Computer-based control of an artificial heart system

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Computer-based control of an artificial heart system

by

David Randolph Carroll

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>LITERATURE REVIEW</td>
<td>5</td>
</tr>
<tr>
<td>Artificial Ventricles and Their Control</td>
<td>5</td>
</tr>
<tr>
<td>APPARATUS</td>
<td>26</td>
</tr>
<tr>
<td>Computer System</td>
<td>26</td>
</tr>
<tr>
<td>Artificial Ventricle</td>
<td>29</td>
</tr>
<tr>
<td>Pneumatic System</td>
<td>31</td>
</tr>
<tr>
<td>Electronic Control System</td>
<td>35</td>
</tr>
<tr>
<td>DETERMINATION OF THE CONTROL ALGORITHM</td>
<td>53</td>
</tr>
<tr>
<td>Manipulated Variables</td>
<td>55</td>
</tr>
<tr>
<td>Controlled Variables</td>
<td>70</td>
</tr>
<tr>
<td>Controller</td>
<td>81</td>
</tr>
<tr>
<td>Gain Constants</td>
<td>93</td>
</tr>
<tr>
<td>EVALUATION OF PERFORMANCE</td>
<td>98</td>
</tr>
<tr>
<td>In Vitro</td>
<td>98</td>
</tr>
<tr>
<td>In Vivo</td>
<td>104</td>
</tr>
<tr>
<td>CONCLUSIONS AND RECOMMENDATIONS</td>
<td>117</td>
</tr>
<tr>
<td>LITERATURE CITED</td>
<td>122</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>135</td>
</tr>
<tr>
<td>APPENDIX: SOFTWARE</td>
<td>136</td>
</tr>
<tr>
<td>Program Abstracts</td>
<td>136</td>
</tr>
<tr>
<td>Subroutine Abstracts</td>
<td>140</td>
</tr>
<tr>
<td>Program Listing</td>
<td>145</td>
</tr>
</tbody>
</table>
INTRODUCTION

The past decade has been a period in which great progress has been made toward a better understanding and treatment of cardiovascular diseases. Advances have been made in the detection and control of cardiac arrhythmias with drugs and electrical pacing. The advent of the heart-lung machine made possible the open heart procedures for correction of inborn and acquired heart diseases. Advances in materials research have made possible the fabrication of reliable, and biologically compatible artificial heart valves to replace those too badly damaged to be repairable. Artificial arteries of synthetic materials have been developed to replace diseased arteries.

In spite of this work, however, cardiovascular disease remains the number one killer in the United States today. There were over one million deaths from diseases of the cardiovascular system in the United States in 1969. Of these deaths, more than 600,000 were from myocardial failure or ischemic heart disease due to coronary insufficiency (Statistical Abstracts, 1971). It has been estimated that possibly half of these people could have been helped by some sort of mechanical circulatory assistance if it had been available (DeBakey, 1971a).

Cardiologists have long recognized the therapeutic value of rest to the acutely insulted heart. The period of rest
allows the heart to recuperate by reducing its workload. The rationale behind this therapy is that failure of the heart results from an imbalance in the energy expended by the myocardium and the energy supply available to the myocardium. The period of rest prescribed by the physician acts to reverse myocardial failure by reducing the myocardial energy expenditure (Galletti, 1967).

The usual case, however, is that a patient who has suffered an acute myocardial infarction arrives at the hospital in a state of cardiogenic shock (Hall, 1967). The mortality rate of such patients is understandably very high. The myocardium has degenerated to the point where its ability to pump blood is not sufficient to supply its own needs nor that of the other organs of the body. The heart has been caught up in the positive feedback of cardiac failure. That is, the impending heart failure results in a decreased aortic pressure which results in a decreased coronary circulation which further reduces the viability of the myocardium.

For this class of patient there is little clinical alternative but to provide some mechanical assistance to the failing heart. Such assistance must provide circulatory support for the body as well as sufficient coronary perfusion to reverse the myocardial failure.

The type of assistance provided would depend upon the
degree of pump failure and could range from simple assist
techniques such as intra-aortic balloon pumping to total
heart replacement. Determination of the device to be used
depends largely on the extent of the damage to the myo-
cardium. The more severe the damage, the more assistance
is required. If the myocardial damage is severe enough to
warrant total heart replacement, there are only two possi-
bilities. The first is the cardiac allograft or transplant
and the second is the artificial ventricle.

The transplanted heart would seem to be preferred
over an artificial ventricle because of its ideal size,
shape, efficiency, and inherent controllability (Shumway, 1967). However, the still serious problem of tissue rejec-
tion by the recipient body remains to be satisfactorily
overcome. Furthermore, the limited number of suitable
donors as well as the legal and moral issues which are
raised by the removal of a vital organ from a human being
act to severely limit the usefulness of the cardiac allograft
as a prosthetic device (Kolff, 1965; Shumaker, 1968).

The artificial ventricle, unfortunately, is not with-
out problems of its own. The primary problems are related
to pump design, pump control, materials research, and
power source design (DeBakey, 1971a, 1971b; Hall, 1967;
Koss, 1971a). There does not appear to be any reason to
think that any of these problems are without solution. In
fact, year by year, important advances are being made by multidisciplinary research groups with members from both the biological and physical sciences. The feasibility of the idea of an artificial ventricle as a prosthesis has been amply demonstrated by the ability to maintain animals on a total mechanical heart for periods in excess of 100 hours (Kwan-Gett, 1971; Takano, 1971; Kawai, 1971) and even more dramatically by Dr. Cooley who used two mechanical ventricles to support the circulation of a human adult for 64 hours (Cooley, 1969a). Much work remains to be done, however, before the artificial ventricle becomes a useful clinical tool.

This dissertation documents the development and evaluation of a computer-based control and instrumentation system for an artificial ventricle. The system uses a small general purpose digital computer which has been programmed to input the pertinent physiological data, perform the required calculations and issue the necessary commands to alter the fluid output of the artificial ventricle. The electronic circuitry necessary for this system, as well as the computer software, has been designed for maximum flexibility so that the system is more suited as a research vehicle than as a clinical tool. This flexibility enables the researcher to make changes in the control algorithm even as an experiment is in progress.
LITERATURE REVIEW

Artificial Ventrices and Their Control

An artificial ventricle system is composed of four essential elements (Mrava, 1970). These elements are the energy source, the power conversion unit, the pumping element and the system controls. This dissertation is primarily concerned with the system controls, although of necessity in work of this nature, the other elements must be considered as well. The purpose of this chapter, then, is that of presenting a review of the literature as it pertains to the control of the artificial ventricle. It is necessary, however, to present a brief review of the energy sources, power conversion units and pumping elements in order to adequately relate the system controls to the overall artificial ventricle system.

The pumping element of the system is that which transmits the propulsive energy to the blood. Typically, the pumping element is a variable-volume container. Pumping takes place by reducing the volume of the container. This action imparts a force to the blood causing it to flow into the arteries against the arterial pressure head. At the completion of the pumping cycle, the container will increase in volume resulting in its filling. This filling may be passive or it may be enhanced by a suction effect.
If the variable volume container is a compliant sac, the system is termed a sac heart. If it is a rigid container divided by a compliant membrane, it is called a diaphragm pump. If it is a tube in which the fluid is massaged from one end to the other, it is termed a roller pump or collapsing tube pump depending upon the means of forcing the blood along the tube. The use of an ordinary centrifugal or impeller pump has also been reported (Bernstein, 1970).

Electrical energy has been used to power the majority of artificial heart devices although radioisotope heat sources have recently been used (Hastings, 1970). Power conversion is normally accomplished mechanically with a gearing arrangement, pneumatically by compressing a gas, hydraulically with a liquid in a closed system, or thermally with a heat engine. To illustrate the above concepts, representative systems from the literature will be cited.

One of the earliest artificial ventricles, constructed and used by Kusserow in 1958, was termed a diaphragm-type blood pump although it more closely resembled a piston-type pump. Kusserow's diaphragm was made of a stainless steel disc with a thin peripheral rim of flexible rubber. The center disc, which was much larger than the rim of rubber, insured positive displacement of fluid during each stroke. The diaphragm was actuated by a small AC
motor which was directly coupled by a mechanical assembly to convert the rotary motion of the motor to the alternating translational motion necessary for pumping action.

A later version of the same pump was powered by an electromagnetic solenoid (Kusserow, 1959). The movable core of the solenoid was attached directly to the pumping diaphragm. This resulted in a simpler and more durable drive mechanism than was previously used.

In an attempt to obviate the requirement for wires or tubes passing through the body wall, Kusserow (1960) later designed an artificial ventricle system in which the completely implanted pumping element could be powered without the use of any direct connections through the body wall. The implantable pump was identical to his diaphragm pump described earlier (1958). In the improved system, the electric motor was replaced by a permanent Alnico bar magnet which was attached in such a manner that its rotation produced the pumping action of the diaphragm. Rotation of the pump magnet was produced by its interaction with an externally generated rotating magnetic field. The external magnetic field was produced by a motor-driven Alnico magnet placed near the skin overlying the implanted pump.

Most piston-type blood pumps utilized a rolling diaphragm or Bellofram to join the piston to the cylinder
wall. The piston and Bellofram moved in a loose fitting cylinder with the Bellofram creating the blood seal. Such an arrangement reduced both friction and consequent damage to the cellular elements of the blood.

Because a piston-type artificial ventricle with a direct connection to its driving motor is a fixed displacement pump, subatmospheric pressures may be developed during diastole if the return flow of blood to the pump is insufficient. This low pressure may result in collapse of the veins or the introduction of an air embolism and ensuing death. On the other hand, if the venous pressure is allowed to become too high, pulmonary or systemic edema will occur (Pierce, 1962). Pierce et al. (1963) and Burney et al. (1963) used a venous pressure transducer and servo-mechanism to control the speed of a drive motor in a positive displacement pump in order to maintain a physiological level of venous pressure. Burns et al. (1965a) used a piston type pump which was driven by a variable-speed motor and a mechanical arrangement so that stroke volume could be varied independently of rate. Adjustment of cardiac output was made manually by a change in rate or stroke volume.

A commercially available centrifugal pump driven by an electric motor was tested by Saxton in 1960. During in vitro pumping, they found that this pump caused some damage to the red blood cells as evidenced by a reduction
in hematocrit. They also noted that the output of the pump was sensitive to both the output and input pressures. This suggested to them that no external regulating mechanism would be necessary for long-term use of pumps of this sort. During in vivo trials involving two such pumps in a total heart replacement, however, they found that it was absolutely essential to monitor both atrial pressures and to make manual adjustments to the pumps until approximate balance of right and left atrial pressures was established. They found that in order to keep the left atrial pressure below 20 cm H$_2$O, they were required to reduce the rate of right ventricular flow, presumably at the expense of right atrial pressure.

An improved centrifugal pump for artificial heart work was reported by Bernstein et al. in 1970. The design of this pump emphasized the minimization of pump surface area exposed to blood and the reduction of turbulent flow. This open impeller pump produced a significant reduction in blood cell destruction. The energy source utilized was a small DC electric motor. The power transmission was effected by a magnetic coupling through the chest wall similar to that of Kusserow (1960). Preliminary in vivo evaluation of the pump was carried out in calves in a left ventricular bypass configuration with promising results (Dorman, 1969).
Roller pumps have been used for artificial heart work (Esmond, 1961; Pierson, 1962, 1965; Pierce, 1967; Turner, 1967). Their widespread use can probably be attributed to their structural and operational simplicity. Because of the roller pump's design, however, there can be appreciable backflow unless it is operated either at high speed or with a high degree of occlusion. Both of these conditions result in a high level of hemolysis (Pierson, 1965).

In an attempt to protect the blood cells from damage, a roller pump was built which attempted to cushion the cells (Akutsu, 1960a). This pump employed a small roller which rotated within a larger housing lined with a sheet of polyurethane foam. Within the housing, between the roller and the foam, were two polyurethane ventricles. The ventricles were placed opposite one another within the housing so that each was compressed alternately as the roller passed. The foam against the housing wall provided a yielding surface against which the ventricles were compressed, thereby minimizing damage to blood cells.

Another improvement in the roller pump was obtained by the use of flat rubber tubing in which the interior was segmented into small chambers by bicuspid valves (Pierson, 1965). The use of this tubing increased the efficiency of the roller pump by minimizing backflow, thus allowing a reduction in input power. Because less complete occlusion
of the valved tubing was necessary, damage to the blood cells was reduced.

It has been stated that one serious disadvantage of a roller pump is that the fluid output is of a nonpulsatile nature and quite unlike the pulsatile output of the natural heart (Many, 1968; Nakayama, 1963; Mandelbaum, 1965). Hoffman (1970) reported the use of a roller pump which did produce a pulsatile flow. The roller pump was driven by a DC motor which was electronically controlled so that rate, systolic duration, and stroke volume could be independently varied.

Another type of artificial ventricle which has been widely used is the sac-type. Saxton in 1959 described an early sac-type artificial ventricle which was fairly typical of later ventricles of this type. The ventricles were constructed with semi-rigid plastic outer casings enclosing pliable blood sacs. During diastole, blood flowed into the distensible sacs. During systole, the introduction of a fluid under pressure into the space between the rigid outer wall and the pliable blood sac acted to eject the blood from the sac. Energy was imparted to the working fluid by a pumping system consisting of two pistons driven in tandem by an electric motor. A mechanical linkage maintained a 2:1 ratio of diastole to systole and permitted a variable stroke volume. The use of a closed hydraulic
driving system resulted in a fixed displacement pump. Because there was no way to accurately match the output of the pump to venous return, in vivo trials ended in death due to air embolism.

The use of a sac-type ventricle which utilized an arrangement of electromagnetic solenoids to provide energy to pump the blood has been described (Norton, 1970). The pump was a dual ventricle device in which the blood flowed into distensible blood sacs during diastole. During systole, the solenoids forced oil, by means of a diaphragm arrangement, against the blood sacs. This action of the oil forced the blood from the sacs into the arteries. The only control of this device was by means of a timer circuit with which rate and duty cycle could be set. Disadvantages of this system included its size, weight and heat production (During in vivo trials, the temperature of the implanted system reached 47°C.)

Another early version of a sac-type heart (Akutsu, 1960, 1961; Houston, 1960) utilized a mechanical compression of the compliant ventricles to eject the blood. The ventricles were suspended within a rigid housing with a pendulum between them. A small electric motor and gearing arrangement caused the pendulum to swing back and forth within the rigid housing. With each oscillation, the pendulum compressed each ventricle alternatively against
the housing causing ejection of the blood.

Burns et al. (1965b) reported the development of another sac-type artificial ventricle which utilized a closed hydraulic driving system. This system consisted of an electric motor and pump which supplied hydraulic fluid, under pressure, to a main fluid switching valve. The valve directed the fluid to the two ventricular chambers where it acted to expel the blood. During the diastolic portion of the cycle, the hydraulic fluid was returned to a reservoir.

Pneumatically driven sac-type artificial ventricles have become widely used (Nakamura, 1969; Serres, 1970). One advantage in using compressed gas as a driving mechanism is the lack of complexity and the ease of control. It has been found that a smooth and easily regulated pumping effect can be obtained from a pneumatically-operated chamber whose source of power is a compressed gas (Hufnagel, 1958).

A sac-type artificial ventricle can be extremely light, compact and reliable (Seidel, 1961). Because the power source need not be contiguous with the ventricle, the size and shape of the sac-type heart can be made to closely approximate the natural heart. This configuration facilitates intra-thoracic implantation.

The pneumatic systems utilized in gas driven ventricles can be either open or closed systems (Liotta, 1962). In
a closed system, air or other suitable gas is pumped in alternate directions by a mechanical pump. The action of the periodically compressed volume of gas on the compliant blood sac ejects the blood. The closed pneumatic driving system is similar to the hydraulic driving systems previously discussed.

An open pneumatic system relies on a source of high pressure gas which, during systole, is applied to the pumping chamber of the ventricle to eject the blood. During diastole, the pumping chamber of the ventricle is vented to the atmosphere to exhaust the air chamber and to allow the blood sac to refill. A ventricle with an open pneumatic driving system is not a fixed displacement pump. Filling pressure, to a great extent, determines the degree of filling of the ventricle (Kwan-Gett, 1970). If the driving system is adjusted properly, the result can be a self-regulating system. In order to enhance the filling of a ventricle utilizing an open pneumatic driving system, a moderate vacuum may be applied to the air chamber of the ventricle during diastole. This aids in exhausting the driving air and applies a gentle suction to the venous blood.

A disadvantage of an air-driven ventricle is that the output of the pump is related to the output pressure as well as the input pressure. Since the output is inverse-
ly proportional to systemic blood pressure, it becomes necessary then, to regulate the driving air pressure in response to cardiac output and peripheral resistance changes (Wakabayashi, 1970; Kwan-Gett, 1969; Seidel, 1961).

An example of a sac-type ventricle which utilized a closed pneumatic system was one in which an electric motor alternately compressed and expanded a polyethylene bellows (Kimoto, 1964). The positive or negative pressure in the bellows was transmitted to the artificial ventricle through vinyl tubing.

A major disadvantage of the sac-type artificial ventricle is that it may produce high rates of red cell hemolysis (Kwan-Gett, 1970). This is thought to be due to the opposite walls of the highly compliant sacs coming into contact as they collapse during systole. Those cells trapped between the walls are subjected to physical injury. This contact could be avoided by the use of controls to avoid complete emptying of the sac but this would add to the complexity of the system.

It is possible to design a blood pump using a diaphragm rather than a sac as the compliant element. If the size and shape of the blood chamber and diaphragm are chosen so that it is impossible for the diaphragm to come into contact with the opposite wall, damage to the blood cells due to such crushing may be avoided. Kwan-Gett et al.
(1970) felt that such a design would retain the basic simplicity of the sac-type ventricle in both the prosthesis and the driving system.

A relatively atraumatic pump was described by Akers et al. in 1966. The pump was designed for minimum trauma to the blood. In order to reduce the possibility of thrombus formation, the inner surfaces were lined with nylon velour. This material tended to anchor fibrin deposits and rapidly produced a lining of living cells within the pump.

The use of diaphragm pumps has been relatively successful in *in vivo* trials (Liotta, 1967; Kwan-Gett, 1970, 1971; Ross 1971b; Lyman, 1971) and in clinical cases (DeBakey, 1971b).

The use of a diaphragm-type ventricle with a mechanical-hydraulic driving arrangement has been used by the Edinburgh Artificial Heart Group (Knight, 1971). They felt that the control of a pneumatically driven ventricle was needlessly complicated. Their driving mechanism consisted of a mechanical actuator whose motions were transmitted to the end plates of a pair of bellows. The force imparted to the bellows was transmitted via an incompressible fluid to the driving chamber of the blood pump.

A disadvantage of most of the artificial ventricles discussed so far is the requirement for valves to insure
the unidirectional flow of blood. Most artificial heart valves contribute to thrombus formation within the ventri­cle (Nose, 1967b). In an effort to overcome some of the disadvantages of conventional artificial heart valves, the "Wave Pulsating Blood Pump" was built (Mrava, 1969). This device consisted of a compliant blood tube within a rigid housing. The introduction of air under pressure in the space between the tube and the housing compressed the tube and expelled the blood within the tube. To insure unidirectional flow, the outflow end of the tube was sur­rounded by a pneumatic element which was inflated during diastole, thus occluding the outflow end of the tube and preventing retrograde flow. The compliant tube was con­structed so that at the onset of systole, the inflow end of the tube collapsed first, preventing backflow. The collapse of the tube proceeded in a wavelike manner forcing the fluid through the now-relaxed outflow valve.

A two-ventricle "Wave Pulsating Total Heart" was de­signed using the principle of the "Wave Pulsating Blood Pump" except that an overall shape similar to that of the natural heart was used (Klain, 1970). Advantages of this device included its improved hemodynamic performance, reduction in thrombogenic sites, and its size and shape which permitted implantation within the pericardial sac.

An interesting and novel approach to the design of
artificial ventricles was reported in 1971 by Sawyer et al. Human cadaver hearts were used as mold masters to form polymer pumping chambers in the exact form of the natural heart. Actuation of these ventricles was achieved by artificial muscle segments. These muscle segments were made of a contractile alloy. A major limitation in this particular ventricle was the cycle time of approximately five seconds for the contractile segments. *In vitro* tests indicated a capability of flow of approximately one half liter per minute at physiological pressures.

The early literature on the use of artificial ventricles included very little on the control of such devices. This was perhaps partially due to the construction of some of these pumps which made them inherently self-compensating. Akutsu and Kolff, in 1958, described an air-driven artificial ventricle which exhibited self-regulation. The filling of this pump was entirely passive and related to the input blood pressure. The air driving pressure was adjusted to insure complete emptying of the ventricle each cycle. The stroke volume then, was a function of venous return. In order that a pump of this type be sensitive enough for good regulation, the resistance to blood flow into the ventricle must be very low. This inflow resistance is equal to the sum of the resistance of the inflow valve, the resistance of the blood sac to flexion and the resist-
ance presented to the exhausting gas or hydraulic fluid (Kwan-Gett, 1970).

Fry in 1961 discussed the necessity of a flexible blood chamber to compensate for variations in venous return. He reported the use of a pump in which the flexibility of the blood chambers resulted in a variable stroke volume even with a prime mover of fixed stroke.

The design of the compliant chamber or blood sac is extremely important, then, in obtaining an artificial ventricle which is sensitive to atrial pressure. Kwan-Gett et al. (1969) plotted cardiac function curves for ventricles with highly compliant and less compliant blood sacs. These curves emphasized the lack of sensitivity of a ventricle with the less compliant sac.

Hastings et al. (1961) developed a ventricle which was sensitive to return flow. This group recognized that venous return under normal conditions varied significantly and that any pump with a fixed displacement was not suitable to meet the demands of normal variations in venous return. Their pump was a two-chambered diaphragm-type pump with a stroke volume greater than that of a large dog (50 ml). In order to enhance filling at low atrial pressures, a slight negative pressure (10-15 cm H₂O) was applied to the diaphragm by spring tension. To allow adequate time for filling, the diastolic period was approximately six times
as long as the systolic period.

In order for a self-regulating, constant stroke volume ventricle to function properly, the rate must be adjusted for the greatest anticipated value of venous return. If this is not done, it is possible that the pump will not be able to accommodate all of the venous return under conditions of high flow and the venous pressure will increase. Newman in 1958 described an artificial ventricle with a rate control which made the system responsive to venous return without continuous operation at a high rate. The ventricle described by Newman was a diaphragm-type pump driven by compressed air. A switch contact was attached to the diaphragm so that when the ventricle was full and the diaphragm was extended, a solenoid valve was actuated which permitted the air under pressure to eject the blood from the pump. A second contact caused the solenoid valve to be inactivated and the air exhausted from the ventricle at the completion of the pumping cycle.

A similar arrangement was used by Kwan-Gett et al. (1969, 1970). They used a driving system which was activated by a signal from a switch within the ventricle. The driving system activated the pneumatic system to provide a pulse of air of fixed duration and amplitude. The stroke volume remained constant then, while rate varied as a function of the venous return.
The use of the EKG signal to synchronize an artificial ventricle in a partial bypass configuration has been quite common (LaFarge, 1968; Akutsu, 1968; Fuller, 1968). Normally, a timing circuit is set to trigger the ventricle on the R wave of the EKG signal. Delay circuits were frequently incorporated so that the artificial ventricle could be activated at any time in the heart cycle. If a reliable control signal could not be derived from the EKG due to movement artifact or fibrillation, the artificial ventricle could be operated at a fixed rate and the natural heart could be paced with the same triggering signal (LaFarge, 1968; Mrava, 1970).

The most common method of closed-loop control of an artificial ventricle has been by means of varying the pump output in response to venous return. The most prevalent method of transducing venous return has been by a direct measurement of atrial pressure.

Pierce et al. (1962) used an electronic servomechanism to add or subtract a given increment of pump speed when atrial pressure exceeded or fell below certain preset values. This same servomechanism was later used to control an implantable roller pump (Pierce, 1967). Burney et al. (1963) created an error signal by comparing atrial pressure with a reference atrial pressure. This error signal was used to vary the speed of a pump which, in turn, reduced
the error signal to zero.

Klopp et al. (1969) used the integral of the atrial pressure to vary the systolic duration of a pulsatile roller pump. Pulse rate and peak flow were held constant. In 1971, Klopp et al. reported the use of a similar system to control the rate of a hydraulically actuated blood pump.

In an attempt to obtain an aortic pressure waveform which was similar to that created by the natural heart, a variable waveform pressure generator was built (Miller, 1962). Compressed air was routed to the artificial ventricle via variable area orifices or servovalves. The area of the servovalve was proportional to an input current. A programable electronic function generator provided the current input to the servovalve. It was possible to create an electronic waveform which, when applied to the servovalve, resulted in the desired air pressure waveform and, ultimately, the desired aortic pressure waveform.

Nose' et al. (1967a) used a similar pressure servomechanism in a closed loop control system with atrial pressure as the controlled variable. The error signal, which was the difference between the actual and desired atrial pressures, modulated the amplitude of the waveform applied to the servovalve. Thus, the driving air pressure was varied in response to the atrial pressure.
Although this system was highly responsive to venous return, oscillations in atrial pressure and pump output were observed under certain conditions (Wildevuur, 1968). In an attempt to eliminate the oscillatory behavior of the system, the control algorithm was changed to include integral as well as proportional control. This allowed the proportional gain to be reduced while still eliminating the steady state error. The artificial atrium used by this group exhibited a nonlinear compliance characteristic. As a result there was a nonlinear relationship between atrial volume and pressure. Since the system was to be responsive to venous return or atrial volume, a linear relationship between atrial volume and pressure was desired. In an attempt to establish a true atrial volume sensor, conductive rubber was used in the construction of the atrium. The resulting volume measurements were found to be lacking in linearity and repeatability.

The use of a fluid amplifier led to the development of a control system for an artificial ventricle which was responsive to venous return. It provided the switching logic for the system with no additional requirement for power other than the driving air pressure (Woodward, 1966). Flow rate of the pump was governed by the rate of filling of the ventricle. Because of the extreme inherent simplicity of the fluid amplifier control system, it exhibited
high reliability. A series of *in vivo* experiments with calves showed the system to be extremely sensitive to venous pressure (Nose, 1970).

The use of arterial pressure as a control parameter was reported by Kwan-Gett *et al.* (1968). The system described used both atrial and arterial pressure as controlled variables, each acting to vary cardiac output according to its own requirements.

The use of venous oxyhemoglobin concentration in conjunction with atrial pressure as control parameters was reported by Cholvin *et al.* (1966, 1967), and Erickson *et al.* (1966). The advantage of such a control scheme was that the oxyhemoglobin concentration gave an indication of the metabolic needs of the tissues while the atrial pressure insured proper balance of blood between the pulmonary and systemic circulations.

With the increase in the availability of the small dedicated mini-computer, its use in the control of the artificial heart seems assured. Indeed, a computer-based optimal controller for a class of cardiac assist devices, the intra-aortic balloon pump, is already a reality (Kane, 1971). Furthermore, the use of an optimal controller for an artificial ventricle has been studied (Spyker, 1968, 1970, 1970a).

Kane *et al.* (1971) applied the techniques of optimal
control theory to obtain the desired clinical goals of intra-aortic balloon pumping. The system attempted to maximize mean systemic pressure by means of diastolic augmentation and to control end-diastolic ventricular pressure at an appropriate value. The control system realized these goals by proper timing of the inflation and deflation of the balloon. When evaluated on a mock circulation, the control system was able to achieve a better performance than that obtained by conventional open loop control schemes using the EKG signal for the timing of balloon inflation and deflation.

Spyker (1970a) studied the optimal control problem as it related to an artificial ventricle used in a left heart bypass configuration. He utilized a computer simulation of both the cardiovascular system and the artificial ventricle to develop the control algorithm. By using cardiac output, pump output, time tension index and flow work in the performance criteria, he was able to determine optimum timing of the bypass ventricle.
APPARATUS

The experimental apparatus described in this chapter includes the artificial ventricle which pumps the blood, the pneumatic air system which provides power to the ventricle, the electronic control circuitry which actuates the valves of the pneumatic system in the proper way so as to cause the ventricle to pump at the proper time with the necessary force, and finally the computer which exercises overall control over the entire system. The system has been designed with a great deal of flexibility in order to enhance its usefulness as a research tool.

Computer System

The basic element of the control system to be described is a small digital computer with its associated peripheral equipment. The computer is a general purpose, 12 bit machine available for off-the-shelf purchase and commonly referred to as a minicomputer because of its small size and portability. The basic memory of the machine consists of eight thousand words of magnetic core memory complemented by a cartridge-type magnetic tape unit. The unit has two tape cartridges each with two loops of tape up to 150 feet in length. This results in a storage capacity of approximately 240 thousand 12 bit words when recorded in blocks of 32 words.
The primary communication between the digital computer and the rest of the control system is by means of analog to digital (A/D) and digital to analog (D/A) conversion circuits. These circuits enable data to be converted between the analog and digital forms. Four D/A converters transform a ten-bit word of digital data into an analog voltage at a level of zero to ten volts. The A/D converter inputs analog data from one of sixteen signal lines or potentiometers and converts it into a ten-bit digital word. The time required for the A/D converter to sample the analog data, convert it to digital form and store the digital word in memory is approximately 15 μsec. The D/A conversion sequence requires approximately 4 μsec (Swift, 1972).

Additional signal input capability exists by means of six sense lines. Machine instructions exist which allow the signal level at a particular sense line to be tested by the computer. If the signal level at that line is below one volt, the program skips one instruction. This feature allows clocking or synchronization by an external signal. There are also six sense switches on the front panel of the computer. Machine instructions exist which allow a program skip when a sense switch is off. This allows some element of on-line program control by the operator who may direct the computer to execute certain segments of the program by the positioning of the sense switches.
Data may be displayed visually in several different ways depending upon the speed of display and the permanence of the record required. A storage oscilloscope which operates under program control provides a rapid and continuous display of data. The presentation of data on the storage oscilloscope is enhanced by a character generation capability which permits labeling of the display with alphanumeric characters. A more permanent display is provided by use of a strip chart recorder or an X-Y recorder driven directly by the D/A converter lines. A teletype is also available for display and is used primarily for the display of typewritten communications with the operator.

Six software-controlled relays with front panel mounted indicator lights are available. If desired, the lights may be used without the relays to output information. A typical use might be to indicate when the computer is executing a particular segment of the program.

The primary timing capability is provided by a hardware clock which operates under program control. The clock may be operated in an interrupt mode such that when a predetermined time has elapsed, the computer program is interrupted or it may be operated in a free running mode where the computer program must query the clock to determine elapsed time between two events.
The computer, with its computational, data handling, and timing capability, provides the essential nucleus for control of the entire system.

Artificial Ventricle

The artificial ventricle used in this study is a hemispherical, diaphragm-type pump utilizing compressed air as the energy source (Figure 1). The artificial ventricle system which included the valves, tubing and atrium was designed for maximum efficiency and minimum blood trauma (Spehr, 1972). The inflow side included a highly compliant atrium and a disc valve. A Gott valve was used in the outflow tract. The diaphragm, molded in a parabolic shape, was made of a polyurethane material which is very durable and has very atraumatic surface properties (Akutsu, 1967). The use of polyurethane in artificial hearts in vivo indicated that polyurethane was nonthrombogenic and was blood compatible (Lyman, 1971). The back surface of the air chamber was made of transparent plexiglass so that the movement of the diaphragm could be visually observed. The inner surface of the pump was coated with medical grade Silastic to reduce damage to the blood. The tubing used with the artificial ventricle was made of a molded polyurethane reinforced with stainless steel wire using the technique recommended by Boretos et al. (1971). This tubing
Figure 1. Schematic drawing of artificial ventricle
was made with a 22 mm inside diameter and was heat set to the required curvature. The dimensions of the pump were such that the diaphragm would not contact the wall of the ventricle during normal pumping. This eliminated one possible source of damage to the cells of the blood. The priming volume of the ventricle was 167 ml with a stroke volume of 100 ml. In tribute to the designers and manufacturers of the ventricle it should be pointed out that in the approximately 300 hours that the system has operated, there has never been a failure of an integral part of the pump, nor has an experimental animal ever been lost due to pump failure.

Pneumatic System

The pneumatic power system and electronic control system is based on a system designed by Swift (1968). The pneumatic power system shown in Figure 2 is designed to meter air under pressure to the air chamber of the artificial ventricle. The compressed air provides the energy to eject the blood from the ventricle. Because the high pressure air source and regulator act as a non-ideal source, variations in air flow delivered to the artificial ventricle result in variations in air pressure at the ventricle. This load dependency of the system has been minimized by use of the accumulator and bypass valve. The accumulator,
Figure 2. Artificial ventricle pneumatic system
which acts as a volume reservoir of compressed air, reduces pressure changes due to load variations. The bypass valve acts as a shunt path for an air flow which is greater than the flow to the ventricle. Because flow to the ventricle is only a part of total flow, variations in pressure due to variation in load will be minimized. In spite of these modifications, the pneumatic system still exhibits a degree of load sensitivity. One reason for this is that the total air capacity of the system is limited by the source so that the flow through the bypass valve is only slightly greater than the flow to the ventricle. The implications of this load sensitivity will be discussed later.

The solenoid air valve is a three-way electromechanical valve which, when energized, meters compressed air to the air chamber of the artificial ventricle. When the solenoid is in the unenergized state, the valve blocks the flow of air to the artificial ventricle and vents the air chamber of the artificial ventricle to the atmosphere. This state of the valve corresponds to the diastolic period of the heart, during which time filling with blood takes place. When the solenoid is energized, air under pressure is pulsed to the air chamber of the artificial ventricle and to the parallel bleed-air valve. This state of the valve corresponds to the systolic period of the heart when ejection of blood from the ventricle takes place.
The pneumatic system is an open system as defined by Liotta et al. (1962). The volume of air used during systole escapes from the ventricle to the atmosphere during diastole. No means is provided for measuring the volume of air pulsed to the artificial ventricle.

The bleed-air valve is placed in the system to enable the driving air pressure delivered to the ventricle to be varied. The valve is a two-way type with approximately ten turns from fully open to fully closed. When the valve is completely open, a portion of the available air is bypassed to the atmosphere so that there is less pressure available to actuate the ventricle. When the valve is completely closed, no air is bypassed and the maximum pressure is available at the ventricle. The valve is driven by a DC motor so that the driving air pressure is continuously variable between limits which are determined by the source pressure. If the regulator is adjusted to deliver air to the air chamber of the artificial ventricle at 100 mm Hg pressure when the valve is fully open, the delivered air pressure is increased to 195 mm Hg with the valve fully closed. It is expected that driving air pressures within the range of 100 to 195 mm Hg will normally be adequate to meet the needs of the system. If not, the pressure may be easily adjusted to the desired value by the regulator knob on the front panel of the controller.
With this pneumatic control system then, there are three possible manipulated variables: rate and duty cycle which are determined by the operation of the solenoid driver valve, and driving air pressure which is determined by the position of the bleed-air valve. Duty cycle is defined as systolic duration divided by heart period.

Electronic Control System

The existing electronic control circuitry as described by Swift (1968) was modified so that the entire system would be compatible with the digital computer. The existing circuitry to operate the solenoid air valve consisted of a control section and a driver section. The control section was essentially a rectangular wave generator with rate and duty cycle independently adjustable by means of panel mounted potentiometers. The driver section consisted of a solid state switching circuit to switch power to the electromagnetic solenoid. The control voltage for the switching circuit was the rectangular wave of the control section. Thus, when the voltage output of the control section was low, the switch was off and the electromagnetic solenoid was unenergized corresponding to the diastolic phase of the heart cycle. When the control section voltage changed to the high state, the solenoid was energized and the systolic phase was begun.
The circuitry to control the bleed-air valve consisted of a power operational amplifier which acted as a driver for the DC motor which operated the valve. The input to the amplifier was a control signal which could be proportional to venous pressure, atrial pressure or oxyhemoglobin concentration.

The output of the operational amplifier was a constant times the input so that the speed of the motor was proportional to the input. There was no feedback from the valve, however, so that the system had no knowledge of the valve position.

In order that the system might be responsive to commands from the computer, as manifested by voltage levels at the output of the D/A converters, circuitry was designed and built which would enable rate, duty cycle and driving air pressure each to be controlled over its entire dynamic range by a computer-supplied voltage from the appropriate D/A converter.

The design criteria of the rate and duty cycle control circuitry were (1) the input was to be a DC voltage from zero to ten volts in magnitude, (2) the output was to be a rectangular wave voltage of proper level so as to be compatible with the existing electromagnetic solenoid driver circuit described above, and (3) the circuit must exhibit a free running characteristic such that, for a
nonchanging voltage at the D/A output, the circuit would continue to output a signal to the solenoid driver circuit at the desired rate and duty cycle. The reason for this requirement was to take advantage of the manner in which the computer handled the D/A voltage output. After the computer performed a D/A instruction and applied a voltage to the D/A output, that voltage remained at the output until another D/A instruction was performed. This last criterion reduced the role of the computer to that of ordering changes in rate and duty cycle only as they were needed rather than being involved in the beat by beat generation of control signals. This left the computer free to perform other essential tasks. The control circuit then, exhibited its own inherent rhythmicity similar to the natural heart and the computer acted to increase or decrease the tone of the system much as the central nervous system behaves in the natural animal.

These design criteria were met by the circuit of Figure 3. This rate control circuit is essentially a sawtooth waveform generator of a variable period which is determined by an external voltage \( V_{HR} \) applied at the reference input of the comparator. The sawtooth waveform is a series of ramp waveforms generated by the integrator as it acts on the DC input taken from the potentiometer. The slope of each ramp is a function of the circuit elements as well
Figure 3. Artificial ventricle rate circuit
as the level of the input voltage. In this case, the circuit elements and the input have been chosen so that the output rises from zero to ten volts in two seconds.

During the time that the waveform is rising, the field effect transistor (FET) is pinched off by the voltage from the inverted output of the monostable multivibrator. During this time, the FET appears as a very large resistance in parallel with the feedback path and has negligible effect on the operation of the integrator. The action of the comparator is to terminate the integrating action and reset the output of the integrator to zero, thus ending the cycle. A comparator is an electronic device which may be used to mark the instant when an arbitrary waveform attains some reference level (Millman, 1965). The integrator is reset then, when the ramp which is applied to the input of the comparator rises above the level of the reference voltage ($V_{HR}$) which is provided by the digital computer. At this time the output state of the comparator changes from low to high and triggers the monostable. The inverted output of the monostable then drops low allowing the FET to conduct, resetting the output of the integrator to zero. The timing elements of the monostable were chosen so that the output pulse is just wide enough to accomplish the reset but no wider. Figure 4 shows the relationship of the waveforms to one another as a function of time.
Figure 4. Waveforms associated with heart rate circuit
Because the ramp input to the comparator is a linear function of time, there is a direct relationship between this voltage and the elapsed time since that particular cycle began. Selection of a given value of voltage ($V_{HR}$) to be applied to the reference input of the comparator corresponds to the selection of a given period of the sawtooth waveform. Since the range of the D/A outputs of the computer is limited to zero to ten volts, the period of the sawtooth waveform theoretically may range from zero to two seconds. In actual practice, the minimum period is limited by the on time of the monostable or the reset time of the integrator to five msec. The actual range in rate is 0.5 to 200 hz. If desired, the lower limit of the rate may be changed by adjusting the potentiometer which determines the input voltage to the integrator. This then, would increase or decrease the slope of the ramp.

The duty cycle circuitry of Figure 5 is based on the same principle as that of the rate circuit. The input to this section is the periodic sawtooth waveform generated by the rate circuitry. This waveform is amplified by an amplifier (gain=2) so that the ramp rises from zero to ten volts in one second. The reason for this increase in slope of the ramp will be pointed out later. The comparator is configured so that its output (Figure 6) goes high
Figure 5. Artificial ventricle duty cycle circuit
Figure 6. Waveforms associated with duty cycle circuit
at the beginning of each cycle and remains high until the ramp reaches the reference voltage \( V_{DC} \). At this time the comparator drops low until the beginning of the next cycle. The output of the comparator is the control signal which is applied to the electromagnetic solenoid driver circuit which opens the solenoid air valve to initiate the systolic period of the ventricle.

Since the ramp input to the comparator rises to ten volts in one second and the maximum output of the D/A converters of the computer is ten volts, the maximum systolic duration is one second. Since the maximum period is two seconds, the maximum duty cycle is 50\% at the minimum rate of 30 beats per minute (BPM). It was not expected that a duty cycle greater than 50\% would be desirable, hence the amplifier (gain=2) was introduced. This allowed the use of the full output range of the D/A converters and resulted in greater resolution and finer control over the duty cycle.

The duty cycle then is determined by the duty cycle reference voltage, \( V_{DC} \), which determines when the solenoid driver control voltage should be turned off. The heart rate is determined by the rate reference voltage, \( V_{HR} \), which determines when the cycle should begin again and turn the control voltage back on.

It should be noted that there is no direct relation-
ship between the duty cycle reference voltage \( V_{DC} \) and duty cycle. Rather, that relationship exists with the systolic period of the heart cycle. Therefore, it is not possible to change rate without causing a change in duty cycle because the systolic period remains constant. This situation necessitates some form of feedback control if a constant duty cycle is to be maintained in the face of rate changes. The transducers for heart rate and duty cycle are, however, essentially integrating circuits with RC time constants so that a finite amount of time is required to detect changes in either of these parameters.

In order for the control system to respond as quickly as possible to changes in the controlled variables, the system does not rely on the output of the rate and duty cycle transducers for error signals. Rather the relationship between the rate and duty cycle reference voltages \( V_{HR} \) and \( V_{DC} \), and the timing of the heart cycle are employed.

For each value of \( V_{HR} \) there is a unique heart rate which is determined by the timing ramp of the control circuit. A similar relationship exists with \( V_{DC} \) and systolic duration. These relationships may be described by the following equations

\[
V_{HR} = K_{HR} T_{HR}
\]

\[
V_{DC} = K_{DC} T_{DC}
\]
where \( T_{HR} \) and \( T_{DC} \) are respectively, the periods of the rate and duty cycle control waveforms. \( K_{HR} \) and \( K_{DC} \) are the slopes of the waveforms, and \( V_{HR} \) and \( V_{DC} \) are the applied reference voltages from the computer.

Since \( K_{DC} = 2 K_{HR} \) and defining \( DC = \frac{T_{DC}}{T_{HR}} \),

where \( 0 \leq DC \leq 1 \),

we can write \( DC = \frac{T_{DC}}{T_{HR}} = \frac{0.5V_{DC}}{V_{HR}} \)

or \( V_{DC} = 2(DC)(V_{HR}) \).

The advantage of computing \( V_{DC} \) for each value of \( V_{HR} \) is speed and stability. The alternative would be a feedback control system in which duty cycle changes would have to be detected and then corrected. The computation of the necessary value of \( V_{DC} \) allows systolic duration to be changed with rate so that duty cycle remains unchanged.

Because certain of the waveforms which must be sampled vary with the artificial heart cycle, it is necessary that the sampling be synchronized so that it occurs at the same time in each cycle. The synchronization circuit must output a timing pulse just prior to the end of systole. This pulse is applied to one of the sense lines of the instrumentation system. When the program calls for a sample to be taken, the computer queries the sense line
until the pulse appears. At that time, the sample is taken. It is important that the synchronization pulse be narrower than the time required for the computer to complete the sampling and return to query the sense line.

The synchronization circuit is shown in Figure 7. The reference voltage applied to the comparator is slightly less than $V_{\text{DC}}$ because of the voltage divider. At the onset of each systolic period, the output of the comparator is low and the monostables are both off (Figure 8). When the ramp output of the amplifier rises to the value of the reference voltage, the comparator changes state. The first monostable triggers on the rising waveform of the comparator and turns on. The output of the first monostable is then used to turn on the second monostable. The two monostables are necessary because the rise time of the signal which triggers the first monostable is greater than the desired pulse width of the synchronization signal. The intermediate monostable is included as a pulse shaper. It presents an input with a fast rise time to the second monostable.

Control of the ventricular driving air pressure required that a DC voltage from the computer cause the motor to drive the valve to a desired position and stop. The existing circuitry was inadequate to accomplish this because it was designed as a continuous-data system whereas
Figure 7. Artificial ventricle synchronizing pulse circuit
Figure 3. Waveforms associated with synchronization circuit
the system utilizing the digital computer was a sampled-data system. If the sample time were made small with respect to the response time of the motor and bleed-air valve, the system as it existed could have been used.

However, a key element of the system under development was to be flexibility. It was desired that the control system need not rely on the computer for beat to beat guidance, but rather be an autonomous system accepting commands from the computer as necessary to change the operating characteristics to meet the physiological demands of the animal. To meet this criterion, some form of feedback was necessary to give an indication of the position of the valve. It was necessary to convert the system into a position-regulating servomechanism.

In order to transduce the position of the valve, a ten-turn potentiometer was mounted so that the shaft of the potentiometer and the shaft of the valve were coupled by means of a gearing arrangement. A voltage was applied across the potentiometer so that the position of the valve was indicated by the voltage at the output of the potentiometer. The voltage indicating the actual position of the valve and the voltage indicating the desired position \(V_{AP}\) are summed at the summing junction of the operational amplifier of Figure 9. If the valve is not at the position desired by the computer, the voltage at the summing junction
Figure 9. Driving air pressure control system  
(The dotted lines indicate a mechanical linkage.)
is not zero. The output of the operational amplifier thus applies a voltage to the motor which drives the valve to the desired position. As the valve approaches this position, the voltage at the summing junction becomes smaller causing the motor to slow and finally stop when the valve reaches the desired position.

Once the computer has issued the command for the driving air pressure to be changed by requesting a change in the position of the bleed-air valve, the computer is free to go about other tasks. It is not necessary for the computer to monitor the progress of the valve.
DETERMINATION OF THE CONTROL ALGORITHM

With the components of the system now assembled, the requirement was to integrate them into a functional control system. Since it was the digital computer which would direct the action of the system, the above requirement was in effect one of determining the software routines required to convert the apparatus described in the previous chapter into an operable system. In order to write the software routines, it was necessary to know the dynamic characteristics of the various parts of the system and how the blocks would interact when assembled as a complete system.

A block diagram of the elements of the system is shown in Figure 10 and indicates something of the philosophy of the control of the system. The block labeled "controller" is the software program of the computer. The input signal to the controller, e, is the error or difference between the desired value and the actual value of the controlled variable. The input to the controller may be a single variable or multiple variables. The controller determines the signal, m, to be applied to the actuator. The actuator in this system is the ventricle with its power and control system. The actuating signal may consist of more than one variable, but in this system it is constrained to include rate, duty cycle and driving air pressure or a combination
Figure 10. Block diagram of the artificial ventricle-animal system
of these. The output of the actuator, $a$, is fluid flow. When the flow is applied to the plant, which represents the recipient of the artificial ventricle, it may be manifested as systemic arterial pressure, oxyhemoglobin concentration, venous pressure, atrial pressure or even blood flow. Any of these variables or others which represent a relationship between the actuator and the plant may be utilized as the controlled variable.

In order to determine which physiological variables to use as the controlled variables, something must be known of the animal and its interreaction with the actuator. In order to determine which of the actuator's parameters to use as the manipulated variables, something must be known of the dynamic characteristics of the ventricle and its power and control systems. The next two sections discuss the determination of the manipulated and controlled variables.

**Manipulated Variables**

In order to determine the dynamic characteristics of the ventricle and its relationship to the pneumatic power and electronic control circuitry, a mechanical analog of the circulation was constructed. This mock circulation was not designed to mimic the natural circulation in every way, but rather to provide a realistic test stand as far
as the physiological demands on the pump were concerned. In other words, provision was made for independent variation of the preload and afterload, or input and output pressures.

A block diagram of the mock circulation is shown in Figure 11. The artificial atrium and ventricle are configured exactly as they would be when attached to an animal. The peripheral resistance is simulated by a Starling resistor. This device consists of a section of compliant tubing within an airtight chamber. The pressure within the chamber is transmitted to the fluid flowing in the compliant tubing. This pressure is controlled by varying the height of a column of water (Figure 12). The pressure head of the water column is then transmitted to the airtight chamber and the compliant tubing by a section of air-filled tubing. The water level in the column is varied by means of a roller pump which transfers water between the column and a reservoir as needed.

The venous reservoir (in Figure 11) is an open vessel which can accommodate temporary imbalances in flow. The circulating fluid is returned to the artificial atrium by means of a variable speed roller pump. The combination of the venous reservoir and the roller pump allow the simulated venous return to be varied independently of the output of the artificial ventricle.
Figure 11. Block diagram of the mock circulation
Figure 12. Schematic drawing of Starling resistor used in mock circulation.
The circulating fluid used in the system was physiological saline. Input and output pressures were measured in the atrium and in the outflow line of the ventricle using fluid-filled catheters and strain gage transducers. Fluid flow was measured in the system using a flowthrough, electromagnetic flowmeter.

The first step in the characterization of the pump was to determine a function curve of the artificial ventricle. This was accomplished by varying the input pressure while maintaining a constant rate, duty cycle, driving air pressure and afterload. The results of one such set of data is shown in Figure 13. This curve resembles very closely data obtained by Patterson and Starling (1914a) in heart-lung experiments in open-chest dogs. In the dog, this ability of the cardiac output to increase with increased input pressure was explained on the basis of the increased contractility of the myocardium as a result of the increased filling. The increased contractility was due to the increased fiber length at the end of diastole (Patterson, 1914b). In the artificial ventricle, it was observed that increased filling occurred with increased input pressure. This was due to the orientation of the ventricle, the finite resistance of the input valve and the resistance of the paraboloid diaphragm to collapse to accommodate increased filling. The flattening of the
Figure 13. Artificial ventricle output vs. atrial pressure
(Rate=90 BPM, duty cycle=40%, driving air pressure=125 mm Hg, Starling resistance=100 mm Hg)
curve at higher input pressures was due to the fact that the maximum effective stroke volume was being approached.

The implication of this data is that the artificial ventricle is self-regulating and any control system would be redundant. In the case of this particular ventricle, it is self-regulating provided that it is operating at a high enough rate and driving air pressure. At other operating points, where the pump is operating closer to capacity, the cardiac output tended to saturate at a lower level. The requirements for inherent controllability then include a ventricle with a large enough stroke volume and operating at a high enough power drain to accommodate the maximum expected cardiac output. This is a high price to pay when considering a totally implantable artificial ventricle system.

Since the primary function of an artificial ventricle is to replace or augment the pumping capability of the natural ventricle, the artificial ventricle should respond to variations in return flow as the natural heart does. That is, a variation in return flow must elicit a rapid response by the system to compensate for the variation in flow in order to maintain atrial pressure at a normal physiological level. In order to determine which of the three control parameters (rate, duty cycle, driving air pressure) of the pump might be most suitable in compensating
for variations in return flow, studies were carried out on the mock circulation. During these tests, two of the control parameters were held constant while the third was varied over its normal range. Return flow was adjusted so that input pressure remained constant during the entire procedure. Each test was repeated for different values of afterload as well as for the two control parameters which remained constant.

Typical data for flow as a function of rate, duty cycle and driving air pressure are shown in Figures 14, 15, and 16. These data indicated that the system was more responsive to variations in driving air pressure (Figure 16) than to rate or duty cycle. The increased driving air pressure resulted in increased work being done on the ejected fluid. Furthermore, the pump became more efficient at higher driving air pressures in that the ventricle emptied more completely causing the diaphragm to be stretched. Then, at the beginning of diastole, the stretched diaphragm acted to force the air from the air chamber as well as to suck blood into the blood chamber. This action of the diaphragm at higher air pressures resulted in more efficient filling of the ventricle.

The response of flow to rate and duty cycle (Figures 14 and 15) was apparent although less pronounced. The maximum of the rate curve occurred at that point where
Figure 14. Artificial ventricle output vs. heart rate
(Duty=cycle 40%, atrial pressure=0 mm Hg, driving air pressure=130 mm Hg, Starling resistance=100 mm Hg)
Figure 15. Artificial ventricle output vs. duty cycle
(Rate=100 BPM, atrial pressure=0 mm Hg, driving air pressure=125 mm Hg, Starling resistance=100 mm Hg)
Figure 16. Artificial ventricle output vs. driving air pressure (Rate=90 BPM, duty cycle=40%, atrial pressure=0 mm Hg, Starling resistance=100 mm Hg)
filling and ejection times were optimized. Filling of the ventricle was not a linear function of time. At the onset of diastole, the inflow rose rapidly to its maximum value and then fell more slowly. At lower rates, filling was somewhat enhanced so that stroke volume was actually increased but total flow was reduced because of the lower rate. The opposite was true at higher rates where stroke volume was reduced and not compensated for by increased rate.

The response of output flow to duty cycle changes exhibited the same dependence on filling and ejection. The peak of the duty cycle curve occurred where filling and ejection times were optimized.

The artificial ventricle was a load-dependent pump and, as such, the output was related to the output pressure. For this reason, if rate or duty cycle were to be used as manipulated variables, the driving air pressure had to be at a sufficient level for the greatest expected load or, alternatively, driving air pressure would have to be used as a secondary manipulated variable to account for changes in afterload. If maximum speed of response were desired, the use of rate or duty cycle control to meet changing flow demand would be preferable since changes in these two parameters occurred electronically. Driving air pressure, on the other hand, was changed electromechanically.
by a motor turning a valve so that the speed of response was slower. This longer response time was partially compensated for by the nature of the system. The elapsed time from the initiation of a command to change rate or duty cycle and the change to be manifested was on the order of one heart period. Thus, at a rate of 90 beats per minute (BPM), 666 msec elapsed before a change in rate or duty cycle could take place. In this time, the bleed-air valve could turn sufficiently to realize a three mm Hg change in driving air pressure. Reference to Figure 16 shows that a three mm Hg change in driving air pressure could produce a change in flow of approximately 300 ml/min when operating at the typical values of Figure 16.

A further argument in favor of using the driving air pressure as the manipulated variable is the fact that the driving air pressure at the ventricle varies as rate and duty cycle vary. Figures 17 and 18 show, respectively, the changes in driving air pressure as rate and duty cycle are varied. These changes are due to the nonideal air pressure source discussed in the chapter on Apparatus. The implication of this data is that if rate or duty cycle were used as the manipulated variable, driving air pressure would have to be controlled as well. Thus, any benefits accruing from speed of response would be negated and the controller would, of necessity, be more complex in order
Figure 17. Driving air pressure vs. heart rate (Duty cycle = 40%)
Figure 18. Driving air pressure vs. duty cycle (Rate=100 BPM)
to stabilize air pressure.

If driving air pressure is to be used as the manipulated variable, the air pressure control system must be well defined. Driving air pressure was determined as a function of the air pressure control voltage \( V_{AP} \) and plotted in Figure 19. The response of driving air pressure to \( V_{AP} \) is reasonably linear between two and ten volts. Below two volts, the curve reverses direction. In order to avoid this region of nonlinearity, the system was allowed to vary only between two and ten volts, and the bleed-air valve was limited to eight turns rather than ten.

The time response of the system was investigated by changing the air pressure control voltage and noting the time required for the change in air pressure to take place. This procedure was repeated for several initial and final values of \( V_{AP} \). Typical curves are shown in Figure 20. The average rate-of-change response was 2.5 sec/volt.

Based on the foregoing discussion, driving air pressure was chosen as the manipulated variable.

**Controlled Variables**

The sole known function of the myocardium is to provide the necessary energy or force to pump or to circulate blood (DeBakey, 1966). The function of the artificial
Figure 19. Driving air pressure vs. air pressure control voltage, $V_{AP}$ ($V_{AP}$ is linearly related to the bleed-air valve position.)
Figure 20. Response of driving air pressure to a step increase in voltage ($V_{AP}$). The initial and final values of $V_{AP}$ are indicated. The timing marks occur each second. The event marker indicates the occurrence of the step increases in $V_{AP}$. 
ventricle was to substitute its pumping ability for that of the myocardium. In order that the artificial ventricle accomplish this function effectively, it should not only be able to pump sufficient blood, but it should be able to mimic the natural heart in the way that it pumps blood. In other words, the interface between the animal and pump should be the same as between the animal and the natural heart.

In order to design an artificial ventricle system then, much must be known about the interface between the animal and the natural heart. This interface is, of course, enormously complex and only incompletely understood. The complete understanding of this interface is equivalent to answering the following two questions. 1) How does the natural heart change its output? 2) What is the control mechanism which prompts the natural heart to change its output?

An early attempt to address the first question was embodied in Starling's law of the heart which stated "that the energy of contraction, however measured, is a function of the length of the muscle fibers" prior to contraction (Starling, 1918). Starling's law established a relationship between cardiac output and the filling pressure of the heart or mean atrial pressure (Richards, 1955). The Starling principle, however, was based on studies of isolated hearts.
and its applicability to the intact heart has been questioned (Rushmer, 1955). Following the measurement of left ventricular diameter and pressure in intact, unanesthetized dogs, Rushmer proposed an alternative law of the heart. This law stated that the output of the heart was determined by at least five factors: the effective filling pressure, the distensibility of the relaxed ventricle, the contractility of the myocardium, the systemic arterial blood pressure, and the heart rate. In addition to these five factors he believed that a number of other factors may also have important roles in the control of cardiac output. Katz (1955) investigated the neurogenic and humoral factors in the regulation of the performance of the heart and concluded that they, too, play a role in the control of cardiac output. It seems reasonable to say, then, that Starling's law described a fundamental property of the myocardium which may be modulated by a variety of intrinsic and extrinsic factors (Lorber, 1955; Richards, 1955).

Much important work has been done in recent years in an attempt to determine how the natural heart responds to its stimuli. No attempt will be made here to review all of this work. However, in light of the fact that the artificial ventricle is similar in many respects to the denervated heart, pertinent data should be considered.

Experiments with denervated and autografted hearts
indicated that the heart, when deprived of its reflex connections, continued to function automatically (Hamilton, 1955; Dong, 1964). The myocardium had some ability to adjust its performance to various levels. The level of performance was reduced in such preparations, but nevertheless, within this reduced level, there was some regulation which was partially dependent upon the stretch response and was sensitive to changes in preload and afterload.

Stone et al. (1967) was able to separate the sympathetic and parasympathetic effects on the myocardium by fluid infusion in cardiac-denervated and cardiac-sympathectomized conscious dogs. By rapidly infusing Tyrode solution into the right side of the heart and measuring cardiac output, heart rate, and stroke volume, it could be shown that the chronically cardiac-denervated animal changed its cardiac output solely by a change in stroke volume, while the animal with partial nervous innervation responded to cardiac stress by a change in rate rather than stroke volume. Again the level of performance was reduced in both the denervated and cardiac-sympathectomized dogs.

These findings would seem to indicate that the increased stroke volume was the more primitive response, being activated only when the rate response was insufficient.

The question of how the heart responds then would seem to be best answered by saying that it is through a complex
interaction of functional and architectural factors influenced by nervous and hormonal factors. The functional and architectural factors are described by Starling's law of the heart. The neural and hormonal factors include variations in rate and contractility due to sympathetic and parasympathetic nervous stimulation and circulating catecholamines.

There are two concepts which could explain the control mechanism by which the output of the natural heart is controlled. The cardiac concept holds that the heart regulates its output to provide the correct blood flow to the peripheral circulation. That is, the heart itself controls cardiac output. The peripheral concept of cardiac output regulation holds that the heart acts to pump all of the blood which is returned to it. The heart, according to this concept, is merely a tool which exercises no control at all over cardiac output.

The concept of the heart as a regulator of cardiac output has been supported by several investigators (Stead, 1947; Warren, 1945, 1948; Hamilton, 1955). The theory assumed that there was always ample blood available at the input side of the heart to be pumped as necessary. The heart, then, acted to regulate the cardiac output by selective pumping of this ample blood supply as indicated by its neural and humoral influences.
The concept of the heart responding to the venous return assumed that the normal heart had the capability to pump all of the blood which was presented to it. If this was the case, then the primary factor in the control of the cardiac output was the action of the peripheral circulation as it affected venous return. The neural and humoral influences of the heart, then, enabled it to better carry out this function. Guyton (1963) pointed out that both the cardiac and the peripheral concepts of cardiac output regulation were valid and both must be considered in discussing the regulation of cardiac output. Using data presented by Guyton (1963), Crosby (1970) concluded that normally the peripheral concept was paramount and the dominant factor in the regulation of cardiac output was venous return. Crosby found that, for example, 81% of the increase in cardiac output in moderate exercise was due to increased venous return. The peripheral concept of cardiac output regulation implied that the control of the cardiac output was directly related to the metabolic needs of the body. The heart may be likened to a pump which is normally capable of pumping out all the fluid presented to it.

The fact that cardiac output could be changed by a changing metabolic need has been demonstrated by experiments in which the hearts of dogs with atrio-ventricular block (due to destruction of their atrio-ventricular nodes
by electro-cautery) were externally paced. The dogs were exercised on a treadmill at three miles per hour while their heart rate was varied from 80 BPM to 240 BPM. At this constant level of exercise, cardiac output remained fairly constant for different heart rates (Warner, 1960). When the level of exercise was increased by increasing the speed of the treadmill, the cardiac output also increased. Rate control in the natural heart then, is seen not to be an essential element of the overall scheme of cardiovascular control.

With the advent of improved implantable measurement devices which made possible the recording of cardiovascular data in unanesthetized and unrestrained experimental animals, a body of data has begun to be accumulated. With this data, mathematical models have been formulated which give further insight into the regulation of the heart and the cardiovascular system.

One such model was developed by Scher et al. (1967) to investigate the regulation of stroke volume in the resting dog. The model attempted to analyze stroke volume on a beat by beat basis and admitted three parameters of control; the interval between beats, the ventricular filling pressure and the pressure against which the heart ejected blood. This model indicated that in the resting dog the influence of the sympathetic nervous system in the regu-
lation of stroke volume was unimportant. The three parameters which did appear to be important (heart period, input pressure, output pressure) were all directly related. That is, as the heart period increased, ventricular filling pressure had to increase due to the damming of the blood in the atrium and the afterload had to decrease due to increased runoff time. This study suggested that in an artificial ventricle operating at a constant heart interval or rate, stroke volume could be controlled by utilizing the atrial pressure and aortic pressure as the controlled variables. Unfortunately, however, a controller based on these variables could face the impossible situation so often seen in patients in shock; that is, a low arterial pressure accompanied by a low atrial pressure due to reduced venous return. The arterial pressure would be calling for increased stroke volume while atrial pressure would be calling for the opposite response. Without suitable safeguards, such a controller based on Scher's model could lead to subatmospheric atrial pressures. With a diaphragm-type ventricle such as the one used in this research, stroke volume is increased by increasing the driving air pressure and hence, the diaphragm travel. If venous return is insufficient to fill the ventricle, subatmospheric pressures could be induced in the atrium by the suction effect of the diaphragm returning to its unstretched position.
Therefore, a controller based on Scher's model must make use of suitable weighting factors for each of the controlled variables. Scher's paper did list weighting factors for each variable, but since the data was taken in normal, healthy dogs, they probably must be modified for an animal undergoing the trauma associated with the attachment of an artificial ventricle.

Another model which gives some insight into the regulation of the cardiovascular system was a mechanical analog to the heart and cardiovascular system (Osborn, 1967). Conclusions drawn from studying this model supported the view that the regulation of cardiac output was a multivariable process but that some hierarchy of control existed. The model showed that Starling regulation determined and maintained the balance of the circulation on a beat-by-beat basis. Relative volumes of the pulmonary and systemic circuits were maintained because any unbalance of these volumes resulted in a change in atrial pressure. Major changes in cardiac output could be accomplished by changes in mean circulatory pressure which caused return flow to vary. Rate could be adjusted to obtain the greatest efficiency for a set of circulatory factors. Again the implication to artificial heart work was that rate control was not necessary, whereas some method of regulating stroke volume was.
If it can be assumed that the control of the peripheral circulation remains virtually intact when the natural heart is replaced by an artificial ventricle, then it can be assumed that the requirement of the tissue beds for an increase in blood flow will be evidenced by an increased flow of blood to the heart (Guyton, 1963). The requirement of any heart, natural or artificial, is that it have the ability to respond quickly to the increased input by pumping the increased volume presented to it.

The selection of an appropriate controlled variable, then, is based upon the primary requirement of meeting the demands imposed upon it by the return flow. There are, of course, several ways of transducing venous return to the artificial heart. These have been discussed in the Literature Review chapter. The direct measurement of blood pressure in the artificial atrium results in a straightforward and uncomplicated indication of venous return. Therefore, the pressure in the artificial atrium will be used as the controlled variable.

Controller

The controller of the artificial ventricle system has been defined as the computer software program which establishes the relationship between the error signal and controlling signal applied to the actuator. The equations
which define the relationship between the error signal and controlling signal will be developed in this section. The computer program is listed in the appendix.

The entire closed-loop artificial ventricle-animal system is shown in Figure 21. The error signal applied to the controller is the difference between the actual and desired values of the controlled variable. The controlling signal is applied to the actuator which drives the manipulated variable to the desired value.

For the artificial ventricle system, the controlled variable has been determined to be atrial pressure and the manipulated variable to be driving air pressure. The block labeled "plant" in Figure 21 is the artificial ventricle which responds to the change in air pressure with a concomitant variation in flow.

The element in the feedback loop labeled "atrial capacitance and transducer" is the artificial atrium and pressure transducer with its associated electronics. A volume change in the atrium is related to a pressure change by the characteristics of the atrium as well as of the transducer system. Figure 22 shows the relationship between volume changes and pressure changes in the atrium. The electronics of the pressure transducer include a low pass filter with a cutoff frequency of 0.1 Hz.

Variation in atrial volume and the consequent variation
Figure 21. Block diagram of artificial ventricle-animal system (Solid lines indicate electrical signal paths, dotted line indicates pneumatic path and dashed lines indicate blood flow paths.)
Figure 22. Compliance of artificial atrium
(Data courtesy of Spehr, 1972)
in atrial pressure is attributable to the difference between the venous return and the flow from the atrium. The system of course, exercises no control over the peripheral circulation which is depicted by the block entitled "delay and storage". As the venous return varies, the net flow into the atrium varies. This volume variation is transduced as a pressure variation which is then used to determine the error signal. The effort of the controller then is to cause the outflow of the atrium to be altered in response to the inflow so that the net flow accumulation remains zero.

The task at hand is to design the controller so that an unbalance in the net flow into the atrium will result in a controlling signal which, when applied to the actuator, will cause the unbalance to be corrected in a desirable manner. Such a design must be based on a knowledge of all of the other elements of the control loop because the controller must compensate for the undesirable dynamic performance of those other components. Normally in a problem of this nature, one writes the transfer functions of the actuator, plant and feedback element, and then using control theory techniques, determines a transfer function for the controller using the criteria of stability, sensitivity, transient and steady state response. If any of the elements of the loop happen to be nonlinear, the
above determination is less straightforward. Methods exist for studying nonlinear systems but a common practice is to consider the nonlinear element as linear and proceed as above. In the system at hand, the elements labeled "actuator", "plant" and "atrial capacitance and transducer" have been previously characterized (Figures 19, 16, 22). Because of its complexity, however, it is not possible to completely characterize the element labeled "delay and storage". Therefore, the design of the controller must be based upon empirical considerations.

Since the mandate under which the controller was conceived was to provide a system with which to study the control of artificial hearts, it was felt that a controller should be designed with sufficient flexibility so that its parameters could be varied easily in order to be able to investigate the application of different controllers.

Certain requirements for the controller were dictated by the physiological requirements of the animal and the dynamics of the system. The system must respond to variations in atrial pressure and the response should be proportional to the magnitude of the error. This requirement indicated the use of a proportional control system. A limitation or disadvantage of this type control system is that a compromise is often necessary in selecting the proper gain constant so that the size of the steady state error
and the maximum overshoot are minimized. It may not be possible, however, to select a gain constant such that both steady state error and overshoot are within acceptable limits.

The performance of the system may be improved by the addition of integral control or derivative control or both. Integral control improves the steady state response of the system by introducing a signal to the controller which is proportional to the time integral of the error. This has the effect of causing a correction to be made whenever an error exists. Derivative control improves the transient response of the system by introducing a signal to the controller which is proportional to the time derivative of the error. Derivative control measures the rate of change of the error and anticipates the overshoot before it occurs. The controller then makes the proper correction before the overshoot occurs.

In the artificial ventricle system, the presence of a small steady state error is not a disadvantage so integral control is not necessary. Because of the inherent phase lag in the motor and valve of the air pressure control system, however, phase lead must be introduced to improve the system's dynamic performance. The use of derivative control satisfies this requirement. The equation which defines the controller, then, is:
\[ m = k_1 \ e + k_2 \frac{de}{dt} \]  

(1)

where \( m \) is the correction applied to the bleed-air valve circuitry and \( e \) is the difference between the actual and desired atrial pressures. The desired or reference atrial pressure must be determined from physiological considerations and the dynamic characteristics of the ventricle and is typically between zero and five mm Hg. The gain constants \( k_1 \) and \( k_2 \) must be determined experimentally.

In spite of the fact that the dynamic range of the driving air pressure is approximately 95 mm Hg and the normal range of 100 to 195 mm Hg is usually adequate, it is possible that the controller could call for pressures outside of this dynamic range. A momentary occlusion of the inflow or outflow tracts or massive hemorrhage could result in a large deviation of atrial pressure. The control algorithm could then attempt to call for a value of \( V_{\text{AP}} \) greater than ten or less than two volts. In order that this never occur, the controller is limited so that it will not output a voltage greater than ten or less than two volts. Instead, it will limit the output to two or ten volts and illuminate one of the relay panel lights. The light will indicate to the operator that the bleed-air valve is at its limit of travel. The operator may then ignore the light if it is obvious that the situation is
momentary, or he may adjust the air pressure with the regulator on the front panel.

A disadvantage of the controller as described thus far is that when the desired driving air pressure drops below the mean systemic pressure, stroke volume essentially drops to zero because of the load dependency of the pump. Rather than allow this to occur, provision is made to reduce the rate of the pump when the driving air pressure drops below a certain value. This increases the heart period and allows the atrium to fill more completely between beats.

Reference was made earlier of the importance of arterial pressure as a control parameter for stroke volume. It is essential that arterial pressures be maintained at an adequate level because of the reduced tissue perfusion and the cessation of kidney function at reduced pressures. Because kidney function decreases sharply at arterial pressures below 60 to 70 mm Hg, the minimum allowable systemic blood pressure should be no lower than 70 mm Hg (Guyton, 1967; Burton, 1965).

Initial feasibility studies of the artificial ventricle in vivo indicated that the pump was operating in a filling-limited mode. It was capable of pumping a greater volume of fluid, but the poor venous return was the limiting factor. Since the output was limited by the input, it was
not possible to increase arterial pressure by means of increased pumping activity.

There are several possible means of maintaining systemic pressure by other ways such as the infusion of drugs and fluids. It is known that there is a definite tendency for fluid shifts to take place during cardiopulmonary bypass (Nazari, 1970; Longnecker, 1969). The exact location of the fluid uptake was determined by Gianelli et al. to be the splanchnic bed (1960). More recent studies by Rudy et al. (1970, 1971) made use of microspheres labeled with radio­nuclides to determine distribution of systemic blood flow during total cardiopulmonary bypass in primates. This work showed an increased flow to the intestine during bypass procedures.

Klain et al. (1971) performed autopsies on a series of calves which had undergone total artificial heart implantation for periods of up to 76 hours and on a group of control animals. Pathological findings indicated that splanchnic congestion was an almost universal response to total artificial heart implantation. They concluded that no improvement in cardiac output could be expected if low venous return in the animal was not treated.

A logical solution to this loss of circulating blood volume would be to prevent its occurrence. The means of realizing this solution, however, is not at the present
time available. A second solution which attacks the symptom but not the cause is to replace the lost fluid. The infusion of a low molecular weight dextran and bicarbonate has been reported to be effective in increasing the venous return in calves with total artificial hearts (Nose, 1966).

The capability of infusing fluids under computer control has been included in the system for use in long-term animal trials. A voltage-controlled, variable-speed infusion pump can be used to infuse fluids into the animal at a precise rate. The pump uses dual 50 cc syringes for a total capacity of 100 cc of fluid. The nominal output of the device may be varied by a gearing arrangement. The actual output may then be varied within a range of 0 to 110% of nominal by the application of an external voltage.

The computer determines the voltage \( V_{FL} \) to be applied to the infusion pump according to the relationship:

\[
V_{FL} = \begin{cases} 
0 & \text{PAS} > P_2 \\
V - k(PAS) & P_1 \leq PAS \leq P_2 \\
10 & PAS < P_1
\end{cases}
\] (2)

where PAS is the mean systemic arterial pressure, \( P_1 \) and \( P_2 \) define the limits of pressure over which the controller operates (Figure 23), \( k \) is the slope of the function between \( P_1 \) and \( P_2 \) and \( V \) is the intercept of the extension of the function past \( P_1 \). The values of the pressures representing \( P_1 \) and \( P_2 \) may be easily changed by a slight
Figure 23. Fluid infusion control function
modification to the software but normally are set at 75 and 100 mm Hg, respectively. In operation, when the mean systemic arterial pressure is 100 mm Hg or greater, $V_{FL}$ is zero and the infusion pump is not operating. If the arterial pressure falls to 75 mm Hg or less, $V_{FL}$ is ten volts and the maximum infusion of approximately 50 ml/min is realized. At any value of systemic pressure between 75 and 100 mm Hg the infusion rate is a linear function of the pressure.

Gain Constants

The initial determination of the gain constants $k_1$ and $k_2$ of equation (1) of the previous section was accomplished on the mock circulation by means of a transient analysis of the system. The procedure was to establish an operating point of the system with respect to rate, duty cycle, air pressure, atrial pressure and mean systemic pressure. Optimum values of rate and duty cycle were chosen based on the experimental data of Figures 14 and 15. Air pressure, flow and mean systemic pressure were selected based on physiological considerations. Atrial pressure, arterial pressure and driving air pressure were measured using strain gage transducers. Fluid flow was measured using an electromagnetic flowmeter. These three variables were recorded and observed on a strip chart recorder.
A true step-function error signal was applied to the control system and the response of the system was observed. The step-function input was realized by inactivating the controller while increasing the return flow. The change in flow resulted in a change in atrial pressure. When the atrial pressure reached its new steady state value, the controller was reactivated. An indication of the ability of the controller to respond is given by the atrial pressure waveform.

Many combinations of the gain constants $k_1$ and $k_2$ were tried before a satisfactory response was obtained. It was found that if the value of $k_1$ was too large and $k_2$ too small, the system became unstable and tended to oscillate. If both $k_1$ and $k_2$ were too small the response was slow and lightly damped. With the gain constants set at 1 and 10 respectively, the system response was fast and exhibited near-critical damping.

Figure 24 shows the system response to a step function input. The atrial pressure was forced to a value of 18.5 mm while the controller was inactivated. When the controller was turned on, the atrial pressure was returned to its reference value of 0 mm Hg within 18 sec. The rise time, which is the time it takes the waveform to go from 0.1 to 0.9 of its final value, was six seconds. It is expected that these characteristics would enable the system to
Figure 24. Response of system to a step function input. (Chart speed 2.5 mm/sec)
respond to normal variations in flow in vivo.

An attempt was made to produce a sinusoidal variation in atrial pressure by means of a sinusoidal variation in flow. The sinusoidal flow was superimposed upon normal return flow by a voltage-controlled, variable-speed infusion pump. A sinusoidal control voltage of 0.01 Hz applied to the pump produced the sinusoidal flow which resulted in a nearly sinusoidal atrial pressure pattern. The controller was able to respond to this input signal by maintaining a relatively constant atrial pressure (0 to 1.5 mm Hg). With the controller turned off, the atrial pressure varied over a much wider range (-6 to +1 mm Hg).
EVALUATION OF PERFORMANCE

In Vitro

The in vitro evaluation of the artificial ventricle-control system was accomplished on the mock circulation by simulating changes in venous return. The entire system including the heart rate control and arterial pressure control segments were evaluated as an integrated system.

A steady state value of cardiac output of 1.7 L/min was established. Return flow was increased from 1.7 to 3.6 L/min by a step increase in the speed of the roller pump (Figure 25). The increase in venous return was indicated by the increase in atrial pressure. The response of the control system and ventricle produced an increase in flow from 1.7 to 4 L/min within six seconds before settling to the steady state value of 3.6 L/min. The atrial pressure reached a maximum of 2.7 mm Hg. The overshoot in flow was due to the temporary pooling of blood in the artificial atrium. The rise time of the system was 2.6 sec.

When the return flow was decreased to 1.9 L/min, the system again responded to match the output of the pump to the input. The response time for the decrease in flow was longer (7 sec) than for the increase. The rise time also lengthened to 4 sec. Furthermore, the change in atrial
Figure 25. Response of system to an increase in flow followed by a decrease. (Chart speed 2.5 mm/sec)
Atrial Pressure (mm Hg)

Flow (L/min)

Driving Air Pressure (mm Hg)
pressure was proportionally less for the decrease than the increase. This difference may be explained on the basis of the nonlinear artificial atrium. The plot of atrial compliance of Figure 22 shows a change in slope at the system operating point of zero mm Hg. Because of this compliance characteristic, a net inflow of fluid in the atrium results in a greater change in pressure than does a net outflow of the same magnitude. Since the system is directly responsive to pressure rather than flow, the response is a function of the operating point.

The further variation of return flow beyond normal physiological values resulted in the activation of the heart rate controller (Figure 26). The upper and lower limits of driving air pressure had been set at 145 mm Hg and 75 mm Hg. When the increase in return flow resulted in an increase in driving air pressure to the upper limit of 145 mm Hg, further increases in return flow were accommodated by increases in rate rather than in air pressure. A decrease in return flow below normal physiological values, on the other hand, resulted in a decrease in the rate after the air pressure dropped to 75 mm Hg.

The arterial pressure controller was evaluated by reducing the value of the Starling resistance. This resulted in a reduction in the mock circulation arterial pressure. The reduced arterial pressure resulted in an
Figure 26. Response of system to a stepwise increase in flow. Activation of the heart rate control occurs when the driving air pressure reaches 145 mm Hg. (Chart speed .25 mm/sec)
infusion of fluids into the system. The physiological effect of the infusion of fluids was not seen on the mock circulation. That is, the arterial pressure was not affected by the increased flow because at the flow rates involved, the pressure is principally determined by the Starling resistance rather than the flow.

The in vitro evaluation established that the system was capable of responding to an approximate doubling of venous return from normal physiological levels within six seconds. This response compared favorably with that of the natural heart.

In Vivo

The in vivo testing was accomplished with the pump attached in a left ventricular replacement configuration. The animals used were mongrel dogs, both male and female ranging in weight from 18 to 27 kg. Food was withheld from the animals for 24 hours prior to each experiment although water was allowed. Sterile surgical procedure was followed throughout. Anesthesia was induced by the administration of Surital and maintained by Metofane which was administered with 100% oxygen by means of a respirator.

Preliminary surgery included surgical exposure of the femoral artery and vein with cannulations for arterial blood pressure measurements and intravenous fluid infusion.
A catheter also was passed down the jugular vein into the anterior vena cava for the measurement of central venous pressure.

A transthoracic approach via the fifth intercostal space was made into the thoracic area. Hemorrhage was controlled by ligating or cauterizing all potential hemorrhage points.

Attachment of the artificial ventricle to the recipient animal was made through the myocardial wall at the apex of the left ventricle and to the descending thoracic aorta. In order to minimize the time involved in making the attachment, specialized fittings were developed to expedite the procedure.

The attachment of the outflow tract of the artificial ventricle to the aorta was made by using a stainless steel T-connector. An incision was made in the aorta to accommodate the T-connector which was then secured by tying with umbilical tape. The artificial ventricle was mounted adjacent to the open chest by means of a gimbal arrangement. The outflow line was attached to the aortic T-connector and clamped. The entire ventricle was primed with warm saline.

Attachment to the left ventricle was made by means of a stainless steel cannula of 18 mm inside diameter. A sharpened penetrating tool was placed within the cannula
and was used to puncture the wall of the ventricle. The stainless steel cannula was inserted through the puncture wound into the ventricle and secured with a purse-string suture. The penetrating tool was withdrawn and the inflow line of the artificial ventricle was attached to the cannula. The pumping action of the artificial ventricle was begun immediately after the connection to the natural ventricle had been made. The fact that a virtual left heart bypass was achieved was confirmed by manually occluding the ascending aorta distal to the coronary arteries. Within minutes, the myocardium weakened and fibrillated. The failure of the myocardium after it was deprived of perfusion from the artificial ventricle indicated that left heart bypass was complete.

The physiological parameters which were monitored included systemic arterial pressure, central venous pressure, EKG, natural heart rate, body core temperature, blood flow and blood pressure in the artificial atrium. The three parameters of the artificial ventricle (rate, duty cycle and driving air pressure) were also monitored. All parameters were recorded continuously on a 12 channel strip chart recorder and were periodically sampled and stored in digital form on magnetic tape. Arterial and venous blood samples were taken periodically and analyzed for $P_{O_2}$, $P_{CO_2}$, pH, hematocrit and hemoglobin concentration.
The final evaluation of the system was carried out with five dogs. The total pumping time varied from three and a half hours to four and a half hours with the average being three hours forty five minutes. Perturbation of the system was accomplished by means of hemorrhage, infusion of fluids, mechanical manipulation and the administration of vasoactive drugs. All of these means were used to cause the venous return and, as a result, the atrial pressure to vary. The response of the system was noted. Small changes in the gain constants were made and these effects were also observed.

Hemorrhage and reinfusion experiments were carried out by means of a catheter passed up the femoral artery. The catheter was connected to a reservoir via a roller pump so that blood could be rapidly withdrawn and reinfused. Figure 27 shows the reduced atrial pressure which has resulted from a hemorrhage of 300 ml of blood. The air pressure valve was at its lower limit of 90 mm Hg so that the controller was unable to make further corrections. Re-infusion of the blood resulted in an increase in venous return which caused an increase in atrial pressure. This rise in atrial pressure was compensated for by an increase in air pressure.

Figure 28 shows the results of complete stoppage of the artificial ventricle by removing the air hose from
Figure 27. Response of system to reinfusion of 300 ml of whole blood
Figure 28. Response of system to complete stoppage of ventricle
(Chart speed 100 mm/min)
the air chamber of the ventricle. That the ventricle was not functioning is indicated by the driving air pressure, atrial pressure and systemic arterial pressure. The controller was turned off before the air hose was removed so there would be no attempted reaction to the increased atrial pressure. When the atrial pressure reached 22 mm Hg, the air line was replaced and the controller turned on simultaneously. The response of the system is seen to be rapid with a slight over-correction before bringing the atrial pressure back to its reference level.

Figure 29 shows the effect of an IV injection of 0.5 cc of epinephrine on a dog in the terminal stage of an experiment. (The choice of epinephrine as a drug to increase the return flow to the artificial ventricle was justified by the fact that the right heart of the experimental animals was generally in a weakened state as evidenced by an elevated central venous pressure. Epinephrine acts on the peripheral circulation to increase the venous return. It also has a positive inotropic and chronotropic effect on the right heart to enable it to increase its cardiac output. The overall result is an increased return to the artificial left ventricle.) Because of inadequate return flow, the atrial pressure had decreased below the desired value and the bleed air valve had reached its full open limit of travel. The injection of the epinephrine was followed by an increase in venous return as evidenced by an increase in atrial
Figure 29. Response of system to IV injection of 0.5 cc epinephrine (Chart speed 100 mm/min)
ATRIAL PRESSURE (mm Hg)

DRIVING AIR PRESSURE (mm Hg)

MEAN AORTIC PRESSURE (mm Hg)
pressure. When the atrial pressure exceeded the reference value of one mm Hg, the driving air pressure increased to maintain the desired value of atrial pressure. As the effect of the drug diminished, venous return again declined, and the driving air pressure decreased to maintain the desired atrial pressure.

To illustrate the efficiency of the control system, the injection of epinephrine was repeated with the control system turned off. Figure 30 shows the response of atrial pressure uncompensated by the control system. The pressure rose from -1 mm Hg to +3.5 mm Hg and remained at that value. One minute later, the controller was turned on as indicated by the increase in air pressure and the decrease in atrial pressure. The rise time of the artificial ventricle-animal system in response to this input was approximately four seconds.

The in vivo animal trials produced satisfactory results as far as all aspects of the artificial ventricle and its control system were concerned. These trials indicated that the system was capable of maintaining the homeostasis of the animal in the face of severe perturbations.
Figure 30. Response of system to IV injection of 0.5 cc epinephrine while controller is inactivated. Reactivation of controller is indicated by the increase in driving air pressure (Chart speed 100 mm/min)
CONCLUSIONS AND RECOMMENDATIONS

The development of a computer-based control system for an artificial ventricle has been documented. The system was designed to be used with a specific ventricle in a left ventricular replacement configuration. The control algorithm takes advantage of the dynamic characteristics of the ventricle and its pneumatic driving system and is responsive to the physiological needs of the recipient.

Evaluation in vitro and in vivo has demonstrated the ability of the system to respond to variations in venous return limited only by the driving air system. In vivo trials have been accomplished only with open chest, anesthetized dogs. It is recognized that a true test of the system should include experiments with closed chest, unanesthetized, ambulatory animals.

The ability of the system to respond to variations in venous return is limited by the size of the orifice of the bleed-air valve. This may be easily rectified by the use of a valve of greater dimensions or perhaps a modified driving system utilizing a servo-driven orifice. Such an arrangement will allow a greater range of control than is now available.

The use of driving air pressure as the primary manipulated variable is a compromise forced in part by the lack of a well-regulated source of compressed air. An improve-
ment in the regulation of the air source would allow greater flexibility in the use of rate as an additional manipulated variable.

The arterial pressure controller is included because of the need for the infusion of fluids to maintain a viable animal preparation. The design of the controller was based on the philosophy that the control of the peripheral circulation of the recipient would remain intact and the artificial ventricle need only respond to the venous return as an indication of the metabolic needs of the animal. Unfortunately, this did not seem to be the case as evidenced by the eventual death of such animals (Klain, 1971; Takano, 1971). The use of the portion of the controller to infuse fluids in response to the arterial pressure is an expedient, intended as an aid in maintaining the homeostasis of the animal. When, and if, it is possible to replace the natural heart and maintain the peripheral circulation intact, control of the arterial pressure via cardiac output should be considered.

All improvements to this system should be made with the future and possible implantation in mind. This implies a controller which minimizes the energy expenditure of the entire system. This must be achieved by the use of a suitable control algorithm which will minimize the power usage of the ventricle. It is expected that such a control algorithm
would make use of changes in driving air pressure to realize large changes in flow while changes in rate would compensate for minor changes in flow.

In order to obtain a good interface between the animal and the ventricle, the use of physiological signals in the control loop should be considered. One possibility is the use of the rate information of the natural EKG signal as a controlled variable. It may also be advantageous to consider the use of a variable reference level for the atrial pressure. If arterial pressure were utilized as an additional controlled variable, both reference levels would need to be variable.

The question of whether a control system for an artificial ventricle is necessary at all, is as yet unanswered and will probably be a subject of controversy for some time. There is no denying that an artificial ventricle can be built that exhibits a great deal of self-regulation. To obtain such inherent regulation, however, requires some compromises. Such compromises may not be acceptable when considering an artificial heart for chronic human implantation.

The inherent regulatory capability of an artificial ventricle manifests itself in its cardiac function curve (Figure 13). The slope of the cardiac function curve of the normal right heart is 4.3 L/min/mm Hg while that of
the left heart is 1.2 L/min/mm Hg (Nose, 1967a). In order
that a pneumatically driven artificial ventricle exhibit
such sensitivity to atrial pressure over a wide range, it
must be physically large, the diaphragm or blood sac must
be extremely compliant and the inflow resistance to blood
flow and the outflow resistance to the driving gas must
be low. In addition, the driving system must operate at
a high enough pressure to pump blood against the highest
anticipated arterial pressure. Furthermore, the rate at
which the pump operates must be high enough so that the
ventricle can accommodate the maximum cardiac output antici-
ipated. A ventricle so described must be characterized as
large, fragile and inefficient. Failure to provide a ven-
tricle which meets the above criteria would result in
abnormally high atrial pressures under conditions of in-
creased venous return.

It is obvious that the requirement for a large ventricle
operating at a high power consumption is not conducive to
a totally implantable artificial heart. However the re-
quirement for a thin compliant diaphragm is perhaps more
dangerous. In the search for a highly compliant diaphragm,
it must be remembered that the diaphragm must cycle on the
order of 100,000 times a day for years without failure.

The use of a control system such as the one described
in this dissertation will allow the use of a smaller ven-
tricle, with a stronger diaphragm, operating at a lower power consumption.
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A special appreciation is due my family: my wife, Mary-Elizabeth, for her understanding, patience and time devoted to the typing and proofreading the manuscript; and to my three children who tolerated the lack of time devoted to them.
APPENDIX: SOFTWARE

The programs which have been used to realize the control algorithm have been written using PDP 8/e symbolic language. The programs are well commented to aid the reader in following the logic. A brief abstract of the control program is included on a section-by-section basis to augment the comments. Other routines such as the SIO driver, multiply and divide are not included because they are modifications of programs available from the manufacturer. Table 1 lists the parameters which are able to be varied by means of the panel-mounted potentiometers. Table 2 lists the function of each sense switch.

Program Abstracts

1600-1611

If sense switch 6 is up, input the desired values of heart rate (HRWANT) and duty cycle (DCWANT) from A/D potentiometers 0 and 1. Store the desired rate in memory location VHR and prepare to compute $V_{DC}$. If switch 6 is down, the value of rate will be determined by the heart rate control (HRCON) segment.

1612-1636

Output VHR on D/A channel 1. Jump to multiply
subroutine to multiply $V_{HR}$ by the desired duty cycle (DCWANT). Output the result ($V_{DC}$) on D/A channel 2 and store in memory location VDC.

1637-1641

Return to 1600 if switch 1 is up. If down, continue. This segment allows the pumping system to be started up under manual control and locks out the control segment of the program.

2001-2007

Input a new value of $K_3$ (attenuation factor) if switch 4 is up, and shift the value of error at the last sample time to the location $E_1$ in preparation for determining the derivative of the error at the new sample time.

2010-2016

Input the reference value of left atrial pressure (PLAREF) and take its two's complement in preparation for subtraction. Wait for the synchronization pulse.

2017-2025

Input the driving air pressure (APRESS) and the systemic arterial pressure (PAS).
Input the left atrial pressure (PLA) and subtract the reference value (PLAREF). Divide the result by $2X(K_3)$ by a right shift instruction. Negative values of $E$ are temporarily made positive. Deposit the result in memory location $E$. (This portion of the program is normally not used. It was included so that the sensitivity of the atrial pressure signal could be increased.)

Input a new value of $K_1$ if switch 2 is up. Enter multiply subroutine to multiply $E$ by $K_1$.

Input a new $K_2$ if switch 3 is up. Compute the derivative of the error ($DEDT$). Jump to multiply subroutine to multiply $DEDT$ by $K_2$.

Jump to the arterial pressure control subroutine (PASCON) if switch 5 is down.

Compute the new value of VAP by adding the old
value of VAP, K1E and K2DEDT. Store temporarily in memory location VAPTEM.

2110-2111
Skip the heart rate control segment (HRCON) if switch 6 is up.

2112-2121
If the air pressure is below the minimum allowed, decrease the heart rate.

2122-2130
If the air pressure is above the maximum allowed, increase the heart rate.

2131-2152
Get the new value of VAP from location VAPTEM. Determine if it is outside the range of 1777 (10V) or 300 (2V). If so, limit the new value of VAP to 1777 or 300 and jump to subroutine UNDER or OVER to alert the operator that the limits have been reached. If within the normal range, output the new driving air pressure reference voltage ($V_{\text{N}}$).
Subroutine Abstracts

UNDER (2200)

The computed value of VAP was less than 300. Output the minimum value of VAP of 300 (2v), turn on relay light 4 to alert the operator and jump to DELAY to allow time for the regulator valve to be adjusted.

OVER (2211)

The computed value of VAP was greater than 1777 (10v). Output the maximum value of VAP of 1777. Alert the operator with relay light 2 and jump to DELAY.

LOADK1 (2222)

The program halts to allow the operator to set the switch register to the desired value of K1. When this has been done, the operator depresses the continue switch and the value of the switch register is stored in K1.

LOADK2 (2230)

The value of K2 is read in and stored in the same manner as K1.
LOADK3 (2235)
The value of K3 is read in. Because K3 is used as a counter, it is complemented before being stored in K3.

DEHR (2242)
This portion of the HRCON subroutine decreases the heart rate if the driving air pressure is below the minimum value as set on potentiometer 4.

INHR (2266)
This is the portion of the HRCON subroutine which increases the heart rate if the driving air pressure is above the maximum value as set on potentiometer 5.

DELA (2313)
The delay subroutine holds the computer in a nonfunctional loop for an adjustable time period. This routine is entered when the limit of travel of the bleed-air valve of the pneumatic controller has been reached. The delay allows the operator time to adjust the air pressure regulator on the controller panel.
SHIFT (2327), NEGAT (2356)

Since the multiplication subroutine is valid only for positive numbers, the SHIFT and NEGAT routines are used to enable negative numbers to be multiplied. It should be mentioned that the product of the multiplication subroutine occupies two words. Since in normal use, the actual product will not overflow into the second word, it is ignored. This could be a possible source of error if large values of K1 and K2 are used.

PASCON (2400)

When PASCON is first entered, initialization is accomplished by instructions 2405-2411 and the skip instruction at 2403 is deleted. Each subsequent time the subroutine is entered, the running total of the value of PAS is augmented. When 64 values of PAS have been totaled, their average is determined by means of the divide subroutine. VFL is computed on the basis of $VFL = 4(600 - PAS)$ for values of PAS between 75 and 100 mm Hg. Otherwise, VFL is set to 0000 or 1777 according to Figure 18.
Table 1. Parameter indicated by potentiometer

<table>
<thead>
<tr>
<th>Potentiometer</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Desired heart rate.</td>
</tr>
<tr>
<td>1</td>
<td>Desired duty cycle.</td>
</tr>
<tr>
<td>3</td>
<td>Reference value of left atrial pressure (PLAREF).</td>
</tr>
<tr>
<td>4</td>
<td>Minimum value of driving air pressure allowed. Heart rate control is activated at this point.</td>
</tr>
<tr>
<td>5</td>
<td>Maximum value of driving air pressure allowed. Heart rate control is activated at this point.</td>
</tr>
</tbody>
</table>
Table 2. Function of sense switches

<table>
<thead>
<tr>
<th>sense switch</th>
<th>Function when up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inactivates the entire controller but provides for the variation of heart rate and duty cycle.</td>
</tr>
<tr>
<td>2</td>
<td>Directs the computer to load a new value of $k_1$ from the switch register.</td>
</tr>
<tr>
<td>3</td>
<td>Directs the computer to load a new value of $k_2$ from the switch register.</td>
</tr>
<tr>
<td>4</td>
<td>Directs the computer to load a new value of $k_3$ from the switch register.</td>
</tr>
<tr>
<td>5</td>
<td>Activates the arterial pressure controller (PASCON) to infuse fluids in response to arterial pressure.</td>
</tr>
<tr>
<td>6</td>
<td>Activates heart rate controller (HRCON).</td>
</tr>
</tbody>
</table>
Program Listing

/PLACON
/INPUT DESIRED HR & DC
*1603
1603 7030 POT, NOP /SET NEW HR & DC IF SW 6 UP
1604 6506 6506
1605 5212 JMP DCCOMP
1606 6560 6560
1607 7233 CLA
1608 1242 TAD DCVANT
1609 3221 DCA MUL
1610 1242 TAD VHR
1611 6541 6541 /OUTPUT VHR
1612 3221 DCA MUL, 0333
1613 7030 NOP

/DROP BITS RIGHT OF OCTAL POINT
1623 0035 AND C1777 /MASK SIGN
1624 7106 CLL RTL
1625 7334 RAL
1626 3032 DCA REG1
1627 1425 TAD I MPl
1628 0841 AND C7003
1629 7032 7032 /SWAP BYTES
1630 7112 CLL RTR
1631 7310 RAR
1632 1032 TAD REG1
1633 6542 6542 /OUTPUT VDC
1634 3043 DCA VDC /DESIRED DC

/PROGRAM HOLD
1635 6531 6531 /HALT IF SENSE SJ 1 UP
1636 5200 JMP POT
1637 5430 JMP I PLACO
1638 6600 DCWANT, 3633
/LEFT ATRIAL PRESSURE CONTROL OF AP

*2002
2000 7003 PLA CON, NOP
2001 7299 CLA
2002 6554 6554 /LOAD K3 IF SW 4 UP
2003 4503 JMS I LOADK3
2004 1072 TAD K3
2005 3175 DCA COUNT1
2006 1063 TAD E
2007 3064 DCA E1
2010 6563 6563 /INPUT PLAREF
2011 0335 AND C1777
2012 7041 CIA
2013 3062 DCA PLAREF
2014 6511 6511 /WAIT FOR SENSE LINE
2015 7410 SKP
2016 5214 JMP -2

/INPUT APRESS, PLA & PAS
2017 7030 NOP
2022 6572 6572 /INPUT APRESS
2021 2035 AND C1777
2022 3065 DCA APRESS
2023 6574 6574 /INPUT PAS
2024 0335 AND C1777
2025 3104 DCA PAS

/COMPUTE ERROR
/ERROR = PLA-PLAREF
2026 6575 6575 /INPUT PLA
2027 2035 AND C1777
2030 1062 TAD PLAREF /THIS IS THE ERROR
2031 3332 DCA REGI
2032 1032 TAD REGI
2033 0337 AND C4000 /CHECK FOR SIGN
2034 3051 DCA SIGN
2035 1051 TAD SIGN
2036 7449 SZA
2037 4503 JMS I NEG
2039 1232 TAD REGI
2041 2375 ISZ COUNT1
2042 7413 SKP
2043 5246 JMP +3
2044 7113 CLL RAR /DIVIDE E BY 2*K3
2045 5241 JMP -4
2046 3032 DCA REGI
2047 1051 TAD SIGN
GET K1 IF SV 2 IS UP

LOAD K1

MULTI

ENTER SHIFT WITH E IN ACC

/COMPUTE DERIVATIVE OF ERROR
/DEDT = E-(E-1)

GET K2 IF SW 3 IS UP

LOAD K2

MULTI

/THIS IS DEDT

PAS CONTROL
/PASCON IF SW 5 DOWN

PASCO

/DETERMINE VAP
/VAP = VAP + K1E + K2DEDT

VAP

K1E

K2DEDT

/THIS IS VAP

VAPTEM

HRCON IF SW 6 DOWN

APCON

CHECK FOR PRESSURE BEYOND RANGE

HRCON, NOP

INPUT MIN APRESS

C1777

CIA
2117 1065 TAD APRESS
2120 7513 SPA I DECHR
2121 5453 JMP

2122 7280 CLA
2123 6565 6565 /*INPUT MAX APRESS
2124 0035 AND C1777
2125 7041 CIA
2126 1065 TAD APRESS
2127 7500 SMA
2130 5454 JMP I INCHR

2131 7000 APCON, NOP
2132 7200 CLA
2133 1061 TAD VAPTEM
2134 3344 DCA VAP
2135 1244 TAD VAP

/*CHECK FOR VALVE BEYOND RANGE
2136 7300 NOP
2137 0040 AND C6900
2140 7440 SZA /*SKIP IF BEYOND
2141 5477 JMP I OVE

2142 7200 CLA
2143 1344 TAD VAP
2144 1273 TAD M302
2145 7513 SPA
2146 5476 JMP I UNDE

2147 7200 CLA
2150 1044 TAD VAP
2151 6543 6543 /*OUTPUT VAP
2152 5427 JMP I POTS

*2200
2200 7230 UNDER, NOP
2201 7202 CLA
2202 1074 TAD C0333
2203 6543 6543
2204 3044 DCA VAP
2205 6521 6521 /*RELAY LIGHT 1 = UNDER
2206 4447 JMS I DELAY
2207 6531 6531
2210 5427 JMP I POTS

2211 7323 OVER, NOP
2212 7200 CLA
2213 1035 TAD C1777
2214 6543 6543
2215 3044 DCA  VAP
2216 6522 6522 /RELAY LIGHT 2 = OVER
2217 4447 JMS  I DELAY
2218 6532 6532
2221 5427 JMP  I POTS
2222 3000 LODK1, 3000
2223 7422 HLT
2224 7604 LAS
2225 3070 DCA  K1
2226 5622 JMP  I LODK1
2227 0300 LODK2, 3000
2230 7402 HLT
2231 7634 LAS
2232 3071 DCA  K2
2233 5627 JMP  I LODK2
2234 3000 LODK3, 3000
2235 7402 HLT
2236 7604 LAS
2237 7043 CMA
2240 3272 DCA  K3
2241 5634 JMP  I LODK3
2242 7303 DEHR, NOP
2243 7200 CLA
2244 1261 TAC  VAPTEM
2245 7341 CIA
2246 1344 TAD  VAP
2247 7510 SPA
2250 5455 JMP  I APCO /RETURN IF INC ADDRESS
2251 7200 CLA
2252 1042 TAD  VHR
2253 1265 TAD  DECR
2254 3032 DCA  REG1 /CHECK FOR MIN HR
2255 1932 TAD  REG1
2256 3340 AND  C6903
2257 7442 SZA
2260 5427 JMP  I POTS
2261 7200 CLA
2262 1332 TAD  REG1
2263 3042 DCA  VHR
2264 5427 JMP  I POTS
2265 3010 DECR, 10
2266 7323 INHR, NOP
2267 7200 CLA
2270 1344 TAD  VAP
2271 7340 CIA
2272 1361 TAD  VAPTEM
2273 7510 SPA
2274 5455 JMP I APCO /RETURN IF DEC APRESS
2275 7200 CLA

2276 1042 TAD VHR
2277 1312 TAD INCR
2280 3032 DCA REG1 /CHECK FOR MAX RATE
2281 1032 TAD REG1
2282 7041 CIA
2283 1356 TAD C3400
2284 7500 SMA
2285 5427 JMP I POTS
2286 7200 CLA
2287 1232 TAD REG1
2290 3342 DCA VHR
2291 5427 JMP I POTS
2292 7770 INCR, -10

2303 0300 DELA, 3000
2304 7200 CLA
2305 1324 TAD OUTE
2306 3326 DCA OUTER
2307 2325 ISZ INNER /INNER LOOP
2308 5317 JMP -.1 /18.432 MSEC
2309 2326 ISZ OUTER
2310 5317 JMP -.3
2311 5713 JMP I DELA

2314 7700 OUTE, 7700
2315 0000 INNER, 0000
2316 0000 OUTER, 0000

2327 0000 SHIFT, 0000
2328 3032 DCA REG1
2329 1032 TAD REG1
2330 2037 AND C4000 /CHECK FOR SIGN
2331 3051 DCA SIGN
2332 1051 TAD SIGN
2333 7440 SZA /SKIP IF POS
2334 4500 JMS I NEG
2335 7200 CLA
2336 1032 TAD REG1
2337 4424 JMS I MULT
2338 3001 MULT2, 3001
2339 7000 NOP
2340 7300 CLA CALL
2341 1425 TAD I MPI
2342 7312 TAP
2343 3332 DCA REG1
2344 1051 TAD SIGN
2345 7440 SZA
2346 4500 JMS I NEG
2353 7200 CLA
2354 1032 TAD  REG1
2355 5727 JMP  I SHIFT

2356 0000 NEJAT, 0000
2357 7200 CLA
2360 1032 TAD  REG1
2361 7241 CIA
2362 3032 DGA  REG1
2363 5756 JMP  I NEGAT

/\OFF PAGE POINTERS

*1923
3223 7496 CFIO,  7496
3221 3226 SAMPLE, 0226
3222 5777 LOC,  5777
3223 3420 PAGE2,  3420
3224 3630 MULT,  3630
3225 3631 MPI,  3631
3226 3640 DIVIDE, 3640
0327 1620 POTS,  1620
3223 2322 PLACC, 2322
3231 0330 SAV,  0330
3232 0330 REG1, 0330
3233 7774 FOUR,  7774
3234 2330 SKIP, 2330
0235 1777 C1777, 1777
3236 2303 C2303, 2303
3237 4320 C4020, 4320
3242 6322 C6322, 6322
3241 7322 C7322, 7322
3242 6400 VHR,  6400
3243 6420 VCC,  6420
3244 1233 VAP,  1233
3245 3203 COUNTR, 3203
3246 2403 PASCO, 2403
3247 2313 DELAY, 2313
3251 2327 SHIFT, 2327
3351 3330 SIGN,  3330
3352 2342 MULTI, 2342
3353 2242 DECHR, 2242
3354 2266 INCHR, 2266
3355 2131 APCO, 2131
3356 3433 C4333, 3433
3257 1233 C1233, 1233
3269 3330 VFL,  3330
3261 3333 VATEM, 3333