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Atrial Fibrillation Signal Analysis

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by

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DEDICATION

To my parents and my sister.

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ABSTRACT

Atrial fibrillation (AF) is the most common type of cardiac arrhythmia encountered in clinical practice and is associated with an increased mortality and morbidity. Identification of the sources of AF has been a goal of researchers for over 20 years. Current treatment procedures such as Cardio version, Radio Frequency Ablation, and multiple drugs have reduced the incidence of AF. Nevertheless, the success rate of these treatments is only 35-40% of the AF patients as they have limited effect in maintaining the patient in normal sinus rhythm. The problem stems from the fact that there are no methods developed to analyze the electrical activity generated by the cardiac cells during AF and to detect the aberrant atrial tissue that triggers it.

In clinical practice, the sources triggering AF are generally expected to be at one of the four pulmonary veins in the left atrium. Classifying the signals originated from four pulmonary veins in left atrium has been the mainstay of signal analysis in this thesis which ultimately leads to correctly locating the source triggering AF. Unlike many of the current researchers where they use ECG signals for AF signal analysis, we collect intra cardiac signals along with ECG signals for AF analysis. AF Signal collected from catheters placed inside the heart gives us a better understanding of AF characteristics compared to the ECG.

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In recent years, mechanisms leading to AF induction have begun to be explored but the current state of research and diagnosis of AF is mainly about the inspection of 12 lead ECG, QRS subtraction methods, spectral analysis to find the fibrillation rate and limited to establishment of its presence or absence. The main goal of this thesis research is to develop methodology and algorithm for finding the source of AF. Pattern recognition techniques were used to classify the AF signals originated from the four pulmonary veins. The classification of AF signals recorded by a stationary intra-cardiac catheter was done based on dominant frequency, frequency distribution and normalized power. Principal Component Analysis was used to reduce the dimensionality and further, Linear Discriminant Analysis was used as a classification technique. An algorithm has been developed and tested during recorded periods of AF with promising results.

CHAPTER 1

INTRODUCTION

1.1 Overview of Atrial Fibrillation

This research brings into limelight the technical and methodological aspects of using signal processing to analyze cardiac signals sans the old school of thoughts which concludes from the interpretations of the medical results.

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice and is associated with an increased mortality and morbidity. It currently affects more than 2.5 million Americans. The occurrence of AF increases with age. The prevalence in individuals over the age of 80 is about 8% in developed countries. It is estimated to increase drastically due to increase in older population [1]. It is estimated to affect 5.6 million Americans by the year 2050 [1].

In a healthy heart, periodic electrical propagation's are initiated by the sino–atrial node (SAN). SAN also known as pace maker is located at the top of the right atrium. AF occurs due to disorders in the genesis or in the conduction of the electrical propagation carrying the information of muscular contraction throughout the whole heart.

Identification of the sources of AF has been a goal of researchers for over 20 years, but has been looked at with renewed interest since the advent of curative therapies for AF aiming at destroying the sources initiating AF. Medical therapy has reduced the incidence of strokes, the most feared consequence of AF, but has limited effect in returning and

maintaining the patient in normal sinus rhythm. Radio-frequency ablation (RFA) has become a widely used procedure to identify and destroy tissue involved in the initiation of AF. In the ablation procedure, a catheter is guided into the heart and the tip of the catheter delivers radiofrequency energy that heats and destroys the tissue. In multiple clinical trials this procedure has shown to be superior to medical therapy in restoring and maintaining sinus rhythm. Nevertheless, success rate of RFA in the treatment of AF is well below the success rate of other arrhythmias. The reason is that identifications of arrhythmic tissue are far less precise in AF than in the majority of supra-ventricular arrhythmias.

The intra-cardiac or Electrocardiogram (ECG) signals during AF are characterized by an apparent randomness and complete disorganization preventing a meaningful interpretation with usual methods of analysis. Signals during atrial fibrillation represent multiple fronts of activation occurring at the point of recording during a highly disorganized rhythm. The recorded signal is, therefore, highly variable in voltage, morphology and rate and this prevents the identification of its different components.

Key to targeting the correct location for ablation is to understand the pathological and electrophysiological arrhythmia mechanism. Analysis of the frequency content of the signals has been the mainstay of signal analysis in this thesis. Left to right atrium gradient of frequencies and the observation of greater activation frequencies or dominant frequencies in the former chamber suggests a preferential origin of AF in the left atrium (LA). Clinically, the approach of RFA to AF has always been to target the four pulmonary veins in the left atrium. Hence, the main objective of the thesis is the

processing and characterization of signals from the four pulmonary veins in the LA using frequency domain analysis and statistical pattern recognition.

1.2 Motivation and Goals of this Thesis

In clinical practice, there is no test available that can predict the source of AF and the outcome of treatment. Current treatment plans for AF include (RFA), multiple drugs or medical procedures such as pulmonary vein isolation, electrical cardio version or atrial pacemaker to restore a normal heart rhythm. During RFA, atrial tissue is destroyed in areas felt to be responsible for the induction of AF. This procedure is not guided by clear identification of these arrhythmic sources, instead by the probability that specific regions of the heart are likely to be involved. The ablation is therefore far less precise than if guided by true knowledge of the mechanism of induction of AF. In pulmonary vein isolation, a targeted destruction of cardiac tissue is performed using a small catheter introduced into the heart. It is possible that pulmonary vein isolation effectively modify AF substrate skin to a surgical maze procedure. Nevertheless, treating all chronic AF patients with similar approach has one conspicuous weakness that every patient with AF does not have the same characteristics. So, treating every patient to the same ablation set is not valid and likely results in many unnecessary lesions. Hence the treatment is only successful in approximately 35-40% of patients. The problem stems from the fact that there are no methods developed to analyze the electrical activity generated by the cardiac cells during AF and to detect the aberrant atrial tissue that triggers it. Intra-cardiac signals through catheters are recorded practically from all patients undergoing AF treatment. It is desirable, to identify the sources of AF to help physicians in deciding which appropriate location in atria is to be burnt by characterizing the AF signal.

This study was aimed at developing a novel method and algorithm for identifying the sources of AF. The proposed research work includes the following research goals:

- *State of the Art.* A comprehensive review of the state of the art of characterization of AF signals, frequency tracking of AF and atrial signal processing to navigate AF ablation will be carried out.
- *Characterization.* Collection of intra-cardiac signals through catheters using a particular protocol. Further analysis will be carried out to characterize atrial signals generated from different areas of the LA.
- *Classification.* To develop a method to classify the signals from four pulmonary veins through statistical pattern recognition techniques. Clinically, the sources of AF are anticipated to be at the four pulmonary veins.
- *Verification of experimental results.*

1.3 Challenges

The anticipated challenges towards reaching the goal are

- Correctly quantifying the characteristics of the AF signal as it propagates through the tissue from the four pulmonary veins to the catheters.
- Identification of AF waveforms due to a single source.

Identifying signal features or characteristics by applying different signal processing techniques to accurately deduce the signal origin. The characteristics of the AF signal vary between different patients. They also vary in the same patient over time. One important challenge is to track such changes in long-term AF signal recordings. Hence, the development of robust signal processing methods is essential.

1.4 Contributions and Organization of this Thesis

Most commonly accepted hypothesis identifies a number of fast discharging arrhythmic triggers are mostly located in LA. Clinically, the approach of Radio Frequency Ablation to AF has always been to target the four Pulmonary Veins in the LA. Hence, in the main body of this thesis, our work primarily focuses on developing a method to characterize the signal traveling from pulmonary veins to catheters. Frequency analysis has been the mainstay for the characterization of these AF signals. Further, the classification of AF signals obtained from pulmonary veins was done based on dominant frequency, frequency distribution, normalized power. The feature set dimension was reduced by using Principal Component Analysis (PCA). The first component generated by PCA accounts for maximum variability in the data, and each succeeding component accounts for as much of the remaining variability as possible. Further, AF signals from the four pulmonary veins in LA were classified using a statistical pattern recognition technique, Linear Discriminant Analysis (LDA).

This chapter presents the motivation and goal of this thesis along with the challenges to achieve those goals. The rest of the thesis is organized as follows:

Chapter 2 presents the extensive introduction to anatomy of the heart, Electrocardiogram (ECG), and AF mechanisms. It also presents recent approaches to identifying the sources of AF.

Chapter 3 covers several widely used ECG signal processing techniques including Fast Fourier Transform (FFT), PCA and LDA are discussed. The mathematical derivations of the algorithms and their underlying assumptions are presented. This chapter would give readers a basic idea of the mentioned techniques and their advantages or disadvantages.

Hence this chapter provides the background for understanding the signal processing techniques used in this research of identifying AF sources.

Chapter 4 presents a new methodology for characterization of AF signals. The main concept of classification of AF signals from four pulmonary veins and the proposed directional algorithm to identify the sources of AF are discussed. This chapter also includes data acquisition protocol, summary of proposed new methodology, simulation results, verification and discussion.

Chapter 5 gives the conclusion and proposes suggestions for future research work.

CHAPTER 2

ATRIAL FIBRILLATION

2.1 Anatomy of the Heart

The human heart is the most essential organ of the human body as it supplies blood to all parts of the body. Blood acts as a medium for transporting substances such as oxygen, nutrients, enzymes, antibodies, as well as collecting end result of multiple metabolic process as toxic byproducts for disposal. The heart is situated in the chest cavity posterior to the sternum and costal cartilages and rests on the superior surface of the diaphragm. The basic anatomy of the heart is shown in Figure 2.1.

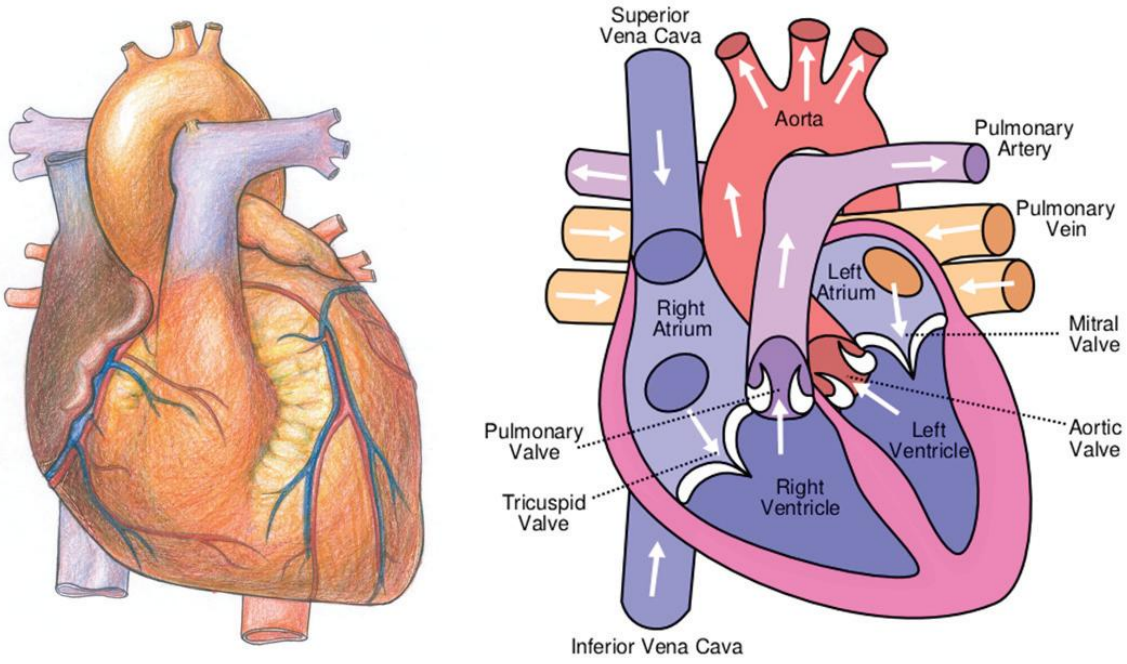

Figure 2.1 Anatomy of the Heart.

The heart has four chambers: two upper chambers (atria) and two lower chambers (ventricles). A muscular septum divides the heart internally into left half and right half. The two upper chambers LA and right atrium (RA) function as collecting chambers. The lower two chambers left ventricle (LV) and right ventricle (RV) pump blood. In general, de-oxygenated blood in the right atrium collected from all veins of the body (except from the veins of the lungs) is pumped into the right ventricle. Contraction of the right ventricle pumps the blood to the lungs through the pulmonary arteries. In the lungs oxygen is supplied to the blood making it oxygenated blood. Both the left and right pulmonary veins carry the oxygenated blood from lungs to LA. Further the blood in the LA is pumped into the left ventricle. Upon the contraction of the left ventricle, the blood through the aortic artery and its branches is supplied to all tissues in the body. Oxygen is used by the cells to produce energy and carbon dioxide is generated as a byproduct. Oxygen poor, carbon dioxide rich blood collected by the superior and inferior vena cava empties into the right atrium. The direction of the blood flow is controlled by atrioventricular valves between the atria and the ventricles, and the pulmonary and aortic valves between the ventricles and the arteries.

During one heart beat or cardiac cycle, a sequence of electrical and mechanical events takes place. Under normal conditions, heart contractions are very rhythmic and synchronized. The contraction of the heart muscle is due to the electrical impulse generated spontaneously by SAN. Hence, SAN is called the “pacemaker” of the heart. The electrical stimulus from SAN spreads through both atria and reaches the atrioventricular node (AVN). The impulse from AVN will reach ventricles via left and right bundles of HIS. In general, bundle of HIS extends into the septum where it

forms two branches, giving rise to Purkinje network. The impulse now spreads rapidly in both ventricular chambers as Purkinje fibers conduct impulses faster than ordinary cardiac muscles. Hence both the ventricles contract almost simultaneously. The basic heart conduction system explained above is shown in Figure 2.2.

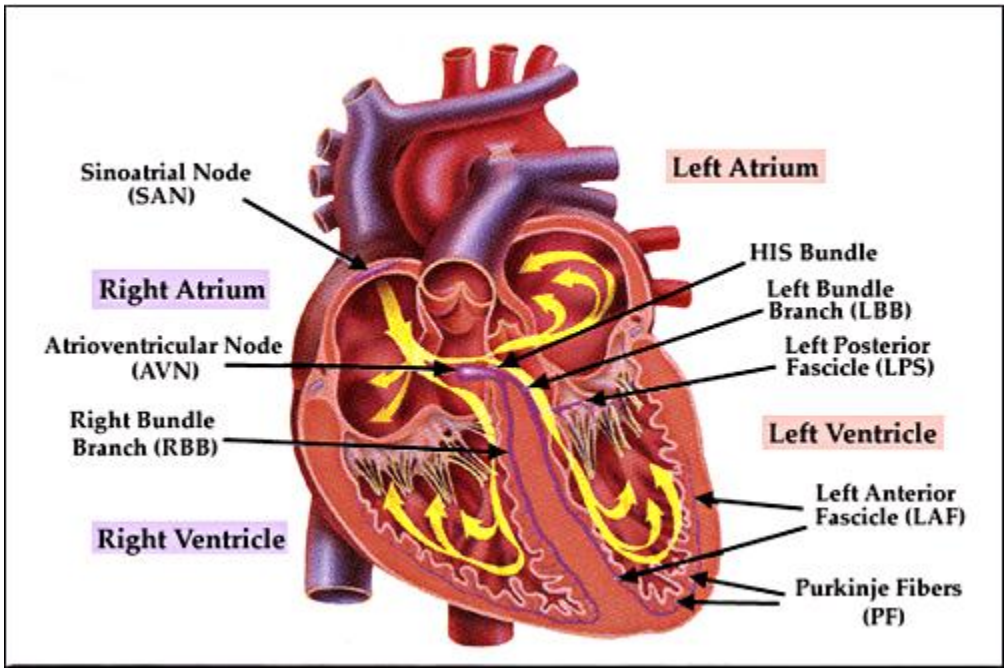

Figure 2.2 Heart Conduction System [2].

2.2 Atrial Fibrillation

AF is the most common type of cardiac arrhythmia. It is a problem associated to abnormal rate or rhythm of the heartbeat. It currently affects more than 2.5 million Americans. The occurrence of AF increases with age. The prevalence in individuals over the age of 80 is between 10 to 15% in developed countries and it is estimated to increase drastically due to increase in the older population [1]. It is estimated to affect 5.6 million Americans by the year 2050.

2.2.1 Symptoms of AF

AF is often asymptomatic and it is not in itself generally life–threatening. AF may result in fainting, chest pain, or congestive heart failure. Symptomatic AF is characterized by irregular and rapid heartbeat, dizziness, sweating and chest pain, shortness of breath, and fatigue while exercising. Patients with AF are therefore at increased risk of stroke between two to seven times the age matched individuals in sinus rhythm. AF is therefore one of the leading causes of stroke [3].

2.2.2 Electrophysiology of AF

A normal heart rate at rest varies from 60 to 80 beats per minute. A normal heart beat is rhythmic as the impulse generated by SAN is very periodic as shown in left figure of Figure 2.3. In AF, the impulse is generated from the sinus node and multiple random signals ‘fire off’ from different abnormal tissues in the atria as shown in the right figure of Figure 2.3.

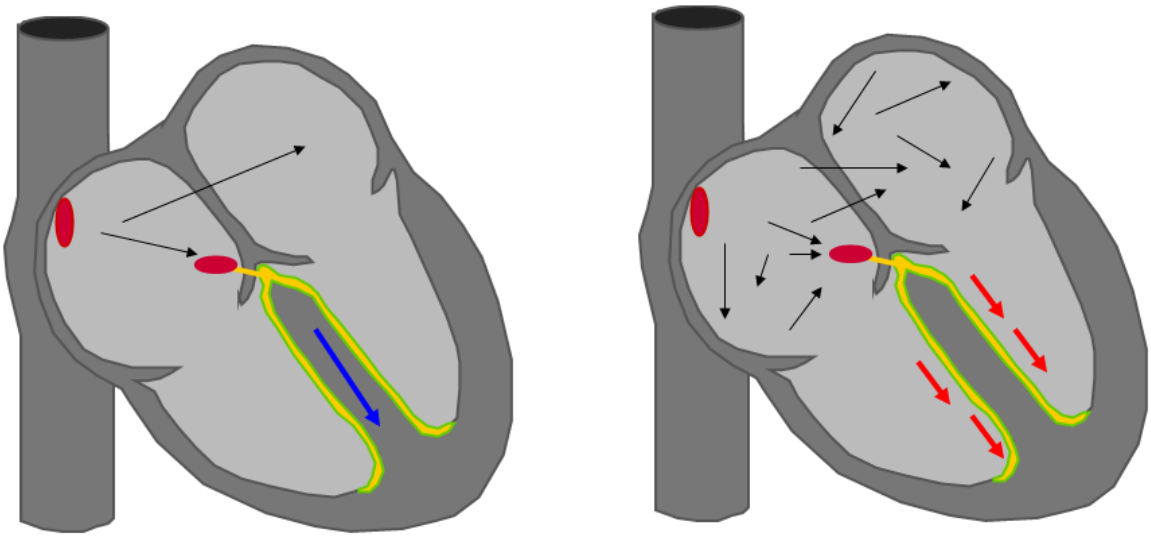

Figure 2.3 Sinus Rhythm and AF in Heart.

Due to the presence of multiple disorganized electrical impulses in the heart, the atria begin to quiver or fibrillate, so they no longer effectively pump blood into the ventricles. Such ineffective contraction induces stagnation of the blood in low flow areas of the atria potentially leading to blood clotting. Small pieces of the clot can break off causing occlusion of small arteries and hence stroke or peripheral artery occlusion (peripheral infront). Hence, during AF, ventricles stimulated by fibrillating atria beat irregularly with varying frequencies. Ventricular function becomes impaired causing heart failure. It is therefore not surprising that AF is associated with an increased risk of death [4].

2.2.3 Classification of AF

Various classifications of AF were made based on ECG pattern, cardiac activity and clinical features. The American Heart Association (AHA) classified heart basically into three types: Firstly detected AF, recurrent AF, Long standing AF. If the AF episode was detected for the first time in a patient, it is called "*Firstly Detected AF"*. If A-fib appears two or more times, then it is considered as "*Recurrent AF*". This can be paroxysmal AF or persistent AF. In paroxysmal AF, the heart changes from sinus rhythm to AF periodically. It returns to the sinus rhythm on its own after lasting for few seconds, hours or days. These are therefore self-terminating episodes lasting for variable time. The patient may only have one episode a year, but the essential feature is that most episodes terminate spontaneously. This is often uncomfortable to the patient as the heart will always be switching between regular and irregular rhythm. One in four people suffering from paroxysmal AF eventually go to permanent AF. Persistent AF does not stop spontaneously, but sinus rhythm can be restored by medication or by applying electrical shock to the heart. The first detected AF can be either paroxysmal or persistent AF. The

third type is "*Long standing AF*", the arrhythmia is sustained for more than one year. In some cases, it progresses to permanent AF. Permanent AF is present all the time. In this case, restoring sinus rhythm is either not possible or not deemed appropriate. These three AF categories are not mutually exclusive.

2.2.4 Diagnosis and Treatment of AF

AF is generally diagnosed with the ECG. The medical history of the patient is also considered. AF is diagnosed as one of the three types paroxysmal, persistent and permanent as discussed in the above section [5]. Treatment options take into consideration the history of arrhythmia and the clinical status of the patient. The main decision regarding AF treatment is whether to return the patient to sinus rhythm or leave AF and control the ventricular rates. Sinus rhythm can be restored by DC cardioversion, drugs, RFA or surgery. Anti-arrhythmia medications are drugs which change the electrical properties of the heart. Usage of these drugs is often complicated by side effects including often more serious cardiac arrhythmias. Cardio-version with direct current is an electrical shock delivered across the chest of the patient for terminating AF and restoring sinus rhythm. But pharmacological cardio-version is ineffective for AF longer than seven days [6]. Major adverse events and deaths occur in patients suffering with permanent AF [7]. RFA, atrial pacing and surgical procedures will be employed in case of permanent AF [8]. The 3D visual display of burnt tissues in atria during RFA is shown in Figure 2.4a and surgical maze procedure in Figure 2.4b.

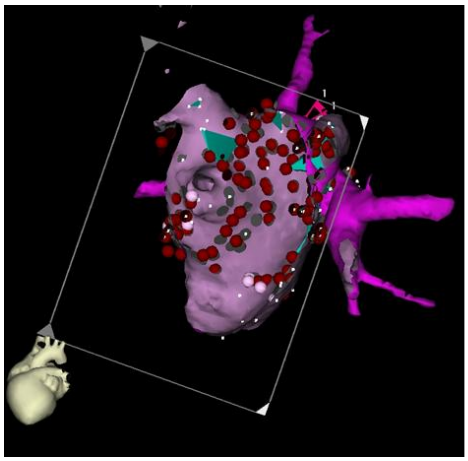

Figure 2.4 Burnt Tissues during RFA

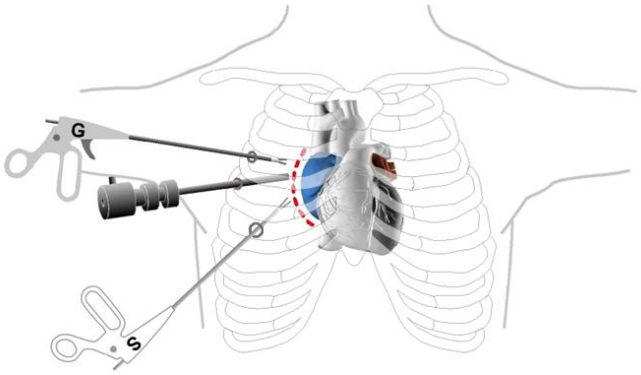

Figure 2.5 Surgical Maze Procedure.

RFA is invasive catheter based procedure where selected atrial tissue is exposed to cautery from inside of the heart (endocardiac). This eliminates areas inducing or maintaining AF restoring sinus rhythm. Surgical approaches vary from open heart compartimentization of the atria to the thorcoscopic ablation of selected atrial regions from outside of the heart (epicardially).

2.3 Electrocardiogram (ECG)

The ECG is a diagnostic tool that measures and records the electrical activity of the heart. ECG is captured by attaching a number of electrodes to the body surface. A graphic representation of the electrical activity can be obtained by using a standard 12 lead ECG. Six of these leads are known as Limb Leads since they are placed on arms or legs. The remaining six leads are Precordial Leads as they are placed on procordium. There are two types of leads- unipolar and bipolar. The following are the 12 leads and their placements.

Lead I is placed in between the right arm and left arm electrodes. The left arm is referred to be positive. Lead II is placed between the right arm and left leg electrodes, the left leg being positive. Lead III is placed between the left arm and left leg electrodes, the

left leg being positive. Lead I, II, III are bipolar leads. The chest electrodes V1-V6 are unipolar leads, and they are placed as follows (shown in Figure 2.5)

V1: Fourth intercostal space to the right of the sternum.

V2: Fourth intercostal space to the Left of the sternum.

V3: Directly between leads V2 and V4.

V4: Fifth intercostal space at midclavicular line.

V5: Level with V4 at left anterior axillary line.

V6: Level with V5 at left midaxillary line.

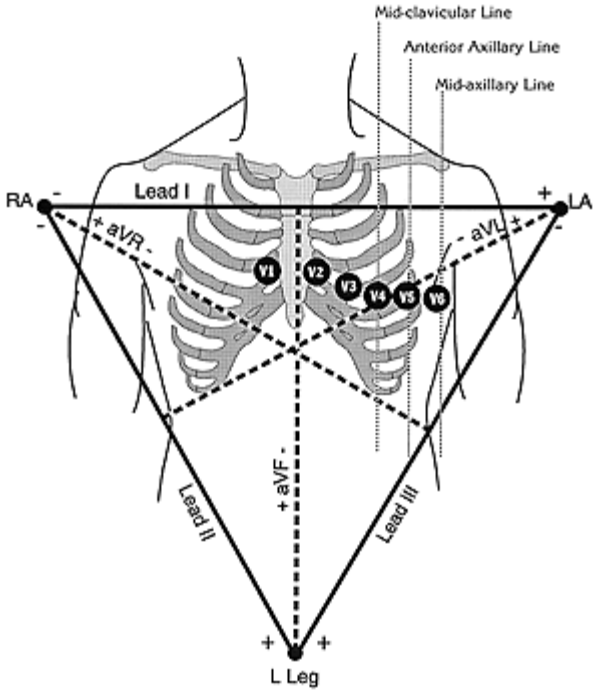

Figure 2.6 Schematic Representation of 12 Leads Around the Heart [9].

Leads aVR (Augmented Vector Right Arm), aVL (Augmented Vector Left Arm), and aVF (Augmented Vector left leg) are known as augmented limb leads. Lead aVR is placed between RA and LA and Left foot (LF)] with RA as positive. Lead aVL is placed between LA and [RA & LF] with LA being positive. Lead aVF is placed between LF and [RA & LA] with LF as positive. The augmented leads are placed as shown in Figure 2.6.

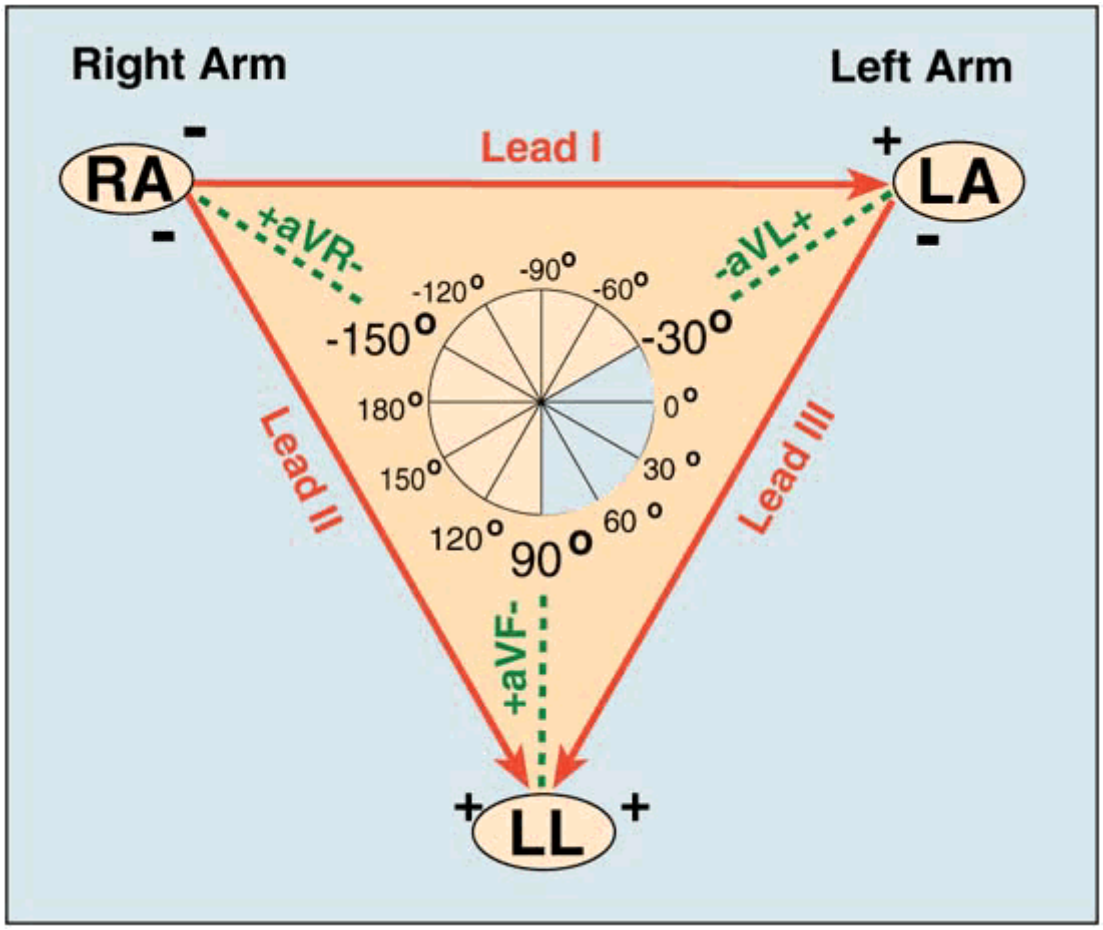

Figure 2.7 Einthoven's Triangle.

2.4 Sinus Rhythm and Arrhythmias

A typical ECG which records bioelectric currents generated by heart is shown in Figure 2.7. The peaks of this ideal ECG waveform are named as P, Q, R, S, T, U. The P wave indicates that the atria are stimulated to pump the blood to ventricles. This process is called atrial depolarization. It occurs when pacemaker (SAN) produces an action potential which depolarizes the atria. In a normal ECG, the P wave should be upright in lead II. If this is so, the ECG is said to be "Normal Sinus Rhythm" (NSR). Each P wave will be followed by QRS complex.

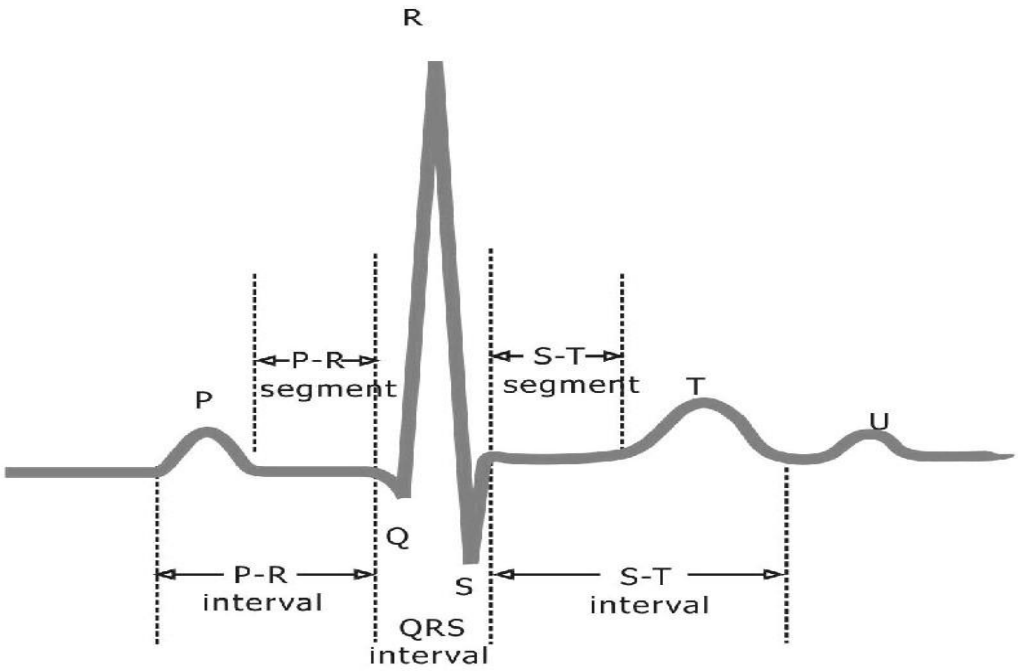

Figure 2.8 Typical ECG signal

The QRS complex represents the ventricular depolarization. This occurs when the signal generated from SA node travels through the AV node to ventricles. The T wave which occurs after the QRS complex is a result of the ventricular repolarization. U waves are produced by repolarization of the Purkinje cells. T waves are asymmetric and must be upright in all leads except the aVR and V1. The PR, QRS and ST intervals are shown in Figure 2.7. The atrial rate can be found by measuring the frequency of P-waves.

2.4.1 Normal Sinus Rhythm

For normal sinus rhythm (NSR),

- Atrial rate during NSR is 60-100 beats per minute (bpm).
- Both atria and ventricles have a regular rhythm.
- P waves occur before QRS and they are upright and uniform.
- The length of the PR interval is about 0.12-0.20 secs.
- All QRS complex will look alike and their length will be less than 0.12 secs.

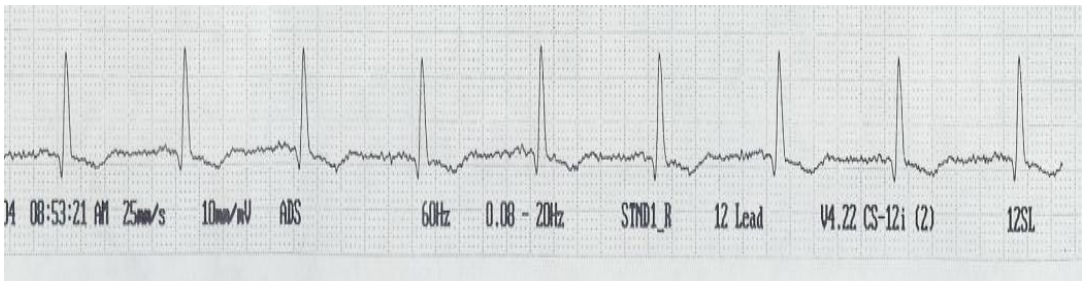

Figure 2.9 ECG of Sinus Rhythm

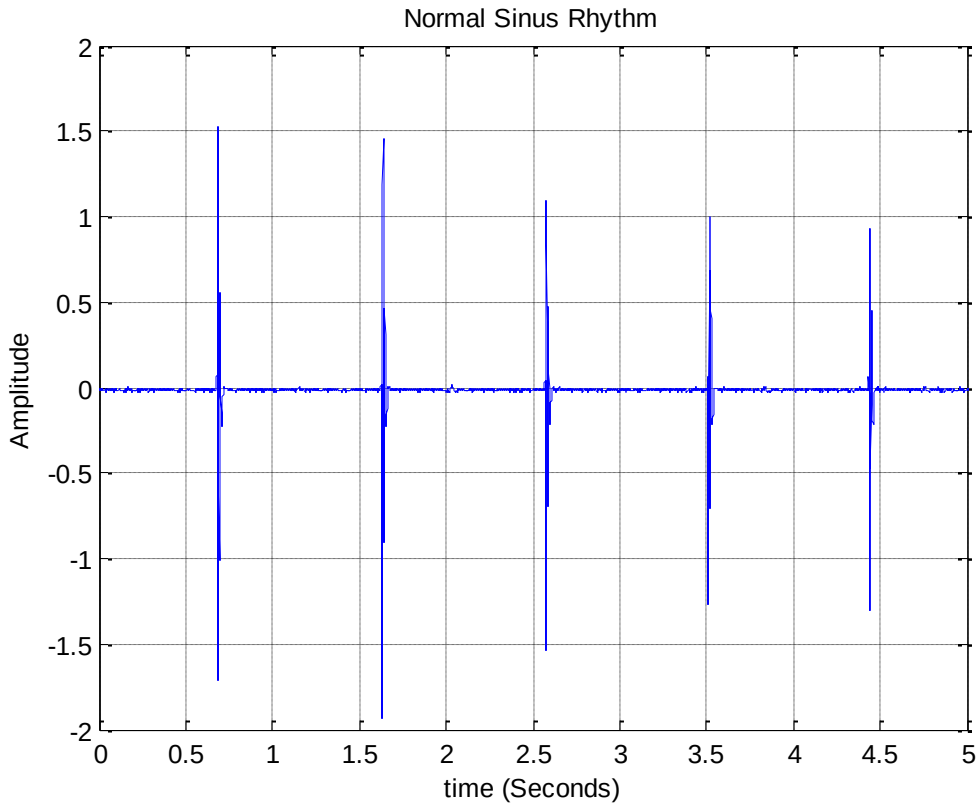

Figure 2.10 Normal Sinus Rhythm

The NSR observed by ECG and measured by the catheters placed in the LA of the heart at coronary sinus are shown in Figures 2.8. and 2.9, respectively. The signal collected through the catheters collects the total activity occurring near the tissue of the catheter. This gives us a more detailed view of the signal compared to that of the ECG signal. Changes in the normal ECG tracing can represent arrhythmia. The heart can function in NSR or might be affected with atrial rhythms. There are three types of atrial rhythms

namely Atrial Flutter, AF and supraventricular Tachycardia. Atrial rhythms occur when atrial tissue or areas other than SA node start generating impulses.

2.4.2 Atrial Fibrillation Signal Characteristics

AF occurs when electricity in atria is flowing in rapid, disorganized way. The atria start to quiver and will not be able to pump blood to the ventricles properly. Thereby, The conduction of atrial and ventricular rate is not 1:1. It is generally 2:1 or 4:1 and it can vary.

- Atrial rate during AF is 350-450 bpm and the ventricular rate is variable.
- Atria have an irregularly regular rhythm, this effects ventricular depolarization.
- Normally P waves are absent and they are replaced with F-waves (saw tooth).
- The length of the PR interval is not discernable.
- All QRS complex will look-alike and their length will be usually less than 0.12 secs.

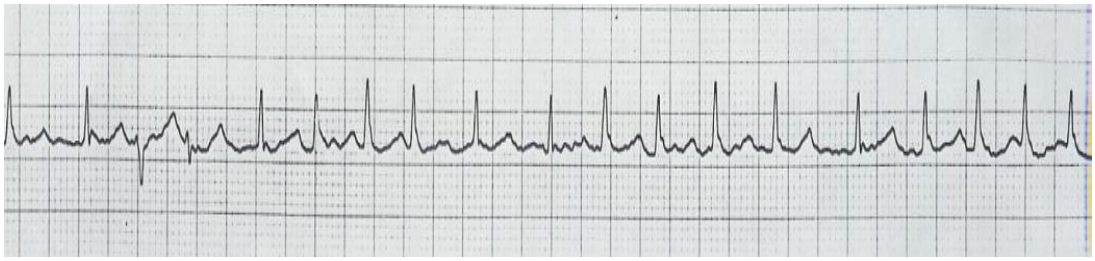

Figure 2.11 Atrial Fibrillation Signal in ECG

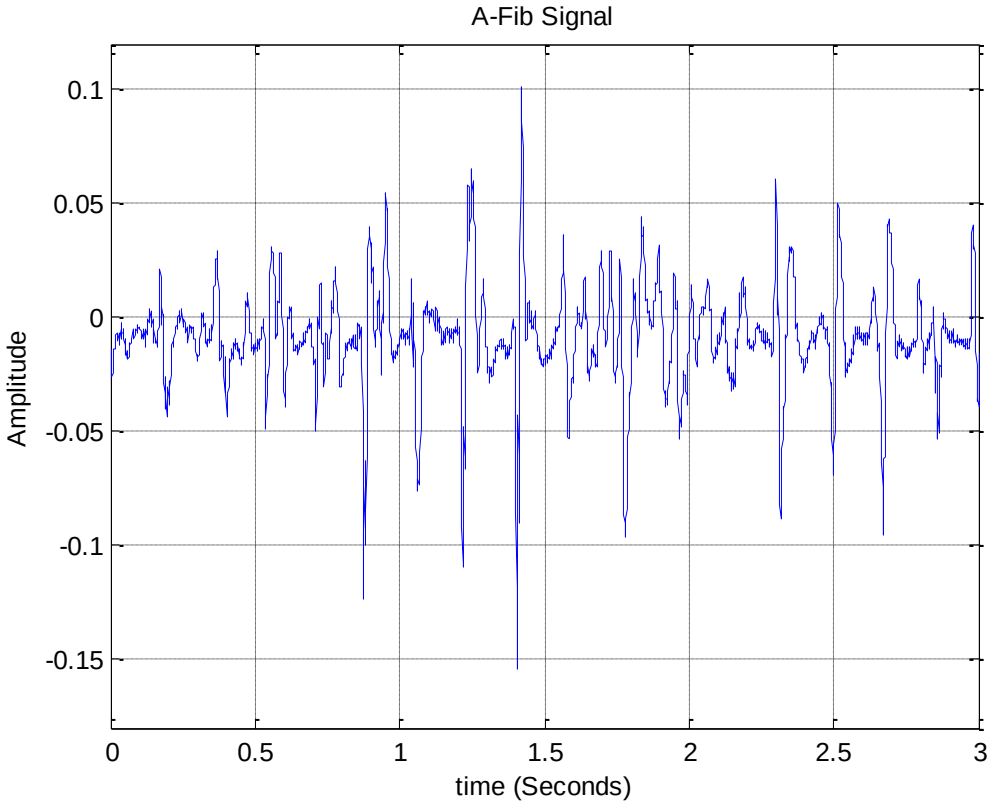

Figure 2.12 Atrial Fibrillation Signal

Figures 2.10 and 2.11 show the AF signal observed by ECG and the AF signal measured by the catheters placed in the LA of the heart, respectively.

2.4.3 Atrial Flutter Signal Characteristics

Atrial Flutter is the abnormal heart beat, in this the atria are depolarizing at an extremely rapid rate. The P wave looks like a saw-tooth wave. These P waves are called flutter waves.

- Atrial rate during atrial flutter is 250-300 bpm and the ventricular rate is variable. The conduction of atrial and ventricular rate is not 1:1. It is generally 2:1 or 4:1and it can also vary.

- Atria have a regular rhythm where as ventricles can be in either regular or irregular rhythm.
- Normally P waves are absent and they are replaced with F-waves (saw tooth).
- The length of the PR interval is not measurable.
- All QRS complex will look-alike and their length will be less than 0.12 secs.

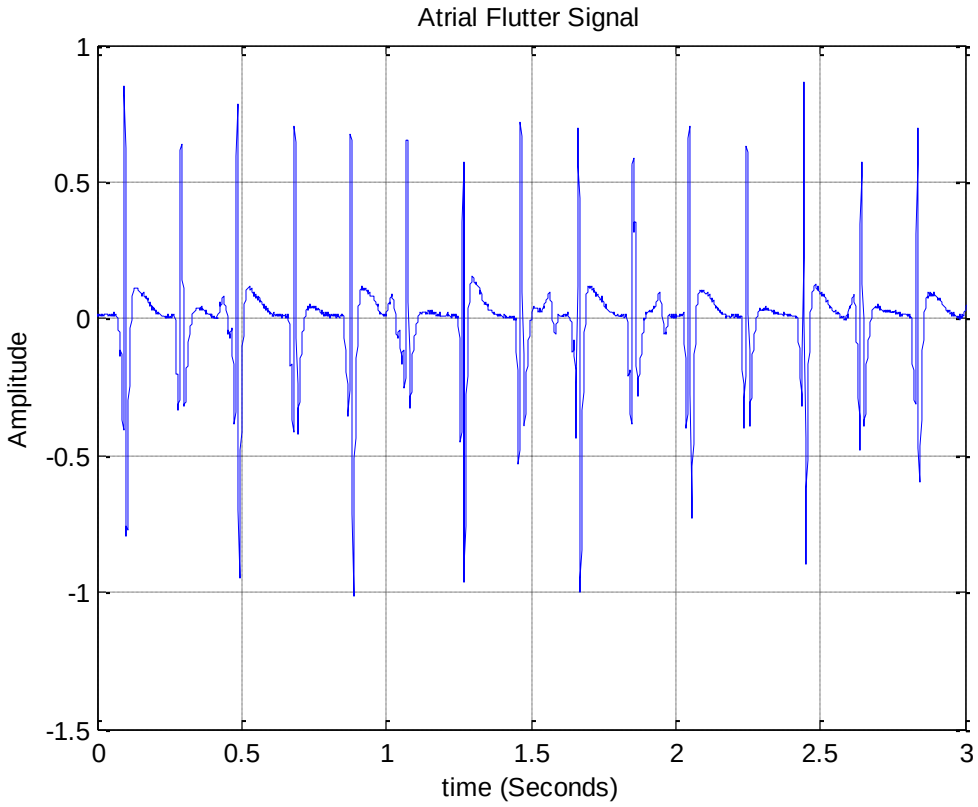

Figure 2.13 Atrial Flutter Signal

Atrial Flutter signal measured by the catheters placed in the LA of the heart is shown in Figure 2.12.

2.4.4 Atrial Tachycardia Signal Characteristics

In Atrial Tachycardia,

- Atrial rate is 150-250 bpm and the ventricular rate is same as that of the atrial rate.
- Atria have an irregularly regular rhythm.
- Normally P waves are absent and they are replaced with F-waves (saw tooth).
- The length of the PR interval is not discernable.
- All QRS complex will look-alike and their length will be less than 0.12 secs.

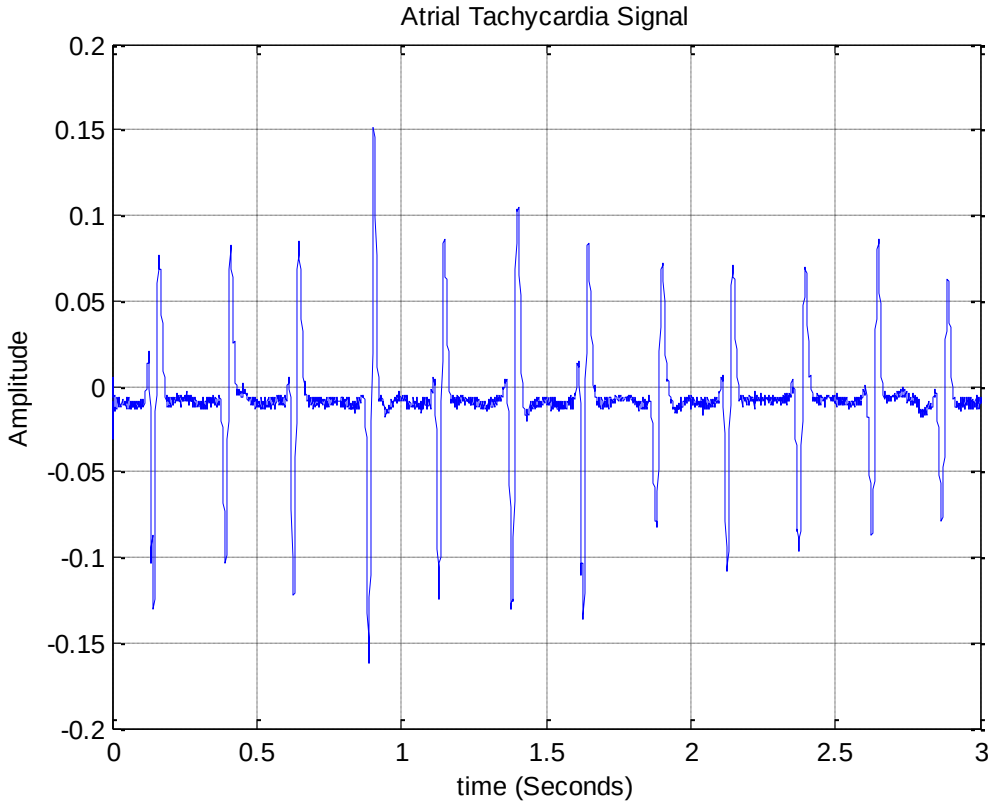

Figure 2.13 Atrial Tachycardia Signal

Atrial Tachycardia signal measured by the catheters placed in the LA of the heart is shown in Figure 2.13.

2.5 Current State of the Art

Initial research on AF started with development of signal processing techniques to distinguish AF and atrial flutter [10], identify AF among several other rhythms [11]. Atrial activation during AF had for a long time been described as random, with no particular pattern. Hence, time domain analysis of AF signals was found to be difficult. So, researchers employed frequency domain analysis to characterize the AF signal [12]. In most studies, spectral analysis techniques were applied to standard 12 lead ECG recordings to obtain atrial fibrillatory rate [13]. Waktare et al suggested to analyze lead V1 when standard ECG was used. This is because, the accuracy of frequency analysis techniques is strongly based on the availability of largest possible atrial activity in ECG signal [14]. As the atrial and ventricular activities occur in a very synchronized way, they overlap spectrally. Hence, general filtering techniques cannot extract the atrial or fibrillatory signal from the surface ECG. Instead, atrial activity extraction was performed using various methods, including source separation methods [15], average beat subtraction methods [16] and spatiotemporal QRST cancellation [17].

Researchers employing spectral analysis techniques demonstrated that certain regions of the atria can have higher activation frequencies than other regions. This suggests that these areas may be the drivers that maintain AF. They could be sources of AF and hence can be target sites for AF ablation [18]. In a study by Konings *et al.* [19], the right atrium was investigated. Three types (I, II, III) of right atrial activation during AF were identified. When the analysis was made on these types, the frequency and irregularity of AF increased from type I to type III. Also the incidence of continuous electrical activity and reentry became higher from type I to type III, [20]. Many other signal processing

techniques such as *Time-frequency analysis* [21], and *Hilbert Huang Transform* [22], were employed by which the second-to-second variations in fundamental frequency and waveform morphology of AF can be studied.

Most of the past AF signal processing researchers use ECG for diagnosis of AF. Also, algorithms for extraction of atrial activity and spectral analysis were applied to ECG to find the fibrillation rate. Hence, the current state of research is limited to establishment of AF presence or absence. This thesis aims at identifying the source of atrial fibrillation through intra-cardiac signals rather than ECG. Compared to ECG, intracardiac signals collected by the insertion of catheters into the heart provides better signal efficacy at the expense of being more invasive. Intra-cardiac signals are more likely to detect silent AF episodes as they are close to atrial tissues. These signals can detect PQ and ST segments better that ECG signal. They also avoid the risk of false positive and negative readings. Hence in this research, better and more accurate AF data compared to ECG was used to analyze the AF signals.

CHAPTER 3

SIGNAL PROCESSING METHODS

3.1 Introduction

In the past, signal processing techniques were used for ECG analysis to remove noise, compress data, and to extract basic features to detect diseases in the heart. Frequency analysis was employed to get the periodicity of ECG. Dominant frequency (Chapter 4) was used for mapping of AF signals, suggesting a rich diversity of frequency components in data. Signal processing plays a very important role for AF source identification. In this chapter, FFT, PCA and LDA methods will be presented. The main focus is on feature extraction, selection and classification methods.

3.2 Frequency Analysis

The intracardiac signals during AF represent multiple fronts of activation occurring at the point of recording during a highly disorganized rhythm. The recorded signal is, therefore, highly variable in voltage, morphology, and rate and this prevents the identification of its different components. Because of these features, methods estimating the frequency content of the signals have been the mainstay of signal analysis in AF.

Basically, the frequency domain offers a way to visualize and describe the complex AF signals about their rate and rate of activation without the measure in the time domain analysis. Dominant frequency analysis is commonly used to find areas of rapid activations, estimation of atrial activation rates [23]. Fast Fourier Transform (FFT) is

frequent method used for finding the dominant frequency which is the sinusoidal waveform with the highest amplitude. Left to right atrium gradient of frequencies and the observation of dominant frequencies in the LA suggest a preferential origin of AF in the LA.

The Fourier transform maps a time series signal into series of frequencies. Discrete Fourier Transform (DFT) converts the discrete time domain signal into a discrete frequency domain representation while Discrete Time Fourier Transform (DTFT) is continuous in frequency domain. DTFT is defined as [24]

$$H\left(e^{j\omega}\right)=\sum_{n=-\infty}^{\infty}h(n)e^{-j\omega n} \tag{3.1}$$

For a fixed-length time series with N samples this becomes:

$$H\left(e^{j\omega}\right)=\sum_{n=0}^{N-1}h(n)e^{-j\omega n} \tag{3.2}$$

From the expression for the DTFT shown in equation (3.2), it is clear that calculating each term for a real time series requires N multiplications of a real number and a complex exponential or $2N$ multiplications. Now all, N terms require $2N^2$ operations which is reduced to N^2 when we remember the symmetry properties of the Fourier transform. The FFT is an optimized algorithm for computing DFT. The DFT is defined as [25] :

$$H(k) = \sum_{n=0}^{N-1} h(n)\, e^{-j2\pi nk/N} \; for \; 0 \leq k \leq N-1 \tag{3.3}$$

The equation (3.3) is the same transform as defined in equation (3.1), but evaluated at N equally-spaced points from $\omega = 0$ to $(N-1)2\pi/N$. The frequency units are normalized with 2π being the angular sample rate. When N is a power of 2, symmetries in the

transform can be exploited to reduce the computational complexity. FFT can be computed in only $N \log_2 N$ operations when the number of samples is a power of 2 (i.e., $N = 2^M$ where M is an integer).

3.3 Filtering and Rectification

In Digital Signal Processing (DSP), the main purpose of the digital filter is to remove the noise and obtain the necessary signal by separating the unwanted components. Lowpass, highpass, bandpass and bandstop are commonly used finite impulse response (FIR) filters. They are classified based on frequency band specifications. In this thesis, bandpass FIR and lowpass FIR filters were used. Low pass FIR filters remove the higher frequency and allows only the low frequency components. Band pass FIR filter allows only certain band of frequencies by attenuating the remaining frequency components. Rectification is to change each waveform into a single positive peak. This is done by a squaring operation. The squarer always produces peaks and volleys. The signal after rectification will generally have low frequency components. Hence rectifier is generally followed by a low pass filter.

3.4 Principal Component Analysis

PCA is considered as a covariance regularization technique. Moghaddam and Pentland were the first to point out that PCA can be used to compute a Gaussian or regularize one if reducing the dimensionality of the data by throwing away some of the principal components [26]. In computer vision applications, it is rare that one can compute enough principal components to prevent dimensionality reduction. There can only be at most N−1 non-zero eigen values for a data set [27].

Principal Components Analysis (PCA) is a statistical, multivariate procedure used to

reduce the size of the data set while retaining most of the information. PCA rotates the data such that the data is projected onto the axes with maximum variances. PCA finds a projection of the actual data set onto orthogonal axes contained in the space. By employing PCA to set of correlated variables, they are transformed into a set of uncorrelated variables. The criteria being that the first axis "contains" the combination of uncorrelated variables with maximum amount of variance. The second principal component containing maximum amount of variation is obtained on the second orthogonal axis. The second principal component is independent of the first principal component. Similarly, the next highest variance component is obtained on third orthogonal axis. This component is orthogonal and independent to the both the higher principal components. The data with minimum variance can be removed with very minimal loss of information or actual data.

The first principal component is the combination of variables that has the highest variance. The second principal component has the next largest variance and so-on. The second component is independent to the first principal component.

The basic algorithm for applying PCA is as follows:

- Step 1. Data acquisition
- Step 2. Subtract the mean from the original data. This gives us a data with mean zero.
- Step 3. Calculate the co-variance of the obtained matrix
- Step 4. Calculate the eigenvalues and eigenvectors of the covariance matrix.
- Step 5. Choose the principal components and obtain the feature vector. The new data set can be obtained from this vector.

The basic assumption for applying PCA to the signal x is a zero-mean random process. The signal x is characterized by the correlation$R_x = E[xx^T]$. The principal components of x is obtained by applying PCA which is an orthonormal linear transformation $\Psi = [\Psi_1\ \Psi_{2\ldots\ldots}\ \Psi_N]$ to x, [27]

$$w = \Psi^T x \tag{3.4}$$

Hence, the principal component vector elements which become mutually uncorrelated are w= $[w_1\ w_{2\ldots\ldots}\ w_N]^T$. The first principal component w_1 is $w_1 = \Psi_1^2 x$, where the vector Ψ_1 is chosen which satisfies the condition [27]

$$E[w_1^2] = E[\Psi_1^T x x^T \Psi_1] = \Psi_1^T R_x \Psi_1 \tag{3.5}$$

is maximized, when $\Psi_T \Psi_1 = 1$. The maximum variance is obtained when Ψ_1 is normalized eigenvector corresponding to the largest eigenvalue of R_x, as denoted λ_1. Resulting variance is [27]

$$E[w_1^2] = \Psi_1^T R_x \Psi_1 = \lambda_1 \Psi_T \Psi_1 = \lambda_1 \tag{3.6}$$

where w_1 and the second principal component w_2 should be uncorrelated, w_2 is obtained by choosing Ψ_2 as the eigenvector corresponding to the second largest eigenvalue of R_x , and so on until the variance of x is completely represented by w. Accordingly, to obtain the whole set of N different principal components, the eigenvector equation for R_x needs to be solved. [27]

$$R_x \Psi = \Psi \Lambda\,, \tag{3.7}$$

where Λ denotes a diagonal matrix with the eigenvalues $\lambda_1 \ldots\ldots\ldots \lambda_N$. Since R_x is rarely known in practice, the N × N sample correlation matrix, defined by [27]

$$R_x = \frac{1}{M} X X^T \tag{3.8}$$

replaces R_x when the eigenvectors are calculated in (3.8). The eigenvalue associated to the first principal component is much larger than those associated with other components.

3.5 Linear Discriminant Analysis

Linear Discriminant Analysis (LDA) is a well-known classification method. LDA finds a linear transformation of the classes given and maximizes the class variation. It can also be used for dimensionality reduction that project high-dimensional data onto a low dimensional space where the data achieves maximum class separability [Duda *et al.* 2000; Fukunaga 1990; Hastie *et al*. 2001]. The derived features in LDA are linear combinations of the original features, where the coefficients are from the transformation matrix. The purpose of LDA in our thesis is to classify AF signals from four pulmonary veins based on a set of features that describe the signals from four pulmonary veins. PCA can be used to extract features and LDA finds the subspace that best discriminates the given 4 groups.

In LDA, the dependent variable is the group (1, 2, 3, 4) and the independent variables (X) are the object features (Explained in Chapter 4). The assumption for using LDA is, the groups are linearly separable. The groups are said to be linearly separable if the groups can be distinguished by a linear combination of features that describe the objects. The classifier is a plane, if there are three features. In this thesis, five features describe the groups, so the separator is a hyper plane.

If there are many groups, Bayesian rule is to used minimize the total error in classification. This is done by assigning the object to one of the groups which has the highest conditional probability. This means $P\left(\frac{i}{x}\right) > P\left(\frac{j}{x}\right)$ where i and j are two different

groups. But, it is very difficult to find $P\left(\frac{i}{x}\right)$. $P\left(\frac{i}{x}\right)$ is defined as probability of "i- class" given the measurement. But we can find the probability of each feature when the probability is given which is $P\left(\frac{x}{i}\right)$. Further we can use Bayes theorem to find $P\left(\frac{i}{x}\right)$.

$$\text{Bayes equation: } P\left(\frac{i}{x}\right) = \left(P\left(\frac{x}{i}\right) * P(i)\right) / \sum_{ij} \left(P\left(\frac{x}{j}\right) * P(j)\right) \tag{3.10}$$

Hence for the condition $P\left(\frac{i}{x}\right)$. $P\left(\frac{i}{x}\right)$ to be true,

$$\left(P\left(\frac{x}{i}\right) * P(i) > \left(P\left(\frac{x}{j}\right) * P(j)\right)\right. \tag{3.11}$$

In real time, it is very usual that data will have many classes and dimensions of measurement. Hence, the computation of conditional probability $P\left(\frac{x}{i}\right)$ requires a lot of data. So in practicality, we assume that the data come from Multivariate Normal distribution.

Simplifying it further, we get the LDA equation as

$$f_i = \mu_i C^{-1} x_k^T - \frac{1}{2} \mu_i C^{-1} \mu_i^T + \ln\left(P(i)\right). \tag{3.12}$$

Equation 3.12 gives a function to assign an object k to group i that has maximum value of f_i.

The optimal projection or transformation in classical LDA is obtained by maximizing the ratio of the between-class variance to the within class variance as described in equation (3.13).

$$J(w) = \frac{w_t S_b w}{w_t S_w w}, \tag{3.13}$$

where w is the transformation matrix, S_b and S_w are the between-class variance and within-class variance, respectively and t represents the transpose operation.

CHAPTER 4

AF SOURCE IDENTIFICATION

4.1 Introduction

In this thesis, statistical recognition methods were used for description and classification of AF signal obtained from four pulmonary veins. The basic block diagram for identification of source of AF is shown in Figure 4.1.

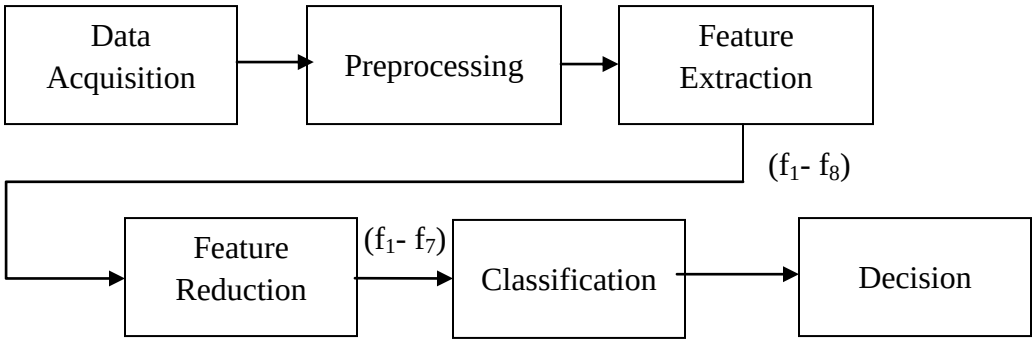

Figure 4.1 Block Diagram for Identification of Single Source of AF.

4.2 Data Acquisition Protocol

Data was collected from patients referred to the Cardiology Arrhythmia Service or Cardio Lab at James Haley Veteran Affairs for RFA of AF. During standard RFA procedure, a number of recording catheters are positioned inside the patient's heart. as shown in Figure 4.2. A catheter shown in Figure 4.3 is defined as small plastic tube that can be inserted into the body cavity, duct or vessels.

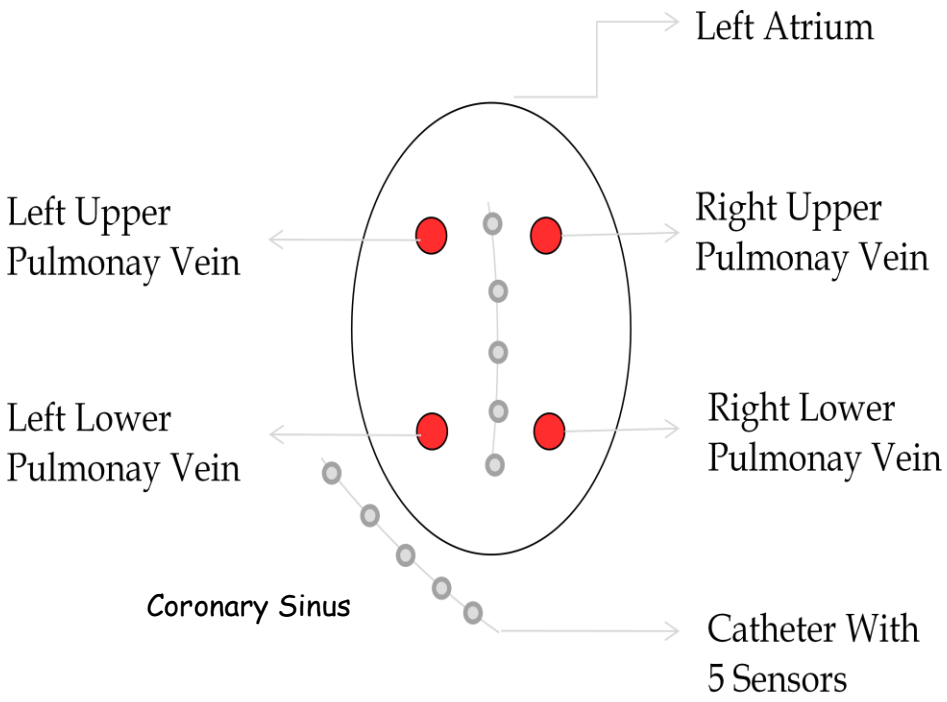

Figure 4.2 Catheter Placement for Data Acquisition

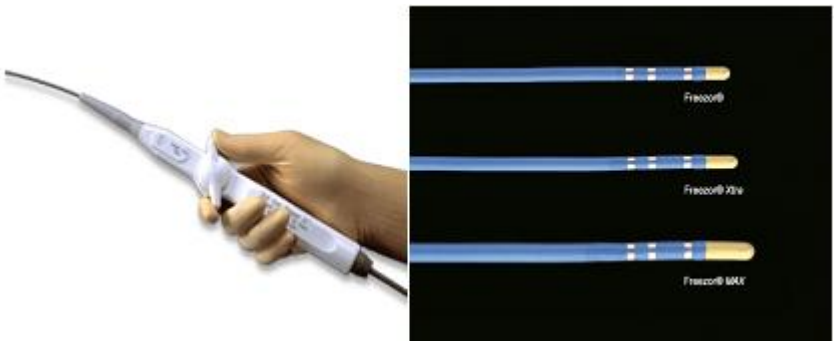

Figure 4.3 Catheters

The catheter in the coronary sinus (a vein in the back of the heart running along the inferior border of the LA) will be selected for study data recording because of its stability. The catheter inserted into the coronary sinus is stable as there will not be any movement in this catheter during the heartbeat. By considering the LA into four segments, the focal activation of AF triggers was stimulated electrically by artificially pacing the method at each of these segments. The coronary sinus recordings during

pacing from these different sites will be analyzed using an algorithm with the purpose of identifying the direction of provenance of the activation and therefore the site of pacing. The AF signals acquired before the ablation procedure were bandpass filtered with 30-400 Hz and sampled at a frequency rate of 977 Hz by Cardio Lab in VA hospital. The data was recorded continuously from catheter. This data collected was stored in digital format and analyzed off-line. In this thesis, AF data was recorded from 18 patients. In all patients, the AF was stimulated at each pulmonary vein and data was measured by catheters.

The inracardiac data measured by the catheters is shown in Figure 4.4

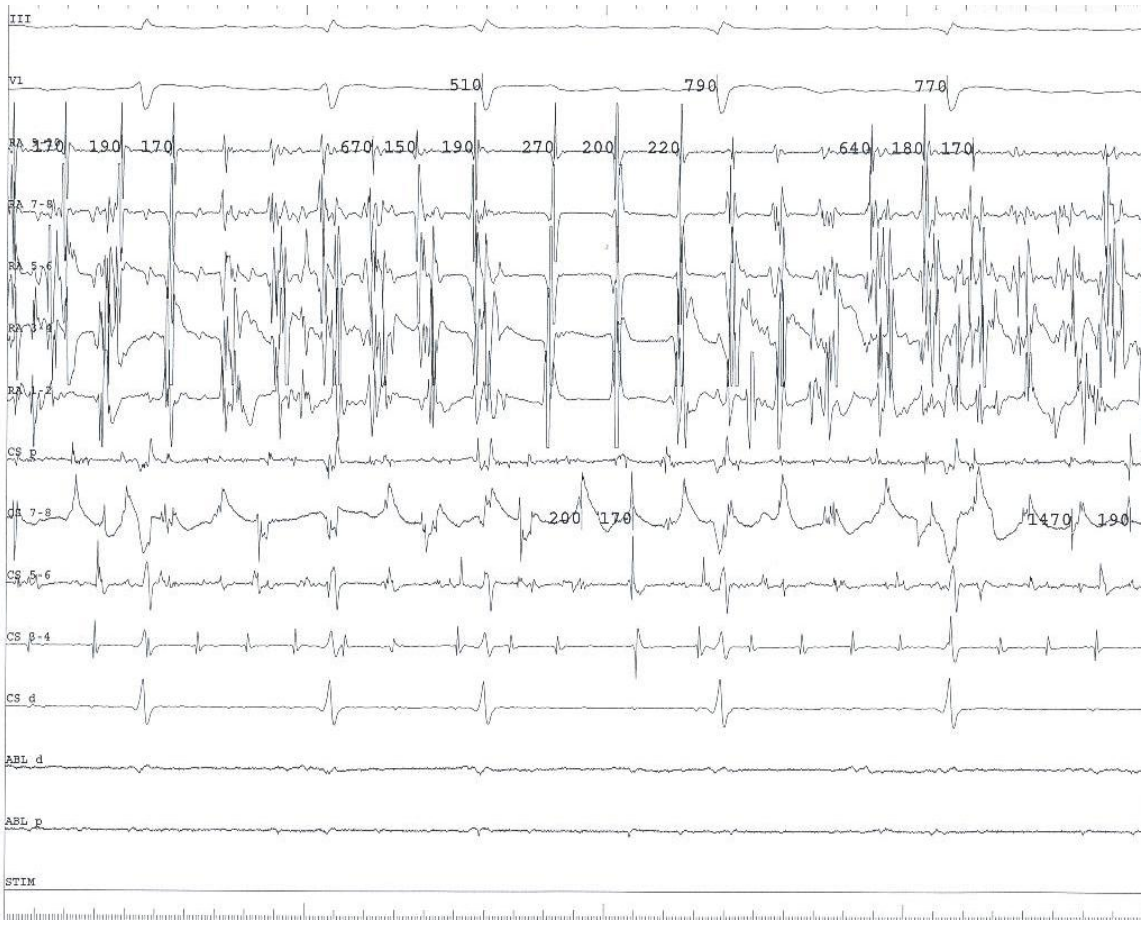

Figure 4.4 ECG and Intra-cardiac Data

Figure 4.4 contains signals from lead III and V1 which are same as in ECG. Further, it contains RA and CS which are data measured by the catheters when placed in right atrium and left atrium, respectively. ABL gives us measured signal from the ablation catheter. Ablation catheter is used to measure the signals as well as to burn the tissues during RFA. The intracardiac signals measured by catheters contain much more atrial activity compared to that of the ECG. Hence AF can be analyzed in a better way with intracardiac signals compared to ECG signal.

4.3 Preprocessing

The following are the preprocessing steps performed in this research. Consider the following notations. Let x be a pattern vector of dimension *N*, x = [x_1, x_2, ...x_n]. The set of original features is the component x_i of x. Sets of features can be compared only when all have the same scales. Hence during preprocessing, the AF signals were normalized. The following scaling of the data is generally used in such cases:

$$x_i' = (x_i - \mu_i)/\sigma_i ,$$

where μ_i is the mean and σ_i is the standard deviation of x_i .

4.4 Feature Extraction

Feature extraction is a way of finding the most informative set of features of the signal. Finding the important feature vectors is the most common way of data representation for classification problems. Each feature is an attribute obtained from a quantitative or qualitative measurement [28]. Then each frame of data is represented by these set of features.

Feature extraction is a way of simplifying the amount of data required to describe a large set of data accurately. The process is to extract features that characterize the signal

and they can be temporal-domain features, spectral domain features and/or parametric features [29].

The features that were extracted in this thesis are shown in Table 4.1

Table 4.1 Features Extracted

f_1	Dominant frequency at each pulmonary vein.
f_2	Frequency at which highest amplitude is obtained in Histogram.
f_3	Frequency at which second highest amplitude is obtained in Histogram.
f_4	Frequency at which the amplitude is 20% of the highest amplitude.
f_5 - f_8	Normalized power.

4.4.1 Dominant Frequency

Generally, frequency domain analysis offers an alternative way to visualize AF signals. Through frequency analysis, we can estimate the activation rate and regularity without measuring the time domain intervals. The Fourier transform is one of the frequently used transforms for frequency analysis. FFT is a fast algorithm to compute DFT. As described in Chapter 3, all continuous signals are decomposed into sum of weighted sinusoidal functions using FFT and thereby converting any discrete time signal to frequency spectrum. FFT provides a spectrum with a range between 0 Hz and half the sampling rate. The most common application of frequency domain analysis is finding the dominant frequency. Dominant frequency analysis is a powerful tool for estimation of atrial rate in AF. It is also used to detect rapid activations areas and changes in the rate [30]. The dominant frequency is defined as the frequency of the sinusoidal waveform with the highest amplitude. Currently, researchers of AF believe that dominant frequency of AF

signal will be in the range of 4 to 9 Hz [31]. Dominant Frequency is calculated by using the following method whose block diagram is shown in Figure 4.5 [32].

- Band pass filtering at 40-250 Hz. Each signal (intra cardiac signals) was filtered with a tenth order zero phase Butterworth filter.
- Rectification
- FFT
- Low Pass Filtering at 20 Hz

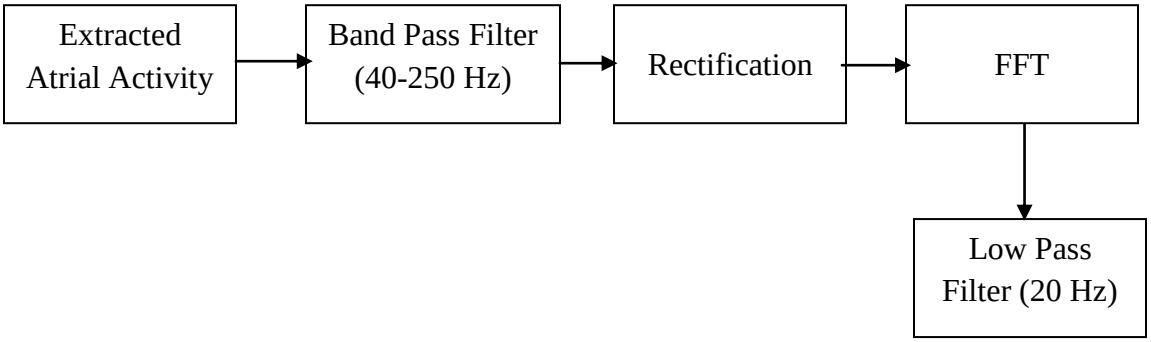

Figure 4.5 Block Diagram to find Dominant Frequency.

Band pass filtering is done to emphasize the signal corresponding to the local depolarization. FFT was used to obtain the power spectrum of the intracardiac signal at each recording site. Rectification is the critical step that will transform the biphasic waveform to a monophasic waveform. Low pass filtered at 20 Hz since the range of AF is around 4 to 9 Hz. The AF signal and spectrum with and without rectification are shown in Figures 4.6 and 4.7, respectively.

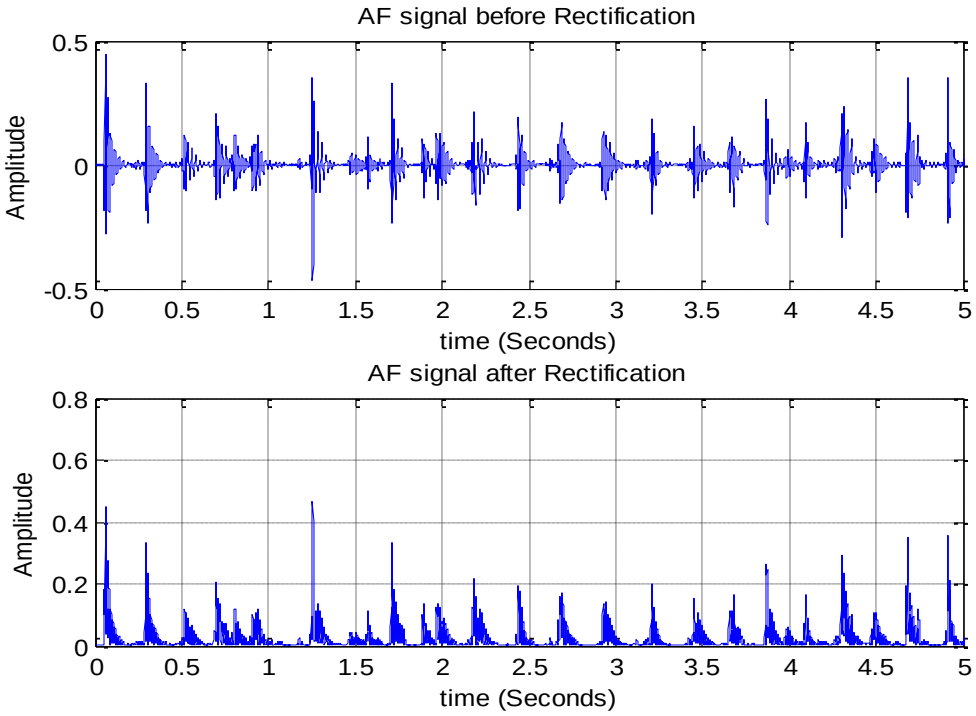

Figure 4.6 AF Signal before and after Rectification

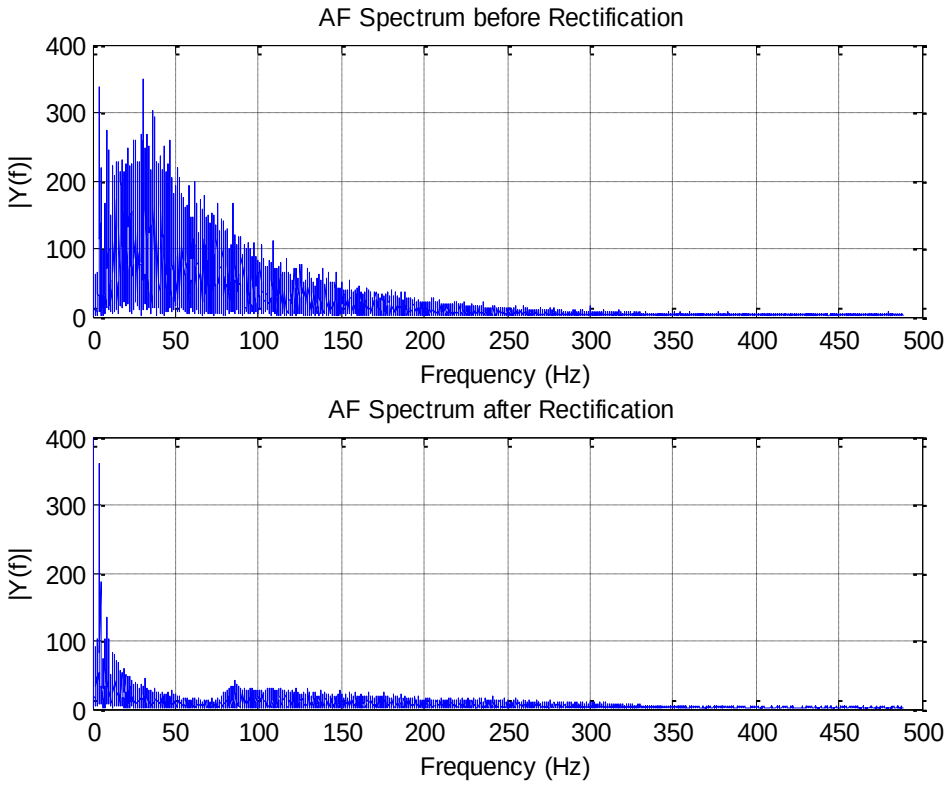

Figure 4.7 AF Signal Spectrum before and after Rectification

The gradient of frequencies from LA to RA confirmed that the origin is generally from LA. In clinical practice, AF is generally believed to have an origin from either one of the four pulmonary veins. The dominant frequency of AF signal and NSR signal is shown in Figures 4.7 and 4.9, respectively. The dominant frequency (f_1) of right superior, right inferior, left superior, left inferior pulmonary veins were found to be 5.307, 4.293, 6.053, and 4.92 Hz respectively (Figure 4.10).

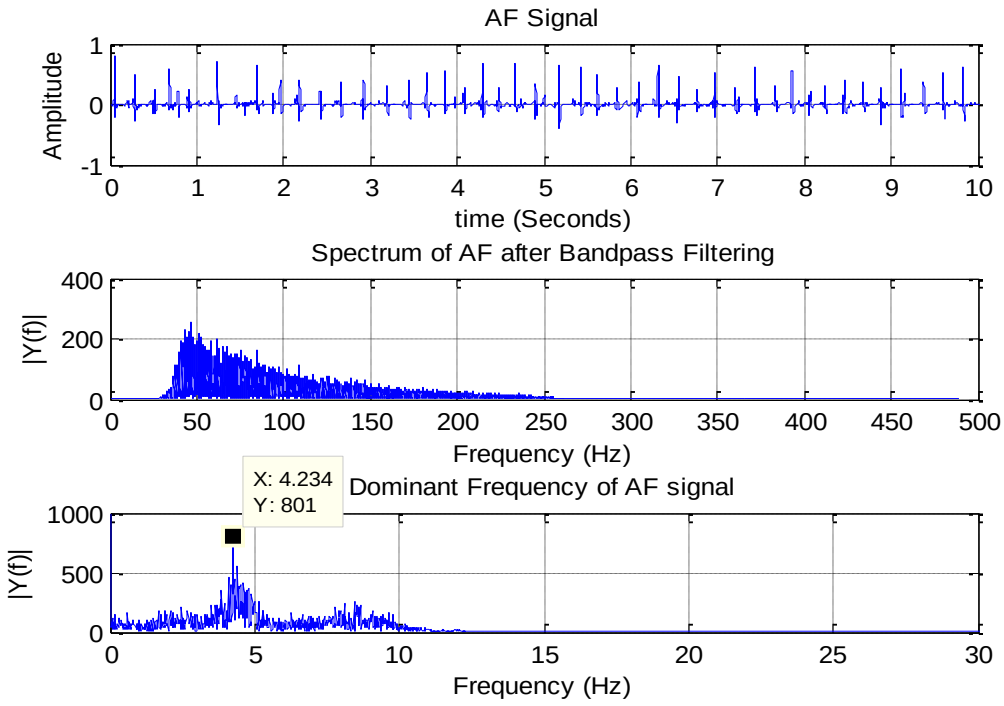

Figure 4.8 Dominant Frequency of AF

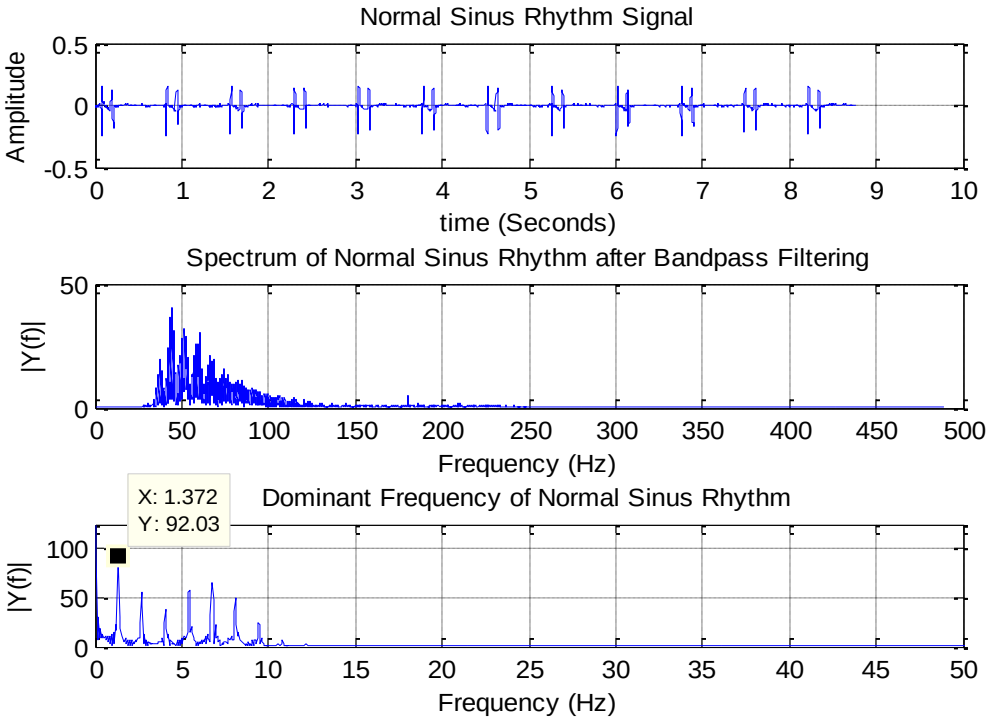

Figure 4.9 Dominant Frequency of Normal Sinus Rhythm

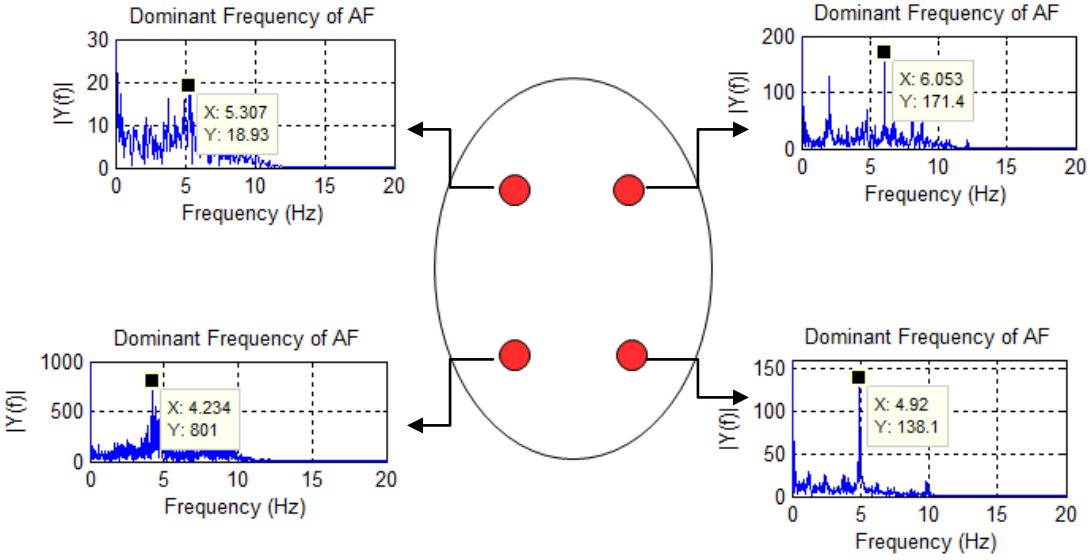

Figure 4.10 Dominant Frequency at Each Pulmonary Vein

4.4.2 Frequency Distribution

A histogram is a graphical representation of data analysis for summarizing the distributional information of a variable. It gives us the frequency distribution which is represented by rectangles or bins whose widths represent class intervals of frequencies. The areas of these rectangles are proportional to the corresponding frequencies. The number of occurrences of the variable is calculated for each bin. In this work, the histogram of band pass filtered AF signal was constructed with 100 bins. In AF, the atrial activity and ventricular activity is found to be in the ratio of 4:1. Hence this atrial activity can be found with the bins of highest amplitude on the histogram.

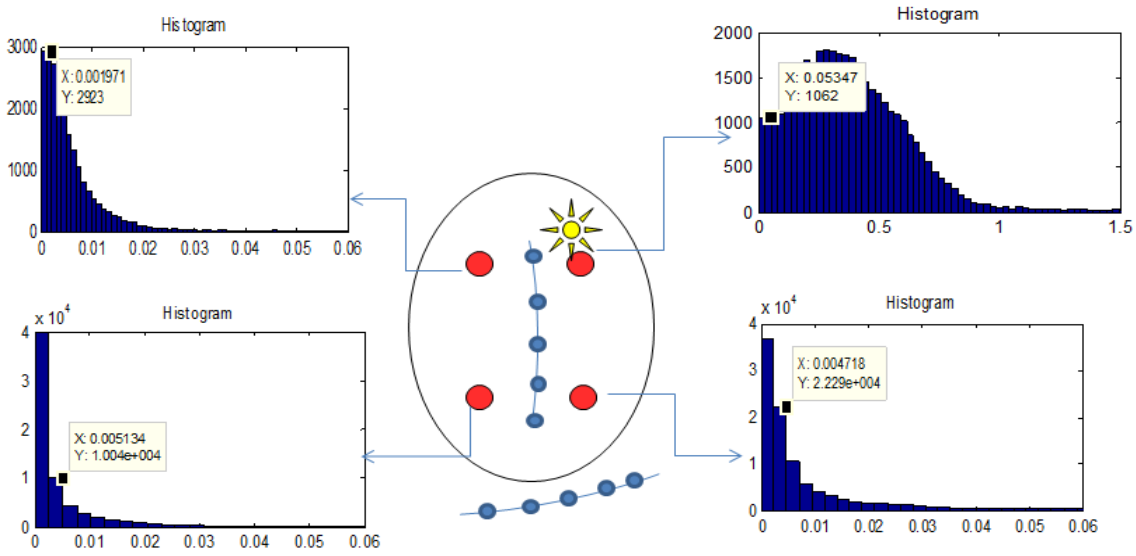

Figure 4.11 Histogram of AF Signal at each Pulmonary Vein

From the histogram of the filtered signal, three features were selected for the classifying the signal originating four pulmonary veins. They are as follows:

- Frequency at which highest amplitude is obtained in the histogram.
- Frequency at which second highest amplitude is obtained in the histogram
- Frequency at which the amplitude is 20% of the highest amplitude.

The histograms when AF is stimulated at right superior, right inferior, left superior, left inferior pulmonary veins are shown in Figure 4.11.

4.4.3 Normalized Power

This section explains how the normalized power is used to classify the AF signals obtained from the four pulmonary veins. A signal is stimulated from one of the pulmonary vein and data is collected at coronary sinus (CS) through CS catheter as explained in the data acquisition protocol. The feature for classifying AF signals is extracted by calculating the power loss as the signal travels from origin (stimulated pulmonary vein) to the destination or final point (CS catheter). The destination point is varied by moving the catheter to other pulmonary veins other than the stimulated pulmonary vein. Initially, power of the stimulated signal along with power of the signal captured at CS catheter was calculated. Further, the power loss of the signal as it travelled from stimulated pulmonary vein to CS catheter can be found by subtracting the power of signal at CS from the power at the stimulated pulmonary vein. Then, the destination catheter is moved to other pulmonary veins to collect the signal at each pulmonary vein (other than the stimulated pulmonary vein). Hence, we can calculate the power at each pulmonary vein, and also the power loss of the signal. Further, each power loss obtained is normalized by dividing with the total power loss of the signal. This gives a set of four features f_5 to f_8.

Example: Assume the signal is stimulated at Right Superior Pulmonary Vein (PV1). The power of the signal is calculated by measuring the average power under the power spectral density curve and assigned as P_1. This signal travels through LA and is captured at CS catheter. Let the power of the component measured at CS catheter be P_{c1}. Power

loss as the signal travelled from PV1 to CS catheter is calculated. This can be found by subtracting P_{c1} from P_1. Let the power loss be P_{L1}. The power of the signal captured at other pulmonary veins as the signal travels from stimulated vein was also calculated ($P_{2,}$ $P_{3,}$ P_4). Further, the power loss from these pulmonary veins to CS catheter was calculated ($P_{L2,}$ $P_{L3,}$ P_{L4}). In real time, every person will not have same heart beat or stimulating energy. So the power loss is normalized by P_{L1}/(P_{L1+} P_{L2+} P_{L3+} P_{L4}). The power loss as the AF signals which are stimulated from P1, P2, P3, and P4 to CS catheter were found to be 3.2, 4.3, 1.6, and 1 respectively. This feature was found to be different for all pulmonary veins and same almost for all patients with little variation.

4.5 Feature Reduction and Classification

Assume an object is an AF signal obtained from one of the pulmonary vein. In this research, LDA is used to classify objects into one of four groups based on a set of features that describe the objects. Before classifying the objects, it is important to determine a set of features that can best determine a group. It is also equally important to find which classification rule or model is best to separate the given groups. These give rise to methods called feature selection and classification. Classification of objects can be done in two methods: *parametric* and *non-parametric* methods.

Parametric methods rely on a probabilistic model of the process of generating the observations in which probability distributions are described in parametric form. Learning is, in this case, the process of estimating the model parameters on the basis of the available observations.

There are two types of non-parametric methods. One of these methods determines the probabilistic model that has generated the data. These methods do not assume a

functional description of this model. Histogram based methods come under this category, whereas, some non parametric methods are based on heuristics. These methods try to minimize a criterion that is dependent on the task instead of directly estimating a model for the data generation. LDA and support vector machines (SVM) are examples of this category.

The total feature set [f_1, f_2 …. f_8] is used to classify the signal originated from the four pulmonary veins. Apart from these features, some other features like mean, standard deviation of R-R (R is a part of ECG signal) intervals, and number of zero crossing points were observed. These features were found to be same in the signals from all 4 pulmonary signals. Hence, these features were not applied to classification. Only features (f_1 to f_8) were applied to PCA. The first principal component contains nearly 52% of the variance. The first component and second component together achieved 74%. Further, as the principal components were added, the variance increased to 81%, 87%, 92%, 96%, 99% and 100%. Data compression can be made by discarding the last feature vector or last principal component. This can be achieved by losing only 1% of the variance. Hence considering the first seven principal components, LDA was applied to classify the AF signals obtained from 4 pulmonary veins. Amongst the AF data recorded from 18 patients, features extracted from 10 patients were used to train the LDA model. While classifying the other 8 patients, LDA was found to have less classification error compared to that of Quadratic Discriminant Analysis (QDA) as shown in Table 4.2. The algorithm was tested clinically on both stimulated and spontaneously generated AF and the source was correctly found. The classification errors for both right and left inferior veins were found to be high as the frequency distributions were similar.

Table 4.2 Classification Error Comparison

Pulmonary Vein	Right Inferior	Right Superior	Left Inferior	Left Superior
Classification Error of LDA	8.1%	5.4%	7.6%	4.1%
Classification Error of QDA	12.5%	9.1%	13.0%	6.2%

4.6 Transition of AF during RFA

In clinical practice, during RFA the AF signals changes to Atrial Tachycardia and atrial further to atrial flutter and finally it goes into normal sinus rhythm. This study was made to observe whether the flutter and tachycardia were induced later during the process or whether they were present from the beginning. The main findings of this were as follows: The spectral components were observed at all different stages of RFA. Some spectral components were found to be similar in all the three AF, AT and AFL. The spectrum of AF and atrial flutter along with their matched components of AF and atrial flutter are shown in the Figures 4.9 and 4.10, respectively. The dominant frequency was found to be decreasing during the process of RFA but the components of the dominant frequency were not completely removed. The amplitude or energy of the signal was found to be reduced by a larger extent. This is shown in Figures 4.12 and 4.13.

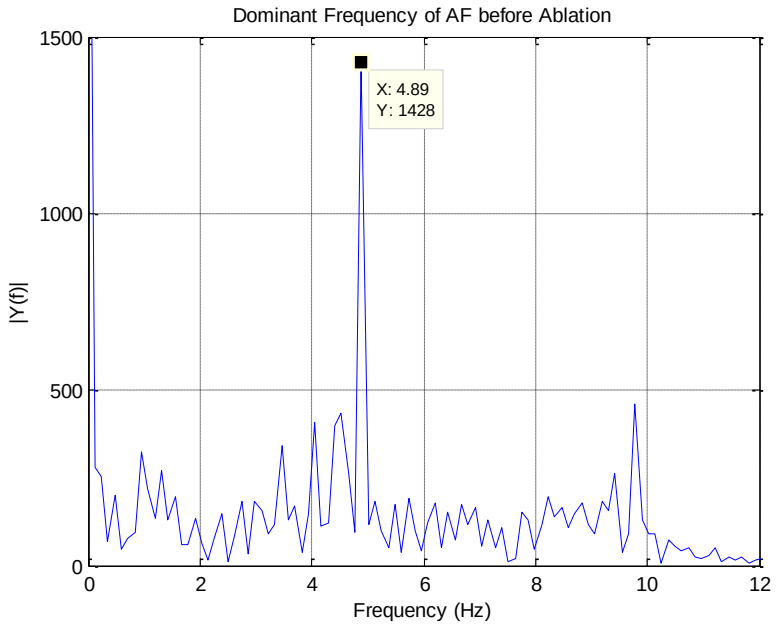

Figure 4.12 Dominant Frequency of AF before RFA

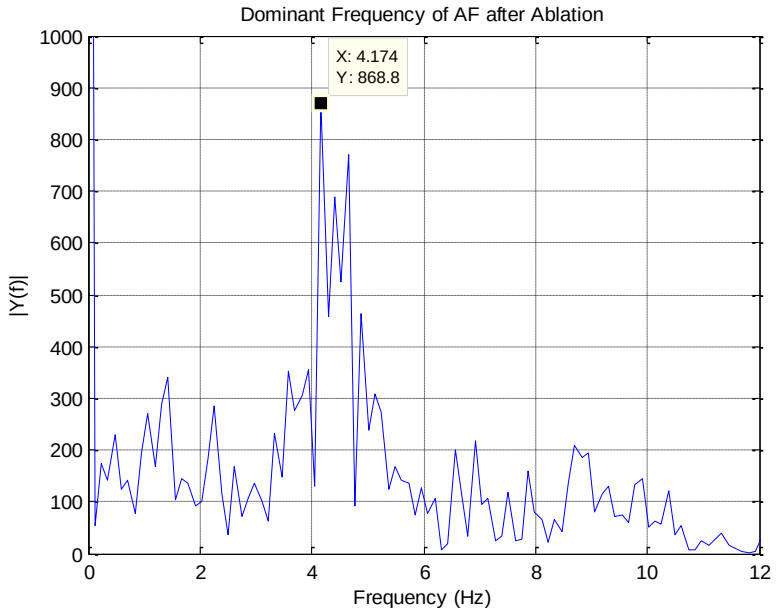

Figure 4.13 Dominant Frequency of AF after RFA

FFT assumes the signal to be stationary and linear. Hence to achieve a better temporal resolution, windowing should be applied. But, this will ultimately reduce the spectral

resolution. To overcome this method Hilbert Huang Transform (HHT) was used for AF signal analysis [33].

4.6.1 Methodology of HHT

HHT has two steps. The first step is to decompose the signal using Emperical Mode Decomposition (EMD). This gives us intrinsic mode functions (IMFs). Further HHT is applied to the obtained IMF's. This transform is particularly applicable for non-linear and non-stationary signals. Huang *et.al* [33] defined IMFs as a class of functions that satisfy two conditions:

- In the whole data set, the number of extrema and the number of zero-crossing must be either equal or differ at most by one.
- At any point, the mean value of the envelope defined by the local maxima and the envelope defined by the local minima is zero.

In the physical world, most signals are not IMFs. So, HHT cannot be applied to original data to get the higher resolution frequency content. Hence, the data should be decomposed into IMF components. EMD process is actually a sifting process, which operates as follows:

- Identify all the local extrema of the given atrial activity, then connect all the local maxima by a cubic spline line. Repeat the same procedure for local minima.
- The difference between the *x(t)* and mean of the above envelopes gives us the first IMF.
- The above two steps are repeated till the IMF's condition gets satisfied. The sifting is considered to be complete when either of the following two conditions is

satisfied: The mean squared error, between two consecutive IMFs, is smaller than a predefined stopping criteria or the residue becomes monotonic.

Consider the data x(t). The mean of the upper and lower envelope is $m1$. The first IMF is defined as $IMF_1 = x(t) - m1$. [33]

HHT is applied to IMf's. HHT is described by the following equation,

$$H[x(t)] = \frac{1}{\pi} \text{ PV } \int_{-\infty}^{\infty} \frac{x(\Gamma)}{t - \Gamma}, \tag{4.1}$$

where PV is principal value of singular integral. When HHT is applied to all IMFs generated, the analytical signal can be defined as

$$z_j(t) = imf_j(t) + HT\left(imf_j(t)\right) = a_j(t)\exp\left(i \int w_j(t)\right)dt. \tag{4.2}$$

After the HHT the original data can be expressed as real function shown in equation 4.3

$$H(w,t) = Re\left[\sum_j a_j \exp\left(i \int w_j(t)\, dt\right.\right] \tag{4.3}$$

The residue is left out as it is a monotonic function. The empirical decomposition of the AF signal is shown in the Figure 4.14. The first component represents the shortest time-scale or high frequency components whereas the last one represents the largest time scale or lower frequency components. Hence, the signal is decomposed in time domain giving us the components with decreasing order of frequency. In this process, the last component c6 (in Figure 4.14) with lesser frequency was found similar to that of the NSR into which the AF has been converted.

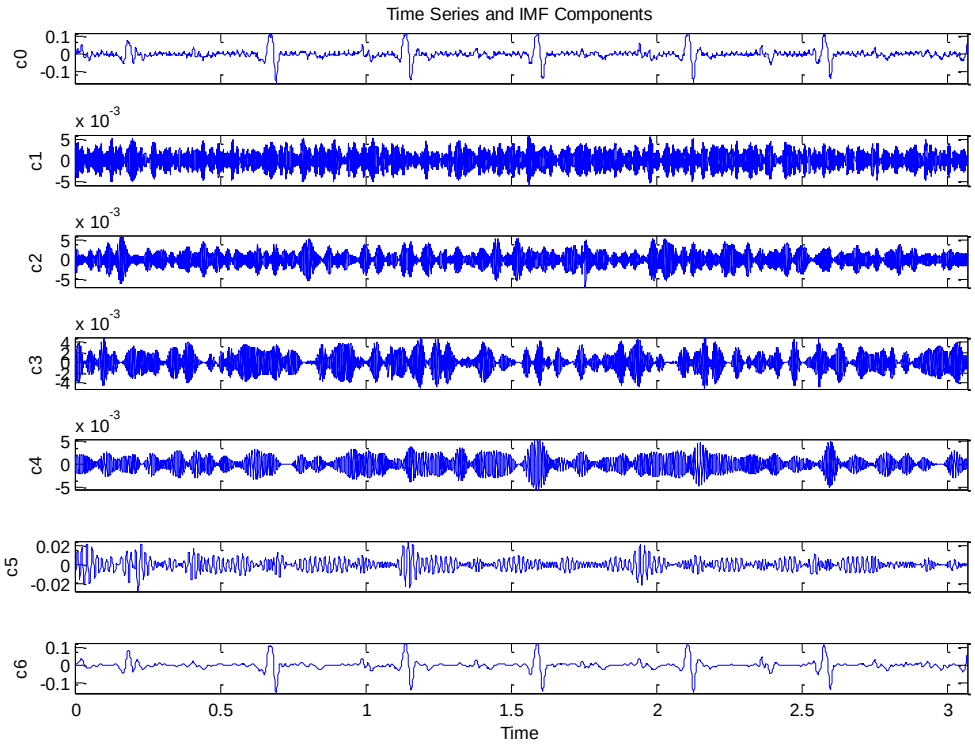

Figure 4.14 IMFs of AF Signal Obtained using EMD

When the signal converts from flutter to tachycardia, the tachycardia was also seen in atrial flutter. Hence, we hypothesize that atrial flutter and atrial tachycardia signals were present during the AF. Hence Emperical Mode Decomposition gives us an very important observation regarding the conversion of AF to atrial flutter and atrial tachycardia.

Figure 4.15 shows better resolution of signals compared to that of the FFT shown in the Figure 4.7. Figure 4.16 shows the analytical signal and its IMF component. When the HHT is applied to IMF's, the instantaneous frequency and amplitude, both the function of instant time, are calculated, and reflect the various features of atrial activity of patients with AF. HHT provides better time and frequency resolution. It also enables us to measure the relationship between peak of the spectrum peak and AF mechanism. Hence,

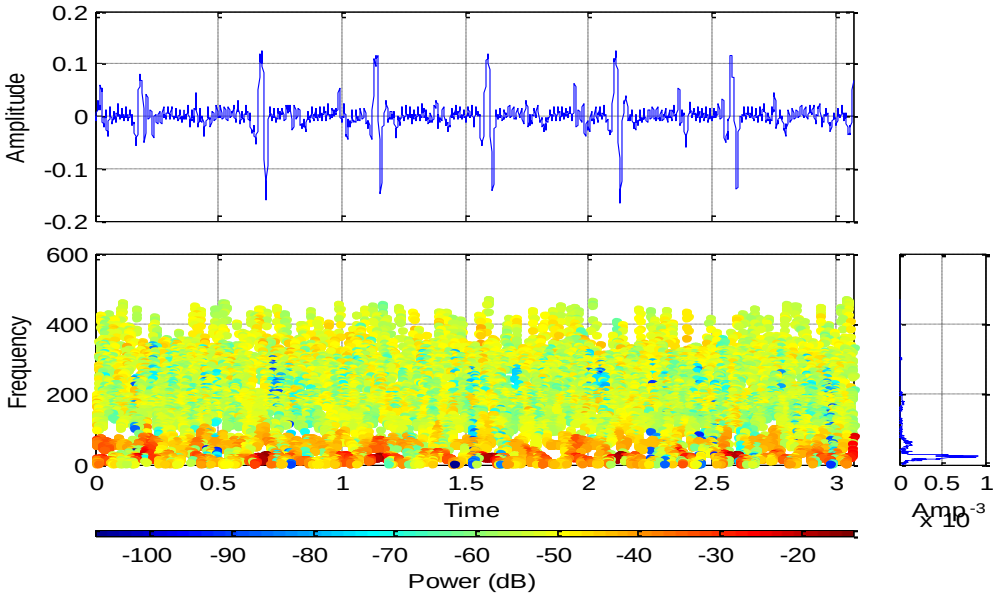

Figure 4.15 Time-Frequency-Energy of AF Signal using HHT

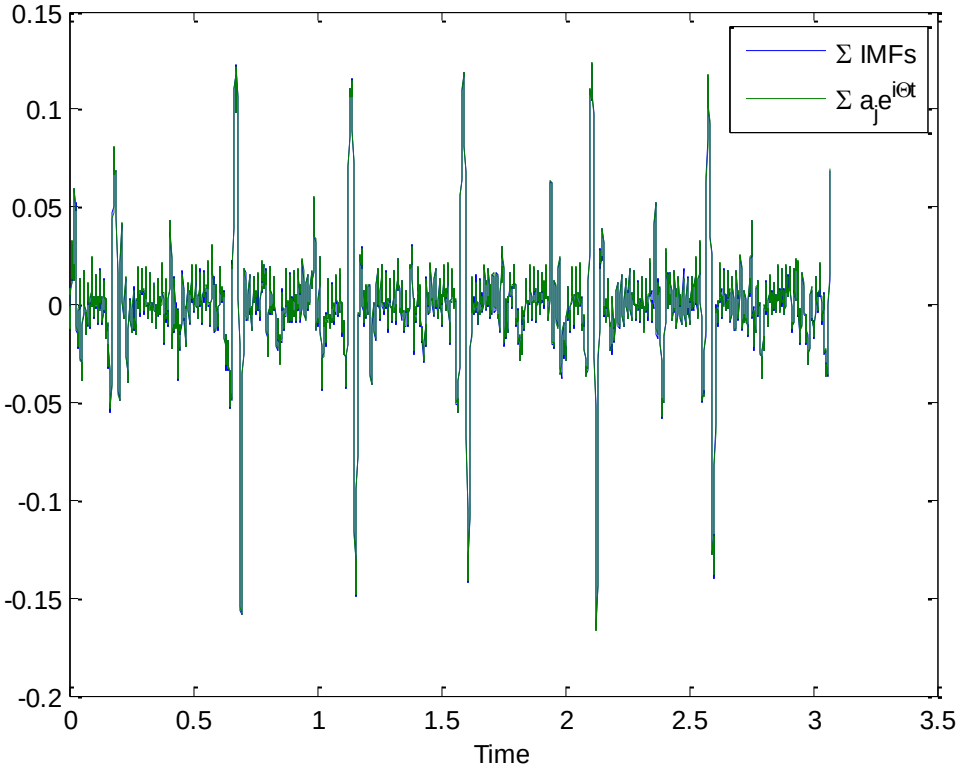

Figure 4.16 IMF and Analytical Signal

We hypothesize that we have developed a multistage algorithm that is able to deconstruct the endocardial recording of atrial fibrillation activity by identifying its components. The comparison of the FFT and HHT is shown in Table 4.3.

Table 4.3 Comparison of HHT and FFT

	FFT	HHT
Basis	*a priori*, theory based	Adaptive, Emperical
Results	Energy- Frequency	Energy-Time-Frequency
Non-Linear	No	Yes
Non Stationery	No	Yes
Number of Computations	$N \log N$	More than 9N
Time Taken for simulation	Very Less (milli seconds)	More (15 minutes)
Spectral Resolution	Acquires 0.01Hz.	Acquires 0.001Hz.
Time Domain Information	No	Yes

4.7 Data Analysis

4.7.1 Dominant Frequency and Ventricular Activity

In this section, the dominant frequency and its dependence on other factors will be explained. The intracardiac activity collected from the coronary sinus is located between the left atrium and left ventricle. Hence, the sensors on catheters collect both the atrial activity and ventricular activity. Dominant frequency is calculated to find the atrial activation rate. Hence to calculate the dominant frequency, ventricular activity must be removed. Figures 4.17 and 4.18 show the effect of ventricular activity on the dominant

frequency. As the ventricular activity always has a higher amplitude compared to atrial activity, the signal can be clipped a certain amplitude to get atrial activity.

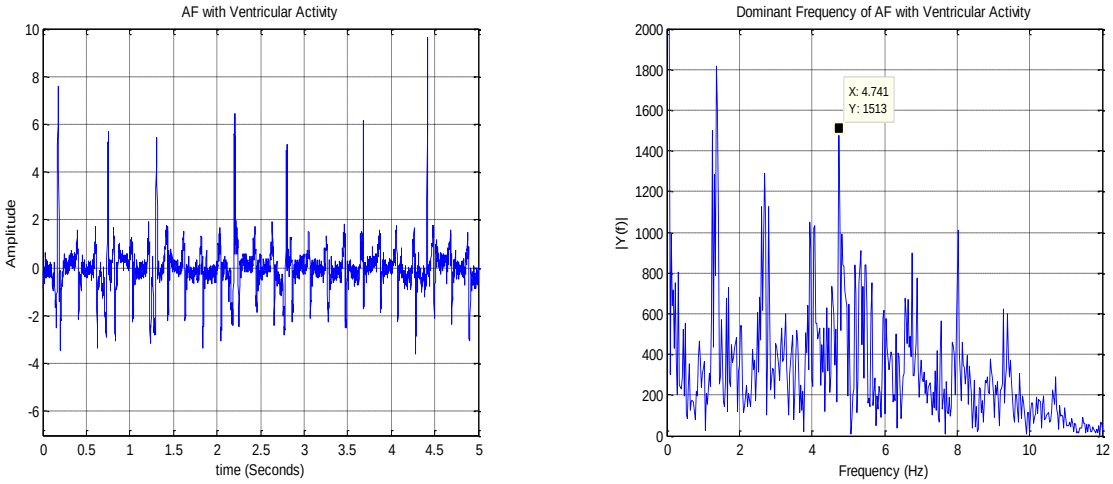

Figure 4.17 AF Signal with Ventricular Activity, Dominant Frequency.

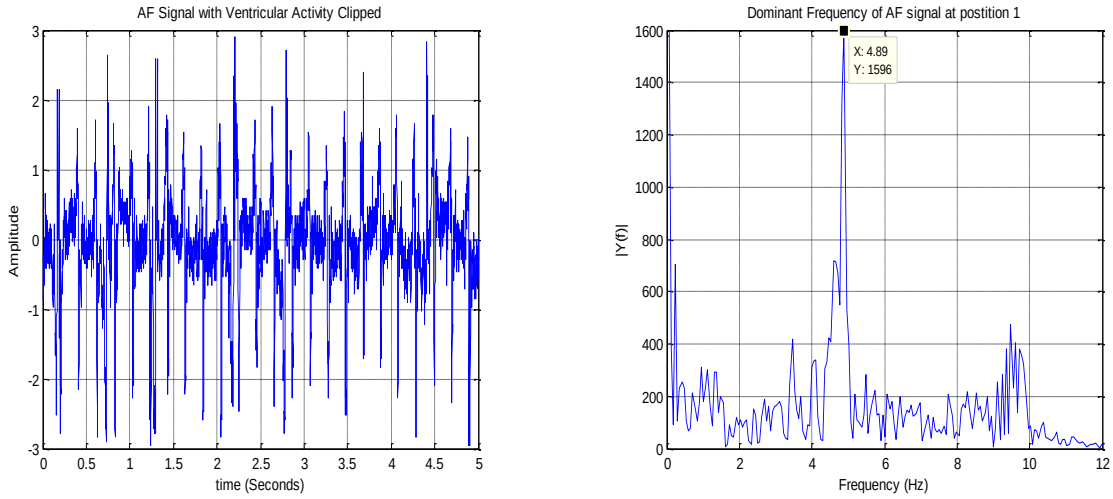

Figure 4.18 Dominant Frequency with AF Signal's Ventricular Activity Clipped.

4.7.2 Dominant Frequency of AF in RA and LA

In this section, the gradient between the left and the right atrium will be explained. During AF, the right atrium was found to have a lesser dominant frequency compared to that of the LA. In this case, it decreased from 4.234 Hz to 1.998 Hz. This is explained

clinically by the fact that the fibrosis tissues are present more in the LA. Fibrosis tissues are assumed to be the main cause of the AF. The amplitude was also found to be reduced in RA. As signal travels from LA to RA, decrease in frequency and energy was observed. The gradient of frequencies from left to right atrium as shown in Figures 4.19 and 4.20 confirm that the origin of AF is from the left atrium.

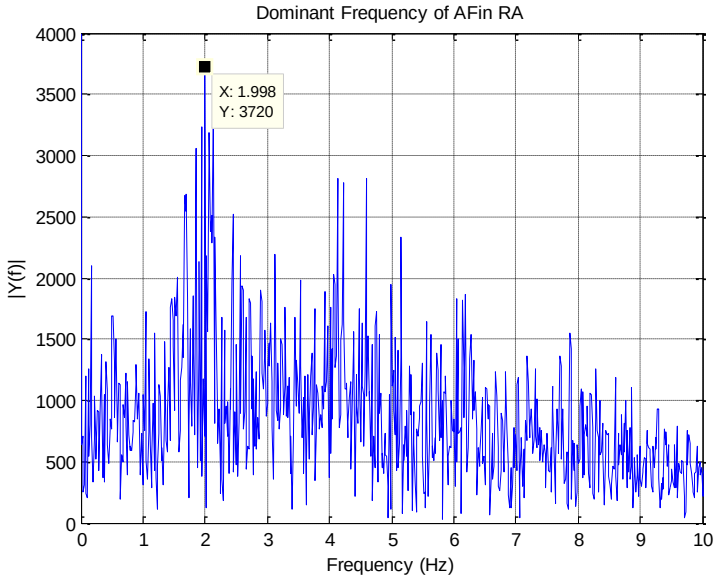

Figure 4.19 Dominating Frequency of AF in RA

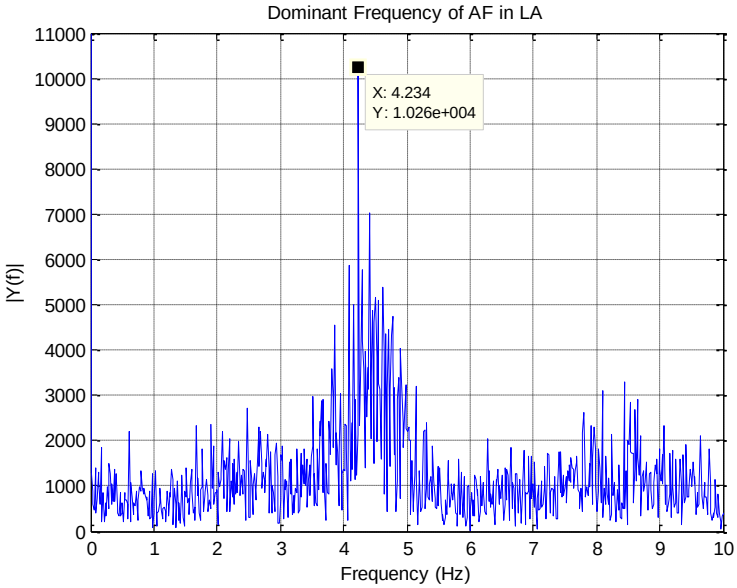

Figure 4.20 Dominating Frequency of AF in LA

4.7.3 Directionality

During AF with one source or in normal sinus rhythm, the signals travel in a particular direction with some delay (Figure 4.21).

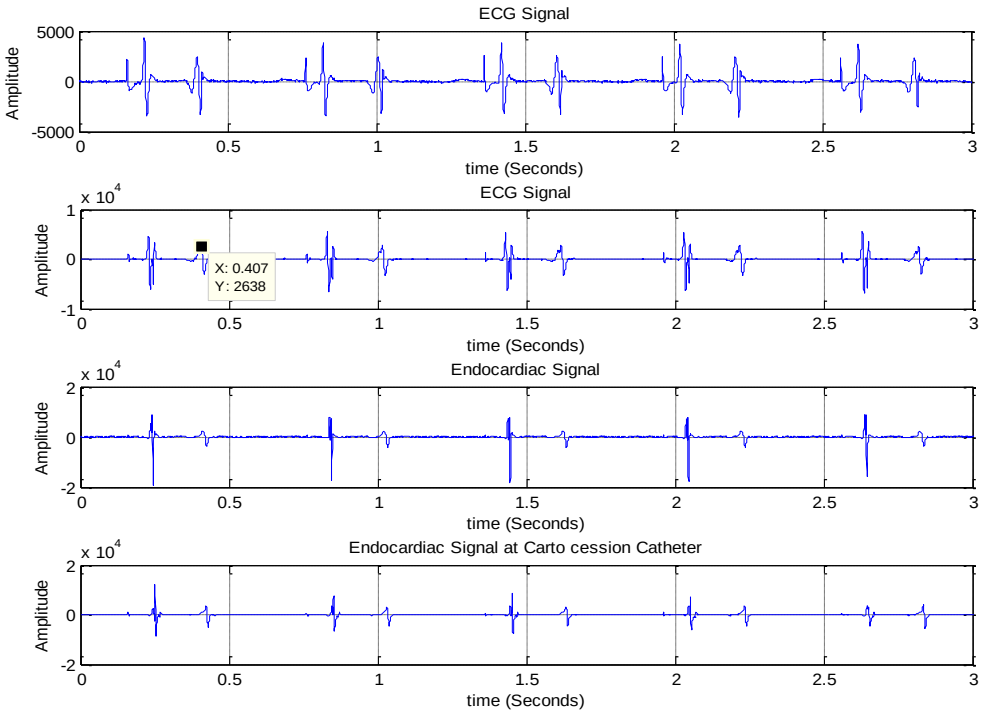

Figure 4.21 Directionality of AF in LA

4.8 Summary

In general, during standard RFA procedure, a number of recording catheters are positioned inside the patient's heart. AF triggers were stimulated by artificially pacing the LA from the four pulmonary veins. The catheter in the coronary sinus was selected for characterizing the data from the four pulmonary veins because of its stability. The coronary sinus recordings during pacing from these different sites will be analyzed using our algorithm with the purpose of identifying the direction of activation and therefore the origin of AF.

The main goal of this research is mainly aims to develop methodology and algorithm for finding the source of the AF. Clinically, the approach of Radio Frequency Ablation to AF has always been to target the four Pulmonary Veins in the LA. Hence the main objective of is to characterization and classify signals from the four pulmonary veins in LA using frequency domain analysis and statistical pattern recognition techniques. The classification of AF signals obtained from pulmonary veins was done based on dominant frequency, frequency distribution and normalized power.

The dominant frequency of PV1, PV2, PV3, and PV4 were found to be 5.307, 4.293, 6.053, and 4.92 Hz, respectively. The normalized power loss for PV1, PV2, PV3, and PV4 were found to be 0.32, 0.43, 0.16, and 0.1 micro watts respectively. The histogram was already shown to be different. These features were applied to PCA. The first component generated by PCA accounts for maximum variability in the data, and each succeeding component accounts for as much of the remaining variability as possible. In our results, the first principal component was found to have nearly 52% of the variance. The first component and second component together achieved 74%. Further, as the principal components were added, the variance increased to 81%, 87%, 92%, 96%, 99% and 100%. Data compression can be made by discarding last component. This can be achieved by losing only 1% of the variance. Further, LDA was applied to classify the signals obtained from the four pulmonary veins.

CHAPTER 5

CONCLUSION AND FUTURE WORK

5.1 Conclusion

In this research work, AF signals were collected from the bipolar catheter placed at coronary sinus during ablation of AF. These signals were specially recorded for the study under specific protocol to understand the characteristics of AF. Forming the protocol to collect data and understanding the data for the study was one of the main parts of this research work. Left to right atrium gradient of frequencies and the observation of dominant frequencies in the LA suggests a preferential origin of AF in the LA. Clinically, the AF is assumed to be originated from pulmonary veins. Hence, a novel methodology has been developed to classify the signals originated from all four pulmonary veins. In this thesis, we hypothesize that we are able to identify direction of their activation wave front and therefore their anatomical location or site of activation. Extensive research has been carried out in the development of synchronous and asynchronous directional. We also hypothesize that we have developed an algorithm able to deconstruct the endocardial recording of atrial fibrillation activity by identifying its component and locate anatomically the origin of these components.

5.2 Future Work

This research work presents promising results that can be used in the future for developing an algorithm to identify multiple sources of AF. These results are only preliminary and need to be confirmed in clinical practice. In future, the initial signal of

AF can be deconstructed to ascertain if the organized rhythm observed during ablation is identified as one of its components. Most of the ablations are performed during spontaneous or induced AF. As atrial tissue is ablated is to observe a reorganization of fibrillation into a more organized rhythm and finally, as ablation is directed to the sources of these rhythms return to sinus rhythm.

Our hypothesis is that these rhythms are the triggers of AF. Their fast stimulation of atrial tissue or possibly the combination of two or more sources induce break down of regular activation into disorganized waves rendering the resultant signal of AF impossible to analyze into their initial components. These components are true initiator of AF and we speculate that, elimination of these sources will terminate the AF and potentially cure it.

Further, Blind source separation (BSS) algorithm can be used to obtain the signal from each source. The number of sources will be applied randomly to the BSS algorithm. Atrial flutter is assumed to be one of the signals present in the AF signal. Hence when one of the signals obtained from BSS matches/coincides to the atrial flutter, the number of sources may be confirmed. Hence the intra cardiac signal is modeled with respect to the number of sources. Finally, the number of sources and signals can be obtained. Hence treating them as a single source the linear discriminate analysis can be applied to find out the number of sources.

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