Valsalva Maneuver for the analysis of interaction hemodynamic – Model study

K. Hemalatha, and M. Manivannan
Indian Institute of Technology Madras, Applied Mechanics, Chennai, India
Email: hemaa75@gmail.com, mani@iitm.ac.in

Abstract—A comprehensive lumped parameter electrical analog model of cardiopulmonary (CP) system to study the interaction between cardiovascular and respiratory system is presented. This model consists of 1) cardiovascular model which integrates four cardiac chambers with valves, pulmonary and systemic circulation, septal and pericardial coupling, and baroreflex control 2) respiratory system with lung mechanics and gas transport at alveolar-capillary membrane. The cardio-pulmonary interaction is realized by intrapleural pressure (Ppl). The governing equations for pressure, volume and flow in each vascular and respiratory compartment are derived from mass balance and continuity principles. Computer simulations are accomplished by numerically integrating the differential equations. Parameters of this combined model are adjusted to fit nominal data, yielding accurate hemodynamic waveforms and validated with literature data. Sensitivity analysis is also performed to individual model parameters. The respiratory influence on aortic pressure is analyzed with pulse pressure (PP) in Valsalva Maneuver(VM). Photoplethysmography is recorded to validate the aortic pressure variations in VM. The maximal percentage changes of PP in phase II of VM shows moderate negative correlation in both simulation and experiment. In summary, this model can be used to analyze cardiopulmonary interactions in normal and pathological states of both the systems.

Index Terms— hemodynamics, pericardium, baroreflex, intrapleural pressure, Valsalva Maneuver, Airways, diffusion, 4th order Runge-Kutta method, Pulse Pressure.

I. INTRODUCTION

Cardiopulmonary (CP) diseases need better understanding of their interactions for diagnosis and treatment. Mathematical models can provide more information regarding both invasive and non-invasive parameters related to cardio-pulmonary system. Our objective is to develop a detail model of CP which can simulate all kinds of diseases related to both the systems and their influence on each other. This model integrates three distinct models, heart with closed loop circulation [1], respiratory system with lung mechanics [2] and gas exchange [3]. Comprehensive survey of mathematical models to study the interaction of cardiovascular and respiratory system varies significantly in their complexity, assumption and objectives. Many authors have constructed separate models to explain cardiovascular and respiratory system behavior in normal as well as pathophysiological conditions [4,5]. The interaction between cardiovascular and respiratory model are incorporated in many models only by modulating intrathoracic pressure with respiratory frequency [4,2] without coupling detailed respiratory model. A comprehensive cardiopulmonary model with detailed circulatory model, lung mechanics and gas exchange has been reported in [7]. However, in their model, the cardiac valves are discrete in nature which has only two states either fully opened or closed. Therefore their model is unable to generate the actual hemodynamics of valves and to simulate valvular diseases which are the most common cardiac diseases. The pericardial coupling between heart chambers is also not addressed in their model and pulmonary vascular compliances are kept as constant, where as time varying elastance is important for studying cardiopulmonary interactions. Our model includes 1) cardiovascular model of four cardiac chambers with proportional valves, pulmonary and systemic circulation, pericardium, septum and baroreflex control, 2) respiratory system with lung mechanics and gas exchange. Our model therefore has the advantages of simulating normal and pathological conditions of both the systems and also their interaction in above said conditions.

II. MODEL FORMULATION

A. Cardiovascular (CV) Model

With the focus of our objective the CV model reported in [2] has been modified. The lumped parameter electrical equivalent of the model is shown in Fig.1.

Heart Model: The viscoelastic nature of heart chambers are characterized by two elements, elastance and resistance. The elastance of four heart chambers are varying with time in a synchronized manner which is the source of the CV model. For Left Ventricle (LV)

\[
\begin{align*}
\varepsilon_h &= \left\{ \begin{array}{ll}
F_L E_{R_{lv}} 0.5 \left( 1 - \cos \left( \frac{\pi}{t_{re}} \right) \right) + E_{R_{lv}} / F_L \\
F_L E_{R_{lv}} 0.5 \left( 1 + \cos \left( \pi \left( t - t_{re} \right) / 0.5 t_{re} \right) \right) + E_{R_{lv}} / F_L 
\end{array} \right.
\end{align*}
\]

Where \( \varepsilon_h \) [mmHg*ml\(^{-1}\)] represent elastance of the LV, \( t_{re} \) is the end ejection time [0.3 sec] and \( \varepsilon_h \) repeats the same pattern for every cardiac cycle (0.855 sec). \( F_L \) is a scaling factor that characterizes the nonlinear volume dependency of elastance.

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Image captions:
- Fig 1. Cardiovascular system Model

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where $V_{max}$ is the maximum cardiac fluid volume of normal human (900ml). In similar way right ventricle elastance can also be written. The coupling septal wall offers direct pressure coupling between left and right ventricles through its constant elastance ($E_s$). Hence the functional elastance of left ventricle is given in Equ.3. Because of the pressure coupling, the net pressure of each ventricle depends not only their volume and elastance but also the coupling pressure from other ventricle. The time varying atrium elastance is given as below.

$$e_a = \begin{cases} E_{lur}, & \frac{1}{2} \left( 1 - \cos \left( \frac{\pi (t - t_{ur})}{\tau_{lur}} \right) \right) + E_{lab} \\ E_{lur}, & \frac{1}{2} \left( 1 + \cos \left( \frac{\pi (t - t_{ur})}{\tau_{lur}} \right) \right) + E_{lab} \end{cases}$$

Where $e_a$ is the elastance of the atrium; $t_{ur}$ [0.855 sec] indicate a cardiac cycle, $t_{ur}$ [0.696 sec] refers to the time when the atrium begins to contract and $t_{ur}$ [0.835 sec] is the time when the atrium begins to relax.

Heart Valves: The nonlinear time dependent behavior of heart valve is realized by three elements. 1) Bernoulli’s resistance (S) models turbulent flow nature at the orifice (valve), 2) Inertance (L) models acceleration in flow at the orifice and 3) Resistance (R) models viscous nature of valve tissue. The opening and closing of the valves are due to forward pressure difference between two anatomical locations where they situate (example if $P_{lu}$ > $P_{lu}$ mitral valve opens).

Systemic and Pulmonary Circulation: The systemic circulation is modeled with 4 elements including constant compliance where as pulmonary compliance is modeled with time varying elastance to achieve effective coupling between cardio-pulmonary.

$$e(t) = E_0 (e^{t/\tau})$$

Where $E_0$ (mmHg·ml$^{-1}$) is the zero-volume elastance, $Z$ (ml) is the volume constant, and $v$ [ml] is volume of the particular pulmonary circulatory unit.

Pericardium: It offers volume coupling among all chambers lie inside the pericardial cavity [2] and hence significant constraint on the filling capabilities of the heart chambers [8]. So the total cardiac fluid volume accounts blood volume and pericardial fluid volume.

Baroreflex Control: The pressure regulating reflex of Atonomous nerves system (ANS baroreflex) is modeled by simply modulating heart rate with systolic peak pressure of aorta ($P_{aos}$) as given below.

$$HR = \left( \frac{K_{baro}}{P_{aos} - 120} \right) + HR_0$$

where $K_{baro}$ is 188.68 based on [9] and $HR_0$ is 70 beats/min.

Governing equations of cardiovascular model are formulated by applying mass balance or force equilibrium at the nodes of Elastance (or $C$) capacitance and inertance. According to mass balance, volume change in any capacitance and elastances can be expressed as follows

$$\dot{v} = \dot{Q}_{in} - \dot{Q}_{out}$$

At inertance node, according to continuity equation flow rate equations are formulated as given below (refer Fig.3).

$$d\dot{Q}/dt = \left( \frac{P_{up} + S_{up}}{R_C} - Q - R_{down} - S_{down} \frac{d\dot{Q}_{down}}{dt} \right) \frac{1}{L}$$

B. Respiratory Model:

The simplified respiratory model (Fig 2.) consists of lung mechanics [2] and gas exchange [3,7]

Lung Mechanics: The respiratory airway is subdivided as peripheral airways (small airways -Rs), collapsible airway (Rc) and upper airway (Ru) and modeled as volume dependent nonlinear resistance [10]. The viscoelastic behavior of lung tissue is characterized by two element Kelvin body which has capacitance and resistance. The pressure equations are reported in [2].The collapsible airway flow is given as

$$Q_{C} = \left( \frac{P_{mouth} - P_{CO}}{R_u + R_C} \right)$$
where \( P_{\text{mouth}} \) is the atmospheric pressure taken as ground and \( P_{\text{co}} \) is the collapsible airway pressure. The small airway flow is the ratio of pressure and resistance
\[
\dot{Q}_S = \frac{P_a}{R_a} \tag{10}
\]
The state equations for collapsible and alveolar volume are written as
\[
\frac{dv_s}{dt} = Q_C - \dot{Q}_S \tag{11}
\]
\[
\frac{dv}{dt} = \dot{Q}_S - \phi_d \tag{12}
\]
where \( \phi_d \) is the flux rate which is the coupling factor between lung mechanics and gas exchange given in equation based on [7].
\[
\phi_d = \frac{\Delta V_p}{P_{STP} - P_{\text{body}}} \left[ P_a - P_b \right] D_L \tag{13}
\]
\( P_{hi} \) represents the partial pressure of gas species \( i \) (\( O_2 \) or \( CO_2 \)) in the pulmonary capillary, \( \Delta V_p \) denotes the blood volume contained in the capillary and \( P_a \) is the partial pressure of corresponding species in alveolar region. The lung and airways are assumed to be enclosed within a rigid-walled thoracic cage, with the airways open to the atmosphere. The spatially averaged time varying intrapleural pressure is driving source.

Gas exchange model: Our gas exchange model is limited to gas transport at alveoli (across the alveolar–capillary membrane) not at tissue level. The following assumptions are made in our model 1) Inspired air is warmed to body temperature (300K) and saturated with water vapor, 2) The gaseous mixture obeys the ideal gas law, 3) Blood is considered as a homogeneous medium, 4) within a control volume, the instantaneous specific reactions are considered to be at equilibrium, 5) Axial directional diffusion is the sole cause of gas transport and the rate of which depends on lung diffusion capacity (\( D_L \)) for the particular species (\( O_2 \) and \( CO_2 \), \( N_2 \) neglected), 6) 35 capillary segments and 35 alveolar units reported in [3] are lumped as single capillary and alveoli. The partial pressure equation for \( O_2 \) in airways are given here, similarly \( CO_2 \) equations can be written.

\[
\frac{dP_{O2}}{dt} = \left\{ \begin{array}{ll} 
Q_a P_{O2_a} - Q_a P_{O2_d} & \text{for } Q_a > 0 \\
Q_a P_{O2_d} - Q_a P_{O2_a} & \text{for } Q_a < 0 
\end{array} \right.
\tag{14}
\]

\[
\frac{dP_{CO2}}{dt} = \left\{ \begin{array}{ll} 
Q_a P_{CO2_a} - Q_a P_{CO2_d} & \text{for } Q_a > 0 \\
Q_a P_{CO2_d} - Q_a P_{CO2_a} & \text{for } Q_a < 0 
\end{array} \right.
\tag{15}
\]

Here, \( P_{O2} \), \( P_{CO2} \) and \( P_{\text{hi}} \) are partial pressures of gas species \( i \) (\( O2 \) or \( CO2 \)) in the upper, middle, and small airways, respectively, \( T_{\text{body}} \) (300K) is the body temperature and \( P_{STP} \) (760 mmHg) is the pressure for standard condition.
### TABLE 1. SENSITIVITY ANALYSIS IN TERMS OF GAIN FOR CV MODEL SIMULATION

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HR, Vb, Vpua, Vvc, MAP, Ppl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rao</td>
<td>-0.1, -0.1, 0.1, 0.1, 0.1, 0.2</td>
</tr>
<tr>
<td>Epa0</td>
<td>NS, -0.1, 0.3, 0.1, 0.1, -0.4</td>
</tr>
<tr>
<td>Epa0</td>
<td>-0.1, NS, -0.3, 0.1, 0.1, 0.4</td>
</tr>
<tr>
<td>Epa0</td>
<td>-0.1, NS, NS, 0.1, NS, 0.2</td>
</tr>
<tr>
<td>Erva</td>
<td>-0.1, 0.1, 0.2, NS, 0.1, 0.2</td>
</tr>
<tr>
<td>Erm0</td>
<td>-0.2, 0.1, 0.2, 0.1, 0.2, 0.5</td>
</tr>
<tr>
<td>Vpco</td>
<td>-0.2, 0.1, 0.1, NS, 0.2, 0.1</td>
</tr>
<tr>
<td>Ppl</td>
<td>-0.3, 0.1, 0.1, NS, 0.2, 0.3</td>
</tr>
</tbody>
</table>

### TABLE 2. CORRELATION OF PP WITH VM PARAMETERS IN PHASE II

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Experiment</th>
<th>Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsava Ratio</td>
<td>-0.467</td>
<td>-0.66</td>
</tr>
<tr>
<td>VM Time</td>
<td>-0.48</td>
<td>-0.61</td>
</tr>
<tr>
<td>VM pressure</td>
<td>-0.32</td>
<td>-0.52</td>
</tr>
</tbody>
</table>

C. Ppl mediated CP interaction:
Intrapleural pressure is the coupling factor between CV and respiratory system. The pleural pressure variations is incorporated in CV system by directly applying it to all compartments lie inside the thorax, which includes vena cava, right heart, pulmonary circulation, left heart, and aorta. In quite breathing Ppl is negative. The CP interaction is typically studied with valsalva maneuver in which the Ppl is kept as a constant positive pressure.

### III. METHODS AND MATERIALS

**A. Experimental protocol:** Data were collected from eight healthy subjects (6 males and 2 females) aged 20 to 34 years for studying the interaction hemodynamics in VM. Plethysmography (PPG) were acquired at wrist with a Bio-Pac MP35 data acquisition system with filter band width of 0.05 Hz to 10Hz. Our experimental method was to allow each subject in relaxed sitting position to exhale through a mouth piece with a restriction to maintain various VM pressures. Exhale pressure is monitored using sphygmomanometer. The effect of pressure is examined with exhale pressure of 10, 20, 30, and 40 mmHg for a period of 15 seconds where as the effect of test duration is examined with 40mmHg for 5, 10, 15, and 20 secs.

**B. Model simulation:** Model parameters are tuned to get accurate hemodynamic waveforms and reported in Fig.3. The quantitative sensitivity of CV model parameters to important hemodynamics is done by increasing them by 10% from control value. The sensitivity gain is the ratio between % change of affected hemodynamics and % change of affecting parameter. The gain ≥0.1 is considered as sensitive (Table.2), and the insensitive parameters are not given in the table. The qualitative sensitivity analysis of respiratory system can be done by changing the functional description of resistances and compliances which is well explored in [3].

### III. RESULTS AND DISCUSSION

Sensitivity analysis shows systemic after load resistance Rao is sensitive because it is the major determinants of aortic pressure. All hemodynamics are more sensitive to ventricular elastances which are the main sources of the pumping action of CV system. Intrapleural pressure (Ppl) has good sensitivity, may be due to it’s direct influence on aortic pressure.

B. CVS Hemodynamics

Fig. 3a and 3b show typical pattern with ventricular filling (phase a), isovolumetric contraction (phase b), ejection (phase c), and isovolumetric relaxation (phase d) clearly [11]. The normal flow across tricuspid and mitral valve (Fig.3c and 3d) show characteristic pattern with initial rapid early flow (E-wave) and a smaller late atrial kick (A-wave) as reported in [12]. Vena cava and pulmonary vein flow patterns [19] show (Fig.3e and 3f) R wave (reverse flow), S wave (systolic forward) flow and D wave (diastolic forward flow).

B. Dynamics of Respiratory model

Respiratory dynamics are simulated for quite breathing in which Ppl is less negative during expiration and more negative during inspiration. The simulation is stated form inspiration phase, at that time alveolar pressure is negative compared with respect to Pmouth and it sucks air from atmosphere. The simultaneous increase in lung recoil pressure compensates Pp changes and equates to Pamb and ends inspiration. The reverse process occurs during expiration. Fig.4 shows changes in dead space volume and alveolar during respiratory cycles [13].

The lung gas exchange occurs due to partial pressure gradient. Fig.5 shows partial pressure of O2 (P_{O2}) and CO2 (P_{CO2}) in upper air way (Dead space) and in alveolar region [14]. During inspiration partial pressure of O2 in airways increases and P_{CO2} reduces and reverse during...
expiration. The slopes of $P_{O_2}$ and $P_{CO_2}$ curve in dead space is higher than alveoli slopes that implies alveolar $P_{O_2}$ and $P_{CO_2}$ is maintained nearly constant to facilitate continuous gas transfer which is achieved by mixing of inhaled air with residual air at alveoli. The high frequency variations in alveoli $P_{O_2}$ and $P_{CO_2}$ (Fig. 5b) represents cardiac frequency.

C. CP interaction

Fig.6 shows the effect of respiratory induced variation in aortic pressure (Pao) in VM. PPG is considered as equivalent of aortic pressure pulse (PP) [15]. The parameter analysed is maximal % change in PP which is calculated using the formula $[(\text{maximal} - \text{basal})/\text{basal}] \times 100$. Both model and experimental waveforms in VM show pressure increase in phase I, recovery of pressure during phase II and phase III, and a brief overshoot during phase IV. Among the four phases of VM, phase II is selected for analysis, because this phase includes complex mechanoreceptor reflex inputs [15]. PP exhibits negative correlation ($p<0.0001$) with VM pressures in both experiment and simulation results (Table. 2). This suggests that arterial baroreflex, which respond mainly to changes in pulsatile pressure. Fig.7 shows baroreflex plays an increasingly important role at higher VM pressures for long duration, due to a progressive decrease in PP. Vasomotor tone and contractility reflex are not considered in model baroreflex so the correlation coefficients are slightly higher than experiment.

D. Model limitations and extension

As in any physical model, our model also has some limitations. 1) The pulse wave propagation phenomena is not addressed 2) whole alveolar units are lumped as a single unit and upper airway bifurcations are not considered, 3) Height variations of anatomical structure is not considered, 4) Coronary circulation is omitted and also not possible to simulate regional disease. However this model has freedom to extent in order to address the above given limitations. It can be used to simulate cardio-pulmonary diseases such as Mitral valve stenosis (MS), mitral regurgitation, heart failure, cardiac tamponade, pulsum paradoxus, asthma, sleep apnea ,emphysema and the influences of one system pathophysiology on the other system.

IV. CONCLUSION

Our objective is to model cardiopulmonary interactions with detailed anatomy involved in both CV and respiratory system. This model combines the advantages of several models previously reported in literature. The parameters of the model are tuned and to match literature data and the basic hemodynamics of CV system and respiratory system responses (pressure, flow, volume and partial pressure of gas species) are simulated for quite breathing. They fit reasonable with literature data for normal human subjects. The CP interaction is simulated in Valsalva Maneuver (VM) conditions. The aortic pressure pulse of the model shows distinct phases in VM as observed in photoplethysmography. The maximal changes of pulse pressure in phase II in VM shows negative correlation with VM parameters both in experiment and simulation. Therefore with this model the CP interactions study can be extended to both the system diseases. In summary our model can be used as a tool to simulate all kinds of CP pathophysiology interaction dynamics. In addition, ANS control over CP can also be implemented in this model.

REFERENCES