A Multichannel Data Acquisition System for RF Ablation of Ventricular Tachycardia

by

Nitza M. Basoco

Submitted to the
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in partial fulfillment of the requirements for the degree of

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Abstract

Catheter ablation, a technique to prevent cardiac arrhythmias from recurring involves the use of a catheter to deliver radio-frequency energy to the site of origin of these arrhythmias. The guidance of the ablation catheter to the site of origin is mainly based on the experience of the cardiac electrophysiologist. As a result, the procedure may last many hours during which the arrhythmia is ongoing. Thus, patients that cannot tolerate this procedure are necessarily excluded. A new methodology developed by the Cohen Lab will allow the use of body surface electrocardiographic (ECG) signals to both identify the site of origin of the arrhythmia in the heart, and guide the ablation catheter to this site.

This thesis deals with the design of the hardware of a 64-channel data acquisition system that will be used to implement the new methodology. It consists of electrode sensor arrays, overvolt protectors, instrumentation/isolation amplifiers, filters and demodulators. The system was designed to achieve low noised level and amplification of a thousand. An eighth-order Bessel low-pass filter was implemented using switched capacitor circuits, so that in a multichannel setup, the rolloff frequency of all channels can be digitally controlled by one clock frequency.

Thesis Supervisor: Richard J. Cohen
Title: Whitaker Professor in Biomedical Engineering

To Rose and Victor Basoco

Your love and encouragement gave me the strength to accomplish my dreams.

Thank you.

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Chapter 1

Introduction

Sudden cardiac death is the leading cause of death in the western civilized world. Arrhythmias, such as ventricular tachycardia (VT) and ventricular fibrillation (VF), are believed to cause half of these deaths. When the heart is in ventricular fibrillation the lower chambers quiver and no blood is pumped. Collapse and sudden death follow unless cardiopulmonary resuscitation is initiated immediately. The only reliable method for termination of VF is defibrillation.

Ventricular fibrillation and tachycardia usually develop during the acute phase of a myocardial infarction, and normally disappear once it stabilizes. However, some patients develop ventricular tachycardia within weeks after the onset of the infarction. VT is dangerous because the heart rate is too fast and unsynchronized to allow effective pumping action by the heart. Often it degenerates into ventricular fibrillation, which again is fatal if untreated.

Prevention and treatment of VT includes 1) anti-arrhythmic drug therapy, 2) implantable cardioverter defibrillator "ICD", 3) surgical ablation and the latest treatment 4) radio frequency catheter ablation. Each of these treatments has its limitations. Anti-arrhythmic drug therapy has not been demonstrated to be effective. ICDs do not prevent VT, but restore the normal heart rhythm after it has become abnormal. In addition, use of the ICD is problematic in individuals with multiple recurrent episodes of fibrillation since internal defibrillation is both traumatic and painful. Surgical ablation, although effective for certain patients, has a mortality rate of 9%-20%.

Catheter ablation involves the delivery of radio frequency energy from the tip of a catheter to the site of origin of the arrhythmia. The ablation process stops the extra impulses that cause the arrhythmia by killing a small region of heart muscle cells (approximately 1/5 of an inch). In order for catheter ablation to be successful the arrhythmia's site of origin has to be identified and the catheter brought to that exact location. Currently the procedure is based on a "trial and error" approach, where success depends on the skills and experience of the cardiac electrophysiologist. The operator must be careful when deciding the correct location, since the patient's condition deteriorates if the wrong piece of tissue is ablated. Thus, the procedure is slow and may take the electrophysiologist hours to find the site of origin of the arrhythmia. Furthermore, the electrophysiologist has to identify the site of the origin while the arrhythmia is occurring, which limits the number of patients eligible for the procedure because not every patient can remain hemodynamically stable throughout the process.

The success of radio frequency catheter ablation for ventricular arrhythmias using the conventional mapping techniques is less than 70%, even in the hands of the best electrocardiologist. A new methodology has been proposed that would allow the cardiac electrophysiologist to use body surface electrocardiographic (ECG) signals to identify the site of origin of the arrhythmia. This new methodology will then enable the cardiac electrophysiologist to use the trajectory of the equivalent cardiac dipole generator to guide the catheter to the focus of the arrhythmia.

Successful catheter ablation of ventricular tachycardia will have a significant impact in reducing sudden cardiac death, the use of defibrillators and potentially harmful antiarrhythmic medications. This new method will have important implications in the patients' quality of life and prognosis, as well as reducing medical cost. This methodology

will also increase the amount of patients eligible for the procedure because it decreases the amount of time the patient has to be in induced arrhythmia.

To implement this new methodology a system that would verify its applicability and accuracy needs to be built. The system would include a personal computer that would perform the following: 1) multi-channel signal acquisition, 2) digital signal processing, 3) estimate the statistical properties of the fit and 4) display the trajectory and spatial error of the equivalent dipole. This thesis deals with the hardware of the multi-channel data acquisition system.

This thesis is organized as follows:

Chapter 2 - Background and Motivation

Chapter 3 – Design

Chapter 4 – Test Procedures

Chapter 5 – Conclusion

Chapter 2

Background and Motivation

2.1 The Heart

2.1.1 Anatomy and Function

The heart functions as a four-chambered pump for the circulatory system. The ventricles supply the main pumping function while the atria are antechambers that store blood while the ventricles are pumping. Diastole is the resting or filling phase of the heart, while systole is the contractile or pumping phase. Each mechanical heartbeat is triggered by an action potential that originates from a rhythmic pacemaker within the heart and is conducted rapidly throughout the organ to produce a coordinated contraction.

2.1.2 The Cardiac Conduction System

All cardiac muscles are electrically excitable and capable of propagating action potentials. The rhythmic cardiac impulses originate in the pace making cells of the sinoartial (SA) node, located at the junction of the superior vena cava and the right atrium as seen in Figure 2.1. Repetitive activity is initiated at this point and propagates to adjoining atrial tissue by means of the local-circuit currents. Activation proceeds from cell to cell until the entire right and left atria are activated. Direct propagation from the atria to ventricles cannot occur because fibrous tissues separate them. Instead activation must follow a path that starts at the atrioventricular (AV) node, in the atria, proceeds through the common and then right and left bundles of His, to the terminal Purkinje fibers. The initial path involves slow conduction in the AV junction, introducing a delay of 70-80ms, that allows atrial contraction to be completed before ventricular contraction begins.

Once the electrical impulse reaches the bundle of His, conduction is rapid and results in the initiation of ventricular activation over a wide region. The Purkinje system

efficiently spreads excitation to the muscle cells of the inner wall of the heart. Activation then spreads slowly from cell to cell through the ventricular myocardium until the entire ventricular muscle mass is depolarized. Excitation begins in the ventricular septum and spreads to the apex, then to the walls of the ventricles and finally to the base of the heart. Depolarization of the ventricles takes about 80ms. Repolarization is not synchronized from cell to cell as is depolarization, and it proceeds in a direction generally opposite to that of depolarization.

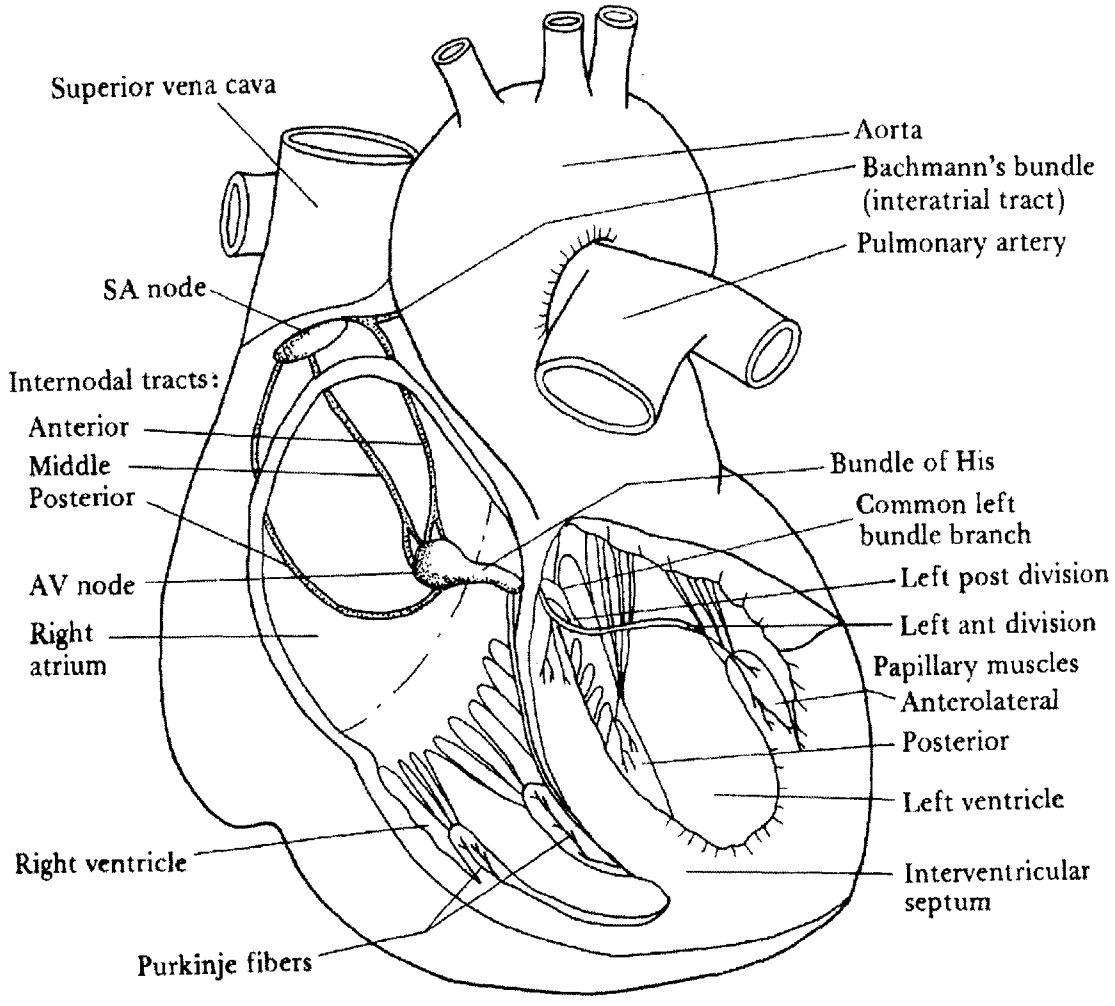

Figure 2.1: Electrical conduction system of the heart [1, p141].

2.1.3 Normal and Abnormal Cardiac Rhythms

2.1.3.1 Natural Excitation of the Heart

The properties of automaticity and periodicity are intrinsic to cardiac tissue. The region that displays the highest order of rhythmicity is the sinoartial or SA node; also known as the natural pacemaker of the heart. Other regions of the heart that initiate beats under special circumstances are called ectopic foci or ectopic pacemakers. Ectopic foci may become pacemakers when 1) their own rhythmicity becomes enhanced, 2) the rhythmicity of the higher order pacemakers becomes depressed, or 3) all conduction pathways between the ectopic focus and those regions with a higher degree of rhythmicity become blocked. A normal heart rate, seen in Figure 2.2, is anywhere between 60-100bpm. The rate is slowed during sleep and is accelerated by emotion, exercise, fever and many other stimuli.

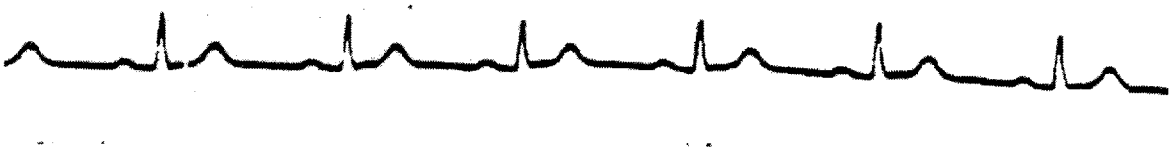

Figure 2.2: ECG of normal heart beat.

2.1.3.2 Pathophysiology of Arrhythmias

Arrhythmias are generally thought to occur on the basis of automaticity, triggered activity, re-entry or a combination of three mechanisms. In general, re-entry is the mechanism of clinical ventricular arrhythmias [1]. In the presence of slow conduction and /or unidirectional block, a "re-entrant circuit" of excitation can be established in the myocardium.

The conditions of reentry are illustrated in Figure 2.3. In each of the four panels, a single bundle (S) of cardiac fibers is seen to divide into a left (L) and a right (R) branch. A connecting bundle (C) runs between the two branches. Normally, the impulse coming

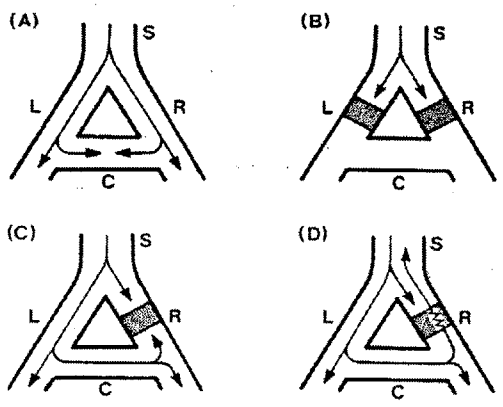

Figure 2.3: The role of unidirectional block in reentry. In panel A, an excitation wave traveling down a single bundle (S) of fibers continues down the left (L) and right (R) branches. The depolarization wave enters the connecting branch (C) from both ends and is extinguished at the point of collision. In panel B, the wave is blocked in the L and R branches. In panel C, bidirectional block exists in branch R. In panel D, unidirectional block exists in branch R. The antegrade impulse is blocked, but the retrograde impulse is conducted through and reenters bundle S [2].

down bundle S is conducted along the L and R branches, as shown in panel A. As the impulse reaches the connecting link C, it enters from both sides and becomes extinguished at the point of collision. The impulse from the left side cannot proceed further because the tissue beyond is in its absolute refractory period. The impulse from the right cannot pass through bundle C for the same reason.

As can be seen in panel B an impulse cannot make a complete circuit if antegrade block exists in the two branches (L and R) of the fiber bundle, and thus reentry is not possible. A necessary condition for reentry unidirectional block -- the impulse is able to pass in one direction but not the other. In panel D the impulse may travel down branch L normally and may be blocked in the antegrade direction in branch R. The impulse that had been conducted down branch L and through the connecting branch C may be able to penetrate the depressed region in branch R from the retrograde direction, even though the antegrade impulse had been blocked previously at the same site. While unidirectional block is

a necessary condition for re-entry it is not a sufficient one. Since the effective refractory period of the reentered region must be less than the propagation time around the loop.

There are two types of re-entrant mechanisms: random re-entry, which can cause atrial or ventricular fibrillation, and ordered re-entry which can cause tachycardias. The difference between the two is in the pathway. During random re-entry, propagation occurs over re-entrant pathways that continuously change their size and location with time, whereas an ordered re-entry implies a relatively fixed re-entrant pathway. For both cases, the wavelength of the impulse in the re-entrant circuit (conduction velocity X refractory period) must be shorter than the length of the circuit, so that the tissue has completed it's refractory period.

Re-entry may occur in patients who have bundles of surviving muscle fibers in healed myocardial infarcts. The interfusion of dead cells and diseased cells creates the anisotropic medium for the development of re-entrant circuits. There are many possible geometric arrangements for such loops which may exist in several sites and locations of the heart [3].

2.1.3.3 Ventricular Tachycardia (VT)

Ventricular Tachycardia arises most frequently in association with the occlusion of a coronary artery and/or electrolyte disturbance. It usually lies in the range from 150-300 beats per minute. Rates above 250 beats per minute fail to provide sufficient cardiac output to maintain life since the rapid rate does not allow sufficient filling of the ventricles. This arrhythmia arises from an enhanced automaticity of re-entry as stated above. It is not possible to unequivocally determine that a tachycardia is of ventricular (and not supra ventricular) origin from the electrocardiogram alone. See Figure 2.4 for VT ECG signal.

Figure 2.4: Ventricular tachycardia

2.1.3.4 Ventricular Fibrillation (VF)

Ventricular fibrillation refers to the seemingly random depolarization of cardiac tissue. The lack of sustained periodic contractions results in an absence of cardiac output making VF a life-threatening condition. The electrocardiographic manifestations are highly irregular continuous waves. The underlying electrophysiology is characterized by reentry loops possibly associated with myocardial damage due to coronary occlusion. See Figure 2.5 for VF ECG signal.

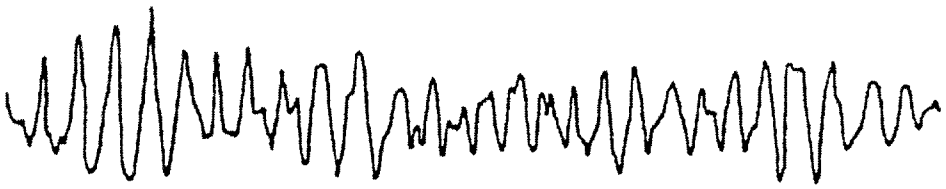

Figure 2.5: Ventricular fibrillation

2.2 Noninvasive Tools to identify Abnormal Arrhythmic Activity

The ability of the physician to guide the catheter to the location is limited by the current technology. Various mapping techniques are in use today and each has it's own limitations.

2.2.1 Fluoroscopic guidance

Common to all clinical catheter ablation strategies is the use of fluoroscopy for the guidance of the ablation catheter, including the beginning of the new methodology. The injection of the radio-opaque dyes into the ventricles makes it possible for the clinician to assess ventricular function. X-ray equipment is used to visualize heart structures and the position of various catheters. The problems associated with fluoroscopy include the following: 1) The inability to accurately associate intracardiac electrograms with their location within the heart. 2) The endocardial surface is not visible, thus the target sites can only be approximated by their relationship with nearby structures. 3) Since fluoroscopy is done in two dimensions navigation is frequently inexact, time consuming and requires multiple views to estimate the three-dimensional location of the catheter. 4) Inability to accurately return the catheter to a previously mapped site. 5) Exposes the patient and medical personnel to radiation. In the new methodology fluoroscopy is necessary to insert the catheter, but then the dyes can be flushed out, decreasing the exposure to radiation.

2.2.2 Electro-anatomical mapping

Electro-anatomical mapping is a non-fluoroscopic catheter mapping tool based on an activation sequence to track and localize the tip of the mapping catheter by magnetic localization in conjunction with electrical activity recorded by the catheter. This technique is fundamentally flawed since it sequentially samples endocardial sites prolonging the mapping process. As mentioned before the patient must be in VT during the mapping pro-

cess and be hemodynamically stable. Thus, the time involved in this procedure greatly limits the amount of patients eligible for the treatment.

2.2.3 Basket Catheter

This approach places a non-contact 64-electrode basket catheter inside the heart to electrically map it. First, high frequency pulses are applied to a standard catheter as the tip is dragged over the endocardial surface. A basket catheter is then used to locate the tip of the ablation catheter, and to trace and reconstruct the endocardial surface of the ventricular chamber. The chamber geometry, the known locations of the basket catheter and the non-contact potential at each electrode on the basket catheter are combined to solve Laplace's equation, and the electrograms on the endocardial surface can be computed. The problem with basket catheter is that the ventricular geometry varies during the cardiac cycle. Also, during systole, the distance between the interelectrodes and the actual recording sites on the endocardium are decreased. This relative movement between the heart and the electrodes limits the accuracy of the mapping method.

2.3 New Methodology

The new methodology considers the heart as a cardiac equivalent dipole. For many arrhythmias, the electrical activity within the heart is highly localized for a portion of the cardiac cycle. For the remainder of the cycle the electrical activity spreads. Normally, it is not possible to reconstruct the three-dimensional distribution of the cardiac electrical sources from a two-dimensional distribution of the ECG signal. However, if the source is localized, then this localized region - the interface of a partially depolarized tissue - can be approximated as a single equivalent moving dipole (SEMD), and its location and moments can be computed.

If the site of the origin of the arrhythmia can be localized during the cardiac cycle, then it can be ablated. The Cohen lab has developed an algorithm that will fit the dipole's location, strength, and orientation to body surface ECG signals [4]. The same inverse algorithm can then be used to find and guide the catheter to the site by applying a low-amplitude bipolar current pulse (~5μA) at high frequency (2kHz - 5kHz) to the tip of the catheter.

The process of guiding the tip of the catheter to the ablation site is summarized in the following steps:

Step 1:Induce the arrhythmia and record a few beats of VT.

Step 2: Reconstruct and plot the dipole locations at each point during the cardiac cycle.

Step 3: Identify the site of origin of the arrhythmia from the these data

Step 4: Apply the bipolar current pulses to the tip of the catheter.

Step 5: Locate the SEMD corresponding to the tip of the catheter on the screen. Using the SEMD location continuous displayed on the screen, the operator will advance the catheter tip to the site of origin of the arrhythmia

Step 6: Apply ablation energy to the tip of the catheter.

The effect of local tissue inhomogeneities have not been taken into account. However, any errors introduced into the system when calculating the position of the site of the arrhythmia and the catheter will be the same. Thus, when the algorithm matches the two sites, they are truly at the same location.

In contrast to the other mapping techniques, the inverse solution can be computed from only a few beats of the arrhythmia eliminating the need for prolonged maintenance. The new methodology will also allow the electrophysiologists to revisit the site and deliver additional radio-frequency energy, once it has been identified. The hardware of this methodology is described in Section 2.7.

2.4 Electrocardiology

The electrical activity of myocardial cells establishes small currents within the body. These lead to potential differences on the body surface, which can be detected. Potential differences are determined by placing electrodes on the surface of the body and measuring the voltage between them. If the two electrodes are located on different equal-potential lines of the electric field of the heart, a nonzero potential is measured. Different pairs of electrodes at different locations generally yield different voltages because of the spatial dependence of the electric field of the heart. Thus, it is important to have certain standard positions for clinical evaluation.

The smallest unit contributing to the ECG is the single cell. At the boundary between normal and depolarized tissue, a small current will flow in the direction of action potential propagation. No net charge is built up by this current, so all current loops in the conductive media close upon themselves, forming a dipole field as seen in Figure 2.6. The heart's total electrical activity at any instant may be represented as a distribution of such current sources, located on the advancing front of depolarization or repolarization.

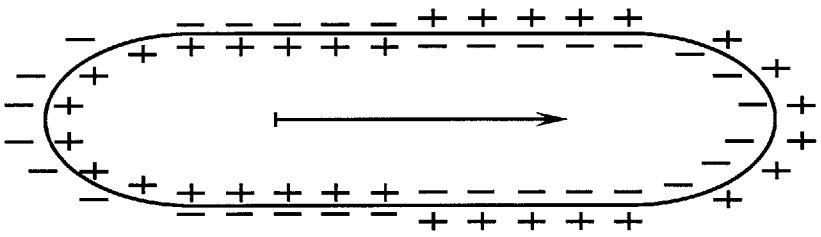

Figure 2.6: Dipole moment of a piece of depolarized tissue.

Imagine the heart suspended in a homogeneous isotropic conducting medium and observed from a distance large compared with its size, then all the individual sources may be assumed to originate at the same point in space. The total electrical activity of the heart may then be represented as a single current dipole whose magnitude and direction are given by the vector summation of all the individual dipole sources. This net vector **M** (t) is

commonly referred to as the heart vector. As cardiac depolarization spreads, this vector changes in magnitude and direction as a function of time.

Body surface potentials may be related to the heart vector. For simplicity, assume that the heart is located at the center of a spherical torso made of homogeneous, isotropic, conducting material [5]. Laplace's equation holds within the sphere and may be solved for the potential distribution on the surface. The result is

$$\Phi(t) = \frac{K|M(t)|}{\sigma R^2}\cos\theta(t) \tag{2.1}$$

where Φ (t) is the potential on the surface of a sphere of radius R and conductivity σ, θ(t) is the angle between the direction of the heart vector and the point of observation and |M(t)| is the magnitude of the heart vector. Equation 2.1 can also be written in vector notation:

$$\Phi(t) = M(t) \cdot OA \tag{2.2}$$

where OA is a vector from the origin to point A on the surface of the sphere.

In general, the potential difference between two points on the surface of the torso would be

$$V_{AB}(t) = M(t) \cdot L_{AB} \tag{2.3}$$

where L_{AB} is the lead vector connecting points A and B on the torso. It is convenient to define a reference central terminal by averaging the potentials from the three limbs:

$$\Phi_{CT}(t) = \Phi_{RA}(t) + \Phi_{LA}(t) + \Phi_{LL}(t) = 0 \tag{2.4}$$

Note that measured potentials contain sources other than the heart (e.g. electrical noise, muscle movement, etc.) Therefore it is necessary that Φ_{CT} (t) = 0 to null out the offsets. Recording from various combinations of limb and chest electrodes generates the standard electrographic lead vectors. In clinical cardiology, more than one lead must be recorded to

describe the heart's electric activity fully. In practice, several leads are taken in the frontal plane (the plane parallel to the ground when you are lying on your back) and the transverse plane (the plane of your body that is parallel to the ground when you are standing erect).

Three basic leads make up the frontal plane ECG. These are derived from the various permutations of pairs of electrodes when one electrode is located on the right arm, RA, the left arm, LA, and the left leg, LL. Often an electrode is placed on the right leg, RL, and connected to a special circuit that helps lower the common voltage. The resulting three leads are lead I, LA to RA; lead II, LL to RA; and lead III, LL to LA. The lead vectors that are formed can be approximated as an equilateral triangle, known as Eindhoven's triangle.

Three additional leads in the frontal plane are routinely taken in clinical ECGs. These leads are based on signals obtained from more than one pair of electrodes, known as unipolar leads. They consist of the potential appearing on one electrode taken with respect to an equivalent reference electrode, which is the moving average of the signals seen at two or more electrodes. The Wilson central terminal is commonly used as the equivalent reference electrode. The signal between LA and the central point is known as VL, that at RA as VR, and that at the left foot as VF. An additional three signals, aVL, AVR, and aVF, are obtained by augmenting the leads, as illustrated in Figure 2.7.

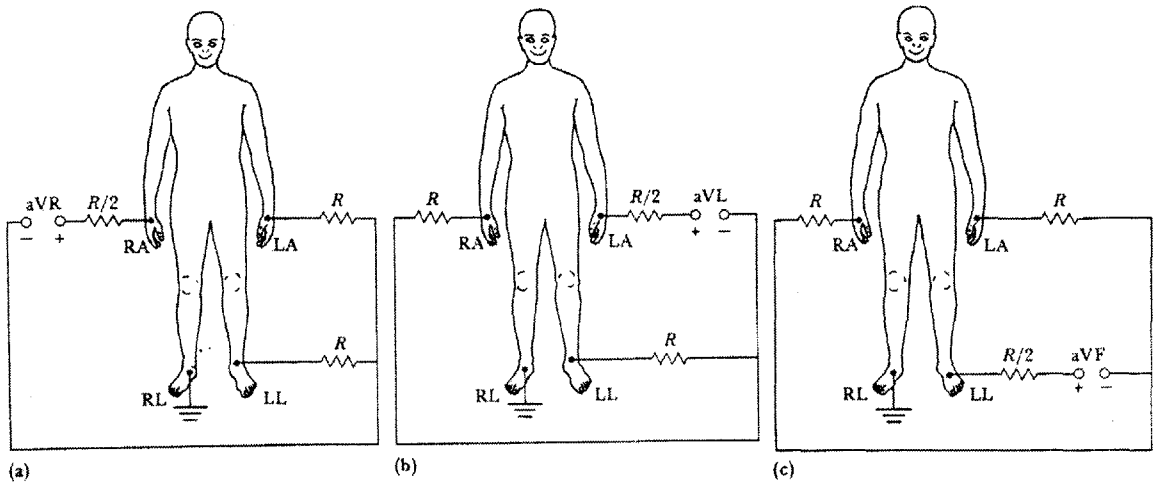

Figure 2.7: Augmented Leads (a), (b), (c) connections of electrodes for the three augmented limb leads [6].

Each cardiac cycle is represented by a sequence of three major waves. The initial low-amplitude P wave reflects atrial depolarization. The next deflection is the QRS complex, corresponding to ventricular depolarization. The final wave is the T wave, which is due to ventricular repolarization. The QRS complex normally masks the manifestations of atrial repolarization. The P-R and S-T intervals are normally at zero potential, the P-R interval being caused mainly by conduction delay in the AV node. The S-T segment is related to the average duration of the plateau regions of individual ventricular cells. A small additional wave, called the U wave, is sometimes recorded temporally after the T wave. It is an inconstant finding believed to be due to slow repolarization of ventricular papillary muscles.

The ECG provides valuable information to clinicians, yet it does have limitations. The three-dimensional distribution of electrical activity in the heart cannot be reconstructed from the potential distribution on the body surface (the inverse problem). Also, the classic ECG electrode array under-samples the distribution of electrical potentials on the torso surface. The precise geometry of the chest and the spatial distribution of conductivities

within the chest are unknown. Information about the cardiac electrical activity is blurred and attenuated in the torso volume conductor, the medium between the heart and the body surface. Furthermore, the standard ECG gives a coarse description of the spatial complexity of cardiac activity. Its interpretation cannot be based on a rigorous biophysical model, but rather must depend on a heuristic match between waveforms and disease state. Despite these limitations, clinical electrocardiography is used because it is safe, inexpensive and a non-invasive way to measure cardiac activity. However, electrode arrays have been used to achieve a denser spatial sampling along with geometrical models of the thorax allowing a better relationship to be established between cardiac electrical activity and torso surface potentials.

2.5 Body Surface Potential Mapping

In contrast to the standard 12-lead electrocardiography (ECG), BSPM depicts the electrical activity of the heart as reflected on the entire surface of the torso. As a consequence, body surface maps may contain important information by which a particular event in the heart may be located. BSPMs contain important clinical diagnostic information for a wide range of cardiac abnormalities including ischemia, infarction, and cardiac rhythm disturbances. While BSPM can reliably identify major single cardiac electrical events, it is limited in its ability to identify and resolve multiple simultaneous electrical events in the heart. In BSPM it is difficult to relate body surface electrical features to specific intracardiac events because the potential at every point on the body surface is a weighed sum of electrical contributions coming from the entire heart. In addition, the volume conductor between the heart and the body smooths and distorts the potential distribution. Many regional events that occur on the cardiac surface do not produce recognizable events on the body surface.

2.6 Noise Effecting the Measurement of the ECG

2.6.1 Interference From Electronic Devices

A major source of interference when recording the ECG is the electric-power system [6]. Besides providing power to the device, power lines are connected to other pieces of equipment and appliances in a typical hospital room. There are also power lines in the walls, floor and ceiling running past the room to other points in the building. These power lines can affect the recording of the ECG and introduce interference at the line frequency in the recorded trace as seen in Figure 2.8a. Such interference appears on the recordings as a result of electric field coupling and/or magnetic induction.

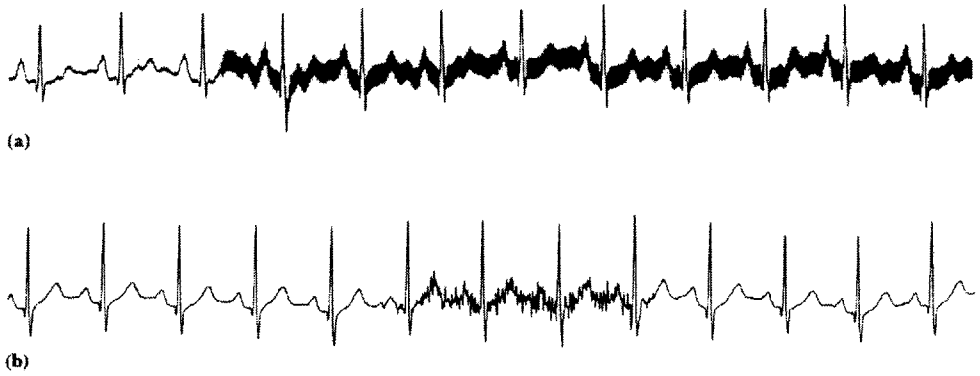

Figure 2.8: (a) 60-Hz power-line interference. (b) Electromyographic interference on the ECG [6].

Electric-field coupling between the power lines, the device and/or the patient is a result of the electric fields surrounding main power lines and the power cords connecting different pieces of apparatus to electric outlets. These fields can be present even when the apparatus is not turned on, because current is not necessary to establish the electric field. These fields couple into the patient, the lead wires, and the device itself. It is as though small capacitors join these entities to the power lines, as show in Figure 2.9.

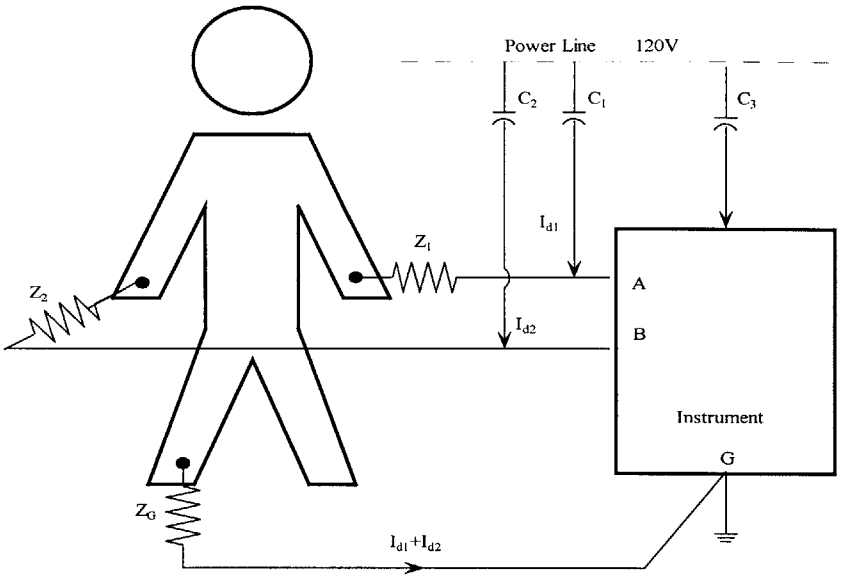

Figure 2.9: Interference from the powerline. Coupling capacitance between the power-line and the lead wires causes current to flow through the skin-electrode impedances on its way to ground

The current through the capacitance C_3 coupling the ungrounded side of the power line and the device itself flows to the ground and does not cause interference. C_1 represents the capacitance between the power line and one of the leads. Current i_{d1} does not flow into the device because of its high input impedance, but rather through the skin-electrode impedances Z_1 and Z_G to ground. Similarly i_{d2} flows through Z_2 and Z_G to ground. Body impedance, which is about 500Ω, can be neglected when compared with the other impedances shown. The voltage amplified is that appearing between inputs A and B, $v_A - v_B = i_{d1}Z_1 - i_{d2}Z_2$. The voltage difference can be up to 120μV, an objectable level of interference. This can be minimized by shielding the leads and grounding each shield at the device. Lowering the skin-electrode impedance is also helpful.

Current also flows from the power line into the body as seen in Figure 2.10. This displacement current i_{db} flows through the ground impedance Z_G to ground. The resulting voltage drop causes a common-mode voltage v_{cm} to appear throughout the body.

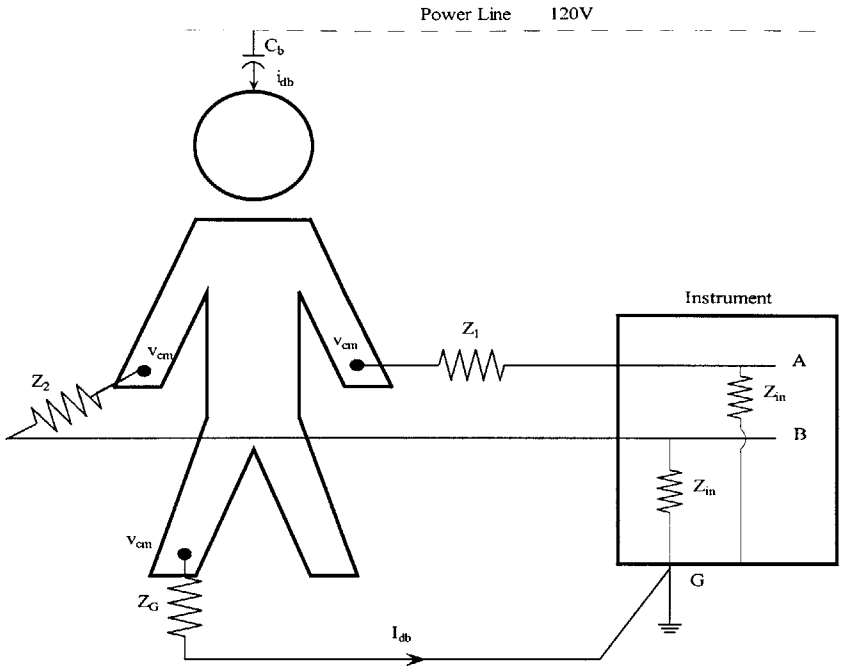

Figure 2.10: Current flows from the power line through the body and ground impedance creating a common-mode voltage everywhere on the body.

In poor electrical environments in which $i_{db}>1\mu A$, v_{cm} can be greater than 50 mV. For an ideal amplifier this would not be a problem, because a differential amplifier would reject the common-mode voltage. However, real amplifiers have finite input impedances Z_{in}. Thus, v_{cm} is decreased because of the attenuator action of the skin-electrode impedances and Z_{in}. That is

$$v_A - v_B = v_{cm}\left(\frac{Z_{in}}{Z_{in}+Z_1} - \frac{Z_{in}}{Z_{in}+Z_2}\right) \tag{2.5}$$

where Z_1 and Z_2 are much less than Z_{in}. A typical voltage difference is around 40mV, which would be noticeable on the ECG. This can be minimized by lowering skin-electrode impedance and raising amplifier input impedance. The difference between the skin-electrode impedances is an important consideration in the choice of biopotential amplifiers.

The other source of interference from power lines is magnetic induction. Current in the power lines establishes a magnetic field in the vicinity of the line. Magnetic fields can also

sometimes originate from transformers and fluorescent lights. If such magnetic fields pass through the instrument, lead wires, and patient, a voltage is induced in this loop. This voltage is proportional to the magnetic-field strength and the area of the effective single-turn coil. It can be reduced by (1) decreasing the magnetic field through the use of shielding, (2) by keeping the device and leads away from potential magnetic-field regions, and/or (3) by reducing the effective area of the single turn-coil. This can be achieved by twisting the lead wires together over as much as possible of the distance between the device and the patient.

2.6.2 Other Sources of Electrical Interference

Electric interference from sources other than the power lines can also affect the ECG. Electromagnetic interference from nearby high-power radio, television, or radar facilities can be picked up and rectified. The lead wires and the patient serve as an antenna. Once the signal is detected the demodulated signal appears as interference on the ECG. Electromagnetic interference can also be generated by high-frequency generators in the hospital itself. Electromagnetic radiation can be generated from x-ray machines or switches and relays on heavy-duty electric equipment in the hospital as well. Something as simple as a flickering fluorescent light can produce serious interference [6].

Electromagnetic interference can usually be minimized by shunting the input terminals to the ECG amplifier with a small capacitor of approximately 200pF. At radio frequencies, its reactance is low enough to cause effective shorting of the electromagnetic interference picked up by the lead wires and to keep it from reaching the transistors in the amplifier.

There is also sources of electric interference located within the body itself that can have an effect on the ECG. The human skin is a source of electrical potentials that can change with physiological causes or with external influences such as movement [7]. In

general, about 25mV of dc skin potential exists at the interface of the recording electrode and the skin, but can be as high as 300mV. This is due in part to the potentials generated by the epidermal layers of the skin and in part to the electrochemical (Nernst) potentials generated by the interface of the electrolytic gel with skin and with the electrode. The dc skin potential can be eliminated by high-pass filters. Another source of interference in the human body are the electromyograms (EMG) - signals generated by muscle movement. It is on the same order of amplitude as ECG signals but occurs at higher frequencies. EMG noise can be reduce by lowering the muscle activity during the ECG reording. Since the recording will be done when the patient is lying down and in surgery the EMG noise should be minimal. Respiration also introduces a low frequency noise.

2.7 Hardware Specifications

The new methodology will allow the cardiologist to use ECG signals to identify the site of the origin arrhythmia and guide the catheter to that site. To accomplish this the catheter ablation device will consist of four parts: the patient interface, signal conditioning, data acquisition and a computer. A block diagram of the device is shown in Figure 2.11.

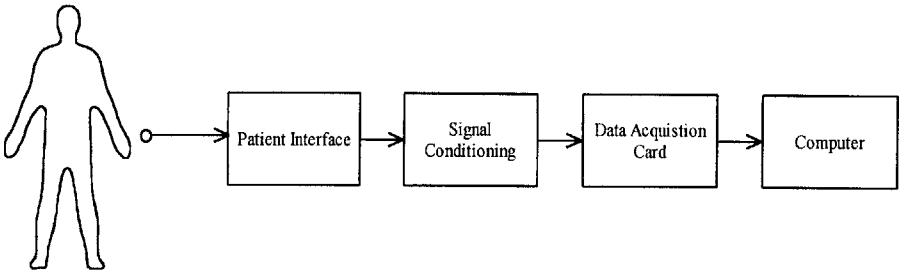

Figure 2.11: Block diagram of complete data acquisition system

The patient interface is made up of sixty-four Ag/AgCl electrodes spread around the chest and back. Two signals are recorded at the electrodes, i) the ECG with frequency range $0<f<250$Hz and ii) the catheter pulses ranging from 2kHz - 5kHz. They are then run

through the conditioning hardware were they are amplified and filtered and separated. The catheter signal is demodulated by a synchronous detector in order to seperate it from the ECG. Once the signals are adequately conditioned they are passed to the National Instrument data acquisition card (AT-MI0-64E-3), where the analog signals are sampled at 2kHz and stored in the computer. The computer then performs the following tasks on the signals: 1) Display of all signals. 2) Digital signal processing, including estimation of the equivalent dipole at each point in the cardiac cycle. 3) Estimate the statistical properties of the fit. 4) Display the trajectory and the spatial error of the equivalent dipole. 5) continuous display of the catheter location

The specifications for the complete device are listed below:

- Number of channels: 64
- Digitizing frequency: 2kHz
- Digital resolution: 12 bits
- Analog frequency bandwidth: 0-50kHz
- Calibration options: Manual or automatic
- Maximum leakage current: 10μA
- Isolation voltage: 3kV AC

Chapter 3

Design

The electrical activity of the human heart can be detected on the body surface and, though quite small (0.5-5.0mV), can be recorded as an electrocardiogram (ECG). In order to safely and accurately measure the ECG and catheter signals care must be taken in designing the conditioning stage of the device. This chapter describes the hardware used to condition the signals.

3.1 Signal Conditioning System Overview

Signals are extracted from 64 unipolar electrodes spaced around the chest and back with high concentration around the heart. Each instrumentation amplifier measures the potential difference between an electrode and a reference signal. The reference signal is chosen to be the Wilson Central Terminal (WCT), the average of the signals from the arms and left leg. This leads to a configuration where the WCT is connected to 64 (inverting) amplifier inputs.

Figure 3.1 shows the block diagram of one channel which is divided into three sections: (i) Common, (ii) ECG and (iii) Catheter. The Common path consists of (1) an overvolt protector, (2) an instrumentation/isolation amplifier, (3) a highpass filter and a (4) Gyrator notch filter to remove the 60-Hz powerline interference. The ECG path includes (1) a lowpass filter with variable cutoff frequency and (2) a gain stage. The Catheter path includes (1) a demodulator (2) a lowpass filter with variable cutoff frequency and (3) a gain stage. The switch at the end of the channel is controlled by computer, and precludes the simultaneous recording of both the ECG and catheter signal.

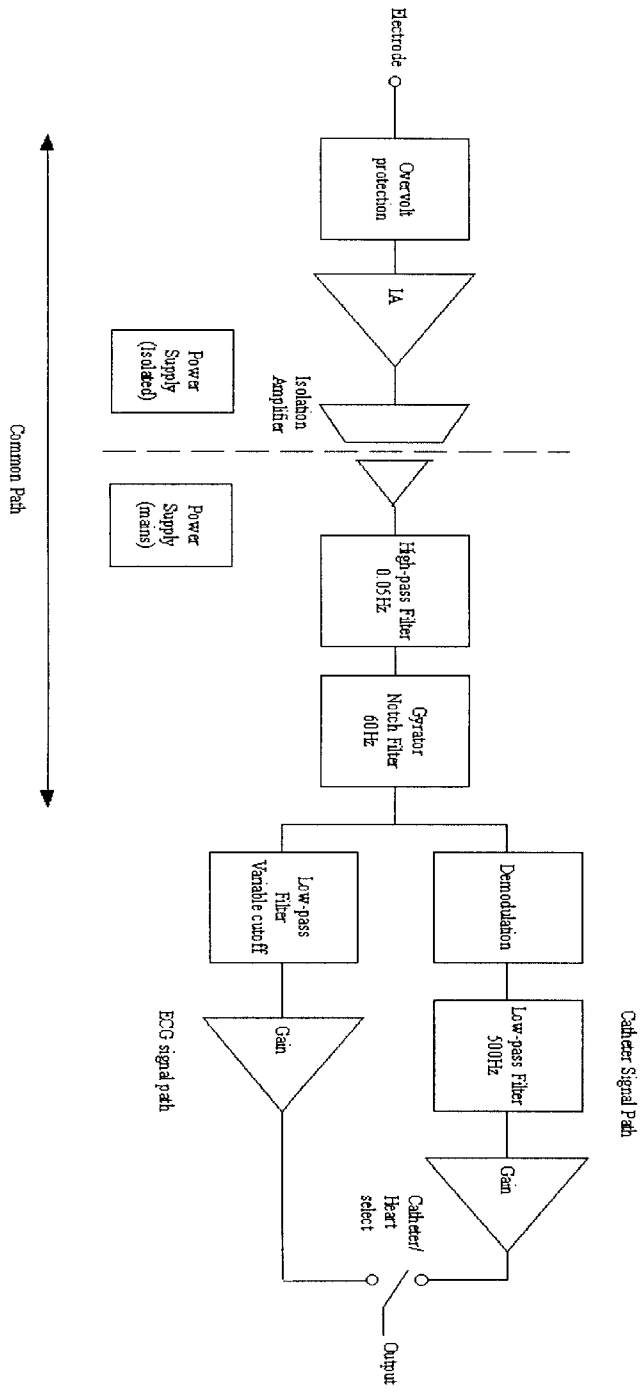

Figure 3.1: Block Diagram of one channel. The channel is separated into three signal paths: (1) Common, (2) ECG and (3) Catheter.

3.2 Common Path

This path is taken by all signals. Its purpose is to provide ample amplification of the signals, isolate and protect the circuit, as well as eliminate the DC offset and 60Hz interference.

3.2.1 Overvolt Protector

The patient as well as the device must be protected from possible hazards. For example, a patient attached to the device may touch the power line. Not only is there a possibility of failure of the electronics, but it is also hazardous to the patient. The data acquisition system must also be suitable for use in an environment, where defibrillators may be used while the instrument is connected to the patient. Therefore, the device is protected from transient voltages as high as 5000V (360J) [8]&[9].

Figure 3.2 shows the circuit used at the front end of the common path to protect the amplifiers of the device. First a series resistors in each electrode lead is used to both limit the current going into the amplifier and attenuate the voltage. The first resistor, R1, is rated for high voltage and power operation. A neon light protects the amplifier from the highest voltage transient. The neon light breaks down at 95V, protecting the following components. Each channel is further protected at lower voltages by means of resistors Rx and Ry and diodes D1 and D2. Depending on the polarity of the high voltage, either D1 or D2 conducts when the voltage at the input is greater than +0.6V or less than -0.6V. The operation of the amplifier is not affected under normal conditions, since the diodes are reverse biased for input signal less than +/- 0.6V. Each of the instrumentation amplifiers (ISO175) has internal overvolt protection of +/- 40V for added protection.

The ISO 175 includes a precision instrumentation amplifier followed by an isolation amplifier and is used as fault protection from defibrillation transients. The ISO175 pro-

vides the first gain stage of the signal. The gain is set to 10, because the absolute dc voltage offset can be as high as 300mV and can cause saturation in the amplifiers.

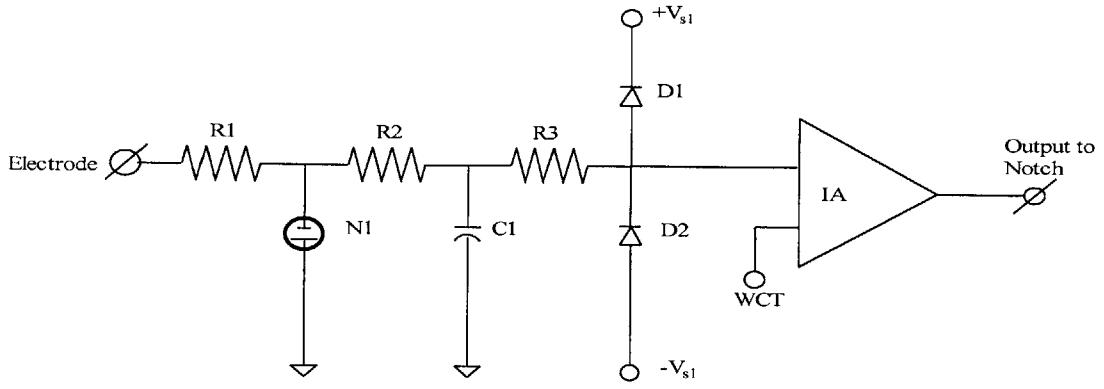

Figure 3.2: Protection Circuit

3.2.2 Highpass Filter

The highpass filter (HPF) removes the large dc offset of the electrodes which permits the ECG signal to be significantly amplified without saturating the amplifiers. It is not placed before the instrumentation amplifier, because the impedances on both sides of the filter will change the cutoff frequency. For example, connecting a 10-kΩ electrode to the HPF would introduce more resistance and change the filter. The system would also require additional highpass filters.

The standard 0.05-Hz single-pole is chosen as the high-pass filter [10]. A higher order filter is not chosen because it would have given nonlinear phase, distorting the shape of the ECG. The circuit is show in Figure 3.3 with a gain of 10. The system function which characterizes this circuit is given as follows:

$$H(s) = \frac{V_{OUT}}{V_{IN}} = \frac{RCs}{RCs + 1} \tag{3.1}$$

Note that the HPF, along with its long time constant, would not be necessary if a higher resolution A-D convertor were used.

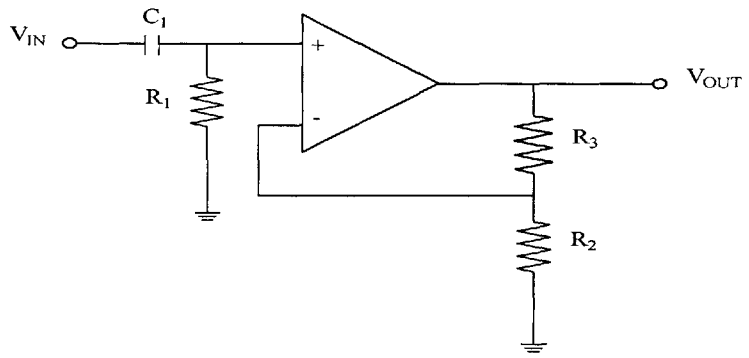

Figure 3.3: Circuit diagram of first-order highpass filter. For cutoff frequency at 0.05Hz: R= 681kΩ, C = 4.7μF

3.2.3 Gyrator Notch Filter

The system noise is required to be less than 30μVp-p RTI, which means that special efforts are needed to reduce the 60-Hz powerline interference. There are a number of steps that can be taken to reduce 60-Hz noise [11]. The most simple is twisting the leads to minimize magnetic induction. Also the use of instrumentation amplifiers with a high common mode rejection ratio is useful since the 60-Hz pickup by the Wilson Central Terminal and the measuring electrode will be cancelled. However, this assumes the input amplifier impedances are equal. In order to completely eliminate the noise, a gyrator notch filter, seen in Figure 3.4, is used. This filter is chosen primarily because of its low sensitivity to component values [12].

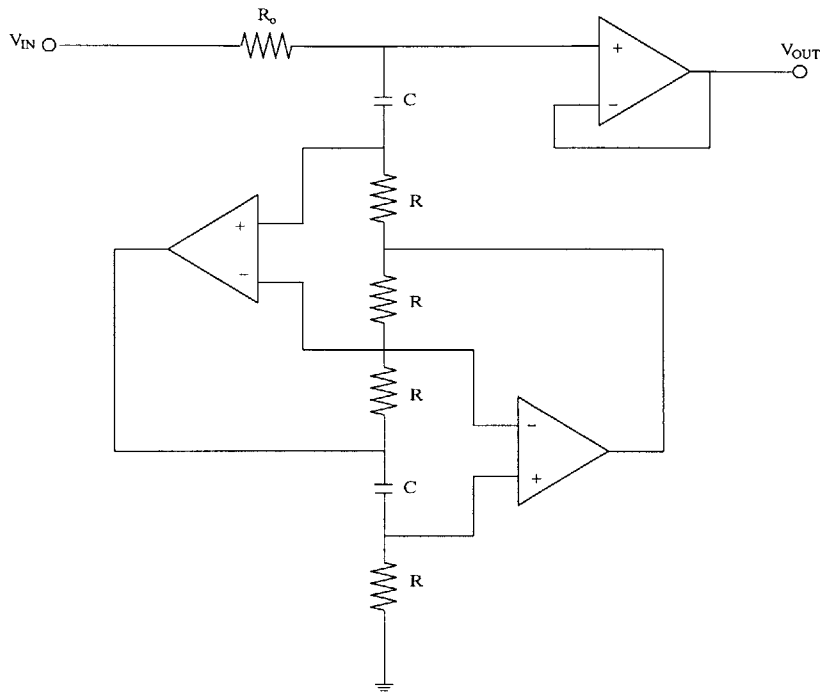

Figure 3.4: 60Hz Gyrator Notch Filter

The notch frequency and the Q value are given as follows:

$$f_{Notch} = \frac{1}{2\pi RC} \tag{3.2}$$

$$Q = \frac{R}{R_o} \tag{3.3}$$

Setting f_{Notch} to 60 and Q to 6, the component values are R = 12.1kΩ and C= 0.22μF. The trade-off to low component sensitivity is a limited input voltage Vin = 2Vp-p. The system function characterizing the notch filter is as follows:

$$H_{Notch}(s) = \frac{V_{OUT}}{V_{IN}} = \frac{1 + R^2C^2s^2}{1 + R_oCs + R^2C^2s^2} \tag{3.4}$$

The notch's calculated frequency response, for Q = 6, is shown in Figure 3.5.

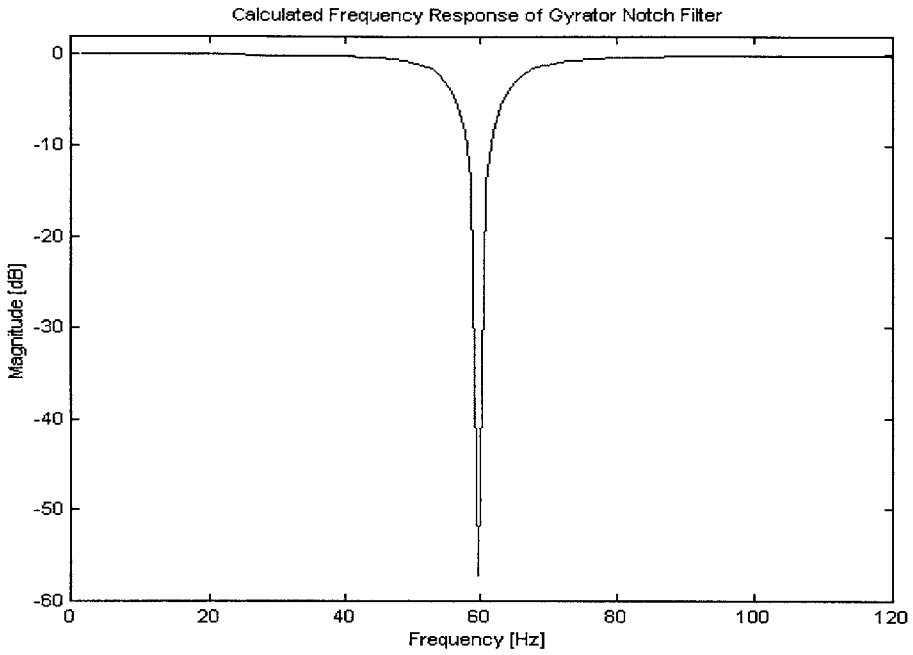

Figure 3.5: Calculated Frequency Response of Gyrator Notch Filter, Q = 6

3.3 ECG Signal Path

3.3.1 Lowpass Filter

The lowpass filter is introduced into the amplifier chain in order to reduce noise power and prevent aliasing. The eighth-order Bessel filter is chosen as the lowpass filter. The Bessel family is chosen because it introduces the least distortions to the ECG. Bessel filters are characterized by almost constant group delay across the entire passband, which preserves the wave shape of filtered signals. They also exhibit short settling time and rise time [12]&[13]. The filter is implemented using an eighth-order switched capacitor (MAX292) because it offers a single line rolloff frequency control for all channels by means of one clock frequency (+5V CMOS logic) [14]. In this way, the rolloff frequency can be controlled by the data-acquisition unit and changed with different sampling rates. Figure 3.6 shows the overall lowpass filter design.

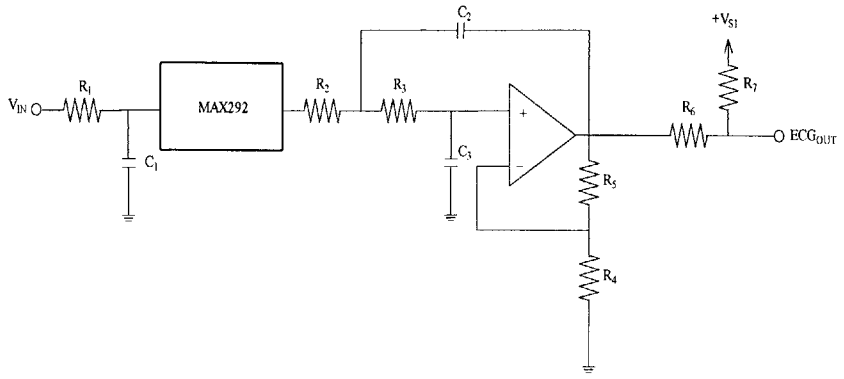

Figure 3.6: Overall Lowpass Filter with simple RC, switched capacitor (MAX292) and 2nd-order Bessel

While the MAX292 offers an attractive solution to single line control of filter frequency in multi-channel applications, it does have some disadvantages. One drawback is the sensitivity of the filter to input signals with a frequency close to the clock frequency. More precisely, any input signal energy at a frequency that differs from that of the clock by an amount corresponding to a frequency in the passband will appear (unattenuated) in the passband. For instance, when using the MAX292 with a cutoff frequency of 100Hz (f_{clock} = 10kHz), any input signal energy in the range of 9.9kHz -10.1kHz will appear in the output band of dc-100Hz and no filter at the output can remove it. Hence, white noise above the Nyquist rate will be aliased into the passband. For example, if the filter cutoff frequency is 100 Hz, then the switched capacitor filter (SCF) samples at 100X100Hz or at 10kHz. Noise above 5kHz (the Nyquist rate) will be aliased to the 5kHz bandwidth represented by the set of samples. Thus, all the noise power will be mapped into the signal spectrum. For these reasons, the simple RC circuit, R1 and C1 as seen in Figure 3.6, is added to limit the bandwidth of the signal before it is applied to the filter section. The 3dB point of the simple RC circuit is set to 4kHz to insure no aliasing for F_{clock}>10kHz (SCF cutoff frequency > 100Hz).

Another disadvantage is clock feedthrough -- the presence of some output signal (typically about 10mV to 25mV) at the clock frequency, that is independent of the input signal. This is easily attenuated with a second-order Bessel filter, seen after the switched capacitor. A cutoff frequency of f_c = 5kHz, is chosen to eliminate all feedthrough for clock frequencies above 10kHz. The system function characterizing this lowpass filter is given as follows:

$$H(s) = \frac{V_{OUT}}{V_{IN}} = \frac{1 + \frac{R_4}{R_3}}{1 + 2RC_2 s + R^2 C_1 C_2 s^2} \tag{3.5}$$

Note that the gain is set by $G = 1 + R_5/R_4$. The gain this stage is ten, bringing the total gain of the channel to 1000. The output voltage range is +/-5V. The purpose of resistors R5 and R6, is to bring the output of the lowpass filter section into the voltage range of the data acquisition card, $0<V_{ADC}<10$.

3.4 Catheter Signal Path

In order to distinguish the catheter signal from the ECG, it is necessary to move the catheter frequency content out of the ECG frequency range (0.05Hz<f<250Hz). Thus, the catheter signal is modulated from low frequency to high frequency. The modulation frequency will range from 2kHz - 5kHz. In order to choose a modulating frequency it is imperative to remember that body impedance is a function of frequency. In particular, an increase in frequency leads to a decrease in impedance. Therefore, it is necessary to keep the modulation frequency sufficiently low such that the catheter and the ECG signals are not at two very different impedances.

In order to modulate the catheter signal, it is necessary to drive the source with a sinusoid source, instead of dc. Then, the spectral density is no longer located at 0 Hz, but

rather is centered at f_0. Therefore, a low-amplitude bipolar current pulse is applied to the tip of the catheter. This method is merely an extension of the chopping technique (turning the source off and on) in order to include both the positive and negative half-cycles [15] & [16].

3.4.1 Demodulation

Since the signal from the tip of the catheter is a square wave, a simple, yet elegant, demodulation technique can be used. Figure 3.9 shows the hardware used to implement this technique [12]. If the input to the demodulation section is only a square wave, then the output will be a dc signal proportional to the signal amplitude. When the control signal is high, or during the positive cycle, signal A is taken to be the output. When the control signal is low, during the negative-cycle signal B is taken to be the output. Figure 3.10 shows the different signals and how the output signal is constructed.

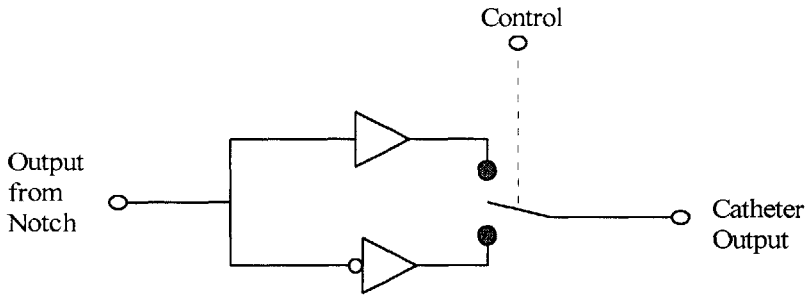

Figure 3.7: Demodulation Hardware

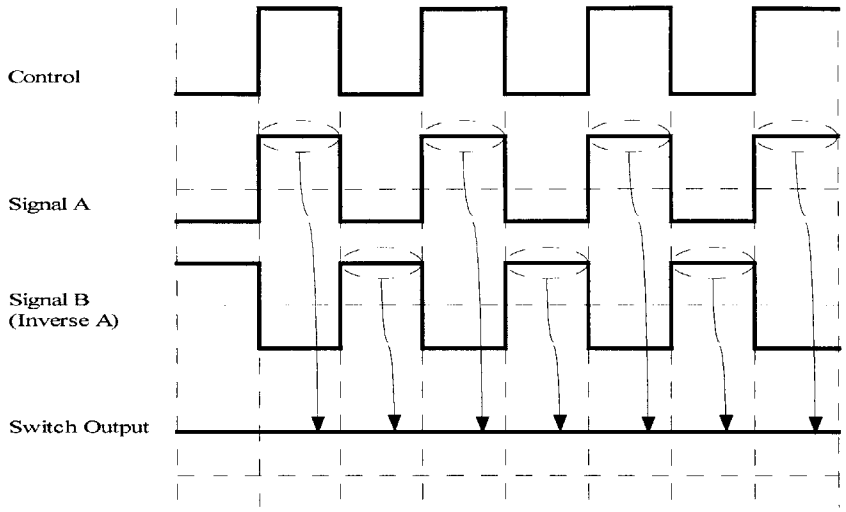

Figure 3.8: Demodulation Signals

From Figure 3.9, it can be seen that the output signal will be incorrect if the demodulator is not synchronized to the carrier signal. The output is dependent on the phase difference, θ, of the carrier and control signal. Instead of the output being $x_{out}(t)$, it would be $x_{out}(t)(1-|2\theta/\pi|)$, where $\theta = 2\pi t/T$. In the extreme case where the control signal is 90^{o} out of phase with the carrier the output would be zero. Hence the signal used to drive the carrier signal in the modulator is used as the control signal to eliminate any phase problems.

In the data acquisition system, the input to the demodulation section is not only a square wave (*i.e.* catheter signal) but also includes the ECG signal. Figure 3.10a shows the signal before demodulation section in which the catheter signal rides on top of the ECG signal. If the signal is lowpass filtered, as done in the ECG signal path, the output is the ECG signal. Figure 3.10b show the signal after the switch, with the ECG signal riding on top of the catheter signal. If this signal is lowpass filtered, then the output will be the catheter signal.

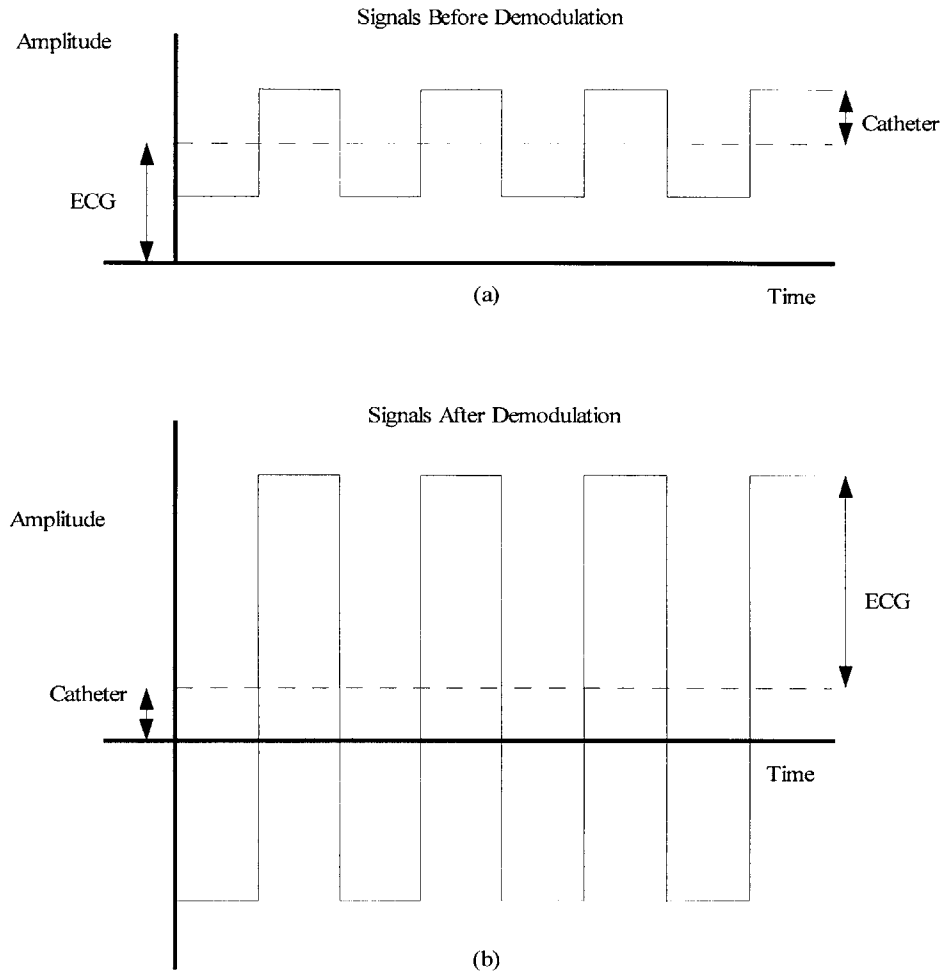

Figure 3.9: (a) Signals before demodulation (b) Signals after demodulation

3.4.2 Lowpass filter and Gain

In order to obtain the catheter signal, the output of the switch needs to be lowpass filtered. The same second-order Bessel filter used after the switch capacitor is used, with a cutoff frequency of 500Hz, since it is not necessary that the cutoff frequency of this lowpass filter be variable. Once again, the Bessel filter is used because of its linear phase and excellent step response (*i.e.* minimal ringing). At this point in time, the gain is set to 10, but may change after the final catheter signal is chosen. Recall that this is easily changed by replacing R4 and R5 such that G = 1+R5/R4 (see Figure 3.6).

Chapter 4

Test Procedures

4.1 Overview

The device will be made up of eight signal conditioning boards and one mother board. Each conditioning board will have eight channels. One channel includes the Common path, ECG path, and Catheter path as discussed in Chapter 3. The mother board will have eight slots where each conditioniing boards will be placed. It will also include the input connections for the electrodes as well as the output connection to the data acquisition card. When the construction of the device is complete it will have to go through various tests. Below is an outline of the test procedures needed to be done on all of the boards and of the complete device.

4.2 Device Specifications

4.2.1 Operating Conditions

The performance requirements of the device will be met under the following ambient environmental conditions [8]:

Table 4.1: Operating Conditions

Line voltage	104-127Vrms
Line frequency	60 +/- 1Hz
Temperature	25 +/- 10oC
Atmospheric pressure	500 to 775 mm Hg

4.2.2 Performance Requirement

Tests for the following performance will be performed after a warm-up of at least 15 minutes [8].

Table 4.2: Performance Requirements

Requirement Description	Min/Max	Units	Min/Max Value
Defibrillation overload protection:			
Overvoltage	max	V	5000
Energy	max	J	360
Engergy reduction	max	%	10
Charge	max	mC	100
Leakage Current	max	uA	10
Input dynamic range:			
Input signal amplitude	max	mV	+/-5
dc offset voltage	range	mV	-300 to +300
System Noise	max	uVp-p	30
60-Hz Tolerance	min	uVp-p	100
Common mode rejection (allowable noise for 20Vrms, 60Hz)	max	mm	10
Frequency Range	range	Hz	0.05 to 50k

4.3 Signal Conditioning

4.3.1 Test Signal

A triangle wave of 1mV at 10 Hz is applied to each channel input in order to verify the output quality of the channel. The ouput should be a triable wave with amplitude 1V. This test will be repeated for the frequecy range of the ECG, 0.05<f<250Hz.

4.3.2 Common Mode Rejection Ratio (CMRR)

The ISO175 is specified to have a CMRR of 115dB at 50Hz. To test it at the ECG frequecy range the an input of 1mV is put in both the electrode input and the WCT input.

4.3.3 60Hz Rejection

The human body there is 60Hz at 20Vrms. To test each channels rejection input a 60Hz sine wave at each input of the instrumentation/isolation amplifier and read the output.

4.3.4 Demodulation

To test the demodulation circuit we have to simulate the catheter pulse riding on top of the ECG signal. To do this a simple square wave with a DC offset will be used. The same square wave will be used as the control signal to the switch of the demodulator.

4.4 Mother Board

4.4.1 Input/Output Connections

Simple tests will have to be done to make sure the signals are interfaces correctly. A test signal of 1V will be placed at the electrode end of the connection. It will then be varified that this signal arrives at the correct slot and node location. A similar procedure will be done at the slot location. A test signal will be place at the output pin of the signal conditioning board and assured that it is connected to the right pin that will be going to the data acquistion board.

4.5 Device

4.5.1 Defibrillation Overload Test

To test if each channel can resist the defibrillation shock a test circuit, as seen in Figure 4.1, must be built whos source storage is a minimum of 5000V, and the energy delievered

360J. It will then be connected such that each of the electrodes and the WCT are tested. R1 is chosen so that the defibrillator enegery delivered to the 100-ohm load is reduced by a maximum of 10 percent relative to the energy delivered to this load with the device connected. To test the device:

- Connect to the test circuit of Figure 4.1
- Operate the device at the normal frequecy response (lowpass filter at 500Hz), so that 10Hz signal is clearly visible when switch S2 is opened
- Charge the capacitor to 5000V, with switch S1 in position A and switch S2 closed. Discharge the capacitor by actuating S1 to position B for a period of 200ms +/- 100ms.
- Immediately after the last discharge for each lead combination, S2 is opened so that the 10Hz test signal can be applied
- After 8 seconds, verify that the test signal appears at the output at an amplitude at least 80 percent of the normal amplitude..

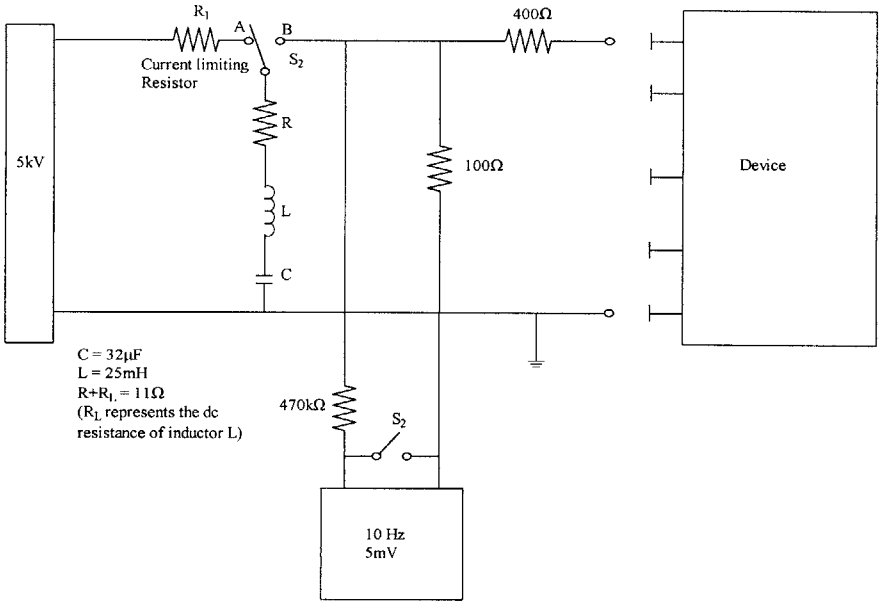

Figure 4.1: Test circuit for defibrillator overload tests.

4.5.2 Leakage Current

The device utilizes isolated patient connections. The risk current flowing to or from the patient through the patient electrode connections, chassis, or monitor controls should not exceed the 10μA.

4.5.3 60Hz voltage tolerance

The maximum peak-to-peak 60Hz sinusoidal voltage amplitude that can be superimposed on a train of QRS signals without exceeding the error limits for individual heart rate accuracy shall be no leass than 100mV p-p.

4.5.4 System Noise

Noise due to patient cables, all internal circuits, and output displays shall not exceed 30μVp-p RTI when all inputs are connected together through a 51kQ resistor in parallel with a 47nF capacitor in series with each patient electrode connection, and when the electrode cable is motionless.

4.5.5 CMRR

The device will have the capability of rejecting 60Hz signal mode interfering voltages as encountered on the surface of the body. A 60Hz signal, with a 200pF source capacitance and a 20Vrms open -circuit voltage, applied from power ground to all patient electrode connections connected to a common node and with a parallel combination of a 51kΩ resistor and 47nF capacitor imbalance impedance in series with each patient lead.

4.6 Data Acquistion

The complete data acquisition system is composed of the device described herein, a data acquistion card (National Instruments AT-MIO-64E-3) and a computer. An important test will be to verify that the signals amplified by the device can be recorded and analysed on the computer.

4.6.1 Signal Capture

Provide signal genertation of 1mV square wave at 10Hz to each electrode input. The signal amplitude at the output to the data acquistion card should be 1V (complete gain of

the system is G = 1000). The input signal should be varied across the signal range of the ECG (0.05Hz<f<250Hz) to make sure that no distortion are evident.

4.6.2 Varying the Lowpass Filter cutoff frequency with Computer Control

The lowpass filter cutoff frequency limited to be greater than 100Hz. The cutoff frquency is controlled by the input clock (+5VCMOS) which is provided by the computer. The clock frequency and cuttoff frequency relation is 100:1. (i.e. for a Fc = 100, Fclock = 10kHz). Though individual test of the lowpass filtered will be done, it will be necessary that single line control of filter frequency in the multi-channel is achieved.

Chapter 5

Conclusion

When complete, the data acquisition system should benefit many people. It should decrease surgery time, allow more patients to have the procedure done, reduce medical costs and increase patient qualtity of life. In a future version of the device, improvements to the hardware should include: variable gain control, guarding and shielding of the input signals and data acquistion through the printer parallel port.

References

[1] M.E. Josephson and C.D. Gottlieb. Ventricular tachycardia associated with coronay artery disease. In Zipes E, editor, From Cell to Bedside, Chapter 63. W.B. Saunders Company, Philadelphia, 1989.

[2] Robert M. Berne, M.D., and Matthew N. Levy, M.D. Cardiovascular Physiology. Fourth Edition. The C. V. Mosby Company, St. Louis, 1981. pages 28-29.

[3] A.H. Harken. Surgical treatment of cardiac arrhythmias. Scientific American, pages 68-74, July 1993.

[4] Antonis Armoundas. A Novel Technique for Guiding Ablative Therapy of Cardaic Arrythmias. PhD THESIS. MIT 1999.

[5] R.G. Mark, "Biological Measurement: Electrical Characteristics of the Heart" in M.G. Singh (ed.), Systems & Control Encyclopedia. Oxford: Pergamon Press, 452-455.

[6] John G. Webster editor, Medical Instrumentation: Application and Design. Third Edition. John Wiley & Sons, INC. 1998

[7] N.V. Thakor, "Electrocardiographic Monitors," in J.G. Webster (ed.), Encyclopedia of Medical Devices and Instrumentation. New York: Wiley, 1988, 1002-1117.

[8] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION, Cardiac Montiors, heart-rate meters, and alarms, ANSI/AAMI EC13-1992

[9] ASSOCIATION FOR THE ADVANCEMENT OF MEDICAL INSTRUMENTATION, American National Standard, Safe Current Limits for Electromedical Apparratus, ANSI/AAMI ES1-1985.

[10] V. de Pinto. Filters for the reduction of baseline wnader and muscle artifact in the ECG. J. Electrocardiol. **25** (Suppl.), 40 (1991).

[11] J. C. Huta, J.G. Webster, "60-Hz interference in electrocardiology." IEEE Trans. Biomed., 1973, BME - 20, 91-101.

[12] Paul Horowitz and W. Hill, The Art of Electronics. Second Edition. Cambridge University Press (1989) Cambridge.

[13] Z.H. Meikson, Complete Guide to Active Filter Design, OP AMPS, & Passive Components. Englewoods, Cliffs, New Jersey: Prentice Hall, 1990.

[14] H.W. Smit, K. Verton and C.A. Grimbergen (1987): A low-cost multi-channel preamplifier for physiological signals. IEEE Trans. BME-34, 307-310.

[15] Stephen D. Senturia, Bruce D. Wedlock. Electronic Circuits and Applications. Krieger Publishing Company, Malabar, Florida1993, 471-497 & 587-594.

[16] William M. Siebert. Circuits, Signals, and Systems. The MIT Press, Cambridge, MA 1986. 507-539.

[17] John Linsley Hood. The Art of Linear Electronics. Butterworth Heinemann Ltd, Oxford, 1993, 324-327.

[18] B.B. Winter and J.G., Driven-right-leg circuit design. IEEE Trans., BME-30, 62-66, 1983

[19] B.B. Winter and J.G. Webster, Reduction of Interference Due to Common Mode Voltage. IEEE Trans., BME-30, 62-66, 1983

[20] A.C. MettingVanRijin, A.P. Kuiper, A.C. Linnenbank, C.A. Grimbergen: Patient isolation in multi-channel bioelectric recordings by digital transmission through a single optical fiber. IEEE Trans., BME-40, March 1993, 302-308.