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A model of mechanical interactions between heart and lungs

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To study the mechanical interactions between heart, lungs and thorax, we propose a mathematical model combining a ventilatory neuromuscular model and a model of the cardiovascular system, as described by Smith *et al.* (Smith, Chase, Nokes, Shaw & Wake 2004 *Med. Eng. Phys.* **26**, 131–139. (doi:10.1016/j.medengphy.2003.10.001)). The respiratory model has been adapted from Thibault *et al.* (Thibault, Heyer, Benchetrit & Baconnier 2002 *Acta Biotheor.* **50**, 269–279. (doi:10.1023/A:1022616701863)); using a Liénard oscillator, it allows the activity of the respiratory centres, the respiratory muscles and rib cage internal mechanics to be simulated. The minimal haemodynamic system model of Smith includes the heart, as well as the pulmonary and systemic circulation systems. These two modules interact mechanically by means of the pleural pressure, calculated in the mechanical respiratory system, and the intrathoracic blood volume, calculated in the cardiovascular model. The simulation by the proposed model provides results, first, close to experimental data, second, in agreement with the literature results and, finally, highlighting the presence of mechanical cardiorespiratory interactions.

Keywords: integrated cardiopulmonary model; pleural pressure; septum;
cardiogenic oscillations

1. Introduction

Clinical diagnosis and treatment decisions taken by health professionals could be improved by using mathematical models. In order to understand the cardiopulmonary interactions so as to contribute partially to diagnosis improvement, we developed a mathematical model that accounts for interactions occurring between cardiovascular and pulmonary systems.

The elaboration of this cardiopulmonary model is one of the parts of the SAPHIR project (‘a Systems Approach for PHysiological Integration of Renal, cardiac, and respiratory functions’). This project (Thomas *et al.* 2008) aims at producing a multi-resolution core modelling environment, along with implementation of a prototype core model of human physiology targeting short- and long-term regulation of blood pressure, body fluids and homeostasis of the major solutes. The goal is to keep the basic core model compact enough to ensure fast

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One contribution of 17 to a Theme Issue ‘From biological and clinical experiments to mathematical models’.

execution time (in view of eventual use in the clinic) and yet to allow elaborate detailed submodels of target tissues or organs while maintaining the system-level regulatory compensations. Rather than starting from scratch, a legacy integrated model has served as the starting point, namely, the classic model of *Guyton et al. (1972)*, which focused on blood pressure regulation. In that model, the pulmonary function is not very detailed. Therefore an extension is proposed here.

(a) *Cardiopulmonary interactions*

Cardiopulmonary interactions are the consequence of the cardiopulmonary anatomy: (i) the cardiac cavities, the pulmonary veins and arteries, as well as a part of the vena cava, are subjected to the intrathoracic (or pleural) pressure, (ii) the right ventricle is connected upstream to the lung, and (iii) both ventricles have a common wall, the interventricular septum. This anatomy, together with the dynamic mechanical properties of organs, ensures reciprocal effects between lung and cardiac volumes and pressures.

Respiration occurs as a result of the reduction or rise in pleural pressure that is transmitted to the intrathoracic organs. This results in pressure and volume changes in the lungs, in addition to similar changes in inner and outer chambers of the left and right heart (*Scharf et al. 1979; Wise & Robotham 1981; Pinsky 1993; Duke 1999; Montebelli 2005*).

Direct ventricular interaction has a significant impact on cardiovascular dynamics and is caused by both the flexible septum and the elastic passive pericardium (*Luo et al. 2007*). Consequently, a rise in right ventricle preload decreases left ventricle filling.

During inspiration, the reduction in pleural pressure yields a decrease in the extramural pressures of the right atrium and right ventricle. This induces their expansion as well as the expansion of the superior and inferior vena cava. Therefore, a rise in pressure gradient occurs, the flow from extrathoracic veins increases and the right ventricle filling (preload) is improved. Then the right ventricle stroke volume (SV) increases via the Frank–Starling mechanism. This increase in the right ventricle SV during inspiration, combined with the direct ventricle interaction via the septum, reduces the filling and the SV of the left heart as well as the systolic blood pressure (*Ruskin et al. 1973; Scharf et al. 1979*). During expiration, the opposite occurs along with a delayed effect of inspiratory rise in right ventricle output (*Guntheroth et al. 1974*). The maximal left SVs occur in the second half of expiration. These variations are accentuated by the increased tidal volume, in other words with the increase in the amplitude of the pleural pressure variations.

To sum up, although the left ventricle SV is, on average, on a respiratory cycle, similar to the right ventricle SV, the ventilation dissociates these values: the left ventricle SV increases during early expiration, whereas the right ventricle SV is decreased.

Simultaneously, the heart mechanical activity induces volume and pressure variations in the rib cage. Two types of volume variations, are non-invasively observable: (i) the rib cage volume variations, observable on plethysmography signal and taken into account by the thoracocardiography (TCG) approach (*Bloch 1998; Bloch et al. 1998, 2002*), and (ii) the volume variations observable on the pneumotachogram and called cardiogenic oscillations (*Dahlstrohm et al. 1945; Hathorn 2000; Bijaoui et al. 2001; Abdulhay & Baconnier 2007*).

Concerning the first volume variations, as the heart is one of the elements of the thoracic cavity content, cardiac volume variations cause rib cage volume variations. Generally, a varying intrathoracic blood volume induces a varying thoracic volume.

The second type of volume variations can be explained. First during cardiac diastole, blood enters the thorax via the vena cava (right heart filling) but no blood leaves the thorax (aorta flow is negligible); second, during systole blood entering the thorax via the vena cava is negligible but blood flows out of the thorax following left ventricle contraction (ejection). Intrapulmonary pressure rise may follow heart filling until the onset of ejection, whereas intrapulmonary pressure fall follows ejection. As alveolar air volume varies in view of the intrapulmonary pressure, an inward air flow following systole and an outward air flow following diastole are expected.

(b) Cardiopulmonary models

Most of the models combining pulmonary and cardiovascular systems (CVSs) do not address their high dynamical interaction. They are mainly either cardiovascular or pulmonary, except two models (Lu *et al.* 2001; Montebelli 2005). The model of Lu *et al.* (2001) combines the important components of the cardiopulmonary system and highlights their interaction, so as to explore how this system responds to disturbances such as during the Valsalva manoeuvre. The heart model used is based on the model of Chung *et al.* (1997) and the respiratory model characterizes the properties of the upper airways resistance and lungs. The model of Montebelli (2005) simulates the cardiopulmonary interactions during spontaneous breathing by healthy individuals and patients with chronic obstructive pulmonary disease (COPD).

In both models, in order to combine the respiratory and cardiovascular models, the alveolar, pleural and abdominal pressures are considered as functional outputs of the respiratory model and they are inserted in the cardiovascular model, where the pressure effect was considered significant. These two models can then help to understand the cardiopulmonary interactions in terms of the effect of respiratory dynamics on the CVS, but not in terms of cardiogenic oscillations.

In this paper, we develop a model that combines a respiratory pattern generator module (Thibault *et al.* 2002) with a simple respiratory model module simulating rib cage internal mechanics and a minimal haemodynamic system model (Smith *et al.* 2004), taking into account cardiogenic oscillations. To achieve our goals, we consider, on the one hand, pleural pressure as the functional output of the respiratory model and we insert it into the CVS where the effect of pleural pressure is considered significant. On the other hand, pericardium, pulmonary artery and pulmonary veins blood volumes are considered as the cardiovascular outputs, and therefore as respiratory inputs.

Figure 1 illustrates the cardiopulmonary anatomy and the elements of the proposed model. The phrenic and vagus nerves take part in some of the interactions, as will be described further with a scheme of the model. Via the vagus nerve, the lungs affect the respiratory rhythm generator that delivers an inspiratory command to the rib cage muscles via the phrenic nerve. Figure 1 shows the heart, contained in the rib cage; according to this position, the heart has an influence on the mechanics of the chest wall but it is also subjected to the volume and pressure variations of the rib cage.

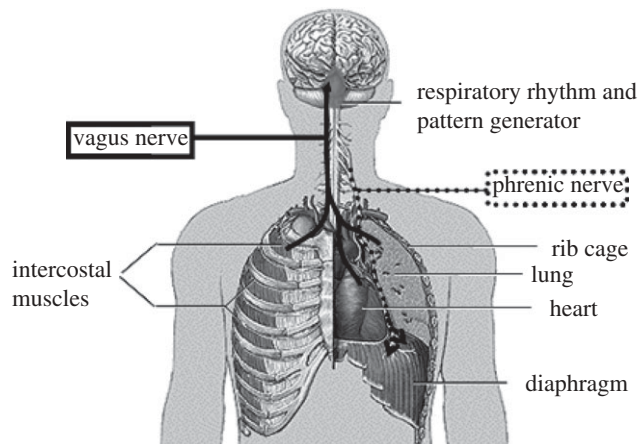


Figure 1. Cardiopulmonary system including the CVS and the neuromuscular ventilatory system.

Although respiratory pressure changes on the outer surface of the intrapulmonary vessels (respectively, on the blood vessels of the abdominal compartment) have some mechanical effects on gas exchange (respectively, on mean systemic pressure), we do not include these in our model.

In §2, we describe the model: starting from a reasonable model of the ventilation, we introduce a realistic pleural pressure (instead of a constant value) in an existing haemodynamic system model (Smith *et al.* 2004). The simulated results, presented in §3, are in agreement with the literature (Guz *et al.* 1987) and with experimental data. In particular, we show that, during inspiration, the SV of the left ventricle decreases and the SV of the right ventricle increases. During expiration, the inverse occurs. This highlights the cardiopulmonary interactions. In §4, the discussion essentially focuses on a review of the minimal haemodynamic system model of Smith *et al.* (2004).

2. Method

The SAPHIR project (Thomas *et al.* 2008) proposes a comprehensive, modular, interactive modelling environment centred on overall regulation of blood pressure and body fluid homeostasis.

In order to fit the SAPHIR philosophy, our proposed model of cardiopulmonary system is decomposed into two modules: a haemodynamic module and a respiratory module. The definition of input and output variables is essential for the future integration of the modules into the SAPHIR core model.

(a) Haemodynamic system

The ‘minimal haemodynamic system’ developed by Smith *et al.* (2004) has been used in this paper (figure 2). This model is intended to be suitable for rapid diagnostic feedback:

- (i) it can be run on a desktop computer in reasonable time,
- (ii) its parameters can be relatively easily determined or approximated for a specific patient,

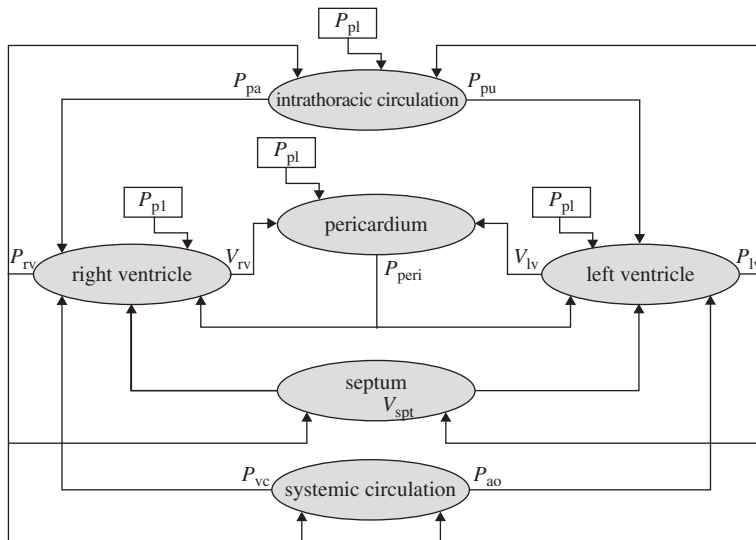


Figure 2. Schematic representation of the minimal closed-loop model of the CVS (adapted from Smith *et al.* 2007).

- (iii) it is stable with minimal complexity, and
- (iv) it uses a minimal number of governing equations, based on a pressure–volume approach.

The CVS is divided into a series of elastic chambers separated by resistances: each elastic chamber (left and right ventricles, aorta, vena cava, pulmonary artery, pulmonary vein, pericardium) is modelled with its own pressure–volume relationship.

The model intends to simulate the essential haemodynamics of the CVS including the heart, the pulmonary and systemic circulation systems, ventricular interaction and valve dynamics. Atria are not designed in the model. This CVS model has been physiologically validated and used by many authors (Hann *et al.* 2005, among others).

This system has been implemented under BERKELEY-MADONNA software (Macey & Oster 2007) based on the equations defined in Smith *et al.* (2004) and the parameter values listed in Smith *et al.* (2007). The simulation of the model gives results, similar to the results of the authors, proposed in Smith *et al.* (2004). Some are presented in figure 3.

In this model, the pleural pressure is a constant parameter. A new equation governing this pressure could then be easily integrated in this haemodynamic system model.

(b) Respiratory system

This system simulates the activity of the respiratory centres, the respiratory muscles and rib cage internal mechanics. It combines a central respiratory pattern generator and a passive mechanical respiratory system (Thibault *et al.* 2002).

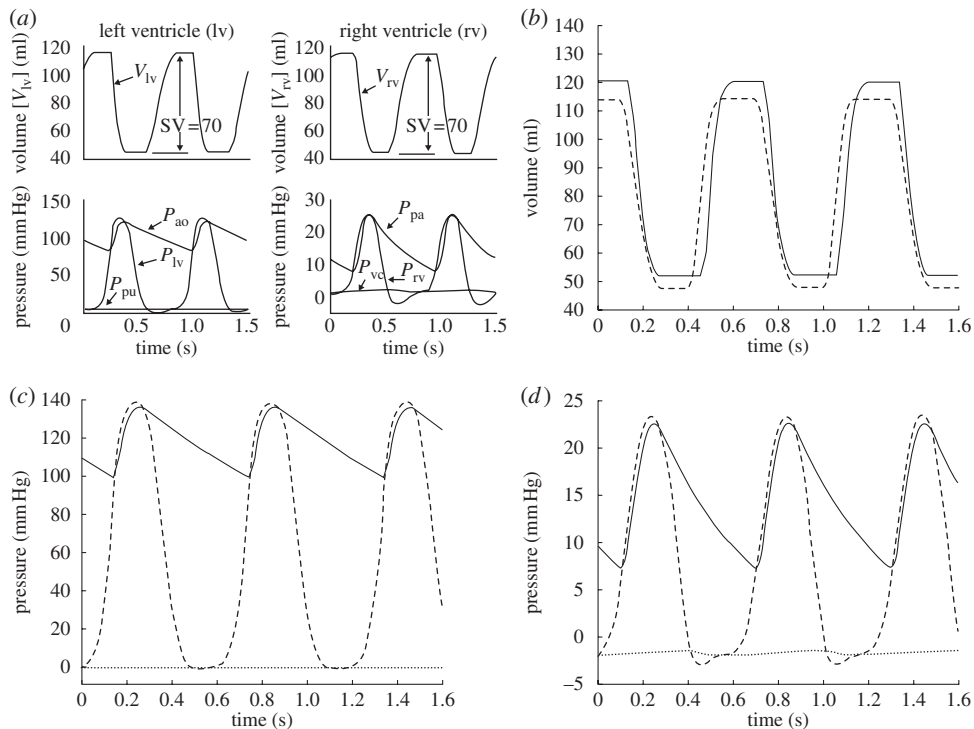


Figure 3. (a) Original simulations of the cardiovascular model (adapted from Smith *et al.* 2004). (b–d) BERKELEY-MADONNA (Macey & Oster 2007) simulations of our implementation of the model. (b) Solid line, V_{lv} ; dashed line, V_{rv} . (c) Solid line, P_{ao} ; dashed line, P_{lv} ; dotted line, P_{pu} . (d) Solid line, P_{pa} ; dashed line, P_{rv} ; dotted line, P_{vc} .

There are two physiological interactions between the central respiratory pattern generator and the mechanical respiratory system:

- (i) the respiratory pattern generator activity is modulated by the lung volume variations, and
- (ii) the lung volume is periodically modified by the respiratory pattern generator activity through the respiratory muscles.

(i) The central respiratory pattern generator

For the central respiratory pattern generator, we do not use the modified Van der Pol oscillator developed by Pham Dinh *et al.* (1983) as in Thibault *et al.* (2002); a Liénard system is proposed as the basis for modelling the respiratory rhythm generator.

Liénard systems (Liénard 1928) are two-dimensional ordinary differential equations: $dy/dt = x$, $dx/dt = -g(y) + xf(y)$, where f and g are polynomials. The use of Liénard systems is universal in biological modelling, especially for physiological processes (Demongeot *et al.* 2007).

The proposed model of the central respiratory pattern generator is then defined by the following equations, where x is a hidden variable, y the activity of the respiratory rhythm generator, V_{alv} the alveolar volume and HB a constant.

This constant refers to the Hering–Breuer reflex (Clark & von Euler 1972; Knox 1973), triggered to prevent over-inflation of the lungs

$$\frac{dx}{dt} = f(x, y) - \text{HB} \frac{d(V_{\text{alv}})}{dt} \quad (2.1)$$

and
$$\frac{dy}{dt} = x. \quad (2.2)$$

In equation (2.1), $f(x, y)$ corresponds to a simple Liénard system

$$f(x, y) = (ay^2 + by)x + (ay^3 + by^2). \quad (2.3)$$

The second term of equation (2.1) allows the effect of the mechanical system state on the central respiratory pattern generator to be taken into account. a , b and HB are respiratory parameters.

The choice of a and b defines the form and the frequency (f_R) of the respiratory oscillations. Moreover, to cover a higher range of respiratory frequencies, we introduce a parameter α in equations (2.1) and (2.2)

$$\frac{dx}{dt} = \alpha \left(f(x, y) - \text{HB} \frac{d(V_{\text{alv}})}{dt} \right) \quad (2.1')$$

and
$$\frac{dy}{dt} = \alpha x. \quad (2.2')$$

When $y < 0$ (respectively, $y > 0$), the oscillator is considered to be in inspiratory (respectively, expiratory) phase.

(ii) The passive mechanical respiratory system

In the absence of respiratory muscle activity, the chest wall is represented by a purely elastic compartment (elastance E_{cw}). The rib cage volume or intrathoracic volume (V_{th}) is driven by pleural pressure (P_{pl})

$$P_{\text{pl}} = E_{\text{cw}}(V_{\text{th}} - V_{\text{th0}}). \quad (2.4)$$

In the presence of muscular activity, the previous equation becomes

$$P_{\text{pl}} = P_{\text{mus}} + E_{\text{cw}}(V_{\text{th}} - V_{\text{th0}}). \quad (2.5)$$

The pressure generated by the respiratory muscles (P_{mus}) is the result of the conversion by the muscles of the respiratory pattern generator output into pressure (figure 4). P_{mus} is then a function of y and it is defined in the proposed model as an integral of the central respiratory activity y generated by the respiratory oscillator and disrupted by the alveolar volume (equation (2.1')) The parameter λ is a positive constant and allows the pleural pressure P_{pl} to be set at physiological values. The parameter μ compensates the leaks so as to keep a constant mean value for the pressure

$$\frac{d(P_{\text{mus}})}{dt} = \lambda y + \mu. \quad (2.6)$$

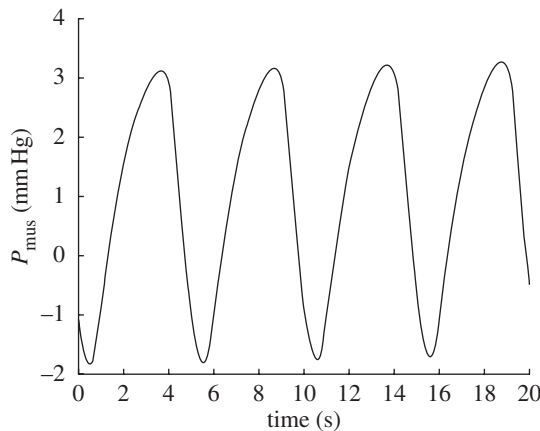


Figure 4. Simulation by the model of the pressure generated by the respiratory muscles (P_{mus}) for 20 s ($f_R = 12 \text{ cycles min}^{-1}$).

The rib cage volume V_{th} is calculated as the sum of the intrathoracic blood volume (V_{bth}) and the alveolar volume (V_{alv})

$$V_{\text{th}} = V_{\text{bth}} + V_{\text{alv}}. \quad (2.7)$$

The human mechanical respiratory system is described by the following equation, where P_{pl} is the pleural pressure, E_{alv} the elastance of the alveola, R_{ua} the resistance of the upper airways and R_{ca} the resistance of the central airways

$$\frac{d(V_{\text{alv}})}{dt} = -\frac{P_{\text{pl}} + E_{\text{alv}} * V_{\text{alv}}}{R_{\text{ca}} + R_{\text{ua}}}. \quad (2.8)$$

Table 1 defines the values of the various parameters and the initial values of the respiratory variables.

(c) *Cardiopulmonary model: interactions between the two previous systems*

The interaction between these two models (haemodynamic system and respiratory system) is carried out by the pleural pressure (P_{pl}) and the intrathoracic volume (V_{bth}).

On the one hand, we insert P_{pl} , calculated by the respiratory system with equation (2.5), into the CVS at the pericardium level, so as to interact on the right and left ventricle surfaces. Note that the pleural pressure is not applied directly on the inferior vena cava and atria.

Moreover, we also consider that the pleural pressure has an influence on the pulmonary vein and artery pressures, and not only on the pericardium, as it is represented in the minimal haemodynamic system model of Smith *et al.* For that purpose, both equations of the CVS model defining the pulmonary vein and artery pressures (P_{pu} , P_{pa}) are modified, by inserting P_{pl} . In equations (2.9) and (2.10), $E_{\text{es},x}$ corresponds to the elastance, $V_{d,x}$ to the volume at zero pressure and V_x to the volume, for x representing either the pulmonary artery (pa) or the pulmonary vein (pu)

Table 1. Initial values of state variables and respiratory parameters values.

| variable | initial value |
|------------------|---------------------------------------|
| V_{alv} | 0.5 l |
| P_{mus} | 0 cm H ₂ O |
| x | -0.6 |
| y | 0 |
| parameter | value |
| E_{alv} | 5 cm H ₂ O l ⁻¹ |
| E_{cw} | 4 cm H ₂ O l ⁻¹ |
| R_{ua} | 5 cm H ₂ O l ⁻¹ |
| R_{ca} | 1 cm H ₂ O l ⁻¹ |
| V_{th0} | 2 l ⁻¹ |
| HB | 1 |
| λ | 1.5 |
| μ | 1 |
| a | -0.8 |
| b | -3 |

$$P_{\text{pa}} = E_{\text{es,pa}} (V_{\text{pa}} - V_{d,\text{pa}}) + P_{\text{pl}} \quad (2.9)$$

and

$$P_{\text{pu}} = E_{\text{es,pu}} (V_{\text{pu}} - V_{d,\text{pu}}) + P_{\text{pl}}. \quad (2.10)$$

On the other hand, we replace the intrathoracic blood volume signal, V_{bth} , previously simulated in two linear phases (Abdulhay & Baconnier 2007) and which is an input of the respiratory system model. The volume of intrathoracic blood (V_{bth}) is now defined as the sum of the pericardium blood volume (V_{pcd}), pulmonary vein and artery blood volumes (V_{pu} and V_{pa}), all volumes calculated by the cardiovascular model

$$V_{\text{bth}} = V_{\text{pcd}} + V_{\text{pu}} + V_{\text{pa}}. \quad (2.11)$$

The interactions between models are shown in figure 5. The black thick and black dotted arrows refer to the phrenic and vagus nerves, respectively, as given in figure 1. The ‘heart and intrathoracic circulatory system’ and the ‘extrathoracic circulatory system’ blocks represent the minimal haemodynamic system model of Smith *et al.* (2004).

All units have been homogenized, especially the pressures, which are all expressed in mm Hg, and the time, expressed in seconds.

Some parameter value adjustments (in table 2) have been necessary so as to get reasonable physiological values for all variables. Most of these changes will be discussed in the last part of the article. The major modification concerns the septum, which is made more flexible by reducing its elastance.

A fourth-order Runge–Kutta algorithm, even with an extremely small step size, is numerically unstable for solving the complete model equations. That is why we use the Rosenbrock variable-step size integration method provided

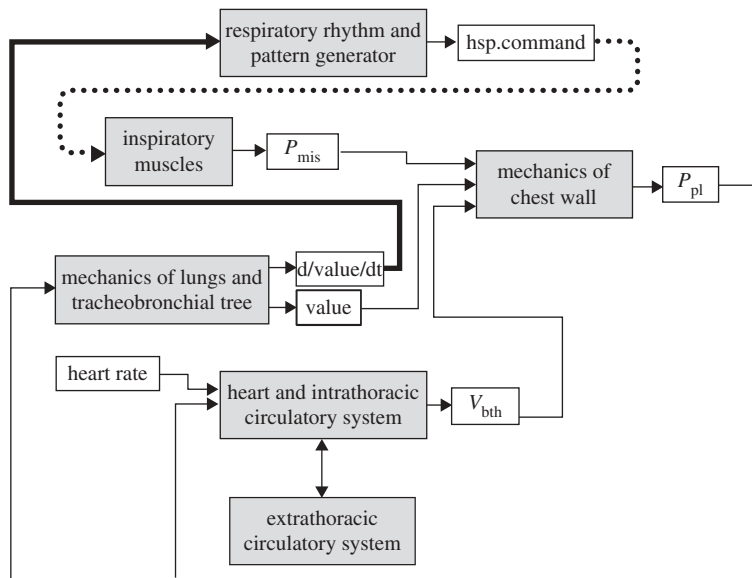


Figure 5. Interactions between the cardiovascular and the neuromuscular ventilatory models.

Table 2. Modified values of some cardiovascular parameters.

| parameter of the cardiovascular model | new value |
|---------------------------------------|----------------------------|
| $E_{es,spt}$ | 3750 mm Hg l ⁻¹ |
| λ_{spt} | 35 l ⁻¹ |
| $E_{es,vc}$ | 2 mm Hg l ⁻¹ |

by BERKELEY-MADONNA (Macey & Oster 2007), which chooses the largest step size consistent with the tolerance and minimum/maximum step size specified. The model can therefore be simulated and the results are presented in the following section.

3. Results

(a) Experimental data

In this article, we use the existing experimental data, recorded for a previous study (Abdulhay & Baconnier 2007) on one male healthy seated volunteer. The subject was asked only to spontaneously breathe. Rib cage and abdomen cross-sectional area changes were recorded with a computer-assisted respiratory inductance plethysmography (RIP) vest (Visuresp, RBI). An electrocardiogram was also recorded. All outputs were connected to an A/D converter connected to a computer. Thorax, abdomen and ECG signals were digitized at a rate of 100 Hz.

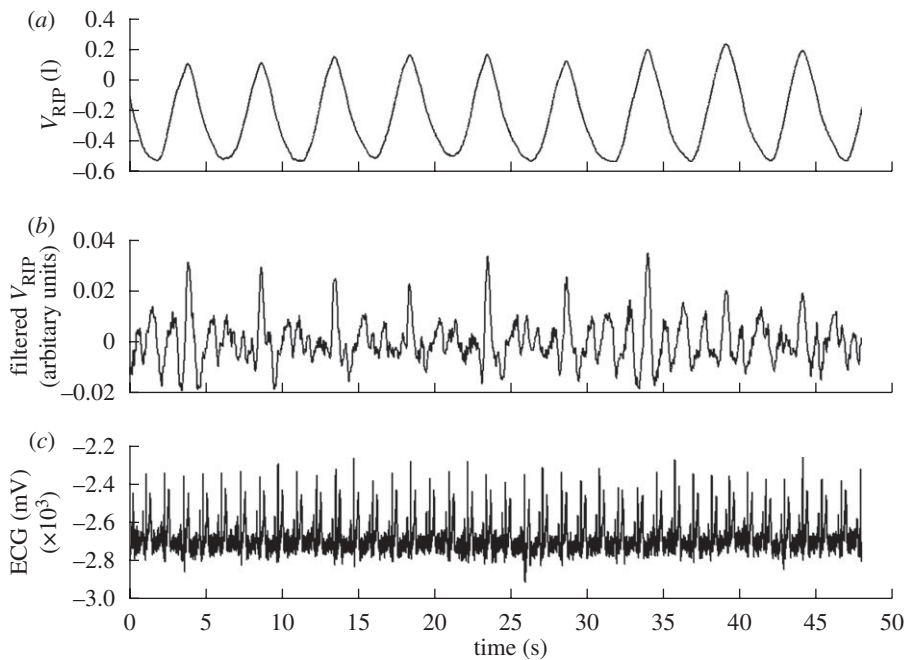


Figure 6. (a–c) Experimental data from RIP and ECG.

The method proposed by Eberhard *et al.* (2001) was applied to obtain a calibrated RIP volume signal, V_{RIP} .

A band-pass filter ($0.7 \times \text{cardiac frequency} - 10 \text{ Hz}$) was applied to V_{RIP} according to Bloch (1998) and Bloch *et al.* (1998, 2002). Indeed, Bloch *et al.* showed that left ventricular volume could be extracted by digital band-pass filtering of respiratory waveforms. These respiratory waveforms were measured by an inductive plethysmography transducer placed transversely around the chest at a level near the xiphoid process. The band-pass filtering suppresses low-frequency harmonics, related to respiration and other body movements, as well as high-frequency electrical noise. This method is called TCG and is supposed to be a non-invasive continuous monitoring of SV and cardiac mechanical performance by inductive plethysmography.

Examples of experimental data are shown in figure 6 for one male subject. First, the calibrated RIP volume signal V_{RIP} is calculated, equivalent to the thoracic volume V_{th} . Then the filtered RIP volume signal was obtained by band-pass filtering, considering the cardiac frequency equals 0.9 Hz (54 cardiac cycles in 1 min according to the ECG signal presented in the last graph). The respiratory frequency has been evaluated to 0.2 Hz (12 respiratory cycles in 1 min).

(b) Temporal and spectral analysis of simulated data

We have simulated the cardiopulmonary system model with frequencies corresponding to the experimental results presented above (heart rate of 54 and respiratory rate of 12). Various simulated volume signals are shown in figure 7: the left ventricle volume (figure 7a), the alveolar volume (figure 7b) and the thoracic volume (figure 7c).

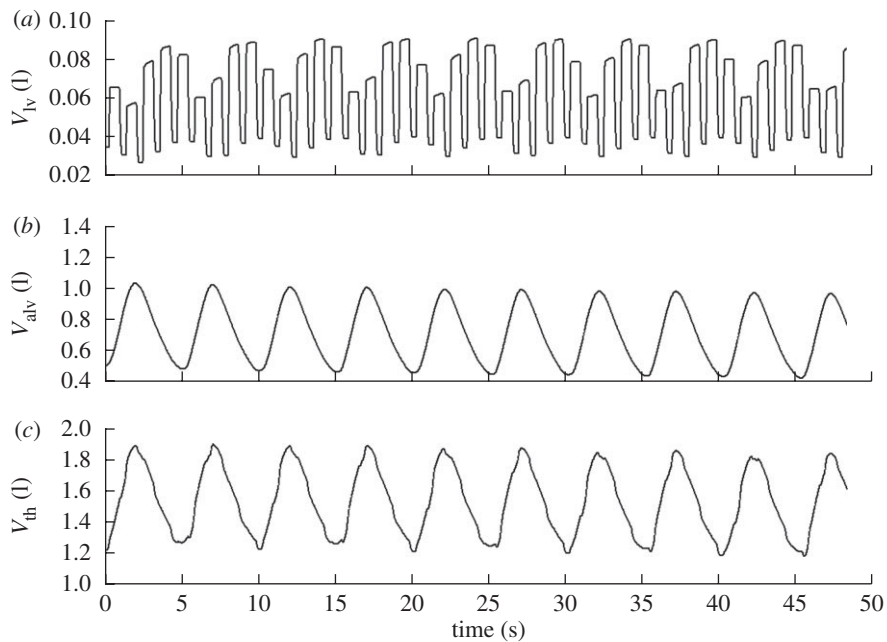


Figure 7. (a–c) Simulated data from cardiopulmonary model ($f_R = 0.2$ Hz, $f_c = 0.9$ Hz).

First we observe that the profiles of the simulated thoracic volume (V_{th}) and of the experimental RIP volume (V_{RIP}) are very similar. Then we observe a low-frequency component on the left ventricle, corresponding to the respiratory frequency as it will be confirmed further with a spectral analysis.

As for the experimental data and according to Bloch (1998) and Bloch *et al.* (1998), the simulated thoracic volume was band-pass filtered. The filtered signal is then compared with the simulated left ventricle volume (V_{lv}) in figure 8. This underlines the presence of a cardiac component or cardiogenic oscillations on the simulated thoracic volume signal.

As proposed by Bloch *et al.*, TCG seems to track changes in left ventricular SV. The beats observed on the filtered V_{th} and on V_{lv} are similar. The frequency is identical and equal to the cardiac frequency. The SV amplitudes are close. A low-frequency component is observed on the left ventricle volume signal: the SV is not constant along a respiratory cycle. We note that this low-frequency respiratory component is synchronous with the thoracic volume signal, but in the opposite direction. As illustrated in figure 9, the simulated left ventricular SV increases during expiration (when the alveolar volume decreases) and decreases during inspiration. The inverse is observed for the simulated right ventricular SV. These results on the cardiac component conform to the properties described by Guz *et al.* (1987) and used by Bloch *et al.* (1998).

In figure 10, spectral representations of simulated signals are represented and point out the cardiopulmonary interactions simulated by the model. For the pericardium and the left ventricle volumes, we observe a component at 0.9 Hz, corresponding to the cardiac frequency, but also another component at

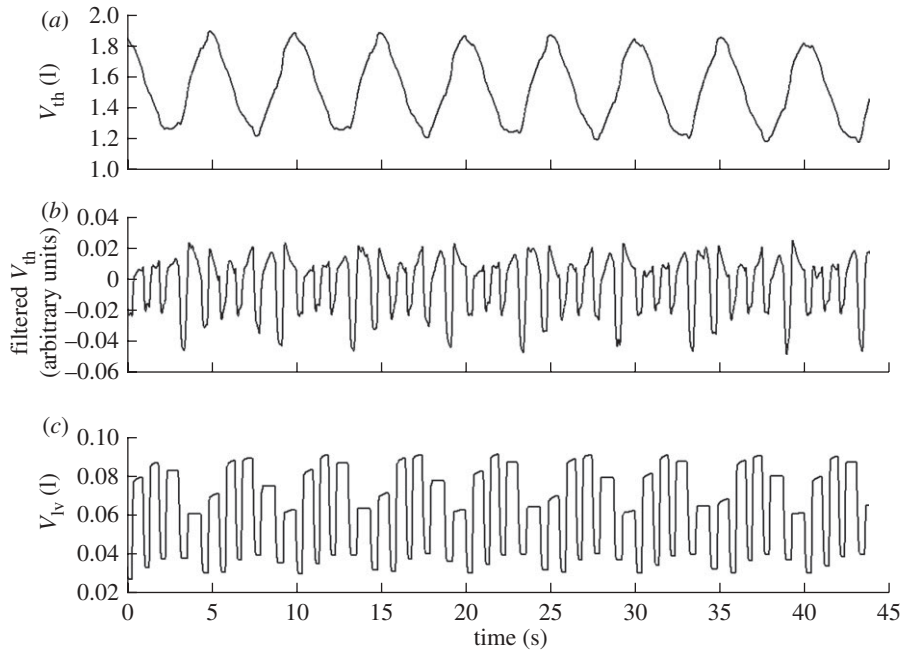


Figure 8. (a–c) The simulated thoracic volume is band-pass filtered and compared with simulations of left ventricular volume.

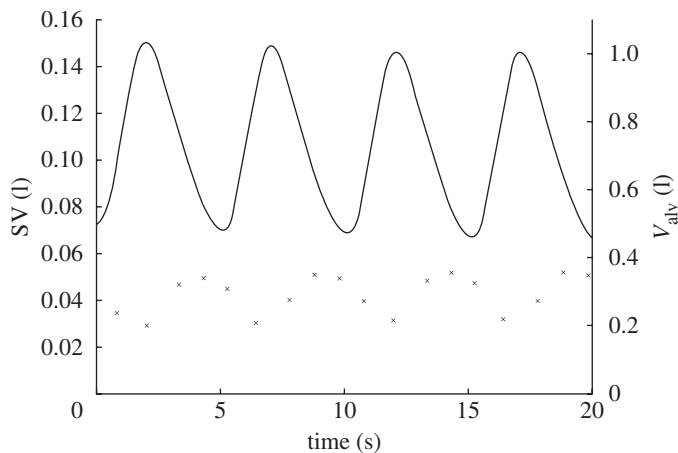


Figure 9. Influence of respiration on left ventricular SV. Solid line, V_{alv} ; crosses, SV.

0.2 Hz, i.e. the respiratory frequency. In the same way, we observe an important component at 0.2 Hz for the respiratory signals such as the airflow (dV_{alv}) or the thoracic volume (V_{th}), and also another component at the cardiac frequency 0.9 Hz.

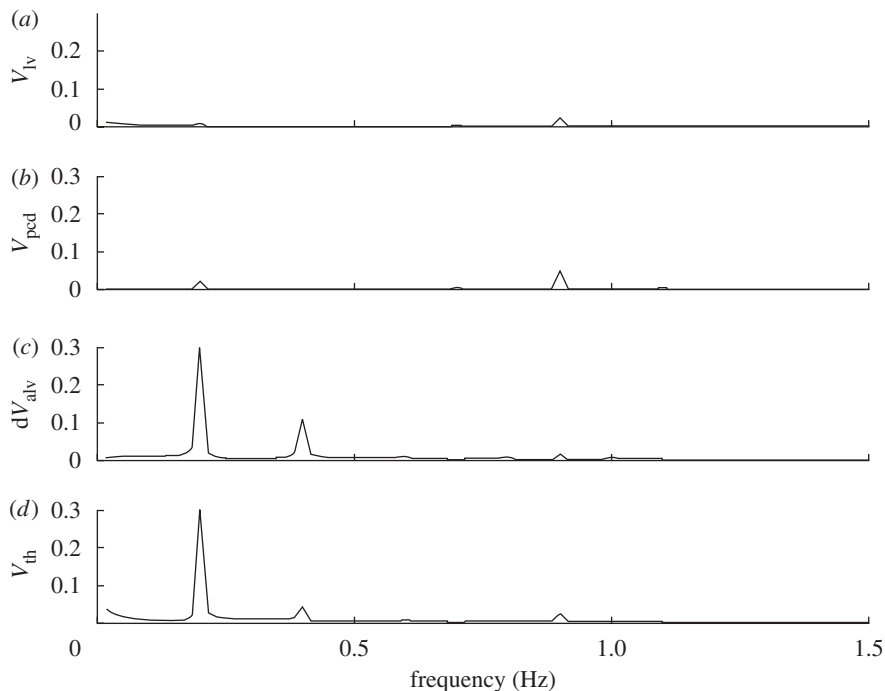


Figure 10. (*a–d*) Spectral representations of cardiopulmonary simulated signals.

4. Discussion

In this work, we have established a mathematical model for studying the interactions between the heart, the lungs and the rib cage. The complete model integrates two models which have been adapted to meet our demands.

First, as described in §2, the respiratory system model includes a respiratory oscillator. Various oscillators have been presented in the literature (Younes & Riddle 1981; Pham Dinh *et al.* 1983; Thibault *et al.* 2002). Younes & Riddle proposed a complete and complex oscillator, but, owing to the great number of parameters involved, their model does not meet our demands. Our proposed oscillator uses the Liénard equation with parameters chosen to provide realistic and reasonable results. Resistance values for the upper and central airways have also been adjusted. The Liénard oscillator has the advantage of being simple, adaptive and easily functional. The simulation of the model for one specific subject can be easily achieved, by simply adjusting a few parameters such as the respiratory frequency.

The cardiovascular part of our model uses the model of Smith *et al.* (2004). However, combined with the respiratory system model, this CVS model cannot, in its original form, simulate the expected cardiopulmonary interactions, described in §1; i.e. the left ventricle stroke volume decreases during inspiration and increases during expiration and the inverse occurs for the right ventricle. A detailed study of the haemodynamic model highlights the important role of the septum for the differentiation of the two ventricle volumes. In the original paper,

the septum was a very rigid wall. This has been modified in our cardiopulmonary model; the septum has been made more flexible and this has allowed more interactions between the two ventricles. The elastance parameters of the septum have been reduced, according to Luo *et al.* (2007).

Moreover, the septum volume computation was complex in the original paper, as this volume was determined as the solution of a nonlinear equation linking the septum pressure to the difference of left and right ventricle pressures. These pressures are all defined from approximations of the end-systolic and the end-diastolic pressure–volume relationships, as in equation (4.1), where $e(t)$ is the cardiac function and x represents the left ventricle, the right ventricle or the septum

$$P_x = e(t)E_{\text{es},x}(V_x - V_{d,x}) + (1 - e(t))P_{0,x}(e^{\lambda_x(V_x - V_{0,x})} - 1). \quad (4.1)$$

This has been simplified (equation (4.2)) by approximating the second term of the previous sum by a linear function. The computation of the septum volume as the solution of the equation linking the septum pressure to the difference of left and right ventricle pressures is then much simpler and therefore the simulation time is highly decreased. Furthermore the simulated results are very little different

$$P_{\text{spt}} = e(t)E_{\text{es},\text{spt}}(V_{\text{spt}} - V_{d,\text{spt}}) + (1 - e(t))P_{0,\text{spt}}\lambda_{\text{spt}}(V_{\text{spt}} - V_{0,\text{spt}}). \quad (4.2)$$

Finally, and as introduced previously, the work is part of the SAPHIR project and the proposed model is aimed at being integrated in the SAPHIR core model. In the philosophy of SAPHIR, we propose new additional modules to determine the respiratory function: a central respiratory pattern generator (coupled to thoracopulmonary mechanics) and a model of cardiopulmonary mechanical interaction including the thoracic haemodynamics and allowing the simulation of alveolar ventilation due to the action of the respiratory muscles.

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