Spatio-Temporal Cardiac Pacing Sites Localization And Time Varying Pericardium Potential Maps Projection Using Ecg Precordial Leads And A Single Moving Dipole Model

Jaime R. De La Cruz
University of Texas at El Paso, jrde@miners.utep.edu

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SPATIO-TEMPORAL CARDIAC PACING SITES LOCALIZATION AND
TIME VARYING PERICARDIUM POTENTIAL MAPS PROJECTION USING
ECG PRECORDIAL LEADS AND A SINGLE MOVING DIPOLE MODEL

JAIME R. DE LA CRUZ
Department of Electrical and Computer Engineering

APPROVED:

__________________________________________
Joseph H. Pierluissi, Ph.D., Chair

__________________________________________
Thompson Sarkodie-Gyan, Ph.D.

__________________________________________
Raymond Rumpf, Ph.D.

__________________________________________
Zainul Abedin, M.D.

__________________________________________
Benjamin C. Flores, Ph.D.
Acting Dean of the Graduate School
Dedication

Quisiera dedicar este trabajo a las siguientes personas. Sin su ayuda, yo no hubiera llegado hasta donde estoy ahora.

Dr. Pierluissi: Thank you for your support and help. Your wisdom words help me to envision a wider world, not only in the scientific plane but also in life. Thank you.

Mis Padres y mis Hermanos: Gracias por hacerme creer que todo es possible, que los sueños son posibles. Gracias por apoyarme en los momentos mas difíciles. Gracias por enseñarme a ser una persona trabajadora y honesta, y a no rendirme ante la adversidad. Este trabajo, y todo lo que yo he hecho con mi vida se los debo a ustedes que son mi orgullo. Gracias.

A mi esposa Grisel: Este trabajo está dedicado a ti. Gracias por estar ahí para apoyarme y entenderme. Gracias por permanecer a mi lado en lo mas difícil y por quererme tal y como soy. Te amo.
SPATIO-TEMPORAL CARDIAC PACING SITES LOCALIZATION AND TIME VARYING PERICARDIUM POTENTIAL MAPS PROJECTION USING ECG PRECORDIAL LEADS AND A SINGLE MOVING DIPOLE MODEL

by

JAIME R. DE LA CRUZ, B.S.E.E

THESIS

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Abstract

A novel non-invasive method for the spatiotemporal localization of the sites of strongest cardiac activity, and for the creation of time varying Pericardium Potential Maps (PPM), with the use of patients’ ECG precordial leads, is proposed in this Thesis study. Compared to previous studies, which analyze electrocardiograms in either time domain or spatial domain, the proposed method has the advantage of a simultaneous spatiotemporal electrocardiograph analysis and a 3-D visualization of pericardium potentials maps, as well as, the pericardium surface polarization patterns during the cardiac cycle. The spatial properties added to the electrocardiogram allow for the analysis of specific regions inside the human heart where potential cardiac malignancies are suspected to occur. In this thesis, the concept of electrocardiography was extended using advanced bioelectromagnetism theory. The proposed MATLAB-based software makes use of the single-moving dipole model, optimized in location and magnitude with respect to the measured precordial leads, and of a realistic Finite Elements Method torso model. The use of the single-moving dipole model allows the specific localization of cardiac pacing sites, i.e the regions within the human heart in which the electrical activity is being generated. The PPMs are displayed simultaneously with precordial leads to allow a 3D visual synchronization between the time varying color coded potential map and the ECG waveforms, which may indicate potential cardiac malignancies. In this Thesis study, the addition of a time dependent visualization of the PPM to the single-moving dipole model resulted in the exact localization of cardiac pacing sites in both space and time. This spatiotemporal analysis is useful for clinical applications since it characterizes the source of the human heart’s electrical activity to a specific region or dipole location inside the heart at a specific moment on the cardiac cycle. Then for each time sample, a single dipole is chosen to be responsible for the generation of the set of precordial signals a function of its moment magnitude. Therefore, the dipole moment location changes in magnitude and origin over time.

The proposed software was implemented in the analysis of 15 normal patients and 15 patients with cardiac abnormalities. For each case, 20 different sites inside the heart were considered as a possible origins of cardiac activity at each instant of time during a complete cardiac cycle. The
hypothesis behind this study is that the dipole with the greatest dipole moment magnitude generates the entire set of precordial signals at a specific time moment. Moreover, the location of the dipole with the greatest dipole moment also indicates the origin of the cardiac activity inside the heart. The logic used to determine whether a patient presents an abnormality relies in the creation of a normal population which provides the necessary parameters for the creation of normal ranges. Those normal parameters establish the expected location of the cardiac activity origin at each one of the sections of a cardiac cycle: the P-wave, QRS-complex, and T-wave. Data are analyzed patient by patient; if a patient is found to have the strongest dipole location out of expected range in one or more cardiac cycle sections, the patient is considered to have an abnormality. Analysis is then fully complemented by the visual inspection of the actual location of the origin of the cardiac activity and the inspection of the polarization and depolarization patterns at the pericardium provided by the PPM projection. Results showed consistently that for normal patients, sources of strongest cardiac activity were located in the atrial region for Q-wave, and the in the ventricle region for both QRS complex and T-wave, whereas for abnormal patients there was no consistency in such locations. The software identified successfully potential cardiac malignancies and their possible locations inside the heart in 93.33% of the abnormal patients’ ECGs. Additionally the inclusion of spectral analysis of the original signals aimed for preliminary arrhythmia detection, signal period calculation and wave segmentation, allowed for robust patient application, since the software parameters needed not to be modified when analyzing different patients. The concepts proposed and explored in this Thesis work provided expected results. Therefore the goals of this research study were successfully achieved.
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Chapter 1: Introduction and Background

1.1 Introduction

Every year more than 5 million patients are diagnosed with some kind of heart disease in the United States [1]. While most of the cardiology procedures presently available can be used to obtain an accurate diagnosis of a patient’s heart condition, they are mostly invasive, time consuming, expensive or cause discomfort to the patient [2]. Non-invasive methods have proved to be as effective as invasive methods, without the disadvantages mentioned [3]. The purpose of the research study being reported is to propose an alternative non-invasive, MATLAB-based method to assist the clinician in a preliminary cardiac health diagnosis, using only the patient’s ECG signals and a realistic Finite Elements Methods (FEM) torso model. The proposed software program provides a graphical visualization of the localization, in both space and time of the sites of major cardiac activity (Cardiac Activation Sites). Compared to previous ECG-based diagnosis methods, which statistically locate sites of strongest cardiac activity within the heart only, the proposed work has the advantage of providing also a visualization of the electrical potentials on the pericardium over the specific patient’s cardiac cycle. As it is well known, inherent limitations of inverse solutions restrict the robustness of approximate solutions, and preliminary diagnostics derived from them would still need verification from other more direct diagnostic methodologies, such as auscultation, x-ray, coronary angiography, clinical chemistry, and others.

From the electrical and biomedical engineering points of view, the heart can be thought as an electric source that induces electric potential on the human torso surface. The surface potentials at the surface of the body can be recorded with the use of electrodes, cables and instrumental amplifiers. Currently in medicine, heart’s electrical activity is recorded and measured at torso’s surface using an electrocardiograph. The electrocardiogram (ECG) represents the trace of the heart’s electrical activity and is widely used by specialists to detect and diagnose cardiac diseases and failures such as hypertrophy, arrhythmia, cardiac infarction, conduction defects, and etcetera. A healthy patient’s ECG is composed of three segments [4]. The first segment corresponds to the initial signal that triggers the
beginning of the cardiac cycle and it is known as the P-wave [4]. The next segment corresponds to blood being pumped out of the heart through the arteries and it is known as the QRS-complex. The last segment, which is called the T-wave, corresponds to the end of the pumping process for blood distribution over the body. Figure 1 shows a healthy patient’s typical ECG and its segments for one cardiac cycle.

![ECG Trace](image)

**Figure 1.** A healthy patient’s typical ECG trace showing its corresponding segments: the P-wave, the QRS-complex and the T-wave.

The ECG is a projection of the electrical activity of the heart on the human torso on the measurement site. When more measurement sites are used, an improved spatial resolution is obtained. When electrodes are placed all over the torso, the recorded signals are no longer called ECG, but Body Surface Potential Maps (BSPM) [5]. A Body Surface Potential Map is a color coded-image of the electric potential over the body. As the heart induces potential on the body surface, ECG can record those potentials; however, this recorded potential is limited only to the location of the measurement sites. If the number of those sites is increased up to a point that surrounds the entire body, virtually the complete spatial electrical activity of the body can be recorded. This is the main idea behind the BSPM concept. A computer generated BSPM is shown in Fig. 2. The main advantage of BSPM over ECG is
that BSPM provides the capability of visualizing, in a three dimensional space, the electrical activity of the heart reflected on the human body’s surface. BSPM and regular ECG (12-lead ECG [6]) are fundamental tools for the study of the inverse problem of electrocardiography. Even though BSPM provides more spatial resolution than 12-lead ECG, the complexity of the mathematical solution, and consequently the error increases dramatically as more measurement sites are added.

**Figure 1.2.** A typical SCIRUN/computer-generated BSPM showing a color coded potential map on a 3D FEM human torso model, accounting for simulated heart electrical activity reflected at the torso [7].

One of the main concepts explored in this thesis study is the use of the 6 precordial leads for the creation of color coded surface potential maps. In this research study color coded surface potential maps at the pericardium (Pericardium Potential Maps) are created by projecting the reconstructed potentials generated by a dipole location after solving the inverse and forward problems of electrocardiography. Projection is made into a 3D FEM model of the human heart. This is accomplished without the necessity of surrounding the torso with several electrodes. As mentioned before, resolution is increased as more electrodes are used to record the ECG; however the complexity of the mathematical solution increases,
as well as, the numerical errors. In this research study color coded surface potential maps are created
with the use of the precordial leads ECG, which utilizes only 6 electrodes. This means that the high
resolution provided by the regular BSPM and its several electrodes usage is achieved by the use of
regular precordial ECG measurements, in which only 6 electrode measurements are needed. Moreover,
the aforementioned mathematical errors are significantly reduced without sacrificing the high spatial
resolution provided by regular BSPM techniques.

1.2 Advanced Concepts in Electrocardiography and Vectorcardiography

Electrocardiography studies the variations in electromotive force generated by the heart,
reflected on the human’s skin surface. Those variations can be measured and recorded in the form of
electric potentials [8,9]. Therefore, the ECG provides a general representation of the cardiac activity
from measurements taken on the surface of the human body, which has as an ultimate purpose the
determination of the health of the heart. In this manner, physicians and, specifically, cardiologists are
able to obtain a diagnosis of the overall condition of this vital organ by simply recording and analyzing
the electrical activity at body’s surface.

ECG analysis is highly dependent on electrodes placement in such manner that recorded
electrical traces will vary according to measurement sites localizations. For instance, one of the first
methods for electrode placements in ECG analysis required the use of three bipolar leads [6,9], which
are placed on the limbs and record the electrical activity of the human heart projected onto the frontal
plane. Subsequent proposed methods for electrode placement added the six precordial leads [10] and the
three augmented leads [11], which resulted in the common 12-lead electrocardiography widely used [6].

The concept of Vectorcardiography or Vectorcardiogram (VCG) is an extension of the ECG
since it allows the study of the heart’s cardiac electrical activity in 3 D. The VCG provides not only
electrical traces in the frontal plane, but also in the transverse and sagittal planes. The main feature of
the VCG is the assumption that the heart behaves as a current source that can be modeled as a current
vector, which is called the Heart Vector [6]. Then, a full vectorcardiographic analysis is composed of
the projections of the magnitude and direction of the heart vector over time onto the frontal, transverse
and sagittal planes. Each projection of the VCG analysis depicts a VCG loop; one for each of segments of the regular ECG. The 3D nature of the VCG allows it to provide additional tools for diagnosis of cardiac illnesses.

1.3 The Standard 6-Precordial leads ECG

As mentioned above, the commonly used 12-lead electrocardiography requires the placement of 12 electrodes in the patient: the bipolar, augmented leads and precordial leads. One characteristic of the limb leads is that they are bipolar [6]. That is, they measure the electric potential difference between two points. The previous statement implies that the measured electric potential will be entirely dependent on the variation of electrical potential in the measurement site; that is, the potential measured will not have a fixed point of reference, i.e. a limb. Therefore, the potential measured between electrodes placed in the chest and one of the limbs will represent changes occurring on the chest and places far from the chest as well. The use of bipolar leads for BSPM projection represents a disadvantage since the potential recorded by electrodes placed in the limbs is propagated by the skin. For BSPM projection purposes, electrical activity generated in the heart is propagated through inner organs and tissue, and is finally recorded in the human torso surface in the form of an electric potential. If a lead records electrical potential between an electrode that measures potential propagated via skin conduction and an electrode that measures potential generated directly from the heart, such leads will not be useful for BSPM construction. They would not reflect cardiac activity in the chest. Because of the aforementioned reasons, unipolar leads, that is, leads that measure potential between a variable point and a fixed point, are needed for BSPM construction since they only measure potential at a single point.

The six precordial leads are ideal for BSPM and PPM construction, given their unipolar nature. Composed of six electrodes located in the fourth and fifth inter-costal spaces, as indicated in Fig. 1.3, the six precordial leads measure potential differences between six electrodes in the chest and a common zero potential point. This latter point is a combination of electrodes placed in the upper and lower limbs, which remains at a constant value throughout the entire cardiac cycle. In this manner the cardiac electrical activity recorded by the six precordial leads accounts only for electric potential at the human
torso. Precordial leads are denoted by $V_1$, $V_2$, $V_3$, $V_4$, $V_5$, and $V_6$. Leads $V_1$ and $V_2$ are placed in the $4^{th}$ intercostal space on the right and left sides of the sternum, respectively. Lead $V_4$ is located in the $5^{th}$ intercostal spaces in the mid-clavicular line, $V_3$ is located midway between $V_2$ and $V_4$. Leads $V_5$ and $V_6$ are located in the $5^{th}$ intercostal space in the interior and mid-axillary lines respectively [12], as seen in Fig. 1.3.

![A SCIRUN/BioPSE generated 3D image showing the location of the six precordial leads in the human torso.](image)

**Figure 1.3.** A SCIRUN/BioPSE generated 3D image showing the location of the six precordial leads in the human torso.
Chapter 2: The Forward and Inverse Problems of Electrocardiography

The purpose of this research study is to propose an alternative non-invasive method to assist in the diagnosis for cardiac illnesses. As mentioned in the previous chapter, the ECG is considered a very good means for diagnosis among the physicians, since by measuring the changes in electric potential in the human torso produced by the heart, cardiac malignancies can be detected by comparing differences in the ECG traces to normal ECG traces. As an extension to regular ECG methods, BSPM provides additional information on the cardiac electrical activity reflected on the human torso. The analysis of ECGs and BSPMs is usually performed with the use of either one of the two problems or approaches of electrocardiography: the inverse problem and the forward problem [13].

2.1 The Inverse Problem of ECG

The inverse problem of electrocardiography refers to the process of analyzing the electric potential at the human torso surface and, from those potentials calculating an equivalent electric current inside the heart as the source for such surface electric potentials. Compared to invasive diagnosis procedures such as cardiac surgery, an inverse analysis provides a non-invasive means for the study and diagnosis of the heart’s condition. Assuming the heart acts as a source of electrical activity [14], the inverse problem of electrocardiography is solved by calculating or inferring the properties of the electric source that generates the electrical activity on the torso.

Given the ill-posed nature of an inverse problem, the inverse problem of electrocardiography has an infinite number of possible solutions [15]. Therefore, it is necessary to have a certain level of knowledge of the expected results in order to be able to discard all the results that do not lie into the expected results category. In other words all the results that are unrealistic or do not have any physical significance must be discarded. In this research study, however, the inverse problem of electrocardiography was structured in such a way that all of the results obtained are real or have a physical significance, and no result is discarded. Results then are classified in terms of their accuracy.

The use of computers and computational algorithms allows the manipulation and analysis of great amounts of data, which allows for the solution of large and complex systems. For the inverse
problem of electrocardiography the use of computer and computational algorithms means the capability
to solve systems with increased number of variables and unknown in the problem definition i.e. torso
surface potential measurements, more resolution for inner body structures and properties [16].
Therefore, the use of computers permits the physicians and the cardiologists to have the possibility of
utilizing computer-aided methods for cardiac illnesses diagnosis. This represents a significant advantage
for cardiologist and physicians in general.

The inverse problem of electrocardiography can be extended to vectorcardiography as well.
From the electric potentials measured at the torso, a source in the form of a vector (the Heart Vector [6])
is calculated as the source of surface electric potential. Therefore, the inverse problem can be used in the
electrocardiogram and in the vectorcardiogram to find the source that generates surface electric
potentials in the torso. As mentioned above, the inverse problem of electrocardiography does not have a
unique solution. Instead, there is an infinite number of possible solutions for such systems [15]. The ill-
posed nature of the inverse problem of electrocardiography and its disadvantages can be eliminated with
the use of an appropriate heart-source model. The most common used heart-source models are the
single-fixed dipole model and the multiple-fixed dipole model. However, in this research a third heart-
source model was developed: the single-moving dipole, which takes the best features of both the single-
fixed and multiple-fixed dipole models but without the disadvantages carried with the two most common
models. Additionally, the inverse problem formulation is very sensitive to small changes in data e.g.
noise added to the original precordial ECG signals. Hence, analyses performed using the inverse
problem of the electrocardiography must be done in such a way that sources of changes in data
(electrical and numerical noises) are reduced to a minimum in order to achieve an acceptable level of
confidence and accuracy in the results.

2.2 The Forward Problem of ECG

Contrary to the inverse problem of electrocardiography in which the source is calculated or
inferred from the torso’s electric potentials, the forward problem of electrocardiography calculates
torso’s electric potentials from known electric source inside the heart. Here, it is assumed that all the
properties of the heart-source model are known and that the torso’s electric potentials can be reconstructed. The forward problem of electrocardiography is divided into two different methods: surface methods and volume methods. In surface methods, surface electric potentials are calculated using the concept of equivalent sources and a generalized form of Green’s second identity [15]. In volume methods the forward problem of electrocardiography is solved using Finite Volume Elements. The forward problem of electrocardiography is used for computer heart modeling, lead vectors calculation, and ECG signal reconstruction [17, 18, 19]. In this research study, the forward problem is used to reconstruct precordial ECG signals generated by dipolar sources in order to determine how well does the calculated reconstruct measure potentials.

2.3 Body Surface Potential Maps and Pericardium Potential Maps

As mentioned before, a BSPM accounts for the electric potential distribution on the human torso. BSPM acquisition requires a large number of measurement sites (electrodes) surrounding the torso. Since according to the inverse problem of electrocardiography formulation, a current dipole source inside the heart generates the electric potentials measured at the human torso, an equivalent dipole source can be calculated out from the BSPM electric potential measurements. Figure 2.1 depicts a standard 128-Lead system intended for BSPM data acquisition.

Figure 2.1. A standard 128-Lead system for BSPM data acquisition [20]. The 128 leads are placed around the patient’s chest in order to record electric potential generated by an equivalent dipole source.
It can be inferred that the spatial resolution and quality of the BSPM increases as the number of measurements sites is increased. This provides more exact information about the electric potential distribution over the torso. However, if the purpose of the BSPM data acquisition is the calculation of an equivalent current dipole source via the inverse problem of electrocardiography, the more measurement sites used the more complex the formulation of the problem grows. This is due to the fact that equivalent dipole sources are calculated by solving linear systems of equations. Therefore, as more measurement sites are used, the matrices in the linear system of equations increase in size. Added to the ill-nature of the inverse problem, a large number of measurement sites can lead to inaccurate, and thus unreliable, results.

In this research the Pericardium potential mapping or maps (PPMs) is introduced as an alternative to traditional BSPMs. PPM accounts for the distribution of electric potential in the pericardium. The pericardium is a sac that contains the heart and the foundations of the venae cavae, the pulmonary artery, the pulmonary veins, the aorta, the brachiocephalic artery, the left common carotid artery among other vessels [21]. The pericardium is divided into two layers: the fibrous and serous pericardium. The fibrous pericardium is composed of two layers as well: the parietal pericardium and the visceral pericardium. Potentials generated by the heart are reflected in the pericardium are measured in the outer layer of the heart tissue, the epicardium, which is part of the visceral pericardium [21, 22]. Knowing the distribution of potential at the pericardium signifies a great advantage in the diagnosis of cardiac malignancies, since it allows for an easier identification of polarization and depolarization patterns throughout the entire cardiac cycle. In such manner, by knowing the segment of the cardiac cycle in which the abnormality is occurring, the origin of the potential cardiac malignancy can be located by identifying which regions of the heart are associated to the cardiac cycle segment in which the abnormality occurs.

Pericardium Potential Mapping, as BSPM and other medical imaging techniques, provide a non-invasive alternative for potential cardiac malignancies detection. Compared to BSPM, the proposed method for PPM data acquisition requires only the use of the six precordial ECG leads for the recording
of the electric potential measurements in the torso. As mentioned before, as more electrodes are used, more spatial resolution is obtained, but the complexity of the problem increases as well. In this research, PPMs obtained had the same high spatial resolution as a multi-electrode BSPM and maintain the low complexity of the problem by using only six electrodes. The reason being for PPMs having high resolution but requiring less computational power is due to the use of the inverse problem of electrocardiography. As mentioned in the previous sections, the purpose of the research study being reported is the localization of equivalent dipole source or cardiac activation sites (CAS) inside the human heart for the aid in cardiac illness diagnosis. Using the inverse problem of electrocardiography and the ECG data provided by electrodes, an equivalent dipolar source is calculated. Given that the system of linear equations used in the inverse problem is over-determined and ill-posed, the more input data used (measurement sites in torso) the more complex and unstable the solution is. The use of the six precordial ECG leads permits the formulation of a smaller and simpler system of linear equations in the inverse problem. Even though that the small system is over-determined and ill-posed, the stability and complexity of the solution decreases significantly. High spatial resolution for six precordial leads ECG PPM generation is achieved by the use signal processing techniques such as digital filtering and spectral analysis. It was found that the application of the mentioned techniques to the signal previous to the formulation of the inverse problem greatly improved the conditioning of the linear system of equations, and consequently the exactitude and resolution of the obtained PPMs. Figure 2.2 depicts a computer generated image of potential distribution on the pericardium.

![Figure 2.2](image)

**Figure 2.2.** A computer generated color coded Pericardium Potential Map posterior and anterior views. Red regions correspond to high electric potential, whereas blue regions correspond to low electric potential.
Chapter 3: Problem Statement and Proposed Solution

3.1 Problem Statement

Unlike most current ECG based research works, which are based either on temporal or spatial properties, the work proposed in this thesis uses both spatial and temporal properties of the ECG for a more accurate and complete analysis. The main goal of this study was propose a non-invasive alternative method to assist in the diagnosis of cardiac illnesses. This is accomplished by the localization in both space and time of the sites with major cardiac electrical activity inside the heart. Additionally, a new concept is introduced for the study of polarization and depolarization patterns occurring at the heart surface tissue during the cardiac cycle: the time-varying Pericardium Potential Maps.

The first problem with ECG analyses is the lack of information regarding the spatial localization of cardiac malignancies. Even though ECG analyses are very useful in detecting cardiac anomalies out from the electric potential measured at the torso, the information regarding the origin of such anomalies inside the heart cannot be provided by regular ECGs. The reason for this lack of spatial properties of the ECG is due to the very definition of the ECG concept itself. The ECG is based on the concept of a single electric source located inside the heart which induces electric potentials measured at the torso. These induced electric potentials are recorded, filtered and amplified so that the electrical traces produced by the heart can be displayed in a monitor for their analyses. Hence it is evident that electrocardiography does not take into account any spatial property regarding the origin of such electric traces, so the localization of any potential cardiac malignancy cannot be determined from the ECG.

The overall goal of all ECG based analyses is 1) the detection of cardiac malignancies, 2) the localization in time of cardiac anomalies, and 3) the localization inside the heart where the abnormalities occur. Additionally, as mentioned before, measured electric potentials in the torso are generated by an equivalent electric source located inside the heart; such electric source can be modeled as a current dipole source. Therefore, the equivalent dipole source can be obtained in the form of a dipole moment vector via the inverse problem of electrocardiography. Since the dipole moment vector has three orthogonal components, the resultant vector has three components as well. Then, for three measurement sites (electrodes), the linear system of equations is well determined and easily solvable. However, most
standard ECG procedures require the placement of 6 to 12 electrodes [6], and 16 to 256 electrodes for BSPM data acquisition [20]. As it has been mentioned before, the more electrodes used the more spatial resolution is acquired. It is evident that using three or few electrodes does not represent any advantage since very poor spatial resolution is obtained, and consequently any result obtained is not physically relevant. Also as described before, as more measurement sites are used, the size and complexity of the linear system of equations associated with the inverse problem of electrocardiography increases, because the linear system of equations becomes over-determined as there are more equations than unknowns. Hence, the dipole moment vector obtained from the torso electric potential measurements has a large margin for errors. For the aforementioned reasons, and the ill-posed nature of the inverse problem solution, it is always a good practice to place a reasonable number of electrodes as according to standard medical procedures [6, 20].

The hypothesis supporting most of the current ECG and BSPM analyses relies in the localization of an single equivalent electric source or a combination of two or more electric source at different locations inside the heart, as being responsible for the induced electric potentials recorded at the torso. The second problem associated with current ECG analyses which involve the localization of equivalent intracardiac electric sources is the balance between the desired spatial resolution, and the complexity and size. Even though multi-electrode BSPM provides an excellent spatial resolution, as more potentials are taken into consideration, the required system of equations for the equivalent dipole moment calculation, is greatly over-determined as the number of equations greatly surpasses the number of unknowns. It is necessary to mention that even though there is a strong correlation between the error of the obtained solution and the number of equations in the system (which is proportional to the number of torso’s measurement sites used), the solution is always subject to inaccuracies no matter the number of electrodes used. However, a balance between system’s complexity and an acceptable spatial resolution is achieved by an intermediate number of electrodes so error of the obtained solution is reduced, but an adequate level of resolution is maintained.

Other problem inherent to ECG analysis involving the usage of the inverse problem of electrocardiography is the physical relevance of the obtained solution regarding: the localization inside
the heart of the equivalent electric source. As discussed in [20] not all the solutions obtained for the localization of the equivalent dipole moment have physical significance and must be discarded. Additionally, previous proposed works for equivalent source localization aimed only for the localization of a single-fixed or multiple-fixed dipolar source in space. That is, a single dipolar source at fixed location inside the heart or a combination of dipolar sources at fixed places inside the heart produced the induced potentials measured at the torso; the dipole moment vector or vectors information for such dipolar sources could be obtained via the inverse problem. However, such aforementioned procedures do not provide any information about cardiac activation sites location changes over the cardiac cycle. Knowing the location inside the heart in which the electrical energy is originated, means a significant advantage not only for detection, but also for localization in space and time of the probable region of the heart in which the malignancy originates. Another inconvenience related to high level ECG-based analysis is the need of high technology and, hence, very high cost equipment, such as CT scans [23], multi-electrode jackets [20], and others. These pieces of equipment are necessary for accurate data acquisition, but their high cost place economical constraints on the development of novel ECG based techniques for the aid in cardiac illnesses diagnosis; the creation of those novel techniques for diagnosis requires to take into consideration the cost of the required materials and equipment, which fosters the research and development of computer based algorithm with a stronger mathematical foundation.

The work developed here is based on robust electrical engineering concepts and was tested under specific conditions with data coming from real patients. However, current available resources do not allow for more clinical testing. Further development and clinical implementation for this algorithm is left for future work stage. Finally, it is important to remark that the work proposed in this thesis is not intended to replace current ECG based studies, nor to fully replace the task of the diagnostician in cardiology. Obviously, diagnosis in medicine is complex and non-trivial. The purpose of this work is to provide an additional tool capable of assisting the physician in obtaining a more accurate and easy diagnosis; ultimately the diagnosis and its outcomes are responsibility of the physician. Furthermore, the algorithm and techniques discussed in this research summary aim for a non-invasive, low cost alternative to invasive procedures.
3.2 Previous Work

As mentioned above the analysis of the ECG is a powerful tool for the detection of cardiac malignancies. Nevertheless, the spatio-temporal properties of electrocardiography had not been fully exploited in previous similar works. Even though there are several publications that address the use of the inverse problem of electrocardiography for the localization of equivalent dipole sources as a non-invasive method for cardiac illnesses diagnosis. However, the results of such research are still in clinical trials and have not reached a greater patient population of cardiac patients. The work presented here is at the same level of the current state of research of the spatio-temporal properties of the ECG. In this section previous published work relevant to the algorithm presented in this thesis will be discussed.

Previous work relevant to this research topic is based on the dipole model of the human heart. The published work titled “Localization of an Equivalent Central Cardiac Electric Dipole for Electrocardiography Applications,” [24] and “Inverse Problem of ECG for Different Equivalent Cardiac Sources” [25] are the starting-point of the work presented here as well as the work presented on the article entitled “Statistical Localization of Arrhythmias Using Precordial ECG Leads” [26]. These articles try to find a solution to the inverse problem of electrocardiography. Their approaches will be discussed in detail the following paragraphs. It is important to mention that the approaches discussed in the first two articles do not include spatial components. Their objective is to explore the reconstruction capabilities of the equivalent central cardiac electric dipole; their goal is to reconstruct the ECG signals.

In the first cited article [24] a detailed description is provided of an optimization method for finding the localization of a central cardiac dipole that provides an optimized equivalent solution [24]. In this article, the authors created their own simulation software that allowed them to obtain simulated surface potentials by using a cardiac dipole as the generating source. Their simulation software utilized a realistic FEM torso model. In this way, the authors claimed that the results yielded realistic results. The optimization method used in this article was the Levenberg-Marquardt method. Using this iterative optimization technique, the authors were able to find an equivalent central cardiac dipole that would optimally reconstruct the ECG signals.
The method published in this article proves to be effective in providing a solution to the inverse problem of electrocardiography. In fact, this approach is a perfect example of an equivalent solution. The method proposed iterates until it finds an adequate solution based on the problem specifications. Nevertheless, the solution found by this system cannot be taken as unique, because of the nature of the inverse problem and the infinite number of solution it can have. In addition, it must be noted that this approach lacks spatial information on ECG signals. The goal was to merely find an equivalent location for the cardiac dipole inside of the human torso, and not to incorporate spatial properties to the cardiac dipole. This method, however, provides a good approximation to the actual solution of the inverse problem of electrocardiography.

The second cited article [25] explores the ECG signal reconstruction properties of the dipole model of the human heart located at the center of the heart. In this article, the authors followed a conventional approach. The research conducted was done using an FEM model of the human torso. The use of an FEM model facilitates the realistic simulation of surface potentials, and for their research purposes it allows the accurate simulation of dipole sources in any given location inside the heart. In their case, their goal was to experiment, through realistic simulation, with the central cardiac electric dipole. However, in order to make a comprehensive study, the results of the central cardiac dipole were compared to simulations of dipoles located in sites other than the central site. For instance, five different dipole locations were used in this article. These dipoles were located in the four heart chambers, respectively, and one on the center of the heart. The method used for reconstruction of ECG signals was least squares with the goal of minimizing the residual between a measured ECG signal and the signal produced from the dipole model. In this article, the ECG reconstruction capabilities of the central cardiac dipole were compared to reconstruction capabilities of dipoles located on other sites inside of the heart. Mainly, the simulation was performed for five different cases as stated in the article [25]. This approach requires that a set of equations for the FEM model, be calculated for every simulation to be performed. Similarly, the ordinary least-squares method is required to be performed for each simulation of any given cardiac dipole. The results show that accurate simulations can be performed using an FEM model, given that realistic conductivity values are incorporated and a least-squares approach is used.
This approach proved efficient to reconstruct ECG signals. However, the reconstruction of ECG signals did show a lack of accuracy. Even the central cardiac dipole showed a considerable difference between the original and reconstructed ECG. The process, as defined in this article, leaves room for improvement on the accuracy of the signal reconstruction.

In the case of the third article [26], even though both spatial and temporal features of the ECG are deeply analyzed, the final result relies entirely in the statistical behavior of the solution of the inverse problem of electrocardiography. Additionally, even though this article aims for the creation of a PPM out from electric potentials measured at the subject’s chest, the results provide only an average distribution of potentials over an entire cardiac cycle and consider only three possible locations for equivalent dipole sources.

The methods and techniques discussed in this section provided the basis for the presented work. It provided a method for modeling the human heart as a dipolar source inducing potential in the torso, a method for signal reconstruction using the dipole model as a source. It has to be mentioned that methods presented in this section were greatly improved in this research summary. Since the goal of this thesis is to improve the current state-of-the-art techniques in ECG analysis, several additions, such as band pass digital filtering, spectral analysis, a new dipole model of the human heart, time dependent PPM projection, were incorporated to achieve such goals.

### 3.3 Proposed Solution

The solution proposed in this thesis for the problems mentioned above, which are inherent to ECG-based analyzed, is partially based on the work done in the cited publications [24, 25, 26]. However, several important modifications were incorporated in order to overcome the difficulties faced in the usage of the methods and techniques discussed in the previous section. The approach taken makes use of the concept of dipole model of the human heart. As mentioned before [20, 26] one common
model is the single-fixed dipole model, in which a single dipole at known fixed location inside the heart induces electric potential in the torso throughout the entire cardiac cycle. The other commonly used model is the multiple-fixed dipole model in which a combination of several dipoles at different known fixed location induce the electric potential measured at the torso. The main disadvantage of these two models is the lack of information about the changes in location of the dipole source over time. The assumption of a fixed location for the origin of cardiac electrical activity does not allow the analysis of the polarization and depolarization patterns of the heart throughout the cardiac cycle.

One of the hypotheses supporting this research work is that potential cardiac malignancies can be detected by anomalies in the trace of the origin of the dipole source during the cardiac cycle. Since a regular ECG trace is composed of three different segments associated with the three main stages in the cardiac cycle: the P-wave, the QRS-complex, and the T-wave [4]. The cardiac cycle begins with the P-wave, which is associated with the depolarization of the atria and indicates the beginning of the cardiac cycle, continues with the QRS-complex, which corresponds to the pumping out process for the distribution of the blood over the body, and ends with the T-wave in which the blood pumping process ends and the heart fibers contract to prepare for the next cycle. Therefore, the location of the origin for cardiac electrical activity, the dipolar source or cardiac activation site, is supposed to change over time during the cardiac cycle. Moreover, each section of the cardiac cycle is associated with a specific region inside the heart; the region of the heart in which the stage of the blood pumping process, associated with the cardiac cycle section, takes place. For a patient with no detected cardiac abnormalities, during the P-wave, the dipole source location moves from the sinoatrial (SA) node towards the atroventricular (VA) node, so the dipole source is expected to be located in the atrial region. During the QRS-complex, the right and left heart ventricles depolarize and pump the blood out from the heart, therefore the cardiac activation site is expected to be located in the ventricular region. Finally, during the T-wave, the ventricles repolarize or regenerate leading the heart’s electricity from the ventricular region to the atrial region; for normal cases the dipolar source is expected to be located between the atria and the right ventricle, around the Bundle of His [27, 28, 29, 30, 31, 32, 33, 34]. For the work presented in this thesis, knowing the expected location of cardiac activation sites or dipole sources inside the heart
provides an enormous advantage since any abnormality or discrepancy between the found location of a cardiac activation site suggest a potential cardiac abnormality.

In order to be able to detect the location over time of the equivalent dipole source inside the heart, a new dipole model for the human heart is introduced: the single-moving dipole model. The newly introduced model combines the advantages of the previously discussed dipole models, without their inherent disadvantages regarding the changing location of the equivalent dipole source over time. In the single-moving dipole formulation used in this work, twenty different possible sites inside the heart are simultaneously considered as possible localizations for a cardiac activation site, at a specific moment in time in the cardiac cycle. Since, as the name of the model implies, a single dipole location inside the heart can be considered as the source inducing the potentials measured in the torso, one dipole location out of the twenty possible locations is selected. This process is called dipole location optimization and it is repeated at each time sample of the patient’s ECG signal selecting the most suitable dipole as the source for cardiac electrical activity. Since the dipole optimization must be performed at every time instant of the cardiac cycle, it is necessary to have the patient’s ECG signals in a digitized for. This is due to the fact that the analysis is performed in a computer, which require data to be inputted in a discrete form. Therefore, all of the patients’ ECG signals to be analyzed need to be sampled and digitized in order to be manipulated by the proposed algorithm. The single-moving dipole model is coupled with a realistic FEM model which takes into consideration all of the inner body properties, such as blood, bones and other organs conductivities, as well as, the complete torso geometry. With the use of the dipole model of the human heart and the FEM model, it is possible to analyze how the energy generated by an equivalent dipole source inside the heart propagates through the bones, blood and organs and is reflected at the human torso in the form of electric potential.
The solution proposed makes use of the inverse problem of electrocardiography as well. Results in the form of dipole moments at different locations inside the heart, are obtained out from patient’s ECG precordial signals after solving an over-determined system of linear equations. This system is ill-posed by nature, which implies that small changes in data, i.e. electrical noise and other signal disturbances in the precordial ECG signals, can signify enormous variations in the results. In this thesis work the incorporation of digital filter to the precordial ECG signals was found to improve the conditioning of the system by the elimination of most of the noise present in the signal. Additionally, the incorporation of spectral analysis to the precordial ECG signals for the detection of out of expected range frequency components is included with two purposes: a pre-analysis capable of detecting overall abnormalities on the patient’s ECG traces, and for the automatic detection of the duration and period of the cardiac cycle.

The proposed solution can be divided into three different parts: the reconstruction of the precordial ECG signals out from obtained dipole moments, the spatio-temporal localization of cardiac activation sites and the projection of time varying PPMs. Signal reconstructions via the forward problem of electrocardiography permits to identify how well the possible dipole locations reconstruct the signal. Since it is assumed that the location of the equivalent dipole source with change along with the cardiac cycle evolution over time, a reconstructed signal from a single dipole cannot be used as a single result for abnormality detection. However, signal reconstruction gives a general idea on how well selected are the possible dipole source locations. On the other hand, the spatio-temporal cardiac activation sites localization provides a solid mean for potential cardiac malignancies detection, since, as explained before, anomalies in the dipole trace over time suggest a malignancy. Moreover, the malignancy location inside the heart can be located by identifying in which segment of the cardiac cycle does the anomaly occurs and its associated cardiac region. This numerical analysis is complemented with the PPM reconstruction and projection over time, which allows for a visual analysis of the potential distribution in the pericardium during the cardiac cycle. As mentioned before PPM is an optimized for of BSMP techniques, more information on BSMP implementation and analysis can be found in [35, 36, 37].
3.4 Clinical Applications

The work presented in this document have multiple potential applications in the clinical practice field. Since the proposed algorithm requires only a medium power personal computer and digitized precordial ECG data, it can be implemented in rural zones in which there is no access to high level technology such CT scanners, x-rays, surgery equipment etc. Additionally it can be implemented in emergency rooms, surgery rooms and cardiology consult/diagnosis rooms as a non-invasive alternative for cardiac malignancies detection and localization. It is important to mention that even though the work, techniques and algorithm presented in this thesis are based on strong engineering, math and physiology concepts, is on a pre-clinical stage, which means that the next stage implies the implementation and clinical testing of such work and concepts in population of clinical patients. The concepts discussed in this paper are intended as an aid in detection and diagnosis of cardiac illnesses, but the final diagnosis and further medical actions are solely responsibility of the diagnostician/cardiologist.
Chapter 4: The Electromagnetic Activity of the Human Heart

4.1 Introduction

The electrical activity that occurs inside the heart has its roots on chemical reactions realized in the heart cells. The electric potential measured in the torso can be explained as the sequential actions of cell membranes [16, 38]. The major working components of the heart in terms of generation and conduction of electrical energy are the SA and AV nodes, the ventricles, conduction cells and pacemaker cells [38]. The cardiac start is triggered by the self excitatory pace maker cells, which are located in the SA node. Once the pace maker cells excite, they excite neighbor conducting cells, which in turn keep exciting other neighbor cells, creating a chain reaction in which electric energy is transferred from cell to cell. Once this excitation chain reaches the right and left ventricles ventricular contraction occurs. Ventricular contraction has two important effects: blood is pumped out of the heart for its distribution over the body and inducing an electromotive force into the surrounding tissues and organs [38]. This electromotive force is ultimately manifested at the torso’s surface in the form of an electric potential. As it has been mentioned before, such electric potentials are recorded by electrodes and read by an electrocardiograph for analysis purposes.

4.2 Maxwell Equations and the Standard six-Precordial Leads ECG

In order to properly analyze the way in which the heart induces electric potentials in the torso’s surface, it is necessary to create a mathematical model describing this physical phenomenon. The electric potential measured at the human torso is generated by chain excitation of heart conduction cells conducting, which ultimately cause the contraction of the ventricles. Therefore, this process can be compared to an electric source enclosed in a propagation medium that induces electric potentials onto the surface of the body. This process is analogous to an antenna, or source, radiating electromagnetic energy through a transmission medium. Such electromagnetic energy ultimately induces electric potentials at a receiving antenna. For the case of the heart generating electric energy, the “receiving antenna” equivalent, would be the body surface, specifically the skin, in which potentials are induced. However, there is a significant difference between an antenna radiating electromagnetic energy and the heart irradiating electric energy. Whereas an antenna propagates energy in free-space, the conducting
medium for heart generated energy is composed of blood, inner organs, lungs, muscle, fat and skin [38]. Therefore, the mathematical model needed for the analysis of the electrical activity of the human heart must take into account all of the mentioned properties. In first place, it must be able to model a radiating source located inside the heart, second it must able to model a conductive medium, and third it must be able to mathematically express the induce electric potential at the conducting medium boundaries, i.e. the torso’s surface.

Arriving to an efficient and realistic mathematical model that describes the electrical activity of the human heart is a very complicated task. The reason for such complexity, that it is caused by the formulation of the dipole model of the human heart itself. As mentioned in previous chapters, the measured torso potentials are a result of the summation of all the small electric currents flowing through the heart muscle fibers and conducting cells [38]. Therefore it is logically implied that incorporating into a mathematical model all of the individual electric currents occurring in the cardiac cycle would be an impossible task. However, one feasible option is to add up all those small electric currents, and model them as an equivalent electric source. The modeling of the transmission medium for the body is a complicated task as well, since such model must take into account not only the geometrical structure of the human body (heart, organs, veins, thoracic cavity, lungs, fat, muscle and skin), but also its conductivity properties.

The use of electromagnetic theory can be applied to find a solution to the analysis of the electromagnetic activity of the human heart. Using Maxwell’s equations, specifically Faraday’s law of induction, it is possible to obtain a complete analytic model of the electromagnetic behavior of the human heart. This can be done because the source, the propagation medium and the induced electric potentials can be modeled and solved by Faraday’s equation. Moreover, Faraday’s law of induction provides an insight of the mathematical relation between the electrocardiogram (ECG) and the vectorcardiogram (VCG) or Heart Vector introduced in [6]. The following detailed derivation of the mentioned relationship is based on the work presented in [20]. The model presented has the purpose of describing the mathematical relation between the heart, the ECG, and the VCG. The derivation begins with the Faraday’s law of induction:
where \( v \) is the electric potential measured at the surface of the body, \( \hat{\mathbf{E}} \) is the quasi-static electric field vector on torso’s surface induced by the dipolar source, \( \hat{dl} \) is the vector differential describing the path of integration from reference point \( p_0 \) on the surface of the torso to the interest point \( p \) located in torso’s surface as well [39]. The use of a reference point is a common practice in ECG analysis, since the potential has to be measured between two different points. In the precordial leads electrode placement, the reference point is a combination of electrodes put at strategic places in the body (limbs) so the combined potential at those places remain constant throughout the cardiac cycle. In the same manner, Faraday’s law of induction, as presented in (4.2) makes use of a zero potential reference point far from the source.

As mentioned above, Faraday’s law states the relation between the ECG and a vector characterizing the VCG. The first step in the analysis of this relation is to assume that the space and, hence, the differential vector, is on Cartesian or rectangular coordinates, as expressed in (4.2):

\[
\hat{dl} = dx \hat{a}_x + dy \hat{a}_y + dz \hat{a}_z
\]  

Similarly, the quasi-static electric field vector is expressed in Cartesian coordinates:

\[
\hat{\mathbf{E}} = E_x \hat{a}_x + E_y \hat{a}_y + E_z \hat{a}_z
\]

Substituting (4.2) and (4.3) into (4.1) yields the following expression:

\[
v = \int_{p_0}^{p} \hat{\mathbf{E}} \cdot \hat{dl}
\]

After some rearrangement of the terms, the next equation is obtained:

\[
v = \int_{p_0}^{x} E_x \hat{a}_x \cdot dx \hat{a}_x + \int_{p_0}^{y} E_y \hat{a}_y \cdot dy \hat{a}_y + \int_{p_0}^{z} E_z \hat{a}_z \cdot dz \hat{a}_z
\]
Since it is assumed that the heart, more specifically the dipole source, is enclosed in a volume conductor the integration path must be considered not only in its vector form, but also in its contribution to the surface potential \( v \). In other words, the medium between the source and the point of interest (the place in the torso where potential is measured) must be taken into consideration as well. In order to do this, it is necessary to assume that the zero potential reference point location is at \((x_0, y_0, z_0)\). If \((x_0, y_0, z_0)\) is assumed to be at \((0,0,0)\), then (4.5) is modified. Now the path of integration is from \((0,0,0)\) to \((x, y, z)\); the equation is balanced by adding the known reference voltage, but since it is assumed to be a zero potential point, the next expression is obtained:

\[
v = \frac{l_x}{l_x} \int_0^k E_x \hat{x} \cdot dx \hat{x} + \frac{l_y}{l_y} \int_0^y E_y \hat{y} \cdot dy \hat{y} + \frac{l_z}{l_z} \int_0^z E_z \hat{z} \cdot dz \hat{z} \quad (4.6)
\]

In order to take into account the contribution to the surface potential of the integration path it is necessary to include a new term. This new term, denoted by \( L = (l_x, l_y, l_z) \), represents the medium between the source and the point of interest in the surface of the body. Therefore, the expression in (4.6) changes to:

\[
v = \frac{l_x}{l_x} \int_0^k E_x \hat{x} \cdot dx \hat{x} + \frac{l_y}{l_y} \int_0^y E_y \hat{y} \cdot dy \hat{y} + \frac{l_z}{l_z} \int_0^z E_z \hat{z} \cdot dz \hat{z} \quad (4.7)
\]

Rearranging terms, a dot product expression in which the contribution of both vectors is obtained:

\[
v = (l_x \hat{x} + l_y \hat{y} + l_z \hat{z}) \cdot \left[ \int_0^k E_x \hat{x} \cdot dx \hat{x} + \int_0^y E_y \hat{y} \cdot dy \hat{y} + \int_0^z E_z \hat{z} \cdot dz \hat{z} \right] \quad (4.8)
\]

Since this is a dot product, (4.8) can be expressed in short notation:

\[
v = \tilde{L} \cdot \tilde{V} \quad (4.9)
\]

where \( v \) is the measured electric potential, \( \tilde{L} \) is the vector that characterizes the medium, linking the reference with the point of interest in which electric potential is to be measured, and \( \tilde{V} \) is the vector modeling the source inducing the measured potentials.
The equation expressed in (4.9) describes the relation between the measured electric potentials at
the body’s surface by the ECG and the heart acting as a generating source, as well as the propagating
medium. Also, (4.9) permits to realize that the vectorcardiogram is an equivalent vector representation
of the heart seen as source inducing potentials onto the surface of the body.

4.3 Dipole Model of the Human Heart

Even though the previous mathematical model completely describes the electromagnetic activity
of the human heart, there is another useful alternative: the dipole model of the human heart. This model
assumes a dipolar source located inside the heart that induces the electric potential measured at the
surface of the chest. The model makes use of Faraday’s law of induction, Ohm’s law and the definition
of the antenna’s dipole moment. Even though the model used in this work is the newly introduced
single-moving dipole model, the derivation of the equations is made based on the single-fixed dipole
model; both multiple-fixed and single moving dipole models are extensions of the single fixed dipole
model. All of the equations derived in this section are based on the work presented in [20].

The first step requires the expression of Faraday’s law of induction in differential form. The
following expression is formulated in terms of the distance, \( r \), between the source and the point of
interest:

\[
\hat{E}(r) = -\nabla \Phi(r) - \frac{\partial \hat{A}}{\partial t}
\]  (4.10)

where \( r \) is the distance of the point of interest, \( \Phi(r) \) is the measured electric potential and \( \hat{A} \) is
the magnetic vector potential. According to [20], the ECG signal being a time-dependent signal implies
that such signals have a frequency, and consequently a wavelength. Since the frequency of ECG signals
is very low, changes in the magnetic vector potentials over time are so small so the second term in (4.10)
drops to zero. This property is called the quasi-static case of Faraday’s law [20]:

\[
\hat{E}(r) = -\nabla \Phi(r)
\]  (4.11)
For this case, Ohm’s law can be used to relate the quasi-static field vector \( \hat{E}(r) \) to the current density in the conductive medium with conductivity \( \sigma \):

\[
\hat{J}(r) = \sigma \hat{E}(r)
\]  

(4.12)

Solving for \( \hat{E}(r) \) in (4.12) and substituting into (4.11) yields the following equation:

\[
\hat{J}(r) = -\sigma \nabla \Phi(r)
\]  

(4.13)

Since it is assumed that the current source inside the heart is dipolar, it is possible to define the current density in the propagating medium. The current density \( \hat{J}(r) \) is given by a monopole described by the following equation:

\[
\hat{J}(r) = \frac{I_0}{4\pi r^2} \hat{a}_r
\]  

(4.14)

where \( I_0 \) is the initial current of the monopole, \( \hat{J}(r) \) is the current density vector, \( r \) is the distance from the source to the observation point [39]. Since the current density vector changes only in function of \( r \), the gradient in (4.13) can be substituted by a partial derivative, and after substituting (4.14) into (4.13) and solving for the partial derivative, the next expression is obtained:

\[
\partial \Phi(r) = -\frac{I_0}{4\pi \sigma r^2} \, dr
\]  

(4.15)

The previous equation is in differential form, so it is possible to integrate the potential in the left side and the distance in the right side. After performing integration, the next expressions are obtained:

\[
\int_{0}^{\Phi} \partial \varphi(r) = \int_{0}^{\frac{1}{R^2}} dR
\]  

(4.16)

\[
\Phi(r) = \frac{I_0}{4\pi \sigma r}
\]  

(4.17)
The expression in (4.17) describes the potential \( \Phi(r) \) at a distance \( r \) produced by a monopolar source. The model of the human heart requires finding the potential \( \Phi(r) \) at a distance \( r \) produce by a dipole. According to [39], a dipole is composed of two monopoles with opposite charges separated by a very small distance. The overall contribution to the point of interest potential of the individual monopoles is found by using the superposition principle [20]. For a dipole, two individual monopoles with distances \( r_1 \) and \( r_2 \) superpose:

\[
\Phi(R) = \varphi_{m+}(R) + \varphi_{m-}(R)
\] (4.18)

\[
\varphi_{m+}(R) = \frac{I_0}{4\pi\sigma r} \left( \frac{1}{r_1} \right)
\] (4.19)

\[
\varphi_{m-}(R) = -\frac{I_0}{4\pi\sigma r} \left( \frac{1}{r_2} \right)
\] (4.20)

\[
\Phi(R) = \frac{I_0}{4\pi\sigma r} \left( \frac{r_2 - r_1}{r_1 r_2} \right)
\] (4.21)

Now, according to [20, 39] the distance \( r_2 - r_1 \) can be approximated by \( d \cos \theta \) and the distance product \( r_1 r_2 \) can be approximated by \( r^2 \) [39]. Then, the expression in (4.21) becomes:

\[
\Phi(R) = \frac{I_0 d \cos \theta}{4\pi\sigma r^2}
\] (4.22)

The moment, \( \hat{m} \), of the dipole \( \Phi(R) \) is defined as the product of the initial current of the dipole and the displacement vector \( \vec{d} = d \cos \theta \). Then, the dipole moment of \( \Phi(R) \) can be easily identified from the numerator of (4.22):
where \( \mathbf{m} \) is the dipole moment of \( \Phi(R) \) and \( \mathbf{a}_r \) is the radial unit vector pointing from the source out to the volume conductor surface. Similarly to (4.8), (4.23) can be expressed in dot product form:

\[
\Phi(R) = v_p = \mathbf{c} \cdot \mathbf{m}
\]  

where \( \Phi(R) \) and \( v_p \) are the same and stand for the potential at the point of interest, \( \mathbf{m} = [m_x, m_y, m_z]^T \) is the dipole moment of the generating source and \( \mathbf{c} \) is the Lead Vector, linking the potential the induced potential at the point of interest, the propagating medium and the source. The Lead Vector function is expanded as:

\[
\mathbf{c} = \left( \frac{A_x}{4\pi\sigma r^2} \right) \mathbf{a}_x + \left( \frac{A_y}{4\pi\sigma r^2} \right) \mathbf{a}_y + \left( \frac{A_z}{4\pi\sigma r^2} \right) \mathbf{a}_z
\]  

4.4 The Single-moving Dipole Model

As described by the equations presented in the previous section, the heart acting as a generating source of electromagnetic activity inducing an electric potential at the surface of the body, modeled as the boundary of the volume conductor enclosing the source, can be modeled as a dipolar source propagating energy in a conductive medium. The single-fixed dipole model of the human heart assumes a single dipolar source at a fixed location inside the heart inducing an electric potential at the boundary of the volume conductor enclosing it. A vector models the medium between the dipolar source and the surface of the body, so the source induces an electric potential at a point in the surface of the body. In a three dimensional Euclidean space, the relation between source’s dipole moment, the vector
characterizing the propagation medium, and the induced potential in a single point on body’s surface is represented by the following equation:

\[ v(x, y, z, t) = \mathbf{c}(x, y, z) \cdot \mathbf{m}(x, y, z, t) \] (4.26)

where \( v(x, y, z, t) \) is the time dependent potential measured at the surface of the body, and it’s the product of the source’s time dependent dipole moment \( \mathbf{m}(x, y, z, t) \) and the vector characterizing the medium of propagation \( \mathbf{c}(x, y, z) \). The single-fixed dipole model of the human heart is assumed to be at a fixed location inside the heart throughout the entire cardiac cycle. The dipole is considered as time dependent since its magnitude and direction change accordingly to the cardiac cycle evolution. Figure 4.1 illustrates the concept of the single-fixed dipole model.

![Figure 4.1](image.png)

**Figure 4.1.** Description of the single fixed dipole model acting as a generating source enclosed in a volume conductor with \( \sigma \neq 0 \). The source \( \mathbf{m} \), induces electric potential at the boundary of the volume conductor, at the point \( v \), i.e. the surface of the body.

Since the position in space of the dipole is assumed to be known, the dipole moment magnitude and orientation are depending only on time. The single-fixed dipole model can be expressed in reduced vector form as:
\[ v(t) = \bar{c} \cdot \bar{m}(t) \]  

The single-fixed dipole model is used then, to represent induced electric potentials. It is important to remark that the cardiac electrical activity is a complex combination of all of the contributions made by all cardiac cells. However, it has been found that using equivalent source model, like the single-fixed dipole model provides a good representation for those distributed potentials and currents occurring in the heart \([40, 41]\). For a single measurement point in the torso, and decomposing the dipole moment and the lead vector into their orthogonal components, the next equation is obtained:

\[ v(t) = \begin{bmatrix} c_x & c_y & c_z \end{bmatrix} \begin{bmatrix} m_x(t) \\ m_y(t) \\ m_z(t) \end{bmatrix} \]  

(4.28)

After performing the dot product of the two vectors:

\[ v(t) = c_x \hat{a}_x \cdot m_x(t) \hat{a}_x + c_y \hat{a}_y \cdot m_y(t) \hat{a}_y + c_z \hat{a}_z \cdot m_z(t) \hat{a}_z \]  

(4.29)

\[ \bar{m} = \begin{bmatrix} 1, 0, 0 \end{bmatrix}^T \]

\[ \bar{m} = 1 \hat{a}_x \]

From the previous equation it can be inferred that the dipole moment components are static in their origin but their magnitudes, and hence the orientation of the vector, are time dependent. On the other hand the lead vector coefficients \(c_x, c_y\) and \(c_z\) do not change over time. The reason for the lead vector and its coefficient not changing over time is due to the fact that a lead vector characterizes the medium between a fixed source in a known location and a single measurement point in the torso’s surface. Therefore, every electric potential measuring site used for ECG/BSPM analysis must have a lead vector linking it to the source inducing the potential. For \(m\) measurement sites in the torso, equation (4.29) becomes:
Assuming vector form, the single-fixed cardiac dipole model can be expressed as follows for \( m \) torso measurements:

\[
\begin{align*}
 v^1(t) &= c^1_x \cdot m^1_x(t) + c^1_y \cdot m^1_y(t) + c^1_z \cdot m^1_z(t) \\
v^2(t) &= c^2_x \cdot m^2_x(t) + c^2_y \cdot m^2_y(t) + c^2_z \cdot m^2_z(t) \\
&\vdots \\
v^m(t) &= c^m_x \cdot m^m_x(t) + c^m_y \cdot m^m_y(t) + c^m_z \cdot m^m_z(t)
\end{align*}
\]  

(4.30)

Another widely used model for modeling the electromagnetic behavior of the human heart is the multiple-fixed model of the human heart, which is an extension of the single-fixed cardiac dipole model. In this model, instead of a single-fixed source in known location inducing potentials at the torso’s surface, several dipole sources at fixed-known locations inside the heart are considered simultaneously. In other words, the induced potential measured at body’s surface is a summation of the individual contributions made by all of the single-fixed dipoles. The multiple-fixed dipole model is characterized by the following equation, for a single measurement site in the torso and \( n \) fixed dipole sources:

\[
v(t) = \bar{c}_1 \cdot \bar{m}_1 + \bar{c}_2 \cdot \bar{m}_2 + \cdots + \bar{c}_i \cdot \bar{m}_i + \cdots + \bar{c}_n \cdot \bar{m}_n
\]

(4.32)

For \( m \) measurements in the torso and \( n \) dipole locations, the multiple fixed-dipole model can be expanded as:

\[
\begin{align*}
 v^1(t) &= \bar{c}_1^1 \cdot \bar{m}_1 + \bar{c}_2^1 \cdot \bar{m}_2 + \cdots + \bar{c}_i^1 \cdot \bar{m}_i + \cdots + \bar{c}_n^1 \cdot \bar{m}_n \\
v^2(t) &= \bar{c}_1^2 \cdot \bar{m}_1^2 + \bar{c}_2^2 \cdot \bar{m}_2^2 + \cdots + \bar{c}_i^2 \cdot \bar{m}_i^2 + \cdots + \bar{c}_n^2 \cdot \bar{m}_n^2 \\
&\vdots \\
v^m(t) &= \bar{c}_1^m \cdot \bar{m}_1^m + \bar{c}_2^m \cdot \bar{m}_2^m + \cdots + \bar{c}_i^m \cdot \bar{m}_i^m + \cdots + \bar{c}_n^m \cdot \bar{m}_n^m
\end{align*}
\]  

(4.33)
In vector product form:

\[
[v(t)]^w = [c]^w_n [m(t)]^w_n
\]  \hspace{1cm} (4.34)

Although the single-fixed and multiple-fixed dipole models provide a strong mathematical representation of the cardiac electrical activity, those models assume a fixed-location for all of dipolar sources during the cardiac cycle. This represents a disadvantage when trying to model the trace that the source leaves throughout the cardiac cycle. In other words and as previously explained, heart’s electrical activity is majorly concentrated in the atrial region during the P-wave, in the ventricular region during the QRS-complex, and in the Bundle of His region during the T-wave. Unfortunately, the single-fixed and multiple-fixed dipole models do not permit to trace the centers of major cardiac activity, since in the single-fixed model a single static dipole generates the induced potential, whereas in the multiple-fixed case, induced potential is a result of the summation of all the contributions made by the fixed dipolar sources at the same time.

The heart’s electrical activity is not limited to a single point inside the heart but is rather concentrated around a cardiac region, it is possible to model the origin of such cardiac electrical activity as a dipolar source located in a specific part of the heart. For the aforementioned reasons and the fact that the two previously described dipole models cannot be used to detect the path left by the dipolar sources during the cardiac cycle, a new dipole of the human heart is introduced: the single-fixed dipole model. This new model is a hybrid combination of the single-fixed and the multiple fixed dipole models. In other words, the new model takes the best features of the other two models in order to be able to solve the problem of dipole path detection. In this model, \( n \) dipoles are assumed to be fixed and distributed all over the heart, in locations such as the AV and SA nodes, the Bundle of His, right and left ventricular areas, Purkinje fibers and all other conducting fibers and cells of the heart. Then at each instant of time during the cardiac cycle, each one of the \( n \) dipoles is assumed to be the solely generating source for the measured potentials in the torso’s surface for that instant of time. For \( m \) measurements in the torso, Eq. (4.31) is solved for \( \bar{m}(t) \) at each one of the \( n \) dipoles. That is, all of the \( n \) dipoles are considered
simultaneously but individually as the generating sources inducing the measured potentials. At each instant of time \( t \), a dipole optimization process is performed and a single dipole location is selected as the single acting generating source for that instant of time only. The process is repeated again for the next instant of time, considering again \( n \) dipoles as possible sources for the induced potentials measured at that particular instant of time. The result of this process is a changing location over time of the sources of major cardiac electric activity in the heart, i.e. the path “left” by the dipolar source as it evolves along with the cardiac cycle.

It can be noticed that the single-moving dipole model is an upgrade to the single-fixed dipole model with features included from the multiple-fixed dipole model. It is called single-moving dipole because it changes in location over time, giving the illusion of a moving source inside the heart. Although the number of possible dipoles used \( n \) is finite by nature and the movement of the dipolar source is by consequence discrete, it can be naturally inferred that as \( n \to \infty \), that is if the number of possible dipole sources is increased in such a way that every single part or region in the heart is covered by a possible dipole source, the movement trace by the equivalent generating source would no longer be discrete but continuous. Another important feature of the single-moving dipole model of the human heart is the necessity to solve for the dipole moment \( \mathbf{m}(t) \) via the inverse problem of electrocardiography for each one of the \( n \) dipoles and at each instant of time \( t \). Thus, for \( t \) time samples and \( n \) dipoles, the inverse problem of electrocardiography needs to be solved \( n \times t \) times. Even though the amount calculations might appear overwhelming at the first sight, it must be remembered that the system needed for single-fixed dipole model is less complex than the system needed for the solution of the multiple-fixed dipole model. Therefore, instead of solving a complex system \( t \) times, \( n \times t \) simple systems are solved.

Since the ECG data used in this research are the precordial ECG data, the number of measurements in the torso is \( m=6 \). Then, the single-moving dipole model requires the solution of the following system \( n \times t \) times, for \( n \) dipoles and \( t \) time samples:

\[
[v]^6 = [c]^6[m]^6
\]  
(4.35)
where $[v]^b$ is a column vector with the induced torso’s potentials, $[c]^b$ is a $6 \times 3$ matrix with the coefficients of the vectors characterizing the medium between the dipolar source and the six measurement sites in the torso, and $[m]^b$ is a $1 \times 3$ matrix with the orthogonal components of the dipole moment at time sample $t$. So, for $t$ time samples and $n$ dipole locations, (4.35) can be also expressed as:

$$
[v(1)]^b = [c(1)]^b[m(1)]^b, [v(2)]^b = [c(2)]^b[m(2)]^b, \ldots, [v(t)]^b = [c(n)]^b[m(1)]^b \\
[v(2)]^b = [c(1)]^b[m(2)]^b, [v(2)]^b = [c(2)]^b[m(2)]^b, \ldots, [v(2)]^b = [c(n)]^b[m(2)]^b \\
\vdots \\
[v(t)]^b = [c(1)]^b[m(t)]^b, [v(t)]^b = [c(2)]^b[m(t)]^b, \ldots, [v(t)]^b = [c(n)]^b[m(t)]^b
$$

(4.36)

4.5 The Concept of Cardiac Activation Sites

As explained above, heart’s electrical activity is not concentrated in a single point within the heart, but rather distributed all over the heart. However, the majority of heart’s electrical activity is concentrated in a region inside the heart, depending on the current segment of the cardiac cycle. This region in which the majority of the cardiac activity is concentrated is called a Cardiac Activation Site [42]. Cardiac activation sites provide time dependent information about the location of the sources of electrical activity on the heart and can be used for potential cardiac malignancies detection.
Chapter 5: A Solution to the Laplace’s Equation for Lead Vector Calculation

The solution to the stated problem requires the use of a realistic FEM model of the human body. Such model includes the geometrical information of the heart, veins, organs, thoracic cavity, lungs, fat, muscle and skin of a human torso, as well as their conductivity values. In the forward problem of electrocardiography, potentials in any part of this model are calculated from a known dipolar source. Therefore, the solution to the forward problem of electrocardiography is obtained from the solution of the volume conductor problem. The mathematical model, the FEM model, the solution to the volume conductor problem, as well as its crucial role in the calculation of the important lead vector, and lead vector coefficients will be discussed in the following sections.

5.1 The Volume Conductor Problem

According to [15], before the introduction of computers, and hence before the creation of computational algorithms, there were only two forms to solve the forward problem, that is to resolve for electric body surface potentials due to equivalent dipole sources. The first was to assume a rectangular or a spherical shape or a cylinder for the body and use the analytical solution previously obtained for a dipole inside the shape. The second, and more complicated algorithm, made use of a physical analog to the human body like an electrolytic tank for the torso to measure the potentials at the surface of the tank produced by a dipole placed inside. However, the creation and development of computer and computation techniques came and revolutionized the way in which the forward problem of electrocardiography was resolved. The appearance of computers into the scientific plane meant to the forward problem the capacity of creating realistic model of the human body. Numerical techniques, then, could be applied for the calculation of surface body potentials.

In general, such approaches can be divided into two main categories: surface methods and volume methods [15]. In surface methods different torso regions are all of isotropic conductivity, and only the interface between the different regions, e.g. boundaries between organs, muscle and skin, etc, are triangularized and represented in the numerical torso model. Any anisotropic region is approximated by an equivalent isotropic region and included in the numerical model. Surface methods calculate
potentials projected into the triangle elements due to internal heart sources. On the other hand, volume methods, the entire 3D torso volume is represented in the numerical model, usually with tetrahedral and hexahedral elements, and the potential is determined everywhere in the torso model, not only on the surface. Volume methods are subdivided into finite elements, finite differences and finite volume methods, and are capable of handling regions with anisotropic conductivity without any further manipulation or processing.

Both surface and volume methods yield results with comparable accuracy. Surface methods use simpler torso numerical models with fewer elements. But the integral equations required for its solution, and the matrix needed to solve for such integrals is fully populated and very complex [15]. Volume methods require more complex torso models, with more elements, and more solutions in the form of electric potential to be computed. However, potentials at each point in the model are expressed in terms of neighboring potentials. Therefore, the matrix needed for the potentials calculations, although larger than the matrix needed in surface methods, is sparse and thus easier to solve [15]. For the aforementioned reasons, even though volume methods require more complex model and a larger formulation, the solution is easier to obtain and is less prone to numerical errors. Additionally, the fact that volume methods solve for the potential in every point on the human torso numerical model represents an enormous advantage for the purposes of this research, since for PPM calculation and projection potentials at the surface of the heart, the pericardium, are needed. More information about volume conductor problem and its solutions can be found in [43, 44, 45].

5.2 The Solution to the Poisson’s Equation

The most common and more robust method in the family of volume methods applied for the solution the forward problem of electrocardiography, is the Finite-Element method [15]. In this method, torso geometry is approximated by a set of contiguous volume elements generally with tetrahedral forms. In this fashion, the model can be subdivided into pieces for its analysis, so the reason for its definition of “finite elements”. The main advantage of this method is the ease in which anisotropies in the volume elements are handled. The finite-elements method solves the following Poisson’s equation:
\[ \nabla \cdot (\sigma \nabla \Phi) = \nabla \cdot J_s = -I_{sv} \] 

(5.1)

where \( \Phi \) is the potential at the nodes of the tetrahedral element, \( J_s \) is the current density, and \( \sigma \) is the conductivity. The boundary conditions of the problem are the continuity of the potential and the normal component of the current at all internal interfaces between the elements. Mixed Neumann and Dirichlet boundary conditions occur at the outer torso interface of the form:

\[ \Phi = \Phi_a \text{ on } S_{01} \] 

(5.2)

\[ (\sigma \nabla \Phi) \cdot \vec{n} dS = J_n dS \text{ on } S_{02} \] 

(5.3)

where \( \Phi_a \) is a known externally applied potential, \( J_n \) is an injected current normal density, \( \vec{n} \) is a unit normal vector, and the union of the disjoint surfaces \( S_{01} \) and \( S_{02} \) equals the entire torso surface \( S_0 \). The solution for (5.1) can be found applying the principle of weighted residuals or Galerkin’s method [46]. Equation described in (5.1) can be approximated by:

\[ \hat{\Phi}(x, y, z) = \sum_{i=1}^{m} \beta_i(x, y, z)\Phi_i \] 

(5.4)

where \( \Phi_i \) is the \( i^{th} \) unknown potential for \( m \) point or nodes in the volume conductor model, \( \beta_i \) are interpolating polynomials. Interpolating polynomials \( \beta_i \), are equal to 1 at node \( i \), and are zero at all other nodes including those nodes in which the potential is known. Substituting (5.4) in (5.1) the following equation is obtained:

\[ \nabla \cdot (\sigma \nabla \hat{\Phi}) + I_{sv} = R \] 

(5.5)
where \( R \) is a residual. The method of weighted residuals attempts to reduce \( R \) to zero, using a weak formulation (Galerkin):

\[
\int_v \nabla \cdot (\sigma \nabla \Phi) + I_{\text{vol}} W_i dV = \int_v R W_i dV = 0 \quad i = 1, 2, \ldots, m
\]  
(5.6)

Since there are \( m \) equations, \( m \) unknown potentials \( \Phi_i \) can be determined. In the Galerkin formulation, the weights \( W_i \) are selected to be the same as the interpolation polynomials \( \beta_i \). The following expression is obtained:

\[
\int_v \beta_i \nabla \cdot (\sigma \nabla \Phi) dV + \int_v \beta_i I_{\text{vol}} dV = 0, \quad i = 1, 2, \ldots, m
\]  
(5.7)

The second integral must be evaluated only over the heart region \( VH \), while the first integral on (5.7) is integrated by parts to obtain:

\[
\int_S \beta_i (\sigma \nabla \Phi) \cdot \vec{n} dS - \int_v (\sigma \nabla \Phi) \cdot \nabla \beta_i dV = -\int_{VH} \beta_i I_{\text{vol}} dV
\]  
(5.8)

Since the potential on \( S_{01} \) is known, the interpolating polynomials are zero there:

\[
\int_S \beta_i (\sigma \nabla \Phi) \cdot \vec{n} dS = \int_{VH} \beta_i I_{\text{vol}} dV + \int_{S_{01}} \beta_i J_{\text{vol}} dV, \quad i = 1, 2, \ldots, m
\]  
(5.9)

Equation (5.9) also holds for each individual volume element, with \( I \) now ranging only \( r \) nodes belonging to that specific element, and with the potential within each element being approximated by:

\[
\hat{\Phi}^{(e)}(x, y, z) = \sum_{i=1}^{r} \beta_i^{(e)}(x, y, z) \Phi_i
\]  
(5.10)
The subscript \((e)\) in (5.10) indicates the equation holds only for an element. The interpolating polynomials \(\beta_i^{(e)}\) are generally selected to be linear and in such a way that the potential is continuous across element interfaces. By substituting \(\hat{\Phi}^{(e)}\) from (5.10), it can be seen that (5.9) for a single element reduces to the matrix form:

\[
A^{(e)}\Phi^{(e)} = F^{(e)}
\]  

(5.11)

where \(\Phi^{(e)}\) is the column vector of unknown potentials, \(F^{(e)}\) is the column vector of the right-hand-side integrals of (5.9), and the elements of the \(r \times r\) matrix \(A^{(e)}\) involve integration of the products of the partial derivatives of the interpolating functions. The single element relations can be assembled into a global matrix equation for \(m\) elements:

\[
A\Phi = F
\]  

(5.12)

where \(A\) is now a \(m \times m\) matrix and \(\Phi\) and \(F\) are \(m \times 1\) column vectors containing the potential at each one of the \(m\) points in the model and the right-hand-side information for each \(F^{(e)}\) in the elements, respectively.

5.3 **The Concept of Lead Vector**

The equation described in (5.12) fully describes the procedure needed to arrive to the solution to the forward problem of electrocardiography. It must be recalled, the in the forward problem a known source inside the FEM volume conductor model of the human torso induces the potentials not only in the surface of the body but also in every single point inside the FEM model. Matrix \(A\) and column vector \(F\) on (5.12) contain the information of the known source and the conductivity information. Therefore, potential at the desired solution space is given by:

\[
\Phi = A^{-1}F
\]  

(5.13)
However, in order to be able to find the dipole moment of the source in Equation (4.31), the matrix \([c]\), with the lead vector coefficients must be calculated. The lead vector characterizes the medium between the source and a single measurement point. The concept of lead vector as the link between the dipole moment and the potential measurement site is now extended to the characterization of the medium between the source and any point or region in the human torso geometry, not only between the source and the surface of the volume conductor. However, it is important to realize that even though equations (4.31) and (5.12) both are intended to solve for the forward problem of electrocardiography, the theory behind such equations is remarkably different.

In the case of equation (5.12), dipole information is entered in vector form and then converted into current source formulation contained in \(A\) and \(F\). On the other hand, the equation described in (4.31) relies on the information provided by 1) the lead vector coefficients and 2) the known dipole moment information. Solving for the electric potential in (4.31) and (5.12) yields for \(m\) points in the model:

\[
A^{-1}F = \bar{v} \cdot \bar{m}
\]  
(5.14)

However, it is not possible to solve for \(\bar{v}\) in (5.14), since it would require calculating the inverse of \(\bar{m}\), which is a column vector. By definition, the inverse of a vector does not exist. Therefore, lead vectors must be calculated using both (5.13) and (4.31) in its expanded form as presented in (4.29) in sequential order. That is, with a known dipole source’s moment the potential \(\Phi\) is obtained. Then, the obtained \(\Phi\) is plugged into (4.29) and solved for \(\bar{v}\). The calculation of the coefficients in \(\bar{v}\) is fully explained and derived in section 6.2.

5.4 Six-lead Time Varying Pericardium Potential Map

Using the Finite-Elements method for solving the volume conductor problem for forward problem solution purposes represents an enormous advantage for PPM creation since, unlike surface methods, potential is calculated in every single point in the model. That is, from a known source electric
potentials both in the torso’s surface and in the pericardium can be calculated. In this research, PPM calculation takes places after obtaining an equivalent dipole moment out from the six-precordial leads ECG. The dipole moment $\vec{m}(t)$ is modeled as a 1-by-3 column vector:

$$
\vec{m}(t) = 
\begin{bmatrix}
  m_x \\
  m_y \\
  m_z
\end{bmatrix}
$$

(5.15)

The potentials at the pericardium are obtained after solving (4.31). The solution space of (4.31) is determined by the number of nodes of a 3D FEM model of the pericardium. This model accounts only for the geometry of the heart’s surface, i.e. the pericardium, and has the purpose of displaying the obtained pericardium potential in a 3D space. Then, for $n$ points or nodes in the pericardium 3D FEM model, the pericardium potentials at time sample $t$ are obtained by:

$$
[v(t)]^n = [c]^n [m(t)]^n
$$

(5.16)

where $[v(t)]^n$ is an $n$-by-1 column vector, $[c]^n$ is a $n$-by-3 matrix containing the orthogonal components or coefficients for $n$ lead vectors, and $[m(t)]^n$ is a 3-by-1 vector with the orthogonal dipole moment components. This equation is for a time instant $t$, therefore the time varying PPM is obtained by solving for (5.16) at each instant of time and projecting the potentials into a triangulated FEM model of the pericardium. The PPM is then a color-coded map that accounts for the potential distribution on the pericardium. As time samples evolve, the PPM permits to analyze the distribution of electric potentials on heart’s surface over time.
Chapter 6: Proposed Methods

The proposed method for identifying the source of major cardiac activity during the cardiac cycle requires the solution to the inverse problem of electrocardiography as means for calculating a moving dipole source inside the heart. As discussed before, in the inverse problem of electrocardiography a known measured body surface electric potential is generated by a dipolar source inside the heart. Then, after solving equation (4.31) for the dipole moment $\vec{m}(t)$ and then performing dipole optimization at each time sample of the precordial ECG signals gives the location in time of the equivalent dipole source. Hence, the trace left by the equivalent source can be calculated and plotted. Additionally, the polarization patterns occurring at the pericardium can be calculated via the forward problem of electrocardiography as presented in (4.31); potentials at the pericardium are calculated from the dipole moment $\vec{m}(t)$, which is in turn obtained out from the six-precordial leads ECG, and then projected in a 3D model of the human heart surface. This process is repeated for every time sample in the ECG signals.

Therefore, the analysis and results presented in this thesis work require the solution of the forward problem as presented in (5.12), the solution of the inverse problem in (4.31), the calculation of the lead vector coefficients for the characterization of medium between the source and the point of interest, a solution for $[m]^m$ in (4.31), which is an over-determined system of linear equations requiring a numerical approximation to the solution. Also, a digitized version for all of the patients’ precordial ECG leads is needed in order to be able to perform the analysis in a computer. In this research project, spectral analysis is applied to the original patients’ ECG data in order to detect the predominating spectral components of the signal. Finally, a 3D model of the human heart’s surface (pericardium) is created out from a cloud of points; the solution for the pericardium potential distribution is projected at each one of the nodes composing the 3D model.

6.1 SCIRUN/BioPSE

The SCIRUN/BioPSE package is an open-source Problem Solving Environment (PSE) software capable of simulating EM fields in any structure or geometrical shape taking into account boundary conditions, conductivity of the media, as well as other features pertinent to EM analyses [7].
SCIRUN/BioPSE is mainly intended for biomedical applications, such as bioelectric field problems. As it can be deduced, SCIRUN is a powerful tool for field analysis. It is module based; that is, placing and interconnecting the appropriate programming modules in the interface window makes the whole data calculation process. In its simplest way of functioning, the process consists mainly of three steps: a read field is placed as an input, processing modules perform all calculations needed for that field, and the result is displayed graphically. Since the main purpose of SCIRUN is to simulate and model bioelectric fields, units to be taken into consideration are conductivity, potentials, electric field, dipole source, current density, and current source density.

Applied to the work presented in this thesis, SCIRUN has the capability of solving the forward problem of electrocardiography as presented in (5.12) and (5.13), which ultimately leads to the capability of calculating the lead vectors coefficients for both the six precordial leads measurement sites and for all of the point forming the pericardium. In order to obtain the values for the coefficients of the lead vectors, a FEM torso model, from SCIRUN/BioPSE software, was used. This model is comprised of inner organs, such as, liver, lungs, heart, bones, blood, fat, and skin. In addition, their conductivities can be set to those of a human torso. The SCIRUN software does not directly provide the values of the lead vectors. Instead, these values must be calculated using the simulated surface potentials calculated by SCIRUN. Having the values of the lead vectors simplifies the computational problem as the forward problem, and consequently the inverse problem, can be expressed in matrix form as presented in (4.31).

6.2 Lead Vector Coefficients Calculation

As it has been previously discussed in this thesis, the lead vectors are a crucial part for the intended ECG analysis and results. As explained in Section 5.3, the lead vector characterizes the conductive medium between the source (expressed in terms of its dipole moment components), and the point(s) of interest for measuring the electric potential (expressed as a column vector). Knowing the lead vector and its coefficients permits, as explained above, express the induced potentials at the point or points of interest in terms of the source’s dipole moment. In other words, the source-surface potential quotient is scaled in both direction and magnitude by the lead vectors.
Lead vectors are calculated by solving the forward problem of electrocardiography in two stages. The first stage requires solving (5.13) for \( \Phi \) in SCIRUN. The second stage requires solving the equation described in equation (4.29). For a single measurement site or point of interest, dipole moment information is inputted into SCIRUN, which provides the induced electric potential at the point of interest. Then, the obtained voltage is substituted into (4.29). The x-component of the lead vector is entered into SCIRUN as:

\[
\vec{m} = \begin{bmatrix} \hat{m}_x, \hat{m}_y, \hat{m}_z \end{bmatrix}^T
\]

\[
\hat{m}_x = 1, \quad \hat{m}_y = 0, \quad \hat{m}_z = 0
\]  

Which is equivalent to:

\[
\vec{m} = 1\hat{a}_x
\]

Then, the obtained electric potential is substituted into:

\[
v(t) = c_x\hat{a}_x \cdot m_x(t)\hat{a}_x + c_x\hat{a}_y \cdot m_y(t)\hat{a}_y + c_x\hat{a}_z \cdot m_z(t)\hat{a}_z
\]

(4.29a)

Therefore, the next expression is obtained:

\[
v(t) = c_x\hat{a}_x \cdot 1\hat{a}_x = c_x
\]

(6.3)

Therefore, the obtained electric potential corresponds to the x component of the lead vector, for that specific point of interest. The remaining lead vector components are calculated as follows:

\[
\vec{m} = 1\hat{a}_y
\]

\[
v(t) = c_y\hat{a}_y \cdot 1\hat{a}_y = c_y
\]
\( \bar{m} = 1 \hat{a}_z \)
\[ v(t) = c_z \hat{a}_z \cdot 1 \hat{a}_z = c_z \] (6.5)

It is important to mention that a lead vector links or characterizes the medium between one single dipolar source and a single point of interest for induced potential measurement. Hence, for \( n \) points of interests \( n \) lead vectors \( c \) are needed. Additionally, since there are \( m \) possible dipole calculations, the total number of lead vectors is \( n \times m \). In this research, the six-precordial ECG leads are measured at the torso’s surface and are labeled as \( V_1, V_2, V_3, V_4, V_5 \) and \( V_6 \). The number of possible dipole source used is 20. Then, \( 6 \times 20 = 120 \) lead vectors are needed for calculating the equivalent dipole moments and for reconstructing the original precordial ECG signals. The following system of linear equations is solved for each one of the 20 possible dipole locations, at each time sample \( t \):

\[
V_1 = c_{1x} \hat{a}_x \cdot m_x \hat{a}_x + c_{1y} \hat{a}_y \cdot m_y \hat{a}_y + c_{1z} \hat{a}_z \cdot m_z \hat{a}_z \\
V_2 = c_{2x} \hat{a}_x \cdot m_x \hat{a}_x + c_{2y} \hat{a}_y \cdot m_y \hat{a}_y + c_{2z} \hat{a}_z \cdot m_z \hat{a}_z \\
V_3 = c_{3x} \hat{a}_x \cdot m_x \hat{a}_x + c_{3y} \hat{a}_y \cdot m_y \hat{a}_y + c_{3z} \hat{a}_z \cdot m_z \hat{a}_z \\
V_4 = c_{4x} \hat{a}_x \cdot m_x \hat{a}_x + c_{4y} \hat{a}_y \cdot m_y \hat{a}_y + c_{4z} \hat{a}_z \cdot m_z \hat{a}_z \\
V_5 = c_{5x} \hat{a}_x \cdot m_x \hat{a}_x + c_{5y} \hat{a}_y \cdot m_y \hat{a}_y + c_{5z} \hat{a}_z \cdot m_z \hat{a}_z \\
V_6 = c_{6x} \hat{a}_x \cdot m_x \hat{a}_x + c_{6y} \hat{a}_y \cdot m_y \hat{a}_y + c_{6z} \hat{a}_z \cdot m_z \hat{a}_z
\] (6.6)

The previous equation can be expressed in matrix-vector multiplication form:

\[
\begin{bmatrix}
V_1 \\
V_2 \\
V_3 \\
V_4 \\
V_5 \\
V_6
\end{bmatrix} =
\begin{bmatrix}
c_{1x} & c_{1y} & c_{1z} \\
c_{2x} & c_{2y} & c_{2z} \\
c_{3x} & c_{3y} & c_{3z} \\
c_{4x} & c_{4y} & c_{4z} \\
c_{5x} & c_{5y} & c_{5z} \\
c_{6x} & c_{6y} & c_{6z}
\end{bmatrix}
\begin{bmatrix}
m_x \\
m_y \\
m_z
\end{bmatrix}
\] (6.7)
At each time sample $t$, (6.7) is solved for $m$, and for all of the 20 possible dipole locations. The previous equation calculates the dipole moment out from the six-precordial ECG leads. For the case of PPM reconstruction and projection, the dipole moment obtained from (6.7), is used to reconstruct the potentials at each one of the points conforming the 3D model of the pericardium. The model of the pericardium from SCIRUN consists of 1329 points or nodes. Therefore, equation (6.7) can be rewritten for PPM reconstruction and projection as follows:

$$
\begin{bmatrix}
V_1 \\
V_2 \\
V_3 \\
V_4 \\
V_5 \\
V_6 \\
\vdots \\
V_{1329}
\end{bmatrix}
= 
\begin{bmatrix}
c_{1x} & c_{1y} & c_{1z} \\
c_{2x} & c_{2y} & c_{2z} \\
c_{3x} & c_{3y} & c_{3z} \\
c_{4x} & c_{4y} & c_{4z} \\
c_{5x} & c_{5y} & c_{5z} \\
c_{6x} & c_{6y} & c_{6z} \\
\vdots & \vdots & \vdots \\
c_{1329x} & c_{1329y} & c_{1329z}
\end{bmatrix}
\begin{bmatrix}
m_x \\
m_y \\
m_z
\end{bmatrix}
$$

(6.8)

As an additional fact, the previously presented pair of equations proves one of the hypothesis presented in this thesis: using only the measurements from the six precordial leads can lead to results with high accuracy without the necessity of placing more electrodes for electric potential measurement. In the equation presented in (6.7), the over-determined linear equation system must be solved numerically for the dipole moment $m$. Since the matrix containing the coefficients for the lead vectors is non-square, the obtained solution $m$ is an approximation only, and then subject to inaccuracies. It is evident from (6.7) that as more measurement points, the system greats more over-determined. As more over-determined the system is, more complex is the solution, more computational power is needed to solve for $m$, and consequently more inaccurate the result is. As a consequence, calculating the dipole
moment out from the six precordial leads, produces a more accurate dipole moment $m$, than calculating it from a multi-electrode jacket with more electric potential measurement sites.

6.3 Time Varying Dipole Moment Magnitude

At each time sample $t$ in the set of precordial ECG measurements, 20 different dipole moments are calculated. Since the primary goal of this research is to calculate the location of the equivalent dipole source at each instant of time, an optimization process in which the dipole which betters reconstruct the original set of ECG measurements is performed. In this optimization process the dipole with the greatest dipole moment magnitude is selected as the equivalent dipole source inducing the potentials measured by the precordial leads. The dipole moment is calculated by:

$$|\vec{m}(t)| = \left[ m_x^2 + m_y^2 + m_z^2 \right]^{1/2} \quad (6.9)$$

where $|\vec{m}(t)|$ is the dipole moment magnitude at time sample $t$. Then, the from the pool of dipole moment magnitudes, the greatest dipole magnitude is selected as the equivalent dipole source at that time sample $t$, and its location $l$ as the location inside the heart of the equivalent dipole source. That is, the strongest dipole is the generating source for the six precordial measurements at time; the location of the equivalent dipole source is the location of the strongest dipole. Since, all of the possible dipole sources are located inside the heart, all of the solutions have physical significance and no solution needs to be discarded. This process is repeated at each time sample. In the end, the spatial coordinates (inside the 3D model of the heart) are stored in an array for further manipulation such as plotting the equivalent dipole location at any time instant of the cardiac cycle. The equivalent dipole and its location are calculated as follows, for 20 possible dipole locations:

$$|\vec{m}(t)|_{eq} = \max(|\vec{m}(t)|_1, |\vec{m}(t)|_2, \ldots, |\vec{m}(t)|_i, \ldots, |\vec{m}(t)|_{20}) \quad (6.10)$$

$$l_{eq}(x, y, z) = (x_{eq}, y_{eq}, z_{eq}) \quad (6.11)$$
where $|\overline{m}(t)|_{eq}$ is the equivalent dipole moment magnitude, $|\overline{m}(t)|_i$ is the dipole moment magnitude of the $i^{th}$ dipole, $l_{eq}$ is the location inside the heart of the equivalent dipole source, and $x_{eq}, y_{eq}$ and $z_{eq}$ are the coordinates of the location of the strongest dipole as obtained from (6.10).

### 6.4 Ordinary Least-Squares Solution

The system of linear equations presented in (6.7) is an over-determined system of equations which, by definition, does not have a unique solution [47] since the coefficients matrix $c$ is non-invertible. Then a numerical approximation is needed in order to arrive to a solution. The ordinary least-squares method provides a very good approximation to the solution of the inverse problem described in (6.7). The equation described in (6.7) can be put as a minimization problem as follows [47, 48]:

Let $f = c \cdot m - v$, minimize $F = \frac{1}{2} \|c \cdot m - v\|^2$ \hspace{1cm} (6.12)

where $f$ is the residual function of the product of lead vector coefficients matrix and dipole moment components column vector minus the column vector with the six precordial potentials. The purpose of the least-squares solution is the minimization of $F$, which is the magnitude of the residual function $f$ divided by two.

The equation presented in (6.12) is solved as:

$$F = \frac{1}{2} \|c \cdot m - v\|^2 = \frac{1}{2} (c \cdot m - v)^T (c \cdot m - v) \hspace{1cm} (6.13)$$

$$F = \frac{1}{2} \left[ (c \cdot m)^T (c \cdot m) - (c \cdot m)^T v - v^T (c \cdot m) + v^T v \right]$$

$$F = \frac{1}{2} \left[ m^T c^T cm - m^T c^T v - v^T cm + v^T v \right] \hspace{1cm} (6.14)$$

49
Since both \( m^T c^T v \) and \( v^T c m \) are both constants we can express \( v^T c m \) as \( m^T c^T v \):

\[
F = \frac{1}{2} \left[ m^T c^T c m - m^T c^T v - m^T c^T v + v^T v \right] \\
F = \frac{1}{2} \left[ m^T c^T c m - 2m^T c^T v + v^T v \right] \\
F = \frac{1}{2} m^T c^T c m - m^T c^T v + \frac{1}{2} v^T v
\] (6.15)

Now, since the target variable of this minimization is \( m \), we take the derivative of \( F \) with respect to \( m \) and set it equal to zero:

\[
\frac{\partial F}{\partial m} = c^T c m - c^T v \\
c^T c m - c^T v = 0 \\
c^T c m = c^T v
\] (6.14)

Then the previous equation is solved for \( m \). The result obtained is an extremum, which can be either a minima or a maxima. This extremum point is expressed as:

\[
m = (c^T c)^{-1} c^T v
\] (6.15)

The previous equation can be either a minimum or a maximum of \( F \). For that reason, the second derivative of \( F \) is calculated to determine whether (6.15) is the minimum of \( F \) or not.

\[
\frac{\partial^2 F}{\partial m^2} = c^T c
\] (6.16)

According to [47, 48] \( c^T c \) is always a positive-definite (all of its eigen-values are positive) square matrix. Then if, \( c^T c \) is positive definite, the solution found in (6.15) is the minimum for \( F \). The equation in (6.15) is the most approximate solution for the system in (6.8), since the residual \( F \) is at its minimum.
6.5 Spectral Analysis

A new inclusion that was not considered in previous and similar ECG analyses is the spectrum of the original ECG signals. In this research the spectrum analysis has two purposes: the identification of the frequency of the ECG signal and, thus the duration of the cardiac cycle. Since the spectral analysis detects all of the frequency components of the precordial ECG signal’s spectrum, the frequency component with the greatest magnitude correspond to the frequency of the ECG signal. If the found predominating frequency in a patient’s ECG signal is found to be extremely high, which has not physical meaning, it suggest that there is a potential abnormality in the patient’s ECG trace. The spectral analysis is based in the following Discrete Fourier Transform (DFT) equation [49]:

\[
F(\omega) = \sum_{n=1}^{N} x(n)e^{-j\omega n}
\]  

(6.17)

where \( F(\omega) \) is the spectral response of the ECG signal, \( x(n) \) is the digitized ECG samples, and \( N \) is the total number of samples in \( x(n) \). The duration of the cardiac cycle was determined by extracting the frequency component with the greatest magnitude from \( F(\omega) \), and then calculating the period of the signal.

6.6 Digitized ECG database

Since the analysis presented is computer-based, all of the input signals, i.e. the patient’s precordial ECG signals must be in digitized form. Additionally, in order to achieve a reliable diagnosis a population of test-patients is necessary. In this research a population of 15 patients with no previously diagnosed cardiac malignancies, and 15 with previously diagnosed cardiac illnesses, sampled at 1000 Hz was obtained from Physionet [50], a medical database. Physionet provides several databases with all types of biosignals intended for research purposes.
6.7 3D Model of the Human Heart

The generation of the time varying color-coded PPMs requires the projection of the calculated pericardium potentials onto a 3D dimensional model of the pericardium. The model used in this research is provided by SCIRUN’s FEM model of the human body. The model consists of a cloud of points in space forming a 3D figure of heart’s surface. As mentioned before, the model consists of 1329 points. In order to be able to project the pericardium potentials in the model, and hence be able to plot the pericardium polarization patterns during the cardiac cycle, the cloud of points must be converted into a 3D convex surface model of the pericardium. This is accomplished by applying the embedded Delaunay’s triangulation algorithm in MATLAB to the cloud of points. The Delaunay’s triangulation algorithm joins each one of the nodes in the cloud of points to their most immediate neighboring nodes. The result is the creation of polygonal planes joining the nodes [51]. Even though the pericardium potential data is stored and projected in the model’s nodes, data is interpolated between nodes in such a way that the faces of the polygons represent the data as well [51]. Figure 6.1 depicts the cloud of points forming the 3D model of the pericardium.

Figure 6.1. The 3D model of the pericardium from SCIRUN’s FEM model of the human torso. The shown model is comprised of a cloud of points modeling the surface of the heart. Unlike the FEM model used for solving the forward problem, this model does not take into account tissue’s conductivity information.
**Figure 6.2.** The convex 3D model of the pericardium after the application of the delaunay’s algorithm. After triangulation, the lines joining the nodes, form the edges of the polygons in which potentials are to be projected on.
Chapter 7: Implementation of the Proposed Algorithm

7.1 Introduction

The theory concepts discussed in Chapter 4 and in Chapter 5 as well as the methods proposed in Chapter 6 were applied to the proposed solution for the analysis of ECG signals. The purpose of the research being reported in this thesis work is the development and implementation of an alternative non-invasive method for the aid in the detection and diagnosis of cardiac malignancies. This objective is achieved by making extensive use of the single-moving dipole model of the human heart, the inverse problem of electrocardiography, the forward problem of electrocardiography, as well as other common electrical engineering concepts such as digital filtering and spectral analysis. Compared to the work discussed in Chapter 3, this work has the following advantages:

1) Reconstructed signals are more accurate than found in literature.

2) The dipole location optimization process provides results with the expected physiological significance and with more accuracy than any previously similar analyses. Additionally, it permits to trace the location of the equivalent dipolar source at any time instant during the cardiac cycle.

3) The addition of the spectral analysis programming modules, signified breakthrough in ECG based analyses, since it permitted a pre-diagnosis by the identification of outstanding frequency components in the ECG signals, which in turn can be interpreted as a preliminary sign of a cardiac malignancy.

4) The presented algorithm requires little computational power and can be implemented in a personal computer. Compared to other methods which, require the use of sophisticated medical equipment, e.g. CT scans, MRI and X-rays, the proposed method requires only an ECG data acquisition unit and a computer.
5) This algorithm permits the simultaneous visualization of any number of precordial leads signals and the equivalent dipole localization inside the heart, which means that abnormalities can be easily identified as well as their location.

6) Finally, the presented algorithm allows the visualization and analysis of the potentials distribution over time occurring in the pericardium as a consequence of the changing location of the equivalent dipole source.

The implementation of the algorithm presented here was clinically tested in two populations of patients: the first test group corresponded to 15 patients with no previously detected cardiac conditions and the second group corresponded to 15 patients with a diagnosed cardiac malignancy. The proposed code was written and implemented in MATLAB and consist of three subsystems executed in sequence: analysis of ECG signals, dipole localization and signal reconstruction, and visualization of results. This algorithm was applied for every patient in the population. Results for individual patients were then compiled in order to establish all necessary ranges for the determination of normality or abnormality of the patients’ ECG signals. All of the programming modules and units, were designed and programmed by the author.

7.2 Signal Filtering and Lead Vectors Loading

Prior to the execution of the aforementioned programming subsystems, all the necessary Lead Vectors (LV) must be calculated from SCIRUN as explained in Section 6.2 and exported to MATLAB. Once in MATLAB, all the necessary LVs are stored in a matrix for easy access. Since the precordial leads’ electrode placement sites and the 20 possible dipole source locations do not change for different patients, this step is performed only once. However, the loading of the lead vectors must be performed whenever the analysis requires the application of either the inverse or forward problems.

The ECG signals available from Physionet contain not only the six precordial leads, but also the remaining leads used in the widely used 12-lead electrocardiography [6]. In this case, the six precordial leads measurements must be extracted from the original file. As previously mentioned, the original set
of precordial ECG measurements must be filtered in order to eliminate unwanted low frequency components coming from mechanical artifacts occurring when taking measurements from the patients, and high frequency components due to electric interference. It was found that eliminating high frequency components from the ECG signal improved the condition of the problem. This was reflected by the level of accuracy of the reconstructed signals. The filtering of the signal was achieved by adding a zero-phase band pass filtering unit to the program’s execution in MATLAB. A first order Butterworth low pass filter with a cutoff frequency of $f_{c1} = 0.5$ Hz cascaded with a first order Butterworth high pass filter with a cutoff frequency $f_{c2} = 100$ Hz, produced a band-pass filter. Figure 7.1 depicts the cascading of the individual filters producing the desired band-pass behavior.

![Flowchart of the filtering process applied to the original set of ECG signals. Two cascaded first order Butterworth filters, a low pass and a high pass, produce a band-pass filter.](image)

**Figure 7.1.** Flowchart of the filtering process applied to the original set of ECG signals. Two cascaded first order Butterworth filters, a low pass and a high pass, produce a band-pass filter.

### 7.3 Analysis of ECG Signals

The first subsystem in the algorithm corresponds to the analysis of the ECG signals. In this module of the algorithm the spectral analysis is applied, inverse problem is performed to locate dipole moment, and original signals are reconstructed via the forward problem out from the obtained dipole moments. The software is designed to accept the six precordial leads signals from a patient as an input signal. The six precordial leads are analyzed in vector form and each one of the lead signals $V_1$ to $V_6$ must have the same number of samples. Since the signals are sampled at 1 kHz, one sample of the signals corresponds to 1 mili-second.

Once the LVs are loaded into the system and the six precordial leads have been extracted, the spectral analysis module detects the duration of the cardiac cycle, by identifying the strongest frequency
component of the spectrum, which in turn corresponds to the frequency of the ECG signal. The duration of the cardiac cycle is useful, since it permits to establish the duration of the signal for analysis as a multiple of cardiac cycles. That is, for a patient the duration of the signal intended for analysis, is in terms of the duration of the cardiac cycle for that patient, i.e. 1, 2 or 3 cardiac cycles. In the next step, the dipole moments for all of the 20 possible dipole locations are calculated at each time sample and stored in an array in memory. This 3-dimensional array is composed of the x, y, and z components of the dipole moments at each time sample, for 20 different dipoles. Therefore, if the ECG signal is $t$ samples in length, the size of the array is $t \times 3 \times 20$. Next, using the 20 different obtained dipole moments, the original set of precordial leads is reconstructed. In the end, 20 different sets of reconstructed precordial ECG signals are available for their visual inspection and comparison to the original set of signals. The programming flowchart of this subsystem is depicted in Fig. 7.2.

**Figure 7.2.** Programming flowchart for the first subsystem. In this stage of the algorithm, the LVs are loaded, the signal is filtered, the duration of the cardiac cycle is determined from the spectral analysis, the dipole moments are calculated for all of 20 possible locations, and the signal is reconstructed.
7.4 Dipole Localization and Optimization

The second subsystem accounts for the calculation of all of the dipole moment magnitudes, and the dipole optimization process. At each time sample the dipole with the greatest magnitude and its location are extracted and stored into a new variable. Since there are 20 different possible locations for the equivalent dipole source, the coordinates are indexed from $I(1)$ to $I(20)$, and $I(i) = (x_i, y_i, z_i)$. It must be remarked that the heart’s coordinate system covers the entire heart geometry and a unit corresponds to 1 mm. So, the indexes of the dipoles are stored in a column vector and can be called by any other programming module at any time. The location of the equivalent dipole over time is then plotted simultaneously with the evolution of the cardiac cycle, so the location of the cardiac activation site is determined at any instant of time. In the next, and using the cardiac cycle duration information provided by the spectral analysis, the ECG signal or wave is divided into equal segment in a process called wave segmentation. The purpose of wave segmentation is to reduce the numerical noise present in the obtained equivalent dipole source vector. The concept of numerical wave segmentation can be only illustrated with an example: the column vector containing the indices for the dipole locations provides the localization in time of the equivalent dipolar source inside the heart. This position is supposed to change as the cardiac cycle evolves, however numerical noises causes very short time variations, with a duration of 5 or less milliseconds, in the position of the equivalent dipolar source. Such small variations have no physical significance and need to be discarded. The solution to this problem is the use of wave segmentation. In wave segmentation the cardiac cycle is divided into $R$ segments of equal duration. The variable $R$ is called the resolution factor, and is assigned values ranging from 1 to $t$, where $t$ is the number of time samples in the cardiac cycle. Then, in each one of the sections of the segmented wave, the dipole with the greatest magnitude and it coordinates, represent the entire wave section. In other words, it is said that the equivalent dipole source inducing the surface potentials during that segment of the wave, is the dipole with the greatest magnitude from that segment. It is important to mention that, the benefits provided by wave segmentation depend entirely on the value of $R$. If $R$ is selected to be 1, the cardiac cycle would be represented by a single segment and consequently by a one dipole location. This contradicts the purpose of this research, which is the identification of the changing location of the
CAS, because if a single dipole location represents the entire cardiac cycle, such location remains the same which has no physical significance. On the other hand, choosing $R$ close to the duration of the cardiac cycle, cancels the effect of the segmentation. For that reason, the resolution factor $R$ is selected to be between 3 and 6. The flowchart for this subsystem is represented in Fig. 7.3.

![Figure 7.3](image)

**Figure 7.3.** Programming flowchart for the second subsystem. In this subsystem, the dipole optimization process and the plotting of the location of the equivalent dipole source, as well as wave segmentation are performed in this stage of the algorithm.
7.5 Projection of Time Varying PPM

The last subsystem or stage corresponds to the reconstruction and projection of the time varying PPMs is performed and the equivalent dipole localizations for the P-wave, the QRS-complex, and for T-wave are calculated. The PPM reconstruction is made from the column vector containing the equivalent dipole locations after wave segmentation. Then, at each time sample the equivalent dipole moment and lead vectors linking the location of the equivalent dipole and the points in the pericardium 3D model are loaded. Once the potentials are reconstructed and calculated for each one of the 1329 points or nodes comprising the 3D model, a color coded potential map is created representing the distribution of the pericardium potentials at that specific time simple. Since the process is repeated for each time sample, for \( t \) samples, the result is \( t \) still images showing the potentials at the pericardium. Those still images are then displayed and recorded in sequential order in such a way that a motion picture or video showing how the potentials change over the cardiac cycle in the pericardium. The distribution of the potentials occurring on the pericardium over time permit the visualization of the polarization patterns on heart surface.

In order to be able to determine whether a patient has a potential cardiac malignancy, normal ranges must be established. Normal ranges are determined by calculating the average localization of the equivalent dipole sources at the P-wave, the QRS-complex, and the T-wave in the normal patients. Therefore, at each one the segments in the cardiac cycle, there is an expected location for the CAS. Then for all patients’ population, both normal and abnormal, the relative position of the CAS’s is determined. Figure 7.3 shows the programming flowchart for this subsystem.
Figure 7.4. Programming flowchart for subsystem 3. In this stage PPMs are created and projected and normal ranges are established.
The previously discussed algorithm was applied on a patient-by-patient basis according to the following flowchart:

![Flowchart](image)

**Figure 7.5.** Complete programming flowchart for the proposed algorithm for Precordial ECG analysis. The three subsystems are executed sequentially and the results displayed and saved.

The proposed algorithm outlined in the programming flowchart was applied to the entire test population. The normal ranges, however, were obtained only in the information provided by the normal patients’ population. That is, for each of the normal patients, the found CAS or equivalent dipole source location coordinates at each one of cardiac cycle segments (the P-wave, the QRS-complex, and the T-
wave) are obtained. The algorithm was written and executed in MATLAB using a modular programming approach. In this approach, each subroutine or module performs each task described in the algorithm. The following flowchart, represent the algorithm outlined in Fig. 7.5, describes the subroutines assigned to perform each one of the required steps needed in order to arrive to a solution.

**Figure 7.6.** Modular programming flowchart for the proposed algorithm. Each one of the subroutines or modules (MATLAB .m files) performs a specific task in the algorithm.
The modules are executed in sequential order and perform a specific task in the algorithm. Next a brief description of the task performed by each subroutine or programming function:

1) *Driver.m*- This is the main driver of the software. All of the subroutines are called from the driver. Patient data and LVs information is loaded from this stage.

2) *Filtering.m*- A digital band-pass filter eliminates unwanted noises and disturbances from the original ECG signal.

3) *Frequency_Analysis.m*- Spectral analysis is applied in order to obtain the duration and frequency of the cardiac cycles.

4) *Precordials_Extractor.m*- The six precordial leads are extracted from patient’s 12-Lead ECG file.

5) *Inverse_Problem*- In this module, the dipole moments are obtained for each one of the 20 possible dipole locations. This is done by solving the over-determined system of equations in the inverse problem of electrocardiography.

6) *Forward_Problem.m*- Original precordial ECG signals are reconstructed for each one of the possible dipole locations.

7) *Matrix_Saver.m*- Saves the input data in matrix-database form. For this particular case, this module saves both all of the obtained dipole moments.

8) *Dipole_Magnitude.m*- The magnitude over time of each one of the 20 possible dipole locations is calculated in this stage.

9) *Max_Dipole.m*- This subroutine performs the dipole optimization process by selecting the dipole location with the greatest magnitude at each sample of time in the ECG signals. CAS’ position in time is plotted simultaneously with one precordial ECG lead.
10) *Wave_Segmentation.m*- This subroutine divides the ECG signal into equal segments. Then the strongest dipole in each segment is selected as the equivalent dipole source or CAS for that particular segment of the wave. Wave segmentation reduces numerical noise and data with no physical significance drastically.

11) *Max_Dip_Mom_Seg.m*- A matrix containing the indices and coordinates of the dipole locations after wave segmentation is created.

12) *Pericardium_Potential_Recons.m*- This subroutine loads the necessary LVs for the reconstruction of potentials in the pericardium. Reconstruction of potentials is achieved by applying the forward problem of electrocardiography equation.

13) *Plot_Original.m*- This module plots the original patient’s precordial ECG signals.

14) *Plot_Recons.m*- In this module the reconstructed precordial lead ECG signals are plotted for visual inspection. For each one of the 20 possible dipole locations, a set six simultaneous reconstructed signals are plotted.

15) *Plot_Dipole_Mag.m*- The 20 possible dipole locations time dependent moments are plotted in this subroutine.

16) *Pericardium_Potential_Proj.m* – This function plots the color-coded time varying PPMs.

17) *Save_Results.m*- In this subroutine all of the numerical results are stored in an exportable database and the PPM movie is created.
The proposed software was tested in a population of 30 patients, 15 patients with no detected cardiac abnormalities and 15 with cardiac abnormalities. The software analyzed a complete cardiac cycle by solving the inverse problem of electrocardiography at each time sample; twenty possible dipole locations were considered simultaneously. Results were interpreted and analyzed in a patient-by-patient basis by properly identifying both graphically and numerically the location of Cardiac Activation Sites, and were complemented with the visualization in time of the PPMs.

The analysis was performed by recording the location coordinates of the strongest dipole at every time sample (Cardiac Activation Site), using the single-moving dipole model in a complete cardiac cycle for all normal patients. This was done in order to establish normal ranges for dipole localization. For this purpose, three points of the cardiac cycle were considered as points of interest, one within each of the P-wave, QRS-Complex and T-wave. Then, for a patient, ECG normality or abnormality at a point of interest was determined by the Euclidean distance between the coordinates of the Cardiac Activation Site and the corresponding average coordinates obtained from the normal patients. If for a specific patient the Cardiac Activation site at the QRS-complex point is found far from the average location, the abnormality was said to occur at the QRS-complex, thus indicating a potential cardiac malignancy. The same criterion was applied for the P and T waves.

Results showed consistently that for normal patients major sources for electrical activity were located at the atrial region for the P-wave, at the Right Ventricle region for the QRS, and at the Bundle of His region for T-wave for normal patients.

8.1 Results for Patients with No Cardiac Abnormalities

The first step in the numerical result process is the analysis of the entire population of normal patients, i.e. patients with no previously known or diagnosed cardiac illnesses. The location of the CAS’s at each one of the points in the cardiac cycle was calculated for each of the normal patients. Then, the average location of the CAS is determined as well, at each one of the points of interest using (8.1).
where \( \bar{L}_p, \bar{L}_{QRS}, \) and \( \bar{L}_T \) stand for the average location coordinates inside the heart geometry of the CAS’ or equivalent dipole sources from the normal patients’ population and \( x_i, y_i, \) and \( z_i \) are the coordinates of the found CAS’ location for the \( i^{th} \) patient, for a particular segment in the cardiac cycle.

The previous equations provide the normal ranges needed for the determination of normality and abnormality, however this criterion is incomplete. The complementary part in the determination of normal ranges requires the calculation, as mentioned above, of the average Euclidean distance between a patient’s CAS location and the calculated average location of the CAS, for a particular cardiac cycle segment. The individual Euclidean distance between a patient’s CASs location and the found CAS location for a cardiac cycle segment is calculated using the following equations:

\[
D_{i,p} = \left[ (\bar{x}_p - x_{i,p})^2 + (\bar{y}_p - y_{i,p})^2 + (\bar{z}_p - z_{i,p})^2 \right]^{1/2}
\]

\[
D_{i,QRS} = \left[ (\bar{x}_{QRS} - x_{i,QRS})^2 + (\bar{y}_{QRS} - y_{i,QRS})^2 + (\bar{z}_{QRS} - z_{i,QRS})^2 \right]^{1/2}
\]

\[
D_{i,T} = \left[ (\bar{x}_T - x_{i,T})^2 + (\bar{y}_T - y_{i,T})^2 + (\bar{z}_T - z_{i,T})^2 \right]^{1/2}
\]
In order to complete the criterion for normal ranges’ determination, the average Euclidean distance at each one the cardiac cycle segments:

\[ \tilde{D}_p = \sum_{i=1}^{15} D_{i,p} \]
\[ \tilde{D}_{QRS} = \sum_{i=1}^{15} D_{i,QRS} \]
\[ \tilde{D}_T = \sum_{i=1}^{15} D_{i,T} \]  

(8.3)

where \( \tilde{D}_p \), \( \tilde{D}_{QRS} \) and \( \tilde{D}_T \) are the average Euclidean distances used for the determination of normal ranges. In simple words, the average Euclidean distance criterion is a sphere with radius \( \tilde{D}_p \) for the P-wave, \( \tilde{D}_{QRS} \) for the QRS-complex, and \( \tilde{D}_T \) for the T-wave. Those spheres are centered at the coordinates of the location of the CASs: \( \bar{x}_p, \bar{y}_p, \bar{z}_p \) for the P-wave, \( \bar{x}_{QRS}, \bar{y}_{QRS}, \bar{z}_{QRS} \) for the QRS-complex, and \( \bar{x}_T, \bar{y}_T, \bar{z}_T \) for the T-wave. Now the normal ranges are fully determined. Table 8.1 summarizes the discussed criterions, the found average locations based on a population of 15 patients with no cardiac abnormalities, as well as the Euclidean distances or spheres’ radii with a 15% tolerance.

**Table 8.1.** Normal ranges in the location of Cardiac Activation Sites during different sections in a cardiac cycle using the single-moving dipole model. Coordinates show the locations inside the FEM model of the human heart.

<table>
<thead>
<tr>
<th>Segment of Cardiac Cycle</th>
<th>Coordinates in Heart’s Geometry (X,Y,Z) [mm]</th>
<th>Average Euclidean Distance for Normal Ranges [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-wave</td>
<td>(-7.33,-27.67, 382.733)</td>
<td>25.95+3.89</td>
</tr>
<tr>
<td>QRS-complex</td>
<td>(2.00,-26.47,355.88)</td>
<td>28.77+4.31</td>
</tr>
<tr>
<td>T-wave</td>
<td>(-5.00,-30.27, 373.27)</td>
<td>31.04+4.65</td>
</tr>
</tbody>
</table>
The following figures depict the found CAS or equivalent dipole source locations, as well as the sphere with radius $\tilde{D}$ centered at that specific location inside the heart. Figures 8.1, 8.2 and 8.2 show the CAS’s location and the spheres for the P-wave, the QRS-complex, and the T-wave respectively.

Figure 8.1. Location of the CAS in the P-wave, the red dot represents the CAS’ location, and the sphere with radius $\tilde{D}_p$ the normal range space. The values for the CAS location coordinates as well as the Euclidean distance or sphere’s radius are presented in Table 8.1.

Figure 8.2. Location of the CAS in the QRS-complex, the red dot represents the CAS’ location, and the sphere with radius $\tilde{D}_{QRS}$ the normal range space. The values for the CAS location coordinates as well as the Euclidean distance or sphere’s radius are presented in Table 8.1.
Figure 8.3. Location of the CAS in the T-wave, the red dot represents the CAS’ location, and the sphere with radius $\hat{D}_T$ the normal range space. The values for the CAS location coordinates as well as the Euclidean distance or sphere’s radius are presented in Table 8.1.

The normal ranges are used for the comparison of the results coming from the population of patients with cardiac abnormalities to test the algorithm ability to detect cardiac malignancies. This will be explained in detail in the following section.

A typical software output for a patient consists of: 1) 20 sets of reconstructed signals, 2) 20 dipole moment magnitudes plots in time, 3) spectrum of the ECG signal, 4) a time dependent CAS location plot and 5) a time varying color-coded PPM. Numerical results, such as the coordinates for the CAS locations are extracted manually for its further processing and collocation in tables. Next, samples of results for patients 2, 3 and 5 are shown. Since all of the reconstructed signals are used composed of 20 sets of reconstructed signals, as well as the time dependant dipole magnitudes, the results shown include only spectral analysis, CAS locations and color coded PPM snapshots at the P-wave, the QRS-complex, and the T-wave. The time varying PPMs, since they are motion pictures or movies, cannot be included in this report, however, captures or snapshots of the PPMs at the cardiac cycle segments. In the color-coded PPM, dark red color represents maximum potentials, whereas dark blue color represents the minimum potential. The output generated by the code in MATLAB for patient 2 is:
Figure 8.4. Results from normal patient 2 consisting of: spectral analysis, CAS during the QRS-complex, and snapshots of the PPM during the P-wave, QRS-complex and the T-wave.
For patient 2, which has no previously diagnosed cardiac illnesses, it can be observed that the location of the equivalent dipole source is in the right ventricular region, as according to the expected flow of electrical current in the heart [30, 31, 32, 33]. From the spectrum of the signal, frequency component was found to be \( f = 1.251 \) Hz, which according to the hypothesis discussed in this thesis, corresponds to the frequency of this patient’s cardiac cycle. If the cardiac cycle has a frequency of 1.251 Hz, the duration of the cardiac cycle would be then \( T = 799.36 \) milliseconds. After inspecting the signal visually and manually measuring the duration of a single cardiac cycle, it was found that the period corresponded to the period calculated from the spectral analysis, with an accuracy of 99.8%. This allows the calculation of the cardiac cycle period (which is needed in wave segmentation) without the necessity of doing it manually. After inspecting the snapshots from the time varying PPM at each of the cardiac cycle segments it can be seen the distribution of the potentials in the pericardium and determine if it corresponds to what is expected from literature. During the QRS-complex and T-wave potentials are high in the pericardium due to the currents flowing during the ventricle contraction, which causes the irradiation of energy from the heart. In the case of the T-wave, cardiac tissues and conducting fibers repolarize and the energy flows back to the atrial regions. On the other hand, during the P-wave the hear is preparing to start a new blood pumping process, so the potentials at the surface are expected to be low.

After inspecting the visual results from patient 2, it can be determined that the precordial ECG signals from this patient correspond to those of a patient with no cardiac abnormalities. The inspection of the ECG signal’s spectrum suggests that the greatest frequency component corresponds to the cardiac cycle frequency, the CAS being located in the right ventricle during the QRS-complex, in the atrial and bundle of His regions during the P-wave and T-wave, respectively (not shown), and the potentials distribution on the pericardium, as shown by the PPM snapshots suggest that the path of the centers of major cardiac activity from this patient, correspond to the data expected from a patient with no cardiac illnesses. Therefore it can be said that this patient does not present any potential malignancy, based on the analysis of the precordial ECG signals. Similar results from patients 3 and 5 are depicted in Fig. 8.5.
and Fig. 8.6. In both cases, the results leaded to the conclusion that both patients had no cardiac abnormalities in their ECG. For the rest of the normal patients, results were consistent as well.

Figure 8.5. Results for normal patient 3. For this patient, the duration of the cardiac cycle is 993.04 milliseconds. The CAS location plot and the PPM snapshots suggest, as with patient 2, that this patient does not have any detected cardiac abnormality, based on the precordial ECG analysis.
Figure 8.6. Results for normal patient 5. For this patient, the duration of the cardiac cycle is 885.73 milliseconds. The CAS location plot and the PPM snapshots suggest, as with patient 2 and 3, that this patient does not have any detected cardiac abnormality, based on the precordial ECG analysis.
8.2 Results for Patients with Cardiac Abnormalities

The analysis of patients with no detected and no diagnosed cardiac abnormalities serves as the basis for the establishment of normal ranges. The normal range or parameters are based on the position of the found CAS location inside the heart, during the segments of the cardiac cycle. Once the normal ranges are determined from the normal population, the population of patients with previously diagnosed cardiac illnesses is subject to a secondary analysis, taking as a reference the normal parameters. For one patient, the CAS locations during the P-wave, the QRS-complex, and the T-wave, are compared to the coordinates in Table 8.1. Then, the each of the three CASs from the patients is analyzed to see if it lies within the normal parameter. In other words, we check if the CAS is inside the spheres depicted in Figs. 8.1, 8.2 and 8.3. If a CAS during a particular cardiac cycle segment is found to be out of range, it is said that there is an abnormality occurs during that particular cardiac cycle segment and, therefore that abnormality is located in the heart’s region or tissues associated to that particular cardiac cycle segment.

The criterion to determine whether a patient has a potential cardiac malignancy is that if at least one CAS location during a cardiac cycle segment is found to be out of range, the patient’s ECG has an abnormality. Furthermore, the patient is said to have a potential cardiac malignancy. This criterion was applied to the entire population of abnormal patients. Table 8.2 summarizes the results obtained after the analysis on abnormal patients.

Table 8.2. Summary of abnormal patients’ analyses and the segments of the cardiac cycle in which a potential cardiac abnormality occurs. “In” signifies the Cardiac Activation Site location was found inside normal range; whereas “Out” means that the Cardiac Activation Site location was found outside normal ranges.

<table>
<thead>
<tr>
<th>Patient</th>
<th>P</th>
<th>QRS</th>
<th>T</th>
<th>Patient</th>
<th>P</th>
<th>QRS</th>
<th>T</th>
<th>Patient</th>
<th>P</th>
<th>QRS</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Out</td>
<td>Out</td>
<td>In</td>
<td>6</td>
<td>Out</td>
<td>In</td>
<td>In</td>
<td>11</td>
<td>In</td>
<td>In</td>
<td>In</td>
</tr>
<tr>
<td>2</td>
<td>Out</td>
<td>Out</td>
<td>In</td>
<td>7</td>
<td>In</td>
<td>Out</td>
<td>In</td>
<td>12</td>
<td>Out</td>
<td>Out</td>
<td>Out</td>
</tr>
<tr>
<td>3</td>
<td>Out</td>
<td>In</td>
<td>In</td>
<td>8</td>
<td>In</td>
<td>Out</td>
<td>In</td>
<td>13</td>
<td>Out</td>
<td>Out</td>
<td>In</td>
</tr>
<tr>
<td>4</td>
<td>Out</td>
<td>In</td>
<td>In</td>
<td>9</td>
<td>Out</td>
<td>Out</td>
<td>In</td>
<td>14</td>
<td>Out</td>
<td>Out</td>
<td>Out</td>
</tr>
<tr>
<td>5</td>
<td>In</td>
<td>Out</td>
<td>In</td>
<td>10</td>
<td>In</td>
<td>Out</td>
<td>In</td>
<td>15</td>
<td>In</td>
<td>Out</td>
<td>In</td>
</tr>
</tbody>
</table>
Since it is of the interest of this research to identify in which parts of the heart does the abnormality occurs, it is necessary to identify which cardiac region is associated with the generation of cardiac electric activity during the different segments of the cardiac cycle. As discussed above, the P-wave is associated with the atrial region, the QRS-complex is associated with the right and left ventricles, and the T-wave is associated with the area surrounding the Bundle of His. Table 8.3 summarizes the found possible regions in which the malignancies are located.

**Table 8.3.** Summary of the results of abnormal patients’ results. This table summarizes the obtained result for each patient and the regions inside the heart in which the malignancy might be located.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Probable Location(s) of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Atria and Ventricles</td>
</tr>
<tr>
<td>2</td>
<td>Atria and Ventricles</td>
</tr>
<tr>
<td>3</td>
<td>Atria</td>
</tr>
<tr>
<td>4</td>
<td>Atria</td>
</tr>
<tr>
<td>5</td>
<td>Ventricles</td>
</tr>
<tr>
<td>6</td>
<td>Atria</td>
</tr>
<tr>
<td>7</td>
<td>Ventricles</td>
</tr>
<tr>
<td>8</td>
<td>Ventricles</td>
</tr>
<tr>
<td>9</td>
<td>Atria and Ventricles</td>
</tr>
<tr>
<td>10</td>
<td>Ventricles</td>
</tr>
<tr>
<td>11</td>
<td>No abnormality detected</td>
</tr>
<tr>
<td>12</td>
<td>Atria, Ventricles, and Bundle of His</td>
</tr>
<tr>
<td>13</td>
<td>Atria and Ventricles</td>
</tr>
<tr>
<td>14</td>
<td>Atria, Ventricles, and Bundle of His</td>
</tr>
<tr>
<td>15</td>
<td>Ventricles</td>
</tr>
</tbody>
</table>

Although Tables 8.2 and 8.3 provide a good foundation in the detection and location of potential cardiac malignancies, it is necessary to inspect the PPMs from a patient and detect any anomalies in the polarization patterns of the heart’s surface. This provides additional information for a stronger a well founded base in the detection and localization of cardiac abnormalities. Next the analysis outputs for abnormal patients 2 and 10 are presented in Figs. 8.7 and 8.8.
Figure 8.7. Output analysis for abnormal patient 2. The output contains the same plots as for the normal patients: spectrum of the ECG signal, the CAS location during the QRS-complex, and PPM snapshots during the P-wave and QRS-complex.
i) Spectral Analysis

ii) CAS location during the T-wave

iii) PPM during the T-wave (front)

iv) PPM during the PPM the T-wave (back)

v) PPM during the QRS-complex (front)

vi) PPM during the QRS-complex (back)

Figure 8.8. Output analysis for abnormal patient 10. The output contains the same plots as for the normal patients: spectrum of the ECG signal, the CAS location during the T-wave, and PPM snapshots during the T-wave and QRS-complex.
Abnormal patient 2 was found to have a cardiac abnormality according to table 8.1. The location of the potential abnormality, as shown from table 8.2, is on the atria and on the ventricles. The CAS location during the QRS-complex was found to be on the atrial region. This location contradicts the expected CAS location during this cardiac cycle segment as according to literature; during the QRS-complex, the CAS is expected to be on the ventricular region. Additionally after inspecting the PPM’s snapshots, it can be seen during the P-wave was found to be at maximum potential and fully polarized, and during the QRS-complex the PPM shows a depolarized heart. As mentioned in the literature, during potentials in the pericardium are expected to be at its minimum since the heart is preparing for the pumping process. On the other hand, during the QRS-complex, the ventricles’ contraction generates a high pulse of radiated energy, so the heart surface is expected to be at maximum potential and fully polarized. Additionally, the predominating frequency component was found to be at \( f = 2.853 \text{ Hz} \), which signifies that the cardiac cycle duration is 350.5 milliseconds. After the visual inspection of the signal, it was found that the actual duration of the cardiac cycle for patient 2 was approximately 730 milliseconds. Hence, if the spectral analysis module is not able to calculate the cardiac cycle period correctly, it can be suggested that spectral analysis works as a preliminary diagnosis tool.

For the abnormal patient 10, the spectrum of the signal suggests that the duration of the cardiac cycle is 208.02 milliseconds. The actual duration of the cardiac cycle was found to be 850 milliseconds. Again, the spectral analysis suggested a potential cardiac abnormality before the full ECG analysis. In this patient, the CAS during the T-wave was found to be located in the upper atrial region, contradicting the expected CAS location during this cardiac cycle segment at the Bundle of His region. The PPMs inspection show that the QRS-complex the heart is at minimum potential and depolarized, thus contradicting the expected literature. These contradictions, suggest an abnormality located in the ventricular region as shown in Table 8.2.
8.3 Discussion of Results

The proposed software was able to successfully identify abnormalities in 93.33% of the abnormal patients. The analysis was complemented with the visualization of the location of the Cardiac Activation Site at a specific time moment during the cardiac cycle, which permitted the identification of the cardiac region in which the Cardiac Activation Site was located. Additionally, the diagnostian can inspect the surface potentials provided by the time-varying PPM and detect any anomaly in the pericardium polarization patterns. Spectral analysis, which is needed for wave segmentation and noise reduction in PPM reconstruction, succeeded in detecting patients’ cardiac cycle duration with a 97% accuracy for all of the normal patients, whereas for abnormal cases spectral analysis successfully detected cardiac cycle duration for only 53.33% of abnormal patients. This discrepancy suggests that spectral analysis provides a preliminary detection of a potential malignancy, since for all normal patients a single predominant frequency component matching the real ECG signal’s frequency is present while for abnormal patients the predominant frequency components are at excessively high frequencies.

Given the over-determined nature of the linear system of equations described in Eq. (6.7), which is by definition ill posed, the related dipole moment calculation is subject to inaccuracies. However, it was found that filtering the signal before solving Eq. (6.7) improves the conditioning of the problem to a great extent; this is reflected in the precision of the reconstructed ECG precordial signals. Solutions obtained in the form of dipole moment magnitudes clearly showed a single maximum dipole moment at a specific location inside the heart, which strongly suggests that the signal measured in the human torso’s surface was generated in that region.

As mentioned above, the spectral analysis provides a preliminary result by the detection of predominant frequency at abnormally large frequencies, which suggests potential arrhythmias. The location of the single-moving dipole, which is selected as function of its magnitude, indicates the possible source of the potential abnormality. Finally, the PPM projection permits the identification of any abnormality in the pericardium’s polarization and depolarization patterns during the cardiac cycle.
The results presented in Table 8.1, show that for all of the normal patients major cardiac activity was located in the atria region during the P-wave segment, right-ventricular region during the QRS-complex, and in the Bundle of His during the T-wave. Also, Table 8.1 provides the mean Euclidean distance in mm of normal patients’ dipole locations from the mean normal dipole location. This provides the necessary conditions for establishing normal ranges of Cardiac Activation Sites locations. Table 8.2 provides a summary of the analysis performed in abnormal patients, which show that abnormalities were detected in 14 out of 15 abnormal patients used for this study, whereas the possible cardiac regions involved in the malignancy occurrence are summarized in Table 8.3. The accuracy of the presented results can be greatly improved by increasing the normal patients’ population since tolerance criteria in Table 8.1 would be reduced. Therefore, abnormalities would be more noticeable numerically. In all of the normal and abnormal cases, CASs were successfully identified and their color-coded PPM showed the corresponding heart’s polarization and depolarization patterns.
Chapter 9: Conclusions and Future Work

9.1 Conclusions and Future Work

The goals of the research experiment reported in this thesis were satisfactorily achieved since a novel, non-invasive alternative method able to detect cardiac abnormalities in patients, as well as the origin inside the heart of such malignancies. The proposed method proved to have an improved level of accuracy in: 1) the reconstruction of the original precordial ECG signals for each one of the 20 possible dipole locations and 2) the localization of equivalent dipole source or CASs. Also, the dipole optimization process is based on the localization of the strongest dipole sources, which implies a stronger physiological significance compared to previous methods which relied on a statistical equivalence in their dipole optimization processes. Additionally, the inclusion of a spectral analysis module was found to be very effective as a preliminary diagnosis tool by identifying abnormalities in the spectrum of patients’ ECG signal. Finally, and perhaps the main contribution to ECG analysis techniques made by in work, is the creation of time varying color-coded Pericardium Potential Maps which permit the visualization and analysis of the electric polarization patterns occurring on the heart’s surface. In such way, potential cardiac malignancies can be identified, additionally to the CAS numerical analysis and reconstructed signal inspection, by detecting anomalies in the potential distribution on the pericardium.

The future work related to this research is the increase on the study population size. By increasing the number of test patients, the normal parameter on Table 8.1 will converge to cardiac regions with more clinical significance, and thus the software will be more sensitive in the detection of cardiac abnormalities. Also, increasing the number of locations of the possible CASs, the spatial resolution of the analysis would be significantly increased. However, the purpose and goal of this research were reached in satisfactory way. Any improvement is left to further stages of this research. As a conclusion, the proposed software properly identified potential abnormalities and their possible locations for 93.33% of the abnormal patients, except for patient in which no abnormality was detected. This leads to the conclusion that the characterization of the cardiac electrical activity with multiple possible dipole locations can lead to a reliable preliminary detection of the origin of cardiac
abnormalities in the ECG. The equivalent single-moving dipole solution, along with signal reconstruction and PPM projection, proved to be valuable assets in a preliminary ECG analysis of a patient.
References


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Appendix

A.1. Example of original six precordial ECG signals (patient 5)

![Original ECG Precordial V1](image1)

![Original ECG Precordial V2](image2)

![Original ECG Precordial V3](image3)

![Original ECG Precordial V4](image4)

![Original ECG Precordial V5](image5)

![Original ECG Precordial V6](image6)

Fig A.1. Original six precordial ECG signals.

A.2. Example of reconstructed ECG signals (patient 5-dipole location 10)
Fig A.2. Original six precordial ECG signals.
A.3. Dipole moment magnitudes in time for patient 5 (Dipole 1-20)
Fig A.3. Dipole moment magnitudes in time.
A.4. Locations of the 20 possible dipole locations inside the heart geometry

Fig. A.4. Location of the 20 possible dipole locations inside the heart
A.5. MATLAB Codes for programming modules.

Driver.m

%%% Jaime De La Cruz    02/09/2011
%%% RESEARCH PROJECT Fall 2010/Spring 2010
%%% Mentor- Dr. Joseph Pierluissi   Electrical and Computer Engineering
%%% The University of Texas at El Paso

% Test Driver-Analysis for patient
%
% This is a test driver code that performs the Inverse Problem of ECG. The
% test signal correspond to a digitized ECG trace, each of the individual
% signals correspond to each one of the 6 precordial leads sampled at 1 KHz
% The output is the current dipole moment corresponding at a specific
% sample of the signal.

clear all;
clc;

% Load patient signals
load patient.mat

% Filter out low frequency modulation present in patient's signal.
patient(:,1)=[];
Dummy_Signal=Filtering(patient(:,11));

% Perform frequency analysis in order to detect the frequency of the QRS
% peaks, and therefore determine the frequency of the signal. This is done
% in order to be able to segment signal into wave sections.

[Frequency, Period]=Frequency_Analysis(Dummy_Signal,length(Dummy_Signal));
Signal=Filtering(patient);

% The signal contains a total of 15 lead signals (Primary, Precordial and
% Frank XYZ leads). Therefore, the 6 precordial leads must be extracted
% from the signal. A time span (t2-t1), that is the length of the portion
% of the signal being analyzed,is defined in miliseconds.

cycles=1.5; % Number of cycles
t1=501;
t2=cycles*round(Period*1000) + t1-1;

[Seg_Signals,V1,V2,V3,V4,V5,V6]=Precordials_extractor(Signal,t1,t2);

% Now, the precordial leads vectors are loaded in order to be able to
% calculate corresponding dipole moment, for a sample of precordial leads
% measurements.

[Dipole_Moments]=Inverse_Problem(Seg_Signals);

% In order to verify which of the obtained dipole moments reconstructs
% initial signal (6 precordials ECG trace), a subroutine that reconstructs
% the signal is executed.

S_L=length(Seg_Signals(:,1));
N_D=length(Dipole_Moments(1,1,:));

[Recons_Signal]=Forward_Problem(Dipole_Moments,S_L,N_D);

% In order to determine which dipole has the greatest magnitude, the
% function Dipole Magnitude is called.

[Dip_Mom_Mag]=Dipole_Magnitude(Dipole_Moments,S_L,N_D);

% Select and plot greatest dipole at each sample of time and its location
% within the heart

[I1]=Max_Dipole(Dip_Mom_Mag,S_L,V5);

% Signal is divided into equal segments for its analysis

[Resolution_Factor,SP,Dip_Mom_Seg]=Wave_Segmentation(Seg_Signals,Period,Dip_Mom_Mag);

% The maximum dipole moment magnitude for each segment of the signal is
% selected.

[I]=Max_Dip_Mom_Seg(Dip_Mom_Seg);

% Now, the potentials are reconstructed at the pericardium taking the
% dipole with the greatest magnitude at each sample of time

[Z,Z_I]=Pericardium_Potential_Recons(Dipole_Moments,N_D,I);

%%% Plotting of results

% Plot of Original Signals
%Plot_Original(Seg_Signals);

% Plot of reconstructed signals
%Plot_Recons(Recons_Signal,N_D);
% Plot the magnitude of the dipole moment over time at each of the dipole
% locations

Plot_Dipole_Mag(Dip_Mom_Mag);

% Project the reconstructed pericardium potentials in a 3D model of the
% heart along all the cardiac cycle

F=Pericardium_Potential_Proj(Z_I,V5);

% Play Obtained movie 1 time

movie(F,1,1000,[-60 -30 0 0]);

% Display the strongest dipole location at a single time t, along with a
% precordial lead V5. No segmentation used

% t=796;
% [X_c,Y_c,Z_c]=Max_Dipole_Single(I1,V5,t);

% Project the reconstructed pericardium potentials in a 3D model of the
% heart at a single time tt

% tt=1;
% Pericardium_Potential_Proj_Single(Z_I,tt,V5);

Filtering.m

function [Signal_Out]=Filtering(Signal_In)

% The original signals is modulated by a low frequency signal. Thus, a high
% pass Butterworth filter is needed to eliminate modulation noise.
% Additionally, a low pass filter is included in order to eliminate high
% frequency noise.

% Set cut-off frequency to 0.5 Hz

wh=0.5/1000;

% Set up filter characteristics

[bh,ah]=butter(1,wh,'high');
sh=filtfilt(bh,ah,Signal_In);

% Set cut-off frequency to 100 Hz

wh2=100/1000;
% Set up filter characteristics
[bh2,ah2]=butter(1,wh2,'low');
Signal_Out=filtfilt(bh2,ah2,sh);

End

Frequency_Analysis.m

function [Frequency, Period]=Frequency_Analysis(V,S_L)

% Perform fft to full-length signal (precardial lead V5) in order to
% extract frequency domain information.
Fs = 1000;                    % Sampling frequency
NFFT = 2^nextpow2(S_L); % Next power of 2 from length of y
Y = fft(V,NFFT)/S_L;
f = Fs/2*linspace(0,1,NFFT/2+1);

% Plot single-sided amplitude spectrum.
figure('Color','w')
hold on
grid on
axis([0 20 0 0.14]);
plot(f,2*abs(Y(1:NFFT/2+1)));
title('Single-Sided Amplitude Spectrum of V5(t)')
xlabel('Frequency (Hz)')
ylabel('|V5(f)|')
[C I]=max(2*abs(Y(1:NFFT/2+1)));
Frequency=f(I);         % Frequency in Hertz
Period=1/Frequency;     % Period in seconds
end

Precordials_Extractor.m

function [Seg_Signals,V1,V2,V3,V4,V5,V6]=Precordials_extractor(Signal,t1,t2)

% Extracts the needed 6 precordial leads in the desired time span in the
% signal.
V1=Signal(t1:t2,7);
V2=Signal(t1:t2,8);
V3=Signal(t1:t2,9);
V4=Signal(t1:t2,10);
V5=Signal(t1:t2,11);
V6=Signal(t1:t2,12);
Seg_Signals=[V1,V2,V3,V4,V5,V6];
end

**Inverse_Problem.m**

function [Dipole_Moments]=Inverse_Problem(Signals)

% This subroutine performs the inverse problem of ECG. The input is the 6
% precordial signals and the output is a vector containing the 3 cartesian
% coordinates for the calculate dipole moment at each sample of the
% signals.

load LV_20_Dipoles.mat    % Load file containing LV Coefficients
Dipole_Moments=zeros(length(Signals(:,1)),3,length(LV_20_Dipoles(1,1,:)));
Signals=Signals';
for k=1:length(LV_20_Dipoles(1,1,:))  % Loop for total number of dipoles
    for jj=1:length(Signals(1,:))
        Dipole_Moments(jj,:,k)=LV_20_Dipoles(:,:,k)
        \Signals(:,jj);
    end
end
% Save obtained dipole momemnt cartesian coordinates into a data base.
[output]=Matrix_Saver(Dipole_Moments);
end

**Matrix_Saver.m**

function [output]=Matrix_Saver(Dipole_Moments_5)

% This function saves input into a database or matrix
save Dipole_Moments_20.mat
output=1;
end
**Forward_Problem.m**

```matlab
function [Recons_Signal]=Forward_Problem(Dipole_Moments,S_L,N_D)

% This subroutine performs the forward problem of electrocardiography. Its
% input is the calculated dipole moment coordinates, while the output is a
% reconstructed signal.

% S_L= Signal Length, N_D=Number of Dipoles used
Recons_Signal=zeros(6,S_L,N_D);
load LV_20_Dipoles.mat    % Load Lead Vectors
for k=1:N_D    % Loop for total number of dipoles
    for jj=1:S_L    % Loop for total length of signal
        Recons_Signal(:,jj,k)=LV_20_Dipoles(:,:,k)*Dipole_Moments(jj,:,k)';
    end
end
[end]
end
```

**Dipole_Magnitude.m**

```matlab
function [Dipole_Strength]=Dipole_Magnitude(Moments,S_L,N_D)

% This subroutine calculates the magnitude of each one of the dipoles'
% over time. This is intended to determine which dipole
% contributes the most for the signal, and thus determine in which area of
% the heart is the origin of the signal.

Dipole_Strength=zeros(N_D,S_L);
for k=1:N_D
    for jj=1:S_L
        Dipole_Strength(k,jj)=sqrt(Moments(jj,1,k)^2+Moments(jj,2,k)^2+Moments(jj,3,k)^2);
    end
end
```

```
Max_Dipole.m

function [Max_Index]=Max_Dipole(Magnitude,S_L,V5)

% This subroutine selects the dipole with the greatest magnitude at each
% sample of time in order to be able to determine the localization of
% heart's electrical activity source.

load LV_20_Dipoles.mat    % Load file containing dipole coordinates

% Localize the index and magnitude of the greatest dipole at each sample of
% time
for k=1:S_L
    [Dip_max(k), Max_Index(k)]=max(Magnitude(:,k));
end

% Now that the index is known, extract the coordinates for that index
for k=1:S_L
    X_max(k)=Dipole_Index(Max_Index(k),2);
    Y_max(k)=Dipole_Index(Max_Index(k),3);
    Z_max(k)=Dipole_Index(Max_Index(k),4);
end

% Load Heart Surface Information
load HeartSurface.mat

% Plot maximum dipole location

% figure
% hold on
% grid on
% plot(V5)
%
% figure
% hold on
% plot3(X_max,Y_max,Z_max,'r');
% plot3(X_h,Y_h,Z_h);
% view(3);
% hold off
%
% figure
% hold on
% pause on
% view(0,0);
%
% for k=1:S_L
%
%     plot3(X_h,Y_h,Z_h);
%     plot3(X_max(k),Y_max(k),Z_max(k),'.r','MarkerSize',25);
%     title([num2str(k)]);
%
%     pause
%     cla
%
% end

Wave_Segmentation.m

function [R,SP,Dip_Mom_Seg]=Wave_Segmentation(Seg_Signals,Period,Dip_Mom_Mag)

% This subroutine segments the precordial signal into equal segments in
% order to ease the localization of the 3 distinct ECG waves (P,QRS and T)
% Then, the maximum dipole magnitude and its location are extracted for
% potential reconstruction and further projection in pericardium's surface.

% Segmentation Period in milliseconds
R=4;
SP=1000*(Period/R);
SP=ceil(SP);

S_L=length(Seg_Signals);
K=floor(S_L/SP);

for k=1:K
    Dip_Mom_Seg(:,:,k)=Dip_Mom_Mag(:,SP*(k-1)+1:(SP*k));
end

end

Max_DipMom_Seg.m

function [I]=Max_Dip_Mom_Seg(Dip_Mom_Seg)

% This subroutine extracts the maximum dipole moment magnitude for each of
% the sections of the Dipole moment magnitude vector. This maximum dipole
% moment and its location will represent the entire segment.
K=length(Dip_Mom_Seg(1,1,:));
SP=length(Dip_Mom_Seg(1,:,1));

for k=1:K
    [a b]=max(Dip_Mom_Seg(:,:,k));
    [c ii]=max(a);
    C(k)=c;
    II(k)=b(ii);
end

for k=1:K
    I(SP*(k-1)+1:SP*k)=II(k);
end

end

Pericardium_Potential_Recons.m

function [Z_v,Z_I]=Pericardium_Potential_Recons(Dipole_Moments,N_D,I)

% This subroutine reconstructs the potential at the pericardium via forward
% problem. The lead vectors for all points in pericardium are multiplied by
% Dipole moments as according to Heart equation.

load LV_Heart_Surf_20.mat
S_L=length(I);
for j=1:N_D
    for k=1:S_L
        Z_v(:,k,j)=LV_Heart_Surf_20(:,:,j)*Dipole_Moments(k,:,j)';
    end
end

for k=1:S_L
    Z_I(:,k)=Z_v(:,k,I(k));
end
Pericardium_Potential_Proj.m

function \([F,h]=Pericardium\_Potential\_Proj(Z\_I,V5)\)

% This subroutine projects the potential generated by dipoles at the
% pericardium in order to see how the activity at heart's surface moves
% along the entire cardial cycle.
load HeartSurface.mat

\(S_{\text{L}}=\text{length}(Z_{\text{I}}(:,1,:));\)
\(X=X_h;\)
\(Y=Y_h;\)
\(Z=Z_h;\)

\(\text{X\_mean}=\text{mean}(X);\)
\(\text{Y\_mean}=\text{mean}(Y);\)
\(\text{Z\_mean}=\text{mean}(Z);\)
\(\text{XX}=X-X\_\text{mean};\)
\(\text{YY}=Y-Y\_\text{mean};\)
\(\text{ZZ}=Z-Z\_\text{mean};\)

\([\text{THETA,PHI,R}] = \text{cart2sph}(\text{XX},\text{YY},\text{ZZ});\)

\(\text{tri= delaunay(THETA,PHI)};\)
\(\text{T=tri'};\)
\(\text{Z\_vector=Z\_I};\)

\(\text{for } k=1:S_{\text{L}}\)
\(\quad \text{for } \text{row}=1:3\)
\(\quad \quad \text{for } \text{col}=1:\text{length}(\text{T}(1,:))\)
\(\quad \quad \quad \text{X\_s(row,col)}=\text{XX}(\text{T(row,col)});\)
\(\quad \quad \quad \text{Y\_s(row,col)}=\text{YY}(\text{T(row,col)});\)
\(\quad \quad \quad \text{Z\_s(row,col)}=\text{ZZ}(\text{T(row,col)});\)
\(\quad \quad \quad \text{C\_s(row,col,k)}=\text{Z\_vector}(\text{T(row,col)},k);\)
\(\quad \end{end}\)
\(\end{end}\)
for k=1:S_L
    h1 = subplot(10,10,1:70);
    fill3(X_s,Y_s,Z_s,C_s,:,:,:k), view(0,0);
    set(h1,'XTick',[],'YTick',[],'ZTick',[]);
    shading interp
    camlight('infinite'); lighting phong;

    subplot(10,10,71:100)
    hold on
    grid on
    axis([0 S_L min(V5) max(V5)]);
    plot(k,V5(k),'.b','MarkerSize',6);
    hold off
    drawnow
    F(k)=getframe(h);
end

end
Vita

Jaime R. De La Cruz was born on April 20th of 1986 in Cd. Juarez, Chihuahua, Mexico. The son of Jaime De La Cruz and Edith L. Vazquez two small business owners and entrepreneurs. He is the oldest of his siblings Mario, Libertad and Maria. He attended public elementary school, public secondary school, and high school in Cd. Juarez before enrolling at UTEP in 2004, where he met his future wife, Grisel Ventura a engineering student. He obtained his bachelor’s degree in Electrical Engineering in 2009 and continued to pursue his Master’s degree under the mentorship of Dr. Joseph H. Pierluissi. He and has two seminar presentations on ECG analysis, two conference presentations on the 2010-2011 period. On March 2011, he achieved his first scientific journal publication in the International Journal of Bioelectromagnetism. Currently he works as an assistant instructor in Electrical Engineering at UTEP.

Permanent address:  514 Tawny Oaks Pl

El Paso, TX, 79912

This thesis was typed by Jaime R. De La Cruz.