametric. Estimation of the classical power spectrum is method based on FFT and The FFT doesn't make assumptions on how the data are generated, hence the classical methods are frequently called as non-parametric while the AR power spectrum methods makes assumptions and referred as parametric. The advantages of nonparametric methodologies include:

- Simplicity of the employed algorithm, in most cases FFT (Fast Fourier Transform).
- Processing speed is high.

The advantages of parametric methods are:

- Easier spectral post processing through an automatic estimation of the power components of lower and higher frequency and easily identifying the each component's central frequency.
- An approximate calculation of PSD even on a less number of samples accurately.

The need for verifying the suitableness of the selected model and the order of the model i.e. its complexity is the basic disadvantage of parametric methods.

3.3.1 SPECTRAL COMPONENTS FOR LONG TERM RECORDINGS

The main spectral components which are recognized within a spectrum estimated over the sequences of NN intervals in the period of 24 hour has been divided into following bands of frequencies:

- ULF :0.0001Hz .$\geq$ ULF < 0.003 Hz
- VLF :0.003Hz $\geq$ VLF < 0.04 Hz
- LF :0.04HZ $\geq$ LF < 0.15 Hz
- HF :0.15Hz $\geq$ HF< 0.4Hz

The biological regulatory mechanisms being recognizably different in nature which contributes to HRV act at confined frequencies approximately within these frequency bands is the main motive for dividing of the spectrum into these frequencies bands. An example showing an approximate calculation of power spectral density (PSD) acquired from the long term interval (24 hours) is shown in Fig.3.1. The components of low and high frequencies only are analogous to the spectrum peaks where as the very low frequency and ultra low frequency cold be estimated on logarithmic scales on both axes by using a line in the plotting. The slope of that line is the 'α' (slope of the linear interpolation of the spectrum in a log-log scale) measure of HRV. The spectral analysis estimated in the whole 24h duration and the spectral outcomes which are acquired from the shorter recordings (5 min) , averaged over the whole 24h duration provides the mean of the modulations attributed to components of LF and HF [1][4]. The long term regulatory mechanisms viz. thermoregulatory systems, humoral factors and the rennin-angiotensin system are thought to be the cause responsible for irregularities below 0.04 Hz in the ULF and VLF bands.

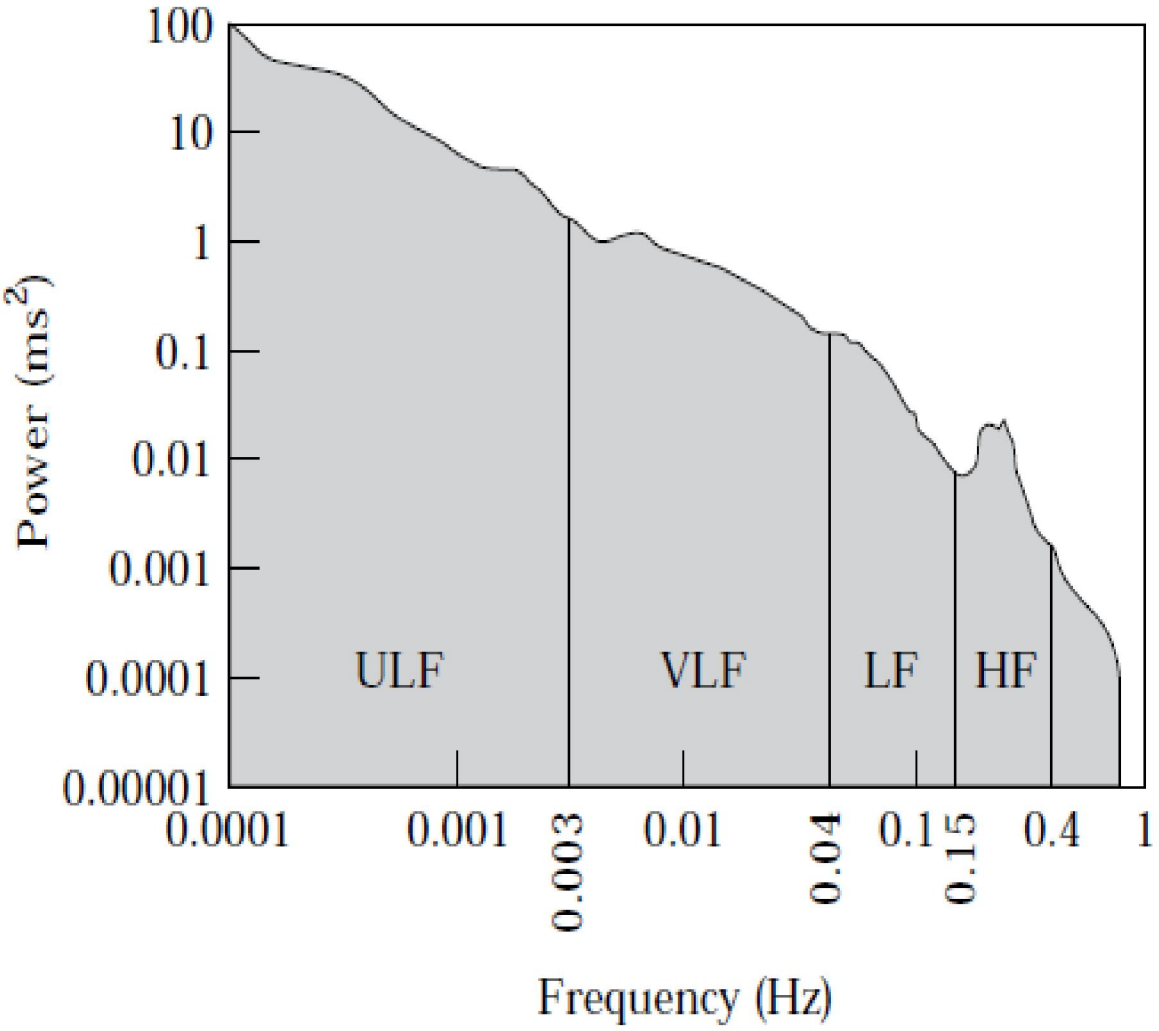


Fig.3.1A typical estimate of PSD of RR interval over long term 24h interval (taken from [1])

3.3.2 SPECTRAL COMPONENTS FOR SHORT TERM RECORDINGS

The main components of spectrum which are dignified in appearance within a spectrum estimated over the sequences of NN intervals for recordings over short term (for 2min to 5 min) are VLF, LF, and HF components. HF power is the measure of parasympathetic activities. LF power is subjected to some controversy that some suggests it as the measure of both parasympathetic and sympathetic activity where as some others suggest it perfect measure of sympathetic activities. For VLF component physiological explanations is much less defined. When explaining the PSD of short term recordings, the VLF evaluated from it (< 5 minutes) is considered having questionable value and must be refrained.

Usually the measurement of power components of VLF, LF, and HF are estimated in absolute values of powers (in ms^2) but normalized units (n.u.) for LF and HF are also measured. The controlled and balanced behavior of sympathetic and parasympathetic branch of ANS is emphasized by representing the LF and HF in the normalized unit (n.u.)[1]. Indices are normalized by dividing the Lf and HF by total power which provides more consistent results for study and comparing subjects having different autonomic stresses[47]. Total power is the summation of VLF, LF and HF and the ratio LF/HF shows sympathovagal balance.

Table3.1 Summary of the selected time domain indices of HRV

Statistical indices		
Variables	**Units**	**Description**
SDNN.	ms	It is the standard deviation of all NN intervals
SDANN	ms	It is the standard deviation of the mean of NN intervals in all segments of 5 min of the whole recordings.
RMSSD	ms	It is the square root of the average of the sum of the squares of differences between adjoining NN intervals
SDNN index	ms	Mean of the standard deviations of all NN intervals for all segments of 5 min of the whole recordings
SDSD	ms	Standard deviation of differences between adjoining NN intervals.
NN50		The Number of pairs of adjoining NN intervals having difference of more than 50 ms in the whole recordings.
pNN50	%	It is obtained as dividing the NN50 count by the total number of all NN intervals
Geometrical indices		
HRV triangular index		It is obtained as dividing the total number of all NN intervals by the height of the histogram of all NN intervals measured on a discrete scale with bins of 7·8125 ms (1/128 s)

TINN	ms	Baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all NN intervals
Differential index	ms	Difference between the widths of the histogram of differences between adjacent NN intervals measured at selected heights (e.g. at the levels of 1000 and 10 000 samples
Logarithmic index		Coefficient φ of the negative exponential curve($k \cdot e^{-\varphi t}$) which is the best approximation of the histogram of absolute differences between adjacent NN intervals

Table 3.2 Summary of the selected frequency domain indices

For analyzing long term (entire 24 hours) recordings			
Variable	**Units**	**Description**	**Frequency range**
Total power	ms^2	Variance of all NN intervals	Approximately ≤ 0·4 Hz
ULF	ms^2	Power in the ultra low frequency range	≤ 0.003Hz
VLF	ms^2	Power in the very low frequency range	0·003–0·04 Hz
LF	ms^2	Power in the low frequency range	0·04–0·15 Hz
HF	ms^2	Power in the high frequency range	0·15–0·4 Hz
A		Slope of the linear interpolation of the spectrum in a log-log scale	Approximately ≤ 0•4 Hz
For analysis of short term (5 min) recordings			
5 minute total power	ms2	The variance of NN intervals over the temporal segment	Approximately ≤ 0•4 Hz
VLF	ms^2	Power in very low frequency range	≤ 0.04 Hz
LF	ms^2	Power in low frequency range	0·04–0·15 Hz
LF norm	n.u.	LF power in normalized units LF/(Total Power–VLF)×100	
HF	ms^2	Power in high frequency range	0·15–0·4 Hz
HF norm	n.u.	HF power in normalized units HF/(Total Power–VLF)×100	
LF/HF		Ratio of LF and HF	

3.4 CORRELATION AND DIFFERENCES BETWEEN THE MEASURES OF TIME AND FREQUENCY DOMAIN

More theoretical knowledge and observations of facts be found on the physiological explanation of the indices in frequency domain as compared to the indices of time domain which is acquired from even the same recording while analyzing the stationary short term recordings. Various variables of time and frequency domain estimated over long term (24 h) portion of time are highly correlated and shown in Table 3.3. Mathematical and physiological relationships both are the reason for these strong correlations[1].

Table3.3 Approximate correlation between measures of time and frequency domain over long term recordings

Time domain measures	**Frequency domain correlate approximately**
SDNN	Total power
HRV triangular index	Total power
TINN	Total power
SDANN	ULF
SDNN index	Mean of 5 min total power
RMSSD	HF
SDSD	HF
NN50 count	HF
pNN50	HF
Differential index	HF
Logarithmic index	HF

3.5 TIME-FREQUENCY METHODS

The Heart rate variability analysis using frequency domain methodologies can provide only the information regarding the distribution of inter beat interval (IBI) signal power in frequency domain while no insight about the temporal evolution of spectrum is provided. Hence, the methods which allows the viewing of both time and frequency information simultaneously are

frequently termed as the time-frequency method. Time-frequency analysis of HRV estimates the measures related to LF, HF and VLF.

The Windowed Fourier Transforms which is also called as Short Time Fourier Transforms (STFT) and Continuous Wavelet Transform are two primary kind of time-frequency analysis method. The term windowed periodogram will be used instead of windowed Fourier transform for including spectral methods other than Fourier transform and generalization of this permits the windowed Burg periodogram and windowed Lomb-Scargle periodogram inclusion.

3.6 NONLINEAR METHODS

Regulation of heart rate can be considered the one of the most complicated or intricate systems in the human being since it is effected by variety of factors viz. respiration, mental load, stress and various physiological and psychological rhythms modulated via autonomic nervous system(ANS)[2]. Hence it is much appropriate for assuming that mechanisms of nonlinearity are comprises in the origin or mode of formation of heart rate variability. Several techniques which have been suggested as per dynamics of nonlinearity applied for analyzing and classification of HRV. The main motivation factor for application of these methods relies on the fact that the high intricacy and the nonlinear influences between the physiological subsystems govern the nonlinear control systems for HRV. There are below mentioned a nonlinear methodology which has been widely applied:

- Measurements of fractality, for example: power-law correlations, detrended fluctuation analysis (DFA), multi-fractal analysis(MFA)
- Measurements of entropy for example approximate entropy, sample entropy, compression entropy
- Correlation dimensions
- The Poincare plot
- Recurrence plot

However, some additional disease or ailment predicting information and complement are provided by the methods from nonlinear dynamics. Contextually analyzing HRV using the Poincare plot method plays a major significant role and having an advantage of being easier for understanding and interpretation and are used in Holter ECG analysis widely. Advancement in technology and the better investigation and explanation of the results obtained by means of non-linear methods are needed for clinical significance of these methodologies[1].

3.6.1 APPROXIMATE ENTROPY

The intricacy or irregularities of the RR interval time series is measured by the approximate entropy. Suppose there is a series having N RR-interval as RR1, RR2, RR3,… RR_N. The series of vectors having length ‘m’ such as X_1, X_2,…,$X_{N-m+1}$from RR intervals is constructed as: X_i =[RR_i,RR_{i+1} ……RR_{i+m-1}].

The d[X_i, X_j] is the distance between vectors X_i and X_j which is described as maximal absolute differences between their relating scalar component. $C_i^m(r)$ is calculated, for each vectors X_i , the relative number of vectors 'X_j' for which the value d[X_i, X_j] ≤ r , where r is the tolerance value[48].

$$C_i^m(r) = \frac{number\{d[X_i, X_j] \le r\}}{N-m+1} \forall j \tag{3.4}$$

Then the index $\Phi^m(r)$ is calculated as:

$$\Phi^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln C_i^m(r) \tag{3.5}$$

Hence, the approximate entropy is calculated as following:

$$AppEn(m, r, N) = \Phi^m(r) - \Phi^{m+1}(r) \tag{3.6}$$

Hence, the AppEn estimation value mainly dependable on the parameters such as length 'm' of vector, tolerance 'r' value, and length 'N' of data. As the length of the data increases the approximate entropy (AppEn) approaches to its asymptotic values. The selection of tolerance 'r' should be done as fraction of SDNN of data. A common selection of m =2 and tolerance(r) is r =0.2SDNN[49].

3.6.2 SAMPLE ENTROPY

For approximate entropy (AppEn), in the determining of number of vectors' X_i' for which the value d[Xi, Xj] ≤ r , the vector X_i itself is included also which ensures that value of $C_i^m(r)$ is always greater than zero and logarithm could be used, but making approximate entropy (AppEn) to be biased. Sample entropy (SampEn) is almost similar to approximate entropy but having difference in computation that self comparison of X_i in sample entropy is eliminated by computing $C_i^m(r)$ as:

$$C_i^m(r) = \frac{number\{d[X_i, X_j] \le r\}}{N-m} \forall j \ne i \tag{3.7}$$

Then, the value of $C_i^m(r)$ are averaged to give

$$C^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} C_i^m(r) \tag{3.8}$$

Hence, the sample entropy is estimated as:

$$SampEn(m,r,N) = \ln(C^m(r) / C^{m+1}(r)) \tag{3.9}$$

Sample entropy (SampEn) was developed for reducing the bias of approximate entropy and it has close accordance with the theory for datasets having probability contents. Sample entropy having value zero implies that consecutive sequence are more likely identical and larger value implies higher complexity[49].

3.6.3 CORRELATION DIMENSION

The correlation dimension (D_2) is one of the methods that are used widespread to measure the complexity, dimensionality of space and strangeness of the time series which is supposed to provide facts or knowledge on minimal number of required dynamic variables for modeling the underlying systems. Time series 'X_i' is formed and $C_i^m(r)$ is calculated similarly as in approximate entropy calculation but in this instance distance function is stated as below:

$$d[X_i, X_j] = \sqrt{\sum_{k=1}^{m} (X_i(k) - X_j(k))^2} \tag{3.10}$$

Here, '$X_i(k)$' and '$X_j(k)$' is the k^{th} element of the series 'X_i' and 'X_j'. Thereafter, the index $C^m(r)$ is calculated by taking average $C_i^m(r)$ over i.

$$C^m(r) = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} C_i^m(r) \tag{3.11}$$

Hence, the correlation dimension (D2) is explained as below:

$$D_2(m) = \lim_{r \to 0} \lim_{N \to \infty} \frac{\log C^m(r)}{\log r} \tag{3.12}$$

These value of limit is estimated fairly accurately by the regression curves slope (log r, log $C^m(r)$). From the linear portions of the log-log plotting the slope is calculated. When the value of m is increased the regression curve's slope tends to saturate on the finite values of D_2. A value of m=10 is most widely selected. Correlation dimension is very useful in measuring the differences between a diseased and healthy person[48]-[49].

3.6.4 DETRENDED FLUCTUATION ANALYSIS

Correlation within the signal is measured by the detrended fluctuation analysis (DFA). For different time scales the correlation is extracted as following: Firstly, the mean of the RR-

interval ($\overline{RR}$) is estimated upon all 'N' samples and then time series of RR intervals is estimated as below:

$$y(k) = \sum_{j=1}^{k} (RR_j - \overline{RR}), k = 1, ..., N \tag{3.13}$$

Next, non overlapping segments having equal length 'n' are obtained by dividing the integrated series. A least square line within each segment is fitted which represents the local trends with a broken line. Suppose these regression lines is denoted by $y_n(k)$. Then by subtracting the local trends within each segment as: $y(k)-y_n(k)$, the integrated series is detrended. The root mean square (RMS) fluctuations for these integrated and detrended time series is estimated as below:

$$F(n) = \sqrt{\frac{1}{N} \sum_{k=1}^{N} (y(k) - y_n(k))^2} \tag{3.14}$$

This estimation is used more than once over distinct length of segments to provide the index 'F(n)' as a function of the length of segment 'n'. More frequently F(n) shows increments with the length of segment. Representation of the Function F(n) in a logarithmic plot (log(F) and log(n)) defines two parameters as: the short term fluctuations (α1) regarded as the regression line slope obtained from 'log(F(n)) to log (n)' plot having ' n' in the range of 4-16, and the long term fluctuations (α2) as the regression line slope obtained from 'log(F(n)) to log(n)' plot having 'n' in the range of 16-64.

3.6.5 POINCARE PLOT

The Poincare plot (PP) analysis is one of the geometrical and nonlinear methods for assessing the HRV. It is an emerging analysis method in which RR intervals are depicted graphically as a function of previous RR intervals where a point in the plot is defined by the values of each pairs of following RR intervals[8]. Temporal correlations occurring inside RR intervals acquired from the ECG recordings are graphically represented by the Poincare plot.

In this plot as shown in Fig.3.2, the current cardiac beat interval (RR_i) is depicted on the x-axis, and the interval of the successive beat (RR_{i+1}) is depicted on the y-axis, therefore each point (RR_i, RR_{i+1}) in the Poincare plotting constitutes for two adjoining heart beats[8]-[21].

The Poincare plot is also referred as Lorenz plot, is a graphically represented tool for the analysis of time series which can visualize both scattering of points clouds and the relation between these data-points[41].

The geometry of the Poincare plot have been shown for distinguishing between normal and diseased person in the clinical settings employing highly skilled and trained persons in specified

fields for visually classifying the plots. The shape of the cloud along the identity line provides useful descriptions of heart rate variability related to clinical significance[47].

It is possible to visualize and quantify the asymmetries of the heart rate viz. the different contributions of decelerations and accelerations of RR intervals to short-term HRV using Poincare plot analysis method.

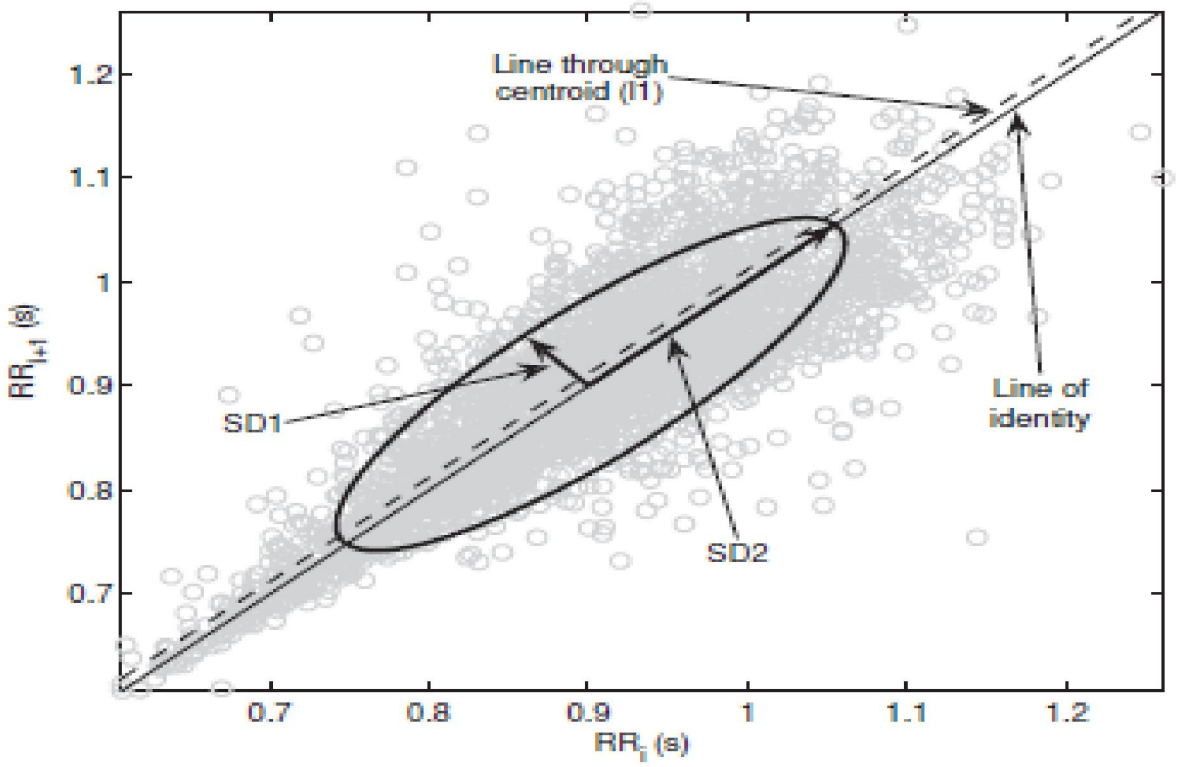


Fig.3.2 A standard Poincare plotting for RR interval of a normal healthy Person [46]

The following descriptors or indices of Poincare plot methods are often used for HRV analysis:

- SD1: It is the standard deviation which measures the distribution of points over a wide area in the Poincare plot across the identity line. All the points in the Poincare plot (PP) are estimated on a line being normal to the identity line, and hence the standard deviation (SD) of the out-coming distribution is evaluated. This characteristic of the Poincare plot is typically stated as a measure for short-term HRV. SD1 has the similar interpretation as RMSSD and considered as good marker for parasympathetic control of heart rate.
- SD2: It is the standard deviation which measures the distribution of points along the identity line. All the points are estimated on the line of identity, and hence the standard deviation is determined. This characteristic is stated as a measure for both short and long-term HRV.SD2 is more strongly related to sympathetic control.
- SD2/SD1: It is obtained as the ratio of SD2 to SD1. The hypothesis is that SD2/SD1 measures the balance between long term and short term HRV analogous to the indices

LF/HF from spectral HRV analysis. The ratio SD2/SD1 has positive correlation with LF while negatively correlated to HF[8].

3.6.5.1 ELLIPSE FITTING TECHNIQUE

Ellipse fitting procedure for characterizing the Poincare plot on the mathematical basis has been adopted by several researchers. The minor axis of the ellipse being fitted is perpendicular to the identity line having slope 135 degree and passing through centre of the mass of the plotting whereas major axis is aligned with identity line having slope 45 degree. Thus, for the fitted ellipse used for the Poincare plot for RR interval series, the major and minor axes could be stated as: $RR_n=RR_{n+1,}$ and $RR_n+RR_{n+1}=2\overline{RR}$.

The distribution of the data points in company with the minor axis estimates the plot width in ellipse fitting technique while distribution of points in company with major axis corresponds to measure plot length. Hence, distance for the ' i^{th}' points of the plotting from major and minor axes could be estimated as below:

$$D_{i(\min)} = \frac{RR_i - RR_{i+1}}{\sqrt{2}} \tag{3.15}$$

And,

$$D_{i(maj)} = \frac{RR_i + RR_{i+1} - 2\overline{RR}}{\sqrt{2}} \tag{3.16}$$

Hence the short term variability and long term variability of the Poincare plot could be calculated as:

$$SD1 = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1} D_{i(\min)}^2} \tag{3.17}$$

and

$$SD2 = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1} D_{i(maj)}^2} \tag{3.18}$$

here, N represents number of RR intervals in the plotting of HRV signals. The pints which are above the identity line corresponds for RR interval which are greater than preceding RR interval ($RR_{n+1}>RR_n$) where as points which are below the identity lines indicates a smaller RR interval than previous($RR_{n+1}<RR_n$).

The motivation for using continuously following RR data-points in the Poincare plot is inherited by the fact that the current occurring RR-intervals significantly influence the successive RR-intervals. Thakre and Smith in their study examined and presented that a curvilinear relationship exists between lag Poincare plot measures for healthy subjects, which is lost in congestive heart failure (CHF) subjects[47].

3.6.5.2 HEART RATE ASYMMETRY ANALYSIS USING POINCARE PLOTTING

Asymmetry is closely related with the irreversibility of the time-series and has been reported higher in systems with healthy physiology and constitutes the availability of complicated nonlinear dynamics in physiological signals. Piskorski, Guzik and Porta et al. have explored that the asymmetries in heart rate must be a common fact or situation that is observed to exists in a healthy heart because the growing and declining RR interval being unequal due to variability in the rates at which the HR increase or decrease[47].

In a particular Poincare plot, asymmetry is an obvious phenomenon with respect to the identity line having slope 45 degree and passing by the origin in plot. Porta et al. in their study have investigated and explored the asymmetries of a Poincare plotting and exhibited the relation to one another among time reversibility, asymmetries in pattern and dynamics of nonlinearity. Mainly the authors have employed asymmetry indices such as Porta's index (PI), Guzik's index(GI) and Ehlers' index (EI)[47],[50].

(i) Porta's index: It is assessed by estimating the percentage of negative ΔRR (difference of successive RR intervals having negative value i.e. ΔRR^{-}) with respect to total number of ΔRR having non-zero value i.e. $\Delta RR \neq 0$ and expressed as below:

$$P_i\% = \frac{N(\Delta RR^{-})}{N(\Delta RR \neq 0)} \times 100 \tag{3.19}$$

(ii) Guzik's index: It is assessed by evaluating the percentage (%) of the cumulative squares value of change in RR interval value having positive value i.e. ΔRR^{+} to the cumulative squares value of all the ΔRR and could be expressed as below:

$$G\% = \frac{\sum_{i=1}^{N(\Delta RR^{+})} \Delta RR^{+}(i)^2}{\sum_{i=1}^{N(\Delta RR)} \Delta RR(i)^2} \times 100 \tag{3.20}$$

For improving the reliability of time irreversibility test based on above measures it was redefined as $P_m\%$ and $G_m\%$. Suppose time series of a heart beat interval are indicated as: x=[x(i);

i=1,2,…..N], here N depicts the number of points of the dataset. The sequential coarse-grained time series by taking the mean of data inside a moving window having τ points was constructed for it where τ is the scale factor.

Then, each elements of a coarse-grained series (x_τ) is estimated as:

$$x_\tau(j) = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i, 1 \le j \le \frac{N-1}{\tau} \tag{3.21}$$

The length of (x_τ) is obtained by dividing the original time series length i.e. N-1 by sale factor τ. Hence the corresponding ΔRR series regarding (x_τ) is evaluated as:

$$y_\tau(k) = x_\tau(k+1) - x_\tau(k), 1 \le k \le \frac{N-1}{\tau} - 1 \tag{3.22}$$

Finally, the indices P_m% and G_m% are defined by evaluating the mean value of P% and G% over each time scales and obtained respectively as:

$$P_m\% = \frac{1}{L} \sum_{\tau=1}^{L} P\%(\tau) \tag{3.23}$$

$$G_m\% = \frac{1}{L} \sum_{\tau=1}^{L} G\%(\tau) \tag{3.24}$$

Here L depicts the maximum scale. When L=1, the value of indices P_m% and G_m% are similar to the original P% and G%, respectively.

Index D: the Euclidean distance from a point in the (P_m%, G_m%) space to the symmetric center can be evaluated as:

$$D_e = \sqrt{(P_m\% - 50)^2 + (G_m\% - 50)} \tag{3.25}$$

A special point referred to as symmetric center explained by the Point (50, 50) in the (Pm%; Gm%) space point-out that its corresponding time series is completely time reversible[50].

(iii) Ehler's index: The first derivative of the series obtained from the RR intervals was used by Ehler et al. for evaluating the asymmetries of the distribution given. Skewness is computed over the first derivative of the signals for estimating the asymmetry for the given distribution[51].

Thus Ehler's index for the time series of RR intervals could be expressed as:

$$EI = \frac{\sum_{i=1}^{N-1} (RR_i - RR_{i+1})^3}{(\sum_{i=1}^{N-1} (RR_i - RR_{i+1})^2)^{\frac{3}{2}}} \tag{3.26}$$

CHAPTER 4

SOFTWARE EVALUATION OF HRV

4.1 OVERVIEW OF KUBIOS HRV ANALYSIS

The Kubios software for analyzing the HRV has been provided by the Bio-signal Analysis and Medical Imaging Group at the Department of Physics, University of Kuopio, Kuopio, Finland. For running Kubios HRV Analysis software the MATLAB Component Runtime (MCR) is required. The software is suitable for researchers and clinicians, sports enthusiasts and anybody wishing to perform detailed HRV analysis because of its distinct varieties analysis methodologies options for HRV analysis and easier user interfaces. This software has been mainly designed for the human HRV analysis. All the widely investigated time and frequency-domain indices of heart rate variability are included in the software. Both the Fourier transform and autoregressive model based spectral computation for frequency domain variables can be evaluated. In addition, the software is well featured for estimating several nonlinear indices and features such as the Poincare plot estimate and sample entropies, detrended fluctuation analysis, recurrence plot analysis, and correlation dimension. The presentation and saving of the analysis results in addition to the usability of the program user interface is well defined in the software[49].

4.2 THE USER INTERFACE

The Kubios software for analyzing the measures or indices of HRV is operated with a single window graphical user interface (GUI) as shown in Fig. 4.1.

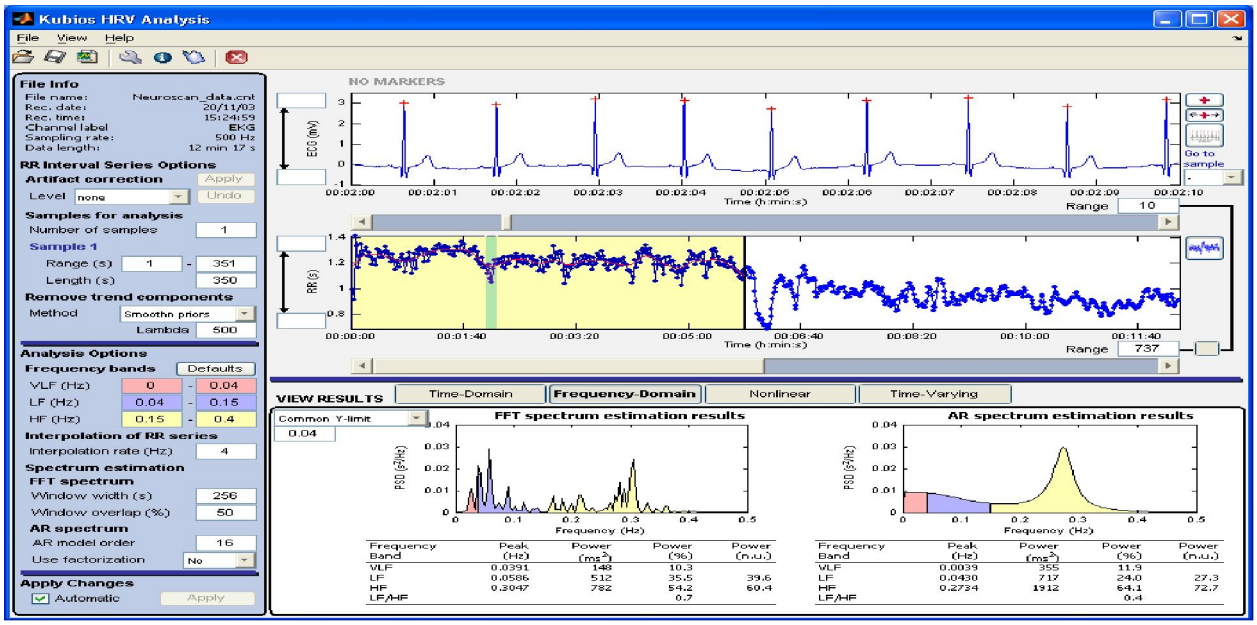


Fig.4.1 The graphical user interface of the Kubios HRV analysis software

The user interface has been separated into four parts such as the options for series of RR interval, data browsing part, option for the analysis and the viewing the results. The version of the Kubios software (Standard or Premium) used decides the available functionalities in the GUI.

4.2.1 RR INTERVAL SERIES OPTIONS

Mainly three functions are included in RR interval series options such as artifact corrections, Remove trends components, and sample for analysis. The options for the series of RR intervals have been depicted in Fig. 4.2.

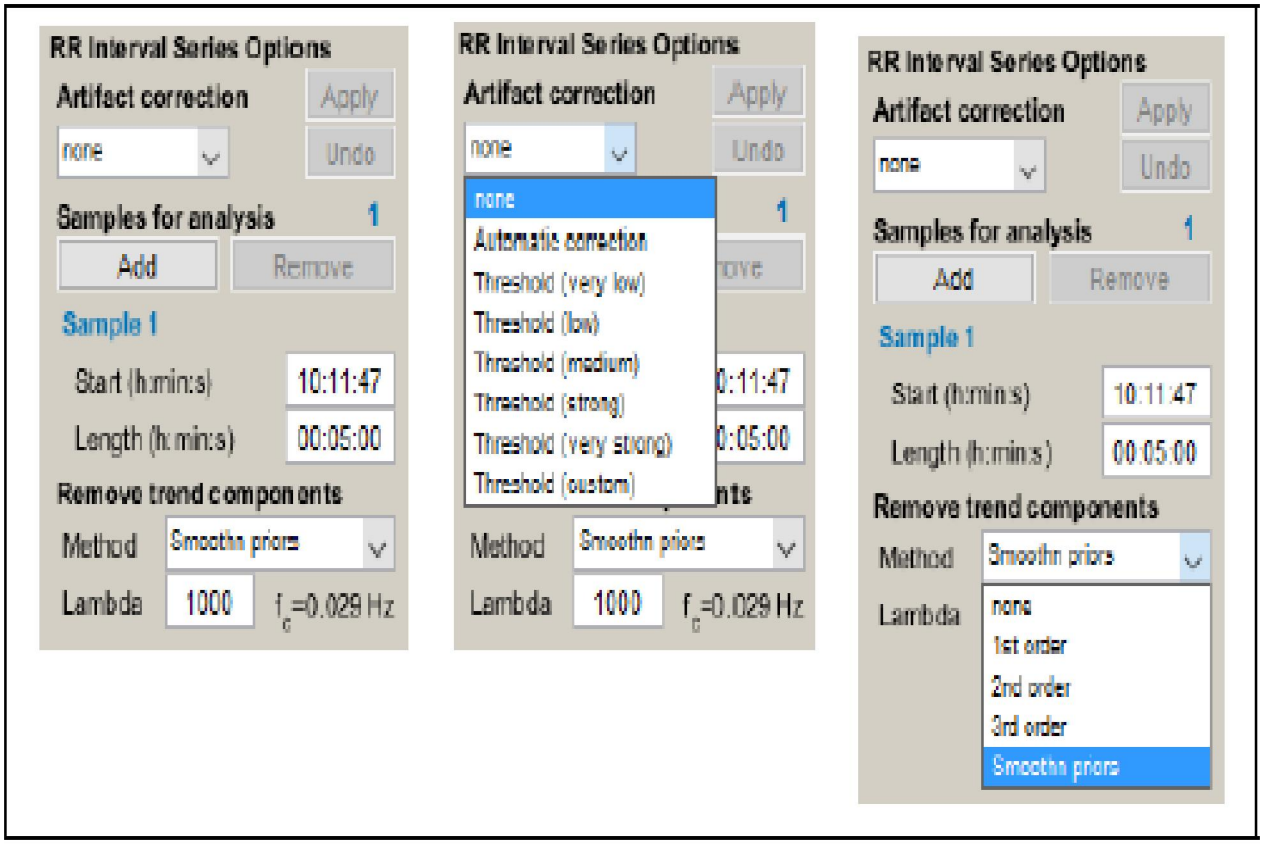


Fig.4.2 Segment of the GUI showing option for the series of RR intervals

4.2.1.1 ARTIFACT CORRECTIONS

For correcting the artifacts from a corrupted series of RR intervals this option can be used. There are various artifacts correction options which can be selected by the users. Additionally, a custom level in second could be set. On the RR interval axis the corrections which have been done on the RR series have been displayed. Methodology used in the corrections is piecewise cubic spline interpolation. It must be noted that dubious values into the series of RR intervals by

interpolation are generated by the artifact correction and hence, may cause distortion into the analysis results.

4.2.1.2 SAMPLE FOR ANALYSIS OPTION

The parts of the RR interval series which is to be analyzed could be selected by editing the number of samples, range, end, and length values in the samples for analysis options. The analysis can be done for both the single samples distinctly and also combining the samples into one before analyzing HRV if more than one sample is selected. Also, the range of the samples can also be changed.

4.2.1.3 REMOVE TREND COMPONENTS OPTION

A disturbing low frequency baseline trend component may sometimes appear in the RR interval time series. The option of detrending can be used for removing these types of trend. Removing of linear trends having order first, second, or third are included in the detrending option along with 'smoothness priors' method. Basically the 'smoothness priors' methodologies could be considered as a time varying high pass filter in which cut-off frequency is approximated by the character Lambda. By editing the lambda values the smoothness criteria of the abolished trend could be approximated. Smoother is the removed trend for bigger the value of Lambda. The trend which is dismissed from the RR interval series is being appeared as a red line over the selected part of the RR interval series.

4.2.2 RESULTS VIEW

In Result view segments the results for selected RR intervals for time and frequency domain and nonlinear methodologies are displayed. By pressing the corresponding option results of each section can be displayed. When we change the setting of analysis the results are by default updated automatically. The time of processing for estimating all the analyzed outcomes results dependent on the ample numbers and lengths. Automatic updating could be disabled by unchecking the 'Auto-refresh results' if it takes too much time for updating of the results.

4.2.2.1 TIME DOMAIN RESULTS

Time domain HRV measures or indices in table along with RR and HR histograms in two axes are displayed in the time domain outcomes. Time domain results viewing have been depicted in Fig.4.3. If detrending is applied most of the findings are estimated from detrended RR intervals data with exceptions of mean of RR and mean of HR visible with asterisk (*) mark. Fixed lower and upper limits values for RR and HR values can be defined in edit box available below the histograms. The histograms according to minimum and maximum values in data are auto-scaled on keeping the edit boxes empty.

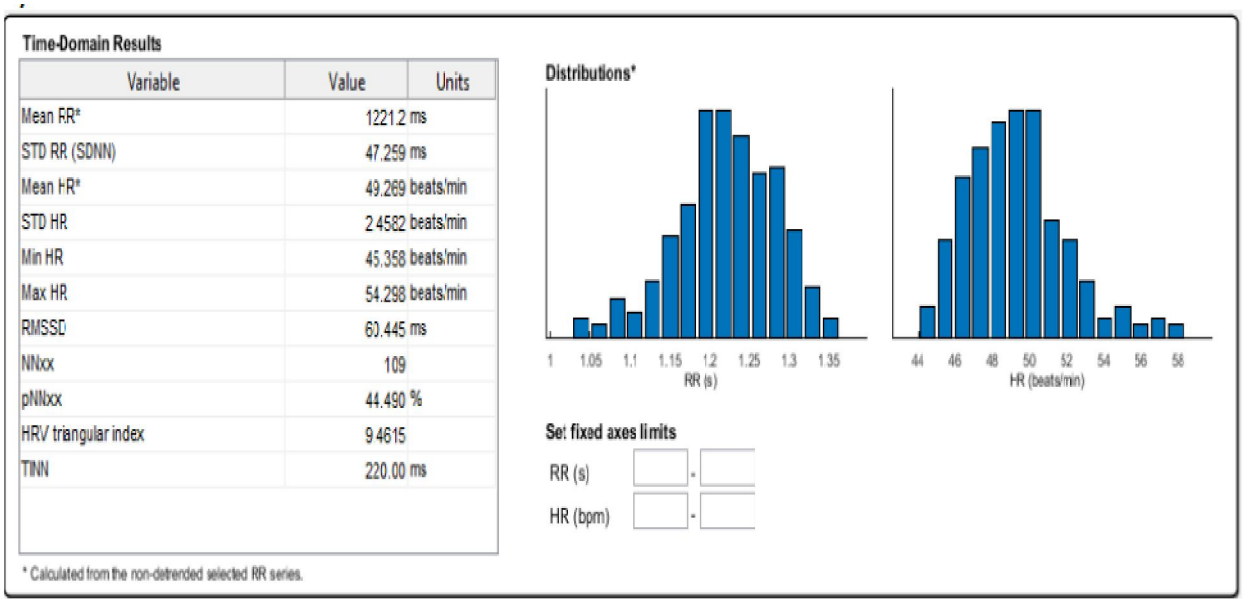


Fig.4.3 Results view segments for time-domain results of Kubios HRV Analysis

4.2.2.2 FREQUENCY DOMAIN RESULTS

The results of HRV measures for both FFT and AR spectrum computation methodologies are displayed in the frequency domain outcomes viewing. Frequency domain results viewing have been shown in Fig.4.4. The frequency axes ranges are 0Hz–0.5 Hz. for the default frequency band settings. Welch's periodogram method for FFT spectrum and AR spectral method has been used for estimation of HRV spectrum in this software.

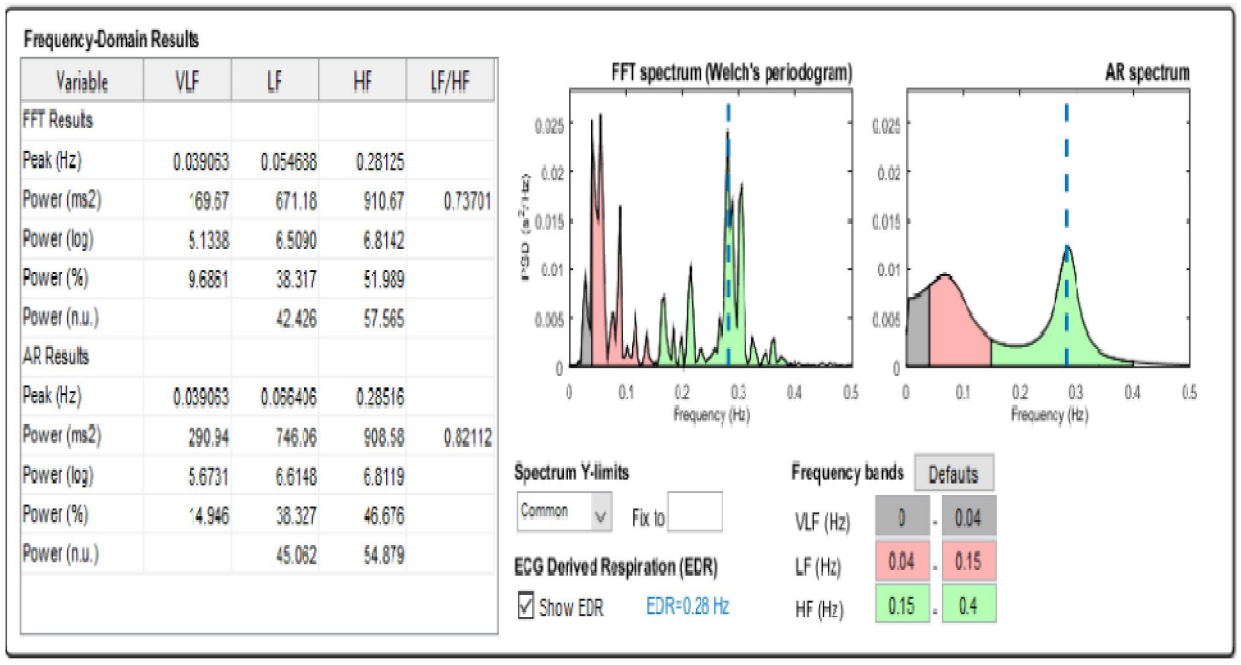


Fig.4.4 Results view segments for frequency-domain results of Kubios HRV Analysis

4.2.2.3 NONLINEAR RESULTS

All the nonlinear measures calculated are displayed in the nonlinear results view. Graphical plots in two axes are also presented for the Poincare plot and detrended fluctuation analysis (DFA) results. The following RR intervals plotting and the SD1 and SD2 measures acquired from the methodology of fitting ellipse are presented in the Poincare plot method where as in DFA plot, the short term and long term fluctuations slopes α1 and α_2 respectively. Poincare plot, approximate and sample entropy, detrended fluctuation analysis, correlation dimension, and recurrence plots measures are analyzed in the nonlinear methods. Nonlinear results view has been shown in Fig.4.5.

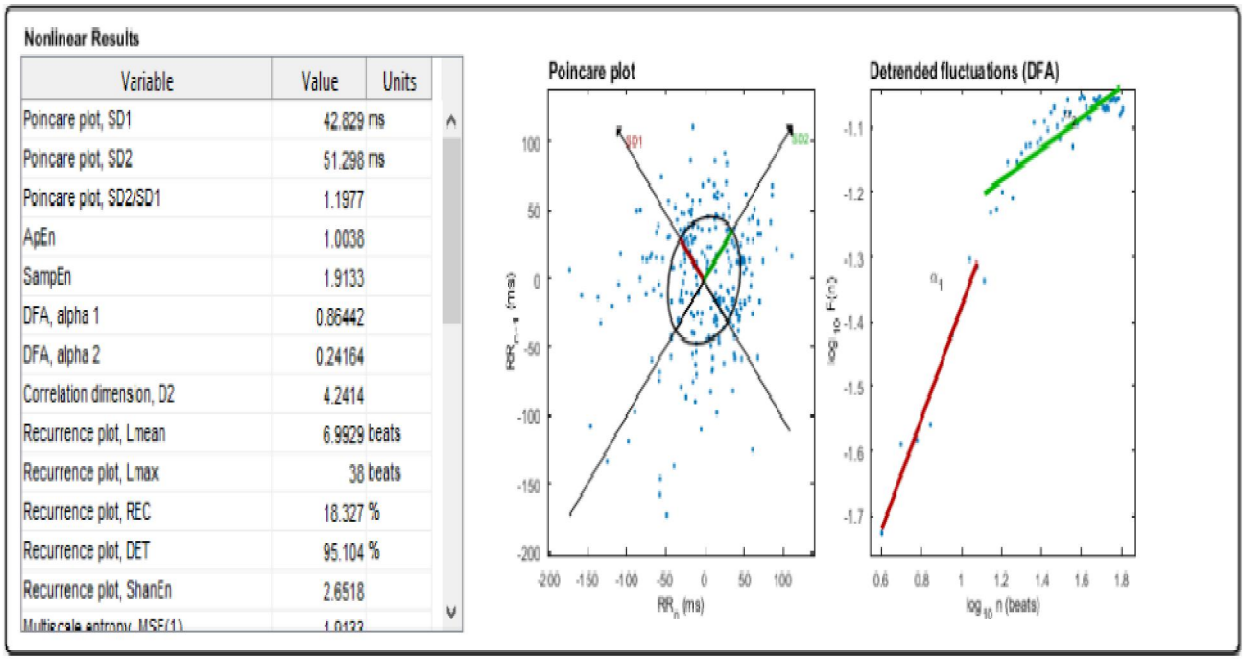


Fig.4.5 Results view segments for frequency-domain results of Kubios HRV Analysis

4.3 SETTING UP THE PREFERENCES

All the options for the analysis which can be approximated in the graphical user interfaces have some pre-selected values and every time when the program is started these preference values are used. Whenever some changes are made on these values in GUI, it applies for the current session only. Sometimes it needed to redefine this preference values. User information, option for analysis, advanced settings, and setting for report are the four categories in which preferences are divided.

4.3.1 USER INFORMATION CATEGORY

In this preference personal as shown in Fig.4.6, the contact information (viz.name, department, and organization) can be set which meant just for pointing out that person who is carrying out the analysis.

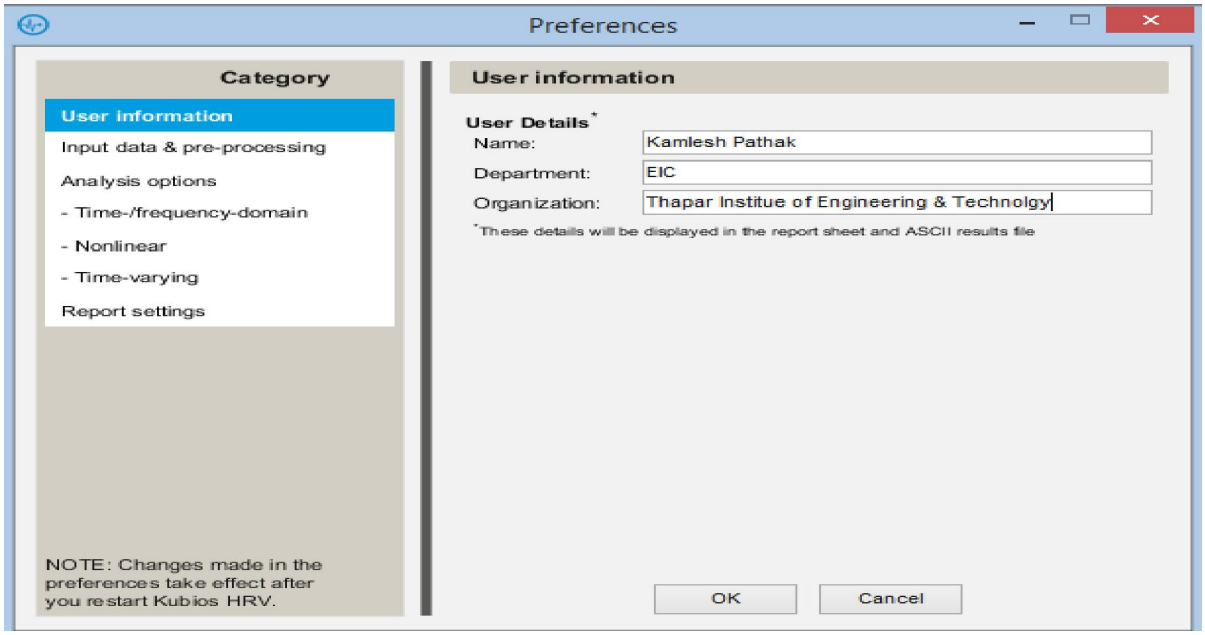
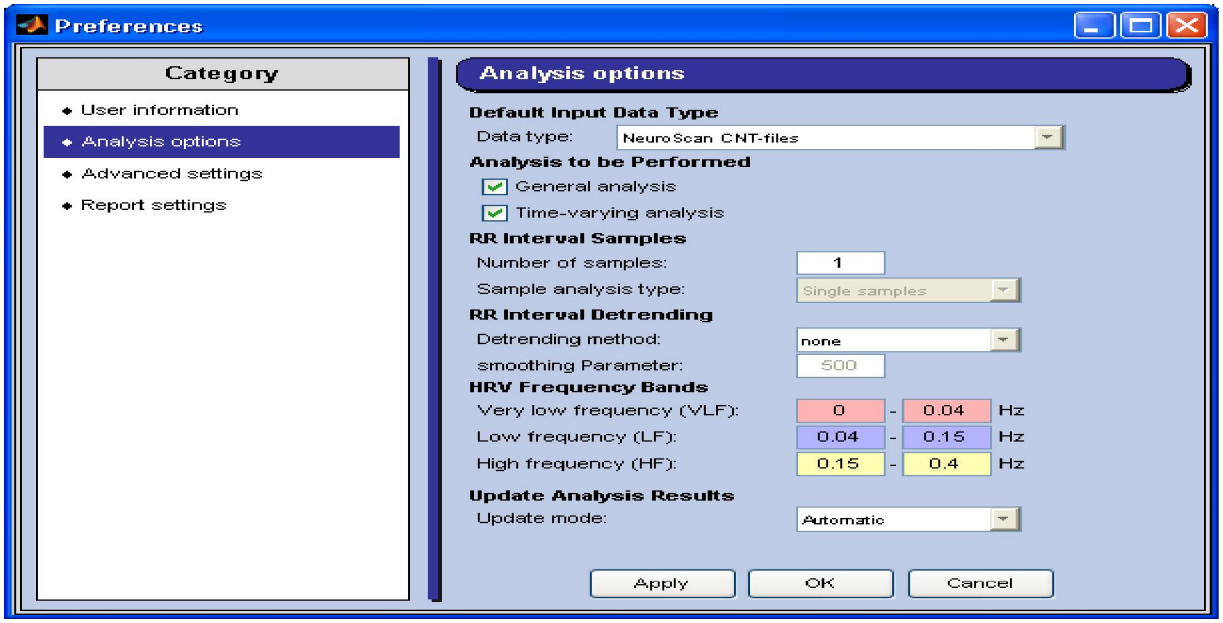


Fig.4.6 Set up preference window for user information category of the software.

4.3.2 ANALYSIS OPTIONS CATEGORY

It includes some basic analysis options such as time domain, frequency domain, and nonlinear analysis and time varying analysis (premium version of software) in which only the selected analysis option will be performed. The Analysis options category has been shown in Fig. 4.7. Additionally, the samples for RR interval, detrending the RR intervals, frequency bands of HRV, and updating analysis outcomes options are included in this analysis options category.



.Fig.4.7 Set up preferences window of the software: Analysis options category.

4.3.3 ADVANCED SETTINGS CATEGORY

This category as depicted in Fig.4.8 comprises the computation options for QRS detection, spectrum estimation, and the time-varying spectrum. The prior guess for the mean RR-interval can be set up in option of QRS detection but this prior guess by default is automatically estimated.

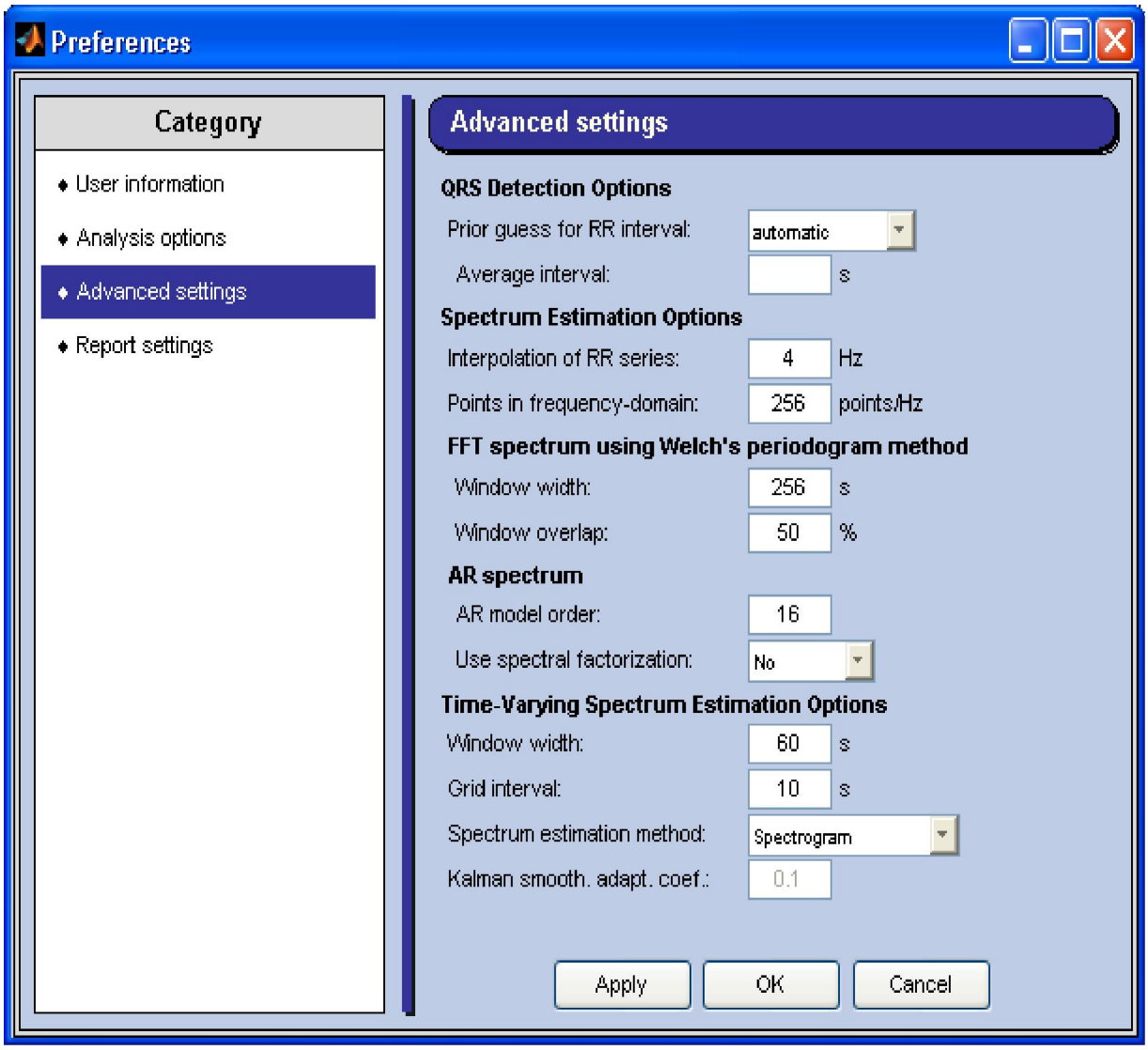


Fig.4.8 Set up preference window for the advanced setting category of the software

4.3.4 THE REPORT SETTINGS CATEGORY

This category as depicted in shown in Fig. 4.9, includes two options i.e. include in report check box and selection of paper size for report generation. By checking the general and time varying results option the content of report sheet can be selected. The size of paper for the report sheet has option to be altered between A4 (210×297 mm) and Letter (8.5×11 inch) size with pre-

selected size of paper is A4. By pressing either the Apply or the OK button all the modifications for the preferences can be saved.

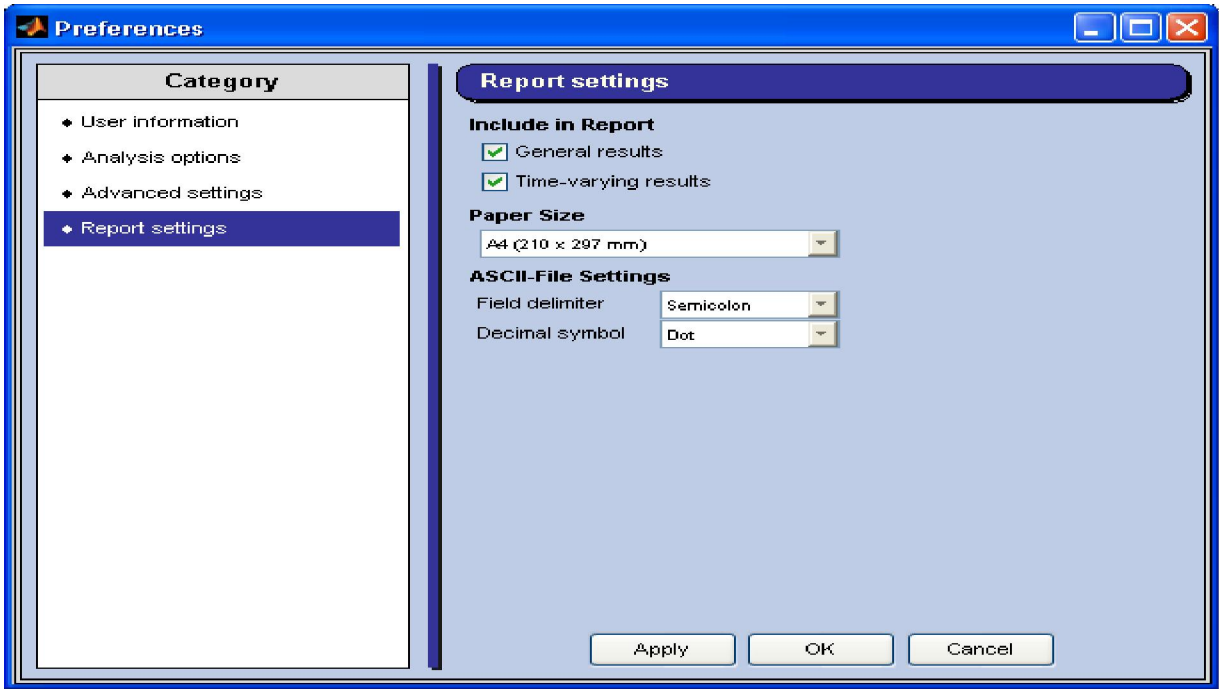


Fig.4.9 Set up preference window for the report setting category of the software

CHAPTER 5

IMPLEMENTATION OF VISIBILITY GRAPH METHOD FOR HRV ANALYSIS

5.1 VISIBILITY GRAPH OVERVIEW

Visibility Graph algorithms belongs to the family of methods which maps time series into networks[10]. The main purpose of visibility graph algorithm is to describe and extract the information regarding the structure of time series, its local states in different time intervals, which are embedded in the segments and their dynamical properties in the graph-theoretical terms[19]. This can be considered a beneficial way to explore the dynamics of heart rate variability by transforming it into the complex networks in which nodes constitute dynamic units and the interaction between the nodes are represented by the edges.

Heart beat interval (IBI) time series can provide information through which several heart diseases can be predicted[39]. We can compute a general class of predictors that could be used for augmenting the previous investigated features used in the analysis of HRV and which shows high predictive power for various types of heart disease solely based on the visibility graph. The statistical significance of the network measures and predictors along with their competitive performances to popularly known indices of statistical, geometric and non-linear methodologies will be estimated. Visibility-graph (VG) algorithm was presented by Lacasa et al. (2008) as a fast estimation methodology for this transformation and demonstrated that several non linear features and measures can be inherited through the visibility graph approach and some of the inherent properties can be estimated through the network measures[34]. A schematic diagram for analysis of HRV data using visibility graph has been shown in Fig.5.1.

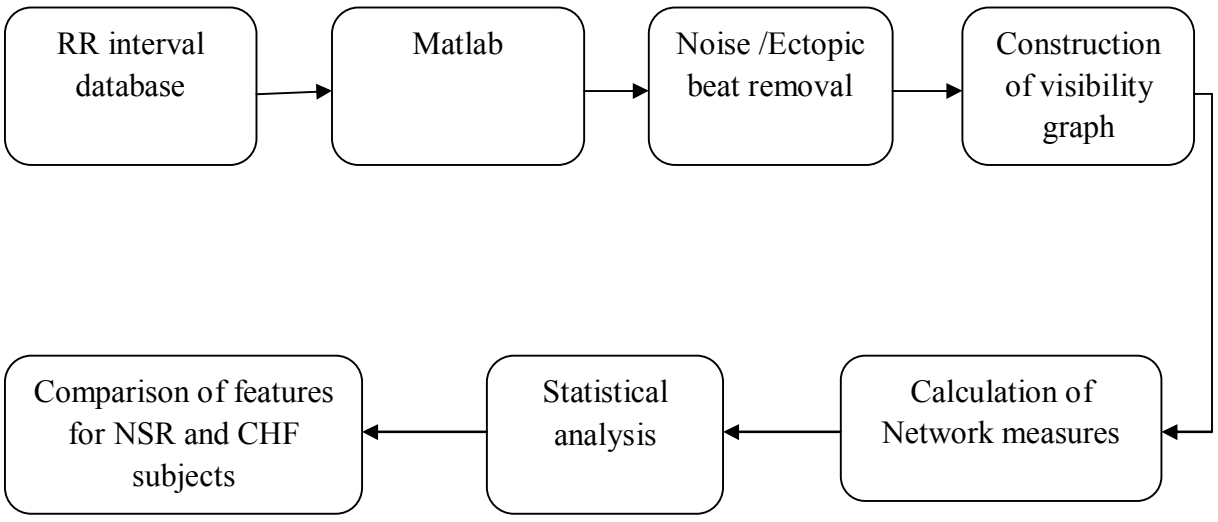


Fig.5.1 Schematic diagram for HRV analysis using visibility graph

5.2 CONSTRUCTION OF VISIBILITY GRAPH

Consider the time series of RR intervals having N points $\{x(i) : 1 \leq i \leq N\}$, then the algorithm for visibility graph (VG) could be described as below. Firstly, take every data points as it is in the same order, in network graph as a corresponding node. For two arbitrary data x(i) and x(j), the criteria to exist the visibility between them is the fulfillment of the following condition.

$$x(l) < x(j) - (j-l)\frac{x(j)-x(i)}{j-i}, \forall l \in (i,j) \tag{5.1}$$

The unweighted and undirected network graph having N nodes is formed by using the visibility criterion. Example of the time series of RR intervals having 20 data points have been shown in Fig.5.2 in which solid lines depicts the visibility criteria. Since the visibility criteria is fulfilled the stem 4 can be perceived from stems 5 and 6 while no visibility exists between stem 14 and 16 because the sight is impeded by stem number 15. The associated graph which is obtained from time series in the Fig.5.2 has been shown in Fig.5.3 using the VG algorithm.

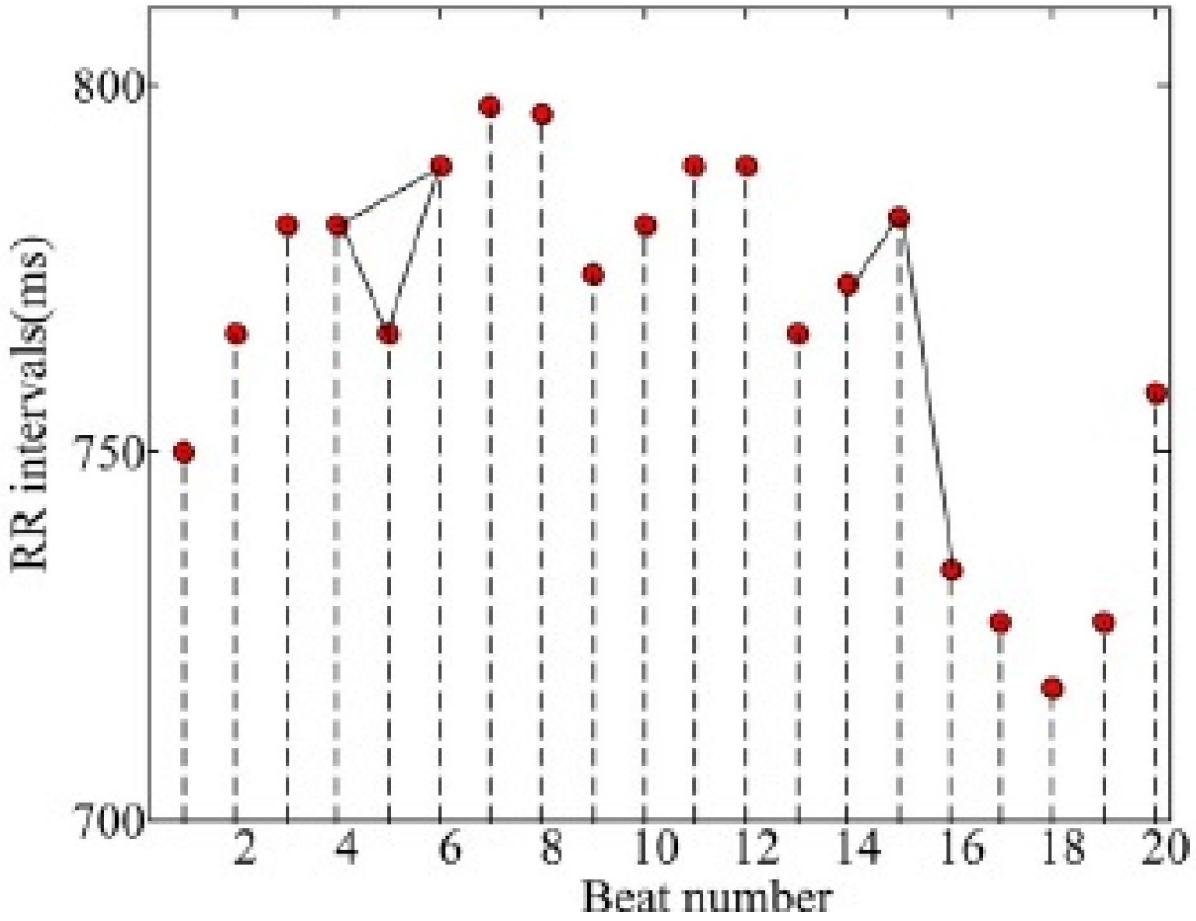


Fig.5.2 Example of the RR-intervals time series having 20 data points[35]

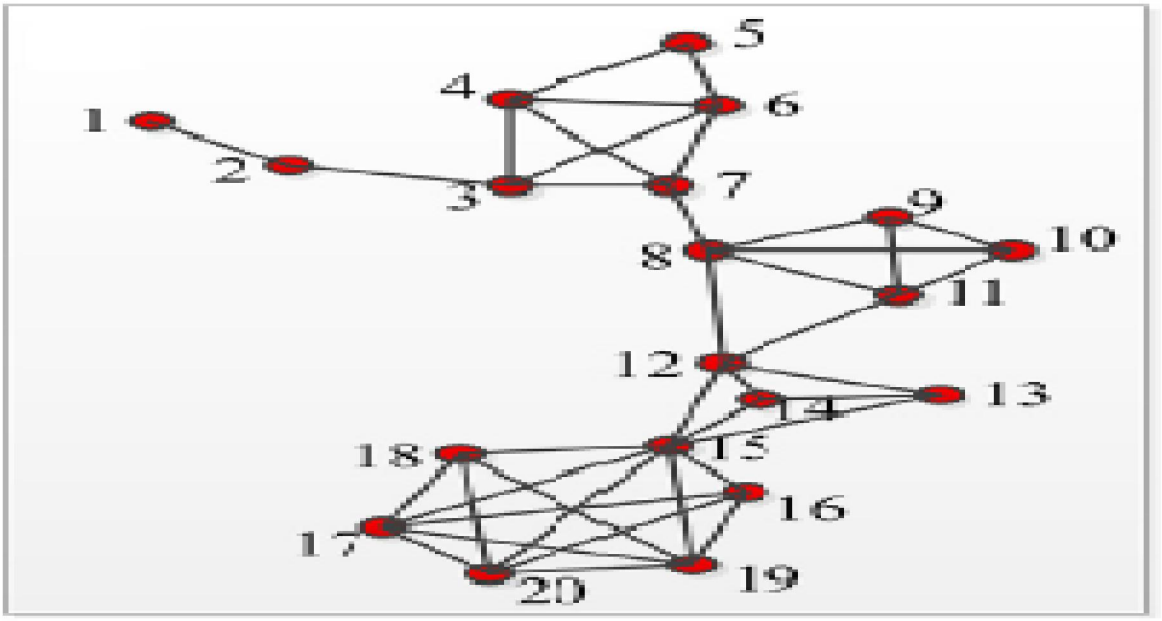


Fig.5.3 The associated graph extracted from time series using the Visibility Graph algorithm [35]

5.3 ESTIMATION OF NETWORK MEASURES

Mainly the network measures such as characteristic path length, clustering coefficient, average degree and entropy of the degree distribution were estimated for each graph.

(i) Characteristic path length (L): It is an estimation of the typical distinction between two nodes in the visibility graph. Characteristic path length (L) is stated as the mean shortest path length considered for all couple of nodes and given as:

$$L = \frac{1}{N \times (N-1)} \sum_{i,j \in v, i \neq j} d_{ij} \tag{5.2}$$

Here, 'v' represents the set of N nodes in the graph, and d_{ij} indicate the shortest path length between the nodes i and j.

For an undirected and unweighted graph, d_{ij} can be defined as the numbers of edges (edges are the interactions between nodes) in the corresponding path. Characteristic path length characterizes the network's internal structure and a well established measure for complex network since shortest path in a network provides easier transport and communication.

(ii) Clustering coefficient (C): It is stated as the evaluating the average of the local clustering coefficient (C_i which expresses to what extent or degree the neighbors of a node will know each other) of each node in the graph. Local clustering coefficient is calculated as: e_i (counting the actual numbers of edges between all the couples of neighbors of node i) / Maximal possible

number of edges between all the k_i neighbors of node i. Hence, the clustering coefficient (C) is estimated as:

$$C = \frac{1}{N} \times \sum_{i \in v} C_i = \frac{1}{N} \times \sum_{i \in v} \frac{e_i}{k_i \times (k_i - 1)} \tag{5.3}$$

The clustering coefficient may be used for determining the extent of a graph to which it is a small world network. To reach any vertex from any other vertex in lesser number of steps is permitted by the small world network.

(iii) Average degree (D_A): The degree of a node is defined as the number of edges (interaction between the nodes) which are incident with the other nodes in a graph. By taking the mean of all nodes in a graph average degree can be evaluated.

(iv) Degree distribution denoted as P (k): The degree distribution of whole networks is stated as the fraction of nodes with degree k in the network graph which is formed from the time series. Hence, P (k) = n_k/n, if there are a total of 'n' nodes the network and out of which ' n_k' of them having degree k.

(v)Entropy of degree distribution (E_{DD}): It is used for quantifying the degree distributions shape and can be evaluated as:

$$E_{DD} = -\sum_{i=0}^{Max(k)} p_i(k) \times \log\, p_i(k) \tag{5.4}$$

Here, p (k) is the fraction of the nodes having degree k in the network graph and max (k) denotes maximal of k. Entropy of degree distribution is similar to the Shannon entropy. A larger value of E_{DD} is contributed by the more uniform probability distribution as well as a wider region of k[34].

5.4 MATERIALS AND METHODS

Physionet database is well acknowledged and characterized digital recordings for physiological signals and related sampled data which is used for validation of developed methodologies by the community of biomedical research worldwide. The Physio-bank includes normal sinus rhythm RR interval datasets and congestive heart failure RR intervals datasets which have been used in dissertation work.

5.4.1 Normal Sinus Rhythm (NSR) RR Interval Datasets:

These databases comprise beat annotation files for 54 long-term ECG recordings of subjects in normal sinus rhythm (30 men, aged 28.5 to 76, and 24 women, aged 58 to 73). The original ECG

recordings (not available) have been digitized at 128 samples per second, and the beat annotations have been achieved by automated analysis with manual review and correction [52].

5.4.2 Congestive Heart Failure (CHF) RR Interval Datasets:

These databases comprises beat annotation files for 29 long-term ECG recordings of subjects with congestive heart failure (NYHA classes I, II, and III) which are aged 34 to 79. Subjects included 8 men and 2 women; and for the remaining 21 subjects gender is not known. The original ECG recordings (not available) have been digitized at 128 samples per second, and the beat annotations have been achieved by automated analysis with manual review and correction [53].

5.5 STEPS FOR VISIBILITY GRAPH ALGORITHM

Step 1: Import file to read the HRV signal.

Step 2: Remove noise from HRV signal.

Step 3: Selecting scale for division of data points within a long time recordings.

Step 4: Getting the list of nodes for varying representation based on graph structure (matrix or cell).

Step 5: Specify graph edges (s, t) in node pairs using G=graph(s, t), where s and t could be numeric, character vectors, or cell arrays of character vectors with the same number of elements.

Step 6: Generate graph vectors using nodes and edges.

Steps 7: Plot the graph.

Steps 8: Convert the graph into adjacency matrix.

Steps 9: Calculation of the network measures.

Steps 10: Statistical analysis on network measures calculated.

5.5.1 ADJACENCY MATRIX

An adjacency matrix is a square matrix which is used for representing a finite graph in graph theory and computer science. The adjacency matrix is a square $|V| \times |V|$ matrix 'A' for a simple graph with vertex set V having its element A_{ij} value equals to one (1) if an edge exists from vertex i to vertex j while zero (0) if no edge is present. Since the edges from a vertex to itself (loops) are not allowed in simple graphs, all the diagonal elements of the matrix are zero. Whether the pair of vertices is adjacent or not in the graph is indicated by the elements of the matrix. An edge between two nodes is specified by the location of each nonzero entry in A such that the value of that entry represents the edge weight. Self-loops or nodes which are joined

together to themselves with an edge may exist if the diagonal element or entry is having nonzero value. For ignoring the diagonal entries use the 'Omit Self Loops' input option [57].

5.6 DATA ANALYSIS

Statistical hypothesis testing can be considered to act as a filter regarding statistical conclusions and method for making decisions for significance of data. It helps in justifying conclusions from statistical point of views and can conclude that the research hypothesis has been supported by the dataset. If a result has been predicted as unlikely to have occurred by chance alone as per a significance level the result is called statistically significant. Statistician Ronald Fisher coined the phrase 'test of significance'.

5.6.1 T-TEST

T-test is used for testing the hypothesis for deciding if we should support or reject a null hypothesis. It enables for deciding if the mean of one condition is really different from the mean of another condition [55]. Larger the difference in the two sample, larger the t-value. The t-test can be used for determining if the two sets of data are distinct significantly from each other [56]. The t-test has been classified as:

(i) Dependent means t-test: This is used when the same subjects take part in both the condition of experiment. This test is also called as **matched-pairs** t-test or **repeated measures** t-test.

(ii) Independent means t-test: This test is used when there are two different groups of subjects and each group is performing different conditions in the experiment. This test is also called as **independent measures** t-test. It has been further classified in equal variance and unequal variance t-tests.

- The "two-sample assuming equal variances'' t-test: This can be used when we know that the variances are the same (either through the question or by analyzing the variance in the data)
- The "two-sample assuming unequal variances'' t-test: This can be used when we know that either the variances are not the same or don't know if the variances are the same or not.

5.6.2 F-TEST

F-test is the statistical test in which the test statistic comprises F-distribution (a continuous probabilistic distributions which arises frequently as the null distribution of a test statistic) under the null hypothesis and most often used for comparison of statistical models which has been fitted to a data set for identifying the model best fitted to the population from which the data had been sampled. George W. Snedecor, in honour of Sir Ronald A. Fisher coined the name F-test [54]. Generally F-test is used for comparing two variances. The equation for comparison of two variances using F-test is given as:

$$F = \frac{s_1^2}{s_2^2} \tag{5.5}$$

Where, s_1 and s_2 is the standard deviations for sample 1 and sample2.

CHAPTER 6

RESULTS AND DISCUSSIONS

6.1 HRV ANALYSIS RESULTS USING VISIBILITY GRAPH

We evaluated the network measures such as average clustering coefficient (acc), characteristic path length (cpl), and standard deviation of shortest path length (cpl std) from the network graphs which has been constructed from the RR-interval segments over long term ECG recordings. All these network measures have been estimated on the normal sinus rhythm RR interval datasets and congestive heart failure RR interval datasets segmented on the scale of different data points. Statistical measures have been estimated using two samples F-test. Mean, variance and P-value hence obtained are shown in the table 6.1-table 6.12 for different scale of data points.

(i) Statistical results using F-test two sample for variance on the scale of 500 data points

Table 6.1 Statistical measures for average clustering coefficient

Average clustering coefficient (acc)		
Variables	CHF	NSR
Mean	0.742539546	0.742506057
Variance	0.000420184	0.000217139
P value	1.91034E-06	

Table 6.2 Statistical measures for characteristic path length

Characteristic path length (cpl)		
Variables	CHF	NSR
Mean	3.287890849	3.331571436
Variance	0.182208622	0.256087254
P value	0.008242721	

Table 6.3 Statistical measures for standard deviation of shortest path length

Standard deviation of shortest path length (Cpl std)

Variables	CHF	NSR
Mean	1.275566828	1.270408973
Variance	0.083401584	0.149715125
P value	2.03909E-05	

(ii) Statistical results using F-test two sample for variance on the scale of 1000 data points

Table 6.4 Statistical measures for average clustering coefficient

Average clustering coefficient (acc)		
Variables	CHF	NSR
Mean	0.745128877	0.739998846
Variance	0.000346953	0.000157796
P value	5.20991E-05	

Table 6.5 Statistical measures for characteristic path length

Characteristic path length (cpl)		
Variables	CHF	NSR
Mean	3.286840684	3.436267627
Variance	0.172550711	0.250270068
P value	0.032206032	

Table 6.6 Statistical measures for standard deviation of shortest path length

Standard deviation of shortest path length (Cpl std)		
Variables	CHF	NSR
mean	1.2802172	1.326950362
variance	0.082873641	0.173070036
P value	0.000140326	

(iii) Statistical results using F-test two sample for variance on the scale of 1500 data points

Table 6.7 statistical measures for average clustering coefficient

Average clustering coefficient (acc)		
Variables	CHF	NSR
Mean	0.742653825	0.739961433
Variance	0.000313731	0.000142199
P value	0.000851312	

Table 6.8 Statistical measures for characteristic path length

Characteristic path length (cpl)		
Variables	CHF	NSR
Mean	3.261267218	3.471665136
Variance	0.197171086	0.262677163
P value	0.125082543	

Table 6.9 Statistical measures for standard deviation of shortest path length

Standard deviation of shortest path length (Cpl std)		
Variables	CHF	NSR
Mean	1.274357969	1.326237557
Variance	0.086673939	0.15482166
P value	0.010344967	

(iv) Statistical results using F-test two sample for variance on the scale of 2000 data points

Table 6.10 Statistical measures for average clustering coefficient

Average clustering coefficient (acc)		
Variables	CHF	NSR
Mean	0.740599914	0.74039966

Variance	0.0003374	0.000135605
P value	0.000805608	

Table 6.11 Statistical measures for characteristic path length

Characteristic path length (cpl)		
Variables	CHF	NSR
Mean	3.310750644	3.387728263
Variance	0.190721094	0.202194597
P value	0.418592361	

Table 6.12 Statistical measures for standard deviation of shortest path length

Standard deviation of shortest path length (Cpl std)		
Variables	CHF	NSR
Mean	1.30960959	1.270900504
Variance	0.083587238	0.115269187
P value	0.129623179	

All the network measures estimated from RR interval segment showed statistically significant result between the subjects having normal sinus rhythm and congestive heart failure(CHF) on different scale of data points except the characteristic path length (cpl) on scale of 1500 data points and cpl, and standard deviation of shortest path length (cpl-std) on 2000 data points.

Characteristic path length (cpl) which is the measure of typical separation between two nodes, was found to be more in normal sinus rhythm subjects and decreased in subjects having congestive heart failure while average clustering coefficient (used for determining the extent of a graph to which it is a small world network. Reaching any vertex from any other vertex by using very less number of steps is allowed by small world network) has increased value in case of congestive heart failure patients. One of the associated graphs for congestive heart failure and normal sinus rhythm subject has been shown in Fig. 6.1 and Fig.6.2.

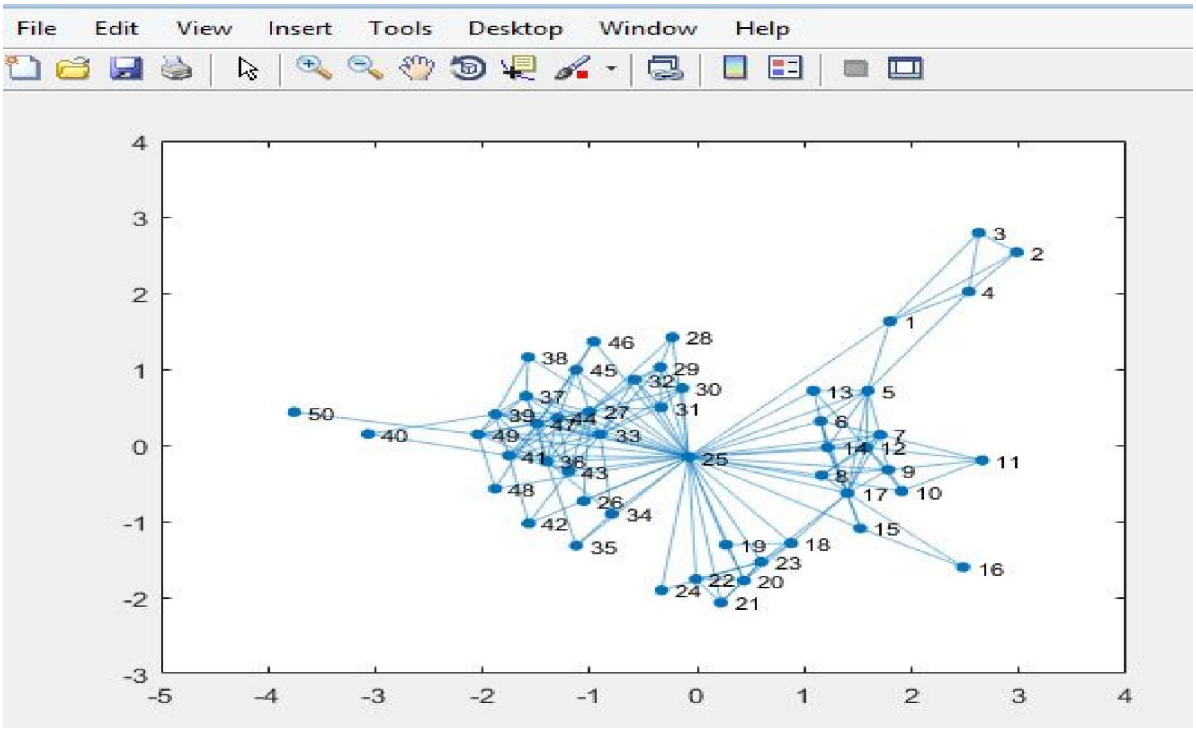


Fig.6.1 Associated network graph for chf2db/chf204 RR interval data

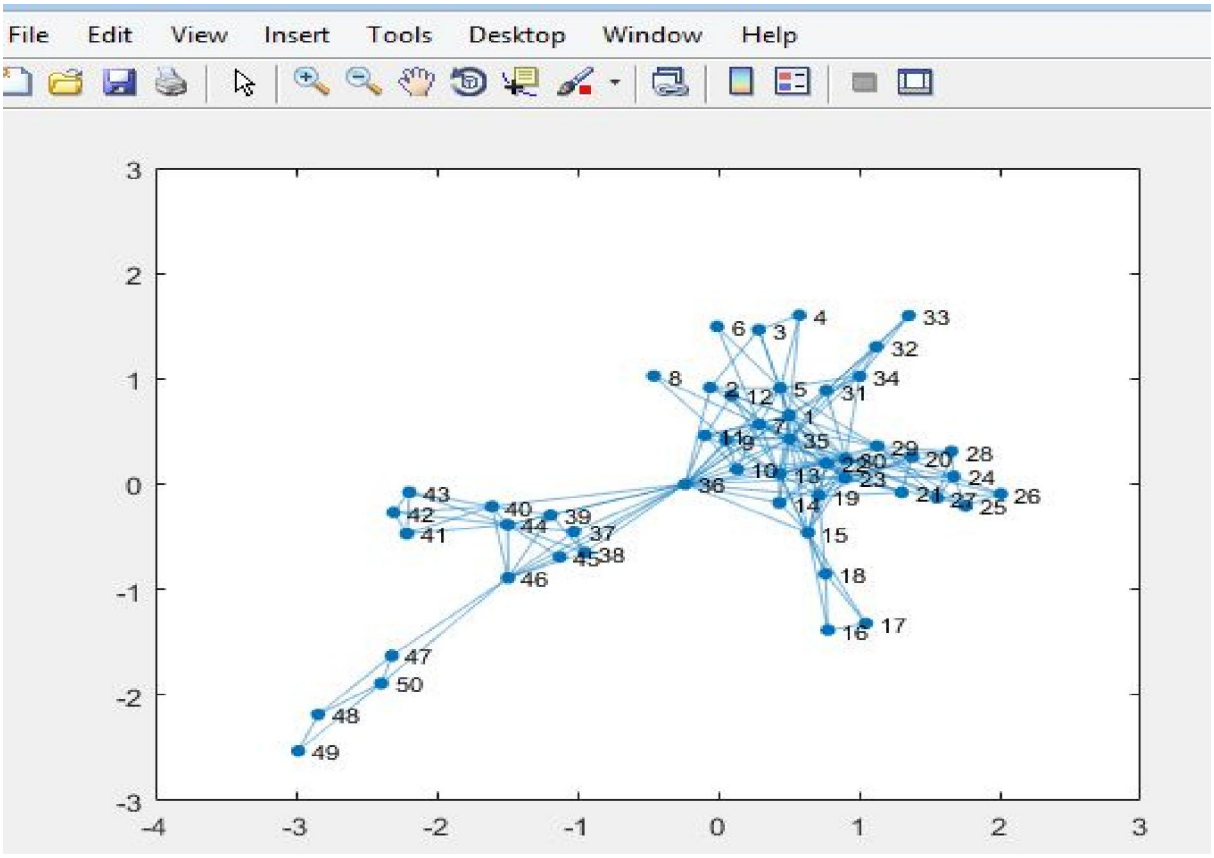


Fig.6.2 Associated network graph for nsr2db/nsr004 RR interval data

6.2 HRV MEASURES USING KUBIOS SOFTWARE

Most of the HRV measures were found to show statistically significant results for the Congestive Heart Failure and the Normal Sinus Rhythm subjects except the peak (LF, and HF), LF and HF power in n.u. and mean HR. The HRV analysis results for time domain, frequency domain and Poincare plot for CHF and NSR database are shown in Table 6.13. Statistics are presented as mean and variance using F-test for Congestive Heart Failure (CHF) and the Normal Sinus Rhythm (NSR) datasets.

Table 6.13 HRV analysis results for time domain frequency domain and Poincare plot

Time domain indices						
Variables	Units	Sig.	CHF		NSR	
			Mean	Variance	Mean	Variance
Mean RR	ms	s	666.8964	10121.9314	714.5428	18692.9906
Mean HR	beats/min	n.s.	91.9575	194.1065	87.15107	317.32011
STDRR (SDNN)	ms	s	0.2857	0.2508	0.4928	3.55624
RMSSD	ms	s	0.310714	0.2595	0.50714	3.54661
Frequency domain results						
VLF (peak)	Hz	s	0.006457143	7.95132E-07	0.006439286	6.55655E-06
LF (peak)	Hz	n.s.	0.042260714	1.07743E-05	0.041185714	5.92497E-06
HF (peak)	Hz	n.s.	0.152846429	7.19517E-06	0.151896429	6.92925E-06
LF/HF power ratio		n.s	8097.509393	1760926.224	8199.029821	1232412.994
Poincare plot measures						
SD1	ms	s	0.221428571	0.148412698	0.375	1.958240741
SD2	ms	s	0.192857143	0.145873016	0.371428571	1.95989418
SD2/SD1		s	0.8455	0.039936481	0.912142857	0.013573683
s=significant, n.s= not significant						

Statistically significant time domain measures as per mean values were found to be lower in CHF as compared to NSR. Frequency domain indices LF/HF power ratio was lower in CHF. For nonlinear analysis using Poincare plot showed lower values of SD1 and SD2 in CHF and higher value of SD1 and SD2 in NSR while SD2/SD1 ratio was found to be higher in NSR as compared to CHF.

Time domain analysis results have shown an increment of HR and reduction of HRV in CHF as compared to NSR and hence, a higher heart rate in combination of lower HRV is a well known indicator of (acute) stress.

CHAPTER 7

CONCLUSION AND FUTURE SCOPE

7.1 CONCLUSIONS

The main focus of this dissertation work is the implementation of the visibility graph method and calculation of network measures which can be obtained from the network graph constructed from RR interval segments over long term ECG recordings. Time domain, frequency domain and nonlinear methodologies for HRV analysis have been studied and reviewed. We evaluated mainly three network measures such as Characteristic Path Length (CPL), Average Clustering Coefficient (ACC), and Standard Deviation of the Shortest Path Length (CPL-STD) of the network graph constructed from the RR interval segment on scale of different data points for congestive heart failure (CHF) and normal sinus rhythm (NSR) database. Time domain, frequency domain and Poincare plot measures for HRV was analyzed using Kubios HRV analysis software. These are the following conclusions obtained from the analysis results:

- All the network measures estimated from RR interval segment showed statistically significant result between Normal Sinus Rhythm and Congestive Heart Failure subjects on different scale of data points except the Characteristic Path Length (CPL) on scale of 1500 data points and cpl, and Standard Deviation of Shortest Path Length (CPL-STD) on 2000 data points.
- Characteristic Path Length (CPL) was found to be more in normal sinus rhythm subjects and decreased in congestive heart failure subjects while Average Clustering Coefficient has increased value in case of congestive heart failure patients.
- Statistically significant time domain measures were found to be lower in CHF as compared to NSR. Frequency domain measure LF/HF ratio was lower in CHF. For nonlinear analysis using Poincare plot showed lower values of SD1 and SD2 in CHF and higher value of SD1 and SD2 in NSR while SD2/SD1 ratio was found to be higher in NSR as compared to CHF.
- Time domain analysis results have shown an increase of HR and reduction of HRV in CHF as compared to NSR and hence, a higher heart rate in combination of lower HRV is a well known indicator of (acute) stress.

7.2 FUTURE SCOPE

This research work has been carried out using the Phisionet database for CHF and NSR subjects. Applying this work directly on real time subjects and recordings may lead to improved diagnosis decision based on HRV. More statistically significant network measures may be explored and investigated which can provide better information from time series.

REFERENCES

[1] Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology,"Guidelines Heart rate variability ," European Heart Journal,17, pp. 354–381, 1996.

[2] R. K. Dishman, Y. Nakamura, M. E. Garcia, R. W. Thompson, A. L. Dunn, and S. N. Blair, "Heart rate variability , trait anxiety , and perceived stress among physically fit men and women," pp. 121–123, 2000.

[3] "HRV Analysis under the usage of different electrocardiography systems (Methodical recommendations)," 2002.

[4] G. D. Clifford and S. C. College, "Signal Processing Methods for Heart Rate Variability," University of Oxford,2002.

[5] J. Niskanen, M. P. Tarvainen, P. O. Ranta-aho, and P. A. Karjalainen, "Software for advanced HRV analysis," pp. 73–81, 2004.

[6] J. A. Healey and R. W. Picard, "Detecting stress during real-world driving tasks using physiological sensors," *IEEE Transactions on Intelligent Transportation Systems*, vol. 6, no. 2, pp. 156–166, 2005.

[7] M. Kumar, M. Weippert, R. Vilbrandt, S. Kreuzfeld, and R. Stoll, "Fuzzy Evaluation of Heart Rate Signals for Mental Stress Assessment," vol. 15, no. 5, pp. 791–808, 2007.

[8] R. Schneider, "Correlations between the Poincaré Plot and Conventional Heart Rate Variability Parameters Assessed during Paced Breathing," no. March 2007.

[9] L. Salahuddin, M. G. Jeong, and D. Kim, "Dependence of Heart Rate Variability on Stress Factors of Stress Response Inventory My ~ feelt," pp. 236–239, 2007.

[10] L. Lacasa, B. Luque, F. Ballesteros, J. Luque, and J. C. Nun, "From time series to complex networks : The visibility graph," 2008.

[11] J. Taelman, S. Vandeput, A. Spaepen, and S. Van Huffel, "Influence of Mental Stress on Heart Rate and Heart Rate Variability," *IFMBE Proceedings*, vol. 22, pp. 1366–1369, 2008.

[12] J. Choi and R. Gutierrez-osuna, "Using Heart Rate Monitors to Detect Mental Stress - bsn09_choi," no.13, May, pp. 221–225, 2009.

[13] C. Schubert, M. Lambertz, R. A. Nelesen, and W. Bardwell, "Effects of stress on heart rate complexity—A comparison between short-term and chronic stress," *Entropy*, vol. 17, no. 3, pp. 325–332, 2009.

[14] J. F. Thayer, S. S. Yamamoto, and J. F. Brosschot, "The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors," *International*

Journal of Cardiology, vol. 141, no. 2, pp. 122–131, 2010.

[15] R. Bail, M. Orini, P. Laguna, S. Member, and O. Meste, "With Time-Varying Threshold : Application to Heart Rate Variability Analysis During Exercise Stress Testing," vol. 58, no. 3, pp. 642–652, 2011.

[16] S. Boonnithi, S. Phongsuphap, and L. Vlf, "Comparison of Heart Rate Variability Measures for Mental Stress Detection," pp. 85–88, 2011.

[17] K. Yoshino and K. Matsuoka, "Correlation between mood and heart rate variability indices during daily life," *Health*, vol. 03, no. 09, pp. 553–556, 2011.

[18] J. Choi and R. Gutierrez-Osuna, "Removal of respiratory influences from heart rate variability in stress monitoring," *IEEE Sensors Journal*, vol. 11, no. 11, pp. 2649–2656, 2011.

[19] R. Article, L. Lacasa, and B. Luque, "Time series irreversibility : a visibility graph approach," 2012.

[20] H. Costin, C. Rotariu, and A. Păsărică, "Mental Stress Detection using Heart Rate Variability and Morphologic Variability of ECG Signals," *2012 International Conference and Exposition on Electrical and Power Engineering (EPE 2012)*, no. Epe, pp. 591–596, 2012.

[21] C. H. Hsu *et al.*, "Poincaré plot indexes of heart rate variability detect dynamic autonomic modulation during general anesthesia induction," *Acta Anaesthesiologica Taiwanica*, vol. 50, no. 1, pp. 12–18, 2012.

[22] J. Choi, B. Ahmed, and R. Gutierrez-Osuna, "Development and evaluation of an ambulatory stress monitor based on wearable sensors bt - special issue of emerging technologies for patient-specific healthcare," *IEEE Transactions on Information Technology in Biomedicine*, vol. 16, no. 2, pp. 279–286, 2012.

[23] H. C. Duc, H. P. Manh, T. N. Duc, and D. N. Viet, "Detecting Congestive Heart Rate Variability Failure Using Pointcaré Trend Analysis Plot," *International Journal of Bioscience, Biochemistry and Bioinformatics*, vol. 3, no. 6, pp. 566–569, 2013.

[24] P. Karthikeyan, M. Murugappan, and S. Yaacob, "Detection of Human Stress Using Short-Term Ecg and Hrv Signals," *Journal of Mechanics in Medicine and Biology*, vol. 13, no. 02, p. 1350038, 2013.

[25] D. Liu and M. Ulrich, "Listen to Your Heart: Stress Prediction Using Consumer Heart Rate Sensors," *Cs229.Stanford.Edu*, 2014.

[26] M. G. Poddar, V. Kumar, and Y. P. Sharma, "Heart rate variability based classification of normal and hypertension cases by linear-nonlinear method," *Defence Science Journal*, vol. 64, no. 6, pp. 542–548, 2014.

[27] G. D'Addio *et al.*, "Fractal behavior of heart rate variability during ECG stress test in cardiac patients," *2014 8th Conference of the European Study Group on Cardiovascular*

Oscillations, ESGCO 2014, no. Esgco, pp. 155–156, 2014.

[28] Mandeep Singh, "Introduction to Biomedical Instrumentation' PHI, Second Edition,2014.

[29] D. H. Patil, G. Kumari, P. Daware, V. Shinde, and A. P. Raina, "Stress Detection by Measuring Heart Rate Variability," no. April, pp. 2083–2089, 2015.

[30] L. Zhang *et al.*, "Automatic recognition of cardiac arrhythmias based on the geometric patterns of poincaré plots," *Physiological Measurement*, vol. 36, no. 2, pp. 283–301, 2015.

[31] M. Bernat and Z. Piotrowski, "Software Tool for the Analysis of Components Characteristic for ECG Signal," pp. 4–9, 2015.

[32] I. Journal *et al.*, "Mental Stress Evaluation using Heart Rate Variability Analysis : A Review," vol. 2, no. 1, pp. 10–16, 2015.

[33] M. Salai, I. Vassányi, and I. Kósa, "Stress Detection Using Low Cost Heart Rate Sensors," vol. 2016, no. i, pp. 1–12, 2016.

[34] D. Bassett, N. Bear, D. Nutt, S. Hood, S. Bassett, and D. Hans, "Reduced heart rate variability in remitted bipolar disorder and recurrent depression," *Australian and New Zealand Journal of Psychiatry*, vol. 50, no. 8, pp. 793–804, 2016.

[35] F. Z. Hou, F. W. Li, J. Wang, and F. R. Yan, "Visibility graph analysis of very short-term heart rate variability during sleep," vol. 458, pp. 140–145, 2016.

[36] A. Bhaduri and D. Ghosh, "Quantitative Assessment of Heart Rate Dynamics during Meditation : An ECG Based Study with Multi-Fractality and Visibility Graph," vol. 7, no. February, pp. 1–10, 2016.

[37] M. K. Moridani, S. K. Setarehdan, A. Motie, and E. Hajinasrollah, "Non-linear feature extraction from HRV signal for mortality prediction of ICU cardiovascular patient," vol. 1902, no. April, 2016.

[38] R. Castaldo, W. Xu, P. Melillo, L. Pecchia, L. Santamaria, and C. James, "Detection of mental stress due to oral academic examination via ultra-short-term HRV analysis," *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*, vol. 2016–Octob, pp. 3805–3808, 2016.

[39] T. Madl, "Network analysis of heart beat intervals using horizontal visibility graphs," pp. 733–736, 2016.

[40] B. Hwang, J. W. Ryu, C. Park, and B. Zhang, "A Novel Method to Monitor Human Stress States using Ultra- Short-Term ECG Spectral Feature," no. 12, pp. 2381–2384, 2017.

[41] N. Bu, "Stress Evaluation Index based on Poincar ´ e Plot for Wearable Health Devices," pp. 0–5, 2017.

[42] S. Sannino, S. Stramaglia, L. Lacasa, and D. Marinazzo, "Visibility graphs for fMRI data : Multiplex temporal graphs and their modulations across resting-state networks," pp. 1–14, 2017.

[43] S. A. Priya, R. Rajalakshmi, and Y. V. Vageesh, "Effect of acute mental stress on heart rate variability in obese adults – A comparative study," *Indian Journal of Physiology and Pharmacology*, vol. 61, no. 4, pp. 357–360, 2017.

[44] M. Saidi, H. Hassanpoor, and A. A. Lari, "Proposed new signal for real-time stress monitoring : Combination of physiological measures," vol. 49, no. 1, pp. 11–18, 2017.

[45] F. Uysal and M. Tokmak, "Evaluation of stress parameters based on heart rate variability measurements," vol. 17, no. 1, pp. 3055–3060, 2017.

[46] D. P. Tobón, S. Jayaraman, T. H. Falk, and S. Member, "Spectro-Temporal Electrocardiogram Analysis for Noise-Robust Heart Rate and Heart Rate Variability Measurement," vol. 5, no. September, 2017.

[47] A. H. Khandoker, C. Karmakar, M. Brennan, A. Voss, and M. Palaniswami, *Poincaré Plot Methods for Heart Rate Variability Analysis*. .

[48] P. Melillo and C. Formisano, "Classification tree for real-life stress detection using linear Heart Rate Variability analysis . Case study : students under stress due to university examination," *World Congress on ...*, pp. 477–480, 2013.

[49] M. P. Tarvainen, J. Niskanen, "User's Guide," Biosignal analysis and medical imaging group, University of Kuopio, Finland, 2006.

[50] F. Hou, J. Zhuang, C. Bian, T. Tong, Y. Chen, and J. Yin, "Analysis of heartbeat asymmetry based on multi-scale time irreversibility test," *Physica A*, vol. 389, no. 4, pp. 754–760, 2010.

[51] H. Search, C. Journals, A. Contact, M. Iopscience, and I. P. Address, "Defining asymmetry in heart rate variability signals using a Poincar ´ e plot," vol. 1227, 2009.

[52] Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PCh, Mark RG, Mietus JE, Moody GB, Peng CK, Stanley HE. Phisio-bank, Phisio-toolkit and Phisionet:Components of a new research resource for complex phisiological signals, Circulation Electonic pages; https://www.physionet.org/physiobank/database/nsr2db/,doi: 10.13026/C2S881

[53] Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PCh, Mark RG, Mietus JE, Moody GB, Peng CK, Stanley HE. Phisio-bank, Phisio-toolkit and Phisionet:Components of a new research resource for complex phisiological signals, Circulation Electonic pages; https://www.physionet.org/physiobank/database/chf2db/, doi: 10.13026/C2F598.

[54] "F-tests", [online]. Available: https://en.wikipedia.org/wiki/F-test, April 4,2018

[55] Research Skills,.Available:http://users.sussex.ac.uk/grahamh/RM1web/t-test,April 5,2018.

[56] T-test, Available: https://researchbasics.education.uconn.edu/t-test/, April 5,2018.

[57] Available:https://in.mathworks.com/help/matlab/ref/graph.html, June 5, 2018

plag2kp

ORIGINALITY REPORT

17%	10%	14%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	F.Z. Hou, F.W. Li, J. Wang, F.R. Yan. "Visibility graph analysis of very short-term heart rate variability during sleep", Physica A: Statistical Mechanics and its Applications, 2016 Publication	1%
2	en.wikipedia.org Internet Source	1%
3	cellinfomed.de Internet Source	1%
4	www.kubios.com Internet Source	1%
5	webcache.googleusercontent.com Internet Source	1%
6	www.lifesciencesite.com Internet Source	1%
7	pdfs.semanticscholar.org Internet Source	1%
8	Melillo, P, and L Pecchia. "Enhanced Remote Health Monitoring : Home Monitoring of	<1%