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Estimation of Pulmonary Gas Exchange in the Human Respiratory System Under Normal and Abnormal Conditions

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The human respiratory system is a collection of organs and tissues that regulate gas exchange in the body. There are millions of alveoli in the lungs surrounded by tiny blood capillaries. By breathing, the body inhales oxygen which moves from the alveoli to the blood capillary, and then exhales carbon dioxide in the air that diffuses across the pulmonary membrane of the blood capillary to the alveoli. We aim to develop a mathematical model of respiratory gas exchange that can handle various situations. A Model should be capable of finding the diffusion rate of oxygen that enters into the capillary from the lungs and dissolves into a different level of hemoglobin. It is also able to give the relationship between oxygen and carbon dioxide concentration with time. Numerical simulation helps us to predict the responses of the cardiorespiratory system during a heavy workout, usual activity, and inactive situations. It also considered the various factors that affect the gas exchange relation between partial pressure and saturation.

Keywords: Gas exchange; Mathematical model; Oxygen; Partial Pressure; Saturation.

The body uses a definite pathway that oxygen enters the lung from the atmosphere. From the atmosphere, oxygen enters the body through the mouth or nostrils of the nose and then proceeds from the nasopharynx to the oral pharynx, and the glottis way it will enter the lung through the trachea.

The lungs are the principal part of the respiratory system, transfer oxygen from the air into the bloodstream and release carbon dioxide from the capillary into the atmosphere. Thousands of narrow tubes end in clusters of tiny air alveoli of the lungs. Covering each sac with blood vessels connects to the veins and arteries that transport blood throughout the body. During external and internal respiration, a group of organs and tissues control gas exchanges in the body.

In the respiratory system, the alveolus diffuses oxygen to the blood capillaries and the oxygen concentration increase in arterial blood. With partial pressure, Oxygen diffusion occurs in the hemoglobin via the pulmonary capillary tube. The oxygen transfers to the body with red blood cells responsible for the supply to the tissue.

Once the oxygen has entered the pulmonary system carried by the blood to the targeted tissues in two distinct forms: (1) Bound to hemoglobin (around 98% of the total blood oxygen content),

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(2) Directly dissolved in the plasma (around 2% of the total blood oxygen content). There are three phases of the respiratory process (1) ventilation which contains the flow of oxygenated air into the alveoli, (2) perfusion, which contains the flow of blood to tissues and organs and (3) diffusion, which contains the movement of gases between alveoli and capillaries across the pulmonary membrane.

The oxygen diffused in the blood is carried in two ways: (1) inside red blood cells and (2) in the dissolved state in plasma. The large surface area of alveoli and the short diffusion pathway of the capillaries play a crucial role in the efficient exchange of oxygen[1]. A substantial part of oxygen (98%) is carried in red blood cells in conjunction with hemoglobin, while a tiny portion of oxygen (2%) combines with plasma as a dissolved form.

Construct a simple mathematical model of the oxygen and carbon dioxide exchange of gases across the pulmonary membrane[2]. That is the most important physical process in the human body. In terms of lung-related structural factors and gas-related transport variables, the model depicts the time course of capillary partial pressure change along the capillary.

Examining the physically dissolved form of oxygen in the blood and the slope of the tangent lines to the oxygen dissociation curve created a mathematical model of pulmonary gas exchange[3,13]. The study has described a mathematical model by breaking down the pulmonary membrane's total oxygen diffusion capacity into two terms describes (1) diffusion across the blood-gas barrier and (2) diffusion associated with oxygen binding to hemoglobin.

For normal individuals, proposed mathematical model of the gas exchange between the alveoli and blood capillaries tubes using cylindrical blood capillaries[4]. They demonstrated the impact of pulmonary membrane surface area, thickness, and cardiac output on gas diffusion.

A mathematical model for the exchange of oxygen from alveoli–capillary calculates the partial pressure profile of oxygen in the capillary tube in normal and abnormal situations[5]. Hill equation establishes the relationship between oxygen partial pressure and concentration at different diffusing capacity levels. The mathematical model estimates the parameters that affect the partial pressures of oxygen and carbon dioxide in an artery[5,6].

Discuss the integrated model for oxygen delivery into the blood and a lumped mechanical model for ventilation[7]. The study focus on the transfer of oxygen into the blood during rest and activity. Also, observed the possible diffusion limitation in oxygen transfer in extreme regimes. Various parameters include alveolar and venous blood oxygen partial pressures, capillary volume, membrane diffusing capacity, and binding by hemoglobin.

Reynolds uses a small section in the lung to replicate gas exchange and the inflammatory reaction to investigate the lung during an inflammatory response[8]. They create a mathematical model to predict the effects of inflammation on ventilation/perfusion distribution and the resulting pulmonary venous partial pressure oxygen level during systemic inflammatory stresses.

Blood oxygen concentration (content), saturation (SO_2), and partial pressure are all factors in the transport of oxygen by arterial blood to human tissues[9]. The hemoglobin-oxygen dissociation curve illustrates the relationship between oxygen saturation and oxygen partial pressure.

Diffuse through a membrane gas needs an equilibrium time long enough to allow equilibrium between the alveoli and the capillary and enough alveoli to allow an adequate volume of gas exchange. 0.25 seconds is required to equalize transfer gradients between the alveoli and the capillary[10].

The respiratory membrane diffusivity is a quantitative expression of the capacity of the respiratory membrane to exchange gas between the alveoli and the pulmonary blood. Diffusivity respiratory membrane is the volume of a gas that will diffuse through the membrane. Heavy workout significantly increases pulmonary blood flow and alveolar air ventilation. The diffusing capacity for oxygen increases in a healthy person to a maximum of about 65 ml/min/mmHg, and the diffusing capacity for oxygen under resting conditions averages 21 ml/min/mmHg[11].

Mathematical Method

We aim to develop the mathematical model of the diffusion of oxygen gas into the pulmonary capillary through the alveolus. In the capillary tubes, oxygen moves with red blood cells that develop a relationship between partial pressure of oxygen and saturation of oxygen in the hemoglobin. The blood transport through the capillary tube and the alveolar air establishes a relation between concentrated oxygen and carbon dioxide with time.

We take the following assumptions

• The entire lung is considered a single unit with an alveolus and capillaries.

• Each Alveolus capillary has the same shape and properties.

• In the alveolar space, the oxygen partial pressure is constant and uniform.

• The rate of blood flow in each capillary tube is constant.

Graham's law[14], the net diffusion of gas occurs from the high concentration to the low concentration. Internal and external respiration both are parts of the respiratory system process. When gas is exchanged between the alveolus and pulmonary capillary is called *external respiration.*

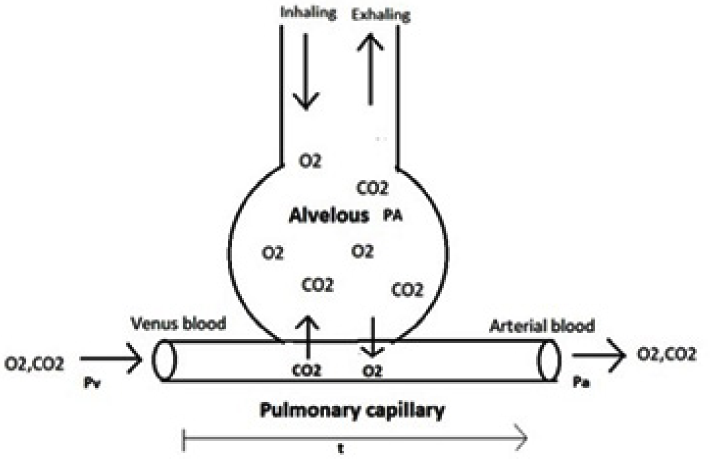

Fig. 1. Presentation of gas exchange through alveolus to blood capillary

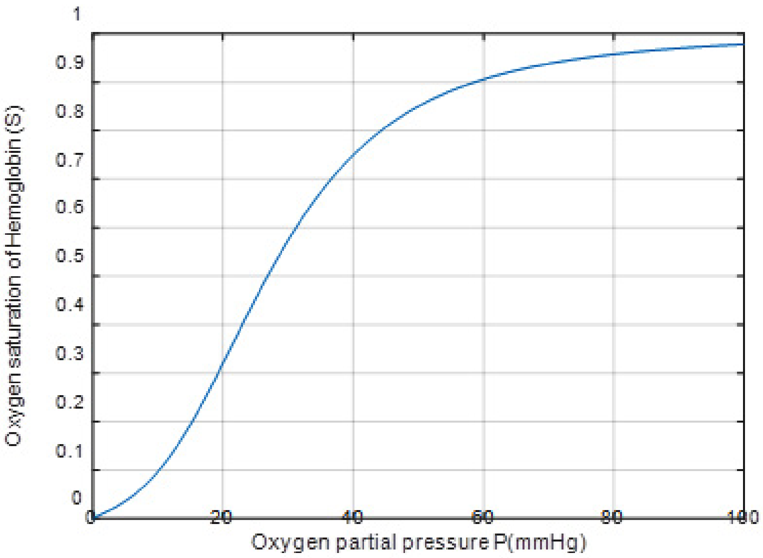

Fig. 2. Oxygen - hemoglobin dissociation curve

Using Fick's Law[15, 16], oxygen diffusion from the alveolus to the blood capillary is described by

$$V'(t)= D_L (P_A-P(t)) \quad ...(1)$$

Where V(t) is the volume of oxygen transmitted across the pulmonary membrane per unit time, D_L is the pulmonary membrane's oxygen diffusion capacity, and P_A & P are the partial pressures of oxygen (P_{O2}) in the alveolus and capillary, respectively.

For simplicity, we considered each capillary is of the same radius, so it is cylindrical with a constant radius. Then the cylinder with

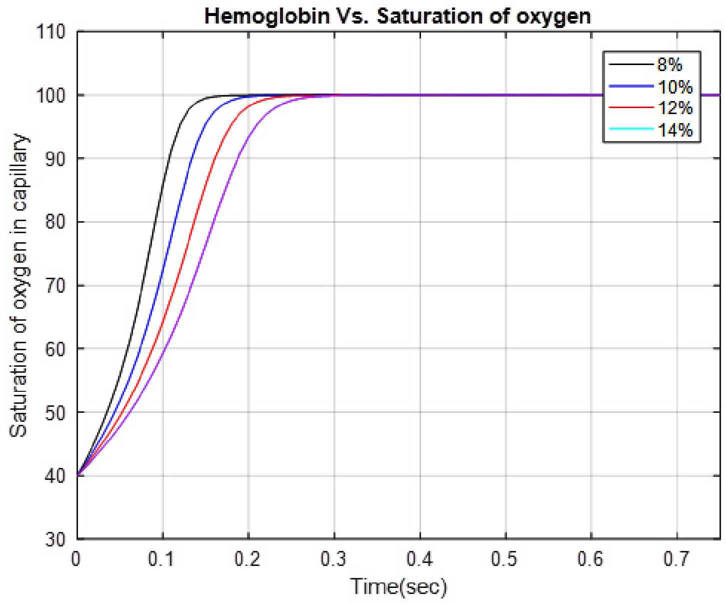

Fig. 3. Oxygen saturation at different level of hemoglobin

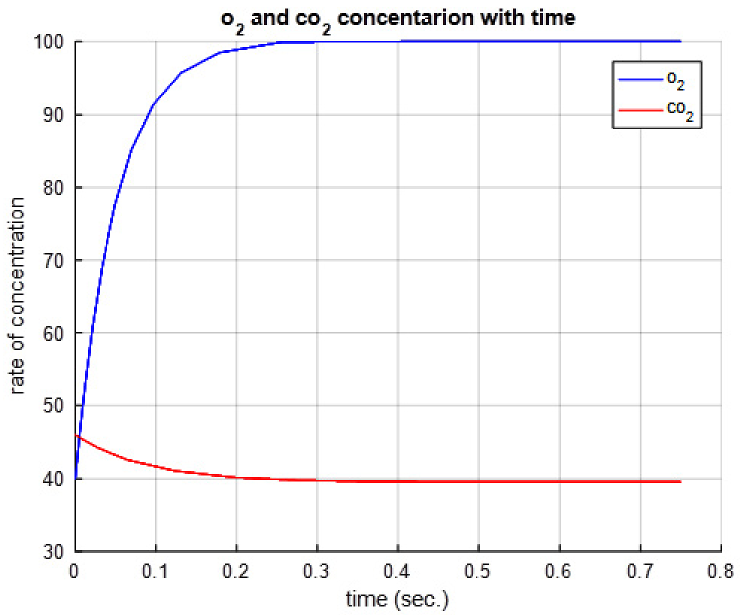

Fig. 4. Oxygen and carbon dioxide concentration curve for normal activity in human

a fixed radius having diffusing capacity can be expressed as:

$$D_L = K\left(\frac{2\pi rh}{T}\right)\left(\frac{\alpha}{\sqrt{M}}\right) \quad ...(2)$$

Where a solubility of oxygen in the blood, M is the oxygen gas's molecular weight, T is capillary thickness, and r is the capillary radius. Apply Fick's law to the blood flow,

$$\dot{V}(t) = V_C \frac{dC(t)}{dt} \quad ...(3)$$

where V_C is the blood volume in the lung capillary and C is the oxygen concentration in the capillary.

Table 1. Values of the model parameters for healthy human

Parameter	Unit	Values
P_A	mmHg	100
P_V	mmHg	40
DL	$mL.min^{-1}mmHg^{-1}$	39
Q	$ml.min^{-1}$	6000
T	Sec	0.75
V_C	mL	75
α	$mL.mL^{-1}mmHg^{-1}$	0.00003
β	$mL . g^{-1}$	134
Hb	$g. mL^{-1}$	0.15

From Eq. (1) and (3), we have;

$$\frac{dC(t)}{dt} = \frac{D_L}{V_C}\left(P_A - P(t)\right) \quad ...(4)$$

The amount of oxygen dissolved in the blood plasma and the chemical reaction that dissociates oxygen from hemoglobin depends on the partial pressure of oxygen in the capillary, which determines the oxygen concentration in the capillary blood.

Millions of hemoglobin molecules contain red blood cells in a *pulmonary capillary tube*. The amount of oxygen moving in the body with red blood cells is called *oxygen saturation.* Oxygen saturation is between 95% to 100% in healthy humans. Hemoglobin inside red blood cells that are in charge of transporting oxygen from the lungs to other parts of the body.

Using Henry's law of respiration, the amount of oxygen dissolved in the circulation is directly proportional to the partial pressure of oxygen in alveolar air. The chemical reaction relates partial pressure of oxygen saturation in hemoglobin.

$$C(t) = \alpha P(t) + \beta.Hb.S \quad ...(5)$$

Where is the solubility of oxygen in the blood, is the oxygen saturation of hemoglobin

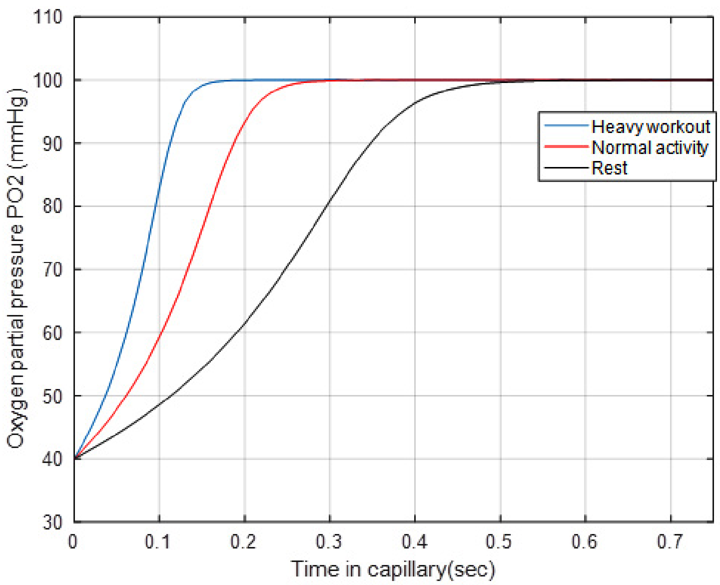

Fig. 5. Oxygen partial pressure in normal and abnormal activities

in the blood, is the amount of hemoglobin per unit volume of blood, and the amount of oxygen contained per unit mass of hemoglobin when 100% is saturated.
From equation (5), we get;

$$\frac{dC(t)}{dt} = \propto \frac{dP(t)}{dt} + \beta Hb \frac{dS}{dt} \quad ...(6)$$

The oxygen moves in arterial blood to the tissues of the body and has several critical determinants including blood oxygen saturation () and partial pressure of oxygen.

The oxygen–hemoglobin dissociation curve (ODC) describes the relationship between oxygen saturation () and partial pressure [9] in figure 2.

$$S(P(t)) = \frac{(P(t))^3 + 150P(t)}{(P(t))^3 + 150P(t) + 23400} \quad ...(7)$$

Above figure represents the relationship between saturation in hemoglobin and partial pressure of oxygen. During zero partial pressure, no oxygen saturation occurs in the hemoglobin. The oxygen partial pressure increases the increase the rate of saturation of oxygen.
From Eq.(4), Eq.(6), and Eq.(7), we get

$$\frac{dP(t)}{dt} = \frac{\frac{D_L}{V_C}(P_A - P(t))}{\alpha + \frac{70200\beta.Hb((P(t))^2+50)}{[(P(t))^3+150P(t)+23400]^2}}, \quad 0 \le t \le T \quad ...(8)$$

Where, T is the time taken by the blood to travel through a capillary in the lung.

Above figure represents the relationship between the percentage of hemoglobin and oxygen saturation in the blood. In the pulmonary capillary, oxygen saturation for various conditions varies according to hemoglobin levels. Less hemoglobin indicates fewer red cells that will take less time for oxygen saturation in the capillary tube. Similarly, if the hemoglobin level is high in the capillary tube, it indicates that more red cells are present in the blood, and it will take more time for oxygen saturation.

For a cardiac output of Q = 6mL/min, 0.75 sec is required. The mathematical model (Eq. (8)) is an initial value problem of an ordinary differential equation with P(0) - $P_{V,}$ where P_V represents the oxygen partial pressure in venous blood as it enters the capillary. When blood exists in the arterial capillary P(T) = P_a, where P_a is the oxygen partial pressure in arterial blood (Figure 1).

The time taken for oxygen and carbon dioxide to diffuse from the alveolus to blood capillaries is called *transit time.* Blood is transported through the alveolar-capillary system in about 0.75 seconds under normal situations.

The rate law is a differential equation that defines the change in reactant concentration (s) as a function of time. The rate law can be integrated using mathematics and get a rate equation that directly represents the reactant concentrations to time. The rate of a chemical reaction regulates by the concentration or partial pressure of oxygen and carbon dioxide with time.

$$\frac{d^2A}{dt^2} = A_0 - \frac{1}{k}\frac{dA}{dt} \quad ...(9)$$

where A_O is the partial pressure of oxygen and carbon dioxide in the venous blood capillary, and k is the diffusivity of oxygen and carbon dioxide in the capillary.

The diffusion of oxygen and carbon dioxide will continue until equilibrium is reached, which takes around 0.25 seconds. As a result, oxygen and carbon dioxide diffusion takes about one-third of the time available.

Simulation result

The derived model is difficult to solve analytically because of nonlinear, so we used the Runge-Kutta algorithm to derive the solution of the differential equation and get the numerical solution with a step size Δt=0.001. The following MATLAB (2016a) code gives the numerical solution of Eq. (8) and plots the result while considering normal and abnormal activities.

```
>>f=inline('(0.008889*(100-p))./
(0.00003+(14636.7*(p.^2 +50)./…
((p.^3+150*p+23400).^2)))','t','p');
>>[t, p]=ode45(f,[0:0.001:.75],39);
>>plot(t, p)
>>grid on
>>axis([0 0.75 30 110])
>>xlabel('Time in capillary(sec)')
>>ylabel('Oxygen partial pressure PO2 (mmHg)')
```

The simulation result shows that the oxygen diffusion increases to a maximum of about 65 ml/min/mmHg during intense work time resulting in increased pulmonary blood flow and alveolar ventilation. Under normal conditions, the oxygen diffusion in young men is about 39 ml/min/mmHg impacts normal pulmonary blood flow and alveolar ventilation. Decrease Oxygen diffusing capacity during rest time is 21ml/min/mmHg reduces pulmonary blood flow and alveolar ventilation.

DISCUSSION

In this study, from Eq(4) and Eq(7) which give the oxygen diffusion into the capillary across the pulmonary membrane that depends on the diffusion capacity of the oxygen (DL), the partial pressure difference between alveolar and capillary blood gas (P_A - P), the solubility of oxygen in the blood (a), the capacity of hemoglobin to carry oxygen (β), and the amount of hemoglobin in the blood (Hb). The level of oxygen in the capillary reaches the oxygen level in the alveoli takes around 0.25 seconds. Using the MATLAB solve the differential equation and simulation the results for normal and abnormal situations.

Since the partial pressure of oxygen in the blood in the capillaries is about 39 mmHg, while the pressure in the alveolar air is 100 , there will be a net oxygen diffusion into the capillary blood. The oxygen diffusion will continue until the concentration equilibrium is reached in the alveolar and capillary. The rate of oxygen diffusion from the alveolus to the blood capillary that regulated by the concentration or partial pressure of both gases oxygen and carbon dioxide with time.

CONCLUSIONS

The exchange of gases in the lungs takes place between alveolar air and blood flowing through the lung capillary by diffusion. Oxygen diffusion through the pulmonary membrane binds with the hemoglobin in red blood cells. The relationship between the hemoglobin level and oxygen saturation in capillary results represents an initial oxygen saturation of 40 mmHg and reaches 100 mmHg at 8% of hemoglobin requires about 0.15 seconds. When hemoglobin is 10% will take 0.20 seconds, and 12% will take around 0.25 seconds. Concludes less hemoglobin indicates a fewer number of red cells and hence that oxygen saturation occurs more quickly in the capillary. The result also established the relationship between oxygen and carbon dioxide concentration with time for usual activity. By defining the relationship, the partial pressure of oxygen in the capillary blood equals the partial pressure of oxygen in the alveolar gas when the blood cover about one-third distance of the lung capillary. Using the Runge-Kutta algorithm (MATLAB function ode45) obtained a numerical solution to the model. The diffusion of oxygen in the capillary tube was described mathematically by oxygen saturation and partial pressure of oxygen. The oxygen diffusing capacity of 65 ml/min/mmHg during a heavy workout takes 0.15 seconds for the oxygen saturation to reach from 40 to 100 mmHg in the lung capillary. The oxygen diffusion capacity is 39 ml/min/mmHg during usual activity takes 0.25 seconds for the oxygen saturation of 40 to 100 mmHg. The maximum time taken for the oxygen saturation of 40 to 100 mmHg during rest time is 0.52 seconds, and the oxygen diffusion capacity is 21 ml/min/mmHg.

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Conflict of interest

The authors declare that there is no conflict of interest involved in this study.

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