International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 7; Issue 4(J); April 2018; Page No. 11974-11977
DOI: http://dx.doi.org/10.24327/ijcar.2018.11977.2092

Research Article

A MATHEMATICAL MODELING OF PULMONARY GAS EXCHANGE IN HUMAN RESPIRATORY SYSTEM

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A R T I C L E I N F O

Article History:

Received 17th January, 2018
Received in revised form 26th February, 2018 Accepted 9th March, 2018
Published online 28th April, 2018

Key words:

Gas exchange, Alveolus, Respiratory membrane, Pulmonary capillary, Oxygen partial pressure, Mathematical model, Numerical simulation

A B S T R A C T

The main function of the human respiratory system is to take fresh oxygen from air and remove waste carbon dioxide from blood. There are millions of alveoli in the lungs which are enveloped by network of capillaries. Inhaled oxygen moves from the alveoli to the blood in the capillaries, and carbon dioxide moves from the blood in the capillaries to the air in the alveoli by diffusion across the respiratory membrane. The diffusion is due to the partial pressure gradient of each *gas*. In this study, a mathematical model of pulmonary gas exchange was developed and numerical simulation was performed for cardiorespiratory parameters responses to breathing at rest in healthy human adult. The two forms of oxygen transport: combined with hemoglobin in red blood cell and in physically dissolved form in the blood were considered in the model. Factors that affect pulmonary gas exchange are shown by the model.

INTRODUCTION

Three processes are essential for exchange of gases between the air in alveoli and the blood in the pulmonary capillaries: ventilation (the filling of the alveoli with oxygen rich-air), perfusion (the flow of blood through capillaries) and diffusion (the passive movement of gases between alveoli and capillaries across the respiratory membrane due to concentration difference). The large surface area of the alveoli and the short diffusion pathway between the alveoli and the capillaries offer favourable conditions for the diffusion [1]. The oxygen diffused in the blood is carried in two ways. A large portion (98%) is carried in combination with hemoglobin inside red blood cells, and a small portion (2%) is carried in the dissolved state in plasma.

Peter D. Wagner [2] developed a simple mathematical model of oxygen and carbon dioxide gas exchange across pulmonary membrane by considering these gases as inert gases. The model describes the time course of capillary partial pressure change along the capillary interms of lung-related structural variables and gas-related transport variables. D. S. Karbing *et al*. [3] developed a mathematical model of pulmonary gas exchange by considering physically dissolved form of oxygen in the blood and the slope of the tangent lines to the oxygen dissociation curve.

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They also developed a mathematical model by decomposing the total oxygen diffusion capacity of the pulmonary membrane into terms describing the diffusion capacity across the blood gas barrier and the diffusion capacity associated with oxygen binding to hemoglobin.

C. Brighenti *et al*. [4] presented a mathematical model of the oxygen alveolo–capillary exchange to provide the capillary oxygen partial pressure profile in normal and pathological conditions. They related the oxygen concentration and partial pressure by the well-known Hill equation. They described oxygen pressure versus capillary normalized distance at different values of diffusing capacity. G. C. E. Mbah *et al*. [5] formulated a mathematical model of gas exchange between the alveoli and blood capillary for normal human. They assumed the respiratory membrane is cylindrical in shape. They showed effects of surface area and thickness of pulmonary membrane and cardiac output on gas diffusion.

S. Martin *et al*. [6] developed an integrated model for oxygen transfer into the blood, coupled with a lumped mechanical model for the ventilation process. They investigated oxygen transfer into the blood at rest or exercise. J. Hughes [7] used a mathematical model to determine factors (age, altitude, chronic obstructive pulmonary diseases) that affect the partial pressures of oxygen and carbon dioxide in artery. A. Reynolds *et al*. [8] modeled gas exchange and the inflammatory response within a small portion of the lung in order to explore the lung during an inflammatory response.

Mathematical model

The following simplifying assumptions were made in this study: (1) The entire pulmonary bed is described as a single unit consisting of an alveolus and a capillary vessel assuming that all alveoli are uniform and have the same shape and the same properties for all capillaries (2) the alveolar oxygen partial pressure is constant and uniform (3) blood flow rate is constant through all capillaries. The simplified model is shown in Figure 1.

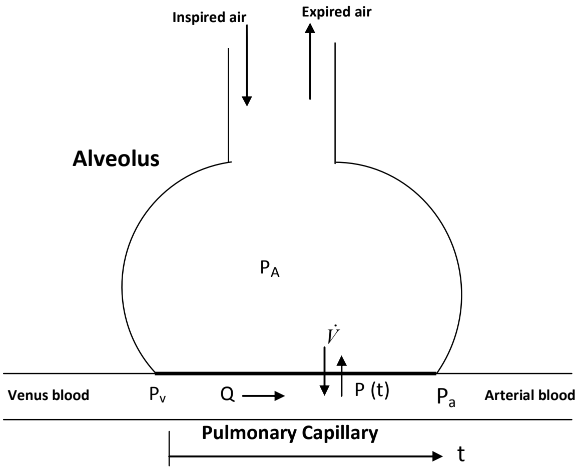

Figure 1 Model showing alveolo–capillary gas exchange

Oxygen diffusion in the pulmonary membrane can be described by the Fick's Law:

$$\dot{V}(t) = D_L(P_A - P(t)) \tag{1}$$

where $\dot{V}(t)$ is the volume of oxygen transferred across the pulmonary membrane per unit time, and D_L is the diffusion capacity of the pulmonary membrane for oxygen, and P_A and P are the partial pressures of oxygen (PO_2) in the alveolus and in the capillary.

If V_c is the total capillary blood volume, applying Fick's principle for blood flow we get

$$\dot{V}(t) = V_c \frac{dC(t)}{dt} \tag{2}$$

where C is the concentration of the oxygen in the capillary blood.

From Eq. (1) and Eq. (2), we have

$$\frac{dC(t)}{dt} = \frac{D_L}{V_c}(P_A - P(t)) \tag{3}$$

The concentration C(t) of oxygen in the capillary blood is resulted from (i) the amount of oxygen dissolved in the blood plasma and (ii) chemical reaction which dissociate of oxygen from hemoglobin, both depend on the partial pressure P of oxygen in the capillary. Applying Henry's Law for (ii) and relating partial pressure to the oxygen saturation of hemoglobin in the blood for (ii), we get the equation [3]

$$C(t) = \alpha P(t) + \beta.Hb.S \tag{4}$$

where α is the solubility of oxygen in the blood, Hb is the amount of haemoglobin per unit volume of the blood, β is the amount of oxygen contained in per unit mass of hemoglobin when 100% saturated and S is oxygen saturation of haemoglobin in the blood. Eq.(4) yield s

$$\frac{dC(t)}{dt} = \alpha\frac{dP(t)}{dt} + \beta Hb\frac{dS}{dt} \tag{5}$$

J. Collins *et al.* [9] related the saturation and the partial pressure from a limited laboratory data as

$$S(P(t)) = \frac{(P(t))^3 + 150P(t)}{(P(t))^3 + 150P(t) + 23400} \tag{6}$$

The relation in Eq.(6) is illustrated in Figure 2 which is obtained by MATLAB R2015a graphics.

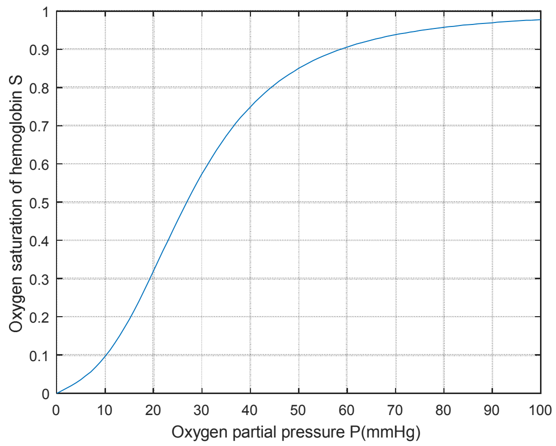

Figure 2 Oxygen - hemoglobin dissociation curve

From Eq.(3), Eq.(5) and Eq.(6), we get

$$\left[\alpha + \frac{3580200\beta.Hb}{\left[(P(t))^3 + 150P(t) + 23400\right]^2}\right]\frac{dP(t)}{dt} = \frac{D_L}{V_c}(P_A - P(t))$$

Or

$$\frac{dP(t)}{dt} = \frac{\frac{D_L}{V_c}(P_A - P(t))}{\alpha + \frac{70200\beta.Hb((P(t))^2 + 50)}{\left[(P(t))^3 + 150P(t) + 23400\right]^2}}, \quad 0 \le t \le T \tag{7}$$

where T is the time taken by blood to pass through capillary at rest which is approximately

0.75 sec for cardiac output of Q = 6mL/min. The mathematical model (Eq.(7)) is an initial value problem of ordinary differential equation with P(0) = Pv, where Pv is the oxygen partial pressure at the venous blood when blood enters the capillary. P(T)= Pa, where Pa is the oxygen partial pressure at the arterial blood when blood exits the capillary (see Figure 1).

Table 1 Values of the model parameters for healthy human adult at rest

Parameter	Unit	values
P_A	mmHg	100
P_v	mmHg	40
D_L	$mL.min^{-1}$ $mmHg^{-1}$	40
Q	$mL.min^{-1}$	6000
T	sec	0.75
V_c	mL	75
α	$mL.mL^{-1}.mmHg^{-1}$	0.0003
Hb	$g.mL^{-1}$	0.15
β	$mL.g^{-1}$	1.39

When we substitute the parameters in the model, P = 100 is the equilibrium solution of the model. The direction field of the model can be plotted using the following Wolfram Mathematica 7.0 command follows.

```
StreamPlot[{0.008889 * (100 − y),0.00003 + (14636.7
        * (y^2 + 50)/((y^3 + 150 * y
        +
23400)^2))}, {x, 0,10}, {y, 0,200}, PlotRange →
{{0,10}, {0,200}}]
```

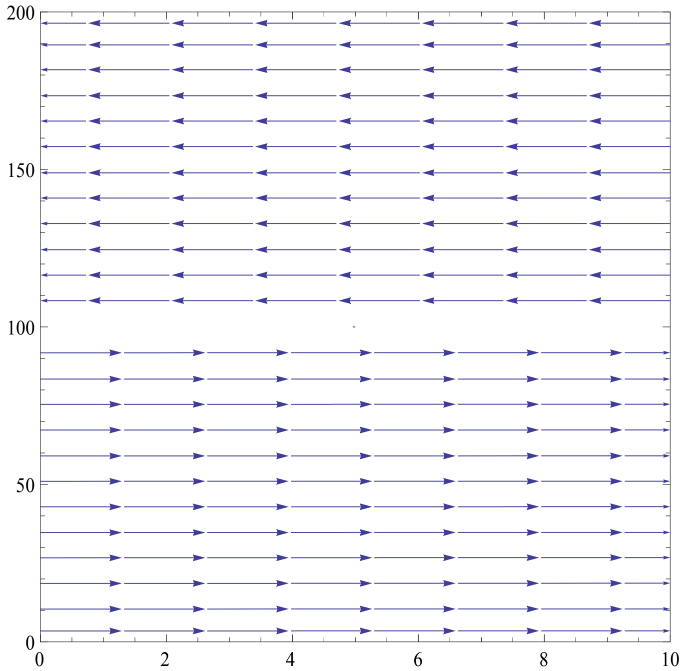

Figure 3 Sketch of direction fields of the model

From the direction field of the model shown in the Figure 3, the equilibrium solution P = 100 is stable. This shows that the primary purpose of the respiratory system, the equilibration of the partial pressures of the respiratory gases in the alveolar air with those in the pulmonary capillary blood, is attained at a certain time.

Simulation results

The model is difficult to solve analytically. We used the Runge–Kutta algorithm (MATLAB R2015a function ode45) to obtain numerical solution for the differential equation with step size $\Delta t = 0.001$. After substituting the parameters with appropriate units, we can solve Eq.(7) numerically and plot the result using the following MATLAB commands including ode45 for breathing at rest.

```
>> 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],40);
>>plot(t, p)
>>grid on
>>axis([0 0.75 30 110])
>>xlabel('Time in capillary(sec)')
>>ylabel('Oxygen partial pressure PO2 (mmHg)')
```

The resulting graph is indicated in Figure 4.

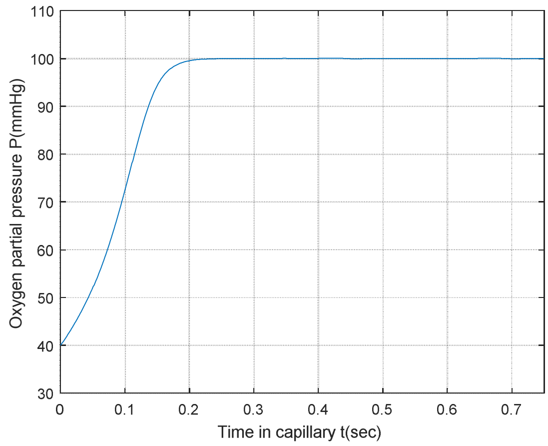

Figure 4 The computed time course of oxygen partial pressure in the pulmonary capillary of human adult breathing at rest

DISCUSSION

From Eq.(3)-Eq. (6), we observed that oxygen diffusion into the capillary across the pulmonary membrane depends on the diffusion capacity of the membrane for the oxygen (D_L), partial pressure difference between alveolar gas and capillary blood gas (P_A-P), the solubility of the oxygen in the blood (α), the capacity hemoglobin to carry of oxygen (β) and the amount of hemoglobin contained in the blood (Hb) . The MATLAB implementation to solve the differential equation enabled us to make sure this fact. Figure 3 shows that the partial pressure of oxygen in the capillary with respect time. The capillary blood reaches the alveoli level within about 0.25 seconds which agrees with [10]. The solution obtained for our model is similar to that the mathematical model developed by D. S. Karbing *et al*. [3].

Since the blood arriving in the alveolar capillaries has a partial pressure of oxygen of, on average, 40 mmHg, while the pressure in the alveolar air is 100 mmHg, there will be a net diffusion of oxygen into the capillary blood. The diffusion of oxygen a will continue until equilibrium is reached. Our model described this real biological process.

CONCLUSIONS

Exchange of gases in the lungs takes place between alveolar air and blood flowing through lung capillaries *by* diffusion. After diffusing into the pulmonary membrane, oxygen is transported by the blood either combined with hemoglobin in the red blood cells or dissolved in the blood plasma. A mathematical model of gas exchange which incorporates the two cases was developed in this study. In the model, previously developed relationship between oxygen saturation and partial pressure was used to describe be the partial pressure of oxygen in the capillary. Runge–Kutta algorithm (MATLAB function ode45) was used to obtain numerical solution for the model. The oxygen alveolo-capillary exchange was expressed numerically using the model.

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How to cite this article:

Endalew Getnet Tsega and V. K. Katiya (2018) 'A Mathematical Modeling of Pulmonary Gas Exchange in Human Respiratory System', *International Journal of Current Advanced Research,* 07(4), pp. 11974-11977.
DOI: http://dx.doi.org/10.24327/ijcar.2018.11977.2092

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