SIMULATION OF THE HUMAN LUNG

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Abstract

A human lung simulator was implemented using a model based on the Fick principle. The simulator is designed to emulate CO_2 production and O_2 consumption in the body and gas exchange in the lung. The implementation consists of hardware and software to control the flow of gases entering and leaving a ventilated test lung. An initial test of CO_2 production qualitatively demonstrated that the lung simulator behaved as expected. Since this project is in its initial stages, additional experimentation and model refinement is necessary for the simulator to accurately represent physiologic responses of a human lung.

Introduction

Modeling and simulation are important means of testing and validating new medical devices without involving live subjects. Human and animal testing is expensive. Furthermore, control of respiratory parameters may be difficult or impossible to obtain during an experiment on live subjects. Creating a model and a simulation may provide the means to validate new instrumentation with less cost and more accuracy. With this in mind, we have created a human lung simulator to validate prototype anesthesia instrumentation. Our simulator is designed to model CO_2 production and O_2 consumption, given a value for cardiac output. Such a simulator may be used to validate medical devices that measure cardiac output non-invasively.

CO_2 production and O_2 consumption

Figure 1 shows a simple representation of blood flow and gas exchange in the body. Oxygen is inspired into the alveoli of the lungs where it diffuses across the alveolar membrane and pulmonary capillary membrane. Likewise, carbon dioxide diffuses from the blood in the pulmonary capillary beds and into the alveoli. Oxygen rich blood is pumped through the right heart and into the tissues where metabolism consumes oxygen and produces carbon dioxide. Thus, CO_2 rich blood is pumped through the left side of the heart and back into the lungs[1].

Cardiac output is related to gas exchange using a mass balance equation, also known as the Fick principle[2]:

$$\dot{Q} = \frac{\dot{V}_{co_2\ produced}}{c_{\bar{v}_{co_2}} - c_{a_{co_2}}}, \qquad (1)$$

where $\dot{Q}$ is cardiac output (liters/minute), $\dot{V}_{co_2\ produced}$ is the amount of CO2 produced by tissue metabolism, (liters/minute), $c_{\bar{v}_{co_2}}$ is the mixed venous CO_2 concentration of the blood (blood flowing into lungs in % volume) and $c_{a_{co_2}}$ is the arterial CO_2 concentration of blood flowing from the lungs (% volume). For our lung simulator, we set the cardiac output to a known value. Thus, we may rearrange (1) so that,

$$\dot{V}_{co_2\ produced} = \dot{Q} \cdot (c_{\bar{v}_{co_2}} - c_{a_{co_2}}). \qquad (2)$$

For every unit of CO_2 produced in the tissues, there is some amount of O_2 consumed ($\dot{V}_{o_2\ consumed}$). CO_2

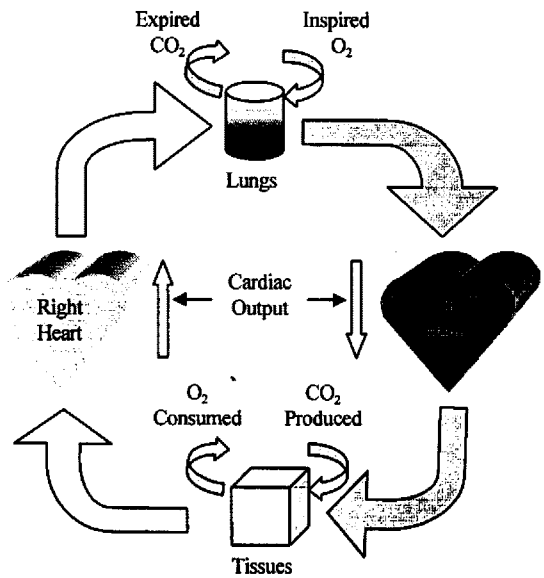

Figure 1: Gas Exchange and Blood Flow in the Human Lung and Body.

production may be related to O_2 consumption by the respiratory exchange ratio, R, where

$$R = \frac{\dot{V}_{CO_2\ produced}}{\dot{V}_{O_2\ consumed}}. \qquad (3)$$

R is a function of metabolism; the body oxidizes fats, carbohydrates, and proteins, where $R_{fat} = 0.7$, $R_{carbohydrate} = 1.0$, and $R_{protein} = 0.8$. For a healthy human, a typical value for R is 0.8.[2]

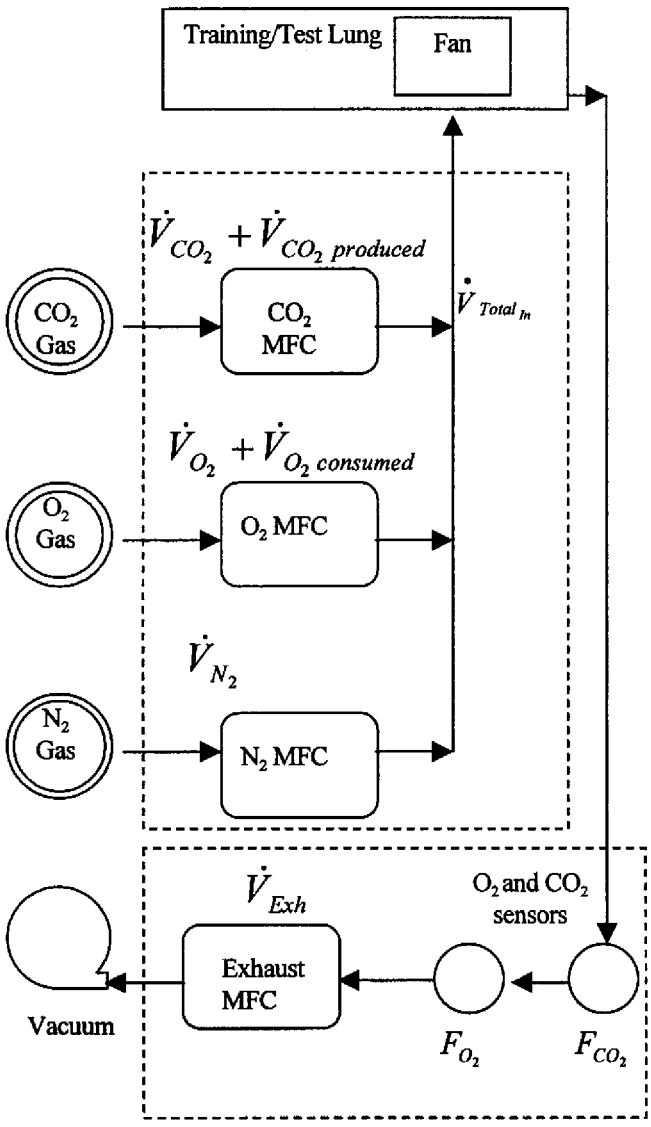

Figure 2: Physical Components of the Lung Simulator

Lung Simulator Implementation

We use equations (2) and (3) as the foundation for our lung simulator. The physical components of the simulator are shown in Figure 2. Since the largest portion of ambient air is composed of N_2, O_2, and CO_2, we use three mass flow controllers (MFCs) to regulate the flow of these gases from pressurized tanks into a ventilated test/training lung (TTL). A fan inside the TTL provides active mixing of the gases from the lung simulator and the ventilator. A vacuum is used to pull the mixed gas from the TTL in which the flow is regulated by the exhaust MFC. O_2 and CO_2 sensors, located in the exhaust flow, record the concentrations of oxygen and carbon dioxide in the lung. A microprocessor controls the flow of the MFCs and receives input from the CO_2 and O_2 sensors. A personal computer communicates with the microprocessor and provides the user with an interface to input cardiac output and $C_{\bar{V}_{CO_2}}$ (see Figure 3).

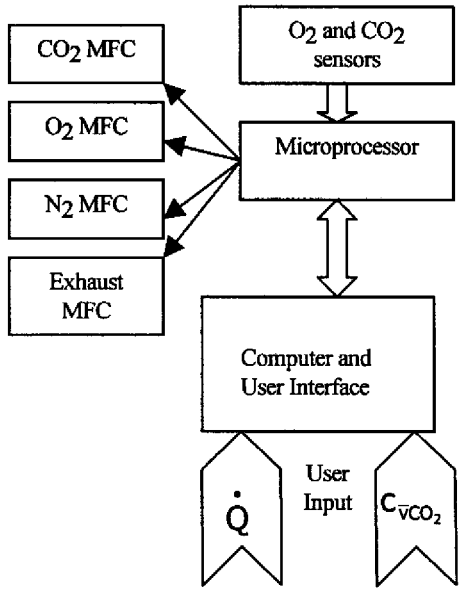

Figure 3: Microprocessor Control and Communication

The lung simulator uses the O_2 and CO_2 sensors to calculate the flow of oxygen $(\dot{V}_{O_2})$ and carbon dioxide $(\dot{V}_{CO_2})$ pulled from the lung by the vacuum. The exhaust flow $(\dot{V}_{Exh})$ is set at a constant rate, so

$$\dot{V}_{O_2} = \dot{V}_{Exh} \cdot F_{O_2}, \text{ (liters/min)} \qquad (4)$$

and

$$\dot{V}_{CO_2} = \dot{V}_{Exh} \cdot F_{CO_2} \text{ (liters/min)}, \quad (5)$$

where F_{O_2} and F_{CO_2} is the fraction of O_2 and CO_2 measured by the sensors in the exhaust flow. Also,

$$\dot{V}_{Exh} = \dot{V}_{CO_2} + \dot{V}_{O_2} + \dot{V}_{N_2} = const. \text{ (liters/min)}, \quad (6)$$

and we may solve for N_2 flow going into and coming out from the lung:

$$\dot{V}_{N_2} = \dot{V}_{Exh} - (\dot{V}_{CO_2} + \dot{V}_{O_2}) \text{ (liters/min)}. \quad (7)$$

In order to calculate O_2 consumption and CO_2 production, we assume that the content of CO_2 in the mixed venous blood, $c_{\bar{v}_{co_2}}$, is constant. To compute $c_{a_{co_2}}$, we first find $P_{a_{co_2}}$, arterial partial pressure (mm Hg), which is a function of barometric pressure, P_{bar} (mm Hg). So,

$$P_{a_{co_2}} = F_{CO_2} \cdot P_{bar} \text{ (mm Hg)}. \quad (8)$$

$P_{a_{co_2}}$ is related to $c_{a_{co_2}}$ by a dissociation curve. Such a curve is empirically derived by Capek and Roy,[3] which also requires the hemoglobin (*Hb*) content of blood in grams per deciliter. So,

$$C_{a_{co_2}}(P_{a_{co_2}}) = (6.957 \cdot Hb + 94.864) \cdot \ln(1 + 0.1933 \cdot P_{a_{co_2}}) \text{ (vol \%)}. \quad (9)$$

This function is plotted in Figure 4.

Using equations (2) -- (9), we may define the flow of gas into the lung, $\dot{V}_{Total_{in}}$:

$$\dot{V}_{Total_{in}} = \overbrace{\left[\dot{V}_{CO_2} + \dot{V}_{CO_2 produced}\right]}^{CO_2 \text{ MFC Flow}} + \overbrace{\left[\dot{V}_{O_2} - \dot{V}_{O_2 consumed}\right]}^{O_2 \text{ MFC Flow}} + \overbrace{\dot{V}_{N_2}}^{N_2 \text{ MFC Flow}} \quad (10)$$

Also, (10) computes the quantity of flow for each gas coming into the lung, which is set by its corresponding MFC as demonstrated in Figure 2.

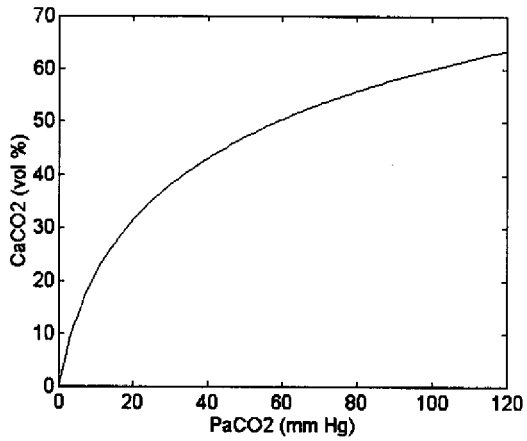

Figure 4 : CO_2 Dissociation Curve With Hb = 15 g/dl

Validation of Lung Simulator

Since this project is a work in progress, we have only begun to validate the simulator. At this time, we have compared CO_2 production in the lung simulator to measured CO_2 production on an anesthesia monitor. This was achieved by comparing $\dot{V}_{co_2\ produced}$, and $P_{a_{co_2}}$ of the lung simulator to CO_2 excretion at the mouth ($\dot{V}_{co_2\ mouth}$, l/min) and end tidal CO_2 (*etCO2*, mm Hg) by the anesthesia monitor. Our TTL may be considered as a single alveolus with 100% perfusion (no parallel deadspace). Under these conditions, alveolar partial pressure of CO_2 ($P_{A_{co_2}}$) is approximately equal to $P_{a_{co_2}}$. $P_{A_{co_2}}$ is related to *etCO2* by:

$$etCO_2 = r \cdot P_{A_{CO_2}\ perfused} + (1 - r) P_{A_{CO_2}\ unperfused}, \quad (11)$$

where *r* is the ratio of perfused to unperfused alveoli.[4] A single alveolus model with no dead space yields

$$etCO_2 = P_{A_{CO_2}} \approx P_{a_{CO_2}}. \quad (12)$$

In addition, under steady state, $\dot{V}_{co_2\ mouth}$ should also have similar values to $\dot{V}_{co_2\ produced}$.

Results

To validate the parameters described in the previous section, we induced changes in the $\dot{V}_{co_2\ produced}$ and $P_{a_{co_2}}$

by changing the set value of cardiac output. For this validation experiment, we decreased cardiac output in one liter/min steps from 6.0 liters/min to 1.0 liter/min. Table 1 describes the times at which cardiac output was altered. Ample time was allowed between each step change so that the system may reach steady state. Figures 5 and 6 show comparisons of $P_{a_{co_2}}$ to $etCO_2$ and $\dot{V}_{co_2\ produced}$ to $\dot{V}_{co_2\ mouth}$ respectively. Unfortunately, these plots should

Cardiac Output (liters/min)	Approx. Time (seconds)
6.0	1830
5.0	2100
4.0	2400
3.0	2690
2.0	2960
1.0	3280

Table 1: Step Decrease in Cardiac Output

be investigated qualitatively because there is a mismatch in the synchronization of the data collection times. There is some inherent delay between the response of the $etCO_2$ signal to a change in alveolar pressure, but it is not on the order of hundreds of seconds.

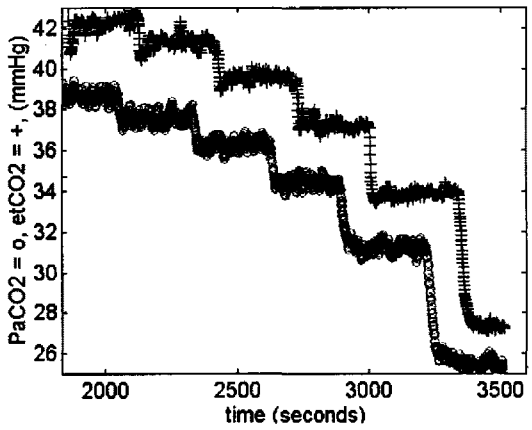

Figure 5: Arterial CO_2 (gray "O") and $etCO_2$ (black "+")

It is apparent from Figure 5 that both signals show a decreasing step change that corresponds to the change in cardiac output. The $etCO_2$ is shifted up from the $P_{a_{co_2}}$ date approximately 3 to 4 mm Hg. The synchronization error is also apparent for the CO_2 production values demonstrated in Figure 6.

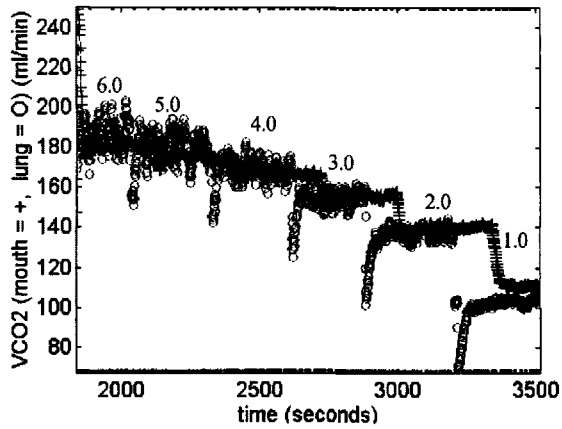

Figure 6: CO_2 Production in the Lung Simulator (lung = gray "O", mouth = black "+"),the numbers in the plot represent the value of cardiac output at that time

Discussion

Due to the limited amount data collected for validation of the lung simulator and difficulties with synchronization of the data collected, no significant conclusions may be made about the accuracy of the lung simulator at this time. It is important to note that this test described in the previous section does not match the physiologic response of a human's lung. That is, even though there was a fall in the CO_2 parameters for the given cardiac output values, they may not correspond correctly for a human response. Additional experiments using human data and comparing it to the lung simulator data are necessary in order to evaluate how well the lung simulator models the human respiratory system. The initial validation tests look promising with respect to the expected behavior of the lung simulator. All CO_2 parameters fell in accordance with a decreasing step change in cardiac output.

The upward shift in $etCO_2$ (Figure 5) may be due to different computation methods for the lung simulator and the anesthesia monitor. For instance, the dissociation curve that is implemented for the simulator is based on empirical data and may not match the computation methods used by the monitor. Examination of the anesthesia monitor's specifications could give insight into how $etCO_2$ is calculated.

Ignoring the effects of the shifted data, there are some transient spikes for the lung simulator's CO_2 production (see Figure 6). The spikes are due to step changes in

cardiac output. The step change in cardiac output causes an instantaneous change in $\dot{V}_{co_2\ produced}$. As $P_{a_{co_2}}$ decreases in response to the change, the CO_2 production rises to a value comparable with the CO_2 excreted at the mouth.

Future Development

While the hardware of the lung simulator requires little additional adjustment, there are many enhancements that still require implementation. As previously stated, more experimentation is required to determine the performance of the lung simulator. For instance, we have yet to validate whether O_2 consumption in our simulator corresponds to the values computed by an O_2 metabolic gas monitor. In addition, experiments that induce rapid changes in cardiac output, hypoxia, and hypercapnia are necessary to determine lung simulator performance.

The current model is based on the Fick principle, which assumes a system in steady state. Thus, the model may yield unpredictable results to the transient responses. Furthermore $c_{\bar{v}_{co_2}}$ is required to be constant in order to solve for $\dot{V}_{CO_2}$ in the Fick equation. This assumption is normally valid since there is a large buffering capacity for CO_2 in the body, especially in fat and muscle.[5, 6] On the other hand, it may not be a valid assumption for patients in septic shock, where most of the blood is flowing to vital organs in which do not store large quantities of CO_2.[6, 7] Finally it is important to notice that the Fick equation does not account for shunt, blood that bypasses the gas exchange occurring in the ventilated alveoli of the lung. Therefore, the Fick equation provides an accurate estimate of cardiac output if shunted blood is not present. Otherwise it measures pulmonary-capillary blood flow.

A more sophisticated model may help to account for these assumptions. Chiari, Avanzolini, and Ursino have proposed a sophisticated respiratory model that simulates the transport of gases to several different compartments including the brain, cerebral spinal fluid, tissues and the lungs. It also accounts for shunt, has chemoreceptor control for ventilation, and incorporates acid/base regulation into its CO_2 dissociation curve[8]. Such a sophisticated model may be incorporated into our lung simulator to improve the accuracy of the model with respect to human respiratory system.

Acknowledgements

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