"Remember that all models are wrong; the practical question is how wrong do they have to be to not be useful." -George E. P. Box

I. Executive Summary

Our team developed a conceptual and mathematical model of the lungs in order to facilitate the creation of an improved Extracorporeal Membrane Oxygenation, or ECMO, machine. We have modeled the entire respiratory system as a multi-unit system that accounts for the holistic changes of air as it progresses through the lungs. Various extensive properties of this air are tracked through a conceptual model and a computational program using MATLAB®. Anatomically, the respiratory system is highly branched and complex (6). However, our model simplifies this system based on function in a way that fosters the engineering of a machine that can efficiently and succinctly exchange gases as the lungs do. Thus, our model primarily focuses on these functions of the respiratory system: humidification, mixing, and diffusion. With inputs such as ambient air composition, our program outputs realistic partial pressures, compositions, and flow rates of each unit in our model as well as the total system. This is accomplished by utilizing a series of conservation equations, iterative calculations, as well as graphical approximations.

The validity of our model is demonstrated by the low percentages of error between accepted values and our program's generated values. The generated values for the composition of alveolar air and exhaled air are all within 2.22% of the accepted values. In addition, the diffusion rates of 0.0035 L/s and 0.0044 L/s, for CO_2 and O_2 in the alveoli respectively, are within 6.2% of accepted values . (7) With our calculated diffusion rates, we arrived at our final values for gas concentrations in blood (15) of 0.198 mL_{O2} / mL_{Blood} and 0.483 mL_{CO2} / mL_{Blood}; these values present a value of less than 2% error. Additionally, our model's output value for the respiratory quotient, RQ, is 0.794, which is within 3.8% of the average person's RQ . All of these outputted values prove our model's overall accurate representation of gas exchange.

Our model is successful in many aspects, but the primary one is its ability to simplify a complex system down to its key critical functions. The relevant output values of our conceptual, multi-unit and mathematical model serve as a basis for the reengineering of an improved ECMO machine.

II. Motivation

Pulmonary gas exchange is essential for cellular respiration in the human body .(7) The respiratory system involves the exchange of carbon dioxide and oxygen between inhaled air and blood. A comprehensive analysis of the respiratory system that provides quantitative and qualitative insight into this complex system is necessary. Specifically, data regarding airflow through the respiratory system can be used to analyze patient lung function and pinpoint deficiencies indicative of abnormalities. The anatomical complexity of this system complicates the experimental collection of relevant data. However, this data can be more easily procured, non-experimentally, through mathematical modeling.

Our team has developed a visual model and computational MATLAB program of the respiratory system in order to facilitate the creation of an improved ECMO machine. ECMO is a machine that provides cardiopulmonary support to help patients manage acute respiratory failure (ARF) . (11) The results of our program serve as an engineering basis for a new ECMO machine that will improve the lives of ARF patients.

In this process, we have two goals: the first is to to represent the average adult male's respiratory system, at rest, as a multi-unit model with inlets and outlets that lect the physiological functions of the system; the second is to design a computational program based off of this model in order to track the flow rate, composition, and partial pressure of air and its components.

In addition to a holistic understanding of respiratory function, our model provides the necessary insight and quantitative data specific to particular regions of the lungs. The utility and applications of these results extend beyond the purpose of improving the ECMO machine; this data provides accurate values for comparison in any analysis of lung function.

III. Introduction to Proposed Model

Figure 1: **[PROPOSED MODEL-insert model image]**

Our team has created a visual, qualitative model of the respiratory system complementary to a mathematical model that provides a quantitative analysis of air flow. Our combined model and program track the flow of air in the discrete time period of one breath, including both an inhalation and exhalation. It accomplishes this by tracking the moles, volumes, composition, diffusion rates and volumetric flow rates of air throughout the respiratory system. These properties are important not only for the accounting equation but also for providing quantitative insight essential to engineering an improved ECMO machine. Our model tracks four constituents: carbon dioxide (CO_2), oxygen (O_2), nitrogen (N_2), and water (H_2O). We chose to track O_2 and CO_2 because they are the primary gases being exchanged with the blood. It is reasonable to track N_2 because it is such a large component of ambient air. Since N_2 is largely uninvolved in gas exchange, its relative stability in concentration throughout the respiratory system serves as a test of reasonableness on our model. Finally, we have chosen to track H_2O through the system because the respiratory system humidifies ambient air.

Although the anatomic structure of the lungs is far more complex than our model lects, our model is fundamentally functionally driven and physiologically accurate. The designation of units in this system is based on the different processes that gases undergo while circulating through the respiratory system. Thus, multiple anatomic parts of the respiratory system, that perform similar functions, are grouped into individual units. Our model relies on several fundamental ideas regarding gas exchange, including the concept of dead space, the plug flow model of mixing as a gradient, a series of equations with complementary assumptions, and an analysis of time as opposed to space. For a comprehensive list of quantitative and qualitative assumptions.

A. Dead Space Air

Before delving into the model, it is first necessary to discuss the concept of dead space. In this paper, the term 'dead space air' ers to air that is not involved in gas exchange in one breath; this air has a volume of 150 mL at any point in the respiratory cycle. (6) The anatomic dead space consists of the nose, mouth, trachea, and bronchi, because these structures are not involved in gas exchange (4) Although the volume of the air is constant, the composition itself changes depending upon whether inhalation or exhalation is occurring. The flow of air through the dead space is highly cyclical. Initially, as inhalation occurs, 150 mL of the inhaled air displaces the previously held 150 mL of dead space air; a 500 mL tidal volume is decreased to 350 mL of oxygenated air engaging in gas exchange.(6) Upon exhalation, 150 mL of the deoxygenated air that has undergone gas exchange then displaces the aforementioned, oxygenated 150 mL, which is incorporated into the expiration. The deoxygenated air is then dead space air for the subsequent inhalation. (6) A portion of dead space air is designated to circulate through our system in the Dead Space Air 1 and Dead Space Air 2 streams.

B. The Plug Flow Model

The periodic displacement and incorporation of dead space air into the main air stream of 350 mL presents complex mixing. In our model the mixing is analogous to the plug flow reactor model of mixing . (6) During inhalation, because the dead space air is anatomically located closer to the alveoli than the nose and mouth, it enters the alveoli before the inhaled air. However, some degree of mixing occurs between the two such that air reaches the alveoli in a gradient from entirely dead space air to entirely humidified, oxygenated air. A similar situation is present upon exhalation, since the 150 mL of dead space air expired upon exhalation is closer to the nose/mouth than the deoxygenated air in the alveoli. Our mathematical program models this mixing, which is analogous to the plug flow model, with logistic curves delineating the volumetric flow rate of the different types of air (dead space air and non-dead space air) over time. Further discussion on dead space and the plug flow model will follow.

C. Governing Equations

Our visual and mathematical model rely on justified assumptions, meant to simplify the respiratory system, as well as equations that analyze airflow and gas exchange. Throughout the model, the conservation equation has been employed. The Ideal Gas Law was used to convert between moles, pressure, and volume of components; deviations are not expected from ideal behavior because the gases are not subjected to extreme pressures or temperatures in the body. We model gas exchange with Fick's

Law of Diffusion, under the assumption that all of our units experience flow along a high to low concentration gradient.

D. Analysis of Time and Space

The flow and diffusion of air through the respiratory system can be considered spatially, with respect to where the air is mixing and diffusing anatomically. They can also be presented chronologically, with respect to the time over which mixing is occurring. Our team has chosen to model the airflow as well as blood flow in the capillaries over a period of time, which is lected throughout our mathematical model as we iterate and integrate over a differential unit of 1 millisecond. Tracking differential units of volume through space in every part of the respiratory system presented too high a level of complexity for our simplified model. Moreover, tracking differential units of volume is impractical to our model, which is based not on anatomic location, but physiological function. The advantages and disadvantages of tracking airflow chronologically will be discussed further in results.

IV. Visual and Mathematical Modeling

A. Humidifier

In our model, the anatomical nose and mouth are represented by the Humidifier unit. A pressure of 759.65 mmHg is assumed to be the overall pressure within the respiratory system throughout the entire period of inhalation . This unit takes in 500 mL of ambient air as the tidal volume, which is the volume of air expired or inspired during each normal breath . (6) The composition of ambient air is assumed to be 20.9% O_2, 0.04% CO_2, 0.5% H_2O, and 78.6% N_2 by volume . (6) This input composition corresponds to typical circumstances of inhalation, however different compositions of air can be input into our computational model.

The purpose of this unit is to humidify the air; the inhaled ambient air mixes completely with water so that the air becomes fully saturated at 6.2% water by volume . (6) We chose to model water used in humidification as inlet stream, labeled H_2O in the figure, despite its continuous presence in the system. Our mathematical model calculates the moles of inlet water needed to achieve complete humidification. The use of the H_2O stream allows us to consider water as an inlet in the mass conservation equations and to avoid any accumulation. The computational program then calculates the moles and molar composition of the humidified air.

The humidified air is split into two outlet streams, Dead Space Air 2 and Humidified Air, which have the same composition. The tidal volume, which includes the volume from both inlets, is 500 mL. The Dead Space Air 2 stream is a bypass stream of 150 mL; this stream will be discussed in the Expirer unit. The remaining 350 mL will continue on to the Mixer in the humidified air stream.

B. Mixer

The Mixer, the next unit in our model, functionally acts as a meeting point for humidified air and dead space air that has already partaken in diffusion. Anatomically this compartment represents the space in the respiratory system including the trachea and 16 generations of bronchi, which are characterized as dead space. (13)The two inlet streams of air, the Dead Space Air 1 and Humidified Air, have different compositions and pass through this unit in a manner analogous to the plug flow reactor model. Additionally, the mixer unit functions continuously over the 2 s time interval of an inhale. In order to determine the composition of the outlet air from the mixer, our model analyzes discrete time intervals of 0.001 s and iterates and integrates over the total 2 s.

The total volume of these streams that enters this unit over the inhale time period is 350 mL of Humidified Air and 150 mL of Dead Space Air 1. The composition of the dead space air is the same as that of the diffuser at the end of the exhale time period , (6) since it originates from deoxygenated air of the previous breath. Dead Space Air 1 has a smaller composition of O_2 and larger composition of CO_2 compared to Humidified Air, since it has completed diffusion in the alveoli. In accordance with the plug flow model, the Dead Space Air 1 and Humidified Air will mix together when and where the two gases physically meet. Thus, to best mathematically represent the concept of a gradient mixture of these two "streams" we chose to model the mixing of Dead Space Air 1 and Humidified Air on two logistic curves, as seen in the figure below.

Figure 1: Mixer Unit, Changing Volumetric Flow Rates Over Time

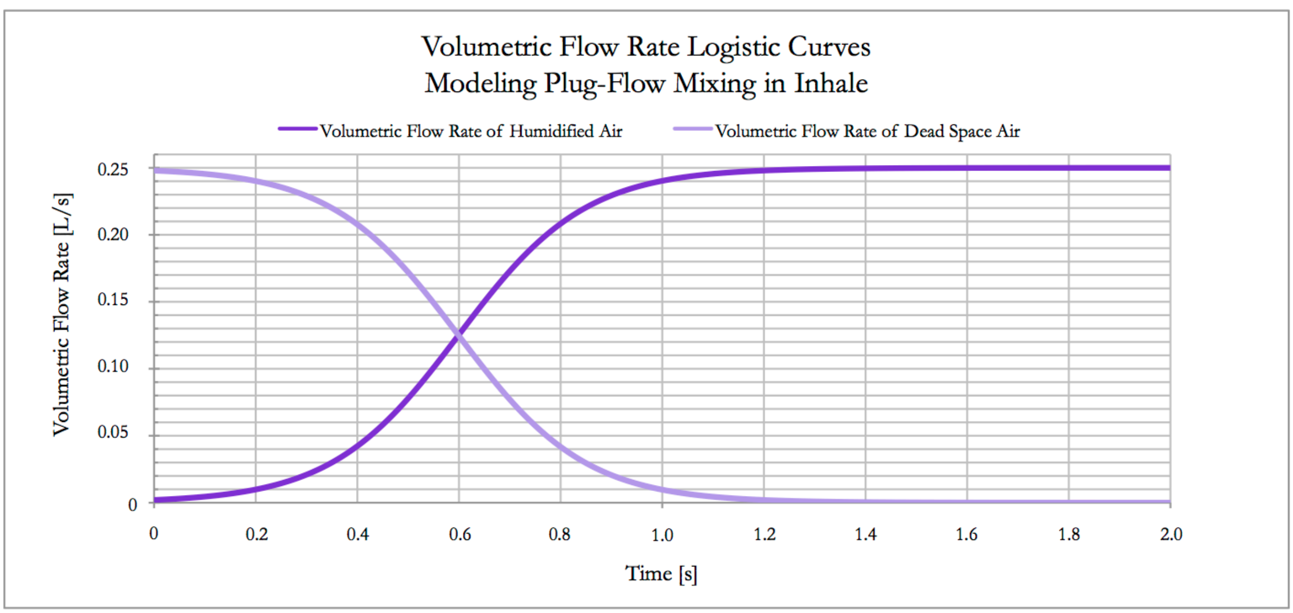


Figure 1 represents the changing volumetric flow rates of both Humidified Air and Dead Space Air 1 as they travel from the Mixer to the Diffuser. Initially, the dead space air enters the Mixer at a maximum rate, which slowly approaches 0 as inhalation is completed. Conversely, initially no Humidified Air enters, but the rate approaches the maximum as inhalation is completed. In summary, this unit accomplishes the specific mixing of dead space air and humidified air, specifying the rate at which each of these are mixed, and outputs the specific moles and composition of each gas component contained in the Transition Air stream at every millisecond upon inhalation. For a detailed mathematical explanation of the logistic graph.

C. Diffuser

The Diffuser of our model anatomically represents all the areas in the lungs where gas exchange occurs: the respiratory bronchioles, interalveolar membrane, and the alveoli. This unit serves two purposes in our model. The first is to mix the entering transition air, which has differing compositions over time, with the functional residual capacity (FRC) air that is initially in the Diffuser. The second purpose is to exchange the O_2 and CO_2 in the air with the Exchanger, which is analogous to the anatomic capillary bed. The FRC air is the 2.3 L of air that is present in the alveoli for gas exchange during exhalation; this allows blood to be continuously oxygenated even during exhalation. (6) The volume in the Diffuser ranges from 2.3 L to 2.8 L within one breath cycle. Since the FRC is mixed with 350 mL of fresh air from each breath during inhalation, but maintains a volume of 2.3 L at the end of exhalation, there is no net accumulation over inhalation and exhalation.

There are two fundamental concepts that govern the Diffuser. The first is the idea that diffusion of gases from the alveoli to the capillaries happens continuously, regardless of the time period in the respiratory cycle. (6) However, the composition of the gas undergoing diffusion changes very slightly depending on the time period in the respiratory cycle. On the inhale, which is represented by a time period of 2 s, the inlet transition air mixes with the continuously present FRC. Our mathematical model iterates such that complete mixing occurs between the transition air and the FRC with every millisecond of entering air. On the exhale, however, mixing has already occurred and no new air is entering the Diffuser; yet, blood is continuously circulating through the capillaries. Theore, on exhalation, diffusion is occurring with air that is a complete mixture of transition air and FRC air. Without the FRC air remaining in the alveoli, diffusion would not occur throughout exhalation and deoxygenated blood would circulate the body.

The second fundamental concept is the way in which the capillary bed and diffusion has been modeled. The diffusion rates of CO_2 and O_2 depend on the difference in their respective partial pressures between the alveoli and the capillaries . (6) We employed two different piecewise function to model the pressure variation for each of these gases, based on research showing how these partial pressures vary along a single pulmonary capillary . (6) However, we made a set of assumptions and designed our model to represent the pressure variation across the entire capillary bed. The pressure gradient varies with time and space in the capillary, since a differential volume or "chunk" of blood take a certain time to traverse the capillary, and experiences a different pressure at each point in the capillary. Our decision to model the flow of blood continuously has advantages and disadvantages. The disadvantage is that our model does not have the capacity to account for spatial variation of partial pressure within the capillaries; this would also be unreasonable because it is significantly more complex to to track a differential unit volume as opposed to a differential unit of time. Although our model is not entirely consistent with the anatomy, it provides an accurate, holistic, and simplified model of the pressure gradient of the capillary bed over the entire time period. The continuous flow of blood and iteration over time permits us to simplify and model the capillary bed with a pressure gradient over its entirety.

With these ideas of gas mixing and diffusion, we modeled the exchange of CO_2 and O_2 using Fick's Law of Diffusion .(6) The Exchanged Air is then a continuous outlet stream of the Diffuser during exhalation, with a known composition and number of moles that may be checked against accepted values of alveolar air composition. The second outlet, which was described as an inlet to the mixer in the previous section, is that of the dead space air that will be displaced by inhaled air in the next breath cycle. There is a pure O_2 outlet stream and a pure CO_2 outlet stream from the Diffuser to the Exchanger to represent the diffusion process.

D. Exchanger

The Exchanger anatomically represents the capillary bed over which gas exchange occurs. It has an outlet stream of pure CO_2 and an inlet stream of pure O_2 to model the physiological function of the capillary bed. There is a continuous flow of blood entering and exiting the Exchanger throughout inhalation and exhalation, so the volume of this blood was calculated over both of these periods. We assumed an initial arterial composition of blood as 0.145 mL_{O2} / mL_{Blood} and 0.532 mL_{CO2} / mL_{Blood}. This total volume of blood was considered in the conservation equations within the program. The mathematical modeling of this unit is different from that of other units because we are considering discrete quantities accounted algebraically. Our mathematical model iterates over the entire 5 second respiratory cycle but does not integrate; the iteration is used to sum up discrete volumes of blood. This unit determines the composition and volume of the blood at the venous end of the capillary bed.

E. Expirer

The Expirer anatomically represents the bronchi, trachea, mouth, and nose, and physiologically models dead space air being mixed with deoxygenated air, and exhaled. There are two inlet streams that mix in this unit: Dead Space Air 2 coming from the Humidifier and Exchanged Air coming from the Diffuser.

As in the mixer unit, the Expirer also employs mixing analogous to the plug flow reactor model. Since the Dead Space Air 2 is anatomically located in the bronchi/trachea region, and the Exchanged Air is located in the alveoli, the Dead Space Air 2 is expired before the Exchanged Air during exhalation. However, the Exchanged Air gradually mixes with the Dead Space Air 2 as it is expired; we chose to model this relationship with a logistic curve. Thus the composition of air in the Expirer changes with time, since the flow rates of the different inlet streams depend on time. Over the course of the exhalation period, which is 3 s (#erence), (6) the volumetric flow rate of the Exchanged Air and the Dead Space Air 2 entering can be modeled by logistic equations. When plotted on a graph, these curves accurately model physical mixing based on the plug flow reactor model.

Figure 2: Expirer Unit Volumetric Flow Rates Over Time

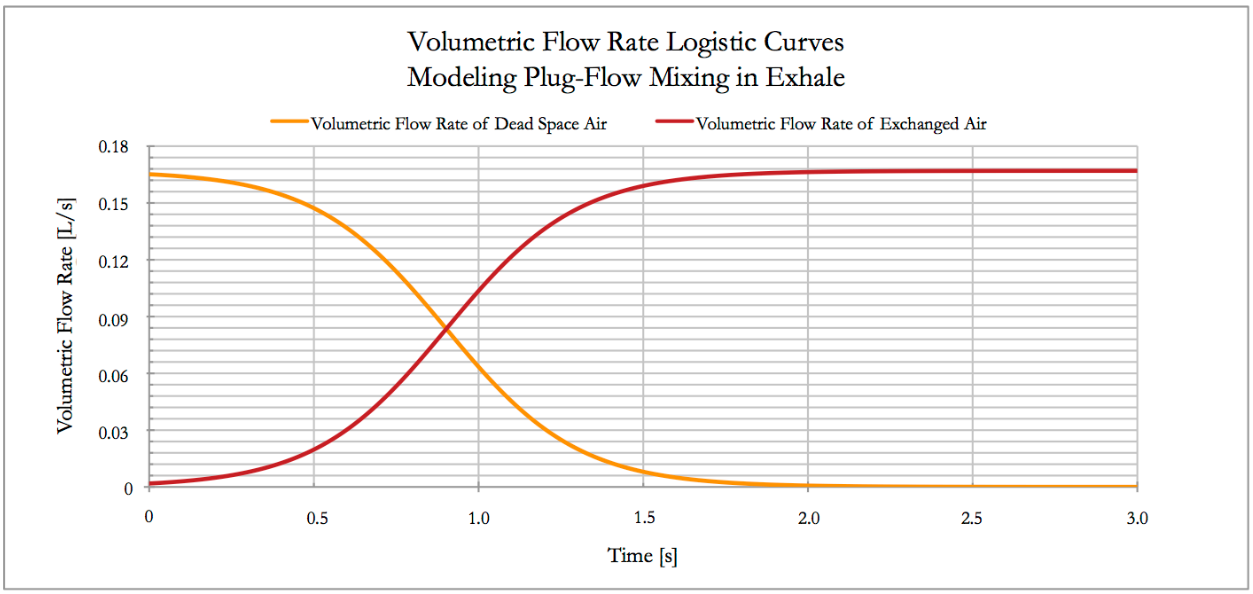


Figure 2 represents the changing volumetric flow rates of both Exchanged Air and Dead Space Air 2, as they enter the Expirer. Initially, the Dead Space Air enters at a maximum rate, which approaches 0 as exhalation is completed. Conversely, initially no Exchanged Air enters, but the rate approaches the maximum as exhalation is completed. The ultimate function of this unit is to account for the variation in the type of air leaving the Expirer over the time of exhalation, with a structure parallel to that of the Mixer. For a more detailed mathematical explanation of this graph..

V. Results

Table 1: Compositions and Percent Errors* of Major Respiratory Gases as

They Enter and Leave the Lung Model

	Atmospheric Air	Humidified Air	Dead Space Air 1† (Exchanged Air)		Exhale Air	
N_2	78.6%	74.1%	74.7%	(0.267%)	74.5%	(0.0%)
O_2	20.9%	19.7%	13.9%	(2.21%)	15.6%	(0.637%)
CO_2	0.04%	0.04%	5.24%	(1.13%)	3.68%	(2.22%)
H_2O	0.5%	6.20%	6.18%	(0.323%)	6.19%	(0.161%)

* When compared to analogous values in Table 39-1 from Guyton & Hall *Textbook of Medical Physiology*, 2000.
† Averaged over the exhale.

This table displays the calculated molar compositions of the four chemical constituents in three key streams. The percent error between our program's outputted values and the accepted values from a textbook (6) are shown. The percent errors for Atmospheric Air and Humidified air are not included because their compositions were inputted into our model or calculated in the model based upon these standardized values.

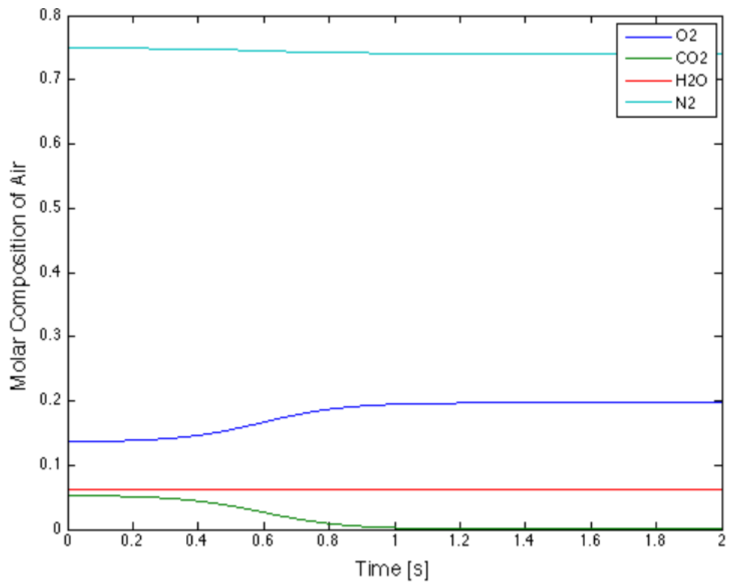
Our program's outputted values for the composition of Dead Space Air 1 and Exhale Air have very low percent errors ranging from 0.0% to 2.22%, demonstrating the validity of our modeling. Moreover, the initial composition for the Dead Space Air 1 was an input of the program, and after one breath cycle, the program is able to generate very similar values. Since the Dead Space Air 1 originates from the Diffuser or alveoli, this indicates that our program has accurately modeled the functions of the respiratory system.

Table 2: Volumetric Flow Rate of Oxygen in Streams Throughout the Lung Model

[redacted]

The table above shows the average volumetric flow rates of O_2 in four different streams. Initially, 0.0522 L/s of O_2 flows into the system in the ambient stream, but mixing with Dead Space Air 1, which is deoxygenated, causes the average flow rate of O_2 to decrease to 0.0447 L/s in the Transition Air. Next, in the Diffuser, O_2 is diffused into the Exchanger, making the volumetric flow rate of O_2 in the Exchanged Air decrease further to 0.0232 L/s. Finally, Exchanged Air mixes with Dead Space Air 2, which did not undergo diffusion and thus has a higher O_2 composition. Consequently, the Exhale Air volumetric flow rate of O_2 increases to 0.0261 L/s.

Figure 3: Molar Composition of Transition Air During Inhale



This figure indicates that we have successfully used the plug flow reactor model as the mechanism of mixing to our Mixer unit. Most significantly, this figure shows the oxygen composition of the Transition Air increases over time and the carbon dioxide composition decreases. The fluctuations in the chemical compositions of the outlet air are indicative of a gradient from fully Dead Space Air 1 to fully Humidified Air.

Since Dead Space Air 1 has undergone diffusion while the Humidifier Air has not, Dead Space Air 1 has a higher molar composition of CO_2 [5.3% > .04%] while Humidified Air has a lower molar composition of O_2 [19.7% > 13.6%].

Consequently, the Transition Air near the beginning of the inhale (mostly Dead Space Air 1) has a higher composition of CO_2, and the Transition Air near the end of the inhale (mostly Humidified Air) has a low concentration of CO_2. According to our model, the molar composition of CO_2 is 5.26% at 0 s, starts decreasing at 0.236 s [5%], plateaus at 0.965 s [.3%], and finally decreases to 0.04% at 2.000 s. The opposite trend is expected and is seen when tracking O_2. In our model, the molar composition of O_2 is 13.7% at 0 s, starts increasing at 0.236 s [13.9%], plateaus at 0.965 s [19.4%], and finally increases to 19.7% at 2.000 s.

Additionally, the figure shows that the composition of the Transition Air near the middle of the inhalation timeframe is a mixture of Dead Space Air 1 and Humidified Air. At 0.599 s, the O_2 and CO_2 concentrations are 16.7% and 2.67%, respectively, which is the exact average of the compositions of the two streams. This is because at 0.599 s, as seen on figure 1, the two logistic curves intersect, indicating the highest amount of mixing.

The molar composition of N_2 decreases slightly because Dead Space Air 1 has a higher concentration of N_2 than Humidified Air [74.9% > 74.1%]. The N_2 compositions of both inlet streams were used as inputs for the program. Thus, since the beginning composition of Transition Air will be mostly Dead Space Air 1, the N_2 composition is higher at 0 s [74.9%]. It proceeds to decrease to 74.1% by 2.000 s, where the Transition Air mostly consists of Humidified Air.

When observing H_2O in the Transition Air, there is no fluctuation in the molar composition, as all the air coming into and going out of the Mixer is fully saturated.

Figure 4: Moles of Oxygen and Carbon Dioxide in Diffuser Over One Breath

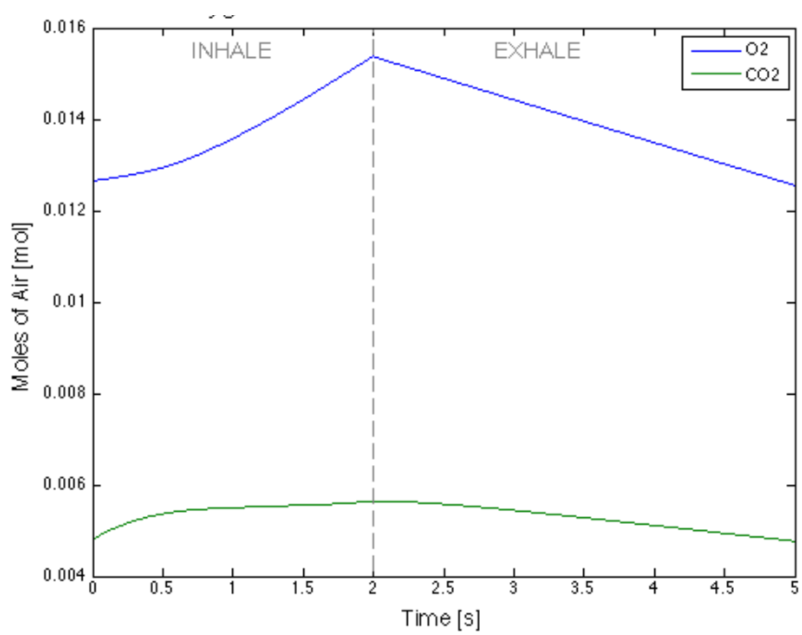


Figure 4 shows the moles of O_2 and CO_2 fluctuating as mixing and diffusion occurs throughout the breath. The first thing to note is that the values of moles of O_2 and CO_2 at the beginning of the breath [0.0127 mol, 0.0048 mol, respectively] and the values at the end of the breath [0.0126 mol, 0.0048 mol] are almost exactly equal, demonstrating that there is no accumulation in the Diffuser unit. The curves of O_2 and CO_2 increase during inhalation to a peak at 2 s [0.0154 mol, 0.0056 mol, respectively], then decrease during exhalation to the initial values. Thus, over the course of one breath it can be calculated that 0.0027 mol of O_2 and 0.0008 mol of CO_2 enter and leave the Diffuser.

The non-linear regions of both curves are caused by simultaneous mixing and diffusion. Transition Air with 17.9% O_2 composition enters the Diffuser at a constant rate and mixes with the FRC air. This process alone would produce a linear increase in the moles of O_2 in the Diffuser, however, since diffusion is occurring simultaneously, O_2 is also leaving this Unit. Thus the curve is not linear but concave.

On the exhale, complete mixing of the Transition Air and FRC air has already occurred and diffusion rates are near negligible, so the curve describing moles of O_2 is primarily caused by the rate at which the air leaves the Diffuser. Thus, the curve appears very nearly linear .

For CO_2, the same reasoning can be applied; however, CO_2 leaves the blood and enters the Diffuser so the curve is concave down. However, the curve still generally increases, peaks at 2 s, and decreases to the original value.

The moles of N_2 and H_2O are not tracked in this figure since they do not take part in diffusion and thus are unaffected when going through the Diffuser.

Figure 5: Partial Pressure of Oxygen and Carbon Dioxide in Diffuser Over One Breath

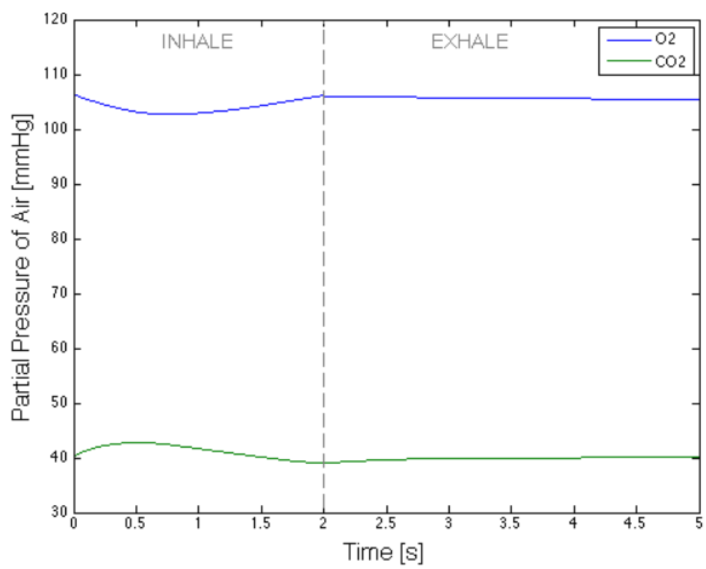


Figure 5 shows that in our computational program, the partial pressures of O_2 and CO_2 in the Diffuser do not fluctuate very widely over the period of an entire breath. Again, since N_2 and H_2O are not involved in diffusion and their values are not affected, their partial pressures are not represented in this figure. Conceptually, this is reasonable because the composition of the 2.3 L FRC air is more influential on the overall partial pressure because its volume is so much higher than the .5 L of Transition Air entering the Diffuser.

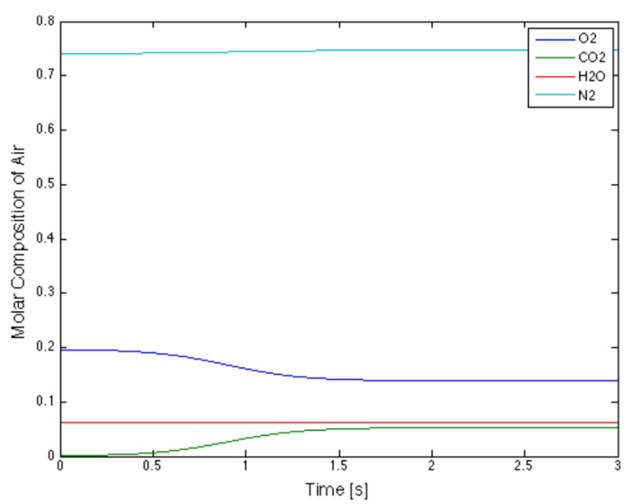
However, digressions from constant partial pressures are observed, especially during the inhalation period. These digressions are reasonable because of the mixing and the varying diffusion rates. The O_2 partial pressure decreases from 106 mmHg to 103 mmHg during the first 0.773 s, since there is such a relatively high rate of diffusion of O_2 out of the Diffuser in the beginning of the inhale. Even though the Transition Air, with an O_2 composition of 17.9%, enters the Diffuser and mixes with the FRC air with an O_2 composition of 13.6%, the diffusion, the effect of adding air with higher O_2 composition is subdued by this high rate of diffusion and the large volume of the FRC air.

Because the diffusion rate decreases at 0.773 s, the addition of the Transition Air becomes apparent; the O_2 partial pressure in the Diffuser increases to 106 mmHg. After 2.000 s, the partial pressure of O_2 begins to decrease very gradually to 105 mmHg. Conceptually, this is reasonable because the inhalation period ends at 2 s such that no new air enters the Diffuser, and the diffusion rates are very low.

The trends for CO_2 are the direct opposite of those for O_2 for the same reasons: mixing and varying diffusion rates. Initially, the partial pressure increases from 40.3 mmHg to 42.8 mmHg since CO_2 is diffused into the Diffuser. As the diffusion rate slows at approximately 0.514 s, the addition of Transition Air becomes apparent. Since the Transition Air has a lower CO_2 concentration than the existing FRC air [1.62% vs. 5.3%], the partial pressure decreases to 48.9 mmHg. After 2.000 s, the CO_2 very slowly increases to 40.1 mmHg. Conceptually, this is explained by the continued diffusion at a very slow rate during the exhalation period.

Overall, the properties of the air in the Diffuser are most similar to that of the overwhelming volume of 2.3L FRC air, and the small addition of 0.5 L of Transition Air does not affect the partial pressures significantly. However, changing diffusion rates across inhalation and exhalation cause small changes in the partial pressure of O_2 and CO_2.

Figure 6: Molar Composition of Air in Exhale Stream During Exhale



This figure lects how the composition of the Exhaled Air stream changes over the course of exhalation, demonstrating the mixing that we modeled after the plug flow reactor model. The concepts that this curve demonstrates are similar to those of Figure 3, *Molar Composition of Transition Air During Inhale*.

According to the program's output, the Exhale Air initially has a higher composition of O_2, which decreases over the course of the exhalation, showing plateauing beginning at approximately 1.37 s. Conceptually, this is accurate because the Exhale Air near the beginning is mostly Dead Space Air 2, which has a higher O_2 composition of 19.7%. erring to the figure, the molar composition of O_2 in Exhale Air is 19.6% at 0 s, and then starts decreasing at 0.435 s where it is 19.2%. The molar composition of O_2 begins to plateau at 1.374 s [14.4%]. This lects the logistic mixing model because at 1.374 s, the components of the air become primarily Exchanged Air. As exhalation ends, the Exhale Air consists of primarily Exchanged Air; thus, the Exhale Air O_2 composition at 3.000 s is equal to that of the Exchanged Air composition, 13.9%.

Conversely Exhale Air initially has a lower composition of CO_2 which increases throughout the exhalation, with a plateauing beginning at 1.37 s. This is accurate conceptually because Exhale Air initially is mostly Dead Space Air 2, which has a lower CO_2 composition compared to Exchanged air [.04% < 5.24%]. The molar composition of CO_2 in Exhale Air is .09% at 0 s, and then increases at .435 s where it is .49%. Then the composition begins to plateau at 1374 [4.8%], as the Exhale Air consists increasingly of Exchanged Air. As the exhale ends at 3 s, the Exhale Air CO_2 composition is equal to that of the Exchanged Air, 5.26%.

Additionally, this figure provides a check on how the Dead Space Air 2 and Exchange Air mix in the logistic curve. At .902 s, the time in which the most mixing of the two streams is occurring according to the input logistic curve for the plug flow reactor model, the O_2 and CO_2 concentrations are 16.8% and 2.64%, respectively, which is the average of the compositions of the two streams.

The molar composition of N_2 increases slightly because Dead Space Air 2 has a lower concentration of N_2 than Humidified Air [74.1% < 74.7%]. The N_2 compositions of both streams were inputted accepted values in the code. Thus, since the initial composition of Exhale Air is mostly Dead Space Air 2, the N_2 composition is lower at 0 s [74.1%]. Then it increases to 74.7% by 2 s, where the Exhale Air is mostly Exchanged Air.

There is not much fluctuation in the molar composition of H_2O in the Transition Air; this is reasonable considering inlet and outlet streams are fully saturated.

Figure 7: Volumetric Flow Rate of O_2 and CO_2 Between Diffuser and Exchanger

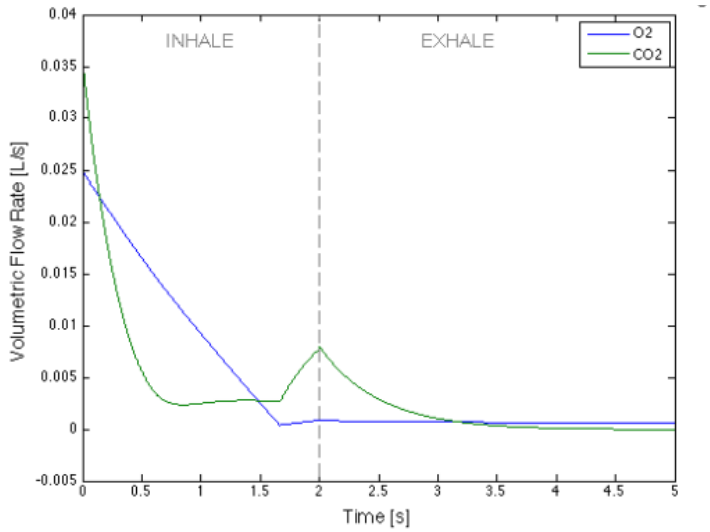


Figure 7 is a graphical representation of our O_2 and CO_2 diffusion rates, which decrease over the course of the breath. The calculated average O_2 and CO_2 diffusion rates are 0.0035 L/s and 0.0044 L/s, respectively,which yields 5.5% and 6.1% error when compared to the accepted average values .(7) This is a holistic check on the overall accuracy of our volumetric flow rate gradients.

The analysis of the graphical trends provides further validation of the Exchanger's accuracy. Overall, the volumetric flow rates of both CO_2 and O_2 are initially high and then drop to a slow sloping state around 1.667 s which is approximately a third of the way through the respiratory cycle. This is consistent with the expected time it takes to fully oxygenate capillary blood. Initially, the O_2 volumetric flow rate is 0.0249 L/s at 0.001 s, and drops in a linear fashion to 0.0004 L/s at 1.67 s. This is a result of the decreasing pressure gradient between the O_2 partial pressure in the Diffuser and the estimated O_2 partial pressures in the Exchanger. From 1.67 s onwards, the volumetric flow rate of O_2 is very low until the end of the respiratory cycle. The volumetric flow rate of CO_2 also follows a similar trend, with a rapid decrease from the initially high diffusion rate of 0.0355 L/s at .001 s, to 0.0027 at 1.67 s, followed by minimal decrease to the end of the respiratory cycle.

The trend of our decreasing diffusion volumetric flow rates is conceptually accurate because our calculated alveolar partial pressures and the modeled capillary partial pressures are converging with time. This convergence causes a decrease in the partial pressure gradient, and subsequently a decrease in diffusion volumetric flow rates of O_2 and CO_2.

However, there is a small spike around the one third mark where we have a period erroneous volumetric flow rates. This inconsistency arises because our approach to obtaining a pressure gradient for Fick's Law is based on two graphs with, although accurate, distinct natures. Within our model, the alveolar partial pressure of CO_2 is constantly being updated with the new pressure changes based on the varying diffusion rates. However, the capillary partial pressures of CO_2 are modeled stagnantly after known accepted values that do not vary with the diffusion rates. These two techniques of deriving partial pressures, although both accurate, do not coincide perfectly. The slight discord causes inaccuracies at places where the two graphs might not be changing in accordance to each other. Although the spike may seem drastic in the graph, this is merely a result of the small scale of the volumetric flow rate; the spike deviates a maximum of 0.0052 L/s from surrounding accurate data points.

Figure 8: Blood Composition of O_2 Over One Breath

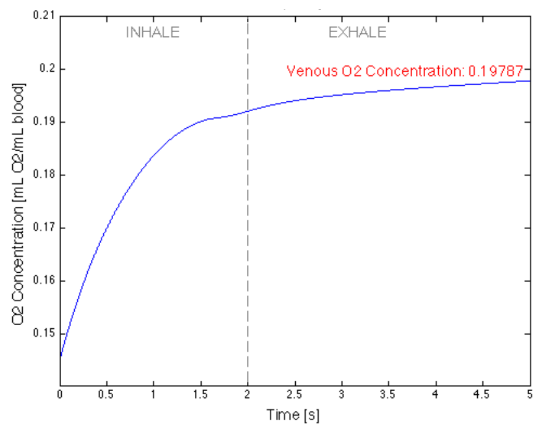


Figure 8 depicts the increasing concentration of O_2 in the blood moving through the capillaries. This is reasonable considering that O_2 is diffusing into the blood from the Diffuser into the Exchanger. The figure shows the rate of increase of the concentration decreasing; this is reasonable conceptually because our diffusion rates decrease according to Fick's Law. At the end of the 5 second breath cycle, the percent composition of O_2 comes out to be 19.8%, compared to 19.5 % for the accepted value .(15) The percent error is 1.5%, demonstrating the validity of our model.

Figure 9: Blood Concentration of CO_2 Over One Breath

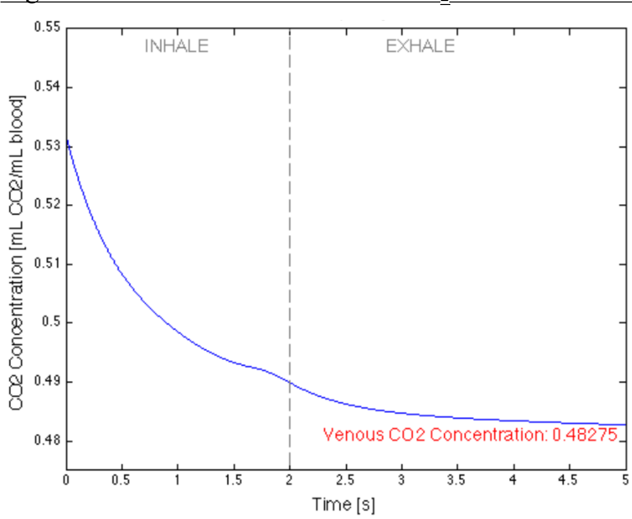


Figure 9 depicts the decreasing concentration of CO_2 of the blood moving through the Exchanger. This is expected since CO_2 is diffusing out of the blood. The rate of decrease of CO_2 concentration also decreases with time, since diffusion rates decrease with Fick's Law. At the end of a 5 second breath, the percent composition of CO_2 in the blood is 48.3%, compared to 49.2%, the accepted value; the percent error is thus 1.8% (15). For a comprehensive table of values discussed in these results, please er to appendix.

VI. Weaknesses and Strengths of the Model

<u>Weaknesses</u>

In order to create a simplified model of such a complex system, a few assumptions had to be made. These assumptions although based on facts, are areas within our model where inaccuracies could occur. One of the assumptions we made is that no chemical reactions occur in any of the units. However, this is not true for the Exchanger, which is involved in maintaining regular pH levels and homeostatic conditions in the body. (4) In order to direct our efforts towards the most important functions of the system, we have chosen to focus only on gas transport and exchange and the changing of various extensive properties of the gas within the respiratory system.

An additional limitation of our model is its inability to adapt to different volumes of inhaled air and varying time parameters for the length of an inhale, outside of our assumed 5 s. We have chosen to set fixed variables for these two parameters because the scope of our analysis is that of a healthy functioning lung in standard conditions, of an average male at rest. Thus, all of our predictive curves such as the logistic curves used for the mixer are based on these particular values and cannot be applied to other volumes and time periods.

The linear approximations of curves, such as the partial pressure of CO_2, present another limitation of our model. This variable situation causes a slight hump in our data compared to the expect trend related to the diffusion of CO_2, this occurs because the change within the values of the curves are not exactly correlated to the calculated changes happening within the different units. These shortcomings of our model, though important are not significant enough to affect the overall accuracy of our results. On a larger perspective we have modeled and made assumptions that account for factors that directly contribute to the aim of our model in simplifying and gathering quantitative data on the lungs.

Strengths

Although our model's accuracy is a result of its numerous strengths we will reiterate a few of the main ones here. One of the most important strengths of our model is that it succeeds in representing the mixing of gases between units both conceptually and mathematically. In order to best demonstrate the mixing of gases in an analogous manner to the plug flow reactor model, we approximated logistic curves in order to generate volumetric flow rates that show a gradient mixing. Though dead space presents a highly complex concept, our model is able to successfully account for the mixing it undergoes. The variation of composition, over time, of the Transition Air and the Exhale streams was modeled using the plug flow reactor model and logistic curves. This allows for the high accuracy, proven by our results.. This is more complex and more representative of respiratory air flow than simply mixing the air linearly or based on average values. Our model also accounts for the recycling of dead air, with both a bypass stream for exhalation, and a returning stream from the diffuser for inhalation on the subsequent breath cycle.

Additionally, our model is able to realistically account for composition of air by accounting for the FRC air within the lungs that remains even after exhalation. This is an essential part of the human respiratory system because it allows for continuous gas exchange; our model has high physiological integrity by accounting for this FRC air while maintaining no net accumulation. Accounting for the FRC air ensures accuracy when tracking the composition of Exchanged Air and Transition Air; because the volume of FRC air is so large the addition of the 500 mL of tidal volume only causes small fluctuations in composition over time.

A series of quantitative checks fortify our model. Our value for the respiratory quotient is 0.7943 and the accepted average value is 0.80 (4) resulting in less than 1% error. Our calculated volumetric flow rates for O_2 and CO_2 are 0.0044 L/s and 0.0035 L/S which are extremely similar to the known values of volumetric flow rates of 0.00417 L/s and 0.0033 L/s, respectively . (7) In addition to the accuracy of our volumetric flow rates, our final blood concentrations of O_2 and CO_2 of 0.198 and 0.483 are have less than 2% error when compared to the accepted average values of 0.195 and 0.492 .(15) These values not only provide accuracy checks for various points in the model but also verification that our model is capable of maintaining the integrity of each units' values throughout the entire system as well as accurately demonstrate the progression of air through the lungs.

VII. Conclusion

To conclude, the results of our conceptual and mathematical modeling support the idea that the respiratory system can be simplified to provide accurate, quantitative data on airflow throughout a breath. Our program used known values and functions as inputs to generate volumetric flow rates, molar compositions, partial pressures, volumes, and diffusion rates of air throughout the system. The Moreover, this reinforces the fundamental idea that because function, not anatomy, drives respiration, machines that replicate the purpose of the respiratory system can be engineered for patients with failing lungs. The results of our mathematical model provide data essential to analyzing lung function and creating a new ECMO machine.