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## **ABSTRACT**

### **IMPACT OF MISSED BEATS ON HEART RATE VARIABILITY USING TIME-FREQUENCY ANALYSIS**

**By**

**Kibrom T Hailu**

ECG recordings, especially during an exercise stress test, are exposed to artifacts. The source of artifacts can be due to technical problems, biological events and errors in the automatic detection. As a result missed beats, extra beats and ectopic beats can occur. In this study analysis of missed beats is performed using time-frequency analysis. Some of the patient's data had missed beats.

Fourier spectral analysis was first applied to the missed beats during the resting state. The impact of missed beats using Fourier spectral analysis is significant, especially, when the missed beats are in a row. The Fourier spectral analysis does not appropriately represent heart rate variability (HRV) during and after exercise because it assumes a signal to be stationary. In addition, Fourier analysis provides information of the heart rate only in the frequency domain. Therefore, there was a need to apply time-frequency analysis to examine the effect of missed beats.

For the purpose of analysis, beats were eliminated in a row and arbitrary. Then time-frequency analysis was applied to the missed beats and the original data by superimposing on each other. Their differences were plotted as error functions. The sizes of the error functions were measured. The results show that the errors due to missed beats do not widely spread throughout the spectrum. That is, missed beats do not affect the entire time-frequency signals. Their effect is local. The errors due to missed beats are reduced when using interpolation.

**IMPACT OF MISSED BEATS ON HEART RATE VARIABILITY  
USING TIME-FREQUENCY ANALYSIS**

**by**

**Kibrom T Hailu**

**A Thesis  
Submitted to the Faculty of  
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In Partial Fulfillment of the Requirements for the Degree of  
Master of Science in Biomedical Engineering**

**Department of Biomedical Engineering**

**January 2006**

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**APPROVAL PAGE**

**IMPACT OF MISSED BEATS ON HEART RATE VARIABILITY  
USING TIME-FREQUENCY ANALYSIS**

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To my beloved family

**“ሕጂ ግና ለምነት ፡ ተስፋ ፡ ፍቅር ፡ ለዘገ ለሰሰተ ለዚላተገ ይነብራ  
ካብዚላተገ ለትግቢ ግና ፍቅር ሊያ =” 1 ቆረ 13:13**

**“And now abide faith, hope, love, these three;  
but the greatest of these is love.” 1 Cor. 13:13**



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## TABLE OF CONTENTS

<b>Chapter</b>	<b>Page</b>
1 INTRODUCTION .....	1
1.1 Scope of the Thesis .....	1
1.2 Thesis Outline .....	3
2 PHYSIOLOGY OF CARDIOVASCULAR SYSTEM .....	4
2.1 The Heart .....	4
2.1.1 Mechanical Activity of the Heart .....	5
2.1.2 Electrical Activity of the Heart.....	6
2.2 The Electrocardiography .....	9
2.2.1 ECG Leads.....	10
2.2.2 Cardiac Action Potential and Corresponding ECG Waves.....	10
2.2.3 Interval Measurements.....	13
3 THE NERVOUS SYSTEM.....	14
3.1 Autonomic Nervous System.....	16
3.1.1 Sympathetic Nervous System.....	17
3.1.2 Parasympathetic Nervous System.....	18
3.2 Heart Rate Variability.....	22
3.2.1 Autonomic Control of the Heart.....	22
3.2.2 Effect of Exercise on Heart Rate.....	24
4 ENGINEERING BACKGROUND FOR HRV .....	25
4.1 Time-domain Method .....	26
4.2 Frequency-domain Method.....	28

**TABLE OF CONTENTS**  
**(Continued)**

<b>Chapter</b>	<b>Page</b>
4.3 Time-frequency Representation.....	32
4.3.1 Short Time Fourier Transform .....	33
4.3.2 Quadratic Time Frequency Representation.....	35
5 METHODS .....	37
5.1 Subjects .....	37
5.2 Equipment.....	37
5.3 Recordings for the Study of HRV .....	38
5.4 Software Used for Data Analysis .....	39
5.5 R Wave Detection .....	40
5.6 Missed Beats .....	41
5.6.1 Motivation.....	41
5.6.2 Methods Used for Missed Beats.....	44
6 RESULTS AND DISCUSSION.....	50
6.1 Effect of Missed Beats Using Fourier Spectral Analysis.....	51
6.2 Effect of Missed Beats Using Time-frequency Analysis .....	53
6.2.1 Effect of Missed Beats in a Raw .....	67
6.2.2 Effect of Arbitrary Missed Beats.....	73
6.3 The Effect of One Extra Beat Using Time-Frequency Analysis.....	78
6.4 Interpolation for the Missed Beats .....	82
6.5 Measurement of Error Functions.....	92
6.5.1 Width of an Error Function .....	93
6.5.2 Height of an Error Function .....	95

**TABLE OF CONTENTS**  
**(Continued)**

<b>Chapter</b>	<b>Page</b>
6.5.3 Area of an Error Function .....	96
6.6 Conclusion and Future Work.....	103
APPENDIX A FOURIER TRANSFORM PROGRAM CODE FOR MISSED BEATS .....	106
APPENDIX B WIGNER DISTRIBUTION PROGRAM CODE FOR MISSED BEATS .....	109
APPENDIX C SHORT TIME FOURIER TRANSFORM PROGRAM CODE FOR MISSED BEATS .....	115
REFERENCE.....	122

## LIST OF TABLES

<b>Table</b>		<b>Page</b>
6.1	Size of LF and HF Error Widths of One to Three Missed beats.....	71
6.2	Original IBI Vs Two Interpolation Missed Beats .....	83
6.3	The Size of the LF and HF Error Width Due to Interpolation for One Subject.....	83
6.4	LF and HF Error Function Measurements of One to Five Missed Beats for Five Patients Using 50sec Window Length.....	97
6.5	LF and HF Error Function Measurements of One to Five Interpolated Missed Beats for Five Patients Using 10sec Window Length .....	99
6.6	One Extra Beat Vs One Missed Beat for Five Patients.....	102

## LIST OF FIGURES

<b>Figure</b>		<b>Page</b>
2.1	Representative mechanical activity of the heart .....	6
2.2	Distribution of impulses through specialized conductive tissues of the heart...	9
2.3	Representative electric activity from various regions of the heart.....	12
2.4	ECG intervals and segments.....	13
3.1	Summary of the Nervous System .....	16
3.2	Sympathetic and parasympathetic nervous system.....	21
4.1	Representative of power spectrum .....	30
5.1	Fourier spectrum for simulated data with 0, 1 and 5 missed beats .....	42
5.2	Example of IBI array and accumulated sum array .....	45
5.3	LabVIEW graphical sum array program .....	45
5.4	Front panel for one beat eliminator .....	46
5.5	One beat eliminator.....	46
5.6	Front panel for the multi-beat eliminator .....	48
5.9	Multi-beat eliminator .....	48
6.1	Power spectrum for a period of 5 minutes clean data during paced breathing..	52
6.2	Power spectrum for one to four missed beats in a row .....	52
6.3	The IIBI plots and their corresponding power spectrum for one to four arbitrary missed beats within a period of 1 to 5 min .....	53
6.4	Time-frequency for original clean data using STFT .....	55
6.5	Time-frequency for one missed beat using STFT .....	56

**LIST OF FIGURES  
(Continued)**

<b>Figure</b>	<b>Page</b>
6.6 The STFT output results for one missed beat during exercise and original clean data together.....	58
6.7 Error functions using STFT.....	59
6.8 TF superimposed plots for one missed beat during exercise on the original data using WD.....	61
6.9 Error functions, 3D and contour plots for one missed beat during exercise using WD.....	62
6.10 TF superimposed plots for one missed beat during paced breathing on the clean data using WD.....	64
6.11 Error functions, 3D and contour plots for one missed beat during paced breathing using WD.....	65
6.12 LF error function with its extreme end values.....	66
6.13 HF error function with its extreme end values.....	66
6.14 TF superimposed plots for two missed beats in a row on the original data using WD.....	68
6.15 Error functions, 3D and contour plots for two missed beats in a row using WD.....	69
6.16 TF superimposed plots for three missed beats in a row on the original data using WD.....	71
6.17 Error functions, 3D and contour plots for three missed beats in a row using WD.....	72
6.18 TF superimposed plots for two arbitrary missed beats on the original data using WD.....	74
6.19 Error functions, 3D and contour plots for two arbitrary missed beats using WD.....	75
6.20 TF superimposed plots three arbitrary missed beats on the original data using WD.....	77

**LIST OF FIGURES**  
**(Continued)**

<b>Figure</b>	<b>Page</b>
6.21 Error functions, 3D and contour plots for three arbitrary missed beats using WD .....	78
6.22 TF superimposed plots for one extra beat on the original data using WD .....	80
6.23 Error functions, 3D and contour plots for one extra beat using WD.....	81
6.24 TF superimposed plots for the two interpolated missed beats on the clean data using WD.....	85
6.25 Error functions, 3D and contour plots for the interpolated two missed beats using WD .....	86
6.26 The superimposed HF error function due to one missed on the error function due to interpolation .....	87
6.27 Expanded view of the superimposed HF error function due to one missed on the error function due to interpolation .....	87
6.28 WD output for three missed beats .....	89
6.29 WD normalized, 3D and contour outputs for three missed beats .....	90
6.30 WD output after interpolation.....	91
6.31 WD normalized, 3D and contour outputs after interpolation .....	92
6.32 Superimposed LF, HF and their corresponding error functions for one missed beat using STFT with 50sec window length .....	94
6.33 Superimposed LF, HF and their corresponding error functions for one missed beat using STFT with 60sec window length .....	95
6.34 Size of the error width of LFs and HFVs Vs the number of missed beats for patient 1 .....	101
6.35 Size of the error height of LFs and HFVs Vs the number of missed beats for patient 1 .....	101
6.36 Size of the error area of LFs and HFVs Vs the number of missed beats for patient 1 .....	102



# CHAPTER 1

## INTRODUCTION

### 1.1 The Scope of the Thesis

The primary goal of this thesis was to study the impact of missed beats on heart rate variability (HRV) analysis. According to Berntson [1], missed beats have been defined as ECGs whose R waves are not detected. This could be due to electrode problems, low amplitude R waves, or other abnormalities of the R waves, and in many instances occurred when patients were moving, such as during exercise studies. The motivation for the analysis of the effect of missed beats on heart rate signals was the ability to include patients that were previously [2] discarded from an exercise study performed at University of Medicine and Dentistry (UMDNJ). The reason they were discarded was that they had several instances of missed beats, and therefore heart rate variability analysis could not be performed. For reasons of comparison, the effects of missed beats on the frequency analysis for the resting state were done. When looking at the entire ECG data, only time-frequency analysis was examined. The resulting signal fluctuations, which are related to autonomic nervous system, would be quantified and plotted.

The first step was to look at the effect of the missed beats during the paced breathing (resting state). In addition to time-frequency analysis, a Fourier analysis of the entire paced breathing period was used. The Fourier analysis method for the paced breathing on the original data and missed beats was examined in this thesis. The two main spectral peaks in the power spectrum are the HF (high frequency) band and the LF (low frequency) band. The interpretation of changes in heart rate variability (spectral)

parameters in terms of the autonomic nervous system (ANS) is far from simple, although the HF peak has been related to the activity of the parasympathetic system while the LF peak has been related to the mixture of both the sympathetic and parasympathetic systems. One of the articles that looked at the effect of missed and extra beats in a resting state is by Berntson [1]. The author examined the effect of the missed and extra beats of a segment of an ECG (within 1-5min) by simply finding the LF and HF. He indicated that even a single missed or extra beat affects the whole heart rate spectrum.

In this thesis the same effects are assessed by applying the time-frequency technique. Unlike the Bernston article, the entire ECG segment can be analyzed using the time-frequency analysis because stationarity is not a consideration. The Fourier spectral analysis method for studying the variability of heart rate during and after exercise states is not valid because the signal is not stationary at those states. Therefore, the time-frequency representation has to be applied to the entire exercise protocol, and was used to assess the effect of missed beats.

Time-frequency analysis is also important to investigate the sympathetic-vagal (LF) and parasympathetic (HF) changes in time and frequency jointly. Some of the time-frequency methods that have been used to analyze the continuous changes in heart rate (HR) are the STFT, Wavelet transform and Wigner distribution. The STFT and Wigner distribution are the methods used in this thesis. The question that will be addressed in this thesis is whether the entire ECG segment's time-frequency analysis would be affected by one or more missed beats, and where the effect of these missed beats ends. The hypothesis was that the error due to missed beats should be localized. To prove whether the hypothesis was correct, TF component signals or activity plots from missed beats

were superimposed on the original non-missed beat data. The errors were then separately plotted as error functions. Measurements for the components of the error functions were taken to observe the correlation between the sizes of the error signals and the number of missed beats in a row. Berntson only used the data on missed beats for his analysis, and did not attempt to interpolate where a missed beat should occur. Using proper interpolation techniques, the error due to missed beats might be minimized. In this thesis, interpolation techniques have been studied as to their effects on the error function.

## 1.2 Thesis Outline

The chapters that are covered in this thesis are categorized as follows:

- Chapter 2 summarizes the physiological background of the cardiovascular system which is important for studying the heart rate variability and heart rate recovery. Since this thesis revolves around heart rate and ECG, the physiological background of the heart and the basic understanding about the ECG are covered.
- Chapter 3 presents the physiological background of the autonomic nervous system and its regulation of the heart rate because the autonomic nervous system is the dominating factor in regulating the rate heart.
- Chapter 4 summarizes the theoretical backgrounds that are useful for analyzing the signals. Since time-frequency representation is useful to examine the HRV in general and the impact of the missed beats in particular, its engineering background is briefly discussed.
- Chapter 5 discusses the methods and protocols used at UMDNJ during the stress test and the data analysis that are used at NJIT.
- Chapter 6 presents all the results, discussions and conclusions of the study. The impact of the missed beats, and the comparison between the original and the missed beats are explained and plotted using TF analyses. Future work is also described.

## **CHAPTER 2**

### **PHYSIOLOGY OF CARDIOVASCULAR SYSTEM**

The cardiovascular system is made up of the heart and the circulatory system. Although the physiology and anatomy of the cardiovascular system is well known, it is difficult to infer the dynamical functioning of the control system from the physiology and anatomy. Moreover, the dynamical aspects of the physiology of the cardiovascular system cannot be fully understood using typical physiological studies. This gap in the scientific knowledge triggered the inclusion of other scientific disciplines into the study of the cardiovascular system, especially the exact sciences, such as engineering and physics.

The extensive knowledge of the theory of control systems in the physics and engineering disciplines spawned a vast interest in applying the methodologies of these disciplines to the study of the cardiovascular system. Indeed, research tools adapted from the exact sciences have proved valuable in the study of the cardiovascular system. One of the most prominent examples of such tools and the subject of this work is the variability of the heart rate – the fluctuations of instantaneous heart rate about its mean value, which result from the activity of ANS on the cardiovascular system [3].

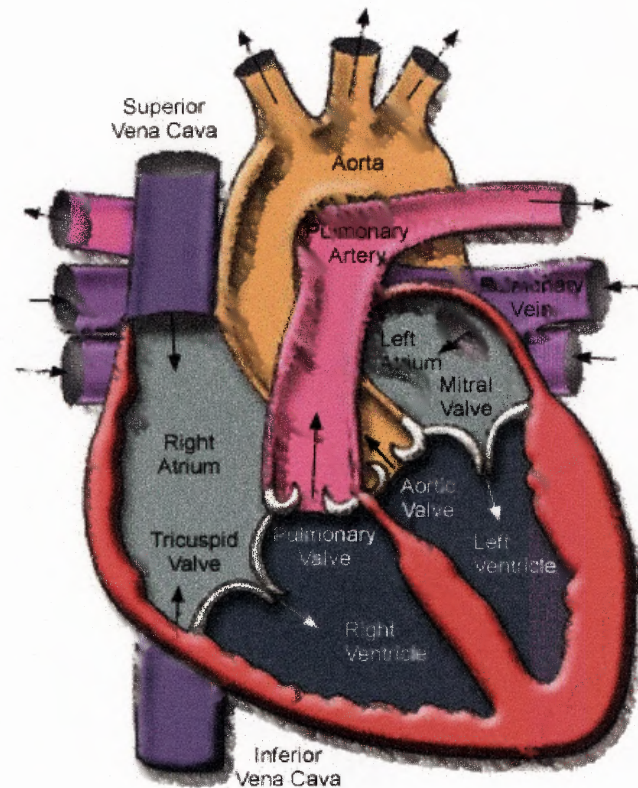
#### **2.1 The Heart**

The heart, the size of your fist, is the central organ of the cardiovascular system. It is located in the middle of the chest, a little tilted to the left. It is a blood pumping muscular organ.

### **2.1.1 Mechanical Activity of the Heart**

The heart consists of four parts called chambers – the right atrium and right ventricle, and the left atrium and left ventricle. The right side of the heart receives blood from the body and pumps it to the lungs to be oxygenated. The left side of the heart on its part receives the oxygenated blood from the lungs and pumps it to the body. The right and left chambers of the heart is separated by a muscle wall called the septum.

All chambers of the heart work together. Blood enters the right atrium through the venous system. After it fills with blood, the right atrium pumps the blood to the right ventricle through the valve called the tricuspid valve. The right ventricle on its part pumps the blood to the pulmonary artery through the pulmonary valve. The blood then enters into the lungs. Since the blood that enters the lungs is not rich in oxygen, oxygen diffuses from the lung's alveoli to the blood and carbon dioxide diffuses from the blood to the alveoli. The oxygenated blood is then returned to the left atrium through the pulmonary veins. Once the left atrium fills with blood, the blood flows to the left ventricle through the mitral valve. The left ventricle, the major pumping chamber of the heart, ejects the blood to the aorta through the aortic valve. All the four chambers of the heart pump the blood by contracting themselves in response to the electrical stimulation which is discussed in the next section [4].



**Figure 2.1** Representative mechanical activity of the heart [5].

### 2.1.2 Electrical Activity of the Heart

The electrical and mechanical activities of the heart are coupled together. It is the electrical activity of the heart that triggers the heart muscle walls to contract. In other words, the pumping activity of the heart cannot occur without organized electrical activity. The electrical stimulation or the propagation of the signals in the heart is not random. The generation of the electric currents, their pathways throughout the heart and their final destination are very regular and specific. It is this situation that makes possible for us to record and investigate the electric conduction of the heart. Although the activity repeats over and over, the heart rate may not be exactly the same at all times. The rate is

affected by many factors such as exercise (physical activity), stress, hormonal activity, and so on. Any physiological system of the body is not independent of other systems. Likewise, the heart is influenced by other systems such as the autonomic nervous system. This will be discussed later in greater detail.

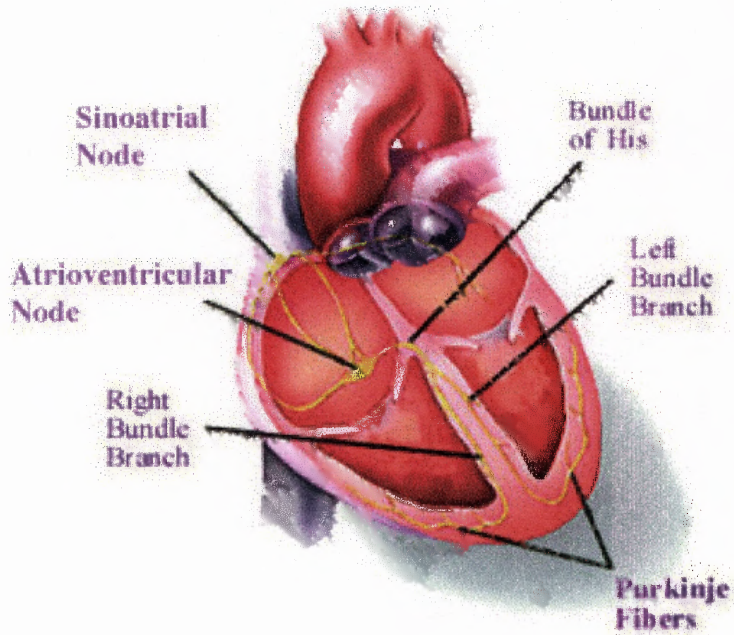
It is important to know the conduction system of the heart before trying to interpret the electrocardiogram. The electric currents that regulate the heart rhythm originate in the heart itself. Under normal conditions, specialized cells in the sinus or sinoatrial (SA) node, also called natural pacemaker, generate the electrical impulses. If the pacemaker's function is disrupted, another part of the conduction system can take over the impulse-firing task [6]. The sinus node is located at the top of the right atrium near the point where blood returns from the upper body. Its specialized cells send out electrical impulses that normally range between 60 and 100 per minute [7]. If the sinus node sends out impulses slower than usual, it is known as sinus bradycardia. On the other hand, if it sends out signals at a faster rate than the usual range, it is called sinus tachycardia. The impulses spread throughout the left and right atria, and stimulate the muscle walls of the atria (myocardium) to contract. The contraction of the atria forces the tricuspid and mitral valves to open and let the blood to flow. The electrical impulses then travel via specialized tracts known as internodal tracts to the atrioventricular node (AV node) [4], the gateway for the impulses between atria and ventricles. The AV node is located in the septum (muscular wall that separates the two major chambers, the ventricles).

The movement of an electrical current is faster than the blood flow and mechanical contraction. Therefore, the AV node delays the impulses until the ventricles

filled with blood that is pumped by the atria. After a little delay in the AV node, the impulses then continue moving into the bundle of His. The bundle of His splits into left and right branches called bundle branches. The impulses through the left branch activate the left ventricle and the right branch activates the right ventricle. Then the impulses enter into the Purkinje network that branch left and right to direct the impulses first to the bottom then up the sides of the ventricles [7]. As a result the ventricles contract and squeeze the blood to flow to the rest of the body. Figure 2.2 shows the anatomical distribution of impulses through specialized conductive tissues of the heart.

The conduction system that has been discussed above produces a single beat. As long as the heart functions properly, the above normal joint process of mechanical and electrical systems repeats over and over again for life. By detecting the electric activity of the heart noninvasively, it has been possible to determine the behavior and nature of the heart beat. In signal point of view, any beat has parts or waves that represent the activities of the conduction system at specific parts of the heart.





**Figure 2.2** Distribution of impulses through specialized conductive tissues of the heart [8].

## 2.2 The Electrocardiograph

As noted in the previous section, the activity of the heart can be detected externally. The electrocardiograph (abbreviated as EKG or ECG) records the electrical activity of the heart. It is often the first test used to follow up the medical history and physical exam because the test is noninvasive, does not entail any risk to the patient, and yields valuable information about a wide variety of heart conditions. It provides information about heart rhythms and electrical configurations that may provide clues to the heart problems, heart attack, irregular heartbeats, or arrhythmias [9].

### **2.2.1 ECG Leads**

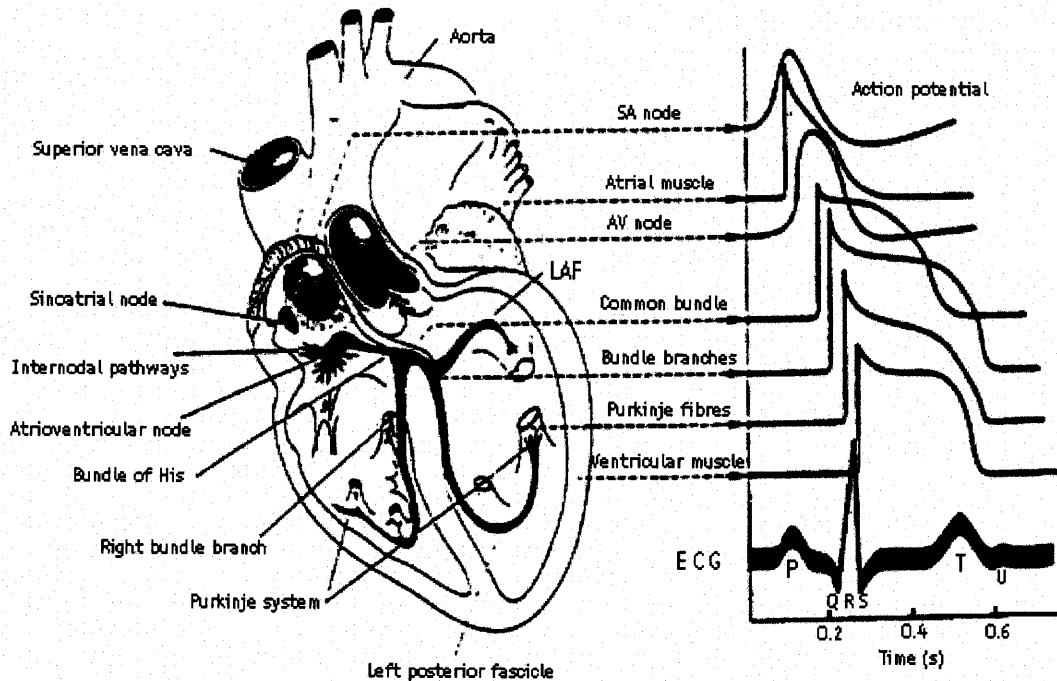
The detection of the electrical events within the heart is achieved by attaching recording electrodes at the surface of the skin. The electric activity of the heart can be approximately represented as a vector quantity. Therefore, the locations at which signals are detected, as well as the time-dependence of the amplitudes of the signals should be known [4]. By convention, electrodes are placed on each arm and leg, and six electrodes are placed at defined locations on the chest. There are two basic types of electrocardiogram (ECG) leads: bipolar and unipolar. Bipolar leads (standard limb leads) utilize a single positive and a single negative electrode between which electrical potentials are measured. Unipolar leads (augmented leads and chest leads) have single positive recording electrode and utilize a combination of the other electrodes to serve as a composite negative electrode [10].

### **2.2.2 Cardiac Action Potentials and Corresponding ECG Waves**

A normal heartbeat in the ECG measurement has waves that correspond to the depolarization and repolarization of the chambers. The cardiac electrical activity is determined by transmembrane potential – the potential, or voltage, difference between the intracellular and extracellular environments. This potential difference can only exist because of the selectively-permeable cardiac cell membrane. This membrane is composed of a lipid bilayer in which are situated specialized proteins that form channels that allow passage of certain ions at specific times between the intra- and the extracellular spaces. Normally, in the resting state the intracellular compartment has more negative than positive ions, and is thus polarized to a negative potential relative to the extracellular

space (about -85 to -90mV for most cardiac cells) [11]. Sodium ( $\text{Na}^+$ ), potassium ( $\text{K}^+$ ), calcium ( $\text{Ca}^{++}$ ) and chloride ( $\text{Cl}^-$ ) are the important ions in cardiac action potentials. At rest the membrane is much more permeable to potassium ions than to sodium and to chloride. Therefore, at rest there is higher concentration of sodium ions on the outside than the inside and a higher concentration of potassium ions on the inside than the outside. But the distribution of these ions is not equal. The resting potential is -90 mV.

An action potential occurs when a cardiac cell membrane is stimulated. The stimulus causes the sodium gates (channels) to open. Then sodium rushes into the cell. The rapid movement of the sodium ions causes the potential to be reversed. The inside part is now more positive and the cell becomes depolarized. When the depolarization reaches about 20 to 30mV, the sodium channels start to close while the potassium and calcium channels start to open. Potassium ions slowly diffuse out and calcium ions slowly move in to the cell. This creates the plateau phase of the action potential that lasts about 250ms. Rapid repolarization occurs as the calcium channels close, and more potassium ions move out of the cell. At this stage the ion concentrations go back to the resting levels and the cell returns to about -90mV.



**Figure 2.3** Representative electric activities from various regions of the heart [12].

The first wave or deflection that is shown in the ECG is called the P wave, corresponds to the depolarization of the upper chambers of the heart, the atria. It should not be higher than 0.3mV in the bipolar leads or 0.25mV in the unipolar leads, or greater than .10sec in duration. When abnormal, the P wave may become inverted, broadened and notched, tall and peaked (exceeds 0.3mV), and replaced by flutter or fibrillation waves [13]. The second combination of waves in the ECG, the QRS complex, corresponds to the depolarization of the ventricles. It should be noted that abnormally broad and deep Q waves are often a feature of myocardial infarction. Normally these Q waves don't exceed .03sec in width, or 0.2mV depth. The average time for the whole complex is usually in the range of .06 to .11sec [13]. The T wave is due to the repolarization or relaxation of the ventricles. Since the repolarization of the atria occurs at

complex, its corresponding wave in the ECG is not seen. Finally, a U wave is sometimes seen in the ECG. Its representation is unknown although there is a claim that it is due to the long repolarization time of the ventricles.

### 2.2.3 Interval Measurements

The intervals and segments in the ECG measurements have great importance as their durations (width in time) increase or decrease may indicate abnormality or disease. Each of the intervals and segments correspond to some kind of physiological activity of the heart. The following are the intervals and segments with their corresponding normal durations [14]:

- PR interval – 0.12-0.2sec
- QT interval – 0.39-0.41sec
- ST Segment – 0.08-0.12sec
- QRS duration – 0.06-0.11sec

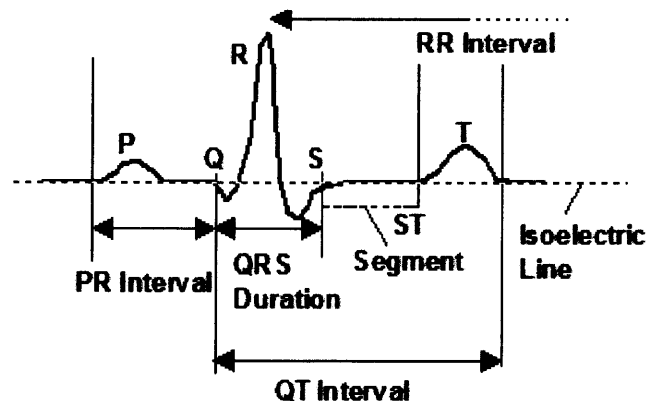


Figure 2.4 ECG intervals and segments [12].

## CHAPTER 3

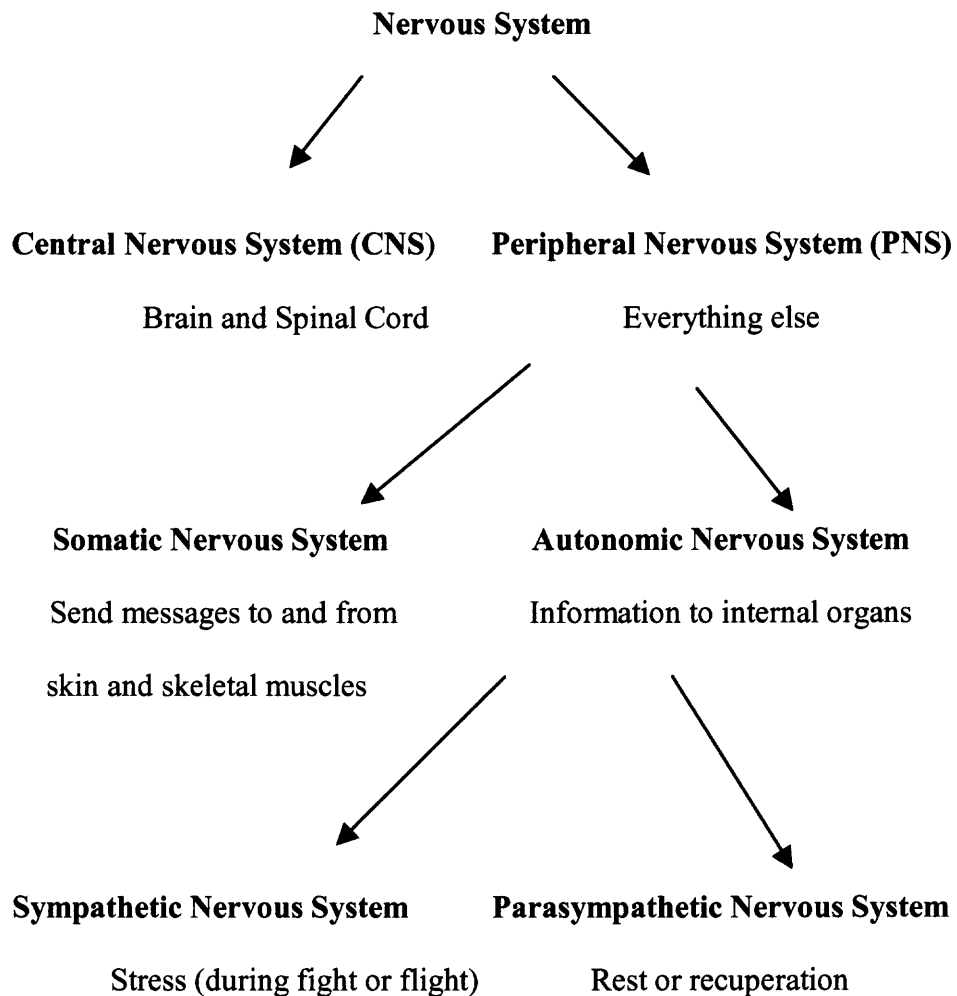
### THE NERVOUS SYSTEM

Humans, like other living organisms, consist of systems that monitor, communicate, and relate them with the environment. The two systems that respond and relate to the environment are the nervous system and the endocrine (hormonal) system. The nervous system coordinates, regulates, controls and instigates many activities of the body. It consists of billions of neurons (nerve cells) that are responsive to stimuli, to communicate, and to conduct electrical signals. Neurons send messages electrochemically. Like the cardiac cells that have been discussed previously, neurons conduct impulses by means of ion distribution. Sodium, potassium, calcium and chloride are important ions in the nervous system as well as the cardiac system.

The central nerves system and the peripheral nervous system are the two divisions of the nervous system. The central nervous system is composed of the interneurons which make up the brain and spinal cord. They relay messages from the sensory neurons to motor neurons. That is, the peripheral nervous system consists of all neurons outside the brain and spinal cord. Sensory neurons are afferent neurons. They send messages from the receptors or sense organs (vision, hearing, touch, smell, and taste) to the central nervous system. The motor neurons, also called efferent neurons, relay messages from the central nervous system to the muscles and the organs.

The efferent (motor neurons) division of the peripheral nervous system consists of the somatic nervous system and the autonomic nervous system. The somatic nervous system is composed of all voluntary nerve fibers that conduct impulses to skin and

skeletal muscles (effectors). All the involuntary activities that are not under conscious control, such as heart rate, blood pressure, gastrointestinal function, temperature, hormone levels, etc are controlled by the autonomic nervous system. All the impulses to the peripheral nervous system that are outside the skeletal muscles, such as the cardiac muscles, smooth muscles and glands are also controlled by the autonomic nervous system. The two branches of the autonomic nervous system are the sympathetic nervous system and the parasympathetic nervous system. Since the autonomic nervous system directly relates to the regulation of the heart rate, it will be discussed in greater detail in the following portion of this study.



**Figure 3.1** Summary of the Nervous System.

### 3.1 Autonomic Nervous System

As briefly discussed above, the autonomic nervous system, a part of the peripheral nervous system, controls the parts of the body that are not under voluntary controls, such as the heart rate, blood pressure, temperature, hormone levels and gastrointestinal functions. It has a great effect in the contraction of the cardiac muscles, contraction and



relaxation of smooth muscles in various organs (such as the intestine, lungs, liver, bladder, and uterus), pupillary size, etc.

The autonomic nervous system is responsible for controlling the heart to beat faster and slower. For example, under stress (physical or mental), the heart's rate increases to facilitate the need of blood and oxygen. On the other hand, under rest or relaxation, the rate decreases to balance the body's need of blood and oxygen. The autonomic nervous system thus controls heart rate. The sympathetic nervous system and parasympathetic nervous system are the two divisions of autonomic nervous system. These two systems have antagonistic effects on the body organs. That is, one dominates the other under different circumstances.

### **3.1.1 Sympathetic Nervous System**

The sympathetic nervous system is active when the body is under stressful situations. It controls, stimulates for response, and mobilizes body systems during emergency or threatening situations (fight or flight). The sympathetic division stimulates the heart to beat faster than normal.

The sympathetic nervous system originates in the spinal cord. The preganglionic neurons are located in the thoracic and lumbar spinal cord. Axons from these neurons project to a chain of ganglia located near the spinal cord. In most cases, these neurons make synapse with other neurons (post-ganglionic neurons) in the ganglion. A few preganglionic neurons go to other ganglia outside of the sympathetic chain and synapse there. The post-ganglionic neurons then project to the "target" - either muscles or glands. The synapse in the sympathetic ganglion uses acetylcholine as a neurotransmitter; the

synapse of the post-ganglionic neuron with the target organ uses the neurotransmitter called norepinephrine. There is one exception: the sympathetic post-ganglionic neuron that terminates on the sweat glands uses acetylcholine [15].

The receptors to norepinephrine in the organs are divided into two subgroups:  $\alpha$  and  $\beta$  receptors. The  $\beta$  receptors are further divided into two types:  $\beta_1$  and  $\beta_2$  receptors. The intricate structure of the ANS is well suited for the functions of its two branches. During stress and emergency, organs must respond in various ways, and moreover, the same kind of tissue (such as blood vessels) located in different places must react differently to the same stimulations. The sympathetic system can stimulate adrenergic receptors by activation of the adrenal medulla, a gland located on the kidney that secretes both epinephrine and norepinephrine into the circulation. Epinephrine and norepinephrine, which are part of a group of substances called catecholamine, have the same effect as that caused by direct neural stimulation, except that their effect lasts for 5 to 10 times as long [3].

### **3.1.2 Parasympathetic Nervous System**

The parasympathetic nervous system is active when the body is at rest. When the parasympathetic division is active the heart rate and other internal organs activities slow down to their normal levels. In times of stress or emergency the sympathetic system prepares the body for “fight or flight” response. The parasympathetic stimulation occurs during relaxation or when the threat is over. Figure 3.2 shows some of the organ parts that are affected by the two divisions of the autonomic nervous system.

The cell bodies of the parasympathetic nervous system are located in the spinal cord (sacral region) and in the medulla. In the medulla, the cranial nerves III, VII, IX and X form the preganglionic parasympathetic fibers. The preganglionic fiber from the medulla or spinal cord projects to ganglia very close to the target organ and makes a synapse. This synapse uses the neurotransmitter called acetylcholine. From this ganglion, the post-ganglionic neuron projects to the target organ and uses acetylcholine again at its terminal [15].

Preganglionic and postganglionic neurons are classified as cholinergic neurons because they release acetylcholine. The two types of cholinergic receptors are:

- Muscarine receptors – receptors that respond to muscarine, an alkaloid produced by poisonous mushroom *Amanita muscaria*.
- Nicotinic receptors – receptors that respond to nicotine, a derivative from the tobacco plant [16].

Nicotinic receptors are found on sympathetic and parasympathetic postganglionic neurons of both the parasympathetic and sympathetic divisions and on the postsynaptic membranes of skeletal muscle cells in the somatic nervous system. Nicotinic receptors respond to acetylcholine released from both sympathetic and parasympathetic preganglion fibers. Muscarine receptors are found on effectors innervated by the parasympathetic postganglionic neurons of the autonomic nervous system. These receptors bind with acetylcholine, which is released from parasympathetic postganglionic neurons and usually inhibits smooth muscle and cardiac pacemaker cells, but excites smooth muscle in other areas [16].

axons that are distributed for short distances to specific areas. The rapid deactivation of acetylcholine by acetylcholinesterase results in a short-term effect by the neurotransmitter [16].

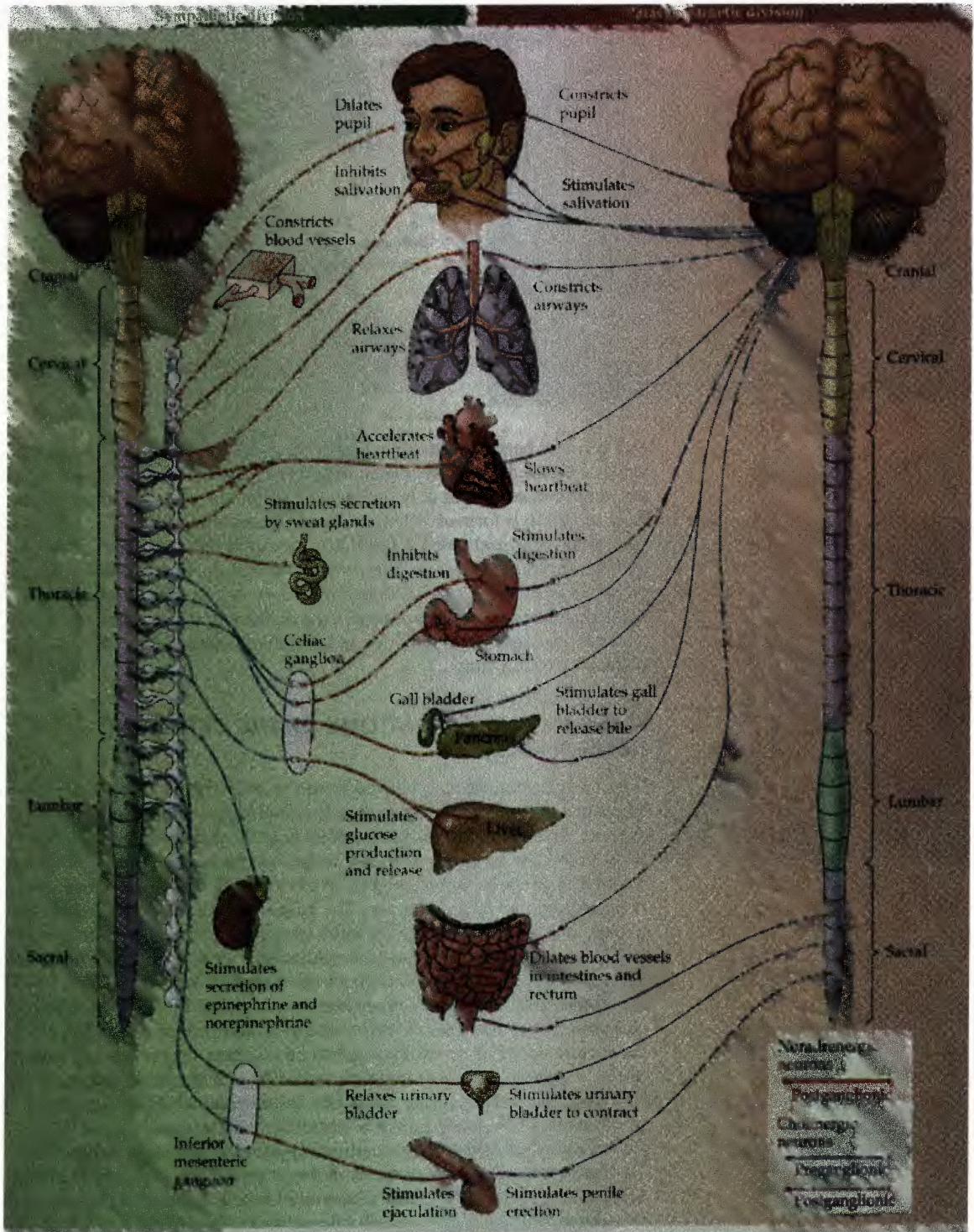


Figure 3.2 Sympathetic and parasympathetic nervous system [17].

## **3.2 Heart Rate Variability**

Heart rate variability (HRV) is a term applied to variations between consecutive heartbeats. That is, it is the variation in beat-to-beat fluctuations around the mean [18]. In HRV analysis either the heart rate as a function of time or the intervals between successive QRS complexes need to be determined. In this thesis when talking about HRV, it actually means the variability of RR intervals (intervals between consecutive R peaks) [19].

### **3.2.1 Autonomic Control of the Heart**

HRV reflects the effects of sympathetic and parasympathetic tone and other physiological control mechanisms on cardiac function. Continuous changes in sympathetic and parasympathetic neural impulses result in changes of heart rate (HR) and cause oscillation around the mean HR [18]. As discussed in the ANS section, the sympathetic activity increases the heart rate, whereas the parasympathetic activity slows it down. Therefore, analysis of heart rate variability is an important tool to understand the activity or function of the autonomic nervous system.

The autonomic nervous system provides innervations for the heart. Although cardiac muscle has an intrinsic mechanism for HR, neural influences superimpose on the inherent rhythm of the myocardium. These influences originate from the cardiovascular center in the medulla oblongata, flow through the sympathetic and parasympathetic (vagal) components of the autonomic nervous system. These divisions are in parallel, but differ from each other due to differences in anatomy, neurotransmitters, receptors, and physiological actions [18].

The parasympathetic nerves are connected to the SA node, the AV conducting pathways, and the atrial and ventricular muscles as well as coronary vessels [20]. The parasympathetic system sends signals to the heart via the vagus nerve. The neurotransmitter acetylcholine is released and binds with muscarinic receptors on the surface of the heart. This results in a decrease in both the heart rate and the force of cardiac contractions [21]. The release of the neurotransmitter acetylcholine is due to the resting or relaxation conditions of the systems of the body. Therefore, under such conditions the variations in heart rate period are largely affected by the parasympathetic (vagal) modulation.

Sympathetic nerve fibers innervate the SA node, the AV conducting pathways, coronary vessels, and the atrial and ventricular myocardium [20]. Sympathetic stimulation occurs via the release of norepinephrine and epinephrine by the adrenal medulla. These neurotransmitters stimulate  $\beta$ -adrenergic receptors, resulting in an increase in the degree and the force of contraction. During resting condition, the parasympathetic system dominates and vessels exhibit a certain amount of vagal tone. Under these conditions changes in heart rate are dependent on vagal modulation. HRV monitors and records these modulations, allowing a more complete understanding of neural functioning [20]. Both divisions of the autonomic nervous system always have some activity which continuously regulates the function of the heart. Heart rate response therefore presents a balance between sympathetic and parasympathetic (vagal) regulation which can be considered also as an antagonist function [21].

### **3.2.2 Effect of Exercise on Heart Rate**

During exercise, heart rate and myocardial contractibility will be increased to satisfy energy demands of working muscles. Its nervous system modulation is considered to be due to the vagal withdrawal at low-intensity exercise and the combination of vagal withdrawal and sympathetic activation at moderate or high-intensity exercise. With the cessation of exercise, the decrease in HR immediately after exercise is mainly thought to be a function of the parasympathetic nervous system. Later, the further decrease in HR to the pre-exercise value depends on the gradual withdrawal of the sympathetic system. Time-frequency analysis of HRV has been proven to be a noninvasive technique capable of providing information on autonomic modulation of the sinus node [22].



## CHAPTER 4

### ENGINEERING BACKGROUND FOR HRV

Some of the reasons for signal processing of physiologic signals are to extract new information, to represent the physiological activities in mathematical and signal forms, and to come up to concrete interpretations. In this chapter the analysis of heart rate variability will be presented in detail. Some of the primary methods of analysis will be discussed. Since this thesis concentrates on the missed beats of the exercise stress test, it is not appropriate to only use time and frequency domains separately. Therefore, the joint time-frequency representation will be used to investigate HRV with and without missed beats. The theoretical backgrounds of the time-frequency techniques, STFT and Wigner distributions will be explained. The work done and the results found using these techniques will be presented in the chapters to follow.

As explained in the previous chapter, heart rate variability is an important noninvasive method for studying the function of autonomic nervous system. The methods of HRV analysis can be divided into: linear time domain methods, frequency domain methods, time-frequency methods and nonlinear methods. Recently, the nonlinear analysis has been evolving as a powerful method for investigating HRV. Although time and frequency domains are important methods in analyzing HRV, neither of them individually gives us information on how energy of a signal is jointly distributed in time and frequency. Therefore, time-frequency representation will be used as the better choice for the analysis.

#### 4.1 Time-domain Method

One of the methods for measuring the variability of heart rate is the time-domain. In this method, the time intervals between consecutive QRS complexes, the so-called normal-to-normal (NN) intervals, are calculated. The interval between two successive QRS complexes is also called inter-beat-interval and is abbreviated as IBI; and the variation between the IBIs is what is called the heart rate variability. All the heartbeat signals are originated from the ECG raw data. Then the R waves are detected to determine the IBIs.

Several time-domain measurements have been used in various studies [23]. Many of them are statistically based time-domain measurements that are derived from IBI variations. The two common measurements are the mean NN (also called RR) interval and the mean heart rate. More complex statistical time-domain measures can be calculated using instantaneous heart rate or cycle intervals, particularly those recorded over long periods of time, usually 24hrs. The simplest variable to calculate is the standard deviation of the NN intervals (SDNN), the square root of the variance. Since variance is mathematically equal to total power of the spectral analysis, SDNN reflects all the cyclic components responsible for variability in the period of recording. In many studies, SDNN is recorded over a 24hrs period and thus encompasses short term HF variations as well as the lowest-frequency components seen in a 24hrs period.

Other commonly used statistical variables calculated from segments of the total monitoring including SDANN, the standard deviation of the average NN intervals over short periods, usually 5min, which is an estimate of the changes in heart rate due to cycles longer than 5min, and the SDNN index, the mean of the 5 min standard deviation

of the NN interval calculated over 24hrs, which measures the variability due to cycles shorter than 5min.

The most commonly used measures derived from interval differences include RMSSD, the square root of the mean squared differences of successive NN intervals, NN50, the number of intervals differences of successive NN intervals greater than 50ms, pNN50, the proportion derived by dividing NN50 by the total number of NN intervals. All these measurements of the short-term variation estimate high frequency variations in heart rate [23].

There are also other geometric measures. The series intervals can be converted into a geometric pattern such as the sample density distribution of RR interval durations, sample density distribution of differences between adjacent RR intervals, Lorenz plot of RR intervals, and so forth [23]. HRV triangular index, TINN and Differential index are some of the common geometric measures. The HRV triangular index is the total number of NN intervals divided by the height of the histogram of all NN intervals as measured on a discrete scale. The TINN, Triangular Interpolation of NN provides the baseline width of the distribution measured as a base of a triangle, approximating the NN interval distribution HRV [24]. Finally, the Differential Index is defined as the difference between the width of the histogram of differences between adjacent NN intervals measured at selected heights (e.g. at the level of 1000 and 10000 samples) [25].

## 4.2 Frequency-domain Method

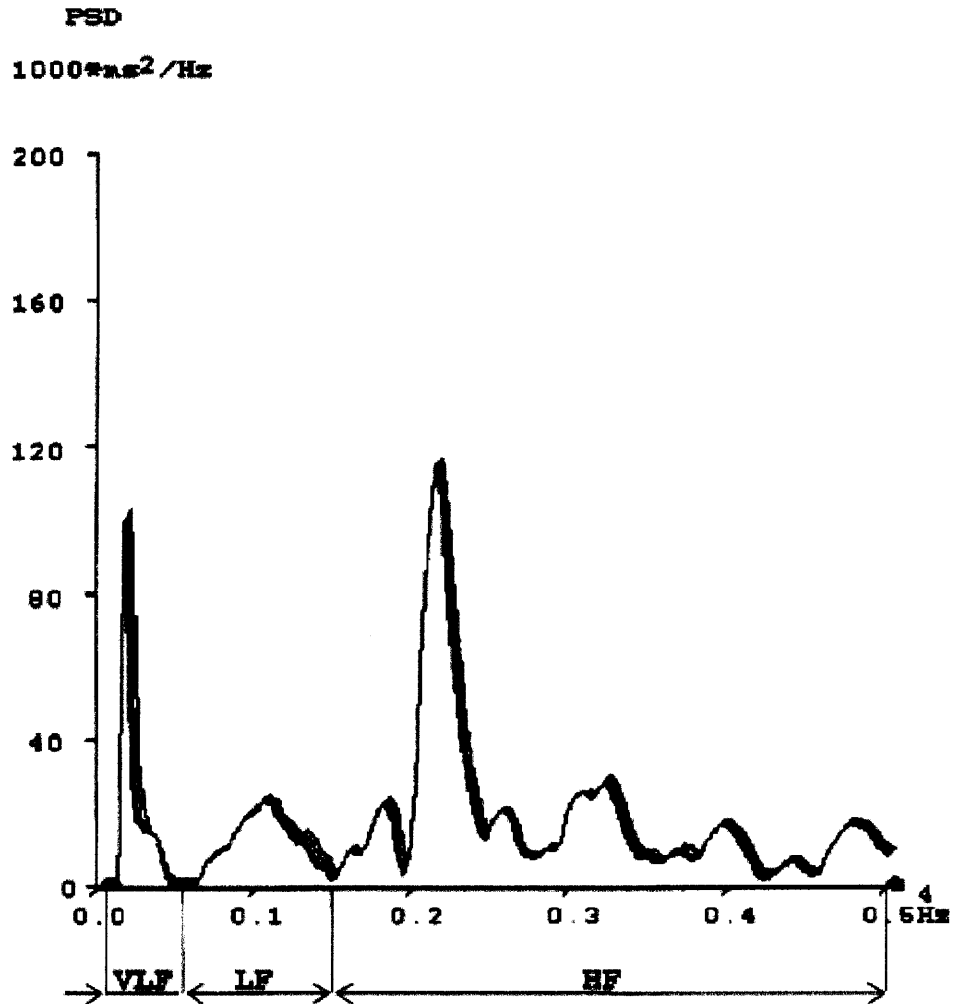
The complexity of the time-domain method for computing the heart rate variability leads to the application of the frequency method of analysis. Pathological conditions are not often easily diagnosed when time domain analysis is performed. By transforming the time domain into the frequency domain, the existence of the pathological conditions can be possibly seen in the frequency domain. The purpose of biomedical engineering research is to develop something that can easily diagnose and treat diseases or illnesses. Transforming time domain into frequency domain has thus been useful in this regard. Heart rate variability is transformed into the frequency domain so that better information may be extracted. Mathematically, the Fourier transform is represented by:

$$F(\omega) = \int_{-\infty}^{\infty} f(t)e^{-j\omega t} dt \quad (4.1)$$

The amplitude of the heart rate fluctuations is seen at different bands of frequencies. This amplitude that is plotted as a function of frequency is called the power spectrum. Power spectrum analysis of heart rate variability is a powerful tool for representing the activities of the autonomic nervous system (both the sympathetic and parasympathetic divisions). In order to perform or to analyze heart rate variability in the frequency domain, the Fourier transform has to be applied to the IIBI (interpolated interbeat interval) of the time-domain. The reason for the interpolation is that the Fourier transform is only applied if the IBI samples are equidistant (evenly spaced). But the IBI timing of the cardiac cycle are inherently irregularly spaced. As previously explained, the IBI is the time interval between two successive R wave peak values of the ECG. Therefore, to obtain the IBI, each if the R waves has to be detected properly. The Fourier

spectral analysis is then applied to the IIBI signal. The detection of the R waves will be explained in Chapter 5.

The power spectral analysis (power density) of the heart rate variability has been studied and its peaks at specific frequency bands are associated with physiological behaviors of the autonomic nervous system. Spectral analysis methods are based on either nonparametric (fast Fourier transform, FFT) or parametric techniques (autoregressive model estimation). In most cases, the results are comparable regardless of the technique applied. The following limits of the frequency bands have been recommended: ultra-low-frequency less than 0.0033Hz (ULF), very-low-frequency from 0.0033 to 0.04Hz (VLF), low-frequency from 0.04 to 0.15Hz (LF) and high-frequency from 0.15 to .4Hz or 0.5Hz (HF). The measurement of different power components is usually made in normalized units, which represent the relative value of each power component in proportion to the total power minus the VLF component [18]. The ULF is the result of a long term recording because a very small number in the frequency domain means a long period of time in the time domain (actually the recording is a sequence of RR intervals in the entire 24hr period).



**Figure 4.1** Representative of power spectrum [26].

The distinct peaks of the frequency spectrum are related with physiological activities. The HF (high frequency band) has been associated with the activity of the parasympathetic nervous system. This is due to the influence of respiration (also known as respiratory sinus arrhythmia). This is the main reason that the HF (when the parasympathetic is more active) occurs at the respiration frequency.

The LF (low frequency band) reflects the activity of the sympathetic nervous system. The parasympathetic nervous system also plays a role on this frequency band. The LF is largely due to the systems regulating blood pressure. According to the Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, the physiological explanation of the VLF component is much less defined and the existence of a specific physiological process attributable to these heart period changes might even be questioned [23].

The LF component in humans has been interpreted as an indicator mainly of sympathetic influence. Consequently, the LF/HF ratio is considered to be a convenient index of sympatho-vagal interaction. Nevertheless, interpretation of LF components is controversial. It is considered by some as a marker of sympathetic modulation (especially when expressed in normalized units) and by others as a parameter that includes both sympathetic and parasympathetic influences [27]. The LF and HF can alternatively be expressed in their normalized units. The normalized units are computed by dividing the absolute power of the LF or HF by the total power as shown in Formula 4.2 and 4.3.

$$NLF = \frac{LF}{LF + HF} \quad (4.2)$$

$$NHF = \frac{HF}{LF + HF} \quad (4.3)$$

where NLF and NHF are the normalized units of the LF and HF respectively.

### 4.3 Time-Frequency Representation

In Section 4.2, it has been shown that by transforming the HRV time domain into the frequency domain and then decomposing the spectrum into components, the activity of the autonomic nervous system can be studied. If an input signal properties do not change over time (i.e. if the signal is stationary), the Fourier spectrum is valid. However many signals of physiological origin are not stationary. It is only for the purpose of study that signals are assumed and approximated in some situations as stationary. For example, signals from the autonomic nervous system during paced breathing are considered as stationary. Practically speaking this is not the case. But since the time variations are not significantly high, the ANS signals are approximated as stationary. Signals are called stationary when their mean and autocorrelation do not change with time. If signals are not stationary, then Fourier analysis is not a good method for the study.

The other thing is that by looking at the time and frequency separately, it is not possible to know when and at what frequency a non-stationary signal event occurs. The Fourier transform doesn't give us time information as to when the frequency components exist. Time-frequency analysis is developed to solve this problem. It is an important method in obtaining joint time-frequency information. When a signal is stationary though, this information is not required because the frequencies occur at all times. In some cases when studying physiological behaviors, one may be interested in what frequency components exist and not at what time these frequencies occur, then Fourier spectral analysis can be used as a choice. But this doesn't mean that the Fourier transform is the most appropriate method.



The most widely used time-frequency representations are the linear and quadratic ones. One example of a linear time-frequency representation is the short time Fourier transform (STFT). The Wigner distribution is among the well known Cohen class quadratic time-frequency representations. The strengths and weaknesses of the above TFRs will be discussed in the sections to follow.

#### 4.3.1 Short Time Fourier Transform

As has been explained the Fourier transform is not a valid analysis unless the input signal is stationary. The question to be asked here is that what if the non-stationary signal is divided into small sections or portions and assumed them as stationary? If a small segment is considered as stationary, it is possible to multiply it with a very narrow moving window that has equal width to the segment, and then take the Fourier spectrum of the product. Therefore, the result of this transformation would be a true frequency representation of the small stationary signal.

The next step would be shifting (moving) the window to another location or to an adjacent small segment and take the Fourier transform of their product. The process is continued until the end of the entire non-stationary signal. Therefore, to overcome the problem when a signal is not stationary, a small section of the signal at a time would be taken using a valid small window. Then the Fourier spectral analysis of the signal at that time would be applied. This method is called short time Fourier transform (STFT). In this case, one has a sense of knowing what frequency components are present in a signal and at what times. Mathematically, STFT of a non-stationary signal  $x(t)$  is represented by:

$$STFT(t, f) = \int_{-\infty}^{\infty} x(\tau)w^*(\tau - t)e^{-j2\pi f\tau} d\tau \quad (4.4)$$

Looking at the above equation, the STFT of a signal is the Fourier transform of the signal  $x(t)$  multiplied by the complex conjugate of the shifted window function  $w(t)$ . STFT has serious drawbacks although it provides some information about both when and at what frequency a signal event occurs. Once a particular size time window is chosen, the window will be the same for all the frequencies. Because of this one cannot know when spectral components occur at what instances of times. Only the existence of band of frequencies of the time intervals can be known, which is a resolution problem. This problem is actually called the Heisenberg Uncertainty Principle [28]. Better time resolution of the STFT requires a short window while better frequency requires a wider window. There is always a tradeoff between time and frequency resolution. The Uncertainty Principle states that the product of the standard deviation in time and frequency is limited by:

$$\Delta\omega\Delta t \geq \frac{1}{2} \quad (4.5)$$

This means that decreasing the deviation in frequency (increasing the frequency resolution) must result in an increase in the deviation in time (decreasing the time resolution) and vice versa. This is the fundamental weakness of the STFT. The boundary of the Heisenberg Uncertainty Principle is reached if a Gaussian window is used [28]. The product of the standard deviation in time and frequency can be reached to equal to  $\frac{1}{2}$  if the Gaussian window is used. Gaussian window is nothing but a window that is normally distributed and is defined by:

$$w(t) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{(t-m)^2}{2\sigma^2}}, \quad (4.6)$$

where  $\sigma$  and  $m$  are the standard deviation and mean respectively.

### 4.3.2 Quadratic Time-Frequency Representations

The quadratic TFRs are used more frequently than the linear TFRs because of their better time-frequency resolution. On the one hand, quadratic TFRs feature disturbing cross-terms making the interpretation of multi-component signals very difficult. An important class of quadratic TFRs is called the Cohen class. The Wigner distribution (WD), the spectrogram, and scalogram are the most well known quadratic TFRs belonging to the Cohen class. Beside the above, there exists a wide variety of quadratic TFRs belonging to the Cohen class that suppress disturbing cross-terms. However, the cross-term suppression is achieved only at the expense of a decreased time-frequency resolution [30]. The WD is defined by the following formula [29]:

$$WD_x = \int_{-\infty}^{\infty} x\left(t + \frac{\tau}{2}\right) x^*\left(t - \frac{\tau}{2}\right) e^{-j2\pi f\tau} d\tau, \quad (4.7)$$

in which  $x(t)$  represents the analyzed signal and  $*$  stands for the complex conjugation. The WD can be thought of as being a squared Fourier transform centered about a point. It features the best time-frequency resolution. However, the WD possesses large amount of the cross-terms. Cross-terms are caused by non-linearity implied in the above formula. That is the sum of two signals is not the sum of their WD. If  $x=x_1+x_2$ , it can be shown that:

$$WD_x(t,f) = WD_{x_1}(t,f) + WD_{x_2}(t,f) + 2\text{Re}\{WD_{x_1x_2}(t,f)\}$$

where the last term is the cross-WD of  $x_1$  and  $x_2$  given by:

$$WD_{x_1x_2} = \int_{-\infty}^{\infty} x_1\left(t + \frac{\tau}{2}\right) x_2^*\left(t - \frac{\tau}{2}\right) e^{-j2\pi f\tau} d\tau \quad (4.8)$$

Because this term reflects the correlation of two signal components, it is named the cross-term. As a result, if a signal contains more than one component in the joint time-

Because this term reflects the correlation of two signal components, it is named the cross-term. As a result, if a signal contains more than one component in the joint time-frequency plane, its WD will contain cross-terms that occur halfway between each pair of auto terms. It is the cross-term interference that prevents the WD from being used for real application, though it possesses many desirable properties for signal analysis. The cross-terms (interferences) in the WD can be attenuated using a distribution called the *pseudo Wigner distribution*. It is the windowed version of WD. That is:

$$PWD_x = \int_{-\infty}^{\infty} h(\tau) x\left(t + \frac{\tau}{2}\right) x^*\left(t - \frac{\tau}{2}\right) e^{-j2\pi f\tau} d\tau \quad (4.9)$$

where  $h(\tau)$  is a window. The drawback with this kind of windowing function is that it is controlled by the short-time window  $h(\tau)$  [30, 31]. In this thesis the PWD is used so that the artifacts due to other than the missed beats would be minimized. The window has been important in determining the size of the width of the peak amplitude errors due to the missed beats.

## **CHAPTER 5**

### **METHODS**

#### **5.1 Subjects**

One hundred subjects from both sexes participated in an exercise stress test, and the protocol will be explained later in this chapter. All the study participants were patients at the University of Medicine and Dentistry of New Jersey (UMDNJ) who were not taking any heart medications. Any subject with a history of heart disease or who had atrial fibrillation, a history of palpitations, a pacemaker, and was 18 years or younger was excluded from the study. This data was taken by a previous student at NJIT [2].

#### **5.2 Equipments**

After preparations of shaving and cleaning on the skin electrode site (chest) with alcohol, electrodes were placed there and the leads connected to a unit called Cardio Card (Quinton QStress) interfaced with the ECG signal cable to a notebook computer. Lead II of the ECG was taken from the rear output of the stress test machine as an analog signal. The ECG signal from the card was then digitized at 250Hz, saved and displayed on the laptop computer with the use of a National Instrument DAQCard-1200 and a program written in LabVIEW 5.1.

### 5.3 Recordings for the Study of HRV

All the tests were performed between 9:00 AM and 12:00 PM. Each subject underwent through three test parts, paced breathing (resting), exercise and recovery. In the resting part, the patient was asked to sit and relax while the continuous ECG was being recorded. To keep the patient's breathing rate at 12 breaths/min (0.2Hz) and to obtain the controlled conditions of ECG recordings, the patient went through inhaling and exhaling process. In order to achieve the regulated breath rate the subject followed a series of moving lights that would move up when the subject should inhale and move down indicating that it is time for the subject to exhale. The participant was asked to follow the rhythm and not to take in deep breaths but to try to keep the volume of air in every breath consistent with normal breathing. The resting state lasted for about 5min [2].

After the 5min of paced breathing, the patient who asked to perform a graded maximal exercise on a treadmill while the ECG was recorded. The exercise test followed the Bruce protocol that involved different stages of exertion. The protocol consisted of 3min warm-up period at a rate of 1.7mph followed by 10% incremental rate at every 3min until the patient reached 85% of his/her maximal heart rate. The 85% maximum heart rate was established by the individual's age, sex, height, and weight. If the patients were exhausted or faced shortness of breath, chest pain, discomfort or cramping before reaching 85% of their maximum heart rate, they would be stopped by the physician.

The last part of the test was the recovery stage. Once the patient completed the exercise, he/she immediately sat down and relaxed for about 4 to 5min while the heart rate was continuously being recorded. The study was then considered complete and the obtained ECG data was converted to ASCII format, which allowed us (NJIT students) to

extract the necessary information for various types of HRV analysis. Although important results have been found, some of the data, especially during exercise had missed beats. In the previous thesis [2], this data was eliminated from the analysis. In this thesis, the impact of these missed beats on HRV analysis is demonstrated.

#### **5.4 Software Used for Data Analysis**

LabVIEW and MATLAB are some of the powerful software environments that are important for engineering and programming applications. All of the computer applications in this thesis were done using both LabVIEW and MATLAB. LabVIEW is an abbreviation for Laboratory Virtual Instrument Engineering Workbench. It is a graphical programming language that uses icons to create applications. It has two parts that link to each other. The first one is the user interface which is called the front panel and the other one is the block diagram similar to a flowchart. The block diagram controls the front panel by adding source code using graphical representations of functions. To edit, create, operate and modify the front panel and block diagram, a Palette is readily available on each of them [32].

LabVIEW is well suited for data acquisition and signal processing. It is easy yet powerful software because it avoids complex, difficult and time consuming of writing codes. Instead, it supports creating blocks that would be properly wired to each other so that a working program will be developed. LabVIEW 7.0 is the latest version that has improved with new features and easier work environments. The other good thing about LabVIEW is that the icon and control panel identifies the VI so that you can use the VI in another VI by importing it. This VI that is imported to another application is called a

subVI. The SubVI is like a subroutine in other text-based programs such as MATLAB. LabVIEW contains built in features that are important to develop solutions for scientific and engineering systems. Applications for HRV use many of the built in features such as power spectral analysis block, Wavelet transform, STFT, statistical blocks and so on.

### **5.5 R wave Detection**

The UMDNJ patients' raw data were analyzed using the LabVIEW programs. All the raw data had to be changed into IBI and IIBI format files for further analysis. The first step to obtain the IBI is to detect each ECG R wave. A program that performs detection of R waves is written in LabVIEW 7.0. This R wave analyzer was developed previously [2].

ECG recordings, especially during an exercise stress test, are exposed to many technical and physiological disturbances which are not easily prevented or controlled, and consequently errors in the automatic detection of the QRS complexes cannot always be avoided. That is, the accuracy of QRS detection can be affected; the detector can miss normal QRS complexes or spuriously detect additional events within normal RR intervals. A missed R wave will lead to an interval, which is approximately twice as long as the average interval, while a detection of an additional event within a normal interval will lead to two shorter intervals, the sum of which equals the real interval. Unfortunately combinations of missed and false detections exist, resulting difficulties in artifact identification.

It can be impossible to tell on the basis of IBI data alone whether the cause of an artifact is physiological or technical. In addition, information is needed on the underlying shape of the ECG signal. Abnormal initiations of the heart beat (ectopic beats) can lead to



a variety of morphologies of QRS complexes and cause difficulties in both their classification and their detection. Abnormally large P or T waves are also other possible potential physiological sources of errors. Movement of electrodes (relative to the skin and heart) or other changes in conductivity between the electrodes and the skin can result in rapid baseline shift. Power line interference and extra peaks originating from the movement of wires or discharges of static electricity when clothes, skin, electrodes and wires chafe against each other in the presence of dry air and skin can also cause disturbances [20].

When the undetected R waves were in the normal positions (i.e. when they form normal intervals), we manually marked them. We also deleted the ones that were falsely detected as R waves. Once the correct detection of R waves was achieved, IBI and IIBI files were saved and their signals were investigated. From these stored IBI and IIBI files, the Fourier spectrum, the STFT and Wigner distribution have been performed.

## **5.6 Missed Beats**

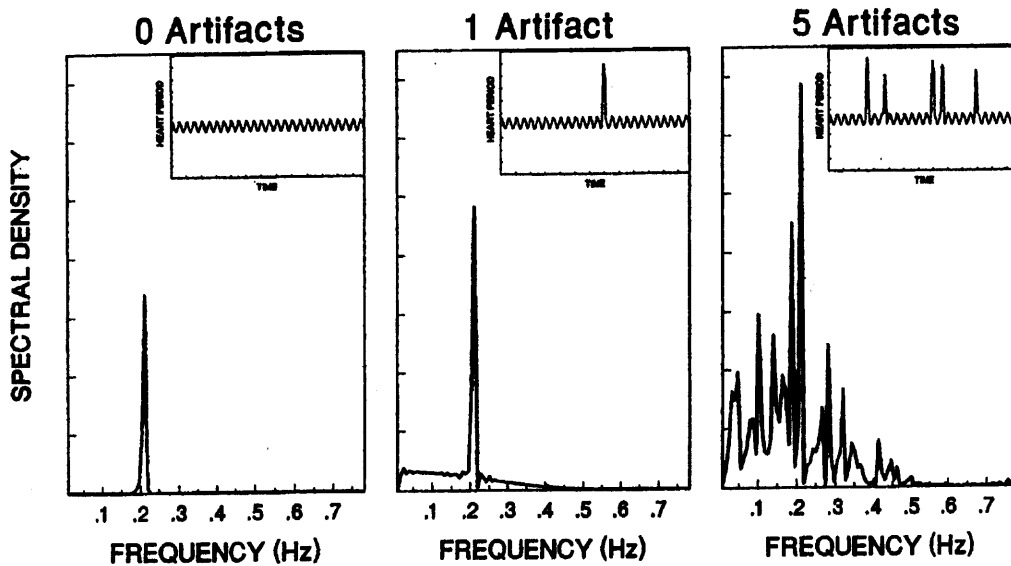
### **5.6.1 Motivation**

There were some patients from the UMDNJ whose R waves were missed due to ECG saturation. To determine whether these patients should be eliminated from the study, especially if the area of the missed beats was significantly apart from the areas of interest in the ECG, simulations of missed beats on "good" data was undertaken to look at their impact using time-frequency analysis. According to Berntson [1], even one missed or extra beat within a certain time interbeat interval series can cause errors in the heart rate variability. Bernston showed that the effect of artifacts (missed or extra beats) on the

power spectrum were significant. He simulated IBI series with 0, 1, and 5 missed beat artifacts. His results indicated that artifacts cannot be ignored in studies of heart rate variability. Berntson evaluated the effects of artifacts on measures of heart period variability by introducing both missed beats and spuriously detected R waves into known series of simulated and actual heart period data. His results revealed that even a single heart period artifact, occurring within a 2-min recording epoch, can lead to errors of estimate of heart period variability that are considerably larger than typical effect sizes in psychophysiological studies [1].

*ECG artifacts*

129



**Figure 5.1** Fourier spectrums for simulated data with 0, 1 and 5 missed beats [1].

In this study, simulations were conducted using time-frequency analysis by intentionally deleting beats at different time marks. Then efforts were made to look at and

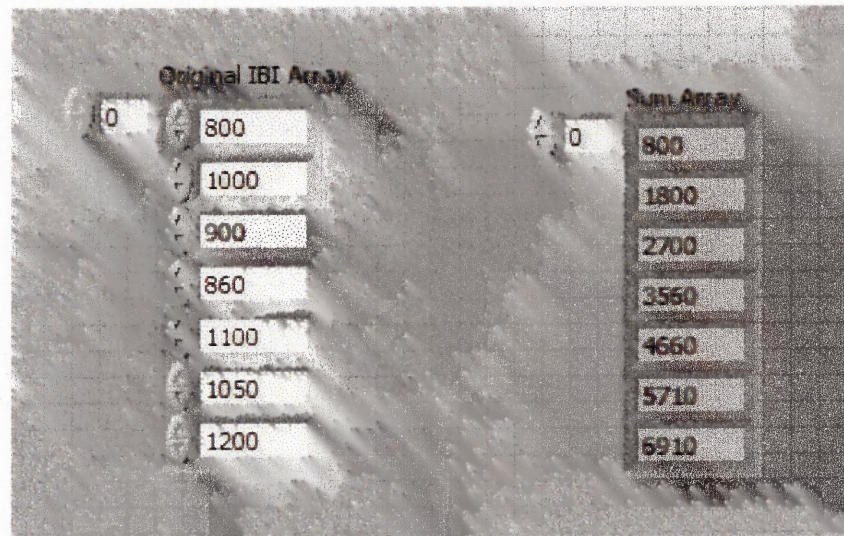
to address the effect of these missed beats using time-frequency analysis. As shown in Figure 5.1, Berntson looked at the overall heart rate variability of the ECG segment in the resting state and plotted the LF and HF values (along with the actual curve). The problem with applying this concept to the UMDNJ study implies that we should simply do a spectral analysis over the entire 10-20 min period. However, to adequately study a long exercise regimen, time-frequency analysis should be utilized. Therefore, the question is whether time-frequency analysis would have the same overall problems with multiple missed beats, or if the effects of missed beats on the spectral analysis are localized to the positioning of the missed beats. If the time-frequency analysis is not affected, then it is possible to add the patients into the study. On the other hand, if the effect is concentrated only around the missed beats, then we can freely study the other sections of the signal. For example, most of the saturations or missed beats in our data occur during the exercise part. Therefore, if the artifacts affect only the exercise part, then we can examine both the recovery and the paced breathing portions of the study.

Berntson also did not perform interpolation for missed R waves, and looked at the effect. Therefore, one of the goals of this thesis is to study the effects of interpolation using time-frequency analysis. If the effect of the missed beats is minimized, then we might be able to study that area of missed beats.

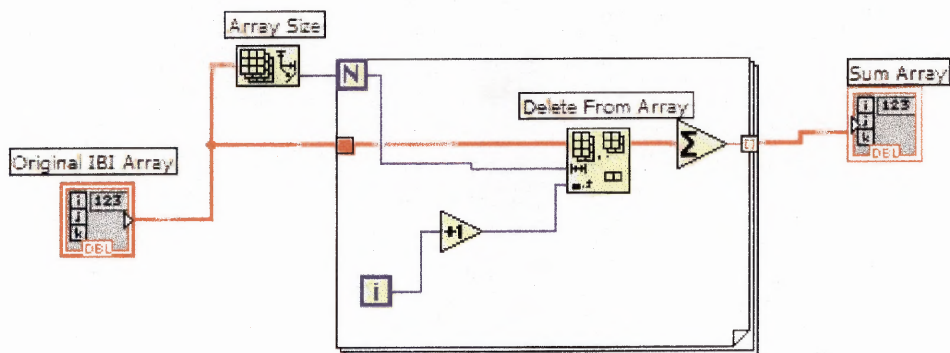
### 5.6.2 Methods Used for Missed Beats

As explained previously, in order to do the analyses on the interbeat interval (IBI), the occurrence of the R waves has to be detected. Once the locations of the heartbeats are detected, the IBI arrays are employed. After the IBI array is obtained, a LabVIEW program that would take the IBI array and simulate missing beats was created. Instead of deleting beats directly from the ECG, they were deleted by working with an IBI.

Initially, a program that has the ability to delete a single beat was created. To delete a single beat, two adjacent intervals have to be combined. Initially this program was tested with a simple array of numbers that was created directly on the front panel, as shown in Figure 5.2. Then the actual IBI was considered for evaluation by importing the IBI text file directly into the program. This program has the ability to delete a beat by a user typing in the approximate time where s/he wants the beat to be eliminated. To search for an approximation as to where each beat is located, an accumulative array from the IBI arrays would be created. This is done by adding each element to the sum of the previous elements. An example of an accumulated array from the corresponding IBI array is shown in Figure 5.2. The LabVIEW program that creates the accumulation is also shown in Figure 5.3.



**Figure 5.2** Example of IBI array and accumulated sum array.



**Figure 5.3** LabVIEW graphical sum array program.

The cumulative array helps the user to know the location of beats. To eliminate a beat (the same as combining two intervals in a row) at the time mark specified the program searches for the point nearest to the time mark. Therefore, the cumulative array is used as a pointer to the original IBI array so that the appropriate interval would be eliminated. The program that is shown in Figure 5.5 is an example of one beat eliminator to the nearest time entered in seconds. It reads the IBI data from the chosen location. It then adds each interval to the sum of the previous elements. It compares the time mark of

beat elimination with the sum array. It combines the two intervals (delete the beat) at the point nearest to the time mark. Finally, it puts the combined interval in the appropriate place of the IBI array. This is just one example because there may be other methods of eliminating a beat. For example, the program that deletes multiple beats should also have the ability to delete a single beat. A program that deletes multiple beats is discussed in the next paragraph.

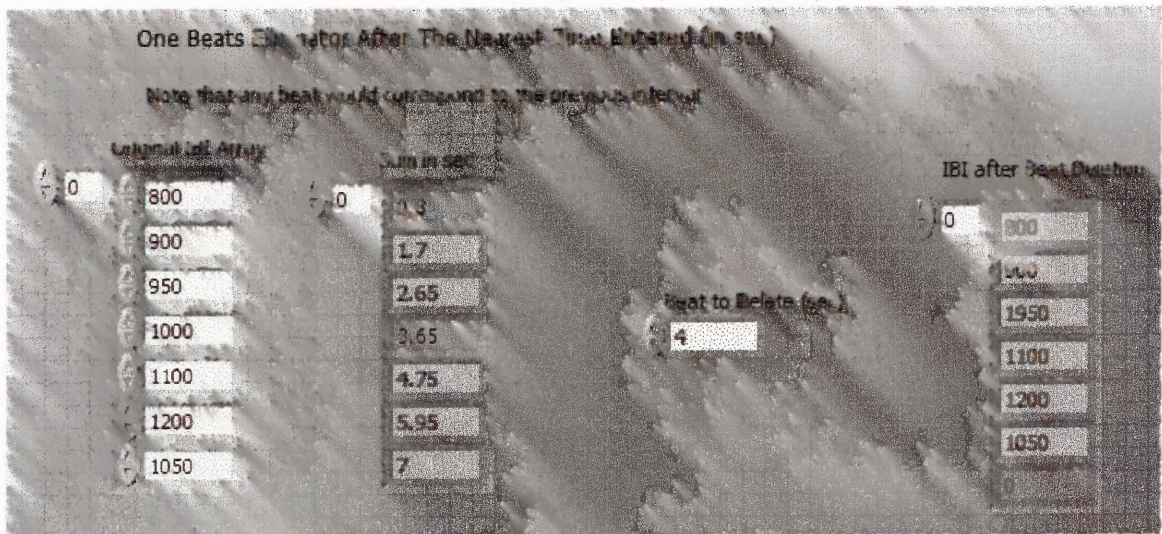


Figure 5.4 Front panel of one beat eliminator.

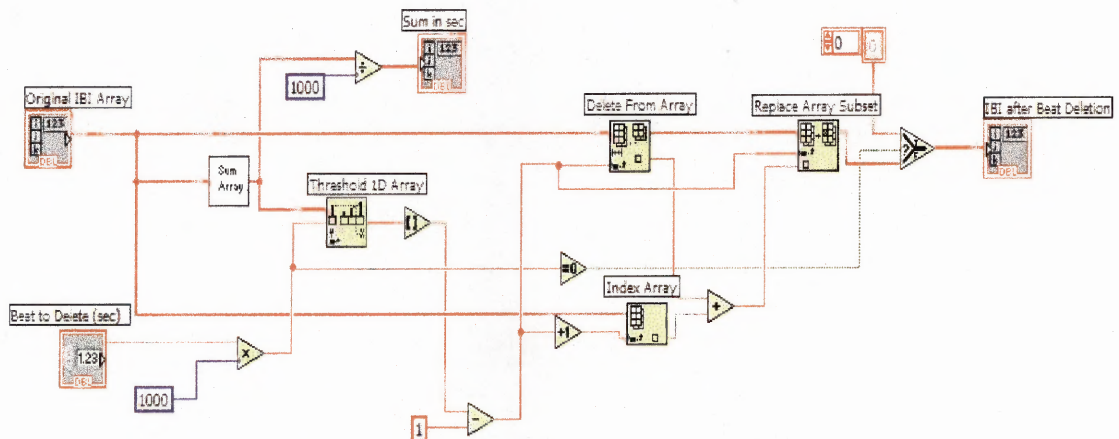
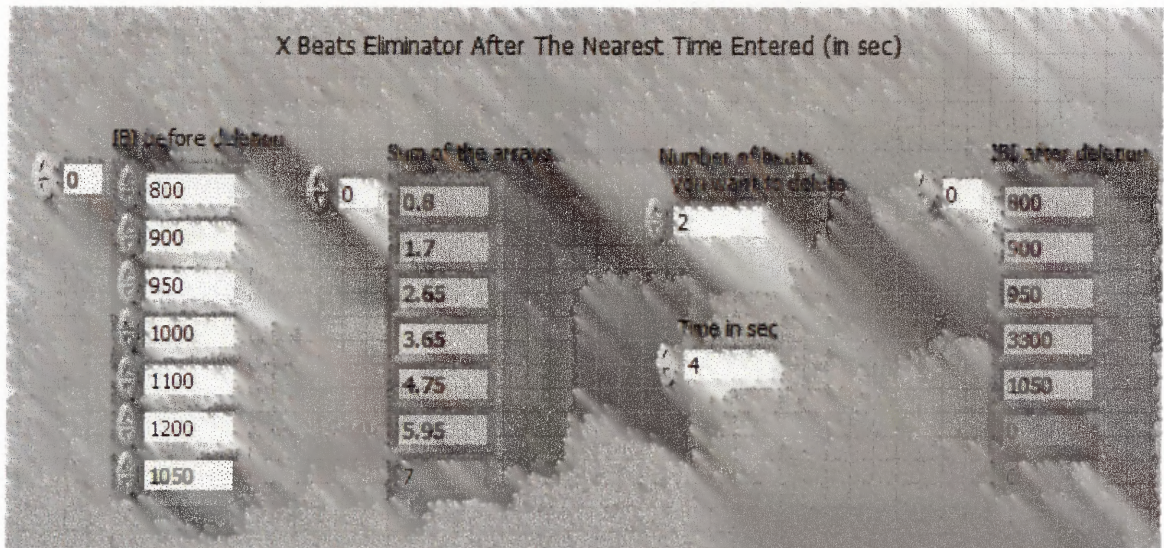


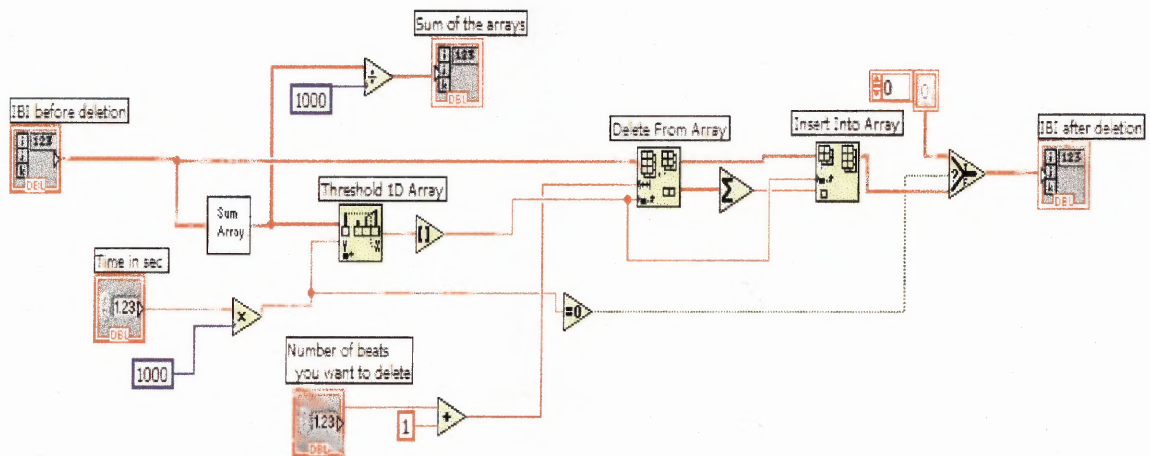
Figure 5.5 One beat eliminator.

In the second approach, the effect of two or more missing beats is examined. In order to examine the effect of multiple missing beats, a program that deletes multiple beats had to be created. As in the first approach, the program should create a cumulative array from the original IBI array and search for the nearest point to the time mark that is entered by the user. The main reason for creating the program that deletes multiple beats is to examine the additive effect of having multiple missing beats for the HRV. An example of a program that has the ability to delete x number of beats in a row is shown in Figure 5.7.

The process is the same as the program that eliminates one beat, except that now the program has the ability to delete more than one beat. The user enters the time mark and the number of beats s/he wants to eliminate. The program searches for the nearest time and goes forward and deletes the number of the beats entered starting from that time mark. For example, in Figure 5.6, the number of the beats to be deleted is 2 and the time mark is 4sec. The program searches for the closest time to 4sec, which in this case is 3.65sec (corresponds to the 1000ms interval of the IBI) and then it goes forward and deletes the two beats (or combines the appropriate intervals). Remember that deleting two beats corresponds to combining three intervals.



**Figure 5.6** Front panel of the multi-beat eliminator.



**Figure 5.7** Multi-beat eliminator.

The resting state (paced breathing part) lasted for 5min. After that, the exercise part followed. One of the assumptions is that during paced breathing, the signals from the ANS can be considered as stationary. This assumption is not appropriate for the exercise part. Therefore, the Fourier transform is valid only for the paced breathing segment. To look at the effect of the missed beats for the HRV of the entire ECG segment, time-



frequency analysis was used. The first thing that was observed was the effect of the missed beats on the LF and HF during the paced breathing using the Fourier spectrum. Then the second approach involved applying time-frequency analysis to the entire ECG by deleting beats in a row and randomly. Finally, a moving average interpolation technique was used on the missed beats that were intentionally eliminated, and the interpolated time-frequency signals were compared with the original clean data. The impact of the missed beats on the LF, HF, LF/HF ratio, 3D, the contour of TF and all other results are discussed in the next Chapter.

## CHAPTER 6

### RESULTS AND DISCUSSION

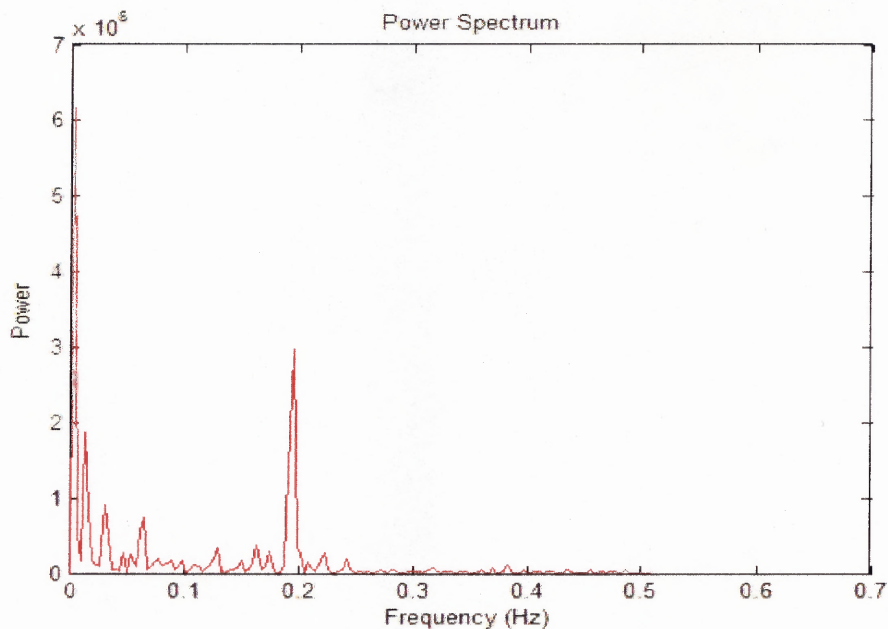
In this chapter the results of the impact of the missed beats will be explained. As indicated in Chapter 5, two protocols have been used to eliminate beats from IBI data. The first one was eliminating the beats that are adjacent to each other (in a row). Two or more beats were deleted. The other protocol was to eliminate beats arbitrarily (sparsely). Both of these protocols were used because some of the patients missed their beats not only arbitrary on the IBI series, but also in a row, especially in the exercise portion. The beat deletions were applied in the paced breathing as well as during the exercise.

For the paced breathing, the results of missed beats were analyzed using the Fourier spectral analysis. This is consistent with the protocol that was used by Berntson [1]. When missed beats are in the exercise or the recovery states, the time-frequency method is used. Comparisons of LF, HF and LF/HF of the original clean data and missed beats are performed by superimposing on each other. The errors are separately plotted. The widths, heights and areas of the error functions are measured and plotted with respect to the number of missed beats. Interpolation or replacement to the missed beats is performed. For the intentionally eliminated beats, comparisons between the interpolated missed beats and the original clean data are done. Finally, the patients who originally have missed beats are looked at, and the moving average is applied to them. Then comparison between the missed beats and the corrected (interpolated) ones is done.

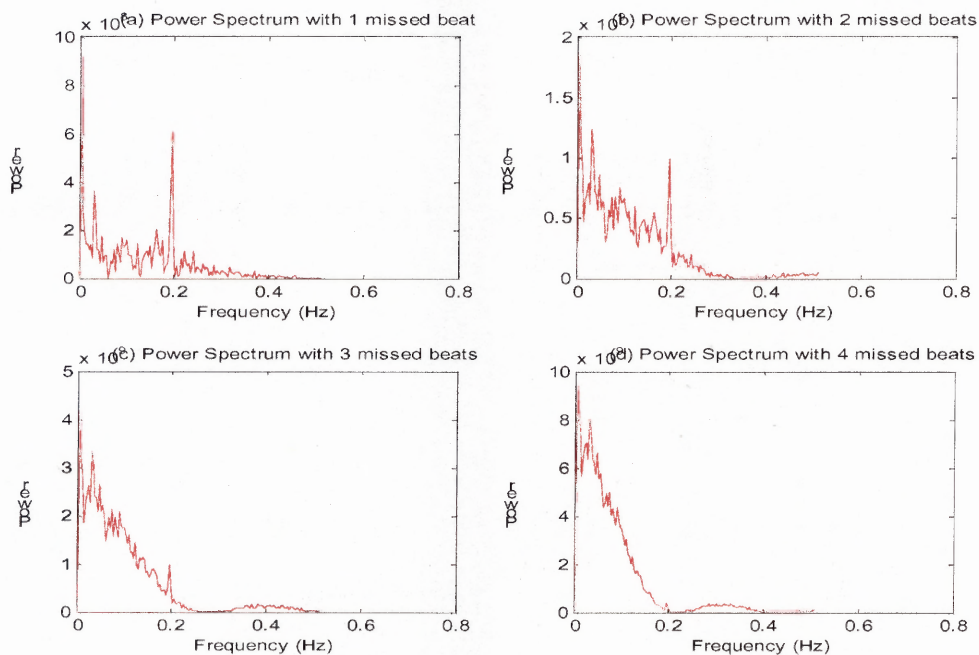
## 6.1 Effect of Missed Beats Using Fourier Spectral Analysis

The power spectrum during the paced breathing is affected due to missed beats as shown in Figures 6.2 and 6.3. At each increment of beat elimination, both in a row and arbitrarily, the powers of the peak components (LF and HF) are increased. Figure 6.1 represents the frequency spectrum for the original clean data during paced breathing, and Figure 6.2 is the result of one to four missed beats in a row. The third figure, Figure 6.3 represents the plots of arbitrary eliminated beats within (between) 10 to 90% of the IBI.

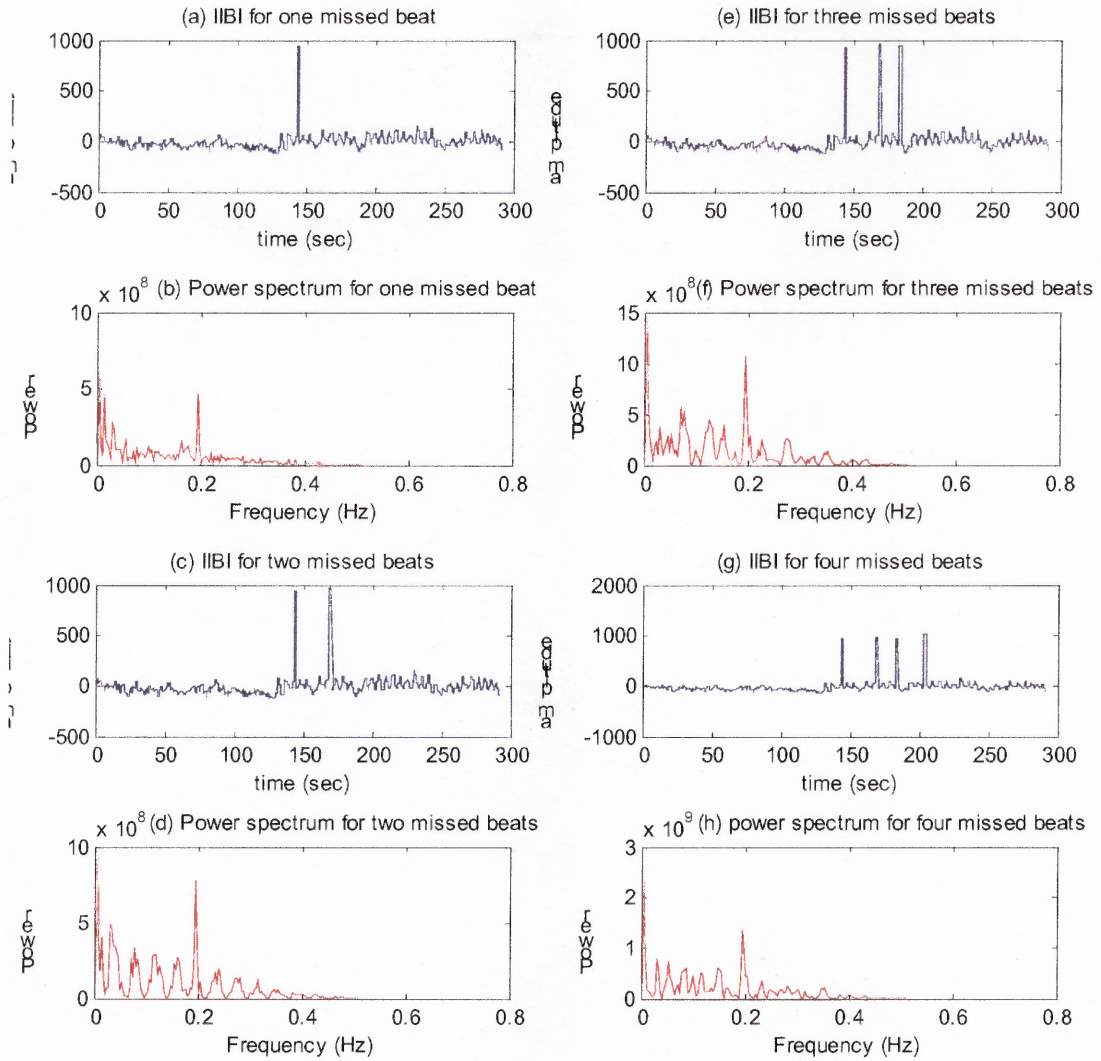
The plots of the IIBI raw data that have one to four arbitrary missed beats are shown in Figure 6.3. The spikes shown in the plots are due to missed beats. One to four beats are eliminated so that the effect of a single beat and cumulative or multiple beats using Fourier spectrum can be compared and analyzed. As can be seen from the graphical results, even one missed beat affects the entire power spectrum of the Fourier analysis. Therefore, regardless of the number of missed beats introduced into the IBI file during the paced breathing, their effect spreads throughout the spectrum. This is consistent with the results from the Berntson paper. The question is what if time-frequency analysis is used? Does the effect still spread across the entire TF spectrum? This will be discussed in the next section.



**Figure 6.1** Power spectrums for a period of 5min clean data during paced breathing.



**Figure 6.2** Power spectrum for (a) one missed beat (b) two missed beats (c) three missed beats (d) four missed beats in a row.



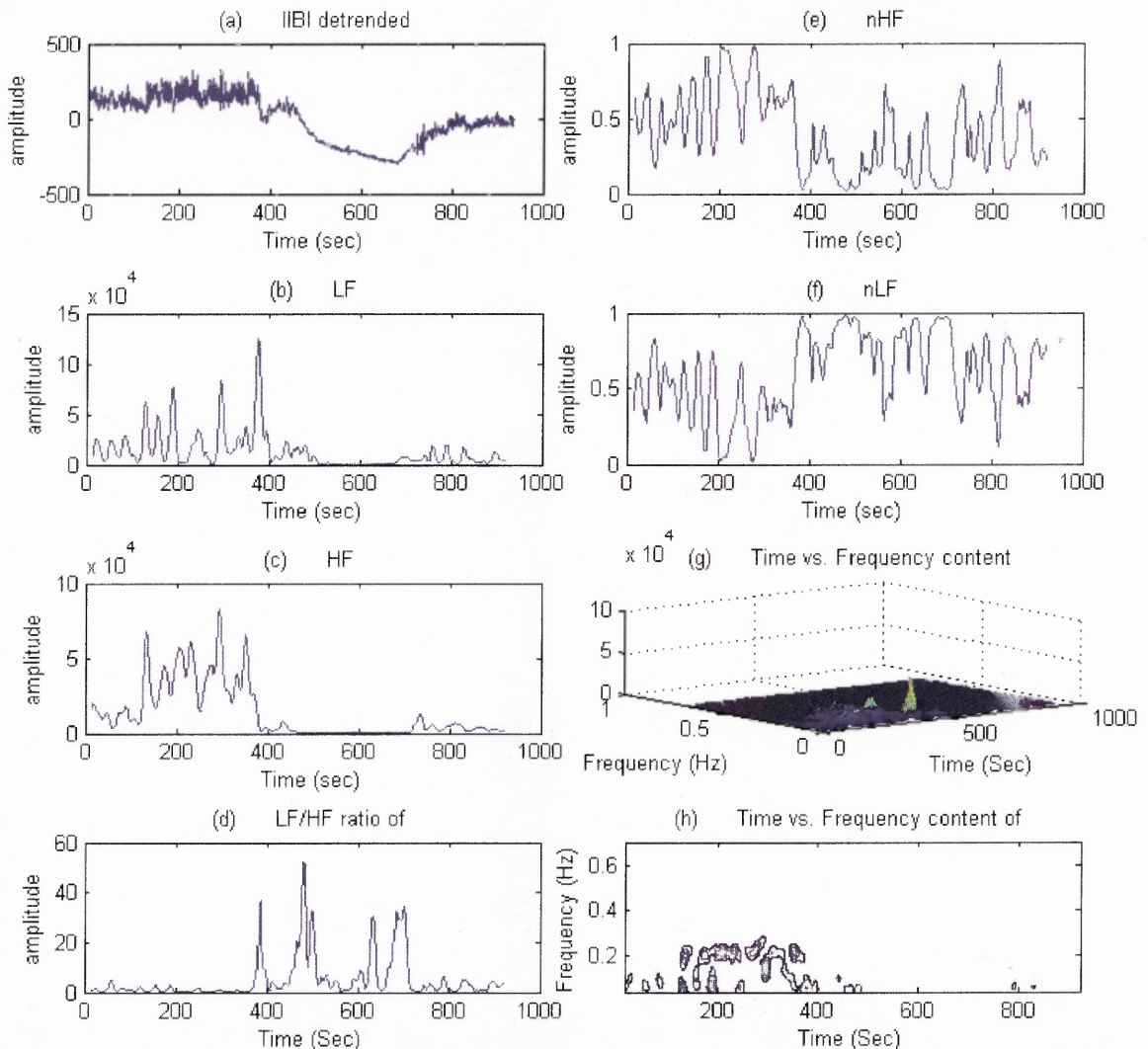
**Figure 6.3** The IIBI plots and their corresponding power spectrum for one, two, three and four arbitrary missed beats within a period of 1 to 5 min.

## 6.2 Effect of Missed Beats Using Time-Frequency Analysis

As mentioned in Chapter one, the original clean data and the missed beats have been analyzed using the STFT and Wigner distribution. Figure 6.4 is the result of original clean data (data that has no missed beats) for the entire exercise stress test. It represents the outcome of the original clean data using the STFT analysis. The LF, HF, (and their normalizations), LF/HF ratio, 3D and contour for the entire exercise stress test are

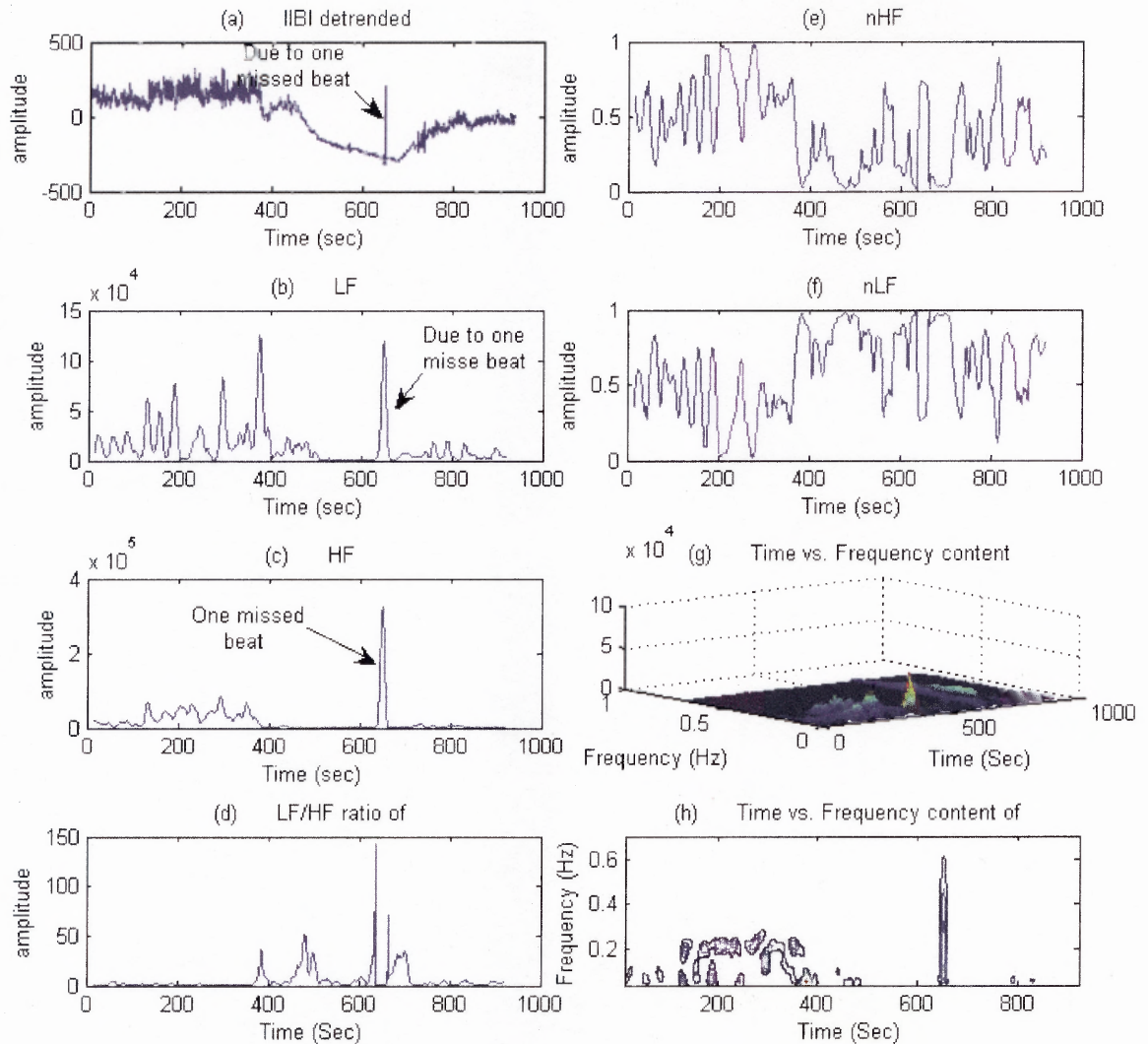
plotted. The plots represent features that are common to most of the clean data files. In figure 6.4(a), the IIBI plot of the data file is shown. The paced breathing is represented by the oscillating plateau. The exercise and recovery parts are indicated by the decrease and increase of the IIBI plot respectively.

Figure 6.4(b), 6.4(c) and 6.4(d) represent the LF, HF and LF/HF respectively. During the resting state the amplitude of the HF band dominates the spectrum because parasympathetic division of the ANS is more active than sympathetic. A decrease in HF and an increase in LF are seen during exercise indicating a reduction in the activity of the parasympathetic portion and an increase in the activity of the sympathetic respectively. An increase in the amplitude of HF band is observed during recovery. The amplitude of LF band is also increased. But the amplitude of their ratio (LF/HF) is small during the paced breathing, increases rapidly during exercise, and stays the same (or oscillates) during the recovery stage. The increase of both HF and LF, and the unchanged (oscillated) plot of their ratio during recovery stage indicate the increase in vagal activity and the slow reduction in sympathetic activity.



**Figure 6.4** Time-frequency for original clean data using STFT: (a) IIBI plot (b) LF (c) HF (d) LF/HF (e) NHF (f) NLF (g) 3D (h) Contour.

Figure 6.5 shows the STFT output for one missed beat at 660sec (11min). In all the activity plots the presence of the missed beat is clearly seen. A spike at 660sec is shown in the IIBI plot of Figure 6.5, indicating the presence of one missed beat. Due to the missed beat, large amplitude is also seen in each of the activity plots. This can be easily observed in the LF and HF components of Figure 6.5.

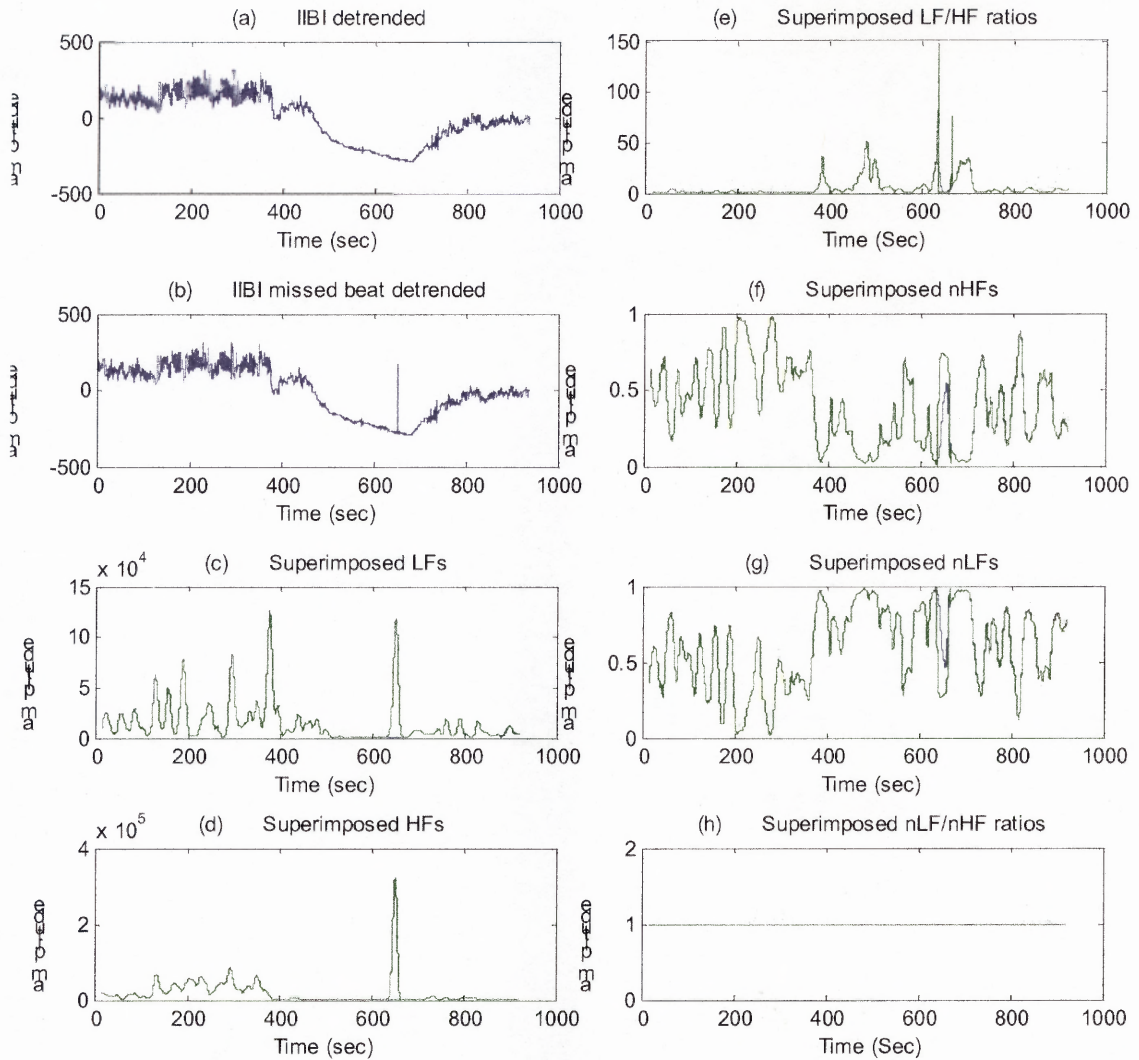


**Figure 6.5** Time-frequency for one missed beat using STFT: (a) IIBI plot (b) LF (c) HF (d) LF/HF (e) NHF (f) NLF (g) 3D (h) Contour.

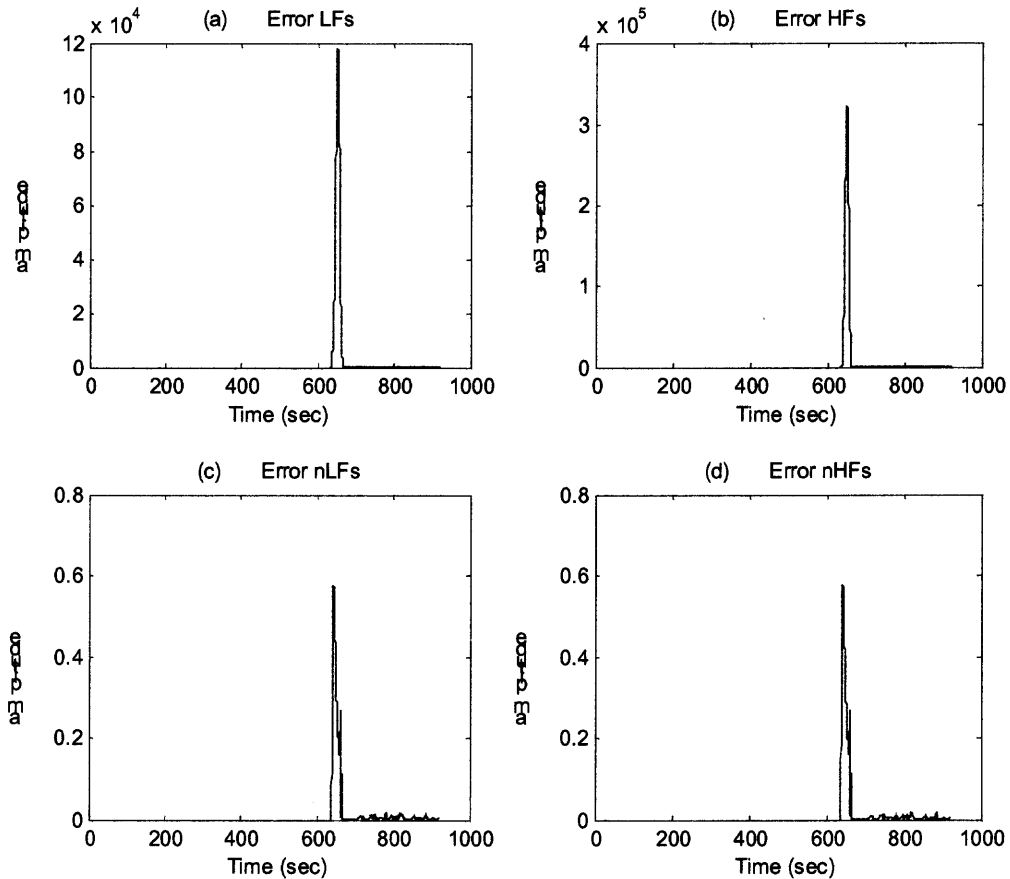
By superimposing or overlapping the missed beat onto the original clean data, it is possible to examine their differences (errors). Then by extracting the differences, they are separately plotted as error functions. This way, it can be observed how far the error functions extend. Figure 6.6 represents the one missed beat TF component plots superimposed on the original data. In each of the superimposed TF components the differences between the two data are clearly seen around the missed beat time mark. As



can be observed from each of the plots, the differences far away from the time mark of the missed beat are zero. That is, the superimposed TF components of the missed beat and the original data are exactly overlapped except around the time mark of the missed beat. This can also be seen from the error function plots in Figure 6.7. A distinct peak amplitude is shown in all of the error function signals. The errors are strictly restricted around the time mark of the missed beat. Beyond the peak amplitudes, the error functions are zero. The size of the LF and HF error widths are measured as 51sec and 49.8sec respectively, and a hanning window has been used. Therefore, one missed beat during exercise does not affect the entire spectrum.



**Figure 6.6** The STFT output results for one missed beat and original clean data together: (a) IIBI plot for clean data (b) IIBI plot for one missed beat (c) Superimposed LFs (d) Superimposed HF power (e) Superimposed LF/HF ratios (f) Superimposed NHFs (g) Superimposed NLFs (h) Superimposed NLF/NHF ratios.

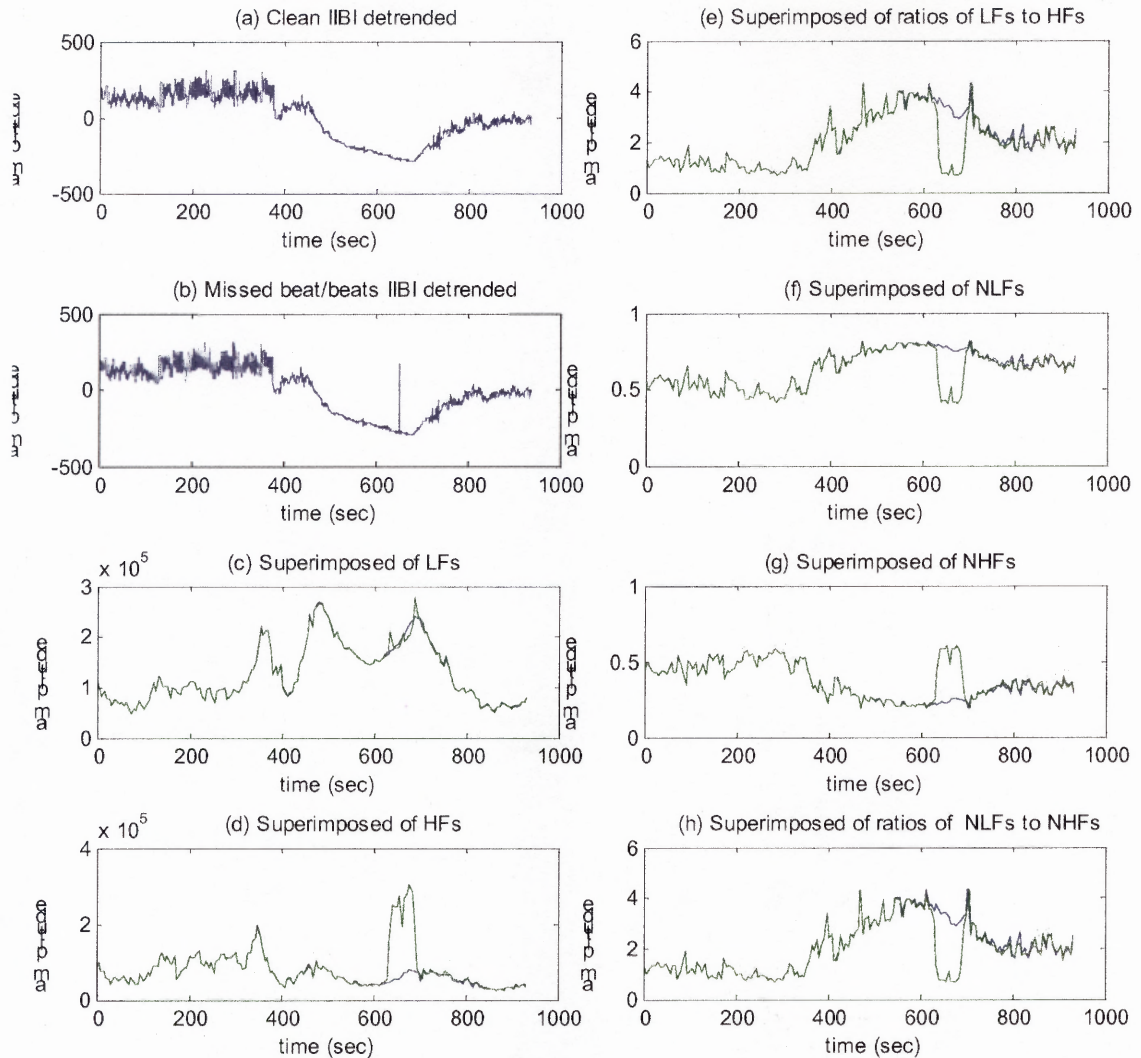


**Figure 6.7** Error functions using STFT: (a) LFs (b) HFs (c) NLFs (d) NHFs.

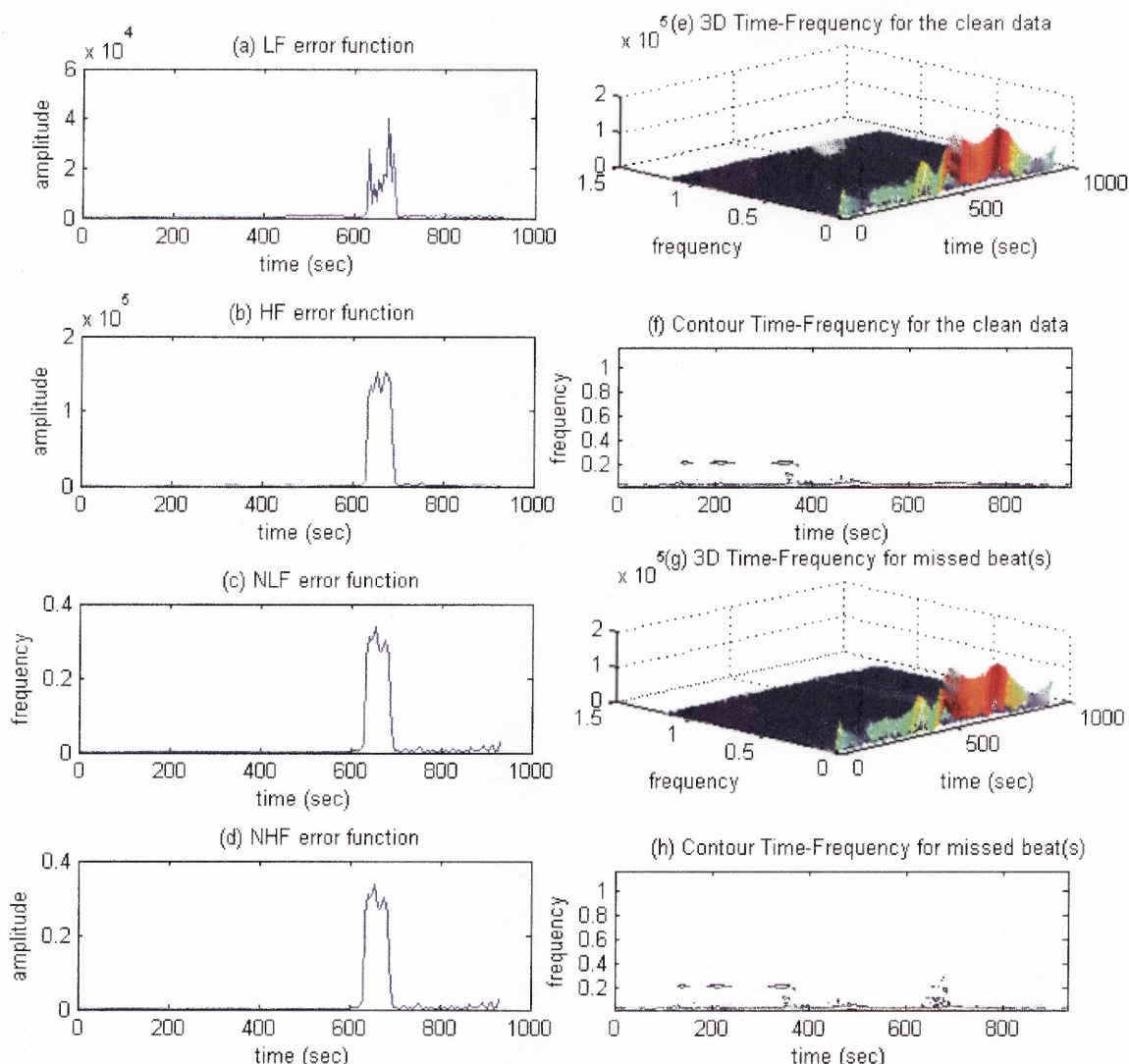
In the previous Figures, STFT was used to plot the TF components. The same result can be found using the Wigner distribution. In the subsequent graphs the one missed beat is analyzed using the WD. Figures 6.8 and 6.9 are the results of data with one missed beat Vs the original clean data. Figure 6.8(a) and 6.8(b) show the IIBIs of the original and one missed beat data respectively. As in previous, in Figure 6.8(b) a spike is shown at 11min or 660sec. This spike indicates the presence of one missed beat at that particular time mark (ie at 11 min). The plots 6.8(c) and 6.8(d) represent the superimposed results of the LF and HF from the one missed beat on the original data. In Figure 6.8(d),

the superimposed HF, upward distinguishable amplitude is seen indicating an error difference between the two plots due to the missed beat at 660sec. The superimposed LF plots from the original and one missed beat data are also shown in Figure 6.8(c). Looking at the superimposed LF and HF plots, the LF error is smaller than HF.

The superimposed plots of LF/HF ratios are shown in Figure 6.8(e). A downward difference is observed. The normalized corresponding plots and the stand alone error differences are also plotted in figure 6.8(f), and Figures 6.8(g), 6.8(h), 6.9(a), 6.9(b) and 6.9(c). As previously discussed using the STFT, the effect of one missed beat using WD is also concentrated around the time mark of that missed beat. It has little effect on the entire plot components. In Figure 6.9, the 3D and contour plots of the original data and one missed beat are shown. As can be seen from the plots, missing only one beat doesn't affect the entire time-frequency plot. In other words, the errors far away from the time mark of the missed beat are negligible. For example, the effect of one missed beat in the exercise portion is local. Therefore, one can study the ANS or the HRV of the exercise segment that is outside the error window, the paced breathing and the recovery portions. In this case, a patient data should not be discarded just because his/her IBI data missed one beat in one of the ECG segments.



**Figure 6.8** TF superimposed plots for one missed beat during exercise on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for one missed beat (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.

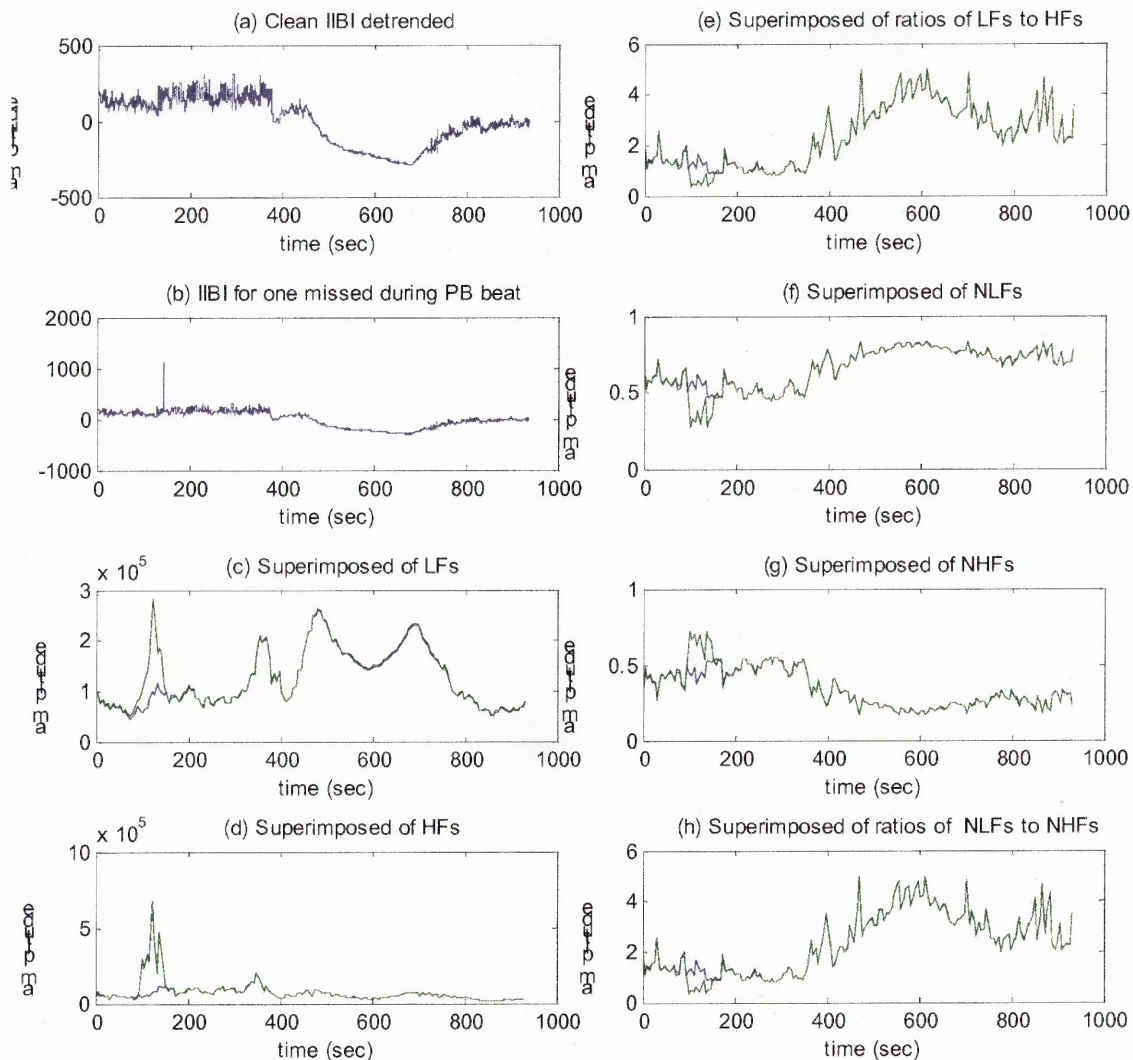


**Figure 6.9** Error functions, 3D and contour plots for one missed beat during exercise using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for one missed beat (h) Contour plot for one missed beat.

As previously explained, the effect of one missed beat during exercise is localized. The errors are strictly bound around the area of the missed beat. The ECG segments outside this region can be used for analysis. The effect of one missed beat during the paced breathing using TF is also localized. Figures 6.10 and 6.11 represent the plots of the original data vs. one missed beat during paced breathing. Figure 6.10(b)

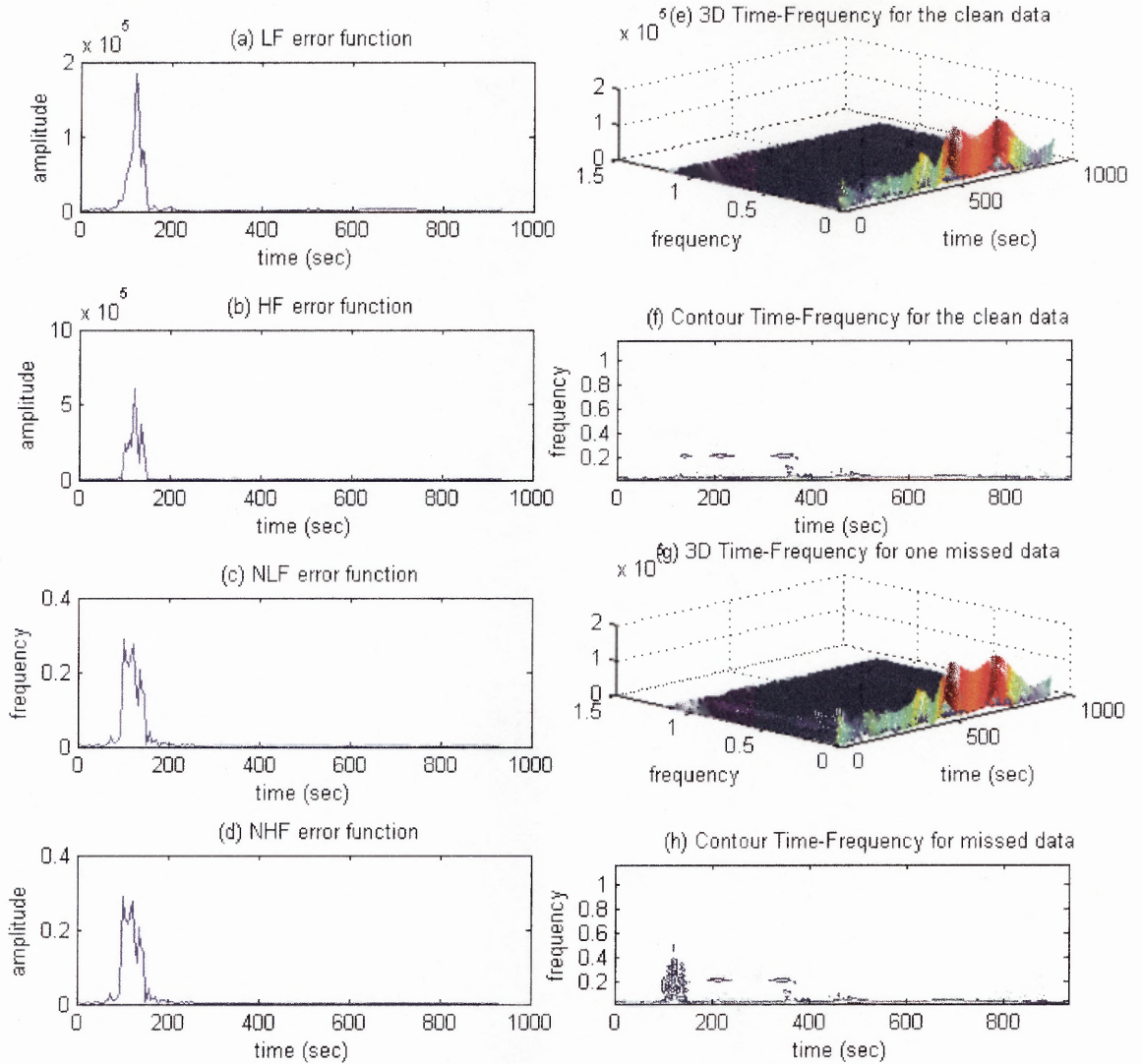
shows one spike during paced breathing at 150sec (2.5min). As can be seen from the superimposed activity plots (Figures 6.10(c)-6.10(h)), there is only one localized amplitude around the area of the missed beat is shown. The portions that are outside this area are not affected. Therefore, they can be considered for study.

The absolute error differences between the original data and one missed beat during the paced breathing are plotted in Figures 6.11(a)-6.11(d). They all show that the errors due to one missed beat do not spread throughout the entire spectrum. The size of the width of the LF and HF error functions is measured as 51.8sec, which is 0.8 and 1sec wider than the LF and HF error function during exercise, respectively. Therefore, one missed beat during paced breathing is consistent with or has the same effect as the one missed beat during exercise. The sizes are computed using STFT since the errors exactly go to zero, as shown in Figures 6.12 and 6.13. The 3D and contour plots of Figures 6.11(g) and 6.11(h) are also illustrated that the effect due to the missed beat is localized. Only the frequencies corresponding to the time mark of the missed beat are affected.



**Figure 6.10** TF superimposed plots for one missed beat during paced breathing on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for one missed beat (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.





**Figure 6.11** Error functions, 3D and contour plots for one missed beat during paced breathing using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for one missed beat (h) Contour plot for one missed beat.

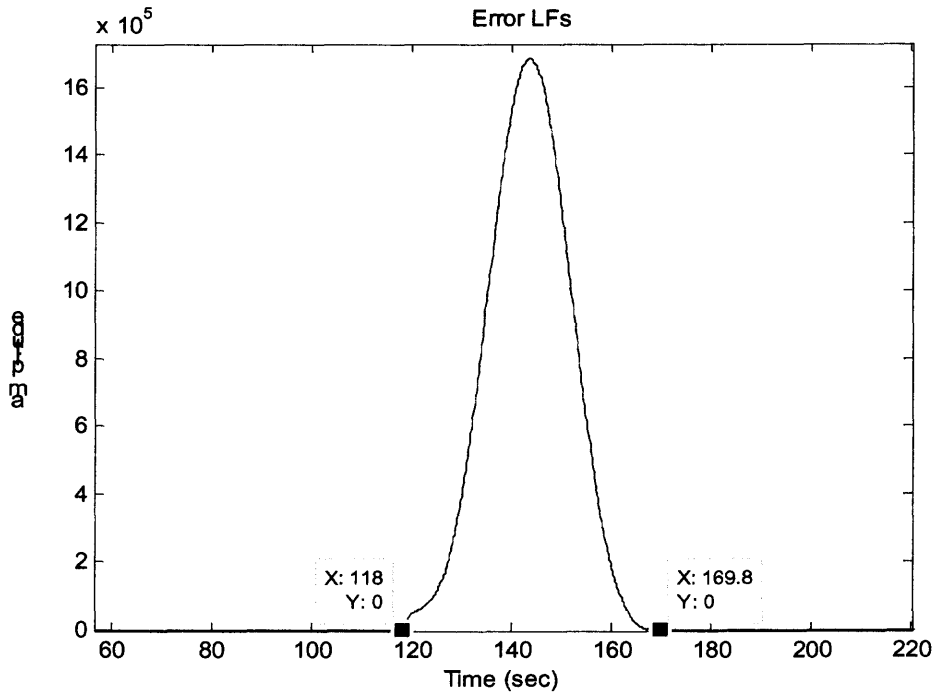


Figure 6.12 LF error function with its extreme end values.

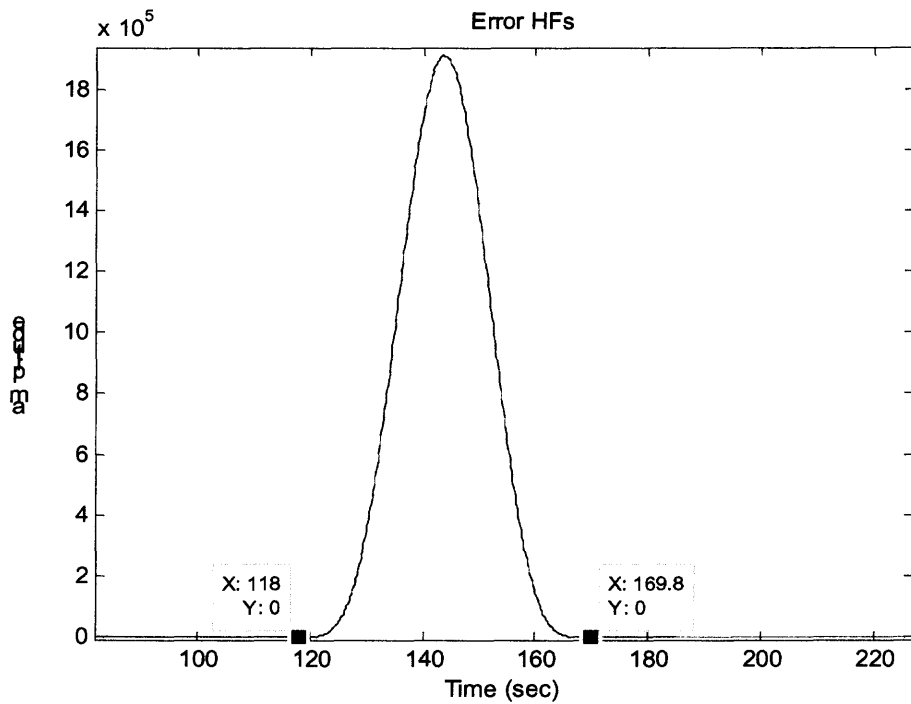


Figure 6.13 HF error function with its extreme end values.

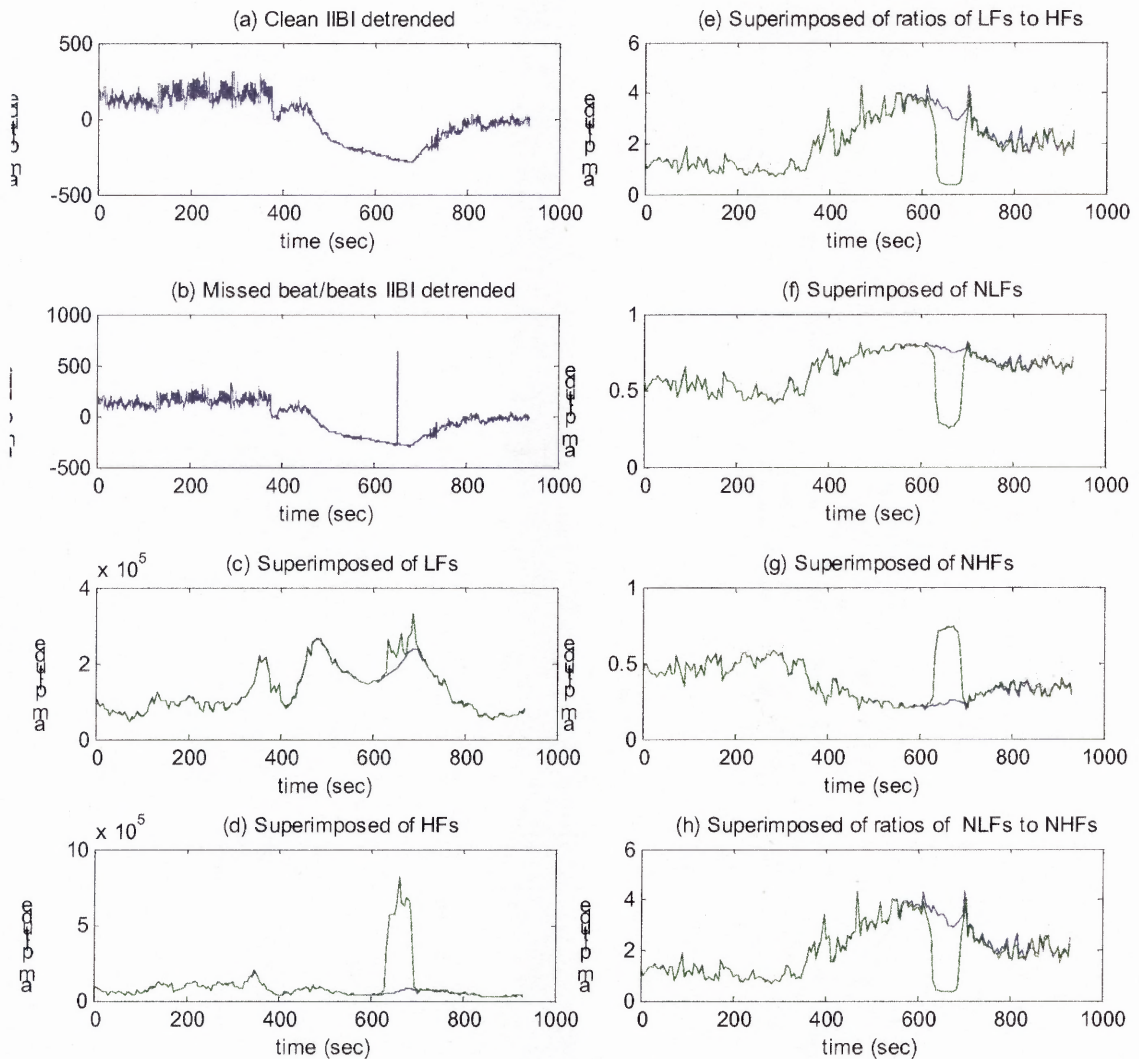
### 6.2.1 Effect of Missed Beats in a Row

In this section the results of two and three missed beats in a row are discussed. Due to similarity between the outputs of STFT and WD, only WD will be used. Figure 6.10 and Figure 6.15 represent the WD signals from the original clean data and two missed beats. Figure 6.14, shows the IIBIs and the superimposed plots. In the subsequent plots of Figure 6.15, the error function, the 3D and contour plots are shown. The effect of two missed beats in a row is also localized.

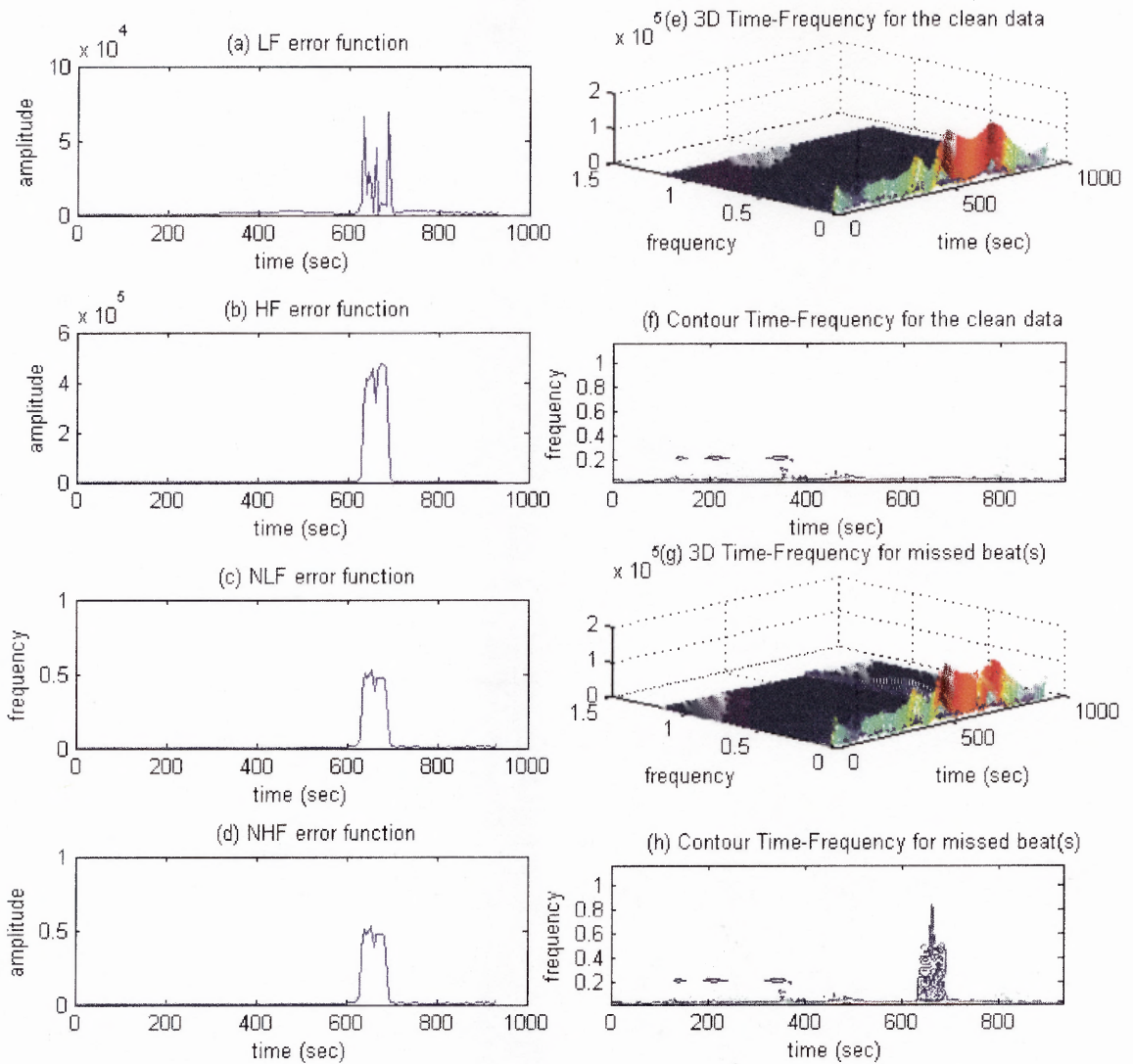
In all of the superimposed and error function plots in Figures 6.14 and 6.15, distinct peak amplitudes are clearly observed. These peak amplitudes are due to two missed beats in a row. There are no other peak amplitudes in any parts of each of the TF components except the one at the time of the two missed beats. This shows that the errors due to two missed beats also do not spread out beyond the location of the two missed beats. Although the heights and areas of the error functions are increased compared to one missed beat, the width is the same size as one missed beat. The size of the width of the error functions is an interesting measurement to look at because it determines how far the error goes beyond the location of the missed beats. The quantitative measurement of these parameters is shown in Table 6.1 and will be discussed in Section 6.5.

The effect of the two missed beats can be shown from the contour plot of Figure 6.15(h). Peaks are also seen around the time mark of the missed beats (at 660sec or 11min). This can also be observed from the 3D TF plot in Figure 6.14g, where the time, frequency and amplitude would be seen clearly. A noticeable peak is covered at all the frequencies at the particular time (at 660sec), which in this case is at the time where the two missed beats are located. The entire frequency of the spectrum, outside the

frequencies corresponding to the time of the missed beats, is not affected. Therefore, the results show that the effect of two missed beats in a row using TF analysis is still localized, and does not change the activities far away from the location of the two missed beats.



**Figure 6.14** TF superimposed plots for two missed beats in a row on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for two missed beats (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.



**Figure 6.15** Error functions, 3D and contour plots for two missed beats in a row using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for two missed beats (h) Contour plot for two missed beats.

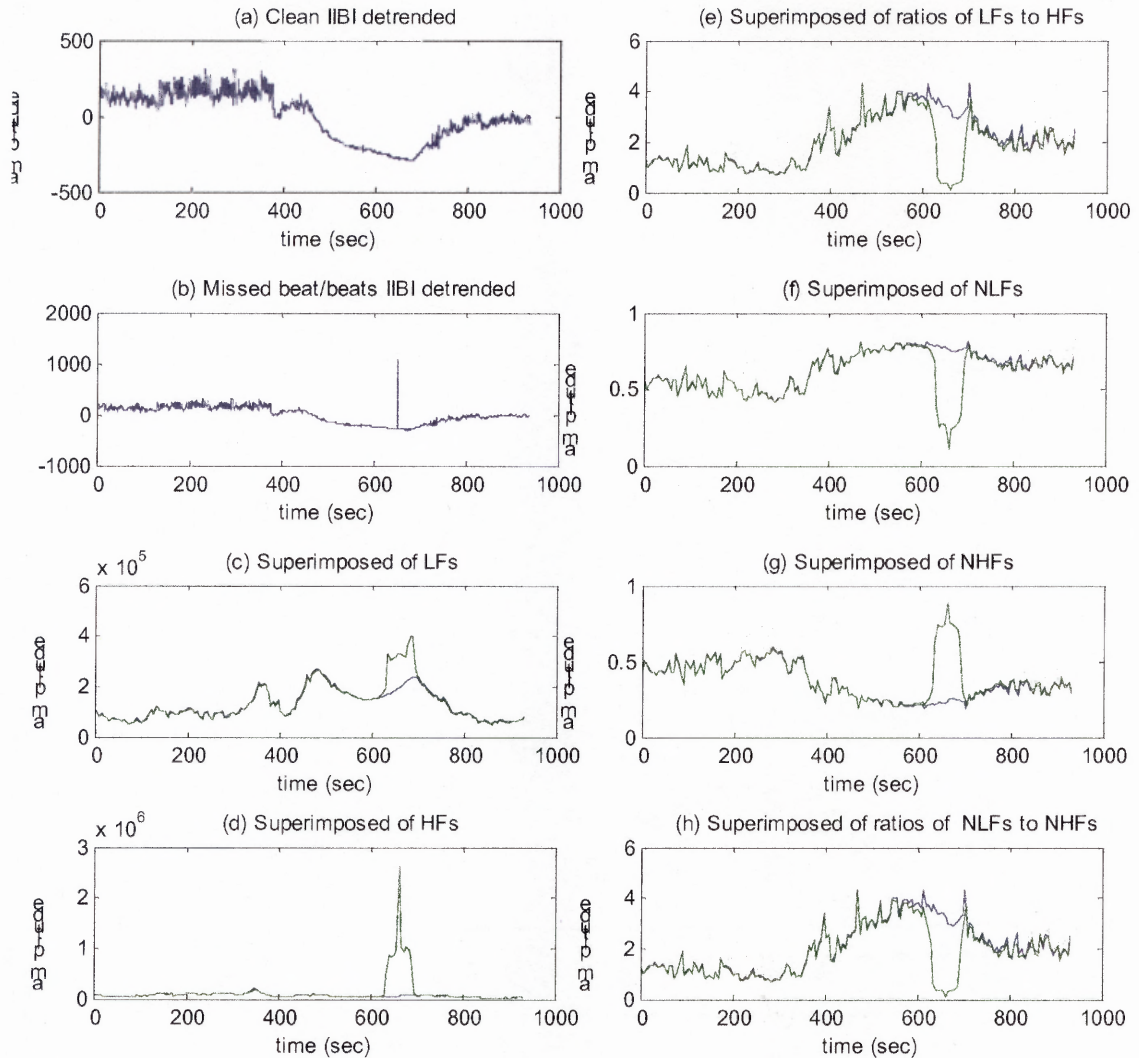
Figure 6.16 and Figure 6.17 represent three missed beats in a row. The same as the one and two missed beats, dominant peak amplitude is shown in all of the component plots. There are no other small or large amplitudes except the one at the time of the three missed beats. Since the height of the peak amplitude due to the three missed beats

increased, the IIBI plot looks small and shrunk. But, the change only occurred at the time of the three missed beats. The size of the error width due to the three missed beats is approximately the same as the error widths due to one and two missed beats. Table 6.1 represents the quantitative measurements of the sizes of the LF and HF error widths of the one to three missed beats that have been discussed. In Section 6.5, measurement of the error functions is addressed.

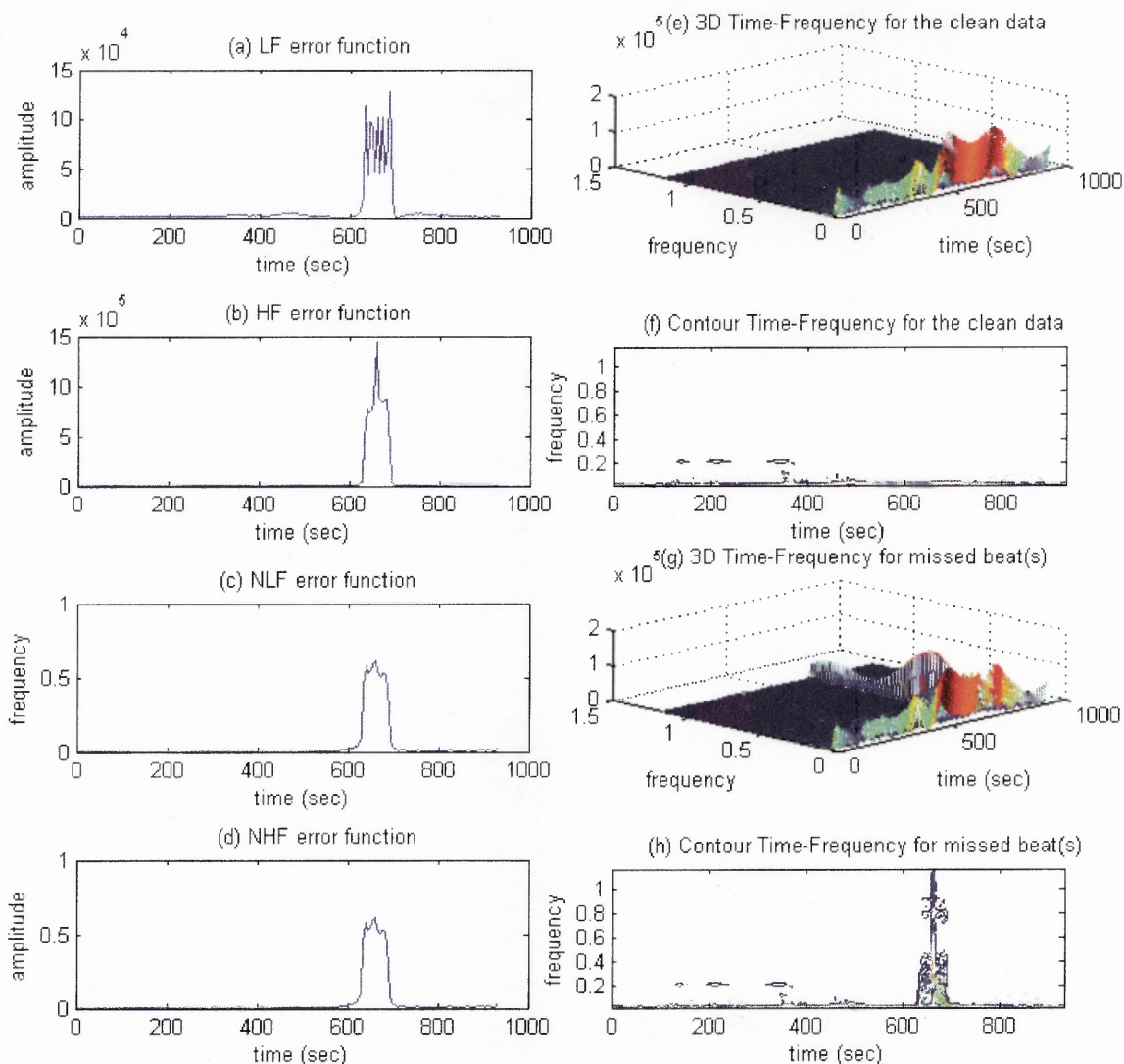
The 3D and contour plots show the increased in amplitude. The frequencies corresponding to the time mark of the three missed beats are greatly affected. But outside the time mark, the changes in frequencies are the same as that of the original clean data. Therefore, as the results demonstrate, the impact of three missed beats in a row is also localized. The signals from the original clean data and the missed beats are the same except at the location that the three missed beats are presented.

**Table 6.1** The Size of LF and HF Error Widths of One to Three Missed Beats

Measurement	No. of Missed Beats	LF Error	HF Error
Width (sec)	1	51.00	49.80
	2	51.40	50.60
	3	52.60	51.20



**Figure 6.16** TF superimposed plots for three missed beats in a row on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for three missed beats (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.



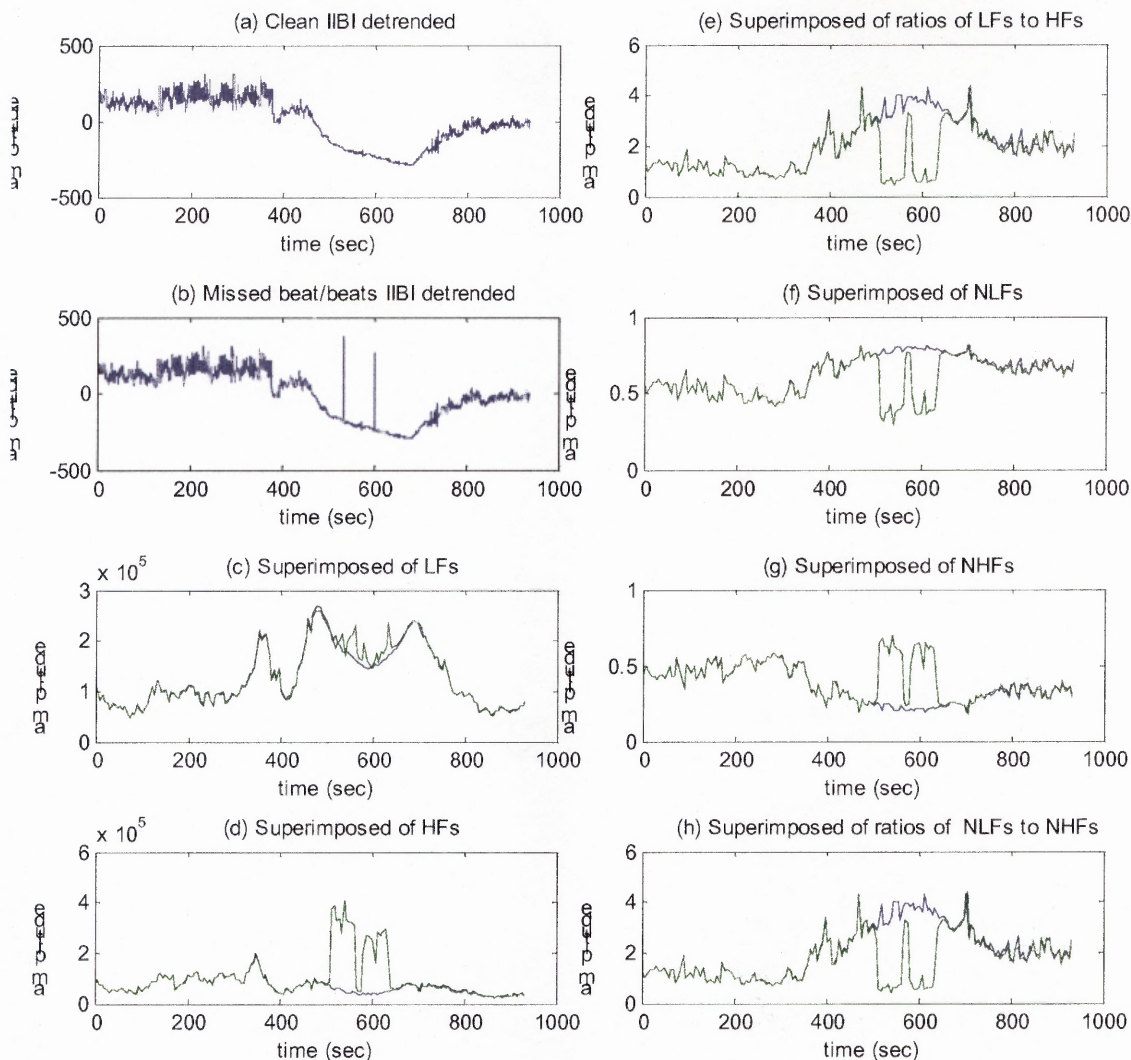
**Figure 6.17** Error functions, 3D and contour plots for three missed beats in a row using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for three missed beats (h) Contour plot for three missed beats.



### 6.2.2 Effect of Arbitrary Missed Beats

In Section 6.2.1, the effect of missed beats in a row has been discussed. It has been shown that the effect of missed beats in a row does not spread throughout the TF spectrum. In this section the impact of arbitrary missed beats (not in a row), especially in the exercise state, is investigated. It was already explained that the effect of one missed beat is bound around the area of the missed beats. To avoid repetition, the results of two and three arbitrary missed beats will be discussed.

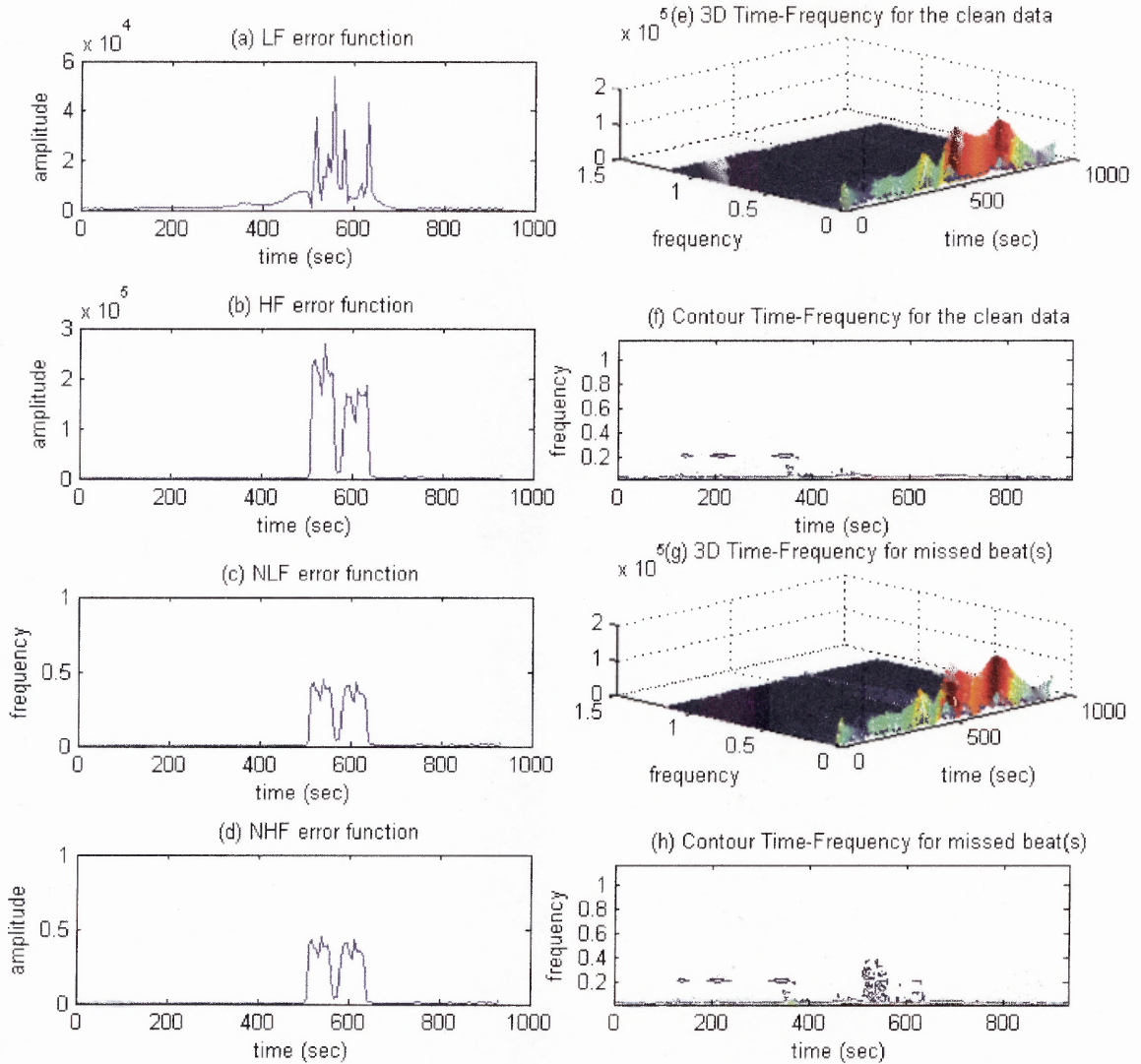
In Figure 6.18(b), two spikes are observed. These spikes are due to the two arbitrary missed beats (not in a row). In the previous section, since the missed beats were in a row, there was only one spike (no matter the number of the missed beats was). But with each increment of the number of missed beats in a row, the spike got bigger and bigger. That was the reason why the IIBI plot looked a somewhat smaller. The superimposed LF, HF and LF/HF ratio from the two missed beats on the original clean data are shown in Figure 6.18(c), Figure 6.18(d) and Figure 6.18(e), respectively. This time, the missed beats are arbitrary distributed across the data. Figure 6.18(f), Figure 6.18(g) and Figure 6.18(h) are the corresponding superimposed of the normalized plots. Unlike the two missed beats in a row, two separate peak amplitudes are seen due to the two scattered missed beats. Like the previous section, the difference between the LFs from the two missed beats and original data is very small compared to the HFs. In Figure 6.19(a), the error of the LFs is small compared to the error of the HFs.



**Figure 6.18** TF superimposed plots for two arbitrary missed beats on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for two arbitrary missed beats (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.

In Figure 6.19, the 3D and the contour plots for the two missed beats and original clean data are shown. Looking at the plots, the differences or errors are small and concentrated around the time mark of the two missed beats, which in this case are at 9 and 10min. It can be concluded that the effects of two missed beats at different time

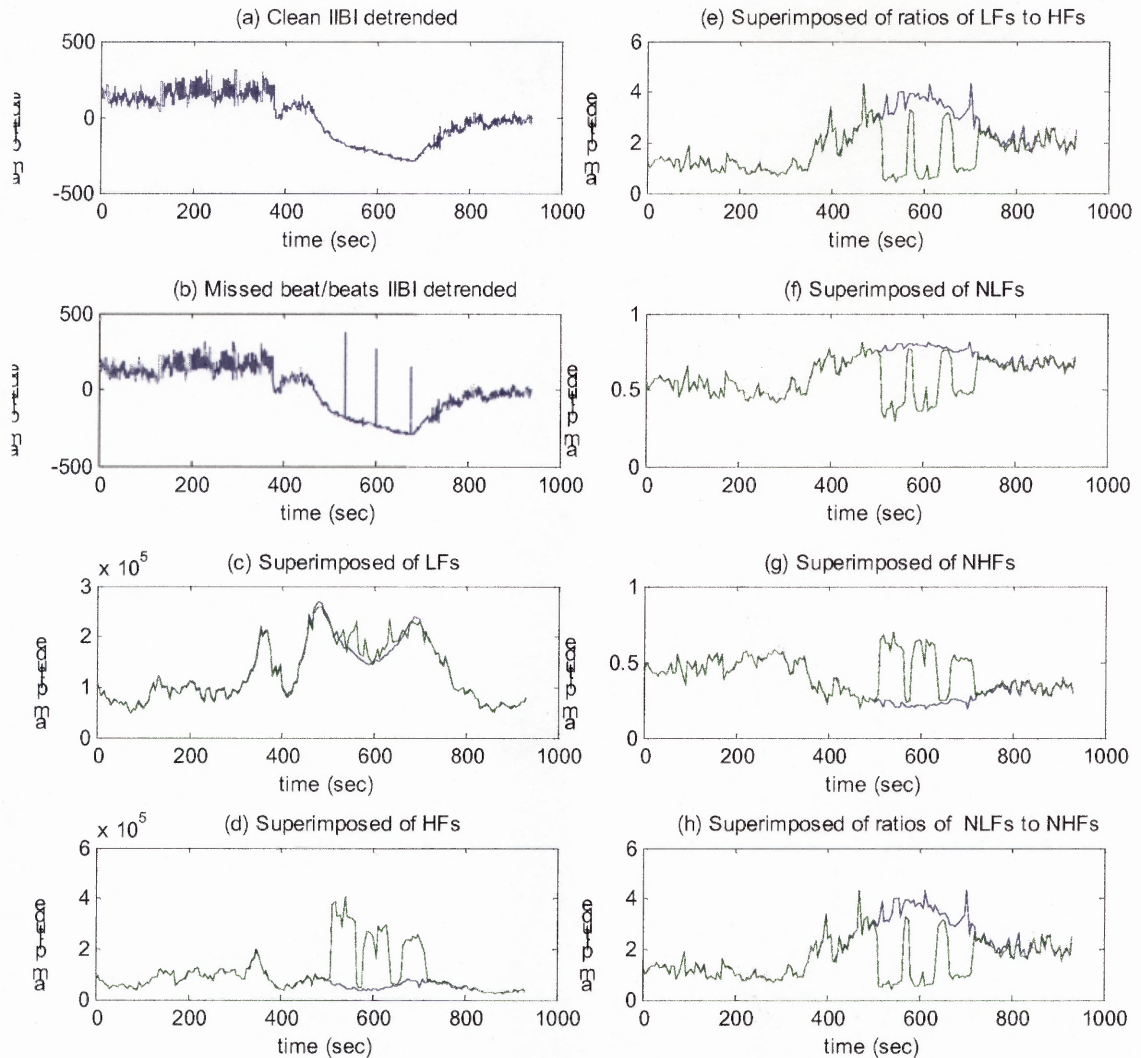
marks are minimum. Their effects are also independent of each other. The errors due to the two arbitrary missed beats do not spread out widely throughout the entire TF plot.



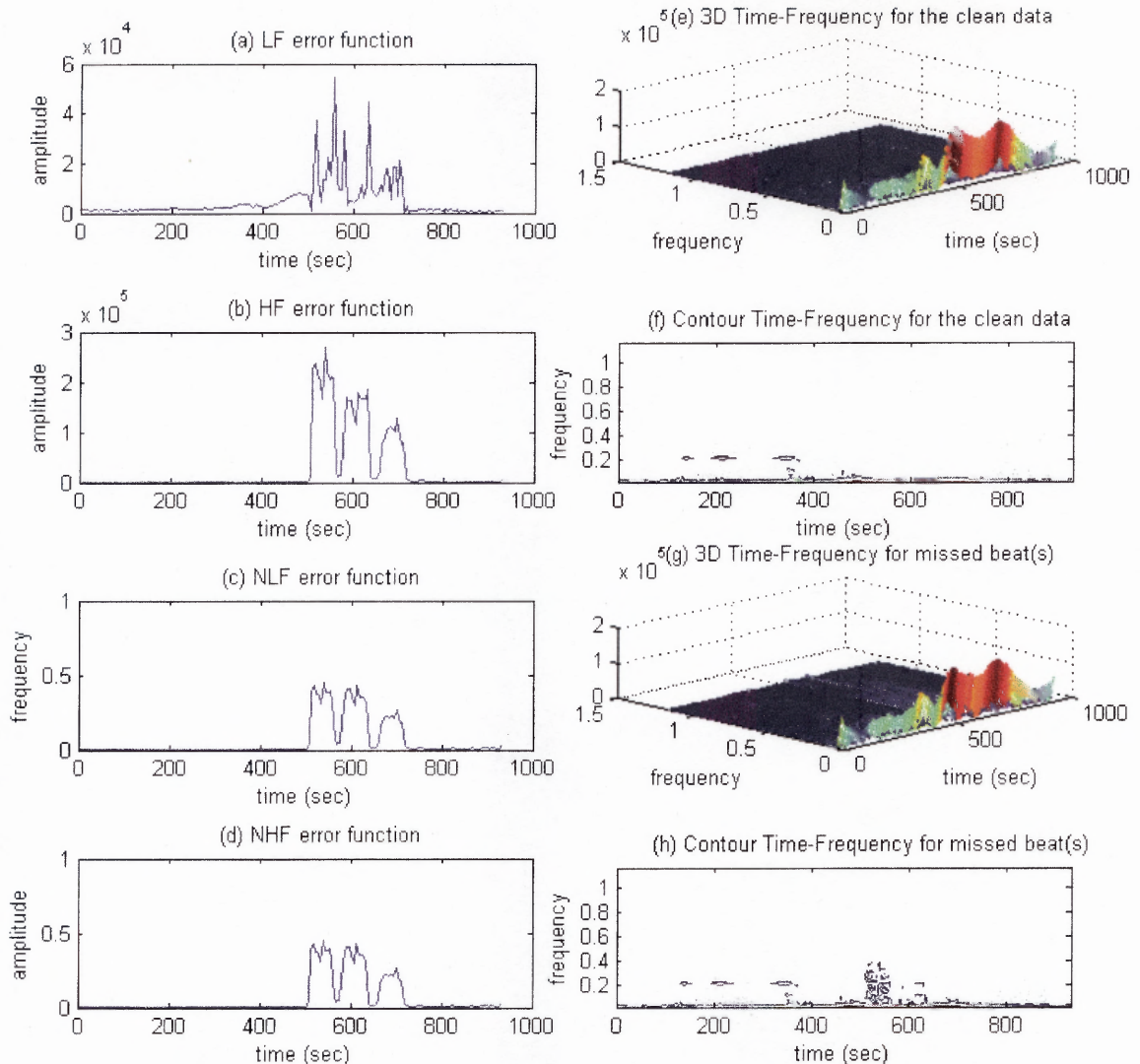
**Figure 6.19** Error functions, 3D and contour plots for two arbitrary missed beats using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for two missed beats (h) Contour plot for two missed beats.

Figures 6.20 and 6.21 represent three arbitrary missed beats vs. the original clean data. Three spikes at different time marks, namely at 9min, 10min and 12min are shown in the IIBI plot, Figure 6.20(b). The subsequent plots of Figure 6.20(c), (d) and (e) show the superimposed plots of LF, HF and LF/HF ratio from the three missed beats on the original clean data. Three amplitudes due to the three arbitrary missed beats are observed in each of the plots. As before, the amplitudes in the superimposed LF plots are very small. Figure 6.21(a) and Figure 6.21(b) are the two errors of the corresponding LFs and HFs. Notice how small the amplitude of the error of the LFs is.

The differences between the plots from the original data and three scattered missed beats are concentrated around where the missed beats are located. The errors do not spread throughout the plots. Therefore, when the missed beats are arbitrary, their effects are also strictly bound around the times of the missed beats. This can be clearly observed in the 3D and contour plots of Figure 6.21. The entire 3D spectrum doesn't look disturbed. The mesh plot (3D) and the contour reveal clearer view of the change of frequencies in time. Looking at the mesh and contour plots, the frequencies corresponding to the time mark of the missed beats are affected. Therefore, the presence of some scattered missed beats across the ECG does not affect the entire HRV signals.



**Figure 6.20** TF superimposed plots of three arbitrary missed beats on the clean data using WD: (a) The IIBI plot without missed beats (b) The IIBI plot for three arbitrary missed beats (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization superimposed LF/HF ratio plot.



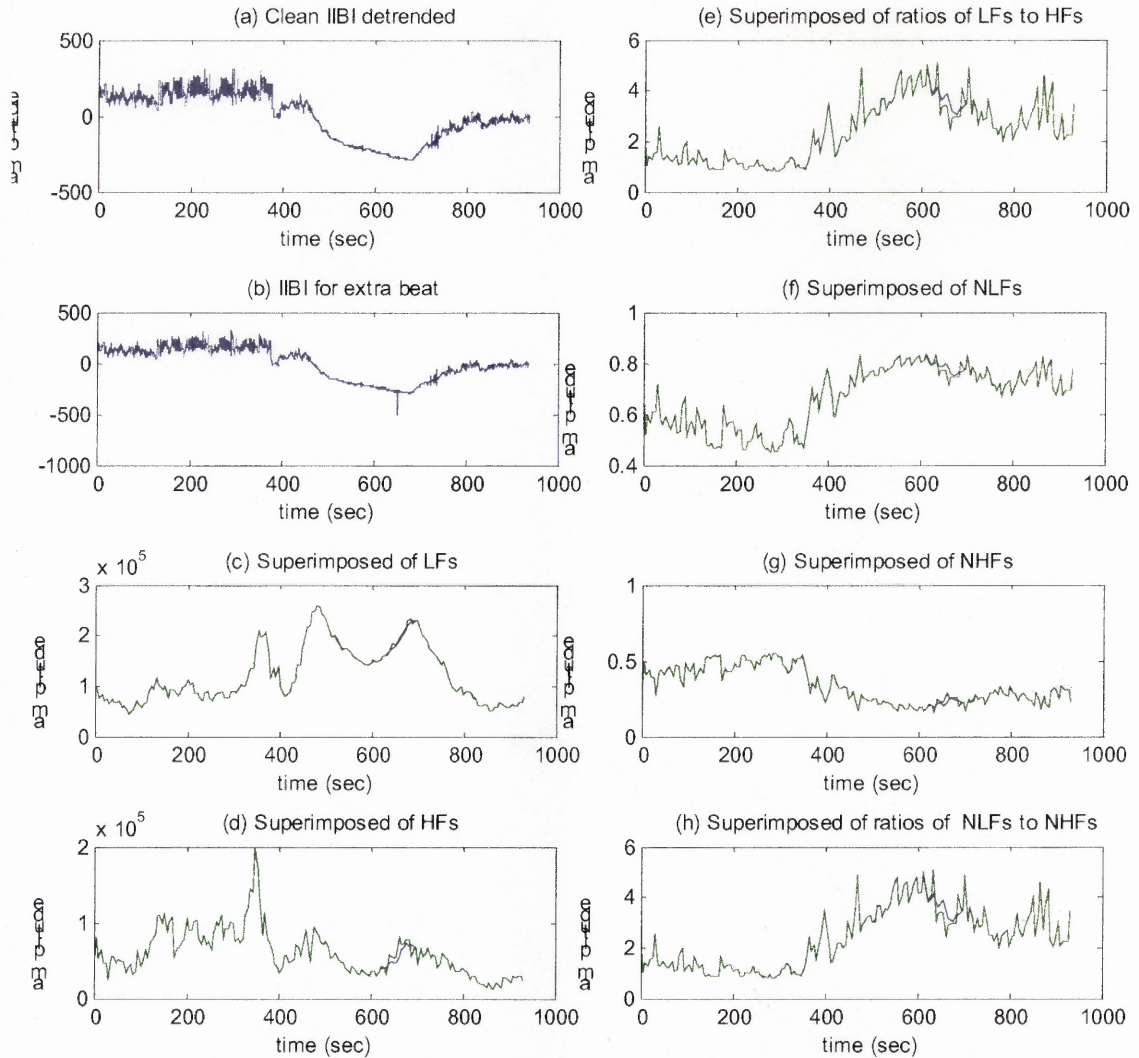
**Figure 6.21** Error functions, 3D and contour plots for three arbitrary missed beats using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for three missed beats (h) Contour plot for three missed beats.

### 6.3 The Effect of One Extra Beat Using Time-Frequency Analysis

The IBI recordings obtained from an exercise stress test often include abnormal intervals. One of such intervals is due to extra beats. Extra beats occur earlier than expected, and might be a result of false positive detection of an R wave, or a ventricular premature beat (VPB). As a result shorter intervals would appear in the IBI data. In the IBI or IIBI plots

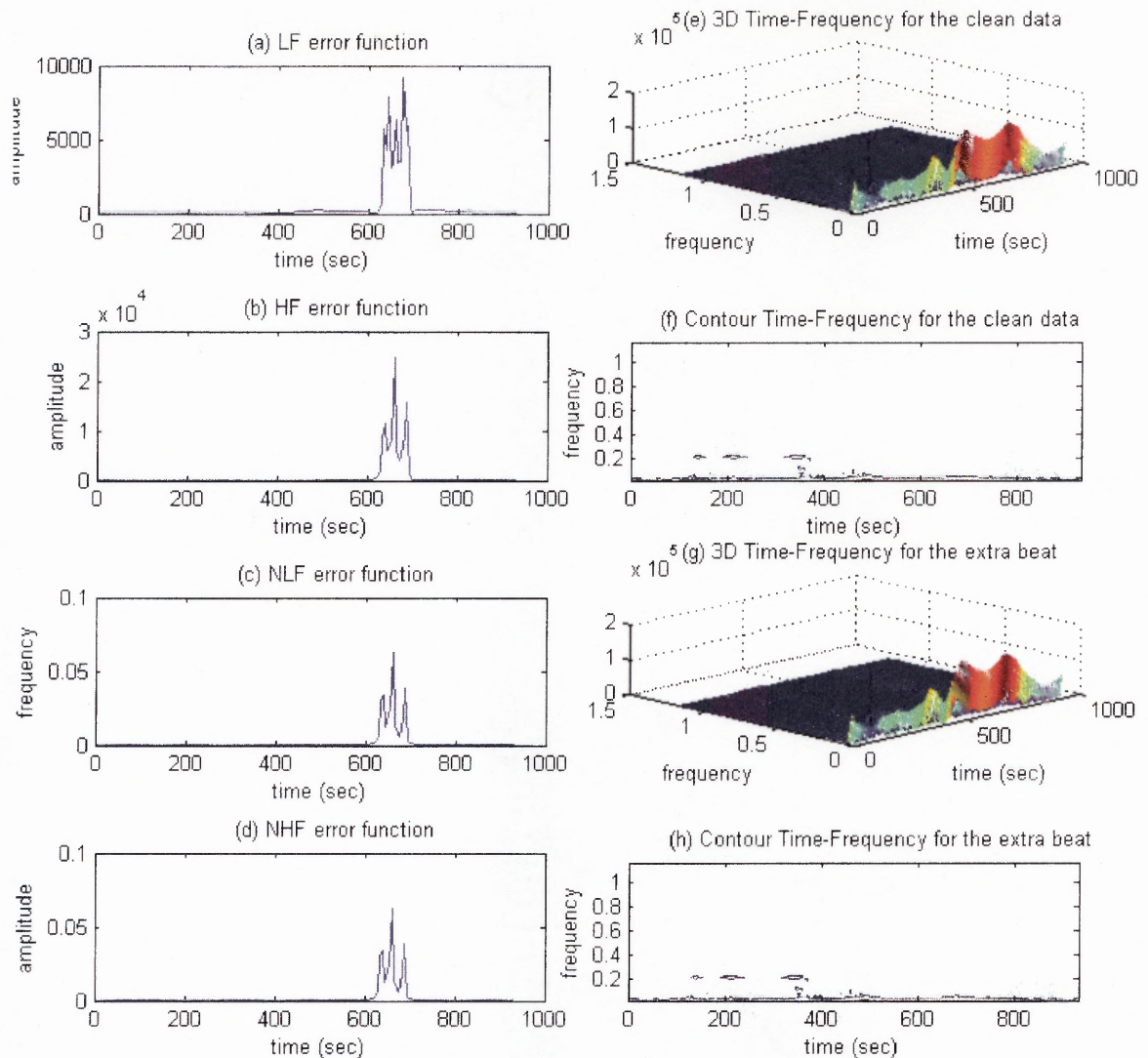
downward spikes are often seen, indicating the presence of extra beats. To compare with one missed beat, one extra beat was put in at the same time mark as that of one missed beat. Like the one missed beat, the errors due to one extra beat are zero except around the time mark that the extra beat has put in. Even at the location of the time mark, the errors are very small compared to the one missed beat.

The widths, heights and areas of the error functions are also smaller than the corresponding one missed beat. Figures 6.22 and 6.23 represent one extra beat vs. the original clean data. Both of the figures show how small the errors due to one extra beat are. The component plots are exactly overlapped except at the time mark of the extra beat. Therefore, the local effect of missed beats is more significant than extra beats although both do not spread throughout the entire spectrum. The error sizes of one extra beat vs. one missed beat are presented in Table 6.3 of Section 6.5.



**Figure 6.22** TF superimposed plots for one extra beat on the clean data using WD: (a) The IIBI plot without extra beat (b) The IIBI plot for one beat (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization superimposed LF plot (g) Normalization superimposed HF plot (h) Normalization superimposed LF/HF ratio plot.





**Figure 6.23** Error functions, 3D and contour plots for one extra beat using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for one extra beat (h) Contour plot for one extra beat.

### 6.4 Interpolation for the Miss Beats

Interpolation is performed to fill-in the missed beats so that a comparison with the original clean data can be performed. The moving average formula that can be used to fill-in the missed beats is:

$$y_m = \frac{\sum_{k=-m}^{k=m} x(n+k)}{2m+1} \quad (6.1)$$

where  $m$  is the number of intervals to be filled-in and  $x(n)$  is the average interval of the missed beats (the total time of the missed beats divided by the total number of the intervals). For example for two missed beats, there are three intervals  $m=1, 2$  and  $3$ .

Therefore:

$$y_1 = \frac{x(n-1) + x(n) + x(n+1)}{3}$$

$$y_2 = \frac{x(n-2) + x(n-1) + x(n) + x(n+1) + x(n+2)}{5}$$

$$y_3 = \frac{x(n-3) + x(n-2) + x(n-1) + x(n) + x(n+1) + x(n+2) + x(n+3)}{7}$$

The  $y_1$ ,  $y_2$  and  $y_3$  are the three interval values. The two missed beats will then be replaced by the values of  $y_1$ ,  $y_2$  and  $y_3$ . The following Figures, Figure 6.24 and 6.25 show the plots of original Vs the interpolated data using the above technique. Two missed beats in a row are replaced using the above moving average technique and then superimposed on the original data. As shown in Figure 6.24, the superimposed plots appear to overlap each other. Figure 6.27 shows that the actual error of the interpolated missed beat is less than 1% of the LF and HF values of the original signal, and the error is localized. There is not any spike in the interpolated IIBI plot. In Figure 6.25, due to very little variation between the original IBIs that form the two missed beats and the IBIs that

are filled-in using the moving average technique, a very small error is seen. In Table 6.2, the quantitative difference between the original and the interpolated IBIs are presented. In Table 6.3, the size of the LF and HF error width due to interpolation for one subject are shown.

**Table 6.2** Original IBI Vs Two Interpolation Missed Beats.

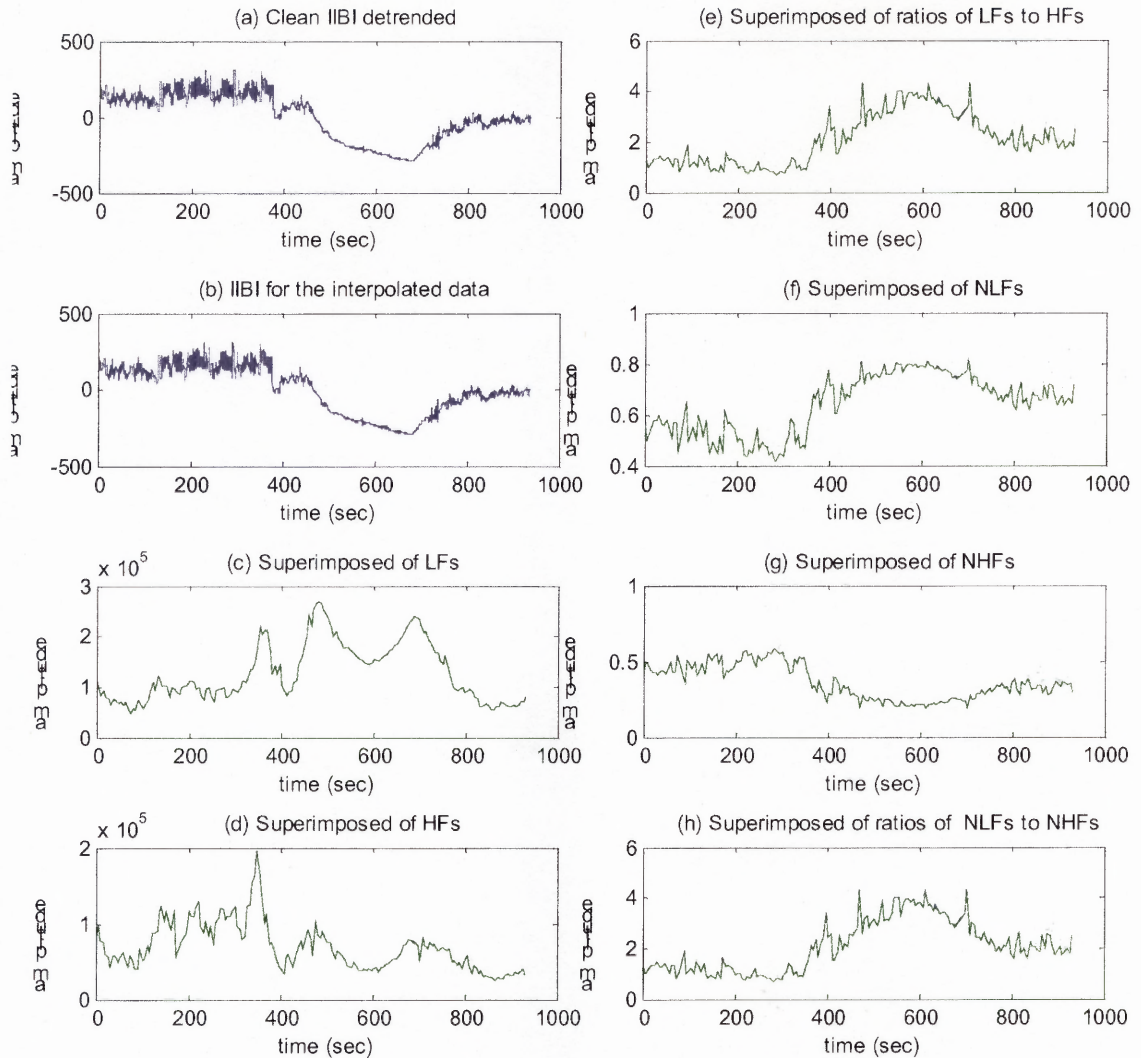
Original IBI data	IBI data with two missed beats	Two interpolated missed beats
624.00	624.00	624.00
624.00	1872.00	627.00
620.00	632.00	626.00
628.00	624.00	624.00
632.00		632.00
624.00		624.00
624.00		624.00

**Table 6.3** The Size of the LF and HF Error Width Due to Interpolation for One Subject.

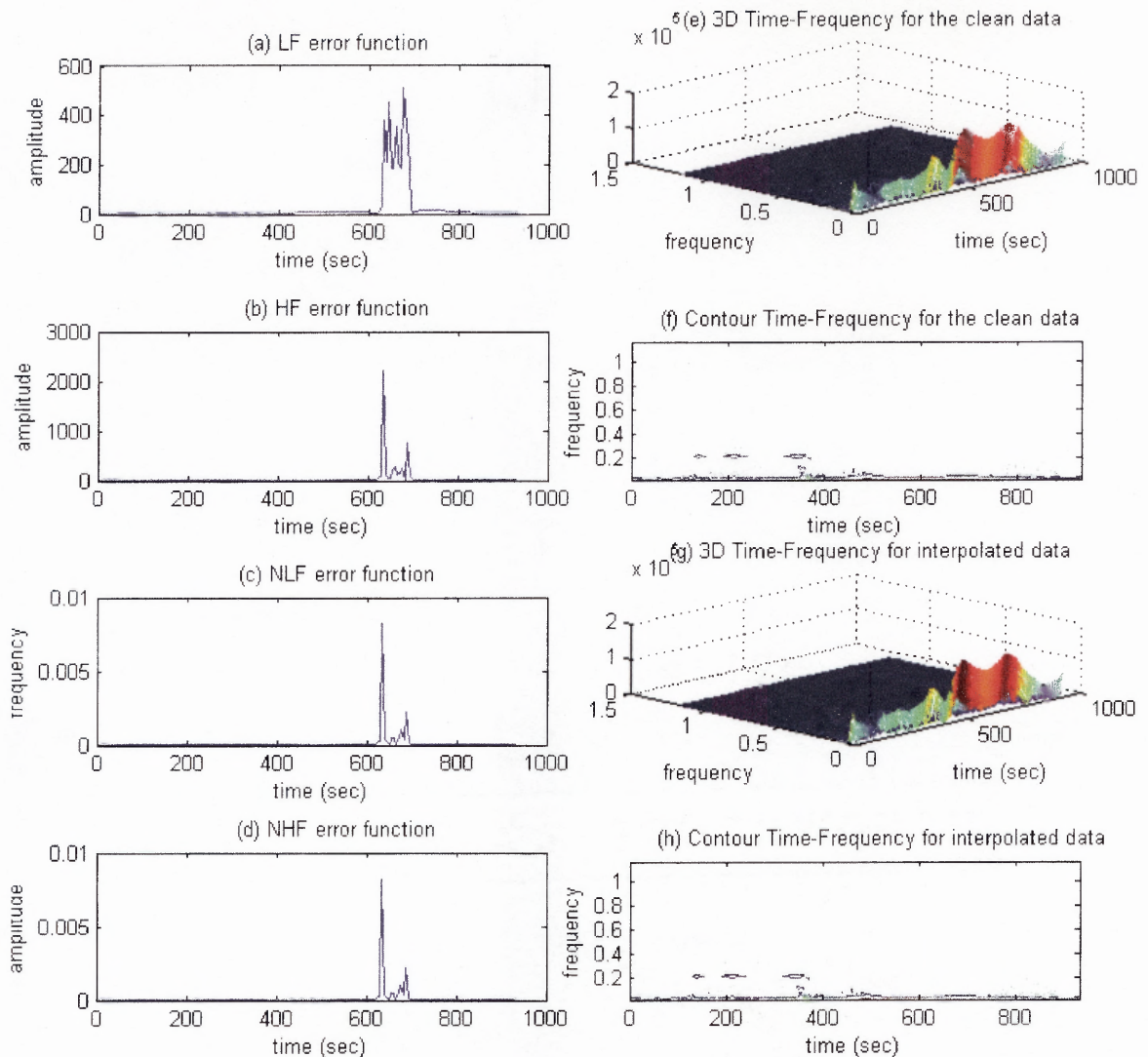
Measurement	No. of Missed Beats	LF Error Due to Interpolation	HF Error Due to Interpolation
Width (sec)	1	11.60	11.60
	2	11.20	11.20
	3	11.60	11.60
	4	12.00	12.00
	5	12.40	12.40

As can be observed from Table 6.3, the interpolation error widths, heights and areas are small compared to the two missed beats that are discussed in Section 6.2.1 and Table 6.1. The moving average technique can also be applied to all the missed beats that have been analyzed in Section 6.2. All the LF and HF error results due to interpolation are approximately the same as shown in Table 6.3. Figure 6.26 shows the superimposed HF error functions due to one missed beat on to the error function due to interpolation. The error function due to the interpolation is negligible, compared to the error function

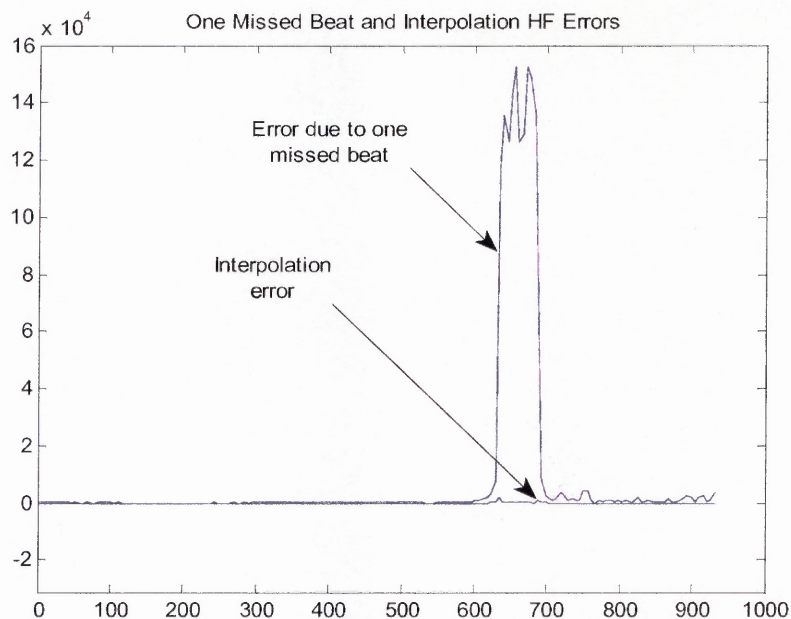
due to one missed beat. Their expanded plot is shown in Figure 6.27. As shown in Table 6.3, the quantitative measurements prove that the errors due to interpolation are very small. The error measurement results of all the missed beats and the corresponding interpolated missed beats for five subjects using the moving average technique are shown in Tables 6.4 and 6.5 (pages 98-101).



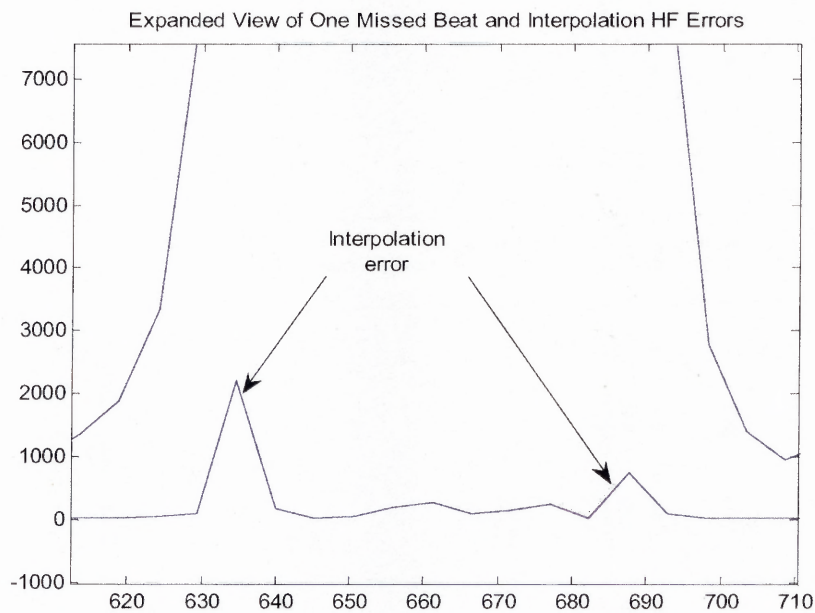
**Figure 6.24** TF superimposed plots for the two interpolated missed beats on the clean data using WD: (a) The IIBI plot for clean data (b) The IIBI plot for the interpolated two missed beats (c) Superimposed LF plot (d) Superimposed HF plot (e) Superimposed LF/HF ratio plot (f) Normalization of superimposed LF plot (g) Normalization of superimposed HF plot (h) Normalization of superimposed LF/HF ratio plot.



**Figure 6.25** Error functions, 3D and contour plots for the interpolated two missed beats using WD: (a) LF error function (b) HF error function (c) NLF error function (d) NHF error function (e) 3D TF plot for clean data (f) Contour plot for the clean data (g) 3D TF plot for the interpolated data (h) Contour plot for the interpolated data.



**Figure 6.26** The superimposed HF error function due to one missed on the error function due to interpolation.

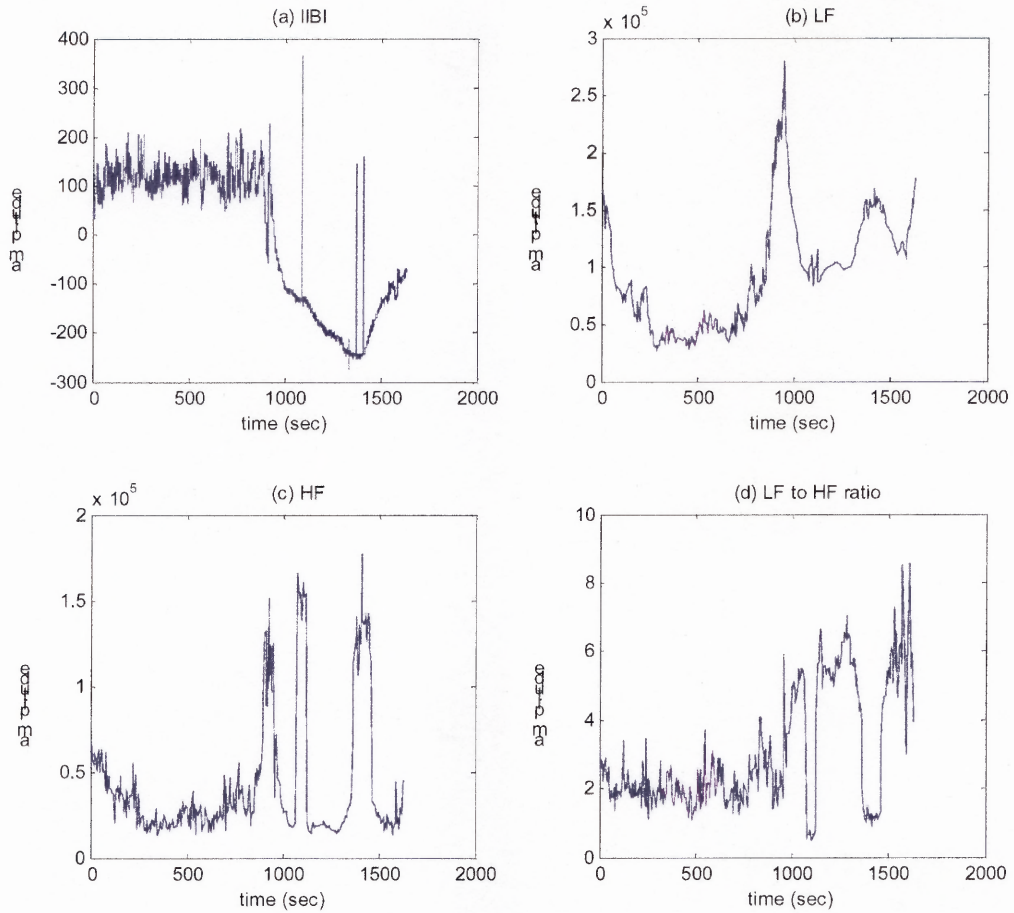


**Figure 6.27** Expanded view of the superimposed HF error function due to one missed on the error function due to interpolation.

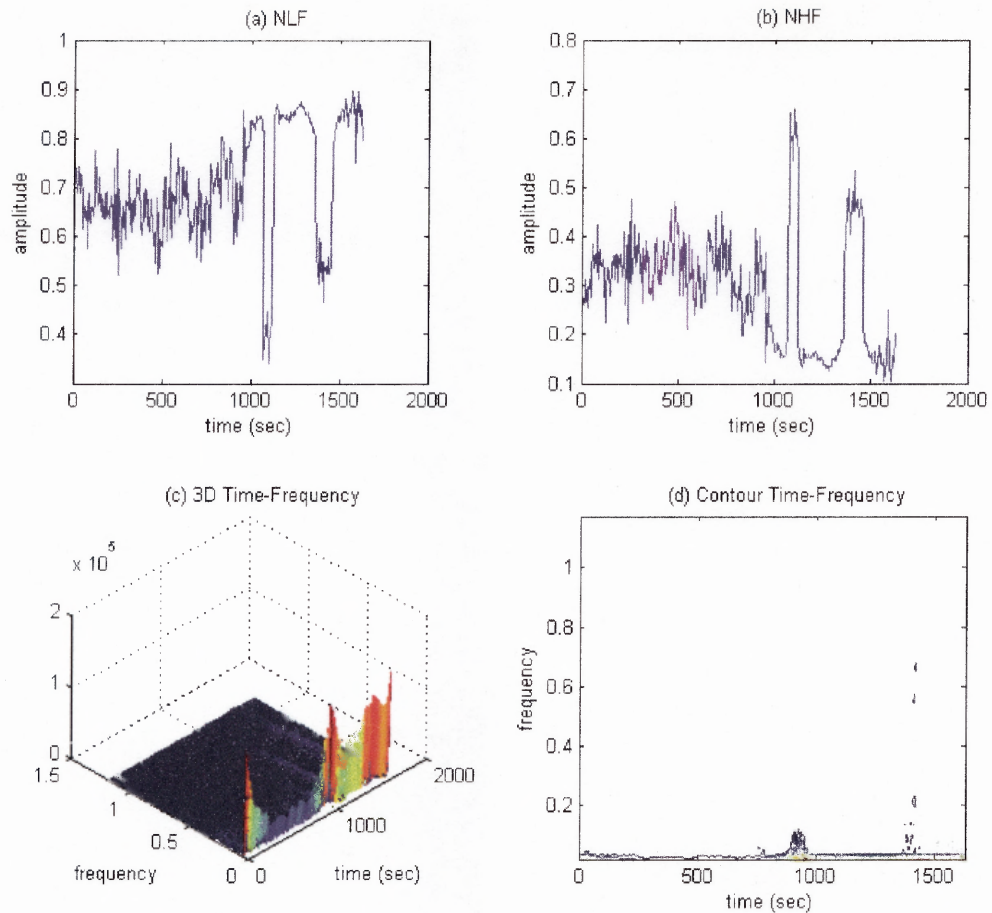
The purpose of all the approaches that have been performed for missed beats on the HRV time-frequency signals is to include the patients that were previously discarded due to missed beats. Using the above moving average interpolation technique, it has been possible to substitute the missed beats with the appropriate IBI intervals. After examining the effect of intentionally eliminated beats using time-frequency analysis, their IBI intervals have been filled-in using the moving average. Then, they are compared with the original clean data. The results show that the differences between the original clean data and the interpolated ones are very small. Based on this fact, the patients that had been eliminated due to missed beats should be considered in further studies. The moving average interpolation is then applied to replace the missed beats.

Figures 6.28 and 6.29 are the WD representations for HRV of one of the patients who missed three beats. The same subject can be examined using the STFT as well, and similar results would be seen. But to avoid repetition, the results are plotted using only one of them, which in this case is the WD. As you can observe from the IIBI plot three spikes are shown. Large amplitude spikes due to the three missed beats are clearly shown in the HF. They are also present in the LF/HF ratio as downward amplitudes. The amplitudes due to the three missed beats in the LF are small. The first large amplitude that is shown in the LF and HF is not due to missed beats. It is due to the fact that the patient stood and walked to the treadmill to perform the exercise after the end of the paced breathing.



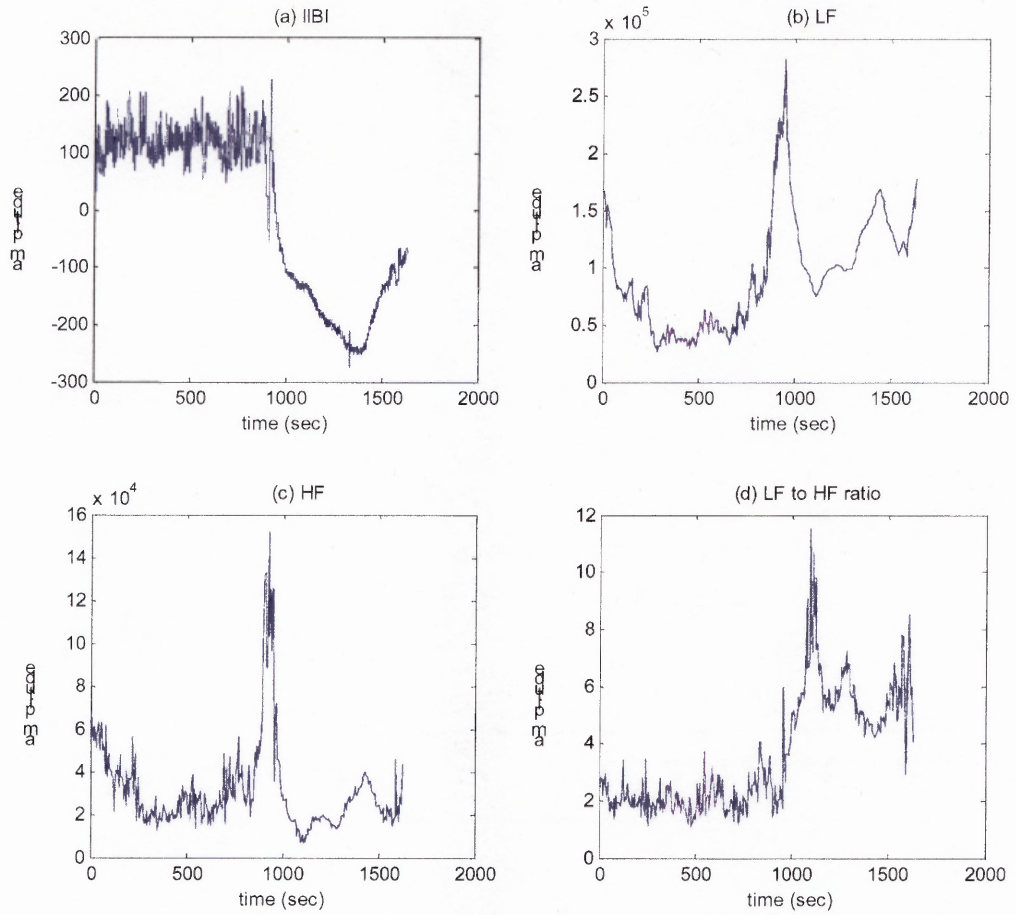


**Figure 6.28** WD output for three missed beats (a) IIBI for the exercise stress test (b) LF (c) HF and (d) LF/HF ratio.

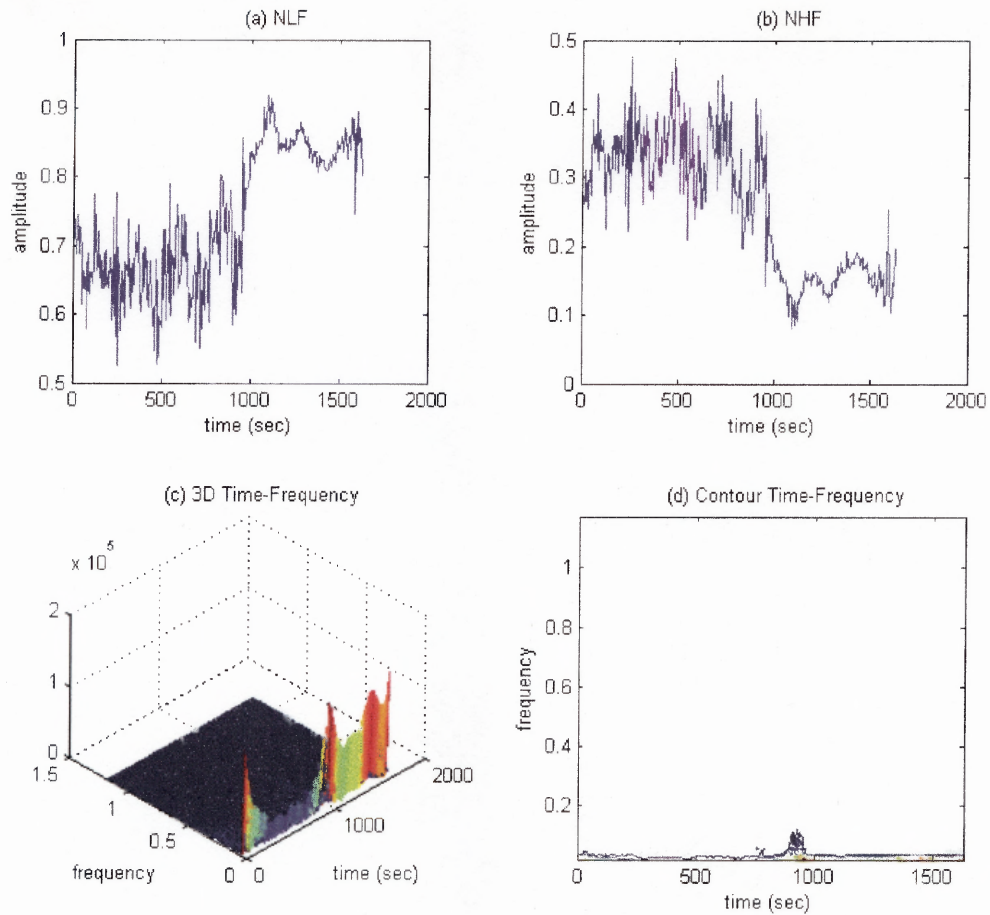


**Figure 6.29** WD output for three missed beats (a) HF normalized (b) LF normalized (c) 3D time-frequency and (d) Contour time-frequency.

The next two Figures, Figure 6.30 and Figure 6.31 represent the corrected or interpolated plots of the same subject. Notice how the spikes and amplitudes due to the missed beats that were seen in Figures 6.28 and 6.29 are now disappeared. As indicated above, the large amplitude that is shown in the previous plots remained there. By comparing the timing of the occurrence of the missed beats and that of the large amplitude, it was observed that the spike is not due to one of the missed beats. The amplitude occurs at the end of the paced breathing and the beginning of the exercise.



**Figure 6.30** WD output after interpolation: (a) IIBI for the exercise stress test (b) LF (c) HF and (d) LF/HF ratio.



**Figure 6.31** WD output after interpolation: (a) HF normalized (b) LF normalized (c) 3D time-frequency and (d) Contour time-frequency.

## 6.5 Measurement of Error Functions

In Sections 6.2.1 and 6.2.2, the original clean data have been superimposed onto the missed beats; and then their differences were extracted and plotted as error functions. In this section, the width, height and area of the error functions are quantitatively measured so that correlation between the sizes of the error functions and the number of the missed beats can be examined.

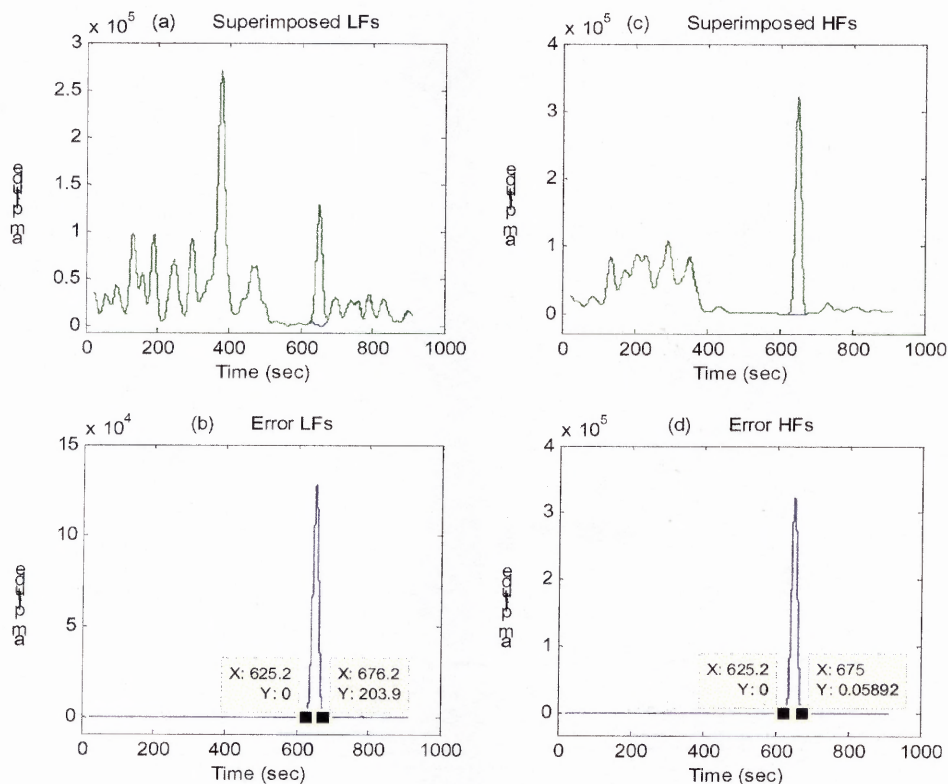
### 6.5.1 Width of an Error Function

The main purpose of this study is to examine and to demonstrate whether the errors due to missed beats spread throughout the TF spectrum or are just localized around the missed beats. In an attempt to find the best estimation of the size of the errors, error functions are separately plotted. Measuring the size of the width of an error function has been one of the focuses of this study. The window length of the STFT and pseudo Wigner distribution are the determining factors for the error functions to go back (settling) to zero. This way, the size of the width can be measured easily and distinctively. For example the size of the window for the STFT was 50sec. This is equal to 250 points (250 samples) because the IIBI signal is sampled at 5HZ. In the WD the size of the FFT computed was 256.

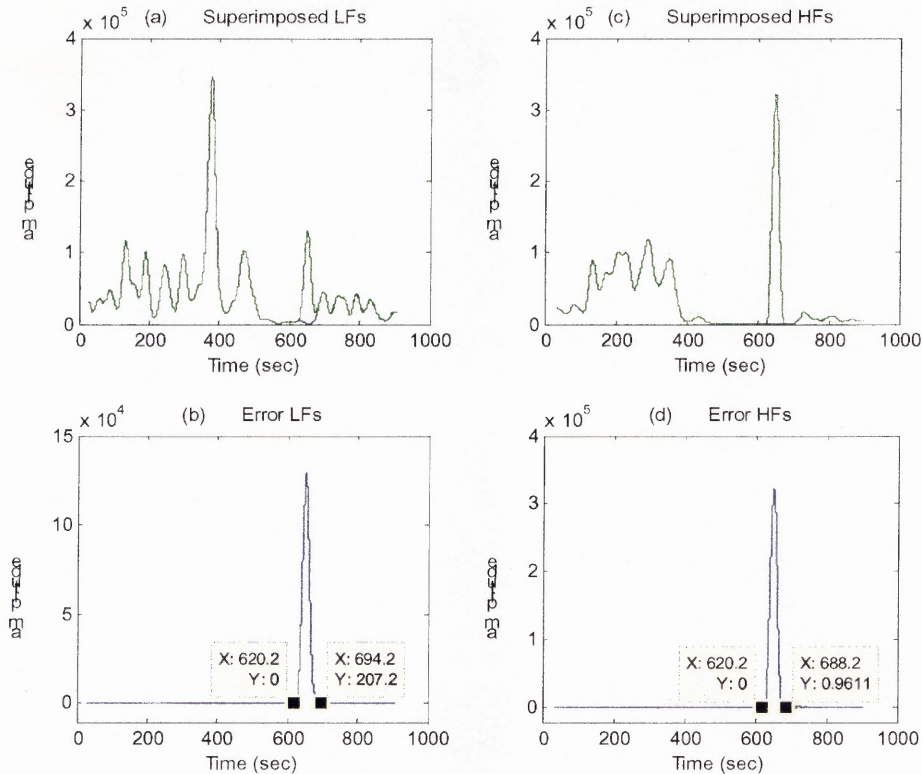
Figure 6.32 represents the superimposed and the corresponding error functions for one missed beat using the STFT. The error width of the LFs starts at exactly 625.2sec and approximately ends at 676.2. Therefore, the difference (51sec) is the size of the width of the error LFs for one missed beat. The size of the error width of the HFs is 49.8sec. The same results can also be found using the WD. The size of the error width for one to five missed beats is shown in Table 6.4. Surprisingly, the quantitative results of the TF analyses show that the sizes of the corresponding TF component widths for all of the missed beats are almost the same. This result is important because it proves that errors due to missed beats are localized. Using the WD, the error functions for two and above missed beats in a row do not exactly go back to zero. But away from the location of the missed beats, the errors are very small. They are negligible, and can be ignored. These

very small errors may not be due to missed beats. They may be due to other interferences or artifacts.

Window functions are important in cutting the errors from spreading throughout the entire signal. As a result, the sizes of the error widths can be known and determined easily. But the size of the error functions change when the window length is changed. This may bias the true sizes of the error parameters. In Figure 6.33, a 60sec window function is used. Because of the increase in the window length, the widths of the corresponding TF components are increased. This time the LF and HF error widths for the one missed beat using 60sec window length are 74sec and 68sec respectively.



**Figure 6.32** Superimposed LF, HF and their corresponding error functions for one missed beat using STFT with 50sec window length, and shows the two end values of error functions.



**Figure 6.33** Superimposed LF, HF and their corresponding error functions for one missed beat using STFT with 60sec window length, and shows the two end values of error functions.

### 6.5.2 Height of an Error Function

Another measurement that has been computed is the height of each of the error functions. To find the height of an error function, the difference between the maximum and minimum amplitude values have to be calculated. The *max()* and *min()* of the MATLAB functions determine the maximum and minimum amplitude values respectively. Obviously, the minimum amplitude is zero. Therefore, the maximum determines the height. As can be noticed from Table 6.4, the height of the error functions of the LFs and HFs are increased with the increment of the number of missed beats. Figure 6.35 shows the error height vs. number of missed beats of both the LFs and HFs. The error height

increases with the increment of the number of missed beats. Measuring the height of an error function is not as important as the width because it only shows how the amplitude of the error function changes with each increment of the missed beats, as opposed to the extent of the error function.

### 6.5.3 Area of an Error Function

When the height of an error function increases, its area also increases. The computed areas of the LF and HF error functions are shown in Table 6.4. In Figure 6.36, the error areas vs. the number of missed beats in a row are plotted. The plots show that moving (increasing) the number of missed beats in time increases the area of the error functions. To measure the areas, the MATLAB function called *polyarea()* can be used. *Polyarea()* determines the area within closed curves. Since the LF and HF curves from the missed beats on the original data are superimposed, the area of the error functions can be found using the *polyarea()* function. The area shows how an error function got bigger when the missed beats are increased. This doesn't indicate how far the errors extend beyond the location of the missed beats. If the increase in the error width was large, the area of an error function would have been a very important parameter.



**Table 6.4** LF and HF Error Function Measurements of One to Five Missed Beats for Five Patients Using 50sec Window Length.

Patient	Measurement	No. of Missed Beats	LF Error	HF Error
1	Width (sec)	1	51.00	49.80
		2	51.40	50.60
		3	52.60	51.20
		4	52.80	52.00
		5	53.20	52.60
	Area ( $10^6$ )	1	2.53	6.06
		2	19.46	30.93
		3	70.65	77.10
		4	178.47	145.76
		5	419.41	227.29
	Height ( $10^6$ )	1	0.13	0.32
		2	0.99	1.64
		3	3.58	4.09
		4	9.03	7.71
		5	21.13	11.97
2	Width (sec)	1	51.20	51.20
		2	51.80	51.80
		3	52.40	52.40
		4	53.00	53.00
		5	53.60	53.60
	Area ( $10^6$ )	1	6.36	12.53
		2	54.49	59.48
		3	203.90	14.61
		4	523.84	246.82
		5	1074.90	350.59
	Height ( $10^6$ )	1	0.32	0.66
		2	2.77	3.15
		3	10.31	7.72
		4	26.37	12.96
		5	53.77	18.24
3	Width (sec)	1	51.20	51.20
		2	51.80	51.80
		3	52.60	54.40
		4	53.20	54.40
		5	54.40	64.40

**Table 6.4** LF and HF Error Function Measurements of One to Five Missed Beats 98  
for Five Patients Using 50sec Window Length. (Continued)

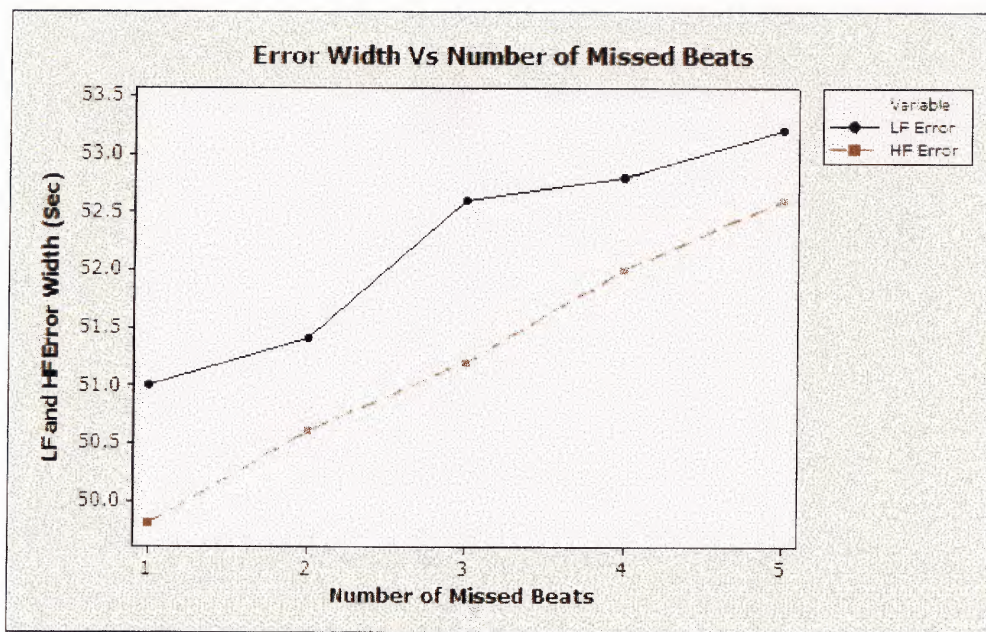
	Area (10 <sup>6</sup> )	1	6.72	13.19
		2	58.14	63.61
		3	251.93	158.42
		4	622.29	257.78
		5	1240.20	364.75
	Height (10 <sup>6</sup> )	1	0.34	0.70
		2	2.95	3.37
		3	12.71	8.35
		4	31.25	13.50
		5	61.87	18.91
4	Width (sec)	1	55.40	50.40
		2	55.40	51.20
		3	55.40	51.20
		4	55.40	52.20
		5	55.40	52.60
	Area (10 <sup>6</sup> )	1	3.64	8.43
		2	33.36	42.89
		3	11.15	10.37
		4	31.11	19.44
		5	677.17	279.88
	Height (10 <sup>6</sup> )	1	0.18	0.45
		2	1.69	2.27
		3	5.64	5.49
		4	15.69	10.25
		5	34.00	14.66
5	Width (sec)	1	51.40	52.80
		2	52.00	52.80
		3	52.80	52.80
		4	53.40	53.00
		5	54.00	53.60
	Area (10 <sup>6</sup> )	1	11.74	17.64
		2	88.36	82.18
		3	342.05	184.06
		4	818.50	297.37
		5	1,598.80	419.66
	Height (10 <sup>6</sup> )	1	0.58	0.94
		2	4.44	4.35
		3	17.16	9.69
		4	40.90	15.53
		5	79.36	21.67

**Table 6.5** LF and HF Error Function Measurements of One to Five Interpolated Beats for Five Patients Using 10sec Window Length.

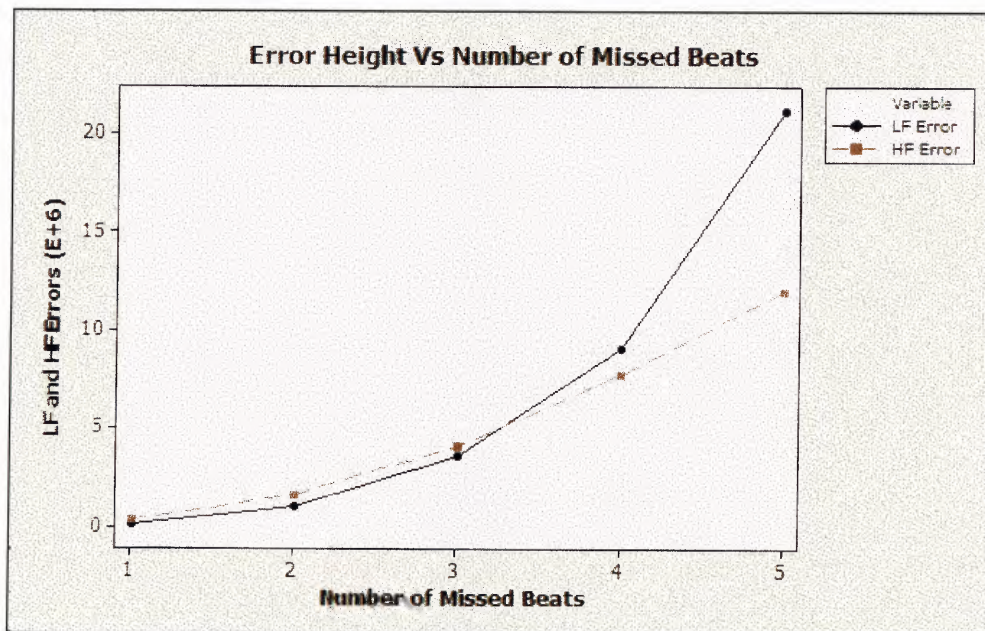
Patient	Measurement	Interpolated Beats	LF Error	HF Error
1	Width (sec)	1	11.60	11.60
		2	11.20	11.20
		3	11.60	11.60
		4	12.00	12.00
		5	12.40	12.40
	Area	1	143.00	90.00
		2	84.30	113.00
		3	24.50	140.00
		4	56.50	293.50
		5	78.00	282.30
	Height	1	29.40	24.10
		2	17.50	30.20
		3	4.80	36.20
		4	11.00	74.00
		5	14.70	72.20
2	Width (sec)	1	11.20	11.20
		2	12.60	11.80
		3	12.40	12.40
		4	13.00	13.00
		5	13.60	13.60
	Area	1	14.09	3.49
		2	69.06	23.76
		3	17.51	20.17
		4	10.49	25.17
		5	13.79	30.18
	Height	1	2.49	0.90
		2	11.96	4.13
		3	3.29	4.72
		4	3.50	6.43
		5	4.00	7.52
3	Width (sec)	1	11.20	11.20
		2	11.80	11.80
		3	12.40	12.40
		4	13.00	13.00
		5	13.00	13.00

**Table 6.5** LF and HF Error Function Measurements of One to Five Interpolated 100 Beats for Five Patients Using 10sec Window Length. (Continued)

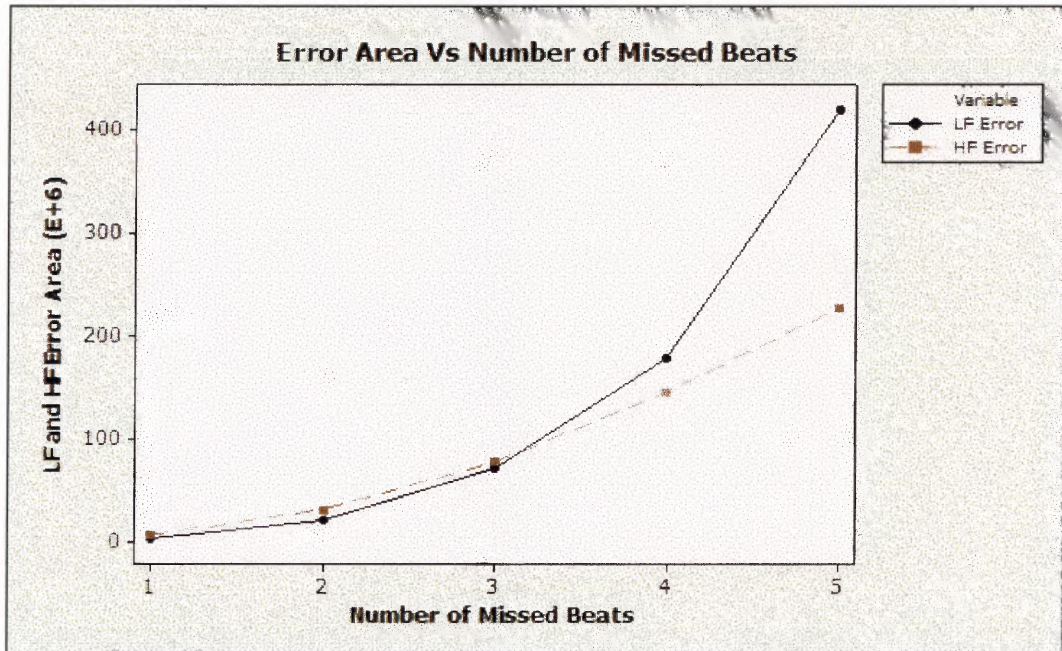
	Area	1	187.56	101.74
		2	183.04	139.18
		3	179.81	403.94
		4	154.26	405.09
		5	118.48	503.71
	Height	1	45.32	29.08
		2	44.23	43.01
		3	39.74	104.49
		4	36.22	104.80
		5	18.29	119.08
4	Width (sec)	1	11.20	11.20
		2	11.80	11.80
		3	12.40	12.40
		4	13.00	13.00
		5	13.60	13.60
	Area	1	306.33	141.85
		2	161.61	176.29
		3	186.78	259.25
		4	200.00	225.24
		5	467.90	404.61
	Height	1	55.87	49.34
		2	31.95	61.52
		3	40.11	89.16
		4	42.90	77.64
		5	93.58	86.84
5	Width (sec)	1	11.20	11.20
		2	11.80	11.80
		3	12.40	12.40
		4	13.00	13.00
		5	13.00	13.00
	Area	1	275.24	914.01
		2	1,572.40	989.68
		3	468.77	2,507.50
		4	559.03	2,469.50
		5	826.40	2,316.20
	Height	1	77.30	211.20
		2	339.08	296.34
		3	105.58	663.84
		4	112.70	657.41
		5	176.38	642.07



**Figure 6.34** Size of the error width of LFs and HFVs Vs the number of missed beats for patient 1.



**Figure 6.35** Size of the error height of LFs and HFVs Vs the number of missed beats for patient 1.



**Figure 6.36** Size of the error area of LFs and HFs Vs the number of missed beats for patient 1.

**Table 6.6** One Extra Beat Vs One Missed Beat for Five Patients

Patient	Measurement	One Extra Beat LF Error	One Extra Beat HF Error	One Missed Beat LF Error	One Missed Beat HF Error
1	Width (sec)	50.40	49.40	51.00	49.80
	Area ( $10^6$ )	0.12	0.43	2.53	6.06
	Height ( $10^3$ )	6.01	22.83	128.00	322.00
2	Width (sec)	50.80	49.60	51.20	51.20
	Area ( $10^6$ )	0.74	2.13	6.36	12.53
	Height ( $10^3$ )	35.98	112.78	323.00	664.00
3	Width (sec)	50.80	49.00	51.20	51.20
	Area ( $10^6$ )	11.15	2.33	6.72	13.19
	Height ( $10^3$ )	40.01	123.10	343.00	701.00
4	Width (sec)	50.20	49.40	55.40	50.40
	Area ( $10^6$ )	0.24	0.54	3.64	8.43
	Height ( $10^3$ )	7.70	28.00	180.00	447.00
5	Width (sec)	50.80	52.20	51.40	52.80
	Area ( $10^6$ )	0.80	2.52	11.74	17.64
	Height ( $10^3$ )	45.36	135.85	583.00	937.00

## 6.6 Conclusion and Future Work

In this study, one to five missed beats are introduced into the IBIs by deleting beats. Deleting beats means combining IBI intervals. First, programs that eliminate beats were created. Then the impact of the missed beats was evaluated. For the paced breathing, the missed beats were analyzed using Fourier spectral analysis. The results showed that even one missed beat affects the entire Fourier spectrum. The effect is much worse when the missed beats are adjacent to each other (in a row). This was consistent with prior research [1].

The primary goal of this thesis was to see whether the missed beats affect the entire exercise stress test. By superimposing the time-frequency components of the missed beats on the original clean data, it has been possible to see how far the differences (errors) extend. The sizes of the error functions were measured. According to TF analyses results the corresponding width for all the missed beats stayed almost the same. This result indicates that the errors due to missed beats are localized to the area of missed beats, when using time-frequency analysis. The height of each of the error functions is increased with the increment of the number of missed beats in a row. As a result, the area under the error function increases. As can be seen from the TF results of all of the missed beats in a row, the errors are clearly distinguishable around the time marks of the missed beats. Beyond these times, the errors are approximately zero and can be ignored.

In an effort to reduce the size of the error functions, an interpolation of a moving average technique was used. The interpolation technique was based on correcting the missed beats by going back and forth from the location of the missed beats in the IBI data. Due to the variation between the original intervals that form the missed beats and

interpolated ones, errors have been observed. If the missed beats were around the area of a quick change of the ECG signals, such as onset of exercise, the variation between the original and interpolated intervals were increased. Therefore, further reduction of the sizes of the errors may be possible by using other methods of interpolation. An extended future study on this regard may be needed to further minimize the errors.

In the present study, the Wigner distribution and STFT methods are applied to analyze the missed beats. The Wigner distribution is a time-frequency method without using a window. As a result the errors do not exactly go back to zero. These errors may be due to other reasons. To avoid the problem, the pseudo WD was used. That is, the Wigner function was multiplied by a window. But the errors for two and above missed beats still didn't exactly go back to zero as expected. Therefore, further study may be needed to look at the WD to solve the problem.

On the other hand, using the STFT the errors go back to zero. In the STFT the window is always fixed. As a result, one cannot know at what instances of times the spectral components occur. Analyzing the missed beats using the STFT may thus misrepresent the true behavior and characteristic of the missed beats. In addition to that, an error width increases, when the window size of the STFT increases. This biases the true sizes of the error functions. Since the wavelet transform uses variable window, better results and information of the impact of missed beats may be found. Time-frequency analysis on the missed beats using the wavelet transform would be interesting to see how much effect the missed beats can have on the spectrum for HRV.

In the present study, in addition to missed beats in a row, arbitrary missed beats were analyzed. When two missed beats were separated by a significant time (wider gap



between the missed beats), distinct peak error amplitudes at the times of the missed beats were observed. If the missed beats moved closer, they created one wider peak error amplitude. Since the size of the width of the error function was largely depended on the window length, the error width was not doubled when the two missed beats were overlapped. This biases the true error size due to missed beats. Further study using time-frequency methods that apply variable window, such as wavelet may be required to determine the true size of the error functions when two missed beats are overlapped.

## APPENDIX A

### FOURIER TRANSFORM PROGRAM CODE FOR MISSED BEATS

This program is written in Matlab to analyze missed beats in the paced breathing.

```
load a.txt    %Original clean data for 5min
load b1.txt   %One missed beat
load c1.txt   %Two randomly missed beats
load d1.txt   %Three randomly missed beats
load e1.txt   %Four randomly missed beats
```

```
sf=5;
x = a;
fftsize=length(x);
x=x-mean(x);
fftx=fft(x,fftsize);
p=fftx.*conj(fftx);
%f=sf*(0:(fftsize/2-1))/fftsize;
f=sf*(0:(fftsize-1))/fftsize;
clear fftx
```

```
x1 = b1;
[row1,col1]=size(b1);
I1=1:row1;
I1=I1(:);
A1=(I1/sf);
```

```
fftsize1=length(x1);
x1=x1-mean(x1);
fftx1=fft(x1,fftsize1);
p1=fftx1.*conj(fftx1);
%f=sf*(0:(fftsize/2-1))/fftsize;
f1=sf*(0:(fftsize1-1))/fftsize1;
clear fftx1
```

```
x2 = c1;
[row2,col2]=size(c1);
I2=1:row2;
I2=I2(:);
A2=(I2/sf);
```

```
fftsize2=length(x2);
```

```

x2=x2-mean(x2);
fftx2=fft(x2,fftsize2);
p2=fftx2.*conj(fftx2);
%f=sf*(0:(fftsize/2-1))/fftsize;
f2=sf*(0:(fftsize2-1))/fftsize2;
clear fftx2

```

```

x3 = d1;
[row3,col]=size(d1);
I3=1:row3;
I3=I3(:);
A3=(I3/sf);

```

```

fftsize3=length(x3);
x3=x3-mean(x3);
fftx3=fft(x3,fftsize3);
p3=fftx3.*conj(fftx3);
%f=sf*(0:(fftsize/2-1))/fftsize;
f3=sf*(0:(fftsize2-1))/fftsize3;
clear fftx3

```

```

x4 = e1;
[row4,col4]=size(e1);
I4=1:row4;
I4=I4(:);
A4=(I4/sf);

```

```

fftsize4=length(x4);
x4=x4-mean(x4);
fftx4=fft(x4,fftsize4);
p4=fftx4.*conj(fftx4);
%f=sf*(0:(fftsize/2-1))/fftsize;
f4=sf*(0:(fftsize4-1))/fftsize4;
clear fftx4

```

```

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

```

figure

```

subplot('position',[0.075 .8 .36 .14]),plot(A1,b1);
title(' (a) IIBI for one missed beat');
xlabel('time (sec)');

```

```

ylabel('amplitude');

subplot('position',[0.075 .55 .36 .14]),plot(f1(1:150),p1(1:150),'r');
%plot(f(1:150),p(1:150)/max(p),'r');
%axis([0 .7 0 1.5]);
xlabel('Frequency (Hz)');
ylabel('Power');
title('      (b) Power spectrum for one missed beat');

subplot('position',[0.075 .30 .36 .14]),plot(A2,c1);
title('(c) IIBI for two missed beats');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.075 .06 .36 .14]),plot(f2(1:150),p2(1:150),'r');
xlabel('Frequency (Hz)');
ylabel('Power');
title('      (d) Power spectrum for two missed beats');

subplot('position',[0.55 .8 .36 .14]),plot(A3,d1);
title('(e) IIBI for three missed beats');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .55 .36 .14]),plot(f3(1:150),p3(1:150),'r');
xlabel('Frequency (Hz)');
ylabel('Power');
title('      (f) Power spectrum for three missed beats');

subplot('position',[0.55 .30 .36 .14]),plot(A4,e1);
title('(g) IIBI for four missed beats');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .06 .36 .14]),plot(f4(1:150),p4(1:150),'r');
xlabel('Frequency (Hz)');
ylabel('Power');
title('      (h) power spectrum for four missed beats');

set(gcf,'position',[5 36 700 662]);

position = findstr('.', File)
if position>=0
File=File(1:position);
end

```

## APPENDIX B

### WIGNER DISTRIBUTION PROGRAM CODE FOR MISSED BEATS

The following program written in Matlab was used to perform time-frequency analysis for missed beats using Wigner distribution on IIBI. Originally, it is written by Sanjay Fernando and Douglas Newandee.

```
[File, Path, FILTERINDEX] = uigetfile('*.*', 'Choose the clean IIBI data file you wish to process');
original_rawdata=load([Path File]);
rawdata=original_rawdata(:);
```

```
[File, Path, FILTERINDEX] = uigetfile('*.*', 'Choose the IIBI data file with missed beat/beats you wish to process');
original_rawdata1=load([Path File]);
rawdata1=original_rawdata1(:);
```

```
%x = decimate(rawdata,10); % decimate data array
x = rawdata;
%N = length(x);
```

```
%order=5;
%freq=0.03;
sample=5;
%nfreq=freq/sample;
dtrendata=rawdata;
[row,col]=size(dtrendata);
I=1:row;
I=I(:);
A=(I/sample); % Time axis in sec
```

```
m=256; % The size of the fft we will be computing.
skip=25; % Number of points we skip to get the next segment.
p=60; % The number of freq vals we will be plotting
k=fix((row-m)/skip); % the number of spectra we compute
%w=rectwin(size(1:m)); % window specification. Can be changed.
%w=w(:);
x=dtrendata;
L=m/2;
l=-(L-1):(L-1);
n=L;
%Z=zeros([p,k]);
for i=1:k
```

```

% Here I think 0 lag is at the Lth point, hence the first
% time location is at LT=128*.001 or .128 sec; hmmm.
g=x(n+1).*conj(x(n-1));
g(2*L)=0;
%y=w.*g;
y=hann(m).*g;      % Apply window to g or kernel.

Y=2/m*abs(fft(y,m)); % evidently because it's analytic
                    % we only need 2/N

Z(:,i)=Y(1:p);
n=n+skip;
end

%LFC = input('Please enter the low frequency range in index numbers. ');
LFC=1:4;
symvag=sum(Z(LFC,1:k));
%HFC=input('Please enter the high frequency range in index numbers. ');
HFC=4:20;
vagal=sum(Z(HFC,1:k));
symtopar=symvag./vagal;

% Normalize

n_symvag=symvag./(symvag+vagal);
n_vagal=vagal./(symvag+vagal);
n_symtopar=n_symvag./n_vagal;

% End normalize

%x1 = decimate(rawdata1,10); % decimate data array
x1 = rawdata;
%N1 = length(x1);

dtrendata1=rawdata1;
[row1,col1]=size(dtrendata1);
I1=1:row1;
I1=I1(:);
    A1=I1/sample;      % Time axis in minutes

m1=256;              % The size of the fft we will be computing.
skip1=25;           % Number of points we skip to get the next segment.
p1=60;              % The number of freq vals we will be plotting
k1=fix((row1-m1)/skip1); % the number of spectra we compute
L1=m1/2;
%w1=rectwin(size(1:m1)); % window specification. Can be changed.

```

```

%w1=w1(:);
x1=dtrendata1;
l1=-(L1-1):(L1-1);
n1=L1;
Z1=zeros([p1,k1]);
for j=1:k1
    % Here I think 0 lag is at the Lth point, hence the first
    % time location is at LT=128*.001 or .128 sec; hmmm.
    g1=x1(n1+1).*conj(x1(n1-l));
    g1(2*L1)=0;
    %y1=w1.*g1;
    y1=hann(m).*g1;      % Apply window to g or kernel.

    Y1=2/m1*abs(fft(y1,m1)); % evidently because it's analytic
                            % we only need 2/N
    Z1(:,j)=Y1(1:p1);
    n1=n1+skip1;
end

%LFC = input('Please enter the low frequency range in index numbers. ');
LFC1=1:4;
symvag1=sum(Z1(LFC1,1:k1));
%HFC=input('Please enter the high frequency range in index numbers. ');
HFC1=4:20;
vagall=sum(Z1(HFC1,1:k1));
symtopar1=symvag1./vagall;

% Normalize

n_symvag1=symvag1./(symvag1+vagall);
n_vagall=vagall./(symvag1+vagall);
n_symtopar1=n_symvag1./n_vagall;

% End normalize

% Plotting commands

J1=((length(x1)/sample)/(k1))*(0:k1-1);
J=((length(x)/sample)/(k))*(0:k-1);

figure

subplot('position',[0.075 .8 .4 .14]),plot(A,dtrendata);
title(' (a) Clean IIBI detrended');

```

```

xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.075 .55 .4 .14]),plot(A1,dtrendata1);
title(' (b) IIBI for the missed beat(s)');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.075 .30 .4 .14]),plot(J,symvag,J1,symvag1);
title(' (c) Superimposed of LFs');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.075 .06 .4 .14]),plot(J,vagal,J1,vagal1);
title(' (d) Superimposed of HFs');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .8 .4 .14]),plot(J,symtopar,J1,symtopar1);
title(' (e) Superimposed of ratios of LFs to HFs');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .55 .4 .14]),plot(J,n_symvag,J1,n_symvag1);
%gtext(top);
title(' (f) Superimposed of NLFs');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .30 .4 .14]),plot(J,n_vagal,J1,n_vagal1);
title(' (g) Superimposed of NHFs');
xlabel('time (sec)');
ylabel('amplitude');

subplot('position',[0.55 .06 .4 .14]),plot(J,n_symtopar,J1,n_symtopar1);
title(' (h) Superimposed of ratios of NLFs to NHFs');
xlabel('time (sec)');
ylabel('amplitude');

set(gcf,'position',[5 36 700 662]);

position = findstr('.', File)
if position>=0
File=File(1:position);
end

```



figure

```
subplot('position',[0.075 .8 .4 .14]),plot(J,abs(symvag1-symvag));
title(' (a) LF error function')
xlabel('time (sec)');
ylabel('amplitude');
```

```
subplot('position',[0.075 .55 .4 .14]),plot(J,abs(vagal1-vagal));
title(' (b) HF error function');
xlabel('time (sec)');
ylabel('amplitude');
```

```
subplot('position',[0.075 .30 .4 .14]),plot(J,abs(n_symvag1-n_symvag));
xlabel('time (sec)');
ylabel('frequency');
title(' (c) NLF error function');
```

```
subplot('position',[0.075 .06 .4 .14]),plot(J,abs(n_vagal1-n_vagal));
title(' (d) NHF error function');
xlabel('time (sec)');
ylabel('amplitude');
```

```
faxis=(1:p)*(.0391/2);
```

```
subplot('position',[0.55 .8 .4 .16]),mesh(J,faxis,Z);
title(' (e) 3D Time-Frequency for the clean data');
xlabel('time (sec)');
ylabel('frequency');
view(-45,45);
```

```
subplot('position',[0.55 .55 .4 .13]),contour(J,faxis,Z);
title(' (f) Contour Time-Frequency for the clean data');
xlabel('time (sec)');
ylabel('frequency');
```

```
subplot('position',[0.55 .30 .4 .16]),mesh(J1,faxis,Z1);
xlabel('time (sec)');
ylabel('frequency');
title(' (g) 3D Time-Frequency for missed beat(s)');
view(-45,45);
```

```
subplot('position',[0.55 .06 .4 .13]),contour(J1,faxis,Z1);
```

```
title(' (h) Contour Time-Frequency for missed beat(s)');  
xlabel('time (sec)');  
ylabel('frequency');  
  
set(gcf,'position',[5 36 700 662]);  
  
position = findstr('.', File)  
if position>=0  
File=File(1:position);  
end
```

**APPENDIX C**  
**SHORT TIME FOURIER TRANSFORM PROGRAM**  
**CODE FOR MISSED BEATS**

The following program written in Matlab was used to perform time-frequency analysis for missed beats using STFT on IIBI. Originally, it is written by Pierre Asselin.

```
clear
%These will open browser window to choose which files to load
[File, Path, FILTERINDEX] = uigetfile('*.*', 'Choose the data file you wish to process');
rawSignal=load([Path File]);

[File, Path, FILTERINDEX] = uigetfile('*.*', 'Choose the data file you wish to process');
rawSignal1=load([Path File]);

%%%%%%%%%%%%%%For original clean
data%%%%%%%%

%Set up the time scale for a 5hz interpolated signal
fs=5;
dtime=1/fs;
time=length(rawSignal)*dtime;
t=[0:dtime:time-dtime];

%this will set up the window length
winSizeSec=50;
winSizeSample=winSizeSec*(1/dtime);

winCent=ceil(winSizeSample/2);

%sets up the DFT with the length of segLength
%makes the fft frequency spike sharper
%since it is a power of 2 this will make the FFT go faster
segLength=2^8;

h = waitbar(0,'Processing FFT...'); %Sets up the %complete

%this will do how much over lap will be with the windowing
%the more overlap the slower the program runs but the better the time vs
%frequency will be
overlap=.9;
```

```

skip=round(winSizeSample*(1-overlap));
skip=1;
%performs the fft on a the set window with 100% overlap
for i=1:skip:length(t)-winSizeSample
    i=(i-1+skip)/skip;    %this will readjust the counter
    winSig=rawSignal(i:i+winSizeSample-1);
    winSig=winSig-mean(winSig);
    winSig=winSig.*hanning(winSizeSample); %adds a hanning window
    winSigMat(i,[1:winSizeSample])=winSig; %constructs a matrix with windowed
signals
    waitbar(i/(round((length(t)-winSizeSample)*2)/skip))    %Marks the Progress of
%complete
end
close(h)    %will close the %done window

%computes the fourier transform of the signal
WINSIGMAT = fft(winSigMat',segLength);

h = waitbar(0,'Processing Power Spectrum..');    %Sets up the %complete
[r,c]=size(WINSIGMAT)
for i=1:c
    %converts the signal to its measure of power at various frequencies
    Pow([1:segLength],i)= WINSIGMAT([1:segLength],i).*
conj(WINSIGMAT([1:segLength],i)) / segLength;
    % Pow= WINSIGMAT.* conj(WINSIGMAT) / segLength;
    waitbar(i/c)    %Marks the Progress of %complete
end
close(h)    %will close the %done window

%this will calculate the frequency energy
lowLF=0.04;
lowLF=round(lowLF*segLength*dtime);
highLF=0.15;
highLF=round(highLF*segLength*dtime);
lowHF=highLF;
highHF=.7;
highHF=round(highHF*segLength*dtime);

%does the sum for the frequency calculation
LF=sum(Pow(lowLF:highLF,:));
HF=sum(Pow(lowHF:highHF,:));

%does the normalization
nLF=LF./(LF+HF);
nHF=HF./(LF+HF);

```

```

%does the LF/HF ratio
LFHFratio=LF./HF;
nLFHFratio=nLF./nLF;

%adds padding to since the windowing cuts off some of the time data
time=winSizeSec/2*fs; %15 seconds of time with a sampling rate of 5 hz
pad=zeros(time,1);
LF=[pad;LF;pad];
HF=[pad;HF;pad];
nLF=[pad;nLF;pad];
nHF=[pad;nHF;pad];
LFHFratio=[pad;LFHFratio;pad];
nLFHFratio=[pad;nLFHFratio;pad];

f = 1/dtime*(lowLF:highHF)/segLength; %this will normalize and adjust the frequency
in the proper range
adjTime=t(winCent+1:skip:length(t)-winCent); %this will crop the time due to the
windowing spacing for the first and last spectrum analysis. this could potentially be
resolved with padding.

startData=length(pad)+1;
endData=startData+length(adjTime)-1;

%%%%%%%%%%%%%%For missed
beat(s)%%%%%%%%%%%%%%
%Set up the time scale for a 5hz interpolated signal
fs1=5;
dtime1=1/fs1;
time1=length(rawSignal1)*dtime1;
t1=[0:dtime1:time1-dtime1];

%this will set up the window length
winSizeSec1=50;
winSizeSample1=winSizeSec1*(1/dtime1);

winCent1=ceil(winSizeSample1/2);

%sets up the DFT with the length of segLength
%makes the fft frequency spike sharper
%since it is a power of 2 this will make the FFT go faster
segLength1=2^8;

h1 = waitbar(0,'Processing FFT...'); %Sets up the %complete

%this will do how much over lap will be with the windowing
%the more overlap the slower the program runs but the better the time vs

```

```

%frequency will be
overlap1=.9;
skip1=round(winSizeSample1*(1-overlap1));
skip1=1;

%performs the fft on a the set window with 100% overlap
for i=1:skip1:length(t1)-winSizeSample1
    i=(i-1+skip1)/skip1;    %this will readjust the counter
    winSig1=rawSignal1(i:i+winSizeSample1-1);
    winSig1=winSig1-mean(winSig1);
    winSig1=winSig1'.*hanning(winSizeSample1); %adds a hanning window
    winSigMat(i,[1:winSizeSample1])=winSig1; %constructs a matrix with windowed
signals
    waitbar(i/(round((length(t1)-winSizeSample1)*2)/skip1))    %Marks the Progress
of %complete
end
close(h1)    %will close the %done window

%computes the fourier transform of the signal
WINSIGMAT = fft(winSigMat',segLength1);

h1 = waitbar(0,'Processing Power Spectrum...');    %Sets up the %complete
[r1,c1]=size(WINSIGMAT)
for i=1:c1
    %converts the signal to its measure of power at various frequencies
    Pow([1:segLength1],i)= WINSIGMAT([1:segLength1],i).*
conj(WINSIGMAT([1:segLength1],i)) / segLength1;
    % Pow= WINSIGMAT.* conj(WINSIGMAT) / segLength;
    waitbar(i/c1)    %Marks the Progress of %complete
end
close(h1)    %will close the %done window

%this will calculate the frequency energy
lowLF1=0.04;
lowLF1=round(lowLF1*segLength1*dtime1);
highLF1=0.15;
highLF1=round(highLF1*segLength1*dtime1);
lowHF1=highLF1;
highHF1=.7;
highHF1=round(highHF1*segLength1*dtime1);

%does the sum for the frequency calculation
LF1=sum(Pow(lowLF1:highLF1,:))';
HF1=sum(Pow(lowHF1:highHF1,:))';

%does the normalization

```

```

nLF1=LF1./(LF1+HF1);
nHF1=HF1./(LF1+HF1);

%does the LF/HF ratio
LFHFratio1=LF1./HF1;
nLFHFratio1=nLF1./nLF1;

%adds padding to since the windowing cuts off some of the time data
time1=winSizeSec/2*fs1; %15 seconds of time with a sampling rate of 5 hz
pad1=zeros(time1,1);
LF1=[pad1;LF1;pad1];
HF1=[pad1;HF1;pad1];
nLF1=[pad1;nLF1;pad1];
nHF1=[pad1;nHF1;pad1];
LFHFratio1=[pad1;LFHFratio1;pad1];
nLFHFratio1=[pad1;nLFHFratio1;pad1];

f1 = 1/dtime1*(lowLF1:highHF1)/segLength1; %this will normalize and adjust the
frequency in the proper range
adjTime1=t1(winCent1+1:skip1:length(t1)-winCent1); %this will crop the time due to
the windowing spacing for the first and last spectrum analysis. this could potentially be
resolved with padding.

startData1=length(pad1)+1;
endData1=startData1+length(adjTime1)-1;

%%%%%%%%%%%%this section does all the
plotting%%%%%%%%%%%%

figure
%Plotting the IIBI signal for the original and missed beat(s) data
subplot('position',[0.075 .8 .4 .14]),plot(t,rawSignal);
title('(a) IIBI detrended');
xlabel('Time (sec)');
ylabel('amplitude');

subplot('position',[0.075 .55 .4 .14]),plot(t1,rawSignal1);
title('(b) IIBI missed beat detrended');
xlabel('Time (sec)');
ylabel('amplitude');

%Plots the superimposed LFs
subplot('position',[0.075 .30 .4
.14]),plot(adjTime,LF(startData:endData),adjTime1,LF1(startData1:endData1));
title('(c) Superimposed LFs');

```

```

xlabel('Time (sec)');
ylabel('amplitude');

%Plots the superimposed HFs
subplot('position',[0.075 .06 .4
.14]),plot(adjTime,HF(startData:endData),adjTime1,HF1(startData1:endData1));
title('(d) Superimposed HFs ');
xlabel('Time (sec)');
ylabel('amplitude');

%this plots the superimposed LF/Hf ratios
subplot('position',[0.55 .8 .4
.14]),plot(adjTime,LFHFratio(startData:endData),adjTime1,LFHFratio1(startData1:endD
ata1));
title('(e) Superimposed LF/HF ratios');
% ylabel('Frequency (Hz)','FontSize',7)
xlabel('Time (Sec)');
ylabel('amplitude');

%Plots the superimposed normalized HFs
subplot('position',[0.55 .55 .4
.14]),plot(adjTime,nHF(startData:endData),adjTime1,nHF1(startData1:endData1));
title('(f) Superimposed nHFs');
xlabel('Time (sec)');
ylabel('amplitude');

%Plots the superimposed normalized LFs
subplot('position',[0.55 .30 .4
.14]),plot(adjTime,nLF(startData:endData),adjTime1,nLF1(startData1:endData1));
title('(g) Superimposed nLFs');
xlabel('Time (sec)');
ylabel('amplitude');

%this plots the superimposed normalized LF/Hf ratios
subplot('position',[0.55 .06 .4
.14]),plot(adjTime,nLFHFratio(startData:endData),adjTime1,nLFHFratio1(startData1:en
dData1));
title('(h) Superimposed nLF/nHF ratios');
% ylabel('Frequency (Hz)','FontSize',7)
xlabel('Time (Sec)');
ylabel('amplitude');

set(gcf,'position',[5 36 700 662]);

position = findstr('.', File)

```



```

if position>=0
File=File(1:position);
end

figure
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%Plots of error
functions%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

symp=abs(LF(startData:endData)-LF1(startData1:endData1-1))
vagal=abs(HF(startData:endData)-HF1(startData1:endData1-1))
nsymp=abs(nHF(startData:endData)-nHF1(startData1:endData1-1))
nvagal=abs(nLF(startData:endData)-nLF1(startData1:endData1-1))

subplot(221),
plot(adjTime,symp);
title('(a) Error LFs');
xlabel('Time (sec)');
ylabel('amplitude');

subplot(222),
plot(adjTime,vagal);
title('(b) Error HFs');
xlabel('Time (sec)');
ylabel('amplitude');

subplot(223)
plot(adjTime,nvagal);
title('(c) Error nLFs');
xlabel('Time (sec)');
ylabel('amplitude');

subplot(224),
plot(adjTime,nsymp);
title('(d) Error nHFs');
xlabel('Time (sec)');
ylabel('amplitude')

set(gcf,'position',[5 36 700 580]);

position = findstr('.',File)
if position>=0
File=File(1:position);
end

```

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