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A Study on Oxygen Diffusion Through Living Tissues

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A STUDY ON OXYGEN DIFFUSION THROUGH LIVING TISSUES
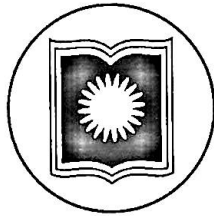
A Thesis submitted to the Department of Mathematics, Rajshahi University, Bangladesh for the Degree of Master of Philosophy.

Submitted By

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July 2009

Dedicated

To

My Beloved Parents

Declaration

I hereby declare that the whole work now submitted as a thesis entitled "A STUDY ON OXYGEN DIFFUSION THROUGH LIVING TISSUES" in the Department of Mathematics, Rajshahi University, Bangladesh for the degree of Master of Philosophy is the result of my own investigation. The thesis contains no material which has been accepted for the award of any other degree or diploma elsewhere, and, to the best of my knowledge, the thesis contains no material previously published or written by another person, except where due reference is made in the text.

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July 2009

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Certificate

This is to certify that the thesis entitled "A STUDY ON OXYGEN DIFFUSION THROUGH LIVING TISSUES" by Abdul Malek in fulfillment of the requirements for the degree of Master of Philosophy in Mathematics, Faculty of Science, University of Rajshahi, Rajshahi, Bangladesh, has been completed under my supervision. I believe that this research work is an original one and it has not been submitted elsewhere for any degree.

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Abstract

A theoretical study of oxygen diffusion process through living tissues and its various consequences have been presented. In this aspect we have reviewed some physiological terms and fundamental lows of diffusion.

A Mathematical model of the partial pressure of oxygen across the alveolar-pulmonary capillary membrane has been determined and expressed in term of membrane thickness due to the oxyhemoglobin dissociation curve. On the other hand, the effect of partial pressure of carbon dioxide has been found to be the function of partial pressure of oxygen. The partial pressure of oxygen along the pulmonary capillary has also been discussed when deoxygenated blood converts to the oxygenated blood taking Hill's modified oxyhemoglobin dissociation equation and Bohr effect. It is found that the partial pressure of oxygen increases with the increasing of capillary length.

The mathematical equations have been developed based on the partial pressure of oxygen in the capillary blood is reached in equilibrium position. It is found that the molar flux decreases exponentially with the increasing of radial thickness of the capillary. Moreover, It is found that the molar flux of oxygen increases linearly with the increasing of diffusion coefficient of oxygen.

A mathematical model of molar flux of oxygen has been developed across the capillary-tissue membrane by neglecting the convective transport across the capillary membrane. We have found that the maximum consumption rate of oxygen increases rapidly at initial stages after that it decreases with the increasing of wall thickness. Moreover, the result indicates that the pressure profile of oxygen along the wall is approximately linear with the increasing of the thickness of capillary wall.

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CHAPTER -1

General Introduction

Summary

This introductory chapter has been described with an overview of the diffusion process of oxygen through living tissues in both external and internal respiratory systems. Since this is the fundamental chapter, so some relevant terms of oxygen diffusion have been discussed.

1.1 Introduction

The primary function of the respiratory system is to transport oxygen and carbon dioxide. Inhaled oxygen enters into the lungs and reaches the alveoli. The alveoli and the surrounding capillaries are in very close contact with each other and there is a membrane between them. This barrier averages about 1 micron ($^1/_{10,000}$ of a centimeter) in thickness. Oxygen passes through this membrane quickly into the blood in the capillaries. The exchange takes place between the millions of alveoli in the lungs and the capillaries that surround them. Inhaled oxygen moves from the alveoli to the blood in the capillaries and similarly, carbon dioxide moves from the blood in the capillaries to the alveoli.

Oxygenated blood travels to the body cell from the lungs through artery. In the internal respiration, this oxygen is relied to the body cells and carbon dioxide is taken from the cells. It happens in much the same way as gas exchange in the lung. Oxygen-deficient and carbon dioxide-rich blood return to the right side of the heart through two large veins, the superior vena cava and the inferior

vena cava. Then the blood is pumped through the pulmonary artery to the lungs, where it picks up oxygen and releases carbon dioxide.
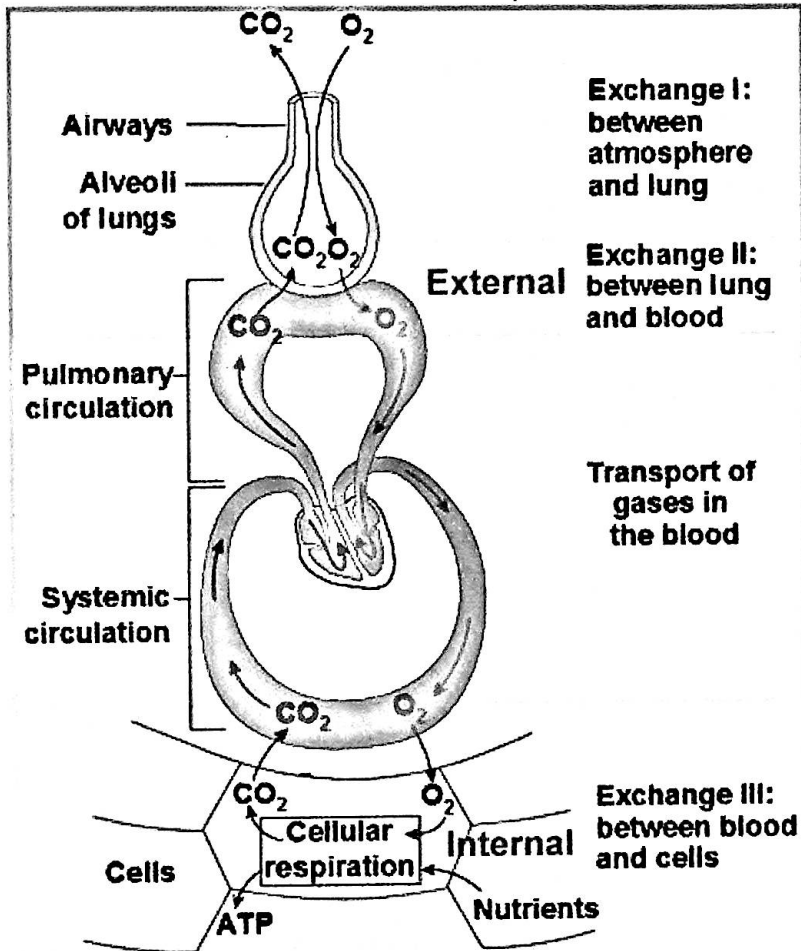
Fig. 1.1. Respiratory system (Source: Internet)

The anatomical features of the respiratory system include airways, lung and the respiratory muscles. Molecules of oxygen and carbon dioxide are passively exchanged, by diffusion, between the gaseous external environment and the blood. This exchange process occurs in the alveolus region of the lungs (Maton et al., 2009). Fenn et al. (1946) discussed the composition of alveolus air of the lung and developed the oxygen-carbon dioxide diagram at high altitude

including the effects of hyperventilation. Kety (1951) developed a governing equation for the exchange of inert gas exchange in the lung and tissues. Pater et al. (1964) designed an electrical analogue of the entire human respiratory system taking the linear system of diffusion of an electrical transmission line. Askanazi et al. (1982) discussed the human respiratory system and delivery of the nutrition and oxygen to the tissues taking clinical investigation. The structure and function of the mammalian respiratory system were discussed by Weibel (1984) and shown that the properties of the respiratory system are potential limiting factor for oxygen flow at all levels of the entire oxygen pathway. Oxygen is required to generate the chemical energy (ATP) to allow muscle contraction. The amount of chemical energy required is directly proportional to the work rate performed and the rate of external respiration equals the rate of internal respiration (Wasserman, 1984).

In this chapter, we have discussed the respiratory system of mammalian body according to the physiological concepts for modeling the diffusing process of oxygen through the living tissue mathematically.

1.2 Mammalian Blood

Medical terms related to blood after begin with hemo-or hemato from the Greek word "haima" for "blood". Anatomically, blood is considered to be a type of connective tissue and it is a suspension of cells or bodily fluid that delivers necessary substances to the body's cells, such as nutrients and oxygen, and transports waste products away from those same cells.

Blood is composed of several kinds of cells. The amount of the cells is about 45% of the whole blood and remaining 55% of whole blood is blood plasma. Blood is liquid medium appearing yellow in color. The normal vale of p^H of human blood is approximately 7.35-7.45.

The blood cells are:

(i) Red blood cells: There are about 96% red cells in whole blood cells. The main function of red blood cell is to transport oxygen from lung to all the cells of the body and to remove of carbon dioxide produced by metabolic processes in the body.
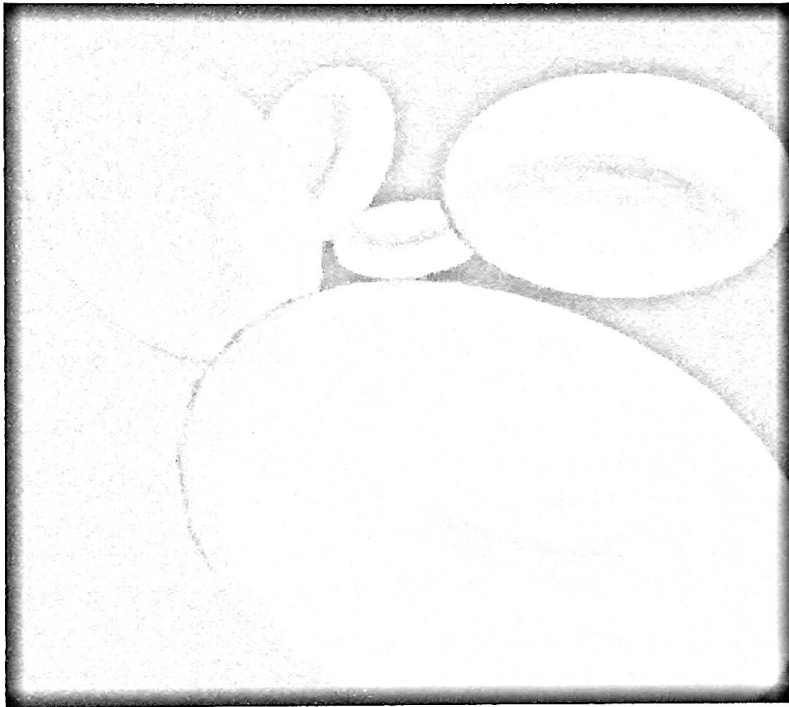
Fig.1.2. Red blood cells (Source: Internet)

Hemoglobin is a pigment and it carries the oxygen as oxyhemoglobin. There are about 25×10^{12} red cells in 5 liters of blood in the human body. The mean life of a red cell is about 120 days and 2.4×10^{9} red cells die per second.

The shape of a red cell is a biconcave disc and an average diameter is about 8 μm and its thickness varies from 1 μm at the center to about 2.2 μm at the ends.

(ii) White blood cells: There are about 3.0% white cells in whole blood cells. White blood cells are part of the immune system and they destroy infection agents.

(iii) Platelets: There are about 1% platelets in blood cells, which are responsible for blood clotting.

Blood plasma is essentially an aqueous solution containing 92% water, 8% blood plasma proteins and trace amounts of other materials. Some components are:

- ❖ Albumin
- ❖ Blood clotting factors
- ❖ Immunoglobulins (antibodies)
- ❖ Hormones
- ❖ Various other proteins
- ❖ Various electrolytes.

Together, plasma and cells form a non- Newtonian fluid whose flow properties are uniquely adapted to the architecture of the blood vessels.

Functions of blood:

- ❖ Supply of oxygen to tissue (bound to hemoglobin, which is carried in red cells)
- ❖ Supply of nutrients such as glucose, amino acids and fatty acids (dissolved in the blood or bound to plasma proteins)
- ❖ Removal of waste such as carbon dioxide, urea and uric acid
- ❖ Immunological functions, including circulation of white cells, and detection of foreign material by antibodies
- ❖ Coagulation, which is one part of the body's self-repair mechanism
- ❖ Messenger functions, including the transport of hormones and the signaling of tissue damage
- ❖ Regulation of body p^H
- ❖ Regulation of core body temperature
- ❖ Hydraulic functions, including creating

1.3 Membrane

We have studied about the membrane of the cell biology because diffusion is occurred through the membrane. Membrane is a thin tissue barrier that separates two organs or spaces and allows diffusion of gases exchanged between the alveolus air and blood of the pulmonary capillary through the alveolus-capillary membrane, and blood to tissue fluid through the tissue-capillary membrane. Plasma membrane or cell membrane is a selectively permeable lipid bilayer found in all cells (Alberts et al., 1994).
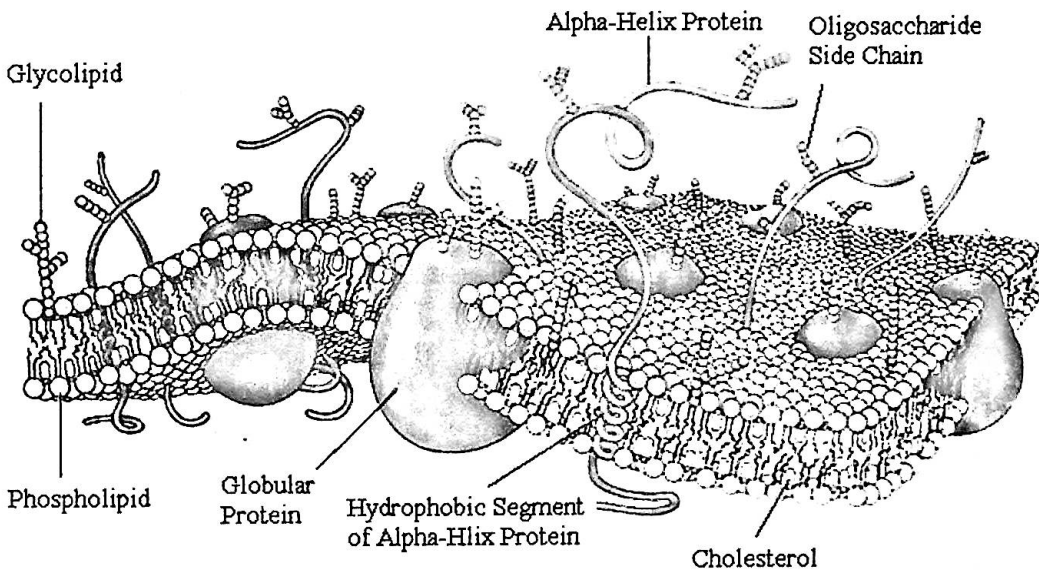
Fig. 1.3. Cross section of mammalian membrane (Source: Alberts et al., 1994)

It is contained of phospholipids, glycolipids, proteins and biological molecules. Membrane is a permeable cell and regulates the movement of materials into and out of cells and the movement of substance across the membrane can be either passive, occurred without the input of cellular energy, requiring the cell to expend energy in moving it.

The arrangement of amphipathic lipid molecules from a lipid bilayer is the architecture of cell membrane and they have hydrophilic polar heads pointing out and hydrophobic portion forming the core, shown in the Fig.1.3. The

arrangement of hydrophilic head and hydrophobic portion of the lipid bilayer prevent polar solutes (that is amino acids, nucleic acids, carbohydrates, proteins, etc.) from diffusing across the membrane, but generally allows the passive diffusion of hydrophobic molecules. One important role of membrane is to regulate the movement of materials into and out of cells, permeability of the membrane, passive transport and active transport mechanisms are considered in the phospholipid bilayer. A cross section of the bilayer is seen in this Fig.1.3. The cell membrane consists of three types of amphipathic lipids: (1) phospholipids, (2) glycolipids and (3) steroils whose depend on the types of the cell, but phospholipids are the major components of amphipathic lipids (Lodish et al., 2004).

The permeability of membrane is a measurement, how easily molecules pass through the membrane. This permeability depends on electric charge, slightly lesser extent, molar mass of the molecule, neutrally small molecules pass the membrane easier than large one.

1.4 Ventilation

The main purpose of respiratory system is to supply oxygen to the cells of the mammalian body and removal of carbon dioxide from the cells produced by cellular activities. This respiratory process can be divided as pulmonary ventilation, external respiration and internal respiration.

Pulmonary ventilation can be divided as breathe in (inspiration) and breathe out (expiration). During inspiration, the volume of lung is expanded by the contraction of the principal aspiratory muscles. In order to increase lung volume, the pressure of the lung decreases. It can be referred as Boyle's law, which states, as at constant temperature, the pressure of a gas in a closed container is inversely proportional to the volume of the container. For this case, the air of the atmosphere enters into the lungs for the pressure gradient. It is mentioned that just before each inspiration, the pressure of air inside the lungs

is equal to the pressure of the atmosphere, which is about 760 mmHg and drops from 760 mmHg to 758 mmHg during inspiration.

Expiration is also occurred for pressure gradient. During the expiration, the volume of the lung is decreased by the relaxation of the muscles. For this reason, the pressure of air of the lungs is greater than the pressure of the atmosphere, normally the pressure is about 763 mmHg. Hence air moves from lung to the atmosphere.
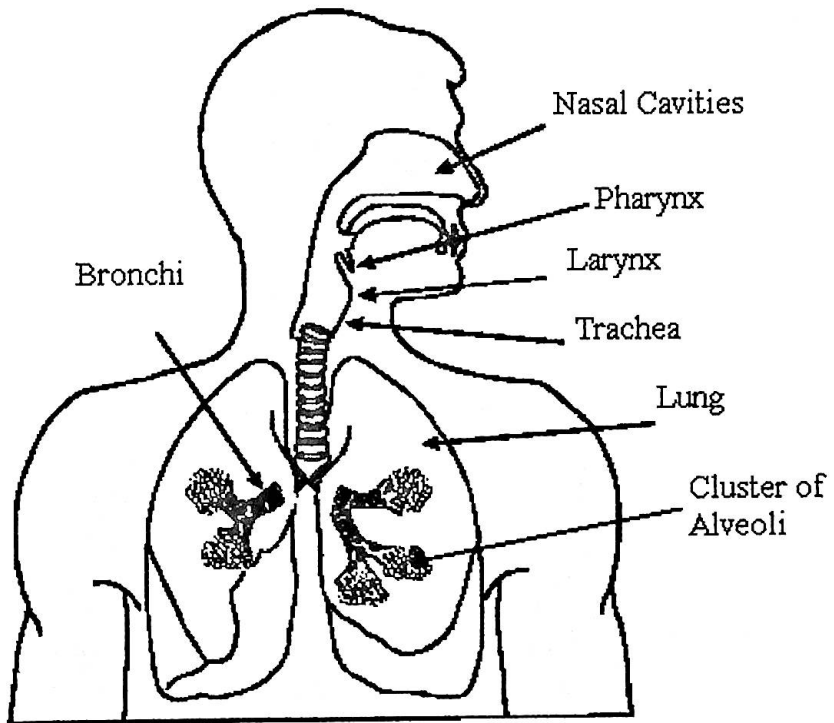
Fig. 1.4. Human ventilation system (Source: Internet)

A healthy adult man inhales about 500 ml of air at each inspiration and 12 times respirations are occurred per minute and same amount of air moves out with unique expiration. But about 350 ml of air actually reaches the alveoli. Other 150 ml of air remains in air spaces of nose, pharynx, larynx, trachea and bronchi.

1.5 External Respiration

External respiration is the exchange of oxygen from alveoli of the lung to blood of the pulmonary capillaries and exchange of carbon dioxide from blood of pulmonary capillaries to alveoli. That is, it is a conversation process of deoxygenated blood to oxygenated blood.
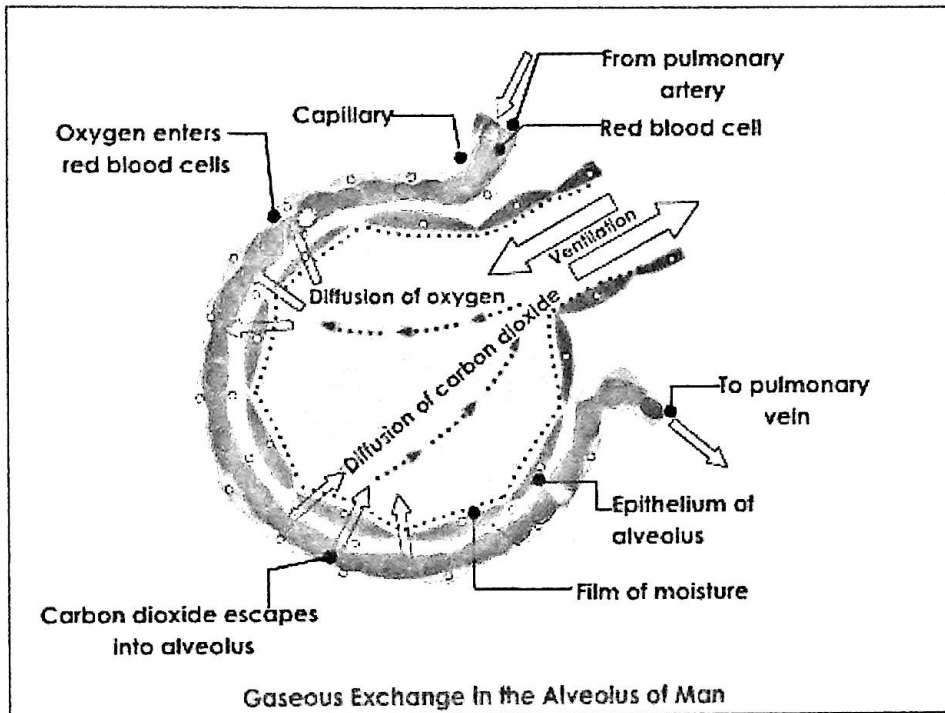
Fig. 1.5. External respiratory system in the lungs (Source: Internet)

The partial pressure of oxygen (pO_2) in the alveolus is 104 mmHg of the air that we inhale and pressure of oxygen is 40 mmHg in deoxygenated blood of the pulmonary capillary. As a result of this pressure gradient, oxygen defuses from alveolus to pulmonary capillary blood until equilibrium is reached and carbon dioxide defuses from capillary blood to alveolus air. Since pressure of carbon dioxide of the deoxygenated blood through the pulmonary capillary is 45 mmHg and that is 40 mmHg of the alveoli air, for this reason, carbon dioxide defuses from blood to alveoli air according to the pressure gradient.

Thus the partial pressure of carbon dioxide (pCO_2) of oxygenated blood leaving the lungs is the same as that of alveolar air. The carbon dioxide that diffused into the alveoli is eliminated from the lung during expiration.

1.6 Internal Respiration

Oxygen is carried with hemoglobin through the blood. In the tissue region, this oxygen exchanges from hemoglobin to tissue fluid and carbon dioxide diffuses from tissue fluid to the blood. This process is called the internal respiration and the oxygenated blood converts to the deoxygenated blood. The pressure of oxygen in the capillary blood is 105 mmHg and that is 40 mmHg in the tissue cell.
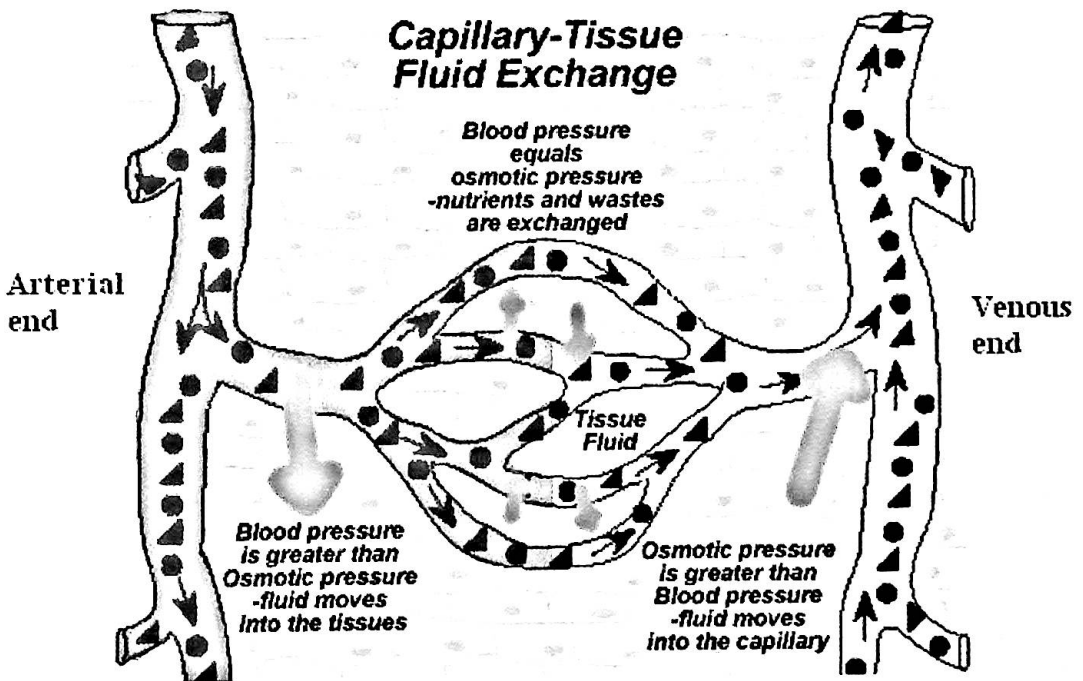
Fig.1.6. Internal respiratory system in the mammalian body (Source: Internet)

For this pressure gradient, oxygen diffuses from capillary blood to the tissue fluid then to the tissue until the pO_2 of the capillary blood is 40 mmHg. But carbon dioxide diffuses in the opposite direction. Normally pCO_2 of tissue

region is 45 mmHg and that is 40 mmHg of the capillary oxygenated blood. As a result, carbon dioxide diffuses from tissue to the blood until the pCO_2 decreases to 40 mmHg in tissue region.

Capillary-tissue fluid exchange depends on blood pressure and osmotic pressure of blood. This exchange is occurred in three steps. At the capillary bed of the arterial end, where blood pressure is 40 mmHg and osmotic pressure of blood is 20 mmHg. As a result capillary blood releases oxygen and nutrients into the tissue fluid of the surrounding cells. It is mentioned that blood cells and plasma proteins cannot cross into the tissue for its big size to leave the capillary.

Middle section of the capillary bed, here blood pressure and osmotic pressure of blood are same, which is equal to 21 mmHg and gas exchanges between capillary blood and tissue fluid for partial pressure of gas called diffusion. Venule side of capillary bed, in this section blood pressure and osmotic pressure of blood are 15 mmHg and 21 mmHg respectively. As a result, additional fluid backs to capillary blood.

1.7 Diffusing Capacity

Oxygen is transferred from alveolus air to pulmonary capillary blood across the alveolus-capillary membrane by diffusion.

$$D_{o_2} = \frac{A\, do_2}{x} \tag{1.1}$$

where D_{o2} is the diffusion capacity, A is the total area of the diffusing surface, x is the thickness of the alveolus-capillary membrane and do_2 is the diffusion coefficient.

By Fick's law, the rate of diffusion is proportional to the pressure gradient. Thus

$$Q'_{o2} = D_{o2} \times p^{(A-B)} \tag{1.2}$$

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where Q'_{o2} is the oxygen uptake per time, $p^{(A-B)}$ is the mean alveolus capillary pressure gradient and D_{o2} is the diffusion capacity. The measurement of partial pressure of oxygen across the membrane requires the determination of Q'_{o2}, where D_{o2} is known but it is hard to estimate the value of $p^{(A-B)}$.
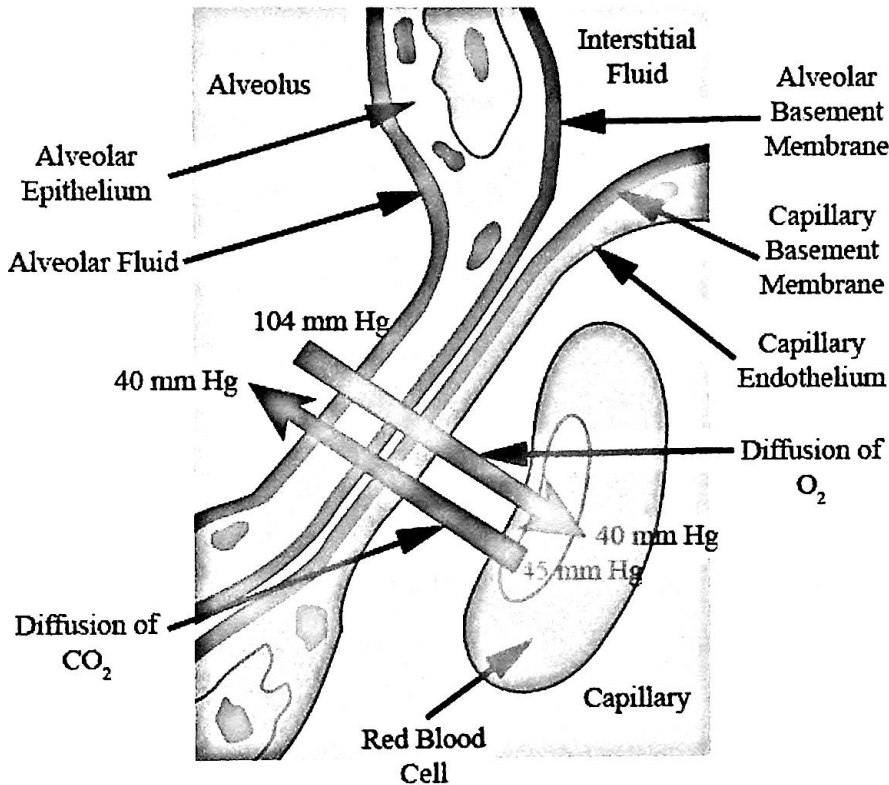
Fig.1.7. Diffusion of oxygen and carbon dioxide through the membrane from alveolus to capillary (Source: Internet)

In chapters 3 and 4, we have determined the partial pressure of oxygen across the alveolus-capillary membrane and the pressure profile of oxygen along the capillary respectively.

1.8 Transportation of Oxygen

The transportation of oxygen between lungs and body tissues is a function of the blood. When oxygen enters into the blood, certain physical and chemical changes occur and that aid to gas transport and exchange. At resting condition, 20% oxygen is contained with blood. Only 3% oxygen is taken up by the blood plasma and remaining 97% of oxygen is carried in chemical combination with hemoglobin of red blood cell.

The reversible reaction of hemoglobin with oxygen is written as

$$Hb + O_2 \leftrightarrow HbO_2$$
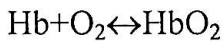
Oxyhemoglobin may be fully saturated or partial saturated, when Hb is completely converted to HbO_2 as called fully saturated and when hemoglobin consists of a mixture of Hb and HbO_2 as known as partially saturated.

Normally a solution of hemoglobin in blood is about 97 % saturated at pO_2 = 100 mmHg. Note that, at high pO_2 hemoglobin binds with large amount of oxygen and is almost fully saturated, and at low pO_2 it is partially saturated with oxygen. Therefore, in pulmonary capillary where pO_2 is high, a lot of oxygen bounded with hemoglobin and in tissue capillary pO2 is low, and oxygen is released from HbO_2 for diffusion into the tissue cells.

The amount of oxygen released from hemoglobin depends on several factors such as p^H, temperature, diphosphoglycerate, etc. In an acid environment, oxygen is released from hemoglobin and low p^H results from the presence of lactic acid, which is generated from contraction of muscle. The blood at limited temperature takes up carbon dioxide, which is inversed to hemoglobin saturation. As temperature increases, oxygen releases from hemoglobin.

In order to discuss the diffusion of oxygen, when oxygen diffuses from capillary to tissue fluid, we have discussed the molar flux of oxygen on the capillary wall in chapter 5 and consumption of oxygen by the capillary wall in chapter 6.

1.9 Outline of the Thesis

To analyze the diffusion process of oxygen in the mammalian body, we need to study the physiological concepts, which are studied above. We have discussed the pressure profile, molar flux and consumption of oxygen mathematically and outline is presented in the following chapters:

Chapter 1 is concerned with the fundamental physiological concepts and discussed some relevant terms of oxygen diffusion through the living tissues.

Chapter 2 is concerned with the mathematical model of diffusion equations and its solutions for microvascular system, such as capillary, artery, vein, etc. In addition, the Krogh's cylinder models of diffusion in the capillary and tissue regions are also discussed.

A simple model of oxygen diffusion across the alveolus-capillary is discussed to estimate the partial pressure profile in chapter 3. The solution of the model in both linear and non-linear conditions according to the effect of carbon dioxide on oxygen has been solved, and the relation between partial pressure of oxygen and alveolus-capillary thickness is presented.

Chapter 4 presents a mathematical model of pressure profile of oxygen in the external respiratory system along the pulmonary capillary including oxyhemoglobin disassociation equations of oxygen. The measurement demonstrates that the pressure is a function of capillary length.

Chapter 5 describes the molar flux of oxygen in the internal respiratory system at the middle section of the capillary when oxygen diffuses from capillary blood to tissue fluid according to the pressure gradient.

But oxygen is consumed by the cell when oxygen diffuses through it. This consumption of oxygen of the microvascular (capillary, artery, vein, etc.) wall has been discussed. Chapter 6 is also concerned with pressure profile and consumption of oxygen at this time.

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CHAPTER -2

Review of Diffusion Equations

Summary

The diffusion equations have been developed for a Cartesian and Cylindrical polar coordinate systems. These equations have been solved to determine the diffusion process of oxygen in the internal respiratory system both in capillary and tissue regions.

2.1 Introduction

Through bio-membrane, oxygen diffusion process is very complicated phenomena. To derive the diffusion equation in bio-membrane, we have used it for different coordinates systems. The different form of diffusion can be modeled quantitatively using the diffusion equation by different names depending on the physical situation. For instance-steady-state bio-molecular diffusion is governed by Fick (1855). Steady-state thermal diffusion was governed by Fourier's law. The diffusion of electrons in electrical field leads essentially to Ohm's law and that was further explained by Einstein relation. Tsang (1961) approximated the solution of Fick's diffusion equation using eigenfunction expression technique. Kass et al. (1966) also solved the Fick's diffusion equation taking diffusion coefficient of the form $D=D_0c^n$, n being an arbitrary positive parameter and some numerical results were presented. Krogh (1919) discussed the mathematical models of oxygen diffusion through living tissue based on the unit structure.

From the above discussion, it is clear that although some researches have been done on the diffusion processes of oxygen and carbon dioxide, this is not sufficient. This study focuses the derivation of diffusion equations through the instance-steady-state bio-molecular membrane and exchanges of oxygen and carbon dioxide through living tissue.

2.2 Diffusion System

Diffusion is the net movement of molecules from an area of high concentration to an area of lower concentration by random molecular motion until both concentrations are equal, as a examples, a sugar cube in a glass of water that is not stirred will dissolve slowly and the sugar molecules will distribute over the water by diffusion (Fig. 2.1).
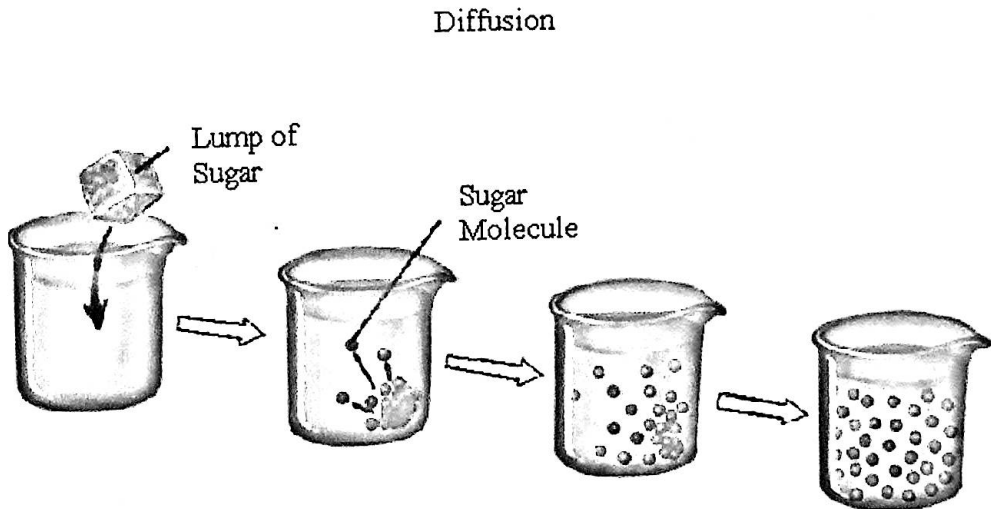
Diffusion

Fig 2.1. Diffusion of sugar molecule in a glass of water (Source: Internet)

It is a physical process rather than a chemical reaction, which requires no net energy expenditure. In cell biology, diffusion is often described as a form of passive transport.

2.3 Facilitated Diffusion (or facilitated transport)

Facilitated diffusion is a process of diffusion, a form of passive transport facilitated by transport proteins. Facilitated diffusion is the spontaneous passage of molecules or ions across a biological membrane passing through specific transmembrane transport proteins. The facilitated diffusion may occur either across biological membranes or through aqueous compartments of an organism.
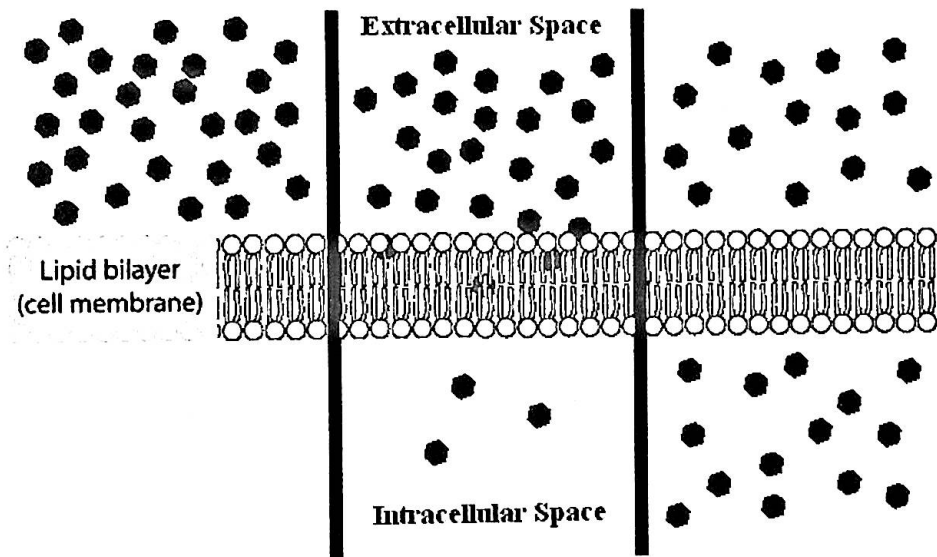
Fig 2.2. Facilitated diffusion of molecule through the membrane

(Source: Internet)

Water, oxygen, carbon dioxide, ethanol and urea are examples of molecules that readily pass either directly through the lipid bilayer or through pores created by certain integral membrane proteins. The relative rate of diffusion is roughly proportional to the concentration gradient across the membrane. For example, oxygen concentrations are always higher outside than inside the cell and oxygen therefore diffuses down its concentration gradient into the cell; the opposite is true for carbon dioxide. Oxygen, carbon dioxide and ethanol are highly lipid soluble and therefore, diffuse across the bilayer.

2.4 Fick's First Law of Diffusion

Fick's first law describes the diffusion and defines the diffusion coefficient (D), was derived by Adolf Fick (1855). Fick's first law is used in steady state diffusion, i.e., when the concentration within the diffusion volume does not change with respect to time ($J_{in}=J_{out}$). The flux J is proportional to the diffusivity and the negative gradient of concentration.

$$J = -D\frac{\partial c}{\partial x} \tag{2.1}$$

where

J is the diffusion flux in dimensions of [parts length^{-2} time^{-1}].

D is the diffusion coefficient in dimensions of [length^2 time^{-1}].

c is the concentration in dimensions of [parts length^{-3}].

x is the position.

The negative sign indicates that J is positive when movement is down the gradient, i.e., the negative sign cancels the negative gradient along the direction of positive flux.

2.5 Fick's Second Law of Diffusion

We have derived Fick's second law from first law of diffusion and the Fick's first law of diffusion can be written as

$$\underline{J} = -D\nabla c \tag{2.2}$$

Now consider a volume V with surface S. The rate of change of amount of solute per unit time is given by

$$\frac{\partial}{\partial t}\int_V c \; dx \; dy \; dz \tag{2.3}$$

The amount of solute that comes out of the surface S per unit time is given by

$$\int_S \underline{J}\cdot\hat{n}\,ds \tag{2.4}$$

where $\hat{n}$ is the normal vector along the outward to the surface. If there is no source or sink inside the volume, we get from Eqs. (2.2), (2.3) and (2.4) using Gauss divergence theorem, which states as a mass-balance relation

$$\frac{\partial c}{\partial t} = -div\,\underline{J}$$

Since, the above equation holds for all volume. Then

$$\frac{\partial c}{\partial t} = D(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}) \tag{2.5}$$

This equation is called as Fick's second law of diffusion.

2.6 Diffusion Equation with Convection Term

When a solute is entrained to a moving fluid, it shares the motion of the fluid. This diffusion is known as convection-diffusion, which involves two current density vectors. Namely,

$$\underline{J}_{diffusion} = -D\nabla c \tag{2.6}$$

$$\underline{J}_{convection} = c\,\underline{v} \tag{2.7}$$

where, c, v, D are the concentration, velocity of the fluid and the diffusion coefficient respectively.

The total current density vector becomes

$$\underline{J} = \underline{J}_{diffusion} + \underline{J}_{convection}$$

or, $\quad \underline{J} = -(D\nabla c - c\underline{v}) \tag{2.8}$

We have from mass balance equation

$$\frac{\partial c}{\partial t} = -div(\underline{J})$$

Thus diffusion equation becomes

$$\frac{\partial c}{\partial t} + (\underline{v} \cdot \nabla)c + c\,(div\,(\underline{v})) = div(D\nabla c)$$

If the fluid is incompressible, i.e., $div(v) = 0$. Then the above equation

becomes

$$\frac{\partial c}{\partial t} + (\underline{v} \cdot \nabla)c = D\nabla^2 c \tag{2.9}$$

In Cartesian coordinate system the above equation can be written as

$$\frac{\partial c}{\partial t} + v_1\frac{\partial c}{\partial x} + v_2\frac{\partial c}{\partial y} + v_3\frac{\partial c}{\partial z} = D(\frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} + \frac{\partial^2 c}{\partial z^2}) \tag{2.10}$$

which is the diffusion equation with convection term.

2.7 Diffusion Equations in Cylindrical Polar Coordinate System

In Cylindrical polar coordinate (r,θ,z), we can convert Eq. (2.10) into Cylindrical coordinate as

$$\frac{\partial c}{\partial t} + v_1(\cos\theta\frac{\partial c}{\partial r} - \frac{\sin\theta}{r}\frac{\partial c}{\partial \theta}) + v_2(\sin\theta\frac{\partial c}{\partial r} + \frac{\cos\theta}{r}\frac{\partial c}{\partial \theta}) + v_3\frac{\partial c}{\partial z} =$$

$$D(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial \theta^2} + \frac{\partial^2 c}{\partial z^2}) \tag{2.11}$$

For the axially symmetric Cylindrical polar co-ordinate, θ is disappeared. Then Eq. (2.11) becomes,

$$\frac{\partial c}{\partial t} + v\frac{\partial c}{\partial z} = D(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}) \tag{2.12}$$

which is the diffusion equation with convection term in Cylindrical polar coordinate.

For steady-state flow $\frac{\partial c}{\partial t} = 0$, so Eq. (2.12) becomes

$$v\frac{\partial c}{\partial z} = D(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}) \tag{2.13}$$

By Hagen-Poiseuille flow, we know the velocity v at the point r is

$$v = v_m(1 - \frac{r^2}{R^2})$$

where v_m is the maximum velocity on the axis of the circular tube and R is the radius of the tube.

Using this, Eq. (2.13) can be written as

$$D(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}) = v_m(1 - \frac{r^2}{R^2})\frac{\partial c}{\partial z} \tag{2.14}$$

This is the diffusion equation with convection term in steady-state case. Similarly, we get Cylindrical non-convective diffusion equation as

$$\frac{\partial c}{\partial t} = D(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}) \tag{2.15}$$

which is the Fick's second law in Cylindrical polar co-ordinates.

2.8 Solution of One-dimensional Fick's Second Law

One dimensional Fick's second law is defined as

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} \tag{2.16}$$

For solving the boundary value problem for which there is no flux at $x=0$ and $x=a$,

i.e., $\quad \dfrac{\partial c}{\partial t} = 0 \qquad$ at $x=0$ and $x=a$ \hfill (2.17)

Let the general solution of the Eq. (2.16) be of the form

$$c(x,t) = X(x)T(t) \tag{2.18}$$

Then the solution of Eq. (2.16) becomes

$$c(x,t) = \sum_k (e^{-k^2 t}(A_k \cos\frac{kx}{\sqrt{D}} + B_k \sin\frac{kx}{\sqrt{D}})) \tag{2.19}$$

Now using the boundary conditions $\dfrac{\partial c}{\partial x} = 0$ at $x=0$ and $x=a$ in Eq. (2.19), we have

$$B_k = 0 \text{ and } k = \frac{n\pi\sqrt{D}}{a} \text{ respectively.}$$

So that

$$c(x,t) = \sum_{n=0}^{\infty} c_n \exp(-n^2\pi^2 Dt/a^2)\cos\frac{n\pi x}{a} \tag{2.20}$$

To determine the constant c_n, we use the initial distribution of concentration $c(x,0)=f(x)$, so that

$$f(x) = \sum_{n=0}^{\infty} c_n \cos \frac{n\pi x}{a}$$

Expanding $f(x)$ in a half-range cosine series, we get

$$c_0 = \frac{1}{a} \int_0^a f(x)dx \qquad\qquad (2.21)$$

$$c_n = \frac{2}{a} \int_0^a f(x)\cos\frac{n\pi x}{a}dx \qquad n=1,2,3,... \qquad (2.22)$$

2.9 Oxygen Diffusion through Living Tissue

2.9.1 The Krogh Cylinder Model

The mathematical models of the transport of molecular oxygen from the blood plasma to the living tissue of skeletal muscle or lung or brain, across the capillary wall are all based on the unit structure given by Krogh (1919).
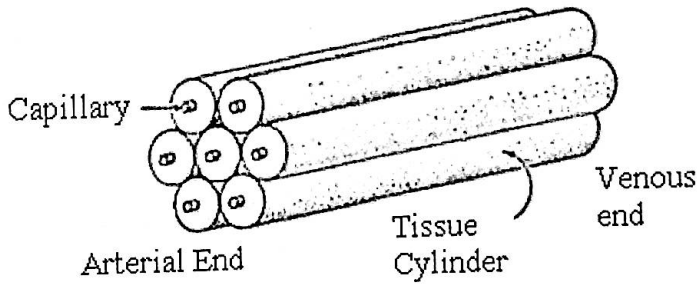
Fig 2.3. Krogh cylindrical model (Source: Internet)

This arrangement postulate that, in a given portion of tissue, all capillaries and surrounding tissue are of equal diameter and are homogeneously dispersed in the tissue. In the capillary region, transport of oxygen takes place both by convection and diffusion, and oxygen is generated due to its dissociation in the hemoglobin in side the red cell and its transport to the blood plasma across the

cell membrane. In the tissue region, there is only diffusion of oxygen and is consumption of oxygen by the tissue cells.

2.9.2 PDE and Bounder Conditions in Capillary Region

Let $c(r,z,t)$ be the concentration of oxygen, r be the radius of a capillary and $v(r,t)$ be the velocity of the blood in the capillary.

We know the diffusion equation with convection term of axially symmetric Cylindrical polar coordinates Eq. (2.12) as

$$\frac{\partial c}{\partial t} + v \frac{\partial c}{\partial z} = D_b (\frac{\partial^2 c}{\partial r^2} + \frac{1}{r} \frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}), \tag{2.23}$$

We also know in the capillary region, the transport of oxygen takes place both by convection and by diffusion, and oxygen is generated due to the dissociation of oxyhemoglobin.

Let $d(c)$ be the rate of generation of oxygen per unit volume due to the dissociation of oxyhemoglobin. Then equation Eq. (2.23) becomes

$$\frac{\partial c}{\partial t} + v \frac{\partial c}{\partial z} = D_b (\frac{\partial^2 c}{\partial r^2} + \frac{1}{r} \frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}) + d(c) \tag{2.24}$$

where D_b is the diffusion coefficient of blood. It is convenient to introduce the average diffusion coefficient D_b as the harmonic mean between these two diffusivities of plasma and hemoglobin. So that

$$\frac{1}{D_b} = \frac{1}{2}(\frac{1}{D_{Hb}} + \frac{1}{D_{plasma}})$$

Equation (2.24) is satisfactory for large capillaries. But for small capillaries, it is preferable to use two diffusivity coefficients, D_r in the radial direction and D_z in the axial direction. Then Eq. (2.24) becomes

$$\frac{Dc}{Dt} = D_b (\frac{\partial^2 c}{\partial r^2} + \frac{1}{r} \frac{\partial c}{\partial r}) + D_z \frac{\partial^2 c}{\partial z^2} + d(c) \tag{2.25}$$

where $\quad \frac{Dc}{Dt} = \frac{\partial c}{\partial t} + v \frac{\partial c}{\partial z}$ and $d(c) = -N \frac{DS}{Dt}$ $\tag{2.26}$

Equation (2.25) can be written

$$\frac{D(c+NS)}{Dt} = D_b\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) + D_z\frac{\partial^2 c}{\partial z^2} \tag{2.27}$$

Here N is the oxygen-bounding capacity of blood and S is the fraction saturation of oxygen given by Hill's equation as

$$S = \frac{Kp''}{1+Kp''} \tag{2.28}$$

where p is the partial pressure of oxygen in equilibrium with a solution of concentration c. But p is proportional to c, i.e.,

$$p = \frac{c}{\alpha}, \tag{2.29}$$

where α is the solubility constant. Now Eq. (2.27) becomes

$$\frac{D}{Dt}\left(c+N\frac{kc''}{1+kc''}\right) = D_b\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) + D_z\frac{\partial^2 c}{\partial z^2} \tag{2.30}$$

This is the required partial differential equation with convective term. For long capillary as compared with radius of capillary, we neglect axial diffusion and Eq. (2.30) can be written as

$$\frac{D}{Dt}\left(c+N\frac{kc''}{1+kc''}\right) = D_b\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) \tag{2.31}$$

which is the required partial differential equation in capillary region.

2.9.3 PDE and Bounder Conditions in Tissue Region

Let $c(r,z,t)$ be the concentration of oxygen and r be the radius of the tissue. We assume the diffusion equation to be axially-symmetric Cylindrical polar coordinate, Eq. (2.15) can be written as

$$\frac{\partial c}{\partial t} = D_t\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}\right), \tag{2.32}$$

where D_t is the diffusion coefficient for oxygen in the tissue. But Krogh Cylinder model in the tissue region, there is only diffusion of oxygen and there is consumption of oxygen by tissue cells.

Let $g(c)$ be the rate of consumption of oxygen per unit volume and usually assumed to follow Michaelis- Menten Kinetics. Then Eq. (2.32) becomes

$$\frac{\partial c}{\partial t} = D_t \left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r} \frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2} \right) - g(c) \tag{2.33}$$

By Michaelis-Menten Kinetics $g(c) = Ac/(B+c)$

If c is large, $g(c)$ can be taken to be constant $g_0 (say)$ and if c is small, it can be taken as kc.

If axial diffusion is neglected, Eq.(2.33) becomes

$$\frac{\partial c}{\partial t} = D_t \left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r} \frac{\partial c}{\partial r} \right) - g(c) \tag{2.34}$$

which is the required partial differential equation in tissue region.

Conclusion

In this chapter, we developed different kinds of diffusion equations and their simplification with convective and non-convective terms. Moreover, we discussed the partial diffusion equations in capillary and tissue region according to the Krogh Cylindrical model to determine the diffusion in the internal respiratory system.

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CHAPTER -3

Transference of Oxygen between Alveolus and Capillary

Summary

The effects of thickness of the membrane have been discussed for the pressure gradient of oxygen theoretically during pulmonary gas exchange. In both cases, the effects of linearity and non-linearity have been discussed. Result shows that the pressure gradient of oxygen has been decreased with the increasing of thickness of the respiratory membrane for constant solubility.

3.1 Introduction

The circulatory system performs a number of essential functions, such that delivery of nutrient, removal of waste products, mass transport, heat exchange, maintenance of fluid balance between blood and interstitium, etc. Oxygen is required for mammalian cell to support the metabolism process, but it cannot be obtained directly from the environment. As blood flow along the pulmonary capillary, oxygen diffuses from alveolus to capillary blood and its partial pressure gradient falls from alveolus to blood stream. On the other hand, carbon dioxide diffuses from blood stream to alveolus air. The composition of the alveolus air is not identical to the dry atmospheric air because (i) air entered to the respiratory system is humidified, (ii) oxygen diffuses from the alveolus to blood and carbon dioxide diffuses from blood to alveolus air and (iii) partial replace of alveolus air with atmospheric air during each inspiration is occurred.

Diffusion is the randomly movement of particles from a high concentration area to a low concentration area, i.e., more molecules leave the high partial pressure area to the low partial pressure area. However, the partial pressure of oxygen in the alveolar air is greater than that of capillary blood. A rate of oxygen diffusion across the respiratory membrane depends on thickness of the membrane, diffusion constant, surface area of the membrane and partial pressure difference.

Several researchers (Krogh, 1919; Longmuir et al., 1960; Grodins et al., 1954; Defares et al., 1960; Milhorn et al., 1965; Longobardo et al., 1966) studied the molecules of gas transport from alveolus to capillary through the respiring tissue. Krogh (1919) obtained the diffusion coefficient of oxygen through the non-respiratory tissue, which was a little lower than that of water. Longmuir et al. (1960) measured the diffusion coefficient of oxygen through the respiratory tissue, which was very similar to that of water. Krogh (1918) assumed that oxygen exchange takes place at the capillaries and described a model for longitudinal and radial gradients at the capillary and surrounding tissue, and provided significant insight the dynamics of oxygen delivery to the tissue. Milhorn et al. (1968) developed a theoretical model of pulmonary capillary gas exchange and venous admixture of human respiratory system. Moreover, he developed a model for pressure gradient in the capillary along the pulmonary capillary.

The process of pulmonary capillary oxygen uptake can be divided into two stages, namely (i) the diffusion of oxygen across the membrane and the plasma, (ii) the diffusion of oxygen into red cell combined with Hb. Conceptually, the total resistance for the oxygen uptake in this path way can be expressed as the algebraic sum of that due to the membrane segment and the RBC segment. Hsia et al. (1995) assumed that these two resistances are independent each other. In this content, we have discussed the effect of membrane during the diffusion process of oxygen through the alveolus-capillary membrane.

3.2 Oxyhemoglobin Dissociation Equations

The oxyhemoglobin dissociation curve describes how the blood carries and releases oxygen. It shows that the amount of oxygen is bounded to hemoglobin at various partial pressure of oxygen in blood and is determined by the hemoglobin affinity for oxygen. The relationship between the partial pressure and concentration of oxygen is developed by Cooney (1976) which is known as Hill equation. Mathematically this equation can be written as

$$c(p) = c_{max} \frac{p^n}{(p_0^n + p^n)} \qquad (3.1)$$

where c_{max} is the maximum value of the oxygen concentration in blood, p_0 is

the value of p at $c = \dfrac{c_{max}}{2}$ and n is the Hill's parameter.

Milhorn et al. (1968) expressed the empirical dissociation relations of oxygen when oxygen and carbon dioxide are simultaneously diffused between alveolus air and capillary blood as

$$c_{O_2} = \frac{1}{100}\left[20 - \exp\sum_{i=0}^{5} a_i p_{o_2}^i\right] + \alpha p_{o_2} \qquad (3.2)$$

where a_0, a_1, a_2, a_3, a_4, and a_5 are the functions of pCO$_2$. The values of the quantities within the range 60-40 mmHg are given in the Table 3.1.

Table 3.1. Values of a_0, a_1, a_2, a_3, a_4, and a_5 for different values of the partial pressures of carbon dioxide for oxyhemoglobin dissociation curve

pCO$_2$	a_0	$a_1 \times 10^3$	$-a_2 \times 10^3$	$a_3 \times 10^5$	$-a_4 \times 10^6$	$a_5 \times 10^8$
10	2.9921	-7.5852	1.3784	-2.8369	-1.3696	-1.2622
20	2.9952	3.6959	2.7301	6.1785	0.68663	0.30361
30	2.995	3.6021	2.3204	4.9006	-2.8396	0.19413
40	2.9957	2.6187	1.9484	3.7880	0.35291	0.12932
50	2.9957	1.6527	1.5995	2.6384	0.20046	0.059417
60	2.9957	3.7759	1.6227	2.7911	0.23294	0.080011
70	2.9958	4.0046	1.4807	2.3793	0.18820	0.063163

3.3 Oxygen Transfer between Alveolus and Capillary

Soluble gasses (oxygen, carbon dioxide, carbon monoxide, etc.) diffuse from alveolus to capillary or vise versa. Normally oxygen diffuses from alveolus to capillary as shown in the Fig.3.1. By Fick's law of diffusion, the diffusion rate of gas across the fluid membrane is proportional to the partial pressure difference and the area of the membrane and inversely proportional to the thickness of the membrane, i.e.,

$$\frac{dv}{dt} = -\frac{Ad}{x}\left(p_a - p\right) \tag{3.3}$$

where x, v, d and A represent the thickness of the membrane, the volume of gas, diffusion constant and total surface area respectively. Moreover, p_a is the partial pressure of gas in the alveolus and p is the partial pressure of gas at any point Q in the pulmonary membrane. The negative sign is taken, as alveolus loses gas.
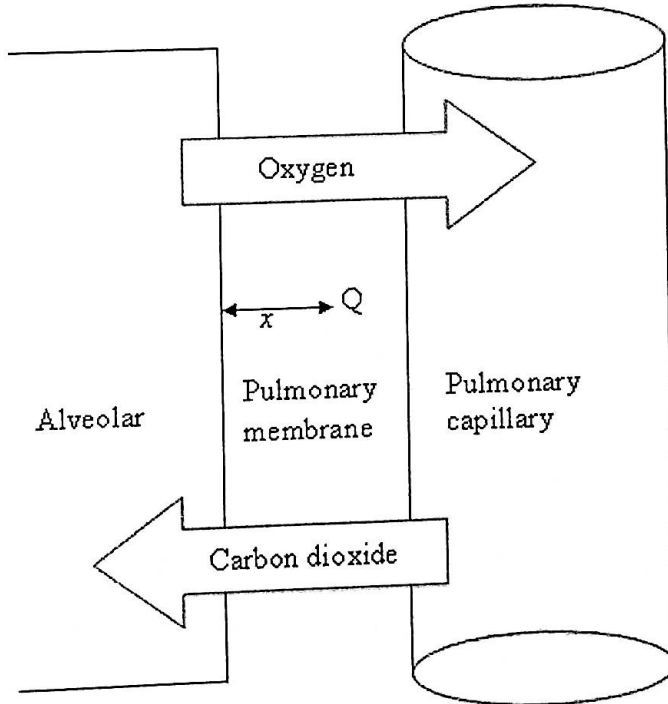
Fig. 3.1. Diffusion of oxygen and carbon dioxide through the alveolus-pulmonary capillary membrane

For simple passive diffusion of molecules, the net movement of diffusing molecules depends on concentration gradient and the rate of diffusion is directly proportional to the concentration gradient by the following expression:

$$\frac{dN}{dt} = PA\frac{dc}{dx} \qquad (3.4)$$

where c, N and P denote the concentration of a gas, number of molecular and permeability constants respectively. The permeability constant depends on the molecular size and lipid solubility. It is defined as the product of diffusion constant and solubility. It can be written as

$$P = \alpha d .$$

Middleman et al. (1972) obtained the solubility of oxygen in the tissue is similar to that of water. At a given temperature, volume of gas is proportional to the number of molecules, yields

$$v = c'N ,$$

where c' is proportional constant. Introducing this in Eq. (3.4), we have

$$\frac{dv}{dt} = Ac'\alpha d\frac{dc}{dx} \qquad (3.5)$$

Now compare the Eqs. (3.3) and (3.5), we get

$$\frac{1}{p_a - p}dc = -\frac{1}{c'\alpha}\frac{1}{x}dx \qquad (3.6)$$

Assume that the membrane is uniform width of thickness x, i.e., for adult healthy human the value of x lies between 0.5 μm and 1.0 μm.

Now integrating Eq. (3.6) in the limits from p_a to p and p_a to p_c when x varies from x_a to x and x_a to x_c respectivly, we get

$$\int_{p_a}^{p}\frac{1}{p_a - p}dc = -\frac{1}{c'\alpha}\int_{x_a}^{x}\frac{1}{x}dx \qquad (3.7)$$

$$\int_{p_a}^{p_c}\frac{1}{p_a - p}dc = -\frac{1}{c'\alpha}\int_{x_a}^{x_c}\frac{1}{x}dx \qquad (3.8)$$

Then from Eqs. (3.7) and (3.8), we obtain

$$\int_{p_c}^{p} \frac{1}{p_a - p} dc = -\frac{1}{c'\alpha} \int_{x_c}^{x} \frac{1}{x} dx \tag{3.9}$$

This is the required diffusion equation of oxygen. Now we can solve it for linear and nonlinear cases.

3.3.1 Linear System

In the linear case, we study the exchange of single gas through the wall of the microvascular. Let there be a single gas (oxygen) inside the alveolus and there exists a partial pressure gradient of this gas between alveolus and capillary. Hence this gas (oxygen) diffuses from alveolus to capillary according to the pressure gradient. Now using this relationship into Eq. (3.1) and put in Eq. (3.9), yield

$$c_{max} \int_{p_{c,O_2}}^{p_{O_2}} \frac{1}{p_{a,O_2} - p_{O_2}} \frac{n \, p_{O_2}^{n-1} \, p_{0,O_2}^{n}}{(p_{0,O_2}^{n} + p_{O_2}^{n})^2} dp = -\frac{1}{c'\alpha} \log \beta \tag{3.10}$$

where $x/x_c = \beta$ and $p(x_c) = p_{c,O2}$

Equation (3.10) can only be solved numerically using the values of the parameters.

3.3.2 Non-linear System

In linear case, we have discussed the exchange of single gas (say, oxygen) through the membrane. But in the lungs, oxygen exchanges from alveolus to pulmonary capillary and carbon dioxide transfers from pulmonary capillary blood to alveolus air. The relationship between concentration and partial pressure of the oxygen in blood is more complicated because the oxyhemoglobin dissociation curve depends on oxygen and carbon dioxide. Thus the partial pressure of oxygen is affected by the partial pressure of carbon dioxide (Haldane effect). Since the exchange of gas is continuous through the membrane and solubility of oxygen is same for membrane, plasma and red blood cell (Federspiel, 1989), so we can assume that the dissociation equation

of oxygen is same for blood and membrane, and these curves of two gases are affected each other in the membrane.
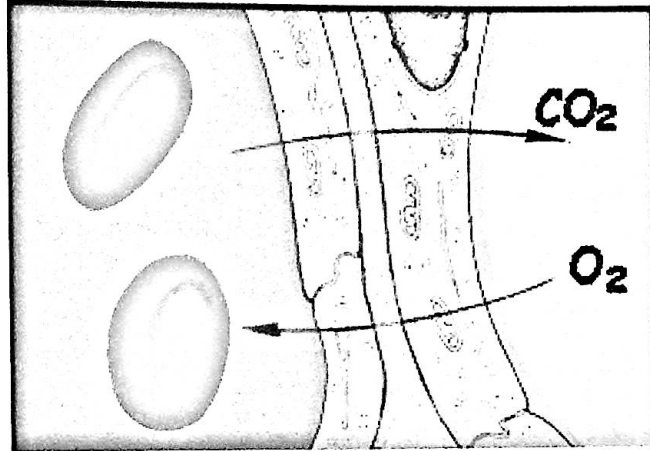
Fig. 3.2. Diffusion of oxygen and carbon dioxide between alveolus and capillary through the membrane (Source: Internet)

We have from Eqs. (3.2) and (3.9)

$$\int_{P_{c,O_2}}^{P_{O_2}} \frac{1}{p_{a,O_2} - p_{O_2}} dc_{O_2}(p_{O_2}, p_{CO_2}) = -\frac{1}{c'\alpha} \log\beta \qquad (3.11)$$

This diffusion equation of oxygen from alveolus to capillary is more complicated, so we can rearrange the above equation in the following form. Now we take the Eq. (3.11) and can be written as

$$\int_{P_{c,O_2}}^{P_{O_2}} \frac{1}{p_{a,O_2} - p_{O2}} \frac{\partial c_{O_2}(p_{O_2}, p_{CO_2})}{\partial p_{O_2}} dp_{O_2} + \int_{P_{c,O_2}}^{P_{O_2}} \frac{1}{p_{a,O_2} - p_{O_2}} \frac{\partial c_{O_2}(p_{O_2}, p_{CO_2})}{\partial p_{CO_2}} dp_{CO_2}$$

$$= -\frac{1}{c'\alpha} \log\beta \qquad (3.12)$$

After simplifying Eq. (3.12), we have

$$\left[\frac{2c_{O_2}}{p_{a,O_2} - p_{O_2}} \right]_{P_{o,O_2}}^{P_{O_2}} - \int_{P_{c,O_2}}^{P_{O_2}} \frac{c_{O_2}}{(p_{a,O_2} - p_{O_2})^2} dp_{O_2} = -\frac{1}{c'\alpha} \log\beta \qquad (3.13)$$

Equation (3.13) can be solved numerically using the values of parameters, whose values are given in the Table 3.2.

Table 3.2. The values of the parameters for the pressure gradient of oxygen

Values of Parameters	Sources
$p_{a.o2}$ = 103 mmHg	Milhorn (1968)
$p_{c,o2}$ = 40 mmHg (capillary blood)	Milhorn (1968)
α = 1.4 n mol-cm^{-3}mmHg^{-1}	Federspiel (1989)
n = 2.7	Cooney (1976)
p_0 = 27.2 mmHg	Cooney (1976)
c_{max} = 0.2 ml of O_2/ ml of blood	Cooney (1976)

3.4 Discussion

The mathematical formulations of pulmonary capillary gas transport have been developed to predict the partial pressure profile of oxygen across the pulmonary capillary membrane for both linear and nonlinear cases. Equation (3.3) suggests that there is a partial pressure difference between the two points in the membrane, otherwise diffusion does not occur. Krogh (1918) assumed that all oxygen exchange takes place at the capillaries. This model is described the pressure gradients of oxygen at the capillary and surrounding alveolus. We have developed a simple pressure gradient equation (Eq. (3.10)) for oxygen through a cell membrane. Our result shows that the partial pressure of oxygen changes in the pulmonary capillary and these pressure profiles of oxygen are exponentially decreased with the increasing of thickness of the membrane. The result also shows that the oxygen uptake depends on the partial pressure of oxygen in the alveolus, which is shown in Figs 3.3, 3.4, 3.5 and 3.6.
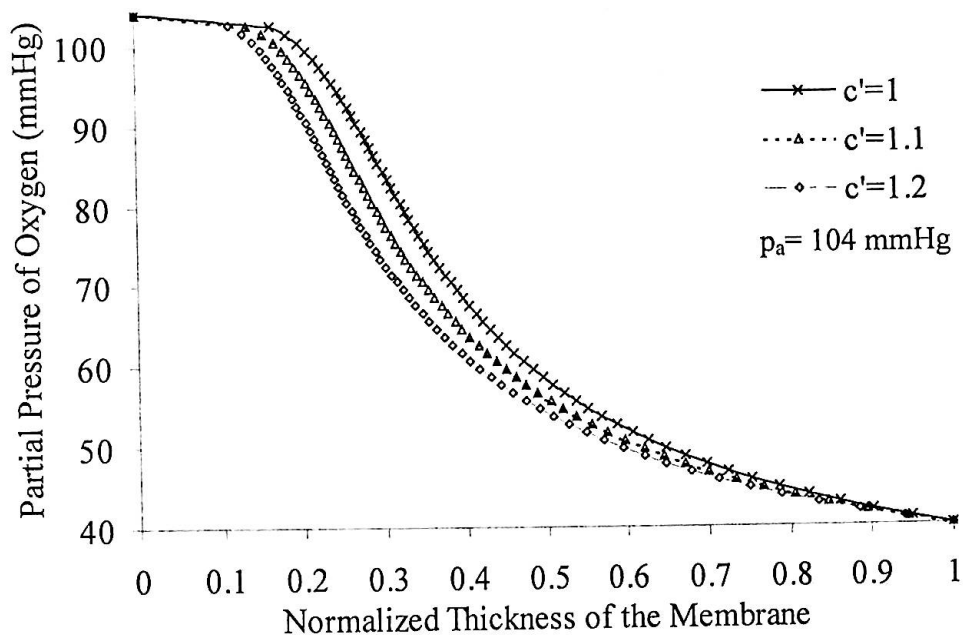
Fig.3.3. Partial pressure of oxygen versus normalized thickness of the membrane with different c'
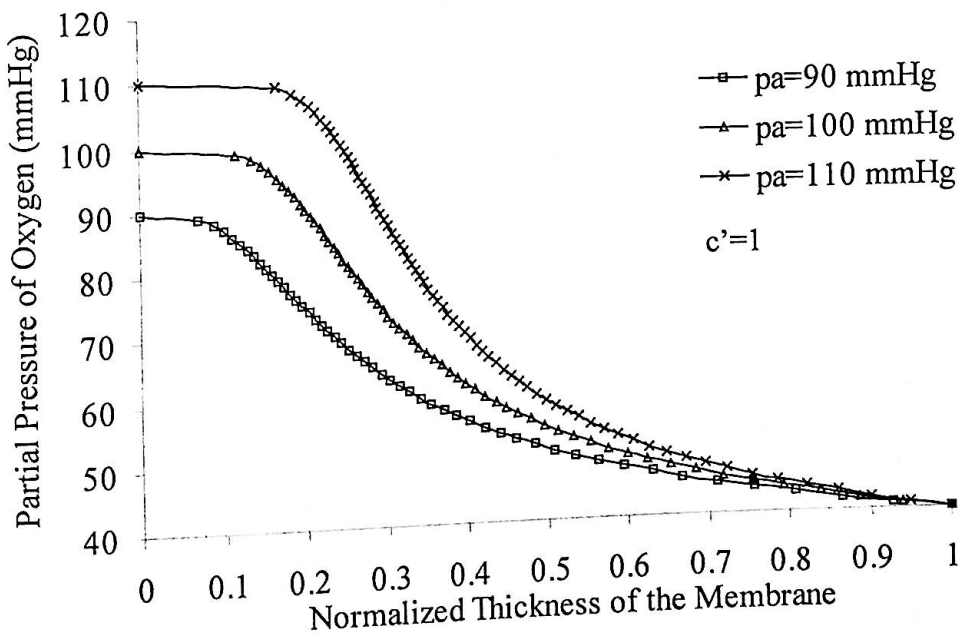
Fig.3.4. Partial pressure of oxygen versus normalized thickness of the membrane with different p_a

Figures 3.3 and 3.4 show that the pressure gradient of oxygen decreases with the increasing of pulmonary membrane thickness for the different values of proportional constant c' and the partial pressure of oxygen in the alveolus. Although alveolar and blood partial pressures of oxygen never reach in equilibrium position, but conveniently, it is considered that the partial pressure of oxygen reaches equilibrium position. The process of equilibrium of alveolus and capillary blood occurs within very short period.

The nonlinear case of oxygen and carbon dioxide is more difficult to study because (i) the dissociation curves of oxygen and carbon dioxide are nonlinear and (ii) oxygen and carbon dioxide are coupled in blood (Bohr and Haldane effects). The solution of the Eq. (3.13) for normal case, β is varied in increments between zero and unity is shown in Figs. 3.5 and 3.6. The difference of pO_2 between alveolus and capillary is taken as ranging from zero to unity.
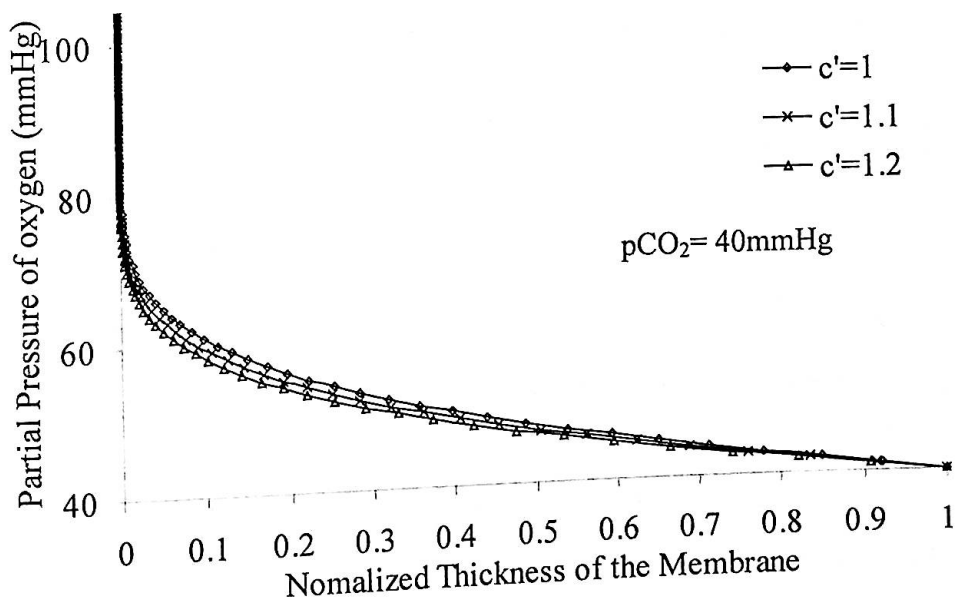
Fig. 3.5. Partial pressure of oxygen versus normalized thickness of the membrane for $pCO_2 = 40$ mmHg
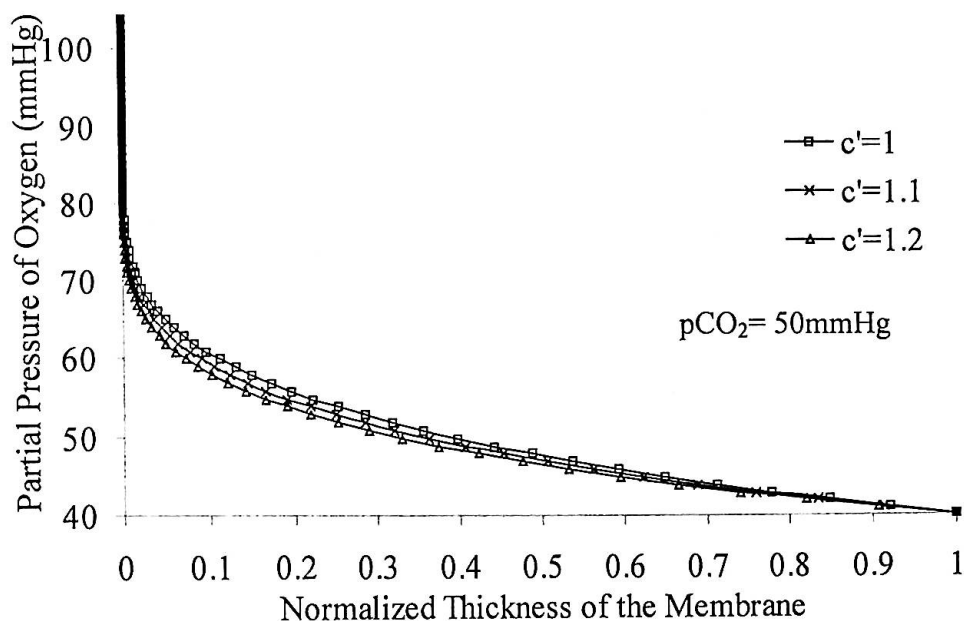
Fig. 3.6. Partial pressure of oxygen versus capillary normalized thickness of the membrane for pCO_2=50 mmHg

Figures. 3.5 and 3.6 also show that the pressure gradient of oxygen decreases exponentially with the increasing of pulmonary membrane thickness for different values of pCO_2. When pCO_2 affects the pO_2, the profiles of pO_2 are shown in Figs. 3.5 and 3.6 for different values of pCO_2 in nonlinear case.

Conclusion

A theoretical analysis was performed to establish the relationship between the partial pressure gradient of oxygen and the thickness of the membrane, when oxygen exchanges from alveolus air to capillary blood. The result of our calculation shows that the partial pressure profile of oxygen was decreased exponentially with increasing of the membrane thickness, when solubility was constant.

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CHAPTER-4

Oxygen Exchange along the Pulmonary Capillary

Summary

A mathematical model of oxygen diffusion along the pulmonary capillary pathway has been developed to predict the pressure profile of oxygen, when it diffuses from alveolar to capillary. Moreover, Bohr effect has been introduced in the model to find out the pressure profile of oxygen along the pulmonary capillary. The results of our calculation show that the partial pressure of oxygen increases with the increasing of the capillary length.

4.1 Introduction

Blood along the pulmonary capillary performs an essential function, it receives oxygen from the alveoli and becomes an oxygenated blood. This transfer of oxygen is occurred by diffusion from a higher to a lower partial pressure area and this diffusion process occurs into two stages, namely (i) due to the membrane segment and (ii) due to the RBC segment. The diffusion across the membrane accounts for both blood-gas tissue barrier and plasma fluid, and the oxygen transport across the RBC segment is the diffusion into red blood cell, where oxygen combines with hemoglobin called oxyhemoglobin. At the end of the artery of the pulmonary capillary, the difference of the partial pressure of oxygen between alveolus and blood is large, as a result oxygen diffuses into the blood and combines with hemoglobin. Thus oxygen partial pressure increases in the pulmonary capillary and reduces the pressure difference. We assume that

at the end of the venous of the capillary, alveolus oxygen partial pressure is equal to the partial pressure of oxygen in capillary.
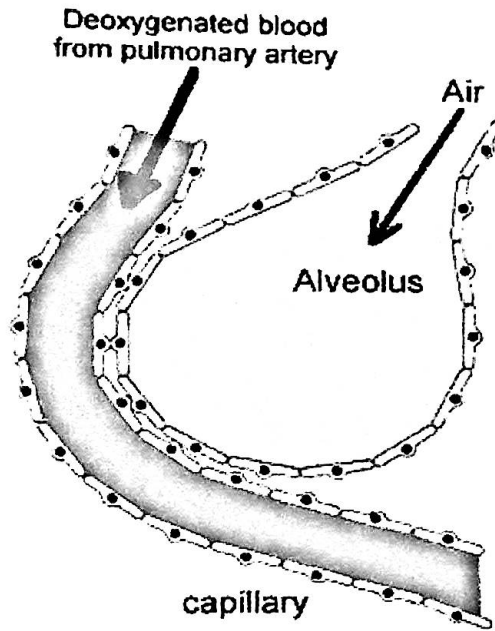
Fig. 4.1. Diffusion of oxygen along the pulmonary capillary (Source: Internet)

Several models of oxygen exchange through the pulmonary capillary were published (Milhorn et al., 1965; Milhorn and Guyton, 1965; Longobardo et al., 1966) using a simple approximation to account for the alveolus-capillary partial pressure difference. Milhorn et al. (1968) developed a model of pulmonary capillary gas exchange considering equilibrium position at the venous end of the pulmonary capillary. Hill et al. (1995) developed the partial pressure of oxygen along the pulmonary capillary by iterative procedures. But this procedure is more complicated. Chiari et al. (1997) developed a complex model assuming pO_2 at the venous end of the pulmonary capillary is equal to the alveolar pO_2. Brighenti et al. (2003) found an approximate solution of the capillary pO_2 profile considering a polynomial approximation of the oxygen hemoglobin dissociation curve using Hill's equation.

In this content, we discuss the pO_2 profile along the pulmonary capillary for simulation purposes using oxygen hemoglobin dissociation curve of oxygen in the pulmonary capillary under physiological conditions.

4.2 Assumptions

To develop a mathematical model of partial pressure of oxygen, we have considered the following assumptions based on Bohr hypotheses:

❖ The alveolus partial pressure of oxygen is constant,

❖ The shape and dimension of all capillaries are considered to be uniform,

❖ The flow rate of RBC is constant through all capillaries,

❖ The diffusing properties of the blood–gas barrier are constant and uniform along the capillaries.

4.3 Mathematical Formulation

The exchange of oxygen between the alveolus and the capillary can be described as the net rate of flow of gas across the surface of the thin cylinder and can be expressed as

$$\frac{dq}{dt} = D(p_A - p(x))dx \tag{4.1}$$

where p_A and p be the partial pressure of oxygen in the alveolus and blood of the capillary respectively. D is the diffusion capacity of blood.

According to the Fick's principle, the net rate of flow of gas across the cylinder must be equal to the blood flow and the gas concentration difference between the ends of the cylinder.

$$\frac{dq}{dt} = f\,dc \tag{4.2}$$

From Eqs. (4.1) and (4.2), we get

$$\frac{dc}{p_A - p(x)} = \frac{D}{f}dx \tag{4.3}$$

Now Integrating Eq. (4.3) from x_v to x and x_v to x_c then the limits of p become from p_v to p and p_v to p_c respectively.

$$\int_{p_v}^{p} \frac{dc}{p_A - p} = \frac{D}{f} \int_{x_v}^{x} dx \qquad (4.4)$$

and

$$\int_{p_v}^{p_c} \frac{dc}{p_A - p} = \frac{D}{f} \int_{x_v}^{x_c} dx \qquad (4.5)$$

where x_v and x_c represent the length of the capillary at artery and venous end of the capillary.

Combining Eqs. (4.4) and (4.5), we get

$$\int_{p_c}^{p} \frac{dc}{p_A - p} = \frac{D}{f} \int_{x_c}^{x} dx = \frac{D}{f}(x - x_c) \qquad (4.6)$$

This is the required equation to find out the partial pressure of oxygen in the pulmonary capillary.

4.3.1 Partial Pressure of Oxygen along the Capillary

The relationship between the partial pressure and the concentration of oxygen in the pulmonary capillary is defined by Hill (1976) as

$$c = c_b s_{Hb}(p) \qquad (4.7)$$

where c_b is the carrying capacity of blood at 100% saturation and the oxyhemoglobin saturation is described based on the Hill's definition.

$$S_{Hb}(p) = \frac{\left(p / p_{50}\right)^n}{1 + \left(p / p_{50}\right)^n} \qquad (4.8)$$

where p_{50} is the pO_2 at which hemoglobin is 50% saturation and n is Hill's constant.

Now simplifying Eqs. (4.6), (4.7) and (4.8), we have

$$x_c + \frac{nf}{p_{50}D}C_b \int_{p_v}^{p} \frac{\left(p/p_{50}\right)^{n-1}}{\left[1+\left(p/p_{50}\right)^n\right]^2 (p_A - p)} dp = x \qquad (4.9)$$

where x_c can be found from Eq. (4.5) and limit of partial pressure becomes from 40 mmHg to 104 mmHg. Thus

$$x_c = \frac{f}{D}\int_{40}^{104} \frac{dc}{p_A - p} \qquad (4.10)$$

where we have considered that the length of the capillary at the artery end is zero ($x_v = 0$), when partial pressure is 40 mmHg.

The Eq. (4.9) represents the partial pressure of oxygen along the pulmonary capillary gas exchange and this equation can be solved using Eq. (4.10).

The values of different parameters are chosen the under physiological conditions and summarized in the Table 4.1 for the pulmonary gas exchange.

Table 4.1. The normal values of the parameters whose are used in the model

Parameters	Values	References
D	8.5 ml.min^{-1}.mmHg^{-1}	Wagner (1972)
f	6 l.min^{-1}	Chiara (1997)
C_b	0.2 ml O_2/ml blood	Chiara (1997)
P_{50}	27.2 mmHg	Hill (1973)
n	2.6	Hill (1973)
p_A	104 mmHg	Milhorn (1968)
p_v	40 mmHg	Milhorn (1968)

4.3.2 Bohr Effect on Partial Pressure of Oxygen

But the situation is more complicated because oxygen and carbon dioxide are mixed together in blood. The partial pressure of carbon dioxide affects the

oxygen dissociation curve according to the Bohr effect (partial pressure of carbon dioxide influences the oxyhemoglobin dissociation curve).

Equation (4.3) can be generalized as

$$\frac{dc(p_{O_2}, p_{CO_2})}{p_A - p(x)} = \frac{D}{f} dx \tag{4.11}$$

Milhorn et al. (1968) expressed the empirical dissociation curve of oxygen by the fact of partial pressure of carbon dioxide as

$$c(p_{O_2}, p_{CO_2}) = \frac{1}{100}\left[20 - \exp \sum_{i=0}^{5} a_i p_{O_2}^i \right] + \alpha\, p_{O_2} \tag{4.12}$$

where α is the solubility of oxygen and $a_0, a_1, ..., a_5$ are the function of pCO$_2$. The values of these parameters are shown in the Table 4.1.

Now integrating and simplifying Eq. (4.11), we get

$$2\left[\frac{c}{p_A - p_{O_2}} \right]_{p_v}^{p} - \int_{p_v}^{p} \frac{c}{(p_A - p_{O_2})^2} dp_{O_2} = \frac{D}{f}\beta x_e \tag{4.13}$$

where $x = \beta x_e$, x_e is the capillary length, c is given by Eq.(4.12) and the Eq. (4.13) equation can be solved with the help of Eq. (4.12) and the values of a_i are taken from the Table 4.2 (Milhorn et al., 1968)

Table 4.2. Values of different parameters of a_1, a_2, a_3, a_4 and a_5

pCO$_2$	a_0	$a_1 \times 10^3$	$-a_2 \times 10^3$	$a_3 \times 10^5$	$-a_4 \times 10^6$	$a_5 \times 10^8$
10	2.9921	-7.5852	1.3784	-2.8369	-1.3696	-1.2622
20	2.9952	3.6959	2.7301	6.1785	0.68663	0.30361
30	2.995	3.6021	2.3204	4.9006	-2.8396	0.19413
40	2.9957	2.6187	1.9484	3.7880	0.35291	0.12932
50	2.9957	1.6527	1.5995	2.6384	0.20046	0.059417
60	2.9957	3.7759	1.6227	2.7911	0.23294	0.080011
70	2.9958	4.0046	1.4807	2.3793	0.18820	0.063163

4.4 Discussion

The mathematical model of the oxygen exchange through capillary has been studied and solved using the values of the parameters given in the Table 4.1.
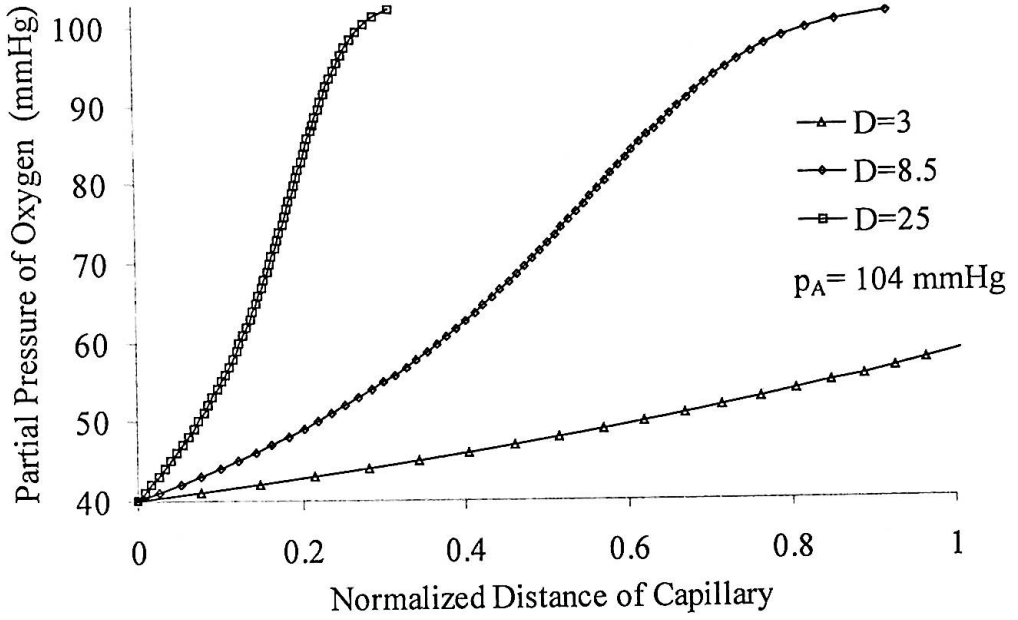
Fig. 4.2. Partial pressure of oxygen along the pulmonary capillary with the normalized distance for different diffusion coefficients
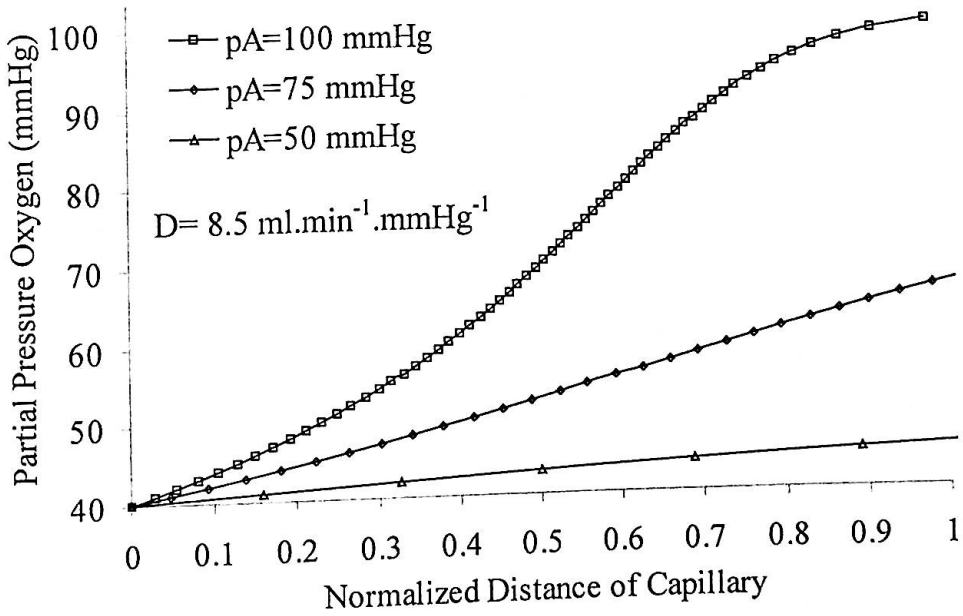
Fig. 4.3. Partial pressure of oxygen along the pulmonary capillary with the normalized distance for different alveolus partial pressures

The model of pulmonary capillary gas exchange was studied theoretically to predict the partial pressure profile of oxygen along the pulmonary capillary represented in Figs 4.2 and 4.3, derived from Eq. (4.9). In Figs. 4.2 and 4.3, the pressure gradient of oxygen increases with the increasing of the length of pulmonary.

Figures 4.2 and 4.3 also show that the pressure profile of oxygen is dominated by both diffusion capacity and alveolus partial pressure of oxygen. Firstly, normal values of the perimeters in alveolus and pulmonary capillary have been used from given the Table 4.1, while the diffusing capacity of the alveolus-capillary membrane has been assumed to be equal to 8.5 and 3 (abnormal and grossly abnormal diffusing capacity respectively). Secondly, the approach is tested considering the normal values of D, p_v and varying p_A from normal to reduced values.

Figure 4.2 shows that the partial pressure of oxygen reaches equilibrium position quickly for large value of diffusion coefficient, i.e., the partial pressure of oxygen equilibrium repeatedly as fast as diffusion process.
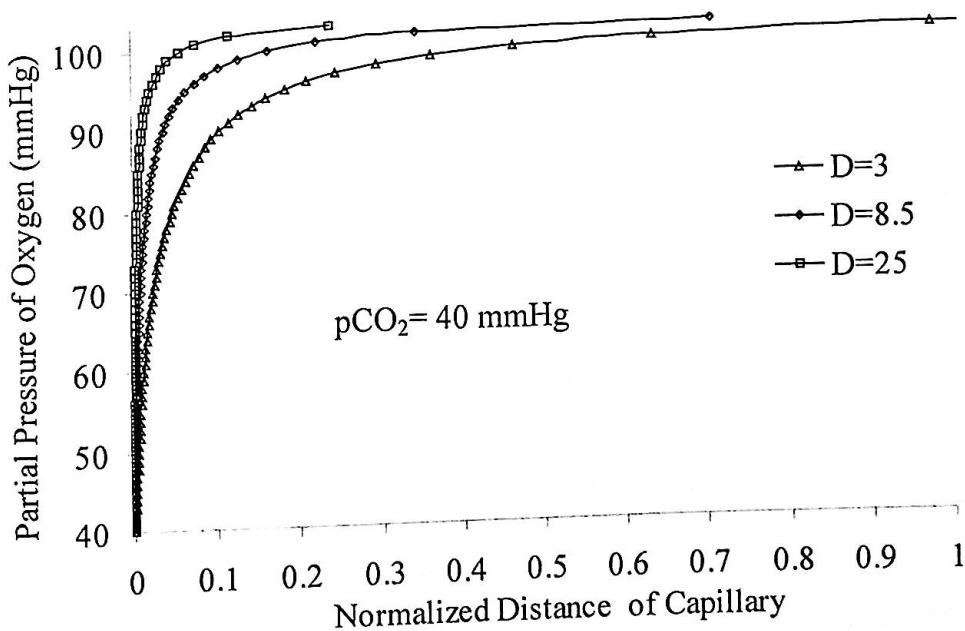
Fig. 4.4. Partial pressure of oxygen along the capillary with the normalized distance of the capillary in different diffusion coefficients for pCO_2= 40 mmHg

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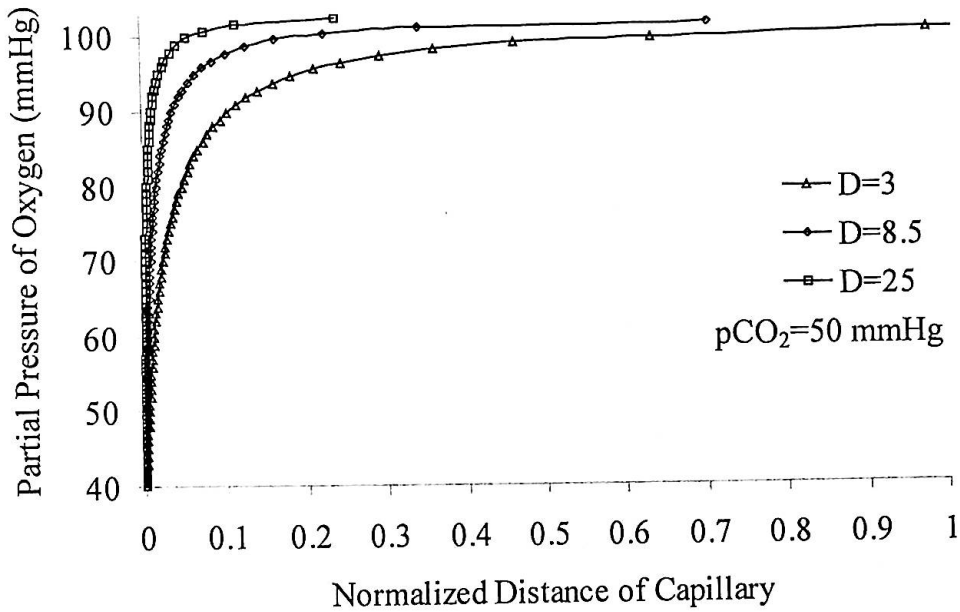
Fig. 4.5. Partial pressure of oxygen along capillary with the normalized distance of the capillary in different diffusion coefficients for $pCO_2 = 50$ mmHg

For complicated case, the effects of the partial pressure of carbon dioxide on that of oxygen are shown in the Figs. 4.4 and 4.5. The pressure profiles of oxygen are shown including the effects of partial pressure of oxygen at 40 mmHg and 50 mmHg.

Moreover, result also shows that the partial pressure depends on the diffusion coefficient. Figures 4.4 and 4.5 show that the partial pressure of oxygen increases repeatedly at initial stages and after that becomes approximately constant with increasing of capillary length along the pulmonary capillary.

Conclusion

A theoretical study of mathematical model of gas exchange was presented, considering the fact that the partial pressure of oxygen at the venous end of the pulmonary capillary and alveolus are same. The result has shown that the profile of pO_2 was increased with the increasing of capillary length. Moreover,

we calculated the pO_2 for complex phenomena on the basis of Bohr effect, which shows that the pO_2 reaches equilibrium approximately at the middle of the capillary.

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CHAPTER- 5

Estimation of Molar Flux of Oxygen in Capillary

Summary

The chapter is concerned with the molar flux of oxygen in the capillary when oxygen diffuses from blood to tissue fluid at the middle section of the capillary bed. The result shows that the molar flux decreases exponentially with the increasing of radial thickness of the capillary. Moreover, it is found that the molar flux of oxygen increases linearly with the increasing of diffusion coefficient of oxygen.

5.1 Introduction

Capillary-tissue fluid exchange occurs in capillary bed where blood and tissue fluids are in proximity enclosed by endothelial cell layer that surrounds all the cells in the body. Blood moves away from the heart, branching off from arteries in arterioles, and then into capillaries, where oxygen and nutrient enter to the tissue fluid from the blood, and carbon dioxide and urea leave the tissue fluid to the blood.

The transport of molecules (oxygen and nutrients) from capillary blood to tissue fluid through the capillary wall is based on the Krogh's cylinder model (Krogh, 1919). The assumptions are, all capillaries and surrounding tissue are equal diameters and they are homogeneously dispersed in the tissue. Transport of oxygen in the capillary region depends on convection, diffusion and rate of

generation of oxygen due to the dissociation of oxyhemoglobin. In the tissue region, there is diffusion of oxygen and the tissue cells consume oxygen. Bird et al. (1960) suggested that temperature gradient and external force also contribute to the diffusion flux, although their effects are usually minor. Brid et al. (2002) also suggested that Fick's equation evaluates the diffusion as a flux measured with respect to the motion of the center of mass, since Fick's law equates diffusion to a gradient relative to the external coordinates. Due to the low Peclet number in capillary blood flow, convective transport can be neglected (Aroesty et al., 1970). Ellsworth et al. (1987) developed the method of the determination of oxygen saturation in red blood cells for use in capillaries in striated muscle but should be generally applicable to the measurement of capillary oxygen saturation in other tissues.

From the above literature, we can see that all the study of molar flux regarding oxygen diffusion concentrated experimentally. But we attempt to solve oxygen diffusion at the middle section of capillary bed theoretically where blood pressure and osmotic pressure of blood are equals and materials such as oxygen, nutrients are moved by diffusion.
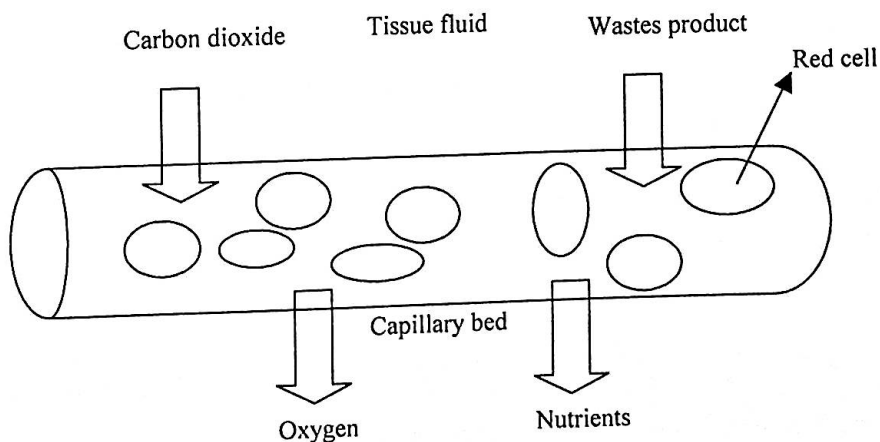
5.2 Capillary-tissue Fluid Exchange

Fig. 5.1. Fluids exchange across the capillary wall between capillary and tissue

Capillary-tissue fluid exchange occurs through a membrane that is one cell thick and allows for rapid diffusion of molecules from blood to tissue fluid and tissue fluid to blood depending on the concentration gradient. Blood pressure and osmotic pressure (the osmotic pressure is due to the plasma proteins) of blood are the major factors for diffusion of molecules. Fluid exchange occurs at three steps. These are:

At the arterial end of the capillary, blood pressure is greater than the osmotic pressure of blood in this region. Thus the result is the net movement of fluid (blood plasma) from the capillary into the tissue fluid. That is, blood discharges oxygen and nutrients like amino acid and glucose in the plasma. The high blood pressure pushes fluid including oxygen, water, amino acid and glucose into the tissue fluid. Large molecular like red blood cell and plasma proteins cannot cross into the tissue.

Blood pressure is equal to the osmotic pressure of blood at the middle of a capillary bed and there is no net movement of fluid from blood to tissue fluid. But nutrients and wastes move with their concentration gradients, which move high concentration to low concentration area. In this area, oxygen and nutrients are in high concentration in the blood and they diffuse from capillary to tissue fluid through the capillary wall. On the other hand, carbon dioxide and other water cells are in high concentration in the tissue fluid than capillary bed, as a result they diffuse from tissue fluid to the capillary bed.

At the venous end of the capillary bed, osmotic pressure of blood is greater than the blood pressure and the result is a net movement of tissue fluid back to the blood. Thus additional amounts of dissolved carbon dioxide, urea, uric acid and other tissue fluid move from tissue fluid to capillary bed.

5.3 Mathematical Formulation

Oxygen transport in the capillary is occurred by passive diffusion. According to Krogh's cylinder model in capillary region, the transport of oxygen depends on

diffusion, convection, and rate of generation of oxygen to the dissociation of oxyhemoglobin. The mathematical expression of above model becomes

$$\frac{Dc}{Dt} = D_b\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}\right) + d(c) \tag{5.1}$$

where c is the concentration of oxygen, D_b is the diffusion coefficient of oxygen in blood as the harmonic mean of hemoglobin and plasma diffusion coefficients. $d(c)$ be the rate of generation of oxygen to the dissociation of oxyhemoglobin. $\dfrac{D}{Dt}$ stands for connective derivative expressed as

$$\frac{D}{Dt} = \frac{\partial}{\partial t} + v\frac{\partial}{\partial z}$$

where v is the velocity of the blood.

But rate of generation of oxygen to the dissociation of oxyhemoglobin can be expressed as

$$d(c) = -N\left(\frac{DS}{Dt}\right) \tag{5.2}$$

where N is the oxygen bounding capacity of blood, and S is the oxygen saturation. By Hill's equation for oxygen saturation (S) in terms of partial pressure (p) is

$$S = \frac{p^n}{p^n + p_{50}^n} \tag{5.3}$$

where p is the partial pressure of oxygen and $p^n{}_{50}$ denotes the partial pressure at 50 % oxyhemoglobin saturation. Considering normal human blood at 37^0C and $p^H = 7.4$, the derived constant p_{50} is 26 mmHg and n is 2.7.

The relation between partial pressure and concentration of a dissolved gas in the liquid is described, called Henry's law, i.e.,

$$c = \alpha\, p \tag{5.4}$$

where α is solubility coefficient.

After simplifying Eqs. (5.3) and (5.4), we obtain

$$S = \frac{c^n}{c^n + (\alpha p_{50})^n} \tag{5.5}$$

Therefore Eq. (5.1) becomes

$$\frac{D}{Dt}\left(c + N\left(\frac{c^n}{c^n + (\alpha p)^n}\right)\right) = D_b\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r} + \frac{\partial^2 c}{\partial z^2}\right) \tag{5.6}$$

Due to the low Peclet number in capillary blood flow, we can neglect the convective transport. Axial diffusion also is neglected because of the ratio of the magnitude of the term containing axial diffusion and the magnitude of the term containing radial diffusion is usually very less than one. Then Eq. (5.6) becomes

$$\frac{\partial}{\partial t}\left(c + N\left(\frac{c^n}{c^n + (\alpha p_{50})^n}\right)\right) = D_r\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) \tag{5.7}$$

where D_r is the radial diffusion coefficient of oxygen.

The concentration gradient is obtained from Eq. (5.7) as steady state case, i.e, neglecting the time dependent terms, we get

$$D_r\left(\frac{\partial^2 c}{\partial r^2} + \frac{1}{r}\frac{\partial c}{\partial r}\right) = 0 \qquad \text{where} \quad r_0 \leq r \leq r_i \tag{5.8}$$

We can find the concentration gradient from Eq. (5.8) by using the following boundary conditions

$$c = c_0 \quad \text{at } r = r_0$$

$$c = c_i \quad \text{at } r = r_i$$

where c_o and c_i are the concentrations of oxygen at r_o and r_i respectively. After simplifying Eq. (5.8) and using the boundary conditions, we obtain

$$\frac{\partial c}{\partial r} = \frac{c_0 - c_i}{r \log\frac{r_0}{r_i}} \tag{5.9}$$

We can obtain the molar flux (J_r) in the capillary blood by using the Fick's first law of diffusion which is proportional to concentration gradient. That can be expressed as

$$J_r = -D_r \frac{\partial c}{\partial r}$$

The negative sign indicates that the concentration increases in the opposite direction of net molar flux. Thus

$$J_r = -D_r \frac{c_0 - c_i}{r \log \frac{r_0}{r_i}} \tag{5.10}$$

Since all capillaries are of equal diameter, so we integrate both sides of Eq. (5.10) from r_0 to r_i, yielding

$$J_r = \frac{D_r}{r_i - r_0}(c_0 - c_i)$$

or, $$\frac{J_r}{(c_0 - c_i)} = \frac{D_r}{r} \tag{5.11}$$

This is the required model for finding the molar flux verses concentration in the capillary taking $r_i - r_0 = r$.

5.4 Results

The molar flux of oxygen in the capillary blood has been studied theoretically. We considered the partial differential equation for capillary region and neglected convective team (the axial diffusion of oxygen from this equation based on small Peclet number) and Fick's first law that produced Eq. (5.11). Figure 5.2(a), which is derived from Eq. (5.11), shows the molar flux ($J_r/(c_0-c_i)$) decreases with the increasing of radial distance of the capillary. On the other hand, Fig. 5.3 shows that the molar flux increases linearly with the increasing of diffusion coefficient. Figure 5.2 shows that $J_r/(c_0-c_i)$ tends to zero at $r \to \infty$ whereas $t=0$ it does not exist. Otherwise, if $(c_0-c_i) = 0$ i.e., there is no concentration difference then Eq. (5.11) shows that, there is no molar flux along the capillary. This suggests that there must be concentration difference, implying that partial pressure difference (by Henry's law) for diffusion of oxygen (gas), otherwise diffusion does not occur.
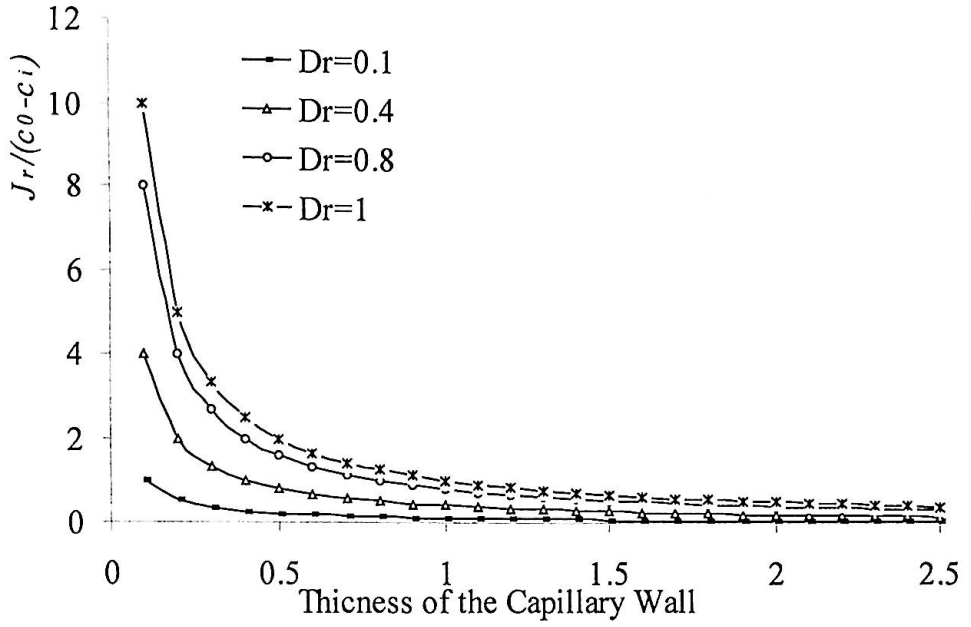
(a)
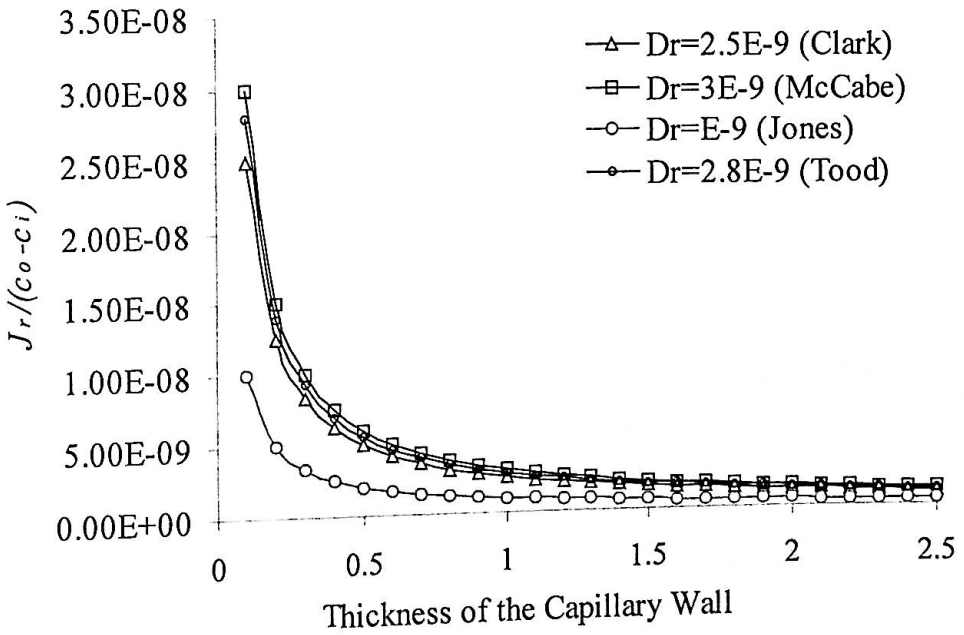
(b)

Fig. 5.2. Effect of radial distance on molar flux for different values of diffusion coefficient
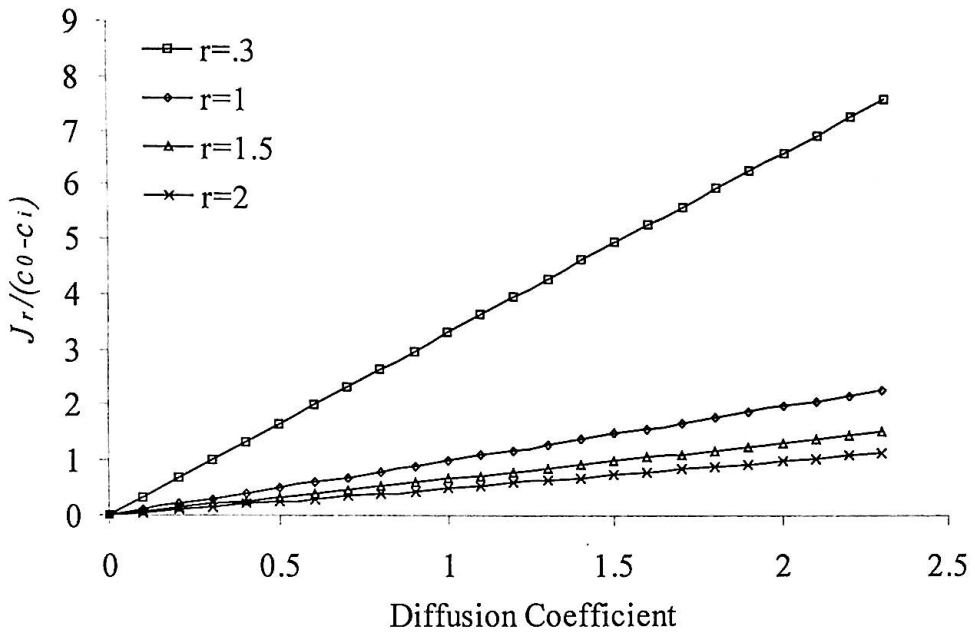
Fig. 5.3. Effect of diffusion coefficient of oxygen on molar flux

We can, therefore, conclude the effect of the radial distance of the capillary on the expression $J_r/(c_0-c_i)$, since it is inversely proportional to the radius. Equation (5.11) also suggests that for diffusion, there must be a membrane between the two media, since Eq. (5.11) does not exist at $r = 0$.

In general, the diffusion coefficient of oxygen through tissue appeared to be equal to that of water by the fraction of the tissue composed of water. Several researchers (Rashevsky (1933), Jones and Kennedy (1982), Jones (1988), Clark (2006), etc.) used different values of diffusion coefficient that are mentioned in the Table 5.1.

Table 5.1. Different values of diffusion coefficients of oxygen in different tissues by several researchers

Diffusion Coefficient For	Values	Researchers
Tissue during hypoxia	$7 \times 10^{-12}\,\mathrm{m^2 s^{-1}}$	Jones and Kennedy (1982)
Water	$2.8 \times 10^{-9}\,\mathrm{m^2 s^{-1}}$	Hewtt (1998)
Blood	$1.8 \times 10^{-9}\,\mathrm{m^2 s^{-1}}$	Hewtt (1998)
Tissue	$10^{-9}\,\mathrm{m^2 s^{-1}}$	Jones (1986)
Bovine & murine cumulus oocyte	$2.5 \times 10^{-9}\,\mathrm{m^2 s^{-1}}$	Clark (2006)
Protoplasm	$11.66 \times 10^{-9}\,\mathrm{cm^2 min^{-1}}$	Rashevsky (1933)
Nafion membrane 1	$5.8692 \times 10^{-7}\,\mathrm{cm^2 s^{-1}}$	Haug (2000)
Nafion membrane 2	$6.4306 \times 10^{-7}\,\mathrm{cm^2 s^{-1}}$	Haug (2000)
Cape cod membrane 1	$4.2231 \times 10^{-7}\,\mathrm{cm^2 s^{-1}}$	Haug (2000)
Cape cod membrane 2	$3.9445 \times 10^{-7}\,\mathrm{cm^2 s^{-1}}$	Haug (2000)

Conclusion

This chapter represented the molar flux of oxygen in the capillary blood flow at the middle section of the capillary bed. Result highlighted that the molar flux decreased exponentially with the increasing of radial thickness of the capillary. Moreover, it was found that the molar flux had increased linearly with the increasing of diffusion coefficient.

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CHAPTER-6

Determination of Oxygen Consumption Rate

Summary

This chapter is focused on the oxygen consumption of the microvascular wall. To determine the consumption of oxygen of the vascular wall, we have determined the intravascular flux and perivascular flux of oxygen of the microvascular. We have found that the maximum consumption rate of oxygen increases rapidly at initial stages after that it decreases with the increasing of wall thickness. Moreover, the result indicates that the pressure profile of oxygen along the wall is approximately linear with the increasing of thickness of the capillary wall.

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6.1 Introduction

One important property of blood is oxygen delivery to the tissue. This transport is occurred through arterioles wall from blood to tissue by diffusion process. This process is studied primarily in microvascular that regulates blood flow and diffusion occurs through the wall. Since at the middle section of the capillary bed, oxygen diffuses into the tissue according to pressure difference of oxygen between blood and tissue, so we have discussed this taking microvascular.

The transport of oxygen from blood plasma to tissue through arterioles wall is based on the Krogh's model (Krogh, 1919). The assumptions are, all capillaries are equal diameters and they are homogeneously dispersed in the tissue. Brid et al. (2002) also suggested that Fick's equation evaluates the diffusion as a flux

measured with respect to the motion of the center of mass. Several researchers (Duling, 1972; Ellsworth et al., 1990; Intaglietta et al., 1996; Bertuglia et al., 2003) discussed the diffusion process in the microvascular and shown that diffusion occurred in the arterioles. Diffusion of oxygen is also occurred in the arterioles provided (Duling, 1970). Vascular wall consumption and intravascular flux of oxygen were estimated by Vadapalli et al. (2000). Tsai et al. (1998) showed in mass balance analysis that oxygen consumption in the microvascular wall causes the oxygen loss from the arterioles in this vascular bed.

Shibata et al. (2005) showed the oxygen consumption rate across the arteriole wall using physiological parameters. Oxygen transport and consumption rate along the skeletal muscle were studied and showed that average oxygen consumption rate is a function of demand (McGuire et al., 2001).

In this chapter, we have used cylindrical model to discuss the pressure profile and consumption rates along the microvascular wall. This model is used to discuss the intravascular, perivascular fluxes and range of oxygen consumption under high demand of oxygen.

6.2 Microvascular

Harvey (1928) stated that blood passes through microscopic channels in circulating from artery to vein. The microvascular is the blood vessels too small to be seen with naked eye and the network of its tiniest blood vessels-arterioles, capillaries and venules. It supplies oxygen and nutrients and removes carbon dioxide and additions waste products from every part of the human body. The network specialized the movement of substances between blood and tissue with a low metabolic rate such as mesentery, hamster cheek and resting skeletal muscle oxygen loss from blood to tissue is largely in the arteriolar network.
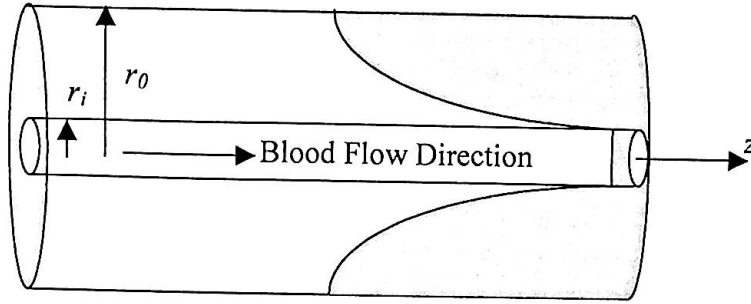
Fig 6.1. Geometry type model of microvascular, inner cylinder represents capillary lumen

6.3 Mathematical Model

The oxygen diffusion model on the capillary wall is represented as one-dimensional diffusion equation by neglecting the convective term and the gas diffuses through the tissue without source or sink.

$$\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial p}{\partial r}\right)=\frac{A_w}{d_w} \tag{6.1}$$

where D_w and A_w are the Krogh diffusion coefficient and oxygen consumption in the wall respectively.

The general solution of Eq. (6.1) is found as

$$p=\frac{A_w}{4D_w}r^2+a\ln r+b \tag{6.2}$$

We consider r_i and r_0 as the inner and outer radii of the microvascular, and p_i and p_0 be the pressure of oxygen at r_i and r_0 respectively.

$p=p_i$ at $r=r_i$

and $p=p_0$ at $r=r_0$

Introducing boundary conditions in Eq. (6.2), we get

$$p=\frac{A_w}{4D_w}\left(r^2-r_i^2\right)+\left[\left(p_i-p_0\right)+\frac{A_w}{4D_w}\left(r_0^2-r_i^2\right)\right]\frac{\ln\dfrac{r}{r_i}}{\ln\dfrac{r_i}{r_0}}+p_i \tag{6.3}$$

Therefore, intravscular flux $J_i = -D_w \left.\dfrac{\partial p}{\partial r}\right|_{r_i}$ can be found by differentiating Eq. (6.3) with respect to r as

$$J_i = \frac{D_w(p_i - p_0)}{r_i \ln \dfrac{r_0}{r_i}} - A_w \left[\frac{r_i}{2} - \frac{r_0^2 - r_i^2}{4 r_i \ln \dfrac{r_0}{r_i}} \right] \tag{6.4}$$

and perivascular flux $J_0 = -D_w \left.\dfrac{\partial p}{\partial r}\right|_{r_0}$ is found by differentiating Eq. (6.3) with respect to r as

$$J_0 = \frac{D_w(p_i - p_0)}{r_0 \ln \dfrac{r_0}{r_i}} - A_w \left[\frac{r_0}{2} - \frac{r_0^2 - r_i^2}{4 r_0 \ln \dfrac{r_0}{r_i}} \right] \tag{6.5}$$

From Eqs. (6.4) and (6.5), we can express A_w as

$$A_w \left(r_0^2 - r_i^2 \right) = 2 r_i J_i - 2 r_0 J_0 \tag{6.6}$$

For a cylindrical segment of blood vassal with a lumenal radius r_i and length Δz, the diffusive loss of oxygen can be estimated as

$$Q[Hb]c_b \frac{\Delta s}{\Delta z} = 2\pi r_i J_i \tag{6.7}$$

where $Q = \pi r_i^2 v$ is the volumetric blood flow rate, v is the mean velocity, [Hb] is the hemoglobin concentration in the blood, c_b is the binding capacity of the hemoglobin, Δs is the saturation difference between the upstream and downstream points along the vessel segment.

The diffusive flux into the tissue is given the boundary condition at the capillary wall as

$$2\pi r_0 J_0 = M_t \left(p_i - p_0 \right) \tag{6.8}$$

where M_t is the mass transfer rate.

After simplifying Eqs. (6.6) and (6.8), we obtain

$$A_w = \frac{1}{\pi\left(r_0^2 - r_i^2\right)} \left[2\pi r_i J_i - M_t\left(p_i - p_0\right)\right] \tag{6.9}$$

From Eq. (6.6), we can obtain maximum consumption of the wall, if all of the oxygen diffusing from lumen is consumed by the wall, i.e., $J_0=0$. Thus

$$\left(A_w\right)_{max} = \frac{2r_i J_i}{\left(r_0^2 - r_i^2\right)} \tag{6.10}$$

Now from Eq. (6.9), we have

$$p_0 = \frac{M_t p_i - 2\pi r_i J_i}{M_t} + \frac{A_w \pi}{M_t}\left(r_0^2 - r_i^2\right) \tag{6.11}$$

Since $p_0 \geq 0$, then Eq. (6.11) can be possible for two cases, where third term of Eq. (6.11) must be positive.

Case 1: $\quad p_i > \dfrac{2\pi r_i J_i}{M_t}$

Case 2: $\quad p_i \leq \dfrac{2\pi r_i J_i}{M_t}$

Case 1 occurs for $p_0 \geq 0$ when A_w varies 0 to $(A_w)_{max}$, i.e., $0 \leq A_w \leq (A_w)_{max}$ then $(p_0)_{min} \leq p_0 \leq (p_0)_{max}$. Then we can get $(p_0)_{min}$ when $A_w=0$ and $(p_0)_{max}$ when $A_w=(A_w)_{max}$ which is obtained in Eq.(6.11). Thus

$$\left(p_0\right)_{min} = p_i - \frac{2\pi r_i J_i}{M_t}$$

and $\quad \left(p_0\right)_{max} = p_i$

Case 2 occurs for $p_0 \geq 0$ when A_w varies from $(A_w)_{min} \leq A_w \leq (A_w)_{max}$ then $0 \leq p_0 \leq (p_0)_{max}$. Then we can get $(A_w)_{min}$ when $p_0=0$ and $(A_w)_{max}$ when $p_0=(p_0)_{max}=p_i$

$$\left(A_w\right)_{min} = \frac{2\pi r_i J_i - M_t p_i}{\pi\left(r_0^2 - r_i^2\right)} \tag{6.12(a)}$$

$$\left(A_w\right)_{max} = \frac{2r_i J_i}{r_0^2 - r_i^2} \tag{6.12(b)}$$

The above expressions represent the minimum and maximum consumption rates of oxygen of the microvascular wall in terms of radii of the

microvascular. The inconsistency of the consumption rates of the microvascular wall can be found as

$$\left(A_w\right)_{max} \Big/ \left(A_w\right)_{min} = \frac{2\pi r_i J_i}{2\pi r_i J_i - M_t(p_i - (p_0)_{min})} \tag{6.13}$$

The ratio of the maximum and minimum consumption rates represents the inconsistency in terms of radius of the microvascular.

6.4 Calculations

We have presented the consumption rate of oxygen of the microvascular wall using the values of the parameters under physiological conditions summarized in the Table 6.1.

Table 6.1. Summary of parameter values used in the models

Parameters	Values	References
p_i	100 mmHg	McGuire (2001)
D_w	9.4×10^{-10} ml O_2.cm^{-1}.s^{-1}mmHg^{-1}	Bentley (1993)
r_i	2 μm	McGuire (2000)
r_0	2.5 μm	McGuire (2001)
M_t	6.8×10^{-8} ml O_2.cm^{-1}.s^{-1}mmHg^{-1}	Murphy (2002)
A_w	1.5×10^{-3} ml O_2.ml^{-1}.s^{-1}	Kjellstrom (1987)
J_i	8.0×10^{-7} ml O_2.cm^{-2}.s^{-1}	Ellsworth (1988)

The partial pressure of oxygen across the microvascular wall is presented in the Fig. 6.2, derived from Eq. (6.3). This Fig. 6.2 shows that partial pressure of oxygen is approximately linearly decreased with the increasing of thickness of the wall measured from the inner side of the wall. The maximum and minimum partial pressures of oxygen on outer side of the wall are determined and those

values are compared with Ellsworth (1988) and Stein (1996) who found the same result for capillary, shown in the Table 6.2.
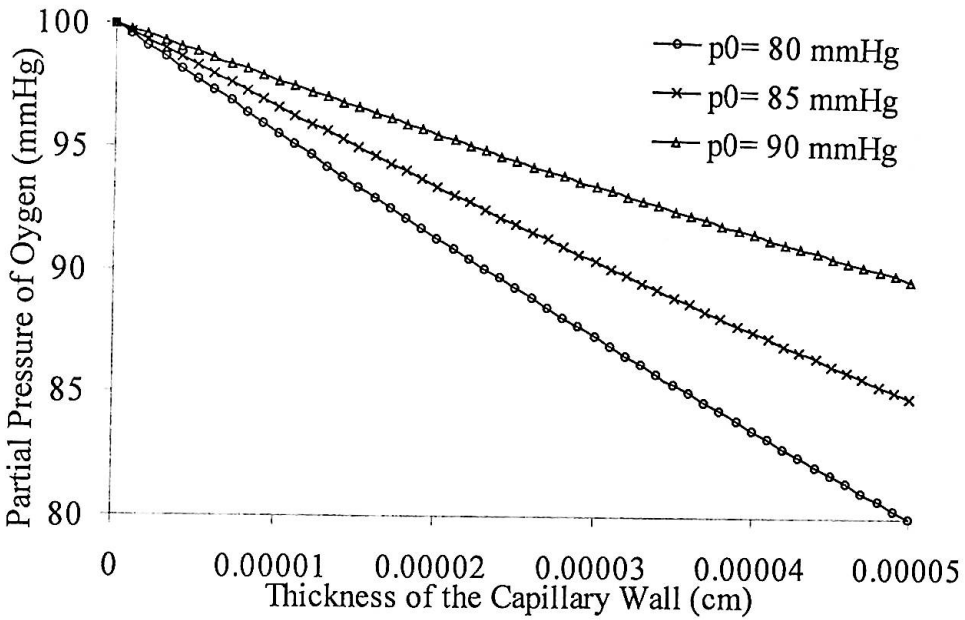

Fig 6.2. Partial pressure of oxygen across the wall over thickness of the wall

Table 6.2. Maximum and minimum partial pressures of oxygen at the outer side of the wall.

$(p_0)_{max}$ mmHg	$(p_0)_{min}$ mmHg	References
30.02	29.99	Ellsworth (1988)
33.05	33.01	Stein (1992)
30.02	30.005	Model (Author)
33.05	33.035	Model (Author)

The effect of the thickness of the capillary wall on consumption of oxygen has been also determined theoretically. The first case is physiological possible, since $(p_0)_{min}$ and $(p_0)_{max}$ are positive and p_0 increases as A_w increasing.
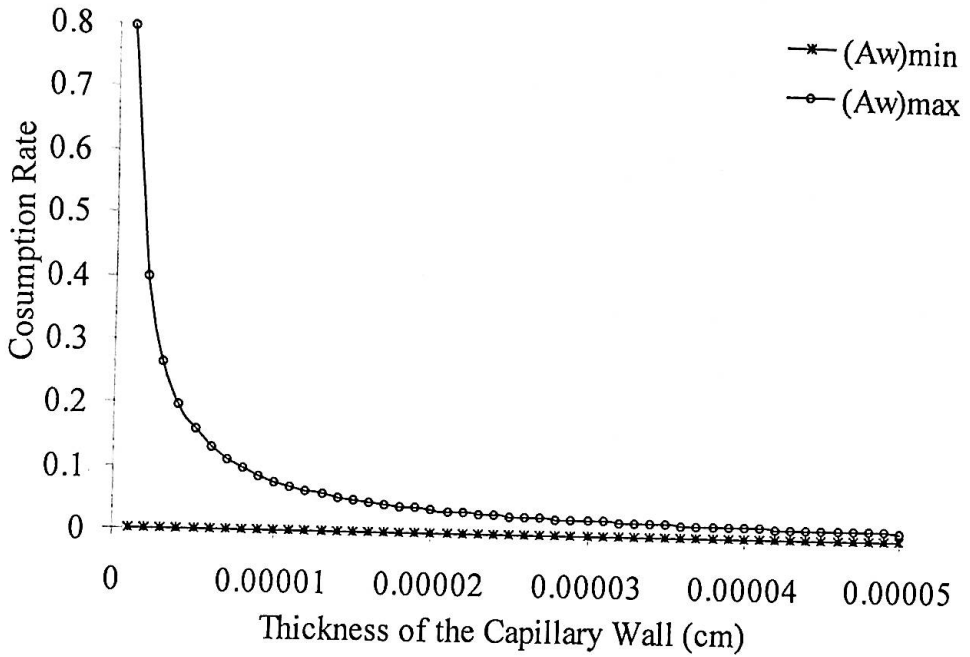
Fig 6.3. Maximum and minimum consumption rates of oxygen along the vascular wall
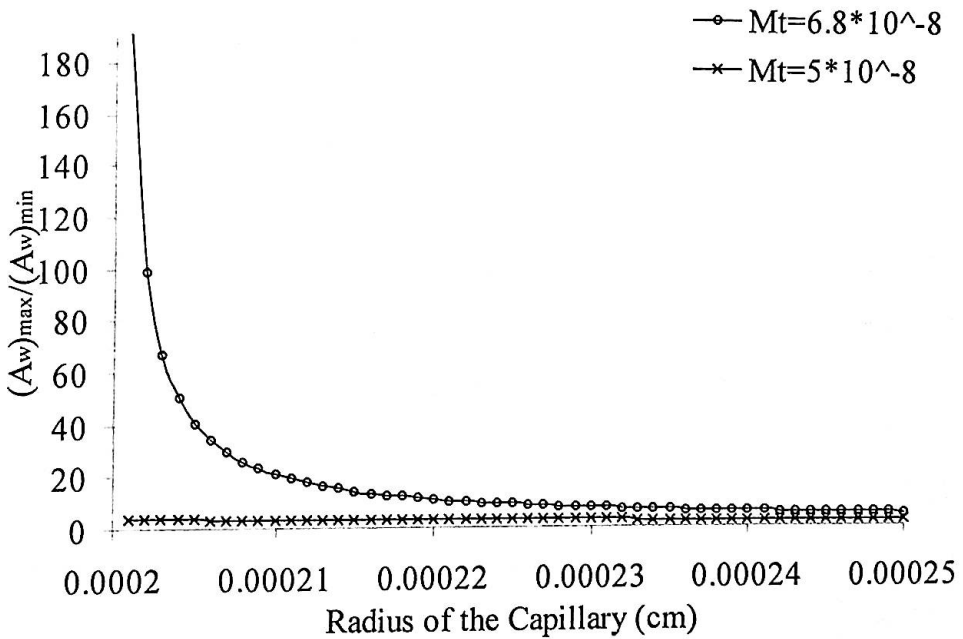

Fig 6.4. Ratio of maximum and minimum consumption rates of oxygen in the vascular wall

Similar behavior will also be seen in case 2. In this case p_0 is negative, when $A_w=0$ from Eq. (6.12(a)) for physiological condition, and it would be $p_0>0$, $A_w>(A_w)_{min}$.

Moreover, we have determined the maximum and minimum consumption rates of oxygen of the microvascular wall for this case and $(A_w)_{min}$ is presented in Eq. (6.12(a)). Here $(A_w)_{min}$ for $p_0=0$ is negative, which is impossible. Hence a $A_w>(A_w)_{min}$. The lower bound of p_0 is a strict inequality, since $p_0=0$ is not possible for finite flux leaving the wall. Then we have found the $(A_w)_{min}$ by putting $p_0=(p_0)_{min}$ in Eq.(6.9).

Finally we have shown the ratio of the consumption rates over thickness of the wall is derived from Eq. (6.13), which is shown in Fig 6.4.

Conclusion

A theoretical analysis was performed to establish the consumption rate of the microvascular wall. Result highlighted that the consumption rate was decreased with the increasing of microvascular wall thickness. Moreover, the inconsistency of the consumption rates has been shown for different values of the mass transfer coefficients.

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