35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Lumped Parameter Model of Cardiovascular-Respiratory Interaction

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Abstract— **The aim of this work was to develop a lumped parameter model of the cardiovascular system and to couple it with a model of respiratory mechanics. In comparison to existing models, modifications and additions have been implemented to include a model of the upper limb vasculature employing the electrical analogy of hemodynamic variables. The model prediction of respiratory effects on arterial pressure was compared with *in vivo* invasive measurement of blood pressure in patients. The model indicates that the inherent coupling between the cardiovascular and respiratory systems can be described by mathematical relationships of physiological parameters with robust predictions. With specification of parameters based on individual measurements of cardio-respiratory variables, the model can be used in the clinical setting of intensive care units to predict hemodynamic changes and to optimize ventilation and volume loading strategies.**

I. Introduction

Evaluation of the hemodynamic profile of a critically ill patient is a crucial step of the process of diagnosis, monitoring and therapy delivery in hospital intensive care units. Hemodynamic assessment allows the optimization of therapy with fluids and medications to regulate tissue and organ perfusion, thus maintaining adequate tissue oxygenation. This assessment requires invasive monitoring of arterial blood pressure and central venous pressure by vascular catheterization. Furthermore, the measure of blood flow (cardiac output) and the calculation of systemic vascular resistance i.e. the loss of pressure load of the system, measured at the extremities of the circulatory system (aortic root - right atrium), require the use of advanced and expensive equipment and specialized operators. In these conditions, models capable of simulation and prediction of hemodynamic changes would improve patient management and assist in titration of therapy.

The aim of this work was to develop and construct a lumped parameter model of the cardiovascular system according to the concept of "elastic chambers" of Smith et al. [1-2] and to couple it with a model of respiratory mechanics such as that presented by Fontecave et al [3]. The output of this model is evaluated both in the time and frequency domains and compared with *in-vivo* invasive measures of blood pressure. In order to make this model more suitable for a validation phase where arterial pressure is measured in the brachial artery, a further modification has been implemented to model the upper limb vasculature following the electrical analogy proposed by Liang et al. [4].

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II. Methods and Models

The primary purpose of this study is to implement a computational model of the cardiovascular and respiratory systems with two main features: (i) being sufficiently detailed for characterization of patient-specific pneumo-hydraulic phenomena underlying structural respiratory mechanics and blood vessels dynamics and (ii) having a relatively low computational burden for practical application. To date, these requirements have restricted the use of finite element models of the cardiovascular system [5], given their complexity and computational times required for useful applications in clinical settings

A. The Hemodynamic System

The reasons that led Smith et al. [1] to choose a model described by a 'minimal hemodynamic system' are the following: (i) the simulation can be run on a personal computer in reasonable time; (ii) it makes use of parameters that can be readily determined or estimated for a specific patient; (iii) the system is stable (robust) while being of minimal complexity; (iv) it is governed by a limited number of equations, based on pressure-volume and pressure-flow relationships.

The cardiovascular system is divided into a series of elastic chambers separated by resistances (and inertia where required). Elastic chambers (ie the two ventricles, aorta, vena cava, arteries veins, lung, pericardium) are modeled with their respective pressure-volume relationship. The resistances describe the effect of loss of pressure by the flowing blood through vessels or valves between each elastic chamber. In this present model, the atria are not taken into account because of their minimal contribution. Activation of the heart muscle is modeled by the use of time-varying elastance [1].The laws that describe the behavior of the two ventricles and the intra-ventricular septum are similar and are all obtained by the blending of a systolic and diastolic relationship between pressure and volume:

$$P_{es} = E_{sys}(V - V_d) \quad (1)$$

$$P_{ed} = A\{exp[\lambda(V - V_0)] - 1\} \quad (2)$$

Equation (1) describes the linear relationship between end systolic pressure (P_{es}) and the difference between the current volume V and that defined at zero pressure V_d [1], determined by the elastance, E_{sys}. Equation (2) describes the non-linear relationship that allows calculation of pressure at the end of diastole (P_{ed}) with known constants A, λ and the unstressed chamber volume V_0. Using the cardiac activation

function, the pressure-volume function is obtained for both ventricles and the cardiac septum between these two limit values.

For fluid flow through the arteries, the governing equations (neglecting inertia) determine the flow rate Q using electrical analogy of the law of Poiseulle:

$$Q = (P_{out} - P_{in})/R \quad (3)$$

where P_{in} and P_{out} are the upstream and downstream pressures of the elastic chamber respectively and R is the Poiseulle resistance, defined as:

$$R = 8\mu L/\pi r^4 \quad (4)$$

where μ is the blood dynamic viscosity and L and r are the length and the mean radius of the blood vessel respectively. The time rate of change of volume V of a chamber with inlet flow rate Q_{in} and exits flow rate Q_{out}, is derived from mass balance as follows:

$$dV/dt = Q_{in} - Q_{out} \quad (5)$$

With regard to the interaction with the pericardium, the pressures inside the ventricles and at the interior of the pericardium are related through the following equations:

$$P_{lv} = P_{lvf} + P_{peri} \quad (6)$$

$$P_{rv} = P_{rvf} + P_{peri} \quad (7)$$

where P_{lv} and P_{rv} represent the left and right ventricular pressure; the "*f*" subscript refers to the transmural pressure contribution and P_{peri} is the pericardium pressure.

Pressure inside the pericardium is given by the sum of thoracic (or pleural) pressure P_{pl} and the intramural pericardial pressure P_{pcd}:

$$P_{peri} = P_{pcd} + P_{pl} \quad (8)$$

Equation (8) determines the intrinsic coupling between the circulatory and the respiratory systems, as P_{pl} can be computed using a respiratory system model.

B. The respiratory system

The breathing pattern is composed essentially of two parts. The combination of a central respiratory rhythm generator and a passive respiratory mechanism with a Liénard oscillator allows simulation of the activity of the respiratory centers, muscle and lung mechanics inside the chest [6-7]. The equations which describe the Liénard model of the respiratory rhythm generator are the following:

$$dx/dt = (ay^2 + by)x + (ay^3 + by^2) - HB \cdot dV_{alv}/dt \quad (9)$$

$$dy/dt = x \quad (10)$$

where the HB constant refers to the Hering-Breuer reflex, triggered to prevent over-inflation of the lungs. The aforementioned relations are then coupled with the relation which describes the lung activation pressure P_{mus}:

$$dP_{mus}/dt = \alpha y + \beta \quad (11)$$

The intrathoracic volume V_{th} is the sum of the intrathoracic blood volume (V_{bth}) and the alveolar volume V_{alv}, which is governed by the following differential equation:

$$dV_{alv}/dt = -(P_{pl} + E_{alv}V_{alv})/(R_{ca} + R_{ua}) \quad (12)$$

In the above equations (9-12), x and y are two auxiliary variables, α and β are two constant coefficients as are *a* and *b*, and E_{alv} is the alveolar elastance. R_{ca} and R_{ua} are the resistances of the central and upper airways respectively. The interaction between the hemodynamic and respiratory systems is caused by P_{pl} and V_{bth}.

The first variable, obtained with the breathing pattern generator, is used in the circulatory system for the

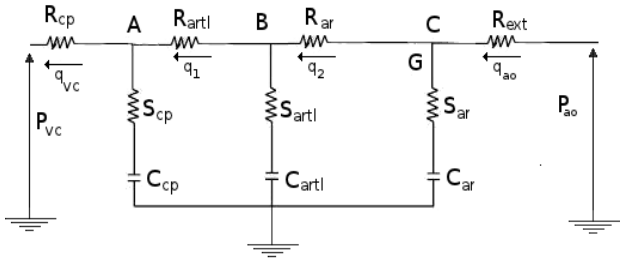

Figure 1 *- Electric circuit diagram of part of the model of Liang et al. [4] representing the upper limb and cerebral circulation. The point 'G' indicates where the pressure is measured at the brachial artery.*

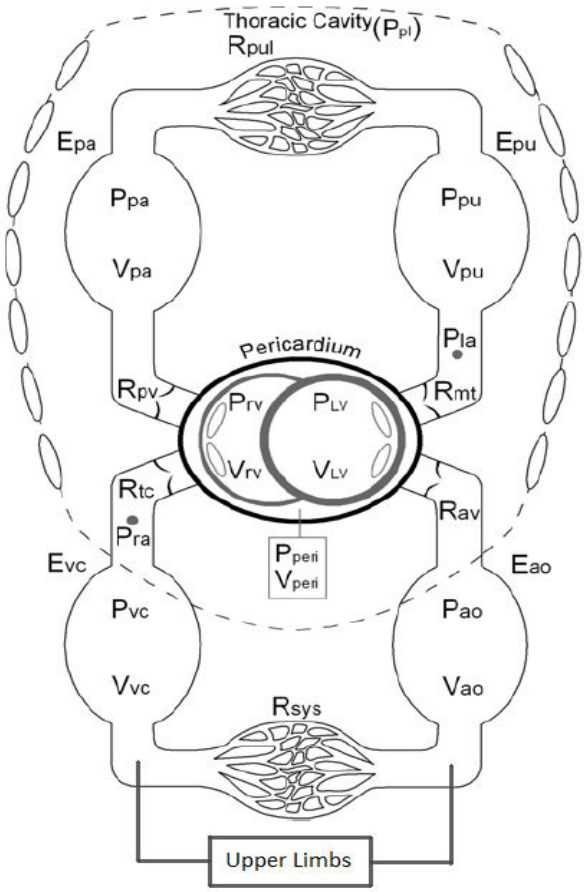

Figure 2 *- Elastic chamber schematic model with the addition of the new upper limbs equivalent part. Parameters defined as in [1-2].*

calculation of pericardial pressure so as to act on the two ventricles and on the pulmonary blood vessels [3]. The intra-thoracic blood volume that appears in the lung model is calculated from the results obtained from the circulatory model using the following equation:

$$V_{bth} = V_{pcd} + V_{pu} + V_{pa} \quad (13)$$

where V_{pu} and V_{pa} are the volumes of pulmonary veins and artery, respectively.

C. Upper Limb Circulation

The inclusion of the upper limb vasculature was to enable comparison with clinical experiments where blood pressure is measured invasively at the brachial artery. Relevant lumped parameter values were obtained from the work of Liang et al. [4] which proposed a complete electrical model of the circulatory system with more than 150 parameters. The upper limb component was adapted for the present model (Fig. 1).

The equations of the model are constructed taking into account the conservation of mass applied to each of the nodes A, B and C (Fig. 1) which implies that, for every point:

$$\Sigma Q_{in} - \Sigma Q_{out} = C \cdot dP/dt \quad (14)$$

where C is a capacitor simulating total arterial compliance of the vascular bed. Pressure is determined by Kirchhoff's law, thus:

$$P = RQ \quad (15)$$

where Q is the volumetric flow rate. (In the upper limb model, the inertial term related to blood mass is neglected, given the relatively small contribution in relation to high mass flow rates in the aorta [8]). The upper limb segment (Fig. 1) is added to the elastic chamber model (Fig. 2).

III. Experimental Setup

Data were collected from patients being treated in the Intensive Care Unit of Ospedale Maggiore Niguarda Cà-Granda (Milan, Italy). Arterial pressure was measured from brachial artery cannulation and signals obtained from monitoring devices (GE Healthcare Clinical Systems SRL). Data were obtained from 27 time histories of 27 patients, with epochs of 1 minute at a sampling frequency of 100 Hz. Analysis was performed using MATLAB and all procedures received institutional approval.

IV. Results

One of the variables that describe the dynamics of the respiratory system is the muscle activation pressure P_{mus}. This physical quantity is a determinant of the breathing pattern. Implementation of this parameter in previous models [3] was not entirely successful. The use of the suggested values for α and β (as described in (11)) leads to an P_{mus}. Modification of these parameters in terms of scaling has produced markedly improved agreement with published results ([3], [6], [7], [9]).

The effect of intra-thoracic pressure on hemodynamics of the systemic circulation [10] is shown in Fig. 3, where the model output signal is represented as the time varying arterial pressure and (Fig. 4) the frequency spectrum of the arterial pressure measured at the brachial artery. The dominant frequency component is the cardiac frequency (around 1 Hz), whereas respiration is represented by that small peak around 0.2 Hz. In the range beyond 1 Hz, the higher harmonics of the heartbeat are also evident. The comparison with the model output of the aortic pressure can be done in terms of the frequency spectrum (Fig. 4, Fig. 5). Generally, the two spectra appear quite similar with regard to the frequency distribution of the peaks, but rather different with reference to the absolute and relative amplitudes. In the brachial artery pressure spectrum (point 'G' of Fig. 1) a general decrease is observed of the absolute values, consistent with the fact that resistances are added to simulate the viscous effect of the vascular wall in the upper limb arteries. Besides, the ratio between the peak amplitudes (aortic and brachial artery pressure) of the same harmonic components changes with increasing frequency (Table I). The ratio of the peak amplitudes at 1 Hz decreases by of approximately 3%, the second harmonic ratio 9%, the third 8% and the fourth relevant harmonic ratio is around 11%. This suggests the presence of an effect which becomes more pronounced with increasing frequency.

A qualitative validation of the results obtained from the cardio-respiratory model can be made by comparison with experimental data. The frequency spectrum of brachial artery blood pressure is shown in Fig. 4 showing the presence of the basic harmonic associated with the heartbeat (around 1 Hz), relevant higher harmonics and a respiratory peak (around 0.2 Hz). These results are in agreement with those of Smith et al. [11] who have reported an experimentally verified cardiovascular model.

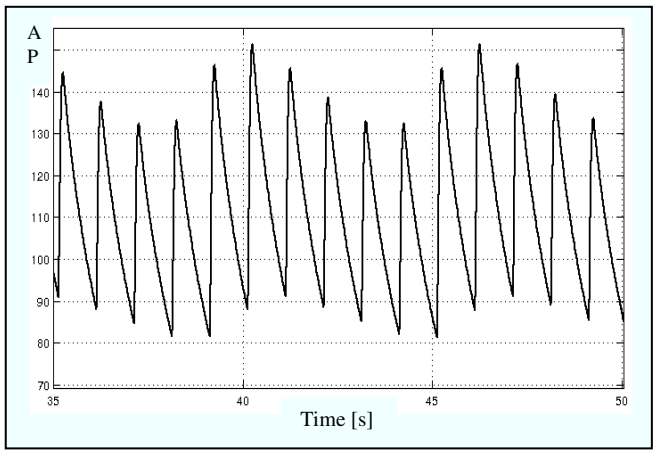

Figure 3 *Arterial pressure AP generated by the coupled cardio-respiratory model. Respiration is clearly seen as a low frequency modulation. Units for vertical axis: mmHg.*

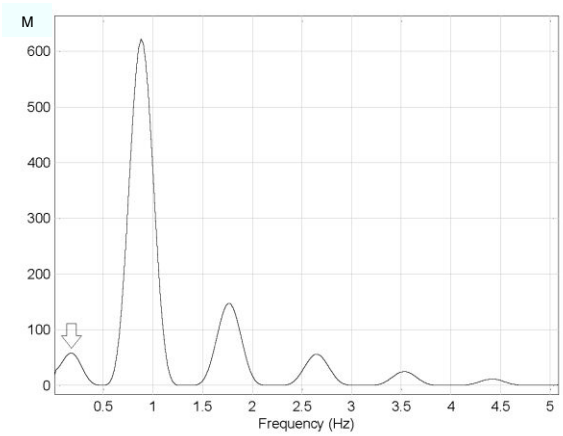

Figure 4 *Magnitude M [dB] of the frequency content [Hz] of the pressure signal calcutated at the brachial artery, as a result of the coupled model (arrow indicates respiratory frequency of 0.2 Hz)*

TABLE I *Comparison of the frequency spectrum of ratio of aortic pressure and brachial artery pressure (single patient).*

Peaks amplitude ratio	**Heartbeat frequency and higher harmonics**			
	1st basic harmonic	***2nd harmonic***	***3rd harmonic***	***4th harmonic***
Percentage value (%)	3	9	8	11

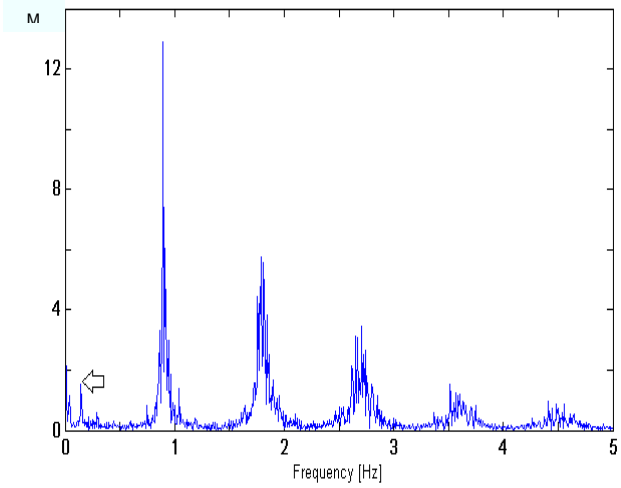

Figure 5 *- Magnitude M [mmHg] of the frequency content [Hz] of the pressure at the brachial artery from in-vivo measurements (arrow indicates respiratory frequency of 0.2 Hz). The ratio of the power of the higher harmonics to that of the first (fundamental) harmonic is quantitatively of the same order as that in the model (Fig 4)*

V. CONCLUSION

The model presented in this investigation indicates that the inherent coupling between the cardiovascular and respiratory systems can be described by mathematical relationships of physiological parameters. The model has shown it can simulate the effects of changes of intra-thoracic pressure due to respiratory activity on the arterial pressure measured at a peripheral limb. With specification of parameters based on individual measurements of cardio-respiratory variables, it is expected that the model can be used in the clinical setting of intensive care units to predict hemodynamic changes and to optimize ventilation and volume loading strategies.

REFERENCES

[1] B.W. Smith, J.G. Chase, R.I. Nokes, G.M. Shaw & G. Wake, "Minimal Hemodynamic System Model Including Ventricular Interaction and Valve Dynamics" *Med. Eng. Phys.*, vol. 26, pp. 131-139, 2004.

[2] B.W. Smith, S. Andreassen, G.M. Shaw , G.M. Jensen, Rees P.L. & J.G. Chase, "Simulation of Cardiovascular Diseases by Including the Autonomic Nervous System into a Minimal Model" *Comput. Methods Programs Biomed.*, vol. 86, pp. 153-160, 2007.

[3] J. Fontecave Jallon, E. Abdulhay, P. Calabrese, P. Baconnier & P. Gumery, "A Model of Mechanical Interactions Between Heart and Lungs" *Phil. Trans. R. Soc* , vol. 367, pp. 4741-4757, 2009.

[4] F. Liang, S. Takagi, R. Himeno & H. Liu, "Multi-scale modeling of the human cardiovascular system with applications to aortic valvular and arterial stenosis" *Med. Biol. Eng. Comput,* Vol. 47, pp. 743–755, 2009.

[5] A. Baretta, C. Corsini, A.L. Marsden, I.E. Vignon-Clementel, T. Hsia, G. Dubini, F. Migliavacca, G. Pennat, "Respiratory Effects on Hemodynamics in patient-specific CFD models of the Fontan circulation under exercise conditions" *European Journal of Mechanics B/Fluids*, vol. 35, pp. 61-69, 2012.

[6] S. Thibault, L. Heyer, G. Benchetrit & P. Baconnier, "Ventilatory Support: a Dynamical Systems Approach" *Acta Biotheor.* , vol. 50, pp. 269-279, 2002.

[7] A. Athanasiades, F. Ghorbel, J.W. Clark Jr., S.C. Niranjan, J. Olansen, J.B. Zwischenberger & A. Bidani "Energy Analysis of a Nonlinear Model of the Normal Human Lung" *J. of Biological Systems*, vol. 8, No. 2, pp. 115-139, 2000.

[8] J. Olansen, J. Clark, D. Khoury, F.. Ghorbel & A. Bidani, "A Closed-loop Model of the Canine Cardiovascular System that Includes Ventricular Interaction" *Comp. Biomed. Res.*, vol. 33, pp. 260-295, 2000.

[9] D.C. Chung, S.C. Niranjan, J.W. Clark Jr., A. Bidani, W.E. Johnston, J.B. Zwischerberger & D.L. Traber, "A Dynamical Model of Ventricular Interaction and Pericardial Influence" *Am. J. Physiol. Heart Circ. Physiol.* , vol. 272, pp. H2942-H2962, 1997.

[10] C. Luo, D. L. Ware, J. B. Zwischenberger, and J. W. Clark Jr. Using a human cardiopulmonary model to study and predict normal and diseased ventricular mechanics, septal interaction, and atrio-ventricular blood flow patterns. Cardiovasc. Eng. 7:17-31, 2007.

[11] B.W. Smith, J.G. Chase, G.M. Shaw & R.I. Nokes, "Experimentally Verified Minimal Cardiovascular System Model for Rapid Diagnostic Assistance" *Control Engineering Practice*, vol. 13, pp. 1183-1193, 2005.