# **PROGRAMMABLE STIMULATOR SYSTEM FOR STUDY OF CARDIAC ARRHYTHMIAS**

**by**

Andrew H. Chung

S.B., Massachusetts Institute of Technology **(1992)**

Submitted to the Department of Electrical Engineering and Computer Science

in partial fulfillment of the requirements for the degree of

### MASTER OF **SCIENCE**

### at the

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 $\mathbf{1}$   $\mathbf{1}$ A uthor .. . . ........... **...... .............** Department of Electrical Engineering and Department of Electrical Engineering and Computer Science August 27, 1993 Certified **by....v...** ......... **.............** Richard **J.** Cohen Professor Thesis Supervisor Accepted **by ...... .......** ......................... Frederic R. Morgenthaler Chairman, Departmental Committee on Graduate Students

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#### **Abstract**

This thesis presents a microcomputer-based stimulator system which is used to produce a wide variety of pacing protocols for the studies of cardiac arrhythmias. The stimulator has two independent output channels: the first channel is for a stimulation through a single-site electrode and the second is for a moderate level stimulation through a multi-site electrodes sock or defibrillation catheters and patches. It is also equipped with an ability to amplify the intracardiac electrogram and synchronize the pacing with the electrical activity of the heart. The control software can be programmed for an induction of cardiac arrhythmias and other variety of pacing protocols.

The stimulator is used to investigate methods for the prevention and termination of lethal cardiac arrhythmias, such as ventricular tachycardia and fibrillation, **by** multi-site pacing. It detects the ventricular premature beats and applies a triggered pacing. This stimulator system is tested in the laboratory animal models of arrhythmias and is shown to function successfully.

Thesis Supervisor: Richard **J.** Cohen Title: Professor

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Most of all, I would like to express my deep love for my parents and my sister. Without their constant love and care, I would not have made it through this far.

# **Contents**



**1** Introduction **10**

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### *CONTENTS* **5**

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# **List of Figures**



 $\label{eq:2.1} \frac{1}{\sqrt{2}}\int_{\mathbb{R}^3}\frac{1}{\sqrt{2}}\left(\frac{1}{\sqrt{2}}\right)^2\frac{1}{\sqrt{2}}\left(\frac{1}{\sqrt{2}}\right)^2\frac{1}{\sqrt{2}}\left(\frac{1}{\sqrt{2}}\right)^2\frac{1}{\sqrt{2}}\left(\frac{1}{\sqrt{2}}\right)^2.$ 



**7**

## *LIST OF FIGURES* **8**



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# **List of Tables**

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# **Chapter 1**

# **Introduction**

Sudden cardiac death victimizes approximately 400,000 people in the United States alone every year. Because the event is both sudden and unexpected, almost two-thirds of the victims die before reaching the hospital [24]. The primary cause of sudden cardiac death in the vast majority of victims is ventricular fibrillation (VF), a disorganized pattern of electrical activity in the principal pumping chambers of the heart. The disorganized pattern of electrical activity results in random contractions and relaxations of cardiac muscle fibers which are ineffectual in pumping blood. Unless cardiopulmonary resuscitation is initiated immediately, death ensues in approximately four minutes from a lack of perfusion of the brain. The only reliable method for termination of VF is defibrillation, the delivery of a sufficiently strong direct current electric discharge to the fibrillating heart to reset the electrical activity of the heart.

Ventricular rhythm disturbances or ventricular arrhythmias, such as fibrillation and tachycardia, are usually developed during the acute phase of myocardial infarction, more commonly known as heart attack. These arrhythmias normally disappear when the infarction stabilizes. However, some patients do develop ventricular arrhythmias usually in the form of tachycardias some weeks or months after the onset of the infarction. Ventricular tachycardia itself is a dangerous rhythm disturbance because the heart rate is usually too fast and too poorly synchronized to allow effective pumping action **by** the heart. Ventricular tachycardia often develops into ventricular fibrillation. Therefore, these tachycardias must be treated. In some cases, antiarrhythmic drug treatment is effective in suppressing such tachycardias. However, current drug therapy are only modestly useful in prevention of these ventricular arrhythmias. Recently, an automatic internal cardiac defibrillator (AICD) has been implanted in high-risk patients. The internal defibrillator senses established VF and automatically administers a large counter electric shock to terminate it. Although the implantable defibrillator is useful for termination of ventricular fibrillation, it is not preventive. In addition, use of the internal defibrillator is also problematic in individuals with multiple recurrent episodes of fibrillation since internal defibrillation is traumatic and painful, and the patient generally loses consciousness prior to defibrillation.

This thesis presents a programmable stimulator system which is used in the studies of electrical pacing methods for the prevention of ventricular arrhythmias, tachycardia and fibrillation. Instead of treating established fibrillation **by** administration of a large countershock, a stimulator system is used to detect the initiation of ventricular arrhythmias and apply an electrical pacing to prevent ventricular tachycardia and fibrillation from developing. In order to study the prevention method, a stimulator is equipped with capabilities to sense the premature ventricular activities and deliver a moderate level stimulation through a multi-site electrode sock. **A** personal computer based system for amplifying the ventricular electrogram and delivering the stimuli of sufficient amplitude is developed. The pacing protocols to prevent and treat ventricular arrhythmias using an epicardial electrode array are studied on the experimental animal models, which are used to duplicate the arrhythmogenic effects of myocardial ischemia.

This thesis is organized as follows:

- **i. A** brief review of the major features of the structure and function of the normal human heart is presented as a reference for subsequent discussion. Also, the most recent theory regarding the initiation of the cardiac arrhythmias is described. (Chapter 2)
- **ii.** An overview of the programmable stimulator system, which consists of commercial components and an integrated system, is presented. The design of the integrated system is presented in detail. (Chapter **3)**
- **iii. A** review of the control program, which is used for the user interface and output control, is presented. Several stimulation protocols used for the experiment are discussed. (Chapter 4)
- iv. Experimental study, where the system is used for induction of arrhythmias and multi-site pacing, is presented. (Chapter **5)**

# **Chapter 2**

# **Background**

In order to lay the groundwork for later description of the pacing system specifications, this chapter is focused on providing the necessary physiological background. The first part of this chapter describes basic anatomy and physiology of the normal human heart. The mechanical events of the heart are then related to the electrocardigrm. Finally, the mechanisms of cardiac arrhythmias, which interfere with the normal functioning of the heart, are discussed and several examples of cardiac arrhythmias are presented.

## **2.1 The Heart**

The human heart is a hollow, thickly muscular organ which facilitates blood flow through the vascular system **by** rhythmic contractions. The heart is responsible for supplying all organs of the body with the necessary life-sustaining nutrition and oxygen.

#### **2.1.1 Anatomy of the Heart**





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The average human adult heart measures 12 cm from apex to base, **9** cm in width at its broadest point, and **6** cm in anterior-posterior dimension **[25]. A** cross-section of the heart is shown in Figure 2-1. Internally, the heart is divided into four distinct chambers; right and left atria, two small upper chambers with thin walls, and right and left ventricles, two lower chambers with thicker walls. The atrium and ventricle on the right side are separated from those on the left **by** a septum. There is an opening between the atrium and ventricle, which is guarded **by** a valve.

#### **2.1.2 Cardiac Cycle**

In a normal cardiac cycle, oxygen-depleted, venous blood returning from the peripheral circulation empties into the right atrium (RA) via the superior and inferior vena cavae (refer to Figure 2-1). From right atrium, blood is pumped through the tricuspid valve into the right ventricle (RV). This is the resting or filling phase of the cardiac cycle and is called diastole. The blood is then pumped from the right ventricle through the pulmonic valve into the pulmonary circulation in a contractile phase called systole. In the luigs, the blood is oxygenated and delivered to the left side of the heart. In parallel with the events on the right, oxygenated blood empties into the left atrium **(LA)** via several pulmonary veins. Left atrial contraction then propels this blood through the mitral (bicuspid) valve into the left ventricle (LV). The left ventricle, **by** far the most muscular of all the heart chambers, pumps blood through the aortic valve into the ascending aorta. From there, blood is distributed through the systemic circulation, eventually to return to the right atrium thereby completing the circuit. The pressures inside of the heart chambers and the aorta during the cardiac cycle are shown in Figure 2-2, with phases of systole and diastole noted. Corresponding heart sounds and electrocardiogram are also provided.



Figure 2-2: Cardiac Cycle (Reproduced from Berne and Levy: Cardiovascular Physiology, **1992)**

### **2.1.3 Cardiac Conduction System**

**A** specialized electrical conduction system normally regulates the steady beating of the heart. The signal giving rise to the cardiac cycle emanates from a cluster of conduction tissue cells collectively known as the sinoatrial node, as shown in Figure **2-3.** This node, located at the top of the right atrium, establishes the tempo of the heartbeat; hence, it is often referred to as the cardiac pacemaker. It sets the tempo simply because it issues impulses more frequently than do other cardiac regions, once about every **830** milliseconds. If something provoks another part of the heart to fire at a faster rate, it would become the new pacemaker. Although the sinoatrial node can respond to signals from outside the heart, it usually becomes active spontaneously, a capability known as automaticity.

Impulses born at a cell in the sinoatrial node speed nearly instantly through the rest of the node, and from there, they course through the entire heart in the span of **160** to 200 milliseconds. Travelling along conduction fibers, they first race across both atria and then regroup at the atrioventricular node, a cellular cluster centrally located atop the ventricles. After a pause, they course down the ventricles along an A-V (His) bundle that divides into two branches known as left and right bundles branches; these further ramify to form arbors of thinner projections called Purkinje fibers. One arborized bundle serves each ventricle, sending signals first along the surface of the septum to the tip of the heart, the apex, and, from there, up along the inner surface of the external or lateral walls to the top of the ventricle.

As impulses from the conduction fibers reach muscle, they activate the overlying cells. Muscle cells, too, are capable of relaying impulses, although more slowly than do conduction fibers. The cells of the inner surface of the wall, the endocardium, depolarizes first and relay the impulses through the thickness of the muscle to the outer surface, the epicardium. Depolarization, in turn, triggers contraction that forces



Figure **2-3:** Electrical conduction system of the heart (RV, right ventricle; LV, left ventricle; LBB, left bundle branch system; A-V, atrioventricular; RA, right atrium; **LA,** left atrium)

blood through the heart and into the arterial circulation.

## **2.2 Electrocardiogram**

The series of mechanical events outlined above can be tracked at the body surface **by** monitoring the surface potentials which are caused **by** the flow of ionic currents within the cardiac structures. The recording of such body surface potentials is known as electrocardiography, and a single recording of the potential difference between two points on the body surface is referred to as an electrocardiogram. Different morphologies of the cardiac action potentials at various locations within the heart are combined to give the electrocardiogram, shown in Figure 2-4. **A** theoretical basis for the relationship between body surface potentials and myocardial transmembrane potentials can be found in major texts [4].

The normal electrocardiogram consists of a P wave, a **QRS** complex, a T wave, and an infrequent **U** wave (refer to Figure 2-4). The P wave, temporally the first component of the **ECG,** is a result of atrial depolarization. The **QRS** complex, which follows the P wave after a delay of approximatley **150** millisecondss (A-V nodal delay), is the result of ventricular depolarization. The T wave, which follows the **QRS** complex **by** a variable period of time, is the result of ventricular repolarization. The repolarization of the atria-is not visible in the surface **ECG** partly because the mass of the atria is relatively small and the time course of the atrial repolarization coincides with ventricular depolarization. The infrequently seen **U** wave is thought to be the result of the repolarization of the His-Purkinje system. It follows the T wave **by** roughly **25** milliseconds because the action potential duration of the Purkinje cells is approximately **25** milliseconds longer than that of ordinary myocardial cells [4].

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Figure 2-4: Schematized **ECG** tracing (Reproduced from Netter FH: Heart, Vol. **5,** The CIBA Collection of Medical Illustrations, CIBA, **1981)**

# **2.3 Arrhythmias**

Disturbances in the heart's electrical activity may cause significant abnormalities in its mechanical function, and are the basis of much cardiac morbidity and mortality. In fact, malfunctiion of the heart's electrical behavior is the principal cause of sudden cardiac death. Arrhythmias are generally thought to occur on the basis of one or a combination of three potential mechanisms: automaticity, triggered activity, or re-entry **[7].**

#### **2.3.1 Pathophysiology of Arrhythmias**

Most evidence suggests that re-entry is the mechanism of clinical ventricular arrhythmias **[17].** In the presence of slow conduction and/or unidirectional block, it is possible to establish in the myocardium a so-called "re-entrant circuits" of excitation, ( as shown in Figure **2-5.** Some workers have subdivided the re-entrant mechanism into two catagories, "random re-entry" and "ordered re-entry". Random re-entry can cause atrial or ventricular fibrillation, whereas ordered re-entry can cause tachycardias. The distinction between the two is that 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. In all configurations, however, The wavelength of the impulse in the reentrant circuit (conduction velocity X refractory period) must be shorter than the length of the circuit, so that the tissue into which the impulse is re-entering has had time to recover its excitability.

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 developement of re-entrant circuits. There are many possible geometric arrangements for such loops which may exist in many locations of



Figure **2-5:** Reentrant Circuit (Reproduced from Smith: Ph.D. Thesis, **1985)**

the heart and in many sizes, both microscopic and macroscopic. It had been proposed that the microscopic re-entrant circuits are the most common form **[15].**

#### **2.3.2 Clinical Examples of Arrhythmias**

As explained earlier, patients who had suffered myocardial infarction are suspectible to ventricular arrhythmias because of the presence of the re-entrant pathways in the surrounding areas of infarct. In this section, some of the clinical ventricular disrhythmias are reviewed.

#### Ventricular Premature Beats

The most common ventricular arrhythmia is the ventricular premature beats (VPB). **A** ventricular premature beats occur when ventricular activation is initiated as a site within the ventricles and not as a result of the normal chain of cardiac activation initiated in the sino-atrial **(SA)** node. Thus, the normal timing of events is disrupted with the result being inadequate time for filling of the ventricles, and consequently decreased ejection of blood into the ascending aorta. As shown in **ECG** in Figure **2-6,** the P wave is absent and the **QRS** complex is quite wide (greater than 0.12 seconds) and bizzare. The width of **QRS** is enlarged due to the VPB not utilizing the His-Purkinje system with its rapid conduction velocity.



Figure **2-6:** Ventricular premature beats (Reproduced from Smith: Ph.D. Thesis, **1985)**

VPB's are often found in otherwise normal individuals and probably have little significance if they are infrequent. In heart diseases, VPB's may be a risk factor for increased incidence of more serious ventricular arrhythmias and sudden death. VPB's which fall on the T-wave of the previous beat are considered particularly dangerous. The period near the T-wave peak is oftern referred to as the "ventricular vulnerable period," as shown in Figure **2-7.** At the time corresponding to the peak of the T-wave, the ventricular myocardium is just beginning to repolarize. Some cells may be in the relatively refractory period, while others may be more fully recovered, and still others quite refractory. The electrical properties of the myocardium are thus quite varied, and conditions favoring re-entrant loops are likely. Thus, an extra stimulus in the form of an isolated VPB which is very early-cycle may trigger a repetitive ventricular ectopic rhythm such as ventricular tachycardia or ventricular fibrillation [4].



Figure **2-7:** Ventricular ventricular period, the time during which ventricular arrhythmias can be induced (Reproduced from Smith: Ph.D. Thesis, **1985)**

#### Ventricular Tachycardia

Another arrhythmia of ventricular origin is ventricular tachycardia, wherein rapid repetitive stimulation and contraction of the ventricles occur in the absence of normal atrially conducted stimulation. The rates of ventricular tachycardia vary from **150** to **300** beats per minute. Rates above **250** beats per minute fails to provide sufficient cardiac output to maintain life since the rapid rate does not permit sufficient filling of the ventricles **[13].** As shown in **ECG** of Figure **2-8,** a train of ventricular complexes similar to VPBs are present, with no coupled preceding atrial activity.

Figure **2-8:** Ventricular tachycardia (Reproduced from Smith: Ph.D. Thesis, **1985)**

#### **Ventricular Fibrillaion**

The last arrhythmia to be reviewed herein, and the one that is most often associated with sudden cardiac death, is ventricular fibrillation. Ventricular fibrillation is characterized **by** asynchronous, chaotic electrical activity resulting in disorganized and ineffectual contractions. Cardiac output during ventricular fibrillation is negligible, and as such the condition is incompatible with life. As shown in Figure **2-9,** ventricular fibrillation is manifested **by** a random oscillation of potential, with no **QRS** complexes.

MMMMMMMMM

Figure **2-9:** Ventricular fibrillation (Reproduced from Smith: Ph.D. Thesis, **1985)**

# **Chapter 3**

# **Programmable Stimulator System**

**A** programmable stimulator system is an essential piece of equipment for the study of arrhythmias. In our studies of arrhythmias, there was a need for a device which produced more than the standard constant current or voltage **S1** pacing train. **A** device is needed to produce a wide variety of pacing protocols, such as induction of arrhythmias, and synchronize the delivery of pulses with the electrical activity of the heart. Also, since some **of** the pacing is done through a multi-site electrodes sock, the system has to provide voltage and current pulses for a moderate level of amplitude. In this chapter, a microcomputer-based stimulator system that can be programmed to produce a wide variety of pacing protocols is presented.

# **3.1 System Overview**

**A** block diagram of the programmable stimulator system is shown in Figure **3- 1.** The programmable stimulator system consists of a **80386** microcomputer with a digital-to-analog board, a software program, called *Pacer,* a stimulator hardware, and monitoring/recording equipments. The stimulator hardware again conisits of three



Figure **3-1:** Diagram of the programmable stimulator system

sub-components: a) a integrated system, **b)** a gain adjuster, and c) a voltage/current amplifier.

Two analog pulses are generated **by** a fast digital-to-analog converter at a rate **of 1,000** samples per second per channel **(DA0** Out and **DA1** Out in Figure **3-1).** The amplitude and timing of the voltage pulses from a digital-to-analog converter are controlled precisely **by** a software and supplied to two inputs of the stimulator hardware **(DA0** In and **DA1** In in Figure **3-1).**

Stimulator hardware converts two voltage inputs to two independent outputs for electrical stimulation. First channel sends current stimuli to a single electrode for pacing and inducing arrhythmias. These current stimuli are generated **by** the voltageto-current converter of the integrated system (STIM **Ch 1** Out in Figure **3-1).** On the other hand, second channel sends either voltage or current stimuli to a multi-site electrodes sock. They are generated **by** the commercial high-performance voltage/current amplifier (STIM **Ch** 2 Out in Figure **3-1).** These pacing stimuli can be applied at a fixed rate or be triggered **by** an external signal. These output pulses are used to stimulate the heart of an open-chest animal.

Following the stimulation, the electrical signal generated **by** the heart is recorded by the electrode placed on the epicardial surface of the heart  $(ECG \pm In\ in\ Figure$ **3-1).** This signal is conditioned **by** the electrocardiogram amplifier of the integrated system, and it is used to detect abnormal electrical activities of the the heart. When abnormal events are detected, a pulse is sent to the external trigger port of a digitalto-analog board to initiate another stimulation of the heart.

In order to monitor and record the animal experiments, all stimuli as well as the electrical activity of the heart can be displayed on the screen of an oscilloscope, and recorded on the analog tape and/or the Astro Med 8-channels chart recorder for hardcopy. In the following sections, various commercial components used in the programmable stimulatr system, as well as the integrated system, will be described.

### **3.2 System Components**

Some of the components used in the development of the programmable stimulator system, such as a digital-to-analog board and a voltage/current amplifer, are **com**mercially available equipments. In this section, some of their specification are given for reference.

### **3.2.1 Digital-to-Analog (D/A) Board**

Data Translation DT **2821** board is used for the digital-to-analog conversion. This board plugs into any IBM compatible microcomputer and contains conversion circuitry for both analog-to-digital and digital-to-analog operations. When used as the digital-to-analog operation, this board produces two voltage outputs, ranging from **-10** to **10** volts, with the resolution of **5** millivolts **[10].** (Refer to the DT **2821** board manual for further information.)

#### **3.2.2 Voltage/Current Amplifier**

**A** Kepco BOP **72-6M** bipolar operational power supply (BOP) is used as a precision voltage or current source for the stimulation through the multi-site electrodes sock. This BOP provides the flexibility to pace **by** voltage or current and a moderate amount of stimulation outputs for multi-site pacing. The output of BOP can be controlled **by** voltage signals. As a bipolar voltage amplifier, the BOP output ranges from **-72** to **72** volts and has a gain factor of **7.2** (V/V). On the other hand, as a bipolar current amplifier, the BOP output ranges from **-6** to **6** amp and has a gain factor of 0.6  $(A/V)$ . Therefore, a  $\pm 10$  volt input signal will program the BOP output as voltage or current through its rated output ranges. Also, built-in preamplifiers, for the voltage and current channels of the BOP, provide the interface with high as well as low impedance signal sources **[19].** (Refer to the KEPCO BOP **72-6M** power suppliy manual for further information.)

## **3.3 Integrated System**

It should be noted that the integrated system, shown in Figure **3-1,** is specifically developed for this study. It cosists of several functional units: a voltage-to-current converter, an electrocardiogram amplifier, and a detector. Special care has been taken to ensure safety of the integrated system **by** preventing electroshock hazards. **By** use of isolation amplifiers, the current pulses are separated from ground guarding against unwanted dangerous interference from the mains.

#### **3.3.1 Current Amplifier**

As mentioned previously, pacing and extra stimuli of channel one are current pulses. Since the **D/A** board generates voltage pulses only, a voltage-to-current converter is needed. The current amplifier, shown in Figure **3-2,** consists of: a) a buffer for impedance matching, **b)** a gain control, c) an isolation amplifier, **d)** a RC circuit to prevent a **DC** shock, e) a voltage-to-current converter, and **f)** a current output monitor with a **LED** indicator.

#### **RC** High-Pass Filter to Prevent **DC** Shock

The voltage pulses of the **D/A** board are fed to an unit-gain buffer, a gain control, and an isolation amplifier. The output of the isolation amplifier is then fed into a simple RC circuit, which acts as a high-pass filer to cutoff **DC** voltage. This RC cirucit protects the experimental animal from the **DC** shock when **DC** is applied accidentally to the current amplifer. The RC circuit and the shape of pulses before and after the



Figure **3-2: A** block diagram of the current amplifier sub-system

RC circuit is shown in Figure **3-3.** Note that the uniform shape of the inputs pulse is modified to the exponentially decaying pulse with the time constant of RC, in this case **10** msec.

#### Voltage-to-Current Converter

The ouput of the RC cirucit is then used to control the current source. The current source uses the xxx transistor . Assuming that the load resistance of the heart during the pacing would be less than 200 ohm, the output of the current source is linear upto about **30** mA.

#### Current Output Monitor

The output of the voltage-to-current converter is monitored **by** recording the voltage developed across **100** ohm resistor. The voltage is recorded on the chart recorder and this enables the investigator to confirm the actual current output delivered to the load at the time of pacing. Isolation amplifier is again used to protect animal



Figure **3-3:** RC circuit used for the **DC** shock protection with pulse shapes before and after the RC cirucit

from fault-ground shock. Also, unity gain buffers are used for impedance matching. In addition, a **LED** display is added to blink at each pacing stimuli.

### **3.3.2 Intracardiac Electrocardiogram Amplifier**

In order to pace the heart based on the electrical activity of the heart, an intracardiac electrocardigram amplifier is needed. This amplifier records the epicardial or intracavitary cardiac signals from the electrode and conditions it as an input the detector.

#### General Description

The intracardiac electrocardiogram **(ECG)** amplifier is used for the amplification of epicardial electrocardiogram, which has a small differential signal riding on a large common mode signal, signals that are common to all the electrodes. For example, if there were a millivolt electrocardiogram signal and a volt of common-mode signal at



Figure 3-4: Circuit diagram of a voltage-to-current converter

the electrodes and transmission along the two wires differed **by 0.1 %,** then a millivolt of differential signal would be developed from the common-mode signal, which is as large as the electrocardiogram itself.

In order to solve these problems involving a common-mode signal, identical conditions have to be imposed on the two signal paths. Each must be exposed to the same noise, same source, and destination impedance. **A** high input-impedance differentialinput amplifier is an ideal choice to solve these problems.

The intra-cardiac electrocardiogram amplifier, shown in Figure **3-5,** is composed of six basic building blocks: a) an overload protection circuit with high pass filter, **b)** a direct-coupled, low gain preamplifier, c) an isolation amplifier, **d)** a high pass filter set at **10** Hz, e) a programmable gain amplifier, and **f)** a low-pass filter set at **70** Hz.



Figure **3-5: A** block diagram of the intra-cardiac electrocardiogram amplifier subsystem

#### Overload Protection Circuit with a High-Pass Filter

An overload protection circuit, shown in Figure **3-6,** prevents damage to the rest of the intracardiac electrocardiogram amplifier in case of cardioversion. The protection circuit clips the input signal when an excessive signal such as defibrillator discharge signal is applied to the input. In addition, the built-in high-pass filter rejects the **DC** (sub-signal) frequencies, especially the half cell potential of several ten or hundreds mV around the surface of electrode.

In the circuit diagram of Figure **3-6,** resistors (R1, R2) and zenor diodes **(D1,** D2) work to protect the differential amplifier from the shock of the defibrillator. Capacitors **(C1, C2)** and resistors (R1, R2, and R3) compose the high pass filter which eliminates the **DC** voltage from the surface of electrodes. Note that R3 must be far greater than R1 and R2 to keep the input impedance of the amplifier high. Capacitor **C3** works as a high cut filter together with R1, R2, **C1,** and **C2.** The characteristics of the filter is adjusted so that the frequency which composes the **QRS**



Figure **3-6: A** circuit diagram of the overload protection circuit with a high-pass filter

complex, **20-50** Hz, can be entirely passed through. Finally, diodes **(D3 - D6)** clip the signal to 1.2 Volts.

#### Differential Amplifier

The direct-coupled, low-gain preamplifier, shown in Figure **3-7,** is a high input impedance differential amplifier with single-ended output. The differential amplifier consists of two stages, a balanced input stage and a differential output stage. The balanced input stage is ideal for amplifying small (range of **10** mV) electrocardiogram signals since it provides: a) high input impednace to minimize differences in attenuation in the two signal paths due to unequal source impedances, **b)** an extremely good common-mode rejection ratio (CMRR) to amplify a small differential signal riding on a large **DC** offset. The balanced input stage's differential output represents a signal with substantial reduction in the comparative common-mode signal. Then, the output stage is connected in the standard differencing amplifier configuration. This configuration of a balanced input stage followed **by** a differential amplifier is called the three op-amp insturmentation amplifier.

CMRR and CMR of the differential amplifier are defined as follows:

$$
CMRR = \frac{Output \text{ due to unit differential} - mode \text{ signal}}{Output \text{ due to unit common} - mode \text{ signal}}
$$
(3.1)

$$
CMR = 20 \log_{10} CMRR \text{ (dB)} \tag{3.2}
$$

Also, the differential gain of the instrumentation amplifier in Figure **3-7** is defined as **follows:**

$$
\frac{V_{\text{out}}}{V_{\text{in}}} = \frac{R_1 + R_2 + R_3}{R_2} \times \frac{R_4}{R_3} \tag{3.3}
$$

This differential amplifier provides CMR of about **50** dB, which is acceptable CMR for electrocardiogram, and has a differential gain of **10.**



Figure **3-7: A** circuit diagram of the differential amplifier
In the circuit diagram of Figure **3-7,** a balanced input stage, which is composed of two operational amplifiers (OP1 and OP2) and three resistors (RI, R2, and R3), is implemented to improve CMRR. Its transfer function is characterized **by** equations 3.4 and **3.5.** The differential gain ADD and ADC are about **10** and **0,** respectively; the common-mode gain A<sub>CD</sub> and A<sub>CC</sub> are 1 and 0, respectively. Matching of R1 to R3 and R4 to R5 affect CMRR. Gain may be adjusted through R2.

$$
V_{02} - V_{01} = A_{DD}(V_{12} - V_{11}) + A_{DC}(\frac{V_{11} + V_{12}}{2})
$$
\nwhere  $A_{DD} = \frac{R_1 + R_2 + R_3}{R_2}$  and  $A_{DC} = 0$ 

\n(3.4)

$$
\left(\frac{V_{01} + V_{02}}{2}\right) = A_{CD}(V_{12} - V_{11}) + A_{CC}\left(\frac{V_{11} + V_{12}}{2}\right)
$$
\nwhere A<sub>CD</sub> = 1 and A<sub>CC</sub> =  $\frac{R_3 - R_1}{2 R_2} = 0$ 

\n(3.5)

**A** differential output stage is composed of one operation amplifier (OP3) and four resistors (R4, R5, R6, and R7). Its transfer function is characterized **by** equation **3.6.** The differential gain A<sub>D</sub> is an unity and the common-mode gain A<sub>C</sub> is ideally 0 for a differential amplifier. However, CMRR is limited **by** the resistor matching of R5 to R7. To improve CMRR, high-precision resistors are used in building the circuit.

$$
V_1 = A_D(V_{02} - V_{01}) + A_C(\frac{V_{01} + V_{02}}{2})
$$
  
where  $A_D = (\frac{R_5}{R_4})$  and  $A_C = 0$  (3.6)

#### **High Pass Filter**

Since the spectrum of the electrocaridogram signal is distributed above **5** Hz, a high-pass filter is built with a cutoff frequency of **10** Hz. The Chebyshev filter with 2 dB ripple in the pass band is chosen for the high-pass filter. Although Chebyshev filter allows some ripples in the passband, it provides the fastest roll-off from passband to stopband. The Sallen-Key circuit with the unity-gain follower, shown in Figure **3-8,** is chosen for the high-pass filter.



Figure **3-8:** Circuit diagram of a 2nd-order Chebyshev high-pass filter with 2dB

#### Low-Pass Filter

The main purpose of the low pass filter is to reduce the noise due to the muscle movements. Since the electrocardiogram signal is distributed below **60** Hz, a low-pass filter is built with a cutoff frequency of **70** Hz. This low-pass filter and the high-pass filter make up a band-pass filter for the electrocardiogram amplifier.

The Bessel filter is chosen for the low-pass filter since it introduces the least distortions to electrocardiogram. The Bessel filter has a phase response which is linearly related to frequency. It also exhibits short settling time and rise time **[1, p.**

**23].** Therefore, when pulses, such as **ECG** signals, are transmitted, the output pulses are of approximately the same shape as the input pulses. The Sallen-Key circuit with the unity-gain follower, shown in Figure **3-9,** is chosen for the low-pass filter. The transfer function of this low-pass filter is shown below, and its frequency response is shown in Figure **3-10.**

$$
H(s) = \frac{1}{1 + s(R_2C_2 + R_1C_2) + s^2(R_1C_1R_2C_2)}
$$
(3.7)

The output of the low-pass filter is the final output of the electrocardiogram amplifier. This signal is then supplied to the input of the detector.



Figure **3-9:** Circuit diagram of a 2nd-order Bessel low-pass filter

### **3.3.3 Detector**

**A** hardware detector, built as a part of the integrated system, uses level detection to trigger a stimulation. This stage receives the filtered electrocardiogram signal from the amplifier and outputs a negative-going (from **10** volt to **0** volt) short duration pulse when the electrocardiogram signal goes above a normal range. This



Figure **3-10:** Frequency response of 2nd-order Bessel low-pass filter

negative-going pulse is provided to the external trigger of the digital-to-analog board for synchronizing the pacing with the abnormal events of the heart. The detector, shown in Figure **3-11** consists of: a) a full-wave rectifier, **b)** a voltage comparator, and c) a trigger generator with a trigger inhibit time.

### Full-Wave Rectifier

**A** full-wave rectifier, shown in Figure **3-12,** converts all negative values to positive values in order to insure detection of all abnormal events. This is necessary since the voltage detector, which follows in the signal path, cannot have two threshold values.



Figure **3-11: A** block diagram of the detector sub-system

When the input is positive, diode **D1** is off and diode **D2** is on. In this case, the first op-amp (OP1) with first two resistors (R1 and R2) becomes an unity-gain inverter. The second op-amp  $(OP2)$  with next three resistors  $(R3, R4, and R5)$  make up an adder with inverting configuration. The output of the second op-amp should follow the input signal to the full-wave rectifier. On the other hand, when the input is negative, **D1** is on and **D2** is off. Then, the first op-amp's output is zero and the second op-amp becomes an unity-gain inverter. The output of the second op-amp should be the opposite of the input signal.

#### Voltage Comparator

The static transfer characteristics of a voltage comparator are shown in Figure 3-13. Voltage comparator has two output levels,  $V_L$  and  $V_H$ . When the input voltage to the comparator goes above the the threshold value,  $V_{TH}$ , the output goes from VL to VH. Note that there is a range of input signals which produce an ambiguous output, called the linear range. It is most optimal to have a minimum linear range to decrease ambiguity. The low and high output levels, VL and VH, are specified **by** the type of logic circuitry which is to be actuated **by** the detector. For the digital-toanalog board, it's the TTL (transistor-transistor-logic) levels, in which less than 0.4 volts is considered logically low, and greater than **2.6** volts is considered high. The threshold voltage,  $V_{TH}$ , is controlled by the potentiometer. This voltage comparator



Figure **3-12:** Circuit diagram of a full-wave rectifier

is realized using **LM311,** an integrated cirucit comparator.

#### Trigger Generator

The output of the comparator is high whenever the input level is higher than the threshold level. Since the digital-to-analog board's output is triggered when the external trigger signal is **low,** a separate trigger ciruit is needed to generate the short negative pulse to the digital-to-analog board. Also, it is desirable not to trigger again for certain time after the first trigger in order to prevent pacing during the refractory time. The trigger generator with the sensing inhibit time, implemented with the retriggable/resettable monostable vibrator, is shown in Figure 3-14 **.**

In the circuit diagram of Figure 3-14, the output of the voltage comparator is connected to the positive input of the first monostable vibrator (MV1). When the input to the positive input of MV1 goes from low to high, it triggers MV1 to output

a negative-going pulse of two milliseconds width. This negative-going pulse is sent to the external trigger port of the digital-to-analog board and it is used to trigger a pacing.

In order to prevent from triggering during heart's refractory time, a sensing inhibit time generator is implemented using the second monostable vibrator (MV2). This generator disables the trigger generator for approximately **70** milliseconds after a trigger signal is sent out. The width of the sensing inhibit time is determined **by** a resistor (R2) and a capacitor **(C2).**



Figure **3-13:** Transfer characteristics of a voltage comparator (Note that the output of the comparator is high wheneve the input level is higher than the threshold level.)



Figure 3-14: Circuit diagram of a trigger generator

# **Chapter 4**

## **Control Program**

The primary function of the control program, *Pacer, is* to provide an easy to use interface for the operator while accurately controlling the output of hardware on the digital-to-analog board. The combination of hardware and software allows for the implementation of many useful features. Preprogrammed stimulation modes are used to limit the number of parameters that the investigator must enter. In addition to the unique modes, there are several functions which can be enabled regardless of the currently selected mode, such as the stoppage of ventricular tachycardia. There is also the ability to receive an trigger signal from an external device, such as the integrated system described in the previous chapter. This trigger signal can be used for synchronous stimulation. *Pacer* is written in **C** using Borland's Turbo **C** development environment.

## **4.1 Program Overview**

**A** flowchart of the control program, *Pacer,* is shown in Figure 4-1. **All** of the features of the program can be accessed from the menu in the command box. The



Figure 4-1: Flowchart of the control program

 $\overline{\phantom{a}}$ 

keyboard key may be used to select items from the menu, and *Pacer* automatically initiates the desired task. The control program, *Pacer,* can be divided into two main parts: a) the user interface where stimulation protocol parameters are selected **by** the investigator, and **b)** the output controller where actual data buffers are written for the outputs of the digital-to-analog board. This separation of two tasks ease the change of stimulation protocols for a constantly evolving investigation.

## **4.2 User Interface**

*Pacer* is especially designed to meet the specific needs of investigators in venrticular arrhythmias study. In this section, it will be explained how parameters of different stimulation protocols in the study of ventricular arrhythmias are inputted **by** the investigator.

### **4.2.1 Pacing Threshold**

For a fixed-rate pacing, a constant current S<sub>1</sub> pacing train is used, as shown in Figure 4-2. Output parameters, such as the **Si** pulse amplitude, **Si** pulse duration, and interstimulus interval **(Si - Si),** of pacing pulses can be adjusted from default values **by** using cursor keys or new parameter values can be typed in using keyboard keys. Once these parameters are set, a series of fixed-rate pacing pulses is generated on the command. While stimulation is active, the pulse amplitude can be in-/decremented **by** the pre-set incremental value using the cursor keys in order to determine the threshold level. On the key pad, number **7** key and number **1** key are used for an increment and decrement of the pacing pulse amplitude, respectively. The interstimulus interval can also be in-/decremented **by** the cursor keys while stimulation is active. Number **6** key and number 4 key are used for an increment and decrement of the interstimulus interval, respectively.



Figure 4-2: Fixed-rate pacing to determine the pacing threshold

### **4.2.2 Mid-Diastolic Threshold**

As discussed in chapter **2,** there is a ventricular vulnerable period roughly coinciding in time with the occurrence of the first half of the T wave in the electrocardiogram, as shown in Figure **2-7.** Since the ventricles are susceptible to re-entrant rhythm disturbances during the vulnerable period, a mid-diastolic (premature) pacing pulse  $(S_2)$  can be used to induce ventricular arrhythmias.  $S_2$  pulse is applied in late diastole of the cardiac cycle, as shown in Figure 4-3. Again, output parameters, such as the  $S_2$  pulse amplitude,  $S_2$  pulse duration, and initial  $S_1$  **-**  $S_2$  interval  $(D_1)$ , can be adjusted. After the fixed-rate pacing is initiated, the mid-diastolic pacing pulse **(S2)** can be applied on the command to determine if a beat is induced **by** the mid-diastolic pacing pulse **(S2 ).** The pulse amplitude can be in-/decremented **by** the pre-set incremental values using the cursor keys and the stimulation can be repeated until the mid-diastolic threshold level is determined. On the key pad, number **9** key and number **3** key are used for an increment and decrement of the pulse amplitude, respectively.

### **4.2.3 Effective Refractory Period**

After the mid-diastolic threshold is determined, the effective refractory period (ERP) is found. During the effective refractory period, there can be no propagated response to the stimuli. The initial  $S_1 - S_2$  interval is decremented until no beat is induced **by** the mid-diastolic pacing pulse **(S2)** and the **Si - S2** interval is noted as the effective refractory period.



Figure 4-3: Mid-diastole pacing to determine the effective refractory period

### **4.2.4 Extra Stimuli for Arrhythmias Induction**

Since more than one mid-diastolic pacing pulses are usually needed to induce ventricular arrhythmias, another mid-diastolic pacing pulse **(S3 )** is added in the same manner as  $S_2$  was added. Again,  $S_3$  pulse amplitude,  $S_3$  pulse duration, and initial **S2 - S3** interval, are adjustable parameters. After the fixed-rate pacing is initiated, the mid-diastolic pacing pulses  $(S_2 \text{ and } S_3)$  are applied on the command to determine if a beat is induced by  $S_2$  and  $S_3$ . The  $S_2$  **-**  $S_3$  interval,  $D_2$ , is decremented until no beat is induced by S<sub>3</sub>. The effective refractory period of S<sub>2</sub> is noted. Then, same procedure is applied for the determination of effective refractory periods for  $S_3$  and  $S_4$ . These premature stimuli delivered during consecutive ventricular vulnerable period are referred to as *extra stimuli.*



Figure 4-4: Extra stimuli used to induce ventricular arrhythmias

## **4.2.5 Burst for Arrhythmias Induction**

In addition to extra stimuli, burst is another type of stimulation pulses known to induce ventricular arrhythmias. Burst is a group of closely placed current pulses in one vulnerable period (approximately **100** milliseconds), as shown in Figure 4-5. Output parameters, such as  $S_2$  pulse amplitude,  $S_2$  duration, length of vulnerable period, and frequency of pulses  $(\frac{1}{\Delta T})$ , can be adjusted for the burst.



Figure 4-5: Burst used to induce ventricular arrhythmias

### **4.2.6 Overdrive Pacing for Arrhythmias Prevention**

Overdrive stimuli refer to the stimuli which are applied after the delivery of premature stimuli in order to prevent the development of ventricular arrhythmias, as shown in Figure 4-6. Ventricular arrhythmias are caused **by** the occurrence of reentrant circuit, and they can **be** terminated if re-entrant circuit can be interrupted **by** the depolarization of the ventricular mass.



Figure 4-6: Overdrive pacing pulses used for the prevention of the ventricular arrhythmias

Either constant current or voltage pacing train can be used for overdrive stimuli. In addition to the usual output parameters (i.e. the pulse amplitude, pulse duration, and interstimulus interval of overdrive pacing pulses), the number of overdrive stimuli and triggering mode can be adjusted. The overdive pacing stimuli can be continued infinitely or specified in any number of overdrive stimuli.

Triggering mode can be either on or off. When triggering mode is off, the overdrive pacing stimuli are applied at a fixed interval after the last premature stimuli. On the other hand, if triggering mode is on, it allows the overdrive pacing stimuli to be applied synchronously with the external event, such as the ventricular electrical activity. When the triggering mode is on, an external trigger port of the digital-toanalog board is sampled to detect the trigger signal. Triggering capability allows the pacing to be applied when premature ventricular beats are detected after the last premature stimulus.

When used with a triggering mode on, a pacing inhibit time must be specified.

**A** pacing inhibit time refers to the period after the last premature stimulus, during which detection is disabled in order to prevent being triggered **by** the artifacts, or transients, **of** the previous stimuli. The pacing inhibit time is implemented using a computer board's internal clock and it can be controlled with the one millisecond resolution.

### **4.2.7 Stimulation Modes**

To reduce the number of parameters that must be entered for an electrophysiologic study **(EPS)** of ventricular arrhythmias, individual stimulation modes for this research have been preprogrammed. Currently, six possible stimulation modes are available. They differ in the types of premature stimuli and overdrive stimuli S<sub>2</sub>. Different stimulation modes are tabulated in Table 4.1. When each stimulation mode is selected, appropriate premature stimuli and overdrive triggering mode are selected and default parameter values are assigned to the output parameters.

	Extra Stimuli	Burst
No Overdrive Pacing	Mode 1	Mode 4
Fixed Rate Overdrive Pacing	Mode 2	Mode 5
<b>Triggered Overdrive Pacing</b>	Mode 3	Mode 6

Table 4.1: Stimulation Modes

## **4.3 Output Controller**

When the investigator initiates a stimulation run, the output controller portion of the *Pacer* program is entered. The parameters that were setup in the user interface are now used to write output buffers for the registers of the digital-to-analog board. Special board driver program, ATLAB, is used to control the outputs of the digitalto-analog board.

### **4.3.1 Initialization and Termination**

The initialization subroutine AL-INITIALIZE must be called before calling any other subroutine. ALSELECT-BOARD and ALRESET are used to reset the currently selected unit. In addition, a first argument of **ALSETUP.DAC** specifies an internal clock to be the timing source for **D/A** conversions and a second argument specifies that two channels are used for writing the data values, one to each channel simultaneously. ALSET\_PERIOD initializes the clock period that affects the conversion rate for **D/A** operations to one millisecond.

ATLAB provides the termination subroutine AL-TERMINATE which performs the functions of termination. AL.TERMINATE must be called before exiting the program to terminate the DMA operation.

## **4.3.2 D/A Operation**

Fixed-rate pacing can be started **by** running a PACING function. When PACING function is called in the program, user data buffers are declared **by** ALDECLARE.BUFFER and linked to the the digital-to-analog board's Buffer Transfer List by AL\_LINK\_BUFFER. After a buffer is declared and linked, output buffer is now filled with data based on the parameter values inputted **by** the investigator. The output buffer contains a twelve bit value which corresponds to the voltage required **by** the stimulator system to produce the desired current and voltage outputs. The analog output board can produce 4096 steps over a **-10** V to **+10** V range: i.e., a digital value **0** refers to output of **-10** V, 2048 refers to output of **0** V, and 4096 refers to output of **10** V.

After the buffer needed for the stimulation has been written, **ALBURST-DAC** is used to produce analog outputs. **AL-BURSTDAC** allows high speed data transfer using the Direct Memory Access (DMA) technique. AL\_WAIT\_FOR\_COMPLETION function synchronizes user program operation with burst mode I/O operation **by** re-

 $\mathcal{L}_{\text{max}}$ 

 $\sim 100$  km s  $^{-1}$ 

 $\sim 0.1$ 

turning the control of the program when  $I/O$  operation is complete. AL\_UNLINK\_BUFFER is called to unlink the buffer from the current unit's Buffer Transfer List after the stimulation. **ALUNDECLAREBUFFER** is used to undeclare the buffer.

Arrhythmias induction and prventive overdrive pacing can be started **by** using a combination of the following functions: EXT.STM, BURST, OVERDRIVE, and TRIGGER. For example, for mode 2 stimulation, functions EXT\_STM and OVER-DRIVE are called; for mode 3 stimulation, functions EXT\_STM and TRIGGER are used. **All** these functions are written in the same structure as the PACING function.

The actual program, called pacer.c, is attached in appendix. The program is written with comments for future modifications. Also, the ATLAB manual can be consulted for more information on the ATLAB functions used in the program **[9].**

## **Chapter 5**

# **Experimental Study**

The programmable stimulator system presented in this thesis is tested in the experimental animal study. Ventricular arrhythmias are induced in a small swine, which has a similar heart size and coronary circulation as humans, and triggered pacing is administered to prevent the arrhythmias from developing. There are two days of surgery involved in this experimental study. The first surgery is a survival surgery, during which myocardial infarction is induced **by** the occlusion of the coronary arteries. The second surgery is an acute procedure for the induction of ventricular arrhythmias and study of triggered multi-site pacing for the prevention of ventricular arrhythmias. (Protocol **# 92-005,** approved **by** MIT Committee on Animal Care)

## **5.1 Survival Surgery**

Using aseptic techniques, a pig of female sex  $(20 \pm 1 \text{ kg})$  is tranquilized with a mixture of ketamine **(10** mg/kg) and xylazine (2 mg/kg) intramuscularly. Anesthesia is maintained using isoflurane gas **by** the vaporizer through the endocardial tude (size **6.5)** placed in the trachea. **A** left thoracotomy at the fourth intercostal space is

performed and the paracardium is dissected open.

Myocardial infarction is induced **by** ligating the second and third diagonal branches from the left anterior descending **(LAD)** coronary artery, permanently obstructing blood flow. Thirty minutes prior to occlusion, a bolus of lidocaine **(1.5** mg/kg) is administered intravenously. The infarct covers approximately **15 -** 20 **%** of the left ventricular myocardium. The pictorial representation of the myocardial infarct is shown in Figure **5-1.**



Figure **5-1:** Myocardial infarct (Reproduced from Netter FH: Heart, Vol. **5,** The CIBA Collection of Medical Illustrations, CIBA, **1981)**

Tygon 16-gauge catheter (Norton Plastics, Akron, Ohio) is implanted in the left azygous vein going into the left atrium for post-operational care (see Figure **5-2** for the anatomy of a **pig** heart). The catheter is externalized on the back of the animal between the shoulder blades. Following the surgery, animal is treated with prophylactic antibiotics (kefflin) and is allowed to recover for seven days before acute surgery.



Figure **5-2:** Cranial view of the swine heart showing the relationships of the blood vessels at the base of the heart. In the bottom view, the great vessels have been severed to reveal the left azygos vein.

## **5.2 Acute Surgery**

### **5.2.1 Surgical Preparation**

The animals is tranquilized (see last section) and anesthized with sodium pentabarbital **(30** mg/kg) intravenously. Tygon 16-gauge catheter is implanted in the femoral vein percutaneously for infusion of **5 %** dextrose ringer solution. And, another **Ty**gon 16-gauge catheter is implanted in the femoral artery percutaneously to record the blood pressure. Phasic arterial blood pressure is measured **by** a pressure transducer connected to the catheter. Lead I electrocardiogram **(ECG)** is obtained through surface electrode needles. **A** sterotomy is performed and the heart is exposed.

One catheter with four unipolar pacing electrodes is passed through a jagular vein and positioned in the apex of the right ventricle, as shown in Figure 5-3. Two distal pacing electrodes are used to deliver current pulses for the single-site pacing and the induction of ventricular arrhythmias. Two proximal pacing electrodes are used for recording the intracavitary electrocardogram. In addition, 56-bipolar electrodes sock array is placed around the ventricle for multi-site pacing of the ventricle, as shown in Figure 5-4. The 56-bipolar electrodes sock array of Bard Electrophysiology has the dimensions of **15** centimeters in perimeter and **8.8** centimeters in length.



Figure **5-3:** Intracavitary lead system used for the experiment



Figure 5-4: 56-bipolar electrodes sock placed around the ventricle

## **5.2.2 Electrophysiologic Study**

Electrophysiologic study is accomplished **by** the programmable stimulator system presented in this thesis. In the following sections, the electrophysiologic study conducted for the prevention of arrhythmias is presented.

### Determination of Single-Site Pacing Threshold

During electrophysiologic study, heart is paced **by** the distal electrodes of the catheter. The distal pole of the pacing bipolar catheter is made cathodal with reference to the proximal pole. Heart rate is maintained at **150** beats/min using constant current rectangular stimuli of two milliseconds duration. The rate is chosen to be **10 %** higher than the intrinsic rate of **135** beats/min. Also, the pulse duration is chosen to be two milliseconds since it is the optimal duration based on the study of the inverse relationship between the pulse duration and pacing threshold **[3].** While

pacing is being performed at the lowest current amplitude possible, the current amplitude is increased at **1** milliamp interval until a ventricular beat is induced. The pacing threshold is determined to be **1** milliamp. The current amplitude of the pacing is then set at four times the value of the pacing threshold, 4 milliamp. The lead I electrocardiogram recorded during the ventricular pacing is shown in Figure **5-5** with stimulator outputs and arterial blood pressure.

#### Induction of Ventricular Tachycardia

Extra stimuli are used to induce ventricular arrhythmias in this experiment. While maintaining a **150** beats/min pacing rate at 4 times pacing threshold, a 2 miliseconds square wave stimulus  $(S_2)$ , producing the first ventricular premature beat, is interposed in late diastole and is moved closer to the T wave of the previous beat in 20 milliseconds intervals until the effective refractory period is reached.  $S_2$  is then set and presented at an interval that is **10** milliseconds longer than the effective refractory period, and a second stimulus  $(S_3)$  is added in the same manner. The  $S_2 - S_3$  interval is shortened progressively in the same fashion until S<sub>3</sub> fails to evoke a propagated response. A third  $(S_4)$  and fourth  $(S_5)$  are added similarly until the desired end point is reached. Ventricular fibrillation is induced when the fourth extra stimulus is added. The animal is defibrillated by **10** Joule energy delivered **by** internal defibrillation paddles. The characteristics of extra stimuli needed to induce ventricular fibrillation is noted. The lead I electrocardiogram during ventricular fibrillation is shown in Figure **5-6** with the stimulator outputs and arterial blood pressure. This protocol is similar to one previously described and utilized in clinical electrophysiologic induction of ventricular arrhythmias [20].



Figure **5-5:** Electrocardiogram and arterial blood pressure during single site pacing using current pulses



Figure 5-6: Ventricular fibrillation induced by four extra stimuli

### Triggered pacing

The extra stimuli of same characteristics is used to induce another ventricularfibrillation, and triggered mulit-site pacing is applied through the mutli-site electrodes sock. The multi-site pacing is applied when two proximal pacing electrodes detect an activity in the right ventricle near the apex. Since the premature activities can be a part of re-entrant circuit, multi-site pacing is applied to prevent arrhythmias **by** deploarizing the ventricular mass. The multi-site pacing is not applied during the pacing inhibit time, 200 milliseconds period right after the previous pacing beat, in order not to trigger pacing **by** the transient of the pacing pulse. The lead I electrocardiogram, one right intracavitary electrogram, stimulator outputs, and blood pressure are shown in Figure **5-7.**

Mutli-site pacing in this experiment did not prevent the development of ventricular fibrillation. The most likely reason for this is that the initial re-entrant site was a very small region and that the multi-site pacing electrodes were not sufficiently close to block the development of re-entry.

## **5.3 Future Study**

To further investigate the preventive methods, the ventricular myocardium where the arrhythmia originate must be depolarized effectively. Other multi-site electrode pacing configurations to achieve this is currently being investigated. The high precision voltage/current amplifier of the current stimlator system can be used for this type of pacing. Also in order to pace only the premature beats, more efficient timing scheme can be programmed into the control program.





# **Chapter 6**

# **Conclusion**

The programmable stimulator system with the control program has provided our laboratory with an easy to use cardiac stimulator for the electrophysiologic study of the prevention of arrhythmias. As new research protocols are created, it is a relatively simple matter to add them into the control program. Also, new hardware components may be added easily into the current system.

 $\hat{\mathcal{A}}$ 

# **Appendix A**

# **Pacer.c**

**\*** *File name* **-- >** *pacer.c* **\*** *Date -------- > 08/22/93* **\*** *Purpose* **---- >** *routine to operate DA board as a stimulator* **\*** #include <stdio.h> **/\*** *standard C I/O header file* \*/ #include <bios.h> **10** #include <conio.h> **/\*** *console I/O header file* \*/ #include <dos.h> **/\*** *command line \*/* #include "atldefs.h" **/\*** *ATLAB function definition file* \*/ #include "atlerrs .h" **/\*** *ATLAB error definition file* \*1 #include "video.h" **/\*** *video display function file* \*/ **\*** *Function prototype* **20** void INIT\_PARAMETER\_SCREEN (); /\* *initialize parameters on the screen* \*/ void READ KEYBOARD-INPUT 0; **/\*** *read keyboard input* \*/ void HIGHLIGHT (char kytmp2); void **FUNCTION** KEY (char kytmp2, int i); void CURSOR (char kytmp2);



**/ \*** *Extra stimuli parameter initial values* **\*/**

#### APPENDIX A. PACER.C



 $\ddot{\phantom{0}}$ Global parameter declarations  $\ast$ 

 $\bar{z}$ 

 $\frac{1}{2}$  parameter declarations for main function \*/

 $=$  {CHP\_DE,CHE\_DE,CHO\_DE};  $int ch[3]$  $=$  {OUTP\_DE, OUTE\_DE, OUTO\_DE};  $int out[3]$ 

68

0

o

0

120



 $\mathcal{L}^{\text{max}}_{\text{max}}$  and  $\mathcal{L}^{\text{max}}_{\text{max}}$ 

 $\sim 10^{11}$ 

#### APPENDIX A. PACER.C

int  $accu = 0$ ;

 $1***$  parameter for waiter \*\*\*/ int intnumber  $= 0x15$ ; union REGS inregs, outregs; long waitval  $= 1024$ ; int clock tics; int clock\_tics1;

```
/**** parameter for readport ***/
int addr = 0x240;
unsigned port_read;
```
 $\min() \{$ 

Parameter assignments 190  $/***$  parameter assignments for function 'PACING' \*\*\*/ int number buffer p; int length\_buffer\_p; int number\_pacing;  $/***$  parameter assignments for function 'PACING PVC' \*\*\*/ int number\_buffer\_pvc; int length\_buffer\_pvc; 200 /\*\*\* parameter assignments for function 'PACING\_NOPVC \*\*\*/ int number\_buffer\_nopvc; int length\_buffer\_nopvc;  $/***$  parameter assignments for function 'EXT\_STM' \*\*\*/ int number\_buffer\_e; int length buffer e; /\* NOTE: this better be fixed to account for 3 ex or 2 ex \*/ 210  $/***$  parameter assignments for function 'BURST' \*\*\*/ int number\_buffer\_b; int length buffer b; /\*\*\* parameter assignments for function 'OVERDRIVE' \*\*\*/ int number\_buffer\_op; int length\_buffer\_op; int number\_overdrive;

180

### APPENDIX A. PACER.C

```
/*** parameter assignments for function 'TRIGGER' ***/
                                              220
int number_buffer_t;
int length_buffer_t;
int number_trigger;
      \pmb{\ast}Initialize video screen
230
CLEAR_SCREEN();
SETUP_SCREEN();
INIT_PARAMETER_SCREEN ();
* Choose from Main Menu
\starProtocol 1 f1 Triggered Multi-Site Pacing
\bulletProtocol 2 f2
                                              240
  Protocol 3 f3
  Protocol 4 14CLEAR_COMMAND (); /* routine to clear command panel */
MAIN_MENU (); /* routine to put protocol menu in command pannel */
READ_KEYBOARD_INPUT (); /* routine to get a keyboard input */
250
* Protocol 1 f1 Triggered Multi-Site Pacing
if ((kytmp1 == 0) & & (kytmp2 == 59)) {
          * Flag definitions
                                              260
     again_fig = 1; /* do it again when it's 1 */
    ex_st_f = 1; /* extra stimuli */
    od flg = 1; /* overdrive */
    out1_flg = CURRENT;
```
71

 $out2_ffg = CURRENT;$ 270 \* Begin protocol 1 loop while(again\_fig)  $\{$ Choose from Protocol 1 Menu: 280 Level 1.1 f1 select mode & channel  $\star$ Level 1.2  $f2$ change output characteristics Level 1.3 cursor change output characteristics Level 1.4 f10 start pacing Level 1.4.1 cursor change output characteristics Level 1.4.2 f1 stop pacing & exit to protocol 1 menu Level 1.4.3 f10 introduce extra stimuli & overdrive Level 1.5 esc exit to the main menu 290 CLEAR\_COMMAND(); PROTOCOL1\_MENU (); READ KEYBOARD INPUT (); \* Level 1.1 f1 select mode & channel 300 if ((kytmp1 == 0) && (kytmp2 == 59)) {  $/* f1 */$ \* Choose from Level 1.1 Menu: \* Level 1.1.1 f1 select mode \* Level 1.1.2 f2 select channel 310 \* Level 1.1.3 esc exit this level 

CLEAR\_COMMAND ();
```
PROTOCOL1_1_MENU ();
READ KEYBOARD INPUT ();
ż
                                                 320* Level 1.1.1 fi select mode
 if ((kytmp1 == 0) \& k (kytmp2 == 59)) { /* f1 */}CLEAR_COMMAND();
       PROTOCOL1_1_1_MENU ();
       READ_KEYBOARD_INPUT ();
        if ((kytmp1 == 0) & & (kytmp2 == 59)) { 330mode_fdg = 1;
               ex_st_f[g] = 1;od_ffg = 1;}
        else if ((kytmpl == 0)
&& (kytmp2 == 60)) {
               mode_{flg} = 2;ex_st\_fig = 1;od_{\text{f}}ig = 2;
       }
                                                  340
        else if ((kytmpl == 0)
&& (kytmp2 == 61)) {
               mode_{\text{Hg}} = 3;
               ex_st_f[g] = 1;od\_fig = 3;}
        else if ((kytmpl == 0)
&& (kytmp2 == 62)) {
               mode_f g = 4;ex_st_ffg = 2;350
               od\_fig = 1;}
        else if ((kytmpl == 0)
&& (kytmp2 == 63)) {
               \text{mode\_fig} = 5;ex_st_f[g] = 2;od\_fig = 2;}
        else if ((kytmpl == 0)
&& (kytmp2 == 64)) { 360
               mode_{\text{flg}} = 6;
               ex_st_f = 2;od_{\text{flg}} = 3;
```

```
}
        else if ((kytmpl == 0) && (kytmp2 == 65)) {
                mode_{fg} = 7;
        }
        if (ex_st_flg == 1) \{ 370
                delays[0] = 200;delays[1] = 0;delays[2] = 0;\text{delays}[3] = 0;sprintf(tmpstr,"4d ms",delays[0]);
                outtext(EXTRAx,D1y,tmpstr,0);
                sprintf(tmpstr,"X4d ms",delays[1]);
                outtext(EXTRAx,D2y,tmpstr,0);
                sprintf(tmpstr,"%4d ms",delays[2]);
                outtext(EXTRAx,D3y,tmpstr,0); 380
                sprintf(tmpstr,"X4d ms",delays[3]);
                outtext(EXTRAx,D4y,tmpstr,0);
        }
        else if (ex_st_f[g == 2) {
                delays[0] = 200; \frac{\dagger}{\dagger} delay before burst train */
                delays\begin{bmatrix}1\end{bmatrix} = 100; /* period for which burst train is on */
                delays[2] = 8; / * delay between burst train */
                delays[3] = 0;sprintf(tmpstr,"X4d ms",delays[0]); 390
                outtext(EXTRAx,D1y,tmpstr,0);
                sprintf(tmpstr,"X4d ms",delays[1]);
                outtext(EXTRAx,D2y,tmpstr,0);
                sprintf(tmpstr,"4d ms",delays[2]);
                outtext(EXTRAx,D3y,tmpstr,0);
                sprintf(tmpstr,"%4d ms",delays[3]);
                outtext(EXTRAx,D4y,tmpstr,0);
} }
                                                      400
          *********************************
 * Level 1.1.2 f2 select channel *
 else if ((kytmpl == 0) && (kytmp2 == 60)) { /* f2 */
        CLEAR_COMMAND();
        PROTOCOL1_1_2_MENU ();
        READ_KEYBOARD_INPUT (); 410
```

```
if ((kytmp1 == 0) && (kytmp2 == 59)) {
        CLEAR_COMMAND ();
        PROTOCOL1.1_2_1_MENU 0;
        READ_KEYBOARD_INPUT ();
        if ((kytmpl == 0) && (kytmp2 == 59)) {
                ch[0] = 1;sprintf(str,"%4d",ch[0]);
                outtext(PACINGx,CHPy,str,0); 420
        }
   \ddot{\phantom{a}}else if ((kytmpl == 0) && (kytmp2 == 60)) {
                ch[0] = 2;sprintf(str,"%4d",ch[O]);
                outtext(PACINGx,CHPy,str,0);
} }
else if ((kytmpl == 0) && (kytmp2 == 60)) { 430
        CLEAR_COMMAND();
        PROTOCOL1_1_2_1_MENU 0;
        READ_KEYBOARD_INPUT ();
        if ((kytmpl == 0) && (kytmp2 == 59)) {
                ch[1] = 1;sprintf(str,"%4d",ch[1]);
                outtext(EXTRAx,CHEy,str,0);
        }
                                             440
        else if ((kytmpl == 0) && (kytmp2 == 60)) {
                ch[1] = 2;sprintf(str,"%4d",ch[1]);
                outtext(EXTRAx,CHEy,str,0);
        }
}
else if ((kytmpl == 0) && (kytmp2 == 61)) { /*f3 *1
        CLEAR<sub>_</sub>COMMAND (); 450
        PROTOCOL1_1.2_1_MENU 0;
        READ_KEYBOARD_INPUT ();
        if ((kytmp1 == 0) && (kytmp2 == 59)) {
                ch[2] = 1;sprintf(str,"%4d",ch[2]);
                outtext(Ox,CHOy,str,0);
        }
```

```
else if ((kytmp1 == 0) & & (kytmp2 ==460)) {
                                             ch[2] = 2;sprintf(str,"%4d",ch[2]);
                                             outtext(Ox,CHOy,str,0);
                                      \mathbf{\}\mathbf{\}\} /* end of level 1.1.2 f2 select channel */
                          470
                          * Level 1.1.3 esc exit this level
                          else if (kytmp1 == 27) {
                                /* don't do anything;
                                  it will automatically go to the protocol 1 menu */480
                         \} /* end of level 1.1.4 esc exit this level */
                   \} /* end of level 1.1 f1 (select channel, extra stimuli \mathcal{B} overdrive) */
                   * Level 1.2 f2 change output characteristics
                    490
                   else if ((kytmp1 == 0) & & (kytmp2 == 60)) { /* f2 */* Begin level 1.2 loop
                          while (1) {
                                                                    500
outtext(2,19, "Which output characteristics do you want to change?",0);
outtext(2,20,"f1 AMPP f2 IAP f3 WP f4 CYCL f5 IC
                                                    ESC Exit",0);
outtext(2,21,"f6 AMPO f7 OD
                        f8 DOD f9 L_E f10 L_O #7 L_B #8 WINDOW #9 WO",0);
      outtext(2,22,"F1 AMPE F2 IAE F3 WE F4 D1 F5 D2 F6 D3 F7 D4 F8 ID F9 EX_ST",0);
```
READ KEYBOARD INPUT ();

CLEAR COMMAND();

```
if (kytmpl == 27) break; /* Ezit level 1.2 loop */
            if (kytmp1 == 0) \{CLEAR_COMMAND (); 510
                  outtext(2,19,"Type in new value for ",0);
                  HIGHLIGHT(kytmp2);
                  outtext(28,19,", followed by RETURN key:",0);
                  KEYBOARD_SCREEN(54,19);
                        / * program to print what's being typed */
                  FUNCTION_KEY(kytmp2,i);
                  /* A LTERMINATE (; *1
            }
      } 520
} /* end of level 1.2 f2 (change output characteristics) */
* Level 1.3 cursor change output characteristics
********************* **************************/
else if ((kytmpl == 0) && (kytmp2 > 70) && (kytmp2 < 82)) { / tfaursor */
      CURSOR(kytmp2);
}|* end of level 1.3 cursor (change output characteristics) */
* Level 1.4 f10 begin pacing
540
else if ((kytmp1 == 0) \&& (kytmp2 == 68)) { /*f10 */}* Initialize A TLAB for DA operation
      1* initialize the A TLAB subroutines *1 550
      ALINITIALIZE ();
      / * select board 1, the first unit */
      AL SELECT BOARD (1);
      /* perform a reset on the device *1
      ALRESET ();
```
 $\frac{1}{2}$  = internal clock, software start  $-1$  - output two values, one to each DAC channel simultanelously  $*/$  $AL$  SETUP\_DAC  $(0,-1)$ ; 560  $/*$  set sample point interval at 1 msec \*/ AL\_SET\_PERIOD (0.001); CLEAR\_COMMAND(); PROTOCOL1\_4\_MENU (mode\_fig);  $again_fg2 = 1;$ 570 \* Begin protocol 1.4 loop \*/ while (again  $fig2)$  {  $*$  Pacing 580  $number_buffer_p = 0;$  $length_buffer_p = cycl;$  $number\_pacing = 99;$ PACING (number\_buffer\_p, length\_buffer\_p, number\_pacing); 590 \* Choose from Level 1.4 Menu: \* Level 1.4.1 cursor change output characteristics \* Level 1.4.2 f1 stop pacing & exit to protocol 1 menu \* Level 1.4.3 f10 introduce extra stimuli & overdrive READ\_KEYBOARD\_INPUT(); 600 \* Level 1.4.1 cursor change amp and cycle

 $\ast$ if  $((kytmp2 > 70) & k\& (kytmp2 < 82))$ CURSOR(kytmp2);  $\mathbf{\}$ 610 \* \* Level 1.4.2 f10 stop pacing else if ((kytmp1 == 0) & & (kytmp2 == 68)) { again\_fig2 = 0; /\* end while loop \*/ 620 CLEAR\_COMMAND (); PROTOCOL1\_MENU ();  $\mathbf{\}$ \* \* Level 1.4.3 f1 extra stimuli & overdrive 630 else if ((kytmp1 == 0) && (kytmp2 == 59)) { \* \* Mode 1: Extra stimuli only \*/ if  $(mode\_fig == 1)$  { 640 \* \* ES for VT induction \*/  $number_buffer_e = 0;$  $/$ \* last pacing pulse width \*/  $length\_buffer_e = width[0];$ for  $(i=0; i$ 650 length\_buffer\_e

 $\mathbf{)}$ 

 $\mathbf{\}$ 

 $\bullet$ 

 $=$  length\_buffer\_e + delays[i] + width[1];  $\frac{1}{\epsilon}$  reset the value to 0 so to avoid the DC shock \*/  $length_buffer_e = length_buffer_e + 2;$ EXT\_STM (number\_buffer\_e, length\_buffer\_e); AL\_TERMINATE (); 660 \* \* Mode 2: Extra stimuli & fixed rate overdrive pacing \*/ else if  $(mod _{e}fig == 2)$  {  $/* ES \& OD *$ /\* 670  $*$  ES for VT induction \*/  $number_buffer_e = 0;$  $length_buffer_e = width[0];$ for  $(i=0; i < ex_st; i++)$ length\_buffer\_e  $=$  length\_buffer\_e + delays[i] + width[1]; length\_buffer\_e = length\_buffer\_e + 2; 680 EXT\_STM (number\_buffer\_e, length\_buffer\_e); /\* \* Fized rate overdrive pacing \*/  $number_buffer_op = 0;$  $length_buffer_op = dod;$ 690 number\_overdrive = od; OVERDRIVE (number\_buffer\_op, length\_buffer\_op, number\_overdrive); AL\_TERMINATE();  $\frac{1}{2}$ \*

```
* Mode 3: Extra stimuli & triggered pacing
                                           700
 else if (mod _{fg} == 3) { /* ES &T & OD */
        /******************************
         * Extra stimuli for VT induction
         *****************************/
                                           710
       number\_buffer_e = 0;length\_buffer_e = width[0];for (i=0; i < ex_st; i++)length_buffer_e
               = length_buffer_e + delays[i] + width[1];
       length_buffer_e = length_buffer_e + 2;EXT_STM (number_buffer_e, length_buffer_e);
              ************************
                                            720
         *
          Trigger
         *****************************/
       number\_buffer_t = 0;length_buffer_t = width[0] + 2;
       number\_trigger = trig;TRIGGER
        (number_buffer_t, length_buffer_t, numberzwigger);
       AL_TERMINATE();
\mathbf{\}********************************
 * Mode 7: Extra stimuli & PVC triggered pacing
 740
else if (mode_f g == 7) { /* ES &T & OD */
             **************************
         * Extra stimuli to induce arrhythmias
         *****************************/
```
 $number\_buffer_e = 0;$ length\_buffer\_e = width $[0]$ ; 750 for  $(i=0; i < ex_st; i++)$ length\_buffer\_e  $=$  length\_buffer\_e + delays[i] + width[1]; length\_buffer\_e = length\_buffer\_e + 2; EXT\_STM (number\_buffer\_e, length\_buffer\_e);

CLEAR\_COMMAND();

outtext $(2,19,$ "Press the space bar to stop PVC triggered pacing",1);

760

/\* \* Wait the pacing inhibit time \* to avoid sensing pacing pulse \* transients \*/

 $\frac{1}{\pi}$  Initialization for waiter \*/ inregs.h.ah =  $0x86$ ;  $integs.x(cx = waitval >> 16;$ inregs.x.dx = waitval & & 0xffff; 770

 $/*$  'clock\_tics' are used to convert the 1.02 KHz clock to 1 KHz clock  $*/$ clock\_tics =  $(int)$  (((long)trig\_locke \*  $(long)1024) / (long)1000);$ for  $(i=0; i <$ clock\_tics;  $i++$ ) int86 (intnumber, &inregs, &outregs);

780

PVC Trigger

\*/

/\* Set up ports 0 & 1 of DT2821 interface board to read in words \*/ outport  $(addr+0x6,0x00);$  $clock\_tics = (int) ((long)(trig\_window-trig\_locke) *$  $(long)1024) / (long)1000);$ 

 $/*$  Start monitoring trigger  $*$ /

 $do { }$ 

for  $(i=0; i <$  clock\_tics;  $i++$ ) { port\_read = inport(addr+0xa);

if (port\_read  $== 0x$ feff) {

*/* **\*** *output triggered pacing pulse \*/* numberbuffer-pvc **= 0; <sup>800</sup>**  $length_buffer_pvc = width[2] + 2;$ PACING\_PVC(number\_buffer\_pvc, length\_buffer\_pvc);

*/* **\*** *wait trig lockout time of overdrive \*/* clock-ticsl **=** (int) (((long)trig-locko **\*** (long)1024) */* (long)1000); for  $(i=0; i <$ clock\_tics1;  $i++$ ) int86 (intnumber, &inregs, &outregs);

*/\* new initialization* **\*/ 810**  $clock\_tics = (int)$   $(((long)(trig\_window-trig\_locko) *$ (long)1024) */* (long)1000);

*/ get out of 'for' loop \*/* break;

*/\* if the end of triggering window is reached \*/*

 $\text{else if } (i == \text{clock\_tics} - 1)$  {  $\text{820}$ 

 $\frac{1}{\sqrt{2}}$  *vait for the spontaneous beat* \*/

 $clock\_tics1 = (int)$   $(((long)(trig\_demand - trig\_window) *$ (long)1024) /(long)1000);

j = **0;**

*}*

do *{* int86(intnumber,&inregs, &outregs);  $j = j + 1;$  **830** port-read **=** inport (addr+Oxa); *}* while **(** port-read **==** Oxffff **&& j <** clockticsl *);*

if  $(j <$  clock\_tics1)  $\{$ 

*/\* wait trigger lockout time of spontaneous beat \*/* clock-ticsl **=** (int) (((long)triglockb **\*** (long)1024) */* (long)1000); for  $(j=0; j <$  clock\_tics1;  $j++$ ) int86 (intnumber, &inregs, &outregs); **<sup>840</sup>**

*/\* new initialization \*/*  $clock\_tics = (int)$   $(((long)(trig\_window-trig\_lockb) *$ 

÷,

*}*

```
(long)1024) / (long)1000);
 /* get out of 'for' loop */
 break;
}
 else { 850
  number.buffer.nopvc = 0;
  length_buffer_nopvc = width[0] + 2;PACING_NOPVC (number_buffer_nopvc, length_buffer_nopvc);
  / * wait trigger lockout time of channel 1 (or ES) */
  clock\_tics1 = (int) (((long)trig\_locke * (long)1024) /
                 (long)1000);
  for (j=0; j<clock-ticsl; j++)
       int86 (intnumber, &inregs, &outregs);
                                                          860
  /* new initialization */
  clock-tics = (int) (((long)(trig-window-trig_locke) *
                (long)1024) / (long)1000);
  /* get out of 'for' loop */
  break;
 }
else { 870
 int86 (intnumber, &inregs, &outregs);
}
                              } /* end of for loop */
                      } while ( !kbhit() );
                      /* kbhit() puts the key hit in register,
                        so need to be removed */
                                                          880
                      getch 0;
                      AL_TERMINATE ();
              } /* end of mode 7*/
                /*************************************
                * Mode 4: Burst only
                                                          890*************************************/
```

```
else if (mode\_fig == 4) { /* Burst */number_buffer_b = 0;length_buffer_b = delays[0] + delays[1];BURST(number_buffer_b, length_buffer_b);
       AL_TERMINATE ();
} 900
       ******************************
 *
* Mode 5: Burst & jized rate overdrive pacing
************ ********************
else if (modejflg == 5) { /* Burst & OD */
       number_buffer_b = 0; 910length_buffer_b = delays[0] + delays[1];BURST(number_buffer_b, length_buffer_b);
       number\_buffer\_op = 0;length buffer.op = cycl;
       number overdrive = od;
       OVERDRIVE
       (number_buffer_op, length_buffer_op, number_overdrive);
       ALTERMINATE 0; 920
}
         **********************************
* Mode 6: Burst & triggered OD
else if \text{(mode fig == 6)} \{ / * B \& T * \}930
       number_buffer_b = 0;length_buffer_b = delays[0] + delays[1];BURST(number_buffer_b, length_buffer_b);
              ***********************
          * Trigger
        *
        *****************************/
```
 $\mathcal{L} \in \mathcal{P}$  , we have

医自主性病 医感染性病

940  $number_buffer_t = 0;$ length\_buffer\_t = width $[0] + 2$ ;  $number\_trigger = trig;$ TRIGGER (number\_buffer\_t, length\_buffer\_t, number\_trigger)

#### AL\_TERMINATE();

- $again_f g2 = 0;$ CLEAR\_COMMAND (); PROTOCOL1\_MENU();
- $\}$  /\* different extra stimuli loop \*/
- $\}$  /\* while loop \*/
- $\}$  /\* end of level 1.4 \*/
- 
- \* Level 1.5: esc  $(e^{zit})$

else if (kytmp1 == 27) {  $/* esc */$ 

ł

 $again_f g = 0;$ 

 $\}$  /\* end of lelve 1.5 esc (exit) \*/

 $\}$  /\* end of while loop \*/

/\*\*\* put in 'EXIT\_HANDLER ()' which resets all outputs to avoid accidential outputs \*\*\*/

 $/*$  end of protocol 1 \*/  $/$ \* end of main.c \*/

¢ Function -------> INIT\_PARAMETER\_SCREEN()

 $Return Type --- > void$ \*

 $\mathbf{H}$ 

}

\* Description  $--->$  routine to put initial parameter values on the screen

86

950

960

970

### void INIT\_PARAMETER\_SCREEN() {

*/\*\*PACING panel \*\**

sprintf(tmpstr,"%4d",ch[0]); outtext(PACINGx,CHPy,tmpstr,O);  $sprint(f(mpst, "4.01 mA", amp[0]/20);$ outtext(PACINGx,AMPPy,tmpstr,0); sprintf(tmpstr," $/4.01$  mA", $ia[0]/20$ ); outtext(PACINGx,IAPy,tmpstr,0); sprintf(tmpstr,"%4d ms",width[0]); outtext(PACINGx,WIDTHPy,tmpstr,O); **<sup>1000</sup>** sprintf(tmpstr,"%4d ms",cycl); outtext(PACINGx,CYCLy,tmpstr,O); sprintf(tmpstr,"%4d ms",ic); outtext(PACINGx,ICy,tmpstr,O);

*/\*\*\* EXTRA STIMULI panel*  ~

 $sprint(f(mpstr,"4d",ch[1]);$ outtext(EXTRAx,CHEy,tmpstr,O); sprintf(tmpstr,'7.4. Of mA"',amp[1]/20); **<sup>1010</sup>** outtext(EXTRAx,AMPEy,tmpstr,O); sprintf(tmpstr," $/4.01$  mA",ia[1]/20); outtext(EXTRAx,IAEy,tmpstr,O); sprintf(tmpstr,"%4d ms",width[1]); outtext(EXTRAx,WIDTHEy,tmpstr,O); sprintf(tmpstr,"'%4d",ex-st); outtext(EXTRAx,EX.STy,tmpstr,O);  $sprint(f(mpstr,"4d ms", delays[0]);$ outtext(EXTRAx,Dly,tmpstr,O); sprintf(tmpstr,"%4d ms ",delays **[1]);** <sup>1020</sup> outtext(EXTRAx,D2y,tmpstr,O); sprintf(tmpstr,"%4d ms",delays[2]); outtext(EXTRAx,D3y,tmpstr,O); sprintf(tmpstr,"%4d ms",delays[3]); outtext(EXTRAx,D4y,tmpstr,O); sprintf(tmpstr,"%4d ms",id); outtext(EXTRAx,IDy,tmpstr,0);

/ *OVERDRIVE panel*  ~

sprintf(tmpstr,"%4d",ch[2]); outtext(Ox,CHOy,tmpstr,O); sprintf(tmpstr," $/4.0f$  mV",amp $[2]$ \*25); outtext(Ox,AMPOy,tmpstr,O); sprintf $(\text{tmpstr,"4d ms",width}[2]);$ 

**990**

```
outtext(Ox,WIDTHOy,tmpstr,O);
       sprintf(tmpstr,"X4d ms",dod);
       outtext(Ox,DODy,tmpstr,O);
      sprintf(tmpstr,"%4d",od);
       outtext(Ox,ODy,tmpstr,O); 1040
       sprintf(tmpstr,"%4d",trig);
       outtext(Ox,TRIGy,tmpstr,O);
       sprintf(tmpstr,"%4d ms",triglocko);
       outtext(Ox,LOCKy,tmpstr,O);
       /** TRIGGER panel *
       sprintf(tmpstr,"%4d ms",trig_locke);
       outtext(Tx,LOCK_Ey,tmpstr,0);
       sprintf(tmpstr,"%4d ms",triglocko); 1050
       outtext(Tx,LOCK_Oy,tmpstr,0);
       sprintf(tmpstr,"X4d ms",triglockb);
       outtext(Tx,LOCK_By,tmpstr,0);
       sprintf(tmpstr,"%4d ms",trig_window);
       outtext(Tx,WINDOWy,tmpstr,O);
       sprintf(tmpstr,"%4d ms",trig_demand);
       outtext(Tx,DEMANDy,tmpstr,O);
}
          / **************************************************************************** 100
 * Function -------- > READKEYBOARDINPUT()
 * Return Type ----- > void
 * Description ---- > routine to read keyboard input *
 void READ KEYBOARD INPUT() { 1070kytmp1 = getch();if (kytmp1 == 0)kytmp2 = getch(); /* ESC, cursors, function keys */
}
      / ****************************************************************************
  * Function -------- > HIGHLIGHT(char kytmp2)
                                                                        1080
 * Return Type ---> void
 * Description ----- >routine to highlight
```


 $\mathcal{L}^{\text{max}}_{\text{max}}$  , where  $\mathcal{L}^{\text{max}}_{\text{max}}$ 

 $\sim$ 

 $\mathcal{O}(\log\log n)$ 

 $\label{eq:2} \frac{1}{2} \int_{\mathbb{R}^3} \frac{1}{\sqrt{2}} \, \mathrm{d} \mu \, \mathrm$ 

break;





```
1230
 * Function ------> FUNCTION_KEY (char kytmp2, int i)
 * Return Type ---> void
 * Description ---> routine to read function key input and do the following
 void FUNCTION_KEY(char kytmp2, int i){
                                                                                   1240
        switch (kytmp2) {
                case 59: if \left(\text{str}[i-1] == 'V'\right) {
                                                                   1 * f1 * 1out[0] = VOLTAGE;amp[0] = new_value / 25;for (i=0; i <strlen(str); i++) {
                                       if (\text{str}[i] == 32) { /* blank space ? */str[i] = \sqrt{0}; /* put in end of line */
                                               break;
                                       }
                                                                                   1250
                               \mathbf{H}sprintf(str, "%4.0f mV ", new_value);
                               outtext(PACINGx,AMPPy,str,0);
                               sprintf(str, "%4.0f mV", ia[0]*25);
                               outtext(PACINGx, IAPy, str, 0);
                     \mathbf{\}else if (\text{str}[i-1] == 'A') {
                               out[0] = CURRENT;amp[0] = new_value * 20;1260
                               for (i=0; i<strlen(str); i++) {
                                       if (\text{str}[i] == 32) {
                                               str[i] = \sqrt{0};
                                                break;
                                       \mathbf{\}}
                               sprintf(str,"%4.0f mA ",new_value);
                               outtext(PACINGx,AMPPy,str,0);
                                sprintf(str, "%4.0f mA ",ia[0]/20);
                               outtext(PACINGx, IAPy, str, 0);
                                                                                   1270
                     \mathbf{)}else \{if (out[0] == VOLTAGE) {
                                        amp[0] = new_value / 25;
```

```
sprintf(str,"%4.0f mV ",new_value);
                        outtext(PACINGx,AMPPy,str,O);
                }
                else if (out[0] == CURRENT) \{amp[0] = new_value * 20; 1280
                        sprintf(str,"%4.0f mA ",new_value);
                        outtext(PACINGx,AMPPy,str,0);
                }
      }
        break;
case 60: if (out[0] == VOLTAGE) { / /* f2 */
                ia[0] = new_value / 25;sprintf(str,"X4.Of mV ",new-value); 1290
        }
        else if (out[0] == \text{CURRENT}) {
                ia[0] = new_value * 20;sprintf(str,"%4.0f mA",new_value);
        }
        outtext(PACINGx,IAPy,str,0);
        break;
case 61: width[0] = new_value; /* f3 */
        sprintf(str,"%4.of ms ",new-value);
        outtext(PACINGx,WIDTHPy,str,0); 1300
        break;
case 62: \text{cycl} = \text{new\_value}; /* f4 */sprintf(str,"%4.0f ms ",new-value);
        outtext(PACINGx,CYCLy,str,0);
      fix\_fig = 2;break;
case 63: ic = new_value; /* f5 */
        sprintf(str,"%4.Of ms ",new-value);
        outtext(PACINGx,ICy,str,0);
         break; 1310
case 64: if (\text{str}[i-1] == 'V') { \neq { \neq } \neq }
                out[2] = VOLTAGE;
                amp[2] = new_value / 25;for (i=0; i <strlen(str); i++) {
                       if (str[i] == 32) { / * blank space ? */
                                str[i] = \sqrt{0}; /* put in end of line */
                                break;
                } }
                sprintf(str,"%4.0f mV ",new value); 1320
                outtext(Ox,AMPOy,str,0);
      }
```

```
else if (\text{str}[i-1] == 'A') {
                out[2] = CURRENT;amp[2] = new_value / 0.3;for (i=0; i<strlen(str); i++) {
                       if (str[i] == 32) {
                              str[i] = '0';break; 1330
                       }
                \mathbf{\}sprintf(str,"%4.Of mA ",new-value);
                outtext(Ox,AMPOy,str,0);
       }
       else {
                if (out[2] == VOLTAGE)amp[2] = new_value / 25;sprintf(str,"%4.Of mV ",new-value); 1340
                       outtext(Ox,AMPOy,str,0);
                }
                else if (out[2] == CURRENT) {
                       amp[2] = new_value / 0.3;sprintf(str,"%4.Of mA ",new-value);
                       outtext(Ox,AMPOy,str,O);
       }<br>}<br>break;
case 65: od = \text{new_value}; / * f7 * / 1350
       sprintf(str,"%4.0f ",new_value);
          outtext(Ox,ODy,str,O);
          break;
  case 66: dod = new_value; /*f8 */sprintf(str,"%4.0f ms ",new_value);
          outtext(Ox,DODy,str,O);
          break;
  case 67: trig_locke = new_value; /* f9 */
          sprintf(str,"%4.Of ",new.value);
          outtext(Tx,LOCK_Ey,str,0); 1360
          break;
  case 68: trig_locko = new_value; / * f10 * /sprintf(str,"%4.0f ",new_value);
          outtext(Ox,LOCKy,str,O);
          outtext(Tx,LOCK_Oy,str,0);
          break;
  case 71: \text{trig\_lockb} = \text{new\_value}; / * \text{#7} */sprintf(str,"%4.Of ",new-value);
          outtext(Tx,LOCK_By,str,0);
          break; 1370
  case 72: trig_window = new_value; / * #8 */
```

```
sprintf(str,"%4.Of ",new-value);
        outtext(Tx,WINDOWy,str,0);
        break;
case 73: width[2] = new_value; /* #9 */
        sprintf(str,"%4.0f ms ",new_value);
        outtext(Ox,WIDTHOy,str,O);
        break;
case 84: if (\text{str}[i-1] == 'V') \{ /* F1 */ 1380
               out[1] = VOLTAGE;
               amp[1] = new_value / 25;for (i=O; i<strlen(str); i++) {
                       if (str[i] == 32) { / * blank space ? */
                               str[i] = \sqrt{0'}; \frac{4}{7} put in end of line */
                               break;
                       }
               }
               sprintf(str,"%4.0f mV ",new-value);
               outtext(EXTRAx,AMPEy,str,O); 1390
               sprintf(str,"'/4.0f mV ",ia[1]*25);
               outtext(EXTRAx,IAEy,str,0);
      }
        else if (\text{str}[i-1] == 'A') {
               out[1] = CURRENT;amp[1] = new_value * 20;for (i=O; i<strlen(str); i++) {
                       if (str[i] == 32) {
                               str[i] = '\0'; 1400
                               break;
                } }
               sprintf(str,"%4.0f mA ",new_value);
               outtext(EXTRAx,AMPEy,str,O);
               sprintf(str,"/4.0f mA ",ia[1]/20);
               outtext(EXTRAx,IAEy,str,0);
      }
      else { 1410
               \mathbf{if} (out[1] == \mathbf{VOLTAGE}) {
                       amp[1] = new_value / 25;sprintf(str, "%4.0f mV ", new_value);
                       outtext(EXTRAx,AMPEy,str,O);
               }
               else if (out[1] == CURRENT) {
                       amp[1] = new_value * 20;sprintf(str, "%4.0f mA ", new_value);
                       outtext(EXTRAx,AMPEy,str,O);
```
 $\label{eq:q} \mathcal{Q} = \mathcal{Q} \left( \mathcal{Q} \right) \left( \mathcal{Q} \right) \left( \mathcal{Q} \right) \left( \mathcal{Q} \right) \left( \mathcal{Q} \right)$ 

 $\hat{f}$  and  $\hat{f}$  and  $\hat{f}$ 

*}*

break;



*}* **1420**

*}*

*}*

*/* **\***

 $\star$ **\*** *Function -------- > CURSOR(char kytmp2)* **1470 \*** *Return Type* **---- >** *void* **\* \*** *Description* **---- >** *routine to do the following actions upon cursor input* **\* \*\*\*\*\*\*\*\*\*\*\*\*\* \*\*\*\* \*\*\*\*\* \*\*\*\*\* \*\*\*\* \*\*\*\*\* \*\*\*\*\* \*\*\*\*\*\*\*\*\* \*\*\*\*\*\*\*\*\* \*\*\*\*\* \*\*\*\*\*\*\*\*\*\*/** void CURSOR (char kytmp2){ switch(kytmp2){ case 71:  $\text{amp}[0] = \text{amp}[0] + \text{ia}[0];$  /\* home \*/ **1480** if (out[0] **== VOLTAGE)** *{* sprintf(tmpstr,"%4.Of mV ",amp[o]\*25); *}*  $else if (out[0] == CURRENT)$  { sprintf(tmpstr,"%4.Of mA ',amp[O]/20); *}* outtext(PACINGx,AMPPy,tmpstr,O);  $fix\_fig = 1;$ break; case 72:  $\text{amp}[1] = \text{amp}[1] + \text{ia}[1];$  /\* up arrow \*/ **1490**  $if (out[1] == VOLTAGE)$ sprintf(tmpstr,"%4.0f mV ",amp[O]\*25); *}* else if  $(out[1] == CURRENT)$  { sprintf(tmpstr,'%4.0f mA ",amp[1]/20); *}* outtext(EXTRAx,AMPEy,tmpstr,O);  $fix_f{fg} = 1;$ break; case 73:  $\text{delays}[\text{ex\_st-1}] = \text{delays}[\text{ex\_st-1}] + \text{id};$  /\* pg up \*/ **1500**sprintf(tmpstr,"%4d ms ",delays[ex\_st-1]);  $if (ex_st == 1) outtext(EXTRAx, D1y,tmpstr,0);$ else if  $(ex_st == 2)$  outtext $(EXTRAN,D2y,tmpstr,0);$ else if  $(ex_st == 3)$  outtext $(EXTRAN, D3y, tmpstr, 0);$ else if  $(ex_st == 4)$  outtext $(EXTRAx, D4y, tmpstr, 0);$ break; */* **\*** *left arrow \*/* case 75:  $\text{cycl} = \text{cycl} - \text{ic};$ sprintf(tmpstr,"%4d ms ",cycl); outtext(PACINGx,CYCLy,tmpstr,O);  $fix_flg = 2;$ **1510** break; case 77:  $\text{cycl} = \text{cycl} + \text{ic};$ **\*** *right arrow* **\*/** sprintf(tmpstr,"X4d ms ",cycl); outtext(PACINGx,CYCLy,tmpstr,O);  $\mathbf{fix} \cdot \mathbf{flg} = 2;$ 

```
break;
               case 79: \text{amp}[0] = \text{amp}[0] - \text{ia}[0]; /* end */
                        if (out[0] == VOLTAGE)sprintf(tmpstr,"%4.Of mV ",amp[O]*25);
                        } 1520
                        else if (out[O] == CURRENT) {
                            sprintf(tmpstr,"X4.Of mA ",amp[O]/20);
                        }
                        outtext(PACINGx,AMPPy,tmpstr,O);
                        \mathbf{fix\_ffg} = 1;break;
               case 80: \text{amp}[1] = \text{amp}[1] - \text{ia}[1]; /* down arrow */
                        if (out[1] == VOLTAGE) {
                               sprintf(tmpstr,"4.Of mV ",amp[1]*25);
                        } 1530
                        else if (out[1] == CURRENT) {
                               sprintf(tmpstr,"%4.Of mA ",amp[1]/20);
                        }
                        outtext(EXTRAx,AMPEy,tmpstr,0);
                        \text{fix}_\text{I}fix\text{fg} = 1;
                        break;
               case 81: \text{delays}[\text{ex\_st-1}] = \text{delays}[\text{ex\_st-1}] - \text{id}; \text{/*} pg \text{down*}/sprintf(tmpstr,"%4d ms ",delays[ex_st-1]);
                        if (ex_st == 1) outtext(EXTRAN, D1y, tmpstr,0);else if (ex_st == 2) outtext(EXTRAx,D2y,tmpstr,0); 1540
                        else if (ex_s t == 3) outtext(EXTRAx, D3y, tmpstr, 0);else if (ex_st == 4) outtext(EXTRAN, D4y, tmpstr, 0);break;
       }
}
                 / ****************************************************************************
 *
 * Function -------> PACING (int number_buffer_p, int length_buffer_p, int number_pacing)
                                                                                  1550
 * Return Type ---- > void
 * Description ---- > routine to produce pacing buffer
 void PACING (int number buffer p, int length buffer p, int number pacing) {
```
 $int BUFFER_P[2000];$ 

/ **\*/** / **\*\*\*** *declare BUFFER\_.P for pacing* \*\*\* / **\*/**

AL\_DECLARE\_BUFFER (number\_buffer\_p, BUFFER\_P, length\_buffer\_p\*2); AL\_LINK\_BUFFER (number\_buffer\_p); 1570 for  $(i=0; i<$  length\_buffer\_p\*2;  $i++$ ) /\* *initialize BUFFER\_P* \*/ BUFFER\_P[i]=2048; for  $(i=ch[0]-1; i$ BUFFER\_P[i]=2048+amp[0]; ;<br>|\*  $1***$  set up output /\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\* 1580  $\frac{1}{2}$  + 0 - internal clock  $AL$  SETUP DAC  $(0,-1)$ ;  $-1$  - output two values to channels 1 & 2 \*/ AL\_SET\_PERIOD (0.001); 1590 if (number\_pacing  $!= 99$ ) { for  $(i=0; i<$ number\_pacing;  $i++$ ) { AL\_BURST\_DAC(); outtext(53,19," \*\* \*\* ",2); outtext(53,20,"\*\*\*\* \*\*\*\*",2); outtext(53,21," \*\*\*\*\*\*\* ",2); outtext(53,22," \*\*\*\*\* ",2); outtext(53,23,"  $",2);$  $\ast$ 1600 AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_p);  $\mathbf{\}$  $\mathbf{\}}$ else if (number pacing  $== 99$ ) { while  $($  !kbhit $()$   $)$   $\{$  $/*$  while key is not hit, repeat \*/ AL\_BURST\_DAC(); 1610

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}

 $\pmb{\ast}$ 

```
1660
     for (i=0; i < (length\_buffer_e*2); i++) /* initialize BUFFER_E */
             BUFFER_E[i] = 2048;for (j=ch[0]-1; j < (width[0]*2); j=j+2) /* last pacing pulse before es */
             BUFFER_E[j] = 2048 + amp[0];\text{accu} = \text{width}[0] + \text{delays}[0];\frac{1}{2} first three extra stimuli */
     for (i=0; i < ex_st - 1; i++) {
             for (j=(ch[1]-1)+(accu*2); j < (accu+width[1])*2; j=j+2)1670
                    BUFFER_E[j] = 2048 + amp[1];accu = accu + width[1] + delays[i+1];\mathcal{Y}for (j=(ch[1]-1)+(accu*2); j < (accu+width[1])*2; j=j+2) /* last es */
             BUFFER_E[j] = 2048 + amp[1];7*** set up output
                                ***/1680
      /* 0 - internal clockAL SETUP DAC (0,-1);-1 - output two values to channels 1 & 2 */
      AL SET PERIOD (0.001);
      /********************************/
      1*** output the extra stimuli ***/
      ,<br>| *********************************/
                                                                         1690
      AL_BURST_DAC();
      AL_WAIT_FOR_COMPLETION (number_buffer_e);
      AL_UNLINK_BUFFERS();
      AL UNDECLARE_BUFFER (number_buffer_e);
        Function -------> OVERDRIVE(int number_buffer_op, int length_buffer_op,
                                                                         1700
                           int number_overdrive)
 Return Type ---> void
* Description ---> routine to do overdrive pacing
```
void OVERDRIVE(int number\_buffer\_op, int length\_buffer\_op, int number overdrive) { 1710 int BUFFER\_OP[2000]; AL\_DECLARE\_BUFFER (number\_buffer\_op, BUFFER\_OP, length\_buffer\_op\*2); AL\_LINK\_BUFFER (number\_buffer\_op); 1720  $/*$  initialize BUFFER\_OP \*/ for (i=0; i<length\_buffer\_op\*2; i++)  $BUFFER_OP[i]=2048;$ for  $(i = (ch[2]-1)+((length_buffer_op - width[0] - 2)*2);$  $/*$  pulse near the end of the cycle length  $*/$  $i < (length_buffer_op - 2)*2; i=i+2)$ 1730  $BUFFER_OP[i]=2048 + amp[2];$ if (number\_overdrive  $!= 99$ ) { CLEAR\_COMMAND(); outtext(2,19,"Press the space bar to stop the overdrive pacing anytime",1); for  $(i=0; i<$ number\_overdrive;  $i++$ ) { 1740 if (kbhit()) break;  $/$ \* stop overdrive pacing if any key is hit \*/ AL BURST DAC (); outtext(65,19," \*\* \*\* ",2);  $outtext(65,20,"******",2);$ outtext(65,21," \*\*\*\*\*\*\* ",2); outtext(65,22," \*\*\*\*\* ",2); outtext $(65, 23,$ "  $",2);$ AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_op); 1750 }  $\mathbf{\}$ else if (number\_overdrive == 99) {



 $/$ \*

 $\frac{1}{2}$ 

AL\_DECLARE\_BUFFER (number\_buffer\_t, BUFFER\_T, length\_buffer\_t\*2); 1810  $/***$  fill BUFFER\_T with triggered pacing stimuli data \*\*\*/  $\frac{1}{2}$  initialize BUFFER\_T \*/

for  $(i=ch[2]-1; i<(width[0])^*2; i=i+2)$ BUFFER  $T[i]=2048 + amp[2];$ 

for (i=0; i<length\_buffer\_t\*2; i++)  $BUFFER_T[i]=2048;$ 

AL\_LINK\_BUFFER (number\_buffer\_t);

 $AL\_SETUP\_DAC(2,-1);$  $AL\_SET\_PERIOD$  (0.001);

 $1***$  set up output \*\*\*/ 

AL\_SETUP\_DAC $(2,-1);$ 

 $\frac{1}{2}$  + 2 – external trigger  $-1$  – output one value to channel 2 \*/

AL\_SET\_PERIOD (0.001);

/\*/ 

if (number\_trigger != 99) { for  $(k=0; k<$ number\_trigger;  $k++$ ) {

if (kbhit()) break;  $/*$  stop overdrive pacing if any key is hit \*/

 $/***$  timer to count 100 msec for trigger lockout. this timer increments in the amount 18.2 Hz (60 msec) \*\*\*/

gettime(&timep); otmp = (timep.ti\_sec \* 1000) + (timep.ti\_hund \* 10); while(1)  $\{$ gettime(&timep);  $tmp = timep.ti\_sec * 1000 + timep.ti_hund * 10;$ if  $((tmp - otmp) >= trig\_locko)$  { break: 1850 }

1820

1830

} \*\*/

 $inress.h.ah = 0x86;$  $integs.x(cx = waitval >> 16;$  $in$ regs.x.dx = waitval && 0xffff; clock<sub>r</sub>tics =  $(int)$  (((long)trig\_locko\*(long)1024)/(long)1000); for  $(i=0; i <$ clock\_tics;  $i++$ ) int86(intnumber,&inregs,&outregs); **1860 AL SET** TIMEOUT **(0);** AL BURST DAC (number\_buffer\_t); outtext(65,19,"\*\*\*\*\*\*\*\*\*",2); outtext(65,20,"\*\*\*\*\*\*\*\*\*",2); outtext(65,21," \*\*\*  $",2);$ outtext(65,22," \*\*\* ",2);<br>outtext(65,23," \*\*\* ",2); outtext(65,23," **\*\*\*** 92); AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_t); 1870 } } else if (number-trigger **==** *99)* { while  $($  !kbhit $()$   $)$   $\{$ **/\*\*\*** *timer to count 100 msec for trigger lockout. this timer increments in the amount*  $18.2$  *Hz*  $(60$  *msec) \*\*\*/* **1880** / **\*\*** *gettime(&timep);*  $otmp = (timep.ti\_sec * 1000) + (timep.ti\_hund * 10); **/$ **/\*** *printf("%d %d %d %d\n", timep.ti hour,timep.ti-min, timep.tisec,timep.ti hund);* \*1 / **\*\*** *while(1)* { gettime(6timep);  $tmp = timep.ti\_sec * 1000 + timep.ti\_hund * 10;$  $if ((tmp - otmp) > = trig\_lockout)$  { **1890** *break;*  $\}$  \*\*/  $\}$ /\* printf("%d %d %d %d\n", timep.ti\_hour,timep.ti\_min, *timep.tisec,timep.ti hund);* \*1  $in$ regs.h.ah =  $0x86$ ;  $\text{integs.x.cx} = \text{waitval} >> 16;$ 

 $\text{integs.x.dx} = \text{waitval} \&& \text{0xffff};$  **1900**  $clock\_tics = (int) ((long)trig\_locko*(long)1024)/(long)1000);$ for  $(i=0; i <$ clock\_tics;  $i++$ ) int86(intnumber,&inregs,&outregs);

*/\* A timeout period 0 causes ATLAB to wait indefinitely \*/* **AL SET** TIMEOUT **(0);** AL\_BURST\_DAC (number\_buffer\_t);



#### AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_t);

} *}* outtext(65,19," **",0); <sup>1920</sup>**



## AL\_UNLINK\_BUFFERS(); AL\_UNDECLARE\_BUFFER (number\_buffer\_t);

**/\*\*\*** *at this point, either there was a intracardiac triggered output or timeout triggered output* \*\*\*/ **<sup>1930</sup>**

#### */* **\* \***

**\*** *Function -------- > PACINGPVC (int number buffer pvc, int length-buffer pvc)*

**\*** *Return Type* **---- >** *void* **\***

*}*

$$
* Description --- -> routine to produce PVC triggered pacing buffer
$$

**\***

**1940**

# void PACING\_PVC (int number\_buffer\_pvc, int length\_buffer\_pvc) {

int BUFFER\_PVC[50];

AL\_DECLARE\_BUFFER (number\_buffer\_pvc, BUFFER\_PVC, length\_buffer\_pvc\*2);

}

AL\_LINK\_BUFFER (number\_buffer\_pvc);

\*/ /\*\*\*\*\*\*\*\*\*\*\*\* 1950  $/***$  fill BUFFER\_PVC with pacing data \*\*\*/ for  $(i=0; i<$  length\_buffer\_pvc\*2;  $i++$ )  $/*$  initialize BUFFER PVC \*/ BUFFER PVC[i]=2048; for  $(i=ch[2]-1; i$ BUFFER\_PVC[i]=2048+amp[2]; 1960  $/****$  set up output  $***/$  $/* 0 - internal clock$  $AL$  SETUP DAC  $(0,-1)$ ;  $-1$  – output two values to channels 1 & 2 \*/ AL\_SET\_PERIOD (0.001); \*\*\*/<br>\*\*\*\*\*\*\*\*\*\*/  $/***$  output the pacing stimuli 1970 /\* AL\_BURST\_DAC(); outtext(53,19,"\*\*\*\*\*\*\*\* ",2); outtext(53,20,"\*\* \*\*  $",2);$ outtext(53,21,"\*\*\*\*\*\*\*\* ",2); outtext(53,22,"\*\*  $",2);$ outtext(53,23,"\*\*  $",2);$ 1980 AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_pvc); /\* to erase the  $P^*$ / outtext(53,19,"  $",0);$  $",0);$ outtext $(53,20,$ " outtext(53,21,"  $",0);$ outtext(53,22,"  $",0);$ outtext(53,23,"  $",0);$ AL\_UNLINK\_BUFFERS (); AL\_UNDECLARE\_BUFFER (number\_buffer\_pvc); 1990 \* Function -------> PACING\_NOPVC (int number\_buffer\_nopvc, int length\_buffer\_nopvc)

á. \* Return Type  $--->$  void \* Description  $--->$  routine to produce no PVC pacing buffer 2000 void PACING\_NOPVC (int number\_buffer\_nopvc, int length\_buffer\_nopvc) { int BUFFER\_NOPVC[100]; AL DECLARE BUFFER (number\_buffer\_nopvc, BUFFER\_NOPVC, length\_buffer\_nopvc\*2); AL\_LINK\_BUFFER (number\_buffer\_nopvc); 2010  $/***$  fill BUFFER NOPVC with pacing data \*\*\*/ for (i=0; i<length\_buffer\_nopvc\*2; i++)  $/*$  initialize BUFFER\_PVC \*/ BUFFER\_NOPVC[i]=2048; for  $(i=ch[0]-1; i$ BUFFER\_NOPVC[i]=2048+amp[0]; 2020  $1***$  set up output \*\*\*/  $/$ \* 0  $-$  internal clock  $AL$ \_SETUP\_DAC $(0,-1)$ ;  $-1$  – output two values to channels 1 & 2 \*/ AL\_SET\_PERIOD (0.001);  $***/$  $\frac{1}{2}$   $\frac{1}{2}$  2030 AL\_BURST\_DAC();  $outtext(53,19,"**$ \*\*\*  $",2);$ outtext(53,20,"\*\* \*\*\*\* ",2); outtext(53,21,"\*\* \*\* \*\* ",2); outtext(53,22,"\*\*\*\* \*\* ",2); outtext(53,23,"\*\*\* \*\* ",2); 2040 AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_nopvc); outtext(53,19,"  $",0);$  $/$ \* to erase the N \*/
## APPENDIX A. PACER.C



#### AL\_UNLINK\_BUFFERS (); AL\_UNDECLARE\_BUFFER (number\_buffer\_nopvc);

```
\mathcal{F}_{\mathcal{A}}* Function -------> BURST(int number_buffer_b, int length_buffer_b)
* Return Type ---> vol* Description ---> routine to produce burst train for VT induction
                                                  2060
```
void BURST(int number\_buffer\_b, int length\_buffer\_b) {

int BUFFER\_E[5000];

AL\_DECLARE\_BUFFER (number\_buffer\_b, BUFFER\_E, length\_buffer\_b\*2); AL\_LINK\_BUFFER (number\_buffer\_b);

for  $(i=0; i < (length_buffer_b*2); i++)$  /\* initialize BUFFER E \*/  $BUFFER_E[i] = 2048;$ 

for  $(j=(ch[1]-1); j < (width[0]*2); j=j+2)$  /\* pacing pulse before es \*/ BUFFER\_E[j] = 2048 +  $amp[1]$ ;

 $\text{accu} = \text{width}[0] + \text{delays}[0];$ 

while  $(\text{accu} < (\text{delays}[0] + \text{delays}[1]))$  {  $/* burst train */$ for  $(j = (ch[1]-1) + (accu*2); j < (accu + width[1])*2; j=j+2)$  $BUFFER_E[j] = 2048 + amp[1];$  $accu = accu + width[1] + delays[2];$  $\mathbf{)}$ 

2050

2080

#### APPENDIX A. PACER.C

 $\bar{z}$ 

}

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for (j=(length\_buffer\_b-2)\*2; j<length\_buffer\_b\*2; j=j+1) /\* to avoid DC shock \*/  $BUFFER_E[j] = 2048;$ 

```
/********************************/
1*** output the extra stimuli ***/<br>|*******************************/
```
AL\_BURST\_DAC();

2100

AL\_WAIT\_FOR\_COMPLETION (number\_buffer\_b);

AL\_UNLINK\_BUFFERS (); AL\_UNDECLARE\_BUFFER (number\_buffer\_b);

# Appendix B

 $\mu_{\rm{max}} = \mu_{\rm{max}}$  , where  $\mu_{\rm{max}}$ 

# Video.c

 $\frac{1}{2} \sum_{i=1}^{n} \frac{1}{2} \sum_{i=1}^{n$ 



 $\sim 10^{-1}$ 

```
int i=0;
     while(i < (MAXX*MAXY<<1)) {
           \text{screenptr}[i++] = \text{'} ';
           screenptr[i++] = FOREGROUND_WHITE| BACKGROWD_ND_LALACK;} }
                   *
* Function -------- > SETUP SCREEN() 40
 *
* Return Type ---- > void
* Description ---- > routine to draw boundaries *
void SETUPSCREEN() { /* outside boundary */
      int j; 50
     char tmpstr[2];
     char *tstr;
      / *** four corners
     tmpstr[1]=0;
     tmpstr[O]=218;
     outtext(0,0,tmpstr,0);
     tmpstr[O]=192;
     outtext(0,24,tmpstr,O);
     tmpstr[O]=217; 60
     outtext(79,24,tmpstr,O);
     tmpstr[O]=191;
     outtext(79,0,tmpstr,O);
     /**** horizontal lines at y = 0,2,18,24 ***/
     tmpstr[O]=196;
     for (j=1; j<79; j++) {
           outtext(j,0,tmpstr,0);
           outtext(j,2,tmpstr,O);
           outtext(j,18,tmpstr,O); 70
           outtext(j,24,tmpstr,0);
     }
/* for (j=35; j<79; j++) {
           outtezt(j,3,tmpstr,0);
           outtezt(j, 10,tmpstr, 0);
     } */
     for j=1; j<34; j++)
           outtext(j,14,tmpstr,O);
```

```
\frac{1}{2} /*** vertical lines at x = 0.17, 34, 79 ***/
         tmpstr[0]=179;for (j=1; j<24; j++) {
                  outtext(0,j,tmpstr,0);
                  outtext(79,j,tmpstr,O);
         }
         for (j=3; j<14; j++)outtext(17,j,tmpstr,0);
         for (j=3; j<18; j++)
                  outtext(34,j,tmpstr,0);
         tmpstr[0]=195; /<sup>*</sup>|- <sup>*</sup>/
         outtext(0,2,tmpstr,O);
         outtext(0,14,tmpstr,O);
         outtext(0,18,tmpstr,O);
/* outtext(34,3,tmpstr,0);
         outtezt(34,10,tmpstr,0); */
         outtext(34,14,tmpstr,O);
         tmpstr[0]=180; /*-| */
         outtext(79,2,tmpstr,O);
/* outtext(79,3,tmpstr,0);outtezt(79, 10,tmpstr, 0); */
         outtext(79,18,tmpstr,O);
         outtext(34,14,tmpstr,O);
         tmpstr[0]=194; /*T */
         outtext(17,2,tmpstr,O);
         outtext(34,2,tmpstr,0);
         tmpstr[0]=193; /* reverse T */
         outtext(17,14,tmpstr,O);
         outtext(34,18,tmpstr,O);
         / *** headings ***/
      tstr="P R 0 G R A M M. A B L
E S T I M U L A T 0 R S Y S T E M";
         outtext(12,0,tstr,1);
         tstr="PACING";
         outtext(2,2,tstr,1);tstr="PREMATURE";
         outtext(19,2,tstr,1);
         tstr="OVERDRIVE";
         outtext(36,2,tstr,1);
/* tstr="WAVEFORM";
         outtezt(52,2,tstr,1);
         tstr="CH 1";
         outtext(36, 3,tstr, 1);
```
**113**

**80**

**90**

**100**

**120**

```
tstr="CH 2";
outtezt(36,10,tstr,1); */
tstr="COMMAND";
outtext(36,18,tstr,1); 130
/*** PA CING panel ***/
tstr="CH =";
outtext(2,3,tstr,O);
tstr="AMP =";
outtext(2,4,tstr,O);
tstr="STEP =";
outtext(2,5,tstr,O);
tstr="WIDTH=";
tstr="CYCL =";
outtext(2,9,tstr,O);
tstr="STEP = ";
outtext(2,10,tstr,O);
/*** PREMATURE panel **
```

```
outtext(2,6,tstr,O); 140
```

```
tstr="CH =";
outtext(19,3,tstr,O);
tstr="AMP =";
outtext(19,4,tstr,O); 150
tstr="STEP =";
outtext(19,5,tstr,O);
tstr="WIDTH=";
outtext(19,6,tstr,O);
tstr="EX_ST=":
outtext(19,8,tstr,O);
tstr="D1 =";
outtext(19,9,tstr,O);
tstr="D2 =";
outtext(19,10,tstr,O); 160
tstr="D3 =";
outtext(19,11,tstr,O);
tstr="D4 =";
outtext(19,12,tstr,O);
tstr="STEP =" 
;
outtext(19,13,tstr,O);
```

```
/*** OVERDRIVE panel **
```

```
tstr="CH ="; 170
outtext(36,3,tstr,O);
tstr="AMP =";
outtext(36,4,tstr,O);
tstr="WIDTH=";
```

```
outtext(36,6,tstr,O);
      tstr="MODE 2 & 6";
      outtext(36,8,tstr,1);
      tstr="OD =";
      outtext(36,9,tstr,O); 180
      tstr="DOD =";
      outtext(36,1O,tstr,0);
      tstr=MODE 3 & 6";
      outtext(36,11,tstr,1);
      tstr="TRIG =";
      outtext(36,12,tstr,O);
      tstr="LOCKO=";
      outtext(36,13,tstr,O);
                                                                        190
      tstr="MDDE 7";
      outtext(53,8,tstr,1);
      tstr="LOCK_E = ";
      outtext(53,9,tstr,O);
      tstr="LOCK_0 =";
      outtext(53,10,tstr,O);
      tstr="LOCK_B =";
      outtext(53,11,tstr,0);tstr="WINDOW =";
      outtext(53,12,tstr,O); 200
      -tstr="DEMAND =";
      outtext(53,13,tstr,O);
}
       / ****************************************************************************
 * Function -------- > CLEARCOMMAND() *
 * Return Type ---- > void
                                                                        210
 * Description ---- > routine to clear command panel
      void CLEAR_COMMAND() {
      char *tstr;
```
tstr=" outtext(2,19,tstr,O); **<sup>220</sup>** outtext(2,20,tstr,O); outtext(2,21,tstr,O);

";

```
outtext(2,22,tstr,0);outtext(2,23, tstr,0);
```

```
\mathcal{F}* Function ------> MAIN_MENU()
                                                            230
* Return Type ---> void
* Description ----> routine to put protocols menu in command panel
    void MAIN_MENU() {
                \sim 100char *tstr;
                                                            240
   tstr="Select the protocol:
                         \mathbf{u}_iouttext(2,19, tstr,0);tstr="f1 Triggered Multi-Site Pacing";
     outtext(2,20, tstr,0);tstr="12":
     outtext(2,21, tstr,0);tstr="f3";
     outtext(2,22,1str,0);tstr = "f4";
     outtext(2,23, tstr,0);250
}
                  **************
* Function ------> PROTOCOL1_MENU()* Return Type ---> void
* Description ----> routine to put protocol 1 menu in command panel
                                                            260
       void PROTOCOL1_MENU() {
     char *tstr;
```
 $\text{tstr} = "11$ select mode and channel";  $outtext(2,19, tstr,0);$  $tstr="f2$ change output characteristics";  $outtext(2,20, tstr,0);$ 

```
tstr=''cursor change output characteristics";
  outtext(2,21,tstr,O);
tstr="f 10 start pacing";
  outtext(2,22,tstr,0);
tstr="esc end the program";
  outtext(2,23,tstr,O);
```

```
/ ****************************************************************************
* 280
* Function -------- >PROTOCOL11MENU() *
* Return Type ----- > void *
* Description ---- > routine to put protocol 1.1 menu in command panel *
```
# **\* \*/**

#### void PROTOCOL1\_1\_MENU() {

char \*tstr;

```
tstr="f1 select mode";
       outtext(2,19,tstr,0);
       tstr="f2 select channel";
       outtext(2,20,tstr,0);
/* tstr="f3 select premature stimuli";
       outtezt(2,21,tstr,0);
       tstr="f4 select overdrive";
       outtext(2,22,tstr,0); */<br>tstr = "esc exit this level";
                 exit this level";
```
}

}

```
*
* Function -------- > PROTOCOL111MENU( *
* Return Type ---- > void
                                                                   310
 * Description ---- > routine to put protocol 1.1.1 menu in command panel
*
***************************************** ********************************
```

```
void PROTOCOL1_1_1_MENU () {
```
outtext(2,21,tstr,O);

char \*tstr;

```
tstr="fI Model (ES & NO) f4 Mode4 (BURST & NO) ";
     outtext(2,19,tstr,0); 320
     tstr="f2 Mode2 (ES & FIXED) f5 Mode5 (BURST & FIXED)";
     outtext(2,20, tstr,0);tstr="f 3 Mode3 (ES & TRIG) f6 Mode6 (BURST & TRIG) ";
     outtext(2,21, tstr,0);щ.
     tstr="f7 Mode7 (ES & PVC TRIG)
     outtext(2,22,tstr,O);
}
   * Function -------- > PROTOCOL112_MENU() 330
* Return Type ---- > void *
* Description ---- > routine to put protocol 1.1.2 menu in command panel
    **************************************************************** *********
void PROTOCOL1_1_2_MENU () {
      char *tstr; 340
     tstr="f1 Pacing channel";
     outtext(2,19,tstr,O);
     tstr="1f2 Extra stimuli channel";
     outtext(2,20, tstr,0);tstr="f3 Overdrive channel";
     outtext(2,21,tstr,O);
}
     350
* Function -------- >PR.OTOCOL12_1_MENU() *
* Return Type ---- > void
* Description ---- > routine to put protocol 1.1.2.1 menu in command panel *
***************** ******************* **************************** *********
void PROTOCOL1_1_2_1_MENU () { 360
```
char \*tstr;

tstr="f1 Channel 1"; outtext(2,19,tstr,O); tstr="f2 Channel 2";

```
outtext(2,20,tstr,0);
}
/* PROTOCOLl13_MENU () and PROTOCOL114_MENU () are obsolete */ 370
  *
* Function -------- > PROTOCOL_1_3 MENU( *
* Return Type ---- > void *
* Description ---- > routine to put protocol 1.1.3 menu in command panel *
380
void PROTOCOL113-MENU() {
     char *tstr;
/* tstr="fl None";
     outtext(2,19,tstr,0);
*/   tstr="f1   Extra Stimuli";
     outtext(2,19,tstr,0);tstr="f 2 Burst"; 390
     outtext(2,20,tstr,O);
}
/ ****************************************************************************
 *
* Function -------- > PROTOCOL114_MENU() *
* Return Type ---- > void-
* Description ---- > routine to put protocol 1.1.4 menu in command panel 400
void PROTOCOL1_1_4_MENU() {
     char *tstr;
     tstr="f1 None";
     outtext(2,19,tstr,O);
     tstr="f2 Fixed rate"; 410
     outtext(2,20,tstr,O);
```
*}*

tstr="f3 Triggered";

outtext(2,21,tstr,O);

```
* Function -------- > PROTOCOL1_4_MENU (int mode) *
* Return Type ---- > void 420
 *
* Description ---- > routine to put protocol 1.4 menu in command panel
 *
************* ********* ***** **** ******************* **** ***** ********* ******/
void PROTOCOL1_4_MENU (int mode) {
      char *tstr;
      tstr="f 1 introduce extra stimuli & overdrive"; 430
      outtext(2,19,tstr,0);
      tstr="cursor change output characteristics";
      outtext(2,20,tstr,O);
      tstr="f 10 stop pacing & exit to protocol 1";
      outtext(2,21,tstr,O);
      if (mode == 1) {
            tstr="Mode 1: Extra stimuli only";
            outtext(2,23,tstr,0);
      else if (mode == 2) {
      } 440
            tstr="Mode 2: Extra stimuli and fixed rate overdrive";
            outtext(2,23,tstr,0);}
      else if (mode == 3) {
            tstr="Mode 3: Extra stimuli and triggered pacing";
            outtext(2,23,tstr,0);
      }
      else if (mod e == 4) \{tstr="Mode 4: Burst only"; 4s0
            outtext(2,23,tstr,0);
      }
      else if (mode == 5) {
            tstr="Mode 5: Burst and fixed rate overdrive";
            outtext(2,23,tstr,O);
      }
      else if (mode == 6) {
            tstr="Mode 6: Burst and triggered pacing";
            outtext(2,23,tstr,O);
      } 460
      else if (mode == 7) {
            tstr="Mode 7: Extra Stimuli and PVC triggered pacing";
```

```
outtext(2,23,tstr,0);\mathbf{R}\mathbf{R}* Function ------> PROTOCOL2_MENU()470
* Return Type ---> vold* Description ---> routine to put protocol 2 menu in command panel
void PROTOCOL2_MENU() {
      char *tstr;
                                                                 480
      tstr="11 induce VT by extra stimuli w/ no overdrive pacing";
      outtext(2,19,tstr,0);tstr="f2 induce VT by extra stimuli w/ fixed overdrive pacing";
      outtext(2,20, tstr,0);tstr="f3 induce VT by extra stimuli w/ triggered overdrive pacing";
      outtext(2,21, tstr,0);/* need to put induce VT by burst w/ no overdrive pacing */
      tstr="f4 induce VT by burst w/ fixed overdrive pacing";
      outtext(2,22,tstr,0);tstr="f5 induce VT by burst w/ fixed overdrive pacing";
                                                                 490
      outtext(2,23, tstr,0);\mathbf{R}Function ------> outtext(int x_coord, int y_coord, char *str, int video flg)
* Return Type ---> void
* Description ---> routine to write characters
                                                                 500
void outtext(int x_coord, int y_coord, char *str, int video_flg) {
```
int off=offset(x\_coord, y\_coord);

$$
\begin{array}{c}\n\textbf{if (video_flg == 0) } {\textbf{\{}} \\
\textbf{while (*str != '\\0') {\textbf{\{}}}} \\
\textbf{screenpt [off+1] =}\n\end{array}
$$

```
FOREGROUND_GREEN|BACKGROUND_BLACK;
                     screenptr[off] = *str++;off += 2;
       } }
       else if (video_flg == 1) \{while (*str := '0') {
                     screenptr[off+1]=FOREGROUND BLACKIBACKGROUNDGREEN; 520
                     screenptr[off] = *str++;\text{off } += 2;} }
       else if (\text{video}_fg == 2)while (*str := \{0\}) {
                     screenptr[off+1]=FOREGROUND_RED|BACKGROUND_BLACK|BLINKING;
                     \text{screenptr}[\text{off}] = * \text{str} + ; 530
                     off += 2;
\left.\vphantom{\raisebox{1.5cm}{.}}\right\} \quad \left.\vphantom{\raisebox{1.5cm}{.}}\right\}/* This main program is used for testing.
main() {
       int z, y;
       init-screen(; 540
       for(y=O;y<MAXY;y++) {
              for(z=O;z<MAXX;z++) {
                     if ((z==1O) 66 (y==O)) {
                            screenptr[offset(x,y)+1] =BLINKING| FOREGR O UND_BLA CK|BACKGR O UND_WHITE;}
                     \text{screenptr/offset}(x,y) = 'B';
              }
} } 550
*/
```
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