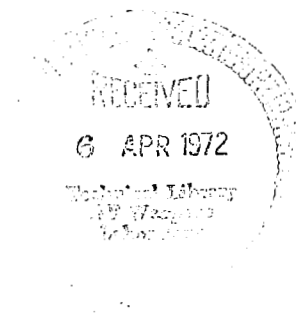# NASA TECHNICAL NOTE

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DESIGN OF A SPECIALIZED COMPUTER
FOR ON-LINE MONITORING
OF CARDIAC STROKE VOLUME

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16. Abstract

The design of a specialized analog computer for on-line determination of cardiac stroke volume by means of a modified version of the pressure pulse contour method is presented. The design consists of an analog circuit for computation and a timing circuit for detecting necessary events on the pressure waveform. Readouts of arterial pressures, systolic duration, heart rate, percent change in stroke volume, and percent change in cardiac output are provided for monitoring cardiac patients. Laboratory results showed that computational accuracy was within 3 percent, while animal experiments verified the operational capability of the computer. Patient safety considerations are also discussed.

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SUMMARY

The design of a specialized analog computer for on-line determination of cardiac stroke volume by means of a modified version of the pressure pulse contour method is presented. The computer is designed to be used for early detection of abnormal recoveries from open-heart surgery and to monitor acutely ill cardiac patients. The pressure pulse contour method is described and implemented by means of electronic circuitry. This circuitry includes an analog circuit for computation of cardiac stroke volume from arterial pressure and a timing circuit for detecting timing events on the pressure waveform. These events are used for resetting integrators and controlling sample and hold amplifiers.

The computer provides continuous readouts of end diastolic blood pressure, dicrotic pressure, systolic duration, heart rate, percent change in cardiac stroke volume, and percent change in cardiac output flow. No calibration for stroke volume or cardiac output is required, since the unit gives percent change from a given point in time. Laboratory experiments indicated that readouts were within 3 percent of hand calculated estimates of cardiac output. The computer detected the proper timing events on a variety of animal pressure waveforms, thus providing a useful monitor. A discussion on patient safety considerations is included.

INTRODUCTION

This report describes the design of a specialized analog computer for on-line monitoring of cardiac stroke volume. The unit was developed as part of the NASA Technology Utilization Program. The work reported herein was done in support of the heart research program directed by Dr. Earle B. Kay and Dr. Akio Suzuki of St. Vincent Charity Hospital, Cleveland, Ohio.

The need for a practical method for continuously monitoring the beat-to-beat stroke volume and cardiac output flow of heart patients with a minimum of discomfort and intervention has led many investigators to study the possibility of using arterial pressure for estimating cardiac output. This approach is motivated by the relative ease of inserting a catheter for measuring arterial pressure as opposed to implantation of an electromagnetic, ultrasonic, or other type of flowmeter, which requires major surgical intervention.

Several methods for obtaining flow from arterial pressure have been studied. One such method, described in reference 1, is the pressure gradient technique. This method computes an estimate of the instantaneous blood velocity from the measured pressure gradient at two points several centimeters apart along the aorta. It has the disadvantage, however, of requiring two pressure measurements that are well calibrated with respect to each other. Reference 2 describes a variation on the pressure gradient technique that eliminates one of the pressure measurements but assumes that the pressure waveform is undistorted and has no reflections. Instantaneous blood velocity is then computed from the time derivative of pressure and the pressure pulse wave velocity.

A more empirical approach is used in the pressure pulse contour methods. These methods use formulas based on simplified arterial models to compute the flow through the vascular resistance. The results obtained with this approach have been useful in applications where qualitative changes in cardiac stroke volume are the main interest. Since 1899, various formulas for this approach have been investigated. One of the more practical and apparently accurate pressure pulse contour methods for estimating cardiac stroke volume for each heartbeat was developed in 1953 by H. R. Warner and colleagues (ref. 3). This method required two pressure signals - the central aortic pressure and the pressure at one peripheral site. For clinical applications, Warner modified the method to require only the measurement of central aortic pressure (ref. 4). He programmed this method on a digital computer for continuous on-line monitoring of cardiac patients. This system, which also included venous pressure measurements, has been successful in detecting complications earlier than would have been the case by the usual methods of monitoring. In reference 4, Warner's method for computing stroke volume was compared to the dye dilution method for measuring cardiac output. Results showed a good correlation between the two methods for large variations in heart rate and peripheral resistance.

The equations for Warner's method were modified and solved by means of a small specialized analog computer which samples and computes about 25 times per minute. This unit would be useful for hospitals which do not have a digital computer facility available for cardiac patient monitoring. The computer described in this report indicates the percent change in the patient's stroke volume from a certain point in time. This capability would be valuable for monitoring changes or trends in a patient's condition, as well as for indicating alarm conditions immediately.

This report presents further detail on Warner's pressure pulse contour method, the analog circuitry used to implement this method, the timing circuits needed for determining timing events, and test results obtained from laboratory and animal experiments.

PRESSURE PULSE CONTOUR METHOD

This section gives the derivation of Warner's basic method, the circulatory model, and the assumptions that are made. The equation resulting from the derivation give stroke volume as a function of the pressure waveform at a peripheral site. These equations are then modified to provide a relation for stroke volume as a function of the aortic pressure waveform. This form is used for computation. Symbols are defined in the appendix.

Basic Method

The pressure pulse contour method devised by Warner for estimating cardiac stroke volume on a beat-to-beat basis assumes that the arterial bed is a distensible tube which terminates in a finite resistance. During systole, when the left ventricle ejects its stroke volume into the arteries, some of this volume is absorbed by the distension of the arteries while the rest flows out of the arteries through the peripheral vascular resistance. During diastole, when the aortic valve prevents return flow from the arteries to the ventricle, the arteries lose some of their stored volume through the peripheral resistance, as indicated by the decay in arterial pressure. Under conditions of steady-state equilibrium, the total volume of blood that passes through the peripheral resistance in one cycle is the same as the stroke volume ejected by the left ventricle during that cycle.

This concept is illustrated by use of the model shown in figure 1, which is similar to the vascular model presented in reference 5. The pressure waveforms at various locations in the model arterial bed are also shown in figure 1. The pressure waveform at the peripheral resistance P_{pr} is assumed to be identical to the waveform in the aorta near the aortic valve P_{ao}. It is also assumed that P_{pr} is delayed from P_{ao} by a fixed time delay τ, which Warner assumes to be 80 milliseconds. (Time delay τ in fig. 1 is exaggerated to show the time-displaced waveforms.) These, of course, are simplifying assumptions and do not reflect the actual waveforms in the arterial system.
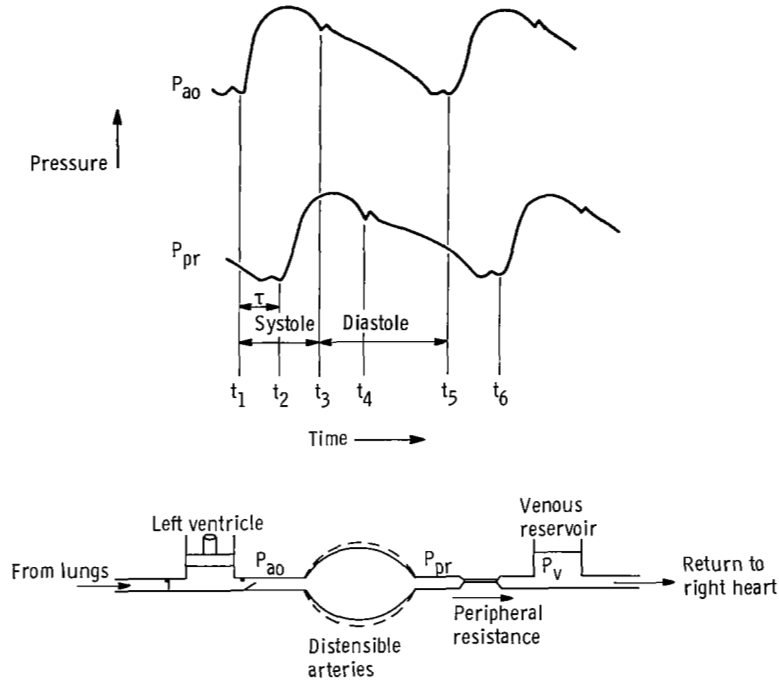
Figure 1. - Arterial pressure waveforms and model used for the pressure pulse contour method.

If the venous pressure P_v is assumed to be constant, then the flow Q through the peripheral resistance at any instant can be described by the equation

$$Q(t) = \frac{P_{pr}(t) - P_v}{R} \tag{1}$$

where R is the peripheral resistance (assumed to be linear), and $P_{pr}(t)$ indicates the time-variant peripheral pressure. The volume flowing through the peripheral resistance during one cardiac cycle would be

$$\Delta V_{pr} = \frac{1}{R} \int_{t_1}^{t_5} \left[P_{pr}(t) - P_v \right] dt \tag{2}$$

The peripheral resistance is considered constant during periods of a few heartbeats and can, therefore, be taken outside the integral. Assuming no net accumulation of blood in the arteries, this would also equal the volume discharged by the heart during one systole, or

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$$\Delta V_{pr} = V_{st} \qquad (3)$$

where V_{st} is the stroke volume.

Since the resistance varies according to body demands, R represents an unknown quantity that cannot be predetermined for calculating stroke volume. However, during diastole, the modeled circulatory system is passive, and the arterial pressure decays in a manner determined by the arterial distensibility and the peripheral resistance. The arterial distensibility is considered to be constant for a given individual over a long period of time. Therefore, a relation can be derived for expressing R in terms of the distensibility and measurable parameters. The arterial distensibility is defined as a hydraulic capacitor which follows the relation

$$\Delta V = Cf(\Delta P) \qquad (4)$$

where ΔV is the change of volume in the capacitor, C is a proportionality constant which will be called capacitance, and $f(\Delta P)$ is a function of the change in pressure. The term $f(\Delta P)$ is empirically obtained by Warner to account for the nonlinear capacitance of the arteries and the time delay in the pressure waveform.

The change in volume in the arteries during diastole is

$$\Delta V_d = V_3 - V_5 \qquad (5)$$

where V_3 is the total arterial volume at the beginning of diastole and V_5 is the total arterial volume at the end of diastole. The change in arterial pressure during diastole ΔP_d is related by equation (4) to give

$$\Delta V_d = Cf(\Delta P_d) \qquad (6)$$

where ΔP_d is defined by Warner as

$$\Delta P_d = \frac{1}{\tau} \left[\int_{t_3}^{t_4} P_{pr}(t)dt - \int_{t_5}^{t_6} P_{pr}(t)dt \right] \qquad (7)$$

For equation (7),

$$(t_4 - t_3) = (t_6 - t_5) = \tau \qquad (8)$$

Therefore, the first integral of equation (7) divided by τ gives the average pressure

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between t_3 and t_4, and the second integral divided by τ gives the average pressure between t_5 and t_6.

Since all of the volume that drains out of the arteries during diastole passes through the peripheral resistance, ΔV_d can also be determined from equation (2) as

$$\Delta V_d = \frac{1}{R} \int_{t_3}^{t_5} \left[P_{pr}(t) - P_v\right]dt \qquad (9)$$

It is now possible to combine equations (6) and (9) to obtain the following equation for R:

$$R = \frac{\int_{t_3}^{t_5} \left[P_{pr}(t) - P_v\right]dt}{Cf(\Delta P_d)} \qquad (10)$$

Then, using equation (10) to replace R in equation (2) yields

$$V_{st} = \frac{Cf(\Delta P_d) \int_{t_1}^{t_5} \left[P_{pr}(t) - P_v\right]dt}{\int_{t_3}^{t_5} \left[P_{pr}(t) - P_v\right]dt} \qquad (11)$$

Since the arterial capacitance C is considered constant, the only independent variable in equation (11) is arterial pressure. Warner found good correlation between this equation and the cardiac output determined by the dye dilution technique when

$$f(\Delta P_d) = \sqrt{\Delta P_d} \qquad (12)$$

and the venous pressure P_v was assumed to be a constant 20 mm Hg (0.27 N/cm^2). By using the areas A_s and A_d under the pressure curve of P_{pr} (see fig. 2) in place of the integrations, equation (11) can be rewritten as

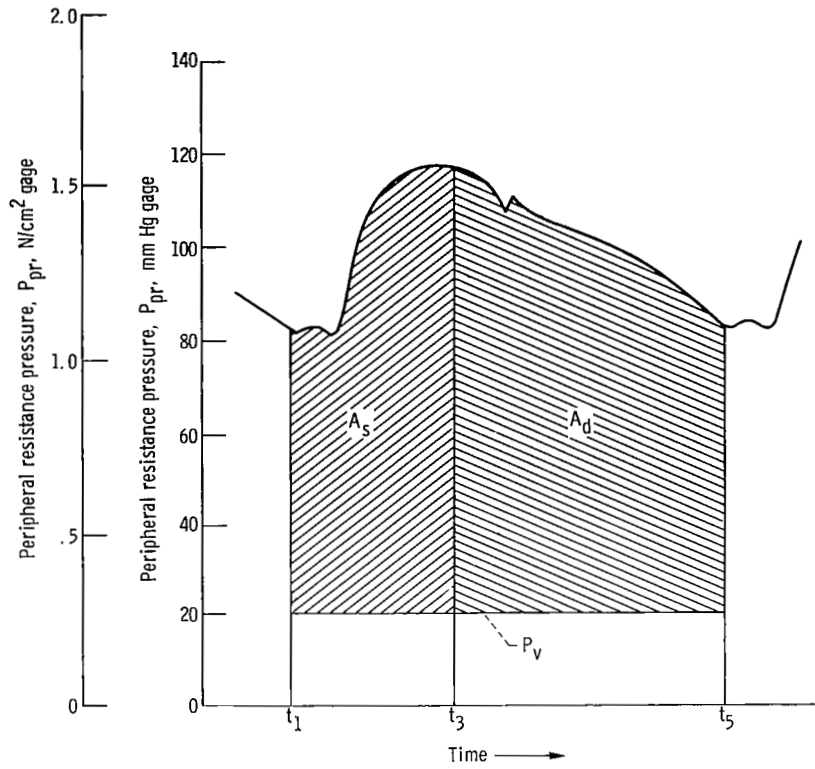$$V_{st} = C\sqrt{\Delta P_d}\left(1 + \frac{A_s}{A_d}\right) \qquad (13)$$

Figure 2. – Areas under the peripheral resistance pressure waveform.

Modifications For On-Line Analog Computation

To implement equation (13) electronically, the times t_1, t_3, and t_5 must be detected. Detection of these times on P_{pr} is difficult as they occur in advance of the two most notable characteristics of the pressure waveform, namely, the pressure rise at the beginning of systole (t_2) and the dicrotic notch (t_4) which occurs at closure of the outflow valve. Therefore, in order to make equation (13) useful for computational methods, some modifications are necessary.

Since it is assumed that the waveforms of P_{ao} and P_{pr} are identical and since it is more convenient to measure pressure in the aorta, P_{ao} will be the waveform used for computation. The points on the waveform of P_{ao} which can be detected are renamed as t_a, t_b, and t_c, as shown in figure 3. The numerator of equation (11) can then be found in terms of P_{ao}. The ΔP_d term in the numerator is approximated as

$$\Delta P_d = P_b - P_a \qquad (14)$$

where P_a and P_b are the pressures at t_a and t_b, respectively. Since the integral

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of one complete cycle remains the same for both P_{pr} and P_{ao},

$$\int_{t_1}^{t_5} \left[P_{pr}(t) - P_v\right] dt = \int_{t_a}^{t_c} \left[P_{ao}(t) - P_v\right] dt \qquad (15)$$
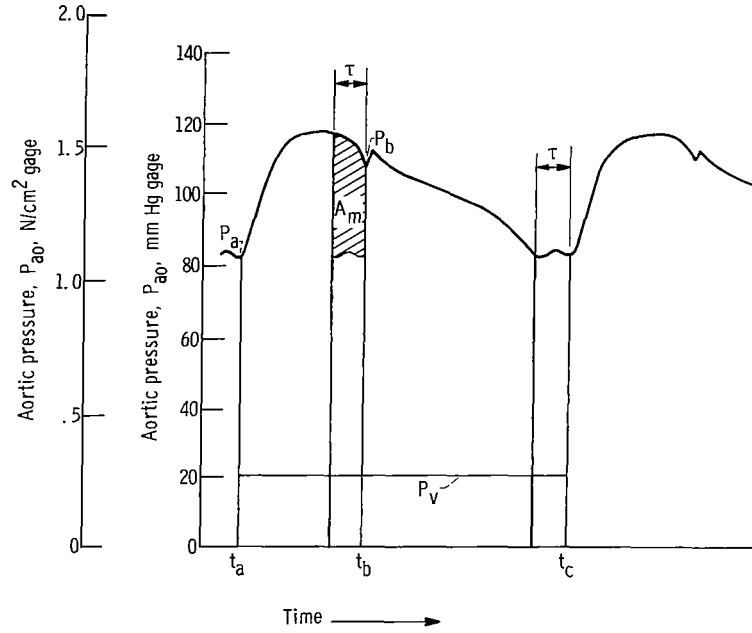

Figure 3. – Area under the aortic pressure waveform and time points used to compute stroke volume.

The denominator of equation (11) can also be obtained in terms of P_{ao} as

$$\int_{t_3}^{t_5} \left[P_{pr}(t) - P_v\right] dt = \int_{t_b-\tau}^{t_c-\tau} \left[P_{ao}(t) - P_v\right] dt$$

$$= \int_{t_b-\tau}^{t_b} \left[P_{ao}(t) - P_v\right] dt + \int_{t_b}^{t_c} \left[P_{ao}(t) - P_v\right] dt$$

$$- \int_{t_c-\tau}^{t_c} \left[P_{ao}(t) - P_v\right] dt \qquad (16)$$

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Figure 3 shows graphically that the first integral on the right side of equation (16) is larger than the third integral and that the difference is an area A_m, where

$$A_m = \int_{t_b-\tau}^{t_b} [P_{pr}(t) - P_v]dt - \int_{t_c-\tau}^{t_c} [P_{pr}(t) - P_v]dt \tag{17}$$

This area can be approximated as

$$A_m = \tau(P_b - P_a) \tag{18}$$

and equation (16) becomes

$$\int_{t_3}^{t_5} [P_{pr}(t) - P_v]dt = \tau(P_b - P_a) + \int_{t_b}^{t_c} [P_{ao}(t) - P_v]dt \tag{19}$$

For computational purposes, it is necessary to express the integral on the right side of equation (19) as

$$\int_{t_b}^{t_c} [P_{ao}(t) - P_v]dt = \int_{t_a}^{t_c} [P_{ao}(t) - P_v]dt - \int_{t_a}^{t_b} [P_{ao}(t) - P_v]dt \tag{20}$$

Substitution of equations (12), (14), (15), (19), and (20) into equation (11) yields

$$V_{st} = \frac{C\sqrt{P_b - P_a} \int_{t_a}^{t_c} [P_{ao}(t) - P_v]dt}{\tau(P_b - P_a) + \int_{t_a}^{t_c} [P_{ao}(t) - P_v]dt - \int_{t_a}^{t_b} [P_{ao}(t) - P_v]dt} \tag{21}$$

The form of this equation is useful for computation. The C in this equation is assumed to be constant (although it is different from patient to patient) and can be considered as a calibration gain coefficient.

ANALOG CIRCUIT DESIGN

The computer described in this report has two primary parts - the analog circuits and the timing circuits. This section discusses the analog circuits for computing stroke volume in some detail, including the means of obtaining an output of percent change in stroke volume.

Computation of Cardiac Stroke Volume

Equation (21) can readily be solved by using an analog circuit coupled to some logic used for timing. A block diagram of equation (21) is given in figure 4. This diagram
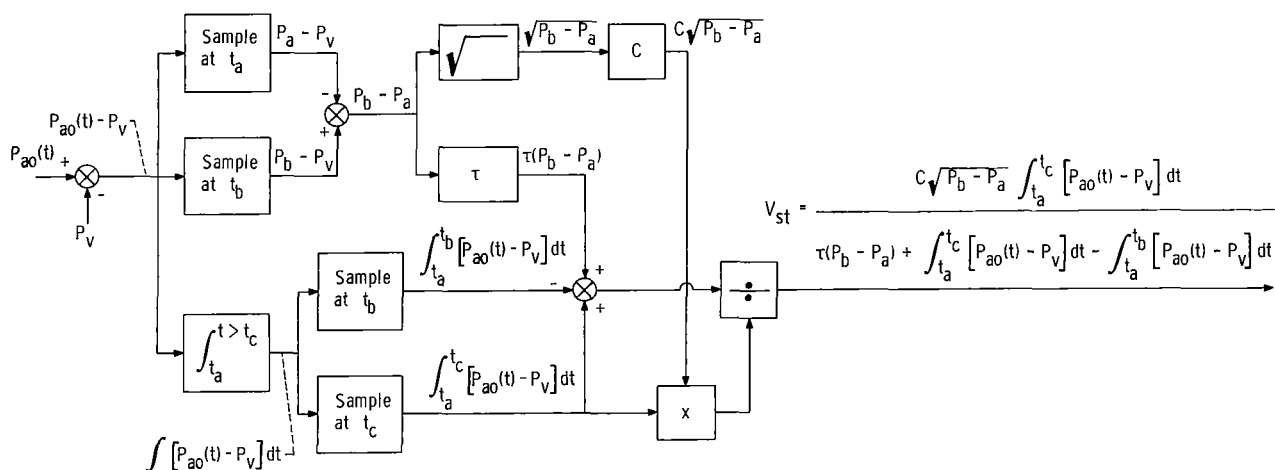

$$V_{st} = \frac{C\sqrt{P_b - P_a} \int_{t_a}^{t_c} \left[P_{ao}(t) - P_v\right] dt}{\tau(P_b - P_a) + \int_{t_a}^{t_c} \left[P_{ao}(t) - P_v\right] dt - \int_{t_a}^{t_b} \left[P_{ao}(t) - P_v\right] dt}$$

Figure 4. - Block diagram of stroke volume equation.

shows that it is necessary to sample the pressure at t_a and t_b to obtain P_a and P_b. Pressure is also integrated, starting at t_a and sampled at t_b and t_c. The denominator of equation (21) is obtained by subtracting the integrals and adding the result to $\tau(P_b - P_a)$. The numerator is obtained by taking the square root of $(P_b - P_a)$, multiplying it by C, and then multiplying this product by the integral over a complete cycle. Finally, carrying out the division on equation (21) yields an output of cardiac stroke volume.

The electrical schematic of the analog circuit is shown in figure 5. The circuit was constructed with operational amplifiers encapsulated in epoxy and with reed relays. The operational amplifiers are inexpensive, general-purpose amplifiers with output current ratings of 5 milliamperes. The multipliers and square-root circuits are also commer-
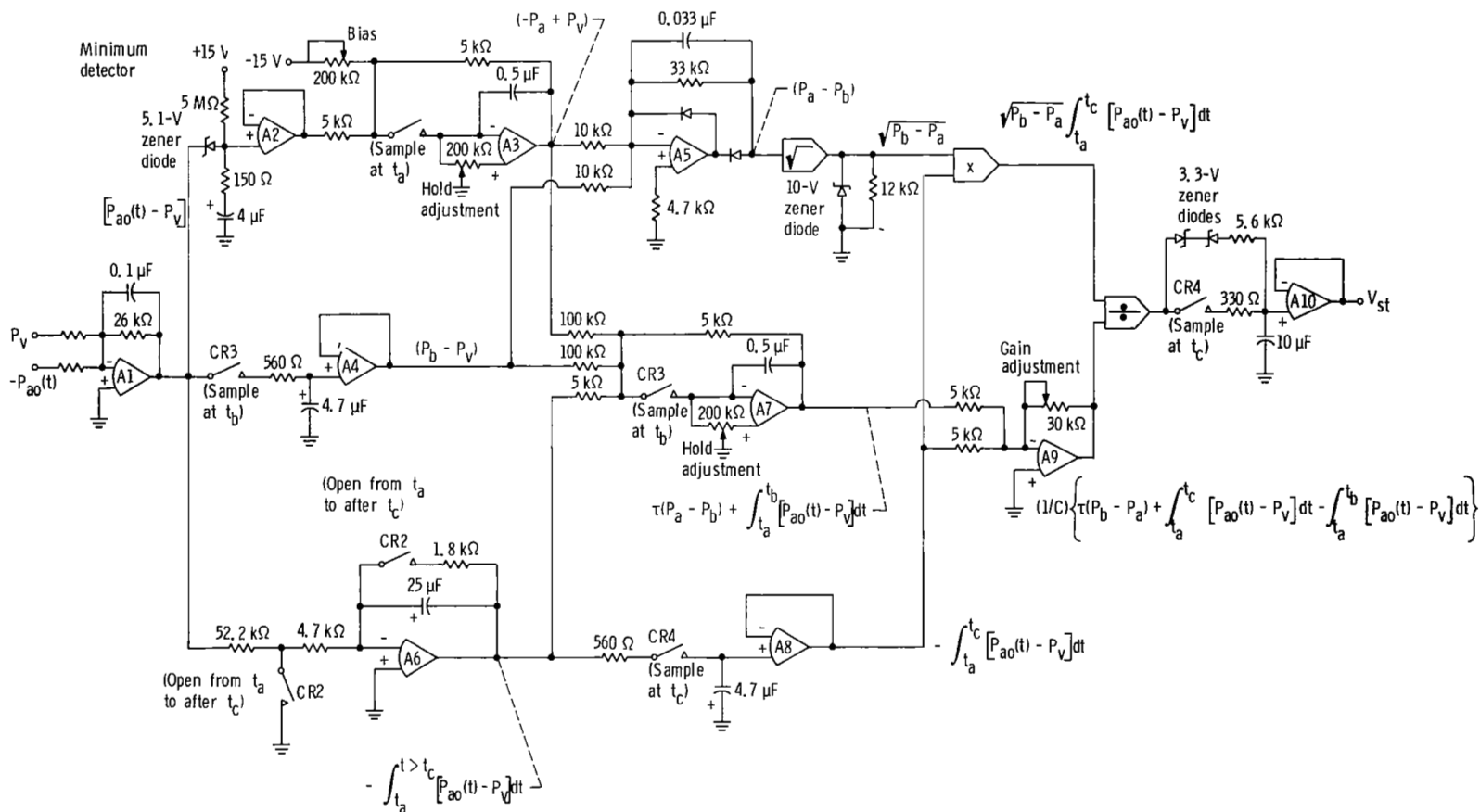
Figure 5. – Simplified electrical schematic diagram of analog circuit for computing stroke volume.

cial, encapsulated units. Although commercial, solid-state, sample-and-hold units are available, the cost was reduced by designing sample-and-hold circuits using operational amplifiers and relays.

The arterial pressure signal is obtained for the computer with a pressure transducer attached to a catheter in the aorta. The instrument amplifier for the transducer bridge was built into the computer. (Safety considerations for patient monitoring will be discussed later in this report.) The output of this amplifier provides the input to amplifier A1 in figure 5. Amplifier A1 is used to subtract the venous pressure P_v from the arterial pressure P_{ao} and smooth the waveform somewhat.

Amplifier A2 is a minimum detector which tracks the pressure in a decreasing direction and holds the minimum pressure. The 5.1-volt zener diode rapidly charges the 4-microfarad capacitor when the computer is initially turned on and resets the minimum detector after sampling P_a. The error in minimum pressure caused by the forward voltage drop across the zener diode is biased out after amplifier A_2.

The output of this amplifier is then sampled at t_a and held by amplifier A_3 to obtain P_a. An inherent delay in the method of detecting t_a necessitates the use of a minimum detector, since the combination of a slight delay in the time at which P_a is sampled and the rapid increase in pressure at t_a could cause a large error in the value obtained for P_a. The dicrotic notch pressure P_b is sampled directly at t_b with amplifier A4.

These two sampled pressures ($-P_a$ and P_b) are summed by amplifier A5. This amplifier is also used as a limiter to prevent the input to the square-root circuit from going positive. If this input did go positive, it would be equivalent to taking the square root of a negative number, in which case the square-root circuit goes into unstable oscillation. The 10-volt zener diode on the square-root circuit output prevents saturation which results in latchup, a characteristic of the particular square-root circuit used.

Amplifier A6 and its circuit are used to integrate the pressure waveform, starting at t_a. This integral is then sampled at t_b with amplifier A7 and at t_c with amplifier A8 to obtain the necessary integrals for equation (21). The $\tau(P_b - P_a)$ term is also added at amplifier A7. The output of A8, which is the integral from t_a to t_c, is multiplied by the output of the square-root circuit to obtain the numerator of equation (21), excluding C. Amplifier A9 is used to add the output of amplifier A7 to the output of amplifier A8 to obtain the denominator of equation (21). The potentiometer in the feedback of amplifier A9 is used to adjust the gain of the denominator, which is equivalent to adjusting the value of the calibration constant C.

Stroke volume is obtained by dividing the output of the multiplier by the output of amplifier A9. The divider output is sampled at t_c by amplifier A10. Because of the limited output current of the divider, the sample-and-hold amplifier A10 cannot track a change greater than 5 volts during the sample time. Therefore, the zener diodes are

used to charge the 10-microfarad capacitor to within 3.3 volts of the divider output when not sampling.

Computation of Percent Change in Stroke Volume

The output of the circuit in figure 5 would give stroke volume in liters if a calibration of the arterial capacitance C would be made for each patient. This is often difficult to determine, since it requires an accurate measurement of cardiac output flow and heart rate. The percent change in stroke volume relative to that at a given time is more easily obtained from this computer and requires no calibration against another measurement. This percent readout is informative about a patient's condition and shows trends in his condition over periods of time. As indicated in reference 6, the stroke volume of the heart for a reclining patient usually remains relatively constant while variations in heart rate achieve needed variations in cardiac output flow. However, monitoring the changes in stroke volume may yield information that is clinically significant for post operative patients.
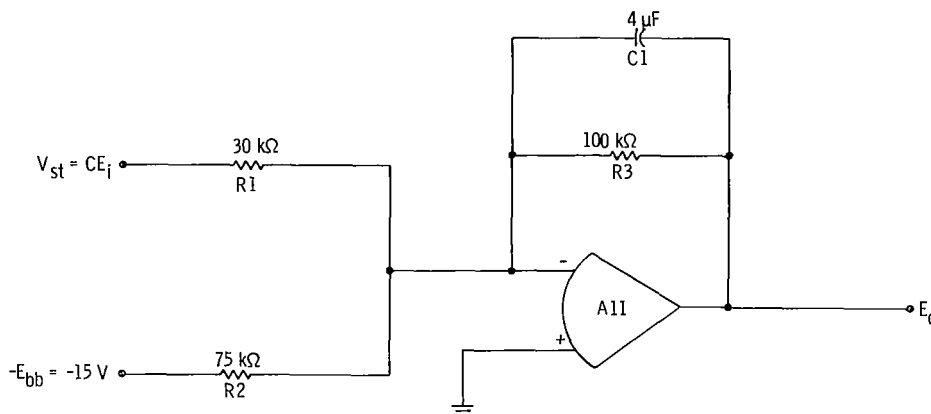

Figure 6. - Circuit for detecting percent change in stroke volume.

To obtain an output from the computer which is a percentage reading, the circuit of figure 6 was used. In this figure, E_i represents the output of amplifier $A10$ in figure 5 with the calibration gain C factored out. The equation describing the steady-state operation of the circuit is

$$E_o = -\left(\frac{R3}{R1} CE_i - \frac{R3}{R2} E_{bb}\right) \qquad (22)$$

If C is adjusted so that initially $E_o = 0$, then

$$CE_i = \frac{R1}{R2} E_{bb} \tag{23}$$

This is the reference value of CE_i at which the percent change in stroke volume is zero. If the stroke volume changes by $C \Delta E_i$ but the setting of C remains the same, the output of the circuit in figure 6 is

$$E_o = -\left[\frac{R3}{R1} C(E_i + \Delta E_i) - \frac{R3}{R2} E_{bb}\right] \tag{24}$$

Solving equation (23) for C and substituting into equation (24) gives

$$E_o = -\left(\frac{R3}{R2} E_{bb}\right)\left(\frac{\Delta E_i}{E_i}\right) \tag{25}$$

Equation (25) is in the form of a gain term multiplied by the percent change in E_i. The resistances R1, R2, and R3 were chosen to give a value of 6 volts for the reference voltage ($R1E_{bb}/R2$) and 20 volts for the gain ($R3E_{bb}/R2$). This results in a full-scale output change of 10 volts when E_i changes by 50 percent. The feedback capacitor C1 is used to smooth the output of the percent-change stage.

TIMING CIRCUIT DESIGN

The design of the analog circuit is dictated by the equations being solved. However, this circuit will not function without proper detection of the time at which events occur on the pressure waveform. This section presents the timing circuits which were designed to operate the relays in the analog circuit. They provide a highly reliable detection of timing events in pressure waveforms containing high-frequency components and low-frequency disturbances caused by breathing effects.

Basic Requirements

The relay contacts of the analog circuit in figure 5 must be closed momentarily at times t_a, t_b, and t_c to sample the various circuit voltages at the appropriate times.
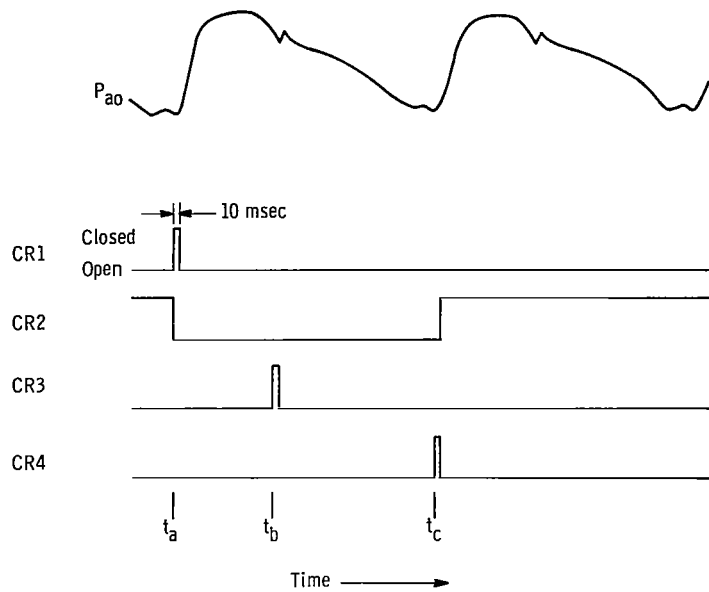
Figure 7. – Relay contact switching required from the timing circuit.

In addition, the integrator must be reset before the next computation cycle. These timing requirements are met with the timing circuit by energizing the relays according to the schedule of figure 7.

Relay CR1 of figure 5 is momentarily energized at the beginning of systole, as shown in figure 7, to sample P_a. Relay CR2 is deenergized at the beginning of systole of the sampled cycle to start integration of the pressure waveform. This relay is then energized after the end of diastole to reset the integrator. Relay CR3 is momentarily energized at the dicrotic notch to sample P_b with one set of contacts and to sample the pressure integral from t_a to t_b with another set of contacts. Relay CR4 is momentarily energized at the end of diastole to sample the pressure integral from t_a to t_c and to sample the computed stroke volume for monitoring. The contacts of all the momentarily energized relays (relays CR1, CR3, and CR4) are closed for 10 milliseconds. This time period is sufficiently long to charge the sample-and-hold circuit capacitors, while it is relatively short with respect to changes in the signal being sampled.

Timing Circuits

In order to obtain these relay driving signals, the timing events t_a, t_b, and t_c must be detected in each sampled cycle. This is accomplished with the circuit shown in block diagram form in figure 8.
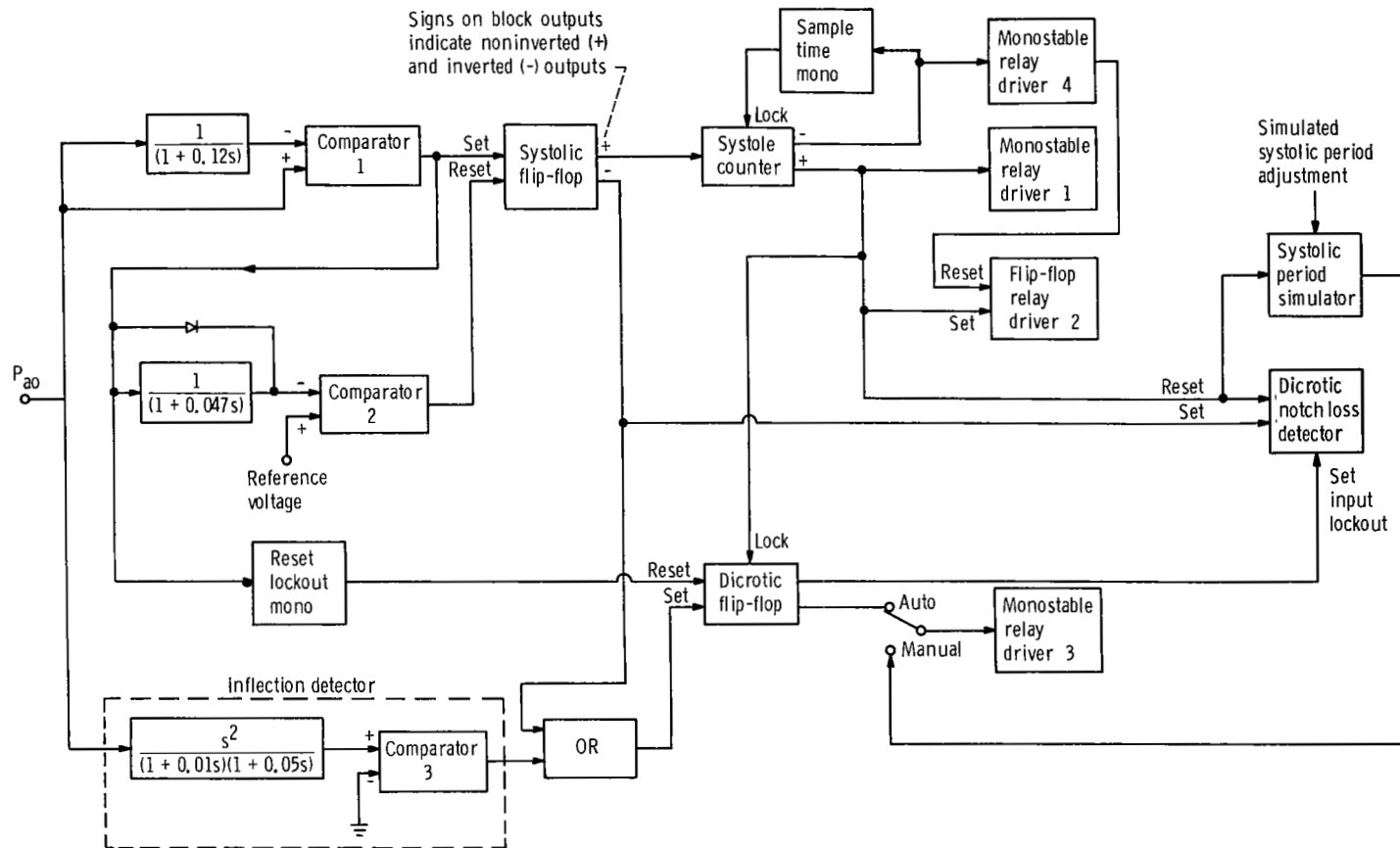
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Figure 8. - Block diagram of timing circuits for cardiac computer.

<u>Detection of the beginning of systole</u>. - In figure 7 it is easy to visually detect the beginning of the heart's cycle as a steep rise in pressure. This could be detected by taking the derivative of pressure and sensing the point at which it crosses from a small negative value to a large positive value. However, most pressure transducer measurements on patients are subject to noise or, as in the case of valve disorders, the pressure waveform is distorted, which could cause false trigger signals.
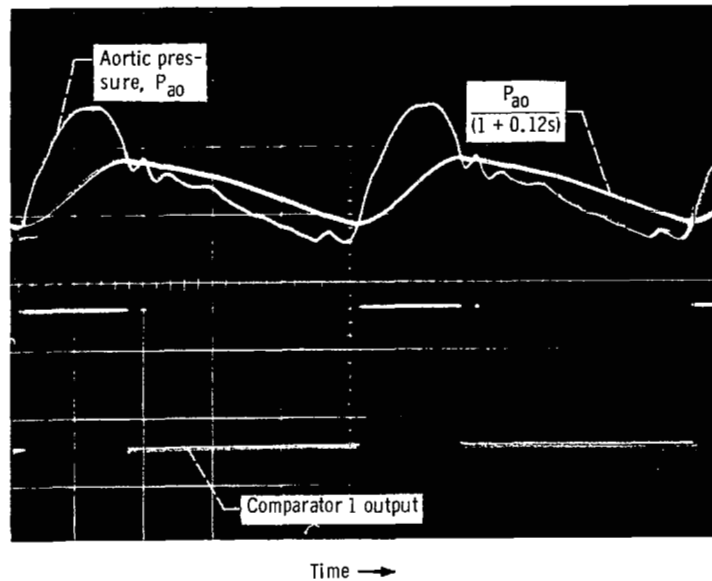
Therefore, the beginning of systole is detected in figure 8 by filtering the pressure waveform with a first-order low-pass filter with a corner frequency of 1.3 hertz. This filtered signal is then compared with the actual pressure waveform by comparator 1. The output of comparator 1 is a square wave that switches whenever the two inputs cross, as shown in figure 9(a). Near the end of diastole, the filtered signal is greater than the actual signal. At the onset of systole, the unfiltered signal rises rapidly and crosses the filtered signal, which is unable to follow the abrupt change in voltage. This crossover, which occurs very near the beginning of systole, provides an indication of both t_a and t_c.

Delay in this detection could cause an error in sampling P_a. However, this is corrected by using a minimum detector before the sample circuit in the analog section, as previously discussed. The error in the integral, also caused by this detection delay, is very small when compared with the total integral value and can be considered insignificant.

One difficulty with this type of detection is the fact that multiple crossovers can occur in one cycle if the pressure oscillations exist near the crossover. One such signal is the dicrotic notch, which has a frequency content of 6 to 15 hertz. If the amplitude of the dicrotic notch is large enough, this portion of the waveform crosses the filtered signal and causes a false output on comparator 1.

To avoid such transients, the output of comparator 1 is filtered with a nonlinear, first-order, low-pass filter, as shown in figure 8. The output of the nonlinear filter follows the output of comparator 1 in the positive direction but decays exponentially when the comparator output switches to a negative value, as shown in figure 9(b). The resultant signal is compared with a reference voltage by means of comparator 2 to obtain a signal that switches to positive in mid-diastole only once each cycle, as is also illustrated in figure 9(b).

In figure 8, if the positive-going output of comparator 2 is used to reset a flip-flop (bistable multivibrator, ref. 6) and the positive-going output of comparator 1 is used to set it, the output of the flip-flop would be set at the beginning of systole and reset late in the diastolic period. The pressure waveform is fairly smooth near the end of diastole and, therefore, the output of comparator 1 is not subject to false crossovers at this point. Once comparator 1 has set the systolic flip-flop, it has no effect until comparator 2 provides a reset input. This prevents false crossovers on comparator 1 from disrupting the timing signal.

(a) Unfiltered pressure waveform compared with filtered pressure waveform.
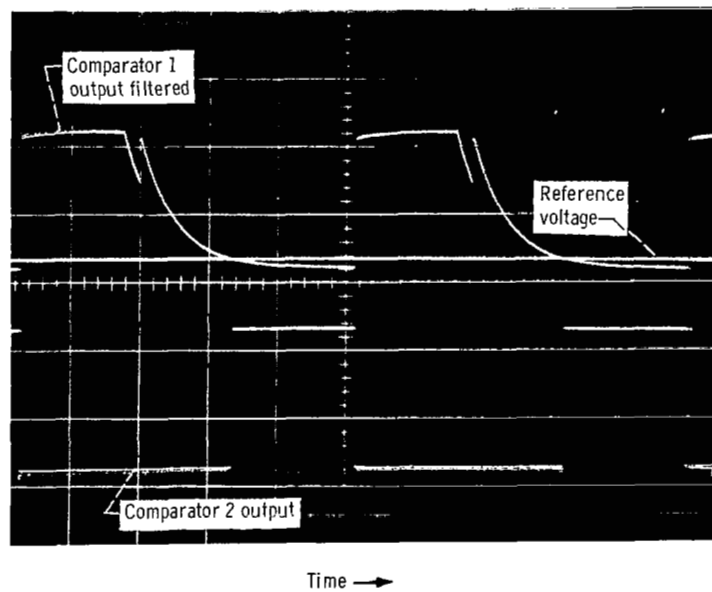
(b) Nonlinear filtered output of comparator 1 compared with a reference voltage.

Figure 9. – Output waveforms of circuits used for detecting the beginning of systole.

It should be noted that this circuit also could be subject to false triggering due to low-frequency pressure signals such as those caused by breathing. Breathing modulates the average arterial pressure level with a 0.25-hertz signal. The circuit just described for detecting the beginning of systole is unaffected by breathing, because the 1.3-hertz corner frequency of the linear, first-order, low-pass filter is well above breathing frequencies. The filtered pressure waveform moves at breathing frequencies with the same amplitude as the unfiltered waveform. When these two signals are subtracted at the input of comparator 1, the breathing signals cancel.

Thus the output of the systolic flip-flop provides a very dependable timing signal for indicating the beginning of systole even in the presence of high-frequency components in the pressure waveform and low-frequency disturbances due to breathing.

Detection of the end of diastole. - The end of the heart's cycle occurs at the beginning of the next systole and can, therefore, be differentiated from the beginning of a measured cycle by counting the positive-going output signal from the systolic flip-flop and assigning the first count as the beginning of a cycle and the second count as the end of the cycle. This is accomplished by using the systole counter, as shown in figure 8. The output of the systole counter and all the outputs of the timing circuit are shown in figure 10.
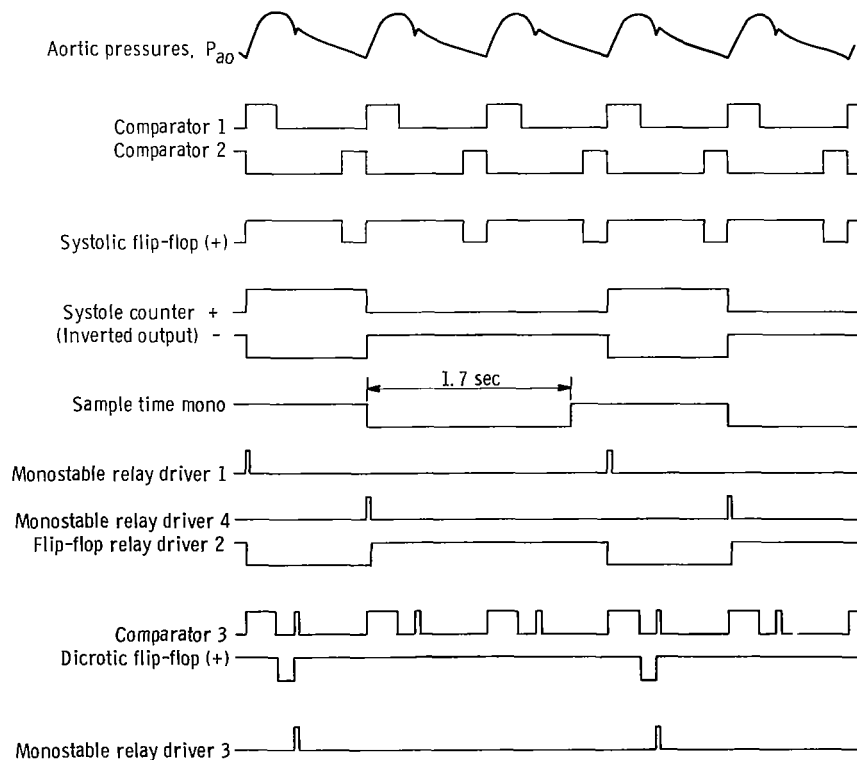

Figure 10. - Timing circuit outputs.

Detection of the dicrotic notch. - The dicrotic notch is detected as the first inflection point on the pressure waveform after the output of comparator 1 switches to the negative direction. This criterion is mechanized in figure 8 with the second-order transfer function and comparator 3. These two blocks comprise an inflection detector with an output that switches at the low-frequency inflection points in the pressure waveform. This signal sets the dicrotic flip-flop when it switches to the positive direction. The flip-flop can be set only after it has been reset by the negative-going slope of the comparator 1 output. Once set, the output of comparator 3 is unable to affect the flip-flop during that cycle.

The reset lockout mono (fig. 8) is a monostable multivibrator used to prevent the output of comparator 1 from resetting the dicrotic flip-flop more than once per cycle. It is triggered into its quasi-stable state by the negative-going output of comparator 1, at which time its output becomes positive and resets the dicrotic flip-flop. The quasi-stable period of this circuit is made sufficiently long to assure that no additional crossovers on comparator 1 will occur for the remainder of that cycle.

Figure 9(a) shows that the slope of the pressure waveform is negative when comparator 1 switches to negative. The next inflection point occurs near the dicrotic notch. This indicates that the output of comparator 3 is negative when the dicrotic flip-flop is reset and then switches in a positive direction, thereby setting the flip-flop at the dicrotic notch. The outputs of comparator 3 and the dicrotic flip-flop are plotted in figure 10 for the normal case.

One additional set input is applied to the dicrotic flip-flop to set the circuit near the end of the cycle. This signal will not affect the flip-flop output when a normal dicrotic notch is detected, because it will have already been set. However, if for some reason the pressure waveform does not have a noticeable dicrotic notch, then the flip-flop is set near the end of diastole. This is done by using the inverted output of the systolic flip-flop. The positive-going slope of this signal is used to set the dicrotic flip-flop. Provisions for detecting and correcting for a missed dicrotic notch will be discussed later.

Sampling rate. - To obtain a fairly continuous monitor, it is desirable to sample as frequently as possible. Since some time is required to reset the integrator at the end of a sampled cycle, it is not possible to sample every cycle. The prospect of sampling every second cycle is good, but may be impractical for patients whose heart-beat alternates (with strong and weak beats). Since only the weak cycles or only the strong cycles would be sampled, an erroneous measure of the patient's condition could be given.

A minimum fixed time interval between samples is obtained by triggering the sample time monostable multivibrator (mono) shown in figure 8 into its quasi-stable state at the end of the sampled cycle. The output of this circuit then locks the systole counter in the state needed before the beginning of systole. This lock is held throughout the

quasi-stable state.   The quasi-stable period of the sample time mono is 1.7 seconds, as indicated in figure 10.

Locking the systole counter prevents it from triggering any output circuits between sample cycles despite the fact that the preceding timing circuits are functioning on every cycle.   The locked output of the systole counter is then used to lock the dicrotic flip-flop between sample cycles, thus preventing any timing outputs from being produced during this period.

Relay driving circuits. - The outputs of the timing circuit are contained in the three
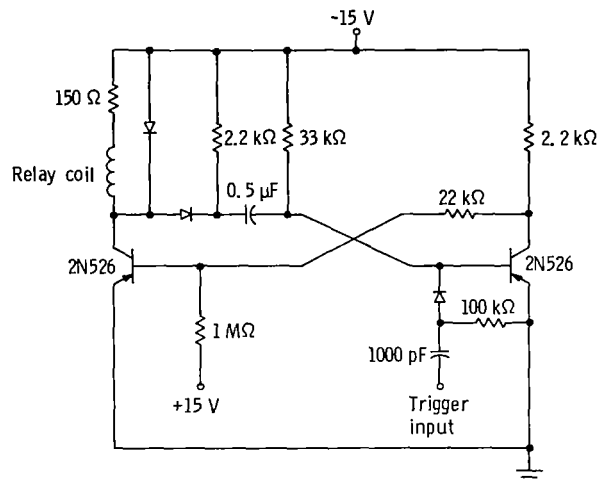
(a) Monostable relay driver (MRD).
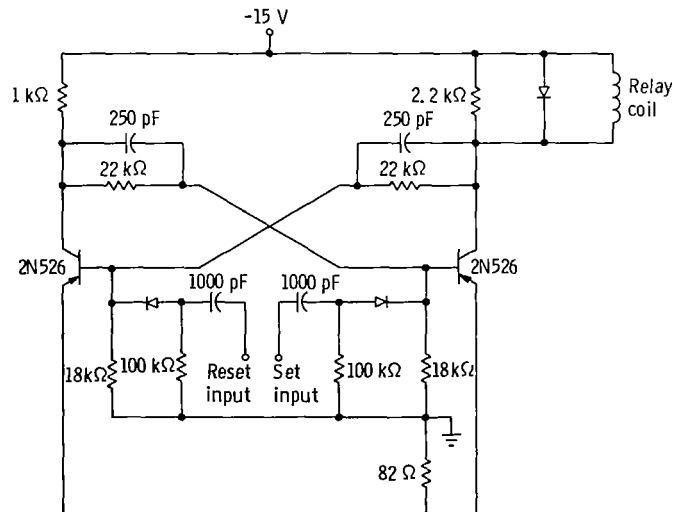
(b) Flip-flop relay driver (FFRD).

Figure 11. - Relay-driver circuits.

blocks in figure 8 labeled monostable relay driver (MRD) and the one block labeled flip-flop relay driver (FFRD). The numbers refer to relay numbers and correspond to those shown in figures 5 and 7.

The monostable relay drivers (MRD's) are basically monostable multivibrators with a relay coil in place of one of the collector load resistors, as shown in figure 11(a). When triggered to its quasi-stable state by the positive-going edge of a square wave input, the multivibrator passes current through the relay coil for the monostable period of approximately 10 milliseconds, after which the multivibrator switches to its stable state. This circuit is used to drive the sample-and-hold circuit relays in figure 5. The contacts on these relays are all normally open.

The flip-flop relay driver shown in figure 11(b) is a bistable multivibrator with a relay coil in place of one of its collector load resistors. This circuit can be set (i.e., the coil can be deenergized) by one positive-going input and reset by a second positive-going input. It is used to drive the integrator relay so that it is set (integrator released) at the beginning of a sampled cycle and reset (integrator output reset to zero) after the end of the sampled cycle. The contacts on this relay are normally open.

The inputs to these relay drive circuits are supplied by the timing circuits discussed earlier in this report. The normal output from the systole counter triggers MRD1 when it switches to positive at t_a. At the same time, this signal is used to set FFRD2. The inverted output of the systole counter switches to positive at t_c and is used to trigger MRD4. This signal also triggers the sample time mono into the locked state, since it indicates the end of the sampled cycle. The FFRD is reset by the inverted output of MRD4, as shown in figure 10. The inverted output of MRD4 is used to reset the integrator after completion of sampling at t_c. The MRD3 is triggered by the normal output of the dicrotic flip-flop at t_b to complete the timing-circuit outputs required by figure 7.

Dicrotic Notch Loss Detection

As mentioned earlier, it is possible that the pressure waveform could be sufficiently damped such that the dicrotic notch does not appear and the time at which the dicrotic notch occurs (t_b) is not detected. If this problem does occur with a patient, it is desirable to indicate this to the operator as a computer error. This is accomplished by using the dicrotic notch loss detector, as shown in figure 8.

The dicrotic notch loss detector circuit is a flip-flop that is reset at t_a. The set input to this circuit is locked out whenever the dicrotic flip-flop is set, as would be the case if the dicrotic notch were detected. If no notch is detected, the loss detector is set late during diastole by the inverted output of the systolic flip-flop. When the loss detector is set, a light is turned on to indicate an error. This light will remain on until

the next sampled cycle, at which time it is turned off by the reset input to the loss detector.

If a detection loss persists, as indicated by the flashing light, a provision is made for manually setting a dicrotic notch with the systolic period simulator of figure 8. This circuit is a monostable multivibrator with an adjustable quasi-stable state. It is manually switched into the circuit with the switch on the input of MRD3. The systolic period simulator is triggered into the quasi-stable state at t_a. At the end of the quasi-stable period, it switches back to its stable state, at which time its output triggers MRD3 to indicate t_b.

To make this adjustment, it is necessary to monitor both the blood pressure and MRD3 output waveforms on an oscilloscope or recorder. This is facilitated in the computer by providing a pressure waveform output terminal that has a spike superimposed on the pressure waveform at the time MRD3 is triggered.

When manually adjusting the dicrotic notch, the spike can be lined up with the visually assumed notch on the waveform. This readout capability also allows the operator to check that the output of comparator 3 is identifying the dicrotic notch correctly when it is being detected automatically.

ADDITIONAL READOUT CIRCUITRY

The computer determines additional basic information concerning the heart's performance which may be as significant as stroke volume. Therefore, readouts of these signals are supplied by means of some additional circuitry.

The circuit of figure 12 is used to obtain systolic period and heart rate. Amplifier A12 integrates a constant input voltage, starting at t_a. The output of A12 is sampled at t_b by A13 to obtain the systolic period. This signal is filtered by A14 to provide a slowly varying signal for a meter readout. Amplifier A15 is used to sample the integral at t_c to obtain the period of one heart cycle. This value is inverted by the divider circuit to obtain heart rate, which is also displayed on a meter readout.

Since cardiac output flow can be found as the product of stroke volume and heart rate, a readout of percent change in cardiac output is obtained by using a circuit similar to that shown in figure 6. Again, this output is in units of percent change from an initial setting and would require calibration by some other method to obtain actual cardiac output.
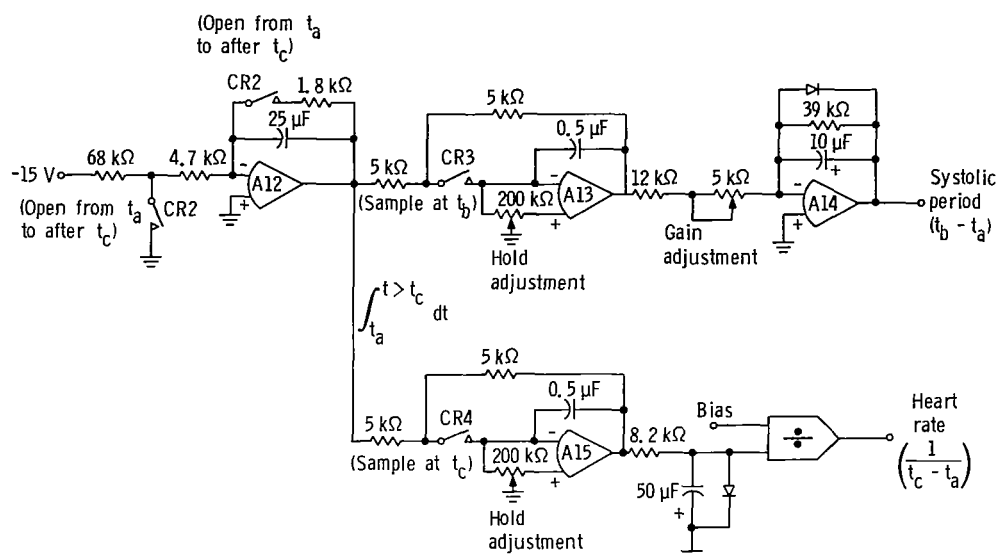
Figure 12. - Simplified electrical schematic diagram for computing systolic period and heart rate.

PACKAGING OF PROTOTYPE COMPUTER

The initial model of this computer, shown in figure 13, was housed in a 25- by 50- by 45-centimeter cabinet and was given the name Pressure Pulse Contour (PPC) Cardiac Computer. Readouts of end diastolic pressure P_a, dicrotic pressure P_b, systolic period $(t_b - t_a)$, heart rate, and percent change in stroke volume are provided by vertical panel meters (fig. 13(a)). The percent change in cardiac output is displayed on a small digital meter. The two potentiometers and the pushbutton on the right are used to zero the percent readouts. The percent change in cardiac output is zeroed by depressing the pushbutton and adjusting the top potentiometer. The percent change in stroke volume is zeroed by adjusting the lower potentiometer.

A toggle switch is provided to the left of the meters for switching from automatic dicrotic notch detection to the manual setting of simulated systolic duration. The simulated period is adjusted using the small potentiometer on the panel. As mentioned previously, an output is provided at the rear of the computer for displaying the pressure waveform with a spike superimposed at the time relay CR3 is energized. The small light between the toggle switch and the potentiometer lights up to indicate that the computer is operating in the manual mode.

Two error lights are provided for indicating that the output being displayed could be in error. The red light (on the left) lights up when any one of the analog operational amplifiers or multipliers goes into saturation. The yellow light (on the right) indicates that the timing circuit has failed to detect the dicrotic notch.
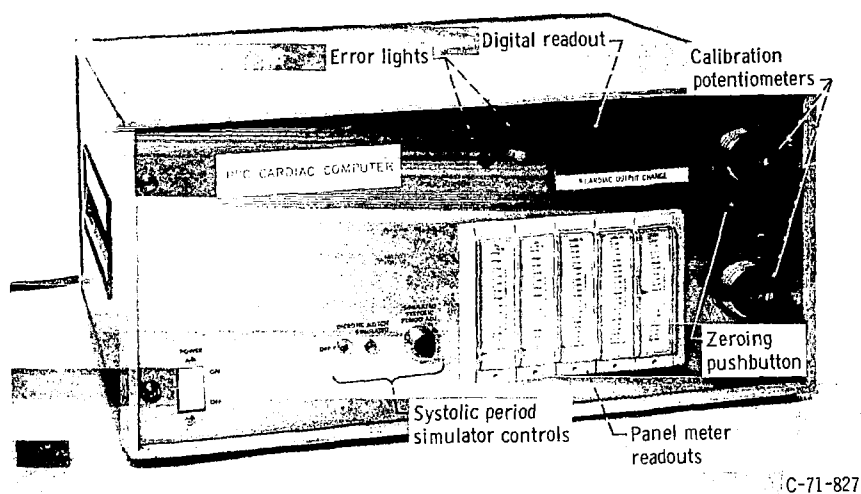
(a) Front view.
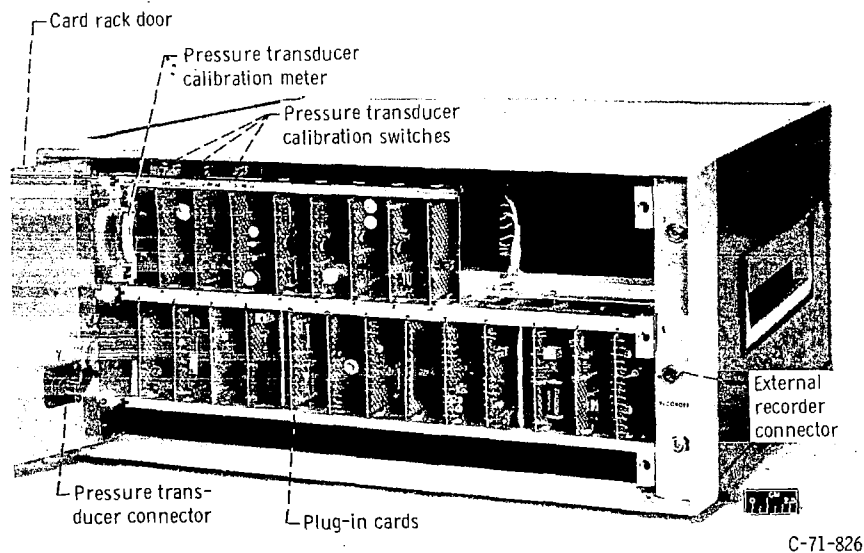
(b) Rear view.

Figure 13. - Pressure pulse contour cardiac computer.

Additional space is provided in this model for the future additions of a small monitoring oscilloscope and a small strip-chart recorder. The circuit components for this unit are mounted on twenty-one 8- by 12-centimeter plug-in cards. These cards slide into a rack which is mounted in the rear of the cabinet, as shown in figure 13(b). The pressure transducer connector is mounted on the door of the rack. Transducer calibration is provided by the switches and vertical meter mounted on the rack. Signals to be used for external monitoring on an oscilloscope or recorder are provided at

25

the connector at the right side of the rack. These signals are the aortic pressure, the aortic pressure waveform with a spike superimposed at t_b, a scope synchronization signal, and a signal ground.

Three power supplies are used with these circuits. A ±15-volt, direct-current, regulated supply with a current capability of ±700 milliamperes is used to power the analog circuits. A 15-volt, direct-current, unregulated supply with a current capability of 1 ampere is used for the timing circuits. The third supply is used for excitation of the transducer bridge.

The transducer supply and instrument amplifier were built into the prototype computer for convenience. However, the patient safety of this input arrangement relies on the electrical isolation of the pressure transducer diaphragm to prevent microshock. To assure safe operation during animal experiments, the electrical isolation of the transducer was checked before and after each experiment. For the transducer used in these tests, the resistance at 200 volts was 120×10^9 ohms, and the capacitance at 60 hertz was 45 picofarads. For 120 volts alternating current at 60 hertz, the maximum leakage current would be 2 microamperes rms. This is below the 10 microampere limit proposed by the National Fire Protection Association for the 1971 National Electrical Code (ref. 7).

When the computer is used to monitor human patients, a commercial pressure monitor system is required to provide the electrical pressure waveform to the analog circuits. It is recommended that a double safety be provided against microshock by using an isolation amplifier or leakage current limiter as well as using an electrically safe transducer. The system should be checked for leakage currents before each usage.

EXPERIMENTAL RESULTS

Results have been obtained with this computer by two methods. The first method provided the computer with an electronically generated waveform in place of the normal pressure transducer and instrument amplifier at the input. Thus, the waveform could be varied to simulate the many possible waveforms to be encountered in actual patient usage. The second method for obtaining results was by experiments with anesthetized animals. These experiments pointed out changes needed in the final development of the computer design and provided added verification of the computer's computational capability.

The timing circuits were tested by the first method to assure that the design criterion was sound. The electronically generated waveform was obtained by using a repetitive diode function generator that provided 50 incremental steps per cycle. This stepwise waveform was applied to a low-pass filter to provide a smooth waveform with a shape similar to a normal aortic pressure waveform.

Electronically generated
waveform for aortic
pressure

Comparator 1

Comparator 2

Systolic
flip-flop (+)

0.1 sec

Systole
counter (+)

Sample
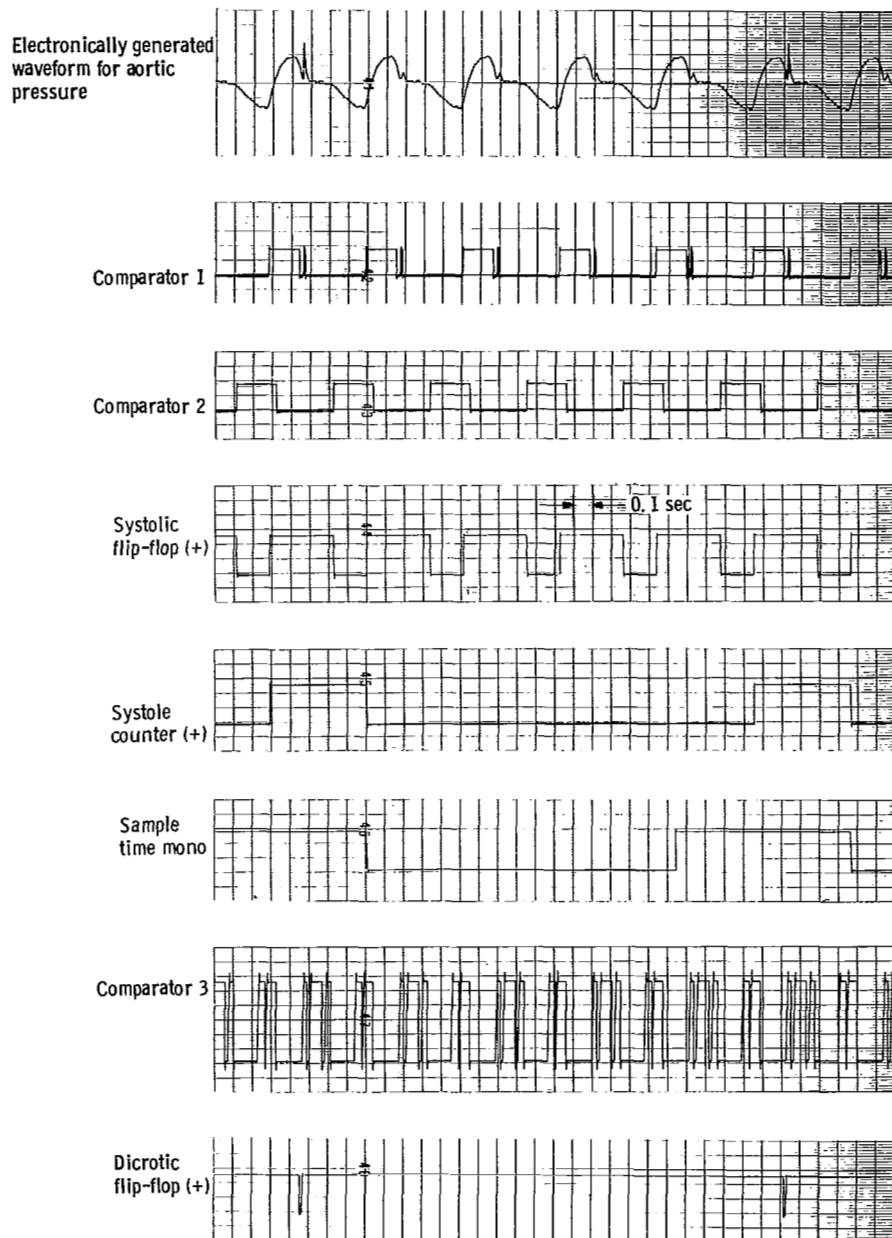time mono

Comparator 3

Dicrotic
flip-flop (+)

Figure 14. - Recording of timing circuit outputs obtained with electronically
generated pressure waveform.

Figure 14 is a recording of the timing-circuit signals as functions of time. For the pressure waveform used here, a false crossover caused the output of comparator 1 to switch more than once per cycle, yet the circuit reliably detected the beginning of systole, as evidenced by the systolic flip-flop output. This illustrates the necessity for comparator 2 to block out false crossovers. The output of comparator 3 switches whenever the slope of the pressure waveform changes polarity. However, this signal only triggers the dicrotic flip-flop once per cycle and only after the first negative-going slope of comparator 1 resets the flip-flop. The point at which the dicrotic notch is determined is displayed by the spike on the pressure waveform.

It is evident from figure 14 that all of the timing signals are functioning as desired and should operate the relay driver circuits in the sequence shown in figure 7. A recording of the relay driver outputs is shown in figure 15 for the same electronically generated waveform. The figure shows that all relay coils are being energized at the appropriate times and demonstrates the inherent delay in detecting the beginning of systole.

The computer accuracy was evaluated by applying a triangular pressure waveform electronically, manually setting the dicrotic notch, and comparing the computer readings for changes in stroke volume and cardiac output with calculated values. Changes
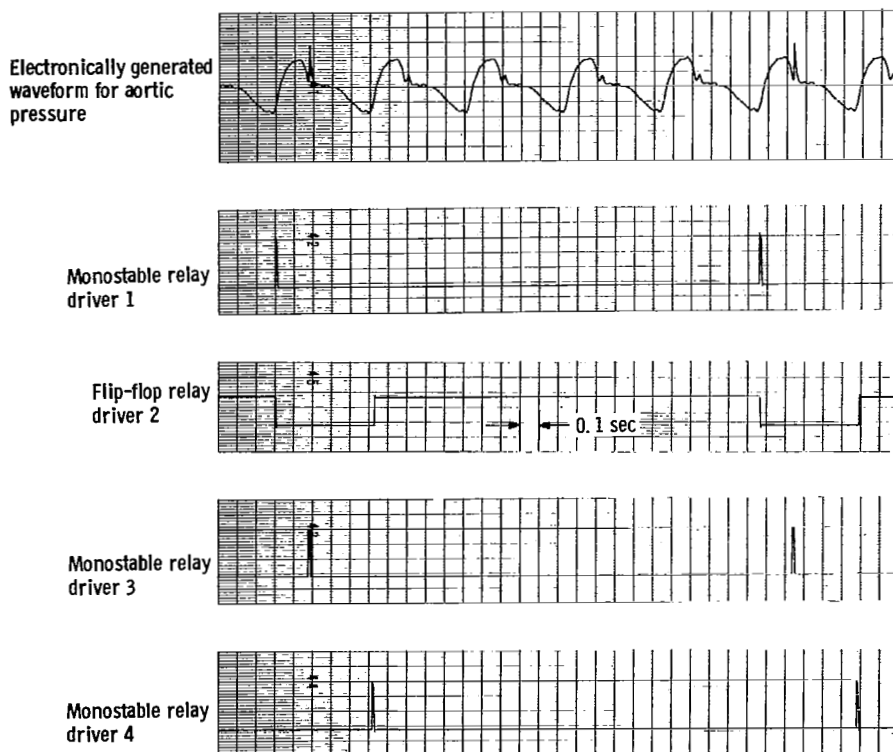

Figure 15. - Outputs recorded from relay driving circuits.

were produced by varying the pulse rate from 60 beats per minute to 180 beats per minute in increments of 20 beats per minute. Pulse rate and systolic duration were measured with a counter to give numbers accurate to within ±0.5 millisecond. The results are given in table I.

TABLE I. - COMPARISON OF CALCULATED

VALUES WITH COMPUTER READINGS

FOR CHANGES IN STROKE VOLUME

AND CARDIAC OUTPUT

Percent change in stroke volume		Percent change in cardiac output	
Calculated value	Computer reading (a)	Calculated value	Computer reading (a)
8.3	9	41.6	43
9.0	9	34.0	35
9.9	10	29.9	30
11.5	12	28.2	28
8.4	9	22.7	24
8.7	9	21.2	22

[a]The computer readings are readable to within ±1 percent.

The meter that shows the percent change in stroke volume can be read to within ±1 percent. All of the measured values for percent change in stroke volume were within ±1 percent of the calculated values. The percent change in cardiac output was also read to within ±1 percent. When compared with calculated values, these computer readings were in error by an average of 3 percent. This error is probably due to component inaccuracies and is acceptable in view of the fact that the method being modeled is an approximation.

Much of the development of this computer was influenced by experiments with anesthetized animals at St. Vincent Charity Hospital, in Cleveland, Ohio. During these experiments, arterial pressure was obtained by inserting a catheter at the femoral artery, with the tip located near the aortic arch. This catheter was filled with saline and was attached to an external pressure transducer which was directly connected to the computer. (The electrical safety considerations for this procedure have been mentioned earlier.)

The experiments with animals helped to further verify the timing circuit operation,

since many different waveforms could be obtained by administration of certain drugs. One such pressure waveform, shown in figure 16, was taken after an injection of isoproterenol. The top trace is P_{ao}, while the bottom trace is the same pressure waveform at a different gain, with the spike superimposed to indicate where the computer has detected the dicrotic notch. Despite the distortion caused by this drug, the computer reliably detected the occurrence of the dicrotic notch, as well as other timing signals. This type of performance may be necessary when monitoring sick patients who require the administration of drugs or have otherwise distorted pressure waveforms.

The experiments with animals were also useful for demonstrating to medical personnel the ease of operation and the readability of computer outputs.
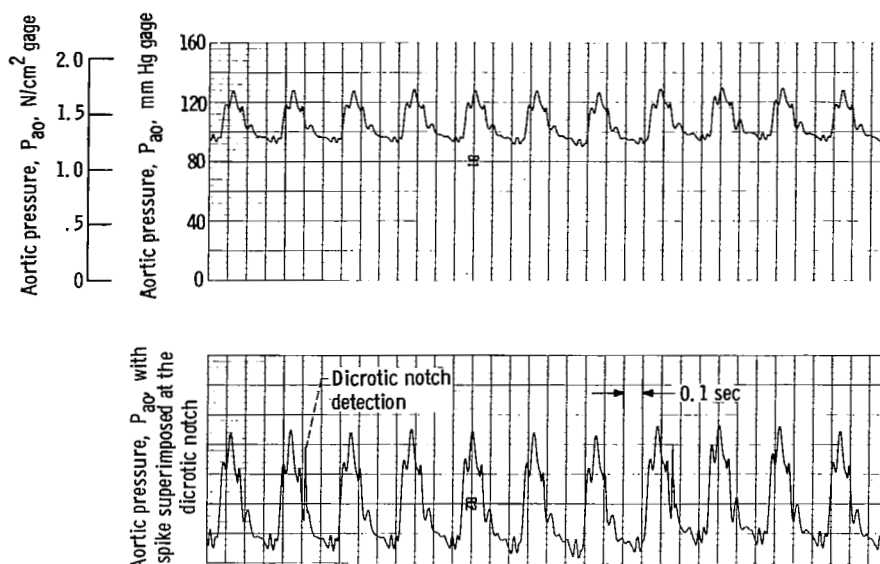

Figure 16. – Arterial pressure waveform and dicrotic notch detection for an animal with isoproterenol injection.

CONCLUDING REMARKS

The design of a specialized pressure pulse contour cardiac computer for use as a patient monitor has been presented. This computer is capable of detecting timing events on-line, even for distorted pressure waveforms, and computing estimates of the percent change in stroke volume and cardiac output with 3 percent computational accuracy. The computer, with its additional readouts of end diastolic pressure, dicrotic notch pressure, systolic duration, and heart rate, is capable of supplying information concerning the condition and trends of patients from a single pressure transducer.

The end result is that it may be possible for many hospitals which do not have extensive monitoring equipment to use such a unit for intensive-care patients, since its size and ease of operation offer a distinct advantage over the use of a general-purpose digital computer for such monitoring.

The experience gained with the design and development of this first prototype can be applied to make further computational improvements. Future models could be made more compact by using integrated circuit technology, and could contain monitoring oscilloscopes and have preset alarms to indicate when the patient is in danger.

Lewis Research Center,
 National Aeronautics and Space Administration,
  Cleveland, Ohio, January 3, 1972,
   764-74.

APPENDIX - SYMBOLS

A	area under pressure waveform curve, $(N)(sec)/m^2$
A1 to A15	operational amplifiers
C	hydraulic capacitance of arterial system, $m^4/\sqrt{N}$
C1	electrical capacitance, F
CR1 to CR4	relays
E	voltage, V
f(P)	function of P
P	pressure, N/m^2
ΔP	change in pressure, N/m^2
Q	flow, m^3/sec
R	hydraulic resistance, $(N)(sec)/m^5$
R1 to R3	electrical resistance, Ω
s	Laplace transform operator, sec^{-1}
t	time, sec
V	volume, m^3
ΔV	change in volume, m^3
τ	time delay, sec

Subscripts:

a	time at beginning of systole (see fig. 2)
ao	aortic
b	time at dicrotic notch (see fig. 2)
bb	supply
c	time at end of diastole (see fig. 2)
d	diastolic
i	input
m	area defined in fig. 2
o	output
pr	peripheral resistance

s	systolic
st	stroke
v	venous
1 to 6	times as defined in fig. 1

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