Personalised Simulation of Haemodynamic Response to the Valsalva Manoeuvre

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Abstract. The Valsalva manoeuvre is a simple and low-risk procedure used for assessing the autonomic nervous system or for diagnosing several heart conditions. The analysis of the cardiovascular alterations occurring during and after the manoeuvre due to the changes of the intrathoracic pressure can be facilitated using mathematical modelling. In this paper we present a method of employing a mathematical model to simulate the haemodynamic response to the Valsalva manoeuvre in a given individual. In particular, we present a method of adapting our own multi-compartmental mathematical model of cardiovascular system (based on standard physiological data from the literature) to reflect the steady state of the cardiovascular system in the given subject before the manoeuvre is started. The structure of our cardiovascular model is also briefly discussed providing some particulars on the used modelling techniques.

Keywords: blood pressure, heart rate variations, baroreflex, autonomic function, mathematical model

1   Introduction

The Valsalva manoeuvre (VM) is often used as a simple, non-invasive, inexpensive and low-risk procedure of diagnosing several heart conditions (including heart failure and heart murmurs abnormalities) [1–5] or for testing the autonomic nervous system [6–9]. The manoeuvre consists in a forced expiratory effort against a closed airway, which increases the intrathoracic and intra-abdominal pressure and causes a specific haemodynamic response [10–12]. The VM triggers several cardiovascular regulatory mechanisms which are based mainly on the activity of baroreceptors (blood pressure sensors), with some influence from slowly adapting pulmonary stretch receptors, as well as central and peripheral

chemoreceptors [13–15, 11] and an almost negligible impact of nonautonomic humoral mechanisms (e.g. angiotensin II) [16].

For assessing the autonomic function, the VM is typically performed with the patient in the supine or sitting position with the intraoral pressure equal to 40 mm Hg maintained for 15 seconds [11, 12]. The diagnosis is based on heart rate variations, which can be recorded with electrocardiography or using a finger cuff device [12].

The changes in arterial blood pressure (BP) and heart rate (HR) during and after the typical VM can be divided into 4 physiological phases, as follows [17] (see Figure 1): (I) onset of strain with a rise of arterial pressure and a slight drop of HR, (II) continued strain with a decrease of arterial pressure, the corresponding tachycardia and ensuing partial pressure recovery, (III) pressure release with a sudden drop of BP and further increase in HR, (IV) arterial pressure overshoot and the resulting bradycardia [12].
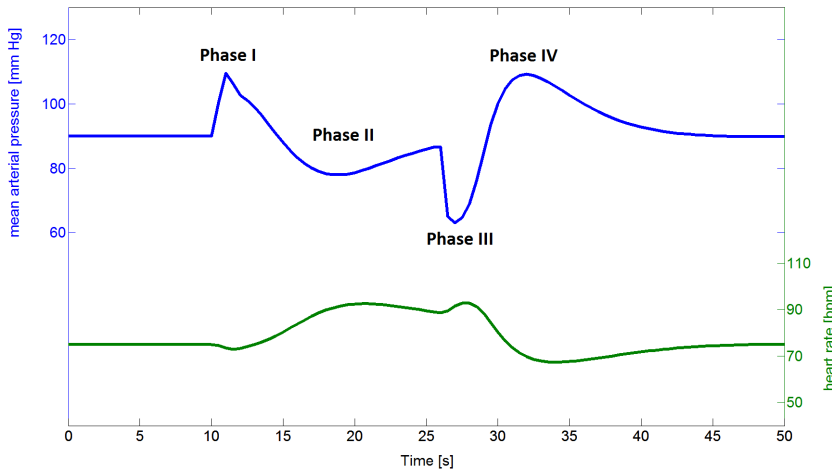

Fig. 1. Simulation of mean arterial pressure and heart rate changes during the Valsalva manoeuvre in a reference patient (the intrathoracic pressure increased to 40 mm Hg for 15 seconds)

2 Mathematical model

2.1 Model structure

We developed a multi-compartmental non-pulsatile model of the cardiovascular system with three baroreflex mechanisms controlling heart rate, peripheral resistance and venous capacity [18]. The proposed model (operating on mean

blood pressures) is much simpler than previously existing multi-compartmental pulsatile models of the VM (describing instantaneous changes of blood pressure with pulse pressure) [19, 20], but still provides a satisfactory representation of the haemodynamic response to the VM. The complete description of the model, its validation and limitations can be found in our previous work [18].

The cardiovascular part of the model involves 7 vascular compartments (aorta, systemic arteries, systemic capillaries, systemic veins, vena cava, pulmonary arteries and pulmonary veins) and 2 cardiac chambers (right heart and left heart, each combining the corresponding atrium and ventricle) [18]. To enable simulation of the VM, 6 intrathoracic compartments (vena cava, right heart, pulmonary arteries, pulmonary veins, left heart and aorta) are connected to a pressure source corresponding to the intrathoracic pressure (see Figure 2) [18]. The vena cava compartment includes both superior and inferior vena cavae. All vascular compartments are modelled as capacitors (representing the volume of blood stored in the compartment at a given pressure) with hydraulic resistances between the compartments corresponding to pressure and energy losses associated with the blood flow (the resistances change dynamically with the changes in the compartment volumes) [18]. With the compartmental structure of the cardiovascular model, we do not describe the continuous blood pressure decline along the blood vessels, but we approximate it instead with a step pressure reduction between the adjacent compartments. Therefore, within each compartment the blood pressure is uniform and equal to the pressure at the entry to the corresponding vasculature.
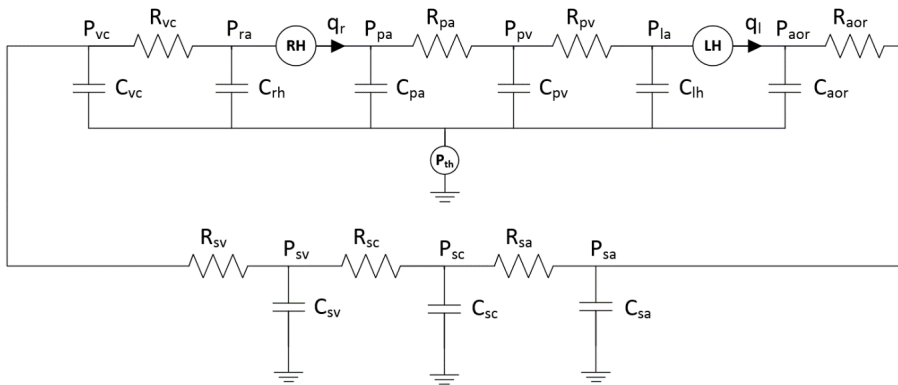

Fig. 2. Electric analogy of the cardiovascular model, where R denotes resistances, P – pressures, C – capacities, q_r and q_l – cardiac outputs from right and left heart ventricles respectively. The meaning of subscripts is: aor – aorta, sa – systemic arteries, sc – systemic capillaries, sv – systemic veins, vc – vena cava, pa – pulmonary arteries, pv – pulmonary veins, rh – right heart, lh – left heart, ra – right atrium, la – left atrium, th – intrathoracic [18].

A slight modification of the representation of vena cava resistance in the model was employed for modelling backflow of blood from right atrium and vena cava during the onset of Valsalva manoeuvre, when the increased intrathoracic pressure compresses these two compartments and pushes some blood back into the systemic veins. Having vena cava resistance represented in the model as a hydraulic resistor between vena cava and right atrium (with the resistance being volume-dependent as described in [18]) distorts the process of emptying of these two compartments, since the significant increase of vena cava resistance (due to volume reduction) impedes emptying of right atrium, while not affecting emptying of vena cava itself. In order to make this process more realistic in the model, for backflow calculations, vena cava resistance was divided in two equal parts localized on each side of vena cava compartment. This way, the blood pushed from the right atrium back to vena cava flows across half of vena cava resistance, while backflow from vena cava to systemic veins takes into account the other half of vena cava resistance (the resistance of systemic veins, being relatively small, was neglected here). This solution was included mainly for technical correctness to avoid unnaturally high differences between pressures of vena cava and right atrium, however it does not affect the results significantly. For normal blood flow (towards the heart) vena cava resistance is always represented as one resistor localized between vena cava and right atrium (see Figure 2).

For all systemic venous compartments (ie. systemic veins and vena cava) nonlinear pressure-volume curves were used due to relatively high lumped compliance of these compartments and relatively high differences in their operating pressures (especially in systemic veins) [18]. For other compartments, linear P-V relationships were used assuming relatively small compliance changes, in which case a linear approximation does not lead to large errors.

A nonlinear (sigmoidal) function was used to describe the relationship between the ventricular stroke volume and atrial pressure (the Frank-Starling law). For the right ventricle we have the following equation [18]:

$$SV_r = \frac{SV_{max,r}}{1 + \exp\left(\frac{-P_{ra}-x_r}{s_r}\right)} a_r \tag{1}$$

where $SV_{max,r}$ represents the maximal right ventricular stroke volume, s_r determines the slope of the sigmoidal function, x_r describes the position of the curve with respect to the atrial pressure axis, a_r is a functional parameter describing the impact of afterload ie. the increase or decrease of stroke volume as a result of decreased or increased pressure downstream the ventricle ([18]).

An analogous equation is used for the left ventricle [18]:

$$SV_l = \frac{SV_{max,l}}{1 + \exp\left(\frac{-P_{la}-x_l}{s_l}\right)} a_l \tag{2}$$

Under the steady-state conditions the cardiac output from both ventricles (calculated as the product of stroke volume and heart frequency) must be equal:

$$q_l = SV_l f = SV_r f = q_r \tag{3}$$

The parameters s and x for both equations are calculated before each run of the model as follows. The parameter s_r is calculated so that when the system is operating at the nominal conditions (ie. at the nominal right atrial pressure $P_{ra,n}$ and the nominal cardiac output q_n) the slope of the SV_r curve (at the nominal operating point) is equal to cardiac output sensitivity to right atrial pressure $sens_r = 35$ ml/min/mmHg/kg [21]. Associating the slope of the curve with the derivative dSV_r/dP_{ra} (from equation 1) and neglecting the impact of afterload, we have hence the following equation for s_r:

$$s_r = \frac{SV_{max,r} \left(\frac{SV_{max,r} f_n}{q_n} - 1 \right)}{k_r \left(\frac{SV_{max,r} f_n}{q_n} \right)^2} \tag{4}$$

where q_n is the nominal cardiac output ($q_n = 80$ ml/min/kg body weight [21]) and k_r is $sens_r$ transformed to ml/mmHg units:

$$k_r = \frac{sens_r BW}{60 f_n} \tag{5}$$

where BW is the patient body weight and f_n is the nominal heart frequency (heart rate) in beats per minute ($f_n = 75$ bpm [22]).

Similarly, we have:

$$s_l = \frac{SV_{max,l} \left(\frac{SV_{max,l} f_n}{q_n} - 1 \right)}{k_l \left(\frac{SV_{max,l} f_n}{q_n} \right)^2} \tag{6}$$

$$k_l = \frac{sens_l BW}{60 f_n} \tag{7}$$

where $sens_l$ is the sensitivity of cardiac output to changes of left atrial pressure ($sens_l = 20.5$ ml/min/mmHg/kg [23]). $SV_{max,r}$ and $SV_{max,l}$ were both given the value 130 ml [22].

The parameters x_r and x_l are set so that at the nominal atrial pressures ($P_{ra,n}$ and $P_{la,n}$) both right and left ventricular outputs (being the product of stroke volume and heart rate) are equal to the nominal cardiac output.

$$x_r = -P_{ra,n} - s_r \log\left(\frac{SV_{max,r}f_n}{q_n} - 1\right) \tag{8}$$

$$x_l = -P_{la,n} - s_l \log\left(\frac{SV_{max,l}f_n}{q_n} - 1\right) \tag{9}$$

Sigmoidal functions were also used to describe the operation of baroreflex mechanisms based on the activity of three groups of baroreceptors – aortic baroreceptors located in the aortic arch, carotid baroreceptors located in carotid sinuses and cardiopulmonary baroreceptors located in the right atrium [18]. All baroreceptors measure continuously the blood pressure in each location and compare the measured values with the normal value for the given location. Based on the weighted sum of pressure deviations from normal levels, the baroreflex mechanisms modify then the controlled parameters (ie. heart rate, peripheral resistance and venous unstressed volume) in order to bring the pressures back to normal [18]. Note that during the VM the aortic transmural pressure measured by the aortic baroreceptors deviates from the normal aortic pressure to a much higher extent than the transmural pressure in the carotid sinuses.

The model is implemented in Matlab® (The Mathworks Inc.) and all simulations are performed using a built-in solver for stiff systems of ordinary differential equations (ode15s) [18].

2.2   Model parameters

The model includes the following parameters: general parameters of the cardiovascular system (nominal cardiac output, nominal HR, total blood volume), parameters related to P-V curves (blood distribution, nominal pressures and compliances, maximal volumes, parameter reflecting the relative level of vascular compliance etc.), parameters of cardiac stroke volume curve (maximal stroke volume etc.) and parameters of all baroreflex mechanisms (amplitudes, gains and time constants) [18].

All model parameters were taken from the literature and correspond to a normal healthy reference patient - an active, but untrained 70-kg mature male individual, as described in our previous work [18]. The initial (nominal) resistances have been calculated from the nominal pressure differences across the adjacent compartments in the normal steady state taking the nominal blood flow across the whole system of 80 ml/min/kg body weight [21].

Note that the nominal pressures used in the model for each compartment (see [18]) are not the average pressures of the corresponding part of the human vasculature, but the pressures at the entrance of the given vascular tree (as described earlier). Therefore the derived pressure-volume curves and their parameters (eg. unstressed volumes) do not necessarily reflect the real values from humans. In the model it is assumed that all the blood stored in a given compartment is subject to the same pressure and that the modelled vessels have a constant cross-section (constant radius) throughout their length. In reality, not

only the blood pressure drops continuously across the length of the vessels (due to friction losses), but also the total cross-section of the vessel (or a group of vessels) is subject to variations. This aspect can be mostly seen in the systemic arteries compartment which includes large arteries, small arteries and arterioles with a significant pressure difference between the beginning (large arteries) and the end of the compartment (arterioles). This issue applies to all compartments used in the model (although in other compartments the pressure differences are much smaller), however, it has no significant impact on the model outcomes.

2.3   Assumptions

The following assumptions were used when developing the cardiovascular model:

1. blood is an incompressible and Newtonian fluid
2. blood flow throughout the system is laminar
3. the body is in the supine position
4. the effects of muscle pump and respiratory pump are negligible
5. normal intrathoracic pressure is equal to the ambient pressure
6. systemic arteries (except aorta), systemic veins (except vena cava) and systemic capillaries are not compressed by the increased intrathoracic or intra-abdominal pressure
7. inertance effects associated with the blood flow are negligible
8. the cross-section of all vessels remain circular at all times (including vena cava during collapse)
9. active response of vascular smooth muscles to pressure changes is negligible
10. vascular viscoelastic effects (stress relaxation) are negligible
11. there is no hysteresis in the vascular pressure-volume curves
12. the pressure waves reflected from vessel bifurcations are negligible
13. there is no blood filtration or refilling across the capillaries
14. the Anrep effect (a mild increase in heart contractility at increased afterload) is negligible
15. there is no pressure "talk" between right and left ventricle (as modelled in [24])
16. the effects of respiration on heart rate variations are negligible
17. there is no time latency in baroreflex operation
18. baroreceptors are not sensitive to the rate of pressure changes
19. there are no other mechanisms controlling blood pressure (eg. chemoreceptors or lung mechanoreceptors)
20. there is no regional blood flow autoregulation (eg. in brain, heart or kidneys)

3   Model adaptation to the individual patient

3.1   Method overview

The main outputs of the VM are the variations of arterial blood pressure and heart rate measured before, during and after the manoeuvre. The same variables

are the main outputs of our model simulations, as shown in Figure 1. Since the model is based on the literature data representing the reference patient, the comparison of model simulations with experimental data from real patients is not straightforward.

Initially (before any changes of the intrathoracic pressure), the cardiovascular system (modelled as described above and in our previous work [18]) is in the steady state. This steady state is characterized by the cardiac output, heart rate, blood pressures, compartment volumes etc. as set for the reference patient. Before simulating the cardiovascular response to the VM in a real patient, one should modify some model parameters in order to better represent the analysed patient in the simulation. More specifically, one should shift the modelled system from the original steady state corresponding to the physiology of the reference patient to a new steady state corresponding, as well as possible, to the haemodynamics of the given patient. Obviously it is not feasible to provide all the individual pressures and blood distribution across all cardiovascular compartments or other physiological parameters. Therefore, we decided to use a simplified approach and concentrate only on two most important physiological parameters for analysing cardiovascular response to the VM. As already mentioned, these are the arterial blood pressure and heart rate, which are both easy to measure in the patient and which are monitored anyway during the VM. Consequently, we wanted to shift the cardiovascular system to the steady state corresponding to the average arterial blood pressure and average heart rate of the given patient measured before the manoeuvre (ideally recorded over a longer period of time in order to smooth out the natural individual variations and to represent as much as possible the normal values for the given patient, assuming that the patient is not overly excited or anxious). At the same time we wanted to keep as much parameters as possible on the level typically reported in the literature. The problem was hence to find a minimal number of model parameters that need to be changed in order to shift the system to a new steady state corresponding to the desired arterial blood pressure and heart rate.

Since heart rate is one of the model parameters (and hence one can set it directly to the desired value), the problem was how to obtain the required steady-state arterial blood pressure. Any steady state of the cardiovascular system is associated with a certain blood flow which must be equal to the output of both right and left heart ventricles. Therefore, in order to shift the system to a new steady state, one has to modify somehow the cardiac output. This can be done by changing the parameters of the relationships between the stroke volume and atrial pressure for right and left ventricles (equations 1 and 2 representing the Frank-Starling law of the heart).

We decided to keep the shape of both stroke volume curves unchanged ie. to keep the slopes (parameters s) and the maximal values (parameters SV_{max}) of both sigmoidal functions at the original level corresponding to the reference patient. To modify the steady state of the system we propose to shift horizontally the right ventricular stroke volume curve by changing the parameter x_r of the Frank-Starling relationship of the right heart (equation 1). Shifting the stroke

volume curve of the right ventricle results in a significant change of the output of the right ventricle. This in turn affects the amount of blood remaining in the right atrium and the amount of blood entering pulmonary arteries. Consequently, it affects blood pressure in right atrium and pulmonary arteries, which in turn affect the blood flow to and from the adjacent compartment and hence the blood flow in all other blood compartments across the whole cardiovascular system. These transient blood flow conditions continue until a new steady state is reached with a new level of blood flow across the system corresponding to the new cardiac output (as determined by the modified stroke volume curve). Using a Matlab built-in function *fminsearch*, which uses the simplex search method [25], we are able to find the value of parameter x_r needed to obtain the desired arterial blood pressure.

Hence, by changing directly only two model parameters i.e. heart rate and parameter x_r we are able to shift the system to a new steady state in which the cardiac output and the blood pressures, blood volumes and resistances of all compartments are modified so that the arterial blood pressure reaches the desired level.

The only other model parameters that can be easily adjusted for the given patient, are the parameters expressed per kg of body weight which can be scaled to the weight of the given patient. These include: nominal vascular compliances, total blood volume or cardiac output sensitivity to right and left atrial pressure changes. All other model parameters are assumed to remain at the original level corresponding to the physiology of the reference patient.

3.2   Case study

Below we present an example of shifting the system from the original steady state for the reference patient with the arterial blood pressure $P_{sa} = 90$ mm Hg and the heart rate $f = 75$ bpm to a new steady state corresponding to the arterial blood pressure $P_{sa} = 110$ mm Hg and the heart rate $f = 70$ bpm. As described above, to reach the new steady state we changed directly the value of heart rate (from 75 to 70 bpm) and we changed the value of parameter x_r (from -1.71 to 3.05), which corresponded to a horizontal shift of the right ventricular stroke volume curve, as shown in Figure 3.

The original steady-state conditions for the reference patient were as follows: right atrial pressure $P_{ra} = 2$ mm Hg, left atrial pressure $P_{la} = 5$ mm Hg, stroke volume $SV = 74.67$ ml, cardiac output $q = 93.33$ ml/s ($q = SVf$). The new steady-state conditions are as follows: right atrial pressure $P_{ra} = $ -1.62 mm Hg, left atrial pressure $P_{la} = 6.93$ mm Hg, stroke volume $SV = 105.55$ ml, cardiac output $q = 123.15$ ml/s.

Figure 4 shows the operating points on the pressure-volume curves for each cardiovascular compartment before and after the changes. In this example we assumed that the new patient has the same weight as the reference patient (70 kg) and hence all model parameters (except heart rate and x_r) are the same as for the reference patient (based on the literature data). In particular, the
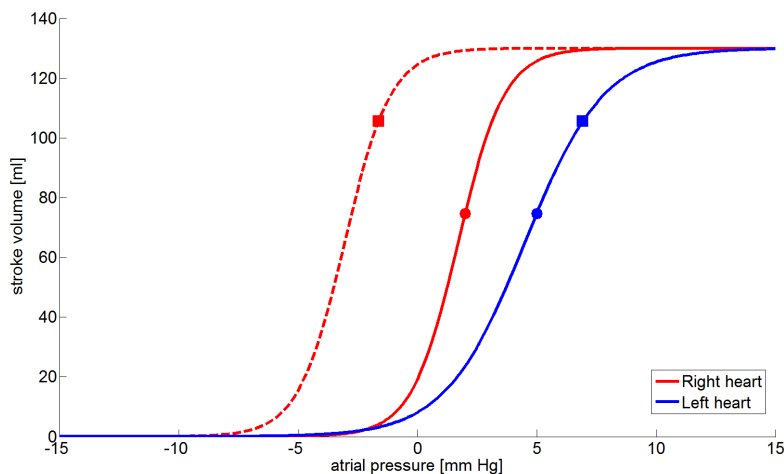
Fig. 3. Frank-Starling relationship between the stroke volume and atrial pressure modelled for a) the reference patient (solid lines with the dots representing the original steady-state conditions), b) the new patient (dashed lines with the squares representing the new steady-state conditions).

parameters of the pressure-volume curves of all cardiac and vascular compartments (ie. unstressed volumes, maximal volumes etc.) are exactly the same as for the reference patient, hence the new steady state corresponding to the new patient is obtained by forcing the model to change the operating points on all pressure-volume curves (ie. to change accordingly the volumes of blood stored in each compartment).

Finally, Figure 5 shows the simulation of the haemodynamic response to the typical 15-s VM (with the intrathoracic pressure increased to 40 mm Hg) starting from both the original steady state of the cardiovascular system in the reference patient and from the new steady state.

3.3   Technical considerations

In order to reach the desired steady state of the cardiovascular system, the baroreflex mechanisms and the stroke volume dependence on afterload have to be temporarily switched off in the model, as these mechanisms depend on the reference pressures set originally for the reference patient. After finding the new steady state of the system and the corresponding pressures and volumes of each compartment, the new steady-state pressures may be then used as the new reference pressures for these mechanisms (aortic, arterial and right atrial pressures for the baroreflex mechanisms; pulmonary arterial and aortic pressures for the afterload impact on the stroke volume of right and left heart respectively), assuming that these pressures represent the normal values for the given patient.
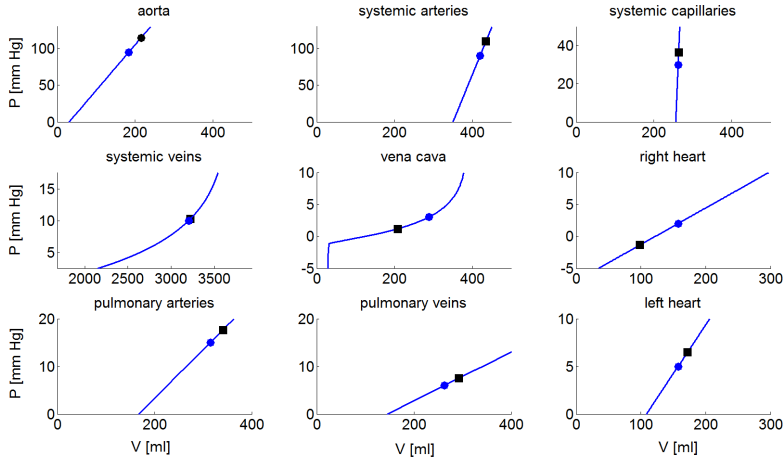
Fig. 4. Operating points on the cardiovascular pressure-volume curves for the original steady-state conditions for the reference patient (blue dots) and for the new steady-state conditions (black squares). The parameters of all pressure-volume curves remained unchanged.

Alternatively, in order not to switch off the baroreflex mechanisms or the impact of afterload, in each modelling step during the transient conditions one could take the current blood pressures as the normal values, thus indicating no deviations of pressure from the normal levels and, hence, effectively disabling the regulatory mechanisms. This approach leads to the same result, however, it is associated with a higher computational cost.

Following the change of heart rate, the minimal and maximal heart rate admissible by the baroreflex control of heart will also change accordingly (these parameters are calculated in the model so that in the steady state conditions the baroreflex operates in the middle point of the sigmoidal curve) [18].

Note that, instead of changing the parameter x_r of the Frank-Starling relationship for the right heart (ie. moving horizontally the curve relating the right ventricular stroke volume to the right atrial pressure), one could change the parameter x_l of the analogous relationship for the left heart. In this study, the former has been changed based on the assumption that any changes in the systemic arterial pressure (with respect to the reference patient) will affect more the right atrial pressure than the left atrial pressure.

As shown in Figure 6, the magnitude of hemodynamic response to the VM simulated in the model depends strongly on the initial state of the system and hence shifting the cardiovascular system to the steady-state conditions corresponding to the mean arterial pressure of the given patient is crucial for simulating the response to the VM. Obviously, the same holds for estimating some physiological parameters of the given patient based on the recorded data on arterial blood pressure and heart rate variations in response to the VM.
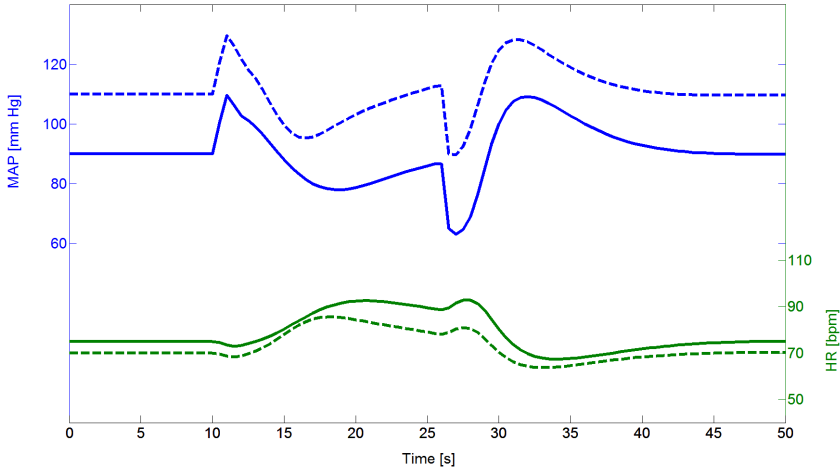
Fig. 5. Simulation of mean arterial blood pressure (MAP) and heart rate (HR) variations in response to the 15-s Valsalva manoeuvre with the intrathoracic pressure increased to 40 mm Hg modelled from the original steady state of the cardiovascular system in the reference patient (solid lines) and from the modified steady state for the given patient (dashed lines).

3.4   Discussion

One should be aware that the new steady state of the system reached using the above approach reflects only the arterial pressure and heart rate of the given patient and most likely does not represent correctly the actual state of all cardiovascular compartments in the given patient and hence such an approach is not ideal. In particular, the new value of cardiac output (equal to the blood flow across the system in the new steady state) will likely not match the real cardiac output of the given patient. Knowing the real cardiac output of the patient (which can be measured invasively or estimated non-invasively), one could change accordingly the values of both x_r and x_l parameters, thus having a better representation of the cardiac function in the modelled patient and reaching the correct steady-state cardiac output. Similarly, knowing the central venous pressure (which again can be measured invasively or estimated non-invasively), one could also change the parameter x_l so that the new steady-state venous pressure in the model would correspond to the measured value.

As far as the parameters scaled to patient's weight are concerned, in the future versions of the model, some of these parameters could depend not only on the weight of the given individual, but also on other anthropometrics, such as height or age. Some parameters, such as the maximal stroke volume (SVmax), could also depend on the physical fitness of the given individual.

All other model parameters (except x_r), as well as all per-kg values of the scalable parameters remain at the levels set for the reference patient (based on
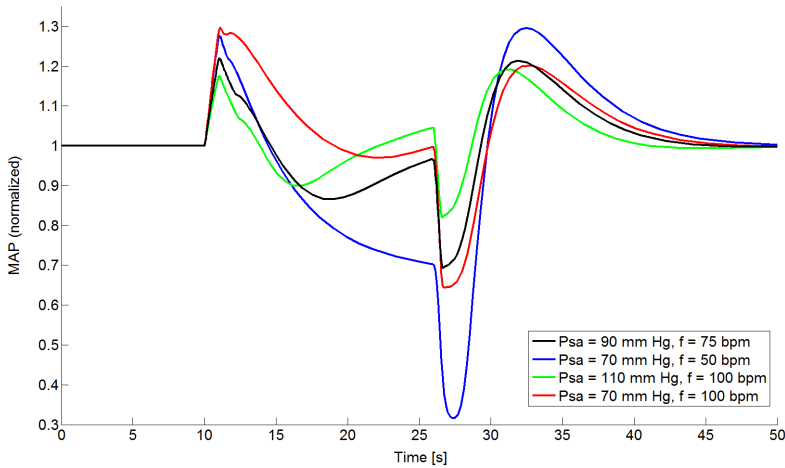
Fig. 6. Model simulations of the normalized mean arterial pressure during the Valsalva manoeuvre in patients with different cardiovascular steady-state conditions.

typical physiological data from the literature), unless one has some particular information or data on the given patient, which would allow changing individual parameters (e.g. decreased vascular compliance due to atherosclerosis).

We would like to point out also that using the presented approach we are not able to shift the cardiovascular system to all possible states. For instance there is an upper limit of the steady-state mean arterial pressure that one can reach in the model using the presented method. This is related to the closed nature of the cardiovascular system. When right and left ventricular outputs are initially increased (following the changes of stroke volume curves), the arterial pressure and the volume of blood in the arterial compartment increase as well. This means that the volume of blood on the low-pressure side of the system (ie. veins, vena cava, right atrium) must decrease and hence the right atrial pressure decreases. This in turn increases the pressure difference between the arteries and right atrium and hence increases the blood flow in the system (which is needed to keep the arterial pressure high). However, lowering right atrial pressure results in reducing the output of right heart ventricle (according to the Frank-Starling law, see equation 1 or Figure 3) which cannot keep up with the high blood inflow to the heart and hence the right atrial pressure starts to increase, which re-increases the right ventricular output, but also reduces the amount of blood in the arteries. This continues until the system finds a steady state and hence there is a maximal arterial pressure that can be reached (approximately 125 mm Hg).

Also, changing significantly the right ventricular stroke volume curve (moving it far left along the atrial pressure axis) is associated with increasing the

right ventricular output to a very high level. Depending on the initial blood distribution in the system this can quickly lead to emptying of right heart, which can compromise the computational efficiency of the model.

The aforementioned parameter SV_{max} (maximal ventricular stroke volume) may also pose limitation in some cases. For instance, it would be impossible to reach a steady state with a very high mean arterial pressure and a low heart rate without changing SV_{max}, as the cardiac output is the product of stroke volume and heart rate and hence it is upper bounded by $SV_{max}f$.

Nevertheless, in most cases the above limitations do not apply and the presented method is effective in the wide range of steady-state conditions of the cardiovascular system. Using this method we were able to simulate haemodynamic response to the VM in several patients (as described in [18]) without any problems. If, however, a need arises to shift the system to an extreme steady state (e.g. a very high mean arterial pressure), one would need to change some other model parameters (for instance, the initial blood distribution across the system).

4   Conclusions

We presented a method of employing our mathematical model for simulating the haemodynamic response to the Valsalva manoeuvre in a given individual. The same method could be used for comparing the simulation results with experimental data (ie. recorded blood pressure and heart rate variations in response to the manoeuvre) to estimate some physiological parameters of the given patient.

The presented method enables simulation of the cardiovascular system of a given subject starting from the steady-state conditions corresponding to the real arterial blood pressure and heart rate of the patient. We acknowledge the fact that this method is not ideal as it uses only two measured parameters, while assuming all other parameters at the standard physiological level (as reported in the literature). As already indicated, measuring additional parameters (such as cardiac output or central venous pressure) could obviously provide better results. Moreover, given any additional information on patient conditions, one can always adjust accordingly the corresponding model parameters to improve modelling accuracy.

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