MODELLING OF RESPIRATORY SYSTEM

A DISSERTATION
submitted in partial fulfilment of
the requirements for the award of the degree
of
MASTER OF ENGINEERING
in
ELECTRICAL ENGINEERING
(Measurements and Instrumentation)

By
JOHN ZACHARIAH

DEPARTMENT OF ELECTRICAL ENGINEERING
UNIVERSITY OF ROORKEE
ROORKEE (U.P.) INDIA
July, 1979

D E D I C A T E D

TO

ALL WHO PURSUE WISDOM

' Acquire Wisdom;

And with all your acquiring,

get Understanding'.
(Proverbs.4:7)

' And to man GOD said,

'Behold, the fear of the LORD,

that is Wisdom;

And to depart from evil is Understanding'.
(Job. 28:28)

' Do not be wise in your own eyes;

Fear the LORD and turn away from evil'.
(Proverbs.3:7)

BIBLE

CERTIFICATE

Certified that the dissertation entitled 'MODELLING OF INDUCTION MOTOR', which is being submitted by Shri John Chandra in partial fulfilment for the award of Master of Engineering in Electrical Engineering (Instruments and Automation), of the University of Roorkee, Roorkee, is a record of bonafide work carried out by him under my supervision and guidance. The matter embodied in this dissertation has not been submitted for the award of any other degree or diploma.

It is further certified that he has worked for a period of 6½ months from January , 1979 to July , 1979 for preparing this dissertation at this University.

(S. C. SAXENA)
READER
DEPARTMENT OF ELECTRICAL ENGG.
UNIVERSITY OF ROORKEE
ROORKEE (U.P.) INDIA

Dated: July 23 , 1979

A C K N O W L E D G E M E N T

I would like to place on record my deep sense of gratitude to Dr.G.C.SAXENA, Reader in Electrical Engineering Department for giving his consent and providing me an opportunity to work under his expert guidance. He has taken very keen interest and much pain in this work and has been very kind to me in devoting much of his valuable time and giving me creative suggestions and encouragement at every stage of the work. He was very nice and free to be approached at any time for discussions, even when he had very tight schedule and problems of his own.

I am also thankful to the teaching and non-teaching members of staff of our Department and Departmental Computer Centre and also to my friends who helped me, directly or indirectly, in completing this work in time.

I am thankful to the Principal, authorities and colleagues of Electrical Engineering Department, of my parent institution-Mar Athanasius College of Engineering, Kothamangalam, for giving me this chance of working here under Quality Improvement Programme and bearing the burden of teaching work there in my absence.

Last, but foremost, I am grateful to my God the Almighty who gave me the privilege to be in this Department and in this University of good tradition and efficient

leadership. I am thankful to Him also for my wife Dr. Mariyemma John, who managed the house-hold matters and our three little children in Kerala in my absense and encouraged me very much in this pursuit for knowledge. So also I am grateful to the Lord for my brethren in different places who were continuously on their knees in their prayers for me during these years' of my studies in this institution.

ROORKEE
JULY 23, 1979

JOHN ZACHARIAH

C O N T E N T S

CHAPTER 1

INTRODUCTION

" The Lord God formed man of the dust from the ground, and breathed into his nostrils the breath of life; and man became a living being". 'He is the Lord of heaven and earth ..... He himself gives to all life and breath and all things'[1]. Life continues in the body of living beings until the breath is taken away.

The human respiratory system is the organism which accepts and utilises this breath for life, sustaining activity of human body. There is a continuous exchange of gases between the pulmonary organism and external environment in the respiratory system and hence it is a pneumatic system. Respiratory system consits of all components required to pass air into and out of lungs, to transfer necessary Oxygen molecules from the air into the blood, to transport this O_2 to and collect the CO_2 from the cells, to carry out the utilisation of O_2 in the cells and the production of CO_2 and other waste products, to transfer the waste products back to the blood and then to transport them to the lungs, to excrete these products into the lung air and finally to exhaust the waste air into the atmosphere.

Gases flow from atmosphere to lungs (breathing), from lungs to blood(diffusion), then to capillaries (fluid flow), to intracellular fluid(transport), to cell membrane (transfer), to mitochondria (cellular respiration), then back to cell (diffusion and membrane transfer), to intracellular fluid (transport), to capillaries (membrane transfer), to blood(fluid flow), to lungs(transport), to alveoli (breathing) and then back to the atmosphere.[2]

Any defect or obstruction in any part of the respiratory organism has its effect on the breathing cycle and hence the

metabolism and connected activities are affected.

Accurate diagnosis and timely treatment of the defective areas of the respiratory organism is the task of the physician. The unaccessibility and difficulty to detect the affected area in early stages of diseases pose the greatest problem in this. Again accuracy of the diagnosis evidently influences the efficiency of treatment.

Proper study of the system and its abnormalities is the essential aspect of better diagnosis and treatment. To study the system behaviour under normal and abnormal conditions, models are used very often in the past two or three decades. Many modifications were made in the simple models and in the method of approach to the problem of system behaviour, in these years. The digging into any system gives more knowledge about the system; but it makes the scientist wonder at the still hidden and vast fields of the system to be understood. Hence there is scope for more detailed and accurate study of the respiratory organism which gives better utility for the diagnosis of the lung diseases.

In this dissertation work, modeling of the human respiratory system with special attention on its diagnosis utility is studied. The essential physiological structures and functions are studied in the second chapter. This gives the basis for the modeling of the system and can be used for further improvement of the model given in this work. In the third chapter the philosophy and the different methods of approach of the modeling are explained. In the fourth chapter, the general modeling of the human respiratory system incorporating our present concepts of the lung are discussed with reference to the recent works in

this field.[3,4] In the next chapter, a more detailed model for pulmonary airway system was developed and studied the system behaviour based on the models developed and data collected by Colden et al,[5] Gupta A.K.,[6] Clark, John W.Jr et al[7] etc. A new diagnostic method to rectify the drawbacks of the previous methods is formulated. The inaccessibility to the innermost parts of the organism and the inaccuracy of measurements in those parts give little idea about the diseases of the silent zone. Using the model developed by the author and utilizing the frequency response technique formulated by Shaffer, F.H.[8] a better solution for diagnosis of this lung tissue obstruction is worked out in chapter six. In the concluding chapter the salient merits and advantages of the work done by the author are briefly discussed.

CHAPTER 2

PHYSIOLOGY OF RESPIRATORY SYSTEM[9-13]

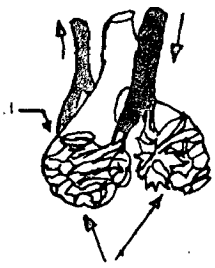
2.1 RESPIRATION[10]

2.1.1 External Respiration.

The interchanges of gases (Oxygen and Carbondioxide) that take place within the lungs is often referred to as the external respiration. The gaseous interchange in the lungs depends on the difference between the O_2 and CO_2 pressures in the pulmonary alveoli and the venous blood flowing to the lungs. The transition of the gases is governed by the definite physical law that if the pressure of a gas in a liquid differs from that of the gas in the surrounding air, the gas passes from the liquid into the air or vice-versa until the pressures are equalized. The partial pressure of O_2 is 100 to 110 mm Hg in the alveolar air and 40 mm Hg in the venous blood and pulmonary capillaries. The partial pressure of CO_2 is 40 mm Hg in the alveoli and 47 mm Hg in the blood. The gaseous interchange is also affected by the cells of the walls of the pulmonary alveoli and of the blood capillaries of the lungs (Fig.2.1).

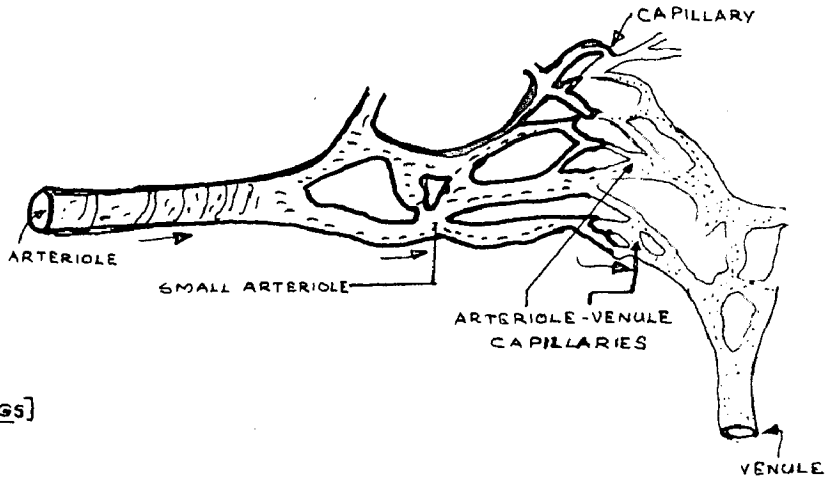
2.1.2 Internal Respiration.

Internal respiration or tissue respiration refers to the exchange of gases in the tissue cells of the circulatory system where metabolism takes place (Fig.2.2). Tissues absorb O_2 only enough to meet the metabolism needs and CO_2 is removed from these cells. Cells are bathed in the tissue fluid which forms the internal environment of the body. The O_2 content of the blood is not increased as the demand for O_2 grows greater



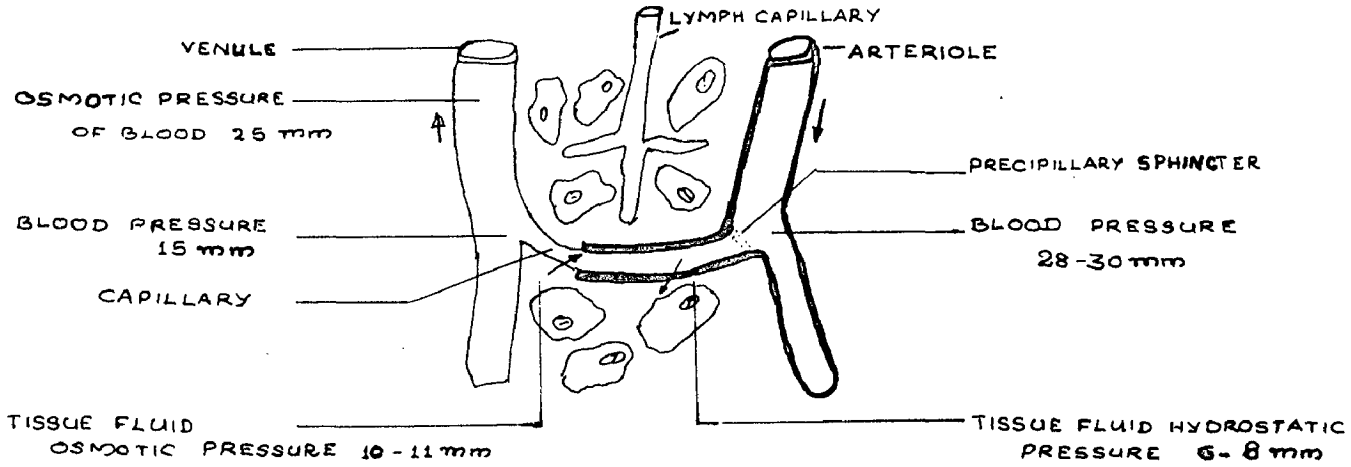
CAPILLARY NETWORK

ALVEOLI ENLARGED

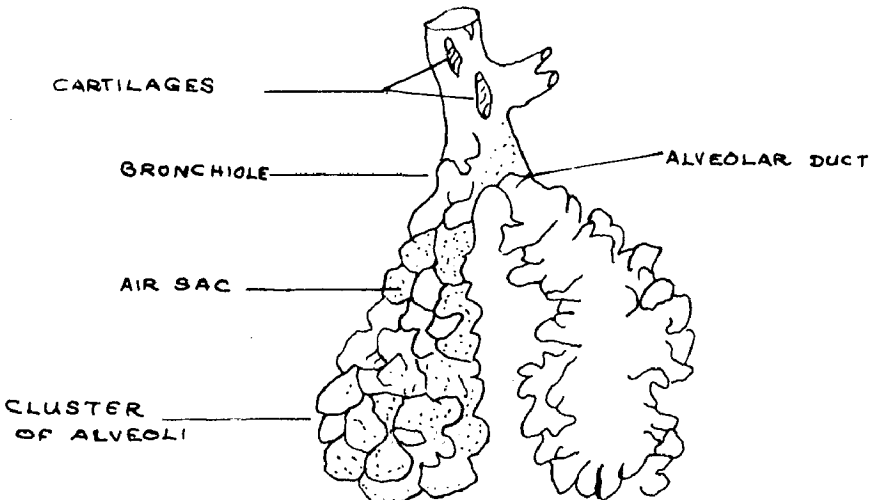


1 EXTERNAL RESPIRATION [IN LUNGS]

2·2 CAPILLARY PATHWAY [INTERNAL RESPIRATION] -IN TISSUES



FIG·2·3 PRESSURE BETWEEN THE CAPILLARY and THE TISSUE SPACES



(a) External appearance (b) Lung tissue partially dissected

FIG 2.5 INTERNAL STRUCTURE

in muscular activity; but because of the dilation of the capillaries, a greater amount of blood flows through the tissues. The CO_2 produced in the cells, having high partial pressure, diffuses through the cell membrane into the fluid of the lymph spaces, then through the capillary wall into the blood plasma and into the red cells to be carried back to the heart and lungs by the venous blood. Cellular metabolism is concerned with the utilization and release of energy from foods.

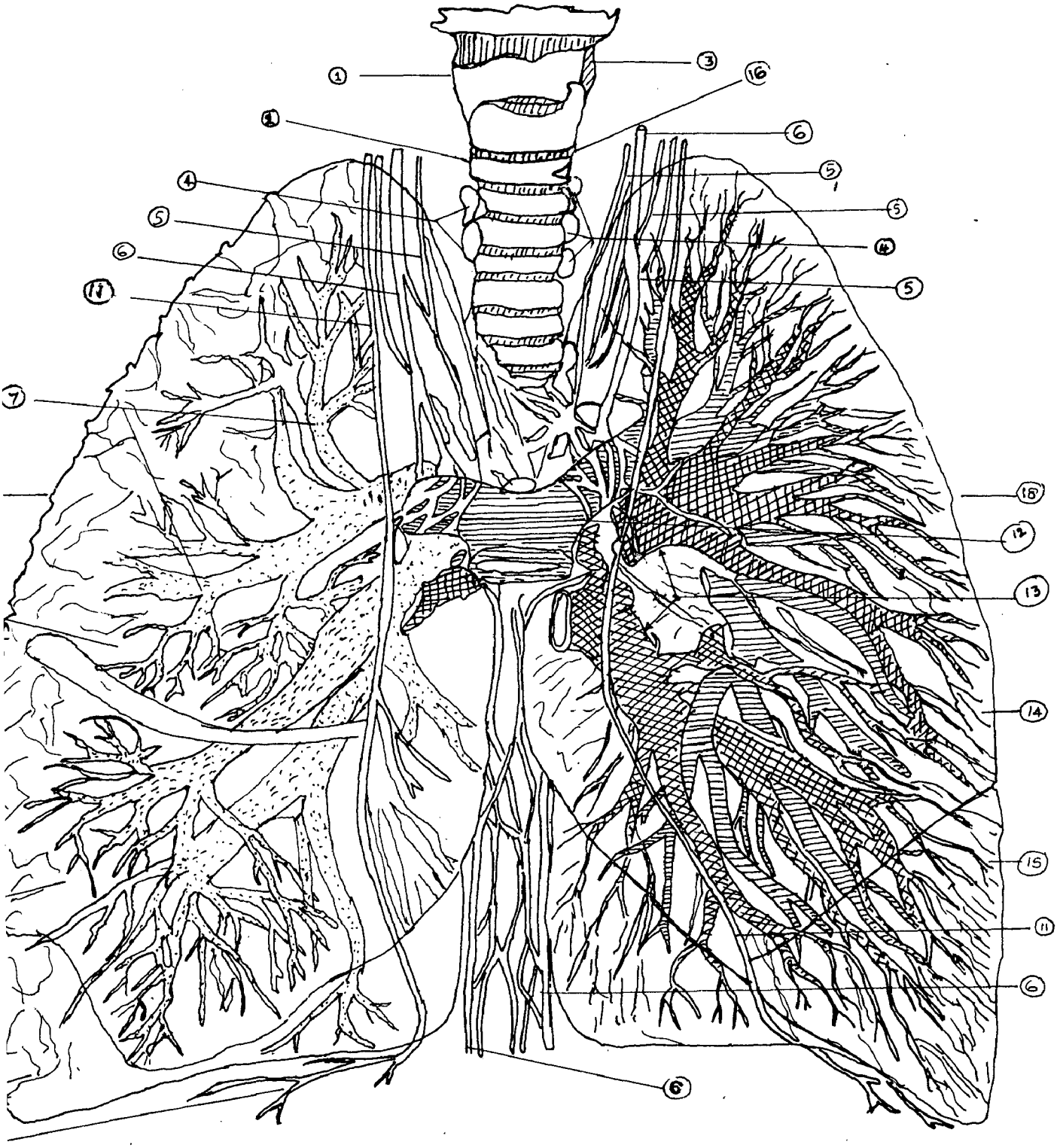
2.2 MOVEMENTS OF FLUIDS THROUGH THE CAPILLARY MEMBRANE[10]

As shown in Fig.2.3, hydrostatic (blood) pressure in capillaries is 28 to 30 mm Hg and in tissue fluid is 6 to 8 mm Hg. Effective hydrostatic pressure is 22 mm Hg which would tend to force the fluid into the tissue spaces. Similarly the effective osmotic pressure is 14 mm Hg (25 mm Hg in plasma proteins and 11 mm Hg in tissue proteins) which attracts fluids towards blood stream. Thus there are two opposing forces regulating the exchange of fluids between the blood and tissues. The difference between the two effective pressures, about 8 mm Hg, represents the filtration pressure which moves the fluid into the tissue spaces.

2.3 RESPIRATORY STRUCTURE[9,12]

Nasal cavities, pharynx, larynx, trachea, bronchi and bronchioles-all form parts of the pulmonary primary airways which lead the air to the lungs and are situated in the thoracic cavity (Fig.2.4). Larynx, a cartilaginous structure at the entrance of trachea, has vocal folds and is protected from above by a movable cartilaginous lid called epiglottis which opens as one breathes and closes when one swallows. The

FIG 2·4 INTERNAL STRUCTURE



1. LARYNX
2. TRACHEA [WITH CARTILAGOUS RINGS]
3. THYROID CARTILAGE
4. TRACHEAL LYMPH NODES
5. CARDIAC NERVES
6. VAGUS NERVES
7. BRONCHIAL BRANCHES
8. UPPER LOBE OF RIGHT LUNG
9. MIDDLE LOBE OF RIGHT LUNG
10. LOWER LOBE OF RIGHT LUNG
11. PHRENIC NERVES
12. PULMONARY ARTERY
13. LEFT PULMONARY VEINS
14. UPPER LOBE OF LEFT LUNG
15. LOWER LOBE OF LEFT LUNG
16. CONNECTING TISSUES
17. RIGHT BRONCHUS
18. LEFT BRONCHUS

glottis leads into the trachea, a long membranous tube supported by rings of cartilage and fibrous connective tissue which gives great flexibility in trachea and yet are strong enough to resist compression.

Trachea is the part of airway from larynx to upper boundary of chest where it is divided into two bronchi. Trachea has the largest diameter of about 1.5 to 2.5 cm and has a length of about 11 cm.

Bronchi branches by over 20 nonsymmetric bifurcations. Bronchi have smaller diameters and bronchioles, the subdivisions of bronchi have still smaller diameters of about 0.1 cm. The diameter decreases in terminal bronchioles (about 0.05 cm) and still decreases in respiratory bronchioles, where some alveoli are attached as small air sacs in the wall of the lung. After some additional branching these air sacs with numerous pouches increase in number becoming the pulmonary alveoli (about 0.02 cm dia and about 300 million in number) as shown in Fig.2.5. Through the walls of capillaries in alveolos, the exchange of gases between blood and the air takes place. The alveolar surface area is about 80 square meters, of which more than three quarters is capillary surface. Unlike the bronchi, the bronchioles have no cartilages or glands in their walls; but like bronchi, they are equipped with smooth muscle fibres. Contraction of these muscle fibres cause spasms (constriction) of the bronchioles.

Upto about the tenth stage of branching, the diameter of the air sacs is more affected by the pressure inside the thorax, called pleural pressure. Beyond this point the bronchioles are embedded within the alveolar lung tissue and their

diameters are affected due to expansion and relaxation by the lung size or lung volume (V_L).

The two lungs occupied in the thoracic cavity vary in size and shape, the right one being larger but about an inch shorter than the left one. A thin serous membrane called the 'pleura' covers each lung and continues over the thoracic wall, the diaphragm and the lateral aspects of the mediastinum. Pleura has two layers. The pulmonary pleura covers the lung; the parietal pleura lines the wall of the chest and covers the diaphragm. The two layers are in contact and the pleural cavity between the two layers is only a potential one.

The lungs also contain a very abundant circulatory tree. The pulmonary arteries (veins) divide into smaller and smaller branches until finally it resolves itself in capillary networks around the bronchioles and alveoli. Pulmonary capillaries anastomose to form tiny venules as the blood leaves the alveoli and give rise to pulmonary veins, which carry freshly oxygenated blood back to the left atrium of the heart. The tissues of the lungs are supplied by bronchial arteries directly from the aorta.

Breathing is accomplished by musculature that literally changes the volume of the thoracic cavity and, in so doing, creates negative and positive pressures that move air into and out the lungs. Two sets of muscles are involved in this. One set of muscles are those which are in and near the diaphragm that cause the diaphragm to move up and down, changing the size of the thoracic cavity in the vertical direction. And the other one are those (external intercostals, internal intercostals etc.) that move the rib cage up and down to change the lateral diameter of the thorax. Breathing occurs

rhythmically. The lungs do not take any active part on respiratory movements.

During inspiration under the influence of nerve impulses the diaphragm contracts (due to diaphragm muscles) and the rib cage outstreches (due to external intercostal muscles) the lungs, giving a resultant increase in thoracic volume and creating internal pressure (negative) of about -4 mm Hg in the thorax which is relieved by air entering the lungs (as the only opening for the closed thoracic chamber is from inside the lungs). The lungs themselves are passive and expand only because of the intercostal pressure of the air in the lungs, which is greater than the pressure in the thorax (pleural cavity) outside the lungs. Normal inspiration is said to be active as it requires the ribs and diaphragm to move from their positions.

Normal expiration is passive (except in forced expiration); for, on release of the inspiratory muscles, the elasticity of the lungs and rib cages, combined with the tone of the diaphragm, reduces the volume of the thorax thereby developing a positive pressure of about +4 mm Hg, forcing the air out of the lungs. During expiration the abdominal muscles move the diaphragm back and the thoracic cage can apply pressures as high as 40 mm Hg on the lung walls.

The pressure signal that drives the respiratory system is the pressure difference between the mouth and the intrathoracic (chest) cavity. Since the mouth pressure (which is the atmospheric pressure) is constant, normal breathing is induced by changes in the intrathoracic pressure. But in forced respiration or artificial respiration, the intrathoracic pressure

remains more or less constant and the mouth pressure is varied.

There are two types of normal respiration; (i) Abdominal (predominates in males) in which the thoracic capacity increases mainly because of the contraction of the diaphragm (increase in vertical size) and (ii) Costal (mainly in females) in which the capacity increases due to contraction of other respiratory muscles.

The ability of the lungs and thorax to expand during breathing is called the compliance, which is expressed as the volume increase in the lungs per unit increase in intra-alveolar pressure. The resistance to the flow of air into and out of the lung is called airway resistance.

2.4 RESPIRATION CONTROL CENTRES[10]

2.4.1 Respiratory Centre.

Different neural mechanisms exert control over breathing. The respiratory centre in the medulla consists of two centres which control the respiratory rate and depth of breathing. They are 'inspiratory centre' and 'expiratory centre'.

Impulses from the inspiratory centre descend through the spinal cord and then through the nerves to the respiratory muscles. Some impulses innervate the diaphragm causing it to contract while others stimulate the 'external intercostal' muscles raising the ribs, thus increasing the thoracic cavity.

The 'internal intercostal' muscles are innervated by a similar set of neurons, but their function is expiratory. They aid in lowering the ribs during a deep or forced expiration. Each of impulses to the inspiratory centre relaxes the muscles.

The inspiratory and expiratory centres exhibit reciprocal inhibition each other. In normal respiration, the inspiratory centre is dominant as it has a lower threshold. But the elastic lung tissues are stretched and the 'sensory receptors' in these tissues are stimulated by the accumulated CO_2 which in turn passes impulses to the respiratory control centre. Since the expiratory centre has a high threshold, the lungs will continue to inflate until the control centre is finally stimulated. The inspiratory centre is then reciprocally inhibited and expiration follows. This afferent mechanism protects the lungs from inflation.

2.4.2 Pneumotaxic Centre.

When vagus nerves are cut, breathing becomes slower and deeper, but still the rhythm is retained, due to the third control area on the upper part called 'pneumotaxic centre', capable of substituting as an inspiratory inhibitory mechanism. In ordinary breathing, afferent impulses from lungs are dominating, but with increased respiratory activity, stimulated by a rise in body temperature, the pneumotaxic centre becomes more dominant.

2.5 FACTORS INDIRECTLY AFFECTING THE RESPIRATORY CENTRE[10]

2.5.1 Chemoreceptors.

Respiration is regulated in accordance with the changes in metabolism due to chemical mechanism. They can affect the respiratory centre directly or through the chemoreceptors located in the carotid and aortic sensory areas. In ordinary breathing chemoreceptors exert only a small regulatory effect, but when the O_2 content in the arterial blood lowers, they become a more important source of stimulation for respiration. They also play a part

the regulation of blood pressure.

2.5.2 Pressoreceptors.

The walls of the carotid sinuses and the arch of the aorta contain receptors that are stimulated mechanically by a rise in blood pressure. These pressoreceptors are primarily concerned with the circulatory regulation, but influences respiration also. A sudden change in blood pressure stretches or contracts the aortic arch and carotic sinus areas, stimulating the pressoreceptor and inhibits the respiration centre reflexly. Pressoreceptors do not appear to be as essential as chemoreceptors in the respiratory regulation.

2.6 FACTORS DIRECTLY AFFECTING THE RESPIRATORY CENTRE[10]

Neurons in the respiratory centre are directly affected by changes in CO_2 concentration, variations in the amount of Carbonic acid, temperature of the blood at medulla and rate of blood flow through medullary tissue.

Only in carefully controlled experiments can one factor be demonstrated to the exclusion of other factors. Ordinarily all chemical and nervous mechanisms are co-ordinated in the control of respiration. If any chemical or physical regulators are to be singled out for special consideration, changes in CO_2 concentration and changes in acidity of the blood are probably the most important in the control of breathing.

A decrease on O_2 inhale does not affect the respiratory rate. As soon as the blood accumulates a certain amount of CO_2, the respiratory (inspiratory) centre becomes excited and an inhalation takes place. During inhalation the lungs expand,

stimulating the endings of the vagus nerve embedded in the tissue of the lungs. The excitation arising in the receptors is transmitted along the vagus nerve to the respiratory (expiratory) centre and inhibits it, with the result that an exhalation occurs. During exhalation the surplus CO_2 is eliminated from the organism and its concentration in the blood decreases. The next inhalation will take place when the CO_2 concentration in the blood is again sufficient to stimulate the inspiratory centre. Thus respiration is automatically regulated; an inhalation stimulates an exhalation, and an exhalation brings about accumulation of CO_2 which stimulates an inhalation.

In addition to the direct effect of CO_2 in the blood on the respiratory centre, an increase in CO_2 increases the acidity of the blood which also acts reflexly on the chemoreceptors controlling the respiration.

An increase in CO_2 in the inhaled gas (due to intense muscular work etc.) excites the inspiratory centre immediately after the exhalation, as the concentration of CO_2 in the blood is already sufficient without further accumulation. In such cases respiration becomes accelerated and dyspnea (laboured breathing) develops which will in turn reduces the excitation of the respiratory centre, bringing the rate to control.

Holding the breath for 30 seconds or so through voluntary nervous control is possible, but soon chemical stimuli overpower all voluntary inhibition and one is forced to take a breath. Breath rate varies considerably with individuals, age, physical activity and emotion and also disease. Average rate at rest in adults is 16 while a new born babe has a rate of about 60.

If totally deprived of O_2 for just a few minutes, certain

nerve cells in the brain undergo irreversible changes. Milder degree of hypoxia may also produce serious effects, when the supply of O_2 is half-normal (Hypoxia) as in air flights at 10,000 feet, headaches, psychological impairment, euphoria, sleepiness and fatigue may occur. Similarly small percentage of CO_2 in the inspired gas (hypercapnia) may result in a five-fold increase in ventilation. At lower levels, where atmospheric pressure is high, in addition to O_2, nitrogen enters the blood. If the pressure decreases rapidly to normal, the N_2 surplus will not be eliminated from the blood immediately and hence bubbles of gas will form in the blood vessels. Joint pains, muscle pains, vomiting are the results and this is called 'Caisson disease.'

If a strong acid is injected into the blood vessels (acidemia), the number of arterial H^+ ions rises, stimulating ventilation. Increase in ventilation decreases arterial PCO_2 below normal, lowering H^+ back towards normal.

'Protective acts' of coughing and sneezing are associated with respiration and are performed reflexly. If the pressure is released through the throat, it is cough. Coughing is the response to irritation of the mucous membrane of the larynx, pharynx or bronchi by particles of dust, food etc., penetrating into the organs. A cough following a deep inhalation expels the air forcefully from the air passages and the irritant in the air passages is also expelled. As the air is expelled, it sets the vocal cords in motion with the characteristic coughing sound. If the air is forcefully directed through the nose, the action is called sneezing, and sneezing is the response to irritation of the mucous membrane of the nose. It works on the

same principle as coughing.

2.7 LUNG DISEASES AND PARAMETERS[2,4,10,14,15]

Respiration system diseases affect the respiration process as they change the characteristics and parameters of airways, alveoli, diaphragm, respiratory muscles and other sub-systems. Quantitative measurement of variables associated with the process in the lungs is important for the physician to perform clinically relevant tasks of assessing the functional status of the respiratory system and intervening in its function. Obstruction of the airways, lack of compliance of the lung tissue, efficiency of transfer of gases from the alveoli to the blood, and measurement of tidal volume have valuable diagnosis meaning.

Dyspnea refers to difficulty in breathing and may be due to cardiac failure, pulmonary edema or emphysema.

In pulmonary edema, the capillary blood pressure rises above that of the plasmaprotein osmotic pressure when congestion happens (due to cardiac failure or pneumonia). Hence fluid begins to fill the alveolar and interstitial spaces and breathing becomes difficult as the lungs must remain dry for smooth respiration.

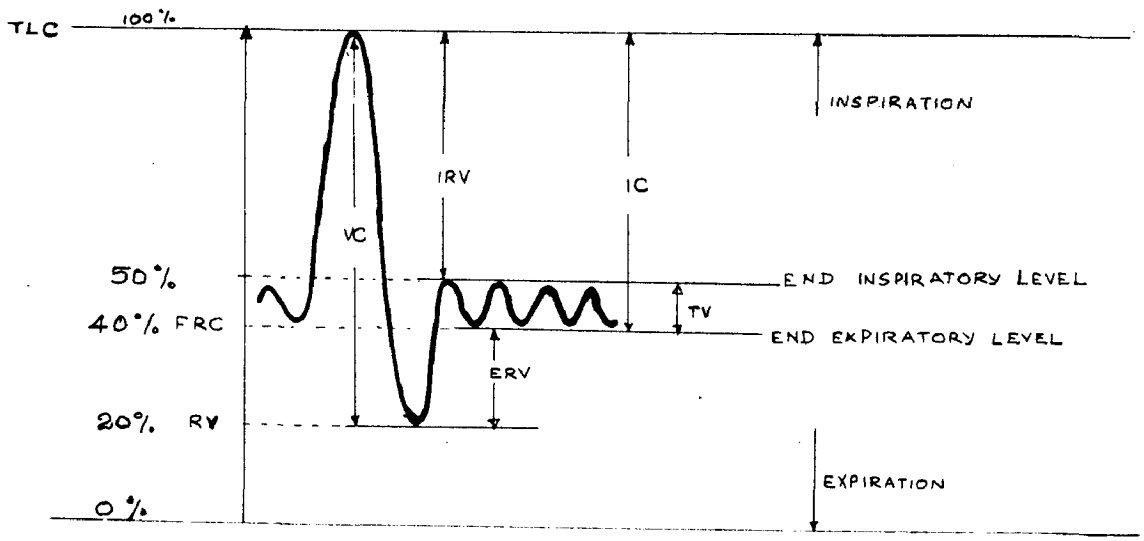
Emphysema is due to the breaking down of alveolar wall progressively, thus reducing the area available for exchange of gases. Hence their capillaries also degenerate tending to rise the pulmonary blood pressure. Smoking increases the likelihood of developing emphysema.

The volume-flow rate and the time integral of volume-flow rate are used to estimate the rate of change of lung volume and the changes of the lung volume, respectively. In addition to

these, the respiratory rate, airway pressures and concentration of CO_2 in the expired gas are the system variables of primary importance. The system also has a number of relatively fixed volumes and capacities which are determinant to the functioning of the system. They are Total Lung Capacity (TLC- the largest volume to which the subject's lungs can be expanded voluntarily and about 6 to 6.5 lit for a 20 to 30 year old male), Tidal-Volume (TV-peak to peak volume change during a quiet breath, about 10% TLC), Residual Volume (RV-the smallest volume to which the subject can slowly deflate his lungs-about 20% TLC), Functional Residual Capacity (FRC-volume of the lungs at the end of a quiet expiration when the respiratory muscles are relaxed-about 40% TLC), Vital Capacity (VC=TLC-RV, the maximum exchange in volume the lungs can undergo during voluntary manouvers-about 80% TLC), Inspiratory Reserve Volume (IRV-additional volume that can be inspired after a normal inspiration - about 50%), Expiratory Reserve Volume (ERV-the additional volume that can be forced out of the lungs after a normal expiration-about 20%) and Inspiratory Capacity (IC=TLC-FRC). The actual amount of air reaching the alveolar interspace is the difference between the tidal volume and volume of the dead space. (Dead space is the volume of various cavities of the air passages which are not subjected to inflation - about 150 ml). (Fig. 2.6) [9]

Static Lung Compliance is the ratio of the difference in lung volumes at two different volume levels and the associated difference on alveolar pressure. Even though compliance is static, dynamic compliance is also measured. It is the ratio of tidal volume to intrathoracic pressures at two instances of zero air-flow. Lung compliance increases with the size of the lungs and decreases with age and disease. Compliances is

TLC - TOTAL LUNG CAPACITY - 6 TO 6.5 LIT (NORMAL ADULT-MALE)
TV - TIDAL VOLUME (ABOUT 10 % TLC)
RV - RESIDUAL VOLUME (" 20 % ")
FRC - FUNCTIONAL RESIDUAL CAPACITY (ABOUT 40% TLC)
VC - VITAL CAPACITY " (" 80 % ")
IRV - INSPIRATORY RESERVE VOLUME (" 50 % ")
ERV - EXPIRATORY RESERVE VOLUME (" 20 % ")
IC - INSPIRATORY CAPACITY (" 60 % ")



FIG·2·6 LUNG VOLUME AND CAPACITIES

assumed constant over the tidal volume.

Airway resistance is the ratio of pressure to flow and is not constant over a respiratory cycle. As pressure in the thoracic cavity becomes more negative, the airways are widened and the airway resistance is lowered (inspiration). In expiration, the intrathoracic pressure is positive and the resistance is increased as airways are narrowed. Most airway resistance measurements are made at or near the FRC level.

The objective assessment of respiratory function is clinically performed on two time scales. One is relatively long, involving discrete observations at various intervals of the order of days to years, observations being made in the form of pulmonary function tests (PFT). Evaluation of parameters of respiratory function by PFT are used,

(i) to screen the general population for disease

(ii) to serve as part of periodic physical examinations, especially of individuals with chronic pulmonary conditions,

(iii) to evaluate acute changes during episodes of disease and

(iv) to follow up after treatment.

The second time scale on which respiratory function is assessed is very short, either continuously or at intervals of the order of minutes to hours. This comes under patient monitoring and is performed in a hospital setting, usually in an intensive care unit (ICU).[4]

CHAPTER 3

PHILOSOPHY OF MODELING OF PHYSIOLOGICAL SYSTEMS

3.1 INTRODUCTION

Modeling is but a part of the overall research programme to gain deeper understanding of the system. Clinical and experimental programmes, though extremely important, are considerably difficult. Modeling cannot provide new knowledge about the system, but can serve to integrate the available knowledge with that from other laboratories. Thus modeling results and actual measurements assist each other to get better contribution to the health and welfare of man.

Generally, a model is constructed by studying the relevant physiology and identifying appropriate input and output variables. Starting with the simplest model which characterizes the general behaviour of the system, model response must be verified with experimental responses at every stage of development. The initial model can be improved to match the specific uses of the model, but it often limits versitility.

A "good model" is one which satisfies three criteria to be useful in education and research.

i) They must agree structurally with the physiological system, but must be of modest size.

ii) Their parameters must be measurable or estimatable and

iii) They must fit computer simulation capabilities.

Obtaining the model parameter values is one of the most difficult tasks to be performed, even for simple models. Parameters may be estimated by performing experiments on the system (measuring time responses), observing steady state values, or

by using computational techniques to optimise values from recorded responses. Often, good 'guesses' must suffice for lack of data.

3.2 MODELS[2,4,15,16]

There are different types of models developed for study and research purposes. Selection of a particular type of model depends upon the easiness and simplicity required, the accuracy needed, the purpose of the study, the data available and such other factors.

3.2.1 Graphical Models.

They are graphical characteristics relating the parameters. This is the simplest model with the data available, but the analysis of the characteristics may require the development of some other type of model, depending upon the complexity of the characteristics.

3.2.2 Mathematical Models. If a mathematical expression could be derived to fit the graphical characteristics, it is called a mathematical model. This would involve much tedious and time consuming work and in view of experimental limitations, the result might be questionable. If the graphical model is subjected to approximation, a crude mathematical model could be developed. This gives less 'exact', but more simpler and rapid procedure. This gives an insight into the system characteristics, though not (exact) one. The mathematical model cannot give more information. But the convenience it gives compensates for the loss of information.

3.2.3 Physical Models.

When approximations or rather linearization of graphical data is accepted, then the data can be represented by a physical model. In the physical or mechanical model, the same dimensions

of the physiological system are adopted, and the model represents the biological system.

3.2.4 Electrical Analog Models.

In electrical analog model, the physical variables are represented by analogous parameters of an electric circuit and the characteristics of the electric circuit will be analogous to the characteristics of the physical or physiological system.

3.2.5 Electronic Models.

Based on the electrical model and taking into account the controlling elements of the system, an electronic model of the physiological system can be developed. This can be used to give the working characteristics of the system in different normal and abnormal conditions, and with more accuracy and easiness.

3.3 MODEL SIMULATION

The basic idea behind the concept of simulation is that, if two systems have graphical similarity for certain aspects of behaviour, one can be substituted for the other in a particular phase of investigation. If the dimensions of both systems are the same, it is called a model simulation; if the dimensions are different, it is an analog simulation.

Simulations can serve two useful purposes. One is the study of how a component of a system may affect the overall operation of the system; the other is to learn more about the system being studied noting how its behaviour differs from that of a known system.

In refined techniques, very close simulations of actual systems are used, particularly when analog and digital computers

are used.

Analog-Circuit representation has physical and mathematical similarity to the actual system. But computer simulation has only mathematical similarity.

3.4 APPROACH AND STRUCTURES

There are two general approaches to the modeling problem - the 'fundamental' and the 'functional'.

3.4.1. Fundamental Model.

Fundamental model is attempted to describe the system mechanics in considerable detail. In lung-airway mechanics, it is useful for study of air flow (for a given set of parameters) of the bronchial tree, from the fluid mechanical point of view.

3.4.2 Functional Model.

Functional model considers the more general aspects of the behaviour of the system and is more clinical oriented and hence contains gross lumpings.

Models may have various physical structures; the most common are Block-diagram models or Transfer Function models (output/input), compartmental models and State Variable models.

3.4.3 Transfer Function Models.

In transfer function models, the physiological system is represented by block diagrams giving the quantitative data, and represents the dynamic response of the system with a well-known input-output relationship. The internal variables need not coincide with any part of the physiological system. The blocks can be simulated electrically (as in analog computer simulation). If the block is non-linearized, the 'operator'

is not constant; if linearized, it will be a constant.

3.4.4 Compartmental Models.

The compartmental model describes the system by a series of interconnected cells or 'compartments' which may or may not be related to the system. Flows between these compartments represent the movement of material, energy or information.

3.4.5 State Variable Models.

The state variable models describe a system using linear or non-linear equations; each equation is related to some part of the physiological system. This model offers the greatest flexibility of the three structures described.

3.5 UTILITY OF MODELS AND ANALOGS[15]

For an engineer, the introduction of a model provides a link between descriptive physiology and the understanding of experimental data. For a student, the existence of a mathematical model provides a means for rapid (simulated) experimentation and understanding of the system functions, which may not be possible otherwise. For those involved in research, a mathematical model provides a method of summarizing what is known about a system and communicating the information to others.

One of the advantages of the model concept is that it can be used as an aid in system studies that involve the interaction between components of the system. Again the model is used as a research tool for which actually a 'perfect model' is required. A perfect model can be built only if everything about the real system is known. Hence a systematic examination

of the gross aspects and then the more subtle proportion of the system is necessary. This implies that a model can not be developed by analysis alone. The process must consist both analysis and experimental work, each complementary to each other. By examining the difference between the postulated model and the real system, the understood portion of the real system is, in effect, 'subtracted out' and attention can then be focussed on more subtle proportion of the system. Thus the models and analogs are used to provide a technique to gain more insight and understanding of system functions.

CHAPTER 4

MODELING OF HUMAN RESPIRATORY SYSTEM

4.1. INTRODUCTION[4]

Ideas about how the respiratory system functions are usually formalized in abstract models. Not only are the variables that are to be measured specified by the models of the respiratory system, but such models also define characteristic parameters of respiratory function and are the basis for the design of experiments to evaluate these parameters. In addition they are used for cybernetic diagnosis of respiratory diseases, and motivate control strategies and devices that are used to produce effective respiratory assistance. The definitions and discussions of lung physiology are based on models of the lungs.

Because it is the respiratory function of living individuals that is to be evaluated, measurements must be minimally invasive, cause minimal discomfort, and be acceptable for use in a clinical environment. This greatly limits the number and types of measurements that can be made and leads to the use of lumped-parameter models. There are two complementary categories of respiratory functions:

(1) Gas transport in the lungs (including extra-pulmonary airways and pulmonary capillaries) and

(2) Mechanics of the lungs and chest wall.

The models describing gas transport deal primarily with changes in concentrations of gas species and volume flow of gas, whereas the models dealing with mechanics primarily relate pressure, lung volume and volume flow of gas.

4.2. GAS TRANSPORT MODEL[3,4]

Models of gas transport, both in the gas phase and across the alveolar-capillary membrane into the blood are developed from mass balances for the pulmonary system depicted as a set of compartments (Fig.4.1). A gas-transport unit of the lung has basically

i) a variable-volume alveolar compartment,

ii) a well-mixed flow-through blood compartment that exchanges gas with alveolar compartment by diffusion and

iii) a constant volume dead space.

Gas moves by convection through the dead space which acts only as a time-delay conduit between its outer opening and its associated alveolar volume (V_A). Abnormal lungs or normal lungs undergoing maximal volume changes have more complicated systems of units in parallel or in series or both.

If a gas 'x' is breathed, (neglecting the chemical reaction), mass balance equation is

$$\left.\begin{array}{l}\text{Rate of mass}\\ \text{accumulation}\\ \text{of 'x' in the}\\ \text{system.}\end{array}\right\} = \left\{\sum_{i=1}^{n} \begin{array}{l}\text{Rate of mass}\\ \text{convection of}\\ \text{'x' through port}\\ i\end{array}\right\} - \left\{\begin{array}{l}\text{Net rate of}\\ \text{diffusion out}\\ \text{of the system}\\ \text{of 'x'.}\end{array}\right.$$

$$\text{In molar balance, No. of moles N} = \frac{\text{mass of 'x'}}{\text{molecular weight (in mass units) of 'x'.}}$$

Molo density (=Moles/Unit volume)

$= \rho_{au}$; $\dot{V}_{au}$ through airway opening,

$= \rho_b$, $\dot{V}_b$ through pulmonary blood.

HUMAN RESPIRATORY SYSTEM MODELS

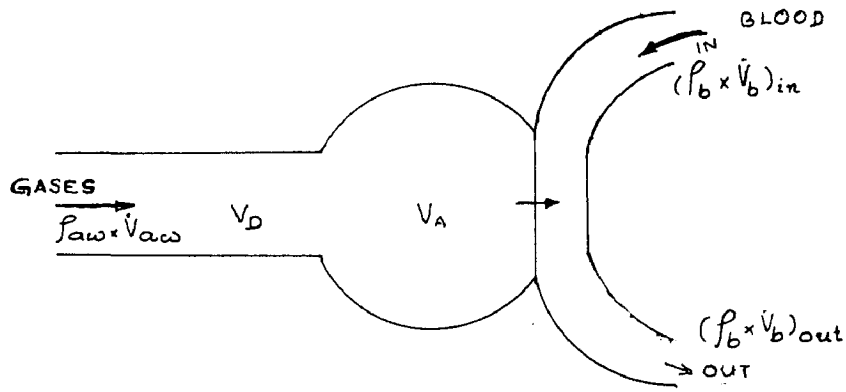


FIG 4.1 GAS TRANSPORT MODEL -NORMAL LUNG
- BASIC GAS TRANSPORT UNIT-

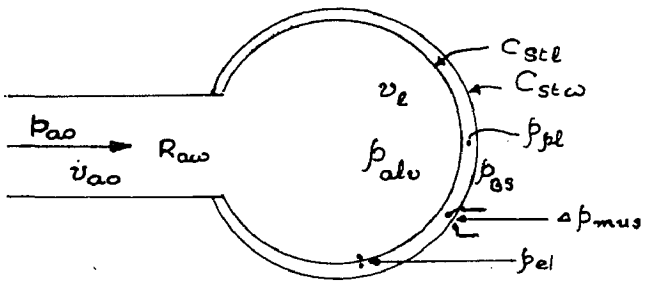
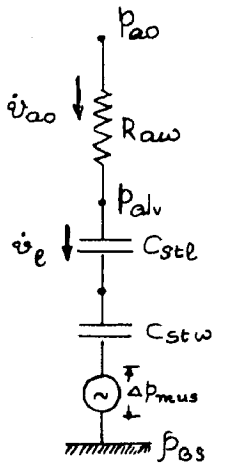


FIG 4.2 MECHANICAL MODEL OF NORMAL VENTILATORY MECHANICS
[FOR SMALL AMPLITUDE, LOW FREQUENCY BREATHING AT RESTING CONDITION]



$\dot{v}_{ao} \simeq \dot{v}_l$

FIG 4.3 ANALOGUS ELECTRICAL MODEL

where ρ_{av}, ρ_b = specific density of airway and blood respectively,

$\dot{V}_{av}, \dot{V}_b$ = Volume flow rate (Volume/unit time) of airway and blood respectively.

$\dot{U}_b$ = Rate of molar uptake/unit x

= Rate of diffusion of moles into the blood.

As per mass balance equation

$\frac{d}{dt}(\Pi_L \cdot x) = \rho_{av} \cdot \dot{V}_{av} - \dot{U}_b \cdot x$ where $\dot{U}_b \cdot x$ = net rate of diffusion of x into the blood.

$\Pi_L \cdot x$ = No. of moles of x in the lungs

= No. of moles of x in the dead space volume + No. of moles of x in alveolar compartment

$= \Pi_D \cdot x + \Pi_A \cdot x = (\Pi_D + \Pi_A)\, x.$

4.3 MECHANICAL AND ELECTRICAL ANALOG MODELS

A general mechanical model of the human respiratory system is shown in [Fig. 4.2] and its analogue electrical model is shown in [Fig.4.3]. This model is from the existing concepts of respiratory organism and based on the latest works and is presented by Frank P.Primiano Jr.[4]. It is an RC model of the lung in terms of resistance to airflow and compliance of the tissues.

The airway is a non-rigid segment having variable resistance to convective airflow. Alveolar space exhibits both elastic and plastic behaviour, and is represented by a single unit taking all the alveoli and terminal airways lumped during a quiet breathing. At high rates of breathing, normal and

abnormal pulmonary systems may require models containing combinations of such units.

Respiratory system can be assumed simply as one compliant element (between lung and pleural cavity) enclosed within another (between pleural cavity and chest cage).

Chest wall includes extrapulmonary structures such as respiratory muscles and abdominal contents which can undergo motions as a result of breathing. The gap between the lung unit and the chest wall represents the liquid filled interpleural space.

When the changes in volumes and their respective time derivations are small (such as those that occur during resting breathing), linear approximations adequately describe the respiratory system. (When they are large, equations describing the mechanical behaviour of the respiratory system are highly non-linear).

Symbols Used

P_{ao} - Hydrostatic pressure at the airway opening

P_{alv} - Representative pressure within the lungs (alveolar pressure)

P_{pl} - Representation of the average force per unit area acting on the pleural surface (interpleural pressure)

P_{el} - Representation of the average force/unit area acting on the tissue wall (tissue pressure difference)

ΔP_{mus} - Representation of the average force/unit area on the chest wall (muscle pressure difference)

P_{BS} - Hydrostatic pressure acting on the body surface, except at the airway opening.

$\dot{V}_{ao}$ - Volume flow of gas at the airway opening.

V_1 - Volume of the gas space in the system, assumed to be entirely within the lungs and airways.

R_{aw} - Total airway resistance.

C_{stl} - Pulmonary (lung) static compliance

C_{stw} - Chest wall static compliance

If alveoli exhibit predominently elastic behaviour, the equations for the model of the mechanics of the respiratory system for normal tidal breath in the atmosphere are as follows:

$$\Delta P_l = P_{ao} - P_{pl}$$

$$P_{ao} = P_{alv} = R_{ao} \cdot \dot{V}_{ao}$$

$$P_{alv} - P_{pl} = \frac{V_1}{C_{stl}}$$

$$\Delta P_{mus} \diamond (P_{pl} - P_{BS}) = \frac{V_1}{C_{stw}}$$ with reference to an operating point.

General definitions of flow resistance through a conduit and compliance of a deformable structure are used to evaluate the parameters of R_{aw}, C_{stl}, and C_{stw}.

$$R = \frac{\partial (P)}{\partial \dot{V}} \quad \text{and} \quad C_{st} = \frac{\partial V}{\partial (P)}$$ where ΔP = pressure difference across the system under study.

$$R_{aw} = \frac{\partial(P_{ao}-P_{pl})}{\partial(\dot{V}_{ao})}$$

Partial derivatives are used to indicate that all other variables must be constant when these parameters are evaluated. In particular, C_{st} can be evaluated only when the system is in static equilibrium i.e. when all flows and rates of change of volume and pressure in the system are zero. In this situation $P_{ao} = P_A$ as $P_{ao} - P_A = 0$

$$\therefore P_{ao}-P_{pl} = P_{alv} - P_{pl}$$

$$C_{st1} = \frac{V_1(t_2) - V_1(t_1)}{\Delta P_1(t_2) - \Delta P_1(t_1)}$$

where $\Delta P_1 = P_{ao}-P_{pl}$ at static condition (i.e. $\dot{V}_1=0$)

= transpulmonary pressure difference and t_1 and t_2 are two instants at which the system is completely relaxed (i.e. $\dot{V}_{ao} = \dot{V}_1 = 0$).

The muscle pressure difference ΔP_{mus} is difficult to measure directly. Hence C_{stw} can be evaluated only when $\Delta P_{mus} = 0$. This occurs by definition when the respiratory muscles are completely relaxed.

Pressure difference across the chest wall

$$\Delta P_w = P_{pl} - P_{BS} \text{ when } \Delta P_{mus} = 0$$

$$\therefore C_{stw} = \frac{V_1(t_4) - V_1(t_3)}{\Delta P_w(t_4) - \Delta P_w(t_3)}$$

where t_3, t_4 are two instants at which the system is static and the respiratory muscles are completely relaxed.

Lung volume changes during respiration. For fast changes in volume, rate of change of volume $\dot{V}_l$ and volume of flow of gas at mouth ($\dot{V}_{ao}$) are not the same. But for normal tidal breathing

$$\dot{V}_{ao} \simeq \dot{V}_l$$

Hence $$P_{ao} - P_{pl} = \frac{V_l}{C_{stl}} + R_{aw} \cdot \dot{V}_l$$

$$\Delta P_{rms} + P_{pl} - P_{BS} = \frac{V_l}{C_{stw}}$$

In the respiratory system, V_l, $\dot{V}_l$, P_{ao}, P_{BS}, partial pressures of gases in the airway and blood and temperature are measurable. Other variables can be inferred or can be measured indirectly.

CHAPTER 5

A RESPIRATORY SYSTEM MODEL FOR AUTOMATIC DIAGNOSIS

5.1 INTRODUCTION [14]

As already stated, lung diseases cause variation in characteristics and parameters of the pulmonary system and its sub-systems rather than varying its basic structure. Hence measurement and estimation of system parameters, together with other informations available to the physician from clinical and laboratory tests, are necessary for the detection of pulmonary diseases. The physiological symptoms may detect the presence of pulmonary mechanical impairment and the intensity of disease, but will not indicate the cause or site of the lung obstruction.

Again in early stages of diseases, the outward manifestations of diseases may be quite similar. In particular, the early detection and clinical diagnosis of emphysema, bronchitis and asthma presents a serious problem, because prognosis and indicated treatment are markedly different for each disease.

Edema and emphysema are characterised by changes in total lung water which modify the permitivity and conductivity of the lung tissue. Hence clear distinction between these diseases will be difficult.

Again emphysema, is a generic term for several respirato-ry diseases (rather than being a specific disease) which are all manifested by an anatomical alteration of the lung characterised by an abnormal enlargement of the air - spaces distal to the terminal, non-respiratory bronchioles.

Centrilobular emphysema is the more common form, characterized by non-uniform appearance in early stages. Panlobular emphysema develops in a more or less uniform fashion. In advanced stages both forms of emphysema may blend together and exhibit a very similar pathology. Hence distinct and precise diagnosis of diseases is difficult.

Prognosis and diagnosis of diseases, and treatment, must be as precise as possible rather than general. Hence a reliable and sufficiently precise method to evaluate the exact site of obstruction and accurate intensity of parameter deviation is necessary for better treatment. Unnecessary medicines must be avoided to the maximum as even the absolutely essential medicines have ill-effects on the human body.

In the attempt to detect diseases in specific terms, one comes across another problem of variation in characteristics and parameters with the body size, weight, age and sex of the individuals. A method to nullify those effects is adopted in the work which follows in this chapter and verified for the available experimental data.

Direct measurement of measurable parameters and indirect estimation of other variables lead to the use of the model for diagnostic purposes. Certain pathological test results could be related to these variables wherever they are found to give additional advantage in specifying diseases.

5.2 MATHEMATICAL MODEL OF PULMONARY MECHANICS

5.2.1 Symbols Used.

For the development of this mathematical model, the following symbols are used.

R_u Upper (large) airway resistance

K_1 Coefficient of the linear term in the Rohrer expression for resistance to airflow in the upper airways.

K_2 Coefficient of the second order term in the Rohrer expression for resistance to airflow in the upper airways.

R_m Resistance to airflow of the mid-airways.

R_{mo} Resistance to airflow of the mid-airways at zero transmural pressure.

V_{mo} Volume of mid-airways at zero transmural pressure.

V_m Volume of mid-airways.

R_l Resistance to airflow of the lower (small)airways which is a function of lung volume.

V_l Alveolar lung volume.

R_{lt} Viscous resistance of the lung tissue.

C_{lt} Static compliance of the lung tissue.

P_u, P_m Pressures (drops) at upper and middle airways with respect to atmosphere.

P_{tm} Transmural pressure across the mid-airway, which is a function of V_m

P_{alv} Representative pressure within the lungs with respect to atmosphere (alveolar pressure)

P_{pl} Representative pressure on the pleural surface with respect to atmosphere

P_{el} Lung elastic recoil or transmural pressure which is a function of lung volume (alveolar space)

C_m Static compliance of the mid airway

$\dot{V}_{ao}, \dot{V}_l, \dot{V}_m$ Average airflow at the mouth, lower airways and mid-airways respectively

P_{opp} is equal and opposite to P_{pl} (applied pressure)

f Frequency of breathing (Breath/Sec)

T_i Time for inspiration (Secs)

5.2.2 Units.

All resistances and K_1 are in Cm H_2O/lit/sec.

All pressures and K_2 are in Cm H_2O.

All airflows are in lit/sec.

All compliances are in lit/Cm H_2O.

All volumes are in lit.

5.2.3 Assumptions and Approximations.

A state variable model characterized by parameters having physiological significance is developed. This model is in accordance with the latest models developed or modified by Golden et al, Gupta et al and others.[4,5,17]

Lumped parameter technique is adopted, not only because of the complexity of the system but also because most clinically flexible measurements can be made only on the system as a whole.

This model is a non-linear mathematical model with due stress on collapsible middle airways and lower airways.

Flow is limited to 5 lit/sec where Rohrer's equation for pressure drop $P_u = K_1 \dot{V}_{ao} + K_2(\dot{V}_{ao})^2$ is valid where

$K_1 \dot{V}_{ao}$ is the laminar flow term containing viscosity of gas and tubular geometry and

$K_2(\dot{V}_{ao})^2$ is significant at higher flow rates where turbulent flow occurs.

In order to simplify the analysis, the interactive effects on lung mechanics by other functional units of respiration such as Blood flow and gas exchange are neglected.

The lumped alveolar space is connected to the mouth by a single non-uniform airway. The alveolar space and most of the airways are surrounded by pleural cavity.

Fig. 5.1 shows the lumped representation of the ventilatory system and its equivalent circuit is shown in Fig.5.2. The airway is divided into three segments, the functional aspects of which are of more importance than their anatomic location.

(i) Upper airways :

This segment is assumed to be rigid due to their cartilage support and consists of the extrathoracic airways from the mouth to the extrathoracic trachea. This account for the non-linearity of flow pressure relationship and is modeled as a resistance = $K_1 + K_2 \dot{V}_{ao}$.

(ii) Middle airways :

The large bronchi composes this segment of the airways. This is of a fixed length and is a collapsible segment in that its resistance to flow changes in abnormals, as its volume changes with the transmural pressure.

(iii) Lower airways :

The small bronchioles (without cartilage support) beyond the tenth stage of branching and those embedded within the alveolar lung tissue compose this section of airways. The resistance offered by this segment is assumed more or less constant except for lesser volume of lung air (V_1). And the lung volume is affected by the expansion and relaxation of the lung.

5.2.4 Nodal Formation.

Upper airways :

The pressure-flow relation between the flow at the mouth $\dot{V}_{ao}$, and the upper airway pressure drop P_u is non-linear

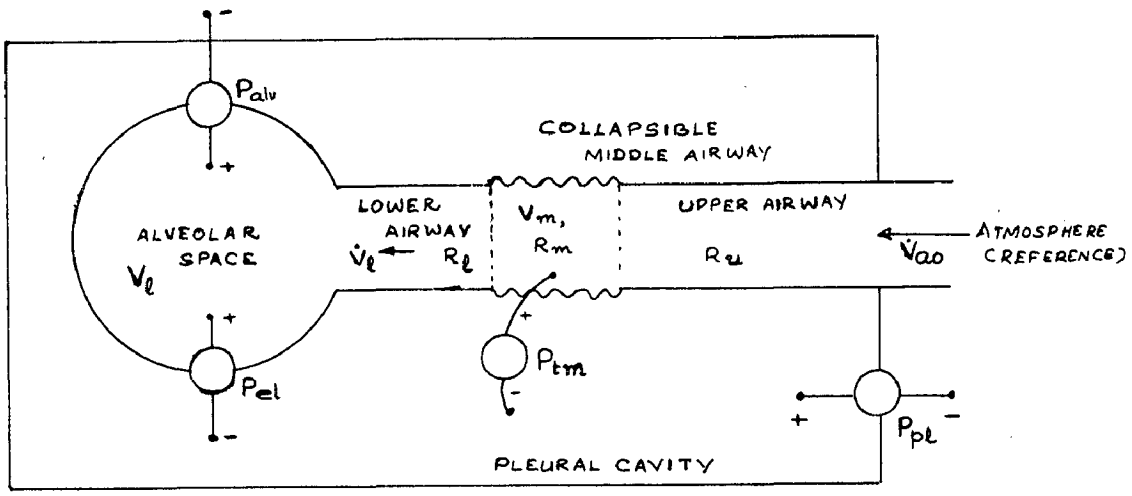


FIG 5.1 LUMPED REPRESENTATION OF PULMONARY AIRWAY SYSTEM

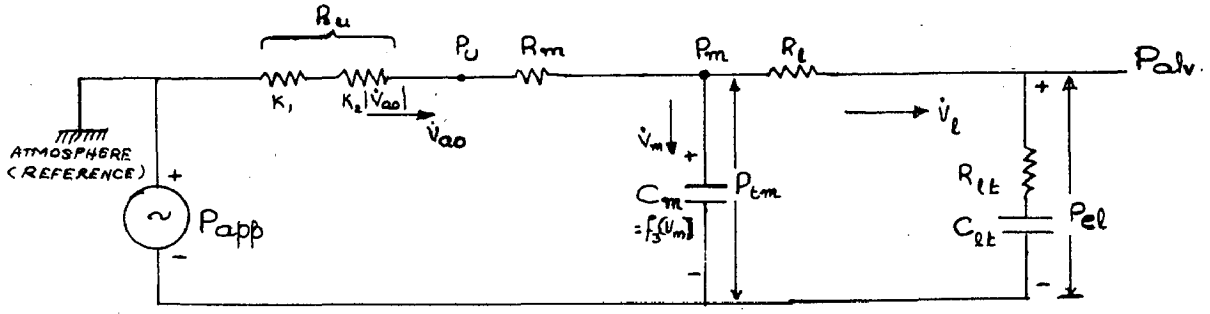


FIG 5.2 EQUIVALENT NON-LINEAR CIRCUIT FOR THE MODEL OF NORMAL VENTILATORY MECHANICS FOR SMALL AMPLITUDE, LOW FREQUENCY (NORMAL LUNGS, RESTING) BREATHING

$$R_u = K_1 + K_2 |\dot{V}_{ao}| \quad \text{.. (1)}$$

$$P_u = K_1 \dot{V}_{ao} + K_2 (\dot{V}_{ao})^2 \quad \text{.. (2)}$$

Middle airways :

$R_m = f_1(V_m)$ where Poiseuille's relationship for resistance to laminar flow in cylinder (here mid-airways) of length L and diameter D is valid.

i.e. $\dot{V}_m = \frac{\Delta P . D^4 \pi}{128 L \rho}$ where ΔP = Pressure difference across the airways

ρ = Coefficient of viscosity of fluid, in 'Poise'.

$$R_m = \frac{\Delta P}{\dot{V}_m} = \frac{128 L \rho}{D^4 \pi}$$

$$R_m = \frac{K}{V_m^2} \text{ where } V_m = \frac{\pi}{4} D^2 L \text{ and } K = \left(\frac{128 L^3 \rho \pi}{16} \right)$$

i.e. the resistance is proportional to the reciprocal of volume squared. Taking the ratios of resting resistance and volume (at zero transmural pressure), to have

$$R_m = R_{mo} \left(\frac{V_{mo}}{V_m} \right)^2 \quad \text{.. (3)}$$

Lower airways :

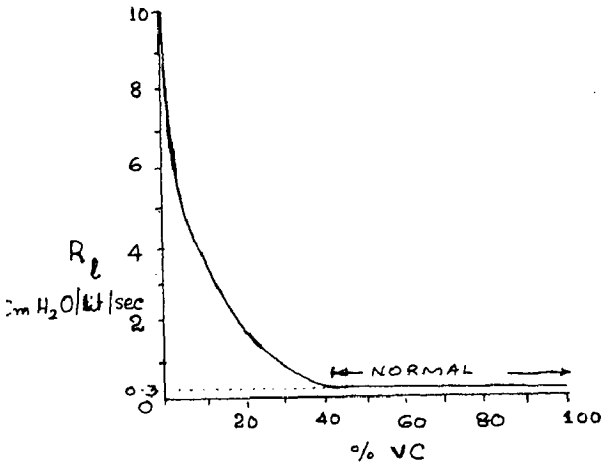
R_l is a function of V_l ie $R_l = f_2(V_l)$

Based on the data published by Macklem and Mead, and Dawhuys[7] as shown in Fig.5.3,

R_l is taken as 0.3 for V_l above 35% TLC

R_l is derived as:-

$$R_l = Y e^{-\left(r_1 \frac{V_l}{TLC} + r_2\right)}$$ where $Y = 10$, $r_1 = 10$ and $r_2 = 0.1$ for $V_l \leq 35\%$ TLC .. (4)



R_l as a function of V_l (∝VC)

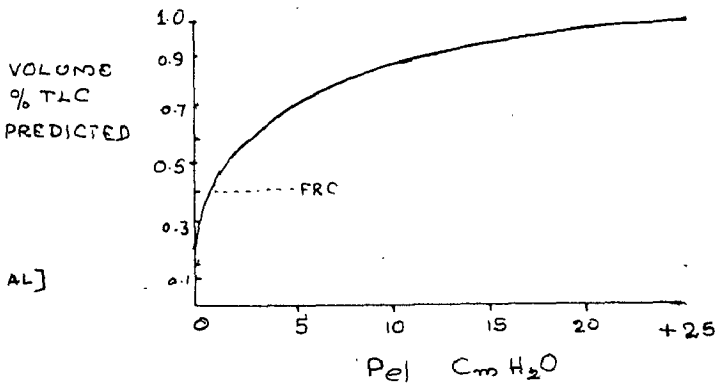
FIG. 5·3 R_l Vs. % VC (LUNG VOLUME)

[BASED ON DATA FURNISHED BY MACKLEM & MEAD, AND BOUHUYS]

FIG. 5.5

LUNG COMPLIANCE CURVE

[BASED ON DATA FURNISHED BY GLAISTEL ET AL AND CLEMENTS ET AL]



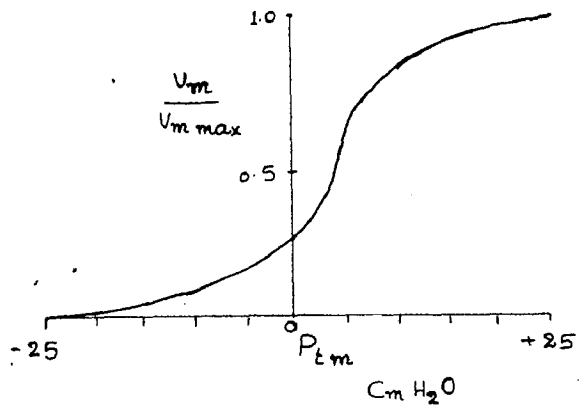


FIG. 5·4 MIDDLE AIRWAY COMPLIANCE CURVE

Middle airway pressure (drop), P_m is calculated from air flow through upper airway and middle airway as

$$P_m = \dot{V}_{ao}\,(R_u + R_m) = P_u + \dot{V}_{ao} \cdot R_m \qquad \text{.. (5)}$$

$$\text{i.e. } P_m = (R_1 + R_2|\dot{V}_{ao}| + R_m)\,\dot{V}_{ao}$$

The pressure that causes the flow of air in the lungs is P_{alv}. It is numerically equals to the sum of pressure across the pleural cavity (P_{pl}) and pressure across the lung tissue(P_{el})

$$\therefore\ P_{alv} = -(P_{pl} + P_{el})$$

$$= -P_{pl} - P_{el}$$

$$= P_{app} - P_{el} \qquad \text{.. (6)}$$

$$\text{as } P_{app} = -P_{pl} \qquad \text{.. (7)}$$

The system forcing function is defined as the pleural pressure or the applied pressure and this is related to alveolar pressure by equation (6). The system forcing function $\xrightarrow{\text{causes}}$ airflow at the mouth $\dot{V}_{ao}$.

Based on the latest experimental data furnished by Olender et al[7], the relationship between P_{tm} and V_m(collapsible compliance curve) is altered from its highly stylized hyperbolic form[5] to the form given in graph (Fig. 5.4). This relationship has the advantage that P_{tm} is given as a function of $V_m/V_{m\,max}$ instead of V_m itself. Hence any abnormal condition in middle airway, though affects the transmural pressure, is considered not to affect the relationship between P_{tm} and $V_m/V_{m\,max}$.

A mathematical equation is derived for this collapsible segment compliance ratio curve i.e. $P_{tm} = f_3(V_m/V_{m\,max})$, based on the data furnished.

Modified Gompertz equation is found to be a suitable solution [18] and is given as

$$P_{tm} = a + ab^{c^{(K_3 x + K_4)}} \qquad \text{where } x = V_m/V_{max.}$$

$\alpha = -25$, $a = 45$, $b = 0.4$

$c = 0.85$, $K_3 = 10$ and $K_4 = -1$

or

$$P_{tm} = -25 + 45\ (0.4)^{0.85^{(10\ \frac{V_m}{V_{m\ max.}} - 1)}} \quad \ldots (8)$$

The flow rate at lower airways $\dot{V}_l$ is derived as

$$\dot{V}_l = \frac{P_{tm} - P_{clt}}{R_l + R_{lt}} \quad \text{where } P_{clt} = \frac{V_l}{C_{lt}}, \text{ the pressure across } C_{lt}$$

$$\therefore \quad \dot{V}_l = \frac{P_{tm}}{R_l + R_{lt}} - \frac{V_l}{C_{lt}(R_l + R_{lt})} = \frac{V_l}{T_l} \quad \ldots (9)$$

Again P_{alv} = The pressure drop at alveoli w.r.t. atmosphere

$$\therefore \quad |P_{alv}| = |P_m| + |\dot{V}_l R_l| = |\dot{V}_{ao}(R_h + R_m)| + |\dot{V}_l R_l|$$

where P_{alv} is negative during inspiration (drop) and positive during expiration.

$$\text{or} \quad |P_m| = |P_{alv}| - |\dot{V}_l R_l| \quad \ldots (10)$$

$$P_{tm} = P_{el} + \dot{V}_l R_l \quad \ldots (11)$$

Static Lung compliance curve for normal case is shown in [Fig. 5.5] as per data furnished by Colebatch et al [7]. A mathematical hyperbolic relation (Sin hx) is derived to suit this characteristic as given below.

$$P_{el} = \beta + l \sin h\ (m \cdot \frac{V_l}{TLC} + n) \quad \text{where } \beta = -0.5,\ l = 12.5$$

$m = 1.45$ and $n = -0.3$

$$\therefore \quad P_{el} = -0.5 + 12.5 \sin h \left(1.15 \frac{V_1}{TLC} - 0.3 \right) \qquad \ldots(12)$$

P_{el} in relation to R_{1t}, C_{1t} is obtained as

$$P_{el} = \dot{V}_1 R_{1t} + \frac{V_1}{C_{1t}} \qquad \ldots(13)$$

$$V_{ao} = \frac{P_m}{R_u + R_m} = \frac{P_{alv} - \left[\frac{P_{tm}}{R_1 + R_{1t}} - \frac{V_1}{C_{1t}(R_1 + R_{1t})} \right] R_1}{K_1 + K_2 |\dot{V}_{ao}| + R_{mo} (V_{mo}/V)^2} \qquad \ldots(14)$$

$$\dot{V}_m = \dot{V}_{ao} - \dot{V}_1 = \frac{P_{alv} - \dot{V}_1 R_1}{R_u + R_m} - \dot{V}_1$$

$$= \frac{P_{alv} - \dot{V}_1 (R_1 + R_u + R_m)}{R_u + R_m} \qquad \ldots(15)$$

$$V_m (t) = V_{mo} + \int_0^t (\dot{V}_{ao} - \dot{V}_1) \, dt \qquad \ldots(16)$$

$$C_m = f_4 (V_m) = \frac{V_m}{P_{tm}}$$

$$\text{or} \quad C_m = \frac{V_m(t_2) - V_m(t_1)}{P_{tm}(t_2) - P_{tm}(t_1)} \qquad \ldots(17)$$

where t_1 and t_2 are two instants at which the the system is completely static and the respiratory muscles relaxed completely.

$$C_{1t} = \frac{V_1(t_4) - V_1(t_3)}{\Delta P_1 (t_4) - \Delta P_1 (t_3)} \qquad \ldots(18)$$

where ΔP_1 = transpulmonary pressure difference
$= P_{alv} - P_{pl}$ at static condition (when $\dot{V}_1 = 0$) and

t_3, t_4 are two instants at which the system is completely motionless.

$$R_{1t} = \frac{P_{el} - \frac{V_1}{C_{1t}}}{\dot{V}_1} \qquad \ldots(19)$$

The volume and flow variables V_1, $\dot{V}_1$ and $\dot{V}_{ao}$ can be measured by using Expirograph and the alveolar pressure P_{alv} can be measured by Plethysmograph. Standard values for K_1, K_2, V_{mo} and R_{mo} are taken for a normal case. And the values of other system variables can be calculated with this data. System parameters are calculated for abnormal cases also where the values of K_1, K_2, V_{mo} and R_{mo} are changed. The values are tabulated and given in Appendix I. In all these calculations the ratio of middle airway volume (V_{mo}) for zero transmural pressure to the middle airway volume ($V_{m\,max}$) for maximum transmural pressure (P_{tm}) is taken as a constant as the collapsible compliance ratio curve is assumed to be applicable to any individual.

5.3 A NEW AUTOMATIC METHOD OF DIAGNOSIS OF DISEASES

The system parameters derived from model equations show the conditions of the different segments of the respiratory system and hence any abnormality can be detected as a variation of these values from the standard values of a normal and healthy person. A major problem encountered in this method already in use, is that these values vary with individuals, according to their size and weight, age, sex etc. and only clearly aggravated cases can be precisely diagnosed. This gives difficulty in prognosing diseases in

their early stages and diagnosing diseases with lesser deviation of values of parameters even in later stages.

A new set of parameters, called 'diagnosis parameters' are derived from the system parameters which give the ratios of certain system parameters. The advantage of these 'diagnosis parameters' is that they don't change considerably from individual to individual in the normal condition. And the variation in abnormal conditions are clearly distinct that diagnosis is precise and distinct. A tabulation of six 'diagnosis parameters' for respiratory diseases derived for 12 persons from the experimental data available are shown in Appendix II.

The ratio $V_a/V_{a\,max}$ is a measure of the amount of middle airway collapse in a given disease for a particular volume of lung air. It is found that for a normal person this ratio $\left(\frac{V_a/V_{a\,max}}{P_{tl}}\right)$ is always in the range of 1.2 to 1.4 and this ratio is an index of bronchial compliance. This indicates the ability of the middle airway to collapse when subjected to compressive stress. But it is found that this ratio depends on the lower airways obstruction also as V_a is a function of the middle transmural pressure (P_{tm}) which is related to R_l.

Hence the middle airway resistance to compliance ratio (R_m/C_a) gives a clearer indication of the obstruction to middle airway independent of lower airway obstruction.

The alveolar pressure depends on the flow rate and obstruction in any part of the airway will affect the alveolar pressure. The ratio (R_u/P_{alv}) gives directly the effect of upper airway obstruction on alveolar pressure and is indicative

of the patient's intrathoracic capacity and strength.

The 'diagnosis parameters' derived indicate a particular combination of deviated values for a particular disease. In the 12 cases under study, the diseases of bronchial asthma, Bronchitis and Emphysema are detected to tally with the clinical observations available in literature.[17] And the subcategories of those diseases can be diagnosed with much accuracy.

The 'diagnosis parameters' can be directly fed to a digital computer so that the deviation of any parameter from the normal range indicates the particular region of the system being affected. The six binary parameters selected for comparison purpose give sixty four combinations, making it possible to automatically categorize sixty four kinds of lung diseases.

One prominent feature in deriving the system parameters necessary for the'diagnosis parameters' is that except for the value of P_{ho}, all other variables needed are measurable (such as V_1, $\dot{V}_1$, $\dot{V}_{eo}$, TLC and P_{alv}). This will enable us to have lesser assumptions and approximations.

CHAPTER 6

FREQUENCY RESPONSE ANALYSIS OF A RESPIRATORY SYSTEM MODEL

6.1 INTRODUCTION

The model described and the diagnosis method derived in the previous chapter, though taken into account the lung tissue resistance and compliance, is not suitable to detect the disease in this silent zone. Since this part of the lungs contribute very low percentage of the total airway resistance (about 5 to 10% only), even advanced obstruction in the tissues can not be diagnosed with normal measurements.

Obstruction in the large and small airways results in frequency dependent behaviour of the lungs as measured by a dynamic compliance test. This frequency dependence can be used as an indirect measure of airway disease in its initial stages. In this analysis, the sensitivity of frequency dependent behaviour to small airway obstruction and distribution is studied in detail.

Thomas H. Shaffer has made a study of the frequency response sensitivity[8] of mechanical parameters such as impedance, dynamic compliance and dynamic resistance as a function of individual airway properties, using a simple three compartmental lung model. In his model, he considered only the system behaviour response to variation in relative compartment resistance and assumed the compartment compliance as constant. Also the variations in lung parameters other than the lung tissue were not considered.

To get a more detailed and accurate frequency response characteristics of the lung mechanical parameters, a model is developed from our model described in chapter 5. The following

are the specific features of this analysis when compared with the analysis done by F.H. Saffer:

(1) The model is more detailed than a simple model.

(2) The total lower airways is sub-divided in this model, into lower airways and lung tissue compartments, as against lumping the whole into one unit.

(3) The system behaviour response to variation in compartment compliance also is considered.

(4) The effect of variations in other parameters like the upper airway resistance, lower airway resistance are also considered in our analysis.

The model is analysed to study frequency response behaviour, using computer programming and the characteristics were discerted to bring out the salient features of this analysis and to be used in diagnostic purpose.

6.2 DEVELOPMENT OF THE MODEL

The equivalent circuit of the model developed for the purpose of analysis of the sensitivity of frequency dependent behaviour of the respiratory system to airway obstruction and distribution in the lung tissues is given in Fig.6.1.

The lung is described as a population of parallel pathways with dissimilar properties. According to Otis et al,[9] the overall behaviour of such a population could vary with breathing frequency while the fundamental properties of the individual pathways remain constant. Therefore the degree of frequency dependence is related to the distribution of mechanical properties in the parallel pathways.[8]

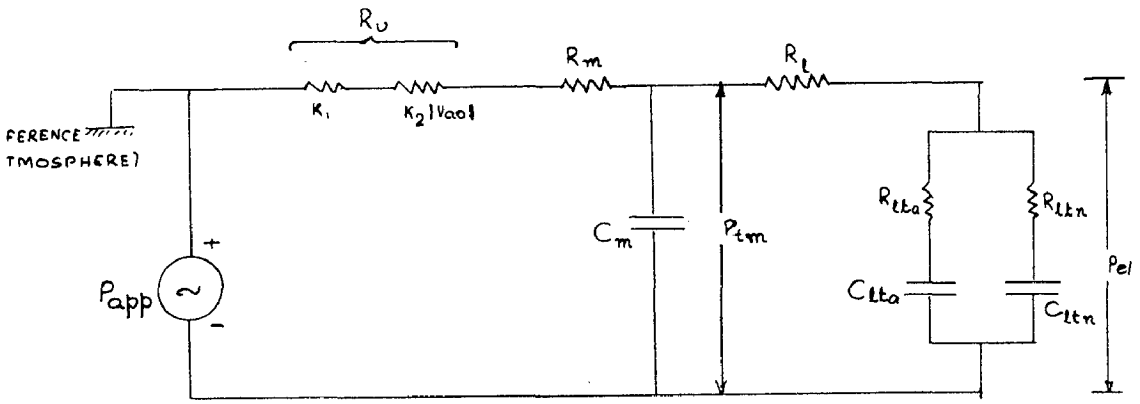


FIG 6.1 EQUIVALENT NON-LINEAR CIRCUIT FOR THE MODEL USED FOR FREQUENCY RESPONSE ANALYSIS

In the model developed here, the lung tissue airways possess two parallel resistive and capacitive pathways which are representative of the mean of all the obstructed and normal lung tissues.

6.2.1 Additional Symbols Used in This Model.

Suffix 'a'	stands for abnormal (obstruction)
Suffix 'n'	stands for normal
D_a	Mean diameter of the obstructed lung tissues
D_n	Mean diameter of the normal lung tissues
R_{lta}	Mean resistance of obstructed compartment which is a function of resistance of each pathway and the number of pathways in that compartment
R_{ltn}	Mean resistance of the normal compartment
C_{lta}	Mean capacitance of the obstructed compartment
C_{ltn}	Mean capacitance of the normal compartment
$R_{lt}(w)$	Dynamic resistance of lung tissues
$C_{lt}(w)$	Dynamic compliance of lung tissues
$Z_{lt}(w)$	Complex impedance of lung tissues
$R_l(w)$	Dynamic resistance of the total small (peripheral airways.
$C_l(w)$	Dynamic compliance of the total small (peripheral)airways
$Z_l(w)$	Complex impedance of the total small (peripheral)airways
$R_{ta}(w), C_{ta}(w)$ and $Z_{ta}(w)$	Dynamic resistance , compliance and complex impedance of the lung system excluding the upper and middle airway resistances

$\bar{R}(v), \bar{C}(v), \bar{Z}(v)$	Dynamic resistance, compliance and complex impedance of the whole lung system
R_{lt}	Resultant lung tissue resistance
C_{lt}	Resultant lung tissue compliance
v	Breathing frequency in Breath/Sec.
τ_o	Time constant of the obstructed compartment
τ_n	Time constant of the normal compartment.

6.2.2 Assumptions and Approximations

The input to the system is assumed to be sinusoidal.

The percentage obstruction depends on the average and mean diameter of the two parallel compartments

$$\text{i.e. } \% OBS = \left(1 - \frac{D_o}{D_n}\right) \times 100 \qquad \text{.. (1)}$$

The resultant lung tissue resistance (R_{lt}) and compliance (C_{lt}) are assumed to be constant

$$R_{lt} = \frac{R_{ltn} \times R_{lto}}{R_{lto} + R_{ltn}} \qquad \text{.. (2)}$$

$$C_{lt} = C_{lto} + C_{ltn} \qquad \text{.. (3)}$$

Hugh Jones P et al [20] shows that flow in the distal airway is laminar (dia 2.5 mm, flow 3.3 lit/sec, Reynolds Number = 719) and that resistance to flow, R, varies as the reciprocal of the fourth power of the diameter,

$$R \propto \frac{1}{D^4}$$

$$\therefore \frac{R_{ltn}}{R_{lto}} = \left(D_n/D_o \right)^4 \qquad \text{.. (4)}$$

The percentage obstruction of obstructed airway relative to the normal can be expressed in terms of the ratio of resistances of the airways. From equations (1) and (4)

$$\% \text{ OBS} = \left[1 - \left(\frac{R_{1tm}}{R_{1tn}} \right)^{0.25} \right] \times 100 \qquad \text{.. (5)}$$

$$\therefore \frac{R_{1tm}}{R_{1tn}} = (1 - \text{OBS})^{4} \qquad \text{.. (5a)}$$

Relationship for OBS in terms of lung tissue compliances :

A relationship is derived for percent obstruction and the lung tissue compliances C_{1tn} and C_{1tm}. The normal and obstructed lung tissue compartments are assumed to be of spherical shape for simplicity of calculations.

$$\text{Compliance } C = \frac{\partial V}{\partial(\Delta P)} \text{ .}$$

$$C_{1tn} = \frac{\partial V_n}{\partial(\Delta P)}$$

$$C_{1tm} = \frac{\partial V_m}{\partial(\Delta P)}$$, assuming same pressure difference across the two parallel compartments at any instant.

$$\therefore \frac{C_{1tm}}{C_{1tn}} = \frac{\partial V_m}{\partial V_n}$$

Again C_{1t} = change in volume of the lung tissue

= $V_1 - V_0$ where V_0 is the initial volume and V_1 is the final volume when variation in pressure difference across the system is $\partial(\Delta P)$.

$$C_{1tn} = V_n - V_{on}$$

$$V_{on} = \frac{4}{3} \pi r^3 = \frac{4}{3} \pi \left(\frac{D_n}{2} \right)^3 = \frac{\pi D_n^3}{6}$$

$$V_{on} \propto D_n^3$$

$\therefore C_{1tm} \propto D_n^3 - D_{on}^3$ where D_{on} is the diameter of normal lung at the initial instance

But $D_n = k_1 \cdot D_{on}$ where k_1 is the % increase in diameter for the pressure difference increase $\delta(\Delta P)$

$\therefore C_{1tn} \propto (k_1^3 - 1) D_{on}^3$

Similarly $C_{1ta} \propto (k_1^3 - 1) D_{oa}^3$, assuming the % increase in diameter to be the same as k_1 in the obstructed airways too.

Hence $$\frac{C_{1ta}}{C_{1tn}} = \frac{D_{oa}^3}{D_{on}^3} = \frac{D_a^3}{D_n^3}$$

$$\frac{D_a}{D_n} = \left(\frac{C_{1ta}}{C_{1tn}} \right)^{1/3} \quad \text{.. (6)}$$

$$\therefore \% OBS = \left[1 - \left(\frac{D_a}{D_n} \right) \right] \times 100$$

$$= \left[1 - \left(\frac{C_{1ta}}{C_{1tn}} \right)^{1/3} \right] \times 100 \quad \text{.. (7)}$$

Hence $$\frac{C_{1ta}}{C_{1tn}} = (1 - OBS)^3 \quad \text{.. (7a)}$$

6.2.3 Model Derivation.

The relationship between obstruction and the ratio of compliances of the two parallel compartments as well as their resistances are given in equations (7a) and (5a) respectively.

For each value of obstruction there will be corresponding values of resistance (R_{1ta}) and capacitance (C_{1ta}) for the obstructed lung tissues and are given by

$$R_{1ta} = R_{1t} \left[1 + \left(R_{1ta}/R_{1tn} \right) \right] \quad \text{.. (8)}$$

$$C_{1ta} = C_{1t} [C_{1ta}/C_{1tn}] \Big/ \left\{ 1 + \left[C_{1ta}/C_{1tn} \right] \right\} \quad \text{.. (9)}$$

Hence $$R_{1tn} = \frac{R_{1ta} \cdot R_{1t}}{R_{1ta} - R_{1t}} \qquad \text{.. (10)}$$

$$C_{1tn} = C_{1t} - C_{1ta} \qquad \text{.. (11)}$$

$$\left.\begin{aligned} \tau_a &= R_{1ta} \cdot C_{1ta} \\ \tau_n &= R_{1tn} \cdot C_{1tn} \end{aligned}\right] \qquad \text{.. (12)}$$

$$Z_{1t}(w) = R_{1t}(w) - j\ X_{c1t}(w) = R_{1t}(w) - \frac{j}{w \cdot C_{1t}(w)} \qquad \text{.. (13)}$$

$$= \frac{\left(R_{1ta} - \frac{j}{w \cdot C_{1ta}}\right)\left(R_{1tn} - \frac{j}{w \cdot C_{1tn}}\right)}{\left(R_{1ta} - \frac{j}{w \cdot C_{1ta}}\right) + \left(R_{1tn} - \frac{j}{w \cdot C_{1tn}}\right)}$$

$$\therefore R_{1t}(w) = \frac{w^2 \tau_a \tau_n (\tau_a C_{1tn} + \tau_n C_{1ta}) + (\tau_a C_{1ta} + \tau_n C_{1tn})}{w^2 (\tau_a C_{1tn} + \tau_n C_{1ta})^2 + (C_{1ta} + C_{1tn})^2} \qquad \text{.. (14)}$$

and

$$C_{1t}(w) = \frac{w^2 (\tau_a C_{1tn} + \tau_n C_{1ta})^2 + (C_{1ta} + C_{1tn})^2}{w^2 (\tau_a^2 C_{1tn} + \tau_n^2 C_{1ta}) + (C_{1ta} + C_{1tn})} \qquad \text{.. (15)}$$

$$Z_1(w) = R_1 + Z_{1t}(w) = R_1(w) - j\ X_{c1}(w) = R_1(w) - j/w \cdot C_1(w) \qquad \text{.. (16)}$$

$$R_1(w) = R_1 + R_{1t}(w)$$

$$= R_1 \cdot A(w) + w^2 \tau_a \tau_n (\tau_a C_{1tn} + \tau_n C_{1ta}) + (\tau_a C_{1ta} + \tau_n C_{1tn})$$

$$R_1(w) = \frac{}{A(w)} \qquad \text{.. (17)}$$

where,

$$A(w) = w^2 (\tau_a C_{1tn} + \tau_n C_{1ta})^2 + (C_{1ta} + C_{1tn})^2 \qquad \text{.. (18)}$$

$$C_1(w) = C_{1t}(w) = \frac{A(w)}{w^2 (r_a^2 C_{1tn} + r_n^2 C_{1ta}) + (C_{1ta} + C_{1tn})} \quad .. (19)$$

$$Z_{tm}(w) = Z_1(w) \parallel X_{C_m} = \frac{Z_1(w) (- j X_{C_m})}{Z_1(w) - j X_{C_m}} = \frac{Z_1(w)(- \frac{j}{wC_m})}{Z_1(w) - j/wC_m} \quad ..(20)$$

$$Z_{tm}(w) = R_{tm}(w) - \frac{j}{w C_{tm}(w)} \quad .. (20a)$$

where,

$$R_{tm}(w) = \frac{R_1(w) C_{1t}^2(w)}{[R_1^2(w). w^2 C_m^2 C_{1t}^2(w) + \{C_m + C_{1t}(w)\}^2]} \quad .. (21)$$

and

$$C_{tm}(w) = \frac{w^2 R_1^2(w). C_m^2 C_{1t}^2(w) + \{C_m + C_{1t}(w) \}^2}{C_m + C_{1t}(w) + R_1^2(w). w^2 C_m. C_{1t}^2(w)} \quad .. (22)$$

$$\bar{Z}(w) = [R_a + R_m + R_{tm}(w)] - \frac{j}{w C_{tm}(w)} = \bar{R}(w) - \frac{j}{w \bar{C}(w)} \quad .. (23)$$

where,

$$\bar{R}(w) = R_a + R_m + \frac{R_1(w). C_{1t}^2(w)}{R_1^2(w). w^2. C_m^2 C_{1t}^2(w) + \{ C_m + C_{1t}(w)\}^2} \quad .. (24)$$

and

$$\bar{C}(w) = C_{tm}(w) = \frac{w^2 R_1^2(w) C_m^2 C_{1t}^2(w) + [C_m + C_{1t}(w)]^2}{C_m + C_{1t}(w) + R_1^2(w) w^2 C_{1t}^2(w) C_m} \quad .. (25)$$

6.3 COMPUTER PROGRAMME FOR THE MODEL

To study the sensitivity of frequency dependent behaviour as a function of airway obstruction, a computer programme was developed from the above electrical model of the lung. The main objective of this study is to assess the effects of the lung tissues rather than other airways. The lung tissue resistance and compliance of the obstructed tissues vary with the percentage obstruction; the resistance (R_{1t}) being increased with the obstruction; and the compliance(C_{1t}) being decreased as seen from equation (4) and (6). For values of R_{1t} and C_{1t} corresponding to each β OBS, values of R_{1t} and C_{1t} of the normal tissues are calculated from equations (10) and (11).

Using the computer model, the lung dynamic impedance $\bar{Z}(v)$, the dynamic compliance $\bar{C}(v)$ and the dynamic resistance $\bar{R}(v)$ were determined as a function of

(i) the breathing frequency (0.1 to 2.0 Hz/Sec)

and (ii) the percent obstruction of the lung tissues.

Again four different cases of lung airways are considered to accommodate the effect of other parameters also in the frequency dependent behaviour of the total impedance, resistance and compliance. They are

(i) when the values of upper airway resistance, (R_u) is large while the lower airway resistance (R_l) is normal

(ii) When upper and lower airway resistances are large

(iii) When upper and lower airway resistances are small and normal

(iv) The condition in which the lung tissue resistance and compliance are also lesser than case (i).

These four cases are considered so that the frequency dependence on $\bar{Z}(v)$, $\bar{R}(v)$, $\bar{C}(v)$ can be studied not only when there is obstruction in lung tissues but also when other parts of the lung system are affected by disease.

Numerical results were obtained from the computer programme (appendix III) with the following algorithm :

(1) Set the values of R_u, R_b, C_b, R_l, R_{lt} and C_{lt}.

(2) Set the value of β obstruction.
(From the β OBS, we will get the corresponding values of R_{ltn}, R_{ltn}, C_{ltn}, C_{ltn}, T_a and T_n).

(3) Give increments to the β obstruction.

(4) Determine $Z_o(v)$, $C_o(v)$ and $R_o(v)$ at $f = 0.1$ Hz/Sec.

(5) Determine the normalised lung parameters $Z(v)/Z_o(v)$, $C(v)/C_o(v)$ and $R(v)/R_o(v)$ over the frequency range 0.1 to 2 Hz/Sec.

6.4 COMPUTER RESULTS

Numerical results of dynamic variables $Z(v)/Z_o(v)$, $C(v)/C_o(v)$ and $R(v)/R_o(v)$ of 4 different cases over the breathing frequency range of 0.1 to 2.0 Hz/Sec are given in Figs. 6.2 to 6.9 . The values of resistance and compliance of the middle collapsible airways are assumed to be constant in all the cases. Each of the variables are normalized about $f = 0.1$ Hz/Sec

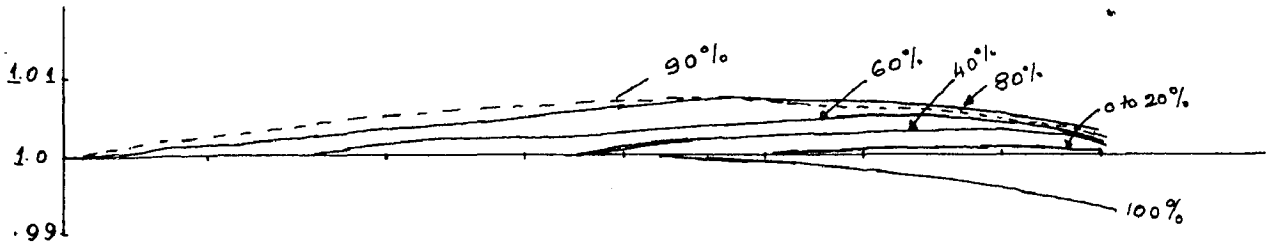
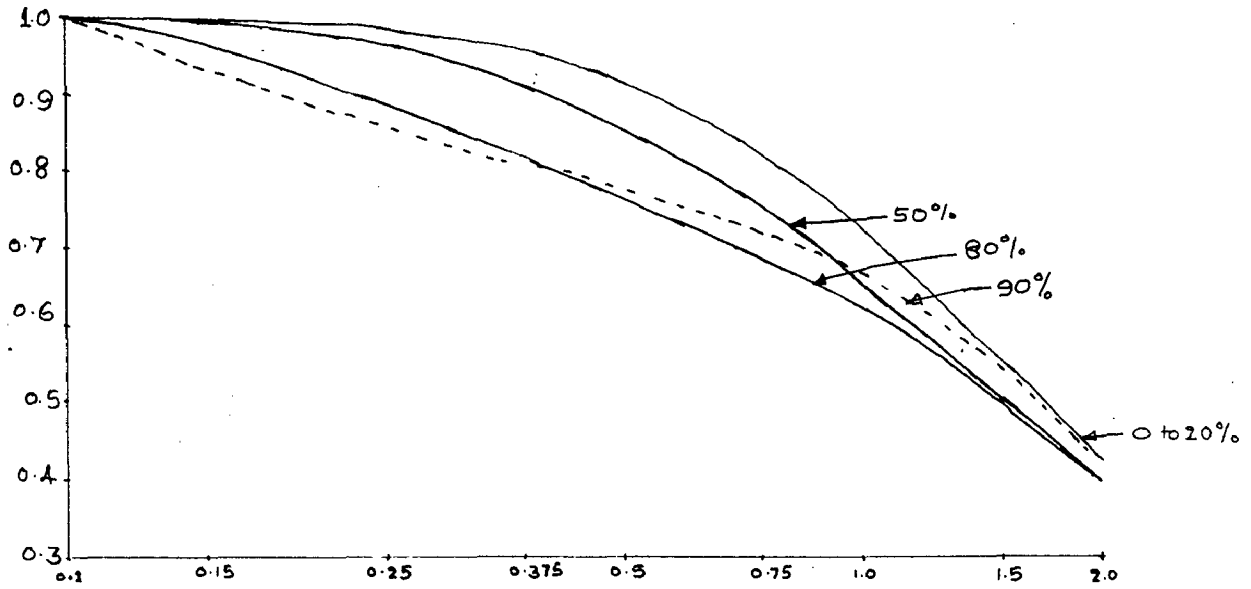


FIG. 6.2(a)



Breathing Frequency (Br/sec)

FIG. 6.2(b)

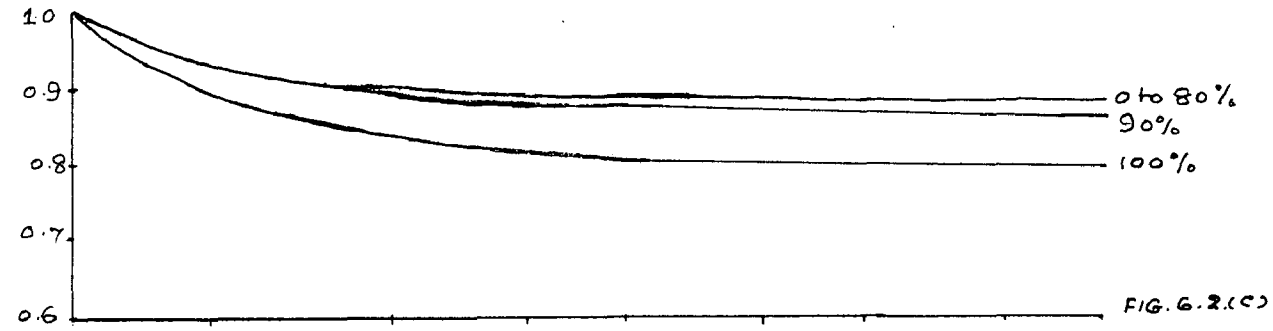


FIG. 6.2(c)

FIG. 6.2. NORMALIZED LUNG PARAMETERS AS A FUNCTION OF BREATHING FREQUENCY FOR DIFFERENT LEVELS OF AIRWAY OBSTRUCTION

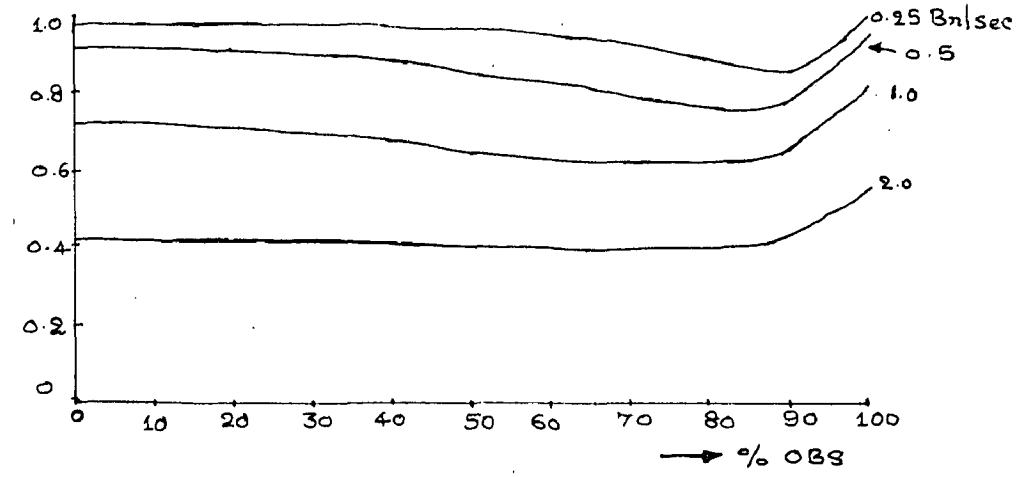


FIG 6.3

DYNAMIC COMPLIANCE AS A FUNCTION OF % OBSTRUCTION FOR CONSTANT BREATHING FREQUENCIES

CASE I

$R_u = 2.25$

$R_\ell = 0.30$

$C_{\ell t} = 0.70$

$R_{\ell t} = 0.175$

$R_m = 0.22$

$C_m = 0.04$

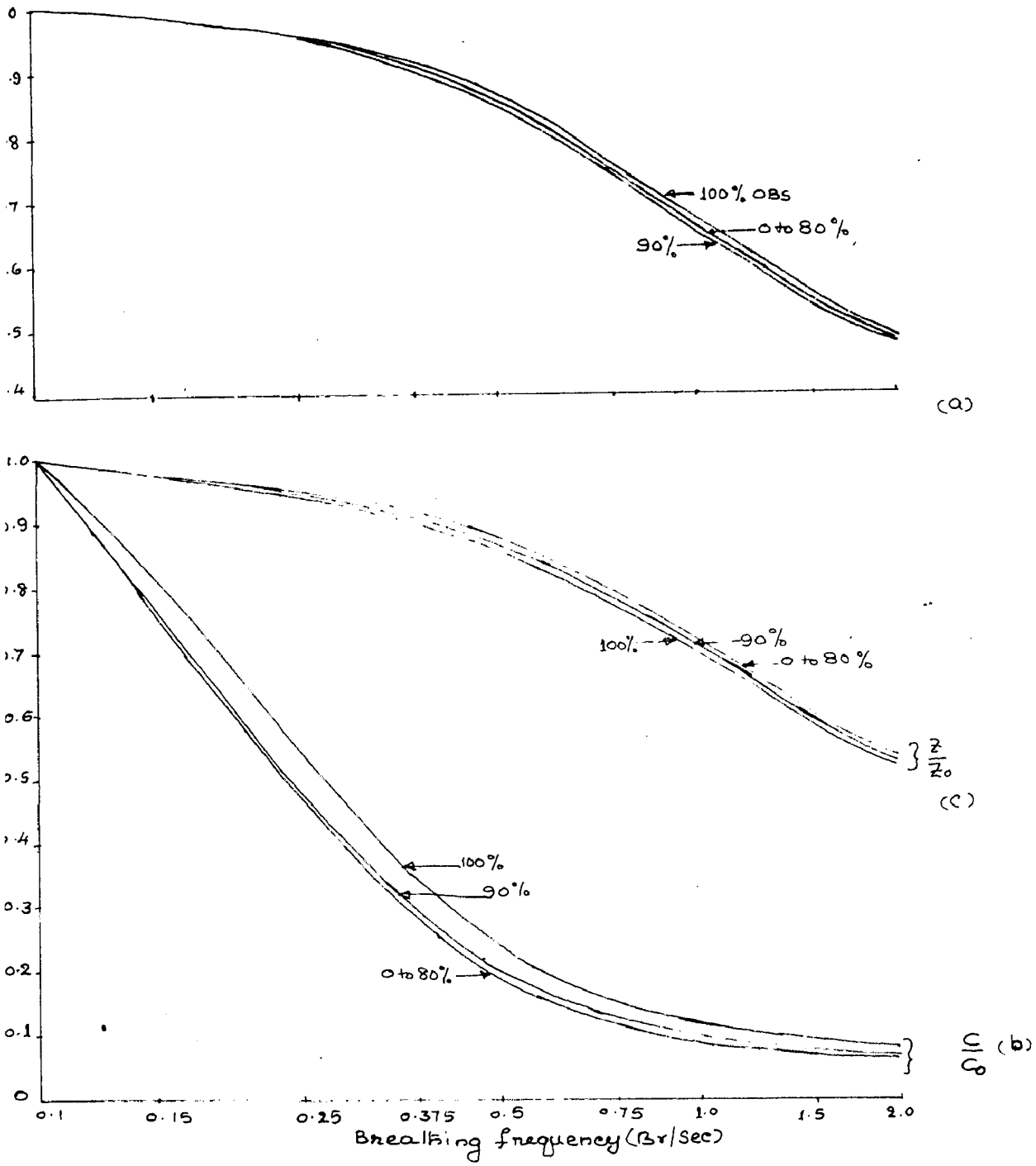


FIG. 6.4 NORMALIZED LUNG PARAMETERS AS A FUNCTION OF BREATHING FREQUENCY FOR DIFFERENT LEVELS OF AIR WAY OBSTRUCTION

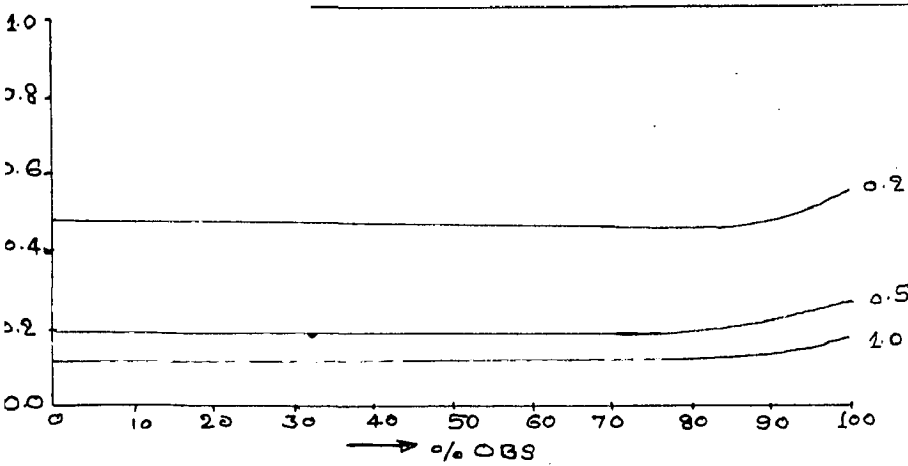


FIG. 6.5 DYNAMIC COMPLIANCE AS A FUNCTION OF % OBSTRUCTION FOR CONSTANT BEATHING FREQUENCIES

CASE II

$R_u = 2.25$

$R_L = 4.30$

$C_{lt} = 0.70$

$R_{lt} = 0.175$

$R_m = 0.22$

$C_m = 0.04$

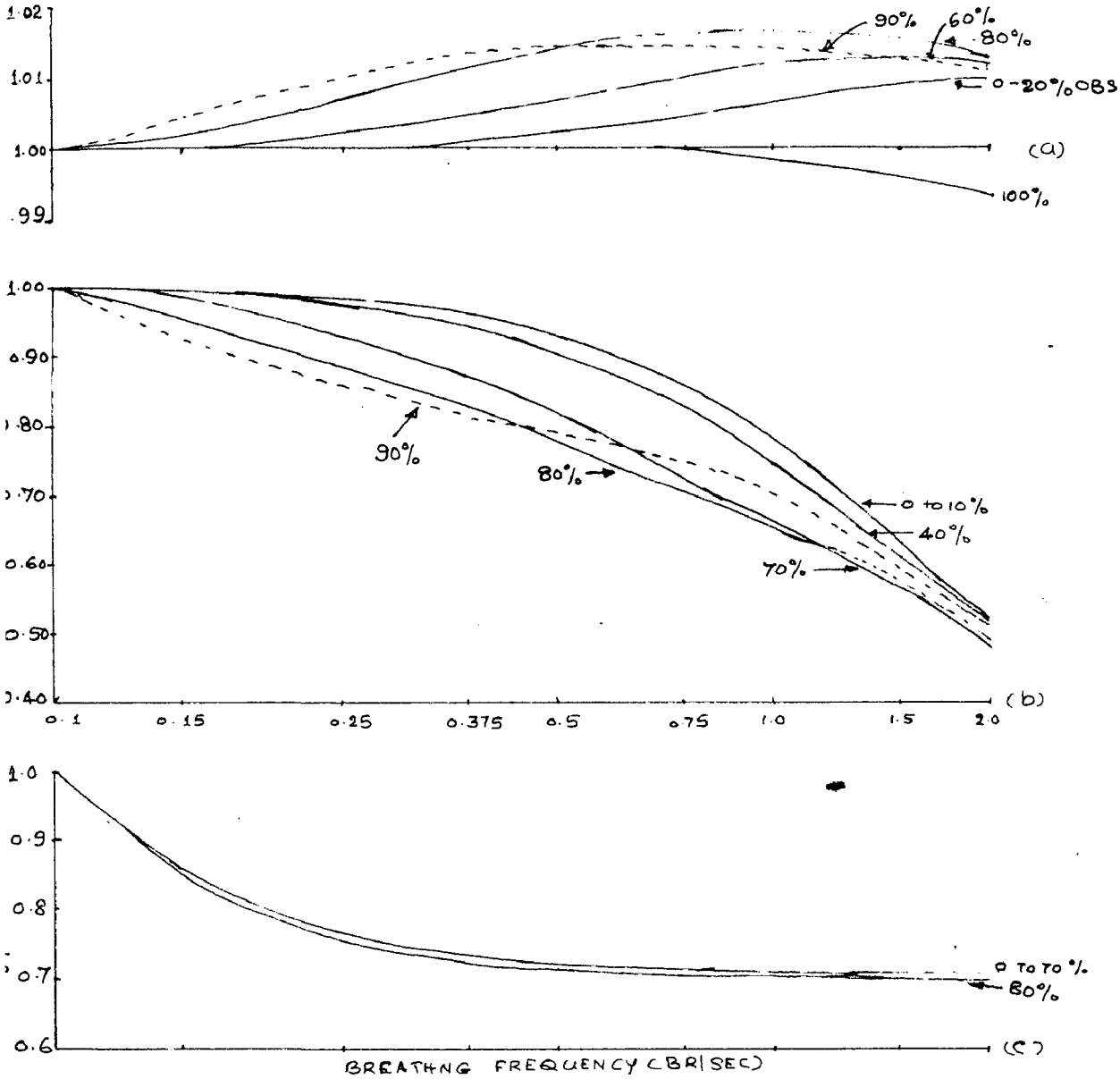


FIG. 6.6 NORMALIZED LUNG PARAMETERS AS A FUNCTION OF BREATHING FREQUENCY FOR DIFFERENT OBSTRUCTION

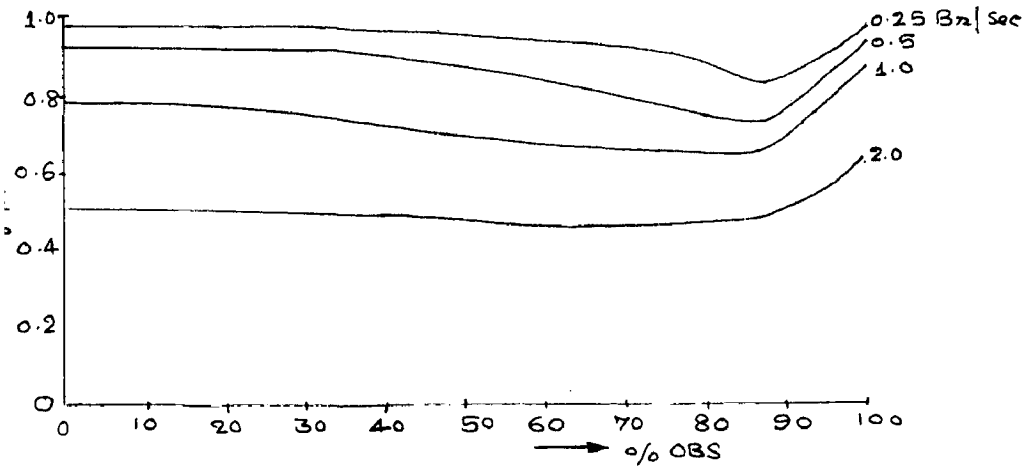


FIG. 6.7 DYNAMIC COMPLIANCE AS A FUNCTION OF OBSTRUCTION FOR CONSTANT BREATHING FREQUENCIES

CASE III

R_u = 1.00

R_l = 0.20

C_{lt} = 0.70

R_{lt} = 0.175

R_m = 0.22

C_m = 0.04

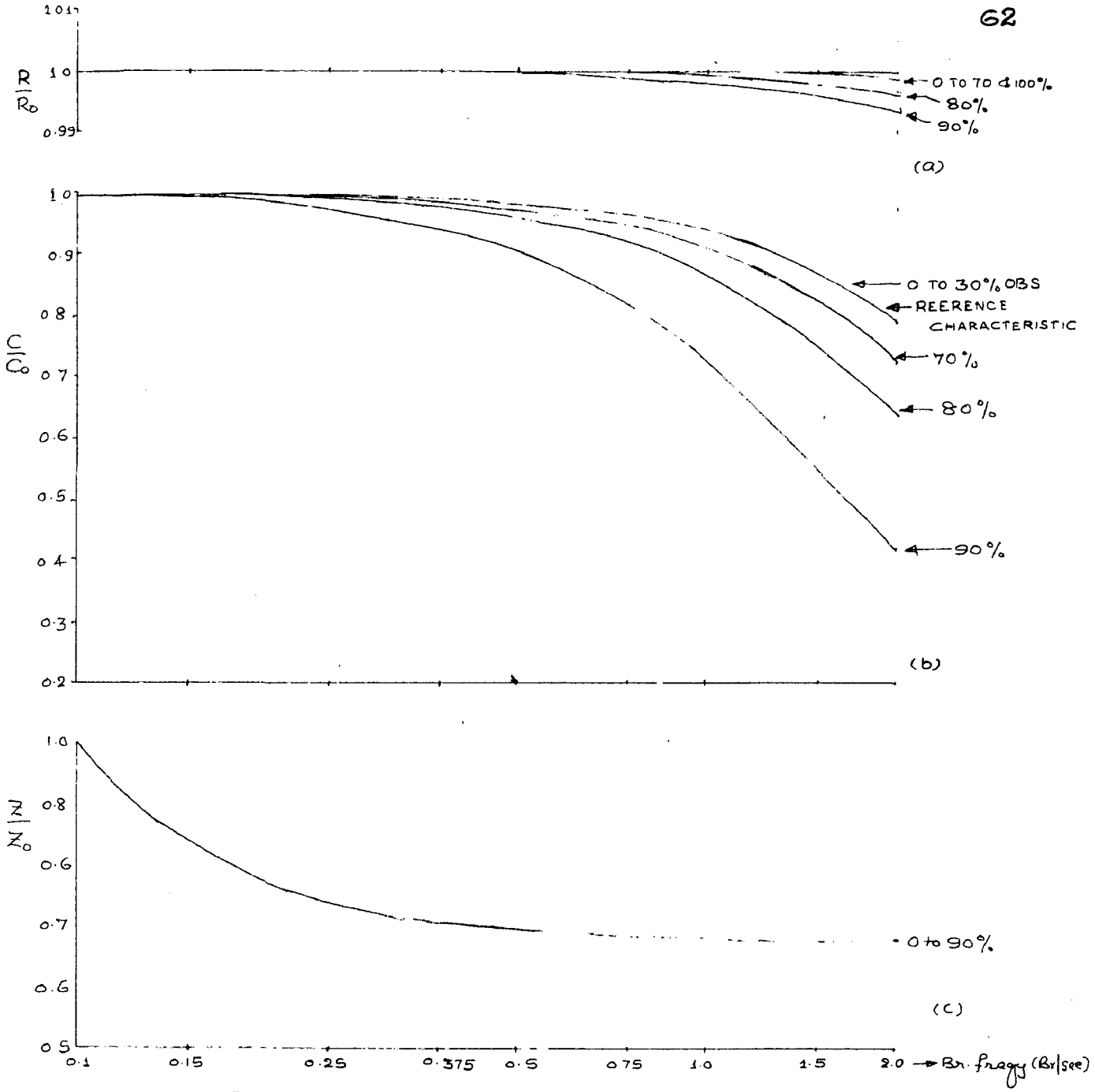


FIG. 6.8 NORMALIZED LUNG PARAMETERS AS A FUNCTION OF BREATHING FREQUENCY FOR CASE IV.

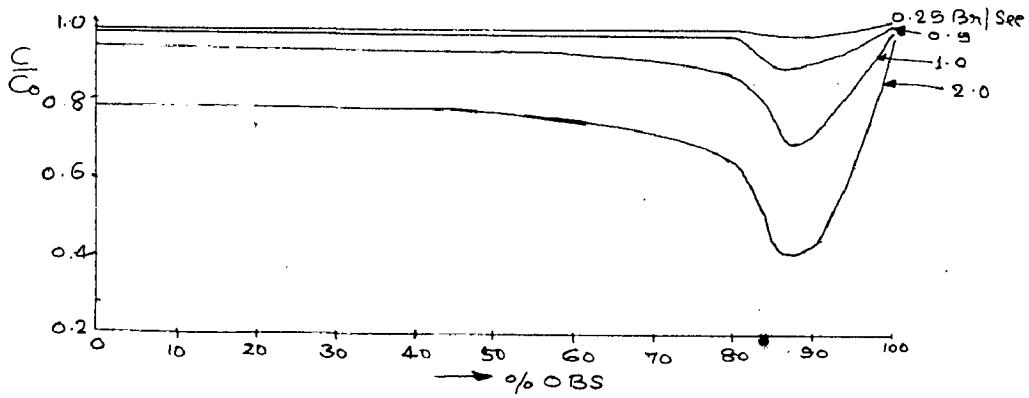


FIG. 6.9 DYNAMIC COMPLIANCE AS A FUNCTION OF % OBSTRUCTION FOR CONSTANT BREATHING FREQUENCIES

CASE IV

R_U = 1.00
R_ℓ = 0.20
$C_{\ell\ell}$ = 0.10
$R_{\ell\ell}$ = 0.10
R_m = 0.22
C_m = 0.04

($v = 0.27$ rad/sec) which represents a quasi-static breathing frequency.

Dynamic Impedance :

In all the four cases the curves $Z(v)/Z_0(v)$ indicate an inherent frequency dependence of dynamic impedance. But in almost all cases the variation of impedance with increasing airway obstruction is very little, especially when the lower airway resistance is comparable with the upper airway resistance. When upper airway resistance is much higher than lower airway and lung tissue resistance, then slight variation(3.5%) in dynamic impedance occurs with increasing airway obstruction. (Fig.6.2, Case I). Hence the variation in impedance can not be taken as a measure of airway obstruction normally.

Dynamic Resistance :

As frequency increases R/R_0 also is found to change but only very little except in case when the lower airway is comparable with the upper airway resistance, (Fig. 6.4). In all cases it is found that the sensitivity is minimum at zero obstruction and at obstruction above 85 to 90% and the maximum sensitivity is found to be between 80 to 90%. It means that when the obstruction is more than about 85%, the two parallel compartments start to behave like a single compartment system and loose its frequency dependent characteristics .

Dynamic Compliance :

Dynamic compliance decreases with increase in frequency, the variation being small at lower frequencies and higher at medium frequencies (between 0.25 Hz/sec and 1.25 Hz/sec) and then lesser, in most cases, in the higher frequency ranges.

But in case IV (Figs. 6.8 and 6.9) the variation of C/C_o is still higher in the higher frequencies but very small even upto 0.4 Hz/Sec. In case II (Figs. 6.4 and 6.5) where the lower airway resistance is much higher than all other resistances, the variation in normalized compliance (or resistance or impedance) is not at all significant and indicative of obstruction of lung tissues. Hence the rate of decrease in compliance depends also upon parameters other than lung tissues. When the lower airway and lung tissue resistance is comparable with upper airways, the variation is not large at higher frequencies. Hence rates of decrease in the value of C/C_o in different cases is indicative of the effects of variation of parameters other than that of lower and lung tissues. Taking into account all the aspects, the suitable breathing frequency range for this model for detection of diseases in the lung tissues is from 0.35 Hz/Sec to 1.25 Hz/Sec

Also the compliance decreases as a function of lung tissue obstruction upto about 85% and then the sensitivity decreases and becomes minimum. The variation of compliance with obstruction of the lung tissues is much more evident than that of the resistance and impedance, but only when the obstruction is above 35%.

T.H. Shaffer, in his analysis[8] has shown that when the system time constants were equal ($\tau_a = \tau_m$) and in the limits $\bar{R}(o)$, $\bar{R}(\infty)$, $\bar{C}(o)$ and $\bar{C}(\infty)$, the system variables $\bar{R}(v)$ and $\bar{C}(v)$ become frequency independent. Physiologically, equal time constants may represent normal lungs with uniform distributions of pulmonary ventilation. Unequal time constants and frequency dependent system behaviour characterize restrictive and obstructive lung diseases.

But in this analysis, the system variables $\bar{R}(v)$ and $\bar{C}(v)$ are found to be frequency dependent even when there is no obstruction at all, (Figs. 6.3, 6.5, 6.7 and 6.9). It is because we have taken into account the compliance of the middle collapsible segment (C_m) which changes the values of $\bar{R}(v)$ and $\bar{C}(v)$ with frequency even when $\%$ OBS = 0. (if C_m were equal to zero, $\bar{R}(v)$, $\bar{C}(v)$ would be frequency independent) Hence variations in the value of middle airway parameters (especially compliance) will change the reference characteristics (i.e. for zero OBS) rather than their relative characteristics.

6.5 DISCUSSION

Model results show that

(i) Dynamic impedance, compliance and resistance of the whole resp. system are sensitive to breathing frequency.

(ii) Dynamic impedance decreases with frequency and becomes almost constant in cases when the lower airway resistance (R_1) is within limits and not affected due to disease. Dynamic resistance variation with frequency is very small in all cases except when lower airway resistance (R_1) is affected by disease. Dynamic compliance variation is large when compared with resistance and impedance.

(iii) Dynamic impedance variation with respect to $\%$ obstruction is not significant in most cases.
Dynamic resistance variation with respect to $\%$ obstruction also is not significant in most cases. Dynamic compliance varies significantly with $\%$ OBS above 35$\%$ and below 90$\%$.

(iv) The sensitivity to frequency variation is maximum for

impedance, resistance and compliance at about 85% of obstruction after which the sensitivity drops back to minimum as in the case of zero obstruction.

(v) In almost all cases the dynamic resistance and compliance variation is more in the frequency range of 0.2 to 1.5 Hz/Sec and dynamic impedance variation is significant in the frequency range of 0.15 and 0.4 Hz/Sec.

(vi) Dynamic compliance is the only parameter which can be related intelligently with the airway obstruction as it has the most sensitivity in a particular range of frequency and obstruction in most cases.

(vii) In case II where the sensitivity of normalized compliance is practically zero, it is not at all indicative of the obstruction, but its variation with frequency is too large and hence is indicative of abnormality in lower airways as a whole (Figs. 6.4 and 6.5).

(viii) The mechanical parameters (especially compliance) in general are found to be more sensitive in the frequency range of 0.35 to 1.25 Hz/Sec and then the percent obstruction of lung tissues is between 35% and 90%.

(ix) The dynamic compliance characteristics for zero obstruction (reference characteristics) is found to be changing in accordance with the compliance of the collapsible segment. The dynamic characteristics for standard values of system parameters (as in case IV - Fig. 6.8) can be taken as the reference characteristic and any deviation from this characteristic is taken as a measure of obstruction.

6.6 USEFULNESS OF MODEL RESULTS FOR DIAGNOSIS PURPOSES

It was difficult to detect the defect or obstruction in the lung tissues using the model analysis and method of diagnosis explained in chapter 5, especially in earlier stages of obstruction. In the analysis done by T.E. Shaffer,[8] the different situation of abnormalities in other parts of the respiratory system were not taken into account when the effect of obstruction on the lower airways was considered. Hence it was not a realistic case.

The variation of the dynamic compliance with frequency as analysed in this chapter gives a more realistic study of the situation in obstructed lung and is a measure of disease in the lung tissues. The analysis is equally useful for detection of obstruction in lung tissues even when the subject has abnormality in other parts of the respiratory system (like the cases of asthma, bronchitis, emphysema). The patient when subjected to a breathing frequency of 0.35 to 1.25 Hz/Sec (which is only a reasonable frequency to be tolerated by a patient) will give sufficiently significant variation in compliance which depends upon the % obstruction.

But even in this analysis, it is found to be little difficult to detect the obstruction in the lung tissues when it is below 35%. Yet this gives better assistance to the detection of disease of the lung tissues in most cases, before the disease is much aggravated.

The variation of compliance is taken with reference to a reference characteristic (Fig.6.8), which is the characteristic of a sound respiratory system of a normal subject with its normal parameters and at zero % obstruction. Fig.6.10 and

6.12 show respectively the dynamic resistance and impedance sensitivity at 70% obstruction with respect to their respective reference characteristics. It is seen that these reference characteristics are not even different from the lung obstructed characteristics of other-wise normal subject (case IV). Thus they are not at all indicative of the diseased condition.

Fig.6.11 shows the compliance variation with respect to frequency (frequency sensitivity) at 70% tissue obstruction of the four cases considered with reference to the reference characteristic of compliance. The deviation of the individual characteristics of each case from this reference characteristic can be studied to analyse the effect of obstruction.

The effect of age, sex, body structure etc. also can be correlated to the reference characteristic of compliance by definite relationship from statistical data and thus generalized reference characteristic can be derived. (And this is beyond the scope of this dissertation work). This has become necessary because in our analysis, the effect of collapsible segment compliance C_m is also considered. (In T.H.Shaffer's analysis C_m was neglected thus getting a constant value for C/C_o for any frequenc at 0% obstruction and this condition is ideal only.).

Eventhough this theoretical model results can be quantitatively compared now with a physical model only, it can be used to give insight into the stage at which the actual physiological system(lung tissue) is affected, in clinical diagnosis. With more accurate methods of measurements of the parameters of the respiratory system and based on data of sufficient number of patients of different types of diseases, this analysis can be use for the effective detection of obstruction in remote parts of the system more accurately and at early stages of diseases.

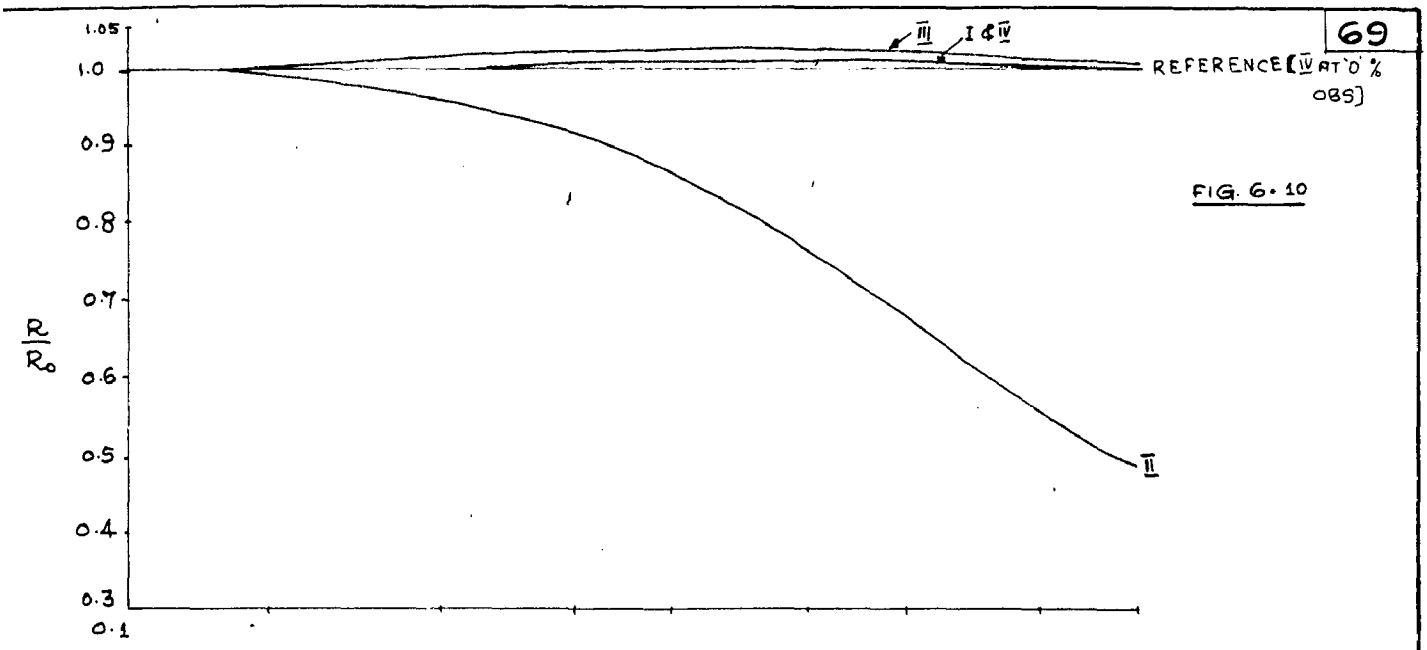


FIG. 6·10

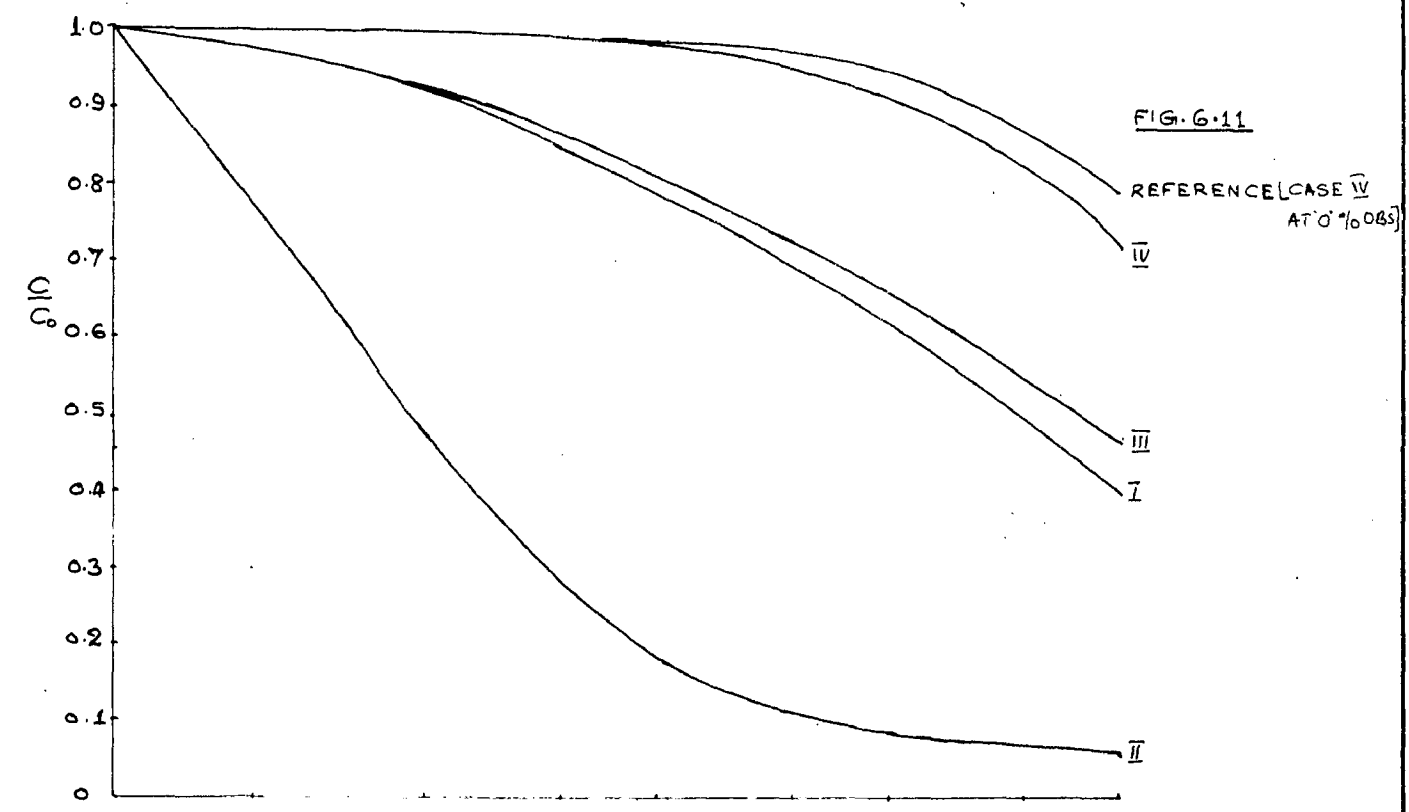


FIG. 6·11

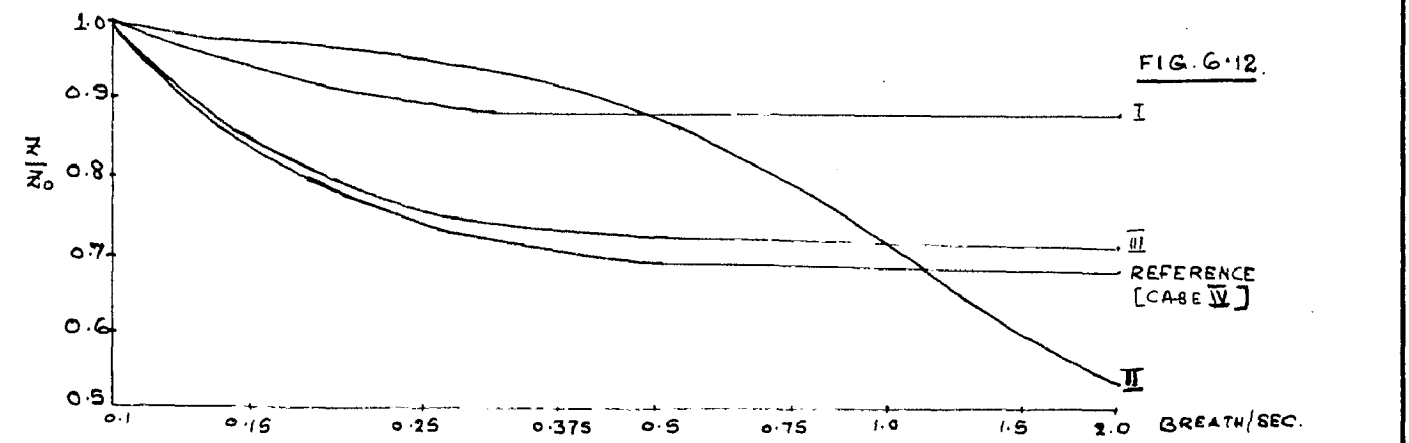


FIG. 6·12

FIGS. 6.10, 6.11 AND 6.12. SENSITIVITY OF LUNG PARAMETERS AT 70% OBS OF THE FOUR CASES UNDER STUDY W.R.T. THE REFERENCE CHARACTERISTICS

CHAPTER 7

CONCLUSION

Modeling of physiological systems and proper techniques to utilize the analysis of the models are challenging fields of research. Models of respiratory system were developed and modified by many and some of them are used for diagnosis purposes.[5,6]

The model developed by Golden et al[5] is used as the reference to the model developed by the author. This model developed by the author is utilized for automatic diagnosis of lung diseases. In this model, the resistance and compliance of the collapsible middle airways, the resistance of the lower airways and the compliance of the lower lung or tissues (or the lung elastic recoil) are considered as non-linear functions of their volumes, based on the most recent and reliable data available. Hence the analysis gives better and accurate values of system parameters, nearer to the actual physiological values. In addition to this, a special set of parameters called 'diagnosis parameters' are derived from the system parameters to be used with computer for automatic diagnosis of diseases. These diagnosis parameters are not affected by the body size, weight, age and sex of the patient, unlike respiratory system parameters. The number of 'diagnosis parameters' selected to be used with the computer will decide the number of different lung diseases that can be diagnosed. In our analysis six binary parameters are selected for diagnosis purpose which gives sixty four combinations of diseases. The method has been tested for available experimental data. The results show that the method is consistent and reliable and can be used on computers directly.

This method solves, to a great extent, the problems faced by physicians in the diagonsis of certain lung diseases, which show quite similar external manifestations or symptoms either at earlier stages or at advanced stages of diseases, but for which the prognosis and indicated treatment are to be markedly different. And the method is more precise and accurate than any of the methods developed so far.

Another advantage of this method is that almost all the variable parameters of the system used in the analysis are measurable and that also to much accuracy.

In this analysis, the defects or obstructions in the lowest part of the pulmonary system namely the lung tissues could not be detected satisfactorily, because its parameters (resistance-compliance combination) is comparatively much lesser than other parameters of the system . Hence its influence on the overall system parameters is insignificant. But its obstruction is significant with respect to the health of the subject.

Frequency sensitivity of the mechanical parameters of the system was devised by Shaffer [8] as a theoretical method to get insight into the percent obstruction of lower airways. In the method developed by the author, more realistic and detailed model is considered and the lung tissue parameters are separated from the lower airways to detect the obstruction even in earlier stages of disease. Also the effect of variation in resistance as well as compliance of the lung tissue is considered. Again different cases where other system parameters affected are taken into account so that this method, to a great extent, gives more realistic and accurate detection of diseases

compliance to frequency variation is found to be a measure of the disease. It is seen that this method gives satisfactory results for diagnosis purposes except in cases where the upper and lower airways are affected to such an extent that the concentration of the physician must be on the whole of the system rather than the lung tissues alone. The disease could be diagnosed in cases where the obstruction is above 35%. Generalised reference characteristics taking into account the sex, age, body structure etc. can be derived from a better statistical data of system parameters.

CAL[illegible]M RESPIRATORY
SYS[illegible]ER FIG. 5.4]

Case No.	MEASURABLE DAT				CALCULATED DATA							
	V_1 / FLC %	V_1	$\dot{V}_1$	$\dot{V}_{oo}$	V_D	$\dot{V}_D$	P_{cl}	P_{tm}	P_{pl}	C_{lc}	R_{lc}	C_D
1	30	1.95	1.3	1.310	0.15	0.018	1.20	1.72	5.2	1.7	0.04	0.087
2	40	2.60	1.3	1.326	0.10	0.026	3.04	3.43	6.8	0.9	0.12	0.052
3	50	3.25	1.3	1.334	0.21	0.084	5.00	5.40	8.7	0.38	0.17	0.039
4	60	3.90	1.22	1.258	0.25	0.038	7.02	7.39	10.3	0.59	0.34	0.034
5	70	4.55	1.2	1.245	0.30	0.045	9.22	9.58	12.4	0.52	0.39	0.031
6	50	3.25	1.3	1.344	0.26	0.044	5.00	5.78	7.9	0.68	0.17	0.045
7	50	3.25	1.3	1.355	0.33	0.055	5.00	5.60	7.4	0.68	0.17	0.059
8	50	3.25	1.3	1.334	0.21	0.034	5.00	5.40	7.1	0.68	0.17	0.039
9	50	3.25	1.3	1.346	0.27	0.046	5.00	5.98	8.8	0.68	0.17	0.045
10	50	3.25	1.08	1.123	0.26	0.043	5.00	7.70	12.7	0.68	0.20	0.033
11	50	3.25	1.08	1.096	0.09	0.016	5.00	7.70	13.5	0.68	0.20	0.012
12	50	3.25	1.08	1.126	0.27	0.046	5.00	8.24	12.6	0.68	0.20	0.033
13	50	3.25	1.08	1.100	0.11	0.020	5.00	8.24	13.0	0.68	0.20	0.014
14	50	3.25	1.08	1.123	0.26	0.043	5.00	7.92	13.2	0.68	0.20	0.032
15	50	3.25	1.08	1.096	0.10	0.016	5.00	7.92	13.9	0.68	0.20	0.012
16	50	3.25	1.08	1.376	0.30	0.057	5.00	9.64	13.1	0.68	0.20	0.031
17	50	3.25	1.08	1.290	0.21	0.041	5.00	9.64	12.8	0.68	0.20	0.022
18	50	3.25	1.08	1.370	0.29	0.054	5.00	9.32	12.3	0.68	0.20	0.031
19	50	3.25	1.08	1.310	0.23	0.043	5.00	9.32	12.2	0.68	0.20	0.025
20	50	3.25	1.08	1.345	0.27	0.046	5.00	8.24	12.7	0.68	0.20	0.032
21	50	3.25	1.08	1.284	0.20	0.036	5.00	8.24	12.7	0.68	0.20	0.025
22	50	3.25	1.08	1.355	0.28	0.050	5.00	8.78	12.0	0.68	0.20	0.031
23	50	3.25	1.08	1.320	0.24	0.044	5.00	8.78	11.9	0.68	0.20	0.028
24	50	3.25	1.08	1.374	0.29	0.056	5.00	9.54	13.7	0.68	0.20	0.031
25	50	3.25	1.16	1.190	0.21	0.030	5.00	5.35	10.7	0.68	0.19	0.039
26	50	3.25	1.16	1.206	0.26	0.046	5.00	7.90	10.6	0.68	0.19	0.032
27	50	3.25	1.30	1.317	0.10	0.017	5.00	8.25	12.5	0.68	0.17	0.012
28	50	3.25	1.30	1.328	0.21	0.028	5.00	5.39	12.6	0.68	0.17	0.039
29	50	3.25	1.30	1.310	0.08	0.010	5.00	5.39	13.7	0.68	0.17	0.014
30	50	3.25	1.30	1.310	0.08	0.010	5.00	5.39	14.3	0.68	0.17	0.014
31	50	3.25	1.16	1.177	0.09	0.017	5.00	7.90	11.5	0.68	0.19	0.012

KEY :-

Anticipated diagnosis
Normal
Asthma
Bronchitis
Emphysema
Miscellaneous

APPENDIX - II

'DIAGNOSIS PARAMETERS' DERIVED FOR 12 SUBJECTS FOR $V_1/TLC = 50\%$ FROM APPENDIX I.

Sl. No.	Case No.	Diagnosis	RANGE OF DIAGNOSIS PARAMETERS I $\frac{V_D/V_{D\,max}}{\Sigma V_1}$	II $\frac{R_m}{C_D}$	III $\frac{R_u}{P_{alv}}$	IV $\frac{R_u}{V_{ao}}$	V $\frac{R_l}{R_u}$	VI $\frac{R_{tm}}{P_{al}}$
1.	6	Normal	1.28	2.89	0.50	1.08	0.40	1.16
2.	7	Normal	1.26	1.45	0.52	0.96	0.36	1.12
3.	8	Normal	1.20	5.66	0.50	0.77	0.25	1.08
4.	9	Normal	1.14	2.90	0.52	1.46	0.38	1.20
5.	11	Asthma	1.50	90.00	0.50	3.86	0.59	1.54
6.	13	Asthma	1.56	51.40	0.45	3.29	0.83	1.65
7.	15	Asthma	1.50	77.40	0.50	4.10	0.60	1.58
8.	17	Bronchitis	1.74	10.10	0.29	1.76	1.90	1.93
9.	19	Bronchitis	1.70	7.35	0.28	1.52	2.01	1.86
10.	21	Emphysema	1.56	8.89	0.41	2.38	0.98	1.65
11.	23	Emphysema	1.62	5.82	0.32	1.65	1.60	1.76
12.	24	Emphysema	1.73	3.57	0.33	2.10	1.46	1.91
Limits for Normals (upper or lower)			≤ 1.40	< 15.00	> 0.50	> 3.00	< 1.50	< 1.50

APPENDIX - III

MODEL EQUATIONS FOR RESPIRATORY FREQUENCY RESPONSE.

$$w = 2\pi f$$

$$\frac{R_{1tn}}{R_{1ta}} = (1 - OBS)^4$$

$$R_{1ta} = R_{1t}\ (\ 1 + R_{1ta}/R_{1tn})$$

$$R_{1tn} = R_{1ta} \cdot R_{1t}/(R_{1ta} - R_{1t})$$

$$\frac{C_{1ta}}{C_{1tn}} = (1 - OBS)^3$$

$$C_{1ta} = C_{1t}\ (C_{1ta}/C_{1tn})\ /\ [\ 1 + (\ C_{1ta}/C_{1tn}\ )]$$

$$C_{1tn} = C_{1t} - C_{1ta}$$

$$\tau_a = R_{1ta} \cdot C_{1ta}$$

$$\tau_n = R_{1tn} \cdot C_{1tn}$$

$$A(w) = w^2(\tau_a C_{1tn} + \tau_n C_{1ta})^2 + C_{1t}$$

$$R_1(w) = [R_1 + w^2 \tau_a \tau_n (\tau_n C_{1tn} + \tau_n C_{1ta}) + (\tau_a C_{1ta} + \tau_n C_{1tn})]/A(w)$$

$$C_{1t}(w) = A(w)/[w^2 (\tau_a^2 \cdot C_{1tn} + \tau_n^2 C_{1ta}) + C_{1t}]$$

$$\bar{R}(w) = [R_u + R_m] + [R_1(w)\ C_{1t}^2(w)]/[R_1^2(w) \cdot w^2 C_m^2 C_{1t}^2(w) + C_m + C_{1t}(w)]$$

$$\bar{C}(w) = \frac{w^2 R_1^2(w) \cdot C_m^2 \cdot C_{1t}^2(w) + [\ C_m + C_{1t}(w)]^2}{C_m + C_{1t}(w) + R_1^2(v) \cdot w^2 \cdot C_m \cdot C_{1t}^2(v)}$$

$$\bar{Z}(w) = [\ \bar{R}^2(w) + \{1/wC_m\}^2]^{0.5}$$

Symbols used in Computer programme

W = w, F = f, P = R_{1ta}/R_{1tn}, RT = R_{1t}, RA = R_{1ta}, RN = R_{1tn},

$Q = C_{1tn}/C_{1tn}$, $CT = C_{1t}$, $CA = C_{1tn}$, $CM = C_{1tn}$, $TA = \nu_0$,

$TM = \nu_n$, $A(I) = A(v)$, $AX = v^2$, $BX = \nu_0 C_{1tn} + \nu_n C_{1tn}$,

$RLA = R_1$, $RL(I) = R_1(v)$, $CL(I) = C_{1t}(v)$; $CM = C_m$, $RM = R_n$,

$RC1 = R_n$, $CZ = v^2 . R_1(v)\, C_{1t}^2(v)$, $AML = C_m + C_{1t}(v)$,

$RC(I) = R_1^2(v) . v^2 . C_n^2 . C_{1t}^2(v) + [\, C_m + C_{1t}(v)]^2$

$R(I) = \bar{R}(v)$, $C(I) = \bar{C}(v)$, $Z(I) = \bar{Z}(v)$,

$RR(I) = \bar{R}(v)/\bar{R}(0)$, $CC(I) = \bar{C}(v)/\bar{C}(0)$, $ZZ(I) = \bar{Z}(v)/\bar{Z}(0)$.

COMPUTER PROGRAMME

```
C    C RESPIRATORY FREQUENCY RESPONSE BY JOHN ZACHARIAH
     DIMENSION A(10), V(10), RL(10), CL(10),AC(10),R(10),
                C(10),Z(10).
     DIMENSION RR(10),CC(10),ZZ(10),F(10)
     READ RT,CT,RLA,CM,RM,RM1,NU
     DO 20 I = 1, NU
     READ F(I)
     V(I)=6.2832 *F(I)
  20 CONTINUE
     OBS=0.
 100 DO 200 I=1,NU
     P=1./((1.-OBS)**4)
     RA=RM*(1.+P)
     RI=RA*RM/(RA-RT)
     Q=(1.-OBS)**3
     CA=CT*Q/(1.+Q)
```

```
      CN=CT-CA
      TA=RA*CA
      TN=RN*CN
      AX=U(I)**2
      BY=TA*CN+TN*CA
      A(I)=AM*BY**2 +CT
      RL(I)=RLA+(AX*TA*TN*BY+TA*CA+TN*CN)/A(I)
      CL(I)=A(I)/(AX*(TA*TA*CN+TN*TN*CA)+CT)
      C2=AM*(RL(I)*CL(I))**2
      AML=CM+CL(I)
      RC(I)=C2*CM**2+AML**2
      R(I)=RU+RM+RL(I)*CL(I)**2/RC(I)
      C(I)=RC(I)/(AML+C2*CM)
      Z(I)=(R(I)**2+1./(W(I)*C(I))**2)**0.5
      RR(I)=R(I)/R(1)
      CC(I)=C(I)/C(1)
      ZZ(I)=Z(I)/Z(1)
      WRITE 12,I,F(I),R(I),C(I),Z(I)
 12: FORMAT(/,I,E,E,E,E)
      WRITE 13,RR(I),CC(I),ZZ(I),OBS
 13: FORMAT(/,E,E,E,E)
200: CONTINUE
      OBS=OBS+.1
      IF(OBS-1.) 300,300,400
300: GO TO 100
400: STOP
      END
```

REFERENCES

1. The Holy Bible - ' The Book of Genesis, Chapter 2 Verse 7' and 'The Acts of the Apostles, Chapter 17 Verses 24 and 25'.

2. Weiss, Marwin D., 'Bio-Medical Instrumentation' - 'Chilton Book Company, Philodelphia (1973), pp. 95-97 and 217-221.

3. Saidal, Gerald M., et al , 'Mass-balance model of pulmonary airway dynamics' - IEEE Trans. on BME, Vol. 19 No. 3 (May 1972), pp. 205-212.

4. Frank P. Primiano Jr., 'Measurements of the Respiratory System' from 'Medical Instrumentation - Application and Design'(Editor - Webster, John G) - Houghton Mifflin Company, Boston (1978), pp. 434 - 510.

5. Golden, James F., et al - 'Mathematical Model of Pulmonary airway dynamics' - IEEE Trans. on BME Vol. 20, No. 6,(Nov.1973), pp. 397 - 403.

6. Gupta, A.K.,et al, 'A System Engineering Approach to Medical Diagnosis' - Proceedings of Fifth National System Conference (NSC - 1978).

7. Clark, John W. Jr., et al, 'Analog Computer Simulation of Maximum expiratory flow limitation' - IEEE Trans. on BME, Vol. 23, No. 6 (Nov., 1976),pp. 445 - 452.

8. Shaffer, Thomas H., 'Limitations of frequency dependance as a measure of airway obstruction' - IEEE Trans. on BME, Vol. 22, No.4 (July 1975), pp. 317-321.

9. Cromwell, Leslie., et al , 'Bio-Medical Instrumentation and Measurements' - Prentice-Hall, Inc., New Jersey (1973).

10. De Coursey, R.M., 'Human Organism', 3rd edition, McGraw Hill Book Co., (1968).

11. Guha, S.K., 'Introduction to Medical Electronics', Bharati Bhawan, Patna,(1969).

12. Tatarinov, V., 'Human Anatomy and Physiology', MIR Publications, Moscow (1978).

13. John Zachariah, ' Seminar Report on Respiratory System Dynamics', U.O.R., Nov. 1978.

14. Peterson P.C., et al, 'Microwave reflection and Transmission measurement of Pulmonary diagnosis and monitoring'- IEEE Transactions on Bio Medical Engineering Vol. 25, No.1 (Jan. 1978), pp. 49-48.

15. Cain, Sudarsh (Editor), 'Mathematical Modeling of Physiological System', Proceedings of the Fourth New England Bio Engineering Conference - Pergamon Press (1976),p.163.

16. Milsum, William R., 'A System Approach to Biomedicine' - McGraw Hill Inc.,(1969).

17. Gupta, A.K., 'Application of Optimization Techniques to Biological Systems', Ph.D. Thesis, University of Roorkee, 1978.

18. Davis, Dale S., 'Nomography and Empirical Equations' (1962), Reinhold Publishing Corporation, U.S.A.

19. Otis, A.B., et al, 'Mechanical factors in distribution of pulmonary ventilation', J. Appl. Physiol. Vol. 8 (1956), pp. 427 - 445.

20. Engh, Jonas P., et al, 'Bronchial Gas Flow', Ciba Foundation Symposium on Pulmonary Structure and Function (1962), pp. 77 - 94.