Assessment of bovine uterine artery hemodynamics using Doppler ultrasound and a computer model

Leroy R. Waite

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Waite, Leroy R., Ph.D.

Iowa State University, 1987
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INTRODUCTION

In the cattle breeding industry, one important component of efficient management is the maximization of conception rates. To obtain this goal it is important to diagnose pregnancy in cattle as early as possible, and to rebreed the non-pregnant cows at the next heat period. Using current techniques there is no practical test which reliably detects pregnancy at less than 30 days after conception.

The research described in this dissertation was initiated several years ago with a general objective to investigate the feasibility of using Doppler ultrasound for early pregnancy diagnosis in cattle. The proposed technique was based on four main concepts (Young and Ford, 1986):

- Blood flow through the middle uterine artery supplying the uterine horn of a cow in which the fetus is developing is significantly different than the flow through the opposite (contralateral) uterine artery at approximately 16 days post-breeding.
- Blood velocity waveforms in the uterine arteries can be measured using ultrasonic crystals placed against the arteries during rectal palpation.
- The difference in blood flow patterns between pregnant and non-pregnant cows can be quantified through an analysis of the velocity waveform.
• The ultrasonic device can be designed and packaged into a simple, inexpensive unit that would be suitable for use by farm personnel on the farm.

The study of blood velocity waveforms has an important role in the field of hemodynamics, and these waveforms are currently used to investigate blood flow in a variety of applications. These applications include prenatal assessment of uterine, ovarian, and umbilical artery blood flow; relating blood flow waveforms to age induced changes in the brachial and carotid arteries; the study of abnormal neonatal cerebral hemodynamics; evaluation of arterial stenoses; and others.

As this project evolved, it became clear that a number of different aspects of blood flow in uterine arteries would need to be considered before the true potential of the use of Doppler ultrasound to diagnose pregnancy could be assessed. Therefore, the project was broken down into several phases. To assist the reader in following these various phases a statement of the objective of each phase is given along with a brief summary.

• The objective of phase 1 was the design, development, and testing of a suitable ultrasonic probe. To accomplish this an ultrasonic probe (Waite, 1985) was designed and built which would fit on an operator's fingertip and could be used
for rectal palpation of the uterine artery. Once this device was available, preliminary data collection began. In this phase Doppler ultrasound blood velocity waveform data were collected from the bovine uterine artery using the new transducer, and a technique for routinely collecting these data was developed (Waite, 1985).

- The objective of phase 2 was to obtain some basic hemodynamic data related to uterine artery blood flow. To characterize bovine uterine artery velocity waveforms, and to relate waveshapes to mean flow, attempts were made to obtain flow waveforms using electromagnetic flowmeters. Electromagnetic flow probes were surgically implanted around the uterine arteries of several cows and some data were obtained. This procedure and some difficulties which were encountered are further explained in the chapter entitled "Materials and Procedures."

- The objective of phase 3 was the design, development, and testing of a microcomputer-based device which could be used to collect and analyze Doppler blood velocity waveforms in the field. This device was designed and constructed in order to provide a means of quickly and efficiently analyzing data at the site of data collection.

- The objective of phase 4 was to collect continuous wave Doppler data in both non-pregnant and pregnant cows, using
the finger probe, and to analyze these data in order to characterize uterine artery blood velocity waveforms. The waveform analyzer noted above allowed for more efficient collection of data and 146 sets of velocity waveforms were collected. During this same time period pulsed Doppler flow probes were implanted on the uterine arteries of four cows and pulsed Doppler velocity waveforms were also collected. These pulsed Doppler waveforms collected in un-bred cattle enabled better characterization of the flow velocity waveform and also provided information concerning variations of the flow waveform over the estrous cycle. Along with the electromagnetic and pulsed Doppler flow data, blood samples were collected in order to measure hormone levels of estrogen and progesterone over the estrous cycle of the cow.

• The objective of phase 5 was to develop and use a computer model of flow in the uterine artery. This model made it possible to study the theoretical effect of various parameter changes on the blood velocity waveform, and to gain a better understanding of the relationship between mean flow and flow velocity waveforms.

• The final objective of the research, phase 6, was to use the results of the foregoing phases to draw some conclusions with regard to the feasibility of early pregnancy detection using Doppler velocity waveforms.
In the following chapters the details of these various phases are described. All animal data used in this research were obtained at the Iowa State University Reproduction Research Farm with the assistance of Dr. S. P. Ford and A. J. Conley of the Department of Animal Science at Iowa State University.
LITERATURE REVIEW

The purpose of this literature review is to provide the reader with a review of some current research as well as some basic background information in the areas of the anatomy of arteries, the assessment of arterial blood flow using blood velocity waveforms, arterial modeling, vascular control mechanisms, and pattern recognition.

The review of the anatomy of arteries provides a basic background of the structure of arteries which is important to the understanding and assessment of arterial blood flow. In reviewing the assessment of arterial blood flow using blood velocity waveforms, a number of examples from the current literature are cited in which blood velocity waveforms were used to study flow in the uterine artery, carotid artery, femoral artery and other arteries. Some basic background information related to computer modeling of arterial blood flow is presented along with a few examples of models which have been used. A review of some basic ideas of vascular control mechanisms is given. This includes neural, humoral and local vascular control. This information is particularly important to the development of the conceptual form of the mathematical model of the artery.

The section on pattern recognition is written to give a background in pattern recognition and define some
terminology which is later used to describe the method of pattern recognition used to collect and analyze blood velocity waveforms.

Anatomy of Arteries

The structure of arteries differs, depending on the size and type of vessel. All arteries are composed of three layers. The tunica intima is the innermost layer and is formed by the endothelium, along with a layer of connective tissue and a basement membrane. The tunica media is the middle layer and is composed of a mixture of smooth muscle fibers and elastic fibers. The tunica externa (or adventitia) is the outermost layer and is composed of connective tissue containing elastic and collagenous fibers. Larger arteries contain vasa vasorum. These are small blood vessels which provide a blood supply to the walls of the arteries.

The larger arteries are called elastic arteries. Elastic arteries have a very thick tunica media with a lot of elastic fibers. In elastic arteries an internal elastic lamina separates the tunica intima from the tunica media and an external elastic lamina separates the tunica media from the tunica externa.
In smaller arteries the tunica media consists almost entirely of up to 40 layers of smooth muscle cells. These arteries are called muscular arteries.

Arterial vessels which are less than 0.5 mm in diameter are called arterioles. Arterioles have a muscular media which contains 1 to 5 layers of smooth muscle cells. There is no external elastic lamina and the tunica externa is narrow and poorly developed.

Capillaries are the smallest blood vessels. They form the connection between the arterial and venous vessels. Capillaries are formed from a single layer of epithelial cells which are rolled in a tube and surrounded by a thin basement membrane of the tunica intima. Two or three cells are generally required to make up the circumference of a capillary. The mean diameter of a capillary is approximately 7-9 μm.

In most capillary networks there are two types of vessels. Thoroughfare channels directly connect arterioles and venules. These thoroughfare channels usually contain some smooth muscle cells and are therefore not true capillaries. True capillaries branch from and rejoin the thoroughfare channels. A ring of smooth muscle surrounds the true capillary at the point where it arises from the thoroughfare channel and is important in the control of
blood flow through the capillaries. This ring is called the precapillary sphincter.

The basic information on the structure of arteries which is given above, is important to the understanding of blood flow in arteries. As the structure of an artery changes, flow conditions can change. Blood flow or velocity waveforms will be different in arteries with different structure, when given the same pressure input waveform. The following section addresses the idea of using the blood velocity waveforms to investigate blood flow in a variety of situations.

Use of Blood Velocity Waveforms and Indices

The study of blood velocity waveforms plays an important role in the field of hemodynamics. One way to investigate blood velocity waveforms is to mathematically quantify the waveshape using a waveform index or a group of waveform indices. Some indices used are, the pulsatility index, rise time, acceleration, height-width index, percent systole, damping factor, diastolic velocity slope, carotid velocity index, Laplace transform coefficients, Fourier coefficients and principal components (Waite, 1985).

Once calculated, it is sometimes possible to correlate the waveform index or indices with a clinical condition,
such as increased placental resistance, or to an arterial characteristic, such as age related changes in an artery. There are a number of examples of the use of blood velocity waveform indices in the current literature and several of these indices are defined as follows.

• The Fourier pulsatility index $PI_F$ (Woodcock et al., 1972) is defined by

$$PI_F = \sum_{i=1}^{n} \frac{V_i^2}{V_0}$$

where $V_i$ is the modulus magnitude of the $n$th Fourier harmonic and $V_0$ is the mean forward velocity.

• The peak-to-peak pulsatility index (Gosling and King, 1974) is probably the most widely used index and has widespread clinical use. This index relates the peak-to-peak amplitude of the velocity waveform to the mean amplitude. It is calculated as

$$PI = \frac{\text{(peak-to-peak amplitude)}}{\text{(mean amplitude)}}$$

Another form of pulsatility index (Skidmore and Woodcock, 1978) which is used is defined by

$$PI_s = \frac{(S-D)}{S}$$

where $S$ is the peak systolic amplitude and $D$ is the end diastolic amplitude.

• The A/B ratio (Trudinger et al., 1985a) is defined as:

$$A/B = \frac{\text{(peak systolic amplitude)}}{\text{(minimum diastolic amplitude)}}$$
• The rise time (Coghlan and Taylor, 1980) is a commonly used index which is measured as the time between the foot of the wave and the systolic peak.

• The acceleration index (Hankner, 1978) is simply the rate of change of the blood velocity with respect to time \((dV/dt)\). The specific parameter measured is normally the systolic acceleration. This may be the average systolic acceleration which can be calculated as:

\[ A = (V_{pk} - V_{ft}) / \text{rise time} \]

where \(V_{pk}\) = maximum pulse velocity, and \(V_{ft}\) = minimum pulse velocity at beginning of rise, or it may be the maximum systolic acceleration which may be easily computed when the velocity-time wave is available in the form of digitized data. Although not dimensionless in this form, acceleration divided by mean or peak amplitude of the velocity-time waveform could be used.

• The height-width index (HWI) (Johnston et al., 1984) may be calculated in the following manner:

\[ \text{HWI} = \frac{\text{PI}}{\text{duration of systolic peak/duration of pulse}} \]

or (Bejar et al., 1982)

\[ \text{HWI} = \frac{\text{peak width (at half peak amplitude)}}{\text{peak amplitude}} \]

• The path length index (PLI) (Johnston et al., 1984) is a measure of the length of the velocity-time trace. When the data are available in digitized form the PLI may be calculated as
PLI = Σ_{i=1}^{n} \frac{((f_{i+1}-f_{i})^2/f_{m}^2) + ((t_{i+1}-t_{i})^2/T^2)}{0.5}

where n = number of samples, f_m = mean amplitude, T = pulse period, f_i = amplitude at t_i, and t_i = discrete time increment.

- Percent systole (McCallum et al., 1978) is the percent of the cardiac cycle which is involved in systole and can be calculated as:

\[ \text{percent systole} = \left( \frac{\text{duration of systole}}{\text{duration of cardiac cycle}} \right) \times 100 \]

- Damping factor (DF) (Johnston et al., 1978) is the relationship between a proximal and distal pulsatility index, and therefore can only be determined from waveforms at two locations along a vessel. It is defined as

\[ \text{DF} = \frac{\text{PI}_{\text{proximal}}}{\text{PI}_{\text{distal}}} \]

- Diastolic velocity slope (DVS) (Bejar et al., 1982) is the acceleration (dV/dt) measured on the diastolic slope of the curve. The average slope is used and can be calculated as

\[ \text{DVS} = \frac{(V_{pk}-V_{ft})}{\text{peak-foot time}} \]

This index is not dimensionless with respect to velocity but could be divided by mean or peak amplitude of the velocity-time waveform to be made dimensionless.

- The carotid velocity index (CVI) (Kreutzer et al., 1982) is defined as
CVI = (peak amplitude - end diastolic amplitude)/peak amplitude

- Laplace transform coefficients are derived using the Laplace transform methods (Skidmore and Woodcock, 1980; Johnston et al., 1984). The heart is assumed to produce a unit impulse input. The output is a third-order velocity waveform which corresponds to the systems unit impulse response. The recorded wave is digitized, and from the digitized data the Fourier transform and Laplace transforms can be calculated using curve-fitting techniques. The system poles are then plotted and compared to poles in normal subjects. It has been shown that peripheral resistance affects the one real pole with increased resistance moving the pole farther from the imaginary axis. The other two poles, which occur in the form of a complex conjugate pair, are related to wall stiffness of the vessel. The general form of the Laplace transform is

\[ H(s) = \frac{1}{[s^2+2\delta \omega s+\omega^2](\delta+\gamma)} \]

- Principal components (Fulton et al., 1983) have been used to analyze blood velocity waveforms. In this method the waveform is approximated by a weighted sum of three component waveforms. The three components are derived statistically from a population of traces. The first component is the population mean \( M(t) \). The other two
components $A(t)$ and $B(t)$ are calculated to account for the greatest degree of deviation by any single wave. The resulting wave can be represented by

$$F(t) = M(t) + aA(t) + bB(t)$$

For each individual waveform the scalar constants $a$ and $b$ are calculated and can be compared to normal values for diagnostic purposes.

- Impedance index ($\text{ImI}$) (Thompson et al., 1986) is defined by

$$\text{ImI} = (\text{maximum velocity}-\text{minimum velocity})/(\text{minimum velocity})^2$$

- The constant flow ratio ($\text{AA}$) (Thompson et al., 1985) can be written as

$$\text{AA} = f_{\text{min}}T/A$$

where $f_{\text{min}}$ is the minimum Doppler frequency shift, $T$ is the pulse period, and $A$ is the area under the frequency versus time curve over one pulse.

- The relative flow rate index ($R$) (Thompson et al., 1985) is defined by

$$R = \frac{A_1/t_1}{A_2(T-t_1)}$$

where $t_1$ is the time from beginning of systole to peak frequency shift, $A_1$ is the area under the curve between beginning of systole and $t_1$, $A_2$ is the area under the curve
between \( t_1 \) and end of diastole, and \( T \) is the period of the pulse.

- The rising slope (RS) (Thompson et al., 1986) is defined by

\[
RS = \frac{f_{\text{max}} - f_{\text{min}}}{(t_1 f_{\text{mean}})}
\]

where \( f_{\text{max}} \) is the maximum frequency shift, \( f_{\text{min}} \) is the minimum frequency shift, \( f_{\text{mean}} \) is the mean frequency shift over the pulse period, and \( t_1 \) is the time period between beginning of systole and \( f_{\text{max}} \).

- Systolic decay time (D) (Thompson et al., 1986) is defined by

\[
D = \frac{t_r}{t_1} \frac{t_d}{t_2}
\]

where \( t_r \) is the rise time from 0.75 \( f_{\text{max}} \) to \( f_{\text{max}} \), \( t_d \) is the decay time from \( f_{\text{max}} \) to 0.75 \( f_{\text{max}} \), \( t_1 \) is the total time of systole, and \( t_2 \) is the total time of diastole.

A large number of indices have been used to quantify waveshape. These indices range from simple to fairly complex and also vary in the amount of information which they provide. There is no general agreement on which index is most useful. This decision can only be made after considering what information is required from the blood velocity waveform and what type of data collection system is being used.
Assessment of uterine and fetal blood flow

Current literature contains several studies in which blood velocity waveforms are being used for the assessment of uterine and fetal blood flow in pregnant women. Many waveform indices have been studied. Erskine and Ritchie (1985) compared the pulsatility index (PI), impedance index (IMI), A/B ratio and the Pourcelot pulsatility index (PR). They determined the PI to be the most useful index in their study and recommended its use.

Thompson et al. (1985, 1986) have compared constant flow ratio (AA), relative flow rate index (R), average rising slope (RS), and systolic decay time (D). They have concluded that the A/B ratio and the PI are the most closely correlated of these indices. They have made use of the A/B ratio in the assessment of uterine and fetal blood flow.

It has been shown that blood velocity waveforms can be used to recognize intrauterine growth retardation and other fetal abnormalities. The arcuate artery flow velocity waveform shows decreased or absent diastolic velocities in most pregnancies complicated by pregnancy induced hypertension (Cohen-Overbeek et al., 1985).

Trudinger et al. (1985a) report increased umbilical artery A/B ratios with reduced or absent diastolic flow in 32 of 43 small for gestational age (SGA) fetuses. They also
found reduced uterine artery diastolic flow in 9 of 12 complicated pregnancies with severe hypertensive disease (1985b).

In 33 twin pregnancies studied, with one or both fetuses being SGA, elevated umbilical artery A/B ratios were reported in 26 case (Giles et al., 1985b). Erskine and Ritchie (1985) report higher umbilical artery PI for growth retarded fetuses. Fleischer et al. (1985) found increased A/B ratios in cases where infants were born with weights less than 25th percentile, and reported high A/B ratios in complicated hypertensive pregnancies (1986).

A comparison of fetal heart rate monitoring and umbilical artery waveform analysis has shown that the assessment of umbilical artery waveforms is more efficient in the recognition of fetal compromise (Trudinger et al., 1986).

Fendel et al. (1984) and Janbu et al. (1985) have studied uterine arterial blood velocity waveforms during labor. They reported velocity decreases, particularly in diastolic flow, during contractions.

Blood velocity waveform analysis has been used to study cerebral hemodynamics in both prenatal and neonatal infants (Evans et al., 1985 and Wladimiroff et al., 1986). In growth retarded fetuses PI decreased in the fetal carotid
artery while increasing in the fetal aorta and in the umbilical artery. This suggests a decrease in vascular resistance to the fetal cerebrum in the presence of fetal hypoxia (Wladimiroff et al., 1986). Neonates with intracranial pathology showed a wider range of the anterior cerebral artery PI than did normal neonates. Principal component analysis was also used and showed similar results.

Assessment of carotid and femoral arterial blood flow

Carotid arterial atherosclerosis has been studied using blood velocity waveforms by Strandness (1986) and Magna et al. (1986). Magna et al. (1986) studied 421 carotid artery segments in 56 patients using angiography and Doppler ultrasound. They used the Doppler frequency ratio (DFR) as a blood velocity waveform index (DFR = maximum frequency shift distal to stenosis/maximum frequency shift in stenosis). DFR was used to predict carotid arterial disease using the formula:

\[(1 - DFR) \times 100\% = \% \text{Stenosis}\]

They recorded 41 true positives from 53 vessels with 75-99 percent stenosis.

Femoral arterial blood velocity waveforms have been studied using PI, Laplace transform analysis (LTA), and normalized transit time to predict femoral arterial disease.
Laplace transform analysis is based on an elastic tube model of an artery. The system response to a unit impulse input is described by a third-order Laplace transform equation. The solutions to this equation are dependent on proximal diameter (LTD), compliance (LTE), and distal resistance (LTR). The values of LTE, LTD, LTR, and PI are calculated from the blood velocity waveform. Plots of LTD versus percent stenosis and PI versus percent stenosis were provided (Capper et al., 1986).

Normalized transit time was used in assessing the femoropopliteal segment. Transit time was calculated as the interval between the onset of flow in the femoral artery and the onset of flow in the popliteal artery. This value was then normalized with respect to mean radial pressure to account for differences in blood pressure. Normalized transit time versus percent stenosis was plotted (Baker et al., 1986).

Other arterial blood velocity waveforms

Blood velocity waveforms have been used to non-invasively study blood flow in other arteries. The PI of the superior mesenteric artery decreased 46%, five minutes after fasting subjects ingested a meal (Quamas et al., 1986). That study included 82 subjects and the mean PI (fasting) was 3.57.
Brachial artery blood velocity waveforms have been quantified using a vector-based approach (Gółzewski and Krajewski, 1987). A vector of Fourier coefficients represented each blood velocity waveform. A relationship was found between vector position and subject age.

Sambrook et al. (1987) have correlated increased mammary blood flow in human females during the menstrual cycle and pregnancy with variations in estrogen, progesterone, and prolactin.

Modeling of Arteries

The purpose of modeling arteries is to enable the researcher to study some behavior or characteristic of the artery which in a living system would be more difficult or impossible to study. Several types of models have been used to investigate arteries. These include:

- direct fluid-mechanical models
- electrical network analogs
- computer (mathematical) models

In this section some of the prominent features of computer models are presented. With the ready availability of digital computers, the feasibility of using this type of model has been greatly enhanced.
The first step in forming a computer mathematical model is the development of the conceptual form of the model. This is followed by a mathematical description of the model and selection of the values for model parameters. The final step is testing and use of the model.

The earliest mathematical model of an artery was by the German physiologist, Otto Frank (Frank, 1899). Frank developed the "windkessel" model based on the comparison between the elasticity of the arterial wall and that of the air chamber of a firetruck.

**Computer mathematical models**

The use of computers to mathematically model arterial hemodynamics is now a commonly used research technique. Although there are many types of models with varying degrees of accuracy and complexity, the basic concept for developing and solving each type of model is similar. A system of equations is written which relates system inputs, system characteristics, and system outputs. These equations are then solved with the use of a computer, since these models normally involve large systems of equations which cannot easily be solved analytically.

**Lumped parameter models**

In a lumped parameter model, a small arterial segment is modeled using a simplified set of equations which is valid over a short
uniform segment. A typical model of a lumped parameter segment of an artery (Dinnar, 1981) is shown in Figure 1. An arterial segment is represented in electrical terms by a resistor in series with an inductor and having a capacitor to ground. Each segment has some input voltage and current.

\[ V_1 \quad R_{i+1} \quad L_{i+1} \quad V_{i+2} \]

\[ I_1 \quad C_{i+2} \]

FIGURE 1. Lumped parameter model of an arterial segment

In this model voltage represents pressure and current represents flow. The three parameters R, L, and C can be related to the flow system through the equations

\[ R = \frac{8\pi \mu l}{A^2} \]

\[ L = \rho l / A \]

and

\[ C = \frac{3A(1+h)^2}{[E(1+2h)]} \]

where \( \mu \) is blood viscosity, \( l \) is segment length, \( A \) is the vessel cross-sectional area, \( \rho \) is blood density, \( h \) is the radius/wall thickness ratio, and \( E \) is the modulus of
elasticity of the vessel wall. These parameters can also have other representations. For example, C may be defined using a known area-pressure relationship such as

\[ A = A_0 [1 + c_0 \cdot (p - p_0)] \]

In this case C can be written:

\[ C = \frac{\Delta V}{\Delta p} = c_0 A_0 \Delta x \]

A number of these segments are combined together to represent a length of artery. The model can be terminated at the distal end with a modified windkessel as shown in Figure 2. This modified windkessel consists of two resistances and a capacitance. From this electrical network, a system of first-order differential equations can be written. There are two equations for each segment plus one for the modified windkessel. This system of first-order differential equations can be solved using a digital computer. Other models have used classical windkessel elements and even a simple resistance element to model capillary beds.

Snyder et al. (1968) used a lumped parameter model to represent the complete human systemic arterial tree. Their model simulated pressure and flow waveforms which compared well with recorded data from normal adult humans. The state variable form of a similar lumped parameter model can be used to describe the human arterial system.
Continuous models

In the continuous model, the artery is modeled using the flow equations for conservation of mass and momentum. This model is also known as the transmission line analogy, since the linearized one-dimensional equations of flow in an elastic tube are identical to the telegraph equations (Dinnar, 1981).

Raines et al. (1974) have developed a computer simulation of arterial dynamics in the human leg. They use the following equations:

\[ \frac{\partial Q}{\partial x} + C(x) \frac{\partial p}{\partial t} = 0 \]

\[ \frac{\partial p}{\partial x} + L(x) \frac{\partial Q}{\partial t} = \frac{\tau \pi D}{A_o} \]

where \( p \) is pressure, \( Q \) is flow, \( D \) is vessel diameter, \( A_o \) is cross sectional area, \( \tau \) is wall shearing stress and

\[ C(x) = \frac{\partial A}{\partial p} \]

\[ L(x) = \frac{\rho}{A_o(x)} \]
The distal end of the model was represented by a modified windkessel. The final equation was an equation of state relating cross sectional area to pressure, \( p \), and distance, \( x \). Raines used the finite difference method to numerically solve these equations.

The finite element method has also been used to simulate pulsatile arterial blood flow (Rooz 1980, Young et al. 1980, Gray 1981, Porenta 1982, Rooz et al. 1982, Rangarajan 1983, Weerappuli 1987). Some examples in which computer modeling has been used include studies of the canine femoral artery; human femoral artery; human radial, brachial, and ulnar arteries; and bovine uterine artery. The models are based on the conservation of mass, conservation of momentum and state equations, with the parameters varied for each case to represent each particular artery.

**Model parameters**

Three parameters which are common to nearly all models of arterial circulation, but are difficult to measure, are arterial compliance, windkessel volume compliance, and windkessel resistance. Arterial compliance is defined as the change in cross sectional area of an arterial segment for a given pressure change. The units of arterial compliance are \( \text{M}^4/\text{N} \).
Simon et al. (1985) indirectly measured compliance in human arteries by measuring vessel diameter and pulse wave velocity. They reported normal arterial compliance to be $2.2 \times 10^{-10} \text{M}^4/\text{N}$ in vessels which are nominally 5-mm in diameter. They also reported decreased compliance in hypertensive patients.

Mergerman et al. (1986) measured arterial compliance in the femoral artery of dogs. They used ultrasonic echo tracking and a pressure catheter to simultaneously measure arterial diameter and pressure. They report values of from 0.05% diameter change/mm Hg to 0.20% diameter change/mm Hg. For a 5 mm diameter vessel, this corresponds to $1.47 \times 10^{-9} \text{M}^4/\text{N}$ to $5.90 \times 10^{-9} \text{M}^4/\text{N}$.

The windkessel volume compliance represents the combined compliance of all arterial branches, arterioles, and capillaries, which are not otherwise modeled. The units of windkessel volume compliance are $\text{M}^5/\text{N}$. Table 1 shows several values of windkessel volume compliance as reported in current literature.

Osberg and Langville (1982) studied arterial compliance in the hind limb circulation of rabbits. In their study they measured mean flow and pressure at the inlet of the artery and calculated capillary bed resistance. Compliance was calculated by measuring the pressure-time curve after
TABLE 1. Values of windkessel volume compliance for arterial branches, arterioles, and capillaries distal to various vessels

<table>
<thead>
<tr>
<th>Author</th>
<th>$M^5/N$</th>
<th>vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snyder et al., 1968</td>
<td>$8.97 \times 10^{-9}$</td>
<td>ascending aorta</td>
</tr>
<tr>
<td>Snyder et al., 1968</td>
<td>$675 \times 10^{-12}$</td>
<td>internal iliac</td>
</tr>
<tr>
<td>Raines et al., 1974</td>
<td>$75 \times 10^{-12}$</td>
<td>tibial artery</td>
</tr>
<tr>
<td>Weerappuli, 1987</td>
<td>$55.3 \times 10^{-12}$</td>
<td>bovine uterine artery</td>
</tr>
<tr>
<td>Weerappuli, 1987</td>
<td>$40-100 \times 10^{-12}$</td>
<td>canine femoral artery</td>
</tr>
</tbody>
</table>

clamping the vessel upstream. They reported compliance values of $1.5 \times 10^{-9}$ to $22.5 \times 10^{-9} \ M^5/N$.

Windkessel resistance represents the lumped resistance of the artery branches, arterioles and capillaries, which are not otherwise modeled. The units for windkessel resistance are $N\cdot s/M^5$. For a given mean input pressure, the value of windkessel resistance determines the mean flow through the capillary bed.

Leodolter et al. (1980) have used a value of $2.0 \times 10^8\ N\cdot s/M^5$ for a model of placental perfusion. Raines et al. (1974) use $4.3 \times 10^9\ N\cdot s/M^5$ for resistance in the capillary beds terminating the tibial vessels in the human leg.
Relation of vessel morphology and model parameters

A number of studies have related normal or pathological arterial changes to changes in model parameters such as arterial compliance and windkessel volume compliance. Simon et al. (1985) found decreased arterial compliance in humans with essential hypertension. They relate this decrease to atherosclerotic lesions and increased collagen to elastin ratios.

Schulman et al. (1986) attribute changes in blood velocity waveforms during pregnancy to changes in compliance, which are due to structural changes in the spiral arteries of the placental bed. Small muscular arteries change to dilated tortuous vessels whose walls are composed of fibrinoid, hyalin, and fibrous tissue with remnants of smooth muscle and elastic tissue (DeWolf et al. 1973).

Vascular Control Mechanisms

The principal hemodynamic effects of control activity in muscular arteries come from changes in vessel diameter and changes in vessel wall compliance. In almost all in-vivo situations, vascular smooth muscle is in tension. The tension developed in these muscle fibers is a function of
fiber length, incoming nerve impulses, catecholamine levels and the chemical environment (Milnor, 1974). The net tension developed in a large group of muscle cells determines the vessel geometry, specifically diameter and thickness, based on the transmural pressure and the mechanical properties of the other vessel wall materials. The compliance is approximately related to this geometry and the mechanical properties by the equation: \(^1\)

\[
C = \frac{\frac{dA}{dp}}{\frac{2\pi r_0^3}{E h_0}}
\]

where \(C\) is the compliance, \(A\) the cross-sectional area, \(p\) is the transmural pressure, \(r_0\) is the initial vessel radius, \(h_0\) is the initial vessel wall thickness, and \(E\) is the incremental modulus of elasticity of the vessel wall.

As muscular tension increases, the vessel diameter decreases while the wall thickness increases. Therefore, if \(E\) remains constant, the compliance decreases with increasing muscle tension. There are several mechanisms which control the net tension in smooth vascular muscle. These include neural control, systemic humoral control, and local control or autoregulation (Milnor, 1974 and Ganong, 1981).

\(^1\)See Appendix A for the derivation of this equation.
Neural vascular control

All blood vessels except capillaries and venules receive motor nerve fibers from the sympathetic division of the autonomic nervous system. The arterioles are the most densely innervated. Based on the chemical transmitters involved, these neurons can be divided into two categories.

Cholinergic neurons use acetylcholine as a transmitting agent. Cholinergic neurons, which end on blood vessels, cause vasodilation when they are activated. These cholinergic neurons are not present on all innervated blood vessels. Specifically, cholinergic innervation is scarce or absent in the uterine artery (Meschia, 1980).

Periarterial sympathetic (adrenergic) neurons, which use norepinephrine as a transmitter, affect two types of receptors on vascular smooth muscle. These receptors include α adrenergic receptors, which cause muscular contraction when activated and β adrenergic receptors which cause muscular relaxation (Milnor 1974). These receptors are classified as α or β depending on their order of potency to adrenergic agonists. The order for α adrenergic receptors is epinephrine > norepinephrine > isoproterenol. The order for β adrenergic receptors is isoproterenol > epinephrine > norepinephrine (Sauer, 1987).
Both types of receptors exist in most blood vessels, and the reaction to catecholamines (e.g., epinephrine and norepinephrine) depends on the relative number of each receptor. If α adrenergic receptors dominate, then smooth muscle contraction and vasoconstriction occurs. If β adrenergic receptors dominate then smooth muscle relaxation and vasodilation occurs.

The uterine arterial vasculature is, as previously stated, innervated by periarterial sympathetic nerves of the autonomic nervous system (Meschia, 1980), but lacks cholinergic innervation. Neural stimulation of the uterine artery causes vasoconstriction and reduced uterine arterial blood flow due to the predominance of α adrenergic receptors. Beta adrenergic receptors play only a minor role in uterine flow control.

**Humoral vascular control**

Epinephrine is a vasoactive catecholamine which is present in the blood supply and is important in vascular control. Epinephrine is secreted by the adrenal medulla during periods of acute stress. It has been shown that infusion of epinephrine into a pregnant animal decreases uteroplacental blood flow (Meschia, 1980).

In addition to normal systemic neural and hormonal vascular control, the uterine blood supply is controlled so
that flow increases during pregnancy and during cyclic variations of flow during the estrous cycle of ewes, cows and sows (Ford, 1982; Lewis et al., 1984; Oakes et al., 1980). Steroid hormones play an important role in this control of uterine blood flow. Estrogen injection has been shown to increase uterine and placental blood flow (Meschia, 1980), and higher estrogen to progesterone ratios are associated with higher uterine blood flow during the estrous cycle of gilts (Ford et al., 1984) and during the estrous cycle and pregnancy of ewes, sows and cows (Ford, 1982). It has been suggested that catechol estrogens block potential sensitive channels (PSC) in the uterine arterial smooth muscle membrane, resulting in decreased tone and increased blood flow (Stice, 1987). Others have suggested that estrogen induced vasodilation may be a result of non-muscular changes in the arterial wall (Moll and Gotz, 1985). While estrogen has a long term effect on uterine arterial tone which controls baseline rate of flow, progesterone mediates short term changes in arterial reactivity. Reactivity is defined as the vessels ability to respond to stimulation by adrenergic agonists with transient reductions in diameter and flow. Tone is defined as the pressure exerted by an artery against an intraluminal flow (Ford and Stice, 1985).
Angiotensin II is a powerful vasoconstrictor which plays an important part in controlling blood pressure and extracellular volume. In pregnant animals angiotensin II has a greater vasoconstrictive effect on systemic arteries than on the uterine vasculature. At physiological doses in pregnant animals angiotensin II increases systemic vascular resistance and mean arterial pressure more than uterine arterial resistance resulting in increased uterine blood flow (Sauer, 1987).

**Local vascular control**

The ability of tissues to locally control their own blood flow is known as autoregulation. The myogenic theory of autoregulation states that smooth muscle cells contract in response to stretch as vessels are distended due to increasing luminal pressure (Ganong, 1981). This action tends to decrease the vessel diameter and keep flow constant.

According to the metabolic theory of autoregulation, vasodilator substances tend to accumulate in areas of decreased flow causing vasodilation and increased flow (Ganong, 1981). As flow is increased the substances tend to be washed away.

Some vasoactive substances which are involved in local control of blood flow include prostaglandins, histamine, and
CO₂ (Ganong, 1981). Increased P<sub>CO₂</sub> causes vasodilation in most beds. There is evidence however that the partial pressure of O₂ and CO₂ does not exert appreciable control on uteroplacental circulation (Meschia, 1980). Prostaglandins are a group of biologically active lipids that exert vasodilator and vasoconstrictor effects (Milnor, 1974), however the role of prostaglandins in regulating uteroplacental blood flow is not well understood (Meschia, 1980). Histamine, which is released in response to injury or antibody-antigen reaction, is a vasodilator. It has a localized effect and is not accompanied by significant amounts of circulating histamines (Milnor, 1974).

**Mechanisms of smooth muscle contraction**

Arterial smooth muscle cell contraction is mediated by specific calcium channels on the cell membrane which, when activated, cause an influx of extracellular calcium. This influx of calcium, causes an increase in intracellular cytosolic free calcium which activates the contractile machinery of the cell (Sauer, 1987). Low intracellular calcium levels are necessary for normal cell function and are maintained by a low cell membrane permeability to calcium and by two ATP dependent calcium pumps which function to remove calcium from the cell.
Uterine arteries exhibit two specific types of calcium channels on the cell membrane which account for the majority of calcium influx mediating contraction: 1) receptor operated calcium channels (ROC) and 2) potential sensitive channels (PSC). Activation of $\alpha$ adrenergic receptors stimulates the opening of ROC and allows for rapid influx of calcium into the cell. PSC are opened by the depolarization of the cell membrane. PSC are important in cells which exhibit action potentials, but are also found in vascular smooth muscle that does not normally produce action potentials. (Sauer, 1987).

In general ROC mediate phasic contractility and PSC mediate vessel tone. This is however an oversimplification and some vessel responses are mediated by both ROC and PSC (Sauer, 1987).

Pattern Recognition of Biological Signals

In order to design and construct a device which collects and analyzes blood velocity waveforms, one must first develop an algorithm which the device can use to detect a blood velocity waveform and to distinguish between separate parts of the waveform in order to perform analysis.
The construction of this type of algorithm is known as pattern recognition. Using methods of pattern recognition, an algorithm can be developed which enables a microprocessor or computer to recognize patterns in collected data, such as blood velocity waveforms.

**Syntactic pattern recognition**

In syntactic pattern recognition a pattern is expressed by a group of components called subpatterns and pattern primitives (Fu, 1979, 1982). Patterns are recognized by applying a set of syntax rules or grammar to these components. This method is somewhat analogous to a language. The pattern is a sentence in a language described by a specified grammar.

Stockman et al. (1976) have used syntactic pattern recognition in the recognition of pressure vs. time pulse waves from the carotid artery. They identified a number of primitives including some shown in Figure 3 below.

The waveform parsing system used by Stockman et al. (1976) was hierarchical. In the hierarchical method the system searches a string of primitives for important combinations of primitives and then other less important combinations until a complete pattern is found. The system begins by searching for a systolic upslope. The grammar then sets a new goal each time a group of primitives is
Figure 3. Primitives used in pattern recognition of carotid pulse waves

found. When the systolic upslope is found, the system searches for a joint between pulses, previous to the systolic upslope, and within a certain time range. This waveform parsing system was coded in Fortran and could analyze 70 seconds of data in 140 seconds, producing 350 pages of formatted output.

**Discriminant pattern recognition**

The method of discriminant pattern recognition makes use of certain pattern "features" which are known a priori and can be extracted. These features are combined into a
feature vector which exists in a feature space. Recognition of patterns is performed by partitioning the feature space.

Features of a pattern can be components of the pattern like primitives used in the syntactic method. Features, however, include other characteristics which are not components, but can be extracted. Some commonly used features include velocity, acceleration, spectral content, and Laplace transform coefficients.

The success of this method is largely dependent on picking features which can differentiate the pattern of interest from all other data or noise. By using more and more features, it is possible to specify a pattern more accurately, but more features also require more processing time.

Evans (1984) has applied the technique of discriminant pattern recognition to the interpretation of ultrasonic Doppler blood velocity signals. Some possible features listed by Evans are the pulsatility index, the Laplace transform coefficients, and principal component coefficients. The pulsatility index is defined as the peak-to-peak velocity divided by the mean velocity. The principal component coefficients are analogous to the Fourier coefficients. Evans used only one- or two-dimensional feature vectors and used a graphical method of
classification or partitioning of the feature space. The partitioning of the feature space was done graphically by plotting the two-dimensional feature vectors and grouping vectors of known diseased state.
This section provides a description of the materials and procedures used to collect data for this project. The first section on continuous wave Doppler data collection includes a section on the design of the fingertip transducer which was used as well as a section on the data collection procedure used to collect Doppler blood velocity waveforms in pregnant and non-pregnant dairy cows. The other sections describe the procedures used to collect pulsed Doppler and electromagnetic flow and velocity waveforms in the uterine artery of un-bred cattle.

Continuous wave Doppler blood velocity waveforms were collected from the uterine arteries of 76 pregnant and non-pregnant cows, between 14 and 36 days after breeding, over a period of six months. Some previous continuous wave Doppler experiments involving 21 cows had been performed to gain experience with the procedure (Waite, 1985 and Young and Ford, 1986).

Data were obtained from four unbred cows, over the course of an estrous cycle, with chronically implanted pulsed Doppler flowmeters and from one unbred cow implanted with an electromagnetic flowmeter, in order to obtain blood velocity waveforms over an estrous cycle in unbred cows.
The purpose of collecting these data was as stated in the introduction, to characterize bovine uterine artery velocity waveforms and to relate waveshapes to mean flow. Another purpose was to provide information concerning variations of the flow waveform over the estrous cycle in un-bred cattle.

Continuous Wave Doppler Data

The method of collecting continuous wave Doppler blood velocity waveforms involved rectal palpation. The operator wearing a fingertip probe palpated the left or right uterine artery.

Probe design

The following criteria were used in specifying requirements for an ultrasound probe to be used in collecting data from the uterine artery of cattle.

Size and shape - The probe must be designed to fit on a finger underneath a rubber glove, and to be small enough to be used in rectal palpation of cows without causing damage to the animal.

Reliability - The probe design must be such that it could be reliably used for periods of at least several weeks of data taking without failure. The probe needed to be designed for use in a high humidity, unclean environment
with varying temperatures and the possibility of rough handling.

Signal strength - The output should be sufficiently large to be processed by the continuous wave Doppler flowmeter with the chosen design.

The probe design uses two, 2 millimeter by 5 millimeter, 10.0 megahertz, piezoelectric crystals. One crystal acts as a transmitter and the other as a receiver. The two crystals lay side by side in a plastic crystal holder (see Figure 4). Each crystal is connected by two 36 gauge (0.009 inch diameter) stainless steel Cooner wires. In some cases these wires were soldered to the crystals at the factory and epoxy coated. In other instances a conducting epoxy (Econobond Solder 56C) was used to attach the wires to the crystals in the laboratory.

The crystal holders were machined on a milling machine from acrylic blocks, and the holder and crystals are mounted on a rubber finger cup which slips over the index finger of the operator. Some earlier model transducers used a velcro strap to hold the probe on the finger. This was acceptable although the finger cup was preferred by the operators involved. The procedure used to build the transducer has been previously described (Waite, 1985). Figure 5 shows a photograph of a transducer which was built using this
FIGURE 4. Transducer crystal mounting drawing
procedure and one which was commercially fabricated. Both probes were used to collect data. One difference in the commercially fabricated probe is that the crystals are parallel to the probe face rather than inclined.

Data collection procedure

The probe was connected to a Parks Model 1010-LA Doppler continuous wave, dual frequency, bi-directional flowmeter with a built in strip chart recorder\(^1\). This flowmeter has a strip chart output, an audio output, and a third output identical to the strip chart input which is connected to a series 115 Tandberg instrumentation tape recorder\(^1\) and/or the microcomputer based velocity waveform analyzer described below.

While the first operator searched for the uterine artery and listened to the audio output, a second operator watched the strip chart recorder and operated the tape recorder and waveform analyzer. The operators attempted to record twenty seconds of repeatable pulses for each data set. Each time, they palpated both the left and right uterine artery. Magnetic tape recordings for each set of data were saved. For each data set, the output of the waveform analyzer was the mean pulsatility index and standard deviation for that set of data.

\(^1\)See Appendix B for equipment specifications.
FIGURE 5. Photographs of a) a transducer built in our lab and b) a commercially fabricated transducer.
Pulsed Doppler Data

Pulsed Doppler flow transducers were surgically implanted around the left and right uterine arteries of four cows. In two cows, pressure transducers were also placed in the internal iliac artery in order to obtain pressure waveforms. The flow transducers were connected to a Valpey-Fisher model PD-1 pulsed Doppler flowmeter. This flowmeter had an audio output, an output to the Tandberg tape recorder, and an output to a strip chart recorder. Data were collected daily on magnetic tape and later processed using the blood velocity waveform analyzer. The pressure transducer was connected to a Milar transducer control unit whose output was connected to the Tandberg tape recorder and to a strip chart recorder. Blood samples were also collected daily and progesterone and estrogen levels were measured from these samples.

Electromagnetic Data

One set of electromagnetic flow data was obtained over the estrous cycle of a cow. An electromagnetic flow probe was implanted around the uterine artery. The flow probe was attached to a Carolina Medical Electronics Model 501D electromagnetic flowmeter\(^1\). The output of the flowmeter was

\(^1\)See Appendix B for equipment specifications.
connected to the Tandberg tape recorder and a strip chart recorder. These data were processed using a data analysis program on a PDP-11/23 digital computer (Waite, 1985). Data were collected daily during one complete estrous cycle. Blood samples were also collected daily and progesterone and estrogen levels were measured.

It should be pointed out that attempts to collect additional electromagnetic flow data did not yield satisfactory data. Electromagnetic flow probes which were surgically implanted in 6 cows failed to provide useable waveforms. In some cases data could be recorded over a period of a few days but in all cases the data were noisy and were considered to be unreliable. The exact cause or causes of the difficulties in obtaining electromagnetic flowmeter data are unknown. However, several possible reasons for this difficulty include, electrically noisy environment, edema around the flow probes due to surgical trauma causing a decrease in the electromagnetic signal strength, and probe failure due to the corrosive effects of the internal environment of the cow.
MICROCOMPUTER BASED WAVEFORM ANALYZER

The purpose of the waveform analyzer was to provide a method of obtaining blood velocity waveform indices quickly and conveniently in the field. The velocity waveform analyzer was designed and constructed using a Micromint BCC52™ BASIC microcomputer/controller. The BCC52 is based on the Intel 8052AH microprocessor. The software for the analyzer is written partially in BASIC and partially in assembly language.

The computer runs a controlling program in a 16 Kbyte read-only memory (ROM) chip. The computer controls the analog-digital (A/D) converter, reads the input signal every 10 microseconds, and stores the data in dynamic random access memory (RAM). After 10-20 seconds of data are collected, the program analyzes the data and calculates the pulsatility index and standard deviation.

As data are collected and stored they are also simultaneously converted to an analog signal and sent to a strip chart recorder for output. When the analyzer has calculated the average pulsatility index, it displays the value using an alphanumeric light emitting diode (LED) device. The waveform analyzer which was built and used in this study is approximately 3 X 7 X 8 inches and is shown in Figure 6 along with two Doppler flowmeters which were used.
FIGURE 6. Photographs of a) Velocity waveform analyzer and b) Doppler flowmeters
Hardware

A block diagram of the velocity waveform analyzer (VWA) is shown in Figure 7. The output of the Doppler flowmeter is input to the VWA at the amplifier/adder. The input to this section is approximately -0.3 to 1.0 volts. The amplifier/adder amplifies the signal and adds a dc voltage to give an output range of 0-2.5 volts. The amplifier/adder circuit uses an LM324 quad operational amplifier chip. The circuit is shown in Figure 8.

The output of the amplifier/adder stage goes into the sample and hold circuit. The purpose of sample and hold is to sample the 0-2.5 volt signal and to keep it constant during the 10 μsec period in which the A/D converter is reading the signal. The sample and hold circuit is controlled by the A/D status line. The sample and hold uses a CD4066 CMOS switch and the circuit is shown in Figure 9.

The output of the sample and hold circuit is the input to the analog to digital converter. This device reads an analog input voltage between 0 and 2.5 volts and outputs an 8-bit binary number between 0000 0000 and 1111 1111 (i.e., between 0 and 255). The sample rate of the A/D converter is controlled by the microcomputer. The A/D converter chip in this device is an Analog Devices AD670 8-bit A/D converter. The A/D converter circuit is shown in Figure 9.
FIGURE 7. Block diagram of velocity waveform analyzer
FIGURE 8. Amplifier/adder circuit diagram
FIGURE 9. A/D converter circuit with sample and hold
The 8-bit output of the A/D converter is the input to parallel port A of the microcomputer. The computer continuously runs a controlling program which is stored in a 16 Kbyte ROM. This program controls the A/D converter, reads the data at port A and stores the data in a RAM. After 10-20 seconds of data are collected, the program analyzes the data and calculates the pulsatility index. Once the PI has been displayed, the program is manually reset by a switch and the program automatically restarts.

At the same time the data are stored in RAM, they are also sent to the digital to analog (D/A) converter. The purpose of the D/A converter is to change the digital signal being stored into an analog signal suitable for a strip chart recorder input. The strip chart provides a valuable visual check on the data being stored. The D/A circuit uses an Analog Devices AD558 DACPORT™. The circuit is shown in Figure 10.

After the analysis program has run, the values for pulsatility index and standard deviation are output to a Litronix DL-1416, 4 digit, 16 segment, alphanumeric light emitting diode display with built in memory, decoder, and driver. This device displays the value of PI and standard deviation. The LED circuit is shown in Figure 10.
FIGURE 10. LED and D/A circuit diagrams
The software for the velocity waveform analyzer consists of two parts. There is an assembly language subroutine which controls the data collection and storage, and a BASIC program which analyzes the stored data. A copy of the assembly language subroutine is provided in Appendix C. The flowchart in Figure 11 illustrates how the subroutine works.

When the VWA is switched on it goes directly to the assembly language subroutine. The subroutine begins by polling the start/stop switch. The switch is connected to bit 1 of port C of the microcomputer. See Figure 12 for a diagram of port configurations.

When the start/stop switch input goes low, the program goes on to a switch debouncing routine. Next, the clock is started and a data address counter is initialized to RAM address 4000H. The clock is then polled and after 10 msec a 0 is sent to bit 4 of port C which is connected to the r/w pin of the A/D converter and a data conversion begins.

Next the microcomputer polls the A/D status at bit 0 of port C and when the status bit equals 0 then the conversion is complete. Data are now stored in external RAM at the address pointed to by the address counter. At the same time, the data are output at port B to the D/A converter.
FIGURE 11. Assembly language flowchart for the waveform analyzer
FIGURE 12. Port configuration for the waveform analyzer
Bit 5 of port C is the output line which signals that the data are intended for the D/A converter and not to the LED. The computer polls the start/stop switch for an interrupt, increments the address counter, and repeats the process.

A listing of the program which controls the VWA is shown in Appendix C. As earlier stated, the program begins by calling the data collection subroutine immediately after initialization. When the start/stop switch signals the end of data collection, the assembly subroutine returns control to the BASIC program.

The analysis begins by finding minimum and maximum values for the data set. Next the program searches for a systolic upslope to signal the beginning of the first pulse. The program then searches for more pulses by looking for systolic upslopes. After the data are divided into a group of pulses, the program calculates the average period and compares each pulse to the average. Pulses which are much longer or shorter than normal are discarded. This process is repeated iteratively until only representative pulses remain.

Once a group of good pulses is obtained, the PI is calculated for each pulse. The average value of PI for the group (\( \bar{\text{PI}} \)) is calculated along with the standard deviation of the PI. The standard deviation is calculated as
\[ S = \left( \frac{\sum_{n=0}^{N} (\overline{P_I} - P_{I_n})^2}{N-1} \right)^{1/2} \]

Once the number of pulses, average PI, and standard deviation have been calculated, the program displays the value of PI on the LED device. When the operator pushes the start/stop switch, the standard deviation is displayed. After one more click of the switch, the number of pulses is displayed. The program continues to display the last value until the program is restarted by the reset switch.

Pattern Recognition

The BASIC program, which is run by the microcomputer in the velocity waveform analyzer, performs the task of recognizing and separating individual pulses. The pattern recognition program combines both syntactic and discriminant pattern recognition methods. Primitives which are extracted are systolic upslopes (acceleration), peaks, and diastolic downslopes (decelerations). A feature which is extracted is the pulse period.

A systolic upslope is defined by a line with a positive slope which crosses a horizontal line drawn at 75% of the peak value for the data set. A peak occurs when a systolic upslope is followed by a line with a negative slope which crosses the same horizontal line. The diastolic downslope is the portion of the wave following a peak and preceding a systolic upslope.
The pattern recognition portion of the program begins by extracting the primitives. The grammar of this pattern recognition program specifies that the parsing of the primitives is done in a left to right template matching fashion (Birman, 1983).

After the data are divided into pulses, the pulse period feature is extracted. The period of each pulse is then compared to the average pulse period. Acceptable pulses are defined as those whose period is between 70% and 140% of the average period for the data set. When unacceptable pulses are discarded, the average is recalculated and the test is performed again. This procedure is performed iteratively until all remaining pulses are acceptable.
COMPUTER MODEL OF UTERINE ARTERIAL FLOW

To aid in the understanding of the waveform data, and the system factors which affect waveforms, a one-dimensional lumped parameter model of unsteady flow in the bovine uterine artery was developed. This model predicts arterial flow based on a pressure input and a given set of arterial parameters. By correlating model results with results from Doppler and electromagnetic velocity and flow data, it was hoped to increase the understanding of how waveforms are changing in relation to parameters of interest, such as mean flow or hormone levels.

Model Description

Figure 13 shows the electrical analog description of the model. The model consists of the uterine artery at the proximal end plus the two branches of the uterine artery at the distal end. The smaller arterial branches, arterioles, and the capillary bed are all modeled as two lumped impedances. One impedance is distal to each branch of the uterine artery.

Figure 1 in the literature review shows the model of an arterial segment which was used, and Figure 2 shows the modified windkessel used to model the distal lumped impedances.
FIGURE 13. Electrical analog of the uterine artery
Two first-order differential equations can be written for each segment:

\[ V_{\text{in}} - V_{\text{out}} = I_{\text{in}} R + L \frac{dI_{\text{in}}}{dt} \]  
\[ I_{\text{in}} - I_{\text{out}} = C \frac{dV_{\text{out}}}{dt} \]

Equation 1 is based on the fluid dynamics equation

\[ \frac{(1+C_1)}{\pi r_0^2} \frac{dQ}{dt} + \frac{C_v \mu}{\pi r_0^4} Q = \frac{dP}{dx} \]

where \( \rho \) = fluid density
\( r_0 \) = artery radius
\( \mu \) = fluid viscosity
\( Q \) = cross sectional mean flow
\( P \) = luminal pressure

The coefficients \( C_1 \) and \( C_v \) account for effects of non-steady flow.

Equation 3 is based on the integral form of the momentum equation. Equation 2 is based on conservation of mass. The analogous fluid dynamics equation can be written as

\[ Q_{\text{in}} - Q_{\text{out}} = \frac{dV}{dP} \times \frac{dP}{dt} \]

where \( V \) is volume, and \( Q \) and \( P \) are defined above. One first-order differential equation describes the modified windkessel. It is

\[ \frac{dI_{\text{in}}}{dt} = \left[ \frac{dV_{\text{in}}}{dt} - \frac{I_{\text{in}}}{C_T} + \frac{V_{\text{in}} - I_{\text{in}} R_1}{R_2C_T} \right] \cdot \frac{1}{R_1} \]

where \( R_1, R_2 \) and \( C_w \) are lumped parameters.
The values of resistance, $R$, capacitance, $C$, and impedance, $L$, for each arterial segment are calculated through the relationships:

$$ R = C_v \cdot \frac{8 \mu \Delta X}{\pi r^4} $$

$$ L = C_u \cdot \frac{\rho \Delta X}{\pi r^2} $$

$$ C = \frac{\Delta V}{\Delta P} = [A_0 c_0 \Delta X + A_0 c_1 \Delta X(p-p_0)] $$

where $\mu$ is viscosity, $\Delta X$ is segment length, $r$ is vessel radius, $\rho$ is blood density, $A_0$ is the initial vessel cross-sectional area at pressure $p=p_0$, and $c_0$ and $c_1$ are experimentally determined constants (Weerappuli, 1987). $C_v$ and $C_u$ are coefficients which are frequency dependent and take into account pulsatile flow effects.

The model can be represented in state-variable form by a system of first order equations:

$$ \frac{dI_1}{dt} = \frac{V_0 - I_1 R_1 - V_2}{L_1} $$

$$ \frac{dV_j}{dt} = \frac{I_{j-1} - I_{j+1}}{C_j} \quad j=2, \text{NASG}^2-2, \text{even} $$

$$ \frac{dI_j}{dt} = \frac{V_{j-1} - I_j R_j - V_{j+1}}{L_j} \quad j=3, \text{NASG}^2+1, \text{odd} $$

\[ \text{See numbering as shown in Figure 13.} \]
\[
\frac{dV_b}{dt} = I_{b-1} - I_{b+1} - I_{b+3}
\]

where \( b \) is two times the number of segments in the main artery. The equations which represent the branches are

\[
\frac{dI_j}{dt} = V_{j-3} - I_j R_j - V_{j+1} \quad j = b+3, \text{ NSEG*2-1, odd}
\]

\[
\frac{dV_j}{dt} = I_{j-1} - I_{j+3} \quad j = b+2, \text{ NSEG*2-4, even}
\]

\[
\frac{dV_{(\dim-4)}}{dt} = I_{(\dim-5)} - I_{(\dim-1)}
\]

\[
\frac{dV_{(\dim-2)}}{dt} = I_{(\dim-3)} - I_{\dim}
\]

The first windkessel equation is

\[
\frac{dI_j}{dt} = \frac{C(j+1) \frac{dV(j-3)}{dt} - I_j (1+R_j/R(j+4)) + V(j-3)/R(j+4)}{(C(j+1)R_j)}
\]

where \( j = \dim-1 \). The final equation is

\[
\frac{dI_j}{dt} = \frac{C(j+2) \frac{dV(j-2)}{dt} - I_j (1+R(j+1)/R(j+5)) + V(j-2)/R(j+5)}{(C(j+2)R(j+1))}
\]

where \( j = \dim \).

NASG is the number of arterial segments in the main branch of the uterine artery, NSEG is the total number of segments in the model and \( \dim \) is the dimension of the state vector which is \((2 \cdot \text{NSEG})+2\). It can be noted that all odd numbered states are flows and even numbered states are pressures except the last two states which are both modified windkessel flows.
Model Parameters

The specific geometry of the model is described in Figure 14. The geometry was determined from available x-ray photographs from several cows. These photographs were provided by Dr. S. P. Ford of the Animal Science Department at Iowa State University, and were also used in a previous study (Weerappuli, 1987). The main branch of the uterine artery is modeled as a 4.7 cm long vessel with a nominal 4.3 mm diameter. The two branch arteries are modeled as one short branch, which is 3.2 cm long and 2.5 mm in diameter and one longer branch which is 6.2 cm long and 3.4 mm in diameter.

The values of $C_Q$ and $c_j$ used to calculate vessel compliance were obtained from in-vitro static compliance tests of uterine arterial segments with data supplied by Dr. S. P. Ford and analyzed by Weerappuli (1987).

Values of $R_1$, $R_2$, and $C_W$ have been estimated by Weerappuli (1987) based on a standard mean flow of 25 ml/min and minimization of reflections from the windkessel. Standard values of $C_Q$, $c_1$, $R_1$, $R_2$, and $C_W$ are given in Table 2.

The pressure input waveform is from a pressure recording of cow 647 on June 2, 1986. At the time the cow was instrumented with a pressure transducer catheter in the
FIGURE 14. Model of the uterine artery in geometric form
TABLE 2. Parameter values used in uterine artery model

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<td>$Kg/M^3$</td>
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<tbody>
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<td>$0.4786 \cdot 10^{10}$</td>
</tr>
<tr>
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<td>$0.4839 \cdot 10^{11}$</td>
</tr>
<tr>
<td>$C_T$</td>
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<td>$0.1793 \cdot 10^{-10}$</td>
</tr>
</tbody>
</table>

left internal iliac artery. The pressure waveform was recorded on magnetic tape and digitized. A digital Fourier transform was performed on the digitized data. The Fourier coefficients and the original recording of the pressure waveform are shown in Figure 15. The Fourier series representation is of the form

$$ P = \sum_{i=1}^{11} A(i) \cos[(i-1)\omega t] + B(i) \sin[(i-1)\omega t] $$

where $P$ is pressure in $N/M^2$, $t$ is time in seconds, and $\omega$ is heart rate in $RAD/S$. 
A(1) = 0.11110 E 3
A(2) = -0.75414 E 1
A(3) = -0.10111 E 2
A(4) = -0.24613 E 1
A(5) = -0.25764 E 1
A(6) = -0.97766 E 0
A(7) = -0.51752 E 0
A(8) = -0.44626 E 0
A(9) = -0.22450 E 0
A(10) = -0.43793 E-1
A(11) = -0.30162 E-1
B(1) = 0.00000 E 0
B(2) = 0.25099 E 2
B(3) = -0.91876 E 0
B(4) = -0.33086 E-1
B(5) = -0.58053 E 0
B(6) = -0.11198 E 1
B(7) = -0.42133 E 0
B(8) = -0.42803 E 0
B(9) = -0.49926 E 0
B(10) = -0.42279 E 0
B(11) = -0.41274 E 0

FIGURE 15. Pressure waveform input and Fourier coefficients

Model Solution

The model is programmed in Fortran 77 and solved on an NAS9 computer. A flowchart of the program logic is shown in Figure 16. A listing of the program is provided in Appendix C.
FIGURE 16. Flowchart of program logic for uterine artery model
The program begins by initializing all constants, calculating initial flow values based on the mean pressure, and calculating initial impedances and resistances for each arterial segment.

The main program then calls a subroutine which solves a system of first-order differential equations using the Runge-Kutta method. This subroutine (RKGS) calls another subroutine (FCT) which contains the system of differential equations to be solved. The equations are written in state-variable form. RKGS sends the state vector, \( \mathbf{x} \), and the time, \( t \), to FCT and FCT returns the derivative vector, \( \frac{d\mathbf{x}}{dt} \), where:

\[
\frac{d\mathbf{x}}{dt} = A\mathbf{x} + \mathbf{b}
\]

is the system of equations which is solved.

At each time increment, a new pressure is calculated along with a new diameter, resistance, inductance and compliance for each arterial segment. RKGS calls subroutine OUTP each time it has solved the system of equations for a specific time. The output subroutine stores each value of pressure, flow and time in an array. RKGS returns control to the main program after it has solved the system of differential equations over the entire time period specified. Next the main program analyzes the flow waveform and calculates the mean flow and the pulsatility index. Finally both pressure and flow waveforms are plotted.
The model was solved for comparison purposes using the subroutine LSODA in the library package ODEPACK. No difference between the two subroutines could be detected in the solution.
RESULTS AND DISCUSSION

Velocity Waveform Analysis Using a Computer Model

The standard solution to the computer model is based on the pressure waveform shown in Figure 15 (used as the proximal pressure) and the parameter values in Table 2. The resulting standard flow waveform can be seen in Figure 17. This waveform represents mean cross sectional flow in the main branch of the artery, proximal to the bifurcation. For the standard case, the mean flow is 25 ml/min and the pulsatility index is 3.94. As stated in the literature review, many indices have been used to assess blood flow. In this study the pulsatility index (PI) has been chosen as the most useful waveform index. The pulsatility index has been chosen because it is easy to calculate from a given set of data and more complicated indices have not been shown to provide more useful information (Erskine and Ritchie, 1985a; Capper et al., 1976; Quamas et al., 1986). It should be noted that this case is designated as the standard flow waveform to provide a baseline for further comparisons. It is based on estimates only of normal model parameters.
FIGURE 17. Standard solution for the uterine artery model
Dimensional analysis

Through the use of dimensional analysis it is possible to analyze a system with a large number of parameters and reduce the number of parameters to some minimum number of $\pi$-term parameters. These $\pi$-terms are dimensionless terms formed from combinations of other parameters.

For the mathematical model of the uterine artery, the pulsatility index can be written as a function of the following parameters:

$$\text{PI} = f(l_1, l_2, l_3, d_1, d_2, d_3, p_0, p_1, c_0, c_1, R_{1A}, R_{TA}, C_{TA}, R_{1B}, R_{TB}, C_{TB}, \omega, \rho, \mu)$$

where $l_1, l_2,$ and $l_3,$ are the length of the three branches,

$d_1, d_2,$ and $d_3,$ are the diameter of the three branches,

$p_0$ is the mean input pressure,

$p_1$ represents the nine Fourier coefficients for the input pressure waveform,

$c_0$ and $c_1$ are coefficients of vessel compliance,

$R_{1}$ and $R_{T}$, are windkessel resistances,

$C_T$ is the windkessel compliance,

$\omega$ is the heart rate,

$\rho$ is the blood density,

and $\mu$ is the blood viscosity.
There are 28 variables, including all 9 Fourier coefficients for the pressure waveform input and including PI. By applying the rules of dimensional analysis, it is possible to write 25 dimensionless π-terms to help simplify the relationship between PI and the other 27 parameters. To begin, it is possible to combine all of the fixed geometric parameters which would not be expected to change under normal conditions in a living animal.

\[
\begin{align*}
\pi_1 &= \frac{l_2}{l_1} \\
\pi_2 &= \frac{l_3}{l_1} \\
\pi_3 &= \frac{d_1}{l_1} \\
\pi_4 &= \frac{d_2}{l_1} \\
\pi_5 &= \frac{d_3}{l_1} \\
\pi_6 &= \frac{\pi_1^2}{\pi_2} = \frac{\pi_3^3}{\pi_4^2} = \frac{\pi_5^5}{\pi_6^4} = \frac{\pi_7^7}{\pi_8^6} = \frac{\pi_9^9}{\pi_10^{10}} = \frac{\pi_11^{11}}{\pi_12^{12}} = \frac{\pi_13^{13}}{\pi_14^{14}}
\end{align*}
\]

π_6 through π_14 can be written as \(\pi_i = \frac{p_i}{p_0}\). These π-terms will be constant for a given pressure input. If it is assumed that \(\rho, \mu, c_0,\) and \(c_1\), are constants, then the following π terms will also be constants:

\[
\begin{align*}
\pi_{15} &= \frac{c_0^2}{c_1} \\
\pi_{16} &= \rho c_0 \\
\pi_{17} &= \rho p_0 d_1^2 / \mu^2
\end{align*}
\]

The following π terms make up the remaining:

\[
\begin{align*}
\pi_{18} &= \frac{C_{TA}}{C_{TB}} \\
\pi_{19} &= \frac{R_{1A}}{R_{TA}} \\
\pi_{20} &= \frac{R_{1B}}{R_{TB}} \\
\pi_{21} &= \frac{R_{TA}}{R_{TB}} \\
\pi_{22} &= \mu \omega / \rho_0 \\
\pi_{23} &= \frac{R_1 d_1}{\rho \omega} \\
\pi_{24} &= \frac{R_{TA} \omega C_{TA}}{R_{TA} \omega C_{TA}} \\
\pi_{25} &= PI
\end{align*}
\]

Therefore, for a constant input pressure waveform, geometry, \(\rho, \mu, c_0,\) and \(c_1\); PI is a function of the remaining π-terms; i.e.,

\[
PI = f\left(\frac{R_{1A}}{R_{TA}}, \frac{R_{1B}}{R_{TB}}, \frac{C_{TA}}{C_{TB}}, \frac{\mu \omega}{\rho_0}, \frac{R_1 d_1}{\rho \omega}, R_{TA} \omega C_{TA}\right)
\]
Figure 18 shows a plot of PI versus $R_{T\omega C}$ obtained from the computer model for varying values of $\mu/\rho_0$ and $R_{td1}/\rho\omega$, while holding the windkessel parameters constant. It can be seen that these latter two $\pi$-terms do not have a large effect on PI.

In the case of a fixed relationship between the two arterial branches (i.e., $R_{TA}/R_{TB} = \text{constant}$ and $C_{TA}/C_{TB} = \text{constant}$) it is possible to further simplify so that

$$PI = f\left(\frac{R_{1A}}{R_{TA}}, \frac{R_{1B}}{R_{TB}}, R_{T\omega C}\right)$$

For Figure 18 $R_{1A}/R_{TA} = 0.07$ and $R_{1B}/R_{TB} = 0.09$. For the case of the fixed relationship in the computer model the single parameter $R_{T\omega C}$ can be taken as $R_{T\omega C}$ for either branch of the model.

The main point shown in Figure 18 is that PI is primarily a function of $R_{T\omega C}$ and relatively independent of $R_1$ and $\mu$. Figure 19 shows a family of 5 curves for PI versus $Q$ at 5 different $R_1/R_T$ ratios. The main point of Figure 19 is to show that the relationship between PI and $Q$ is dependent on the $R_1/R_T$ ratio although $Q$ is chiefly a function of $R_T$. To obtain these data $\omega$ and $C$ remained constant while $R_T$ was varied.
FIGURE 18. PI versus $R_{T \omega C}$
FIGURE 19. PI versus mean flow for various $R_1/R_T$ ratios as obtained from the computer model.
PI as a function of model parameters

Through the use of the computer model, it is possible to obtain PI versus a single parameter while all other parameters are held constant. This is done in Figures 20 and 21 for parameters \( R_T, d, l, C_T \), and \( c_0 \). For the case of varying diameters and lengths, the length or diameter of each branch was varied. From these plots it can be seen that PI is largely a function of \( C_T \) and \( R_T \). Diameter, length and \( c_0 \) also affect compliance, but more weakly than the other parameters. It should be noted that for small diameters the PI has decreased significantly. This decreased PI is accompanied by decreased flow due to the small diameter. In cases where flow remains constant, PI is not strongly affected by changing the diameter.

Bovine Uterine Artery Waveforms

Electromagnetic and pulsed Doppler data

In order to better characterize the flow velocity waveform in the bovine uterine artery and to provide information concerning flow waveform variations over the estrous cycle, electromagnetic and pulsed Doppler blood velocity waveform data were collected. Examples of pulsed Doppler and continuous wave Doppler blood velocity waveforms in the bovine uterine artery are shown in Figure 22. These
FIGURE 20. PI as a function of d, l, and Rₜ
FIGURE 21. PI as a function of $c_o$ and $C_T$
FIGURE 22. Blood velocity waveforms from a) pulsed Doppler and b) continuous wave Doppler flowmeters
waveforms are from two different cows on different days of the estrous cycle.

Blood velocity waveform data were collected over the course of an estrous cycle in 5 cows. In one cow (cow number 520), data were collected using an electromagnetic flowmeter over the course of one complete estrous cycle. Mean flow data were also recorded for this cow. In four other cows data were collected over part of an estrous cycle using a pulsed Doppler flowmeter (cows 801, 905, 127, and 647). Daily hormonal levels of estrogen (estradiol-17β) and progesterone were recorded for all five cows. In this dissertation, estradiol-17β will be referred to as estrogen. In cows 801, 127, and 647 data were recorded from both left and right uterine arteries. In cows 905 and 520 data were recorded from only one uterine artery.

Tables 3 through 6 show the pulsatility index and standard deviation as obtained from the pulsed Doppler blood velocity waveforms. In these Tables PI_l represents the pulsatility index in the left uterine artery and PI_r represents the PI in the right uterine artery. The day of the estrous cycle is defined with respect to day 0 which is the day of the cycle when the cow comes into behavioral estrus. Table 7 shows mean flow for cow 520 and values of pulsatility index as obtained from the electromagnetic blood
velocity waveforms. Figure 23 shows mean flow versus day of the estrous cycle for cow 520. Tables 8 and 9 show values of estrogen and progesterone through the estrous cycle for all 5 cows.
FIGURE 23. Mean flow versus day of the estrous cycle for cow 520
TABLE 3. Pulsed Doppler data from cow 127

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TABLE 4. Pulsed Doppler data from cow 647

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TABLE 9. Progesterone in systemic blood - ng/ml

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**Pulsatility index versus day of the estrous cycle**

Figure 24 shows pulsatility index versus the day of the estrous cycle (based on data from Table 3 through Table 7). Values for pulsatility index are averages calculated from all five cows using both left and right uterine artery data, where both are available. The dashed line in Figure 24 shows a filtered PI (PIF) curve where PIF is a 3 day average value of PI. That is

$$\text{PIF}_d = \frac{(\text{PI}_{d-1} + \text{PI}_{d} + \text{PI}_{d+1})}{3}$$
where d is the day of the estrous cycle.

**PI versus estrogen and progesterone levels**

Concentrations of estrogen and progesterone in systemic blood are important in regulating uterine blood flow (Ford, 1982). Table 10 shows daily values of estrogen to progesterone ratio (E/P ratio), estrogen level, progesterone level and PIF averaged for all 5 cows. A plot of estrogen and progesterone versus day of the estrous cycle can be seen in Figure 25. The values of estrogen and progesterone are average values for cows 520, 801, 905, 127, and 647. Figure 26 shows natural log of the filtered pulsatility index (PIF) plotted versus the estrogen progesterone ratio (E/P) for all 5 cows during the period of day -4 to +4. During this time period estrogen is the predominant hormone and the E/P ratio is relatively high (E/P > 0.01, approximately). There is a significant correlation between PI and E/P. The empirical equation describing this relationship is:

\[ \text{PI} = 2.34 e^{-5.04(E/P)} \]

The correlation coefficient for the linear regression is \( r = -0.95 \). There is no significant correlation between pulsatility index and E/P ratio when taken over the entire estrous cycle, or over the period of day +5 to day 14(-5). Figure 27 shows natural log of filtered pulsatility index versus the progesterone level for all 5 cows during the
FIGURE 24. PI versus day of the estrous cycle
TABLE 10. Daily levels of estrogen, progesterone, PIF, and E/P ratio for 5 cows

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<td>2.35</td>
<td>0.0020</td>
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<td>4.85</td>
<td>2.29</td>
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<td>50.6</td>
<td>3.67</td>
<td>1.95</td>
<td>0.0537</td>
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<td>18</td>
<td>82.4</td>
<td>0.34</td>
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<td>0.2424</td>
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</table>

period of day 7 through day 14(-5). During this time period the estrogen level is low and E/P ratios are generally less than 0.003. A significant positive correlation between ln(PI) and progesterone level can be shown by linear regression. The correlation coefficient is r=+0.94. There is no significant correlation between ln(PI) and progesterone level when calculated over the entire estrous cycle or over the period of -4 to +4 days.
FIGURE 25. Estrogen and progesterone versus day of the estrous cycle
FIGURE 26. Ln(PI) versus estrogen/progesterone ratio

$PI = 2.34 e^{5.04(E/P)}$
FIGURE 27. Ln(PI) versus progesterone level
Pulsatility index versus flow  Figure 28 shows a plot of the natural logarithm of pulsatility index versus natural logarithm of flow, Q, in the uterine artery of cow 520 between day -4 and +4 of the estrous cycle. During this period of the estrous cycle there is a significant negative correlation between ln(PI) and ln(Q). The correlation coefficient for the linear regression is -0.92. The equation describing the logarithmic relationship is

\[
PI = 36.8Q^{-0.71}
\]

The relationship between ln(PI) and ln(Q) for days 7 through 14 is not so strongly correlated. The correlation coefficient is r=-0.75. The null hypothesis is that the two variables are not related. For 6 degrees of freedom, this hypothesis is rejected at the 95% confidence level. It should be noted that in this time period the mean flow is nearly constant and relatively low (Q=30.7 ml/min and s=4.72 ml/min).

Continuous wave Doppler data

The purpose of collecting these data was, as stated in the introduction, to collect Doppler data in both non-pregnant and pregnant cows, to analyze these data in order to characterize uterine artery blood velocity waveforms, and to use the results of the foregoing phases to draw some conclusions with regards to the feasibility of early
FIGURE 28. Ln(PI) versus Ln(mean flow)

PI = 36.8 Q^{-0.71}
pregnancy detection using Doppler velocity waveforms. An explanation of the procedures used to collect these data is given in the Materials and Procedures section in the reference "Use of ultrasonic Doppler waveforms in the assessment of uterine artery blood flow," (Waite, 1985).

One-hundred forty-six data sets were collected over a six month period from cows which were between 14 and 36 days post-breeding. A data set is data collected continuously over a 10 to 20 second period from one artery of a single cow. A sample data set can be seen in Figure 22b. A data pair includes one data set from the left uterine artery and one data set from the right uterine artery of a single cow, collected on the same day. For each data set a pulsatility index and standard deviation were calculated. The data were not used in cases where the standard deviation was greater than one-third of the pulsatility index (s > 1/3 PI). From one-hundred forty-six data sets there were 27 bad sets (s > 1/3 PI). The useable data sets formed 53 pairs of useable data. For the purposes of this work a useable data set was considered to be a set in which the standard deviation of the PI was less than 1/3 of the pulsatility index. A useable data pair is a data pair in which both data sets in a single cow (one from the left and one from the right uterine artery) are useable.
The data were divided into 4 groups according to operator and pregnant versus non-pregnant cows. There is a statistically significant difference between operators. The average PI from data collected by operator 2 (Conley) was 2.90 (s=1.2, n=80). The average PI from data collected by operator 1 (Ford) was 1.40 (s=0.33, n=26).

**Data from operator 1** The average PI for pregnant cows was 1.47 (s=0.30, n=20) compared to 1.18 (s=0.388, n=6) for non-pregnant cows. These data include both left and right uterine artery data. Another index was the PI ratio which can be calculated from the PI values in both the left and right uterine artery. \( \text{PI}_{\text{high}} \) is defined as the higher of the two PI values. \( \text{PI}_{\text{low}} \) is the lower of the values between \( \text{PI}_r \) and \( \text{PI}_l \). PI ratio is then defined by \( \text{Ratio} = \frac{\text{PI}_{\text{high}}}{\text{PI}_{\text{low}}} \). The average PI ratio was 1.21 (s=0.14, n=10) for pregnant cows and 1.72 (s=0.110, n=3) for non-pregnant cows. These data indicate a statistically significant difference between pregnant and non-pregnant cows with respect to both the average PI and the PI ratio.

**Data from operator 2** These data do not indicate a statistically significant difference between pregnant and non-pregnant cows. As a group these data indicate a value for average PI=2.90 (s=1.20, n=80) and PI ratio=1.42 (s=0.36, n=40). It should be noted that the standard
deviation of the mean PI value for this group of data is 1.2 compared to 0.33 for the operator 1 data (pregnant and non-pregnant data combined). Table 11 summarizes the data from operators 1 and 2 in tabular form.

### TABLE 11. Continuous wave Doppler data from pregnant and non-pregnant dairy cows collected by operators 1 and 2

<table>
<thead>
<tr>
<th>Operator</th>
<th>Average PI</th>
<th>PI Ratio</th>
<th>Average PI</th>
<th>PI Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operator 1</td>
<td>1.47</td>
<td>1.21</td>
<td>2.89</td>
<td>1.45</td>
</tr>
<tr>
<td>(s=0.30)</td>
<td>(s=0.14)</td>
<td>(s=1.32)</td>
<td>(s=0.39)</td>
<td></td>
</tr>
<tr>
<td>(n=20)</td>
<td>(n=10)</td>
<td>(n=50)</td>
<td>(n=28)</td>
<td></td>
</tr>
<tr>
<td>Operator 2</td>
<td>1.18</td>
<td>1.72</td>
<td>2.93</td>
<td>1.34</td>
</tr>
<tr>
<td>(s=0.39)</td>
<td>(s=0.11)</td>
<td>(s=0.89)</td>
<td>(s=0.31)</td>
<td></td>
</tr>
<tr>
<td>(n=6)</td>
<td>(n=3)</td>
<td>(n=24)</td>
<td>(n=12)</td>
<td></td>
</tr>
<tr>
<td><strong>Non-pregnant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operator 1</td>
<td>1.40</td>
<td>1.33</td>
<td>2.90</td>
<td>1.42</td>
</tr>
<tr>
<td>(s=0.33)</td>
<td>(s=0.26)</td>
<td>(s=1.20)</td>
<td>(s=0.36)</td>
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<tr>
<td>(n=26)</td>
<td>(n=13)</td>
<td>(n=80)</td>
<td>(n=40)</td>
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</tr>
</tbody>
</table>

Between operator differences It is possible to make some speculations concerning the between operator differences in pulsatility index based on results from the computer model along with other available information. It has been suggested that differences in handling of the
uterine artery during palpation could account for the
difference. The uterine artery wall can contract in
response to touch and may spasm causing significant changes
in vessel diameter. In addition the wall properties such as
compliance are not constant but can change under certain
conditions.

A local decrease in diameter due to arterial spasm may
be an explanation for an increase in PI as measured by
operator 2. The computer model predicts increases in PI
proximal to severe localized constrictions. Compliance of
the artery may also change significantly under these
conditions. Osberg and Langville (1982) have reported
reflex control of arterial compliance in rabbits. This
suggests that it may be possible to have sudden significant
changes in arterial compliance which are neurally controlled
and may be related, for example, to the handling of the
artery during palpation. It can be seen from Figure 21 that
increased windkessel compliance, $C_T$, can account for
significant increases in the pulsatility index.

**Diagnosing pregnancy** Figure 29 shows $P_{I\text{high}}$ versus
$P_{I\text{low}}$ for 13 sets of data collected by operator 1. This
Figure shows that the data can be separated into two groups
using the discriminant line $P_{I\text{high}}/P_{I\text{low}} = 1.52$. All data
which fall above and to the left of this line are data
points from non-pregnant cows. All data below and to the right of this line are from pregnant cows. A similar linear discriminant cannot be found for data collected by operator 2.

Comparison Between Bovine Uterine Artery Data and Computer Model

As described previously, Figure 28 shows a curve relating PI to mean flow for a non-pregnant cow between days -4 and +4 of the estrous cycle. During this time period the PI is related to the estrogen to progesterone ratio. This curve is plotted from electromagnetic flowmeter data and can be described by the equation:

\[
\text{PI} = 36.8 Q^{-0.71}
\]

where \( Q \) is flow in ml/min. Figure 30 shows a number of curves relating PI to mean flow using the mathematical model. It can be seen that the ratio \( R_1/R_T = 0.1 \) corresponds most closely to the measured curve.

During the remainder of the estrous cycle the PI appears to be related to the progesterone level. In one set of electromagnetic flowmeter measurements which were recorded, the flow remained relatively constant between day 7 and day 14 except for a short transitional period of one to three days. Since the mean flow is inversely related to
FIGURE 29. $P_{I_{\text{high}}}$ versus $P_{I_{\text{low}}}$
FIGURE 30. Pulsatility index versus flow

\[ \frac{R_1}{R_T} = 0.02 \]

\[ 0.05 \]

\[ 0.10 \]

\[ 0.20 \]

\[ 0.50 \]

\[ \text{PI} = 3.48 Q^{-0.70} \]
the total resistance, $R_T$, this would indicate that the total resistance is relatively constant and that some other parameter such as changing capacitance would account for the changes in the PI over this portion of the estrous cycle. Since estrogens are minimal during this period and progesterone increases responsiveness of smooth muscle to norepinephrine, it is possible to speculate that changing progesterone levels are having an effect on pulsatility index with little or no change of mean flow; i.e., the pulsatility of the flow waveform is changing but the mean flow is not.

If the windkessel resistances $R_1$ and $R_2$ are considered to model, respectively, the arteriole resistance and capillary resistance of a capillary bed, then windkessel capacitance, $C_T$, can be viewed as the volume compliance of the arterioles, since the capillaries are modeled as rigid tubes. With this view in mind, progesterone acting on the smooth muscle of the arterioles may change the compliance of the arterioles (thereby changing the PI) while having little effect on the total windkessel resistance.

The control of uterine artery blood flow during pregnancy is different from control during the estrous cycle (Ford and Stice, 1985). During pregnancy both estrogen and progesterone are elevated (Ford and Stice, 1985).
Therefore, it could be expected that during pregnancy, although flow is changing, it may not be directly related to a change in PI. For example, it is possible that both mean flow and PI can increase if the ratio of \( \frac{R_1}{R_T} \) decreases or if windkessel capacitance, \( C_T \), increases at the same time that \( R_T \) is decreasing. In the case of the continuous wave Doppler data collected in pregnant cows, it was found that in pregnant cows the PI ratio (\( \frac{P_{\text{high}}}{P_{\text{low}}} \)) was lower in pregnant cows. That fact indicates a smaller difference in PI values between arteries, although previous data (Ford, 1982) suggest the mean flow difference between arteries increases significantly. One possible explanation is that as flow increases (\( R_T \) decreases) to the artery supplying the gravid horn of the uterus, the windkessel capacitance \( C_T \) increases in that artery. Another possibility is that the windkessel capacitance in the artery supplying the non-gravid horn decreases. In either case this could account for the fact that the PI difference decreases while the flow difference increases.
SUMMARY AND CONCLUSIONS

The first stated objective of this study was the design, development and testing of a suitable ultrasonic probe. This objective was achieved and several probes were constructed which were used to collect continuous wave Doppler blood velocity waveforms for this study.

The second objective was to obtain some basic hemodynamic data related to uterine artery blood flow. Electromagnetic, pulsed Doppler and continuous wave Doppler blood velocity waveforms were obtained as well as mean flow data in one non-pregnant cow. Figure 22 shows two sample blood velocity waveforms from bovine uterine arteries.

The third and fourth stated objectives of this study were to design, develop and test a portable microcomputer based device which could be used to collect and analyze Doppler blood velocity waveforms in the field, and to collect continuous wave Doppler data in both pregnant and non-pregnant cows, with a subsequent analysis of these data to characterize uterine artery blood velocity waveforms.

The device was designed, constructed and used to collect 146 sets of continuous wave Doppler blood velocity waveforms in bovine uterine arteries. The pulsatility index was obtained for each of these waveforms.
The fifth objective was to create a computer model of flow in the uterine artery. This model was developed and coded in Fortran. A comparison was made between the results of this model and those of a similar finite-element model of the uterine artery (Weerappuli, 1987) using the same input parameters. The results for the three cases which were compared matched very closely. The output of this one-dimensional time dependent model is a flow or pressure versus time waveform at some specific point in the artery. Figure 17 shows a typical output from this model. The lumped parameter model indicates that for a fixed geometry and a fixed proximal input pressure waveform, the pulsatility index is chiefly a function of the $R_1/R_T$ ratio and $R_T\omega C_T$ where $\omega$ is the heart rate, $R_1$ is the proximal windkessel resistance (see Figure 2), $R_T$ is the total windkessel resistance, and $C_T$ is the total windkessel capacitance.

By comparing PI to estrogen/progesterone ratios and to progesterone level at various stages of the estrous cycle in non-pregnant cows, it appeared that the estrous cycle could be divided into two time periods for the purpose of relating PI to steroid hormone levels. Between day -4 and +4 of the estrous cycle the estrogen/progesterone ratio is negatively correlated ($r = -0.95$) with the natural log of the PI. This
information is based on both pulsed Doppler and electromagnetic flowmeter data collected in a total of 5 cows (Doppler data from 4 cows and electromagnetic data from 1 cow). For this same period, mean flow data in one cow were related to the PI. Figure 28 shows the curve relating pulsatility index to mean flow in cow 520 between day -4 and +4 of the estrous cycle. Figure 30 shows a family of curves, generated by the computer model, for PI versus flow for various $R_1/R_T$ ratios. In the range of 25 to 200 ml/min, which is a representative range of flow in the bovine uterine artery, the curve for $R_1/R_T = 0.1$ closely approximates the curve described in Figure 28. Therefore, the data collected between days -4 and +4 are most closely modeled by a system in which $R_1/R_T = 0.1$ with $R_T$ being varied to change the mean flow and the pulsatility index.

Between day 7 and day 14, the natural log of the PI is more closely related to the progesterone level ($r = +0.94$). Again, this information is based on both pulsed Doppler and electromagnetic flowmeter data. During this time period, the one set of mean flow data which was collected shows that the mean flow remained relatively constant, although the PI varied. Since the mean flow is inversely proportional to the total resistance $R_T$ and mean flow was constant, the data collected for the time period of day 7 to day 14 are most
closely modeled by a system with a constant $R_T$ and varying windkessel capacitance, $C_T$.

The final objective of the research was to use the results of the foregoing phases to draw some conclusions with regard to the feasibility of early pregnancy detection using Doppler velocity waveforms. Figure 29 shows $P_{I_{\text{high}}}$ versus $P_{I_{\text{low}}}$ for 13 pairs of data collected by operator 1. Using a discriminant line $P_{I_{\text{high}}}/P_{I_{\text{low}}} = 1.52$, the data can be separated into two groups. All data which falls above and to the left of this line are data points from pregnant cows. All data below and to the right of this line are from non-pregnant cows. A similar discriminant between pregnant and non-pregnant cow data from operator 2 could not be found. With regard to the final objective, the following points can be made:

- It is feasible to obtain velocity waveforms through rectal palpation using the finger probe which was designed for this study.
- The data can be processed using the portable, microcomputer-based, velocity waveform analyzer.
- It may be possible to diagnose pregnancy in cows using Doppler blood velocity waveforms, but due to the fact that several factors, in addition to mean flow, appear to affect the PI, further work is needed to establish suitable criteria.
Possibilities for Further Investigation

There are a number of areas in which further work on this project are possible. Clearly, in order to make the velocity waveform analyzer a useful tool in diagnosing pregnancy, the problem of between operator differences must be resolved. In this regard, one possible improvement might develop from an investigation of the effect of different probe shapes on the variability of the data. That is, with a probe design that would be easier to use, it may be possible to simplify the obtaining of Doppler waveforms, thus reducing the variability among operators. It would be possible to investigate between operator differences systematically by using a number of operators to collect data.

The relationship between mean flow and PI during the estrous cycle and early pregnancy could be further explored by collecting additional electromagnetic flow data. Additional work with the model and with electromagnetic and pulsed Doppler flow data can be done to further determine various model parameters. Specifically, one could obtain simultaneous pressure and flow recordings from the uterine artery using a pressure transducer and a pulsed Doppler flowmeter. Then using the computer model to match waveforms, it may be possible to estimate parameters such as
$R_T$ and $C_T$. It may then be possible to relate parameters such as $R_T$, $C_T$, and $R_1/R_T$ ratio to hormone levels.

Another possible investigation would be to attempt to measure pulsed Doppler flow velocity waveforms and hormone levels in pregnant cows, in a manner similar to what has been done with non-pregnant cows in this investigation.
BIBLIOGRAPHY


ACKNOWLEDGMENTS

I would like to thank Dr. D. F. Young for his help and guidance on this project. I would also like to thank Dr. S. P. Ford and A. J. Conley for the time and effort which they have invested. A special note of appreciation goes to the Iowa High Technology Council for the funding of this project.

The experimental use of cows in this project conforms to the "Guiding Principles in the Care and Use of Animals", approved by the council of the American Physiological Society. Cattle involved in the project were maintained at the Iowa State Animal Reproduction Farm and the Iowa State Dairy Farm.
APPENDIX A

Derivation of Compliance Equation

Assumptions:
Arterial wall material is incompressible.
Artery length is a constant.

\( p - \) pressure inside artery lumen
\( r - \) inside radius
\( h - \) wall thickness
\( E - \) incremental modulus of elasticity
\( \epsilon - \) strain
\( S_\theta - \) hoop stress

\[ S_\theta = \frac{pr}{h} \quad \quad r_o h_o = rh \]
\[ E = \frac{dS_\theta}{d\epsilon} \quad \quad d\epsilon = \frac{dr}{r} \]

1) \( dS_\theta = d(\frac{pr}{h}) = d[pr(\frac{r}{r_o h_o})] = d(\frac{pr^2}{r_o h_o}) \)

2) \( dS_\theta = Ed\epsilon = Edr/r \)

3) \( d(\frac{pr^2}{r_o h_o}) = 2prdr + r^2 dp \); \( dr \approx 0 \)

4) \( r^2 dp/r_o h_o = Edr/r \); (from equations 1, 2 and 3)

5) \( \int_{p_o}^{P} dp = Eh_o r_o \int_{r_o}^{r} \frac{dr}{r^3} \)
6) \( p - p_0 = \frac{E_{ho}}{2r_0} \left[ \frac{1}{r_0^2} - 1/r_0^2 \right] \)

7) \( p - p_0 = \frac{E_{ho}}{2r_0} \left[ 1 - A_0 / A \right] \)

8) \( \frac{A}{A_0} = (1 - \Delta_p D_0)^{-1} \frac{E_{ho}}{E_{ho}} \)

Polynomial series for \((1-x)^{-1}\) is \(1 + x + x^2 + x^3 + \ldots\)

9) \( \frac{A}{A_0} = 1 + \left( \frac{p - p_0}{D_0} \right) + \left[ \left( \frac{p - p_0}{D_0} \right)^2 \right] + \left[ \left( \frac{p - p_0}{D_0} \right)^3 \right] + \ldots \)

10) \( \frac{dA}{dp} = \frac{A_0 D_0 + A_0 D_0^2}{E_{ho}} \frac{(p - p_0)}{E_{ho}^2} \)

11) \( \frac{dA}{dp} \approx \frac{A_0 D_0}{E_{ho}} = \frac{2\pi R_0^3}{E_{ho}} \)
APPENDIX B

Equipment Specifications

Parks model 909 and model 1010-LA Doppler flowmeters

1. Oscillator frequency: Nominal 10 Mhz or 5 Mhz
2. Power: Rechargable battery - Gel Cell™
3. Filters: 4 pole low-pass active filters; 12 db per octave cutoff at 3.5, 7, 14, of 28 Hz

Biotronex Model BL-610
Electromagnetic Blood Flowmeter

1. Input: Differential with no common mode return except through transducer ground
   a. Impedance: Nominally 10,000 ohms at 1100 Hz
   b. Maximum voltage before distortion at the output of the flowmeter - At least $1 \times 10^{-5}$ V peak-peak at one tenth amplifier gain using sine-wave generator slightly offset from the carrier frequency

2. Outputs: Single ended. One output with high response capability for pulsatile blood flow and another output with damped response for mean flow presentation are located on the rear apron of the power supply and console housing
   a. Output impedance: 2700 ohms.
b. Output capability: 5.33 volts peak-peak at one tenth amplifier gain with $1 \times 10^{-4}$ V input connected as in 1.b.

3. Frequency response: At least 100 Hz (-3dB) measured at the phasic output connector with frequency response switch in maximum response setting of 100.

4. Noise: With input shorted to ground and amplifier at one half gain in 100 Hz frequency response setting, noise is less than 0.5μV

5. Baseline: Fixed zero reference is presented on the outputs. This will not necessarily be an "electronic zero".

6. Flow polarity: Reversible

Tandberg Series 115
Instrumentation Tape Recorder

1. Speed control: Electronic servo controls capstan speed against fixed reference.

2. Tape speeds: 15, 3 3/4, 15/16 ips, electrically switchable. FM carrier frequency and FM reproduce filter bandwidth automatically selected.

3. Input impedance: 40 K ohm/volt, single ended
4. Frequency range and signal/noise ratio:

<table>
<thead>
<tr>
<th>Speed (ips)</th>
<th>Center carrier freq. (hz)</th>
<th>Pass band limits lower</th>
<th>Pass band limits upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>27000</td>
<td>DC</td>
<td>5000</td>
</tr>
<tr>
<td>3 3/4</td>
<td>6750</td>
<td>DC</td>
<td>1250</td>
</tr>
<tr>
<td>15/16</td>
<td>1688</td>
<td>DC</td>
<td>312</td>
</tr>
</tbody>
</table>

5. Output voltage: ±5 V peak for full deviation

6. Output impedance: Less than 1 ohm single-ended

7. Linearity: 0.2% departure from best straight line through zero

Hewlett-Packard

Model 3960 Instrumentation Tape Recorder

1. Tape speed accuracy: ±0.2%

2. Tape speed: 15, 3 3/4, and 15/16 ips

3. Input impedance: 50 k ohms or greater shunted by 200 pF maximum, single ended
4. **Frequency range and signal/noise ratio**

<table>
<thead>
<tr>
<th>Speed (ips)</th>
<th>Center carrier freq. (hz)</th>
<th>Pass band limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
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<tr>
<td>3 3/4</td>
<td>6750</td>
<td>DC 1250</td>
</tr>
<tr>
<td>15/16</td>
<td>1688</td>
<td>DC 312</td>
</tr>
</tbody>
</table>

5. **Output voltage:** ±5 V peak for full deviation

6. **Output impedance:** 140 ohms maximum

7. **Linearity:** ±1% peak-peak output

---

**Hewlett-Packard Model 7402A Oscillograph Recorder**

1. **Input:** Single ended
2. **Input impedance:** One megaohm (nominal)
3. **Input sensitivity range:** 20 mV/div - 5 V/div
4. **Gain accuracy:** Within 0.75% of full scale value
5. **Linearity:** Within 0.6% of full scale value
6. **Frequency response:** Within 2% flat from DC to 40 Hz (less than 3 dB down at 55 Hz)
APPENDIX C

Velocity Waveform Analyzer Program in Basic

10  BAUD 300
20  DIM C0(30), C1(30), C2(30), P(30)
30  READ T0, N1, M0, F0, P0, M1, K1
40  DATA 0, 0, 0, 0, 0, 256, 0
50  REM CALL ASSY LANGUAGE ROUTINE FOR A/D INPUT
60  XBY(0C803H)=91H
65  GOSUB 2000
70  CALL 0B800H
80  REM FIND MAX AND MIN VALUES FOR ALL DATA
90  N=7FFH
100 Z9=1CH
110 FOR J=4000H TO 47FFH
120 IF XBY(J)=255 THEN XBY(J)=XBY(J-1)
130 IF XBY(J)>M0 THEN M0=XBY(J)
140 IF XBY(J)<M1 THEN M1=XBY(J)
150 NEXT J
160 REM FIND FIRST PULSE BY SEARCHING FOR A PEAK
170 IF M1<32. THEN M2=.75*M0 ELSE M2=(M0-M1)*.75+M1
180 FOR J=4000H TO (4000H+N)
190 IF F0=1 THEN 240
200 IF XBY(J)<M2 THEN 250
210 F0=1
220   P = P + 1
230   IF P > 2 THEN 290 ELSE 250
240   IF XBY(J) < M2 THEN F0 = 0
250   NEXT J
260   XBY(0C801H) = OFFH
261   XBY(0C802H) = 20H
262   XBY(0C802H) = 30H
270   STOP
280   REM FIND STARTING POINT OF FIRST PULSE
290   C0(1) = J
300   FOR I = C0(1) TO (C0(1) - 25) STEP -1
310   IF (XBY(I) - XBY(I - 2)) < 0 THEN 330
320   NEXT I
330   IF (C0(1) - I) < 6 THEN 320 ELSE C1(1) = I
340   F0 = 0
350   N0 = 1
360   REM FIND OTHER PULSES BY SEARCHING FOR PEAKS
370   FOR J = C1(1) TO (4000H + N)
380   IF F0 = 1 THEN 430
390   IF XBY(J) < M2 THEN 440
400   N0 = N0 + 1
410   C0(N0) = J
420   F0 = 1
425   J = J + 20
430   IF XBY(J) < M2 THEN F0 = 0 ELSE 440
435  J=J+20
440  NEXT J
450  I=0
460  REM FIND STARTING POINTS OF OTHER PULSES
470  I=I+1
480  J=C0(I)
490  J=J-1
500  IF (XBY(J)-XBY(J-2))<0 THEN 520
510  IF J>(C0(I)-25) THEN 490
520  IF (C0(I)-J)<6 THEN 490 ELSE C1(I)=J
530  IF I<N0 GOTO 470
540  REM INITIAL CHECK OF EACH PULSE PERIOD
550  I=0
560  I=I+1
570  T=(C1(I+1)-C1(I))/100
580  IF T=0 GOTO 630
590  IF T>2 GOTO 630
600  IF T<.3 GOTO 630
610  C2(I)=0
620  GOTO 640
630  C2(I)=1
640  IF I<(N0-1) THEN 560
650  REM CALL SUBROUTINE TO CHECK PULSE PERIODS
660  GOSUB 1320
670  T0=0
N1 = 0
REM FOR GOOD PULSES, FIND MIN, MAX, MEAN, AND PI
FOR I = 1 TO (N0-1)
M2 = 0
3 = 256
IF C2(I) = 1 GOTO 990
FOR J = Cl(I) TO Cl(I+1)
S = S + XBY(J)
IF XBY(J) > M2 THEN M2 = XBY(J)
IF XBY(J) < M3 THEN M3 = XBY(J)
NEXT J
M4 = S / (Cl(I+1) - Cl(I))
M4 = M4 - Z9
M3 = M3 - Z9
M2 = M2 - Z9
IF M4 = 0 GOTO 990
P1 = (M2 - M3) / M4
T = (Cl(I+1) - Cl(I)) / 100
T0 = T0 + T
N1 = N1 + 1
P(N1) = P1
REM OUTPUT INFO. TO CRT AND PRINTER
S = 0
NEXT I
IF N1 < 2 THEN 260
1000 FOR I=1 TO N1
1010 P0=P0+P(I)/N1
1020 NEXT I
1030 IF N1=1 THEN 1090
1040 S1=0
1050 FOR I=1 TO N1
1060 S1=S1+(P0-P(I))**2
1070 NEXT I
1080 S2=SQR(S1/(N1-1))
1110 R=60*N1/T0
1170 X=INT(P0/10)
1180 Y=INT(P0-10*X)
1190 Z=INT((P0-10*X-Y)*10)
1200 Z0=INT((P0-10*X-Y-Z/10)*100)
1210 IF X>0 THEN 2200
1215 IF X>9 THEN 260
1220 XBY(0C801H)=0C0H+30H+Y
1230 GOSUB 1590
1240 XBY(0C801H)=0AEH
1250 GOSUB 1590
1260 XBY(0C801H)=40H+30H+Z
1270 GOSUB 1590
1280 XBY(0C801H)=30H+Z0
1281 GOSUB 1590
1285 Z1=XBY(0C802H).AND.2
1286   IF Z1=0 THEN 1285
1292   X=INT(S2/10)
1293   IF X=0 THEN 1295
1294   GOTO 260
1295   Y=INT(S2)
1296   Z=INT((S2-Y)*10)
1297   Z0=INT((S2-Y-Z/10)*100)
1298   GOSUB 4000
1299   GOSUB 3000
1300   X=INT(N1/10)
1301   IF X>9 THEN 260
1302   Y=INT(N1-10*X)
1303   Z=0
1304   GOTO 2200
1310   REM   SUBROUTINE TO CHECK PULSE PERIOD
1320   N2=N1
1330   N1=0
1340   K=0 ; T0=0
1350   REM   FIND THE AVERAGE
1360   K=K+1
1370   IF C2(K)=1 THEN 1410
1380   T=(C1(K+1)-C1(K))/100
1390   T0=T0+T
1400   N1=N1+1
1410   IF K<(N0-1) THEN 1360
138

1430 REM IF OF PULSES IS SAME TWICE RETURN
1440 IF N2=N1 THEN 1580
1450 K1=K1+1
1460 IF K1>10 THEN 260
1470 K=0
1480 REM CHECK WHICH PULSES FIT THE AVERAGE
1490 K=K+1
1500 IF C2(K)=1 THEN 1550
1510 T=(C1(K+1)-C1(K))/100
1520 C2(K)=0
1530 IF T>(1.4*T0/N1) THEN C2(K)=1
1540 IF T<(.7*T0/N1) THEN C2(K)=1
1550 IF K<(N0-1) THEN 1490
1560 GOTO 1320
1570 XBY(0C801H)=0FEH
1571 XBY(0C802H)=20H
1572 XBY(0C802H)=30H
1580 RETURN
1590 XBY(0C802H)=60H
1600 XBY(0C802H)=70H
1610 RETURN
200 XBY(0C801H)=0
2010 XBY(0C802H)=20H
2020 XBY(0C802H)=30H
2030 FOR J=1 TO 4
2040 XBY(0C801H)=2FH
2050 GOSUB 1590
2060 XBY(0C801H)=4BH
2070 GOSUB 1590
2080 XBY(0C801H)=8FH
2090 GOSUB 1590
2100 XBY(0C801H)=0EFH
2110 GOSUB 1590
2120 PRINT " ",
2130 FOR I=20H TO 0E0H STEP 40H
2140 XBY(0C801H)=I
2150 GOSUB 1590
2160 PRINT " ",
2170 NEXT I
2180 NEXT J
2190 RETURN
2200 XBY(0C801H)=OCOH+3OH+X
2210 GOSUB 1590
2220 XBY(0C801H)=80H+Y+30H
2230 GOSUB 1590
2240 XBY(0C801H)=40H+2EH
2250 GOSUB 1590
2260 XBY(0C801H)=30H+Z
2270 GOSUB 1590
2280 GOTO 1285
3000 XBY(0C801H)=0COH+30H+Y
3010 GOSUB 1590
3020 XBY(0C801H)=0AEH
3030 GOSUB 1590
3040 XBY(0C801H)=40H+30H+Z
3050 GOSUB 1590
3060 XBY(0C801H)=30H+Z0
3070 GOSUB 1590
3080 Z1=XBY(0C802H).AND.2
3090 IF Z1=0 THEN 3080
3100 RETURN
4000 REM DEBOUNCE SUBROUTINE
4010 FOR I=1 TO 1000
4020 I=I+1
4030 NEXT I
4040 RETURN
Data Conversion Subroutine in Assembly Language

B300
ORG 0B300H LOC 2000H
B300

; WAIT FOR HIGH SWITCH VALUE TO
; BEGIN COLLECTING DATA

B300

B300 90 C8 02
START: MOV DPTR, OC802H
B303 E0
MOVX A, @DPTR
B304 54 02
ANL A, 02H
B306 60 F8
JZ START
B308

; SWITCH DEBOUNCING ROUTINE,
; APPX. 5 MSEC DELAY

B308

B308 79 FF
MOV R1, 0FFH
B30A 7A 13
MOV R2, 13H
B30C D9 FE
DEB1: DJNZ R1, DEB1
B30E 79 FF
MOV R1, 0FFH
B310 DA FA
DJNZ R2, DEB1
B312

; WAIT FOR SWITCH VALUE TO GO LOW
; BEFORE GOING ON

B312

B312 E0
FIN: MOVX A, @DPTR
B313 54 02
ANL A, 02H
142

B315 70 FB  JNZ FIN
B317
B317  ; SWITCH DEBOUNCING ROUTINE
B317
B317 79 FF  MOV R1, OFFH
B319 7A 13  MOV R2, 13H
B31B D9 FE  DEB2:DJNZ R1,DEB2
B31D 79 FF  MOV R1, OFFH
B31F DA FA  DJNZ R2,DEB2
B321

; SELECT REGISTER BANK 3, CLOCK 1
; MODEL, DISABLE CLOCK 0, START CLOCK
B321
B321 D2 D3  SETB 0D0H.3
B323 D2 D4  SETB 0D0H.4
B325 75 89 10  MOV 89H, 10H
B328 C2 A9  CLR 0A8H.1
B32A C2 8C  CLR 88H.4
B32C D2 8E  SETB 88H.6
B32E
B32E  ; INITIALIZE 20H:21H TO 4000H
B32E
B32E 75 21 40  MOV 21H, 40H
B331 75 20 00  MOV 20H, 00H
B334
B334 ;INCREMENT 20H,21H
B334
B334 E5 20 CONVERT:MOV A,20H
B336 C3 CLR C
B337 24 01 ADD A, 1
B339 F5 20 MOV 20H,A
B33B E5 21 MOV A,21H
B33D 34 00 ADDC A, 0
B33F F5 21 MOV 21H,A
B341 ;
B341 ;RESET TO 4000H IF 21,20=4800
B341
B341 30 0B 06 JNB 21H.3,CONT
B344 75 21 40 MOV 21H, 40H
B347 75 20 00 MOV 20H, 0
B34A ;
B34A ;TIMING--WAIT FOR CLOCK
B34A
B34A C3 CONT:CLR C
B34B 74 23 WAIT:MOV A, 23H
B34D 95 8D SUBB A,8DH
B34F 50 FA JNC WAIT
B351 C3 CLR C
B352 C2 8E CLR 88H.6
B354 75 8D 00 MOV 8DH, 0
MOV 8BH, 0
SETB 88H.6

;SEND 0 THEN 1 TO BIT 4 OF PORTC
;TO START CONVERSION

MOV DPTR, 0C802H
MOV A, 0
MOVX @DPTR, A
MOV A, l0H
MOVX @DPTR, A

;CHECK STATUS FOR CONVERSION END,
;PORT C BIT 0

CKSTATUS: MOVX A, @DPTR
ANL A, 1
JNZ CKSTATUS

;READ DATA @ PORT A

MOV DPTR, 0C800H
MOVX A, @DPTR

;PUT DATA IN XRAM & D/A AT PORT B
MOV 83H, 21H
MOV 82H, 20H
MOVX @DPTR, A
MOV R1, A
MOVX @DPTR, A
MOVX @DPTR, A
MOVX @DPTR, A
MOV A, 0
MOVX @DPTR, A
MOV A, 10H
MOVX @DPTR, A
MOVX A, @DPTR
ANL A, 02H
JZ CONVERT
CLR 0D0H.3
CLR 0D0H.4
CLR 88H.6
RET
Uterine Artery Model in Fortran

//ARTPLOT JOB ,LEE.R.WAITE
/*JOBPARM DEST=LOCAL,BLOCK=(NIGHT,NIGHT)
//STEP1 EXEC SCRUNC,PARM='L.I3821.ARTDAT'
//STEP2 EXEC SCRUNC,PARM='L.I3821.RDATDAT'
//STEP3 EXEC F0RTVCLG,TIME.GO=4

C THIS PROGRAM MODELS A UTERINE ARTERY USING AN
C UNSPECIFIED NUMBER OF DISCRETE NODES. TO USE THE
C PROGRAM CHANGE NASG AND N1SG TO REFLECT THE
C REQUESTED NUMBER OF MAIN ARTERY SEGMENT AND BRANCH
C ARTERY SEGMENTS (IN EACH BRANCH) RESPECTIVELY.
C THIS PROGRAM PLOTS THE DATA USING THE SIMPLOTTER
C THE PROGRAM STPTIC ALSO GIVES MEAN VALUES FOR FLOW AND
C PRESSURES AS INITIAL CONDITIONS, REDUCING TRANSIENTS.
C
C INITIALIZATION
C
DIMENSION PRMT(5),Y(102),DERY(102),AUX(8,102),PTF(1000),
1PTX(1000),PTP(1000),RD(102),R(102),A(9),B(9)
DIMENSION C(102),DX(102),L(102)
EXTERNAL FCT,OUTP,RADCAL
REAL R,L,C,RHO,MU,EP,H0,LA,LB1,LB2,DXA,DX1,DX2,RD,DX,PRMT,
1DERY,P0,P,PI,PTF,PTP,PTX,Y,AUX,C0,C1,A,B,PAVG
INTEGER NASG,N1SG,N2SG,I,J,K,PTN,Z,ZBEG,ZEND
CHARACTER*20 PULS,PULS2
COMMON/NONARR/EP, H0, P, P0, PI, NSEG, C0, C1, PAVG, *TLAST, MU, RHO, FREQ, CU, CV, PTN *
*, NBN, NASG/ARRAY/C, RD, DX, R, L, A, B, Y, PTP, PTX, PTF

C

PTN = 0
TLAST = 0
PI = 3.14159265
PRMT(1) = 0
PRMT(2) = 3.
PRMT(3) = .01
PRMT(4) = 1.E-1
RHO = 1050.
MU = 0.0045
H0 = .0015
LA = .047
LB1 = .032
LB2 = .062
NASG = 5
N1SG = 5
N2SG = N1SG
P0 = 80.
C0 = .103E-5
C1 = .230E-12
PAVG = .1111E3
**C**

**C** INITIALIZING DER Y AND Y

**C** ALL Y VALUES INITIALIZED TO PAVG AND LATER FLOW VALUES

**C** ARE INITIALIZED TO MEAN FLOW

**C**

**DO 10 I=1,NDIM**

**DERY(I)=(1/FLOAT(NDIM))**

**Y(I)=PAVG**

**10 CONTINUE**

**C**

**C** ASSIGNING R AND C VALUES FOR THE MODIFIED WINDKESSEL
C CHosen to give 50 ml/min flow with the given press input
C
C First value of R is R1A, branch A is upper, shorter branch
   R(NSEG*2+1)=.6813E10/8.E9
C Second R value is R2A, resistance parallel to cap.
   R(NSEG*2+5)=.9052E11/8.E9
C Third R value is R1B
   R(NSEG*2+3)=.4786E10/8.E9
C Fourth R value is R2B, resistance parallel to cap.
   R(NSEG*2+7)=.4839E11/8.E9
C First capacitance value is CTA in weerappuli model
   C(NSEG*2+2)=.96975E-11*8E9
C Second capacitance value is CTB in weerappuli model
   C(NSEG*2+4)=.17929E-10*8.E9
C
C Calculate initial flow values
C
   RATOT=R(NSEG*2+1)+R(NSEG*2+5)
   RBTOT=R(NSEG*2+3)+R(NSEG*2+7)
   RTOT=1/((1/RATOT)+(1/RBTOT))
   YODD=PAVG/RTOT
   YAODD=YODD*RTOT/RATOT
   YBODD=YODD*RTOT/RBTOT
C
C Assign initial flow values
C

ZEND = NASG*2 - 1
DO 16 I = 1, ZEND, 2
Y(I) = YODD
16 CONTINUE
C

ZBEG = NASG*2 + 1
ZEND = NSEG*2 - 3
DO 17 I = ZBEG, ZEND, 4
Y(I) = YAODD
17 CONTINUE
C

ZBEG = NASG*2 + 3
ZEND = NSEG*2 - 1
DO 18 I = ZBEG, ZEND, 4
Y(I) = YBODD
18 CONTINUE
C

C ASSIGNED FLOW VALUES TO THE WINDKESSELS
C

Y(NSEG*2 + 1) = YAODD
Y(NSEG*2 + 2) = YBODD
C

C ASSIGNING VALUES TO THE RADIUS AT EACH NODE
FLAG=0
DO 15 I=1,NDIM,2
IF (I .GT. (NASG*2)) GO TO 12
RD(I)=ARTRD
GO TO 11
12 IF (FLAG.EQ.1) GO TO 13
RD(I)=B1RD
FLAG=1
GO TO 11
13 RD(I)=B2RD
FLAG=0
11 WRITE(6,14)I,RD(I)
14 FORMAT(5X,'RD(',12/ ) = ' ,F6.5)
15 CONTINUE

C
C ASSIGNING DELTA X VALUES FOR MAIN ARTERY AND BRANCHES
C
Z=NASG*2
DO 100 I=1,Z
DX(I)=DXA
100 CONTINUE

C
ZBEG=NASG*2+1
ZEND=NASG*2+N1SG*2+N2SG*2
FLAG=0
DO 200 I=ZBEG,ZEND
IF (FLAG .EQ. 1) GO TO 201
DX(I)=DX1
FLAG=1
GO TO 200
201 DX(I)=DX2
FLAG=0
200 CONTINUE

C
C CALCULATE RESISTANCES AND IMPEDANCES
C

CALL RADCAL
ZEND=NDIM+5
DO 202 I=1,ZEND,2
WRITE(6,203)I,R(I),L(I)
203 FORMAT(5X,'R(',I 2,') = ',F7.4,5X, ' L=',F7.4)
202 CONTINUE

C
C OPEN OUTPUT FILE AND CALL RKGS SUBROUTINE
C

CALL RKGS(PRMT,Y,DERY,NDIM,IHLF,FCT,OUTP,AUX)
WRITE(6,105)IHLF
105 FORMAT(5X,'IHLF=' ,12)
WRITE(6,106)PTN
106 FORMAT(5X, I 4)
C
C FIND A LOCAL MINIMUM TO BEGIN PI CALCULATIONS
C
RCOUNT=2000
DO 600 I=100,(100+RPD*100)
   IF (PTF(I) .GT. RCOUNT) GO TO 600
   RCOUNT=PTF(I)
   IBEG=I
600 CONTINUE
C
C FIND A LOCAL MINIMUM TO END PI CALCULATIONS
C
RCOUNT=200
DO 650 I=(PTN-(RPD*100)),PTN-5
   IF (PTF(I) .GT. RCOUNT) GO TO 650
   RCOUNT=PTF(I)
   IEND=I
650 CONTINUE
   IF(IEND .LE. IBEG)GO TO 1000
651 RLEN=FLOAT(IEND-IBEG)
C
C ROUTINE TO CALCULATE PI
C
RMIN=200
SUM=0
RMAX=0
RPMX=0
PTN=PTN−1
CT=0
DO 500 I=IBEG,IEND
RMAX=AMAX1(RMAX,PTF(I))
RMIN=AMIN1(RMIN,PTF(I))
RPMX=AMAX1(RPMX,PTP(I))
SUM=SUM+PTF(I)
CT=CT+1
500 CONTINUE
RMEAN=SUM/CT
RPI=(RMAX−RMIN)/RMEAN

WRITE (6,701)RMEAN,RPI,RMAX,RMIN
701 FORMAT(5X,'FLOW=',F5.0,', PI=',F5.2,
* ', RMAX=',F5.0,', RMIN=',F5.0)

FLMIN=0
IF(RMIN .GE. 0)GO TO 702
FLMIN=10*AINT((RMIN-10)/10)
702 FLMX=(AMAX1(RMAX,RPMX))*1.25
TMX=PTX(PTN-1)
XSACLE=TMX/6.
YSSCALE = (FLMX-FLMIN) * 1.2/4.5
CALL GRAPH(0,PTX,PTP,100,4,6.0,4.5,XSCLAE,0.0,YSCLAE,
*FLMIN,'TIME','PRESSURE OR FLOW','
* 'XXXXXXXXXXXXXXXXXXXXXXXX',
CALL GRAPHSP(PTN,PTX,PTP,200,104,'PRESSURE'
CALL GRAPHSP(PTN,PTX,PTF,400,104,'FLOW'

C
WRITE(6,1001)PULS,PULS2
1001 FORMAT(5X,'PULS=',A1,5X,'PULS2=',A1)
C
STOP
1000 IBEG=0
IEND=PTN-2
WRITE(6,1002)
1002 FORMAT(5X,'CALCULATION ERROR-LONGER SAMPLE NEEDED')
GO TO 651
END
C
C
C FUNCTION SUBROUTINE SUPPLIES RKGS WITH DIFF. EQ.'S
C
SUBROUTINE FCT(X,DERY)
DIMENSION AREA(102),DERY(102)
REAL Y,DERY,C,L,R,RD,DX,P,EP,H0,P0,PI,PP,C0,C1,F,
*A,B,PAVG
INTEGER I,ZBEG,ZEND,PTN
COMMON/NONARR/EP,H0,P,P0,PI,NSEG,C0,C1,PAVG,
*TLAST,MU,RHO,FREQ,CU,CV,PTN
*,NBN,NASG/ARRAY/C(102),RD(102),DX(102),R(102),L(102),
*A(9),B(9),Y(102),PTP(1000),PTX(1000),PTF(1000)

C
T=X
F=FREQ*T

C CALCULATING THE PRESSURE INPUT AT TIME=T
C
PP=PAVG+A(1)*COS(F)+B(1)*SIN(F)+A(2)*COS(2*F)+
  B(2)*SIN(2*F)+A(3)*COS(3*F)+B(3)*SIN(3*F)+A(4)*COS(4*F)+
  B(4)*SIN(4*F)+A(5)*
  COS(5*F)+B(5)*SIN(5*F)+A(6)*COS(6*F)+B(6)*SIN(6*F)+
  A(7)*COS(7*F)+B(7)*SIN(7*F)+A(8)*COS(8*F)+B(8)*
  SIN(8*F)+A(9)*COS(9*F)+B(9)*SIN(9*F)

P=PP

C CALCULATING THE C VALUES AT EACH NODE AT TIME=T
C
ZEND=2*NSEG
DO 100 I=2,ZEND,2
\[ \text{AREA}(I) = \pi \times \text{RD}(I-1)^2 \]
\[ \text{C}(I) = \text{AREA}(I) \times \text{DX}(I) \times (\text{C0} + \text{C1} \times (\text{Y}(I) - \text{P0}) \times 133.33275) \times 8E9 \]

100 CONTINUE

C

C SYSTEM OF FIRST ORDER DIFF EQ'S

C

\[ \text{DERY}(1) = \frac{(P - \text{Y}(1) \times \text{R}(1) - \text{Y}(2))}{L(1)} \]
\[ \text{ZEND} = \text{NASG} \times 2 + 1 \]
\[ \text{DO} \ 110 \ I = 3, \text{ZEND}, 2 \]
\[ \text{DERY}(I) = \frac{(\text{Y}(I-1) - \text{Y}(I) \times \text{R}(I) - \text{Y}(I+1))}{L(I)} \]

110 CONTINUE

\[ \text{ZEND} = (\text{NASG} - 1) \times 2 \]
\[ \text{DO} \ 120 \ I = 2, \text{ZEND}, 2 \]
\[ \text{DERY}(I) = \frac{(\text{Y}(I-1) - \text{Y}(I+1))}{\text{C}(I)} \]

120 CONTINUE

\[ \text{DERY}(\text{NBN}) = \frac{(\text{Y}(\text{NBN}-1) - \text{Y}(\text{NBN}+1) - \text{Y}(\text{NBN}+3))}{\text{C}(\text{NBN})} \]
\[ \text{ZBEG} = (\text{NASG} + 1) \times 2 + 1 \]
\[ \text{ZEND} = \text{NSEG} \times 2 - 1 \]
\[ \text{DO} \ 130 \ I = \text{ZBEG}, \text{ZEND}, 2 \]
\[ \text{DERY}(I) = \frac{(\text{Y}(I-3) - \text{R}(I) \times \text{Y}(I) - \text{Y}(I+1))}{L(I)} \]

130 CONTINUE

\[ \text{ZBEG} = (\text{NASG} + 1) \times 2 \]
\[ \text{ZEND} = \text{NSEG} \times 2 - 4 \]
\[ \text{DO} \ 140 \ I = \text{ZBEG}, \text{ZEND}, 2 \]
\[ \text{DERY}(I) = \frac{(\text{Y}(I-1) - \text{Y}(I+3))}{\text{C}(I)} \]
CONTINUE

I = NSEG * 2

C CALCULATING THE DP/DT FOR THE LAST TWO ELEMENTS

\[ \text{DERY}(l-2) = \left( \frac{Y(l-3) - Y(l+1)}{C(l-2)} \right) \]

\[ \text{DERY}(l) = \left( \frac{Y(l-1) - Y(l+2)}{C(l)} \right) \]

C CALCULATING THE DQ/DT FOR THE WINDKESSELS

\[ \text{DERY}(l+1) = \left( \frac{C(l+2) \cdot \text{DERY}(l-2) + Y(l-2) / R(l+5) - (1 + R(l+1)) \cdot Y(l+1)}{C(l+2) \cdot R(l+3)} \right) \]

\[ \text{DERY}(l+2) = \left( \frac{C(l+4) \cdot \text{DERY}(l) + Y(l) / R(l+7) - (1 + R(l+3)) \cdot Y(l+2)}{C(l+4) \cdot R(l+3)} \right) \]

RETURN

END

C

SUBROUTINE OUTP IS AN OUTPUT SUBROUTINE WHICH WRITES
THE VALUES FOR TIME, PRESSURE, AND FLOW (MKS UNITS) TO A FILE

SUBROUTINE OUTP(T,DERY,IHLF,NDIM,PRMT)
DIMENSION DERY(102),PRMT(5)
REAL Y,DERY,T,PRMT,PMMHG,FLOW,EP,H0,RD DX,R,L,PI,PAVG,
*TLAST,F
INTEGER COUNT,CHECK,ZBEG,ZEND,PTN
COMMON/NONARR/EP,H0,P,P0,PI,NSEG,C0,C1,PAVG,
*TLAST,MU,RHO,FREQ,CU,CV,PTN
*,NBN,NASG/ARRAY/C(102),RD(102),DX(102),R(102),L(102),
*A(9), B(9), Y(102), PTP(1000), PTX(1000), PTF(1000)

C

C NO OUTPUT IF INCREMENT IS LESS THAN .05

C

CHECK = INT((T - TLAST) * 100.)

IF (CHECK .LT. 1) GO TO 500

TLAST = T

C

C CALCULATE PRESSURE PRIOR TO OUTPUT

C

F = FREQ * T

PP = PAVG + A(1) * COS(F) + B(1) * SIN(F) + A(2) * COS(2*F) +
B(2) * SIN(2*F)

1 + A(3) * COS(3*F) + B(3) * SIN(3*F) + A(4) * COS(4*F) + B(4) *
1 SIN(4*F) + A(5) *
1 COS(5*F) + B(5) * SIN(5*F) + A(6) * COS(6*F) + B(6) * SIN(6*F)

P = PP

C

WRITE (12, 100) T

100 FORMAT(//, ' TIME=', F3.1)

C

DO 200 COUNT = 1, 12

WRITE (12, 201) Y(COUNT), DERY(COUNT), COUNT

200 CONTINUE

201 FORMAT(5X, F6.1, 5X, E9.3, 5X, I2)
PMMHG = P
FLOW = Y(NBN - 1)
WRITE(13, 401) T, PMMHG, FLOW, Y(1), Y(NBN + 1), Y(NBN + 3), PTN
401 FORMAT(5X, F5.2, F5.1, F5.0, F5.0, F5.0, F5.0, I6)
PTN = PTN + 1
PTF(PTN) = Y(NBN - 1)
PTP(PTN) = P
PTX(PTN) = T
WRITE(13, 401) T, PMMHG, FLOW, Y(1), Y(NBN + 1), Y(NBN + 3), PTN

CALL RADCAL TO UPDATE R AND L BASED ON DIAM.
CHANGES DUE TO PRESSURE CHANGES

CALL RADCAL

500 RETURN
END

SUBROUTINE RKGS(PRMT, Y, DERY, NDIM, IHLF, FCT, OUTP, AUX)

DIMENSION Y(102), DERY(102), AUX(8, 102), A(4), B(4),
*C(4), PRMT(5)
DO 1 I=1,NDIM
1  AUX(8,I)=.06666667*DERY(I)
X=PRMT(1)
XEND=PRMT(2)
H=PRMT(3)
PRMT(5)=0.
CALL FCT(X,DERY)

C
C ERROR TEST
IF(H*(XEND-X))38,37,2

C
PREPARATIONS FOR RUNGE-KUTTA METHOD
2 A(1)=.5
   A(2)=.2928932
   A(3)=1.707107
   A(4)=.1666667
   B(1)=2.
   B(2)=1.
   B(3)=1.
   B(4)=2.
   C(1)=.5
   C(2)=.2928932
   C(3)=1.707107
   C(4)=.5
C
PREPARATIONS OF FIRST RUNGE-KUTTA STEP

DO 3 I=1,NDIM
   AUX(1,I)=Y(I)
   AUX(2,I)=DERY(I)
   AUX(3,I)=0.
3 AUX(6,I)=0.
   IREC=0
   H=H+H
   IHLF=-1
   ISTEP=0
   IEND=0

START OF A RUNGE-KUTTA STEP

4 IF((X+H-XEND)*H)7,6,5
5 H=XEND-X
6 IEND=1

RECORDING OF INITIAL VALUES OF THIS STEP

7 CALL OUTP(X,DERY,IREC,NDIM,PRMT)
   IF(PRMT(5))40,8,40
8 ITEST=0
9 ISTEP=ISTEP+1
C START OF INNERMOST RUNGE-KUTTA LOOP

J=1

10 AJ=A(J)
    BJ=B(J)
    CJ=C(J)
    DO 11 I=1,NDIM
        R1=H*DERY(I)
        R2=AJ*(R1-BJ*AUX(6,I))
        Y(I)=Y(I)+R2
        R2=R2+R2+R2

11 AUX(6,I)=AUX(6,I)+R2-CJ*R1
    IF(J-4)12,15,15
12 J=J+1
    IF(J-3)13,14,13
13 X=X+.5*H
14 CALL FCT(X,DERY)

    GOTO 10

C END OF INNERMOST RUNGE-KUTTA LOOP
C
C
C TEST OF ACCURACY

15 IF(ITEST)16,16,20
C
C IN CASE ITEST=0 THERE IS NO POSSIBILITY FOR TESTING
C OF ACCURACY
164

16 DO 17 I=1,NDIM
17 AUX(4,I)=Y(I)

ITEST=1
ISTEP=ISTEP+ISTEP-2
18 IHLF=IHLF+1

X=X-H
H=.5*H

DO 19 I=1,NDIM

Y(I)=AUX(1,I)
DERY(I)=AUX(2,I)
19 AUX(6,I)=AUX(3,I)
GOTO 9

C

C IN CASE ITEST=1 TESTING OF ACCURACY IS POSSIBLE

20 IMOD=ISTEP/2

IF(ISTEP-IMOD-IMOD)21,23,21
21 CALL FCT(X,DERY)

DO 22 I=1,NDIM

AUX(5,I)=Y(I)
22 AUX(7,I)=DERY(I)
GOTO 9

C

C COMPUTATION OF TEST VALUE DELT

23 DELT=0.

DO 24 I=1,NDIM
DELT=DELT+AUX(8,I)*ABS(AUX(4,I)-Y(I))
IF(DELT-PRMT(4))=28,28,25

ERROR IS TOO GREAT

IF(IHLF-IO)=26,36,36
DO 27 I=1,NDIM
AUX(4,I)=AUX(5,I)
ISTEP=ISTEP+ISTEP-4
X=X-H
IEND=0
GOTO 18

RESULT VALUES ARE GOOD

CALL FCT(X,DERY)
DO 29 I=1,NDIM
AUX(1,I)=Y(I)
AUX(2,I)=DERY(I)
AUX(3,I)=AUX(6,I)
Y(I)=AUX(5,I)

DERY(I)=AUX(7,I)
CALL OUTP(X-H,Y,DERY,IHLF,NDIM,PRMT)
IF(PRMT(5))=40,30,40
DO 31 I=1,NDIM
Y(I)=AUX(1,I)

DERY(I)=AUX(2,I)
IREC=IHLF
IF(IEND)32,32,39

C
C INCREMENT GETS DOUBLED
32 IHLF=IHLF-1
ISTEP=ISTEP/2
H=H+H
IF(IHLF)4,33,33

33 IMOD=ISTEP/2
IF(ISTEP-IMOD-IMOD)4,34,4
34 IF(DELT-.02*PRMT(4))35,35,4
35 IHLF=IHLF-1
ISTEP=ISTEP/2
H=H+H
GOTO 4

C
C
C RETURNS TO CALLING PROGRAM
36 IHLF=11
CALL FCT(X,DERY)
GOTO 39
37 IHLF=12
GOTO 39
38 IHLF=13
39 CALL OUTP(X,DERY,IHLF,NDIM,PRMT)
SUBROUTINE RADCAL CALCULATES NEW RADIUS BASED ON PRESSURE AND RECALCULATES NEW RESISTANCE AND INDUCTANCE BASED ON THE NEW RADIUS

SUBROUTINE RADCAL
REAL PI, PO, P, MU, H0, RHO, L
INTEGER PTN
COMMON/NONARR/EP, H0, P, PO, PI, NSEG, C0, C1, PAVG,
*TLAST, MU, RHO, FREQ, CU, CV, PTN
*, NBN, NASG/ARRAY/C(102), RD(102), DX(102), R(102), L(102),
*A(9), B(9), Y(102), PTP(1000), PTX(1000), PTF(1000)
DO 400 I = 1, NSEG
J = 2*I - 1
DUMMY = RD(J)
IF (Y(J+1) .GT. P0) GO TO 401
RDS = RD(J)
GO TO 402

401 TMPRDS = (DUMMY**2*(1+C0*(Y(J+1)-P0)*133.33275**2))
RDS = SQRT(TMPRDS)

402 R(J) = (8*MU*DX(J))/(PI*RDS**4)*CV/8E9
L(J) = (RHO*DX(J))/(PI*RDS**2)*CU/8E9
FORMAT(5X,F10.5,5X,I2,5X,F10.5,5X,F10.5)

IF (IWRFLG .EQ. 1) GO TO 400

IWRFLG=1

WRITE(6,302) RD(J),TMPRDS,RDS,DX(J),MU,RHO,I,J

FORMAT(5X,'RADIUS(J)=',F6.4,5X,F6.4,5X,F6.4,5X,F6.4,5X,F6.4,5X,
*F6.4,5X,F6.0,5X,I2,5X,I2)

WRITE(6,301) J,R(J),J,L(J)

FORMAT(5X,'R(',I 2,' ) = ',F10.5,5X,'L(',I 2,') = ',F10.5)

400 CONTINUE

RETURN

END

C

C BLOCK DATA SUBPROGRAM LOADS DATA BEFORE RUNNING PROGRAM

C

BLOCK DATA

REAL P,PO,PI,PAVG,L,H0

COMMON/NONARR/EP,H0,P,PO,PI,NSEG,C0,C1,PAVG,
*TLAST,MU,RHO,FREQ,CU,CV,PTN

*,NBN,NASG/ARRAY/C(102),RD(102),DX(102),R(102),L(102),
*A(9),B(9),Y(102),PTP(1000),PTX(1000),PTF(1000)

DATA A(1),A(2),A(3),A(4),A(5),A(6),A(7),A(8),A(9)
1 /-.75414E1,-.10111E2,-.24613E1,-.25764E1,-.97766,
1-.51752,-.44626,-.2245,-.43793E-1/

DATA B(1),B(2),B(3),B(4),B(5),B(6),B(7),B(8),B(9)
1 /.25099E2,-.91876,-.33086E-1,-.58053,-.11198E1,
169

l-.42133,-.42803,-.49926,-.42279/

END

//GO.FT13F001 DD DSNAME=L.I3821.ARTDAT,
// DISP=(NEW,CATLG),UNIT=DISK,SPACE=(6200,(3,3),RLSE),
// DCB=(RECFM=FB,LRECL=50,BLKSIZE=6233)
//GO.FT12F001 DD DSNAME=L.I3821.RDATDAT,
// DISP=(NEW,CATLG),UNIT=DISK,SPACE=(6200,(15,3),RLSE),
// DCB=(RECFM=FB,LRECL=50,BLKSIZE=6233)
//GO.FT14F001 DD DSN=&SM,DISP=(NEW,PASS),UNIT=SCRTCH,
// SPACE=(6233,(120,15),RLSE),DCB=(RECFM=VBS,
// LRECL=6229,BLKSIZE=6233)
//SMPLTTR EXEC PLOT,PLOTTER=INCRMNTL