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Instrumentation and Control for a Microprocessor-Based Coronary Perfusion System

Daniel L. Priester
Marquette University

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BY

Daniel L. Priester
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PREFACE

I would at this time like to acknowledgee my committee for all the help given to me and support shown throughout this entire process. I am particularly indebted to Dr. Kristine Ropella and Dr. Lawrence Boerboom for their seemingly unending patience.

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CHAPTER I.

INTRODUCTION

Perfusion systems provide a means of investigating the blood flow to organs in living animals. A coronary perfusion unit is one such type of system. By isolating perfusion of the heart from the systemic circulation, control is gained over coronary pressure and flow, and the response of the heart to certain conditions can be investigated experimentally. As an example of a condition that would be of interest, an occlusion valve could be placed in the perfusion system, allowing the investigator to model the effects of the narrowing of arteries that occurs with heart disease, while accurately controlling the pressure and flow to the arteries.

A control system must be used in order to accommodate the exact control of the pressure and flow to the heart in the coronary perfusion system. A closed loop servo system is one means of accomplishing this control [9]. In a servo system a reference value is input, indicating the

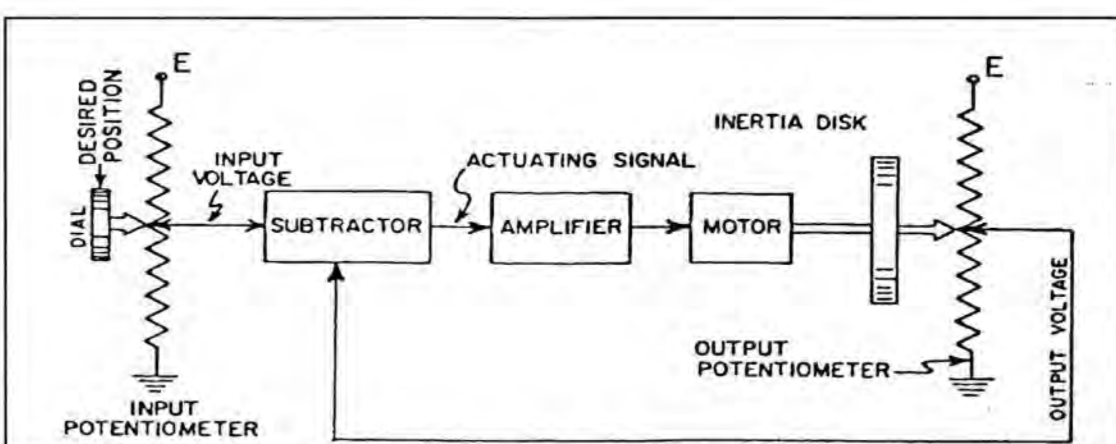

Figure 1- General Components of Closed Loop Servo System.

desired result. A transducer is used to simultaneously obtain a value representing the actual position of the system. These two signals then are subtracted to produce an error signal which drives an actuator and forces the actual position of the system to the input reference level (Figure 1). In a coronary perfusion system the pressure control loop appears as shown in Figure 2, with the controlled variable being the

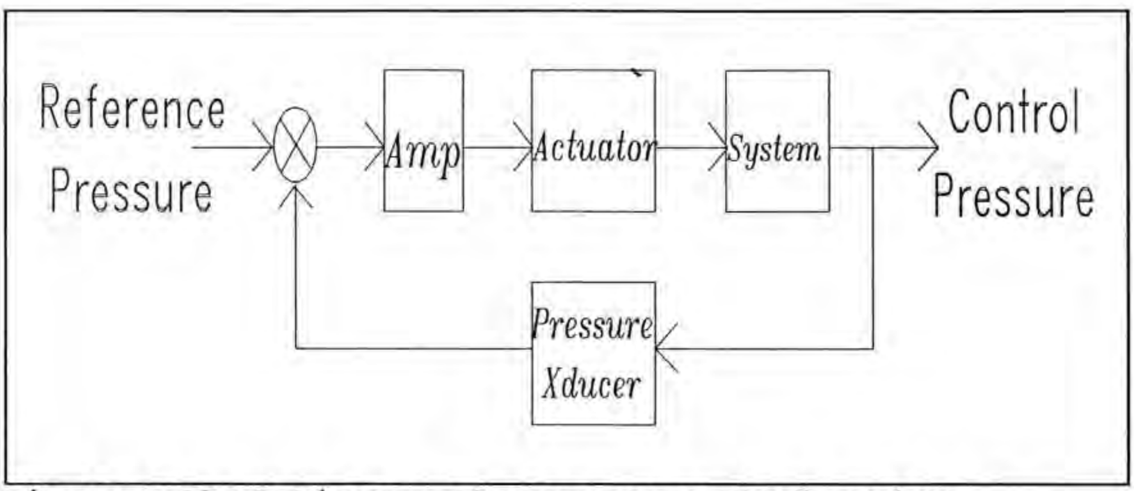

Figure 2-Block Diagram of pressure control system.

coronary pressure.

The actuation or production of the desired pressure could be accomplished by any one of a number of methods. Mohrman [12] proposed an actuator that used a roller pump and varied the pump speed to increase or decrease the coronary pressure. A perfusion system utilizing this actuation method was used by Metting [10] on dogs to study the response of the hindlimb vascular bed to changes in perfusion pressure, and Grant [6] used it in a system to characterize the influence of cardiac output on pulmonary hemodynamics. Another actuation method was first used in dog renal perfusion studies [7], and later adapted to coronary perfusion systems. This method uses a cuff occluder to control the flow and consequent perfusion pressure to the organ of interest. The shortcoming in these methods was their inability to accurately model the pulsatile blood pressure and flow waveforms present in physiological systems. A solution to this was presented by Canty and Mates [4], who proposed a method in which an electrohydraulic servo valve was placed between the perfused heart and a pressurized blood reservoir, thereby making the coronary pressure a function of the relative position of the valve. Figure 3 shows the specifics of the Canty and Mates system that correspond to the general block diagram shown in Figure 2. This system was used for studies aimed at characterizing the relationship of coronary pressure and flow [2,3]. The inherent advantage of this system is its ability to effectively model the coronary circulation for purposes of impedance /capacitance studies [1].

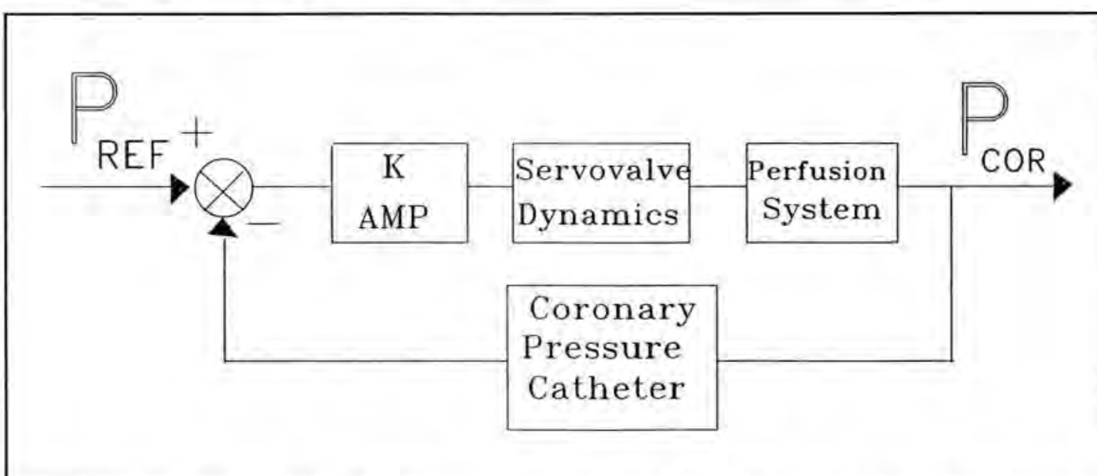

Figure 3- Block diagram of Canty and Mates perfusion system.

The system developed by Canty and Mates had one very distinct disadvantage; it incorporated a control system which was analog-based, and as such was prone to drift and oscillations caused by instability. The control of pressure and flow in coronary circulation requires an extremely fast and accurate system due to the wide variations in load impedance over a single cardiac cycle. A much more efficient and accurate method would be to implement microprocessor-based digital control for the system. Digital control would allow for a faster and more stable system.

Using Canty and Mates work as a basis,it was the focus of this study to develop a microprocessor based coronary perfusion system that would improve the system performance in terms of speed and stability. The improvement of physiological control systems by digital microprocessor control has been demonstrated by Muhlethaler [13] who used microprocessor based control for a brain perfusion system in rats, and Smith,et al. [15] who used microprocessor control to improve the performance of an intra-aortic balloon pump.

Employing microprocessor control of the perfusion system would also allow for the addition of proportional, derivative, and integral controller elements to enhance the time domain characteristics of the system [8]. A preliminary block diagram showing a perfusion system incorporating digital proportional, integral, and derivative control is shown in Figure 4. In this scenario the reference value and feedback value are digitized by an analog to digital convertor. The error signal is then computed using the proportional, derivative, and integral algorithms contained in the microprocessor. The resulting error signal is converted back to analog form by a digital to analog convertor, and the valve moves correspondingly.

One concern in the design of control systems is stability. Canty and Mates noted that "...high frequency oscillations about the mean

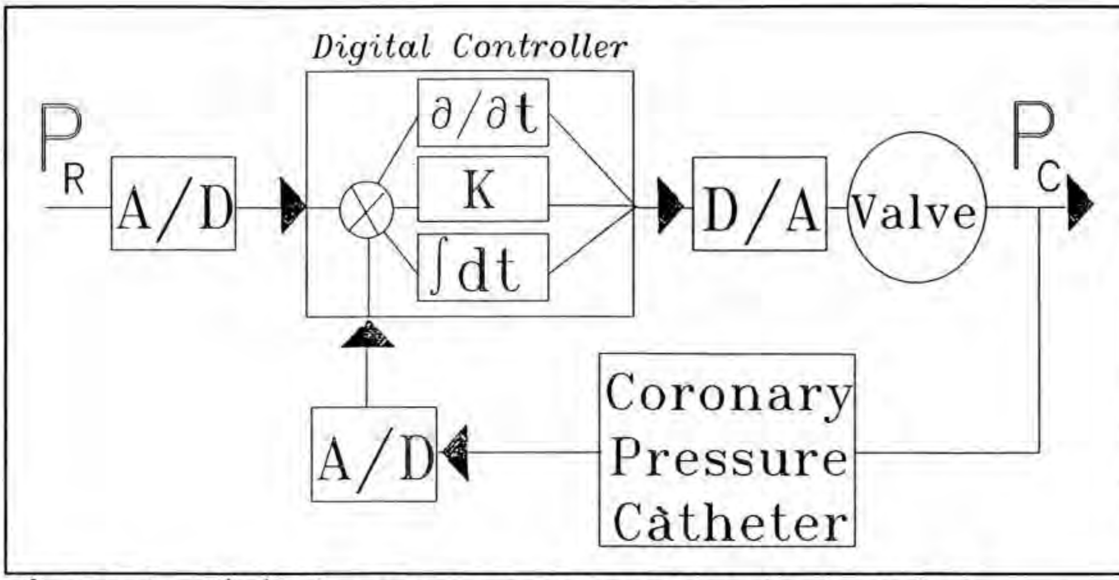

Figure 4- Digital coronary pressure control system incorporating proportional, integral and derivative elements.

pressure..." were observed at higher amplifier gains [4]. The authors are in effect describing a situation of instability, but they make no mention of efforts to characterize this instability. This research attempts to characterize the stability of the digital control system developed. For this reason, a mathematical model is developed for the various parts of the perfusion system and analyzed on the computer. All analog and digital circuits are also modelled and the results of this analysis are compared to actual results obtained from the finished prototype circuit.

Another consideration in the design of the coronary perfusion system is the frequency response of the overall system.

> To accurately reproduce the pressure control signal, the perfusion system must have a natural frequency higher than any significant harmonic component in the desired pressure waveform. Fourier analysis of arterial pressure waveforms has shown that approximately 10 harmonics are necessary to reproduce a pulsatile ascending aortic waveform adequately [5].

The frequency content of the arterial pressure waveforms therefore require that the perfusion system have a frequency response flat to 30 Hz. The various elements of the system are tested in terms of their frequency response to ensure the system has the required specifications. Testing the frequency response of the various components also allows identification of the components in the system which have the most limiting effect on the bandwidth.

The design process for the system implementation could be broken down into 6 main components.

A. **Signal Conditioner**- A circuit was required for excitation of the transducers used, as well as proper conditioning of the outputs of the transducers. This was required for the pressure transducers, as well as the EKG signal.

B. **Data Acquisition System**- A system separate from the control system was required for acquisition and analysis of data pertaining to the perfusion studies to be performed.

C. **Level Control of Blood Reservoirs**- A reliable system needed to be developed to control the level of blood in both the pressurized and auxiliary blood reservoirs used by the system.

D. **Control Loop**- This is the servo loop used to control the pressure. This portion of system consists of analog to digital conversion of the reference and feedback pressures, the actual P,I,D control algorithm, and digital to analog conversion of the command signal.

E. **Servo Valve Driver**- This component interfaces the output of D/A convertor to servo valve actuator. The driver consists of an isolation stage and a voltage to current convertor.

F. **Transit Time Measurement System**- A viable method needed to be developed to measure the absolute transit time of blood in the system. This is necessary for studies utilizing microsphere injections in order to synchronize the arrival of the microspheres with a particular event in the cardiac cycle.

The physical relationship of all the system parts is shown in Figure 5 on the following page.

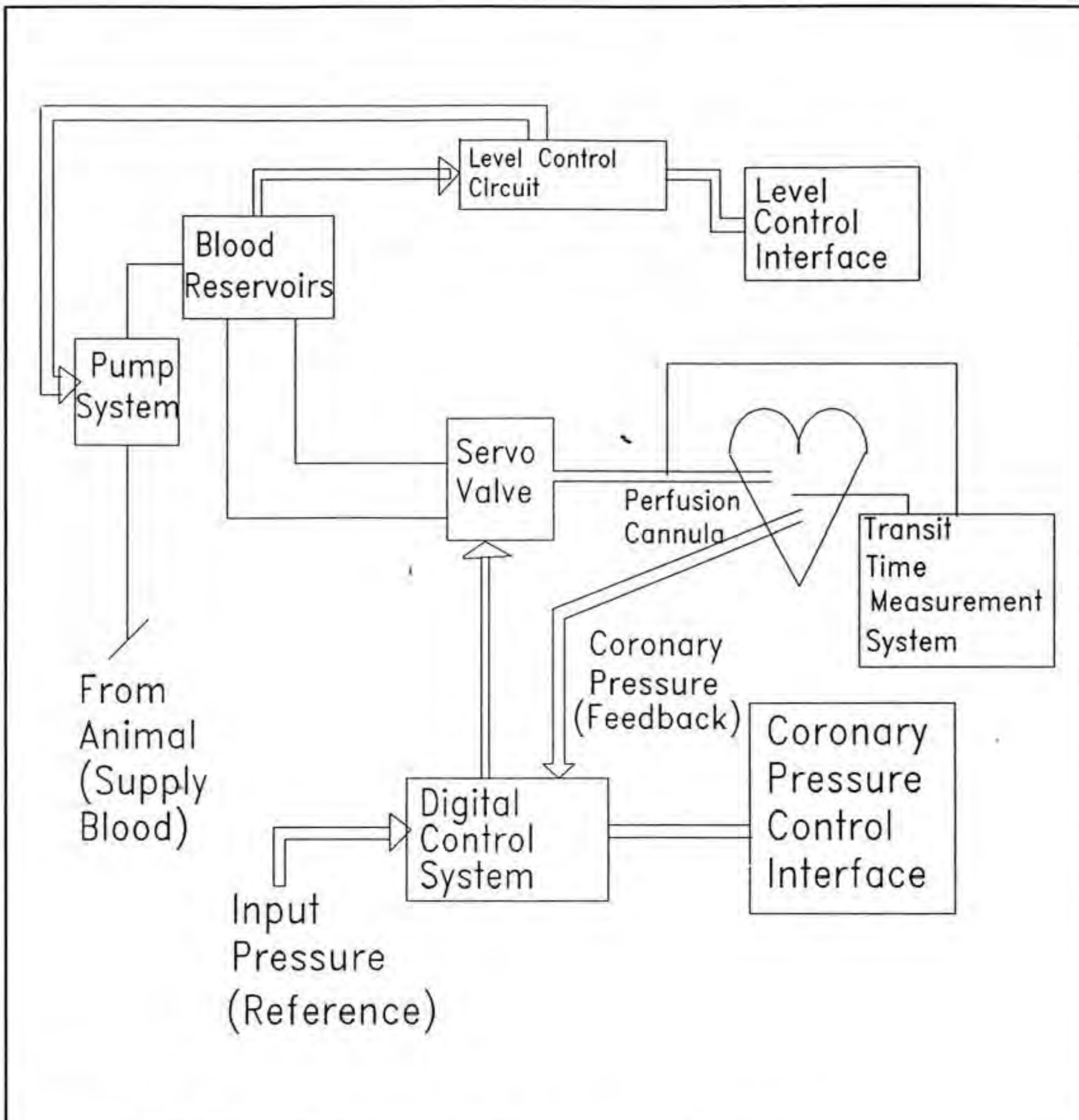

Figure 5- Overall perfusion system diagram.

CHAPTER II.

SYSTEM DESIGN

Section A: Signal Conditioning System:

The Millar pressure transducers (Section II.D) required a signal conditioning system to provide both an excitation voltage for the transducers and amplification of the output signals. A signal conditioning system was developed based on the Analog Devices 1B31 strain gauge conditioner integrated circuit [17]. This modular device provides all conditioning required by the transducer; excitation, amplification, voltage offsetting, and filtering. The IB31 is implemented on a card which fits into a rack mounted card cage. A schematic diagram of a single channel pressure transducer signal conditioner with its external components for controlling gain and offset is shown in Figure 6. The system was designed to have the following specifications:

Bridge Excitation Voltage:	5 volts
Amplifier Gain Range:	2-320
Low Pass Filter Cut Off:	50 Hz

There are 16 channels in the signal conditioning system, 13 of which are dedicated to these pressure signal conditioning modules, 2 of which are dedicated to thermocouple amplifiers (transit time measurement Section II.F), and one channel dedicated to EKG measurement. The EKG amplifier channel schematic is shown in Figure 7. This EKG amplifier system consists of an Analog Devices AD625 instrumentation amplifier followed by an isolation stage with adjustable gain and offset. The outputs of the

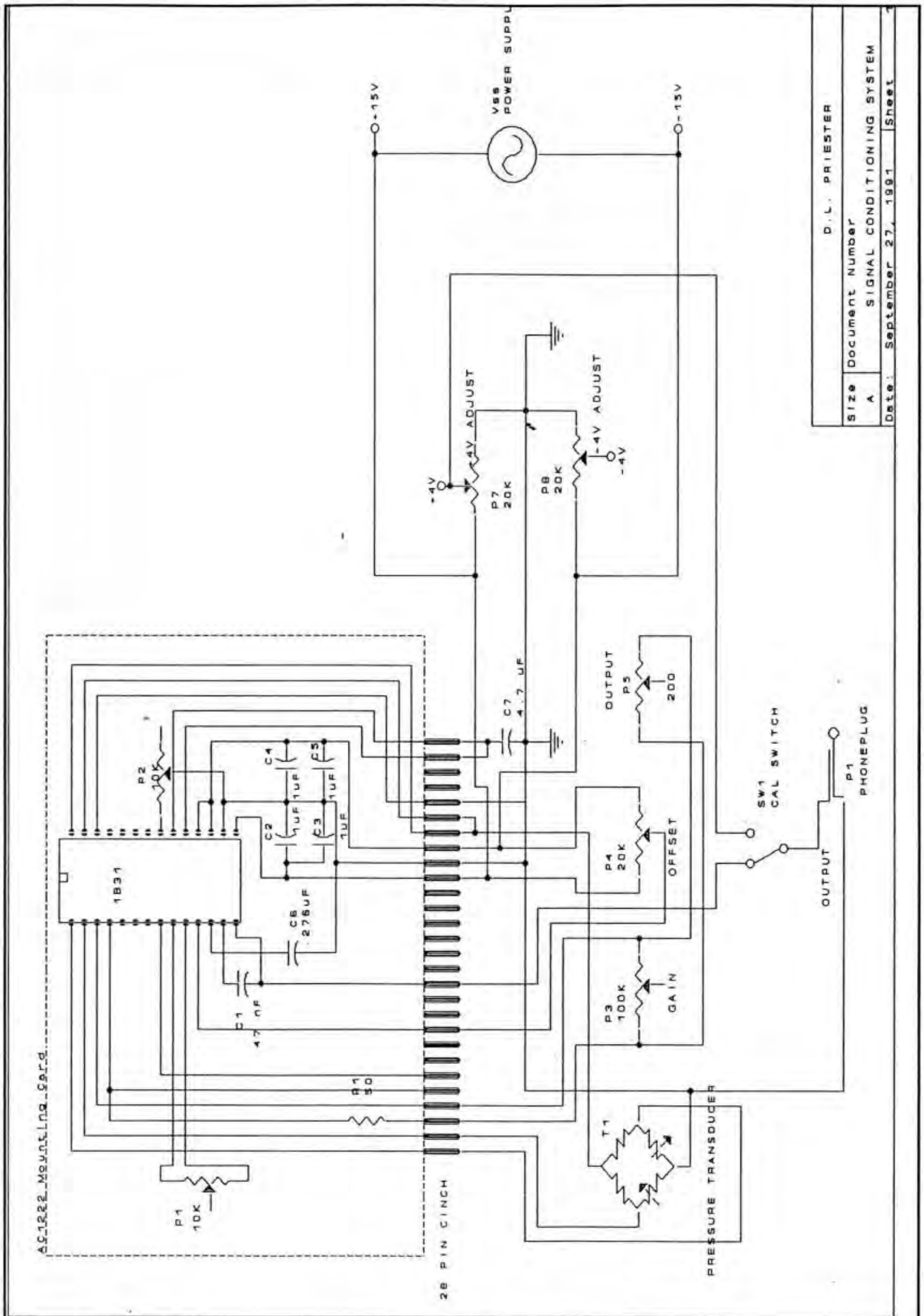

Figure 6- Pressure signal conditioning system circuit.

signal conditioning modules were then input to the data acquisition system (Section II.B) for recording.

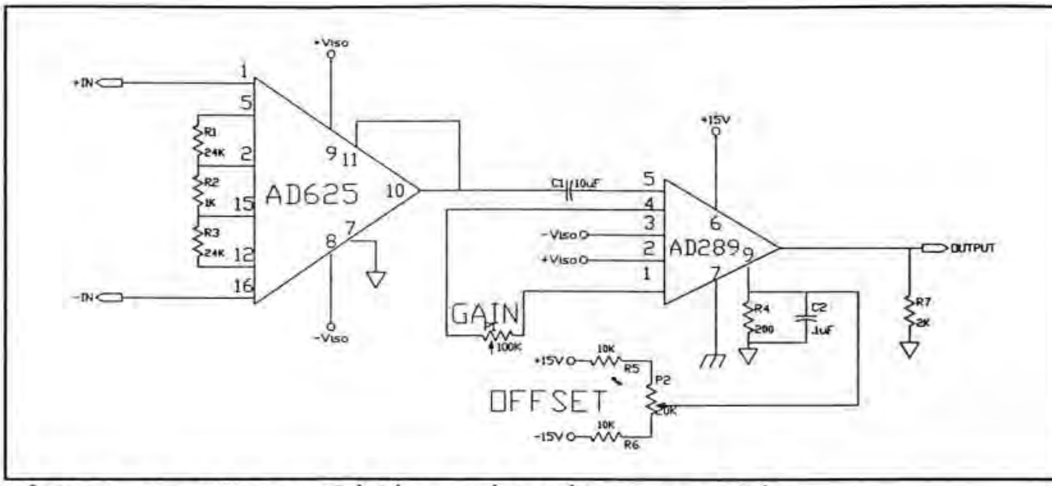

Figure 7- EKG amplifier circuit schematic.

Section B: <u>Data Acquisition System</u>-

In order to accommodate the acquisition and analysis of data pertaining to the perfusion studies, a data acquisition system was employed. This system uses an IBM PS/2 Model 70, which utilizes an 80386 microprocessor running at 20 MHz. A CODAS™ commercial data acquisition system was implemented on the computer.

The hardware portion of this system consists of a 12 bit 16 channel A/D convertor card with a high performance input module. The A/D card is capable of sampling one channel at 50 KHz in continuous mode. The high performance module has a maximum input range of ± 30 volts, and has software programmable gains of 1,2,5,10,50,100,500, and 1000 for each channel independently. The input module has an input impedance of 100M ohms, and nonlinearity of 0.04%.

The software portion of the system consists of a real time display of the data being acquired in record mode. Gain and offset are controlled independently for each channel from the keyboard. The system software also has a playback mode that allows viewing and analysis of the previously acquired data.

Section C: Blood Reservoir Level Control System-

A diagram showing the blood reservoirs and their relationship to the rest of the perfusion system is shown in Figure 8. The level of blood in the pressurized and recirculating reservoirs is controlled by the speed of the two peristaltic roller pumps P1 and P2. In order to effectively control the level of blood in the reservoirs, a system needed to be developed to monitor the blood levels in both reservoirs and run the pumps at an appropriate speed to keep the blood levels at a level chosen by the user.

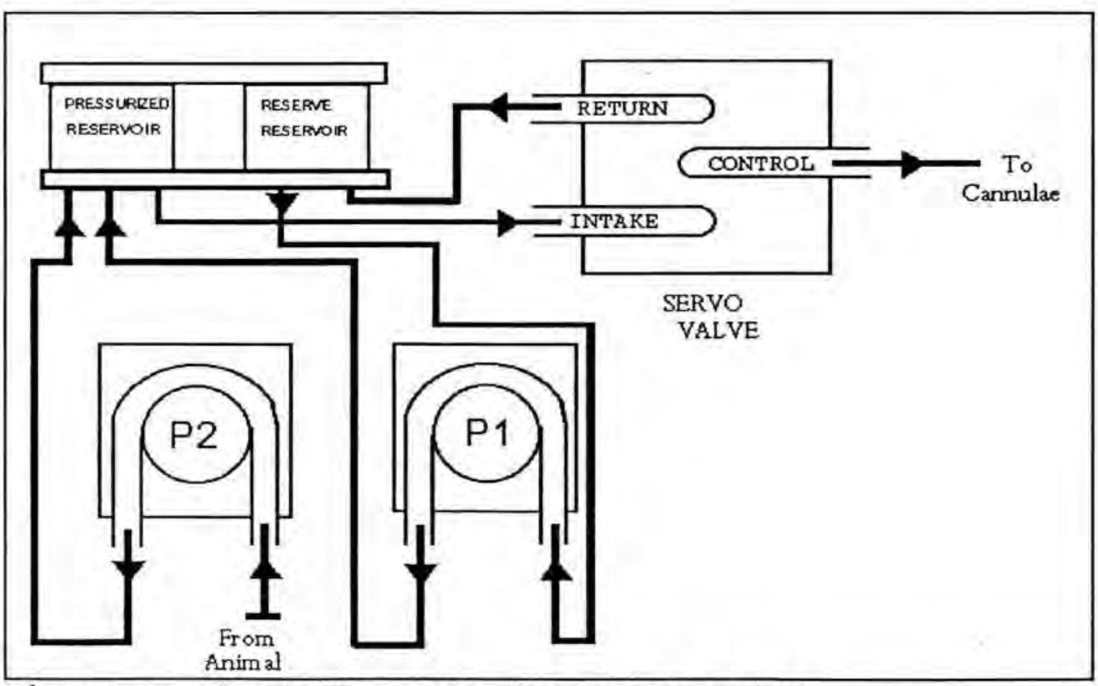

Figure 8- Blood flow path for servo system.

To accomplish the blood level control, a detection system was implemented which uses an impedance method to determine the level of blood in the reservoirs. The system developed is based upon the fact that the impedance between two electrodes placed in the reservoir will vary according to the level of blood in the reservoir. An oscillator signal with a frequency of 1 kHz is applied through a load resistor to the sensing electrode, the other electrode being connected to ground. The voltage measured at the reference electrode varies in response to changes in blood level due to the fact that the impedance between the two electrodes varies inversely with the surface area immersed. The resulting waveform is conditioned to detect the absolute value of the AC signal. This absolute value is then input to the microprocessor circuit in the form of a DC voltage via an A/D conversion port. The schematic diagram of the level detector circuit is shown in Figure 9. The calibration data for the level detector circuit is shown in Figure 10.

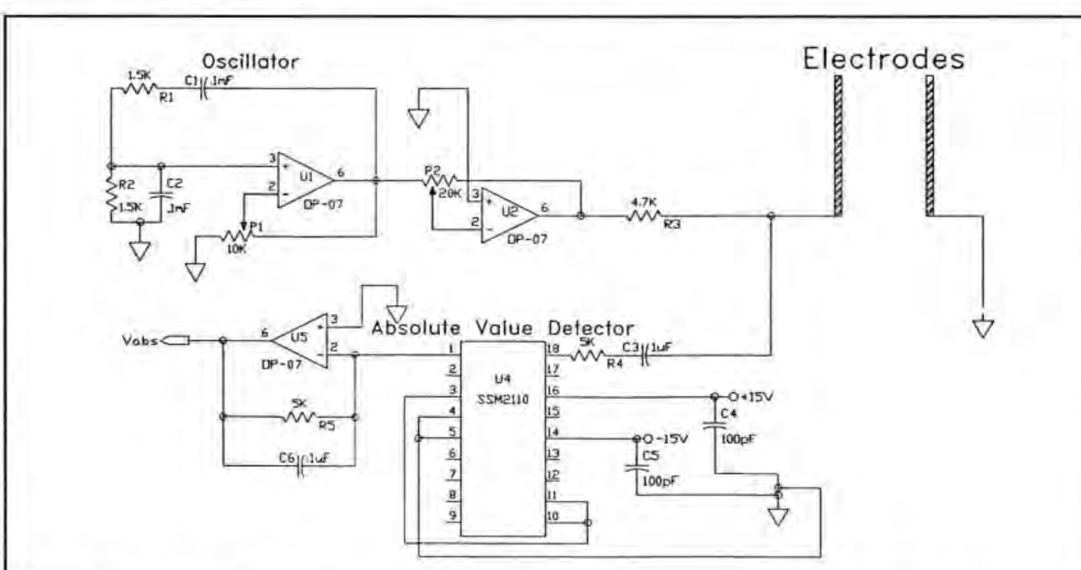

Figure 9- Schematic of blood reservoir level detection circuit.

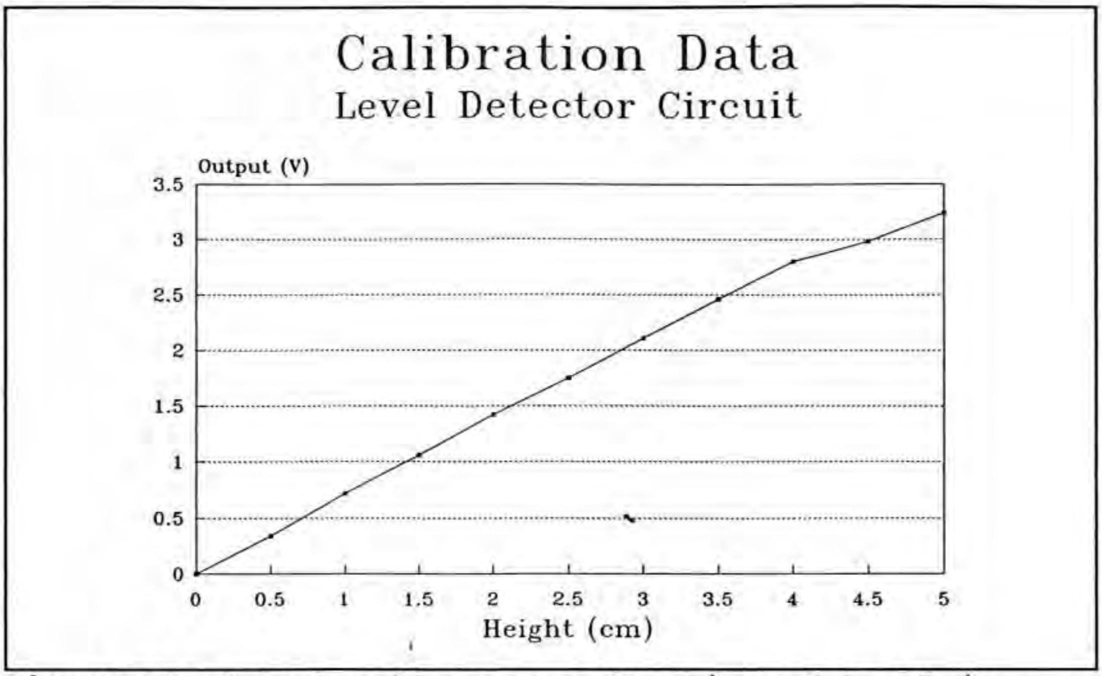

Figure 10- Output voltage as a function of level in reservoir.

The level detector output is read by a microprocessor based circuit which also reads in a value for the desired level (input by user) and determines an appropriate output signal to run the peristaltic roller pumps. The microprocessor circuit is implemented using a 68HC11 single chip microcomputer from Motorola [18]. The control software for the level control is implemented in the form of BASIC11™ commands stored in the EEPROM memory of the 68HC11 controller [18]. The program prompts the user to input levels for the reservoirs through a VT-100 terminal.

The control software subtracts the desired level from the actual level, and the 68HC11 circuit outputs an error value to an 8 bit digital I/O port. A digital to analog convertor and high voltage power amplifier are then used to condition the signal to an appropriate voltage to run the pumps. A diagram of the blood reservoir level control system is shown in Figure 11. Shown in Figure 12 is the power amplifier circuit used to drive the pumps.

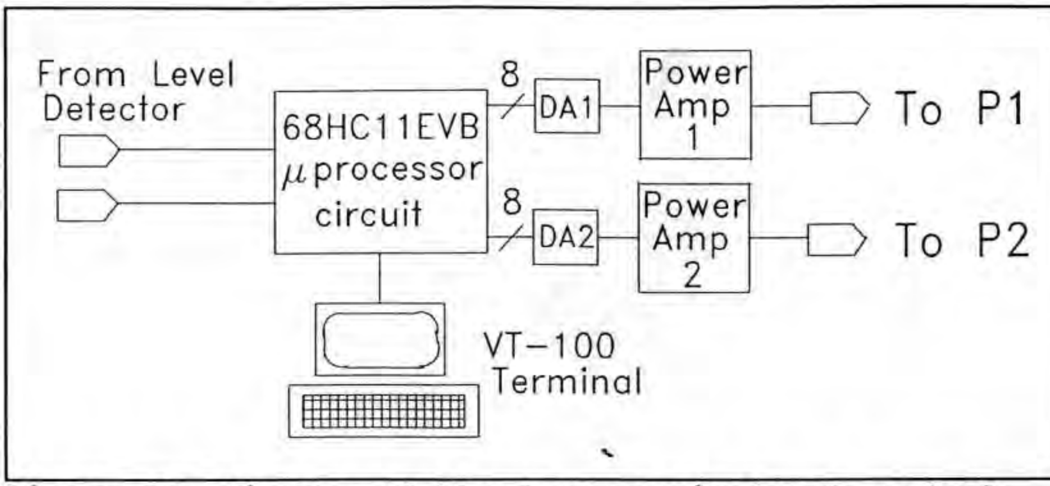

Figure 11- Diagram of blood reservoir level control system

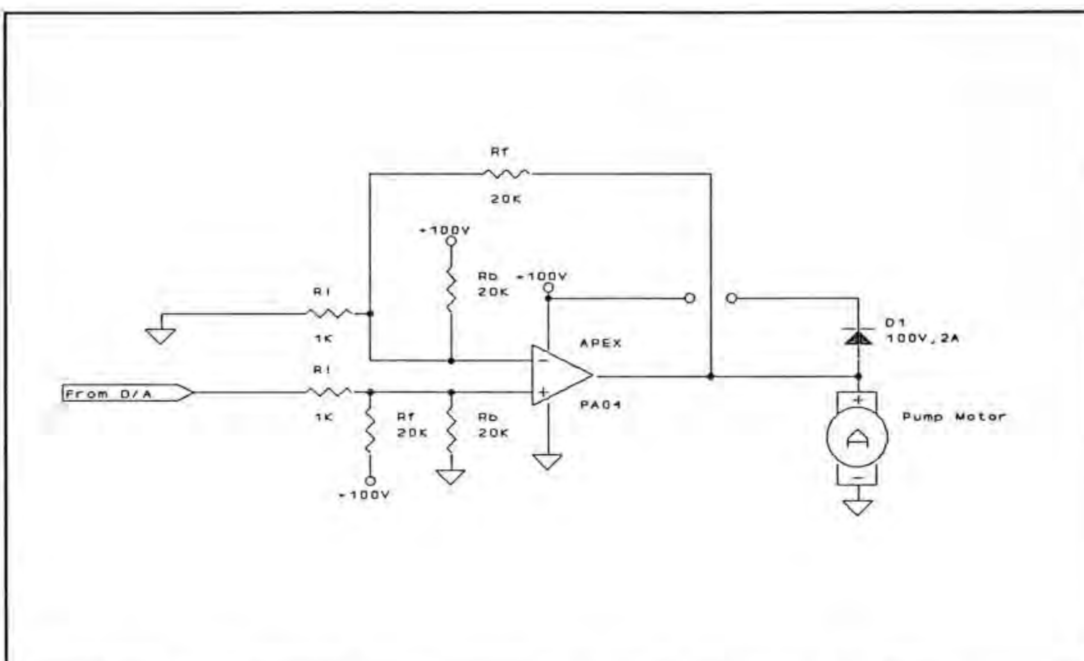

Figure 12- Schematic diagram of power amplifiers.

Section D: <u>P,I,D Control Loop</u>-

The coronary pressure control routine is implemented on an IBM AT compatible personal computer using a Real Time Devices™ ADA2000 board for interfacing analog and digital signals. The computer uses an 80386 microprocessor running at 25 MHz. The ADA2000 employs an Analog Devices™ AD574 A/D integrated circuit, which is a 12 bit successive approximation analog-to-digital convertor with a 35 microsecond conversion time and maximum non-linearity of 1/2 bit [16]. For output of analog signals, the board is equipped with an Analog Devices AD7537 D/A integrated circuit. This digital to analog convertor has 8 bit resolution and maximum non-linearity of ± 1 bit with a settling time of 1.8 microseconds [16].

Millar™ high fidelity pressure transducers were used to obtain values for the coronary and aortic pressures. These transducers employ a miniature strain gauge mounted on the tip of a catheter. The strain gauge is used as a sense arm in a full bridge configuration transducer. The sensitivity of the bridge is given by:

$$V_{out} = 5\ (uV/mmHg) * V_{excitation}$$

The excitation and signal conditioning for these transducers is provided by signal conditioning unit (Section II.A). The outputs are then converted to 12 bit digital form via the ADA2000, and the software routine uses these two values to produce an error signal to drive the servo valve.

Real Time Graphics and Display package by Quinn-Curtis™ was the commercially available software used for the coronary pressure control. This software package consists of different subroutines which are called from a main program to perform the control functions and display pressure values. The main program that calls the subroutines and controls input from and output to the ADA2000 is attached to a interrupt that is generated every .3 milliseconds. The flow diagram for the main program is shown in Figure 13.

The software incorporates a proportional, integral, and derivative control scheme to determine the error signal. The proportional element is the value that is obtained from the direct subtraction of the reference and command signals, while the derivative element takes the derivative of the error signal (which acts to anticipate changes), and the integral element integrates the signal to remove DC error and offset [4]. The transfer function describing a digital proportional, derivative and integral controller is shown below.

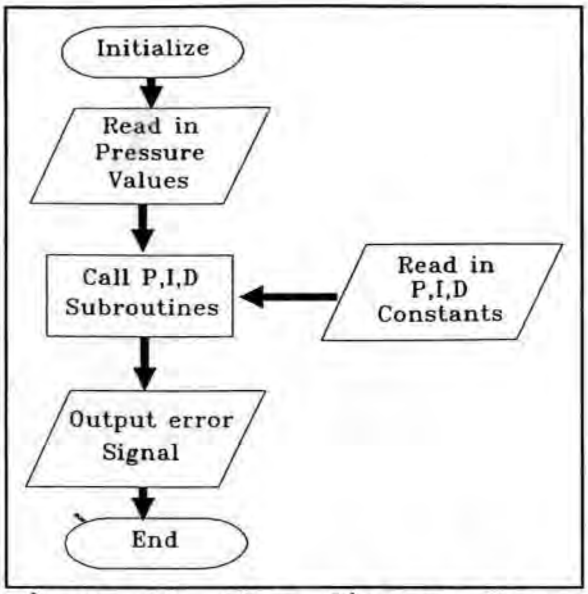

Figure 13- Flow diagram for main control algorithm.

$$G(z)= K_p + K_i(T/2)((z+1)/(z-1)) + K_d((z-1)/T*z)$$

Where: K's are gain constants

z is discrete time frequency plane operator

T is period of the signal

For purposes of the mathematical model to be developed later it can be assumed that the speed of conversion of the ADA2000, coupled with the relatively high frequency of interrupt generation is sufficient to replace the discrete time transfer function with the continuous time transfer function given by:

$$G(s)= K_p + K_i/s + K_d*s$$

Where s is continuous time frequency plane operator.

The method of interrupt generation allows for "on the fly" adjustments of the proportional, integral, and derivative element constants (K_p, K_i, and K_d) as well as real time display of the coronary pressure, aortic pressure, and the error between the two.

Once the final error value has been calculated, the computer outputs the value to the digital-to-analog convertor channel of the ADA2000 board. A detailed block diagram of the pressure control system is shown in Figure 14.

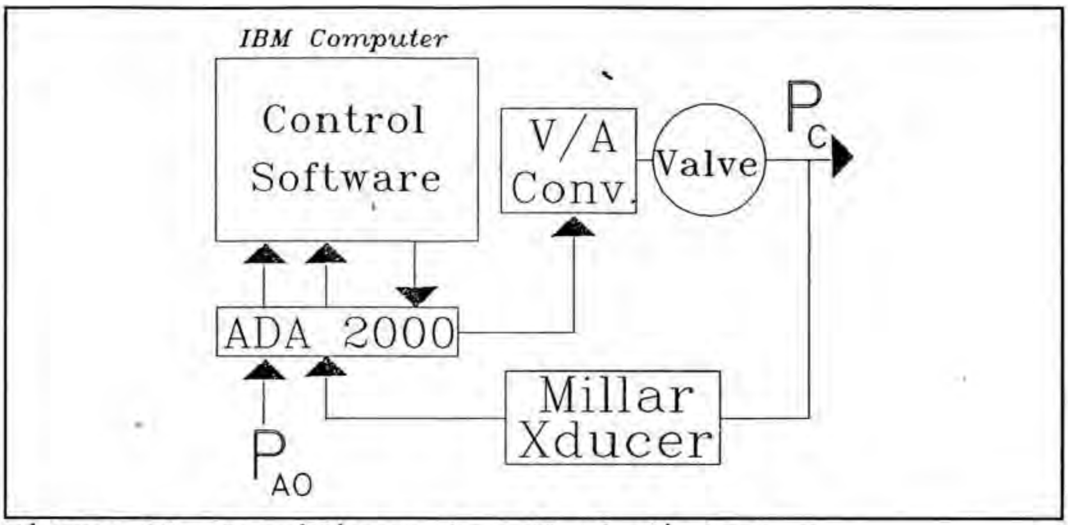

Figure 14- Specific system block diagram.

Section E: <u>Servo Valve Driver</u>-

A circuit was necessary to convert the voltage output of the ADA2000 board to a corresponding current to drive the servo valve. The voltage-to-current convertor implementation is shown in Figure 15. The circuit employs an OP-07 operational amplifier with bipolar junction transistors connected to the output. The amplifier drives the complementary transistors Q1 and Q2, which supply the high current output necessary to drive the servo valve's coil. The 100K ohm resistor provides current feedback for the valve driver, and the 5.1 ohm resistors provide current overdrive limits for the output current.

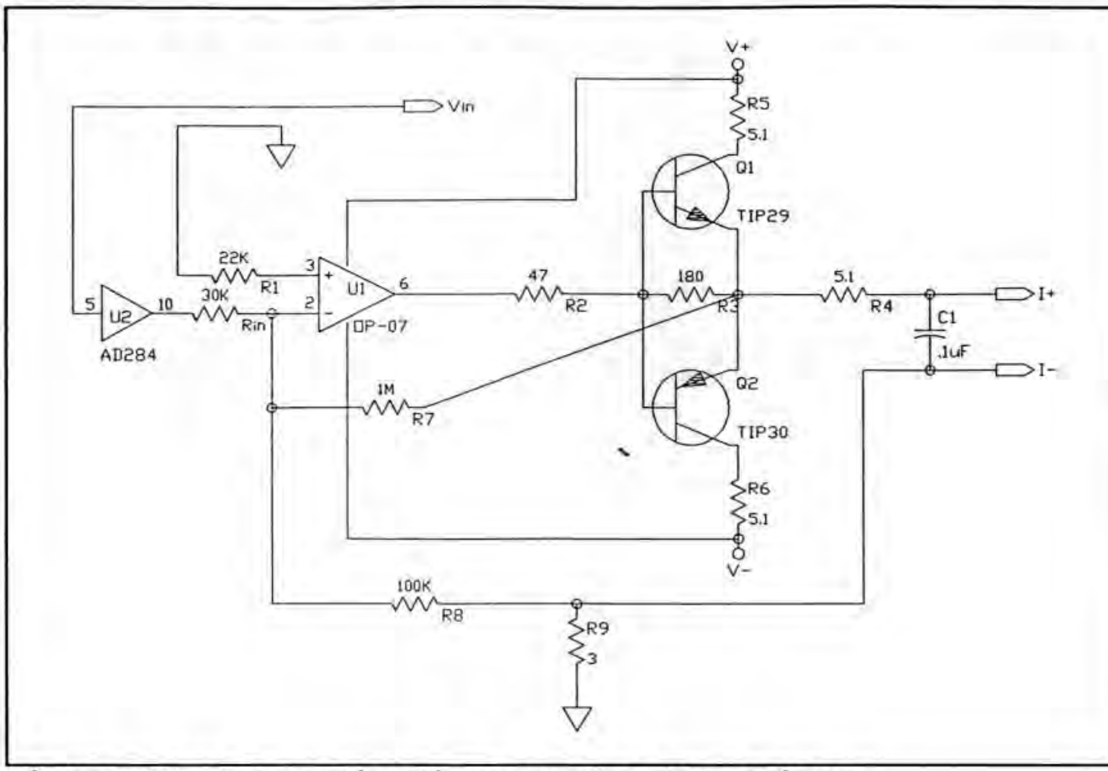

Figure 15- Schematic diagram of valve driver.

On the front end of this voltage-to-current convertor is a unity gain isolation amplifier. This preconditioning stage serves to both reject common mode noise, and isolate the animal from potentially dangerous ground faults.

Section F: <u>Transit Time Measurement:</u>

For perfusion studies utilizing radiolabelled microspheres, it is necessary to determine the transit time for the blood, and subsequently the microspheres in the blood, from the cannula to some predetermined area in the coronary arteries. This is needed because it is often necessary to synchronize the arrival of the microspheres with some specific event in the cardiac cycle.

To accomplish this transit time measurement a system was developed that uses two type T (copper-constantanum) thermocouples to detect the passing of a small amount of cold saline solution that is injected at the tip of the cannula. By placing one thermocouple at the injection site, and one at the area of interest in the coronary artery, a measurement can be made of the absolute transit time between the two points. Since only the presence of the cold saline needs to be detected, not the actual temperature, no linearization is necessary. To make the relatively small voltage output of the thermocouples more discernable, an ice bath reference is used for each thermocouple. A block diagram of the transit time system is shown in Figure 16.

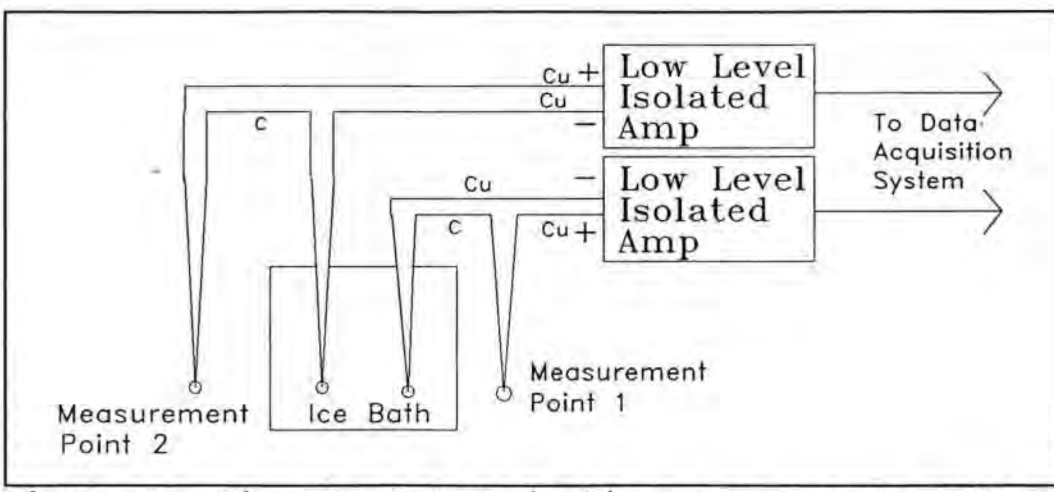

Figure 16- Diagram of transit time measurement system.

The low level isolated amplifiers were necessary to both isolate the animal and to provide amplification of the small "raw" output of the thermocouples. These low level amps were realized by using the 2B50 integrated circuit from Analog Devices [17]. This 2B50 is designed for use exclusively as an isolated thermocouple amplifier, so the implementation was straightforward. The output of these thermocouple conditioners was then input to the data acquisition system (Section II.B) for analysis of the transit time. The output of these thermocouple amplifier circuits is shown in Figure 17. This data was obtained by placing the measurement thermocouple in water heated 5 degrees above room temperature, and recording output in volts.

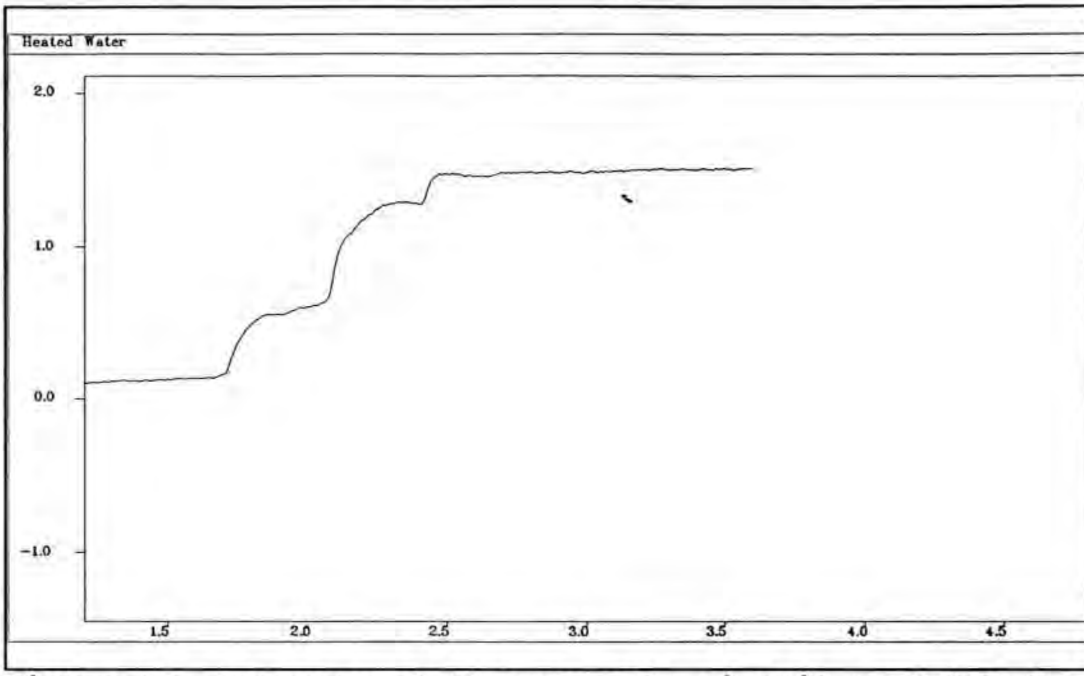

Figure 17- Response of thermocouple circuit to 5 deg C.

This concluded the phase of the design of the system. The system now needed to be tested to ascertain the performance of the system was consistent with the needs specified. This performance analysis of the system is included in Chapter III.

Chapter III.

System Analysis

Section A: Determination of System Transfer Function-

The coronary pressure control system developed in Chapter II can be simplified to the block diagram shown in Figure 18 showing each block's gain. The simplified block diagram assumes the controller and the signals

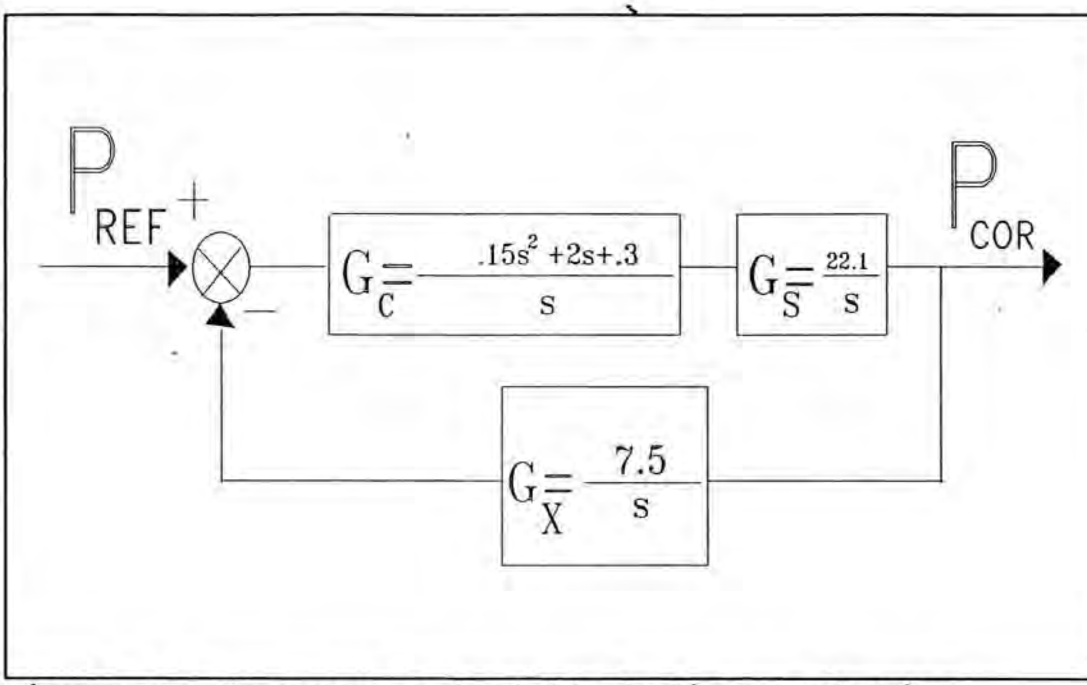

Figure 18- Pressure control block diagram showing individual gains.

are analog in nature, this assumption is valid due to the relatively high speed of the controlling microprocessor, as well as the high speed of conversion of the command, feedback, and error signals. This block diagram will be used in this chapter to develop a mathematical model of the theoretical response of the system in terms of frequency domain, time domain, and stability. These results will then be compared with experimentally determined results.

The actual benchtop results were obtained by testing the system under idealized conditions, using tubing and an adjustable clasp to model the coronary arteries being perfused. The supply pressure was 350 mmHg, and the flow to the tubing being used to simulate the coronary arteries was approxiamtely 100 ml/min.

As discussed in Chapter 2, the transfer function of the controller is given by $G_c = K_p + K_i/s + K_d*s$. To determine the transfer function of the servo valve actuator, it is necessary to look at actual input/output data obtained experimentally from the valve. The inherent nature of the electrohydraulic servo valve is such that the transfer curve is sigmoid in nature and exhibits hysteresis [14]. By assuming that the valve will be working in the relatively linear range of the sigmoid curve, this transfer curve can be fit to a line and assumed to respond linearly to inputs. Figure 19 shows the actual transfer data for the servo valve, as well as the best fit line obtained by linear regression. Using this linearized transfer characteristic, it is possible to obtain the system's overall transfer function by use of the general gain formula. In order to accomplish this, it is necessary to specify actual gains for the P,I, and D gain parameters. The following experimentally determined gains were used; $K_p=2$, $K_i=0.3$, $K_d=0.15$. These gains were determined by varying the gains in the test situation, until the system response was idealized.

Applying the general gain formula to this block diagram yields the following transfer function for the overall system:

$$G(s)= (3.3s^2 + 42.25s + 6.63) / (s^3 + 24.75s^2+316.9s + 49.7)$$

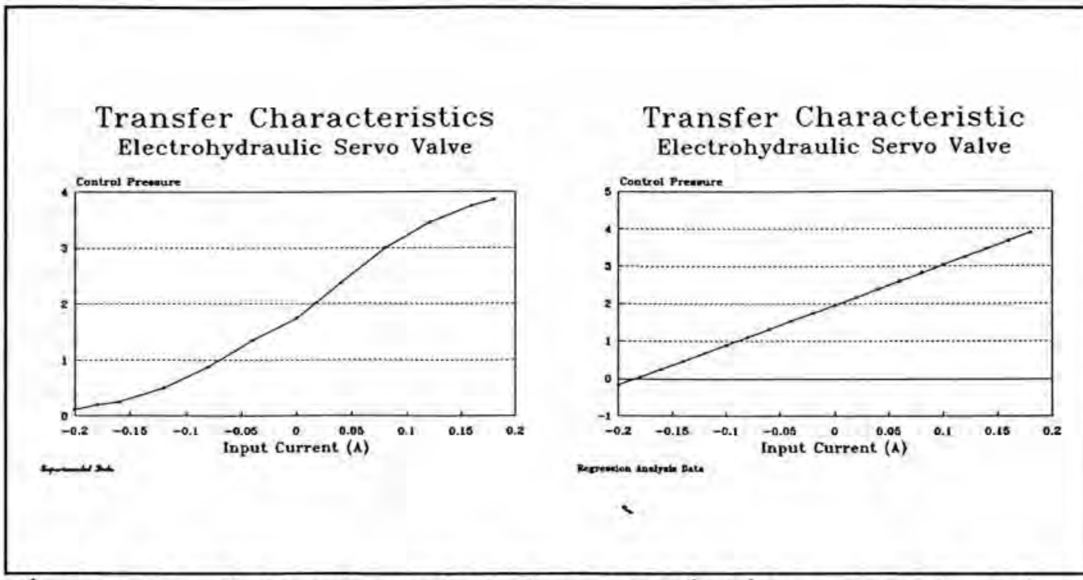

Figure 19- Valve transfer characteristics, actual and linearized.

Section B: <u>Frequency Domain Analysis</u>-

Using the above transfer function it is possible to obtain a theoretical representation of the systems frequency domain characteristics. The theoretical frequency response for the system is shown in Figure 20. This theoretical frequency response was found by inputting the transfer function into Matlab™ computer software. The actual frequency response determined by testing the system is shown in Figure 21.

The results obtained from the frequency response analysis of the model yielded a cut off frequency of approximately 40 Hz. This cut off frequency value corresponds to the value obtained from the actual system, the main difference between the two being that the resonant peak is more pronounced on the theoretical model results.

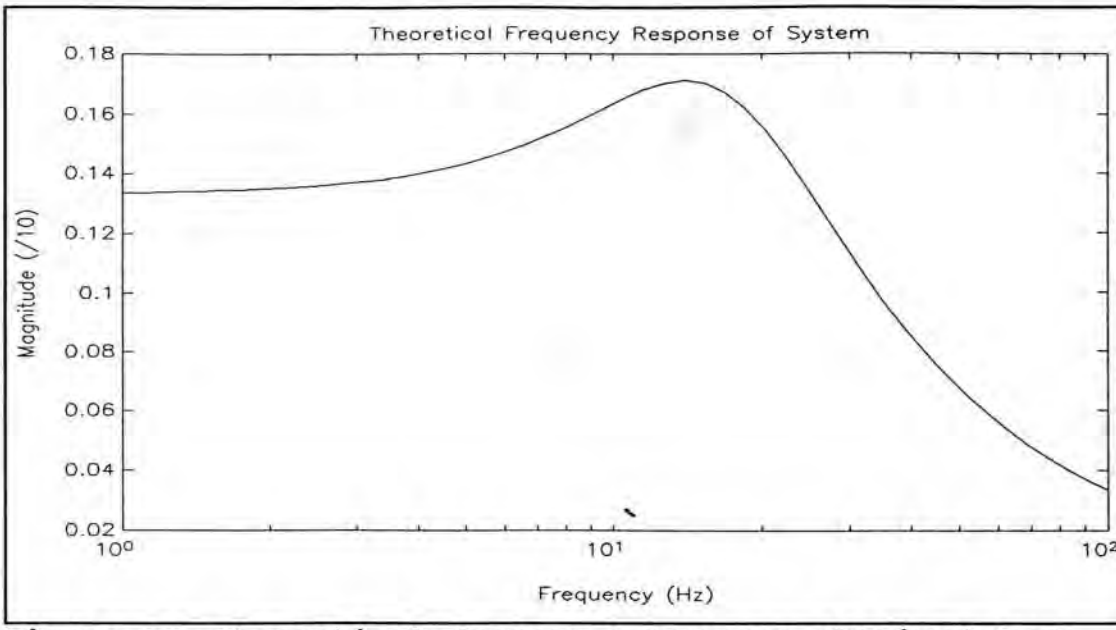

Figure 20- Theoretical frequency response obtained from model.

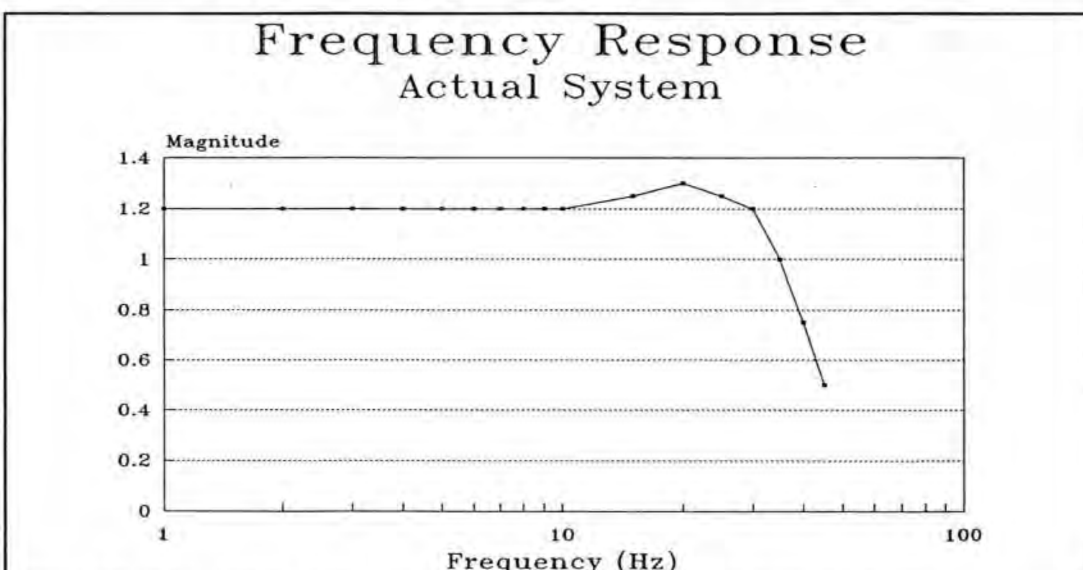

Figure 21- Actual frequency response of system.

Section C: <u>Time Domain Analysis</u>:

Using the mathematical model it is also possible to obtain a theoretical system response in the time domain. A typical measure of a systems ability to respond to inputs is it's ability to follow a step input. The response to the model of the system to a step input is shown in Figure 22. The corresponding actual system response to a step input is shown in Figure 23.

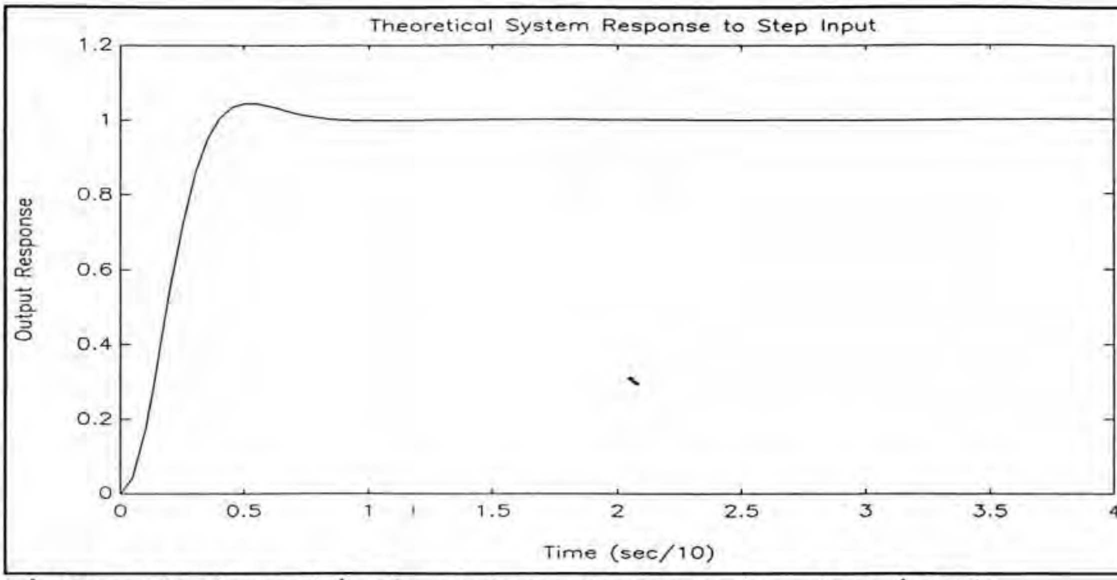

Figure 22-Theoretical system response to step input.

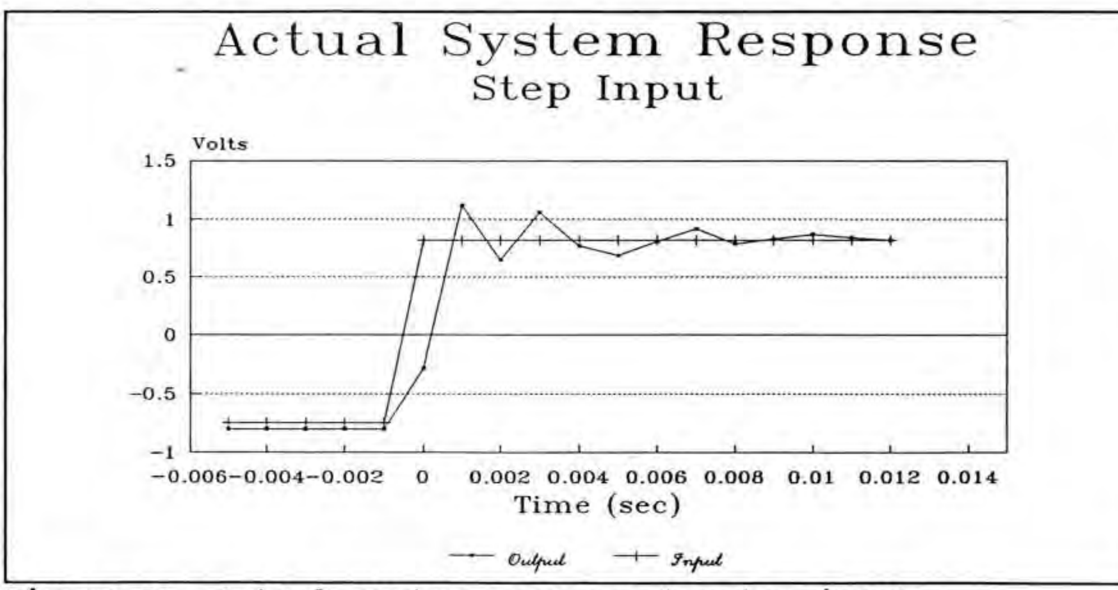

Figure 23- Actual system response to step input.

The step input response analysis showed that the actual system had slightly higher overshoot and a slightly longer settling time than the theoretical system response.

Section D: Stability Analysis:

By examining the denominator of the model for the system, it is possible to obtain the characteristic equation for the system, which can be examined to determine the system's stability. A system is defined as asymptotically stable if for an input of zero, the output of the system goes to zero as time goes to infinity. The Routh-Hurwitz criteria is one means of establishing the stability of the system. By forming the Hurwitz matrix, the number of poles in the right hand plane can be determined, by the number of sign changes in the first column of the matrix. A necessary condition for stability is no poles of the system are located in the right half plane. The Hurwitz matrix for the model of the system is shown below.

s^3:	1	316.9
s^2:	24.8	49.7
	b_1	b_2

Where:

b_1= ((24.8*316.9)-(1*49.7)) / 24.8 = 314.9

b_2= 0

Since the values in the left hand column are all positive, there are no poles in the right hand plane for the system and, for the values and assumptions given, the system is stable.

This concluded the system testing portion. A discussion of the results obtained in this section can be found in the conclusion (Chapter IV).

CHAPTER IV.

CONCLUSION

The system developed showed results that were within the preliminary specifications given for the perfusion system. As discussed in Chapter I, the coronary pressure control system needed a frequency response that would have a cutoff frequency greater than 30 hertz. The analysis in Chapter III showed that the experimentally determined cut off frequency of the actual system was approximately 40 Hertz. Therefore, the frequency response criteria was met.

Another important specification was the stability of the system. The control system for the coronary pressure needed to be asymptotically stable to assure the reliability of the system. The Routh-Hurwitz stability analysis in Chapter III showed that the system was stable for the specified gains. This was verified by experimental data to show the system followed inputs without going into oscillation.

The system showed an actual response to step input that was fairly close to the ideal response shown by the model. This response to step input can be improved by changing some of the gain parameters. The parameter with the greatest effect on the transient response is the derivative gain constant, K_d. However, increasing the derivative gain constant can have an adverse effect on the stability of the overall pressure control system. This is due to the fact that the derivative element is anticipatory in nature and in real world applications tends to amplify the derivative of the noise, along with the derivative of the error signal.

Thus the system was able to be designed to meet all the preliminary design criteria initially set forth, and a workable control system for the coronary perfusion system was successfully developed.

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