Simple Mathematical Models for the Simulation of the Human Respiratory System

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Abstract. *This paper presents an evaluation of the main trends in modeling and simulation of the human respiratory system, focused on the mechanical characteristics of the respiratory physiology – known as pulmonary ventilation – disregarding chemical, neural or cardiovascular aspects and interactions. The benefits of this modeling include aids to research and teaching in the fields of pneumology and respiration physiotherapy, in order to improve understanding and make identification of pathologies and other clinical phenomena easier. Therefore, many aspects related to ventilation were studied, including simulation and analysis of existing models. As a result, we present the most important characteristics and effects that should be considered in the development of a more complete and effective model of the respiratory system. Furthermore, we introduce a didactic simulator capable of illustrating, through a user-friendly graphical interface, the main concepts related to pulmonary ventilation, integrating a basic tool for the simulation of more complex models and concepts.*

Keywords. *Bioengineering, Modeling, Simulation, Multicompartment, Lung ventilation.*

1. Introduction

Human lung ventilation (or external respiration) is a mechanical process that has the main objective of providing oxygen that will be carried by the blood to the cells, where internal respiration takes place, producing energy that will be used in other body processes. This paper focuses on external respiration and related effects, having two main objectives.

The first one consists in the study and critical analysis of some models that present particular aspects of lung ventilation or different modeling techniques. Our intention is to determine the main processes and effects that must be considered in the development of a more complex model of the human respiratory system. Such model could provide better comprehension of clinic phenomena and easier identification of diseases. Though we acknowledge the necessity of the involvement of effects originated from different natures, we consider here only mechanical ventilation characteristics, ignoring, for example, cardiovascular, chemical or neural aspects. Moreover, respiratory system typical heterogeneities must be reproduced, through the use of multiple variables or compartments.

The second objective, which can be thought of as a continuation, or a second phase of the modeling part, consists in the development of a didactic simulator of an artificial ventilator. This simulator is a web based application intended to aid learning and training in respiration physiotherapy and medicine, giving students who do not have a laboratory available the opportunity of testing and improving their ventilation knowledge. We incorporated a two compartment model of the respiratory system connected to a simplified model of an artificial ventilator, providing related information and graphs, and allowing total control of the ventilator and the patient. For now, the simulator reproduces only one ventilation mode, but it is intended to incorporate more ventilation modes, different (more complex) models and tutorials. Also, an algorithm for health improvement is being planned, so that users can actually visualize changes on the patient's state, as well as predict results for new treatments or procedures.

All models presented in this paper were numerically simulated in MatLab by the authors. Further explanations, algorithms and code listings can be provided via e-mail.

2. Respiration Physiology

Human external respiration is a complex process that aims the supply of oxygen to the cells as well as the removal of carbon dioxide from them. It can be divided into four major functional events: (*i*) pulmonary ventilation, consisting on the cyclic exchange of alveolar gas for atmospheric fresh air; (*ii*) oxygen and carbon dioxide diffusion between alveoli and blood; (*iii*) transport of oxygen (from lungs to cells) and carbon dioxide (from cells to lungs) through blood and body fluids; (*iv*) neural regulation of respiration end related processes. This paper focuses on the first event, pulmonary ventilation – specifically on ventilation mechanics.

The most important components of the respiratory system used in our study are presented next. *Airways*: set of branched tubes that transport ambient air to the interior of the lungs; divided into upper airways (mouth, nose, nasal cavities, pharynx, larynx and trachea) and peripheral airways (bronchi and bronchioles). *Alveoli*: sac-like dilations of the alveolar ducts in the lungs, where gas exchange effectively occurs. *Respiratory Muscles*: set of muscles responsible for the inflation and deflation of the lungs. Normal ventilation occurs mainly due to the contraction of the diaphragm, assisted by the elevation of the ribcage – accomplished by the rectus abdominis and the intercostal muscles (Guyton, Hall, 1997).

3. Mechanical Ventilation

Pulmonary ventilation dynamics is characterized by volume, pressure and flow generated in the respiratory system throughout the inspiratory and expiratory cycles. The values of these parameters are determined by a series of intrinsic properties of the respiratory system.

During inspiratory phase, the thoracic volume is increased. According to Boyle's law (pV = cte), this volume increase leads to a pressure decrease inside the chest wall, generating a pressure gradient between the thorax and the atmosphere. The *pleural (or intrapleural) pressure* is measured in the pleural cavity, comprised between the lungs and the chest wall. There is a small vacuum (negative relative pressure) inside this cavity, making the lungs to attach to the chest wall. The *alveolar (or intrapulmonary) pressure* is defined as that existing inside alveoli and airways. The *transpulmonary (or transmural) pressure* is the gradient between alveolar and pleural pressure, i.e., the pressure difference between the interior of the alveoli and the lung surface (Guyton, Hall, 1997). These pressures are shown in Fig. (1), for a normal respiration cycle.

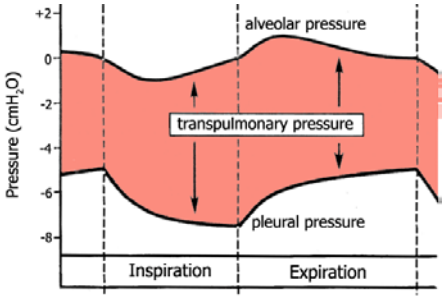

Figure 1. Pressures related to mechanical ventilation, with typical values during a normal inspiration cycle (Guyton, Hall, 1997).

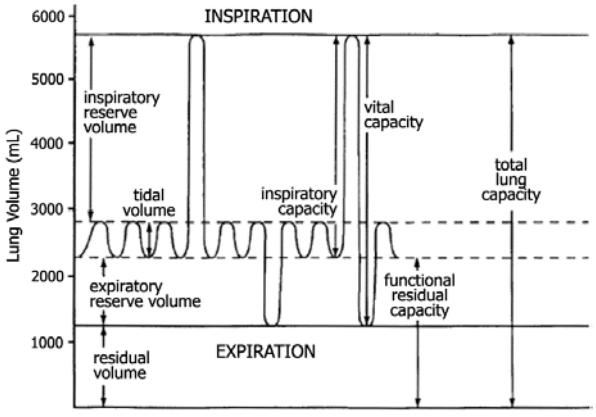

Figure 2. Volumes related to mechanical ventilation.

Figure (2) shows the main volumes and capacities related to mechanical ventilation. *Tidal volume* is the amount of air inhaled during normal ventilation. *Inspiratory* and *expiratory reserve volumes* are obtained, respectively, during forced inspiration and expiration. *Functional residual capacity* is the amount of air which remains in the lungs after a normal expiration, while the *residual volume* is the remaining volume after a forced expiration (it avoids collapse of alveoli). Finally, *total lung capacity* is the total volume that lungs are able to support. Typical values for these volumes can also be seen in Fig. (2), corresponding to a 20 to 30-year-old man (Guyton, Hall, 1997).

Lungs, as well as the chest wall itself, present elastic behavior, so that it is possible to relate the pressure generated by the inspiratory muscles with the amount of air inhaled during inspiratory phase. *Compliance* is defined as the ratio of unity volume expansion of the lungs to unity increase in pressure (pleural, transpulmonary or alveolar). Figure (3) shows the compliance of the lungs, the chest wall and the respiratory system itself. The resistance offered by the respiratory system is caused mainly by friction, due to air movement through the airways. Thus, *resistance* can be

defined as the relation between a pressure difference in the airways and the resultant flow (Bonassa, 2000; Guyton, Hall, 1997).

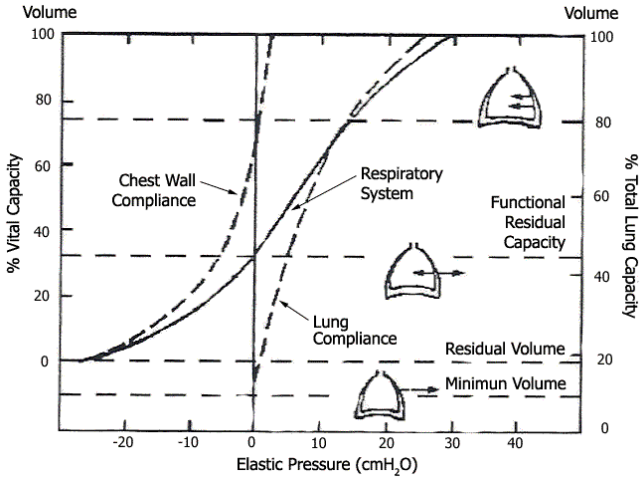

Figure 3. Lung capacities vs. elastic pressure graph, illustrating the compliances of the respiratory system. Note that in the tidal volume region, total compliance is linear, justifying a linear model for compliance.

4. Analysis and Simulation of Ventilation Phenomena

Many models of individual aspects of the respiratory mechanics have been studied, developed and simulated, in order to evaluate their influence on the overall functioning of the respiratory system.

4.1. Gravitational Effects

During normal functioning of the respiratory system a vertical gradient of pressure and alveoli volume occurs in the lungs, due to concentration differences in the intrapleural fluid caused by action of gravity. Although these effects become more relevant only in treatments with liquid ventilation or in pathologies that cause fluid increase in the lungs (because of intensification of density effects), as stated by Tarczy-Hornoch et al (2000), they are also present in normal air ventilation, as shown by the simulations. The volume variation is remarkably important, because hyperinflation of the lungs may lead to trauma in alveoli (Lonardoni, Iwata, 2002).

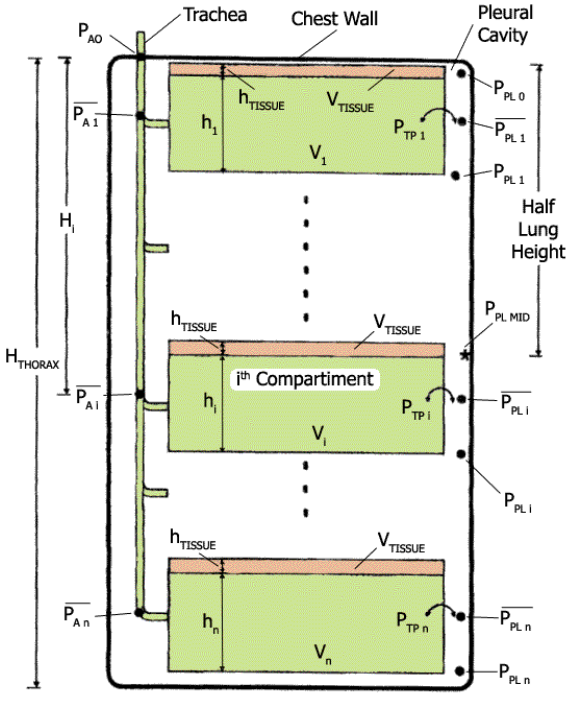

Figure 4. Model for study of gravitational effects (Tarczy-Hornoch et al, 2000).

The simulated model was originally suggested by Tarczy-Hornoch et al (2000) and considers only the elastic properties of the respiratory system (the situations are static, with no flow). The model consists of multiple compartments arranged vertically, without side separation of the lungs, as shown in Fig. (4). Thus, alveolar volume depends only on compartment compliance, residual volume and transpulmonary pressure. Compliance changes with the elastic properties of the tissue and with interfacial tensions between inflating gas and alveolar wall. Linear pressure-volume relations were assumed, as shown in Fig. (3).

Transpulmonary pressure (P_{TP}) is calculated as the difference between alveolar (P_A) and pleural (P_{PL}) pressures. In the inflated lung, P_A is equal to the airway opening pressure (P_{AO}). Pleural pressure P_{PL} in any point results from the pressure on the top of the lung (P_{PL0}) plus the weight of tissue and fluid above that point. The density of the pulmonary fluid and its contents determines the relative pleural pressure gradient.

We have run numeric simulations for many cases, varying the number of compartments, the total lung compliance and the input pressure (airway opening pressure). Results show that, for different compliances, alveolar pressure remains nearly equal for all compartments, while pleural and transpulmonary pressures vary 5 cmH_2O from the bottom to the top of the lung. Furthermore, volume compartment showed a variation of approximately 5% in each simulation. Figure (5) shows results of two simulations: for a healthy individual and for a low compliance one.

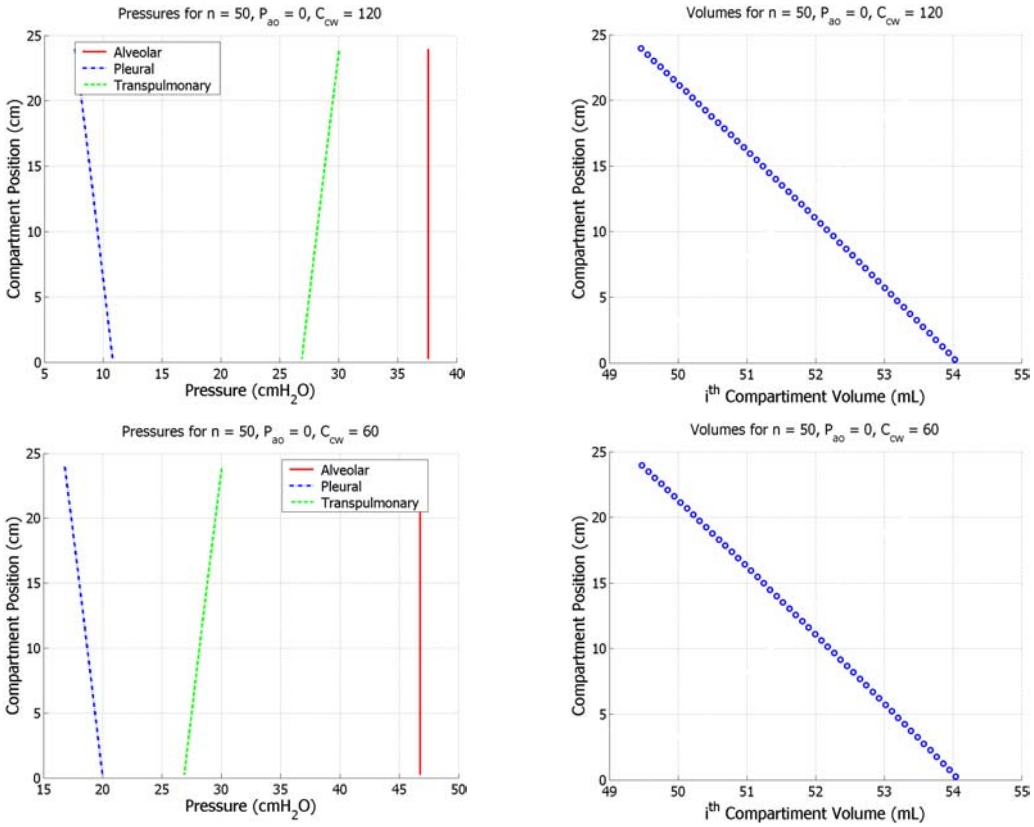

Figure 5. Simulations for a healthy individual (top) and for a low compliance individual (bottom), with no pressure input in the airway opening. The graphs on the right show the volume of each compartment in relation to its relative position (height).

4.2. Inspiratory Pump

The so called inspiratory pump, which comprises the rib cage and the respiratory muscles, translates either automatic or voluntary inspiratory commands in alveolar ventilation through the application of expanding forces to the lungs. It is extremely important for the comprehension of respiration physiology and also of some pathologies. The biggest difficulties in the mechanical modeling of its structure arise from the complex geometric shape of its components.

Among all studied inspiratory pump models, we have found in Ricci et al (2002) an original method to determine inaccessible respiratory parameters. That is accomplished through the use of magnetic resonance imaging (MRI) results over a geometry based mathematical model, so that values can be estimated. This model will not be shown in this paper. Another model (actually a set of models) proposed by Kaye (1997) showed some impressive results. His models, which were originally developed for a finite-element trauma simulator, are based on an interesting mechanical analogy with pistons, springs and actuators, as shown in Fig. (6). Here, we present simulations only for the simpler model, with one degree of freedom – the original dissertation presents at least three evolutions of this model, reaching up to eleven degrees of freedom.

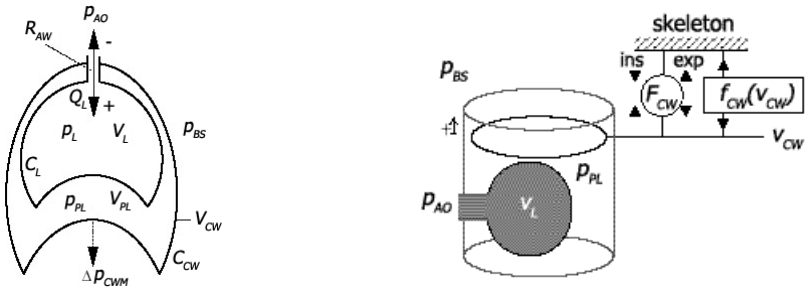

Figure 6. One-degree-of-freedom inspiratory pump (Kaye, 1997).

It is considered, in this model, that any volume change in the chest wall (v_{CW}) is followed by an identical volume change in the lung (v_L), because intrapleural fluid transmits integrally the forces from the chest wall to the lungs, since its contents are incompressible. Thus we can write Eq. (1).

$$v_{CW} = v_L \tag{1}$$

Variables represented in lowercase letters correspond to changes about an operating point. As far as the variations in volume are equal, from Eq. (1), one can infer that the variations in volume rate of the chest wall ($\dot{v}_{CW}$) and of the lung ($\dot{v}_L$) are also equal:

$$\dot{v}_{CW} = \dot{v}_L \tag{2}$$

The next two equations represent the generalized force balance respectively over the chest wall and over the lung.

$$(p_{PL} - p_{BS}) + \Delta p_{CWM} = \frac{1}{C_{CW}} \cdot v_{CW} + R_{CW} \cdot \dot{v}_{CW} \tag{3}$$

$$(p_{AO} - p_{PL}) = \frac{1}{C_L} \cdot v_L + R_L \cdot \dot{v}_L \tag{4}$$

Variables in Eqs. (1) to (4) are also shown in Fig. (6). Volumes are denoted as v, pressures as p, resistances as R and compliances as C. Subscripts indicate L for the lung, CW for the chest wall, PL for the intrapleural space, BS for body surface, AO for airway opening and AW for airway. The symbol Δp_{CWM} represents the muscle effort. These equations result in a first order differential equation with a forced input, as shown in Eq. (5).

$$\dot{v}(R_{CW} + R_L) + v\left(\frac{1}{C_{CW}} + \frac{1}{C_L}\right) = (p_{AO} - p_{BS}) + \Delta p_{CWM} \tag{5}$$

The right side of Eq. (5) represents the forced input. If p_{AO} is positive, we got artificial positive ventilation, with positive pressure being kept in the airway opening. If p_{BS} is positive, we simulate artificial negative pressure, with the patient's body being maintained in an ambient with vacuum (this was the first generation of artificial ventilators, also known as iron lungs). Finally, if Δp_{CWM} is not null, we have normal spontaneous respiration.

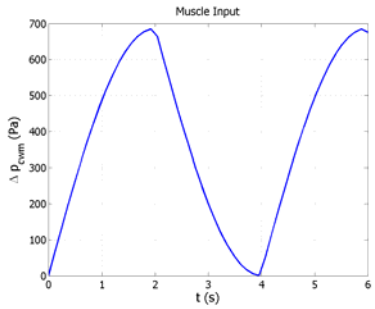

Figure 7. Muscle effort given as input for simulations of Eq. (5).

The simulations demonstrate the inspiratory pump mechanics – the pressure generated by the movement of the chest wall (p_{PL}) result in variation of the alveolar pressure (p_L), which will cause flow in the airways and thus inflate the

lung (volume increase). We used a quarter-sine wave as muscle input, as shown in Fig. (7), which is approximately accurate for a combination of diaphragm and chest wall efforts (Bonassa, 2002). Simulations in Fig. (8) are separated in three rows: the first one represents a healthy individual, the second row corresponds to a low resistance patient, and the last row represents a low compliance patient. Common parameters used in all simulations are R_{CW} (29.4 Pa / Ls^{-1}), C_{CW} (0.00153 L / Pa), p_{BS} (0 Pa) and p_{AO} (0 Pa); other parameters are specified in the subtitle. This model, as well as the remaining ones suggested by Kaye (1997), proved to be very useful in the study of spontaneous ventilation.

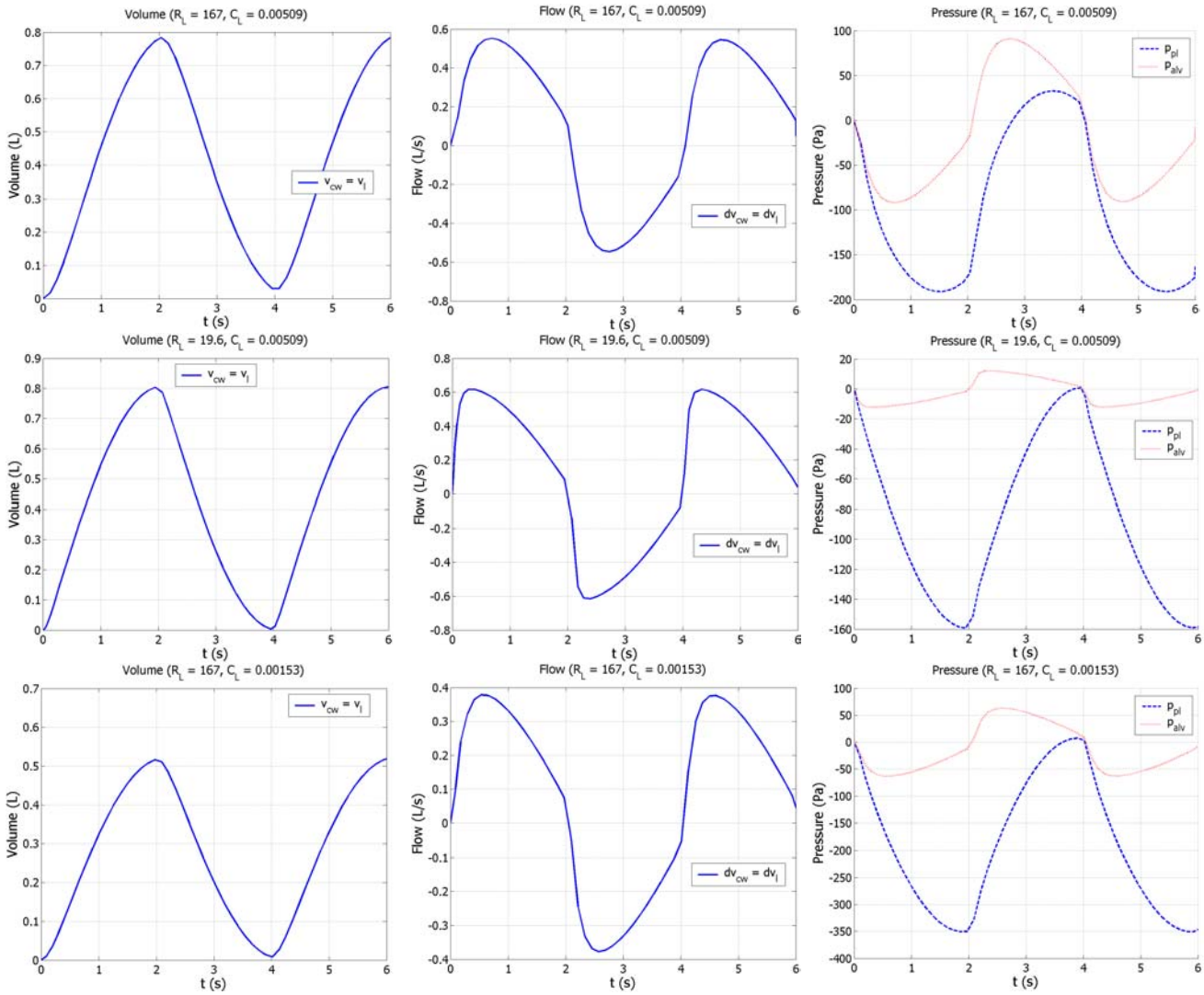

Figure 8. Results (volume, flow and pressure) for the simulation of a quarter-sine muscle input in three different individuals. First row corresponds to a healthy individual (R_L = 167.0 Pa / Ls^{-1} and C_L = 0.00509 L / Pa), second row corresponds to a patient with low resistance (R_L = 19.6 Pa / Ls^{-1} and C_L = 0.00509 L / Pa), and third row resulted from a patient with low compliance (R_L = 167.0 Pa / Ls^{-1} and C_L = 0.00153 L / Pa).

4.2. Artificial Ventilation

Most diseases associated with the respiratory system use artificial ventilators as main treatment. These devices manage forced air flow to a generally sedated patient. In order to better simulate artificial ventilation it is necessary to add to the respiratory system model some new components relative to the ventilator functioning. Bonassa (1996) suggested a one-compartment model based on electric analogy (commonly used in simpler models of the respiratory system) with the objective of studying work of breath (WOB) in patients. The model considers a single lung, with equivalent resistance and compliance. The analog circuit, as well as simulations and equations, will not be shown for this model, but rather for the next one, with two compartments.

5. Didactic Simulator

In order to expand the use of our model, we have developed a didactic simulator dedicated to training in artificial ventilation. This simulator allows the visualization and individual adjustment of all patient and ventilator parameters, as well as volume, flow and pressure graphs.

5.1. Two-Compartment Model

Aiming the development of the didactic simulator, we have proposed a new two-compartment model, so that users could visualize individual results for the two sides of the lung at the same time. This model was based on the one suggested by Bonassa (1996), with only one compartment, as stated above. The new model is still based on electric analogy, as shown in Fig. (9).

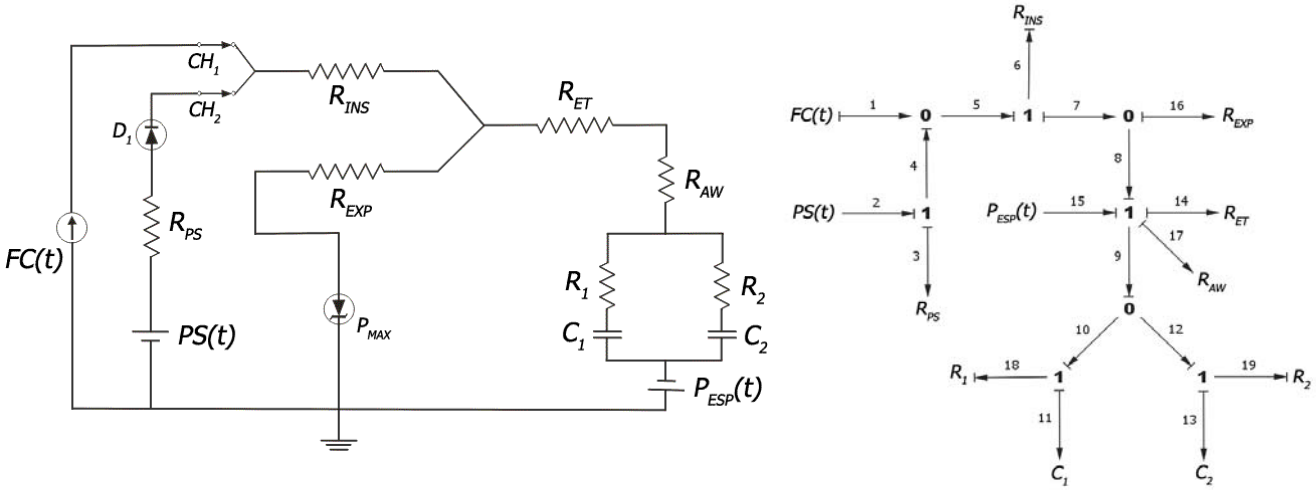

Figure 9. Electric analogy and respective bond-graph of the two-compartment model.

We have chosen to model the lung laterally, as two separate structures, rather than vertically, in order to simplify the model and allow the development of the simulator (see section 5.2). The authors are aware that gravitational effects are indeed important, as shown in section 4.1, and future studies and implementations may incorporate these effects.

The respiratory system is considered to be a viscoelastic structure, thus allowing the lungs to be modeled as two compartments characterized by individual resistance (R_1 and R_2) and compliance (C_1 and C_2). The values of resistance are associated with viscosity and turbulence effects, present in peripheral airways, from bronchioles to alveoli. Upper airways have resistance R_{AW}. As external parameters we have the endotracheal tube resistance, R_{ET} and the inspiratory and expiratory branch resistance, respectively R_{INS} and R_{EXP}, relative to the set of tubes that connects the patient to the equipment. Simulations will be covered on the next issue.

We have chosen to simulate only one ventilation mode, known as controlled volume, in which the ventilator supplies a determined volume with constant flow (FC(t), in the model) and respiratory rate, all set by the operator. Therefore, we could ignore some terms of the original model. These include the terms related to support pressure (PS(t), R_{PS} and D_1), the muscle effort $P_{ESP}(t)$ and the zener diodes switched by CH_3 in the original Bonassa's model. However, we decided to preserve these variables in the model, just setting them to convenient values, in order allow future evolutions of this work.

The system was modeled using the bond graph technique, which allows easy determination of desired variables. The subscripts in the next equations refer to Fig. (9), so that subscripts 1 and 2 correspond respectively to right and left lungs. Thus, V_1 and V_2 are right and left lung volumes, p_1 and p_2 are respective alveolar pressures and $\dot{V}_1$ and $\dot{V}_2$ are right and left bronchi flow. Other subscripts follow the previous descriptions.

The airway flow $\dot{V}_{AW}$ is given by Eq. (6).

$$\dot{V}_{AW} = \frac{\left\{ \frac{PS(t)}{(R_{INS}+R_{PS})} + \frac{FC(t)}{\left(1+\frac{R_{INS}}{R_{PS}}\right)} - R_{EQ}\cdot\left[\frac{V_1}{C_1} + R_1\cdot\dot{V}_1 - P_{ESP}(t)\right]\right\}}{\left[1+R_{EQ}\cdot(R_{ET}+R_{AW})\right]} \tag{6}$$

which still depends on $\dot{V}_1$. Equivalent resistance R_{EQ} is given by Eq. (7)

$$R_{EQ} = \left(\frac{1}{R_{INS}+R_{PS}} + \frac{1}{R_{EXP}}\right) \tag{7}$$

Now we can determine bronchi flow through Eqs. (8) and (9).

$$\dot{V}_1 = \frac{\left\{ \frac{V_2}{C_2} - \frac{V_1}{C_1} + R_2 \cdot \left[\frac{PS(t)}{(R_{INS} + R_{PS})} + \frac{FC(t)}{(1 + R_{INS}/R_{PS})} - R_{EQ} \cdot \left(\frac{V_1}{C_1} - P_{ESP}(t) \right) \right] \right\}}{1 + R_{EQ} \cdot (R_{ET} + R_{AW})} \quad (8)$$

$$R_1 + R_2 + R_1 R_2 \cdot \left(\frac{R_{EQ}}{1 + R_{EQ} \cdot (R_{ET} + R_{AW})} \right)$$

$$\dot{V}_2 = \dot{V}_{AW} - \dot{V}_1 \quad (9)$$

Alveolar pressure for the right lung can be determined by Eq. (10).

$$p_1 = \frac{V_1}{C_1} \quad (10)$$

A similar equation can be determined for the left lung by substituting the subscripts in Eq. (10). Airway pressure, given by Eq. (11), depends on the elastic pressure, on resistive losses and on spontaneous effort. Note that in the next equation the terms related to the right lung (subscript 1) can be replaced with left lung variables (subscripted as 2), because the two lungs are connected in parallel.

$$p_{AW} = R_1 \cdot \dot{V}_1 + \frac{V_1}{C_1} + (R_{ET} + R_{AW}) \cdot \dot{V}_{AW} - P_{ESP}(t) \quad (11)$$

Finally, we can determine the right lung volume V_1 (and similarly V_2) simply integrating flow $\dot{V}_1$ (or $\dot{V}_2$) over time, as shown in Eq. (12).

$$V_1 = \int_{t_0}^{t_1} \dot{V}_1 \, dt \quad (12)$$

Clearly, the equations are interdependent, requiring an iterative solution, so that values calculated in one step are used on the next step. The implementations in the simulator and in MatLab were done considering these aspects.

5.2. Simulator

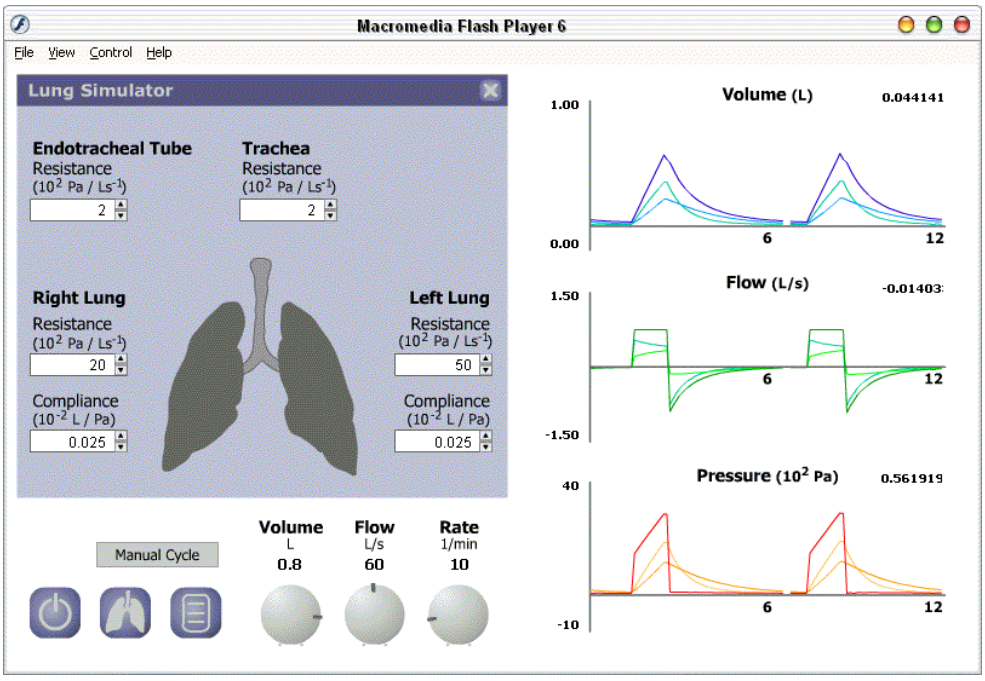

Figure 10. Simulator interface.

The simulator was developed in Flash (Actionscript language), which allows easy creation of graphical interfaces and publishing in the Internet. Figure (10) shows the simulator interface.

It is possible to set all model parameters, either relative to the patient (resistances and compliances) or to the ventilator (volume, flow and respiratory rate). The graphs display not only values calculated on the airway opening (which are familiar to users of graph monitors associated to commercially available ventilators), but also separate graphs for each lung (so that it is possible to visualize what is really happening in the interior of the lungs, as seen in Fig. (10)).

We compared some tests run in the simulator with numeric simulations in Matlab, in order to check the accuracy of the values calculated in real time by the software. Figures. (11) to (13) show graphical comparisons for three usual clinical cases – a healthy individual, a high resistance (obstructive) patient and a low compliance (restrictive) patient.

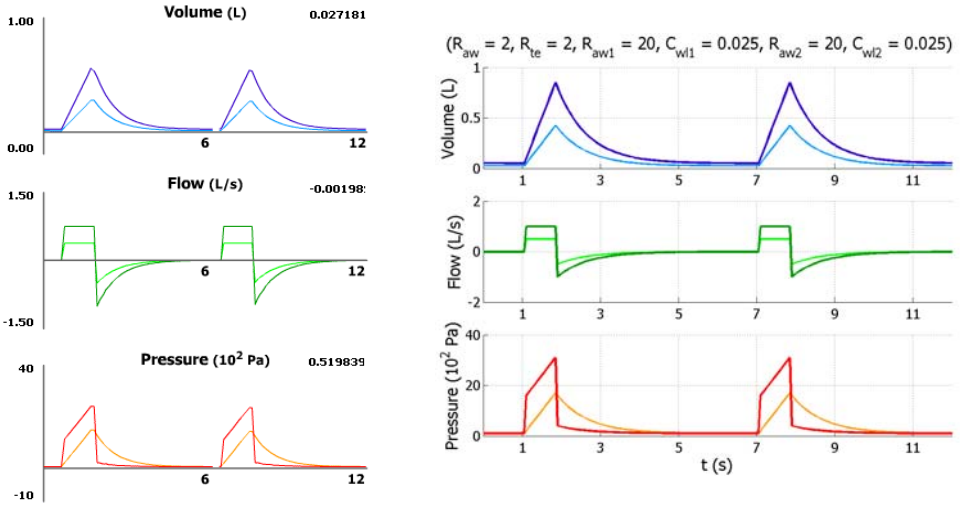

Figure 11. Comparison between results obtained from the Simulator in Flash and numerical simulations run in MatLab. The colors in MatLab were chosen to match the ones used in the Simulator. Parameters are R_{AW} = 2 hPa / Ls^{-1}, R_{TE} = 2 hPa / Ls^{-1}, R_{AW1} = 20 hPa / Ls^{-1}, C_{WL1} = 0.0025 L / hPa, R_{AW2} = 20 hPa / Ls^{-1}, C_{WL2} = L / hPa.

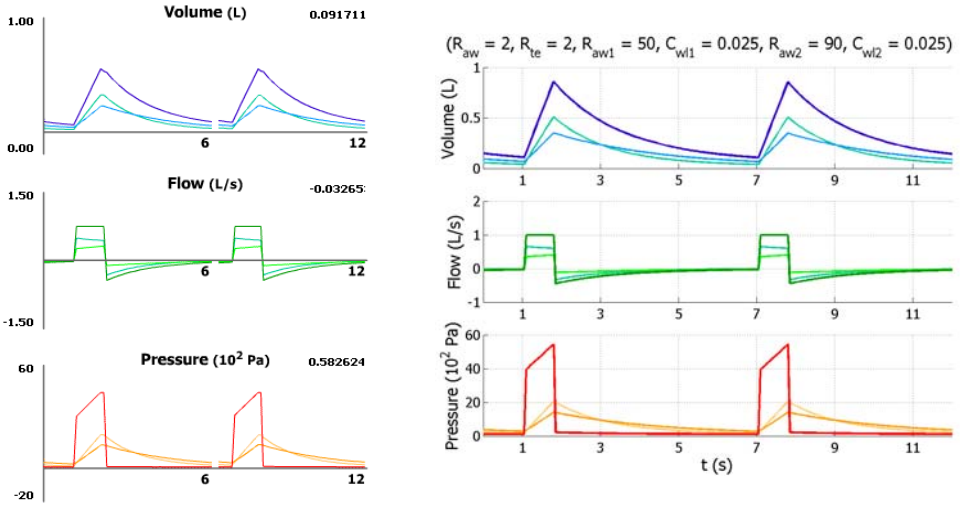

Figure 12. Simulations for an obstructive patient (with high airway resistance). Note that different resistances (50 and 90 hPa / Ls^{-1}) were chosen for left and right compartments, although both are higher than in normal conditions.

Simulations presented in Figs. (11) to (13) show that results obtained in real time from the simulator are accurate to numerical results from MatLab, thus allowing us to say that the simulator is suitable for use as a tool for teaching and training.

We have noticed some decrease in the performance of the simulator on slower machines. However, due to characteristics of the implementation, the evolution of parameters through time was preserved, maintaining the general aspect of the curves without compromise of accuracy.

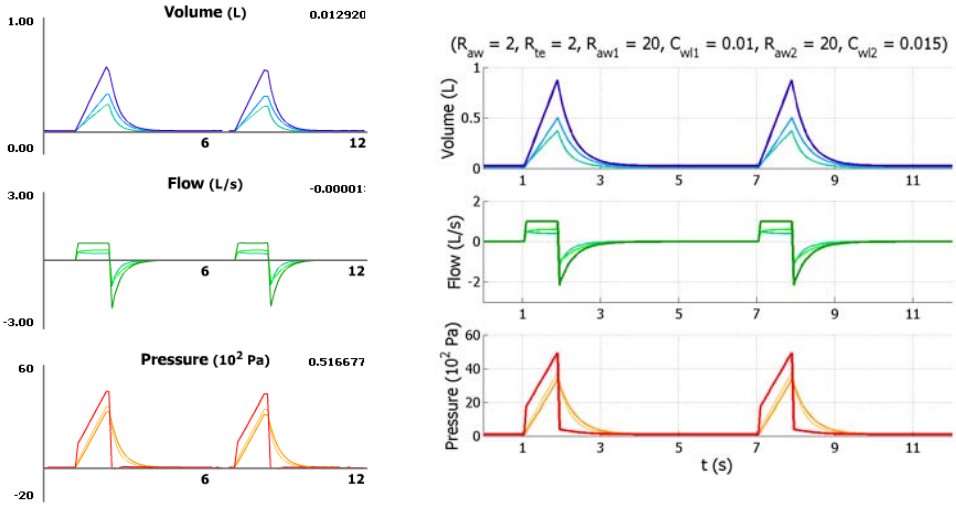

Figure 13. Simulation for a restrictive patient (with low compliance lungs). Once more, different values were used for each compartment (0.010 and 0.015 L / hPa), but both lower than in a healthy patient.

6. Conclusions

This paper has proposed, initially, an analysis of the most relevant aspects (which we have presented here) necessary to the development of a more complete model of the respiratory system mechanics. Certainly, for the development of this highly complex model, there must be a deeper study of these effects and their influences on one other, as well as the involvement of different systems and characteristics. Cardiovascular system influences can be noticed in the rigidity of the mediastinum (changing the mechanical behavior of the inspiratory pump) or in gas exchange in the alveoli. Some studies and developments already point to that direction, presenting very interesting results (Kaye, 1997; Timischl, 1998; Liu, 1998). On the other hand, internal respiration is a very complex process, whose inclusion should lead to very complicated models and poor overall improvement in this phase of our studies.

The didactic simulator has shown excellent results, even being still based on a simple mechanical model. It is already capable of improving comprehension of the main ventilatory parameters, and shall be used in learning and training of professionals.

Based on this first simulator, we intend to develop a more sophisticated and complex one, with the inclusion of more ventilation modes, tutorials and even a patient state evolution algorithm. Also, other models may be tested and incorporated, in order to include effects presented here. However, we have noticed poor performance on slow computers, demanding some optimization of the code. Perhaps a combination of Flash Actionscript language with higher performance languages, such as C++ or Visual Basic, may improve performance, enabling future developments.

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