arterial network

Assume that the arterial network is made up of N vessels, with $N = 0$ as the root and $k \in N$ terminal vessels.

Define the instantaneous average pressure in vessel n as the spatial average pressure

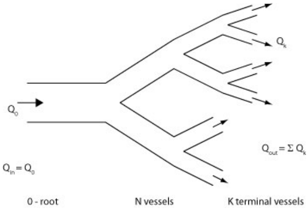
$$P_n = \frac{1}{L_n} \int_0^{L_n} P(x, t) dx$$

where $x = 0$ is the origin of the vessel and $x = L_n$ is its outlet.

Assume that flow out of the terminal vessels is governed by a resistive law

$$Q_k = \frac{P_n - P_\infty}{R_k}$$

where R_k is the resistance to outflow into through the microcirculation and P_∞ is the pressure at which flow through the artery is zero. P_∞ may be different from the venous pressure due to waterfall effects.



- there are N connected arteries
- $n = 0$ is the aortic root
- there are $K \in N$ terminal arteries

conservation of mass

Overall conservation of mass in the arterial network requires

$$\frac{dV}{dt} = Q_{in} - Q_{out}$$

where V is the volume of the arterial system, $Q_{in} = Q_0$ is the flow into the aortic root from the ventricle and

$$Q_{out} = \sum_{n \in K} \frac{P_n - P_\infty}{R_k}$$

is the net flow out of the arteries through the microcirculation.

We assume that the compliance of each artery, $C_n = \frac{dV_n}{dP_n}$ is constant. With this assumption, the conservation of mass equation can be written

$$\sum_{n \in N} C_n \frac{dP_n}{dt} + \sum_{n \in K} \frac{P_n - P_\infty}{R_k} = Q_0$$

This equation relates the average pressures in the different arteries to the flow from the ventricle and will be the basis of the analysis that follows.

Windkessel pressure

The classical Windkessel solution, originally derived by Frank in 1899, follows from this equation. Assume that the Windkessel pressure is a function of time that is uniform throughout the arterial system, $P_n = P_{Wk}(t)$. Substituting in the mass conservation equation

$$C\frac{dP_{Wk}}{dt} + \frac{P_{Wk} - P_\infty}{R} = Q_0$$

where

$$C = \sum_{n \in N} C_n \qquad \text{and} \qquad \frac{1}{R} = \sum_{n \in K} \frac{1}{R_k}$$

are the net compliance and resistance of the arterial system. This is a simple ODE with the general solution

$$P_{Wk} - P_\infty = \frac{e^{-t/RC}}{C}\int_0^t Q_0(\gamma)e^{\gamma/RC}d\gamma + (P_{Wk}(0) - P_\infty)e^{-t/RC}$$

where $P_{Wk}(0)$ is the pressure at $t = 0$, which is taken as the time of the end of diastole and the start of systole.

Note that during diastole when $Q_0 = 0$, the Windkessel pressure decreases exponentially with the time constant $\tau = RC$.

reservoir pressure

We now define the reservoir pressure, $\bar{P}$ as the pressure which satisfies the mass conservation equation and which has a waveform that is uniform throughout the arterial system, but is delayed in vessels n by a delay time τ_n which depends on the time it takes for a wave to travel from the aortic root to vessel n

$$\bar{P}_n(t) = \bar{P}(t - \tau_n)$$

Substituting this definition into the mass conservation equation we obtain the defining equation for $\bar{P}$

$$\sum_{n \in N} C_n \frac{d\bar{P}(t - \tau_n)}{dt} + \sum_{n \in K} \frac{\bar{P}(t - \tau_n) - P_\infty}{R_k} = Q_0(t)$$

This is a time-delay, differential equation with constant coefficients. This type of equation has been studied extensively in the context of control theory. Although there are no general methods of solution for equations of this type existence and uniqueness theorems exist that prove that there is a solution and that the solution is unique.

In the analysis that follows, we only require that the reservoir pressure exists and that it is unique. Given the reservoir pressure, we define the excess pressure, $p_n(t)$, to be the difference between the measured pressure and the reservoir pressure

$$p_n(t) = P_n(t) - \bar{P}(t - \tau_n)$$

ventricular work

The hydraulic work done by the ventricle over a cardiac period T is

$$W = \int_0^T P_0 Q_0 dt$$

where we again define $t = 0$ to the time of end diastole and start of systole. From the previous definition of reservoir and excess pressures, we can divide the hydraulic work into reservoir work and excess work

$$W = \int_0^T \bar{P} Q_0 dt + \int_0^T p_0 Q_0 dt \equiv \bar{W} + w$$

where we assume that the time delay in the aortic root is zero.

The bulk of the following analysis is directed at finding the minimum possible excess work w using the calculus of variations.

minimum excess work

We apply the arguments of the calculus of variations to find the functional form of the excess pressure that minimises the ventricular excess work under appropriate constraints. The constraints are necessary to find non-trivial results from the analysis, since $p_0 = 0$ is obviously gives the minimum possible excess work. The constraints that we chose are that p_0 is integrable, is periodic with period T and that it satisfies the equation for mass conservation. We therefore seek the minimum of the function

$$\chi = \int_0^T (p_o Q_0 + \lambda p_0) dt$$

where λ is a Lagrange multiplier that will be determined by using the assumption of periodicity.

Following the standard methods of the calculus of variations, we assume that χ is minimum when $p_n - \hat{p}_n$ and find this minimising function by considering all functions close to $\hat{p}_n$. In particular, we consider the functions $p_n = \hat{p}_n + \epsilon\eta$, where ϵ is a small constant and η is an arbitrary function with $\eta(0) = \eta(T)$. This final condition follows from our assumption that the cardiac cycle is periodic with period T.

The minimum is found by setting the derivative of χ with respect to the parameter ϵ equal to zero

$$0 = \frac{\partial \chi}{\partial \epsilon} = \frac{\partial}{\partial \epsilon}\Big(\int_0^T p_0 Q_0 dt + \lambda \int_0^T p_0 dt\Big)$$

minimum excess work (2)

The evaluation of this equation depends on our assumption that the mass conservation equation is satisfied. Substituting the definitions of $\bar{P}$ and p_n into the mass conservation equation we see that the derivative of Q_0 wrt to ϵ is

$$\frac{\partial Q_0}{\partial \epsilon} = \frac{\partial}{\partial \epsilon}\left(\sum_{n=1}^{N} C_n \frac{d(\bar{P}(t-\tau_n) + \hat{p}_n + \epsilon\eta)}{dt} + \sum_{k=1}^{K} \frac{(\bar{P}(t-\tau_k) + -P_\infty + \hat{p}_k + \epsilon\eta)}{R_k}\right)$$

$$= C\frac{d\eta}{dt} + \frac{\eta}{R}$$

where we have used the previously definitions for C and R. Similarly, the derivative of p_0 wrt to ϵ is

$$\frac{\partial p_0}{\partial \epsilon} = \eta$$

Substituting into the integral expression we obtain

$$0 = \frac{\partial \chi}{\partial \epsilon} = \int_0^T \left[Q_0\eta + \hat{p}_0\left(C\frac{d\eta}{dt} + \frac{\eta}{R}\right) + \lambda\eta\right] dt$$

where we have neglected terms of $\mathcal{O}(\epsilon)$.

minimum excess work (3)

The term involving the time derivative of η can be rewritten using integration by parts

$$\int_0^T \hat{p}_0 C \frac{d\eta}{dt} dt = \left[\hat{p}_0 C \eta\right]_0^T - \int_0^T \frac{d\hat{p}_0}{dt} C \eta dt$$

We observe that the first term on the rhs is zero because of the assumption that $\eta(0) = \eta(T)$. Thus, the full integral can be written

$$0 = \int_0^T \left[Q_o - C\frac{d\hat{p}_0}{dt} + \frac{\hat{p}_0}{R} + \lambda\right] \eta dt$$

Since η is an arbitrary function, the terms within the brackets must be equal to zero, so that the minimising $\hat{p}_0$ satisfies the equation

$$\frac{d\hat{p}_0}{dt} - \frac{\hat{p}_0}{RC} = \frac{Q_0 + \lambda}{C}$$

where R and C, defined previously, are the net compliance of the arterial system and the net resistance of the microcirculation. This equation can be solved by quadrature using the integration factor $e^{-t/RC}$. Using the initial condition $p_0(0) = 0$, the solution can be written

$$\hat{p}_0 = \frac{e^{t/RC}}{C} \int_0^t Q_0(\gamma) e^{-\gamma/RC} d\gamma + \lambda R\left(e^{t/RC} - 1\right)$$

minimum excess work (4)

The Lagrange multiplier λ can now be evaluated using the periodicity condition $\hat{p}_0(T) = \hat{p}_0(0) = 0$,

$$\lambda = \frac{-e^{T/RC}}{RC\left(e^{T/RC} - 1\right)} \int_0^T Q_0(\gamma) e^{-\gamma/RC} d\gamma$$

Thus, the excess pressure that leads to the minimum excess work is given by

$$\hat{p}_0 = \frac{e^{t/RC}}{C} \int_0^t Q_0(\gamma) e^{-\gamma/RC} d\gamma - \frac{e^{T/RC}\left(e^{t/RC} - 1\right)}{C\left(e^{T/RC} - 1\right)} \int_0^T Q_0(\sigma) e^{-\sigma/RC} d\sigma$$

We see that the minimising pressure $\hat{p}_0(t) = f(t; Q_0, T, R, C)$.

We are now able to evaluate the minimum work that the ventricle can do against the excess pressure in the aortic root $\hat{w}$.

$$\hat{w} = \int_0^T \hat{p}_0 Q_0 dt = \frac{1}{C} \int_0^T Q_0 e^{t/RC} \int_0^t Q_0(\gamma) e^{-\gamma/RC} d\gamma dt$$

$$- \frac{e^{T/RC}}{\left(e^{T/RC-1}\right)} \int_0^T Q_0(\gamma) e^{-\gamma/RC} d\gamma \int_0^T Q_0(\sigma)\left(e^{\sigma/RC} - 1\right) d\sigma$$

We now turn to finding the conditions where the minimum excess work $\hat{w} > 0$.

nondimensional excess work

Before continuing, it is convenient to define nondimensional variables to help us in finding the conditions for which $\hat{w} > 0$. There are several times in the problem, but it seems most convenient to scale time with the arterial time constant $\tau = RC$. The flow rate is most conveniently nondimensionalised by using the stroke volume $V_s = \int_0^T Q_0 dt$, which is the volume of blood ejected by the heart during one cardiac period. Similarly, the work is conveniently scaled by the work V_s^2/C, which is the area of the P-V loop that would be produced if the stroke volume was ejected instantaneously, increasing the pressure by the amount V_s/C. With these scalings the nondimensional variables, denoted by primes are

$$t' = \frac{t}{RC}, \qquad q' = \frac{RCQ_0}{V_s} \qquad \text{and} \qquad \hat{w}' = \frac{C\hat{w}}{V_S^2}$$

The nondimensional equation for the minimum excess work is

$$\hat{w}' = \int_0^{T'} q(t')e^{t'} \int_0^{t'} q(\gamma')e^{-\gamma'} d\gamma' dt'$$
$$- \frac{e^{T'}}{e^{T'} - 1} \int_0^{T'} q(\gamma')e^{-\gamma'} d\gamma' \left(\int_0^{T'} q(\sigma')e^{\sigma'} d\sigma' - 1 \right)$$

where $T' = T/RC$ is the cardiac period measured in units of the arterial time constant.

physiologically meaningful conditions

It is probably useful to remind ourselves of what we are trying to do at this point of the analysis. We have found an expression for the minimum excess work $\hat{w}'$ that can be done for a given ventricular flow rate q' and given arterial resistance R and compliance C. We are trying to find the conditions under which $\hat{w}' > 0$, because these are the conditions under which the reservoir pressure represents the minimum work that the ventricle has to do.

If we consider all possible flow rates q', this analysis becomes so general (and difficult analytically) that it is difficult to understand the results. It is helpful, therefore, to consider what types of flow rates are physiologically reasonable.

- We consider only cases where the stroke volume $V_s > 0$.
- Physiological flow rates involve a period of systole followed by a period of diastole when $q' = 0$.
- For almost all physiological and and clinically relevant cases, the time of systole T_S is short compared to the arterial time constant τ. Therefore, $S' = T_S/RC < 0$.
- Because the heart has to fill before it can eject, the time of diastole is generally greater or, at least, equal to the time of systole. In nondimensional terms this means $\kappa = T'/S' \geq 2$.

For these reasons, we will constrain ourselves to these conditions; in particular to the case $S' < 1$.

general bounds when $S' \ll 1$

For notational convenience, we temporarily drop the primes from the nondimensional variables. This should not cause confusion and we will indicate when we return to dimensional variables.

If $S \ll 1$ we can expand the exponential terms as power series in S. The calculations are quite complex, involving a lot of integration by parts, but are relatively straightforward. The analysis is most conveniently carried out in terms of the instantaneous volume displaced from the heart $v = \int_0^t q dt$, whence the volume flow rate can be written $q = \dot{v}$. We also note that $v(S) = 1$ since we have used the stroke volume V_s to nondimensionalise Q.
As an illustration of the steps in the analysis, we evaluate the indefinite integral term

$$\int_0^t q(\gamma)e^{-\gamma}d\gamma \approx \int_0^t \dot{v}(\gamma)(1-\gamma+...) = v - \int_0^t \dot{v}(\gamma)\gamma d\gamma + ... = v - vt + \int_0^t v(\gamma)d\gamma + ...$$

where the last equation follows from integration by parts.
Using this result, we can evaluate the definite integral

$$\int_0^S q(t)e^{-t}dt \approx 1 - S + S\langle v\rangle + ...$$

where we have used $v(S) = 1$ and defined the average over systole $\langle \cdot \rangle = \frac{1}{S}\int_0^S \cdot dt$.

general bounds when $S' \ll 1$ (2)

Expanding and evaluating all of the terms in the equation for the minimum excess work, we can collect the terms in ascending powers of S

$$\hat{w} \approx \left[\frac{1}{2} - \frac{1}{\kappa} + \frac{\langle v \rangle}{\kappa}\right] + S\left[\frac{1}{2} - \frac{(3\kappa - 4)}{2\kappa}\langle v \rangle + \langle v^2 \rangle - \frac{\langle v \rangle^2}{\kappa} - \frac{\int_0^S vtdt}{\kappa S^2}\right] + S^2[\ldots]$$

As already discussed, the ratio of the cardiac period to the time of systole $\kappa = \frac{T}{T_S} \geq 2$, which says that diastole to is at least as long as systole. Similarly, the assumption that the stroke volume is positive means that the time average volume displacement during systole, $\langle v \rangle > 0$. If both of these assumptions are true then, to $\mathcal{O}(S^0)$, $\hat{w} \geq 0$.

Looking at the $\mathcal{O}(S^1)$ term, we see that things get much more complicated if this term becomes of the same order as the $\mathcal{O}(S^0)$ term. The conditions for which $\hat{w} \geq 0$ depend on several other properties of the volume waveform v as well as the ratio κ: the averages $\langle v \rangle$ and $\langle v^2 \rangle$ and the last term which is related to the first moment of v over S. For any given v, the sign of $\hat{w}$ can be determined fairly easily, but it is difficult to make general statements for such a complex relationship.

Nevertheless, for almost all physiologically and clinically interesting cases we expect $S \ll 1$ so that the conclusions based on the zeroth order term are relevant.

conclusions

From the above arguments we conclude:

For all physiologically and clinically relevant cases: $\hat{w} \geq 0$

The corollary to this is:

The reservoir pressure represents the minimum hydraulic work
that the ventricle can do to generate a given flow
for the given arterial resistance and compliance.

The final conclusion follows that:

The excess pressure represents the excess hydraulic work
that the ventricle does over and above the minimum work
needed for the given conditions.