SOLITONS:

PROPAGATION OF SOLITARY WAVES THROUGH BLOOD

[redacted]

A dissertation submitted in part fulfilment of the requirements for the award of a BSc Honours Degree in Physics

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The University of Leeds

I certify that this work has not been accepted in substance for any degree, and is not concurrently being submitted for any degree other than that of the BSc Honours Degree in Physics. I also declare that this work is the result of my own investigations except where otherwise identified by references and that I have not plagiarised another's work.

Signed **Date**

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I owe the most sincere gratitude to my supervisor, [redacted], for the support and guidance he has shown me throughout my dissertation. It would have not been possible without his encouragement understanding and persistent help.

CONTENTS

Figures, Tables and Graphs	**5**
Introduction	**6**
The Circulatory System	**8**
Blood Pressure Measurements	**10**
Measurement of Cardiac Output	**17**
Soliton Theory	**26**
Conclusion	**36**
References	**37**

FIGURES, TABLES AND GRAPHS

Figure 1	**6**	**Table 1**	**21**
Figure 2	**7**	**Table 2**	**22**
Figure 3	**8**		
Figure 4	**8**		
Figure 5	**9**	**Graph 1**	**26**
Figure 6	**10**	**Graph 2**	**26**
Figure 7	**12**	**Graph 3**	**28**
Figure 8	**17**	**Graph 4**	**29**
Figure 9	**21**	**Graph 5**	**29**
Figure 10	**23**	**Graph 6**	**29**
Figure 11	**23**		
Figure 12	**27**		
Figure 13	**28**		
Figure 14	**30**		
Figure 15	**30**		
Figure 16	**30**		
Figure 17	**30**		
Figure 18	**31**		
Figure 19	**32**		
Figure 20	**32**		
Figure 21	**33**		
Figure 22	**34**		
Figure 23	**34**		

Introduction

The circulatory system is a complicated system. The centre of the system is the heart which can produce magnetic fields. These can be measured by a magnometer. Magnetometry is the measure of the patterns of magnetism in the heart, although it is commonly used in geophysical surveys of soils[4]. When a magnetometer is used to scan the heart, a reading of 4 Hz is recorded, appearing to be a signal from the aorta.

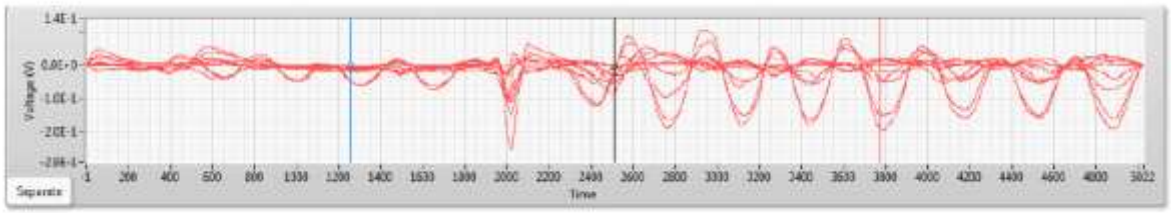


Figure 1: Results from the magnometer to show the 4Hz signal.

The aim and objective of this research project is to explore and review written studies and related articles and journals to decipher if the origin of the signal is the aorta as well as the possible causes of the signal. The resulting literature review determined that many papers could not state the cause of the signal even though it is mentioned or used in some way. Stok et al[6] use a FINAPRES to measure blood pressure at the finger. This FINAPRES was designed by Peňáz[7] in 1973 to measure blood pressure noninvasively. Other papers try to validate a transfer function which is used to convert blood pressure measured on the upper arm, by the cuff sphygmomanometer, into blood pressure of the central arteries[8-10]. The cuff sphygmomanometer is based on the same ideas as the FINAPRES but uses the upper arm instead of the finger. The transfer function incorporates the 4 Hz signal implying that it is too large to be ignored. However the measure of 4 Hz itself is not what is interesting. The interesting part is that when blood pressure and heart rate increase the frequency of the signal increases[6]. The frequency signal is increased during high levels of exercise and stays constant, of around 4 Hz, during low levels of exercise. This means trying to measure blood pressure during high levels of exercise is very difficult[6]. Another method to understand how the blood pressure changes when moving from the central arteries to the peripheries is wave analysis[11,12]. The idea of this is to study the propagation of the pressure wave as it travels.

This can be modelled mathematically, stimulated by a computer model, or can be done experimentally. One model that has been produced is the Windkessel[13], which is a model of the flow of blood around the arterial system. It observes the pressure waveform leading on to the observation of the velocity waveform. The ideas from pulse wave analysis allow blood pressure to be monitored well and can help with diagnosis of disease[12]. Knowing that there is a wave that propagates makes one think that eventually the wave would be critically dampened. However we can feel our pulse in the wrist just as clearly as we can in the carotid artery in the neck. If the wave is being dampened out, why is this so? The answer is that it is a solitary wave, more commonly known as a soliton. A soliton is a nonlinear pulse like wave which can interact and collide with other solitons and will not be altered except by a phase shift[14].

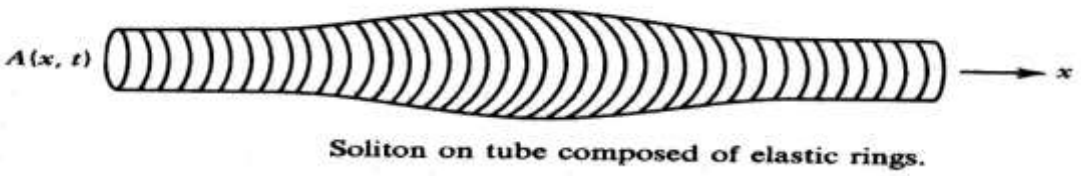


Figure 2: A soliton travelling through an elastic tube[1]

The Circulatory System

Understanding the circulatory system is essential to this project as the role of the circulatory system is to propel blood. 'Blood is a suspension of formed elements in plasma'[15]. These formed elements take up 45% of the blood and contains red blood cells and platelets. The plasma is a solution that contains molecules but can be assumed to be a homogenous fluid. Blood cannot be seen as a homogenous fluid in smaller arterioles and capillaries as the red blood cells are very large compared to the diameter of the vessels. As we are mostly dealing with large blood vessels we will consider blood a homogenous fluid [15]. As blood is propelled around the circulatory system, materials are exchanged through membranes into and out of organs. As the source of the force propelling the blood is the heart, this is the beginning of the cycle. The heart consists of four chambers, which are considered as two pairs of chambers; hence the heart is split into the right heart and the left heart. These act as two separate pumps.

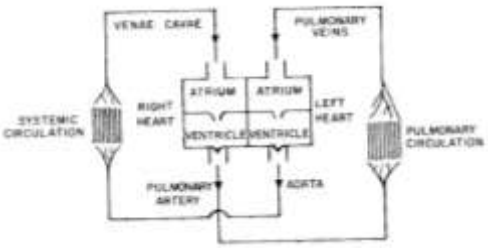


Figure 3: Structure of the heart[3]

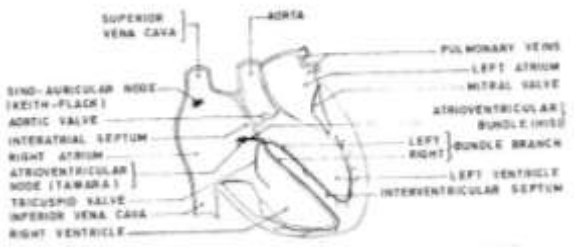


Figure 4: Anatomy of the heart[3]

In each heart there are two valves; in the left heart these are the tricuspid and the aortic valves, and in the right heart there are the pulmonary and the mitral valves. The valves are there to ensure that the blood travels in the correct direction as well as to stop backflow. The arteries are the water pipes of the circulatory system; the blood flows through them around the body, from and back to the heart. [3]

The mechanism of the heart pumping the blood is triggered by an electrical system. This system separates the heart differently to the circulatory system; between the atria and the ventricles.[3] The sino-auricular (SA) node is the pacemaker that generates a periodical electrical impulse. This spreads to the atrial musculature which shortens, as it contracts, so that the atria can pump. The impulse also reaches the atrioventricular (AV) node, which allows a delay before the impulse continues and is conducted through the bundle of His, allowing said impulse to travel to the left and right ventricles and ending at the myocardium. The delay instigated by the AV node allows the heart to pump effectively by ensuring that the atria can finish pumping before the ventricles can begin to pump. [3,16]

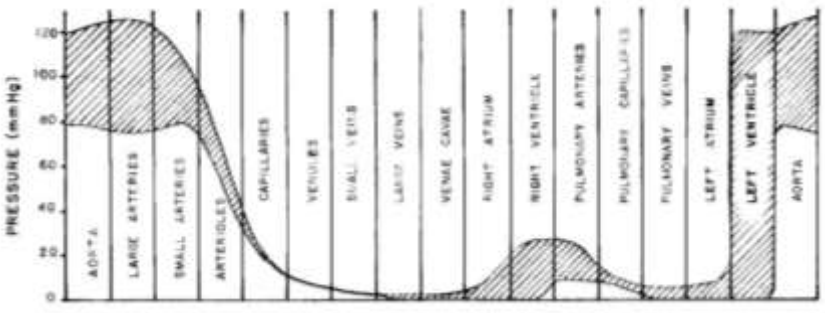


Figure 5: Pressure cycle through the circulatory system[3]

Blood Pressure Measurements

From *Fig. 5* it can be seen that the pressure changes through the cycle and is linked with blood flow. The signal of 4 Hz that is produced appears to be linked with blood pressure. This determines that the measure of blood pressure must be accurate. The blood pressure, being a direct window to the circulatory system, can provide information on the work load of the heart. Blood pressure can be measured invasively as well as noninvasively. It is commonly accepted that the first measurements of blood pressure were done noninvasively by Hales in 1733. Eventually Hales' work led to two techniques which are accepted and known in research laboratories and clinics; needle-manometer and catheter-manometer.[3] Invasive measurement of blood pressure is preferred in research and in the monitoring of patients in intensive care. This is because invasive measurement allows continuous monitoring of blood pressure at any point in the cardiovascular system. It also reduces the chance of errors associated with the cuff[3].

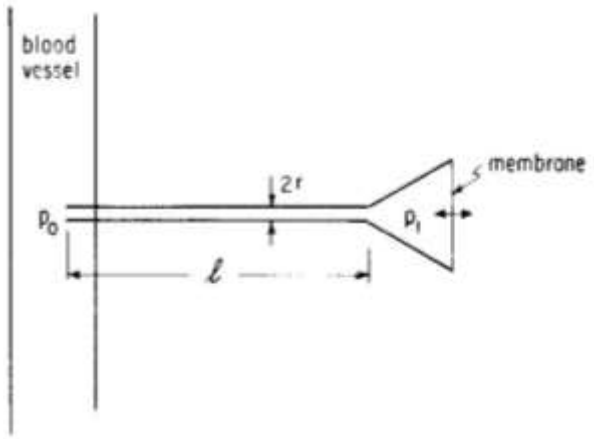


Figure 6: A manometer[3]

A manometer has a needle or catheter connected to it, and both needle or catheter and manometer are filled with fluid. From *Fig. 6* it can be seen that one side of the manometer consists of a membrane. This membrane deforms as the pressure of the manometer changes. This deformation can be measured by various methods[15].

In the needle-manometer system, the needle is inserted into a blood vessel where the pressure measurement is required. If the membrane deforms easily then the signal measured is large. If the measured signal is too large, the blood will flow into the needle, which will deform the signal. This has led to a compromise of a large compliance of the manometer

without interfering with the frequency. This system is useful as it allows pressure to be measured at various places in the cardiovascular system. The concern with this system is that it cannot be used for measuring blood pressure in the central area around the heart, which led to the production of the catheter-manometer system.

The catheter-manometer system was first established by Chaveau and Marey.[17] The equipment comprises of a water-filled tube, with balloons attached at either end. Pressure changes in one balloon cause a change to the volume of water in the other balloon. As the volume changes, a tip attached to the balloon causes a curve to be etched on paper. This method can measure ventricular pressure although it is inadequate for atrial pressure. The current method used is derived using 'Forssmann's[18] ideas on how to inject fluid and drugs into a vein close to the heart.'[3] A catheter is 'a hollow flexible tube for insertion into a body cavity, duct, or vessel to allow the passage of fluids or distend a passageway.'[14] It contains a radioactive substance in order to be seen with x-ray imaging. This allows the catheter to be placed into an exact location while being monitored. This system has many similarities to the needle-manometer system.[3]

There are non-invasive methods to measure blood pressure, which are useful when a quick and safe measurement it required. The common cuff used clinically today, was first mentioned by Riva-Rocci[19] in 1896. The mechanism behind the cuff is to compress an artery, leading to the effect of the compression then being measured. This was extended by Korotoff[20] with the use of Korotoff sounds. These sounds are audible when pressure is between systolic and diastolic pressure. Pressure from the cuff is increased until the sounds cannot be heard, which is at a much greater pressure than the systolic pressure, and is then reduced until the sounds can be heard again.[3,15] Another method to non-invasively measure pressure was derived by Peňáz[7]. The aim of experiment implemented by Peňáz was to measure the blood pressure in the most efficient way possible. The pressure of a finger cuff is controlled by an electro-pneumatic system. 'The photoelectric plethysprogram is recorded at cuff pressure.'[7] This allows one to measure blood pressure as it is directly linked to arterial

flow. From this paper it appears to be an estimation measure of the blood pressure, using a graph, not dissimilar to the current method of using a transfer function. The cuff pressure is controlled by a signal. It is increased to the pressure of the arterial blood vessels at the 'unloading' stage. Peňáz realised that although the advantage of this method was that blood pressure could be measured non-invasively, there would be a significant difference between peripheral and central blood pressure[7].

Similarly there are two other, less used, methods to measure blood pressure noninvasively. Ultrasound can be used by placing a transducer under the cuff, so that Doppler signals can be recorded as the artery opens and closes. It allows systolic and diastolic pressure to be measured for many patients[3].

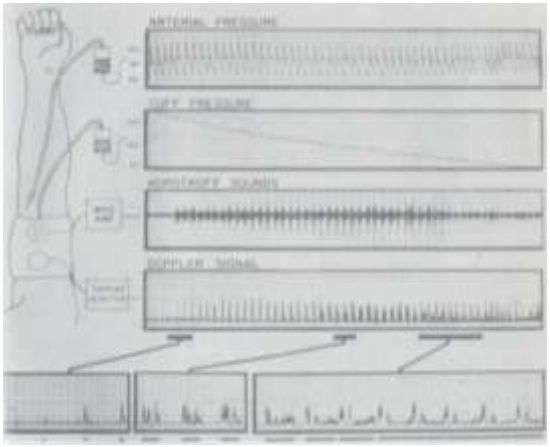


Figure 7: Measurement of pressure using the cuff compared with Doppler[3]

Ultrasound is much more costly compared to the cuff, yet it is not possible to measure the blood pressure continuously. The Valsalva manoeuvre also cannot be used for continuous blood pressure measurements as it requires the patient to blow against a manometer for 30 seconds whilst maintaining a pressure of 40mmHg. A recording is then made which tends to be very close to the central blood pressure. This method however can cause blood clots to detach, resulting in cardiovascular arrest, myocardial infarction, or other serious risks. These are rare but possibly fatal risks, hence the use of this method is a last resort[4].

There have been many research papers that have looked at the difference between the peripheral blood pressure and the central blood pressure. A transfer function is used to translate the pressure measured at the finger or the upper arm, using the cuff, to the central blood pressure. In 2006, Wim J Stok et al wrote a paper titled "Changes in finger-aorta pressure transfer function during and after exercise".[6] This paper investigates the use of a

transfer function to reconstruct the aortic pressure from finger pressure measured by the Peňáz technique. Blood pressure was measured non-invasively, using the Peňáz technique, and a transfer function was used to find the aortic blood pressure, for comparative purposes. This particular paper questions the use of the transfer function during and after exercise. The transfer function was calculated using an autoregressive exogenous model method, predicting the aortic pressure. The predicted estimate was compared to aortic pressure which had been measured invasively. The results concluded that the transfer function changes during exercise as oppose to during rest, determining it. This is an expected outcome as there is a rise in blood pressure due to an increased heart rate during exercise. A generalised transfer function is not exceptionally useful in making precise measurements however it has use during periods of rest. An individualised transfer function is best, as there are less or no calibration errors. This is of course is not possible when using the transfer function in small finger cuffs that are sold to public, for instance in exercise machines. The outcome of this paper with regard to the signal of 4 Hz, is that this signal is used as a control in calculating transfer functions, seeing as the signal tends to be the same in every individual when at rest, increases only with blood pressure.

A further to this study, in 2011, Wim J Stok et al wrote another paper[21], "Aortic pressure wave reconstruction during exercise is improved by adaptive filtering: a pilot study", in which Stok investigated the use of individualised transfer functions at various levels of exercise. Although the generalised transfer function worked for rest periods and low energy exercise, the reasoning behind the newer paper was to improve the aortic pressure reconstruction for a more accurate pressure by the use of adaptive filtering. The aortic pressure was invasively measured as before along with the finger pressure measure. As before the data was determined from rest as well as during exercise, and the transfer function calculated using the same model. The transfer function was filtered to then calculate Fpeak. The Fpeak calculated appeared to be the 4 Hz signal detected by the magnetometer. This

paper shows that during exercise cardiac output (CO) and this signal have a linear relationship.

$$Fpeak = 0.32 * pcCO + 2.68 \quad [1]$$

There is also correlation with heart rate, pressure with respect to time, and mean arterial pressure, but these are negligible compared with pulse contour estimation of cardiac output. The error within this equation is that it suggests that a heart completely at rest i.e. dead, has a frequency of 2.68Hz, which is clearly not the case.

One of oldest papers found on comparing finger pressure and arterial blood pressure was written by Parati et al[22]. In this paper the FINAPRES that was designed by Peňáz is tested. Parati et al wanted to determine the accuracy of the FINAPRES, parallel to the 2006 Stok paper[6]. Parati et al found that the FINAPRES produced similar results for finger and intra-arterial blood pressures. Parati et al states that the Valsalva manoeuvre gives good results for blood pressure, even when the pressure is changing rapidly. This is not the case with FINAPRES. The Valsalva manoeuvre method however is not used due to the risk of cardiovascular events as discussed previously.

In addition to the 2011 Stok paper[21], there has been further research into the transfer function. Gallagher et al[10] did a study to validate the use of the standard generalised transfer function. Although it is convention to use this transfer function, more data was required in order to confidently use the transfer function for an entire population. The generalised transfer function is used to calculate the aortic pressure from the radial artery pressure, and it involves calibration errors for correction of the distortions in the arm.

In this paper the signal of 4 Hz is apparent, and it is used in producing the transfer function. The measurement of aortic pressure is done invasively and compared with aortic pressure predicted using the transfer function. The population of the study was varied and diverse in terms of gender, age, and pathology. No significant difference was observed in the use of the transfer function. Other studies have been approved for research of the transfer function in

different conditions, for example in populations of subjects with long term health conditions, or in subjects using regular medication.

The conclusion reached is that the transfer function itself is accurate to use, yet the error lies with the cuff. The solution to this is to utilise the cuff as well as pressure pulse waveform. The use of pressure pulse waveform will later be discussed in this project.

Other than the generalised transfer function, there is an individualised transfer function which can be compared with the generalised transfer function. A study undertaken by Sharman et al[9], with similarities to that of Stok[21] and Gallagher[10], used pulse wave analysis. It has been shown by some studies that knowing the aortic blood pressure during exercise can provide better prognostic information than at rest[12] as it can indicate or predict disease. Stok[6] shows that at high levels of exercise the cuff or FINAPRES can become limited, hence the usage of pulse wave analysis in addition to the cuff, aids in measuring the central blood pressure more accurately. This study has determined that there are differences between the central and peripheral pressures, and that the use of tonometry and pulse wave analysis together can record blood pressure during high levels of exercise.

Arterial blood pressure is much more useful for diagnosis of cardiovascular complications than the peripheral blood pressure. There are many various methods of determining the transfer function, including the Fourier analysis used by Stok at al[21], and in Karamangolu et al[23], the use of a model of segments of the arterial tree. These methods are all debatable and have been validated by some clinical trials, yet this validation is not accurate as different researchers use variable methods. Westerhof at al[8] investigates 'the influence of arterial, blood and load parameters on the transfer of pressure.'[8] This study found that the transfer functions from the aorta to the brachial artery were the most alike. It also determined that at rest, a generalised transfer function can be used, and that measuring the velocity of the blood flow enhances the accuracy of the transfer function for exercise. From all these papers, it can be concluded that a generalised transfer function can be used for the population, as a whole,

to measure blood pressure as rest. When exercise is taken into account however, the 4 Hz signal changes, causing a change in the transfer function, regardless of how it is calculated. This is due to the change in blood flow which is directly linked to the work load of the heart, the blood pressure, and the structure of the arteries themselves. The length of time of the heart cycle varies, explaining why the transfer function used by Stok et al and others are not useful during strenuous exercise.

Measurement of Cardiac Output

Like pressure, flow velocity of the blood is very difficult to measure which is problematic as it is a main interest. The most desired measurement is cardiac output and thus far it cannot be measured with satisfactory accuracy. There are several well-known methods in measuring cardiac output; The Flick Principle, The Stewart Principle, The Windkessel, thermodilution, echocardiography, pulse contour cardiac output, Doppler ultrasound and others. [3,24]

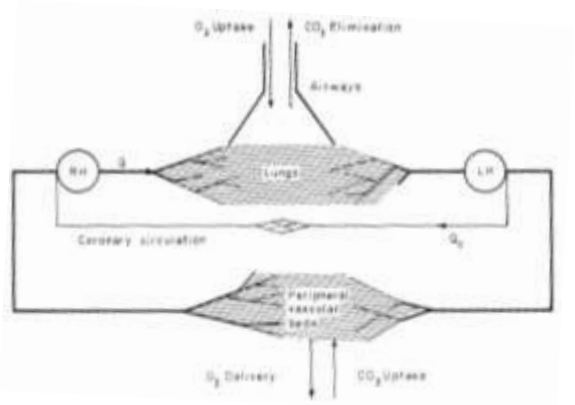


Figure 8: The Fick Principle[3]

The Flick principle (1876) being one of oldest, makes use of the circulatory system. Fig. 8 shows the blood flow through the lungs and the gas exchange between the blood and the air. The O_2 uptake into blood and CO_2 diffusion into the alveoli in the lungs allows cardiac output to be determined. It can be recorded in two ways; the direct Flick technique or the indirect Flick technique. The direct Flick technique uses O_2 uptake which can be easily found by analysing the air that is inspired and expired. Oxygen in the pulmonary venous blood is estimated from samples taken from an artery for equation [2], below; the oxygen in the pulmonary arterial blood needs to be measured. For this a catheter is inserted into the pulmonary artery. A similar method is used for equation [3].

$$\mathrm{CO} = \frac{O_2 \text{ consumption per unit time}}{O_2 \text{ content in the pulmonary venous blood minus } O_2 \text{ content in pulmonary arterial blood}} \quad [2]\,^{3}$$

$$\mathrm{CO} = \frac{CO_2 \text{ elimination per unit time}}{CO_2 \text{ content in the pulmonary arterial blood minus } CO_2 \text{ content in pulmonary venous blood}} \quad [3]\,^{3}$$

The indirect Flick technique was developed to eliminate the use of the invasive measurements required in the direct Flick technique. To measure oxygen in the pulmonary venous blood, it is assumed that O_2 in alveolus air is equal to oxygen in the blood in the

pulmonary capillaries which can be estimated from analysing air that is expired. The oxygen in the pulmonary arterial blood can be estimated as being equal to the oxygen in the blood that leaves the lung to the oxygen in the blood that enters the lungs. For this, a patient will breathe into a bag of which volume of air is known. Once the equilibrium is achieved, an air sample can be taken for the estimation. [3]

The Stewart principle is modified from Hering[25]. Hering suggests that if an identifiable substance is injected into moving fluid, the detection of the substance at a later point will allow flow velocity to be measured. Stewart[26] introduced a new principle which is used to measure cardiac output. If a substance with a steady rate, m, is injected into a fluid and mixes with the fluid homogenously, its concentration, c, is equation 4.

$c=m/CO$ [4] [3]

When the system is in a living animal, the injected substance must be small enough to not affect the system. Stewart[27] provides an alternative, a bolus injection i.e. a rapid injection, causing m to become a function of time, giving equation 5.

$c(t) =m(t)/CO$ [5] [3]

This relationship does not consider error due to mixing. All of the injected substance passes the sampling site; therefore the integral below can be used:

$$Q \int_{c=0}^{\infty} c(t)dt = \int_{c=o}^{\infty} m(t)dt \quad [6]^3$$

As the total volume of substance injected is known, M, m(t) can be eliminated.

$$Q = M/\int_{c=0}^{\infty} c(t)dt \quad [7]^3$$

The application of this equation can be difficult as the concentration curve is not as predicted due to the fact that recirculation starts before the concentration curve can reach a plateau. There are modifications which can be made to help model this.

The Windkessel model can be used to determine cardiac output quickly and noninvasively by using equation 8.

$CO = v_s f$ [8][3]

V_s is the stroke volume and f is the heart rate. As stroke volume is linked with blood pressure, the ease of cardiac output depends on the non-invasive measurement of pressure. As previously discussed, this is inaccurate, determining the cardiac output also inaccurate.

The Windkessel model is very important in modelling the arterial system. Westerhof et al[13] discussed the Windkessel model, named after its original inventor Frank Windkessel. The model describes the flow of blood around the arterial system. It is most accurate when used for approximation of the ventricular afterload. The first model was a lumped model i.e. it does not consider spatial variability.

It is known and widely accepted that Hales was the first to measure blood pressure, finding it inconstant. Frank Windkessel formulated the two-element Windkessel model which states that resistance is inversely proportional to (blood vessel radius)[4] meaning that small arteries have the most resistance. The summed resistance will find the systemic vascular bed resistance, also known as peripheral resistance, R, which would be calculated by the mean pressure of the aorta / cardiac output.[13] The two-element model predicts, in diastole (where the aortic valve is closed), that pressure decays exponentially with a time delay of RC. This time delay can be used to determine CO.

The two-element model needed to be improved which provided a gateway to the three-element Windkessel. For this model, a Fourier analysis and a calculation of impedance are required, the new element being impedance. It is shown that phase change does not change the wave shape. In actual fast the wave shape is changed by the time delay. These models contained many errors therefore in order to reduce said errors the four-element Windkessel was created. The fourth element is the total arterial inertance which is a measure of pressure gradient in a fluid required to cause a change in flow rate with time. It affects only mean

term and low frequency of impedance and is very hard to calculate. As a result the three-element model is the preferred.

In order to model blood flow in arteries correctly, not only the understanding of how it propagates through the arterial system is essential, but also how the arterial system affects the propagation of the blood. Blood vessels behave with viscoelastic properties, demonstrating viscous and elastic properties, affecting blood flow. To understand these effects the viscoelastic behaviour needed to be studied further. The biophysicist Thomas Young was renowned worldwide as the main contributor to physics of elasticity and the relation between the arteries and the velocity of the arterial pulse. In addition to the viscoelastic properties of blood vessels, another significant consideration is that since 1950, the arterial system has been treated as a steady-state oscillation produced by the heart beating.

To start modelling the arterial system, an artery is thought of as a long cylindrical tube with a steady flow along it. It is now known that the blood is not actually a like neo-Newtonian liquid; its flow rate varies so there is a Reynolds number to demonstrate this.[2] Blood flow can be turbulent, which is when the steady flow is disturbed[14]. This disturbance increases until it comprises of all the liquid.[2] When turbulent flow occurs, a murmur is present which is hypothesized to come from the aorta. This can actually only be heard in a person with aortic valve stenosis in which the valve does not fully open[15]. From this turbulence it can be assumed that this is significantly related to the arterial wall material. Turbulence also has a tendency to occur after peak systole and disappears rapidly afterwards[15]. This is likely due to hydrodynamic instability, and this knowledge can aid in diagnosis of arterial disease.[15] Blood flow is also thought to be pulsatile, making it difficult to model due to the heartbeat generating pulses.[28]

When modelling, branching also needs to be incorporated into the cylindrical tubes. To do this simply, the following assumptions need to be made; pressure stays constant, the overall

length of the branches is the same and fluid resistance stays the same in an individual branch[2]. This would mean that the vascular resistance increases in each branch and is determined by the radius of the vessels. Thus the pressure drops from arteries to capillaries and peripheral resistance will equal mean aortic pressure – mean right arterial pressure / CO.[2]

Vessel	Radius (cm)	Mean flow velocity (cm/sec)	Shear rate at wall (sec^{-1})
Ascending aorta (man)	1·25	25	80
Ascending aorta (dog)	0·50	25	200
Inferior vena cava (man)	1·75	12	28
Arteriole (small artery)	0·01	1·0	400
Capillary	0·0005	0·5	400

Table 1: Change in flow velocity as the radius of the vessel changes2

Table 1 shows how flow velocity changes with the radius sixe decreasing. It shows that the 4Hz could be produced from the aorta. As blood is a non-Newtonian liquid; the viscosity of blood depends on the tube size, and as blood has oscillatory flow, the effects of this need to be known[15]. It was deciphered that blood still has stable flow with some turbulent flow, which can be observed in *Fig. 9.* [2]

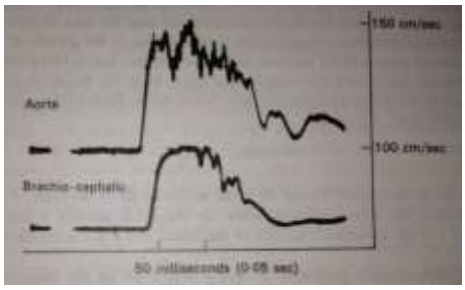


Figure 9: Arterial flow pulses [2]

It is not enough to just model an artery as a cylindrical tube as arteries are elastic and so have varying diameters. The velocity of the pulse propagation relies on the elasticity of the wall, but as previously discussed, the arteriole is more complicated due to its viscoelastic properties[15]. Elastic substances have an elastic modulus which can explain how a substance deforms[2]. In the arterial wall the elastic modulus increases as the circumferential strain increases.[2] This allows blood vessels to maintain stable as the pressure changes. When arterial stiffness occurs, the elastic modulus increases and can cause serious damage as the blood vessels will not remain stable. As the elastic modulus increases at a constant rate, the pressure increases with the rate of increase of blood volume, eventually leading the elastic

modulus to reach infinity causing the artery to burst[2]. In a viscoelastic substance it is difficult to model the arterial wall as viscosity is a mathematical abstraction, [2] thus trying to mimic the dynamic elastic behaviour of the arterial wall is improbable. The wall elasticity determines the velocity of the propagation of the pressure-waves[15].

M Karamanoglu et al investigated 'the influence of the large arteries and the peripheral load on pressure wave propagation'.[23] To do this they had to create 'an anatomically realistic multibranched model'[23]. In other words they created an accurate model of the human upper arm to mimic what would happen in physical blood vessels. The large arteries and peripheral load properties are represented as windkessels.

Other papers[29,30] have stated that there are differences in central and peripheral blood pressures; meaning the pressure wave in the upper arm would be different to the central pressure. Karamanoglu's model takes wave propagation and reflection into consideration to make the observations more accurate. The 'pressure transfer functions and peripheral pressure waves'[23] were analysed, with a representation of an artery being a viscoelastic thin and tethered tube with negligible nonlinear properties This was used to calculate pressure wave transmission from which *Table 2* was compiled.

	l, cm	$2r$, cm	h, cm	E, $\times 10^6$ dyn/cm^2 Young	Old	Θ, degrees
Ascending aorta	4.00	2.90	0.16	6.58	13.29	4.41
Aortic arch	2.00	2.24	0.13	6.98	14.43	4.64
Brachiocephalic	3.40	1.24	0.09	7.28	11.65	5.81
Subclavian	6.80	0.80	0.07	7.28	10.19	7.00
Internal mammary	15.00	0.20	0.03	10.40	14.56	12.00
Vertebral	14.80	0.19	0.05	10.40	14.56	21.05
Costocervical	5.00	0.40	0.05	10.40	14.56	10.00
Suprascapular	10.00	0.20	0.02	10.40	14.56	8.00
Thyrocervical	5.00	0.20	0.03	10.40	14.56	12.00
Axillary	6.10	0.72	0.06	8.58	12.01	6.67
Thorocoacromial	3.00	0.30	0.04	20.80	29.12	10.67
Axillary	5.60	0.62	0.06	8.58	12.01	7.74
Subscapular	8.00	0.30	0.04	20.80	29.12	10.67
Brachial	6.30	0.56	0.05	9.74	13.64	7.14
Circumplex scapular	5.00	0.20	0.03	20.80	29.12	12.00
Profunda brachii	15.00	0.30	0.04	10.40	14.56	10.67
Brachial	6.30	0.52	0.05	9.55	13.37	7.69
Superior ulnar collateral	5.00	0.14	0.02	20.80	29.12	11.43
Brachial	6.30	0.50	0.05	9.56	13.38	8.00
Inferior ulnar collateral	5.00	0.12	0.02	20.80	29.12	13.33
Brachial	4.60	0.48	0.05	9.73	13.62	8.33
Ulnar	6.70	0.42	0.05	10.40	14.56	9.52
Radial	11.70	0.32	0.04	10.40	14.56	10.00
Ulnar	8.50	0.38	0.05	10.40	14.56	10.53
Interossea	7.90	0.18	0.03	20.80	29.12	13.33
Radial	11.70	0.32	0.04	11.55	16.17	10.00
Ulnar	8.50	0.38	0.05	11.14	15.60	10.53

l, Length; r, radius; h, thickness; E, Young's modulus; Θ, phase.

Table 1: Changes in E from young to old and the change in E with the variable l [23]

Table 2 concludes that the older the subject, the larger the value of the elastic modulus, E, therefore an increase in velocity is assumed[23]. A signal of 4 Hz can clearly be seen as E increases and pressure rises at a point in time, which is where the blood reaches the aorta in *Fig. 10*.

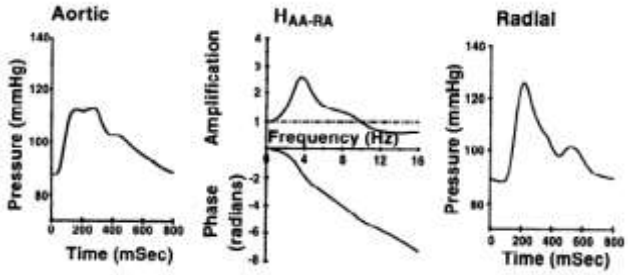


Figure 10: Pressure pulses in aorta and peripheral [23]

There is little or no longitudinal movement of the arteries as a pulse passes through due to the artery being anisotropic[2]. Naturally arteries are subjected to some longitudinal stress, although trying to model this with the current models, such as the spring and dashpot, is very difficult. It is obvious that when trying to determine the thickness of the arterial wall, a dynamic and static Young's modulus are required[2].

Fig. 11. shows that around 2-4Hz there is an apparent increase in the Young's modulus which is also be seen in Karamangolu et al[23]. This implies that viscosity is inversely proportional to frequency, which is unlike the spring and dashpot model.[2] When trying to measure viscoelastic properties of the arteries, Gow and Taylor[31] analysed the pressure and dilation curves using harmonics as the arterial wall had been found to show non-

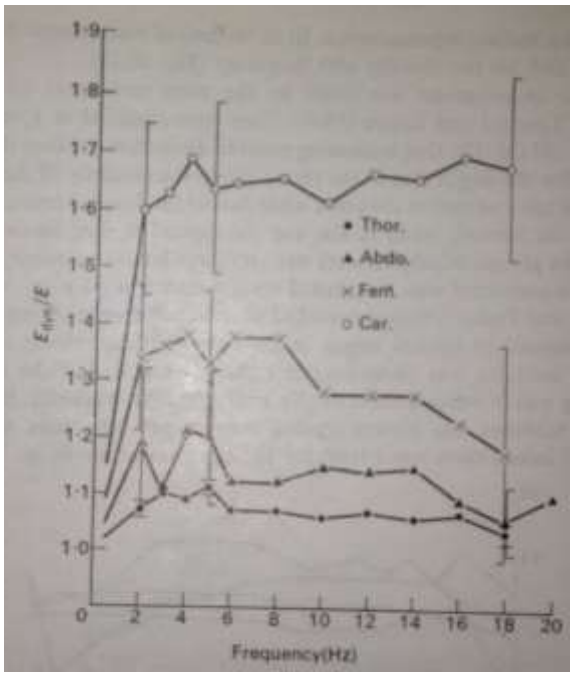


Figure 11: Ratio of Edyn to Estat in arteries[2]

linear behaviour. Using equipment to measure elastic modulus, the wave velocity can also be measured as there is a direct comparison between results from radial dilation and wave velocity[32].

Wormersley[28] developed a model of the circulatory system involving an elastic tube with longitudinal restraint, and walls loaded by a mass. This model has been modified to include viscoelastic behaviour and this has been tested on a rubber model. The rubber model includes; a perfectly elastic wall, a long wavelength compared with the circumference of the tube which is infinite on either side of the region of study implying that there is no entrance or end effect.[2] The assumption for perfectly elastic walls is not a good assumption and also as it is not infinite on either side, wave reflections do take place[33]. For a more accurate model there are considerations of; longitudinal and radial movement of the wall, pressure-flow relationship, the propagation of the wave and the equations being non-linear[2].

Thus far in the models wave reflection has been ignored, yet it does take place as arteries are not infinite tubes as they have been modelled. The arterial tree acts as an almost perfect sound-absorber due to internal damping of the system which can be seen in the rubber model[3]. This means that reflected waves that are produced in the peripheries of the arterial tree are dampened out quickly. The ideas of these wave reflections are included in the later elements of the Windkessel and in pulse wave analysis[12].

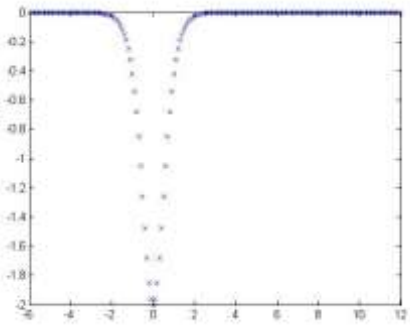
O'Rourke et al[12] look into the history and theory of the use of the arterial pulse pressure measured by the blood pressure cuff to find the pressure wave from the ascending aorta. It is widely known that Fredrick Akbar Mohammad was the founder of pulse wave analysis. For pulse wave analysis, pressure first needs to be recorded, the pressure waves need to be consistent with the pulse beat, and the greatest amplitude is preferable[11]. The measuring of pressure noninvasively is still an issue and O'Rourke at al suggest that this is due to neither the upper arm length, and the pulse wave velocity, not being too variable in comparison to age[12]. This paper clearly shows that there are a number of factors that can affect the arterial

pulse; ‘growth and development, ageing, physical fitness, food, heart rate, exercise, body height and gender’[12] along with disease. The arterial stiffness previously discussed can occur due to ageing. It is a degenerative process and the increase in pressure is known as hypertension. Hypertension is known to cause an increase in the speed of degeneration of the aorta and can cause pressure changes[3]. The generalised transfer function can be used when this is the case[10]. Heart failure can be detected using pulse wave analysis but not all diseases can be screened using this as not all diseases will affect the arteries. Some effects of drugs can also be analysed[12] using this method. Currently, pulse wave analysis is used for diagnostic purposes, which is the desired use for the 4 Hz signal, and with the correct research the diagnosis of disease could be achieved using this 4 Hz signal. The rationale behind the thinking that using this signal will be better than pulse wave analysis is that it will not use the cuff to noninvasively measure pressure and therefore may be more accurate. Segers et al[34] have also delved into pulse wave analysis leading to the idea of the pulse being a solitary wave or a soliton.

Soliton Theory

A description of a soliton is 'a pulse like wave that can exist in nonlinear systems, does not obey the superposition principle, and does not disperse'[4]. In other words it a short single pulse[2] which propagates with a constant amplitude and does not change if it collides or interacts with another soliton. Lamb's[1] book on soliton theory has provided equations that have allowed for mathematical modelling of soliton interacts. First a single soliton needs to be modelled and this has been done using the Korteweg-de Vries equation to provide a solution for a steady-state pulse.

$$U = -\frac{c}{2} sech^2[\frac{\sqrt{c}}{2}(x - ct)] \quad [9]^1$$

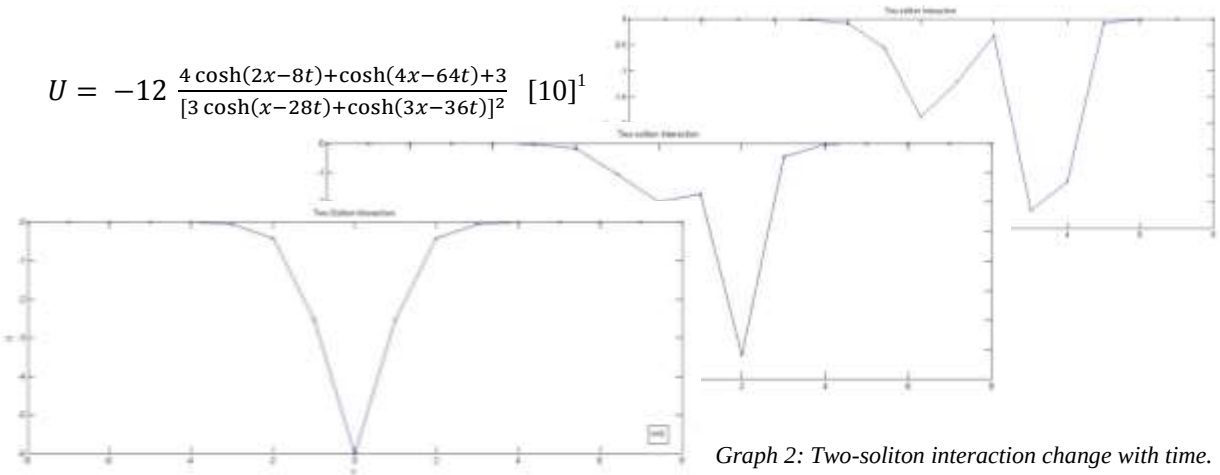


Graph 1:Single soliton movement

Graph 1 shows the movement of a soliton along x vs U at t=0. As the time changes the soliton does not change, it propagates along at the same amplitude.

The two-soliton solution:

$$U = -12 \frac{4\cosh(2x-8t)+\cosh(4x-64t)+3}{[3\cosh(x-28t)+\cosh(3x-36t)]^2} \quad [10]^1$$



Graph 2: Two-soliton interaction change with time.

Graph 2 shows solitons before and after interaction. This has also been modelled by Bastani[35] for a two-soliton interaction. It is assumed that the arterial pulse is dicrotic and that a steepening in arterial pulse wave is related to an increase in pulse-wave velocity.

There are also reflections and transmissions in the arteries which have been ignored for modelling purposes. These models can be produced but are much more complicated. The simplest case has been considered by McDonald[2] which is injecting fluid into one end of a water filled rubber tube, an experimental model to show the reflections.

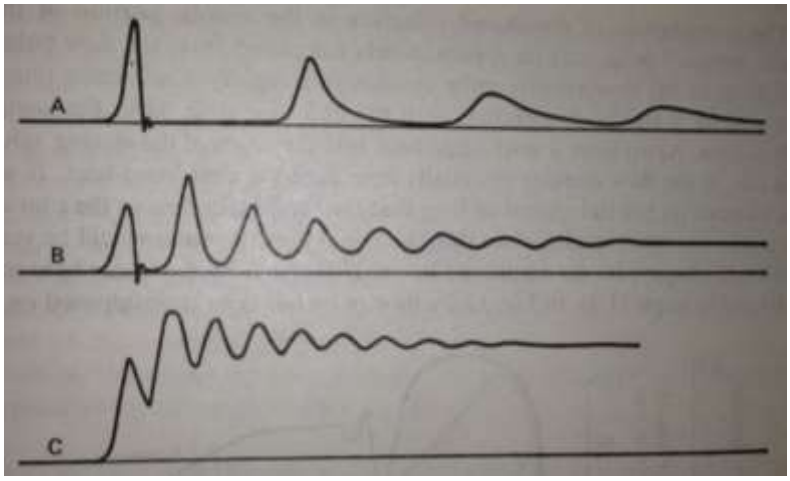


Figure 12: The behaviour of pressure pules at varying lengths, due to an injection of liquid[2]

Fig.12 shows interaction between incident and reflected waves in differing sized tubes. *Fig.12(A)* shows a tube that has been clamped at a far distance. The initial soliton has completed and the pressure has stabilised before the reflection has returned. *Fig.12(B)* shows a tube that is clamped at a smaller distance than *Fig.12(A)* but still the original soliton is not affected by the reflections. *Fig.12(C)* shows a tube that has been clamped at a closer distance than *Fig.12(B)*, so the reflected soliton returns before the initial soliton is completed. Knowing this, it becomes easier to see that the joining of the solitons will give a curve similar to the systolic pressure of the aorta. From this figure in *A* it can be seen that the waves are altered in shape and amplitude when they are reflected, this is because the soliton is made up of a spectrum of frequencies and the wave velocity will vary with frequency. This is known as dispersion and can be seen in *Fig.12(A)*.

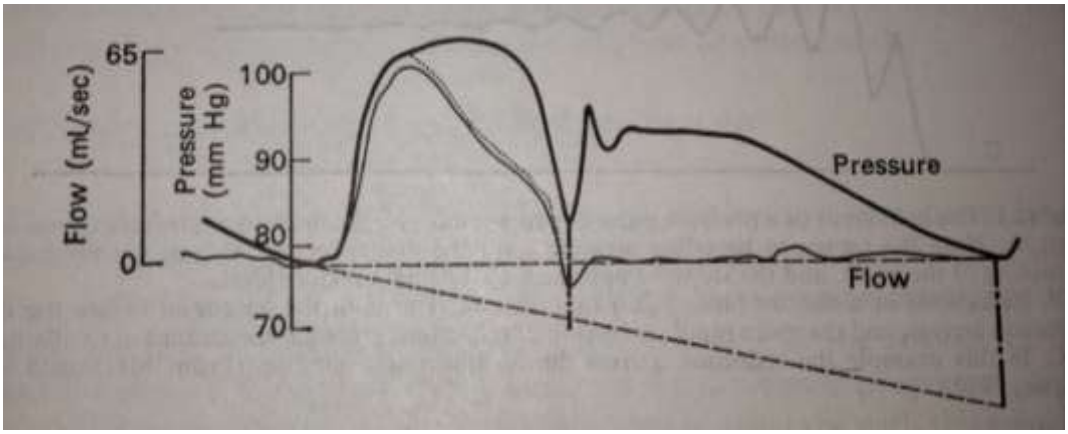
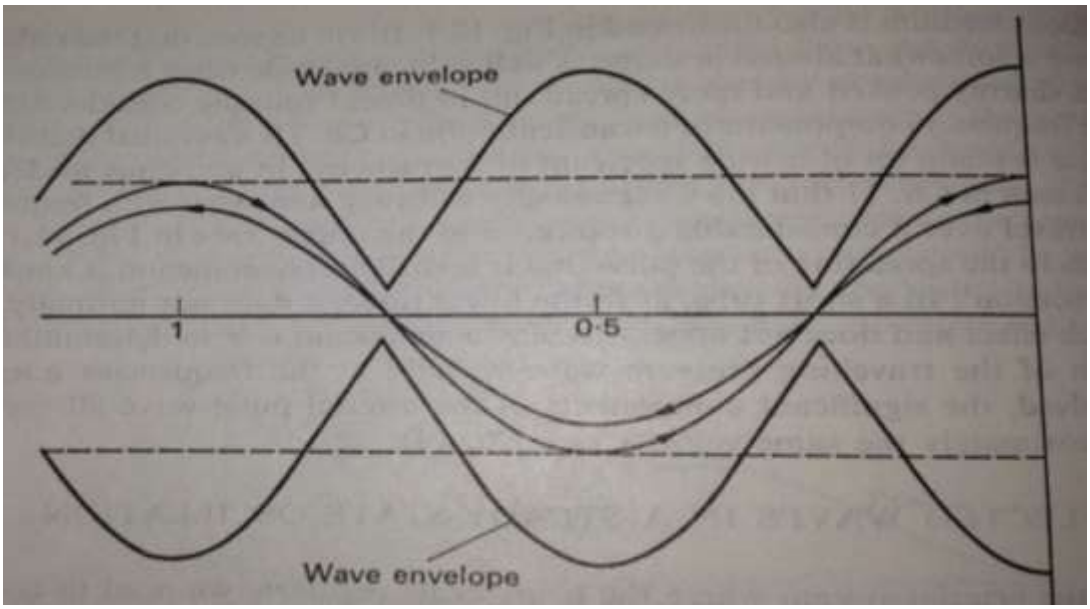


Figure 12: Pressure curve of aorta superimposed with aortic flow[2]

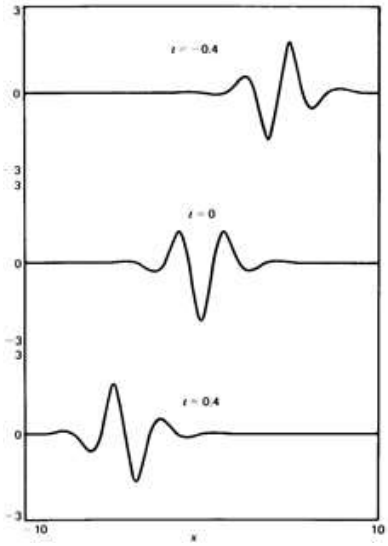
Fig.13 shows that a rise in pressure beyond systole is due to the reflection wave. There is no doubt that the reflection wave contributes to the arterial pressure. The question that remains is if this reflected wave and the 4 Hz signal can be used for diagnostic purposes.

As the arterial system involves a regular beat from the heart, the reflections are in steady-state oscillations, which as modelled in FIG the solitons are not changed if they propagated forever. Yet let us consider a tube which is closed at one end. There will be an incident and reflected wave to give a graph as below:

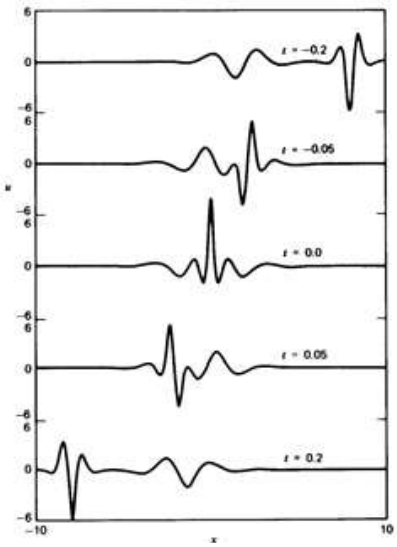


Graph 3: Interaction of centrifugal and reflected wave at closed end

This can also be modelled using a modified version of the Korteweg-deVries equations:

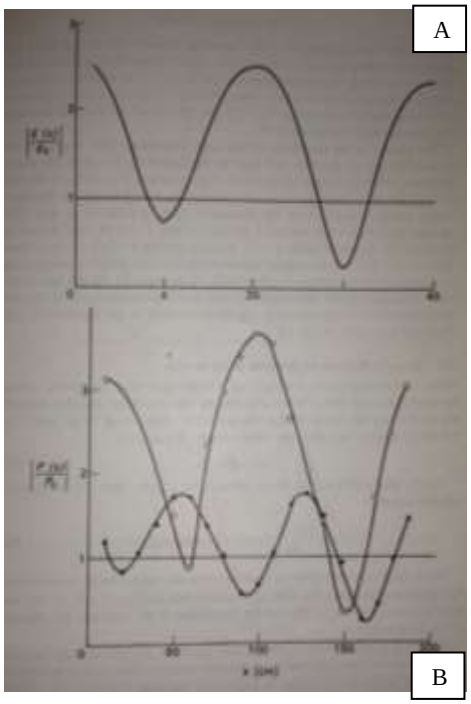


Graph 4: Solution for modified Korteweg-deVries equation [1]



Graph 5: Solution for modified Korteweg-deVries equation, for the interaction of two-solitons [1]

The maxima become infinitely larger and the nodes remain zero. This is due to resonance, and a standing wave is produced. However damping is involved so the reflected wave will always be smaller in amplitude than the incident wave. The arterial system does not have a closed end so the mathematical analysis is not completely identical with the system and is done using an electrical transmission line which is thought to be analogous with the arterial system.



Graph 4:
A-Variation in modulous of voltage for a transmission line l=40
B- Actual pressure in a rubber tube [2]

A shows the variation in voltage along the transmission line and B shows the there is a 7Hz resonance at 7,400cm/s when there is a pump frequency to simulate the heartbeat, the tube resonates. This could be the reason for the 4Hz signal produced in humans.

When there are reflections, the apparent phase-velocity varies like the amplitude of the pressure

oscillation with an exception. This exception is it rises at an open end rather than falling as the pressure oscillation does. In addition, within the previously discussed arterial tree there is branching and there is a reflection coefficient that changes. It is difficult to know the coefficient as all point making computer simulation very important. When looking at the reality of the arterial tree behaviour, the percentage of the amplitude of the reflected wave compared with the incident wave is observed in (A). (B) shows how the reflected wave has a phase difference from being closed at 0˚ and open at 180˚.

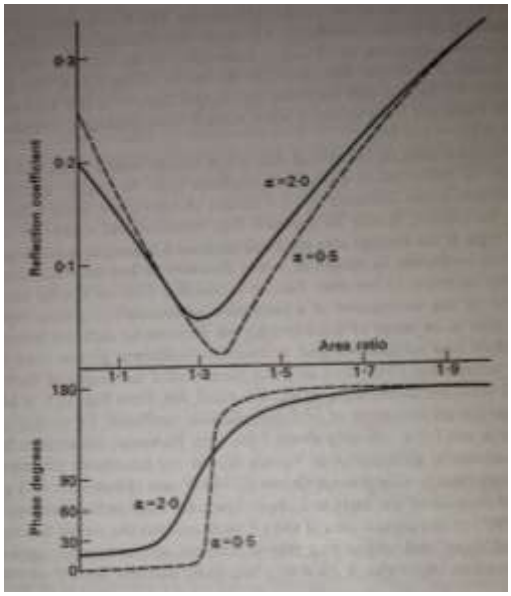


Figure 14: Theoretical magnitude of reflection when there is a bifurcation[2]

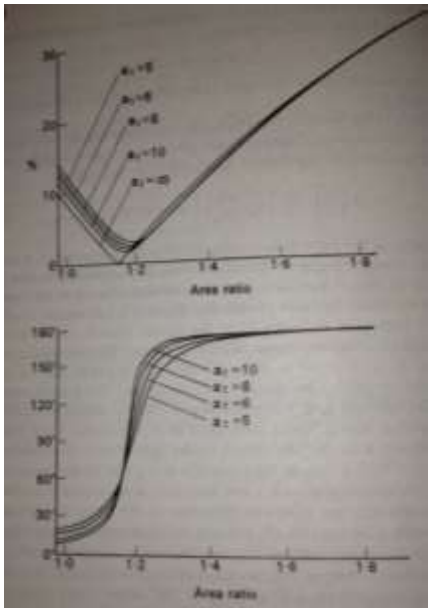


Figure 13: Magnitude of reflection when there is a bifurcation.[2]

Fig. 14 shows the theoretical curves at bifurcation of reflections for smaller vessels than in *Fig. 15*. It can be assumed from these figures that reflection will always be the closed type.

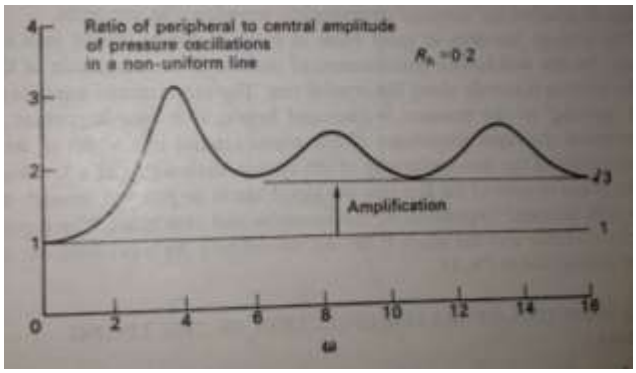


Figure 15: Amplitude of reflections in a non-uniform line[2]

Fig.16 shows how the amplitude of the reflection changes in a non-uniform line. The frequency reduces and the wave-velocity increases. From this is can be seen that as the soliton travels through the arterial tree its amplitude rises. Wen-Shan

Duan et al[36] have concluded that when there is an arterial branch, only one soliton is transmitted into each branch and the amplitude of the soliton is larger than the initial transmitted wave. This change in amplitude is due to the varying radius of the vessels. Therefore disease can be observed from the pulse blood waveform due to changes in the amplitude and velocity. Depending on the type of bifurcation parameters a reflection can be considered negligible; however inserting prosthesis will change the reflection coefficients which can change the propagation of the soliton. As a result these changes could be measured using pulse wave analysis or the 4 Hz signal.[37,38]

In living animals, the analysis of wave-reflection is more complex than the previously discussed single harmonic oscillation and the soliton. When a large vessel bifurcates there is a constant reflected wave that is known. Reflection at the smaller vessels i.e. arterioles, are more varied hence making it more difficult predict behaviour.[2] As discussed by O'Rourke et al[12] , measuring the wave is useful in diagnostics. To further the understating of pulse wave analysis, McDonald[2] looks at pulse in dogs and the effect on blood flow.

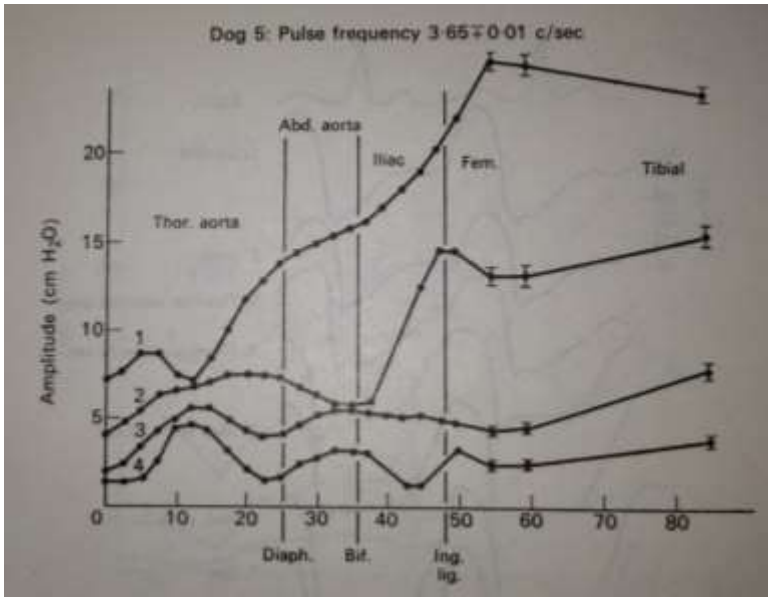


Figure 16: The distance from aorta outwards with amplitude of pressure [2]

Fig.17 shows a pulse frequency of 3.65±0.1Hz. The pressure is measured invasively and then a Fourier analysis done.

Fig.18 shows an analysis of the first four harmonics over the entire arterial tree. There is a time delay between the zero line and the beginning of the systolic rise which is due to three things; the time of electrical excitation that occurs in the left ventricle when the muscle fibres shorten; the time between the AV

valve closing to the opening of the aortic valve; the time for the pressure wave to propagate to wherever the measurement of pressure is being made, the most prominent reason. This can be made more accurate by measuring the pressure at simultaneous times at points between which the distance is known.[2]

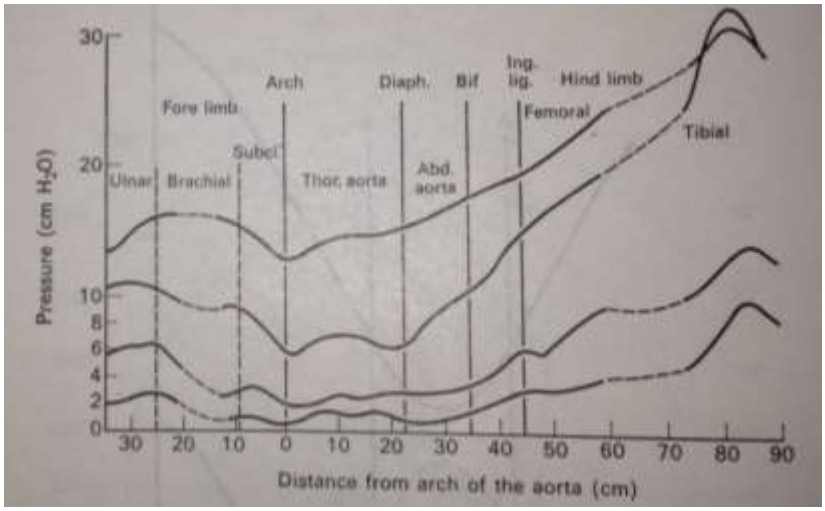


Figure 17: Analysis of first four harmonics[2]

To understand the reflected wave and the transmission wave better, impedance needs to be considered. In physics, impedance is a measure of the opposition of flow in any system.[4,14] It is mostly known in circuits. It can also be used to study the flow of pulsatile liquids in relation to a pressure-gradient. The term 'input impedance'[2] is used to distinguish impedance at the origin, which has been modified by reflected waves, from impedance due to transmission of the artery.

Seeing the changes in pressure and flow waves simultaneously is the first step to understanding the effects of impedance.

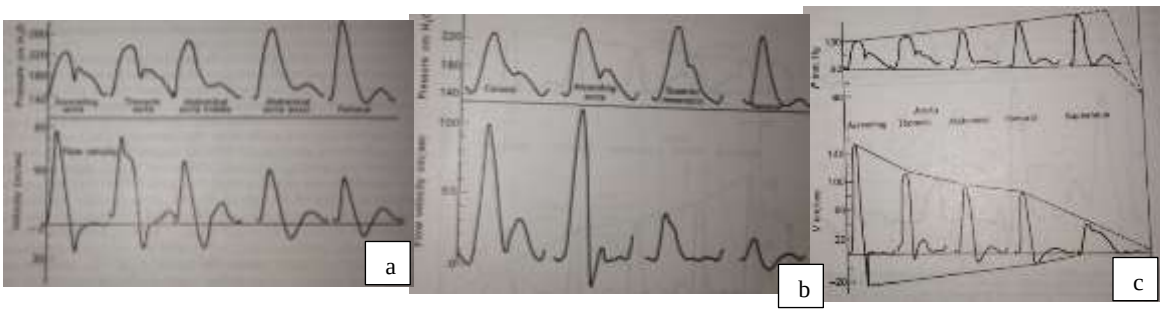


Figure 18a,b.c: Pressure and velocity pulse[2]

Fig.19 shows that pressure increases as velocity decreases when moving away from the heart. This is because impedance increases as the distance from the heart increases. *Fig.19c* shows that the capillaries are pulsatile. It also shows that in the peripheral vessels the reflection waves have a very marked effect. In the centre due to attenuation from the peripheries, the effects of reflection are reduced. The input impedance is important when thinking about work load on the heart.

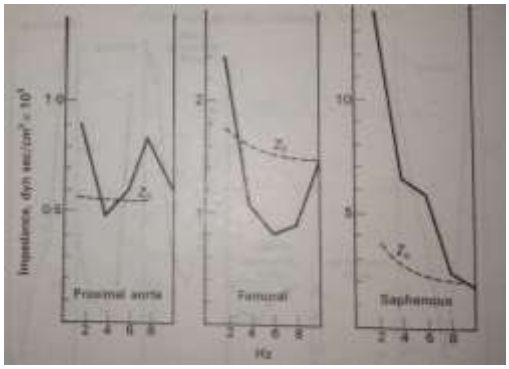


Figure 19: Impedance in the arteries[2]

The femoral artery is taken to be what is typical of peripheral branch arteries as it is the most studied. *Fig.20* shows that impedance increases in the peripheral arteries. Measuring the input impedance in the ascending aorta is done as it shows the 'output load on the left ventricle'[2]. The impedance has a shallow minimum around 5 Hz for a dog, and this minimum represents a quarter wave-length minimum of the reflected waves from the short arterial system. As it is known, a rise in pressure causes the minimum to shift to higher frequencies. The phase becomes close to zero at 4-5 Hz. This is the case in dogs, but as we know in humans, the aorta is longer so the frequency measured is reduced to 4 Hz. This appears to be the cause of the 4 Hz signal that is measured.

The wave is reflected from the lower part of the body and is returned to the aorta arch. Above 15 Hz the input impedance becomes constant, so at high frequencies it should be close to zero. In peripheral arteries the reflected wave effects reduce due to attenuation.

Attenuation is important to the wave velocity and the true wave velocity is 'the velocity of the centre of area of the group'[2], where the group is a set of waves. To determine the velocity of the flow the blood flow itself needs to be measured with methods previously discussed. The simplest method to measure flow velocity is an invasive procedure which requires a vessel to be cut and for blood to flow into a cylinder during a known time.[3]

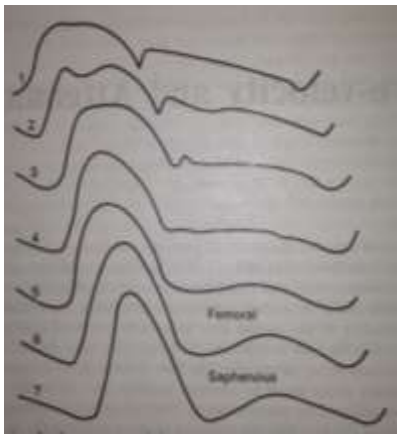


Figure 20: Pulse waves along arterial tree [2]

Another type of velocity is phase velocity; this is much easier to measure as it varies with frequency. This also means that is closely related to impedance. An increase in the mean arterial pressure will cause an increase in the pulse-wave velocity. From *Fig.21* it is clear that even when pressure is the same at point the velocity is not the same. A foot-to-foot velocity correlates with mean arterial pressure. Wave velocity that is measured using mean phase velocity is derived using the whole wave. It is only affected by the blood flow velocity. This is very low when compared with pressure wave-velocity.

The wave velocity is affected by attenuation which is caused by the viscous like properties of the arterial wall. As a wave travels it dissipates energy which is seen as attenuation. It can only be seen by experiments and is too difficult to model. Knowing this, if an arterial wall is damaged, it will affect the attenuation and this affect can be measured.

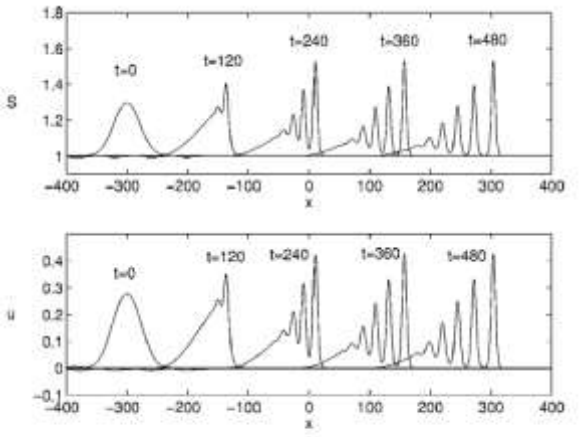


Figure 22: Profile of tube and velocity at different times [5]

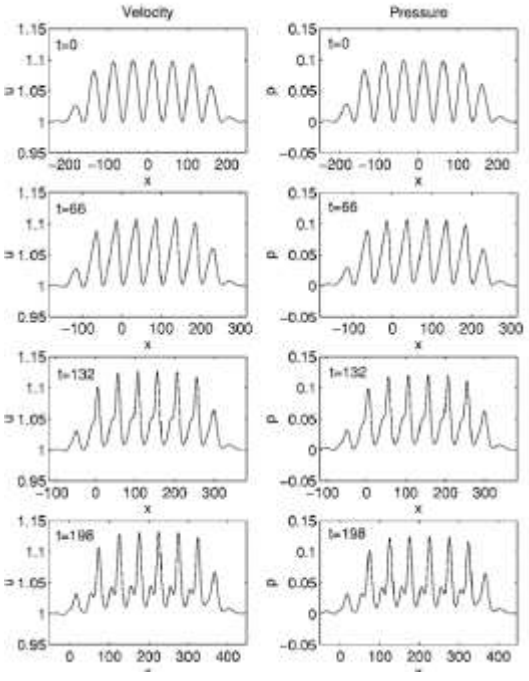


Figure 21: Flow velocity and pressure at different times[5]

A more complex model of the soliton propagation has been produced by Eliasson et al[5] to show how solitons behave as they propagate through the arterial system. *Fig.22* shows that the soliton breaks up into oscillations as it propagated and that a few solitons with large amplitudes have been produced. *Fig.23* shows the relationship between the velocity and the pressure as time increases. This model, along with the understating of the wave propagation can allow for analysis of the propagation of the blood to demonstrate the efficacy of the arterial system.

Conclusion

The 4 Hz signal can be seen in every individual and is used for transfer functions to measure blood pressure. The signal changes with variations in blood pressure, heart rate and the arterial walls. This is due to the direct correlation between an increase in blood pressure, an increase in heart rate, causing an increase in blood flow. The velocity of the blood flow causes the 4 Hz signal to increase as the soliton is moving faster therefor will break up more rapidly. When the arterial wall changes, that is to say it becomes stiffer, the signal will increase due to the pressure increase. Any form of change to the arterial wall tends to be caused by disease. These diseases all cause an increase in blood pressure, therefore increasing the signal. The signal can show how the blood pressure has changed from a healthy patient to a patient with a cardiovascular disease. It can also show whether a stenois has blended well with the arterial wall to keep the pressure at the correct number. To use the signal effectively there needs to be further study. An example of a future study would be to measure the signal change in a patient experiencing increased levels of stress. This can be compared with an invasive measurement of blood pressure. Increasing the level of stress can be achieved by performing different levels of exercise. Using the changes in the signal to measure blood pressure is more efficient than the previous methods as it allows for a continuous measurement, noninvasively. This could be very useful during long surgeries as any change in blood pressure can be caused by complications in the arterial system, such as a burst artery. An accurate, continuous, non-invasive measurement of blood pressure will allow for an accurate measurement of cardiac output. This will give information on the oxygen around the body, also providing additional information on any disease that can affect the circulatory system.

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