Mathematical model of the circulation under hypergravity

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Abstract

In these notes, we present a linear model of the human circulatory system to predict a subject's tolerance to hypergravitational forces. Key features of this approach include feedback control elements to model the autonomic nervous system's regulation of heart rate and reserve volume, compartmentalization of the upper and lower circulation to allow for gravitational acceleration in the vertical direction to be incorporated, and the inclusion of partial collapse of the systemic veins. We adopt a steady-state modeling approach, the simplicity of which enables us to predict an individual's tolerance to high gravitational acceleration analytically.

1 Introduction

The biophysical processes underlying haemodynamics and the regulation of blood flow are complex and nonlinear. They involve the pulsatile contractions of the heart chambers, which are regulated by the pacemaker in the sino-atrial node in healthy individuals, and the morphology and plasticity of the vascular system. The rate of the heart's contractions is in turn mediated by baroreceptors located in the carotid sinus and aortic arch which detect changes in pressure. The pulsatile contractions of the heart, smooth muscle and skeletal muscle, along with the compliance of blood vessels, regulate the flow of fluid throughout the vascular system. Several phenomena are known to cause temporary changes in blood flow, causing reduced blood flow to the brain and resulting in a loss or alteration of consciousness. These include amongst others: orthostatic hypotension, transient ischemic attack, and loss of blood volume.

Of particular interest to us is gravity-induced loss of consciousness (G-LOC), which occurs when the sudden increase in the vertical acceleration, G_z, causes blood to pool in the lower extremities. To investigate the relationship between high G_z and hyper-gravity induced pathologies such as G-LOC, we designed a mathematical model which incorporates the effects of gravitational acceleration and studied its numerical behavior using Python. While the effects that vertical and lateral acceleration have on the body are fundamentally non-linear, we postulate that this linear model is sufficient for granular tasks, such as predicting an individual's G-tolerance.

Studies on the effects of centrifugation-induced hypergravity typically focus on post-facto gravity-induced changes on the circulatory system. To our knowledge, this is the first steady-state model with feedback control that includes partial venous collapse, and the first mathematical study of the effect of high Gz on the maintenace of homeostasis on the circulation. Further novelty of this work comes from the calibration of model parameters to a subject's centrifuge simulation data and monitoring,

2 Model Derivation

In this section, we present the model used in this work. The following subsections describe a steady-state flow model which incorporates the effects of gravity in the vertical direction, G_{z}, on hemodynamics. A unique feature of this model is the inclusion partial collapse of the systemic veins. We additionally (describe) a method for feedback control in the circulation to allow for the model to appropriately respond to changes in its parameters.

2.1 Blood Flow Model

We divide the circulation into compartments and divide the vascular compartments into compliance chambers and resistance elements. Each compartment is identified with a unique index i. We assume the following relation between the compliance C_i, the pressure difference between the interior and exterior of the vessel P_i, and the volume V_i:

$$V_i = V_i^0 + C_i P_i = V_i^0 + C_i(P_i^{\text{interior}} - P_i^{\text{exterior}}). \tag{1}$$

Compliance is the ability of a structure to change shape as a function of volume and pressure. The contractions of cardiac chambers result in the compliance values periodically oscillating between a minimum and maximum value during the phases of systole, when the chamber contracts, and diastole, when the chamber relaxes, respectively. The dead volume, V_i^0 is equal to the residual chamber volume at zero pressure. We will interchangeably refer to dead volume as reserve volume, since a reduction in V^0 may compensate for a loss in total volume. The total volume, V_{total} is the sum of the volumes in all compartments:

$$V_{\text{total}} = \sum_i V_i, \tag{2}$$

and similarly, the total reserve volume, V_{total}^0 is the sum of each of the reserve volumes:

$$V_{\text{total}}^0 = \sum_i V_i^0. \tag{3}$$

Subtracting equation (3) from (2) and substituting (1) yields:

$$V_{\text{total}} - V_{\text{total}}^0 = \sum_i C_i P_i. \tag{4}$$

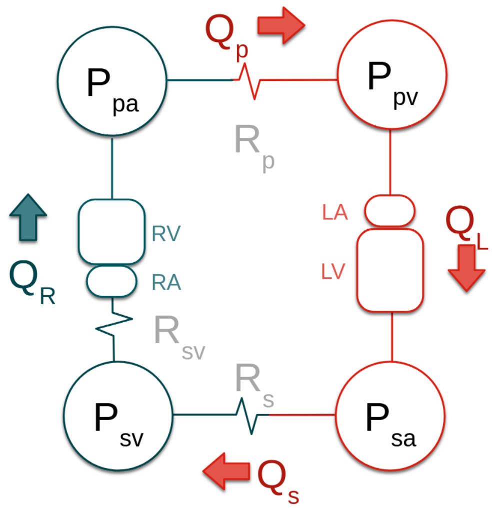

Figure 1: Schematic of the compartmentalization of the circulation used in this model. (u = upper, l = lower, p = pulmonary, s = systemic, pv = pulmonary veins, sv = systemic veins, sa = systemic arteries, pa = pulmonary arteries, RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle)

In a resistance vessel, the flow is proportional to the pressure difference from one end of the vessel to the other. Thus any flow through a resistance vessel between chamber i and j, Q_{ij} is given by Ohm's Law/Poiseuille's Equation:

$$Q_{ij} = \frac{P_i - P_j}{R_{ij}}. \tag{5}$$

We model the systemic arteries (sa), systemic veins (sv), pulmonary arteries (pa) and pulmonary veins (pv) as compliance vessels and tissues and organs as resistance vessels.

In order to simplify the modelling process we average over the cardiac cycle, effectively reducing the pulsatile flow to a continuous flow. Moreover, as the model descrives the system at steady-state, the pressures, flows, and volumes are all time-independent. See Figure 1 for schematic of the connectivity of the described elements.

Cardiac output or systemic flow is defined as the volume of blood delivered to the systemic circulation over time and can be computed by:

$$Q_{\text{sa,sv}} = F V_{\text{stroke}} \tag{6}$$

where $Q_{\text{sa,sv}} = Q_{\text{s}}$ is the flow between the systemic arteries and systemic veins, F is heart rate in beats per unit time and stroke volume V_{stroke} is the volume of blood ejected by the left ventricle per heart beat.

Letting t be time, and recalling our steady-state assumption of time-independence for all chambers i:

$$\frac{\mathrm{d}V_i}{\mathrm{d}t} = \sum_{j=1}^{n} Q_{\mathrm{ji}} - \sum_{k=1}^{m} Q_{ik} = 0 \tag{7}$$

or in other words, the total flow entering a vessel is equal to the flow exiting a vessel. Thus, we may drop the subscript on Q_{ij} for any i and j and simply refer to Q as flow in general.

For most of the systemic circulation, the external pressure is that of the atmosphere, which we denote as zero pressure. For the pulmonary circulation and both sides of the heart, the external pressure is the intrathoracic pressure, denoted as P_{thorax}, which varies during the cycle of breathing and is lower during inspiration and higher during expiration.

On average, the value of P_{thorax} is negative and is to be thought of as the pressure in the tissue surrounding the lungs. The lungs are elastic and tend to collapse and a pressure difference between the air in the lungs and the air in the surrounding tissue is needed to keep them open. Negative intrathoracic pressure is generated by contraction of the diaphragm.

Since F is the same for both the left and right side of the heart (as a result of there being a single pacemaker, known as the sino-atrial node) the stroke volumes of the left and right heart are equal and are approximated by using equation (1) for the volume in a ventricle at the end of diastole (and considering the volume remaining in the ventricle at the end of systole to be negligible):

$$V_{\mathrm{stroke}} = C_{\mathrm{LVD}}(P_{\mathrm{RA}} - P_{\mathrm{thorax}}) \tag{8}$$
$$= C_{\mathrm{RVD}}(P_{\mathrm{pv}} - P_{\mathrm{thorax}}) \tag{9}$$

where C_{LVD} and C_{RVD} are the left and right ventricular diastolic compliances respectively. Combining equations (6) with (8) and (9), respectively, yields the following:

$$Q = FC_{\mathrm{LVD}}(P_{\mathrm{RA}} - P_{\mathrm{thorax}}) \tag{10}$$
$$= FC_{\mathrm{RVD}}(P_{\mathrm{pv}} - P_{\mathrm{thorax}}) \tag{11}$$

Additionally, by equation (5) and the steady state assumption, we have pulmonary flow given by:

$$Q = \frac{P_{\mathrm{pa}} - P_{\mathrm{pv}}}{R_{\mathrm{p}}} \tag{12}$$

2.2 Incorporation of Gravity

To incorporate the effects of gravity in the vertical direction, $\mathrm{G_z}$, we compartmentalize the systemic circulation into an upper and lower component, each with their own pressure, flow and resistance values. See Figure 2 for a visual schematic of this compartmentalization. Then, by equation (5),

$$Q_{\mathrm{s}}^{\mathrm{u}} = \frac{P_{\mathrm{sa}}^{\mathrm{u}} - P_{\mathrm{sv}}^{\mathrm{u}}}{R_{\mathrm{s}}^{\mathrm{u}}} \tag{13}$$

$$Q_{\mathrm{s}}^{\mathrm{l}} = \frac{P_{\mathrm{sa}}^{\mathrm{l}} - P_{\mathrm{sv}}^{\mathrm{l}}}{R_{\mathrm{s}}^{\mathrm{l}}} \tag{14}$$

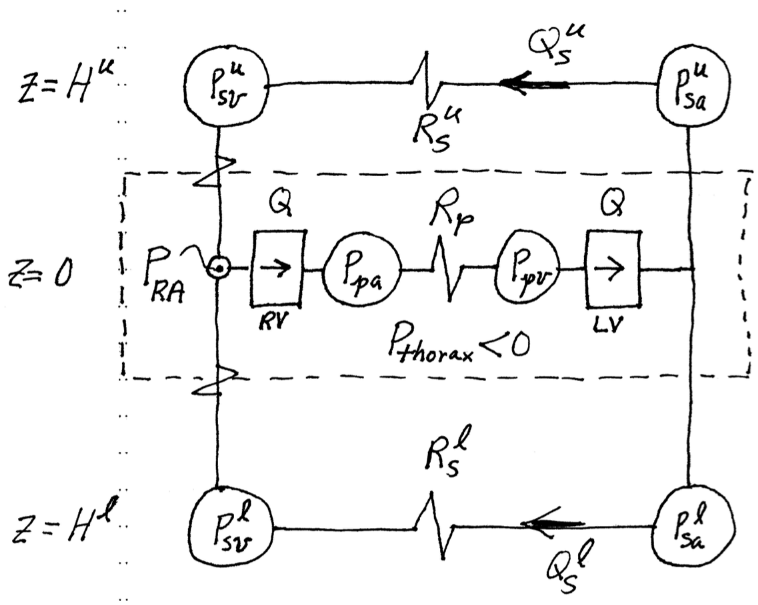

Figure 2: Compartmentalization of the circulation into upper, lower and thoracic components. (H = height, u = upper, l = lower, p = pulmonary, s = systemic, pv = pulmonary veins, sv = systemic veins, sa = systemic arteries, pa = pulmonary arteries, RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle).

In the systemic circulation, there are multiple tissues and organs connected in parallel; their flows add to give the total systemic flow:

$$Q_{\text{sa,sv}} = \sum_j Q_{\text{s}_j} \tag{15}$$

Note that by equation (15),

$$Q = Q_{\text{s}}^{\text{u}} + Q_{\text{s}}^{\text{l}} \tag{16}$$

Then, we are able consider the blood between the upper and lower compartment of the systemic circulation as a fluid-filled column and use Bernouli's equation to obtain the following relationship:

$$P_{\text{sa}}^{\text{l}} - P_{\text{sa}}^{\text{u}} = \rho g (H^{\text{u}} - H^{\text{l}}) \tag{17}$$

where, ρ is the density of blood, g is the gravitational acceleration, and H^{u} and H^{l} denote upper and lower heights respectively such that

$$H^{\text{u}} > 0 > H^{\text{l}}. \tag{18}$$

2.3 Partial Venous Collapse

The heart chambers are lumped into one chamber which we choose to be the right atrium. Depending on right atrial pressure, P_{RA}, we get the following equations

$$P_{\text{sv}}^{\text{u}} = \max\{0, P_{\text{RA}} - \rho g H^{\text{u}}\} \tag{19}$$

$$P_{\text{sv}}^{\text{l}} = \max\{(0, P_{\text{RA}}) - \rho g H^{\text{l}}\} \tag{20}$$

which give rise to three cases.

Case I:

$$P_{\text{thorax}} < P_{\text{RA}} < 0 \tag{21}$$
$$P_{\text{sv}}^{\text{u}} = 0 \tag{22}$$
$$P_{\text{sv}}^{\text{l}} = \rho g(-H^{\text{l}}) \tag{23}$$

Case II:

$$0 < P_{\text{RA}} < \rho g(-H^{\text{l}}) \tag{24}$$
$$P_{\text{sv}}^{\text{u}} = 0 \tag{25}$$
$$P_{\text{sv}}^{\text{l}} = P_{\text{RA}} + \rho g(-H^{\text{l}}) \tag{26}$$

Case III:

$$\rho g(H^{\text{u}}) < P_{\text{RA}} \tag{27}$$
$$P_{\text{sv}}^{\text{u}} = P_{\text{RA}} - \rho g(-H^{\text{u}}) \tag{28}$$
$$P_{\text{sv}}^{\text{l}} = P_{\text{RA}} + \rho g(-H^{\text{l}}). \tag{29}$$

Cases I and II observe a localized partial collapse of the systemic veins, just upstream of their entry into the thoracic compartment. This is referred to as partial venous collapse. Case III exhibits no partial collapse of the systemic veins. We now have a linear system of equations that we can solve analytically for each of the three cases. In the uncontrolled case, our parameters are the total reserve volume, compliance and resistance values of the arteries and veins, stroke volume, the upper and lower compartment heights, total volume, gravitational acceleration, blood density, and heart rate. The need for feedback control can be clearly seen by considering the example of what occurs during exercise. When we begin to exercise, the blood vessels in our systemic circulation dilate to increase blood flow to the tissues that are being depleted of oxygen. This dilation results in the radius of the vessel increasing and thereby reducing the systemic resistance. Clearly, by equations (13) and (14), this will cause the systemic arterial pressure to drop. Baroreceptors detect this drop in blood pressure from a set value and adjust the heart rate accordingly to improve cardiac output. Because heart rate is a fixed parameter in the uncontrolled model, and the cardiac output is directly proportion to heart rate, Q will not increase sufficiently.

2.4 Idealized Controller

In this subsection, we attempt to remedy the issues of the uncontrolled circulation by considering F and V_{total}^{0} to be unknown variables rather than parameters, so that Q can be proportionally adjusted during dynamic changes to the circulation. Since total volume is still fixed, the reduction of total reserve volume serves to increase the volume of distributed blood between the chambers, thereby increasing flow. We assume that the autonomic nervous system is able to make adjustments to heart rate and total reserve volume to maintain specific target values of P_{sa}^{u} and also the pressure difference that stretches the wall of the right atrium, ΔP_{RA}. Thus, we have new parameters $(P_{\text{sa}}^{\text{u}})^*$ and $(\Delta P_{\text{RA}})^*$ defined as

$$P_{\text{sa}}^{\text{u}} = (P_{\text{sa}}^{\text{u}})^* \tag{30}$$

$$P_{\text{RA}} - P_{\text{thorax}} = (\Delta P_{\text{RA}})^* \tag{31}$$

For the model to be valid, V_{total}^0 must be nonnegative as a working system always has some venous reserve volume. We will derive analytical solutions for F and V_{total}^0 for each case separately, with the following procedure:

1. Identify the case defining condition for validity on P_{thorax}.
2. Use the upper and lower systemic venous pressures and the control equations (30) and (31) to solve for the lower systemic arterial pressure.
3. Solve for the upper and lower systemic flows with the appropriate systemic pressure values to obtain an expression for Q.
4. Use Q from the previous step to obtain F as a function of parameters.
5. Solve for pulmonary pressures knowing Q and write total reserve volume V_{total}^0 as a function of parameters.

2.4.1 Case I

Since $P_{\text{RA}} = P_{\text{thorax}} + (\Delta P_{\text{RA}})^*$ by equation (31), the condition for validity of case I can be stated as follows:

$$P_{\text{thorax}} \leq -(\Delta P_{\text{RA}})^* \tag{32}$$

Substituting the controlled value for P_{sa}^{u} into equation (17) yields

$$P_{\text{sa}}^{\text{l}} = (P_{\text{sa}}^{\text{u}})^* + \rho g (H^{\text{u}} - H^{\text{l}}) \tag{33}$$

Using equations (13), (14) and (33), the systemic pressures specify the flows

$$Q_{\text{s}}^{\text{u}} = \frac{1}{R_{\text{s}}^{\text{u}}} (P_{\text{sa}}^{\text{u}} - P_{\text{sv}}^{\text{u}}) \tag{34}$$

$$= \frac{1}{R_{\text{s}}^{\text{u}}} (P_{\text{sa}}^{\text{u}})^* \tag{35}$$

$$Q_{\text{s}}^{\text{l}} = \frac{1}{R_{\text{s}}^{\text{l}}} \left(P_{\text{sa}}^{\text{l}} - P_{\text{sv}}^{\text{l}}\right) \tag{36}$$

$$= \frac{1}{R_{\text{s}}^{\text{l}}} ((P_{\text{sa}}^{\text{u}})^* + \rho g H^{\text{u}}) \tag{37}$$

With both upper and lower systemic flows known, the cardiac output is simply their sum by equation (16):

$$Q = \left(\frac{1}{R_{\text{s}}^{\text{u}}} + \frac{1}{R_{\text{s}}^{\text{l}}}\right) (P_{\text{sa}}^{\text{u}})^* + \frac{\rho g H^{\text{u}}}{R_{\text{s}}^{\text{l}}} \tag{38}$$

Then, by using equation (11) and substituting (31) and (38), an equation for heart rate as a function of parameters can be obtained:

$$F = \frac{Q}{C_{\mathrm{RVD}}\left(P_{\mathrm{RA}} - P_{\mathrm{thorax}}\right)} \tag{39}$$

$$= \frac{\left(\frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\right)\left(P_{\mathrm{sa}}^{\mathrm{u}}\right)^{*} + \frac{\rho g H^{\mathrm{u}}}{R_{\mathrm{s}}^{\mathrm{l}}}}{C_{\mathrm{RVD}}\left(\Delta P_{\mathrm{RA}}\right)^{*}} \tag{40}$$

The pulmonary pressures can be solved for by setting equations (8) and (9) equal to each other and substituting equation (31):

$$C_{\mathrm{LVD}}(P_{\mathrm{pv}} - P_{\mathrm{thorax}}) = C_{\mathrm{RVD}}\left(\Delta P_{\mathrm{RA}}\right)^{*} \tag{41}$$

$$P_{\mathrm{pv}} - P_{\mathrm{thorax}} = \frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}\left(\Delta P_{\mathrm{RA}}\right)^{*} \tag{42}$$

We know from equation (12) that $P_{\mathrm{pa}} - P_{\mathrm{pv}} = QR_{\mathrm{p}}$ and adding this quantity to both sides of (42) results in:

$$P_{\mathrm{pa}} - P_{\mathrm{thorax}} = \frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}\left(\Delta P_{\mathrm{RA}}\right)^{*} + QR_{\mathrm{p}} \tag{43}$$

Using equation (4) and our case I assumptions, we also arrive at an expression for total reserve volume as a function of parameters:

$$V_{\mathrm{total}}^{0} = V_{\mathrm{total}} - C_{\mathrm{p}}\frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}\left(\Delta P_{\mathrm{RA}}\right)^{*} - \left(T_{\mathrm{p}}G_{\mathrm{s}} + C_{\mathrm{sa}}\right)\left(P_{\mathrm{sa}}^{\mathrm{u}}\right)^{*} - \left(\frac{T_{\mathrm{p}}}{R_{\mathrm{s}}^{\mathrm{l}}} + C_{\mathrm{sa}}^{\mathrm{l}}\right)\rho g H^{\mathrm{u}} - C_{\mathrm{s}}^{\mathrm{l}}\rho g - H^{\mathrm{l}}) \tag{44}$$

where the arterial compliance is the sum of the compartment compliances:

$$C_{\mathrm{sa}} = C_{\mathrm{sa}}^{\mathrm{u}} + C_{\mathrm{sa}}^{\mathrm{l}}, \tag{45}$$

the conductance term G_{s} is the sum of the upper and lower conductances (reciprocal resistances):

$$G_{\mathrm{s}} = G_{\mathrm{s}}^{\mathrm{u}} + G_{\mathrm{s}}^{\mathrm{l}} = \frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}, \tag{46}$$

the pulmonary time constant T_{p} is

$$T_{\mathrm{p}} = C_{\mathrm{pa}}R_{\mathrm{p}} \tag{47}$$

and the pulmonary compliance, C_{p} is

$$C_{\mathrm{p}} = C_{\mathrm{pa}} + C_{\mathrm{pv}}. \tag{48}$$

2.4.2 Case II

Similarly, case II is defined by the following inequality:

$$0 < P_{\mathrm{RA}} < \rho g H^{\mathrm{u}} \tag{49}$$

which can be rewritten as

$$-(\Delta P_{\mathrm{RA}})^{*} < P_{\mathrm{thorax}} < \rho g H^{\mathrm{u}}. \tag{50}$$

by equation (31). Since $P_{\mathrm{RA}} < \rho g H^{\mathrm{u}}$, there is partial collapse of the upper systemic veins (not extending all the way down to the heart). Thus, similar to case I, we have that $P_{\mathrm{sv}}^{\mathrm{u}} = 0$, but because right atrial pressure is nonnegative, there is no systemic venous collapse below the heart, yielding the following:

$$P_{\mathrm{sv}}^{\mathrm{l}} = \rho g(-H^{\mathrm{l}}) + P_{\mathrm{RA}} \tag{51}$$

$$= \rho g(-H^{\mathrm{l}}) + P_{\mathrm{thorax}} + (\Delta P_{\mathrm{RA}})^{*} \tag{52}$$

The upper and lower systemic arterial pressures are the same as in case I, given by equations (30) and (33), and the upper and lower systemic flows follow:

$$Q_{\mathrm{s}}^{\mathrm{u}} = \frac{1}{R_{\mathrm{s}}^{\mathrm{u}}}\left((P_{\mathrm{sa}}^{\mathrm{u}})^{*} + \rho g(H^{\mathrm{u}} - H^{\mathrm{l}})\right) \tag{53}$$

$$Q_{\mathrm{s}}^{\mathrm{l}} = \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\left((P_{\mathrm{sa}}^{\mathrm{u}})^{*} + \rho g\left(H^{\mathrm{u}} - H^{\mathrm{l}}\right)\right) - \rho g(-H^{\mathrm{l}}) - P_{\mathrm{thorax}} - (\Delta P_{\mathrm{RA}})^{*}\Big) \tag{54}$$

$$= \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\left((P_{\mathrm{sa}}^{\mathrm{u}})^{*} + \rho g H^{\mathrm{u}} - P_{\mathrm{thorax}} - (\Delta P_{\mathrm{RA}})^{*}\right) \tag{55}$$

Adding the upper and lower systemic flows together yields the cardiac output:

$$Q = \left(\frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{u}}}\right)(P_{\mathrm{sa}}^{\mathrm{u}})^{*} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\left(\rho g H^{\mathrm{u}} - P_{\mathrm{thorax}} - (\Delta P_{\mathrm{RA}})^{*}\right) \tag{56}$$

which in turn allows us to solve for heart rate by equation (31) and (56) into (11):

$$F = \frac{\left(\frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{u}}}\right)(P_{\mathrm{sa}}^{\mathrm{u}})^{*} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\left(\rho g H^{\mathrm{u}} - P_{\mathrm{thorax}} - (\Delta P_{\mathrm{RA}})^{*}\right)}{C_{\mathrm{RVD}}}(\Delta P_{\mathrm{RA}})^{*} \tag{57}$$

The pulmonary pressures can be solved by setting equations (8) and (9) equal to each other after solving for pressure difference:

$$C_{\mathrm{LVD}}(P_{\mathrm{pv}} - P_{\mathrm{thorax}}) = C_{\mathrm{RVD}}(\Delta P_{\mathrm{RA}})^{*} \tag{58}$$

$$P_{\mathrm{pv}} - P_{\mathrm{thorax}} = \frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}(\Delta P_{\mathrm{RA}})^{*} \tag{59}$$

We know from equation (12) that $P_{\mathrm{pa}} - P_{\mathrm{pv}} = QR_{\mathrm{p}}$ and adding this quantity to both sides results in:

$$P_{\mathrm{pa}} - P_{\mathrm{thorax}} = \frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}(\Delta P_{\mathrm{RA}})^{*} + QR_{\mathrm{p}} \tag{60}$$

$$= \frac{C_{\text{RVD}}}{C_{\text{LVD}}} + R_{\text{p}} \left(\left(\frac{1}{R_{\text{s}}^{\text{u}}} + \frac{1}{R_{\text{s}}^{\text{u}}} \right) (P_{\text{sa}}^{\text{u}})^* + \frac{1}{R_{\text{s}}^{\text{l}}} (\rho g H^{\text{u}} - P_{\text{thorax}} - (\Delta P_{\text{RA}})^*) \right) \tag{61}$$

Following the same procedure from case I, we can solve for V_{total}^0 in terms of parameters using equation (4) and our case II assumptions:

$$\begin{aligned} V_{\text{total}}^0 = V_{\text{total}} - C_{\text{p}} \frac{C_{\text{RVD}}}{C_{\text{LVD}}} (\Delta P_{\text{RA}})^* - (T_{\text{p}} G_{\text{s}} + C_{\text{sa}}) (P_{\text{sa}}^{\text{u}})^* - (T_{\text{p}} G_{\text{s}}^{\text{l}} \\ + C_{\text{sa}}^{\text{l}}) \rho g H^{\text{u}} - C_{\text{s}}^{\text{l}} \rho g (-H^{\text{l}}) - (C_{\text{sv}}^{\text{l}} - T_{\text{p}} G_{\text{s}}) (P_{\text{thorax}} + (\Delta P_{\text{RA}})^*) \end{aligned} \tag{62}$$

2.4.3 Case III

Repeating the procedure from the previous two cases, we can derive analytical solutions for heart rate and total reserve volume in case III where there is no venous collapse. The defining inequality for this case is

$$\rho g (H^{\text{u}}) < P_{\text{RA}} = P_{\text{thorax}} + (\Delta P_{\text{RA}})^* \tag{63}$$

which subsequently gives the condition for validity on P_{thorax}:

$$\rho g H^{\text{u}} - (\Delta P_{\text{RA}})^* \leq P_{\text{thorax}} \tag{64}$$

The upper and lower systemic venous pressures are defined as:

$$P_{\text{sv}}^{\text{u}} = P_{\text{RA}} - \rho g (-H^{\text{u}}) = P_{\text{thorax}} + (\Delta P_{\text{RA}})^* - \rho g (-H^{\text{u}}) \tag{65}$$

$$P_{\text{sv}}^{\text{l}} = P_{\text{RA}} + \rho g (-H^{\text{l}}) = P_{\text{thorax}} + (\Delta P_{\text{RA}})^* + \rho g (-H^{\text{l}}) \tag{66}$$

The upper and lower systemic arterial pressures are the same as the other two cases as given by given by equations (30) and (33) and combining them with equations (13) and (14) result in:

$$\begin{aligned} Q_{\text{s}}^{\text{u}} &= \frac{1}{R_{\text{s}}^{\text{u}}} ((P_{\text{sa}}^{\text{u}})^* - (P_{\text{thorax}} + (\Delta P_{\text{RA}})^* - \rho g H^{\text{u}})) \\ &= \frac{1}{R_{\text{s}}^{\text{l}}} ((P_{\text{sa}}^{\text{u}})^* + \rho g H^{\text{u}} - (P_{\text{thorax}}) - (\Delta P_{\text{RA}})^*) \end{aligned} \tag{67}$$

$$\begin{aligned} Q_{\text{s}}^{\text{l}} &= \frac{1}{R_{\text{s}}^{\text{l}}} \big((P_{\text{sa}}^{\text{u}})^* + \rho g (H^{\text{u}} - H^{\text{l}})) - (P_{\text{thorax}} + (\Delta P_{\text{RA}})^* + \rho g (-H^{\text{l}})) \big) \\ &= \frac{1}{R_{\text{s}}^{\text{l}}} ((P_{\text{sa}}^{\text{u}})^* + \rho g H^{\text{u}} - (P_{\text{thorax}}) - (\Delta P_{\text{RA}})^*) \end{aligned} \tag{68}$$

Since the upper and lower pressure differences are the same, the sum of the upper and lower systemic flows results in the following equation for cardiac output:

$$Q = \left(\frac{1}{R_{\text{s}}^{\text{u}}} + \frac{1}{R_{\text{s}}^{\text{l}}} \right) ((P_{\text{sa}}^{\text{u}})^* + \rho g H^{\text{u}} - (P_{\text{thorax}}) - (\Delta P_{\text{RA}})^*) \tag{69}$$

Then, heart rate is given in the same way by rearranging equation (11) and plugging in Q from equation (69):

$$F = \frac{\left(\frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\right)\left((P_{\mathrm{sa}}^{\mathrm{u}})^* + \rho g H^{\mathrm{u}} - (P_{\mathrm{thorax}}) - (\Delta P_{\mathrm{RA}})^*\right)}{C_{\mathrm{RVD}}\,(\Delta P_{\mathrm{RA}})^*} \tag{70}$$

Then, we use the pulmonary pressures from (59) and (60) and plug in our case III value for Q from equation (69) into the latter:

$$P_{\mathrm{pa}} - P_{\mathrm{thorax}} = \frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}\,(\Delta P_{\mathrm{RA}})^* + \left(\frac{1}{R_{\mathrm{s}}^{\mathrm{u}}} + \frac{1}{R_{\mathrm{s}}^{\mathrm{l}}}\right)\left((P_{\mathrm{sa}}^{\mathrm{u}})^* + \rho g H^{\mathrm{u}} - (P_{\mathrm{thorax}}) - (\Delta P_{\mathrm{RA}})^*\right) R_{\mathrm{p}} \tag{71}$$

Finally, we can write the total reserve volume for case III with the following familiar expression from equation (4):

$$\begin{aligned} V_{\mathrm{total}}^{0} = V_{\mathrm{total}} - C_{\mathrm{p}}\frac{C_{\mathrm{RVD}}}{C_{\mathrm{LVD}}}\,(\Delta P_{\mathrm{RA}})^* - (T_{\mathrm{p}}G_{\mathrm{s}} + C_{\mathrm{sa}})\,(P_{\mathrm{sa}}^{\mathrm{u}})^* - (T_{\mathrm{p}}G_{\mathrm{s}}^{\mathrm{l}} + \\ C_{\mathrm{sa}}^{\mathrm{l}} - C_{\mathrm{sv}}^{\mathrm{u}})\rho g H^{\mathrm{u}} - C_{\mathrm{s}}^{\mathrm{l}}\rho g(-H^{\mathrm{l}}) - (C_{\mathrm{sv}}^{\mathrm{l}} - T_{\mathrm{p}}G_{\mathrm{s}})(P_{\mathrm{thorax}} + (\Delta P_{\mathrm{RA}})^*) \end{aligned} \tag{72}$$

Note that when the equality

$$P_{\mathrm{thorax}} + (\Delta P_{\mathrm{RA}})^* = \rho g H^{\mathrm{u}}. \tag{73}$$

holds, we are in the borderline between case II and III. Setting equations (57) and (70) equal gives:

$$F = \frac{G_{\mathrm{s}}(P_{\mathrm{sa}}^{\mathrm{u}})^*}{C_{\mathrm{RVD}}(\Delta P_{\mathrm{RA}})^*}. \tag{74}$$

Setting the total reserve volume equations for these two cases, (62) and (72), equal to each other, it is clear that they only differ with the terms $\rho g H^{\mathrm{u}}$ and $P_{\mathrm{thorax}} + (\Delta P_{\mathrm{RA}})^*$. Thus, heart rate and total reserve volume are continuous functions in the transition between case II and III.