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**AUTOMATIC CARDIAC PACING TECHNIQUE
FOR ELECTROPHYSIOLOGIC INVESTIGATIONS:
MEASUREMENT OF MYOCARDIAL EXCITABILITY
IN THE DOG DURING EXPOSURE TO +G_z**

Leonid Hrebien
Air Vehicle and Crew Systems Technology Department
Naval Air Development Center
Warminster, PA 18974

DECEMBER 1987

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Prepared for
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Warminster, PA 18974

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AUTOMATIC CARDIAC PACING TECHNIQUE FOR ELECTROPHYSIOLOGIC INVESTIGATIONS:
MEASUREMENT OF MYOCARDIAL EXCITABILITY IN THE DOG DURING EXPOSURE TO +G_z

ABSTRACT

The objective of this effort was to quantify changes in the excitability of the heart muscle during exposure to various G acceleration profiles. Dogs were catheterized with cardiac pacing electrodes which were inserted into the ventricle of the heart. The exteriorized end of the catheter was protected by a cloth and tape collar allowing the animals to reside in ordinary cages with experimentation taking place for at least 3-4 weeks.

A microcomputer-controlled pacemaker was designed, built, and programmed to pace the heart with a basic rhythm established with periodic suprathreshold pulses (S1), and a test stimulus (S2) inserted at a frequency (typically every tenth beat) chosen by the investigator. Other parameters which can be varied by the investigator include pulse amplitudes, durations and S1-S2 delay.

The automated equipment described, has been used to collect experimental data on dogs undergoing +G_z forces on the NAVAIRDFVCEN animal centrifuge. The threshold of stimulation levels are plotted as a function of +G_z. We have demonstrated a system in which an animal with a chronic pacing catheter and a computer-based instrument have been combined to provide a useful model in which cardiac threshold of excitability changes can be observed in response to stressors such as +G_z.

BACKGROUND

Modern high-performance aircraft are capable of producing and sustaining complex accelerative forces that can alter the physiology and exceed the tolerance limits of their human operators. Cardiac rhythm anomalies are caused by accelerative forces and are aggravated by straining maneuvers used by aircrew to increase their G-tolerance. These anomalies can also be observed when subjects are exposed to G loads on a human centrifuge (13). The arrhythmias themselves may not be particularly harmful when they occur as single occasional events (premature ventricular contractions or PVC's). However, a sequence of several PVC's (ventricular tachycardia or VT) can be dangerous for the aircrew since they significantly reduce the heart's efficiency to pump blood. This results in decreased flow of oxygenated blood to the brain which can cause vertigo (dizziness), functional incapacitation, or syncope (loss of consciousness).

Arrhythmias occur when the ventricular muscle becomes irritable or more excitable due to various disease states or physically stressful

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conditions such as exposure to increased G loads. An understanding of the irritable response of the ventricular muscle during exposure to G is necessary to explain the etiology of PVC's and VT under these conditions.

Numerous studies at the USAF School of Aerospace Medicine (USAFSAM) and observations of records from +G_z exposures on our own Dynamic Flight Simulator confirm that these rhythm anomalies do indeed occur in significant numbers. In a recent study at USAFSAM, 544 individuals who underwent +G_z exposures on 2,100 different occasions showed PVC's on 1,073 separate episodes (11)(12). Figure 1 shows three contiguous strips taken from a two channel, ambulatory EKG recording while a subject was exposed to +G on the NAVAIRDEVGEN human centrifuge. This recording shows seven PVC's during a time span of only 18 seconds.

To date, various mechanisms for the increased cardiac excitability, and thus the generation of arrhythmias under G loading, have been proposed, but none have been experimentally confirmed or quantified. Some of these are: elevated heart rate due to excessive sympathetic activity (1)(2)(10)(12), increased metabolites (12), autonomic imbalance due to fluctuations in baroreceptor stimulation (4)(12)(15), myocardial ischemia (2)(3)(10), cardiac filling changes (2)(3)(10)(14), cardiac displacement (2)(3)(4)(10)(12), mechanical stress on the cardiac muscle (2)(10)(16), and respiratory straining maneuvers (2)(10)(15)(16).

INTRODUCTION

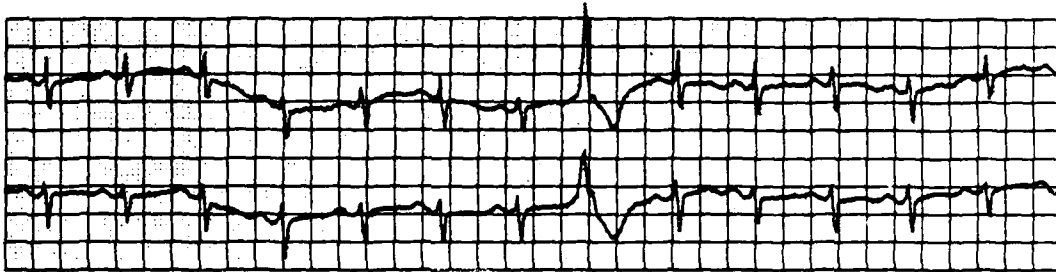
The objectives of this research are to quantify the changes in the excitability of the heart muscle during exposure to various G profiles and ultimately to correlate these changes with variations in other physiological parameters such as those mentioned above. The changes in heart muscle sensitivity or irritability due to exposure to G loading were measured by a technique proven in previous studies (5)(7)(8). Invasive techniques were required so animal models rather than human volunteers were used in this study. The relationship between G loading and ventricular excitability was measured by determining the minimum energy required to stimulate the heart under different G profiles. This was accomplished through the use of standard pacemaker electrodes implanted in or on the animal's ventricular myocardium and brought out through the skin (5).

A microcomputer-based cardiac stimulator was designed in which specific stimulation waveforms could be programmed, and either modified from the computer keyboard, or modified under program control in response to physiological events. The ability to have program control of a parameter in response to changes in physiological signals is essential in dynamic interactive experiments such as the one in which this equipment was used. Specifically, the experiment was conducted with conscious dogs on an animal centrifuge. Each trial entailed several hundred cardiac cycles which required an operator decision at 10 beat intervals. Clearly, with heart rates in the 150 beat per minute range, manual control of pacing parameters by a human operator would be difficult. This report will

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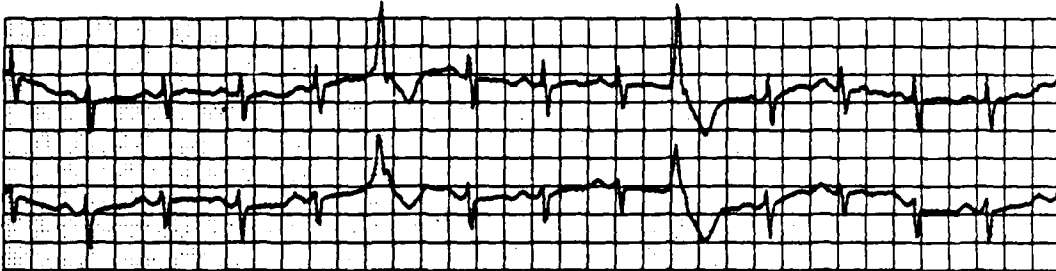
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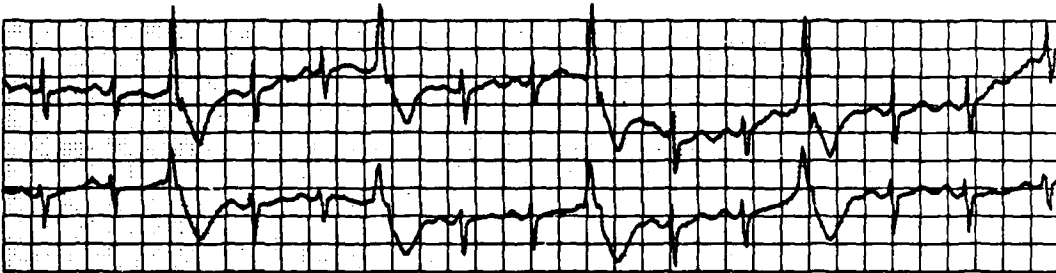


Figure 1 - Two channel Holter recording showing ventricular premature beats (VPS) recorded during acceleration on a human centrifuge.

describe the hardware and software used in this experimental apparatus as well as the experimental results.

A manual version of the test stimulator used in these studies was tested in the laboratory. This experimental pacemaker produced two sets of stimulating pulses. One set, (S1), stimulates the heart at a regular physiologic rate and the other, (S2), stimulates the heart every tenth interval to simulate a PVC. Both sets of stimuli have independent controls for rate, amplitude, duration, and time separation between the two sets of stimuli. Figure 2 shows the timing relationships for these pulses. Threshold determinations were done using the double pulse technique. Here the animal was paced at normal physiologic rates with the S1 stimuli and threshold determinations made by slowly increasing the amplitude of the S2 test pulses until premature responses just began to occur on the EKG as seen in Figure 3. The amplitude of this threshold stimulus was taken as the measure of cardiac excitability.

The sensitivity of this technique for measuring changes in cardiac excitability was tested in the laboratory using a dog preparation as described above. The animal was suspended in a canvas sling and a series of threshold determinations were made for different stimulus durations to generate a stimulus strength-duration curve. This was done twice: once as a control and a second time after administration of a common diuretic drug (furosimide) known to decrease cardiac excitability. The curves thus generated are shown in Figure 4. These curves indicate that changes in cardiac excitability can indeed be measured using the above described technique. (The furosimide curve shows higher threshold stimulus strength indicating lower excitability than the control curve) (6).

HARDWARE SYSTEM DESCRIPTION

The hardware configuration of the microcomputer-based cardiac stimulator is shown in Figure 5. The heart of the apparatus is an 8085 based laboratory microcomputer, the IMSAI PCS-80/30, which features the MPU-B, single board microcomputer, dual 8 inch floppy disk drives with controller board, a keyboard and CRT display. This machine has the S-100 buss and additional plug-in cards complete the system. They are: IMSAI RAM-III-32, 32 K dynamic RAM, Cromemco D+7A I/O analog-to-digital and digital-to-analog interface and the Cromemco TU-ART digital interface. The MPU-B, is an 8-bit, single-board microcomputer which features a small amount of RAM and ROM memory, the S-100 Buss interface, parallel and serial I/O and three programmable 16 bit timers.

An interface was designed to couple the I/O portion of the microcomputer system to the experimental animal. The 0 to 2.5 volt stimulation pulses were made available at the output of the D/A converter of the microcomputer system. The interface accomplishes two things: the voltage pulse output was converted to a constant current pulse and the interface output, which connects directly to the experimental animal's cardiac tissue, was electrically isolated from ground. This provides a measure of safety against extraneous electrical currents being conducted directly through the heart muscle.

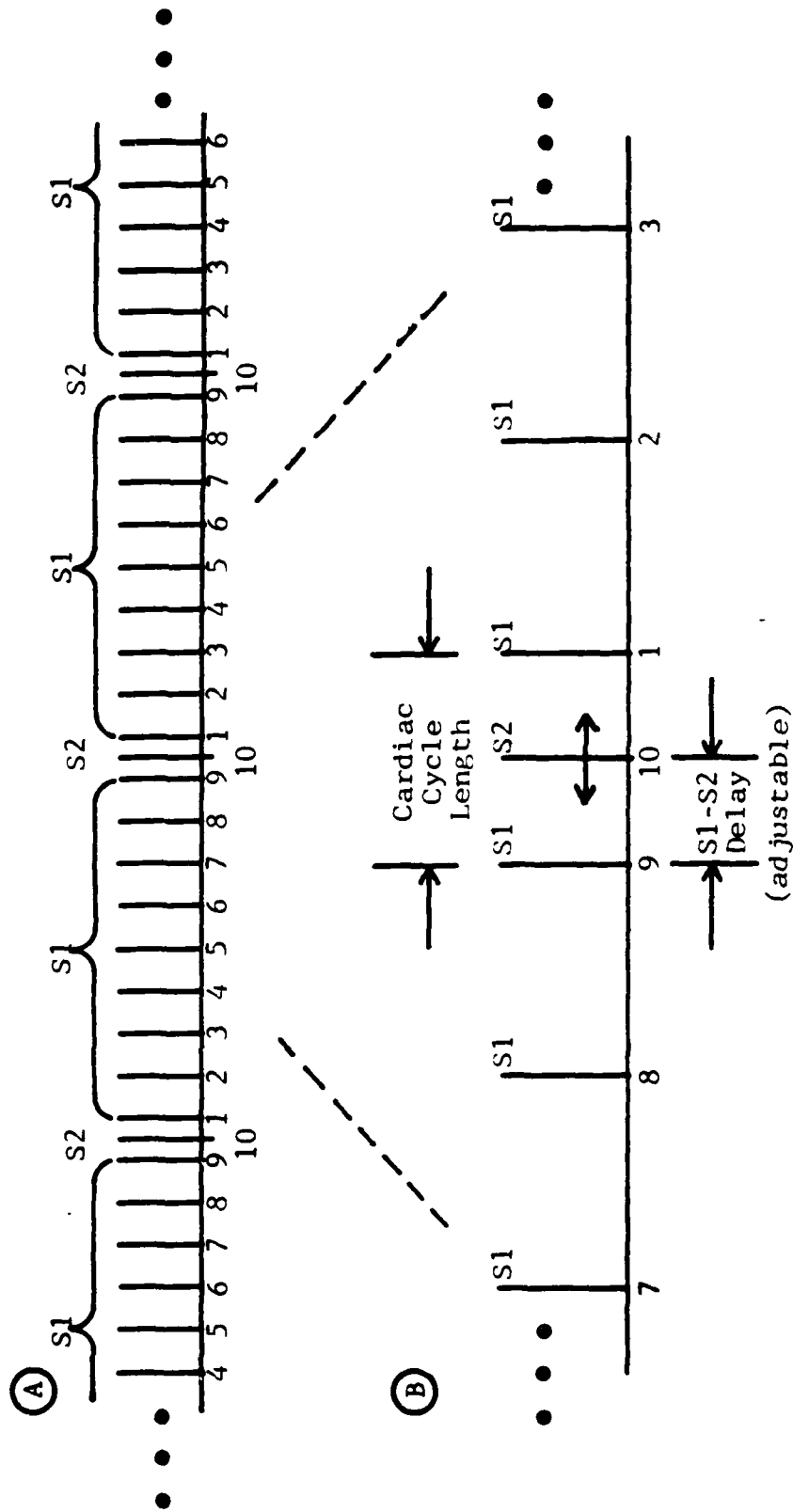


Figure 2 - Timing relationships for S1 and S2 pulses from the double pulse pacemaker.

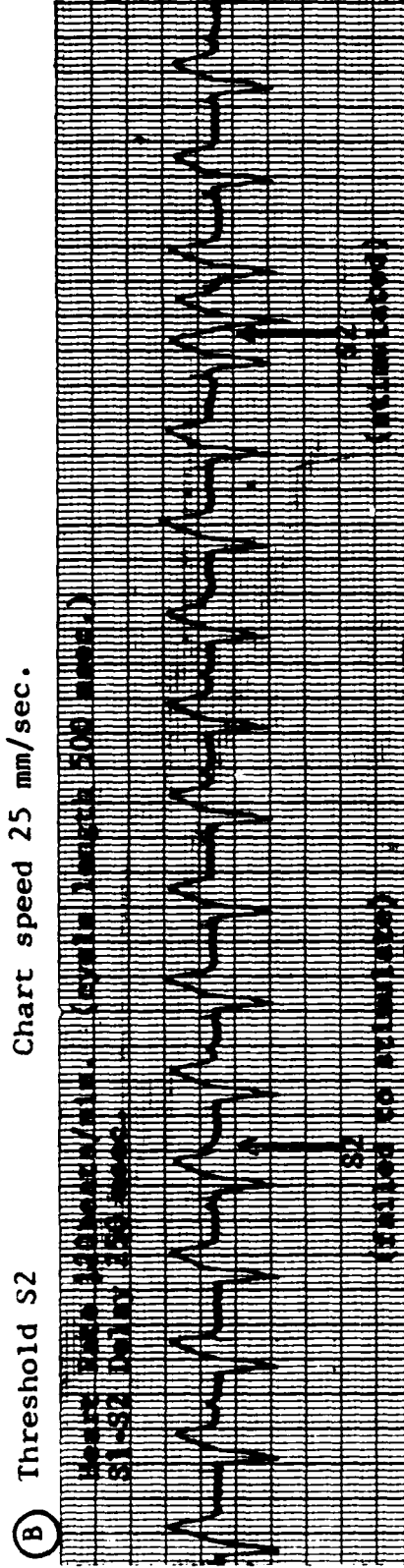
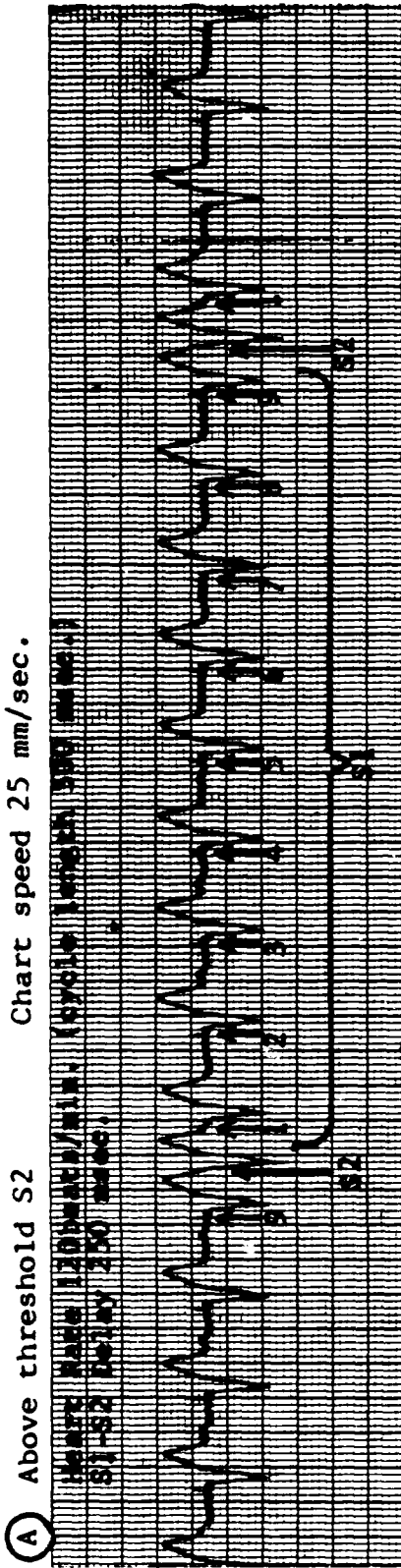


Figure 3 - EKG tracings showing double pulse pacing, (A) above threshold and (B) at threshold.

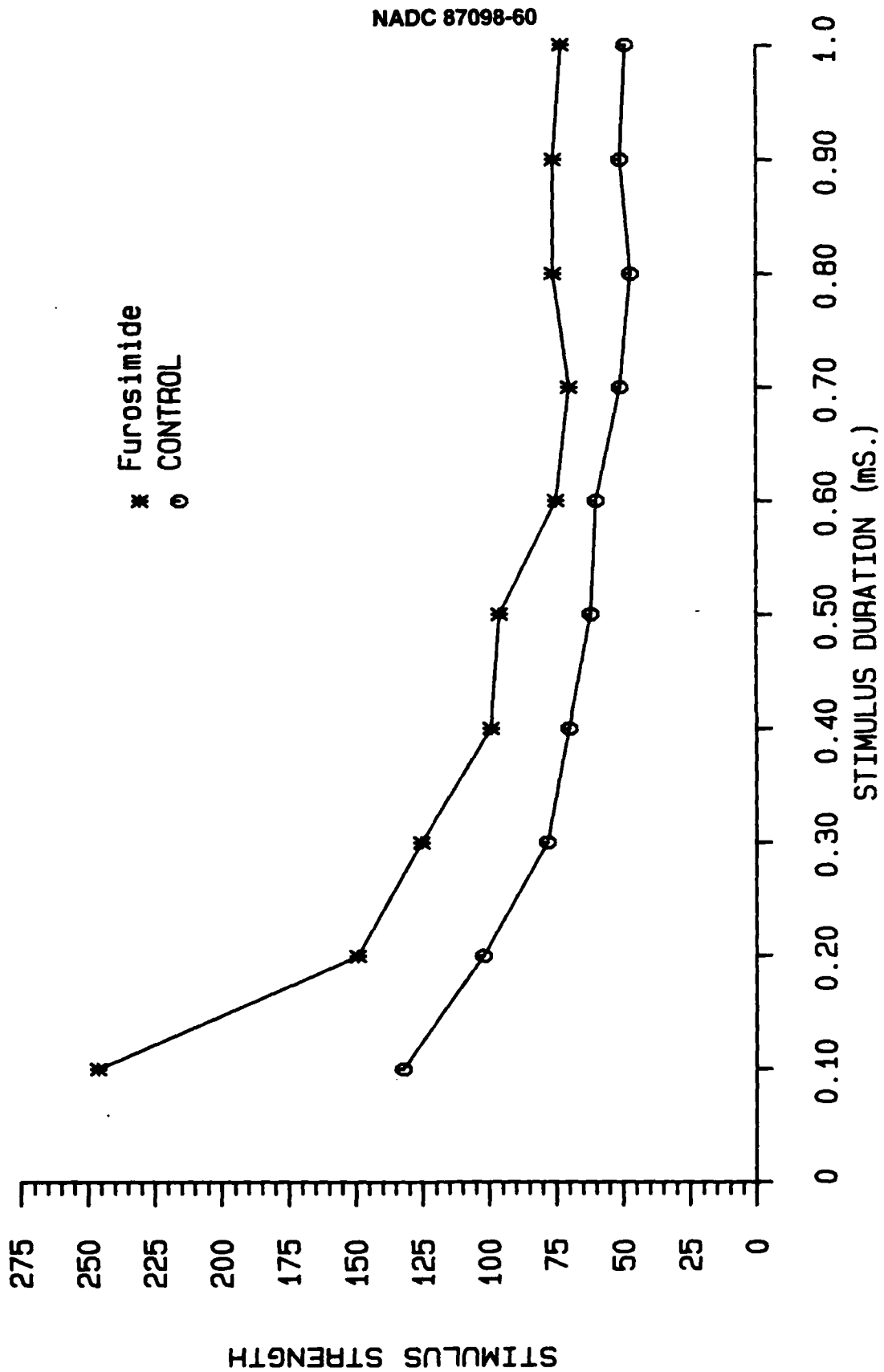


Figure 4 - Strength-duration curves showing ability of double pulse pacing to detect changes in cardiac excitability.

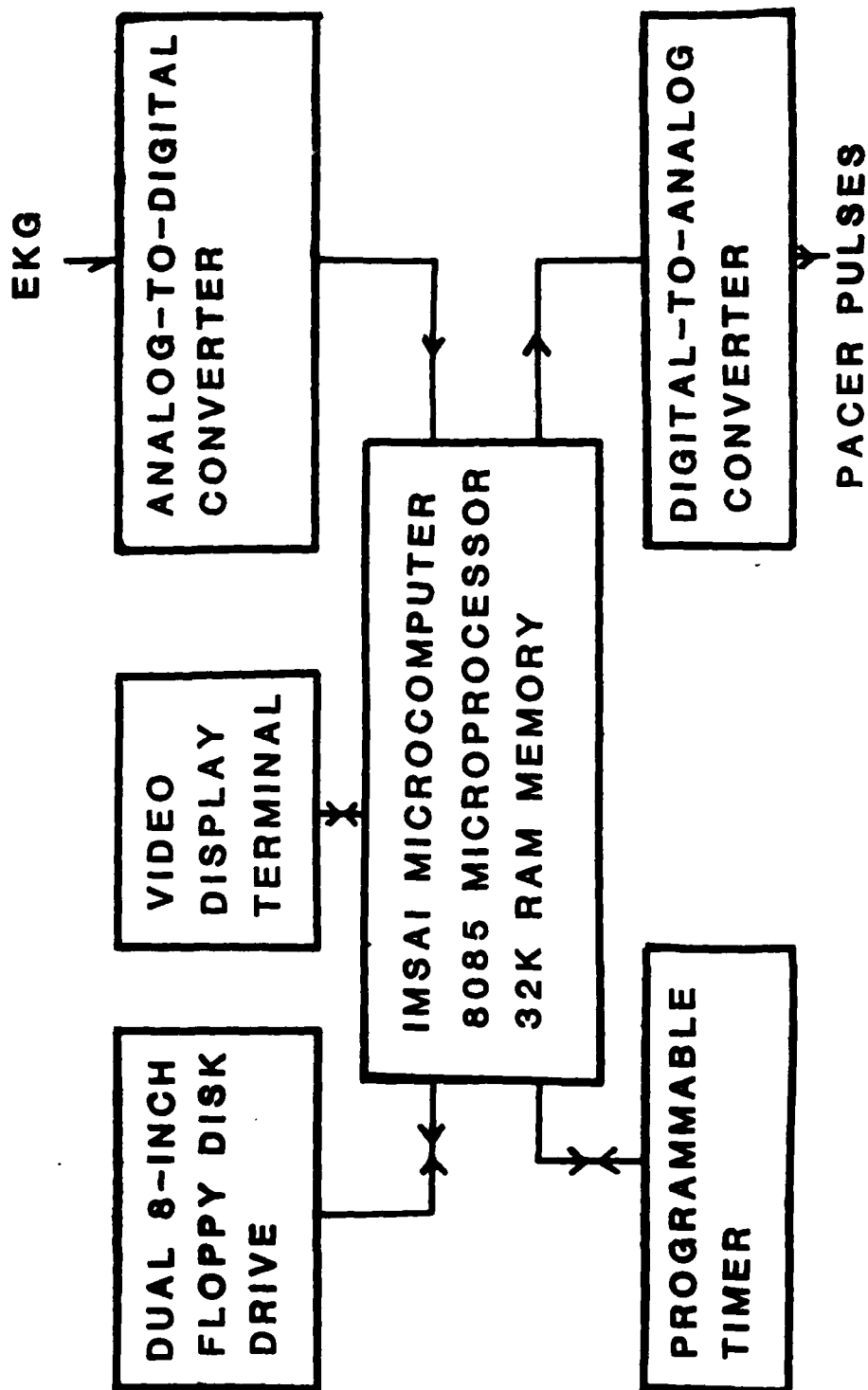


Figure 5 - Computer system block diagram.

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Figure 6 is a schematic drawing of the interface circuitry. An Analog Devices, Model 284J, isolation amplifier is used to provide an isolated power supply of + or - 8.5 volts and to provide an isolated output channel to monitor either the voltage or current at the pacing electrode terminals. Electrical isolation is maintained on the input side with an optocoupler. The transistor on the output side of the optocoupler is used in a mode in which the light-coupled signal is the current across the reverse-biased collector-base junction. This mode has a high degree of linearity, high speed, and low thermal drift characteristics.

The isolated signal is amplified by operational amplifier A, which has a dc-offset trimmer, R7, to cancel out the dc bias voltage introduced by the optocoupler. Operational amplifier D is a voltage-to-current converter which is set up to provide 1 milliamp/volt. Capacitor C1 is provided to prevent any tissue-damaging flow of DC current, however, it presents a problem when monopolar pulses are delivered. The capacitor eventually becomes charged to the maximum supply voltage and current flow ceases. The solution to this problem is to allow a discharging current between pulses, by providing a small offset with trimmer R7.

SYSTEM SOFTWARE DESCRIPTION

The software for the programmable stimulator can be broken up into functional modules as shown in Figure 7. The software which controls the operator interface (the video display terminal and keyboard), is written in Fortran (see Appendix A). The first function of the Fortran program is to call the subroutine INIT which sets up and starts the S1 and S2 timers and defines the interrupt vector. More details on INIT are provided in Appendix A. Primarily, the Fortran program prompts the operator with a series of messages to the screen asking for the various pulse parameter values. These values are then transferred to the data value storage area of the assembly language interrupt service routine by a call with multiple parameters to the subroutine called STPVAL. STPVAL is explained in more detail in Appendix A. The use of Fortran makes mathematical conversions very easy - for instance beats per minute is the obvious parameter for the operator to enter and can easily be converted to the proper number of 10 millisecond interrupts for the assembly language program.

The other program modules are written in assembly language, and they make up the interrupt service routine. Since waveform generation essentially involves performing operations at specific time intervals, a means must be established to generate an accurate time base. In this case, one of the programmable, 16 bit timers on the MPU-B microcomputer board is used to generate interrupts at 10 millisecond intervals. Each time an interrupt is generated, the interrupt service routine is executed, and by keeping track of the number of interrupts, the elapsed time between events can be tabulated. Then it is a simple matter of comparing a running total of the number of interrupts to fixed values representing the waveform time intervals. When the two values are equal, a waveform event is generated. For instance, the heart rate is determined by the S1 pulses which are generated continuously forming the basic loop of the program.

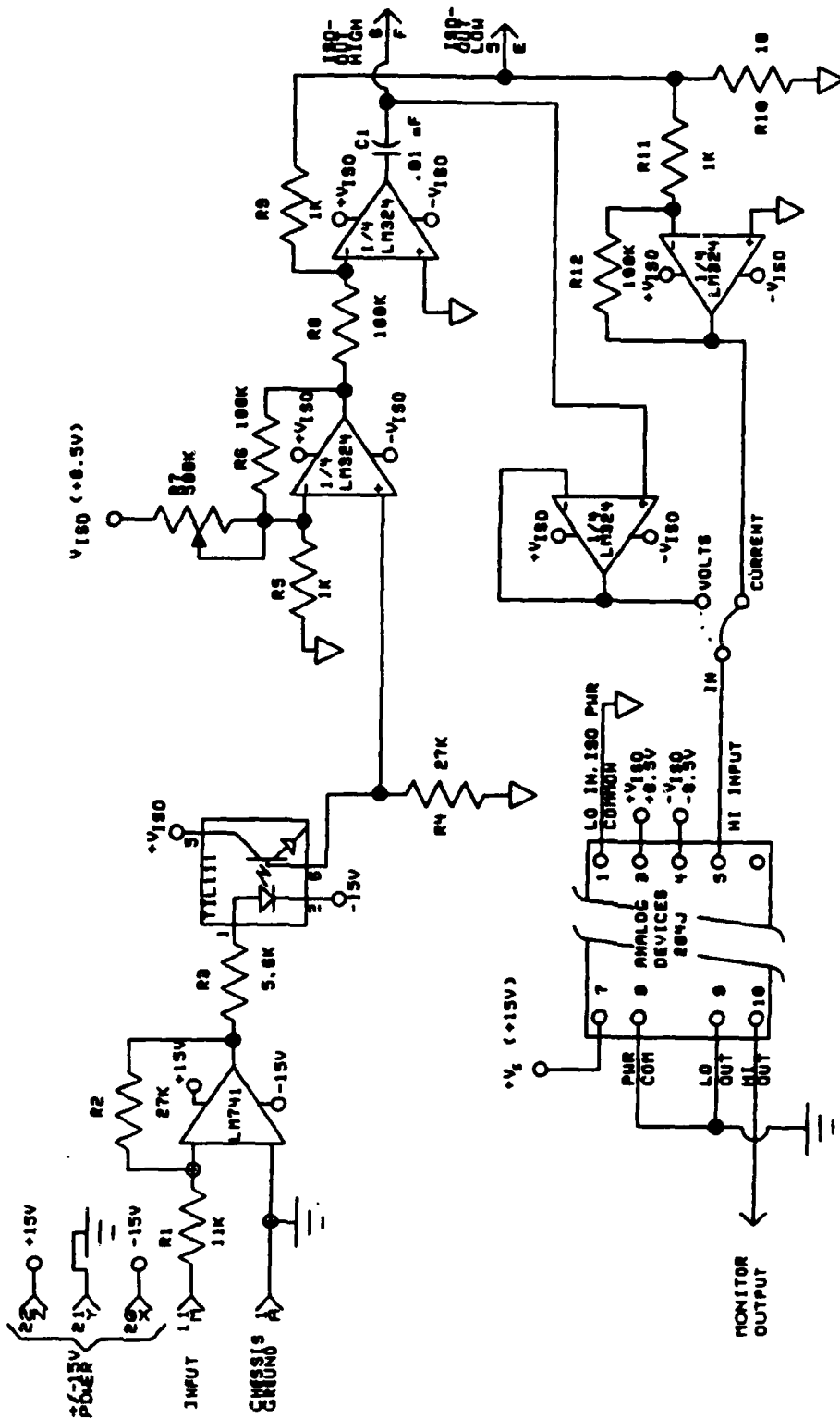
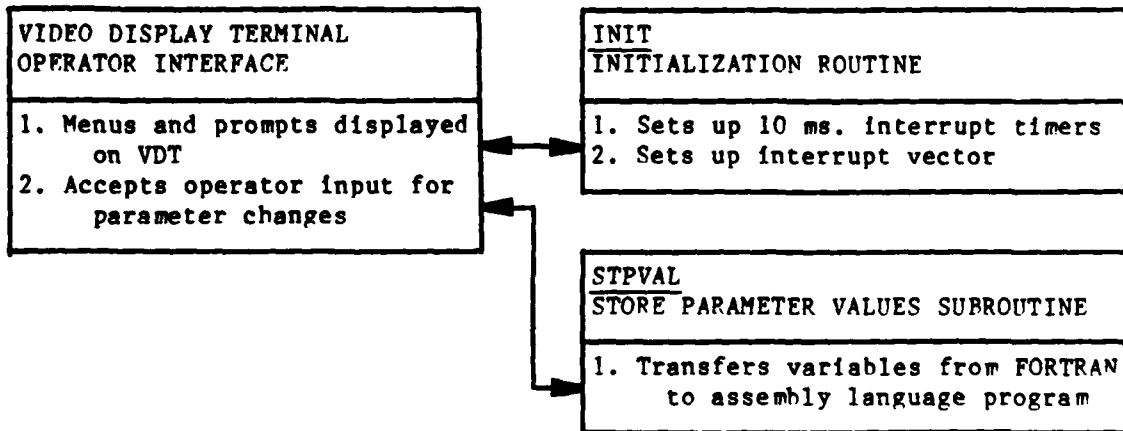


Figure 6 - Cardiac stimulator isolated interface schematic diagram.

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OPERATOR I/O MODULE (FOPTRAN)



10 ms. interrupts determined by hardware clock

INTERRUPT SERVICE ROUTINE
(Relocatable Macroassembler)

Analog EKG input

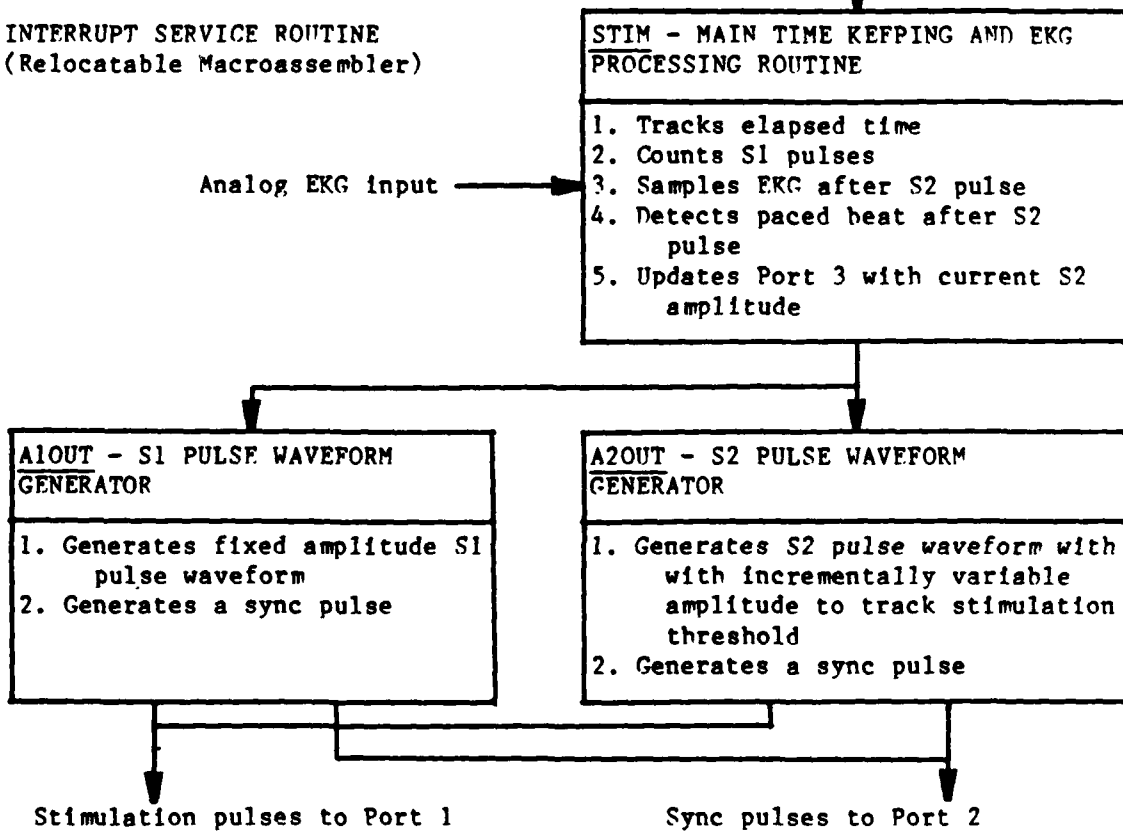


Figure 7 - Program modules

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As can be seen in Figure 7, the main time-keeping and processing module receives input from the analog input EKG amplifier, and within the module, sampling of the EKG takes place at the interrupt interval of 10 milliseconds, corresponding to a rate of 100 samples per second. As part of the main loop of the interrupt service routine, the analog EKG samples are compared to a threshold level during a period after the S2 pulse, and a software flag is set if a beat is detected (threshold is exceeded). In this way, the output waveform can be modified in response to events detected by the EKG module. Specifically, whenever a paced beat is detected, the amplitude of the S2 pulse is decreased and, conversely, when an S2 pulse fails to stimulate the heart, the amplitude of the next S2 pulse is increased. Thus, the S2 amplitude inversely tracks the excitability level of the heart.

METHODS

The double-pulse stimulator described above was used to study the changes in heart muscle sensitivity or irritability due to G loading. Since invasive techniques were necessary, the mongrel dog was chosen as the animal model for this experiment. With pacing electrodes placed in the ventricular muscle of the heart, the relationship between G loading and ventricular excitability was measured by determining the minimum energy required to stimulate the heart under different G profiles.

To prepare the animals for this study, bipolar pacing catheters were introduced into the jugular vein and the tip was guided into the right ventricle of the heart with the aid of fluoroscopy. A technique was developed for bringing the pacing electrode wires through the skin at the back of the animal's neck so the animal is completely unencumbered and remains instrumented for several months. As shown in Figure 8, a special body sling was designed to restrain the dog within a metal framework mounted on the NADC animal centrifuge. EKG electrodes were placed above and below the dog's heart on the mid-sternal line with the reference electrode placed to one side on the lower portion of the rib cage. A commercially available animal vest (Alice King Chatham, Chatsworth, CA) was used to hold the electrodes in place. A battery-operated EKG amplifier (MED Associates, Inc., East Fairfield, VT) was mounted on the centrifuge arm, and the amplified signal passed through the slip rings to the computer and recording equipment. The pacing pulses were applied through the slip rings and connected to the catheter wires at the back of the dog's neck. The animal was restrained, but unanesthetized during the experiment. A pacemaker rate was established which would override the dog's normal rate. Since no tranquilizers or anesthetics were used, a rate of about 175 beats/minute was required. Threshold of stimulation for the S2 pulse was determined, then the centrifuge was brought smoothly up to the +Gz level of interest and maintained until a new stimulation threshold was found, and then brought down to a stop for a determination of post +Gz threshold. The data recorded on the chart recorder and magnetic recorder included the EKG, the pacer output pulse train, the +Gz level and the S2 amplitude as an indication of myocardial excitability.

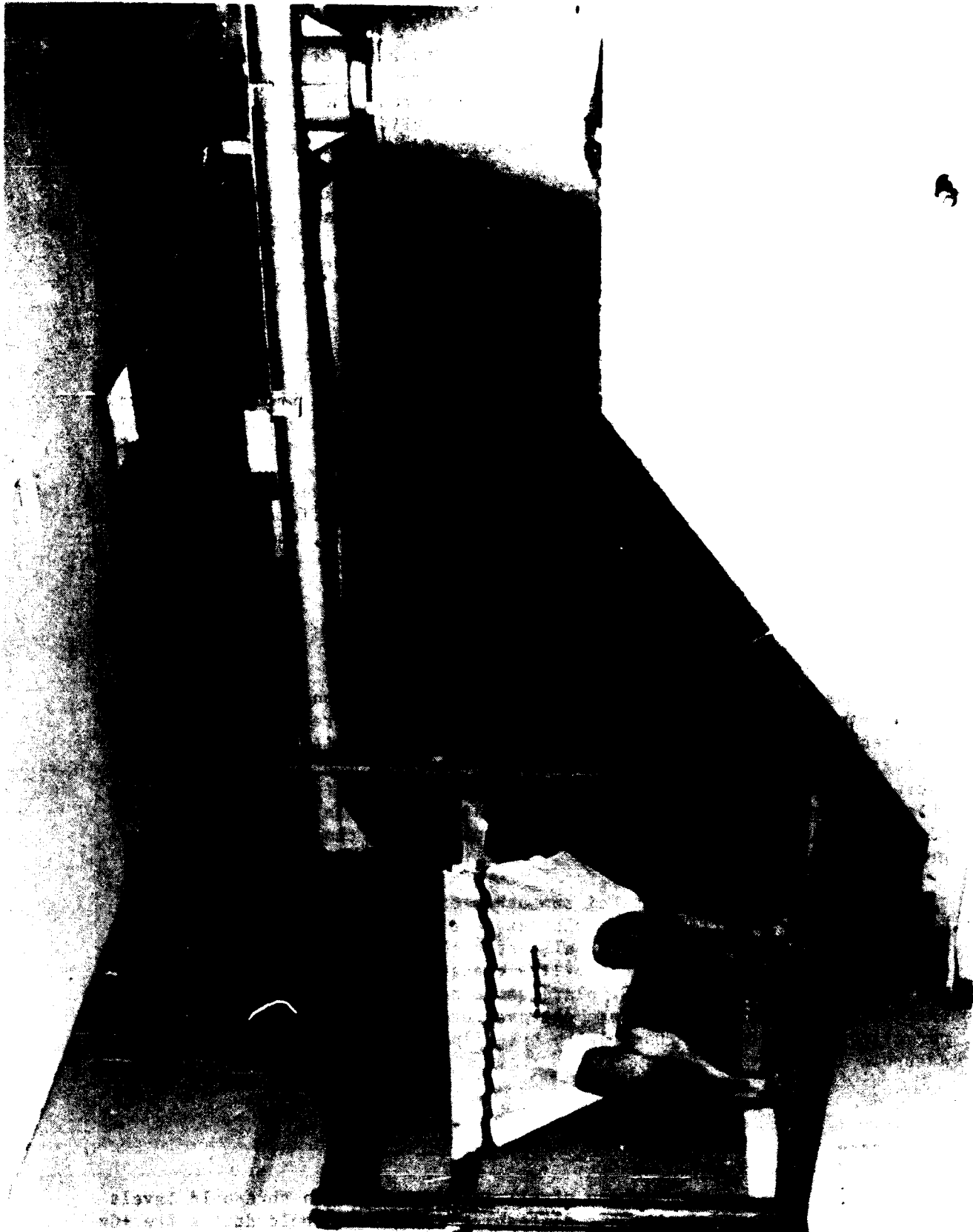


Figure 8 - Dog suspended in animal centrifuge.

Figure 9 shows a portion of recorded EKG which demonstrates the difference between normal EKG and EKG signal which results when the heart is paced at a rate which overrides the normal rate. The S2 pulses are producing a premature ventricular contraction (PVC) waveform indicating that the S2 amplitude exceeds the threshold of excitability of the heart.

Figure 10 shows a strip-chart recording with automatic threshold determination and tracking. During threshold determination, the amplitude of the S2 stimuli increased or decreased with each test interval until threshold stimulation was accomplished. A stable threshold of excitability is characterized by a series of S2 positive responses (pacing) alternating with S2 negative responses (non-pacing).

The data strip from a run to +3G is shown in Figure 11. Notice that before the G profile is applied the threshold of the ventricle is being tracked by alternating pacing and non-pacing S2 stimuli. When the G profile is applied, the threshold of stimulation goes down, indicating an increase in cardiac excitability until a new threshold level is found during the G plateau. Following this, the G profile is removed and the threshold is tracked back to a higher level, at or near that determined before the G profile was applied. This procedure was repeated for different G plateau levels with threshold measurements taken before, during, and after each plateau.

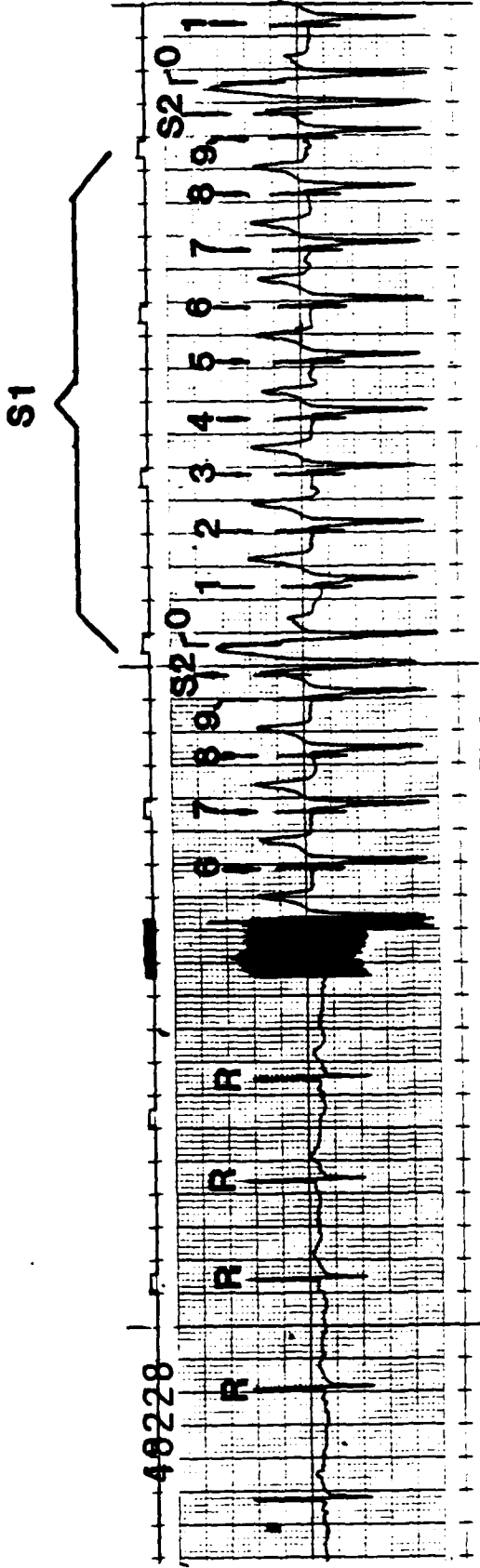
RESULTS

Figure 12 shows the results of two experiments conducted on different days, using the same dog. In both cases, there were three runs to +3Gz and a decrease in S2 threshold (increase in myocardial excitability) was seen during the acceleration plateau. After the acceleration plateaus, the excitability levels returned to values near the base line levels. Although this same pattern of myocardial excitability changes is seen for each +Gz plateau, the base line levels and the magnitudes of the changes can vary greatly.

Figure 13 shows results of two other experiments on two different dogs and at three different +Gz plateau levels. The same pattern of excitability changes is seen for all three +Gz levels (+2Gz, +3Gz, +4Gz) but the magnitudes of the excitability changes do not correlate with the +Gz level. That is, higher +Gz plateaus do not necessarily cause greater excitability changes. These same observations are made even clearer by normalizing each of the runs to the base line values (before +Gz plateau) as shown in Figure 14.

DISCUSSION

Figure 15 is a compilation of all data showing mean threshold levels for the base line before the +Gz plateau, the mean threshold during the +Gz plateau, and the mean threshold level after the +Gz plateau was turned off. This series of experiments clearly shows that threshold of stimulation

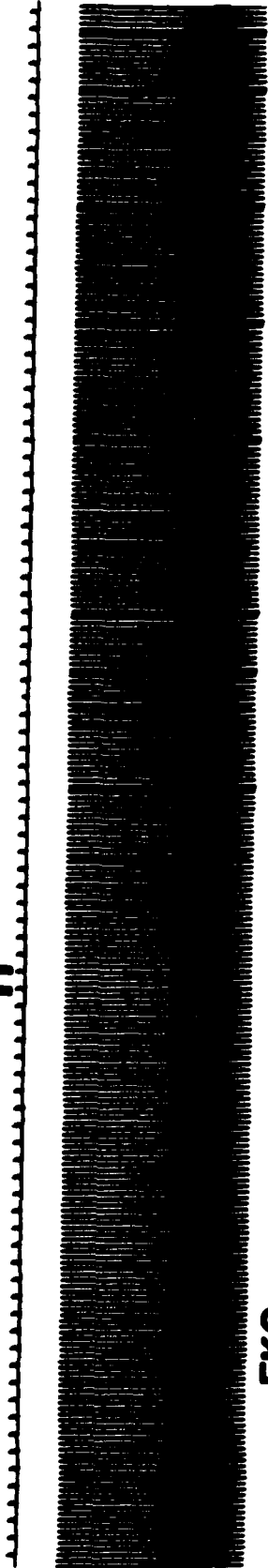


**NORMAL EKG
 PACED AT 176 BEATS PER MINUTE**

**NORMAL EKG FOLLOWED BY PACED BEATS
 WITH S2 ABOVE THRESHOLD**

Figure 9 - Normal and paced EKG.

1 sec.



EKG

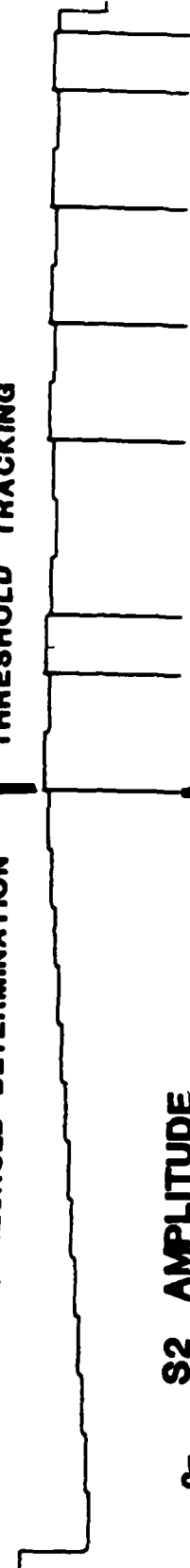


S1 - S2 TIMING

250-

THRESHOLD DETERMINATION

THRESHOLD TRACKING



S2 AMPLITUDE

INDICATES S2 PACED

Figure 10 - Data recording showing automatic S2 threshold determination and tracking.

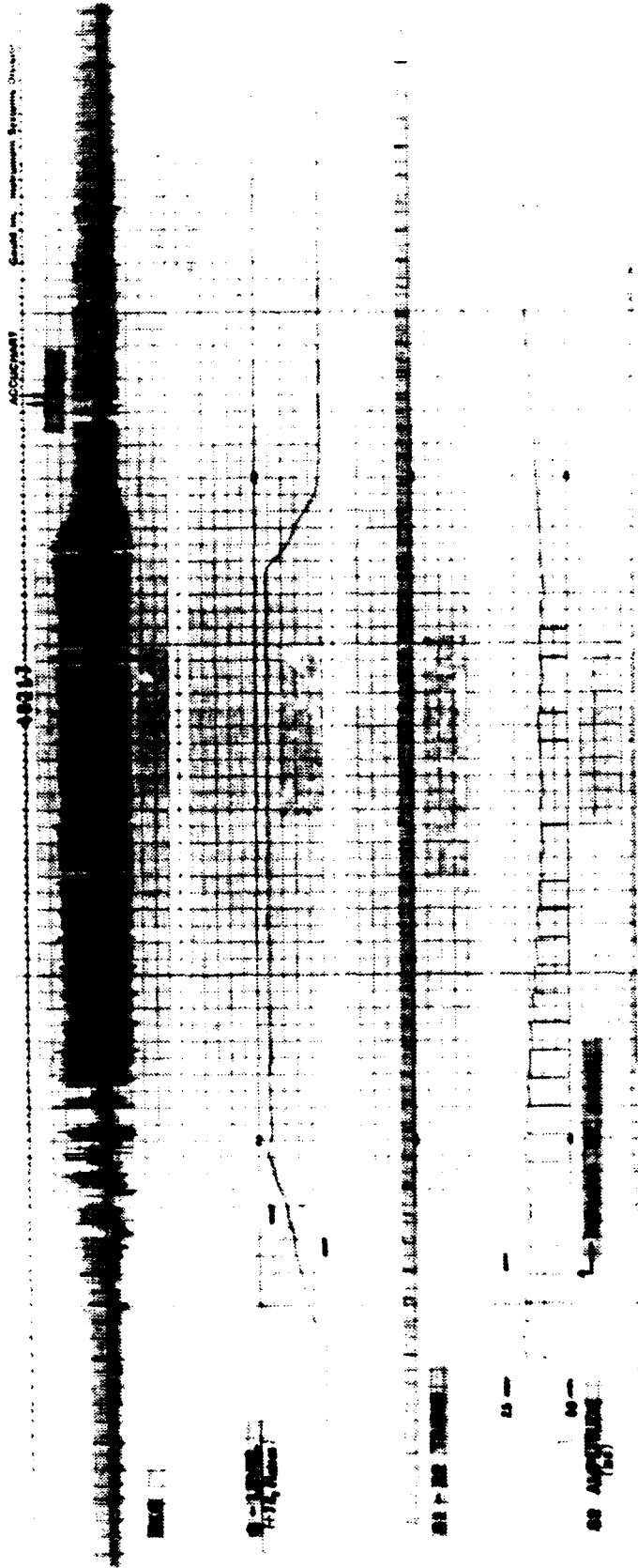
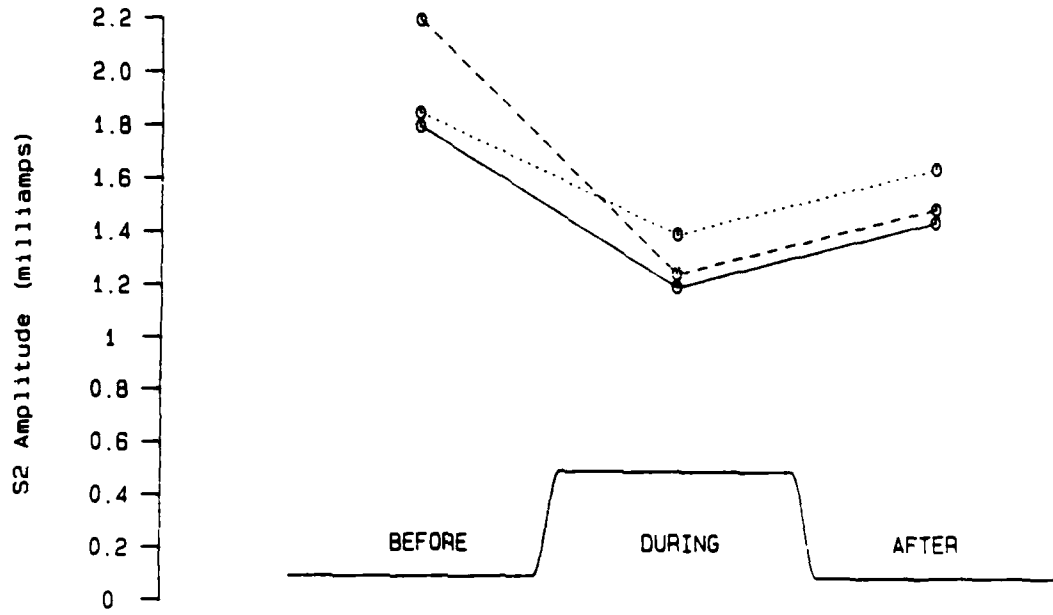


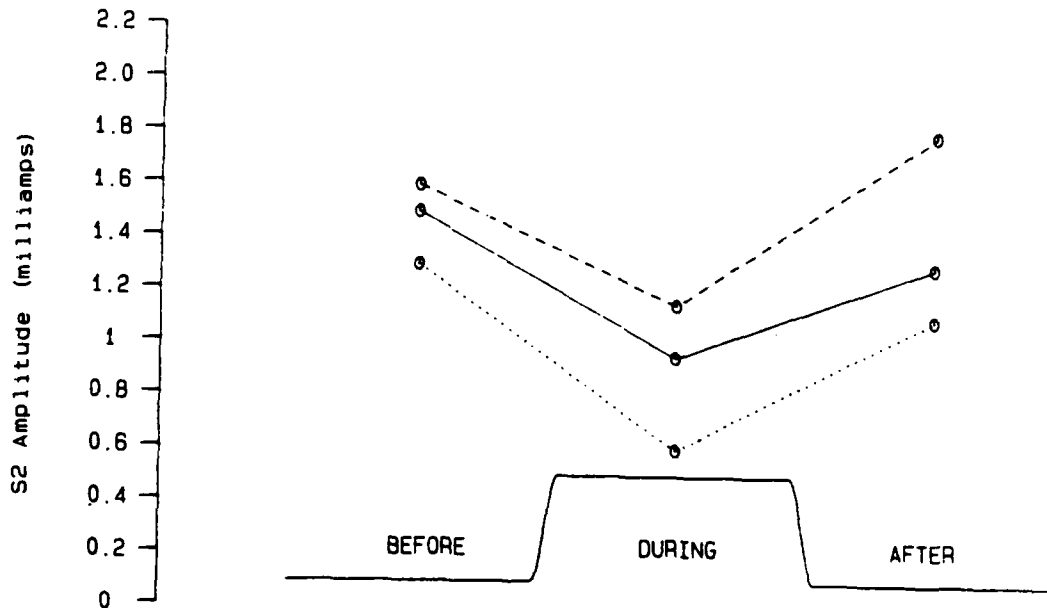
Figure 11 - Data recording showing automatic S2 threshold determination and tracking before, during, and after a +3 Gz exposure.

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+Gz Acceleration Profile

Animal D - 3 experiments on 10/16/86

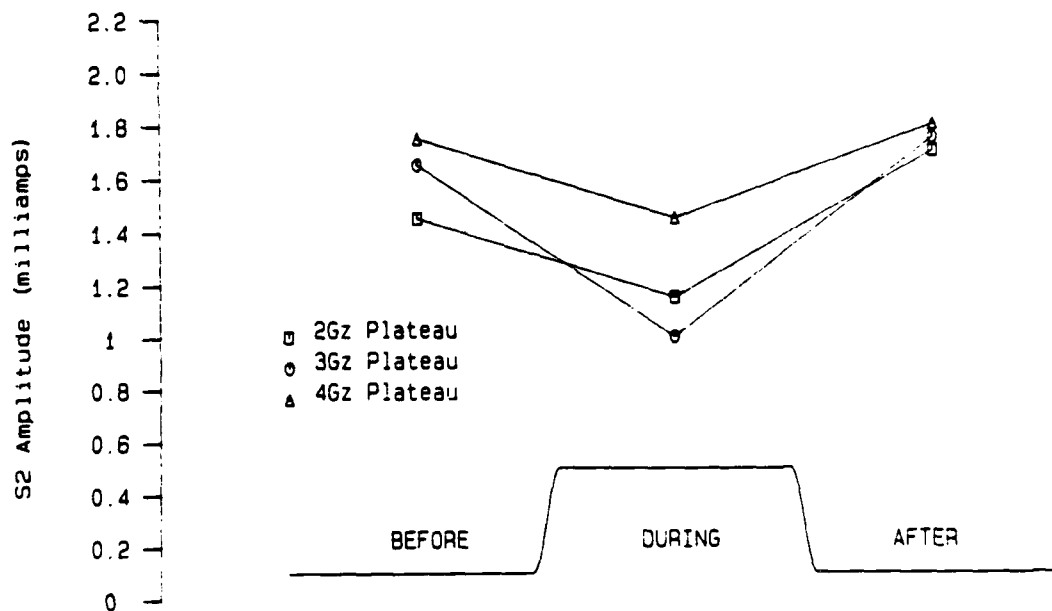


+Gz Acceleration Profile

Animal D - 3 experiments on 10/17/86

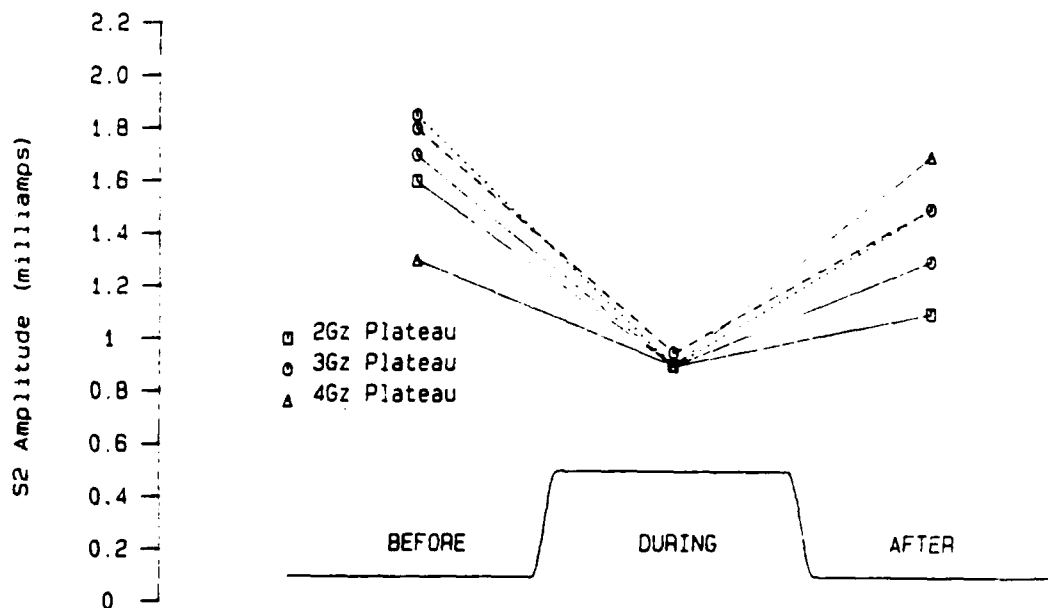
Figure 12 - Experimental results showing S2 stimulation threshold values before, during, and after exposure to +3 Gz (same animal on two different days).

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+Gz Acceleration Profile

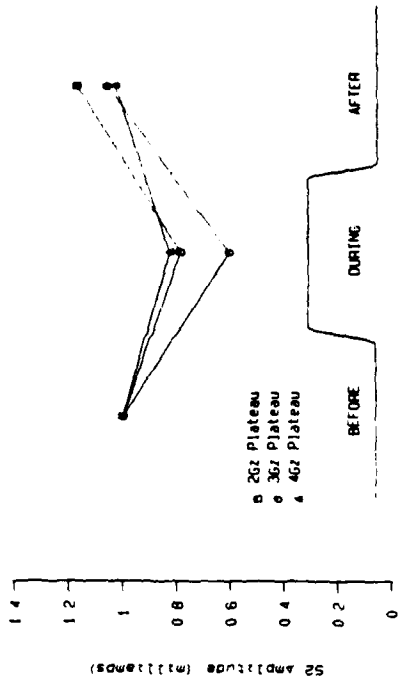
Animal B - 3 experiments on 4/85



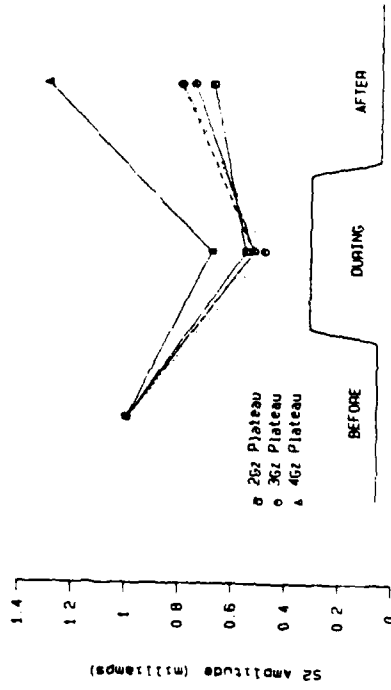
+Gz Acceleration Profile

Animal D - 5 experiments on 10/15/86

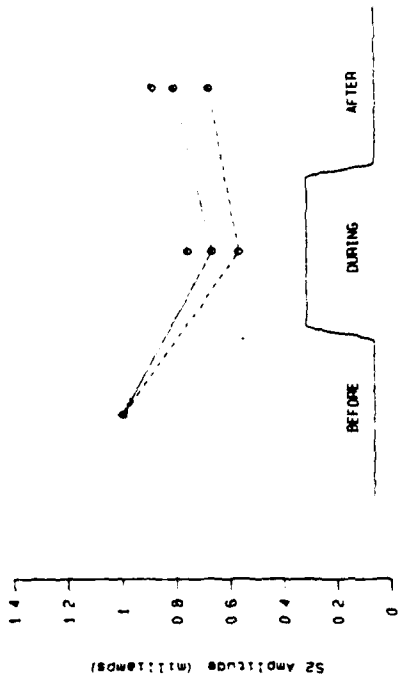
Figure 13 - Experimental results showing S2 stimulation threshold values before, during, and after exposure to +2 Gz, +3 Gz, and +4 Gz (two different animals).



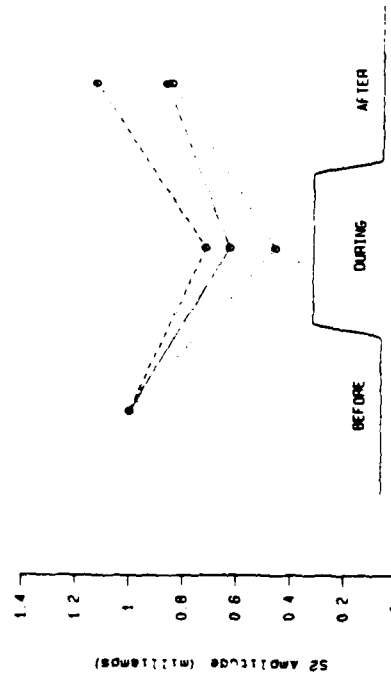
+Gz Acceleration Profile
Animal B - 3 experiments on 4/85



+Gz Acceleration Profile
Animal D - 5 experiments on 10/15/86

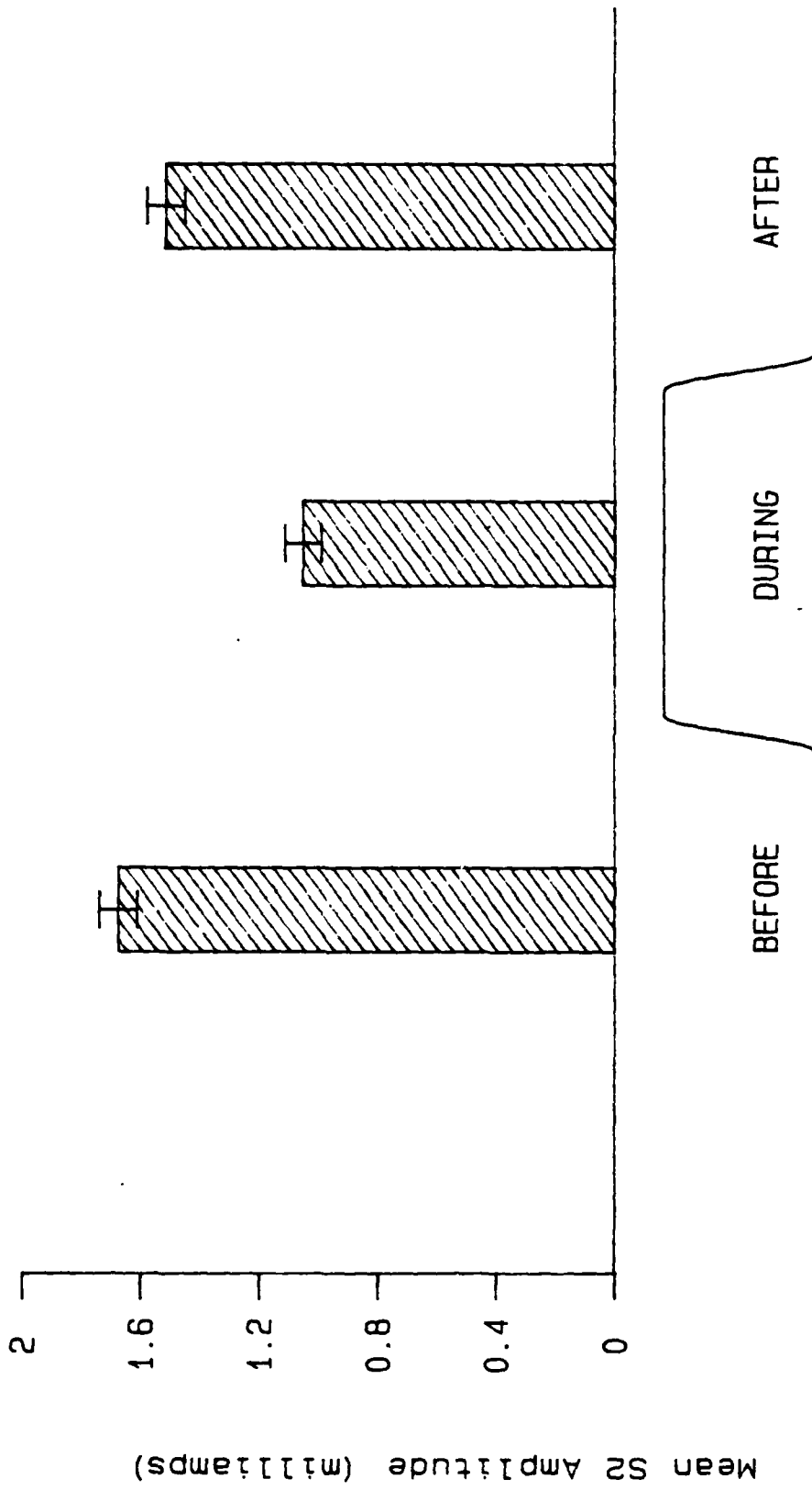


+Gz Acceleration Profile
Animal D - 3 experiments on 10/16/86



+Gz Acceleration Profile
Animal D - 3 experiments on 10/17/86

Figure 14 - Normalized results (data from Figures 12 and 13 normalized to the "before" values).



+Gz Acceleration Profile

Figure 15 - Mean S2 stimulation thresholds before, during, and after exposure to +Gz (shown + S. F. M.).

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decreases (myocardial excitability increases) when the animals are exposed to +Gz and returns to base line levels when the +Gz is removed. Although myocardial excitability always increases with +Gz, there seems to be no clear relationship between the level of +Gz and the magnitude of the S2 threshold change.

Although an increase in myocardial excitability during exposure to +Gz is expected and explainable as discussed in the introductory sections of this report, the fact that the degree of excitability change does not correlate with the level of +Gz exposure is an unexpected result. Previous work seems to indicate that the rate of occurrence of PVC's during exposure to +Gz goes up with increased G level (9). PVC's are generated due to increased myocardial excitability and therefore conditions that cause higher rates of PVC's would be expected to cause greater increases in myocardial excitability.

A possible explanation of this apparent discrepancy is that the range of +Gz exposure (+2Gz - +4Gz) used in these experiments may not have been great enough to have caused measurable differences in excitability increases. Additional experimentation using carotid flow probes, rheoencephalogram, doppler velocimeter, infrared plethysmograph, pressure catheters, etc. is planned for the future with a wider range of +Gz exposure.

ACKNOWLEDGEMENTS

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This research was done in accordance with the Animal Welfare Act and in adherence to the principles enunciated in NIH 80-23, 'Guide for the Care and Use of Laboratory Animals.'

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APPENDIX A: Program descriptions, flow diagrams and Assembler listings

The initialization routine enables the timer on the MPU-R board and loads the timer with a digital value. In addition, the interrupt system is enabled and the interrupt vector is programmed.

First, the timer must be enabled through the control port located at a single I/O mapped address, F3h. It is a write-only port and only bits 6 and 7 are active.

bit 6 = 1 system memory at 0000 to 007Fh; = D, onboard 2KROM
at 0000 to 007Fh

bit 7 = 1 system memory at D000 to DFFFh; = 0, 2KROM at D800
to DFFFh 256 byte RAM at D000 to D0FFh TIMERS appear
at D100 to D103h

The TIMER control byte is at D103 and has the following format:

bit	7	6	5	4	3	2	1	0
	SC1	SC0	RL1	RL0	M2	M1	M0	BCD
	Select Counter		Read/Load		Mode			

In this case, D103h is loaded with 74h (01110100b) which programs counter 1 to be loaded LSB first, then MSB, and to operate in mode 2 (programmable rate, pulse generator) counting in binary.

Then, the location for timer 1, D101, is loaded first with the least significant byte (LSB), 20h, and second with the most significant byte (MSB), 4Eh.

The counter is then loaded with 4E20h which equals 20,000d and it starts to countdown at a 2 megahertz rate. After 10 milliseconds, the counter will generate an interrupt, RST 7.5, and the counter will automatically reload and start counting down again. The result is an interrupt generated at precise, 10 msec intervals.

The following assembler code appears in the initialization routine:

```
MVI    A,1BH
DB     30H
```

This is a special instruction of the 8085 microprocessor called SIM(30h). The accumulator must contain a control word (in this case, 1Bh) when SIM is executed. The control word has the following format:

Bit:	7	6	5	4	3	2	1	0
	SOD	SDE	XXX	R7.5	MSE	M7.5	M6.5	M5.5

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1Bh 0 0 0 1 1 0 1 1

This is interpreted as follows: Bits 7 and 6 are for serial communications and are not used, bit 5 is a don't care, bit 4 resets the RST7.5 interrupts and the remaining bits enable the RST7.5 interrupt. See page 3-61 of Intel 8080/8085 Assembly Language Programming Manual for additional information.

When timer 1 reaches zero, which has been programmed to occur at 10 msec intervals, a RST7.5 interrupt occurs. This is a vectored interrupt and the 8085 program counter is set to 003Ch. Therefore, a JUMP instruction to the interrupt service routine, called STIM, must be located at memory location 3Ch. The code to do this and the results in the computer memory are shown below:

	<u>CODE</u>	
MVI	A,0C3H;	MOVE C3h (code for JMP) to Accumulator
STA	3CH;	STORE in memory location 3Ch
LXI	H,STIM;	LOAD HL register pair with address of STIM
SHLD	3DH;	STORE contents of HL register pair in two successive bytes of memory starting at 3Dh

<u>MEMORY LOCATION</u>	<u>CONTENTS</u>	
003C	C 3	Code for JUMP
003D	L L	Lower order address bits
003E	H H	Higher order address bits for program called STIM

In this program it was desirable to use a FORTRAN program to provide a user interface and perform some calculations. The main program is the interrupt service routine for interrupts from timer 1 and needs the various parameters specified by the user. Thus, parameters must be passed from the FORTRAN program to the assembly language program. The method used is discussed in the FORTRAN-80 Reference Manual - Appendix C - Subprogram Linkages.

The parameter actually passed is the address of the low byte of the argument so the parameters are always two bytes long. Parameter 1 is passed in the HL register pair, parameter 2 in register pair DE and parameters 3 through N in a contiguous block with register pair BC pointing to the low byte of this block (low byte of parameter 3). \$AT is a system subroutine for transferring parameters to a local data area. Before it is called, register pair HL must point to the local area; register pair BC points to the 3rd parameter and the accumulator contains the number of arguments.

After \$AT is run, the variables P1 through P8 contain the low byte of the address of the eight parameters which are passed when the subroutine STPVAL is called from the FORTRAN program. The variables P1 through P8 are correlated with the variables of the assembly language programs as follows:

P1 : A1 P5 : T2

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P2 : A2 P6 : T3VAL
P3 : TVAL P7 : INC
P4 : T1 P8 : THLDST

The passed variables are all integer values, which are two bytes in length, and which would allow a maximum positive value of 32.767d. Most of the variables used are only one byte (less than 255d).

The variables in the assembly language program are updated with the following sequence:

LHLD P1; address of first variable in H-L pair,
MOV A,M; value of first variable into accumulator,
STA A1; store in location A1 in assembly language data
 area.

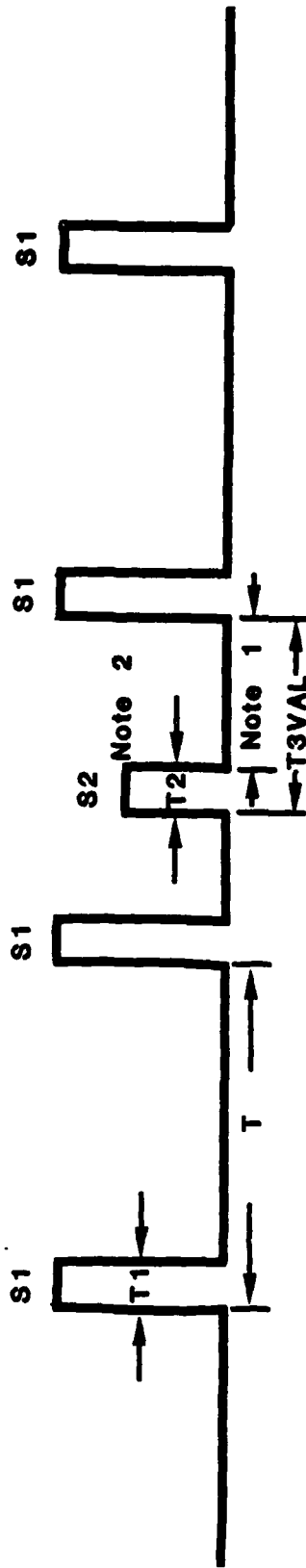
This is an example where the variable is one byte.

For a two byte transfer:

LHLD P4; load HL with address of T1; a 2 byte variable,
MOV A,M; low byte of T1 value into accumulator,
STA T1+1; store in low byte storage space for T1 in
 assembly language program,
INX H; increase HL by one,
MOV A,M; get high byte of T1 value into accumulator,
STA T1; store in high byte storage space in assembler
 program.

The main software routine is the interrupt service routine called STIM which is diagrammed in flow chart form in Figure A2. This flow chart is made more understandable by referring to the diagram in Figure A1, which shows the significance of the various program variables in determining pulse timing relationships. STIM is entered whenever an interrupt is generated by timer 1 on the MPU-B board. This occurs at an interval of 10 milliseconds. Each time the interrupt occurs, the memory location specified by the label T is decremented. If [T] = 0, then there is a branch to A1OUT which is the module which generates the S1 pulse. If [T] is greater than zero, SICNT is checked for zero value by loading the contents of this memory location into A and performing ORH A. If SICNT is zero, then a S2 pulse must be generated in the current interval. Assuming SICNT is zero, T is compared to T3VAL to ascertain when the S2 pulse should be generated. The shaded area in Figure A1, described by NOTE 1 and defined by $T3VAL > T > 5$, indicates the period when sampling of the EKG occurs during each interrupt cycle. The sample is checked for negative value by doing the OR-Immediate instruction with a zero operand and checking for a one in bit 7 of the result in the accumulator. If the sampled value is greater than THLDST, then a paced beat has occurred and several things result.

- 1) FFh is stored in SYSFLG.
- 2) A short, audible "beep" is generated on the keyboard speaker.



Note 1: Sampling of the EKG occurs during this time to determine if a paced beat was elicited by S2.

Note 2: Amplitude of S2 increases by increment (INC) if previous S2 failed to stimulate, or decreases by INC if S2 succeeded in stimulating the heart.

Figure A1 - Computer generated cardiac stimulation waveforms.

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- 3) FFh is put out on part 3 (-2.5 volts) for a period of 4 msec.

Figure A3 is a flow chart for the program segment which defines the generation of the S2 pulse. The code for the S2 pulse, labeled A2OUT, first checks the contents of the variable SYSFLG to determine if the last S2 pulse successfully stimulated the heart. If it did, then the current S2 amplitude (variable A2) is decremented, and, if it did not, then A2 is incremented. The value stored in the variable INC determines the magnitude of the change, and the resultant A2 value is checked to see if it is within the range of 00_h to 7F_h. If either the upper or lower bound is exceeded, the variable A2 is set to whichever bound was exceeded, either 7F_h or 00_h, respectively. Next, the software flag SYSFLG is reset. SYSFLG would have been set by the detection of a paced beat in the main routine, STIM. The rest of the routine produces a pulse output on Port 1 with amplitude A2, and a duration determined by the two-byte variable, T2. The level on port 1 is returned to zero at the end of the routine. In addition, a sync pulse is generated on port 2 which has +2.5 volt magnitude and beginning 0.5 milliseconds before the S2 pulse and extends 2 milliseconds after.

The S1 pulse is generated in a very similar manner to the S2 pulse with the exception that the amplitude is not variable, but remains fixed at a level which has been set by the operator. The variable ,A1, in the assembly language module contains a fixed amplitude for the S1 pulse.

The time delay described above, as well as the time delays for the S1 and S2 pulses, is generated using the subroutine, LOOP. In this subroutine, a programmed LOOP is formed in which the BC register pair is decremented and checked for zero, continually, until BC is equalled to zero when a return from the subroutine is executed. The instructions shown below, which decrement BC and check for zero, take about 8 microseconds to execute.

LOOP:	DCX	B	6	X	1/3	=	2
	MOV	A,R	4	X	1/3	=	1 1/3
	ORA	C	4	X	1/3	=	1 1/3
	JNZ	LOOP	10	X	1/3	=	<u>3 1/3</u>
		TOTAL					8 msec

Therefore:

$$T_d (\text{time delay in microseconds}) = 8 \times [\text{value in BC register pair}]$$

For example, if a 1 msec delay is desired:

$$1 \text{ msec} = 1000 \text{ msec} = 8 \times [X]$$

$$X = 1000/8 = 125d = 7Dh$$

The subroutine BEEP causes the speaker on the keyboard to emit a short "beep". In the program, this coincides with detection of a paced beat, and it is a useful auditory feedback for the operator. This function, described on page KEY-21 of IKB-1, Intelligent Keyboard Users Guide, is performed by sending a command string to port 2 with bit 0 set to zero.

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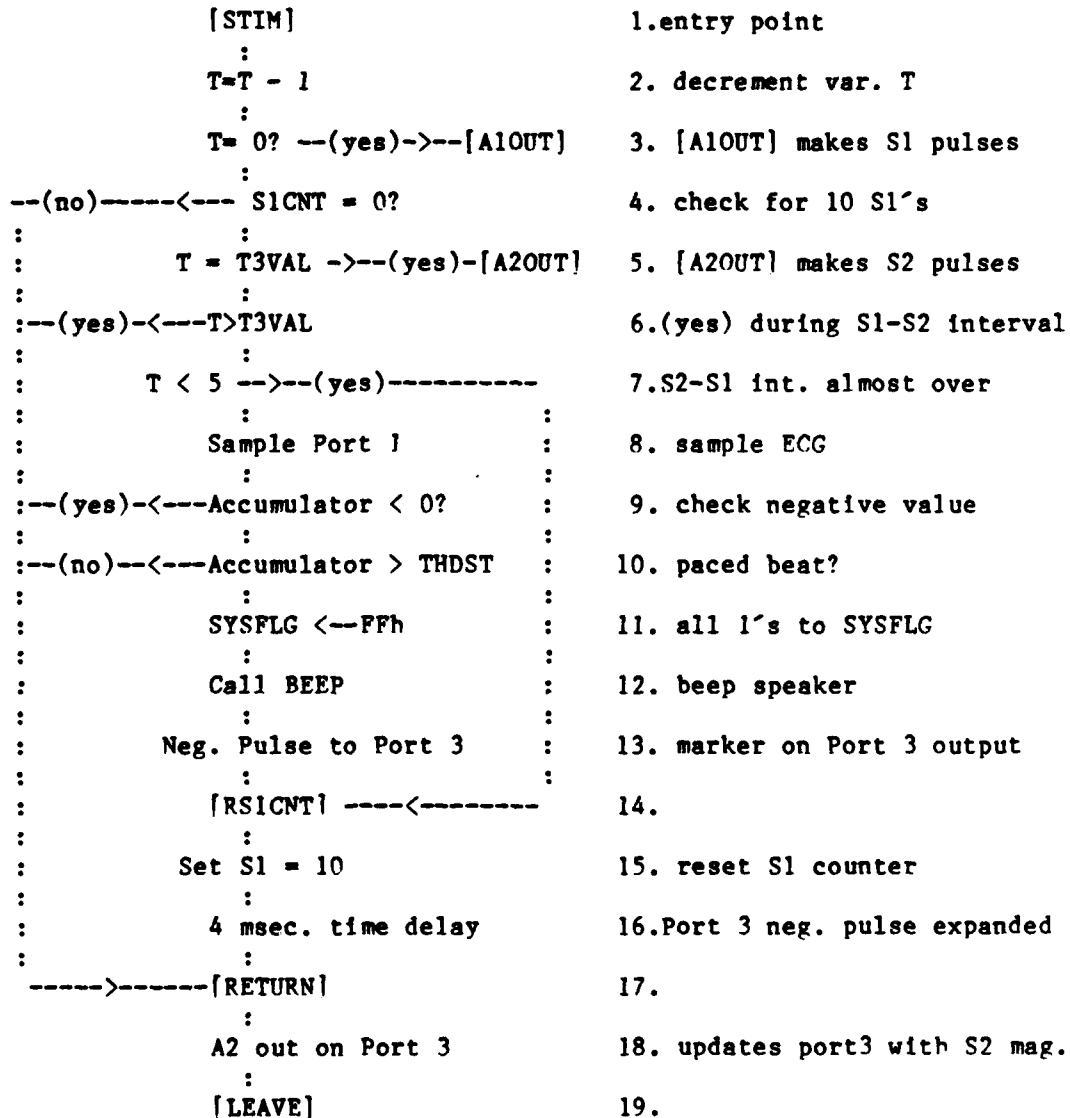


Figure A2: Flow chart of the basic loop of the interrupt service routine.

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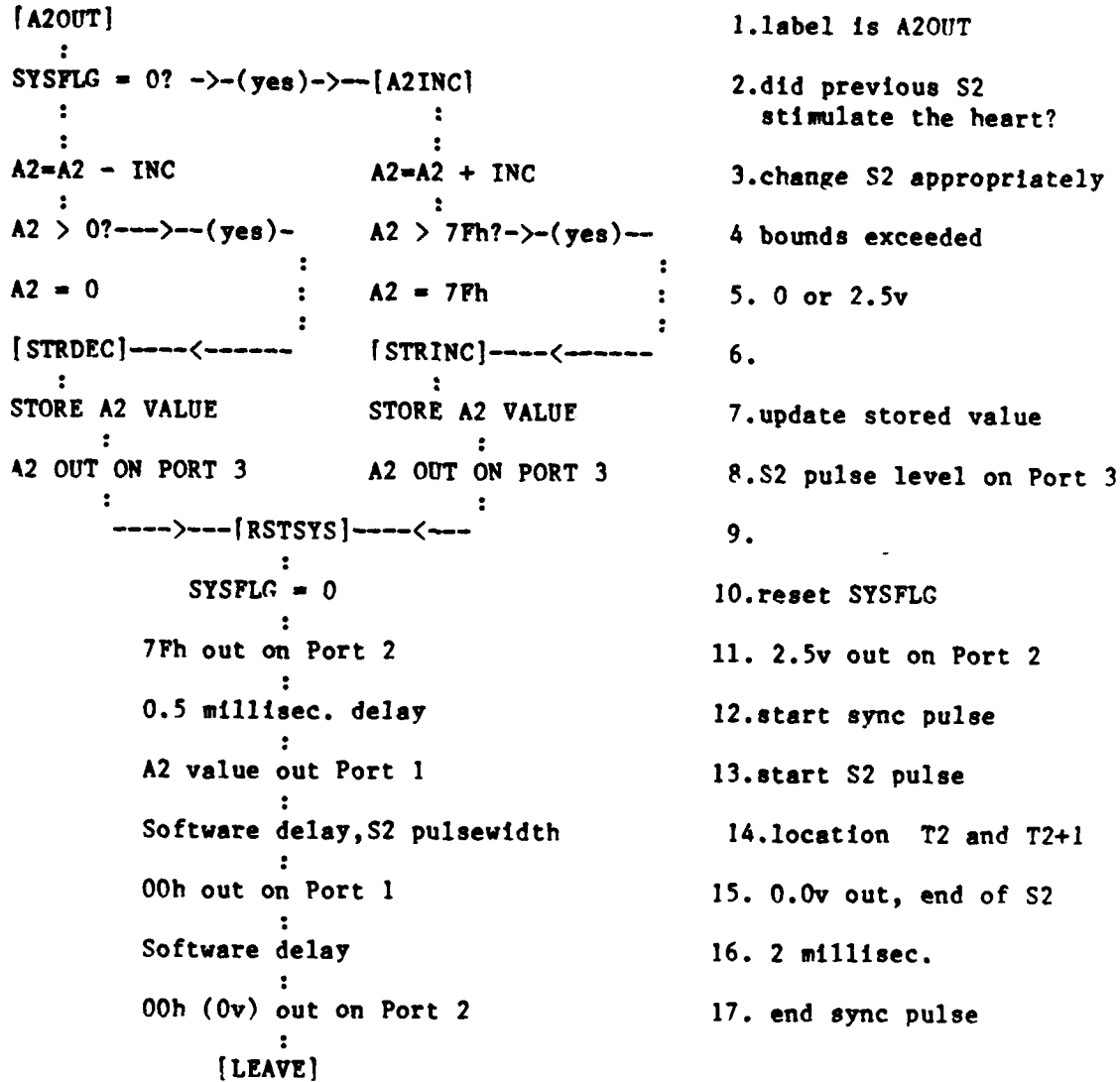


Figure A3: Flow diagram for the assembly language program (A2OUT) for generation of the S2 pulse. The flow diagram for the assembly language program, A1OUT is very similar to steps 11 through 17 of this figure.

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```

C
C
C
C PAGE 1 - STIM.FOR
C
C
C
C MAIN PCER PROGRAM
C ALL VARIABLES ARE INTEGERS
C CALL TO INIT INITIALIZES THE ASSEMBLY LANGAUGE PROGRAM
C (SETS UP THE TIMERS, SETS UP THE INTERRUPT, ENABLES INT.)
C   INTEGER A1,A2,TVAL,T1,T2,T3VAL,THLDST,RR,RATE,S2DELY,PWTH1,PWTH2
C   CALL INIT
C WRITE PROMPTS TO SCTEEN AND READ AMPLITUDE VALUES
C (0-127 CORRESPONDS TO 00 TO 7FH AND 00 T TO 2.5 VOLTS)
1   WRITE (3,10)
    READ (3,50)A1
    WRITE (3,12)
    READ (3,50)A2
C READ THE PULSEWIDTH IN MICTOSECONDS
C DELAY LOOP IS 8 MICROCEC., THEREFORE, DIV. BY 8
    WRITE (3,22)
    READ (3,50)PWTH1
    T1=PWTH1/8
C SAME AS ABOVE FOR S2 PULSE
    WRITE (3,24)
    READ (3,50)PWTH2
    T2=PWTH2/8
C THE VARIABLES TVAL AND T3VAL REPRESENT THE S1 TO S1
C PERIOD AND THE S2 TO NEXT S1 PERIOD RESPECTIVELY.
C THE NUMBERS LOADED MUST BE THE NUMBER OF 10 MSEC. INTERRUPTS
C REQUIRED TO GENERATE THE PERIOD.
C
C RATE INPUT BEATS PER MINUTE
C
C  $TVAL(\text{INTERRUPTS}/S1 \text{ PULSE}) = [6000 (\text{INTERRUPTS}/\text{MIN.})] / [\text{RATE} (S1 \text{ PULSES}/\text{MIN})]$ 
    WRITE (3,20)
    READ (3,50)RATE
    TVAL=6000/RATE
C
C RR IS THE TIME IN MILLISECS BETWEEN PULSES
C
C   RR=TVAL*10
    WRITE(3,40)RR
C S2DELY IS THE TIME IN MILLISECS BETWEEN S2 AND PREVIOUS S1
C THE S2 PULSE IS GENERATED WHEN T IS DECREMENTED UNTIL T=T3VAL,
C SO THE NO. OF INTERRUPTS IN S2DELY (S2DELY / 10)
C

```

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```
C
C PAGE 2
C
C
C MUST BE SUBTRACTED FROM TVAL (MAX. VALUE OF T IS TVAL)
C TO GET THE PROPER VALUE OF T3VAL
  READ(3,50)S2DELY
  T3VAL=TVAL-S2DELY/10
C READ THE INCREMENT FOR S2 PULSES. FOR INSTANCE,
C WHEN INC=1, THE CHANGE IN THE VOLTAGE OUTPUT
C ON PORT 1 WOULD BE 2.5/127 OR .02 VOLTS
  WRITE (3,60_
  READ(3,50)INC
C READ THE LEVEL FOR DETECTION. ONLY POSITIVE VALUES, SO
C RANGE IS 0-127, CORRESPONDING TO 00 TO 7FH OR 0 TO 2.5 VOLTS.
  WRITE(3,70)
  READ(3,50)THLDST
  CALL STPVAL(A1,A2,TVAL,T1,T2,T3VAL,INC,THLDST)
10  FORMAT(' A1 AMPLITUDE (0-125)=' )
12  FORMAT(' A2 AMPLITUDE (0-125)=' )
20  FORMAT(' PULSE RATE (PULSES/MINUTE)=' )
22  FORMAT(' S1 PULSEWIDTH (MICROSECONDS)=' )
24  FORMAT(' S2 PULSEWIDTH (MICROSECONDS)=' )
30  FORMAT(' PULSE DELAY (MSEC)=' )
40  FORMAT(' RR INTERVAL (MSEC)=' ,I8)
50  FORMAT(I8)
60  FORMAT(' S2 AMPLITUDE INCREMENT (0-10)=' )
70  FORMAT(' LEVEL FOR DETECTION (0-125)=' )
  PAUSE
  GO TO 1
  END
```


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TITLE PAGE S1-S2 PACING ROUTINE

```

        EXT      $AT
        ENTRY   INIT,STPVAL,STIM
;THE INITIALIZATION ROUTINE TAKES CARE OF
;SETTING UP TIMER 1 ON THE MPU-B BOARD,
;(PROGRAMMABLE RATE, PULSE GENERATOR,
;BINARY COUNT)
;IT ENABLES THE 7.5 INTERRUPT USING THE
;SPECIAL 8085 SIM INSTRUCTION
;AND A JUMP INSTRUCTION IS INSERTED AT
;MEMORY LOCATION 3CH (RST 7.5)
INIT:   MVI     A,40H      ;ENABLE TIMER 1
        OUT     0F3H
        MVI     A,74H      ;LSB FIRST, MODE 2
        STA     0D103H    ;
        MVI     A,20H      ;LSB FIRST
        STA     0D101H
        MVI     A,4EH      ;THEN MSB
        STA     0D101H
        MVI     A,1BH      ;ENABLE 7.5 INTERRUPT
        DB      30H
        MVI     A,0C3H     ;SET UP THE JUMP
        STA     3CH       ;C3 INTO [003C]
        LXI    H,STIM     ;LOAD HL REG. PAIR WITH
                           ;ADDRESS OF "STIM"
        SHLD   3DH       ;[H] TO [003D]
                           ;[L] TO [003E]

        EI
        RET
;STORE PARAMETER VALUES
STPVAL: DI

        SHLD   P1        ;SAVE PARAMETER 1
        XCHG
        SHLD   P2        ;SAVE PARAMETER 2
        MVI    A,6        ;NUMBER OF PARAMETERS LEFT
        LXI    H,P3      ;POINTER TO LOCAL AREA
        CALL   $AT       ;FORTRAN TRANSFER ROUTINE
;PARAMETER ADDRESSES
P1:    DW
P2:    DW
P3:    DW
P4:    DW
P5:    DW
P6:    DW
P7:    DW
P8:    DW
;LOAD NEW VALUES INTO THE VARIABLES
;DEFINED IN THE ASSEMBLY PROGRAM
;GET THE ADDRESS FROM THE TABLE
;DEFINED WITH P1: TO P8: NOTE:
;MOST VALUES ARE ONE BYTE
;BUT SOME HAVE TWO BYTES

```

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```

LHLD    P1          ;GET FIRST ADDRESS
MOV     A,M         ;GET FIRST VALUE
STA     A1          ;STORE AS A1
LHLD    P2
MOV     A,M         ;STORE PARAMETER
STA     A2          ;2 AS A2

LHLD    P3

MOV     A,M         ;STORE PARAMETER
STA     TVAL        ;3 AS TVAL
LHLD    P4          ;ADDR. OF P4 INTO [HL]
MOV     A,M         ;LOW BYTE OF 2-BYTE VAR.
STA     T1+1        ;STORE IN LOW BYTE OF T1
INX     H           ;INCREMENT HL
MOV     A,M         ;HIGH BYTE TO [A]
STA     T1          ;STORE IN LOC. T1
LHLD    P5          ;STORE FIFTH AS T2
MOV     A,M
STA     T2+1
INX     H
MOV     A,M
STA     T2
LHLD    P6          ;STORE PARAMETER 6 AS T3VAL
MOV     A,M
STA     T3VAL
LHLD    P7          ;STORE PARAMETER 7 AS INC
MOV     A,M
STA     INC
LHLD    P8          ;STORE PARM. 8 AS THLDST
MOV     A,M
STA     THLDST

EI
RET
;BEGINNING OF THE INTERRUPT ROUTINE
;ENTERED WHENEVER TIMER 1 TIMES OUT
;
STIM:   DI          ;DISABLE INTERRUPT
;STORE REGISTER VALUES ON STACK
        PUSH       PSW
        PUSH       B
        PUSH       D
        PUSH       H
        LXI        H,T          ;LOAD HL WITH T ADDRESS
        DCR        M           ;T=T-1
        JZ         A1OUT        ;IF T=0, THEN JUMP TO A1OUT
;IF SICNT NE ZERO, THEN JUMP TO RETURN
        LDA        SICNT
        ORA        A
        JNZ        RETURN
;COMPARE T3VAL AND T
;(HL REG. STILL CONTAINS ADDRESS OF T)

```

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```

;IF T =T3VAL, THEN JUMP TO A2OUT
;IF T GT T3VAL, THEN JUMP RETURN
    LDA    T3VAL
    CMP    M
    JZ     A2OUT
    JC     RETURN
;THIS CODE EXECUTED WHEN T IS LT T3VAL
;(S2 HAS OCCURRED). PURPOSE IS TO SAMPLE THE
;EKG UNTIL JUST BEFORE NEXT S1
    MVI    A,5      ; ALMOST TIME FOR NEXT S1?
    CMP    M        ;COMPARE T TO 5
    JNC    RS1CNT   ;IF T LT 5 JUMP TO RS1CNT
    IN     PORT1    ;SAMPLE THE EKG
    ORI    00H      ;UPDATE FLAGS
    JM     RETURN   ;CHECK FOR NEG. VALUE
;THE POSITIVE SAMPLE IS COMPARED TO A THRESHOLD
;IF GT, SYSFLG IS SET TO FFH
;KEYBOARD SPEAKER IS BEEPED, AND
;-2.5V OUTPUT ON PORT 3
;JUMP OUT TO RS1CNT

    LXI    H,THLDST;H-L GETS THLDST ADDRESS
    CMP    M        ;IF EKG SAMPLE LT THLDST,

    JC     RETURN   ;THEN JUMP TO RETURN
    MVI    A,0FFH   ;SET SYSFLG=FFH
    STA    SYSFLG
    CALL   BEEP     ;BEEP THE KEYBOARD SPEAKER
    MVI    A,0FFH
    OUT    PORT3    ;-2.5 V OUT ON PORT 3
    JMP    RS1CNT   ;EXIT TO RS1CNT

;A2OUT GENERATES THE S2 PULSE
;S2 AMPLITUDE IS DETERMINED BY
;RESULTS OF PREVIOUS S2 REFLECTED
;BY THE CONTENTS OF SYSFLG
;IF SYSFLG=00,THEN A2=A2+INC
;IF SYSFLG=FFH, THEN A2=A2-INC
A2OUT: LDA    SYSFLG ;GET VALUE (00 OR FF)
    CPI    00H
    JZ     A2INC    ;IF SYSFLG=00, JUMP A2INC
;PERFORM A2=A2-INC
    LXI    H,INC    ;GET ADDRESS OF INC IN H-L
    LDA    A2       ;GET A2 VALUE

    SUB    M        ;A2=A2-INC
;IF A2 GOES NEG., THEN SET A2=0
    JP     STRDEC   ;IF A2 GT ZERO, JUMP STRDEC
    MVI    A,00H   ;PUT 00 IN ACCUMULATOR

STRDEC: STA    A2    ;STORE ACCUM. IN A2
    OUT    PORT3    ;NEW A2 VALUE OUT ON PORT 3

    JMP    RSTSYS  ;JUMP TO RESET PART

```

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```

;PERFORMS A2=A2+INC
A2INC: LXI    H,INC    ;GET INC ADDRESS IN H-L
        LDA    A2
        ADD    M        ;A2=A2+INC
;IF THE RESULT OF THE INCREMENT EXCEEDS 7FH
;THEN 7FH SHOULD BE STORED IN A2
        JP     STRINC   ;A2 BETWEEN 00 AND 7F, JUMP

        MVI    A,7FH    ;7F INTO ACCUMULATOR
STRINC: STA    A2        ;STORE ACCUM. IN A2
        OUT    PORT3    ;A2 VALUE OUT ON PORT 3
;SYSFLG IS RESET BEFORE ACTUAL S2 GENERATED
RSTSYS: MVI    A,00H    ;RESET SYSFLAG
        STA    SYSFLG

;NEXT SECTION OF CODE GENERATES A 2.5V
;OUTPUT (PORT2) FOR A PERIOD OF TIME
;DETERMINED BY: 0040H X LOOP TIME
;0040H=64D, LOOPTIME=8MICROSEC.
;THEREFORE THE LOOP SUBROUTINE
;GENERATES A DELAY OF 512 MICROSEC.
        MVI    A,7FH
        OUT    PORT2
        LXI    B,0040H
        CALL   LOOP

;THIS IS THE CODE WHICH DETERMINES
;THE DURATION OF THE S2 PULSE.
;THIS CODE LOADS THE TWO-BYTE
;VALUE FROM T2 INTO THE B-C PAIR
        LDA    T2        ;LOAD B WITH T2 MSB
        MOV    B,A
        LDA    T2+1      ;LOAD C WITH T2 LSB
        MOV    C,A
        LDA    A2        ;FORM S2 PULSE
        OUT    PORT1
        CALL   LOOP      ;TIME DELAY
;ON RETURN FROM LOOP, THE ACCUMULATOR
;CONTAINS ZERO AND THIS IS OUTPUT
;TO PORT1 TO FINISH OFF THE S2 PULSE
        OUT    PORT1
;ANOTHER TIME DELAY IS GENERATED
;WHICH DETERMINES HOW MUCH LONGER THE
;PULSE ON PORT 2 EXTENDS BEYOND
;THE S2 PULSE
        LXI    B,0100H
        CALL   LOOP
        MVI    A,00H
        OUT    PORT2
        JMP    LEAVE     ;EXIT THE PROGRAM

;THIS SUBROUTINE IS A DELAY LOOP
;WHERE EACH ITERATION TAKES 8
;MICROSEC. AND THE NUM. OF ITER-
;ATIONS IS IN BC INITIALLY
LOOP:   DCX    B        ;DECREMENT BC PAIR
;B AND C ARE OR-ED TOGETHER AND

```

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;THE RESULT IS ZERO ONLY WHEN BOTH
;B AND C ARE ZERO

```

MOV    A,B
ORA    C
JNZ    LOOP
RET

```

;THIS SUBROUTINE BEEPS THE SPEAKER OF THE
;KEYBOARD. THIS IS DONE BY WRITING
;A CONTROL WORD TO PORT 2
;WITH THE LS BIT=0

```

BEEP:  PUSH    PSW
        MVI    A,00H
        OUT    02H
        MVI    A,0FFH
        OUT    02H
        MVI    A,00H
        OUT    02H
        POP    PSW
        RET

```

;THIS CODE GENERATES THE S1 PULSE
;IT IS SIMILAR TO THE A2OUT CODE
;WHICH GENERATES THE S2 PULSE.

```

A1OUT: MVI    A,7FH    ;2.5V OUT ON PORT 2
        OUT    PORT2
        LXI    B,0040H ;DELAY FOR 512 MICROSEC.
        CALL   LOOP
        LDA    TVAL    ;RESET THE VAR. T TO TVAL
        STA    T
        LDA    T1      ;LOAD BC WITH T1, MSB FIRST
        MOV    B,A
        LDA    T1+1
        MOV    C,A
        LDA    A1
        OUT    PORT1   ;START THE S1 PULSE
        CALL   LOOP
        OUT    PORT1   ;FINISH S1 PULSE
        LXI    H,S1CNT ;DECREMENT S1CNT
        DCR    M
        LXI    B,0100H ;SET UP DELAY
        CALL   LOOP
        MVI    A,00H
        OUT    PORT2   ;ENDS AFTER S1
        JMP    LEAVE

```

;S1CNT IS RESET AND A TIME DELAY OF
;ABOUT 4 MILLISEC. IS GENERATED
;THE PURPOSE IS TO ALLOW TIME
;FOR THE -2.5 PULSE GENERATED WHEN
;A SYSTOLE IS DETECTED

```

RS1CNT: LDA    S1CVAL ;RESET S1CNT
        STA    S1CNT
        LXI    B,01F4H
        CALL   LOOP

```

;THE CURRENT A2 LEVEL IS PUT OUT ON

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```

;PORT 3 AS AN INDICATION OF THE
;LEVEL REQUIRED FOR STIMULATION
;EACH TIME A SYSTOLE IS DETECTED
;A -2.5V PULSE IS PUT OUT ON PORT 3
RETURN: LDA      A2
          OUT     PORT3
LEAVE:  POP      H
          POP     D
          POP     B
          POP     PSW
          EI
          RET

SYSFLG: DB      00H      ;SYSTOLE?YES=FFH,NO=00H
INC:    DB      5        ;INCREMENT OF S1 AMPLITUDE
THLDST: DB      3FH     ;THRESHOLD SET,0 TO 7FH
S1CNT:  DB      0AH     ;S1 COUNT, VARIABLE
S1CVAL: DB      0AH     ;S1 COUNT VALUE, 10
T:      DB      32H     ;TIME, VARIABLE
TVAL:   DB      32      ;TIME VALUE (RATE)H
T1:     DW      7DH     ;S1 DURATION
T2:     DW      7DH     ;S2 DURATION
A1:     DB      3FH     ;S1 AMPLITUDE
A2:     DB      7FH     ;S2 DURATION
A2SET:  DB      3FH
T3VAL:  DB      19H

;INPUTS                                OUTPUTS
PORT1   EQU     19H      ;EKG                                PACER
PORT2   EQU     1AH      ;S2 LEVEL                            SYNC PULSE
PORT3   EQU     1BH      ;                                       A2 LEVEL
PORT4   EQU     1CH      ;                                       A2 SET LEV.
PORT5   EQU     1DH
PORT6   EQU     1EH
PORT7   EQU     1FH
END

```

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