

Modeling and Understanding the Dynamics of Pressure and Flow in the Aorta for Individuals on Cardiopulmonary Bypass

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Introduction

Cardiopulmonary bypass (CPB) is used during heart surgery to oxygenate and circulate the blood independent of the heart. This allows surgeons operate on the heart while maintaining tissue oxygenation. Venous blood is drained out of the right side of the heart passively and brought to a reservoir where mixing and addition of drugs can occur. After collection in the reservoir, blood is oxygenated, heated, filtered, and then returned to the patient. Blood is typically returned to the aorta of the patient, but can be returned to different vessels depending on the particular surgery and patient.

Different types of pumps are utilized to return blood to the patient. There are centrifugal pumps and roller pumps, which can deliver continuous and pulsatile flows, respectively. [1] There are many other components involved in the cardiopulmonary bypass system, as can be seen in Figure 1 [1].

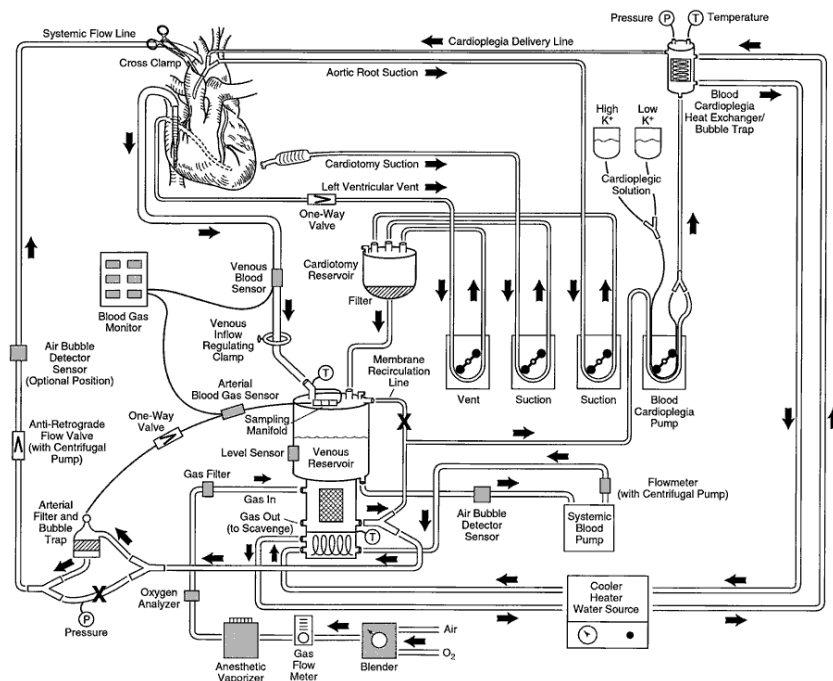


Figure 1. Diagram of the components of cardiopulmonary bypass. As the figure shows, there are many components involved in successful cardiopulmonary bypass. The key components are the heat exchange components, pump elements, filters and reservoir. Figure from Hessel et. Al.[1]

Placing a patient on cardiopulmonary bypass can lead to the development of many complications. The main complications are myocardial injury, brain injury, impaired renal function, colonic ischemia or hemorrhage, endocrine disturbance, catecholamine release, and the activation of immune cascades. The input perfusion pressure and time to establish flow on cardiopulmonary bypass can contribute to these adverse effects, as is the case for brain, renal, and some gastrointestinal injury. This is because decreased perfusion pressure leads to decreased tissue oxygenation, hypoxia, and ischemia. Electrical brain activity stops after 30 seconds of total hypoxia and irreversible cell death and damage occurs after minutes. [6] Time to irreversible injury is similar for the heart and kidney. [9] Initial hypoxic injury due to lack of blood flow constitutes the primary injury, but secondary injury in surrounding tissues due to inflammatory cells

and apoptosis can increase the total area of tissue damage. Damage due to secondary injury can continue to increase over the course of hours in situations where there is decreased, but not zero, perfusion pressure. [6] In other cases of adverse effects, the main cause is due to the lack of pulsatile flow. This mechanism of injury has been documented to contribute to hormonal disturbances, catecholamine release, and some gastrointestinal injuries. [2].

Many parameters of cardiopulmonary bypass are currently undecided. For example, no flow pattern (pulsatile or continuous) is preferred. Continuous flow is the standard due to historical development of CPB. [2,3] A pulsatile flow may have protective effects on the body while on CPB, but the reports of benefit in the literature are conflicting [2,3]. The perfusion pressure attained in the aorta should be between 50 - 150 mmHg. [2] The perfusion pressure required has been determined with respect to brain injury, but not with respect to other organs. Required inlet flow has been determined as at least 1.6 L/min/m² in order to avoid renal and brain injury.[2] Although values can be found in the literature, there is still much debate over the appropriateness of the values and which values are most important.

Modeling of the aorta and systemic circulation on bypass may be of use to help elucidate which pump settings could be most beneficial to the patient on cardiopulmonary bypass.

A common model that has been used to describe pressure and flow relationships in the aorta and systemic circulation for a given driving input is the Windkessel model. [4] The 2, 3, and 4 element Windkessel models are shown in figure 2.

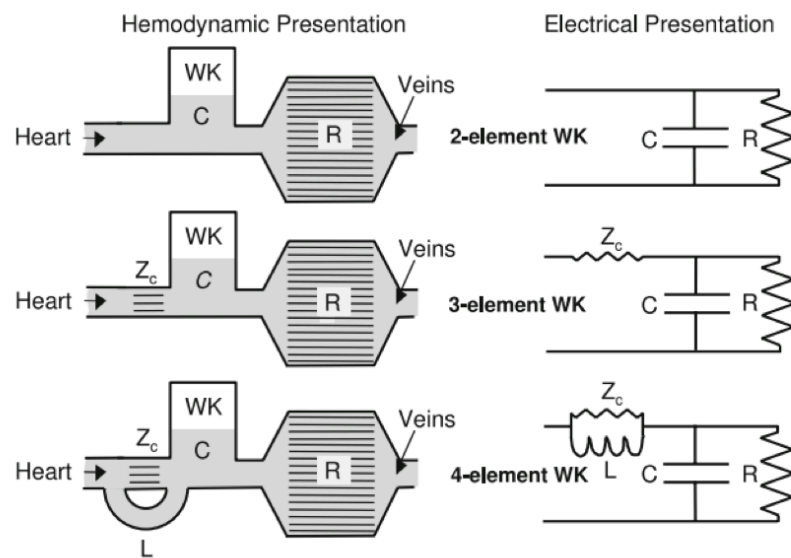


Figure 2. Schematic of the 2, 3 and 4 element Windkessel models that are used to model pressure and blood flow in the aorta. Figure from Westerhoff. [4]

Traditionally, the elements of the Windkessel model are used to represent the resistance of the arterioles and small arteries in the systemic circulation (R), the compliance of the of the aortic vessel wall (C), the impedance of the aorta and resistance through the aortic valve (Z), and the inertance (L) of the blood. Impedance of the aorta is based on the vessel stiffness, which can vary as the vessel diameter changes. The diameter of the vessel will change over the course of a cardiac cycle. Many models assume this value to be constant to simplify calculations. [4, 5]

Problem statement

There is currently no preference of one CPB input flow scheme over another. Our goal is to model the dynamics of a patient hooked up to cardiopulmonary bypass. Specifically, we will examine how the aortic perfusion pressure and time to equilibrium pressure after connection to CPB vary with different flow input waveforms (pulsatile vs continuous) and amplitudes (5L/min vs 2.5 L/min). We use analytical and numerical methods to solve a modified 3 element Windkessel model to view the dynamics of the aortic pressure for a given input. Then, using numerical methods, we will expand our simulation to a modified 4 element Windkessel model to see if that provides more insight on the pressure dynamics in the aorta for pulsatile versus constant flow and different input maximum flow rates.

Methods

For our problem, we are interested in the perfusion pressure in an aorta connected to cardiopulmonary bypass. We are curious what the effects of varying pump type (pulsatile or continuous) and maximum flow input will be on the perfusion pressure provided to the aorta. We want to determine the perfusion pressure in the aorta to draw conclusions about which flow regime may be more beneficial for minimizing patient adverse effects. To achieve this, we use the general set up of the 3 and 4 element Windkessel models, but modify the branch resistance term to consider the effects of the heart's attachment to cardiopulmonary bypass in addition to resistance in the aorta.

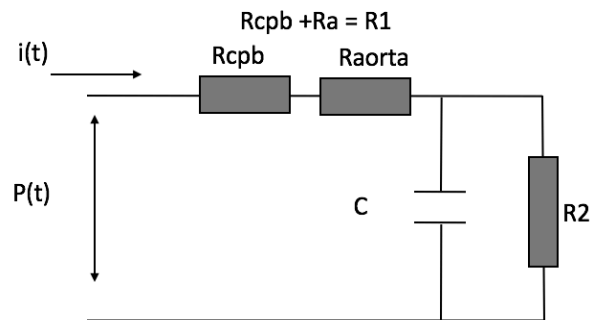


Figure 3. Modified 4 element Windkessel model

$R1$ is a combination of resistances due to the tubing coupling the aorta to the cardiopulmonary bypass machine (R_{cpb}) and the resistance of the aorta (R_a). C and $R2$ keep similar values to those in the standard 3 element Windkessel model, being the compliance of the aorta and the systemic resistance, respectively. $i(t)$ is the driving flow provided from the CPB pump.

For the modified 4 element Windkessel we have:

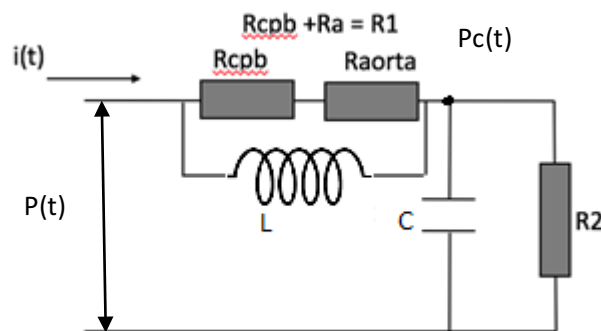


Figure 4. Modified 4 element Windkessel model

In this model, $R1$, $R2$, and C represent the same values as they do in the three element Windkessel model. An inductance element is added parallel to $R1$. This inductance allows the model to better account for the inertial forces in the blood.

Assumptions

Because the systemic circulation is disconnected from its pump source (the heart) by drainage of the venous fluid before connection to cardiopulmonary bypass, the current and pressure in the aorta before application of the CPB pump flow is zero. At the instant the pump starts applying a driving blood flow, the pressure may still be assumed to be zero. It is assumed that at $P(0)$, the aorta has not yet had a chance to fill and respond to the input flow. This makes our initial conditions of the system $\mathbf{P(0) = 0}$.

As is done for many other aortic flow models, we assume that the impedance of the aorta (R_a) is constant. [4, 5] To keep resistance of the systemic circulation (R_2) constant, we assume that the vasoconstriction and vasodilation due to myogenic auto-regulation and the sympathetic nervous system do not influence vessel diameter or resistance. The sympathetic nervous system takes approximately 100s to affect the mean arterial pressure after pressure changes and baroreceptor stimulation. [10] This is longer than the window of ischemia and tissue damage, so it is reasonable to ignore this effect for our cardiopulmonary bypass model, since we care about how quickly perfusion can be established before tissue damage occurs. It is unknown how inclusion of the autonomic nervous system would effect the model. Cardiac surgery has been shown to increase autonomic stress hormone release, which might cause vasoconstriction. [14] But in disease states that have a pump failure, like would be seen when a patient is being switched onto bypass, patients can experience massive vasodilation and autonomic dysregulation [15]. Additionally, the autonomic nervous system responses have been shown to be impaired during and after cardiopulmonary bypass [16]. It is unclear which of these factors would have the predominant effect on the autonomic nervous system output, so it is unknown how the autonomic nervous system would affect the perfusion pressure. Auto-regulation from the myogenic response of arterioles occurs at organ inflow pressures of 60 – 80 mmHG. [11] These pressures are achieved in organs only after a non-ischemic perfusion pressure is reached, making it a valid assumption to ignore these effects when establishing the perfusion pressure. Considering the myogenic response in the model would be expected to be similar to adding a PID controller to the model that functions to keep input pressure in the range of 60 – 80 mmHg for a given organ.

We assume any drug effects are constant. At the point during which the patient is being transferred onto cardiopulmonary bypass, their administered medications and anesthetics are in the maintenance phase of anesthesia. Inhaled anesthetics frequently given during the maintenance phase of anesthesia have half lives of 3 – 4 minutes. [12] Even though these medications have vasodilation effects, the half-life is outside of the window of interest (ischemic injury window) for our cardiopulmonary bypass model, allowing us to treat their effects as constant. Other drugs that are important to consider are vasopressors and vasodilators used to stabilize patient blood pressure. All of these drugs have half lives that are greater than 100 seconds, so their effects can also be considered constant for our model. Vasopressors will decrease the time required to reach an appropriate perfusion pressure, while vasodilators will increase the time required to reach a specified perfusion pressure. [13]

Calculation of Constants R_1 , R_2 and C

The constants for the model elements were calculated from physiological parameters referred from the literature and standard physiologic values. The calculations are listed below.

Table 1 at the end of this section summarizes the parameters used in the model. All values were found in SI units and converted to mmHg after simulation. IO values were based off of cardiac output values (L/min) but were also converted to SI units for the model.

R1:

$R1 = \text{resistance of the aorta} + \text{resistance of tube that couples aorta to CPB} = R_{\text{tube}} + R_z$

$$R1 = \frac{PWV * \rho_{\text{blood}}}{Area_{\text{aorta}}} + \frac{8\eta_{\text{blood}}L_{\text{coupling}}}{\pi r^4}$$

$$R_{\text{tube}} = \frac{8\eta L}{\pi r^4}$$

$\eta = \text{viscosity of the blood @37}^\circ\text{C} = 1.8 * \text{viscosity of water} = 1.8 (0.6913)\text{mPa/s}$

$L = \text{Length of the Tube} = 50 \text{ cm} = 0.5 \text{ m}$

$r = \text{radius of the tube} \sim \text{radius of the Aorta} = 2 \text{ cm} = 0.02 \text{ m}$

$$R_{\text{tube}} = \frac{(8 * 1.8 (0.6913) * 0.5)}{\pi * 0.02^4} = 9.9021 * 10^3$$

$$R_z = R_{\text{aorta}} = \frac{\text{Pulse wave Velocity} * \text{Density of Blood}}{\text{Area of the connecting surface}}$$

$\text{Pulse wave equation} = 10 \text{ m/s}$

$\text{Density of Blood} = 1050 \text{ kg/m}^3$

$A = \pi * r^2$

$$R_z = \frac{1050 * 10}{\pi * 0.03^2} = 3.7136 * 10^6$$

R2:

$R2 = \text{systemic resistance} = \text{Mean Arterial Pressure} / \text{Cardiac Output}$

$$= \frac{95 \text{ mmHg}}{5 \text{ L/min}}$$

$$= \frac{1.26656 * 10^4}{8.33 * 10^{-5}} = 1.52 * 10^8 \text{ Pa s/m}^3$$

C:

$$C = \text{Compliance} = 1.125 * 10^{-7} \text{ m}^3 / \text{Pa} \text{ [8]}$$

I0:

I0 was calculated by converting the standard cardiac output (5L/min) into units of m³/s.

$$I0 = 8.33 * 10^{-5} \text{ m}^3/\text{s}$$

I: Inertance of the blood was taken to be 100x less than the resistance in the aorta to match inertance values in other models [4, 5]

Table 1. Summary of parameter values

Parameter Name	Meaning	Value	unit
PWV	Pulse wave velocity; proxy for aortic stiffness	10	m/s
p blood	density of blood	1050	kg/m ³
nu blood	viscosity of the blood	1.24434	mPa/s
Lcoupling	Length of tube coupling CPB machine to the patient	0.5	m
Area Aorta	Area of the descending Aorta after the aortic arch	0.00008478	m ²
r	diameter of coupling tube	0.02	m
MAP	Mean Arterial Pressure	12.7	kPa
Cardiac Output	Cardiac Output	$8.33 \cdot 10^{-5}$	m ³ /s
R1	resistance of the aorta + coupling tube	$3.7 \cdot 10^6$	Pa.s/m ³
R2	resistance of the systemic circulation	$1.52 \cdot 10^8$	Pa.s/m ³
C	Compliance of the aorta	$1.125 \cdot 10^{-7}$	m ³ /Pa
L	Inertance of blood	$1 \cdot 10^5$	kg/m ⁻⁴

Analytical Solution

The voltage equations for the 3 element Windkessel model were written out by applying Kirchoff's laws and ohm's laws to the model. Analytical solutions were calculated for two types of driving flow: 1) a continuous driving flow and 2) a sinusoidal driving flow.

Writing the node equation for the node voltage of $P_c(t)$ in the 3 element Windkessel Model:

Current through the Capacitor = Initial Current – Current through the R2 branch

$$C \frac{dP_c(t)}{dt} = i(t) - \frac{P_c(t)}{R_2} \quad (1)$$

Voltage across the network = Voltage Drop across R1 – Voltage drop across R2 and C

$$P(t) = i(t)R_1 + P_c(t) \quad (2)$$

$$P_c(t) = P(t) - i(t)R_1$$

Taking Derivative on Both sides,

$$\frac{dP_c(t)}{dt} = \frac{dP(t)}{dt} - \frac{di(t)}{dt} R_1$$

$$C \frac{dP_c(t)}{dt} = C \left(\frac{dP(t)}{dt} - \frac{di(t)}{dt} R_1 \right) = i(t) - \left(\frac{P(t) - i(t)R_1}{R_2} \right)$$

Rearranging the above equation,

$$C \frac{dP(t)}{dt} - \frac{di(t)}{dt} CR_1 = \frac{R_2 * i(t) - P(t) + i(t) * R_1}{R_2}$$

$$C \frac{dP(t)}{dt} - \frac{di(t)}{dt} CR_1 = \frac{-P(t)}{R_2} + i(t) \left(1 + \frac{R_1}{R_2} \right)$$

$$C \frac{dP(t)}{dt} = \frac{-P(t)}{R_2} + i(t) \left(1 + \frac{R_1}{R_2} \right) + \frac{di(t)}{dt} CR_1 \quad (3)$$

We are solving the equation in Two cases, a) When the input flow $i(t)$ is constant

b) When the input flow is sinusoidal

a) If $i(t)$ is constant (I_0), $\frac{di(t)}{dt} = 0$, The equation Becomes,

$$C \frac{dP(t)}{dt} = \frac{-P(t)}{R_2} + I_0 \left(1 + \frac{R_1}{R_2} \right)$$

Taking Laplace Transform on both sides,

$$C(sP(s) - P(0)) = \frac{-P(s)}{R2} + \frac{\left(I0 \left(1 + \frac{R1}{R2}\right)\right)}{s}$$

Taking the initial Pressure Conditions as $P(0) = 0$,
(at the time of Coupling the CBP and the aorta),

$$sCP(s) + \frac{P(s)}{R2} = \frac{\left(I0 \left(1 + \frac{R1}{R2}\right)\right)}{s}$$

$$P(s)(sR2C + 1) = \frac{\left(I0 \left(1 + \frac{R1}{R2}\right)\right)}{s}$$

$$P(s) = \frac{\left(I0 \left(1 + \frac{R1}{R2}\right)\right)}{s(sR2C + 1)}$$

Taking Inverse laplace Transform,

$$P(t) = I0 (R1 + R2)(1 - e^{-\frac{t}{R2C}}) \quad (4)$$

It can be observed from equation (4) is that the pressure that is achieved by the constant flow input is an increasing exponential. The aortic perfusion pressure starts at 0, which is our initial condition, and increases over time to reach a stable perfusion pressure.

a) If $i(t)$ is a sinusoidal input

The system was also given a pulsatile input, modeled as a sinusoidal input flow. The sinusoidal input to the system can be characterized by the following equation.

$$I(t) = I0 \sin^2\left(\pi * \frac{t}{Tp}\right) \rightarrow \frac{di(t)}{dt} = I0 \frac{2\pi}{Tp} \cos\left(\pi * \frac{t}{Tp}\right) \sin\left(\pi * \frac{t}{Tp}\right)$$

The equation Becomes,

$$C \frac{dP(t)}{dt} = \frac{-P(t)}{R2} + I0 \sin^2\left(\pi * \frac{t}{Tp}\right) \left(1 + \frac{R1}{R2}\right) + I0 \frac{2\pi}{Tp} \cos\left(\pi * \frac{t}{Tp}\right) \sin\left(\pi * \frac{t}{Tp}\right) CR1$$

Rearranging and Taking laplace transform on both sides,

$$L\left(C \frac{dP(t)}{dt} + \frac{P(t)}{R2}\right) = L\left(I0 \sin^2\left(\pi * \frac{t}{Tp}\right) \left(1 + \frac{R1}{R2}\right) + I0 \frac{2\pi}{Tp} \cos\left(\pi * \frac{t}{Tp}\right) \sin\left(\pi * \frac{t}{Tp}\right) CR1\right)$$

$$sCP(s) - CP(0) + \frac{P(s)}{R2} = \frac{2 * I0 * \left(1 + \frac{R1}{R2}\right) \left(\frac{\pi}{Tp}\right)^2}{s \left(s^2 + 4 \left(\frac{\pi}{Tp}\right)^2\right)} + \frac{2\pi^2 I0 CR1}{Tp^2} \left(\frac{1}{\frac{4\pi^2}{Tp^2} + s^2}\right)$$

Applying the Initial Condition, $P(0) = 0$

$$sCP(s) + \frac{P(s)}{R2} = P(s)(sCR2 + 1) = \frac{2 * I0 * \left(1 + \frac{R1}{R2}\right) \left(\frac{\pi}{Tp}\right)^2}{s \left(s^2 + 4 \left(\frac{\pi}{Tp}\right)^2\right)} + \frac{2\pi^2 I0 CR1}{Tp^2} \left(\frac{1}{\frac{4\pi^2}{Tp^2} + s^2}\right)$$

Taking Partial fractions and Inverse Laplace transform, We arrive at the solution:

$$P(t) = \frac{A - (B1 + B2) - C}{D}$$

$$\text{where, } A = \frac{I0(R1 + R2)}{2}$$

$$B1 = Tp^2 * I0 * \cos\left(\frac{2\pi t}{Tp}\right) (R1 + R2)$$

$$B2 = 2C * I0 * R2^2 \pi \left(2CR1\pi \cos\left(\frac{2\pi t}{Tp}\right) + Tp \sin\left(\frac{2\pi t}{Tp}\right)\right)$$

$$C = \frac{2C^2 * I0 * R2^3 \pi^2 e^{-\frac{t}{CR2}}}{4\pi^2 C^2 R2^2 + Tp^2}$$

$$D = 8\pi^2 C^2 R2^2 + Tp^2$$

Numerical Solution:

The numerical Solutions to the 3 and 4 element Windkessel models were obtained using Euler's method in Matlab. Euler's method is a technique where an ode is solved as a finite difference approximation. The pressure values are calculated in very small steps of time and are aggregated to attain and characterize the function.

Results and Analysis

Continuous Flow:

Perfusion pressure in the aorta for a continuous flow input of 5L/min is shown below. 5 L/ min was initially chosen as the driving function because it corresponds to an input flow that is the same value as the normal cardiac output in an adult.

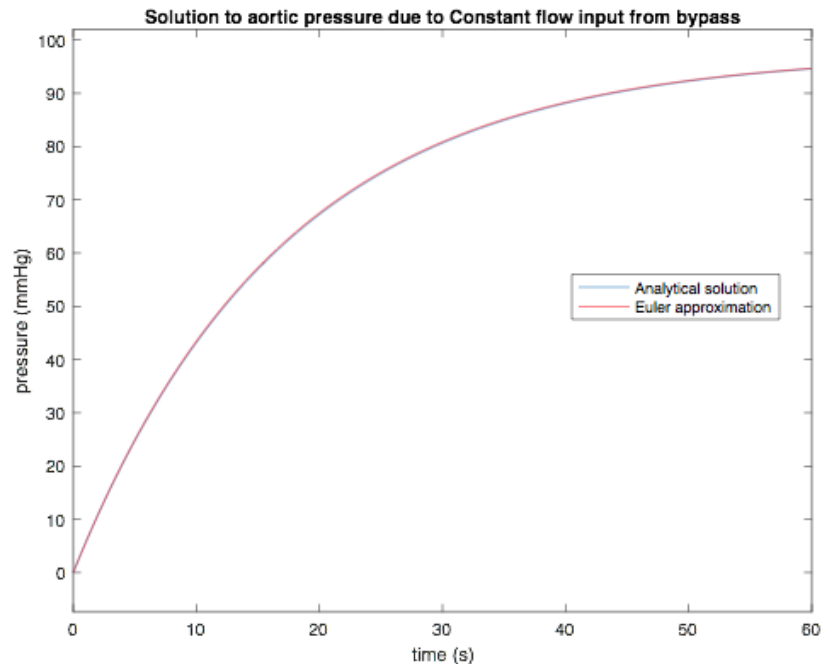


Figure 5. The Analytical and Numerical solution for perfusion pressure in the aorta for a continuous flow input. Input flow rate from CBP was set to be 5 L/min for a 3 element Windkessel model.

It can be seen that for a driving blood flow of 5 L/min, a perfusion pressure of 95 mmHg is reached. This pressure would provide adequate perfusion to all the tissues, assuming the gas exchange portions of the CPB machine are functioning. After connection to cardiopulmonary bypass, it takes 13 seconds for the aorta to reach a perfusion pressure greater than 50 mmHg and takes 30 seconds for the perfusion pressure in the aorta to reach 90% of its final value. There appears to be very good agreement between the true solution and the Euler's method approximation of the solution.

Perfusion pressure in the aorta for a continuous flow input of 2.5L/min is shown below. 2.5 L/ min was chosen as a driving flow to assess the perfusion pressure resulting from lower values of input flow.

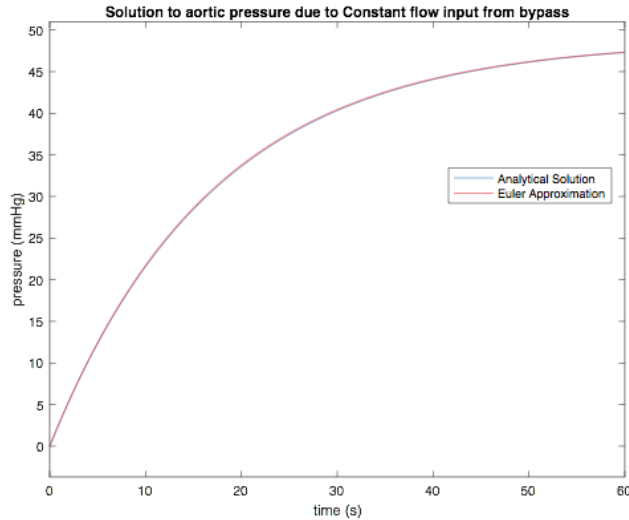


Figure 6. The Analytical and Numerical solution for perfusion pressure in the aorta for a continuous flow input. Input flow rate from CBP was set to be 2.5 L/min for a 3 element Windkessel model.

It can be seen that for a driving blood flow of 2.5 L/min, a perfusion pressure of 47 mmHg is reached. This pressure is probably not high enough to perfuse the tissues, as the lower bound for acceptable perfusion pressure presented in the literature is 50 mmHg. After connection to cardiopulmonary bypass, it takes 30 seconds for the perfusion pressure in the aorta to reach 90% of its final value. As expected, changing the magnitude of the input flow does not affect the time it takes to obtain the steady state peak pressure.

Pulsatile Flow

The first input flow assessed for a pulsatile pump was a sinusoidal driving pressure with maximum amplitude of 5L/min. Like in the continuous flow model, this flow was chosen to determine the perfusion pressure when the driving flow is the same as a normal cardiac output.

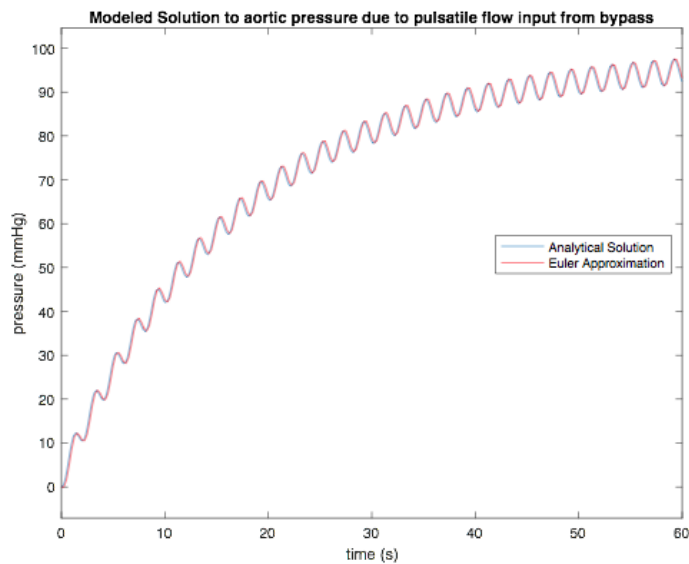


Figure 7. The true and Euler approximation solutions for perfusion pressure in the aorta for a pulsatile flow input. Input flow rate from CBP was set to be 5 L/min for a 3 element Windkessel model.

It can be seen that for a driving blood flow of 5 L/min, a peak perfusion pressure of 98 mmHg is reached. The steady state mean perfusion pressure is 94 mmHg, which is 1 mmHg lower than that achieved in the for the continuous flow model. This pressure would provide adequate perfusion to all the tissues, assuming the gas exchange portions of the CPB machine are functioning. The pulse pressure of the system is 12 mmHg. This pulse pressure is much smaller than the physiologic pulse pressure of 40 mmHg. After connection to cardiopulmonary bypass, it takes 13 seconds for the aorta to reach a perfusion pressure greater than 50 mmHg and takes slightly greater than 30 seconds for the perfusion pressure in the aorta to reach 90% of its final value. This slight delay compared to the continuous flow model is likely due to the oscillating values that accompany the pulsatile input, which cause the average to climb slightly slower. There appears to be very good agreement between the true solution and the Euler's method approximation of the solution.

The next input flow assessed for a pulsatile pump was a sinusoidal driving pressure with maximum amplitude of 2.5L/min.

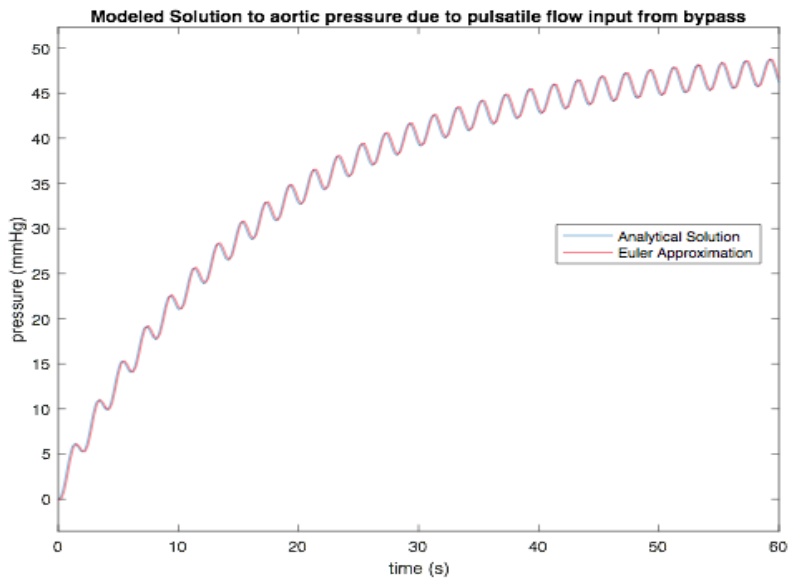


Figure 8. The true and Euler approximation solution solution for perfusion pressure in the aorta for a pulsatile flow input. Input flow rate from CBP was set to be 2.5 L/min for a 3 element Windkessel model.

It can be seen that for a pulsatile driving blood flow of 2.5 L/min, a peak perfusion pressure of 49 mmHg is reached, which is higher than that attained for the continuous flow pump. The steady state mean perfusion pressure of 46 mmHg is slightly lower than that achieved for the continuous flow model. As is seen with the continuous flow model, the input flow of 2.5 L/min does not create a large enough perfusion pressure to oxygenate the tissues. The pulse pressure of the system is 6 mmHg. This pulse pressure is smaller than that seen for the 5 L/min pulsatile input, and is much smaller than the physiologic pulse pressure of 40 mmHg. After connection to cardiopulmonary bypass, it takes takes slightly longer than 30 seconds for the mean perfusion pressure in the aorta to reach 90% of its final value. This slight delay compared to the continuous flow model is likely due to the oscillating values that accompany the pulsatile input, which cause the average to climb slightly slower. There appears to be very good agreement between the true solution and the Euler's method approximation of the solution.

4 Element Windkessel with pulsatile flow

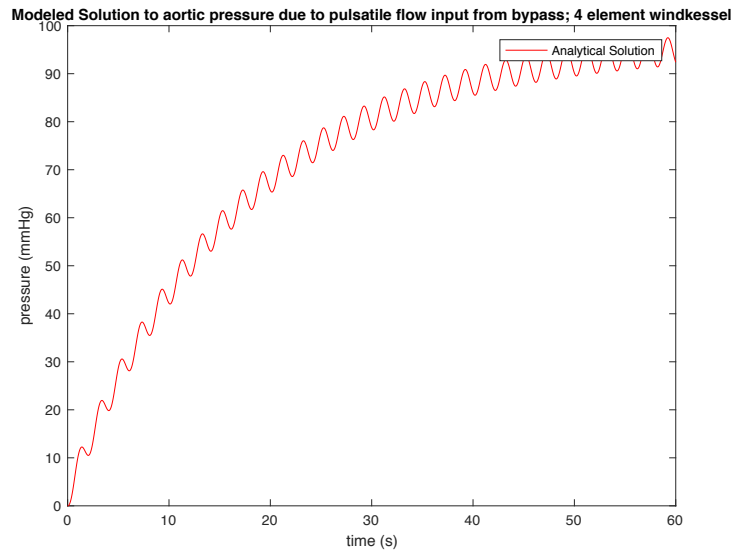


Figure 9. The Euler approximation solution solution for perfusion pressure in the aorta for a pulsatile flow input. Max input flow rate from CBP was set to be 5 L/min for a 4 element Windkessel model.

The perfusion pressure in the aorta for the 4 element Windkessel with pulsatile input of max amplitude 5 L/min agrees well with the perfusion pressure obtained from the corresponding 3 element model. It can be seen that for a driving peak blood flow of 5 L/min, a peak perfusion pressure of 98 mmHg, mean perfusion of 94 mmHg and pulse pressure of 12 mmHg is attained. After connection to cardiopulmonary bypass, it takes 13 seconds for the aorta to reach a perfusion pressure greater than 50 mmHg and takes slightly greater than 30 seconds for the perfusion pressure in the aorta to reach 90% of its final value, which is also consistent with the 3 element model. There is no change in the perfusion pressure wave form between the output for the 3 and 4 element Windkessel models.

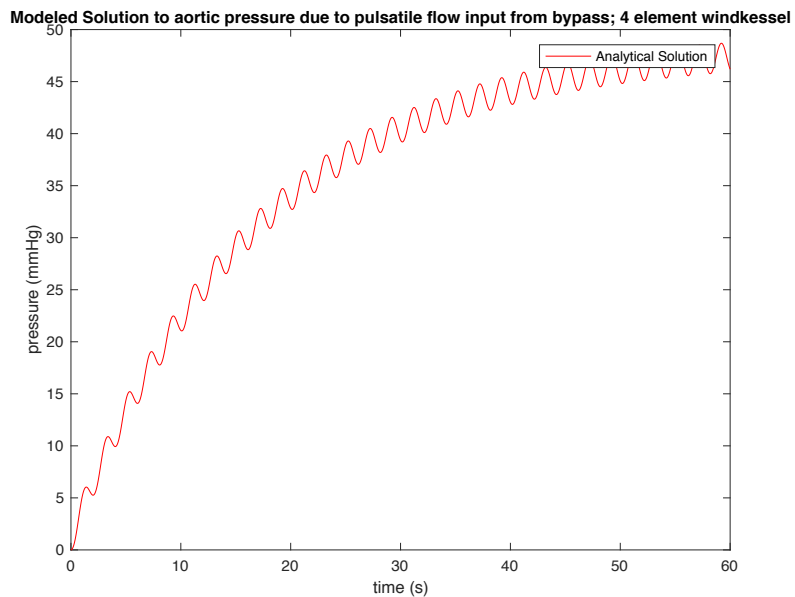


Figure 10. The Euler approximation solution solution for perfusion pressure in the aorta for a pulsatile flow input. Max input flow rate from CBP was set to be 2.5 L/min for a 4 element Windkessel model.

The perfusion pressure in the aorta for the 4 element Windkessel with pulsatile input of max amplitude 2.5 L/min agrees well with the perfusion pressure obtained from the corresponding 3 element model. It can be seen that for a driving peak blood flow of 2.5 L/min, a peak perfusion pressure of 49 mmHg, mean perfusion of 46 mmHg and pulse pressure of 6 mmHg is attained. The mean perfusion pressure never gets above 50 mmHg, which is also consistent with the 3 element model. There is no change in the perfusion pressure wave form between the output for the 3 and 4 element Windkessel models.

Conclusions and Discussion

Both the pulsatile and continuous flow CPB models with a driving flow of 5 L/ min lead to mean perfusion pressures that were 97 mmHg and 96 mmHg respectively. Both of these values were reached within 30s of switching the patient onto CPB. These values are high enough (> 50 mmHg) to sustain appropriate oxygenation to the brain, kidneys and other tissues of the patient [2]. It took about 15 seconds for both perfusion pressures to become greater than 50 mmHg. 15s of hypoxia is under the threshold of 30s, which is when brain injury starts occur. [6]

For the driving flow conditions of 2.5 L/ min, the mean perfusion pressures reached were 47 mmHg and 46 mmHg for the continuous and pulsatile flow models, respectively. Neither of these values is greater than the 50 mmHg required to prevent brain and kidney damage, but they are close. They agree well with the lower bounds of input flows reported in the literature. [2] It is reported that the lowest acceptable input flow is 1.6 L/min.m^2 . The average adult surface area is 1.8 m^2 [7], making the average lowest acceptable flow about 2.9 L/min.

The pulse pressure in pulsatile input models is 12 mmHg and 6 mmHg for the 5 L/min and 2.5 L/ min inputs, respectively. Both of these values are lower than the normal pulse pressure of 20 - 40 mmHg. The literature suggests that the tubing coupling the CPB system to the aorta may dampen the pulsations applied by the driving flow. [2] Our model agrees with this finding. Both the model and literature suggest that a pulsatile driving function of the pump is not enough to guarantee pulsatile behavior in the aorta of the same magnitude. A pulsatile pump alone may not be enough to restore some of the beneficial effects of pulsatile flow to individuals on CPB. The pulse pressure did increase with increasing driving pressure. This suggests that a pulsatile input may be of more use for higher driving pressure systems.

There is no difference in the perfusion pressure waveform between the 3 and 4 element Windkessel models for pulsatile blood flow inputs. It has been reported in previous simulations that the 4 element Windkessel's wave form produces a dichroitic notch [4], which is absent in our model. The presence of the dichroitic notch in the pulse pressure waveform is due to the closing of the aortic valve, and bulging of the aortic valve into the aorta. Given that our model bypasses the heart and its valves, the absence of a dichroitic notch makes sense. The agreement between the Windkessel 4 element and 3 element models is exact for our model and parameters. This is true for many different values of inductance (data not shown). This suggests that for the parameters of our model, the inertial contributions of blood flow is less important than the other parameters. Looking at the equations derived for our model, it appears that the pressure in the aorta is most heavily influenced by the resistance due to the aorta and its coupling to CPB (R_1) and the capacitance of the aorta (C).

This model agrees with the prevailing opinion that there is not a large difference between pulsatile or continuous driving flow for maintaining aortic perfusion pressure. The mean perfusion pressure and time required to reach steady state is similar for both models. For low input flows, it seems it would be best to stick with the standard of using continuous flow pumps. The pulse pressure produced for pulsatile pumps at low flow conditions is too low to promote their use over continuous flow pumps. As the input flow increases, the pulse pressure exhibited by the aorta also increases. Because of this increase in pulse pressure, an argument could be made that pulsatile flow pumps may produce more pulsatile behavior at larger inflow rates and could provide more protective benefit than continuous flow pumps in these situations.

The next problem we would like to expand our model to solve, is the development and maintenance of cerebral perfusion pressure during cardiopulmonary bypass surgery. To achieve this goal, we would first have to modify our model to look at the resistances of the cerebral vessels separately from the rest of the systemic circulation. After we have a simple, modified model that looks at the cerebral circulation, we would like to add in the effects of cerebral auto regulation and different vasoactive drugs

on the maintenance of the perfusion pressure. Auto-regulation would likely act on the system in a similar manner to a PID controller that functions to keep cerebral perfusion pressure within a given pressure range. Consideration would have to be taken to determine how to best represent the different vasoactive substances and their effect on the cerebral circulation. The patient would likely have multiple different drugs in their system, with different half-lives, leading to a vascular resistance that could vary as a function of time due to the varying pharmacokinetics of the different drugs.

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Appendix: Matlab Code

The following matlab function was run repeatedly for varying values of I0

```
clear all;
close all;

%parameters of system

syms tt xx;

%my parameters
f = 8.33e-5;
r1 = 3.7e6;
r2 = 1.52e8;
C = 1.125e-7;
Tp = 2;
I0 = 2*(( 8.33e-5)/2);
f = (8.33e-5)/2;
L = 1e5

%Ptest = 0.25* exp(2*tt) - 0.5*tt - 0.25;

P = (f*(r1 + r2) - f*exp(-tt/(C*r2))*(r1 + r2) ) /133;

PS = ((I0*(r1 + r2))/2 - (Tp^2*I0*r1*cos((2*pi*tt)/Tp) +
Tp^2*I0*r2*cos((2*pi*tt)/Tp) + 4*C^2*I0*r1*r2^2*pi^2*cos((2*pi*tt)/Tp) +
2*C*Tp*I0*r2^2*pi*sin((2*pi*tt)/Tp))/(8*pi^2*C^2*r2^2 + 2*Tp^2) -
(2*C^2*I0*r2^3*pi^2*exp(-tt/(C*r2)))/(4*pi^2*C^2*r2^2 + Tp^2))/133;
```

```

figure(1)
ezplot(P, [0 60])
title ('Solution to aortic pressure due to Constant flow input from bypass')
xlabel('time (s)')
ylabel('pressure (mmHg)')
hold on
%ezplot(PS, [0, 60])

%derivatives of interest
%DPC = ( ( (1 + R1/R2)*F + C*R1(0) ) - p/R2)/C;
%DPW = ( ( (1 + R1/R2)*sin(pi*t/Ts) + C*R1*pi*t*Tscos(pi*t/Ts) ) - p/R2)/C;

step = 0.025;
n = 60;
m = n/step + 1;
p = zeros(1, m);
t = zeros(1, m);
ysin = zeros(1, m);
yinL = zeros(1, m);

nl = 1;

%Initial conditions
p(1) = 0;
ysin(1) = 0;
pt(1) = 0;
yinL(1) = 0;
tnot = 0;
t(1) = tnot;

%
%
%
%
for i = tnot + step : step : n
    %3 models
    p(nl + 1) = p(nl) + step* ( ( (1 + r1/r2)*f ) - p(nl)/r2)/C;
    ysin(nl + 1) = ysin(nl) + step * ( ( I0*(1 + r1/r2)*sin(pi*t(nl)/Tp).^2
+ 2*I0*C*r1*(pi/Tp)*sin(pi*t(nl)/Tp)*cos(pi*t(nl)/Tp) ) - ysin(nl)/r2)/C;
    %pt(nl + 1) = (2*(pt(nl)) + t(nl)) * step + pt(nl);
    it = I0*sin(pi*t(nl)/Tp).^2;
    dit = I0*(2*pi/Tp) * cos(pi*t(nl)/Tp)*sin(pi*t(nl)/Tp);
    ddit = (2*pi^2/(Tp^2)) * (cos(pi*t(nl)/Tp).^2 - sin(pi*t(nl)/Tp).^2)*I0;
    derp = ( (1+r1/r2)*it + (r1*C + L/r2)*dit +L*C*ddit - yinL(nl)/r2)/C
    yinL(nl + 1) = yinL(nl) +step*derp;

```

```

%4models

    t(nl+ 1) = t(nl) +step;
%
    nl = nl+1;

end
yinL = yinL./133

pm = p./133
yinm = ysin./133
%figure%(2)
plot(t, pm, 'r')
hold on
%plot (t, ysin)
% ezplot(Ptest, 'b')
legend('Analytical Solution', 'Euler Approximation')

hold off
figure(2)
ezplot(PS, [0 60])
title ('Solution to aortic pressure due to pulsatile flow input from bypass')
xlabel('time (s)')
ylabel('pressure (mmHg)')

hold on
plot(t, yinm, 'r')
title ('Modeled Solution to aortic pressure due to pulsatile flow input from
bypass')
xlabel('time (s)')
ylabel('pressure (mmHg)')
legend('Analytical Solution', 'Euler Approximation')
hold off

figure(3)
plot(t, yinL, 'r')
title ('Modeled Solution to aortic pressure due to pulsatile flow input from
bypass; 4 element windkessel')
xlabel('time (s)')
ylabel('pressure (mmHg)')
legend('Analytical Solution', 'Euler Approximation')

% figure(3)
% ezplot(PS, [45 60])
% title ('Solution to aortic pressure due to pulsatile flow input from
bypass')
% xlabel('time (s)')
% ylabel('pressure (mmHg)')
%
%
%

```

```

%
% % figure(4)
% % plot(t, yinm)
% % title ('Modeled Solution to aortic pressure due to pulsatile flow input
from bypass')
% % xlabel('time (s)')
% % ylabel('pressure (mmHg)')
%
% IN = f*(sin(tt * pi/Tp).^2)
% figure(5)
% ezplot(IN, [0 60])

a = mean(yinm(1:400));
b = mean(yinm(410:800));
c = mean(yinm(810:1200));
d = mean(yinm(1210:1600));
e = mean(yinm(1610:2000));
f = mean(yinm(2010:2401));
meanP3 = [a b c d e f]

aaa = mean(yinL(1:400));
bbb = mean(yinL(410:800));
ccc = mean(yinL(810:1200));
ddd = mean(yinL(1210:1600));
eee = mean(yinL(1610:2000));
fff = mean(yinL(2010:2401));
meanP4 = [aaa bbb ccc ddd eee fff]

```