AN ANALYSIS OF PRESSURE ENERGY HARMONIC PROPAGATION IN THE
ARTERIAL SYSTEM BY A DIGITAL COMPUTER
Fourier Technique

Dissertation

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Robert Lucas Farrow, B.S., M.S.
The Ohio State University
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Approved by

Ralph W. Stacy
Advisor
Department of Physiology
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## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td><strong>Survey of the Literature</strong></td>
<td></td>
</tr>
<tr>
<td>A. Early Theoretical Studies</td>
<td>5</td>
</tr>
<tr>
<td>B. Recent Theoretical Studies</td>
<td>9</td>
</tr>
<tr>
<td>C. Periodic Nature of the Circulation</td>
<td>14</td>
</tr>
<tr>
<td>D. Physical Analysis</td>
<td>16</td>
</tr>
<tr>
<td><strong>Methods and Procedures</strong></td>
<td></td>
</tr>
<tr>
<td>A. General Approach</td>
<td>23</td>
</tr>
<tr>
<td>B. Animal Preparation</td>
<td>25</td>
</tr>
<tr>
<td>C. Instrumentation</td>
<td>26</td>
</tr>
<tr>
<td>D. Analytical Procedures</td>
<td>28</td>
</tr>
<tr>
<td>E. Experimental Procedures</td>
<td>34</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td>37</td>
</tr>
<tr>
<td><strong>Discussion</strong></td>
<td></td>
</tr>
<tr>
<td>A. Fourier Analysis</td>
<td>44</td>
</tr>
<tr>
<td>B. Periodic Forcing and Genesis of Harmonics</td>
<td>46</td>
</tr>
<tr>
<td>C. Harmonic Content of Arterial Pulses</td>
<td>48</td>
</tr>
<tr>
<td>D. Addition of Reflected Waves</td>
<td>51</td>
</tr>
<tr>
<td>E. Apparent Phase Velocity and Reflection</td>
<td>52</td>
</tr>
<tr>
<td>F. Physiological Significance of Results</td>
<td>63</td>
</tr>
<tr>
<td><strong>Summary and Conclusions</strong></td>
<td>74</td>
</tr>
<tr>
<td><strong>Figure</strong></td>
<td>76</td>
</tr>
<tr>
<td><strong>Tables</strong></td>
<td>77</td>
</tr>
<tr>
<td><strong>Autobiography</strong></td>
<td>91</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>76</td>
</tr>
</tbody>
</table>

1. Typical Record of Aortic Pulses
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>Numerical Method for Fourier Analysis Using 24 Ordinates</td>
</tr>
<tr>
<td>II.</td>
<td>Flow Diagram of IBM 650 Program to Calculate Fourier Analysis and Apparent Phase Velocity</td>
</tr>
<tr>
<td>III.</td>
<td>Percent Contribution of the Modulus of Each Harmonic from the Average of 343 Pulse Pairs</td>
</tr>
<tr>
<td>IV.</td>
<td>Modulus and Phase Angle of the First Eleven Harmonics - Average for 343 Pulses</td>
</tr>
<tr>
<td>V.</td>
<td>Average Values of the Apparent Phase Velocity Calculated for the First Six Harmonics in a Series of 343 Pulse Pairs</td>
</tr>
<tr>
<td>VI.</td>
<td>Average Values for the Modulus and Phase Angle of Pressure Gradient Calculated for 343 Pulses</td>
</tr>
<tr>
<td>VII.</td>
<td>A Comparison Between the Effects of Nor-Epinephrine, Acetylcholine, Bilateral Femoral Occlusion and 43 Control Pulses</td>
</tr>
<tr>
<td>VIII.</td>
<td>Comparison Between the Mean Pressure and Apparent Phase Velocity Averaged over Intervals in a Series of 343 Pulse Pairs</td>
</tr>
<tr>
<td>IX.</td>
<td>Comparison Between Apparent Phase Velocity of the Fundamental and Pulse Wave Velocity as Measured from the Pulse Wave Foot</td>
</tr>
</tbody>
</table>
INTRODUCTION

With the evolution of animals and the specialization of cells, a system was required to bring nutrients and oxygen to the cells no longer exposed to the nutrient bearing environment. At the same time it also became necessary to dissipate the waste products of cellular metabolism.

The circulatory system of animals consisting of the heart, blood and blood vessels is a system that subserves the above functions. In this system, the heart functions as a pump which periodically propels the nutrient and oxygen carrying blood through a network of closed tubes called arteries and veins.

The exchange of nutrients takes place across the thin walls of the capillaries that are interposed between the arteries carrying the blood from the heart and the veins returning the blood to the heart. The total number of capillaries in medium sized mammals has been estimated to be about 1,200,000,000.\(^1\) The energy required for the hydrostatic filtration process that takes place at the proximal end of the capillaries is derived from the heart.

In order to understand the transfer of energy from the heart to the periphery of the circulatory system it is necessary to study the hydrodynamics and transmission characteristics of the system.

The heart, as the prime mover of the blood, functions by periodically forcing a quantity of blood (known as the stroke volume) from the low pressure pulmonary circuit into the high pressure systemic circulation, by alternately contracting and relaxing. In this manner it imparts both kinetic and potential energy to the blood. The kinetic fraction of the energy is expressed by the product of the mass of the blood ejected by the heart times the velocity it is accelerated squared. The potential energy fraction of the blood is expressed by the product of the mass of the blood and the pressure to which is raised in the artery.

The movement of the blood down a vessel results from the blood passing from a region of relative high pressure to one of a lower pressure. Thus, the measurement of the pressure gradient between two points in the system gives some information concerning the driving forces involved in the movement of the blood.

In any system transmitting energy where there is a discontinuity in the characteristics of the transmitting medium, a certain portion of the transmitted energy will be reflected back. This is analogous to the reflected sound or echo in the mountains resulting from the interposition of a mountainside of different transmission characteristic than that of the transmitting medium, or air. Similarly in telegraphic lines or radio frequency couplings between the transmitter and antenna, where the terminating impedance is differ-
ent from the characteristic impedance of the line, some of the energy will be reflected back toward the source or input end of the line. If a transmission line is sufficiently long or the transmitted frequency sufficiently high, a standing wave will be produced where the reflected component adds in phase to the transmitted wave. An anti-node is also produced under similar circumstances when the reflected component adds to the transmitted wave out of phase.

It is therefore of interest to examine the arterial system from the viewpoint of determining whether a reflected component of the arterial pulse appears and if so, whether it is possible to change the amount and phase of the reflected energy by changing the terminal impedance of the system. Since the driving action of the heart is periodic, it is possible to treat the pressure pulses by Fourier analysis, breaking them into their harmonic constituents and a constant or D.C. term. Thus, if one makes pressure tracings at two separate points in the descending aorta, it is possible to analyze both pulses simultaneously and calculate the velocity for each harmonic component. If when doing this one causes the terminal impedance to change by either dilating or constricting the terminal arterioles, it should be possible to detect changes in each harmonic velocity resulting from changes in the amount and phase of energy reflected back from the
periphery of the arterial system. From this information it should be possible to make some deductions concerning reflection and its effect upon the contour and magnitude of the pressure pulse as it travels down the arterial tree.
A. Early Theoretical Studies

As early as 1808, Young\textsuperscript{1} published an equation in which he expressed the transmission of pulses in a distensible fluid filled system with added mass. He gave the velocity of wave propagation as

\begin{equation}
\frac{\partial^2 \xi}{\partial t^2} = \frac{Ee_0}{\rho r'} \frac{\partial^2 \xi}{\partial Z^2}
\end{equation}

where $E$ is the modulus of elasticity of the wall, $e_0$ is the thickness of the wall, $r'$ is the internal radius of the tube, $\xi$ is the radial displacement of the wall, $Z$ is the axial distance, and $\rho$ is the density of the fluid. This equation is known as the Young-Korteweg equation, since some 70 years later Korteweg published an equation which was the exact equivalent of Young's. The coefficient of the right hand side of equation (1) is equal to the square of the wave velocity.

Apparently the first published reference to the pulse wave velocity was made by Weber\textsuperscript{2} in 1834. From his observations he estimated the pulse wave velocity to be about 94.2 cm/sec between the temporal and dorsal pedis artery.

The first published theoretical observations upon

\textsuperscript{1}T. Young, "Hydraulic Investigations," Phil. Trans., London, 1: 164, 1808.

the transmission of the pulse was made by Resal\textsuperscript{1} who made a computation of the wave velocity. Based upon these observations Moens\textsuperscript{2} in 1878 proposed an equation expressing the pulse wave velocity by using a dimensionless, empirical constant to modify the Young-Korteweg expression:

\[ v = K \sqrt{\frac{E_0 e_0}{2pr^2}} \]  \hspace{1cm} (2)

This relationship makes certain tacit assumption; namely, that the wall material exhibits a linear elasticity and that the wall thickness does not change. If a correction is made to take this into account the Moens equation will yield a value for the velocity that is higher than the Young-Korteweg expression.

Late in the last decade of the nineteenth century Frank\textsuperscript{3} proposed the "Windkessel" theory to explain the contour of the pressure pulse. He defined the energy storage capacity of the arterial system in terms of a "volume elastic modulus," \( k \), defined by the following equation:

\[ k = \frac{dP}{dV} \cdot V \hspace{1cm} (3) \]

\begin{flushright}
\textsuperscript{2}A. I. Moens, Die Pulskurve, Leiden, E. J. Brill, p. 90, 1878.
\end{flushright}
in which \( P \) is the pressure and \( V \) is the volume. The volume-elastic modulus is then related to the density of the blood \( \rho \) and the pulse wave velocity \( C \) in the following manner:

\[
k = \rho C^2; \quad C = \frac{k}{\rho}
\]

In the case of a cylindrical tube with a volume \( V = Q1 \), Frank defines the coefficient of elasticity \( E' \) as

\[
E' = \frac{dP}{dV} = \frac{k}{V} = \frac{\rho C^2}{Q1}
\]

The pressure gradient is then related to the viscosity and distensibility of the system by the equation:

\[
\frac{dP}{dZ} = -\rho \cdot \frac{dV}{dt}
\]

and the course of the pressure is related to the elasticity and distensability by the equation:

\[
\frac{dP}{dt} = -k \frac{dV}{dZ}
\]

From the foregoing he then derived the so-called wave motion as

\[
\frac{dP}{dt} = -C \frac{dP}{dZ}; \quad \frac{dV}{dt} = -C \frac{dV}{dZ},
\]

in which the proportionality factor is the pulse wave velocity.

In 1922, Bramwell and Hill\(^1\) decided to examine the

Moens equation. In order to slow the wave velocity and verify this relationship with accuracy, they decided to use mercury with a density of 13.4 times that of water (i.e., blood). They were able to simplify the equation to

\[ \text{PWV} = 0.357 \sqrt{\frac{dP}{dV}} \cdot V, \quad (4) \]

where \( V \) is the volume of the artery.

It is evident from the Bramwell-Hill velocity equation that the velocity will be proportional to the square root of the rigidity of the artery.

One of the first studies involving the transmission of energy in elastic tubes was made by Lamb\(^1\) in 1898. From his observations of sound in rigid tubes and water in rubber tubes he derived a "frequency equation" for the velocity in terms of the tube dimensions and the elastic constants of the tube wall. It was shown that when the wavelength was long as compared with the circumference of the tube, the velocity of propagation will be independent of frequency. This then describes the case of an incompressible, inviscous fluid (i.e., an ideal fluid). The velocity obtained in a water filled india rubber tube was found to have the same value as that calculated by Resal.\(^2\)

\(^1\)H. Lamb, "On the Velocity of Sound in an Elastic Tube as Influenced by the Elasticity of the Walls," Mem. Manchester Lit. and Phil. Soc., 42; Number 9, 1898.

\(^2\)Resal, loc. cit.
B. Recent Theoretical Studies

The modern concepts of the transmission of pulse waves date from the work of Witzig\(^1\) published in 1914. In this paper Witzig derives an approximate solution for the equations of a viscous fluid motion while he neglected the non-linear terms. In addition he deduced a frequency equation from which he was able to derive the wave velocity in terms of the thickness and radius of the tube, its elastic constants, the viscosity of the fluid and the frequency of the waves. However, Witzig neglected to take into account the vibrations of the wall of the tube, and the forces applied to the wall from the traction of the pulsatile flow of the fluid within and the inertial terms of the fluid flow.

Recently, Branson\(^2\) has been able to show mathematically that the classical equations for viscous flow can describe blood flow in the femoral artery. By assuming the non-viscous case he derives Moens equation for the pulse wave velocity in terms of the density and elasticity of the arterial system.

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Karreman\(^1\) has derived the relation between the propagation velocity and the geometrical and elastic properties of a branched tube. In this, he assumes the walls of the tube to exhibit Hookean behavior (which is not the case\(^2\)) and the fluid to be incompressible. If \(D\) is the wall thickness, \(E\) the modulus of elasticity, \(r\) the radius of the tube and \(p\) the fluid density, the velocity is:

\[
c = \sqrt[4]{\frac{DE}{2rp}}
\]  

(5)

This equation is a special case used for the propagation of pressure waves in the theory of the water-hammer phenomenon— that is, for an incompressible fluid. The general case was derived for the first time by Korteweg\(^3\) in 1878.

By extending Witzig's\(^4\) analysis of an unbranched tube in order to take into account of its flexural rigidity Karreman gives an approximation for the pulse wave velocity in

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\(^4\)Witzig, op. cit.
terms of kinematic viscosity and frequency. The real part of the velocity is given as

\[ \text{Re} \left[ c \right] = \left( \frac{Eh}{\sqrt{R\rho}} \right) \left( 0.8 - 0.03R \right) \sqrt{\frac{\omega}{\gamma}} \]  

(6)

In this case, \( \gamma \) is the kinematic viscosity \( \mu/\rho \), where \( \rho \) is the density, \( E \) the elastic modulus, \( R \) the radius, and \( h \) the wall thickness. This equation differs only slightly from equation (5) in that the numerical coefficient in front of the square root is different.

In a later publication, Karreman\(^1\) derived the reflection characteristics of a tube with a local constriction based upon the continuity of pressure and mass flow on both sides of the constriction. He concluded that the wave velocity is proportional to the square root of the radius. In Karreman\(^2\)'s third paper of the series, he calculates the reflection coefficient for a branched tube of changing areas. He concludes that the amplitude of the reflected component in physiological branching may be about 4 percent or less of the amplitude of the initial wave and therefore may not be detectable.

The most recent and complete mathematical treatment

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of pressure and flow in elastic tubes is that given by Womersley. 

In this unified theory he develops a very important non-dimensional parameter that characterizes the motion of the fluid:

\[ a = R \sqrt{\frac{n}{v}}, \]

where \( R \) is the radius of the tube, \( n \) is the circular frequency (i.e., the frequency in cycles per second multiplied by \( 2\pi \)), and \( v \) is the kinematic viscosity of the liquid.

Whereas the previously cited workers have obtained solutions for very large and very small diameters, and therefore either extreme in magnitude of \( a \), Womersley has given most of his attention to the solution of his theory in the range likely to be encountered in a biological system.

This is the first time any one worker has unified the relationships between the velocity of wave propagation, the pressure-flow for the motion of the liquid, and the pressure-diameter relationship.


\[ 2 \] J. R. Womersley, "Method for the Calculation of Velocity, Rate of Flow and Viscous Drag in Arteries when the Pressure Gradient is known," ibid., 127: 553, 1955.

Since the pressure pulses in the arterial side of the circulation are periodic in nature it is possible to describe the pressure pulse in terms of a Fourier series. Thus, Womersley\(^1\) is able to describe the velocity of each harmonic component of the pulse wave by expressing it in terms of the harmonics of the pulse wave and the harmonics of the pressure gradient in the presence of a reflected wave.

From the experimental data of McDonald\(^2\) he has calculated the oscillatory flow and the reflection coefficient in modulus and phase in the femoral artery of the dog by using the pressure gradient.

However, Womersley\(^3\) has pointed out that if reflections are present, the calculation of phase velocity leads to an "apparent phase velocity." The magnitude of the apparent phase velocity then depends upon the magnitude and phase of the reflected harmonic. In addition, he mentions that in order to calculate the reflection coefficient it is necessary to take into account the complex damping of both the transmitted and reflected components. He did not include these in the mathematical descriptions in the work cited.

\(^1\)J. R. Womersley, ibid.


\(^3\)J. R. Womersley, Personal Communication, 1958.
C. The Periodic Nature of the Circulation

A general review of the theories of pulsatile flow and pressure of the circulatory system based upon physical models of elastic systems is given by Aperia\(^1\) and Wetterer.\(^2\) The former has a discussion of both the physics and mathematics of vibration, acoustics and hydrodynamic studies.

It has previously been shown\(^3\) that many biological systems exhibit rhythmic or periodic behavior. This type of activity is therefore amenable to Fourier analysis. Such analysis will then reveal the periods or frequencies of the perturbing influences. For example, it becomes possible to separate a diurnal cycle and lunar cycle which interact to change the skin coloring of certain marine animals. These problems are extensively reviewed by Kleitman.\(^4\)

As late as 1940, Broemser\(^5\), by means of Fourier analysis described a method for the calculation of the fundamental


\(^{2}\)E. Wetterer, "Die Wirkung der Herztätigkeit auf die Dynamik des Arteriensystems," Verh. Dtsch. Ges. f. Krieslauf-

\(^{3}\)P. Broemser, Die Bedeutung der Lehre von der erzwungenen Schwingungen In der Physiologie: München, 1918.


period of oscillation of blood produced by its mass and inertial resistance, the elasticity of the arterial system and the peripheral resistance of the circulatory bed. Essentially he used simultaneously recorded central and peripheral pressure pulses. He subjected the resulting Fourier analyses of the pulses to theoretical treatment in terms of Frank's "Windkessel" theory and found the fundamental frequency of the oscillating blood column which he converted into the reciprocal time period.

Other workers have also applied Fourier analysis to the cardiovascular system. Porje used Fourier analysis on sphygmograms from intact human subjects in an experimental study of isthmus stenosis (coarctation) to determine its effect upon the pressure pulse form. Ranke has applied this type of analysis to pressure pulses to find damping coefficients in the arterial system. Müller using the same methods has extended Ranke's work and has shown the artery to have a damping coefficient that is very highly frequency dependent. This entire field of the periodic nature of the cardiovascular system has recently been extensively reviewed by Wetterer.

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4. E. Wetterer, loc. cit.
D. Physical Analysis

It is fruitful to treat the arterial system by analogy with physical transmission systems such as a telegraph line.

Theoretically, if a line has no resistance, no leakage, and no loss of energy through radiation, the successive periodic conversions of energy would occur with no dissipative loss and the energy would be divided, at any instant of time, and at any point along the line, between the two fields. For a given frequency the wave-length constant will be fixed and the velocity of propagation will be equal to that of light. The current and voltage will then be distributed in time and space, in which case each is called a standing wave. The standing wave may be defined as waves in which all of the energy is reactive in character, that is, the energy is stored in the line. At any point along the line where the voltage is at a maximum, the current and its associated magnetic field will be zero. The converse is also true, so the relationship between the current and voltage is 90°.

If we now consider a line of finite length loaded at its end with any definite impedance, we find that the energy wave upon reaching the end of the line experiences either a

1A. Aperia, loc. cit.

total or partial arrest. This results in a partial or complete reversal of energy transfer called reflection. The exception to this condition is the case where the terminating impedance of the line is equal to that of the characteristic impedance of the line. In this case the line acts as an infinite line and the energy is transferred into the load with no losses, that is, with no reflection of energy.

The two boundary conditions are those of an open circuited and short circuited line. In the former case, the current at the remote terminus of the line is zero but maximal at the entrance and the voltage is maximal but minimal at the entrance. The magnetic field associated with the current is not dissipated but converted to a voltage. This results in an increase in potential at the line termination which is higher than the point immediately preceding it causing a reversed displacement. The reversed displacement of energy is then the reflected component of the energy. In the case of the short circuited line, the current flow will be maximal and the voltage minimal. The high current flow with its associated magnetic field produces a potential at a point in the line immediately preceding the termination. This results again in a reversal of electric displacement and a transfer of energy in the reverse direction.

It now can be readily seen that when a transmission line is not optimally loaded the energy transfer into the
load is inefficient and a part of the transmitted energy will be reflected back along the line.

When certain parameters of a line are known it becomes possible to calculate the reflection coefficient in modulus and phase form. The magnitude of the modulus of the reflection coefficient varies from zero (no reflection) to 1.0 (complete reflection). The phase of the reflection coefficient can vary from zero degrees (no phase shift) to 180° (complete reversal of reflected wave).

In complex systems it may be too difficult to measure the parameters required for the calculation of the reflection coefficient. Therefore, in order to determine the efficiency of energy transfer from the transmission line to the terminal load, especially in ultra high frequency applications, the voltage standing wave ratio (VSWR) is measured. This is the ratio of the voltage value measured at antinodes to that measured at the nodes (i.e., the ratio of maximum to minimum values obtaining along the line). As the VSWR increases from a value of one, the energy transfer is less optimal and the magnitude of the reflected component is greater. In the cardiovascular system the analogous measurement would be the pressure standing wave ratio (PSWR).¹

The behavior of simple physical systems analogous to arterial transmission have been studied by several investigators.

¹Womersley, ibid.
The first of these is Jochim.\textsuperscript{1,2} In these studies the effects of injections of epinephrine and histamine on the contour and time relationship of the pressure and flow curves were made. He then excited an electrical network consisting of a shunt capacitor representing arterial compliance, a series resistance representing the resistance to flow and an inductance representing the blood mass. When this network was pulsed with half-sine waves corresponding the cardiac ejection pulses, similar relationships between the analog and the circulatory system were noted. With the inductance in the network, the current peaks either preceded or followed the voltage peaks, depending upon the relative values of the parameters. In the dog a similar phenomenon was observed when the peripheral vascular resistance was changed by the injection of epinephrine or histamine. When the latter was injected, the flow peak was delayed so that in some cases it actually followed the pressure peak. When the resistance of the electrical network was lowered the analogous phenomenon was observed.

Taylor\textsuperscript{3} has recently (1957) examined the nature of the arterial system by analogy using telegraph equations applied to


\textsuperscript{2}Jochim, \textit{ibid}, 8: 82, 1949.

\textsuperscript{3}Taylor, \textit{op. cit.}
an attenuating line. From this study he derives the apparent phase velocity over a finite interval of a line and the modulus of the reflection coefficient in terms of the apparent phase velocity as a function of distance from the closed end.

In another paper, Taylor examined the frequency response characteristics of a water filled rubber tube. By using a mechanical relay resolver he was able to obtain the sine and cosine terms of the pressure oscillations in the tube. From these measurements the input impedance of an occluded tube was calculated as a function of its length from 4-12 cycles per second. True standing waves were not present in the tube, although the pressure moduli exhibited minima. The phase velocity of the occluded tube varied above and below the value found for the un-occluded tube. Near the origin the apparent phase velocity was about 30 percent above or below the un-occluded value. However, as the measurements were taken more closely to the terminal end of the tube, the apparent phase velocity deviated by more than 300 percent of the unoccluded value.

The large deviation in this simple case is of course the result of the addition of the reflected component and is the analogous situation that one would expect to find in the aorta for the very same reasons.

In physical vibration studies the forcing of the system may not be truly sinusoidal. However, non-sinusoidal

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1M. G. Taylor, ibid., II. Fluid Oscillations in an Elastic Pipe, In Press.
forces which are periodic may be expressed as a series of sinusoidal forces with a harmonic relationship by Fourier analysis. The response of the system may also be analyzed by the same procedure provided the superposition theory holds. Manley\(^1\) has stated that the impedance offered to forcing at the frequency of each harmonic has a magnitude equal to the ratio between the magnitude of the forcing component and the magnitude of the system response at each frequency.

By using Fourier analysis, Broemser\(^2\) has studied the characteristics of the aorta by calculating the Fourier harmonic series components of the central and peripheral pulses. A comparison of their relative amplitudes revealed the nature of the system damping of the central pulse. He concludes that the damping is predominantly viscous.

Peterson\(^3\) has also examined the nature of the aorta by transient analysis. With the aid of a mechanical injector he was able to inject known volumes of fluid into the aorta with reproducible force patterns. From these studies he concluded that the vascular pulse pressure is influenced by the effective arterial mass, viscous friction and distensibility all of which are non-linear.


\(^2\)Loc. cit.

In order to study the harmonic content of the pressure pulses in the cardiovascular system, the fidelity of the reproduction of the pulses is of first order importance. The recent development of pressure analog devices of inherent high frequency response and extremely low mass displacement insures that this first criterion will be met. The use of extremely linear strain-gage amplifiers and high frequency response recording optical galvanometers permits the accuracy of the analysis of the pulse to be as reliable as the physical measurement of the height of the recorded pulse can be made.

It can therefore be appreciated that the limiting factor in the harmonic analysis of the pulse is not in the transducer and associated recording devices, but rather is a result of the error in estimating the fractional part of a millimeter in measuring the height of the pulse above zero pressure.
METHODS AND PROCEDURES

A. General Approach

The problem of interest in these studies was to examine the transmission of pulse wave in the abdominal aorta. No attempt has been made to evaluate the physical factors involved in this system, nor was it possible to calculate the reflection coefficient. The reasons for this are given in detail later.

The method of approach was to utilize the regular periodic cardiac ejections of blood as the forcing element. As has been pointed out previously, as this pressure wave reaches discontinuities of the aorta such as the major branches, a certain amount of the energy will be reflected back up the aorta toward the heart. In addition, there can also be other reflections from the more peripheral portions of the vascular system. Depending upon the state of the peripheral vessels at any one instant, the reflected wave will add into the transmitted wave, and depending upon its phase and distance from the point of reflection, each harmonic will either advance or retard the phase of the corresponding harmonic in the transmitted wave in a linear system.

The complicating factor is that the reflected wave will appear in the pulse as recorded toward the heart and also in a different phase in the same pulse as recorded a short distance below this point. However, because of damping of the reflected wave during its retrograde travel, the magnitude that appears in the lower pulse recording will be greater.
At the same time if the reflected wave adds vectorially one should expect to find the lower recorded pulse "sharpened" as one finds in comparing aortic pulses to those recorded, for example, in the lower femoral artery.

By recording the pressure pulses from two rather close locations in the abdominal aorta, it will be possible to measure the phase velocity of each harmonic over this known interval. In addition, by subtracting the lower pulse from the upper pulse, one obtains the pressure gradient which is the driving force over the interval between the two recording sites along the aorta. This distance was measured at the end of the experiment during post mortem examinations.

Since the waveform of the pressure pulse was determined by the animal's own heart rate and stroke volume and rate of ejection, a series of pulses were not uniformly identical one with each other but showed slight irregularities. The pulse, however, should be rich in harmonic content. Because it is possible to analyze the pressure waveform of just one cardiac cycle into its harmonic sinusoidal components, one may therefore obtain the frequency spectrum of this waveform at two separated sites along the aorta and the frequency spectrum of the pressure gradient.

By altering the peripheral resistance of the terminal vascular bed, it follows that the magnitude and phase of the energy reflected back into the aorta will be altered. In this manner the influence of reflection upon the harmonic content
and phase velocity of the aortic pulse can be detected. The greatest disadvantage is that the fundamental frequency is limited to that of the heart rate of the animal.

B. Animal Preparation

Mongrel male and female dogs ranging from 18 to 25 kg body weight were given, by vein, a general anesthetic in the amount of 30 mg of veterinary pentobarbital sodium (Nembutal, Abbott Laboratories, Chicago, Illinois) per kilogram of total body weight. The trachea was exposed and cannulated. The left carotid artery was also exposed and cannulated with a 15 cm, size 11 urethral cannula. The tip of this cannula was advanced to the point where the carotid artery joined the aortic arch. This was accomplished by advancing the cannula until it touched the opposite wall of the aorta and then withdrawing it one-half an inch. The purpose of this was to insure that all of the injected materials entered the arterial blood stream. Heparin sodium (in a dose of 30 mg) was given each animal to retard blood clotting. In addition, Heparin in the amount of 5 units/cc was added to Ringer's solution used to fill the pressure transducers and associated cannulae to prevent occlusion due to clot formation in the lumen of the cannulae.

The left renal artery and the inferior mesenteric artery were then exposed by an abdominal incision and cannulated with metal cannula, each made from an 18 gauge, 3 inch hypodermic needle. Both needles were cut flat on the ends to the
same exact length to cancel any distortion of the pressure wave they might introduce. The tip of each cannula was carefully advanced until it reached, but did not protrude into, the aorta as determined by palpation of the tips.

Before and after each experiment the pressure transducer (Statham type P-23-D) were calibrated with a mercury manometer, extreme care being exercised to insure that (a) both transducers gave a linear output over the pressure range of 15 to 230 mm Hg, (b) the output of each transducer corresponded to 5 mm galvanometer deflection for every 10 mm Hg pressure and (c) the light spots from each galvanometer were superimposed one upon the other at the plane of the photographic recording paper over the pressure ranges stipulated above. This last provision assumed great importance since the pressure gradient was to be determined and a large error would be incurred if equivalent blood pressures did not correspond to the same vertical height on the recording. This last step would not be necessary if the Fourier analysis were to be performed only on the two pulse tracings, since a constant shift in the zero base line would only increase or decrease the constant (or so-called D.C.) term of the series leaving the oscillatory terms unaltered.

C. Instrumentation

The blood pressure measurements were made with a pair of Statham P-23-D pressure transducers. Initially both transducers were checked for relative phase shift by attaching two
carefully matched cannulae to them and displaying the output of one transducer on the Y-axis of an oscilloscope and the other on the X-axis. With a set of perfectly matched cannulae there was no detectable phase difference between the two transducers up to 30 cps.

Initially it was thought that polyethylene tubing would serve as a cannula; however, it was found that the slight distensibility of the tube walls and the fact that the pressure pulses tended to straighten the slight curvature in the tubing produced very pronounced transient spikes in the recorded pulses. In addition, it was very difficult to flush minute bubbles from the tubing since they adhered tenaciously to the inner wall of the polyethylene. Therefore, rigid cannulae were made in matched pairs of 15, 16, and 18 gauge, 3 inch hypodermic needles. A small rounded drop of solder was placed on the needle shank to prevent the cannula from slipping out of the artery.

Preliminary experiments were carried out with a Sierra Electronics Corporation airborne carrier amplifier because the gain of each amplifier could be adjusted continuously. The carrier frequency of this amplifier was 2500 cps. Later experiments were made with a model 1-118 Consolidated Engineering Corporation (Pasadena, California) carrier amplifier operating on 3000 cps. The output of the carrier amplifier was fed into two Hathaway oil-damped, light galvanometers with a sensitivity of 315 mm/ma/M, and a natural frequency of 125 cps. The
frequency response is flat to better than three times the maximum frequency of the highest harmonic of any pulse wave.

The pulses were recorded on photographic paper by a Hathaway Instrument Company (Denver, Colorado) type S-14C oscillograph. The paper speed for short runs was maintained at 20 in/sec, while for continuous recordings the speed was set at 10 in/sec. This made the shortest recorded pulse, about three and one-half inches long.

All electrically operated equipment was run from a constant voltage transformer to minimize the effect of changes in line voltage.

D. Analytical Procedures

The simultaneous recordings of blood pressure from the two selected sites in the aorta were used as the source of data for each experiment. Since the pressure pulses are complex periodic functions of time they are not easily described by any simple mathematical relationship. To enable their expression in a quantitative manner they were analyzed into a series of harmonically related sine wave components by Fourier analysis.

Fourier's theorem states that any periodic function of time can be represented as the sum of a single constant term plus a series of harmonically related sine and cosine terms. This theorem may be stated as

\[ y = A_0 + a_1 \cos w_1 t + a_2 \cos w_2 t + \ldots + b_1 \sin w_1 t + b_2 \sin w_2 t + \ldots, \] (7)
where \( A \) is the constant term, \( a_1 \) and \( b_1 \) are the respective magnitudes of the cosine and sine term for the fundamental frequency \( w; \) \( a_2 \) and \( b_2 \) for the second harmonic, and so forth.

Since the sum of a sine function and a cosine function can be expressed in terms of a sine function with an associated phase angle, by trigonometric identities, equation (7) can be written as

\[
y = A_0 + A_1 \sin (wt + \theta_1) + A_2 \sin (2wt + \theta_2) + \ldots\ldots
\]

in which \( A_m = \sqrt{a_m^2 + b_m^2} \), which is the modulus of the \( m^{th} \) harmonic, and the associated phase angle \( \theta_m = \arctan \frac{a_m}{b_m} \).

In order to evaluate the modulus and phase angles of the sinusoidal terms of each pulse wave, a numerical method as illustrated by Manley\(^1\) was used. The general method will be discussed here.

To obtain the coefficients of any term in the series it is first necessary to multiply both sides of equation (8) by the sine or cosine factor which one desires to evaluate. Hence, for the \( m^{th} \) harmonic term,

\[
y \sin mwt = A_0 \sin mwt + a_1 \sin wt \sin mwt + \ldots
\]

and second, it is necessary to integrate both sides of the

\(^1\text{Manley, loc. cit.}\)
equation obtained with respect to the angle (i.e., \( wt, 2 wt, \ldots \)) between the limits of 0 and \( 2\pi \) (one cycle). Hence:

\[
\int_{0}^{2\pi} y \sin mwt \, dwt = A_0 \int_{0}^{2\pi} \sin mwt \, dwt +
\int_{0}^{2\pi} \sin wt \sin mwt \, dwt + \ldots \ldots a \int_{0}^{2\pi} \sin^2 mwt + \ldots \ldots
\]

(10)

All of the first order sine and cosine terms will integrate to zero for one complete cycle of the fundamental leaving only the squared term which integrated to \( \pi \). Third, evaluate the coefficient of the term of interest:

\[
\int_{0}^{2\pi} \sin mwt \, dwt = \pi a_m
\]

(11)

and rearrange to form

\[
a_m = \frac{1}{\pi} \int_{0}^{2\pi} y \sin mwt \, dwt
\]

(12)

This last expression is that which must be evaluated in order to obtain the modulus of any given sinusoidal harmonic component. The integration of equation (11) is performed appro-
expressions measured for twenty-four 15° intervals of a given cardiac cycle. The magnitude of each of the twenty-four ordinates (y) of the cycle being analyzed is multiplied by the sine (or the cosine for the cosine terms in the series) of the angle of the cardiac cycle it represents for that harmonic, i.e., \( \sin m\omega t \); and this product in turn is multiplied by the angle interval between the ordinates, i.e., 15°. This multiplication must be repeated for the constant term A and each sine and cosine term in the series.

From a practical viewpoint, it is not necessary to make separate computations for all of the sine and cosine terms of all of the frequencies of interest. Numerical tables have been designed which minimize the number of redundant and duplicate computations. This form is the result of arranging the various calculations into a format to facilitate numerical analysis. Inspection of the tables, however, does not reveal the basis of the evaluation.

Table I, which is that given by Manley, indicates the manner in which the twenty-four ordinates are arranged and handled in order to perform the integrations of equation (11) for the constant term and the first eleven harmonics of the sine and cosine terms.

The pulse wave to be analyzed is divided into twenty-four even spaces. A typical recording prepared for analysis is shown in Figure 1. An ordinate is erected from the base line (zero pressure) to the corresponding point on the pulse wave.
tracing. The initial ordinate is marked \( y_0 \), the next, \( y_1 \), etc. The numerical value of each ordinate is then arranged in tabular form as shown in the first two columns of Table I. They are then summed and subtracted horizontally in pairs producing columns \( V \) and \( W \), respectively. In turn, columns \( V \) and \( W \) are likewise arranged, as indicated, and summed and subtracted to produce columns \( P \), \( Q \); and \( R \), \( S \). Columns \( L \) and \( M \) are the results of summation and subtraction respectively of column \( P \). The odd terms such as \( C \), \( D \), \( F \), \( J \), \( T \), \( X \), and the \( E \)'s and \( U \)'s are calculated from the proper values from the table.

Separate tables are arranged for the sine and cosine coefficients of each harmonic. This is accomplished by multiplying the calculated values from the table by the constants in column \( (Z) \). Each vertical column is then summed and divided by twelve. This provides the sine and cosine terms for the first eleven harmonics. The modulus and phase of each harmonic is then calculated by the following relationships:

\[
A_m = \sqrt{a_m^2 + b_m^2}, \quad \text{and} \quad \arctan \theta_m = \frac{a_m}{b_m},
\]

where \( A_m \) and \( \theta_m \) are the modulus and phase angle, respectively, of the \( m^{th} \) harmonic.

Since the value of the arctangent as it stands does not indicate in which quadrant the vector is located, it is necessary to determine this by an examination of the sign of the two coefficients. Thus, if both are positive, the angle will lie between \( 0 - 90^\circ \); if the sine is positive and the cosine
is negative, between 90-180°; if both are negative, between 180-270°; and when the sine is negative and the cosine positive, between 270-360°.

To verify the correctness of a given analysis the identities indicated in Table I must be used. If the checks show that an error has been committed, a considerable amount of time can be lost trying to find the error. In any event, it takes on the order of two hours to complete a single Fourier analysis with a modern desk calculator even when no mistakes are made. Since this method is time consuming and laborious it was decided to program Manley's method for the IBM 650 digital computer. The program was written in the Bell Floating Decimal Interpretive system, devised by V. M. Wolontis.1 Once the program was checked out by using previously hand-calculated Fourier analyses and the identities shown in Table I, one could expect results accurate to the eighth place had input data of that significance been used. To take advantage of a high-speed random access storage unit added to the 650 computer, after the problem was started, the Bell Interpretive system was rewritten. This reduced the running time for a given set of data by 28 percent. The final running time to compute the Fourier analysis of the two recorded pulses and the Fourier analysis of the pressure

gradient was 1 minute and 35 seconds. The flow chart for
the program is given in Table II. It should be noted that
the arctangent subroutine of the Bell system develops only
the principal angle of the argument, and a logic program had
to be devised to examine the signs of the two coefficients
so that the phase angle would be expressed as a rotation
through $360^\circ$.

The sum of the constant term and the sinusoidal com-
ponents when added together will provide a curve that will
pass through the twenty-four original pressure ordinates
used.

E. Experimental Procedures

Three types of experiments were performed to determine
the effects of reflection upon the harmonic content and appa-
rent phase velocity of the transmitted pressure wave in the
aorta. In two animals bilateral digital occlusion of the
femoral arteries in Scarpa's triangle was performed to deter-
mine whether an occlusion known to cause a reflection in rub-
ber tube models would indeed alter the oscillatory components
of the pulse wave. Two other experimental maneuvers employed
consisted of intra-arterial injections of acetylcholine chlor-
ide ($0.005$ mg/kg) and nor-epinephrine ($0.0015$ mg/kg) which
produce vasodilation and vasoconstriction respectively.¹

¹L. S. Goodman and A. Gilman, The Pharmacological
Basis of Therapeutics, Ed. 2, The MacMillan Co., New York,
These maneuvers were performed on a series of six dogs, and a total of 343 pairs of pulses were analyzed. All of these pulses were later averaged together and the standard error of the mean calculated for each harmonic of both pulses on the IBM 650 computer.

The pulses were recorded on Kodak linagraph paper. The zero pressure point is indicated by a line which is made by an unused galvanometer. The finished records are aligned in a horizontal line on a drafting board and two vertical lines are erected at the start and end of the renal pulse. The interval between the two vertical lines is marked off into twenty-four evenly spaced ordinates running from the zero base line and intersecting the highest pulse. Each ordinate then represents a 15° interval of the total pulse cycle. The first ordinate is marked \( y_0 \), the second \( y_1 \), etc., to \( y_{23} \). Each ordinate is then measured from the zero pressure line to its intersection with the pulse recording, with a pair of dividers which are read on a steel ruler to the nearest 0.1 mm. The second or mesenteric pulse is measured in a like manner from \( y_0 \) to \( y_{23} \).

The period of the pulse is measured by reading the \( y_0 \) ordinate to the nearest 0.01 of a second and obtaining the time interval between this and the \( y_0 \) ordinate of the next successive pulse (i.e., the second vertical line marking the end of the pulse).

The raw data are tabulated on forms made for this
purpose and when a sufficient number have been accumulated they are punched on IBM cards with a unique number to identify each experiment and pulse.

When a series of pulses have been accumulated they are read into the IBM 650 computer which first multiplies all the data by a factor of two to convert the measurements into mm Hg. The next step is then to subtract the corresponding ordinates of the mesenteric pulse from those of the renal pulse and divide each by the measured distance between the two recording sites. This process manufactures the ordinates of the pressure gradient which are stored until called for by the internal program on the computer.

The calculation of the apparent phase velocity was made by evaluating the following equation using the phase angles of the first ten corresponding harmonics of the renal and mesenteric pressure pulses:

\[ \text{APV} = \frac{S}{\left[ \frac{\theta_1 - \theta_3^1}{3} \right]} \times T \]  

(13)

\( S \) is the linear distance between the two recording sites in cm, \( T \) is the period of the pressure pulse, \( \theta_1 \) and \( \theta_3 \) are the phase angles of the \( m^{th} \) harmonics of the renal and mesenteric pressure pulses, respectively.
RESULTS

Table III contains the relative percent that the modulus of each of the first eleven harmonics contributes to the peak oscillatory pressure of each pressure pulse recorded from the left renal artery ($F_1$) and the inferior mesenteric artery ($F_3$) in the dog. These values were calculated from the average values of the moduli of the harmonics from 343 separate pairs of pressure pulses. In the last column is the percent increase or decrease of the average values of the modulus of each harmonic in the mesenteric pulse with respect to the corresponding harmonic in the renal pulse. The average heart rate for all 343 pulses is 2.62 beats per second (i.e., 157.4 beats per minute).

It is apparent that there is a marked increase in the amplitude of each harmonic as the pressure pulse travels toward the periphery in the aorta. The largest increase is to be found in the fourth harmonic, which amounts to a 77.5 percent increase in amplitude over the fourth harmonic in the renal pulses. The least change in the harmonic energy is found in the eighth harmonic, where it appears that this harmonic in the mesenteric pulses suffered a decrease of almost 13 percent of the corresponding harmonic of the renal pulse.

The total amount that the harmonic moduli has increased was 31.57 percent as the pressure pulse has traveled about 10 cm in the lower part of the abdominal aorta in the dog. Inspection of Table III shows that slightly more than 76 percent
of the total oscillatory energy of the pressure pulses is contained within the first four harmonic components of the pulse.

Table IV contains the moduli, in mm Hg, and the phase angle, in degrees, of the first eleven harmonics of 343 pairs of aortic pulses with their associated standard error of the mean. The SEM was calculated by using the relation

\[ \text{SEM} = \sqrt{\frac{(X - \bar{X})^2}{n(n-1)}}. \]

The SEM tends to be larger than one would expect for the total number of pulses averaged. However, it should be noted that these data are obtained from the Fourier analysis of the aortic pulses recorded under all degrees of vascular activity. At either extreme is the marked vasodilation induced by intra-arterial injections of Acetylcholine, and the vasoconstriction resulting from the injections of Nor-epinephrine. It can be seen from Table IV that the least variation is to be found in the fifth harmonic. On the other hand, as one would suspect, the maximum variability is found in the fundamental frequency of the mesenteric pulse. In this case, the average modulus of the fundamental is 23.8 mm Hg ± 2.17, while the phase angle is 198.9 ± 115.0 degrees.

Table V contains the average values of the apparent phase velocities for 343 determinations under all conditions with their SEM. Only the first six are given since the
distance between the recording transducers along the aorta becomes an appreciable fraction of the total wave length at the higher harmonics and the values obtained are without significance. For example, if we calculate the wave length by the well known relation \( V = n\lambda \) where \( V \) is the velocity, \( n \) is the frequency and \( \lambda \) is the wave length, by assuming a value of 10 M/sec for the velocity and a heart rate of 3 beats per second, then the wave length of the sixth harmonic will be approximately 50 cm. When the distance between the two transducers is 10 cm, it is slightly less than one-quarter of the wave length of the sixth harmonic.

As expected from finding the great variability in the phase angle of the fundamental of the mesenteric pulse, Table V shows the apparent phase velocity of the fundamental to be 3774.9 ± 2240 cm/sec, while the average phase velocity of the second harmonic is 902.1 ± 85.2 cm/sec. The next highest velocity is exhibited by the fourth harmonic, or 400.5 ± 92.0 cm/sec.

Table VI exhibits the average value of the Fourier components of the pressure gradient. It will be noticed that two-thirds of the total oscillatory energy is found in the first five sine wave components. The modulus of each harmonic is expressed in mm/Hg/cm, and the phase angle is in degrees/cm. The largest of these is the fundamental which is 0.658 ± 1.39 mm Hg/cm. The next largest is the third harmonic with a modulus of 0.506 ± 1.17 mm Hg/cm, while the
fourth harmonic modulus is $0.475 \pm 1.26$ mm Hg/cm. These particular three harmonics also exhibit the largest standard error which expresses their great variability. If the standard deviation is expressed as a percent one finds the variability to be the largest for the fourth harmonic (265 percent), the third harmonic (231 percent) and the fundamental (213 percent). The harmonic showing the least change is the second with a modulus of $0.447 \pm 0.024$ mm Hg/cm.

This indicates that 65 percent of the values for this harmonic fell within plus or minus 5.3 percent of the mean value. These percent deviations for the remaining harmonics are listed in the third column in Table VI.

It is of interest to examine the effects of drugs which cause peripheral vasoconstriction and vasodilation. Table VII shows, for the first six harmonics, a comparison between the modulus, phase angle and apparent phase velocity for the average values of 45 control pulses and for a smaller series of analyses of pulses taken at the maximum effect of Nor-epinephrine, Acetylcholine or during manual bilateral femoral occlusion. It can be readily seen that at the maximum effects of both drugs, the pulses are much richer in harmonic content as expressed by the moduli of the first six harmonics. The moduli of the fundamental frequencies are almost double those of the control values. On the other hand, the moduli of the series of femoral occlusion pulses exhibit a relatively smaller amount of harmonic pressure energy.
The comparison of the apparent phase velocities of the same series of pulses very dramatically demonstrates the effects of the above maneuvers in altering the shape of the transmitted pressure pulse. Thus, it can be seen that two entirely different methods of producing an increase in peripheral resistance, that is, by intra-arterial injections of Nor-epinephrine and by digital femoral occlusion, cause the phase angle of the first harmonic (fundamental) to be retarded by such an amount as to give rise to negative values for the apparent phase velocity for that harmonic. Thus, in the case of femoral occlusion the starting value of \(-177.8\) meters/sec is obtained. It should be noted that the average value of the modulus for this harmonic is but a few percent less than the same value for the control series. By contrast, it can be seen that the vasodilation induced by intraarterial injections of Acetylcholine causes the phase angle of the fundamental of the mesenteric pulse to be retarded so that it approaches the absolute value of the phase angle for the same harmonic in the renal pulse thus giving rise to a large positive apparent phase velocity.

It should also be noted that the apparent phase velocities of the second harmonic are raised above the values for the same harmonic in the control series. The remaining phase velocities do not exhibit a significant difference with the exception of the large value obtained for the phase velocity of the fourth harmonic in the femoral occlusion series.
The percent of the standard error of the mean in every case did not exceed 20 percent, so that the differences shown for the fundamental frequency between the control values and the experimental values are significant.

Table VIII shows the apparent phase velocity for the first five harmonics and the mean pressure of the renal pulses averaged over intervals of approximately every 20 mm Hg in a series of 343 pulses. It can be seen from this table that the velocity as calculated varies in a manner proportional to the mean pressure. However, the average values of the other harmonics exhibit only very slight changes and appear to have no relationship to the mean pressure.

There can be no doubt, however, that the apparent phase velocity of the fundamental is related in some complex manner to the mean pressure. In this case, the mean pressure is derived from the so-called constant term of the Fourier series, which represents a mean value in mm Hg upon which the oscillatory terms are superimposed. Because of the manner in which these values were arrived at, no statistical treatment was attempted.

As a result of finding both large positive and negative values of phase velocity for the fundamental frequency in various pulses, it is of interest to learn the effects of the shift of the phase angle upon the determination of the pulse wave velocity. The pulse wave velocity was calculated by finding the distance between the foot of each pulse pair with a micrometer
microscope and converting this value to time. Table IX shows how the values obtained in this manner compare with the value of the apparent phase velocity for the first three harmonics. It is evident that as the phase angle of the fundamental is retarded, giving rise to a large negative phase velocity for the fundamental, the distance between the foot of each pressure pulse will be relatively large. Hence the calculation of the pulse wave velocity based upon measurements from these apparently identical points will yield a value that is very low. However, as the apparent phase velocity of the fundamental becomes more positive, the distance between the foot of each pair of pressure pulses decreases, giving rise to a higher value for the pulse wave velocity. As this happens it can be seen that upon inspection the rate of rise of the mesenteric pulse becomes greater and at the largest fundamental phase velocities appears to be greater than the rate of rise of the renal pulse. There is only a slight correlation between the measured pulse wave velocity and the apparent phase velocities of the second and third harmonics.
A. **Fourier Analysis**

A Fourier representation is a method by which an unknown function of time can be decomposed into an infinite series of sinusoidal waves. The resulting infinite series describing these component waves is known as a Fourier series.\(^1\) In order for this representation to be valid, certain criteria must first be met. The first of these is the assumption that the wave to be decomposed is periodic. Theoretically, this implies that the periodic wave existed from the beginning of time and will exist to the end of time.\(^2\) The second criterion is that the wave under consideration be continuous within all finite intervals. Conversely, if a wave has an infinite period it is considered to be non-periodic. A function may be said to be continuous in a finite interval if that interval can be divided into a finite number of subintervals and that inside of each subinterval the function is continuous and has finite limits as the function approaches either boundary of each given subinterval from the interior.

It can be seen therefore that the cardiac pressure waves essentially fulfill these requirements. From the standpoint of the analysis of a single pressure wave one must consider the results from the viewpoint that they represent the

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situation rigorously only when the cardiac stroke volume remains constant, terminal impedance does not change and the heart rate remains identical for the previous and succeeding pulses. However, from a practical standpoint no two successive cardiac pressure waves are identical nor do the other cardiovascular parameters remain constant. This deviation from the ideal situation required for Fourier analysis permits at best only an approximation, although such an approximation may be extremely close.

The value found in using this type of analysis is that it expresses complex waveforms as a series of sinusoidal components in terms of modulus and phase. This is at once unique. Because one is familiar with the real sinusoidal wave form output of oscillators and other types of electronic wave generators, it becomes easy to visualize a Fourier series. In addition, sine waves are the simplest functions that can be generated and the behavior of these waves is thoroughly described. Thus, it becomes a relatively simple matter to treat the behavior and transmission of individual sinusoidal components rather than a complex waveform of unknown function such as the arterial pressure pulse.

It should be pointed out that the use of a medium size digital computer contributed immensely toward the examination of the harmonic content of central pulses under varying conditions of peripheral resistance. The total number of Fourier analyses performed was 1,029. Of these, 686 were
actually hand measured, while the remaining third were synthesized by the machine program from the hand-measured data as the pressure gradient.

The use of the computer not only speeded the treatment of the raw data, but also insured the accuracy of the results to approximately that of 0.5 percent. Since the intermediate values in the analysis were carried to the eighth decimal place round-off errors were negligible, which would not have been the case if the analysis had been carried out using a desk calculator.

In addition, it was possible to analyze the output data from the computer statistically. Since there were three Fourier analyses each containing eleven harmonics in modulus and phase plus the constant term, or 23 different items per analysis, the total number of Fourier items to be treated statistically amounted to 69. This number was increased by 10 apparent phase velocities so that the computing machine actually calculated the average and standard error of the mean for 79 items of data for each pulse analysis. To perform these analyses by hand would require a formidable amount of work as to make the problem impractical from the standpoint of time consumed.

B. Periodic Forcing and Genesis of Harmonics

One can think of the periodic forcing of the arterial system by the cardiac ejection as being similar to that of a half-wave rectifier. When such a rectifier is connected
to a purely resistive load, it can be shown that the output consists of each alternate positive half of the sine wave input to the rectifier. In this case, each positive sinusoidal half-wave is separated from each adjacent half-wave by an interval during which no current flows. This interval corresponds to the negative half of the input wave during which time the rectifier does not conduct. When viewed on an oscilloscope, the output then appears as alternate sinusoidal "domes" separated from each other by horizontal lines. If we now place a capacitor in parallel with the resistive load, the output wave form of the rectifier is markedly altered. Instead of the voltage falling to zero between the alternate pulses, it decreases toward zero exponentially until the next positive half cycle of rectifier conduction occurs.

In general appearance, this type of wave form fairly closely approximates the wave form found in the aorta. Although a rectifier with a resistive-capacitative load is a rather oversimplified analog of the heart and arterial tree, there are some obvious similarities between both systems.

When one examines the output wave form of either system it becomes evident that the source of the harmonic is due to the nature of the periodic forcing. In an ideal system where no distortion occurs, when the forcing is purely sinusoidal, a graphical plot of the energy spectrum will consist of a single, fine line corresponding to the amplitude
of the sinusoidal forcing and located at the frequency of the forcing wave form. When the forcing consists of a single one-half cycle of a sinusoid, the frequency spectrum spreads over all frequencies. The height of the spectrum is greatest at zero frequency. At the frequency corresponding to that of the sinusoid, the energy will be 0.62 of the magnitude at zero frequency. The shorter the duration of the pulse, the more uniform will be the distribution of the energy spectrum. In the case of a single pulse of negligible width its frequency spectrum will extend to infinite frequency at a constant height.

C. Harmonic Content Of Arterial Pulses

The transmission of the pulsatile energy in the cardiovascular system is accomplished by the propagation of energy in the form of a pressure wave and by the propagation of a flow of blood. As a result of viscosity and imperfect elasticity, energy will be lost from the system as heat resulting from the internal friction of the blood and incomplete conversion to kinetic energy from the potential energy stored in the elastic elements. There are several causes of distortion of the transmitted pressure wave. Among these are amplification resulting from a gradual tapering of the vessel walls, damping of the wave by visco-elastic elements in the

vessel walls, retrograde reflections from discontinuities and junctions in the arterial tree, and the variation in propagation rate of different harmonics, if these are propagated at unequal velocities.

Because a reflection can occur with a shift in phase, it should be expected that reflections in the cardiovascular system will add vectorially into the transmitted wave and thereby cause not only an increase or decrease in the amplitude but also in the phase angle of the harmonic components of the transmitted wave. If there is a significant retrograde reflection in the arterial system due to a difference between the characteristic impedance of the transmitting line and the terminal impedance, and if these reflected waves are not fully damped, changes in the latter will result in distortion of the transmitted wave depending upon the magnitude and phase of the components that are reflected. Because of the high order of damping found in the arterial system, the greatest amount of the reflected component will be found in the pulse recorded closest to the point of reflection. In the work reported here, it has been shown (Table III) that in a series of 343 pulse pairs, the pulse closest to the point of reflection contains harmonics, the moduli of which are all greater than the corresponding harmonics of the pulse recorded at a greater distance (with the exception of the eighth harmonic). In addition, to this, we find that the more peripheral

\footnote{P. Broemser, \textit{loc. cit.}}
pulse also is richer in harmonic sinusoidal components as one would expect if it contained a greater amount of a reflected wave than did the pulse recorded farther away from "the point of reflection". This corresponds to Broemser's findings in the dog, from which he calculated the damping of the pulse in the arterial system.

That the damping of the reflected wave is rather high, on the order of 10 percent per 10 cm of travel (calculated theoretically by Womersley²), is shown by the relatively small standard error of the harmonic components of the pulses recorded farthest from the point of reflection. These data are compared to the corresponding harmonics of the pulses that are closer to the point of reflection, as shown in Table IV. Because the average values in Table IV are derived from pulses recorded over all degrees of terminal vascular activity, one would expect the addition of varying amounts of reflection at different phases to cause the standard error to be large. That this is true only for the pulses recorded near the point of reflection and not for the pulses recorded farther from the point of reflection means that the perturbating influence of the reflection is damped as it travels toward the heart.

The rather large standard error for the fundamental frequency indicates its great variability over a large range.

¹Ibid.
²J. R. Womersley, loc. cit.
of peripheral resistance and shows that it, of all the sinusoidal components of the pressure wave, is reflected to the greatest degree. From the relatively small variations found in the other harmonics one would be tempted to conclude that these components of the pressure waves are negligibly reflected. However, as an alternate explanation for these results one is faced with the dilemma of frequency dependent damping such that the higher harmonics are damped to a greater degree. Under these circumstances, the higher harmonics would contribute little to the distortion of the central pressure pulses and would provide similar results.

From a practical viewpoint the greatest apparent mismatch between the characteristic impedance of the aorta and the terminal impedance of the arterioles occurs in the range of the fundamental or heart rate frequency. The effect of a large magnitude of reflection at the fundamental frequency upon the measured pulse wave velocity will be discussed later.

D. Addition of Reflected Waves

We may represent a complex wave propagated in modulus and phase in the form

\[ A e^{i\omega (t - z/c)} \]

where \( A \) is the modulus, \( \omega \) is the "circular frequency" \( (2\pi f) \), \( t \) is the time, \( z \) is the distance along the tube and \( c \) is the complex velocity of propagation. Here the minus sign indicates the direction of travel, that is, away from the point
of observation toward the point of reflection. Now let us say that as this wave reaches the point of reflection, one-tenth of the energy will be reflected back along the tube and the rest of the energy will continue onward. The reflected wave can now be written as

\[ \frac{1}{10} A e^{i\pi(t + z/c)} \]

and the resultant of these two waves may well be described as

\[ A e^{i\pi(t - z/c)} + \frac{1}{10} A e^{i\pi(t + z/c)} \]  (14)

Equation (14) is the sum of the incident wave and a wave of one-tenth its amplitude traveling in the opposite direction. It can now be seen that the reflected wave will add vectorially into the incident wave.

E. **Apparent Phase Velocity and Reflection**

Porje\(^1\) who has recorded arterial pulses from normal human beings calculated the apparent phase velocities for several harmonics after completing a Fourier analysis on the pulses. Although his recordings were non-sanguinary, since he used piezo-electric transducers pressed down upon the skin over the desired artery, his calculated apparent phase velocities of the fundamental frequency were much higher than

\[^1\]I. G. Porje, *loc. cit.*
expected. This he attributed to a retrograde reflection containing this frequency to the exclusion of reflected components at the second and third harmonics since the phase velocities for these latter frequencies were rather constant. This also has been found to be the case in the work reported here as can be seen from the small values for the Standard Error of the Mean of the phase velocities of harmonic calculated for 343 pulse pairs in Table V. For a large variation of peripheral resistance, it is seen that the second and fifth harmonic phase velocities are the most consistent. It is felt that the rather large variation in the third harmonic phase velocity is the result of these extremes in peripheral resistance imposed during experimental maneuvers which Porje did not attempt to investigate.

Because the elaborate mathematical descriptions published by Karreman¹, Womersley² and others³ predict the presence of reflection in the aorta resulting from branching and discontinuities in the arterial tree, it was of interest to attempt to demonstrate that an occlusive discontinuity, such as may be produced by manual pressure on the femoral arteries,

¹G. Karreman, loc. cit.
²J. R. Womersley, loc. cit.
would give rise to a reflection phenomenon similar to that arising from constriction of the terminal arterial bed by Nor-epinephrine. Both of these maneuvers cause the apparent phase velocity of the fundamental frequency to assume a negative value. That this is not due merely to changes in pressure is seen from the fact that the average mean pressures of these pulse groups are all of the same approximate magnitude.

At this point it is well to consider the findings of Hamilton who states that injections of acetylcholine in the dog weakens the reflected wave and causes the collapse of the "standing wave" reported in an earlier work. This worker also stated that the reflection could be re-established after vasodilation by injecting epinephrine or by manually occluding the animal's leg. Because of the finding of a large apparent phase velocity for the fundamental frequency after injections of acetylcholine in the work reported here, the data presented here strongly contradict Hamilton's conclusion that the reflection is abolished by vasodilation. The data, however, do lend substantial support to the hypothesis that the radius of the arterioles plays a major role in the production of the reflected waves.


Recently Landowne\textsuperscript{1} used a 48 ordinate Fourier analysis scheme (23 harmonics) from which he calculated the apparent phase velocity from different locations in the aorta and between the aorta and peripheral arteries in human subjects. His findings are in fairly close agreement with those reported here. He states that in 23 pulses analyzed, the moduli of the harmonics above the third were less than 5 mm Hg and those above the fifth were less than 2 mm Hg. In several subjects he found the brachioradial pulse to be richer in higher harmonics as compared with the aortic pulse. In addition, he states that the phase velocities were found to be consistently higher for the lower harmonics; this is verified by the findings reported here.

In an earlier work, Landowne\textsuperscript{2} reported the velocity of externally produced sinusoidal pressure waves in the arterial system. These results showed that the velocity of propagation, not phase velocity, was markedly frequency dependent. When the frequency was about 5 cps, the velocity was between 5 to 9 M/sec, whereas at 60 cps the velocity rose to values between 13-22 M/sec. These wave amplitudes were on the order of 10-30 mm Hg. When the amplitudes were increased, the velocity also increased, but not to the same degree as


changes in frequency exhibited. Thus it is evident that the transmission velocity will be a complex function of both frequency and pressure. In the same report, it is stated that the damping of the externally induced sinusoidal waves is also frequently dependent, for it was found that 50 percent attenuation occurred in the range of 15-40 cps, while it exceeded 90 percent in the range of 60-140 cps. This finding suggests the reason for the relative absence of higher harmonics in the reflected waves. That is to say, when high frequency components are reflected it is probable that they will be detected only if the recording is made close to the point of reflection.

The pressure gradient as noted before is a measure of the local driving force responsible for blood flow over the distance interval over which the gradient is measured. When the pressure wave is transmitted without change, the pressure gradient will always be positive (that is, referred to the direction of flow from the heart toward the periphery) during the rising phase of the pressure. This is due to the fact that there is a propagation delay as the pressure pulse travels down the artery. During the falling phase of the pressure pulse, the pressure gradient will become negative for the same reason. In certain cases, however, the negative portion of the pressure gradient may exceed the positive value, especially when the interval over which it is recorded is large, or the pulse pressure in the peripheral pulse is large. Such was found
to be the case by Hamilton\(^1\) in comparing the pulses obtained from the femoral and dorsalis pedis arteries. Theoretically, this would suggest a large back-flow of blood, which has not been observed,\(^2\) although small back flows have been observed in the rabbit aorta by McDonald.\(^3\)

The theoretical relation between oscillating pressure and flow is described in detail by Womersley\(^4\) based upon the Fourier analysis of pressure gradient. Since the calculation of flow is based on a summation of the harmonic terms of the pressure gradient, it gives only the oscillating values and over one cycle these will sum to a mean of zero. However, since there is a net forward flow of blood, it is necessary to superimpose the constant flow upon the oscillatory flow. The former can be calculated by using Poiseuille's Law and assuming the flow to be linear. This type of calculation has been made by McDonald\(^5\) for flow in the dog's

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femoral artery. This calculation was not performed in the work reported here because of the necessity of using a special Bessel function in calculating the flow by Womersley's method. Such a subroutine was not available for the IBM 650 digital computer at the time the program was written.

Let us now examine the factors determining the apparent phase velocity. By inspection of equation (13) it is evident that the phase velocity will be a hyperbolic function of the difference between the two phase angles. When the apparent phase velocity is plotted against the difference between the phase angles for several different periods derived from the heart rate, it is found that the phase velocity asymptotically approaches a low positive or negative value as the difference between the corresponding phase angles approaches 360°. However, as the difference becomes smaller, the value for the velocity rapidly approaches positive or negative infinity. Thus, for very small differences between the corresponding phase angles, the error becomes appreciably magnified. As the heart rate increases, the period becomes smaller, which causes the hyperbole to become flatter. Under these circumstances, the apparent phase velocity does not approach large values so rapidly, and the error is then correspondingly less. Therefore, greater reliability can be placed in the calculations of apparent phase velocities at higher heart rates.
When a comparison is made between the mean pressure derived from the Fourier analysis (i.e., the constant term) and the apparent phase velocities, it is at once manifest that as the mean pressure increases, the phase velocity for both the fundamental and second harmonics increases. As seen in Table VIII the increase of the fundamental phase velocity rapidly approaches a very high value apparently in an irregular manner. On the other hand, the phase velocity of the second harmonic increases in what appears to be a double exponential function as the mean pressure increases, whereas the values for phase velocities of the remaining harmonics remain relatively constant. Qualitatively these results correspond to those obtained by Landowne\(^1\) using human subjects.

In general, other workers have calculated the pulse wave velocity by measuring the time interval between two simultaneously recorded pressure pulses by using what they considered as being equivalent points on either pulse wave. Bramwell and Hill\(^2\) have stated that the pulse wave velocity is proportional to the square root of the ratio of the pressure change to the volume change. They feel that the pulse wave velocity is proportional to the diastolic pressure.\(^3\)

\(^1\)M. Landowne, _op. cit._


Other workers\(^1,2,3\) disagree and relate the pulse wave velocity to the systolic pressure. These differences are undoubtedly due to the different criteria used to select what the investigator thought were equivalent points on both pressure pulses. To avoid this ambiguity Kraner and Ogden\(^4\) have recently calculated the pulse wave velocity in the femoral artery in the dog by measuring the time interval between the recorded electrical differential of the pressure pulse with respect to time. They cite values from 7-9 M/sec which are similar to those found by McDonald\(^5\) and Landowne.\(^6\)

The determination of the pulse wave velocity by such methods is actually a measure of the group velocity, that is, the velocity of a pressure pulse composed of a large number of harmonic components, all of which travel at different


\(^4\)J. C. Kraner and E. Ogden, In press.

\(^5\)D. A. McDonald, loc. cit.

\(^6\)M. Landowne, loc. cit.
velocities dependent upon their frequency. One would therefore expect that if a reflected wave were present to a greater degree in one of the pulses used for this measurement than in the other, the accuracy of the method would suffer deterioration depending upon the shift of the foot and change in the rate of rise of the pressure wave due to the reflection. Table IX shows the comparison between the group velocity (so-called pulse wave velocity) and the phase velocities of the first three harmonics of 9 different pulses. It is strikingly evident from a comparison of the fundamental phase velocity and that of the measured group velocity. With a large amount of reflection and a correspondingly large negative phase velocity for the fundamental, the time interval between the simultaneously recorded pressure pulses is lengthened. This gives rise to an unusually low group velocity. At the other extreme of reflection, a very high positive fundamental phase velocity shortens the time interval between the two pulses, giving rise to a high group velocity. Upon visual inspections of these pulses it can be quite clearly seen that when there is a large negative fundamental phase velocity; the rate of rise of the pulses is diminished. Conversely, the high positive fundamental phase velocity causes the rate of rise of the pulse closest to the reflection to be markedly increased. In these cases the second pulse contour is much "sharper" than the more centrally recorded pulse.
It now becomes obvious that when there is a significant amount of retrograde reflection in a pair of pulses, the calculation of a group velocity will bear little relationship to the theoretical pulse wave velocity. Unfortunately, use of the time interval between the two first differentials of pressure with respect to time will not solve this problem, since this gives only the rate of pressure change with respect to time. Because of the very slow rate of change in pressure with respect to time as seen in the recordings of pulses with a negative fundamental phase velocity, the time intervals between the two first differentials will still be prolonged, especially if one uses their peak. The converse is true in those instances where a reflection gives rise to a large positive fundamental phase velocity. It would appear from the data in Table IX that the group velocity will approximate the pulse wave velocity only when the reflection is at a minimum, i.e., when the phase shift of the fundamental due to reflection is minimal and is only a function of the travel time between the two recording sites.

Because of the rather close correlation of group velocity with pressure, one can speculate whether the rigidity of the vessels is as important as it has been thought to be in determining the so-called pulse wave velocity. It certainly appears that reflection plays a significant role in determining the group velocity. A more analytical study of this problem is needed to define the part played by each of these contributing factors.
F. Physiological Significance of Results

(1) The Pulse Wave Contour.

Because the contour of the pressure pulse upon analysis will determine the magnitude and phase relationships of the harmonic components that characterise it, it is of interest to examine some of the physiological factors having an immediate effect upon the genesis of the pulse contour.

Of the several physical factors influencing the shape and duration of the pressure pulse, that of the rate and force of systolic ejection is of primary importance. The rate of ejection of blood from the ventricle into the aorta will determine the rate at which the systolic pressure will rise from the end diastolic pressure of the previous pulse. Both this rate of rise and the subsequent rate of pressure fall toward the diastolic level will determine to the largest extent the broadness of the spectrum of the higher harmonic components. Because the heart rate per se determines the fundamental frequency it is evident that the faster is the heart beat, the correspondingly greater will be the frequencies of the harmonics. When the end diastolic pressures of adjacent pulses are not the same a discontinuous step is introduced into the Fourier analysis. The effect of this discontinuity is to increase not only the magnitude of the high order harmonics but also to increase the number of these harmonics. This type of error, fortunately, adds only to the unreliability of those components having little influence in the pulse wave contour.
The pressure to which the mass of ejected blood is raised plus the acceleration given to the blood will, of course, determine the peak of systolic pressure as well as the time course of the first part of the pressure wave. Hence, the greater the force of ejection the greater will be the magnitudes of the first several sinusoidal harmonic terms of the pressure. It should be apparent that if a given fraction of this pressure energy will be reflected, because of the damping in the cardiovascular system, the effectiveness of reflections in altering the pulse contour will be enhanced at greater systolic ejection forces because it will appear in larger amounts at a given location in the system. Recent work by Starr has shown that even with identical stroke volumes over identical periods of time the pulse contour can vary markedly. He therefore considers that the acceleration imparted to the blood is the most important factor in determining the time course of the pulse wave.

Another factor that will influence the harmonic content of the pressure pulse is the rate of diastolic run-off. When the peripheral resistance is low and the rate of run-off is high, not only will the pulse pressure be greater but the systolic pressure will fall toward the end diastolic pressure more rapidly. When the diastolic pressure is markedly reduced due to vasodilation it is possible to obtain a "pistol shot"

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type of pulse. This type of pulse approximates a square wave and is extremely rich in high order harmonic components. Usually, one sees a highly damped oscillation on the anacrotic limb of such a pulse and presumably it is this transient that produces the characteristic sound of this pulse. The fact that the pulse sound is so sharp is indicative of its high harmonic content.

When one considers that the aorta has numerous branches along its length, it becomes evident that the contour of the pulse will be altered in its peripheral travel as a result of the loss of low frequency flow components. Under normal conditions Ryan and his co-workers have shown, by tying-off these branches, that they exert little influence. This is surprising since the flow requirements of these branch vessels are great.

Another important factor that will influence the time course of the pulse wave is the arterial elasticity. During systolic ejection the blood that is propelled into the aorta distends the vessel walls. The elastic recoil of the walls then acts as a "Windkessel" and forces the blood toward the periphery after the systolic discharge. This effect of the walls tends to damp out the higher frequency harmonics of the pulse. When this elastic recoil is diminished, the effect is not unlike a pressure pulse traveling in a lead pipe. In this

case, the flow would be transmitted at a high velocity and would appear across the periphery almost instantaneously. This, in turn, would cause the pressure to rise extremely rapidly to a high value and just as quickly fall to a very low value. The harmonics that such a pulse contains are of large magnitude and of high orders of frequency.

From the foregoing it can be seen, neglecting reflection, that the most significant physiological factors influencing the pulse contour and hence the harmonic content of the pulse are vigor of systolic ejection, the resistance to flow and, lastly, the arterial elastic recoil.

Because of the reflection from the periphery, one would expect that as a result of the high damping, as the transmitted pulse approached the point of reflection it would contain larger amounts of reflected pressure. This in itself is sufficient to explain the difference in the contour of the pulse as it travels peripherally. The results suggest that this physiological phenomenon is the manifestation of reflection rather than the effects of a frequency dependent velocity that would cause the harmonics to "pile-up" similar to an ocean wave (c.f. page 52).

(2) The Effect of Reflections on Cardiac Work.

Because of the pulsatile nature of the flow in the arterial tree and the production of retrograde reflections, it is of interest to determine the terminal vascular impedance for
the sinusoidal harmonics of the blood flow. If the impedance is high for some harmonics and not for others this would indicate that reflection of these harmonics would occur. Randall has recently calculated the mechanical impedance to the first four harmonics of blood flow in the hind leg of the dog. His impedance vs frequency curve shows a pronounced dip in the region of the second and third harmonics. This is in accord with the findings reported here that the second and third harmonics evidence little reflection.

What these findings mean in terms of cardiac work is that at those harmonic frequencies where little reflection occurs, the energy transfer into the periphery is optimal. However, at lower and higher frequencies a mismatching occurs and a portion of the energy that normally would produce useful flow is reflected back toward the heart. Therefore, the amount of work that the heart is required to perform to maintain a given flow will be of necessity in excess of the actual amount needed. This inefficiency of transmission will be in proportion to the amount of energy reflected back from the periphery. It would be expected to rise with extremes of vasoconstriction and vasodilation or very rapid and very slow heart rates. The energy thus lost for the performance of useful work eventually contributes to the increase of entropy of the system as heat.

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Pulsatile Flow in the Cardiovascular System.

The pulsatile nature of the cardiovascular system precludes the measurement and calculation of flow based on the linear Poiseuille relationship. There are two types of blood flow to be reckoned with in the artery. The first is the constant or D.C. flow and the second is the oscillatory flow. As can be expected, the flow velocity in the large arteries lags the pressure velocity. Broemser\(^1\) has measured the flow velocity in the abdominal aorta in dogs where he found it to be 18 cm/sec, while Machella\(^2\) found the flow velocity in the carotid and femoral arteries to be 14 cm/sec. However, McDonald\(^3\) recently calculated the flow velocity in the femoral artery of the dog and obtained a value of 120 cm/sec. The discrepancy between these results is because the latter calculation was based upon oscillatory flow calculated from the Fourier analysis of the pressure gradient. Because the flow occurring locally is the result of the driving forces of the pressure gradient, the oscillatory flow thus generated probably will always have a retrograde component. This phenomenon undoubtedly

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\(^3\)D. A. McDonald, loc. cit.
contributes a certain amount of ineffeciency to the work of the heart.

(4) The Bearing of Results on Pressure Velocity Measurements.

It is evident that the physiologist has three pressure velocity measurements that he can make. The first and most important for a theoretical treatment of pulse transmission is the true wave velocity. Unfortunately, this is a very difficult measurement to make since it requires for its solution a knowledge of the modulus of elasticity of the vessel wall, the traction of the moving blood upon the wall, and the resulting movement of the constrained vessel, etc. The second measurement is the group velocity which actually is a measure of the transmission velocity of a complex wave-form all of whose harmonic components are moving with different velocities. It is this phenomenon that is unique to the cardiovascular transmission system as compared to other hydraulic systems and also is the factor that makes study of the system so difficult. It is certainly manifest that these two measurements are not interchangeable unless some correction can be made to equate them. The third measurement is that of the phase velocity. The fundamental phase velocity should be equal to the pulse wave velocity when no distortion during transmission occurs and when no reflection exists. However, because these ideal conditions do not exist in the arterial system, it is not possible to measure a true phase velocity. From the
addition of a reflection into the transmitted wave, which results in a phase shift of the various harmonics, one instead obtains an apparent phase velocity. This immediately suggests that one could correct group velocity measurements for the presence of reflection by harmonic analysis of two pulses and resynthesis of the pulses after an appropriate shift of the harmonics followed by a recalculation of the velocity from the synthesized pulses.

(5) Some Reflections on Future Cardiovascular Research.

This work was initially undertaken in order to provide experimental information to verify the "Elastic Tube Theory of Pulse Transmission and Oscillatory Flow in Arteries" developed by J. R. Womersley. Aperia and Porje have both underscored the lack of a constant theory that takes into account the reflections that probably occur in the cardiovascular system. The lack of such a theory has prevented a logical and systematic investigation and understanding of cardiovascular hemodynamics. Thus, any experimental verification of a mathematical description will provide cardiovascular physiologists with a solid framework in which to expand investigations.

1J. R. Womersley, loc. cit.
2A. Aperia, loc. cit.
3I. Porje, loc. cit.
Under the conditions of branching flow, one may calculate the steady flow in each branch from a linear relationship similar to Ohm's Law. It is usual to speak in terms of the resistance when calculating the steady flow, and the summation of the action of all the resistances in the branches in a manner analogous to direct current circuit computations. With an oscillating pressure in a branched system, however, phase relationships are introduced in addition to the dimensions of the flow. Unfortunately, the theory governing the fluid flow under these conditions is considerably more complex than those governing the flow of alternating currents at low frequencies where the size of the conductor may be disregarded. Womersley's theory, that has been previously cited, is fundamentally the same as that determining the flow of very high frequency currents. This has the important result that the Bessel functions necessary for its solution have previously been computed and tabulated.

The data presented here comprise the first step required for the solution of Womersley's mathematical description of the pulsatile pressure and flow in the cardiovascular system. It should now be possible to calculate the ratio of the harmonic velocities in blood to their equivalent velocities in a perfect fluid in the same vessels. Next, it will be necessary to determine the amount of damping at each frequency. To be useful these values have to be found in complex form. Previous investigators have given only the real part
of this function. With these values it will then be possible to find the general solution for pulsatile transmission in the aorta.

In order to obtain the quantitative values for the above mentioned parameters, it is necessary to obtain the Fourier analysis of a pulse and pressure gradient immediately in front of a point where reflection is known to occur. Thus, one will know the distance over which the reflected wave travels. With this information it becomes a simple matter to solve the equation on a computer for a value of the harmonic velocity in a perfect fluid which gives a consistent ratio for all harmonics as found experimentally. Knowing this, the equation can be written for the complex solution to the damping coefficients for all harmonics. Then by writing the general equation for the computer in a form so that it can be set equal to zero, the general solution can be obtained by successive iterations to find the unknown distance from the site of recording to the point of reflection. The solution to the general equation would then provide information concerning the amount and phase of reflection at different frequencies from which one could calculate the energy transfer across the terminal impedance for every harmonic.

After this has been accomplished, it should be possible to evaluate such factors as arterial stiffness, aberrant vaso-motor activity, changes in arterial diameter, etc., in selected
cases of cardiovascular disease. Some insight into such basic mechanisms of normal cardiovascular pulse transmission is highly desirable since knowledge of these permits one to treat disorders rationally rather than by symptomatic or empiric methods.
SUMMARY AND CONCLUSIONS

The first eleven harmonic components of aortic pressure pulses, recorded simultaneously at two different sites, and the pressure gradient have been determined.

The aortic pulses recorded toward the periphery have a richer harmonic content than do the same pulses recorded nearer the heart. This is attributed to energy reflected from the periphery which is attenuated as it travels back up the aorta toward the heart.

A little over 76 percent of the oscillatory energy of the pulse was found to be contained within the first four harmonics. Above the sixth harmonic, the energy contribution to the pressure pulse is negligible.

From the phase angles obtained by Fourier analysis, the apparent phase velocities were calculated for the first ten harmonics of the pressure pulse. The velocity decreases in proportion to the order of the harmonic.

The relationship between the apparent phase velocity and the state of the arteriolar constriction or dilation was examined. When the peripheral resistance is high, the apparent phase velocity of the fundamental harmonic may reach a very large positive value. When the peripheral resistance is low, the fundamental phase velocity can assume a very large negative value. This effect is related to the reflected wave that adds vectorially into the transmitted pulse.
and causes a change in the phase angles of the constituent harmonics.

The effect of large positive and negative values of the fundamental phase velocity on the measured group velocity (pulse wave velocity) was determined. A large negative velocity causes the measured group velocity to have a low value, whereas a large positive fundamental phase velocity causes the group velocity to be higher. Under extreme conditions, this effect would tend to invalidate the results of measured pulse wave velocity.

The relationship between harmonic apparent phase velocity and mean pressure has been examined. It is shown that the velocities of the first two harmonics is only roughly proportional to the mean pressure.
Fig. 1. Typical Record of Aortic Pulses. The period is divided into 24 equally spaced intervals at ordinates erected at each point. (Redrawn actual size).
### TABLE I

**Numerical Method for Fourier Analysis using \( 2L \) Ordinates**

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<th>V</th>
<th>Sum ( P )</th>
<th>Diff. ( Q )</th>
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<th>Sum ( L )</th>
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\[
C = N_1 + N_2 \\
D = N_1 - N_2 \\
E_o = Q_o - Q_4 \\
E_1 = Q_1 - Q_3 - Q_5 \\
F = G_0 + G_1 \\
J = H_o - H_1 \\
T = M_0 - M_2 \\
X = K_1 - K_3 \\
U = R + R - R \\
U = R - R \\
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TABLE I (PART 2)
Cosine Coefficients

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<td>Q_1</td>
<td>M_0</td>
<td>E_0</td>
<td>H_0</td>
<td>Q_0</td>
<td>T</td>
<td>Q_0</td>
<td>G_0</td>
<td>E_0</td>
<td>M_0</td>
<td>Q_0</td>
<td>J</td>
</tr>
<tr>
<td>1.00000</td>
<td>Q_0</td>
<td>M_0</td>
<td>E_0</td>
<td>H_0</td>
<td>Q_0</td>
<td>T</td>
<td>Q_0</td>
<td>G_0</td>
<td>E_0</td>
<td>M_0</td>
<td>Q_0</td>
<td>J</td>
</tr>
</tbody>
</table>

Sum of Columns gives $12a_k$

Sine Coefficients

<table>
<thead>
<tr>
<th>Z</th>
<th>X</th>
<th>2X</th>
<th>3X</th>
<th>4X</th>
<th>5X</th>
<th>6X</th>
<th>7X</th>
<th>8X</th>
<th>9X</th>
<th>10X</th>
<th>11X</th>
<th>12X</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25882</td>
<td>R_1</td>
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<td>R_5</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td>R_1</td>
</tr>
<tr>
<td>0.50000</td>
<td>R_2</td>
<td>K_1</td>
<td></td>
<td></td>
<td>R_5</td>
<td></td>
<td></td>
<td></td>
<td>K_1</td>
<td></td>
<td></td>
<td>R_2</td>
</tr>
<tr>
<td>0.70711</td>
<td>R_3</td>
<td>U_1</td>
<td></td>
<td></td>
<td>R_3</td>
<td></td>
<td></td>
<td>U_1</td>
<td></td>
<td></td>
<td></td>
<td>R_3</td>
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<td>R_4</td>
<td>K_2</td>
<td></td>
<td></td>
<td>R_4</td>
<td></td>
<td></td>
<td></td>
<td>R_4</td>
<td></td>
<td></td>
<td>R_4</td>
</tr>
<tr>
<td>0.96593</td>
<td>R_5</td>
<td>K_3</td>
<td>U_2</td>
<td></td>
<td>R_1</td>
<td>X</td>
<td>R_6</td>
<td></td>
<td>U_2</td>
<td></td>
<td></td>
<td>R_6</td>
</tr>
<tr>
<td>1.00000</td>
<td>R_6</td>
<td>K_3</td>
<td>U_2</td>
<td></td>
<td>R_1</td>
<td>X</td>
<td>R_6</td>
<td></td>
<td>U_2</td>
<td></td>
<td></td>
<td>R_6</td>
</tr>
</tbody>
</table>

Sum of Columns gives $12b_k$

Checks:
1) $y_0 = A_0 + a_k$
2) $1/2 (Y_1 - Y_{23}) = 0.2588 (b_1 + b_{11}) + 0.5 (b_2 + b_{10}) + 0.7071 (b_3 + b_9) + 0.8660 (b_4 + b_8) + 0.9659 (b_5 + b_7) + b_6$
TABLE II

Flow Diagram of IBM 650 Program to Calculate Fourier Analysis and Apparent Phase Velocity

Read-in ordinates $F_1$ and $F_3$

Initialize all variable addresses and switches

Move $F$ to storage

Calculate ordinates for $F_2$

$(F_1 - F_3) = F_2$

Calc. $-dP/dZ$

$F_1 = F_3 / S$

$S$ distance between $P_1$ and $P_2$

Invert ordinates from $y_{12}$ to $y_{23}$

Add: $y_k + y_{13-k}$ store $V$

is $k = 12$?

YES

Subtr: $y_k - y_{13-k}$ store $W$

NO

is $k = 12$?

NO

YES

Invert $V_7 = V_{12}$

Add: $V_k + V_{7-k}$ store $P$

is $k = 6$?

YES

Subtr: $V_k - V_{7-k}$ store $Q$

is $k = 6$?

NO

NO

increase $k$ by 1

increase $k$ by 1
TABLE II (PART 2)

Compute L and M

Compute G and H

Invert W = W

Add:

W + W

k 7-k

store R

is k = 6?

YES

NO

increase k by 1

Subtr:

W k 7-k

store S

is k = 6?

YES

Compute K and M

Compute miscellaneous factors: C, D, E₀, E₁, F, J, T, X, U₁, and U₂

NO

increase k by 1

Compute cosine coefficients and store in sequence

Compute sine coefficients and store in sequence

(go to coefficient evaluation program)
TABLE II (PART 3)

Coefficient Evaluation

- **Calc**: $\sqrt{a_k^2 + b_k^2} = A_k$ and store
- **is $b_k = 0$ zero?**
  - **YES**: store contents (000) in $L(Q_m)$
  - **NO**: continue
- **is $a_k = 0$ zero?**
  - **YES**: set $Q_m = 0$
  - **NO**: continue
- **is $a_k = 0$ zero?**
  - **YES**: set $Q_m = 270^\circ$
  - **NO**: set $Q_m = 360^\circ$
- **increase $k$ by 1**
- **set $\alpha = a_1$**
- **set $\alpha = a_2$**
- **set $\alpha = a_3$**
- **is $k=11$?**
  - **YES**: **exit to switch**
  - **NO**: continue
- **Calc**: $\arctan a_k/b_k$ and store in location [000]
- **add nothing** to (000)
- **add $180^\circ$** to (000)
- **add $360^\circ$** to (000)
TABLE II (PART 4)

1. Initialize Fourier and coefficient test prog. for $F_2$
   - set $\Theta = B_2$
   - move $F$ to loc $F_1$
2. Initialize Fourier and coefficient test prog for $F_3$
   - set $\Theta = B_3$
   - move $F_3$ to loc $F_1$
3. Initialize the C program
   - subtr: $\Theta = m - m_3$
   - $\frac{Q_m - Q_m}{360^\circ}$
   - $\left[ \frac{Q_m - Q_m}{360^\circ} \right] \times T$
4. Increase $m$ by 1
   - NO: is $m = 10$?
5. Unconditional transfer to READ

Punch $F_1$, $F_2$, $F_3$, and $C_m$ and store

(A) Unconditional transfer to start of Fourier prog.
TABLE III
Percent Contribution of the Modulus of each Harmonic from the Average of 343 Pulse Pairs

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>$F_1$ Percent of Total</th>
<th>$F_3$ Percent of Total</th>
<th>Percent Change of $F_3$ from $F_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40.35</td>
<td>37.94</td>
<td>23.7</td>
</tr>
<tr>
<td>2</td>
<td>19.20</td>
<td>17.67</td>
<td>21.1</td>
</tr>
<tr>
<td>3</td>
<td>9.63</td>
<td>11.23</td>
<td>53.5</td>
</tr>
<tr>
<td>4</td>
<td>7.28</td>
<td>9.81</td>
<td>77.5</td>
</tr>
<tr>
<td>5</td>
<td>5.84</td>
<td>6.68</td>
<td>50.5</td>
</tr>
<tr>
<td>6</td>
<td>3.45</td>
<td>3.16</td>
<td>20.6</td>
</tr>
<tr>
<td>7</td>
<td>3.60</td>
<td>3.33</td>
<td>21.5</td>
</tr>
<tr>
<td>8</td>
<td>3.45</td>
<td>2.27</td>
<td>-12.7</td>
</tr>
<tr>
<td>9</td>
<td>2.85</td>
<td>2.79</td>
<td>29.4</td>
</tr>
<tr>
<td>10</td>
<td>1.72</td>
<td>1.80</td>
<td>37.8</td>
</tr>
<tr>
<td>11</td>
<td>2.57</td>
<td>3.25</td>
<td>65.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47.70 mm Hg</strong></td>
<td><strong>62.77 mm Hg</strong></td>
<td><strong>31.6</strong></td>
</tr>
</tbody>
</table>

Average Heart Rate is 2.62 Beats Per Minute
TABLE IV

Absolute Values for the Modulus and Phase Angle of the First Eleven Harmonics
Average for 343 Pulses

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>$F_1$</th>
<th>$F_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mod. mm Hg</td>
<td>SEM</td>
</tr>
<tr>
<td>1</td>
<td>19.2</td>
<td>0.45</td>
</tr>
<tr>
<td>2</td>
<td>9.2</td>
<td>0.24</td>
</tr>
<tr>
<td>3</td>
<td>4.6</td>
<td>0.50</td>
</tr>
<tr>
<td>4</td>
<td>3.5</td>
<td>0.67</td>
</tr>
<tr>
<td>5</td>
<td>2.8</td>
<td>0.48</td>
</tr>
<tr>
<td>6</td>
<td>1.7</td>
<td>0.04</td>
</tr>
<tr>
<td>7</td>
<td>1.7</td>
<td>0.48</td>
</tr>
<tr>
<td>8</td>
<td>1.6</td>
<td>0.68</td>
</tr>
<tr>
<td>9</td>
<td>1.4</td>
<td>0.48</td>
</tr>
<tr>
<td>10</td>
<td>0.8</td>
<td>0.03</td>
</tr>
<tr>
<td>11</td>
<td>1.2</td>
<td>0.48</td>
</tr>
<tr>
<td>Constant</td>
<td>130.6</td>
<td>1.30</td>
</tr>
</tbody>
</table>
TABLE V

Average Values of the Apparent Phase Velocity Calculated for the First Six Harmonics in a Series of 343 Pulse Pairs

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>Apparent Phase Velocity (cm/sec)</th>
<th>Standard Error (cm/sec)</th>
<th>Percent of Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3774.8</td>
<td>2240.4</td>
<td>59.3</td>
</tr>
<tr>
<td>2</td>
<td>902.2</td>
<td>852</td>
<td>9.4</td>
</tr>
<tr>
<td>3</td>
<td>183.9</td>
<td>66.6</td>
<td>36.2</td>
</tr>
<tr>
<td>4</td>
<td>400.5</td>
<td>920</td>
<td>22.9</td>
</tr>
<tr>
<td>5</td>
<td>252.7</td>
<td>22.9</td>
<td>9.1</td>
</tr>
<tr>
<td>6</td>
<td>107.7</td>
<td>86.1</td>
<td>79.9</td>
</tr>
</tbody>
</table>
TABLE VI
Average Values for the Modulus and Phase Angle of Pressure Gradient Calculated for 343 Pulses

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>Modulus (mm Hg/cm)</th>
<th>SEM</th>
<th>Phase angle (deg)</th>
<th>SEM</th>
<th>Percent of Standard Error of Modulus</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.658</td>
<td>1.390</td>
<td>254.4</td>
<td>188.33</td>
<td>213.0</td>
</tr>
<tr>
<td>2</td>
<td>0.447</td>
<td>0.024</td>
<td>240.6</td>
<td>1.96</td>
<td>5.4</td>
</tr>
<tr>
<td>3</td>
<td>0.506</td>
<td>1.178</td>
<td>195.1</td>
<td>1.56</td>
<td>231.0</td>
</tr>
<tr>
<td>4</td>
<td>0.475</td>
<td>1.266</td>
<td>192.9</td>
<td>1.65</td>
<td>265.0</td>
</tr>
<tr>
<td>5</td>
<td>0.384</td>
<td>0.087</td>
<td>168.4</td>
<td>1.63</td>
<td>22.6</td>
</tr>
<tr>
<td>6</td>
<td>0.189</td>
<td>0.230</td>
<td>157.9</td>
<td>2.57</td>
<td>12.1</td>
</tr>
<tr>
<td>7</td>
<td>0.235</td>
<td>0.057</td>
<td>139.9</td>
<td>1.91</td>
<td>24.2</td>
</tr>
<tr>
<td>8</td>
<td>0.156</td>
<td>0.025</td>
<td>123.5</td>
<td>2.56</td>
<td>16.0</td>
</tr>
<tr>
<td>9</td>
<td>0.226</td>
<td>0.061</td>
<td>133.9</td>
<td>3.44</td>
<td>26.9</td>
</tr>
<tr>
<td>10</td>
<td>0.149</td>
<td>0.020</td>
<td>126.2</td>
<td>4.19</td>
<td>13.4</td>
</tr>
<tr>
<td>11</td>
<td>0.258</td>
<td>0.069</td>
<td>147.0</td>
<td>4.42</td>
<td>26.7</td>
</tr>
<tr>
<td>A°</td>
<td>0.197</td>
<td>0.094</td>
<td>--</td>
<td>--</td>
<td>17.7</td>
</tr>
</tbody>
</table>
TABLE VII (PART 1)

A Comparison between the Effects of Nor-epinephrine, Acetylcholine,
Bilateral Femoral Occlusion and 45 Control Pulses

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>Control</th>
<th>Nor-epinephrine</th>
<th>Femoral Occlusion</th>
<th>Acetylcholine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Modulus (mm Hg)</td>
<td>Phase (Degrees)</td>
<td>Modulus (mm Hg)</td>
<td>Phase (Degrees)</td>
</tr>
<tr>
<td>1</td>
<td>13.5</td>
<td>37.4</td>
<td>24.7</td>
<td>5.2</td>
</tr>
<tr>
<td>2</td>
<td>8.8</td>
<td>263.3</td>
<td>11.8</td>
<td>333.3</td>
</tr>
<tr>
<td>3</td>
<td>3.7</td>
<td>277.1</td>
<td>9.3</td>
<td>315.7</td>
</tr>
<tr>
<td>4</td>
<td>1.7</td>
<td>260.1</td>
<td>5.3</td>
<td>287.3</td>
</tr>
<tr>
<td>5</td>
<td>1.6</td>
<td>298.6</td>
<td>2.9</td>
<td>283.1</td>
</tr>
<tr>
<td>6</td>
<td>1.4</td>
<td>257.8</td>
<td>2.3</td>
<td>268.4</td>
</tr>
<tr>
<td>Mean Pressure</td>
<td>136.6± 1.8</td>
<td>156.1± 8.1</td>
<td>149.9± 6.6</td>
<td>145.6± 12.0</td>
</tr>
<tr>
<td>Number of Pulses</td>
<td>45</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Number of Animals</td>
<td>6</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>
TABLE VII (PART 2)

Apparent Phase Velocity in cm/sec.

<table>
<thead>
<tr>
<th>Harmonic</th>
<th>Control</th>
<th>Nor-epinephrine</th>
<th>Femoral Occlusion</th>
<th>Acetylcholine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1524.1</td>
<td>-3640.8</td>
<td>-17788.6</td>
<td>14834.9</td>
</tr>
<tr>
<td>2</td>
<td>676.7</td>
<td>6985.3</td>
<td>2345.8</td>
<td>1149.1</td>
</tr>
<tr>
<td>3</td>
<td>300.9</td>
<td>508.2</td>
<td>389.0</td>
<td>412.6</td>
</tr>
<tr>
<td>4</td>
<td>277.5</td>
<td>388.3</td>
<td>6435.8</td>
<td>401.6</td>
</tr>
<tr>
<td>5</td>
<td>228.4</td>
<td>282.6</td>
<td>271.4</td>
<td>500.0</td>
</tr>
<tr>
<td>6</td>
<td>126.9</td>
<td>426.4</td>
<td>143.9</td>
<td>261.2</td>
</tr>
</tbody>
</table>
# TABLE VIII

Comparison Between the Mean Pressure and Apparent Phase Velocity Averaged Over Intervals in a Series of 343 Pulse Pairs

<table>
<thead>
<tr>
<th>Mean Pressure (mm Hg)</th>
<th>( C_1 )</th>
<th>( C_2 )</th>
<th>( C_3 )</th>
<th>( C_4 )</th>
<th>( C_5 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>88.2</td>
<td>671.7</td>
<td>312.2</td>
<td>290.4</td>
<td>268.3</td>
<td>160.3</td>
</tr>
<tr>
<td>111.5</td>
<td>9430.6</td>
<td>390.0</td>
<td>266.0</td>
<td>246.2</td>
<td>144.6</td>
</tr>
<tr>
<td>130.4</td>
<td>4498.7</td>
<td>436.4</td>
<td>-50.9</td>
<td>601.5</td>
<td>247.5</td>
</tr>
<tr>
<td>147.7</td>
<td>3302.4</td>
<td>1088.9</td>
<td>386.0</td>
<td>367.2</td>
<td>307.2</td>
</tr>
<tr>
<td>176.6</td>
<td>24089.2</td>
<td>2301.7</td>
<td>459.4</td>
<td>408.7</td>
<td>260.2</td>
</tr>
<tr>
<td>PWV</td>
<td>$C_1$</td>
<td>$C_2$</td>
<td>$C_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>233.6</td>
<td>-19162.2</td>
<td>276.2</td>
<td>190.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>402.1</td>
<td>-7435.4</td>
<td>286.6</td>
<td>178.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>501.3</td>
<td>-1954.7</td>
<td>239.4</td>
<td>224.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>793.1</td>
<td>-686.7</td>
<td>-14.0</td>
<td>1556.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>709.3</td>
<td>-25.5</td>
<td>172.6</td>
<td>199.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>522.1</td>
<td>3320.4</td>
<td>-14.9</td>
<td>175.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2214.3</td>
<td>8424.3</td>
<td>1047.5</td>
<td>635.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1173.4</td>
<td>13761.4</td>
<td>1919.7</td>
<td>626.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2733.1</td>
<td>28744.6</td>
<td>2200.4</td>
<td>765.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All Values are cm/sec.*
I, Robert Lucas Farrow, was born in Green Bay, Wisconsin, March 5, 1924. I received my secondary school education in the public schools of Shaker Heights, Ohio. My undergraduate training was obtained from John Carroll University from which I received the degree Bachelor of Science in Natural Science in 1948. From Georgetown University, I received the degree Master of Science in 1951. My major subject was Physiology. In the fall of 1951 I matriculated in the Graduate School at the Ohio State University and was appointed a Graduate Assistant in the Department of Physiology. In 1957 I received an appointment as Research Fellow in the Department of Physiology. I held this position for one year while completing the requirements for the degree Doctor of Philosophy.