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DECLARATION

I do hereby declare that this thesis has been composed by myself and it is a record of my own work under the supervision of Prof. M.A. Rashid. The matter embodied in this thesis has not been submitted for the award of any other degree.

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B.Sc. (Agra.), B. Ed., M.Sc. (Alig)

JULY, 1992.

CERTIFICATION

This thesis entitled "Mathematical Modelling and Optimization for Respiration and Dialysis" by Masood Hasan Khan meets the regulations governing the award of the degree of Doctor of philosophy (Ph.D) of Ahmadu Bellow University and is approved for its contribution to scientific knowledge and literary presentation.

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DEDICATION

Dedicated to my father inlaw

(Late Hameed Ahmed Alhashmi)

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ABSTRACT

MATHEMATICAL MODELLING AND OPTIMIZATION FOR RESPIRATION AND DIALYSIS

There has been a remarkable development in the field of system and control theory, its application in almost all the systems including biological system have been realized.

The aim of the present work is to use system techniques to the modelling and controlling of the physiological systems. For this purpose, the patients respiratory system and the artificial kidney system are analysed in this thesis.

In the first part of the thesis, an analysis of controlled ventilation has been carried out for patients, whose breathing is controlled by an external means such as artificial ventilators. The basic design parameters of the ventilators are obtained by minimization of the average alveolar pressure, subject to the maximum ventilatory work capacity of the patients. The optimal input pressure wave form is decided on the basis of average and peak alveolar pressures and the inspiratory time. We discuss four such models namely, Rectangular, Ramp, Sine and Gamma pressures input and that the Ramp pressure input wave form is the best choice.

Haemodialysis has been a widely accepted as the mode of therapy for the treatment of chronic kidney failure. Although there is no doubt about the clinical efficacy of the method, however the planning of the haemodia1ysis for individuals is done on empirical grounds. The physicians are not even aware, except in a general sense[1], of how the various parameters of the dialyser operation effectively control the patients dialysis. Despite satisfactory results, it is still far from an optimal procedure and is both time consuming and expensive.

The second part of this thesis deals with the development of optimal control policies for haemodialysis. This is done by considering a mathematical model of the patient coupled to an artificial kidney system. The body fluids are represented by three compartments with uniform mixing. It is assumed that all the cells are lumped together as a cellular compartment. The blood plasma and interstitial fluids are lumped together as extracellular, compartment. The brain fluid compartment is added for simulating the cerebral pressure transients.

It is desirable to remove the biological waste as fast as possible in order to minimize the treatment time. However, with increasing dialysis rates, the cerebro spinal fluid pressure undergoes large dynamic over shoots, causing much discomfort to the patient. The dialysis has to be so controlled that the treatment time is minimized and the discomfort to the patient avoided. The rate of urea loss is

optimized by varying both the dialysate flow and the flow of the patient's blood.

The objective of minimi zing the treatment time is achieved by devising a time optimal control policy to the above problem. Application of this policy reduces the treatment time to an over all minimum. However, the dialysate feed requirement increases substantially and unless the dialysis facility is to be utilized for two shifts. this policy probably cannot be of much use.

To reduce the quantity of fresh dialysate, the recycling of the diaysate has been sugested. It has been observed that by recycling a portion of the dialysate. the amount of fresh make up needed could be reduced substantla1ly and considerable reduction in treatment time affected. An optima] policy pertaining to blood flow rate and dialysate freshmake up rate has been developed in the thesis for this system. Although reduction in treatment time with the reeve liner scheme is not large, but when considered with the daily operating schedule or a dialysis centre the potential cost; saving tor the patient **may** be substantial.

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CHAPTER ONE

INTRODUCTION

Since last two decades, there has been a remarkable development in the field of system theory, which has resulted in its application to almost all the systems including the biological systems. Mathematical description of biological systems has become more and more useful and of far-reaching importance.

Models can be used to predict the effects of alternative treatment procedures and thus help the physicians to select the most efficient one and avoid unnecessarily experimenting with the patient. The design of assistive devices and operating treatment, which control some physiological systems artificially should be based on natural performance principles. As such this may turn out to be of practical importance in future, when more and more complex and automatically operating devices are developed e.g. artificial organs. In clinical practice, the mathematical models can be used as diagnostic aids in the early detection of abnormal responses and in the subsequent recovery processes.

To emphasize the importance of system theory application to biological systems, the human respiratory system and the excretory system have been discussed in the following work. The study is related to the excretory system, and optimal control of the artificial kidney system is used to design an external assistance.

1.1 RESPIRATORY SYSTEM:

Patients during surgery or with respiratory insufficiency are incapable of performing spontaneous breathing. In such cases, external assistance to respiration is provided - usually by means of intermittent positive pressure ventilators (IPPV). Intermittent positive pressure ventilation is contrary to the normal physiological mode of respiration and if not used properly, may lead to several side effects such as circulatory interference and mechanical damage to the lung tissues. Several ventilator designs based upon the minimization of the harmful effects of positive pressure ventilation have ben proposed. However, the investigators have not minimized the ventilatory work, the physiological importance of which is well established for natural respiration. A ventilator designed to minimize the ventilatory work and the harm caused by positive pressure ventilation, will provide optimal assistance to the patient and create conditions similar to those prevailing in natural respiration.

1.2 ARTIFICIAL KIDNEY SYSTEM:

The kidneys in the human body excrete the waste metabolites and toxins. If the kidneys cease to function, there is an accumulation of the toxic substances in the organism for which the treatment is provided by a suitable artificial kidney to the patient. This technique is called Haemodialysis.

Haemodialysis has been in use for about 25 years to treat patients with severe renal failure. Urea is quantitatively the major metabolite to be removed from the human body. Its transfer in different body fluid compartments has been investigated because it may result disequilibrium syndrome. Investigators have formulated two compartments (Intra cellular/Extra cellular) patient model to simulate the transfer of Urea and plasma Urea. The studies of various investigators are conflicting in regard to the value of transcellular mass transfer coefficient[16]. These models fail to simulate the cerebral pressure transients, which are often experienced by patients during haemodialysis. A model of the patient artificial - kidney system must be adequate to simulate the effects of various dialyser operating variables, namely the dialysate flow rate, the blood flow rate through the dialyser, and dialysis time etc. The effect of these variables can be visualised experimentally. The unguided experimental programme is very much expensive and time consuming. In such cases it would be necessary to have some theoretical guide lines.

A mathematical model concerning the patient's artificial kidney system would be the one, which can predict the changes in the solute concentration as a function of dialyser operating parameters and thus attempt to optimize on the dialyser operation. For the treatment of chronic Uraemia, the combined diffusive and convective transport process has been recommended. The increase in the flow rate of the fluid

on both sides of the membrane of the dialyser, the convective transport, can be enhanced. As resistance to the transport declines, the time required to remove the waste products would also reduce. During the haemodialysis, feeding the fresh dialysate to the system is very costly and the large value of blood flow and dialysate flow rates lead to disequilibrium - syndrome which causes discomfort to the patient. These symptoms are due to an osmotic imbalance between blood plasma and cerebro spinal fluid (CSF) - from the fact that the urea is removed from the plasma at a greater rate than that at which it can be removed from the (CSF).

The cost of the dialysis and the effectiveness of the treatment are very significant to the patient. The cost of the bed, the personal charges and the charges of the clinical centre become a burden to the patient[2]. Thus it will be desirable to remove the waste products from the body as fast as possible so that the time of dialysis can be saved subject to minimal discomfort to the patient.

To bring down the cost of therapy, a portion of the dialysate is recycled and thus the quantity of fresh dialysate required for the dialysis can be reduced. However, the quality of the treatment by recycling the portion of the dialysate is not as good as in case of feeding the fresh dialysate. Therefore a control policy which will regulate the make up rate of the fresh dialysate and the patient's blood to the dialyser, need be devised, so as to minimize the discomfort to

the patient and provide a cheap dialysis facility. Normally the kidneys of an average patient weighing 70kg receive over 1700 litres of blood per day of the plasma contained in that blood, the glomerulus filters approximately 180 litres of fluid per day containing among other substances, about 30 gram of Urea, 0.6 gram of creatinine, 0.9 gram of uric acid and minor quantities of other waste products in about 1.5 litres of urine[21]. It is apparent that urea is quantitatively the major substance removed from the body. Therefore, urea is generally used as an indicator of renal function, and dialysis effectiveness. Renal function or structure can be obtained by following the passage of a radio-labelled tracer through the kidneys by external scintillation counting (renography) or imaging (gamma - camera). With a modern computerized gamma - camera system it is possible to select an "area of interest" and obtain an activity-versus-time output from that region, thereby combing the advantages of the imaging system with the quantitative assessment of the scintillation counter. There are a wide variety of markers and radiolabels: Hippuran is selectively concentrated by renal tubular secretion: diethylenetriaminepentracetate (DTPA) are filtered by the glomerulus and not reabsorbed: dimercaptosuccinate (DMSA) binds to proximal tubule cells and very little appears in the urine. The standard renogram usually employs an injection of 131 I Hippuran with scintillation detectors placed over each kidney recording the activity with time. It is very helpful to have a third detector injection, there is a rapid increase in activity over

the kidney as the bolus injection arrives (first phase). This has little diagnostic importance. There follows a more gradual tubule cells and thence to the tubular lumen where it is concentrated by water reabsorption and passes down the nephron. This second phase achieves a peak at about 3 minutes and is followed by the third phase coincident with the appearance of Hippuran in the bladder. During this latter phase Hippuran is still being abstracted from the plasma by proximal tubular cells, concentrated in tubular fluid and passed down the nephron, but there is also removal of the transported Hippuran by the renal collecting system. It is thus a complicated function of plasma levels, secretion, tubular fluid reabsorption, transit and removal. However, normal renograms have almost simultaneous and quite well delineated peaks. In unilateral renal vascular disease the affected kidney shows a delayed peak and an impaired third phase. This pattern in a hypertensive patient indicates the need for further diagnostic tests in search of a correctable renal arterial lesion. The interpretation of the renogram is difficult in patients with oliguria. Thus in pre-renal and renal causes of acute renal failure there is an impaired third phase but a similar picture can be produced in bilateral outflow obstruction. Obstruction is rarely perfectly symmetrical, however, and a difference between the two kidneys is used as an indication of a post-renal cause, but the use of the gamma-camera improves the diagnostic accuracy in this circumstance.[25]

If the kidneys cease to function, there is an accumulation of toxic substances in the organism. This is called uraemia and is characterized by a rise in blood urea concentration. Uraemic symptoms include thirst and nocturia (failure to concentrate), nausea, anorexia and diarrhoea impaired level of consciousness and convulsion, airhunger (acidaemia), bone pain, tenderness and gastrointestinal haemorrhage. In case of renal failure, the patient can be treated either by an artificial kidney or with kidney transplantation. A successful kidney transplant is a permanent cure but the patient's life is circumscribed by the tissue rejection reaction. Until the difficulties pertaining to the replacement of natural kidneys are overcome, the treatment of patients with chronic renal inefficiency must be provided by a suitable artificial kidney.

Among the various methods of blood purification, haemodialysis has proved to be clinically satisfactory method of treatment. Despite satisfactory results, it is still far from an optimal procedure. There is a need for a large quantity of accurately controlled dialysate, hampering the portability of the artificial kidney and hence the patient's mobility, cost of the treatment is of paramount importance.

1.3 HAEMODIALYSIS:

Artificial kidneys have now been used for about 25 years to treat patients with severe renal failure.

The basic principle of the artificial kidney is to pass blood through very minute blood channels bounded by thin membrane. On the other sides of the membrane is a dialysing fluid into which unwanted substances in the blood pass by diffusion.

The figure (3.1)[7] illustrate an artificial kidney in which blood flows continually between two thin sheets of cellophane, out side of the sheets is a dialysing fluid. The cellophane is porous enough to allow all constituents of the plasma except the plasma protein to diffuse freely in both directions - from plasma into dialysing fluid and from the dialysing fluid back into the plasma. If the concentration of a substance is greater in the plasma than in the dialysing fluid, there will be a net transfer of the substance from the plasma into the dialysing fluid. The amount of the substance that transfers depends on:

(i) The difference between the concentrations on the two sides of the membrane

(ii) The molecular size of the toxins, the smaller molecules diffusing more rapidly than the larger one.

(iii) The time that the blood and the fluid remain in contact with the membrane. In normal operation of the artificial kidney, blood continually flows from an artery, through the kidney, and back into the vein. The total amount of blood

in the artificial kidney at any one time is usually less than 500 ml. The rate of flow may be several hundred ml per minute and the total diffusion surface is usually between 10,000 and 20,000 square centimetres. To prevent coagulation of blood in the artificial kidney heparin is infused into the blood as it enters the "kidney". Then, to prevent bleeding in the patient as a result of the heparin an anti-heparin substance protaminé is infused into the blood as it is returning to the patient.

1.4 DIALYSING FLUID:

Table (1.1)[7] compares the constituents in a typical fluid with those in normal plasma and uraemic plasma. The constituents of the dialysing fluid are chosen so that those substances in excess in the extracellular fluid in uraemia can be removed at rapid rates, while the normal electrolytes remain essentially normal.

1.5 BODY FLUID COMPARTMENTS:

Most of the models which have been proposed to date have considered the body to consist of two-well mixed uniform compartments. Haemodialysis patients sometimes experience headache, nausea, mental confusion during the treatment[19,30]. These symptoms have been collectively referred to as the disequilibrium syndrome. According to some investigations[1,19,30], these symptoms are related to an

increase in (CSF) pressure which generally takes place during dialysis. The present study pertains to simulation of haemodialysis and its optimal control, a cerebro-spinal fluid (CSF) compartment has been included to simulate the cerebral pressure transients.

1.5.1 THE INTRACELLULAR COMPARTMENT:

About 25 litres of the 40 litres of fluid in the body are inside the approximately 75 trillion cells of the body and are collectively called the intra cellular fluid. The fluid of each cell contains its own individual mixture of different constituents which are reasonably similar from one cell to another. For this reason, the intracellular fluid of all the different cells is considered to be one large fluid compartment.

1.5.2 THE EXTRA CELLULAR COMPARTMENT:

All the fluids outside the cells are called extracellular fluids, and these fluids are constantly mixing. The fluid flowing through the spaces in between the cells (intra cellular fluid has a very large solute transfer rate with the intra vascular fluid (blood plasma). The characteristics of the two fluids are also the same except for the proteins in plasma, so the two fluids could be lumped into an extra cellular compartment.[19]

1.5.3 THE CEREBRO SPINAL FLUID:

The Cerebro Spinal Fluid (CSF) comprises all the fluid in the ventricles of the brain and in the subarachnoid

TABLE 1.1 TYPICAL VALUES OF THE CONSTITUENTS OF THE NORMAL PLASMA, DIALYSING FLUID AND UREMIC PLASMA

CONSTITUENTS	NORMAL PLASMA	DIALYSING FLUID	UREMIC PLASMA
a)Electrolytes (m Eq/litre)			
Na^+	142	142	142
K^+	5	5	7
Ca^{++}	3	3	2
Mg^{++}	1.5	1.5	1.5
Cl^-	107	107	107
$(HCO3)^-$	27	27	14
$Lactate^-$	1.2	1.2	1.2
$Hp04_^-$	3	0	9
Urate	0.3	0	2
$Sulphate^{--}$	0.5	0	3
b) Non- Electrolytes mg/dℓ			
Glucose	100	125	100
Urea	26	0	200
Cretinine	1	0	6

spaces surrounding both the brain and spinal cord. The entire cavity enclosing the brain and the spinal cord has a volume of approximately 1650 ml and about 150ml of this volume is occupied by cerebro spinal fluid.[7]

The normal pressure in the (CSF) system when one is lying in a horizontal position averages 130mm water (10mm Hg) though this may be as low as 70mm water or as high as 180mm water even in the normal person. The cerebro spinal fluid pressure is regulated by the product of, first the rate of fluid formation and second the resistance to absorption through the arachnoidal villi. When either of these is increased, the pressure rises and when either is decreased the pressure falls.

1.6 THE CHARACTERISTIC OF THE BODY:

(i) The body fluid compartments may be treated as uniform well mixed pools. ([29])

(ii) Metabolic production of solutes is assumed to exist only in the intra-cellular compartment. While produced chiefly in the liver component of this compartment, Urea production is assumed to occur in the entire pool.[20] Transfer of solutes such as urea takes place from the tissue cells to the intracellular fluid, from intracellular fluid to the interstitial fluid and from interstitial fluid to the intravascular spaces (blood).

(iii) Only specy contributing to the change of the osmolarities in the fluid compartment is Urea.

(iv) The brain is a sensitive and important part of the human system and the rate of transfer of urea to the (CSF) is expected to be different from the rate of transfer of Urea to the intracellular space, thus a third compartment corresponding to the (CSF) has been added to the model[3].

(v) The mechanism which controls the concentration gradient between the blood and the brain are not completely understood and have been collectively referred to as the blood brain barrier. It has been observed that the steady state - concentrations of some of the substances like urea, in the (CSF) is lower then their concentration in plasma. When (CSF) flow is stopped, the concentration becomes equal in the (CSF) and the plasma[27]. This suggests that the transfer mechanism is reversible and passive for these substances. In the presence of bulk flow, there is insufficient contact time to reach equilibrium with the blood plasma. Therefore, urea transfer in the (CSF) has been assumed to result from two mechanisms:

(i) a reversible diffusive transport from the cerebral - capillaries into the brain interstitial and cerebro spinal fluid spaces.

(ii) the transport of urea from the cerebral space by bulk flow of the (CSF) into the venous blood.

1.7 SCOPE OF THE WORK:

The considerations as discussed lead to the present investigations with the following objectives:

(i) To develop a rational analysis of controlled ventilation and therefrom predict ventilator designs which would provide an optimal respiratory assistance so as to minimize the harmful effects of positive pressure ventilation and constrain the ventilatory work on the patient within the permissible capacity.

(ii) To devise a time optimal control policy in terms of the system valuable for the clinical centres with an aim to minimize the treatment time.

(iii) To establish an optimal control policy for the patient - artificial kidney system with dialysate recycle, so as to minimize the penalty for the dialysate cost reduction.

(iv) The use of computer in physiology and medicine have been well documented.[11] Also mathematical models for the Hepatic Handing of Hexose sugars using a computer assisted model has been reported. [13,14] A physiological nomogram for the use of sucrose as an extracellular reference marker in the liver has been established. [12,15,16]

1.8 INTERMITTENT POSITIVE PRESSURE (IPPV):

The lungs are inflated with air or oxygen intermittently; this requires a deriving force or pressure greater than that in the lungs which is atmospheric pressure. This explains the origin of the term intermittent positive pressure ventilation. During inflation of the lungs, the trachea pressure is positive i.e above atmospheric. Normal respiration is called negative pressure ventilation since the trachea pressure falls during inspiration.

The pulse is produced through the machine, having knobs that read different important parameters namely, W_g (work capacity of the patient). P_i (inspiratory period), T_i (inspiratory time) P_{ip} (Peak alveolar pressure); P_A (Average alveolar pressure) etc.

In case of producing different pressure inputs namely, Rectangular, Ramp, Sine and Gamma pressures input, the knobs are set on the required values of the parameters in the machine according to the tables (2.5 - 2.8) respectively. The machine gives the digital display of all the input parameters; and the required pulse is produced by the machine automatically. The latest (1ppv) machine has the capability to produce a graphic display of the pulse on the monitor and the input parameters are fed through the computer.

1.9 ACHIEVEMENTS:

Normally after 12 hours of treatment time the concentration of urea in the blood decays to a value of 0.1099 g/l. The application of the policy given in this work. by recycling a portion of fresh dialysate to the system at a constant rate of 500ml/min and keeping the blood flow rate constant, results in 11% reduction in time and 37.1% reduction in the amount of fresh dialysate feed. By using this policy the dialysis centres may be used in double shift.

CHAPTER TWO

Optimization of Artificial ventilators

2.1 INTRODUCTION:

The function of the human respiratory system is the transfer of oxygen from the inspired air to the blood stream and at the same time to remove carbon dioxide from the venous blood and exhaust it out of the body. This is achieved by the activity of the respiratory muscles. In some cases of surgery or with patients having respiratory insufficiency, spontaneous breathing is not possible and an external assistance usually by means of Intermittent Positive Pressure Ventilators (IPPV) is used to ensure proper ventilation of patients.

In the normal physiological mode of respiration, a slight negative pressure exists in the lungs whereas a positive pressure is applied to ventilate the lungs in (IPPV). The alveolar and intrathoracic pressures are considerably higher in (IPPV), as compared to those in natural breathing. This indicates that intermittent positive pressure ventilation, if not properly used, may lead to several harmful side effects. In addition to causing uneven ventilation and metabolic effects, positive pressure ventilation interferes with the pulmonary blood flow, leading to the reduction of the cardiac output and mechanical damage to the lung tissues due to excessive pressures. These effects indicate the necessity of

maintaining a properly regulated (IPPV), system for the patient.

In designing (IPPV) systems, special precautions are therefore required to ensure that patient's ventilatory demand are properly met, while the constraints posed by the harmful effects of positive pressure ventilation are simultaneously satisfied. This is particularly important for those patients, who are incapable of tolerating the minor upsets. The positive pressure developed by the ventilator during the inspiratory phase is applied to patient's lung via the upper air ways and trachea-bronchial tree which offer resistance to the flow of air and the ventilator has to do work on the patient in overcoming the air ways resistance and against the elastic recoil of the lungs and thorax.

Attempts have therefore been made to study the operational dynamics of the ventilation technique and develop suitable designs to minimize harmful effects of the method[12, 32]. One of the earlier studies in this direction was done by Mead[23].

By assuming a continuous sinusoidal flow pattern, they determined the optimum frequency to give a minimum average pressure over a breath. Otis, Fenn and Rahn [26] observed that minimum ventilatory work done during inspiration is obtained at normal breathing frequencies. But these investigations are not applicable directly to (IPPV) because sinusoidal flow pattern exists only in spontaneous breathing.
With externally assisted respiration, the flow

pattern depends on the wave form of the external pressure applied which is in general not sinusoidal. Wald at al[32] gave an analytical study of the controlled ventilation. By considering average alveolar pressure as an index of the effects of alveolar positive pressure on pulmonary circulation, they showed that for a particular dead space and alveolar ventilation, there is a minimum value of average alveolar pressure, which gives a corresponding tidal volume and breathing frequency. Based upon the criteria of minimum average alveolar pressure, ventilator designs have been proposed for several wave forms of pressure inputs.

A critical study of the design criteria used by early investigators indicate that, some of the factors ignored by Wald et al [32], vitally affect physiological conditions during actual ventilator operation. The two major factors are low arterial carbondioxide tension caused by hyperventilation and necessity to minimize the ventilatory work. The hyperventilation effects are caused by long term use of mechanical ventilation[4]. Suwa and Bendexin[28] have determined the amount of additional mechanical dead space necessary to maintain the arterial carbondioxide tension at the normal value. Optimally controlled ventilators which minimize the harm due to (IPPV) and provide desired ventilation have also been designed by Mitimura at el[24], and Jain and Guha[17]. Early studies did not pay much attention to

minimize the ventilatory work because it had been assumed to be a mechanical parameter related to the ventilator.

The physiological importance of minimizing ventilatory work in natural respiration has been well established by the work of Otis[26], Mead[23], Yamashio and Grodins[33]. Since the provision of (IPPV) therapy substitutes the functions of the impaired respiratory system, minimizing the ventilatory work would amount to creating conditions similar to natural breathing. Jain and Guha[18] have included the ventilatory work in the formulation of the design equations and have tried to simultaneously minimize both average alveolar pressure and ventilatory work with a compromise in the selection of optimal design parameters for the ventilator. They have not used any optimization technique and it may result in values of ventilatory work exceeding the permissible capacity of the patient.

In the following work;

(i) The average alveolar pressure is minimized

(ii) The ventilatory work is constrained within a maximum allowable work capacity of the patient.

2.2 MATHEMATICAL MODELLING OF VENTILATORS:

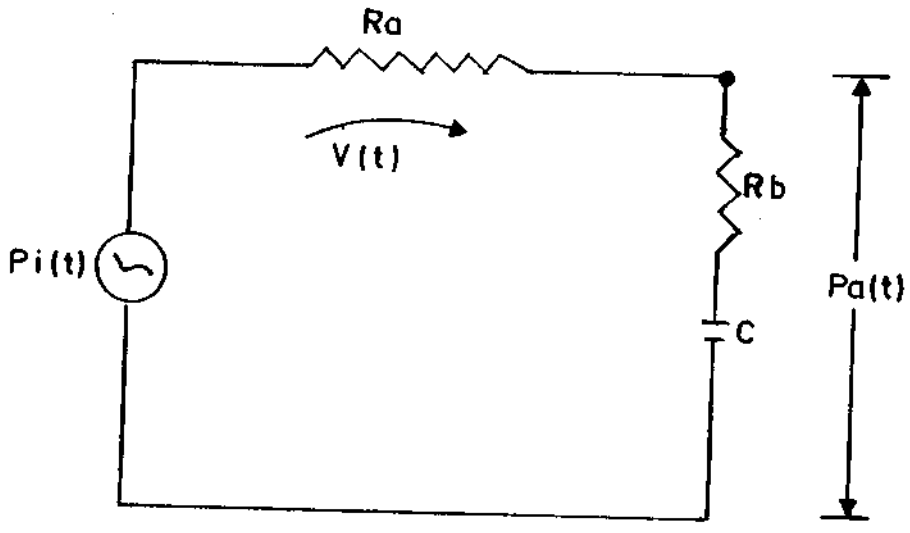
2.2.1 Model of Respiratory System:

A model which includes all aspects of the respiratory process is not quite known at present. Several different models have been proposed to study different aspects of the

respiratory process. Lumped parameter Lung Model[8] has been widely use to explain the mechanism of respiration. The mechanical parameters concerned with ventilation are airway resistance, resistance of lung tissues, chest wall, the compliance and inertia of the lung tissues.

The inertial terms are very small and can be neglected[28]. The remaining parameters can be adequately incorporated in a simplified resistance compliance lung model shown in figure (2.1). Parameters are taken as linear, lumped, deterministic and time variant. Gas inertial effects, effect of turbulence, surface tension, stress adoption and non linearities of the parameters with the lung model have been neglected. Ventilation in a patient is controlled by the application of intermittent positive pressure to the airway, which causes the flow of inspiratory gases. To study the effect of positive pressure a simulated pressure pulse is applied at the input of the respiratory analog model. Expiration is assumed to commence immediately after the end of an applied pressure pulse.

In this work our problem which is of fluid mechanical nature is cast in Electrical Engineering analogy. The terms in the two areas are related as given in the Table (2.1).



Ra = Upper Airway Resistance
Rb = Lung and Chest wall Resistance
C = Lung and Chest wall Compliance
Pi = Applied Pressure Input
Pa = Pressure in Alveoli

FIG-2-1 : ANALOG MODEL FOR CONTROLLED VENTILATION

TABLE 2.1: COMPARATIVE ANALYSIS OF ELECTRICAL AND FLUID MECHANICAL TERMINOLOGIES

ELECTRICAL TERMINOLOGIES	FLUID MECHANICAL TERMINOLOGIES
V Potential in volts	P Pressure in CmH20
Q Charge in coulombs	V volume in litres
t in seconds	t in seconds.
$I=\frac{Q}{t}$ in Coulomb/second	$\dot{V} = v/t$ in litres/seconds
$R=\frac{V}{I}$ in ohms.	$R = P/\dot{V}$ in CmH_2o/litres/second

The input impedance Z_I for the model shown in Figure (2.1) is

$$Z_I = R_a + R_b + \frac{I}{SC}.$$

Using $C = \frac{T}{R_a+R_b}$

$$Z_1=(R_a+R_b)\ \frac{S+\frac{1}{T}}{S}\ .$$

Inspiration gas flow is given by

$$\dot{V}_1(S)\ \frac{P_1(S)}{Z_I}=\frac{1}{R_a+R_b}.\frac{S}{S+\frac{1}{T}}\ P_1(S)$$

In the following work four models have been studied Figure (2.2) shows these models.

In any of these models, alveolar pressure differs from applied pressure by, pressure drop-across upper airway resistance.

Figure (2.2) also shows representative curves of alveolar pressure super imposed on the applied pressure curves.

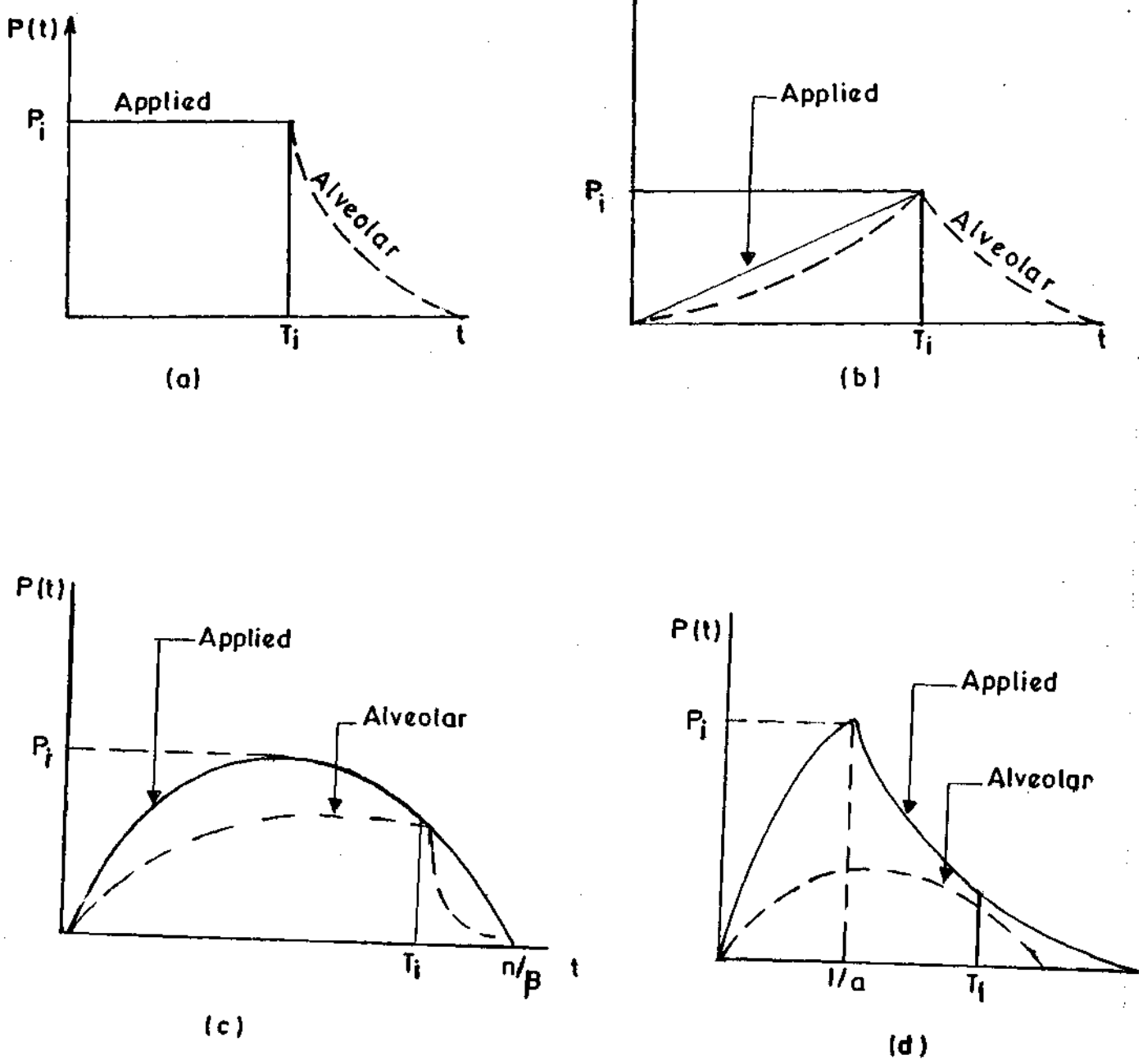
TABLE 2.2 SYMBOLS AND UNITS

S/NO	QUANTITY	SYMBOLS	UNITS
1-	Time period for in inspiratory-cycle	T_i	Seconds
2-	Time period for expiratory-cycle	T_e	Seconds
3-	Frequency	f	breath/minute
4-	Upper airway resistance	R_a	c.mH20/litres/second
5-	Lung and chest wall - resistance	R_b	c.mH20/litres/second
6-	Lung and chest wall - compliance	C	litres/cmH20
7-	Alveolar ventilation	$\dot{V}_A$	litres/second
8-	Pressure at inspiration	P_i	cm H20
9-	Pressure at expiration	P_e	cm H20
10-	Average alveolar pressure	$\overline{P_A}$	cm H20
11-	Peak alveolar pressure	Pa_p	cm H20
12-	Tidal volume	V_T	litres
13-	Flow rate during inspiration	$\dot{V}_I$	litres/second
14-	Flow rate during expiration	$\dot{V}_e$	litres/second
15-	Constant	C_1	Dimension less.
	Constant	C_2	litres.

S/NO	QUANTITY	SYMBOLS	UNITS
-	Constant	K_{DS}	Dimension less
-	Constant Constant	β G	Per second litres/cmH20 second
16-	Vital capacity	V_c	litres
17-	Work done in the expiratory cycle	W_1	litres cm H20
18-	Work done in the expiratory cycle	W_2	litres cm H20

TABLE 2.3 THE NUMERICAL VALUES OF THE RESPIRATORY PARAMETERS AND CONSTANTS FOR AN ADULT PATIENT

S/NO	NAME OF THE PARAMETERS OR CONSTANTS	SYMBOL	VALUE
1-	Upper Airway resistance	R_a	1.5cmH20 seconds/litre
2-	Lung and chest wall resitance	R_b	1.2cmH20 seconds/litre
3-	Lung and chest wall compliance	C	0.1 cm H20
4-	Alveolar Ventilation	$\dot{V}_A$	0.1 litres/second
5-	Time period	T	0.27 seconds.
6-	Vital capacity	V_c	4.0 litres
7-	Resistance	R	2.7 CmH20 seconds/litre
8-	Constant	C_1	I
9-	Constant	C_2	0.148 litres
10-	Constant	K_{DS}	0.005
11-	Constant	K	0.555



FIG·2·2 : WAVE FORMS FOR APPLIED PRESSURE AND ALVEOLAR PRESSURES FOR THE VARIOUS MODELS

2.2.2: VENTILATORY PARAMETERS:

The main variables in (IPPV) are tidal volume ventilatory rate, applied pressure, resistance and compliance. These parameters are inter related with each other. The resistance and compliance are assumed constant for a particular patient. The tidal volume is fixed by the applied pressure. Thus there are only two independent parameters - the applied or peak alveolar pressure and ventilatory rate or inspiration and expiration time. Mathematical relationship between the physiological functions e.g average alveolar pressure and ventilatory work done on the patient are obtained in terms of these parameters for various input pressure wave forms namely, Rectangular, Ramp, Sine and Gamma distribution.

2.3 DESIGN EQUATIONS

2.3.1 RECTANGULAR PRESSURE INPUT

For a rectangular pressure pulse of amplitude P_i in the figure 2.2 (a) applied at the input of the respiratory systemanalog, the total instantaneous flow rate $V_i(t)$ inspiration is given by

$$\dot{V}_i(t) = \alpha^{-1}[\dot{V}(s)]$$

where α^{-1} is the inverse Laplace transforms.

$$= \mathcal{L}^{-1}\left[\frac{P_I}{R} \cdot \frac{S}{S+\frac{1}{T}}\right] or$$

$$\dot{V}_I(t) = \frac{P_I}{R} Exp(-t/T) \qquad \ldots(2.1)$$

The tidal volume, which is the volume of the gas contained in the lungs at the end of the inspiration phase, is

$$V_T = \int_o^{T_I} \dot{V}_I(t)\, dt \qquad \ldots(2.2)$$

$$= \frac{P_I}{R} [Exp(-t/T)\ (-T)]_o^{T_I}$$

$$= \frac{P_I}{R} T(1-EXP(-T_I/T))$$

where T = RC and T_i is inspiratory period in seconds or the total time for which the positive pressure is applied. Thus,

$V_T = P_i\ C\ (1 - EXP(-T_i/T))$. ...(2.3)

The alveolar pressure during inspiration is

$P_{ai}\ (t) = P_i - R_a\ V_i\ (t)$ ...(2.4)

and the expiratory flow rate is

$$\dot{V}_e(t) = \frac{V_T}{T} EXP(-t/T) \qquad \ldots.(2.5)$$

The alveolar pressure during expiration is

$P_{ae}(t) = R_a\ \dot{V}_e(t)$. ...(2.6)

The average alveolar pressure P_A is given by

$$\overline{P_A} = \frac{f}{60}\left[\int_o^{T_I} P_{aI}(t)\,dt \; t \int_o^{T_e} P_{ae}(t)\,dt\right] \qquad \ldots(2.7)$$

$$\int_o^{T_I} P_{aI}(t)\,dt = \int_o^{T_I} (P_I - R_a \dot{V}_I(t))\,dt$$

$$= P_I \,|t|_o^{T_I} - R_a \int_o^{T_I} \frac{P_I}{R}\, EXP(-t/T)\,dt$$

$$= P_I(T_I) + \frac{R_a P_I T}{R}\, (EXP(-T_I/T - 1)$$

The above becomes on using Eq. (2.3)

$$\int_o^{T_I} P_{aI}(t)\,dt = P_I\,(T_I) - R_a\, V_T \qquad \ldots(2.8)$$

Also, $\int_o^{T_e} P_{ae}(t)\,dt = R_a \int_o^{T_e} \dot{V}_e(t)\,dt$

$$= \frac{R_a}{T}\int_o^{T_e} V_T\, EXP(-t/T)\,dt$$

from Eq. (2.5), which gives

$$\int_o^{T_e} P_{ae}(t)\,dt = R_a V_T\,(1 - EXP(-T_e/T)) \qquad \ldots(2.9)$$

On substituting from Eqs. (2.8) and (2.9) in Eq. (2.7), we have.

$$\overline{P_A} = \frac{f}{60}\,[P_I T_I - R_a V_T\, EXP(-T_e/T) \qquad \ldots(2.10)$$

where f = respiratory frequency, breaths/minute, and

T_e = expiratory period in seconds.

The dead space varies considerably for large tidal volumes in positive pressure ventilation. This is because

positive pressure ventilation tends to cause uneven ventilation leading to an increased physiological dead space[4,11]. The relationship between dead space and tidal volume is not exactly linear but can be approximated by a straight line for the usual range of tidal volumes. One such relationship as reported by Grey et al[9] is given by

$$V_D = D_{S_0} + K_{D_S} V_T \qquad \ldots(2.11)$$

where $D_{S_0} = 0.037 \times V_C$,

Vc = Vital Capacity

$K_{DS} = \frac{D_{SO}}{8}$.

Tidal volume can be described in terms of alveolar-ventilation and dead space as

$$V_T = \frac{\dot{V}_A}{f/60} + V_D \qquad \ldots(2.12)$$

Where V_A = Alveolar ventilation litres/minute.

From Eq. (2.11)

$$V_T = \frac{\dot{V}_A}{f/60} + D_{SO} + K_{DS} V_T$$

$$or\ V_T = \frac{\dot{V}_A}{f/60(1-K_{DS})} + \frac{D_{SO}}{(1-K_{DS})}$$

$$Putting\ C_1 = \frac{1}{(1 - K_{DS})}$$

$$and \qquad C_2 = \frac{D_{SO}}{(1 - K_{DS})}$$

We have

$$V_T = \frac{C_1}{f/60}\dot{V}_A + C_2 \qquad \ldots(2.13)$$

where f = respiratory frequency breaths/minute,

Now, time period = $(T_i + T_e)$ seconds,

$$= \left(\frac{T_i + T_e}{60}\right) \textit{minutes.}$$

$$\textit{or } f = \frac{60}{T_i + T_e}, \textit{ Per minute}$$

Putting this value of f in Eq.(2.13) we have,

$$V_T = C_1\dot{V}_A(T_i + T_e) + C_2 \qquad \ldots(2.14)$$

The peak alveolar pressure attained at the end of the inspiratory phase is given by

$$P_{ap} = P_i\ (1 - K\ EXP(-T_i/T)) \qquad \ldots(2.15)$$

where $K = R_a/R$

From Eq.(2.3) namely

$V_T = P_i\ C(1 - EXP(-T_i/T))$

using Eq. (2.14), we have,

$C_1\dot{V}_A(T_i + T_e) + C_2 = P_i\ C(1 - EXP(-T_i/T))$

or

$$P_i = \frac{C_1\dot{V}_A\ (T_i + T_e) + C_2}{C(1 - EXP(-T_i/T))} \qquad \ldots(2.16)$$

$$P_{ap} = \frac{C_1\dot{V}_A\ (T_i + T_e) + C_2}{C(1 - EXP(-T_i/T))}\ x\ (1 - K\ EXP(-T_i/T)\,.$$

From Eq. (2.16)

$$T_e = \frac{CP_I\,(1 - EXP(-T_I/T)) - C_2}{C_1 \dot{V}_A} - T_I. \qquad \ldots(2.17)$$

During inspiration, work is done on the patient by the ventilator in overcoming the airway resistance and against the elastic recoil of the lungs and thoracic cage. The work done against elastic recoil of lungs and thorax is stored as potential energy and is made available during expiration. The expiratory work is therefore taken as negative while calculating the total work. The inspiratory work done by the ventilator per cycle is

$$W_I = \int_o^{T_I} P_I \dot{V}_I(t)\,dt = P_I V_T \qquad \ldots(2.18)$$

from Eq. (2.2)

The expiratory work per cycle is given by

$$W_e = \int_o^{T_e} P_e(t)\,\dot{V}_e(t)\,dt \qquad \ldots(2.19)$$

$$But\ P_e(t)\,\dot{V}_e(t) = \frac{V_T}{C} EXP(-t/T) \cdot \frac{V_T}{T} EXP(-t/T)$$

$$= \frac{V_T 2}{CT} EXP(-2t/T)$$

where $P_e(t)$ is the expiratory driving pressure, given by

$$P_e(t) = \frac{V_T}{C} EXP(-t/T).$$

$$\dot{V}_I(s) = \frac{1}{R}\frac{S}{S+\frac{1}{T}} \cdot \frac{P_I}{T_I}\frac{1}{S2}$$

$$= \frac{P_I}{T_I R} \cdot \frac{1}{S(S+\frac{1}{T})}$$

$$\dot{V}_I(s) = \frac{P_I}{T_I}\frac{T}{R}\left(\frac{1}{s} - \frac{1}{s+\frac{1}{T}}\right)$$

$$\dot{V}I(t) = \frac{P_I T}{T_I R}\,\mathcal{L}^{-1}\left(\frac{1}{S} - \frac{1}{S+\frac{1}{T}}\right)$$

$$\dot{V}_I(t) = \frac{P_I T}{T_I R}\,(1-EXP(-t/T)) \qquad \ldots.(2.23)$$

From Eq. (2.2), the tidal volume i.e the volume of the gas contained in the lungs at the end of the inspiratory period is given by

$$V_T = \int_0^{T_I} \dot{V}_I(t)\,dt$$

Substitution from (2.23)

$$= \int_0^{T_I} \frac{P_I T}{T_I R}\,(1 - EXP(-t/T))\,dt$$

$$= \frac{TP_I}{R}\left[1 - \frac{T}{T_I}\,(1 - EXP\,(-T_I/T))\right]$$

By using T = RC,

$$V_T = CP_i \left[1 - \frac{T}{T_i} \left(1 - EXP(-T_i/T)\right)\right] \qquad \ldots(2.24)$$

The average alveolar pressure P_A is given by

$$\overline{P_A} = \frac{f}{60} \left[\int_0^{T_i} P_{ai}(t)\,dt + \int_0^{T_e} Pa_e(t)\,dt\right]$$

From Eqs. (2.4) and (2.6)

$$\overline{P_A} = \frac{f}{60} \left[\int_o^{T_i} P_r(t)\ R_a\ \dot{V}_i(t)\,dt + \int_o^{T_e} R_a\ \dot{V}_e(t)\,dt\right]$$

Using Eqs. (2.22), (2.2) and (2.5) we have,

$$= \frac{f}{60} \left[\frac{P_i T_i}{2} - R_a V_T + R_a V_T \left(1 - EXP(-T_e/T)\right)\right]$$

Thus

$$\overline{P_A} = \frac{f}{60} \left[\frac{P_i T_i}{2} - R_a V_T\, EXP(-T_e/T;\right] \qquad \ldots(2.25)$$

From Eq. (2.4)

$$P_{ai}(t) = P_i - R_a \dot{V}_i(t)$$

$$= P_i - R_a \left[\frac{P_i T}{T_i R} \left(1 - EXP(-t/T)\right)\right]$$

$$P_i \left[1 - R_a \left\{\left(\frac{T}{T_i\, R} \left((1 - EXP(-t/T)\right)\right\}\right]\right.$$

When $t = T_i$ then $P_{ai}(t) = P_{ap}$ i.e, the Peak alveolar pressure is given by

$$P_{ap} = P_i \left[1 - \frac{R_a}{T_i} \left\{\frac{T}{R} \left(1 - EXP(-T_i/T)\right\}\right]\right.$$

$$P_{ap} = P_1 \left[1 - \frac{R_a}{T_1} C(1 - EXP\ (-T_1/T))\right] \qquad \ldots(2.26)$$

From Eqs. (2.14) and (2.23) we have,

$$CP_1 \left[1 - \frac{T}{T_1} (1 - EXP(-T_1/T))\right] = C_1 V_A (T_1 + T_o) + C_2$$

or

$$P_1 = \frac{C_1 \dot{V}_A (T_1 + T_o) + C_2}{C\left[1 - \frac{T}{T_1}(1 - EXP(-T_1/T))\right]} \qquad \ldots(2.27)$$

From Eq. (2.27)

$$CP_1 \left[1 - \frac{T}{T_1} (1 - EXP(-T_1/T))\right] = C_1 \dot{V}_A (T_1 + T_o) + C_2$$

$$T_o = \frac{CP_1\left[1 - \frac{T}{T_1} (1 - EXP(-T_1/T))\right] - C_2}{C_1 \dot{V}_A} - T_1 \qquad \ldots(2.28)$$

From Eq. (2.18)

$$W_1 = \int_o^{T_1} P_1 \dot{V}_1(t)\, dt = \int_o^{T_1} P_r(t) \dot{V}_1(t)\, dt$$

From the Eqs. (2.22) and (2.23) we have

$$W_1 = \frac{P_1}{T_1} \int_o^{T_1} t \frac{P_1 T}{T_1 R} (1 - EXP(-t/T))\, dt \qquad or$$

$$W_1 = \frac{P_1^2}{T_1^2} C\left[\frac{T_1^2}{2} + TT_1\, EXP(-T_1/T) + T^2 (EXP(-T_1/T) - 1)\right]$$

$$W_1 = \frac{P_1^2}{T_1^2} C\left[\frac{T_1^2}{2} + T(T_1+T)\, EXP(-T_1/T) - T^2\right] \qquad (2.29)$$

From Eq. (2.19)

$$W_e = \int_0^{T_e} P_e(t)\, \dot{V}_e(t)\, dt$$

$$\text{and } P_e(t) = \frac{V_T}{C}\ EXP(-t/T),$$

By using Eq. (2.5) we have,

$$W_e = \frac{V_T^2}{2C}\ (1 - EXP(-2T_e/T)). \qquad \ldots(2.30)$$

The total work done W_{tf} is given by

$$W_{tf} = f\ (W_i - W_e)$$

From Eqs. (2.28) and (2.29) we have

$$W_{tf} = f[\frac{P_i^2}{T_i^2}C\{\frac{T_i^2}{2} + T(T_i+T_e)\,EXP(-T_i/T) - T^2\}\frac{V_T^2}{2C}\ (1-EXP(-2T_e/T))]$$

$$\ldots(2.31)$$

2.3.3 SINE PRESSURE INPUT

In this model, the input pressure varies as shown in the Figure 2.2(c) and is given by,

$$P_f(t) = P_i \sin \beta t$$

where β is a constant.

Then the Laplace transform of $P_f(t)$ is given by

$$P_1(s) = \int_o^{\infty} P_1\, EXP(-st)\ Sin\, \beta t\, dt$$

$$= P_1\ [\frac{\beta}{s^2+\beta^2}]$$

We have

$$\dot{V}_1(s) = \frac{1}{R} \cdot \frac{s}{s+\frac{1}{T}} P_1 \frac{\beta}{s^2+\beta^2}$$

$$= \frac{P_1\beta}{R} \left[\frac{s}{s+\frac{1}{T}(s^2+\beta^2)}\right]$$

$$= \frac{P_1\beta}{R} \left[\frac{-T^2}{(1+T^2\beta^2)(ST+1)} + \frac{TS + T^2\beta^2}{(1+T^2\beta^2)(S^2+\beta^2)}\right]$$

$$= \frac{P_1\beta}{R} \left[\frac{-T}{1+T^2\beta^2} \cdot \frac{T}{ST+1} + \frac{T}{1+T^2\beta^2} \cdot \frac{s}{s^2+\beta^2}\right.$$

$$\left. + \frac{T^2\beta}{1+T^2\beta^2} \cdot \frac{\beta}{S^2+\beta^2}\right]$$

Thus

$$\dot{V}_1(t) = \frac{P_1\beta}{R} \alpha^{-1} \left[\frac{-T}{1+T^2\beta^2} \frac{T}{(ST+1)} + \frac{T}{(1+T^2\beta^2)} \frac{S}{S^2+\beta^2}\right.$$

$$\left. + \frac{T^2\beta}{1+T^2\beta^2} \frac{\beta}{S^2+\beta^2}\right]$$

Or

$$\dot{V}_1(t) = \frac{P_1\beta}{R} \left[\frac{-T}{1+T^2\beta^2} EXP(-t/T) + \frac{T}{1+T^2\beta^2} cos\ \beta t + \frac{T^2\beta}{1+T^2\beta^2} \sin \beta t\right]$$

$$\dot{V}_1(t) = \frac{P_1\beta}{R} \left[\frac{-T}{1+T^2\beta^2} EXP(-t/T) + \frac{T}{\sqrt{1+T^2\beta^2}} cos(\beta t - \phi)\right] \quad ...(2.33)$$

where.

$$cos\ \phi = \frac{1}{\sqrt{1+\beta^2T^2}} \quad or \quad \phi = tan^{-1}\ \beta T.$$

Now by putting.

$$G = \frac{\beta C}{1+\beta^2 T^2} \text{ and } D = \frac{\beta C}{\sqrt{1+T^2\beta^2}}$$

where T = RC,

Eq. (2.33) becomes,

$$\dot{V}_I(t) = P_I\,[-G\,EXP(-t/T) + D\,\cos(\beta t - \phi)] \qquad \ldots(2.34)$$

From Eq. (2.2), now the tidal volume i.e the volume contained in the lungs at the end of the inspiratory period, is given by

$$V_T = \int_o^{T_I} \dot{V}_I(t)\,dt$$

which from Eq. (2.34) becomes,

$$V_T = \frac{P_I D}{\beta}(\sin(\beta T_I - \phi) + \sin\phi) - TGP_I(1 - EXP(-T_I/T)) \qquad \ldots(2.35$$

The average alveolar pressure P_A is given by

$$\overline{P_A} = \frac{f}{60}\left[\int_o^{T_I} P_{AI}(t)\,dt + \int_o^{T_e} P_{Ae}(t)\,dt\right].$$

Using Eqs. (2.4) and (2.6),

$$\overline{P_A} = \frac{f}{60}\,[\int_o^{T_I}(P_I(t) - R_a\,\dot{V}_I(t)\,dt + \int_o^{T_e} R_a\,\dot{V}_e(t)\,dt].$$

Using Eqs. (2.32), (2.2) and (2.5)

$$\overline{P_A} = \frac{f}{60}\,[\int_o^{T_I} P_I \sin\beta t\,dt - R_a V_T + \frac{R_a V_T}{T}\int_o^{T_e} EXP(-t/T)\,dt]$$

Thus,

$$\overline{P_A} \quad \frac{f}{60}\,[\frac{P_I}{\beta}(1 - \cos\beta T_I) - R_a V_T EXP(-T_e/T)] \qquad \ldots(2.36)$$

From Eq. (2.4).

$$P_{al}(t) = P_l(t) - R_a\dot{V}_l(t) = P_x(t) - R_a\dot{V}_l(t)$$

Now From Eq. (2.32),

$$P_{al}(t) = P_l \sin\beta t - R_a\dot{V}_l(t)$$

Finally from Eq. (2.34)

$$P_{al}(t) = P_l[\sin\beta t + R_a G\, EXP(-t/T) - R_a D(\cos(\beta t - \phi))]$$

When $t = T_1$, the $P_{al}(t)$ becomes P_{ap}, the peak aveolar pressure, and is given by,

$$P_{ap} = P_1\left[\sin\beta T_1 + R_a G\, EXP(-T_1/T) - R_a D\cos(\beta T_1 - \Phi)\right]$$

From Eqs. (2.14 and (2.35), Equating the two expression for V_T.

$$\frac{P_l D}{\beta}(\sin(\beta T_l - \phi) + \sin\phi) - TGP_l(1 - EXP(-T_l/T) = C_1\dot{V}_A(T_l + T_e) + C_2$$

or

$$P_l = \frac{\beta(C_1\dot{V}_A(T_l+T_e)+C_2)}{D(Sin(\beta T_l - \Phi)+Sin\,\Phi) - \beta TG(1-EXP(-T_l/T))} \qquad \ldots(2.38)$$

Which gives,

$$T_e = \frac{P_l D/\beta(Sin(\beta T_l - \phi) + Sin\,\phi) - P_l TG(1 - EXP(-T_l/T)) - C_2}{C_1\dot{V}_A} - T_l$$

$\ldots(2.39)$

From Eq. (2.18)

$$W_1 = \int_o^{T_1} P_1(t)\, \dot{V}_1(t)\, dt = \int_o^{T_1} P_r(t)\, \dot{V}_1(t)\, dt$$

which becomes using Eqs. (2.32) and (2.34),

$$W_1 = \frac{P_1^2 D}{4\beta}\left[\cos\phi - \cos(2\beta T_1 - \phi) + 2\beta T_1 \sin\phi\right]$$

$$+ \frac{P_1^2 \beta G}{\beta^2 + \frac{1}{T2}}\left[EXP(-T_1/T)\left(\cos\beta T_1 - \frac{1}{\beta T}\sin(\beta T_1)\right) - 1\right] \quad ..(2.40)$$

From Eq.(2.19)

$$W_e = \int_o^{T_e} P_e(t)\, \dot{V}e(t)\, dt$$

where $P_e(t) = \frac{V_r}{C} EXP(-t/T)$

Substituting from Eq. (2.5) we have,

$$W_e = \int_o^{T_e} \frac{T}{C} EXP(-t/T) \cdot \frac{V_r}{T} EXP(-t/T)\, dt$$

or

$$W_e = \frac{V_r 2}{2C}(1 - EXP(-2T_e/T)) \qquad ...(2.41)$$

Now, the total work done W_{tf} is given by

$W_{tf} = f\ (Wi - W_e)$

$$W_{tf} = f\left[\frac{P_1^2 D}{4\beta}\{\cos\phi - \cos(2\beta T_1 - \phi) + 2\beta T_1 \sin\phi\}\right.$$

$$+ \frac{P_1^2 \beta G}{\beta^2 + \frac{1}{T^2}}\{(EXP(-T_1/T)(\cos\beta T_1 - \frac{1}{\beta T}\sin(\beta T_1)) - 1\}$$

$$\left. - \frac{V_r 2}{2C}(1 - EXP(-2T_*/T))\right] \qquad \ldots(2.42)$$

2.3.4 GAMMA PRESSURE INPUT:

In this model, the input pressure varies as shown in the Figure 2.2(d) and is given by,

$$P_r(t) = P_i \text{ at } EXP(-at) \qquad \ldots(2.43)$$

where 'a' is a constant

Thus

$$P_1(S) = \int_0^{\infty} P_1\, EXP(-St)\ at\ EXP\ (-at)\, dt$$

Now, we have

$$\dot{V}_1(S) = \frac{1}{R} \cdot \frac{S}{S+\frac{1}{T}}\ P_1\ \frac{a}{(S+a)^2}$$

which becomes taking, $b = \frac{1}{T}$,

$$\dot{V}_1(S) = \frac{P_1 a}{R}\left[\frac{-b}{(a-b)^2(S+b)} + \frac{b}{(a-b)^2(S+a)} + \frac{a}{(a-b)(S+a)^2}\right]$$

or

$$\dot{V}_I(t) = \frac{P_I a}{R}\alpha^{-1}\left[\frac{-b}{(a-b)^2(S+b)} + \frac{b}{(a-b)^2(S+a)} + \frac{a}{(a-b)(S+a)^2}\right]$$

$$= \frac{P_I a}{R}\left[\frac{-b}{(a-b)^2}\,EXP(-bt) + \frac{b}{(a-b)^2}\,EXP(-at)\right.$$

$$\left. + \frac{a}{(a-b)}\,t\,EXP(-at)\right]. \qquad \ldots(2.44)$$

The tidal volume of the gas i.e the volume of the gas contained in the lungs at the end of the inspiratory period is given by.

$$V_T = \int_o^{T_I} \dot{V}_I(t)\,dt$$

From Eq. (2.43) we have

$$V_T = \frac{P_I a}{R}\int_o^{T_I}\frac{-b}{(a-b)^2}EXP(-bt)\,dt + \frac{P_I a}{R}\int_o^{T_I}\frac{b}{(a-b)^2}EXP(-at)\,dt$$

$$+ \frac{P_I a}{R}\int_o^{T_I}\frac{a}{(a-b)}\,t\,EXP(-at)\,dt$$

or

$$V_T = \frac{P_I a}{R(a-b)^2}\left[EXP(-bT_I) - EXP(-aT_I)\,(1+T_I(a-b))\right]. \qquad \ldots(2.45)$$

The average alveolar pressure P_A is given by

$$\overline{P_A} = \frac{f}{60}\left[\int_0^{T_I} P_{aI}(t)\,dt + \int_o^{T_e} P_{ae}(t)\,dt\right].$$

From Eqs. (2.4) and (2.6) we have,

$$\overline{P_A} = \frac{f}{60}\left[\int_o^{T_I}(P_r(t) - (R - R_a)\,\dot{V}_I(t)\,dt) + \int_o^{T_e} R_a \dot{V}_e(t)\,dt\right]$$

Using Eqs. (2.43), (2.2) and (2.5)

$$\overline{P_A} = \frac{f}{60}\left[P_1 a \int_o^{T_1} t\ EXP(-at)\,dt - R\int_o^{T_1}\dot{V}_1(t)\,dt + R_a\int_o^{T_1}\dot{V}_1(t)\,dt\right]$$

$$+ \frac{R_a V_T}{T}\int_o^{T_e} EXP(-t/T)\,dt\Big]$$

$$= \frac{f}{60}\left[P_1 a\left(-\frac{T_1}{a}EXP(-aT_1) + \frac{1}{a^2}(1 - EXP(-aT_1))\right)\right.$$

$$\left. - R\ V_T + 2\ R_a\ V_T - R_a\ V_T\ EXP(-T_e/T)\right]$$

$$= \frac{f}{60}\left[-P_1\ EXP(-aT_1) + \frac{P_1}{a}(1 - EXP(-aT_1))\right.$$

$$- \frac{P_1 a}{(a-b)^2}\{EXP(-bT_1) - EXP(-aT_1)\,(1+T_1(a+b))\}$$

$$\left. + \frac{2KP_1 a}{(a-b)^2}\{EXP(-bT_1) - EXP(-aT_1)\,(1+T_1(a+b))\}\right.$$

$$\left. - R_a\ V_T\ EXP(-T_e/T)\right] \quad , \qquad where\ K = \frac{R_a}{R}$$

$$= \frac{f}{60}\left[\frac{P_1 a(2k-1)}{(a-b)^2}\ EXP(-bT_1) + \frac{P_1}{a} + \frac{P_1 a}{(a-b)^2}EXP\ (-aT_1)\right.$$

$$- \frac{2KP_1 a}{(a-b)^2}\ EXP(-aT_1) - \frac{P_1}{a}\ EXP(-aT_1)$$

$$+ \frac{P_1 a T_1}{(a-b)}\ EXP(-aT_1) - \frac{2KP_1 a T_1}{a-b}EXP(-aT_1)$$

$$\left. - P_1 T_1\ EXP(-aT_1) - R_a V_T\ EXP(-T_e/T)\right] \qquad ...(2.46)$$

Now, collecting the terms not containing a factor T_1 namely,

$$\frac{P_1 a}{(a-b)^2}\ EXP(-aT_1) - \frac{2KP_1 a}{(a-b)^2}\ EXP(-aT_1) - \frac{P_1}{a}\ EXP(-aT_1)$$

$$= \frac{P_1}{(a-b)} EXP\ (-aT_1)\ \{\frac{1}{a(a-b)}\ (2ab - b^2 - 2a^2K))\} \quad ...(2.47)$$

Now from Eq. (2.45) collecting the terms containing T_i as a factor,

$$\frac{P_1 aT_1}{(a-b)} EXP\ (-aT_1) - \frac{2KP_1 aT_1}{(a-b)} EXP(-aT_1) - P_1 T_1\ EXP(-aT_1)$$

$$= \frac{P_1}{(a-b)} EXP(-aT_1)\ T_1\ (b - 2aK) \quad ...(2.48)$$

Substituting from Eqs. (2.46) and (2.47) in (2.45) we have,

$$\overline{P_A} = \frac{f}{60} [P_1 \frac{a(2k-1)}{(a-b)^2} EXP\ (-bT_1) + \frac{P_1}{a} - R_a V_T\ EXP(-T_e/T)$$

$$+ \frac{P_1}{(a-b)} EXP(-aT_1)\{\frac{1}{a(a-b)}\ (2ab - b^2 - 2ak) + T_1 + T_1(b - 2ak)\}] \quad ...(2.49)$$

Next from Eq. (2.4)

$$P_{ai}(t) = P_1 - R_a \dot{V}_1(t)$$

$$= P_r(t) - (R - R_a)\, \dot{V}_1(t)$$

which becomes using Eq. (2.43)

$$P_{ai}(t) = P_1 at\ EXP(-at)\ - R\dot{V}_1(t) + R_a \dot{V}_1(t)\,.$$

Usng Eq. (2.44).

$$P_{ai}(t) = P_1 a[tEXP(-at) + \frac{b}{(a-b)^2} EXP(-bt) - \frac{b}{(a-b)^2} EXP(-at)$$

$$- \frac{a}{(a-b)} t\, EXP(-at) - \frac{kb}{(a-b)^2} EXP(-bt)$$

$$+ \frac{kb}{(a-b)^2} EXP\,(-at) + \frac{ka}{(a-b)} t\, EXP(-at)]$$

At, $t = \frac{1}{a}$, P_{a1} becomes P_{ap}. Hence

$$P_{ap} = \frac{P_1 ab}{(a-b)^2}(1-K)\{\exp(-b/a) - EXP(-1)\}$$

$$- \frac{P_1(b-ak)}{(a-b)} EXP(-1) \qquad \ldots(2.50)$$

From Eqs. (2.14) and (2.44)

$$\frac{P_1 a}{R(a-b)^2}[EXP(-bT_1) - EXP(-aT_1)\{(1+T_1(a+b))\}]$$

$$= C_1 \dot{V}_A (T_1+T_e) + C_2,$$

or

$$P_1 = \frac{C_1 \dot{V}_A (T_1+T_e) + C_2}{EXP(-bT_1) - EXP(-aT_1)\{(1+T_1(a-b)\}} \times \frac{R(a-b)^2}{a} \qquad \ldots(2.51)$$

which becomes,

$$T_e = \frac{P_1 a[EXP(-bT_1 - EXP(-aT_1)\{(1+T_1(a-b)\}] - C_2}{R(a-b)^2 C_1 \dot{V}_A} - T_1. \qquad \ldots(2.52)$$

again,

$$W_1 = \int_o^{T_1} P_1 \dot{V}_1(t)\, dt = \int_o^{T_1} P_r(t)\ \dot{V}_1(t)\, dt$$

$$= \int_o^{T_1} \frac{P_1^2 a^2}{R(a-b)^2} \{ - bEXP(-(a+b)t)\, t + bEXP(-2at)\, t$$

$+ a(a-b)^2 t\ EXP(-2at)\}dt,$

Using Eqs. (2.43) and (2.44)

$$W_1 = \frac{bEXP(-(a+b)T_1)}{(a+b)} + \frac{EXP(-(a+b)T_1)}{(a+b)^2} - \frac{b}{(a+b)^2} + \frac{b}{4a^2}$$

$$- \frac{bT_1\ EXP(-2aT_1)}{2a} - \frac{bEXP(-2aT_1)}{4a^2} + a(a-b\{\frac{T_1}{-2a}\ EXP(-2aT_1)$$

$$\frac{T_1}{2a^2} EXP(-2aT_1) \quad - \frac{1}{4a^3} EXP(-2aT_1) + \frac{1}{4a^3}\}$$

$$or \quad W_1 = \frac{P_1^2 a^2}{R(a-b)^2} [\frac{b}{(a+b)^2} EXP(-(a+b)T_1)\{(a+b)T_1+1)$$

$$- \frac{a-b}{2} T_1^2 EXP(-2aT_1) - \frac{T_1}{2} EXP(-2aT_1) - \frac{1}{4a} EXP(-2aT_1)$$

$$+ \frac{(a-b)^2}{4a(a+b)^2}] \qquad \ldots(2.53)$$

From Eq. (2.19) we have,

$$W_e = \int_o^{T_e} P_e(t)\ \dot{V}_e(t)\, dt$$

$$and\ P_e(t) = \frac{V_T}{C} EXP(-t/T)$$

Substituting from the Eq. (2.5) we have

$$= \int_o^{Te} \frac{V_T}{C} EXP(-t/T) \frac{V_T}{T} EXP(-t/T)\, dt,$$

or

$$W_e = \frac{V_T 2}{2C} \ (1 - EXP(-2T_e/T) . \qquad \ldots(2.54)$$

Now, the total work done W_{tf} is given by,

$W_{tf} = f(W_i - W_e)$

$$W_{tf} = f \ [\frac{P_1^2 a^2}{R(a-b)^2}\{\frac{b}{(a+b)^2} EXP(-(a+b)\,T_1)\ (1+(a+b)\,T_1)]$$

$$- \frac{a-b}{2} T_1 2 \ EXP(-2aT_1) \ - \frac{T_1}{2} \ EXP(-2aT_1)$$

$$- \frac{1}{4a} \ EXP \ (-2aT_1) \ + \frac{(a-b)^2}{4a(a+b)^2}\}$$

$$- \frac{V_T 2}{2C} \ (1 - EXP \ (-2T_e/T))] . \qquad \ldots(2.55)$$

2.4: NOTATIONS USED IN THE COMPUTER PROGRAMMING:

The notation used for the Programming of all the four models namely, Rectangular, Ramp, Sine and Gamma pressure inputs are given below:

TABLE 2.4:

MODEL - NOTATIONS	COMPUTER NOTATIONS
P_i	P1
$\overline{P_i}$	P2
P_{ap}	P3
T_i	T1
T_c	T2
f	F
V_T	V
V_{max}	V2
R_i	R1
β	B
Φ	M

2.5 COMPUTER PROGRAMMES

2.5.1 RECTANGULAR PRESSURE INPUT:

```
25   REM *** RECTANGULAR PRESSURE INPUT ***
1Φ   S = 9999
2Φ   T = 27:R1=1.5:C2 = .148:R = 2.7:C = .1:K =.555
3Φ   W12 = Φ: P12 = Φ:V12 = T12 = Φ:T13 =Φ: F12 = Φ
4Φ   FOR P1 = 7 TO 8 STEP .Φ25
5Φ   FOR T1 = .3 TO .4 STEP .Φ25
6Φ   X = 1 - EXP (-T1/T)
```

```
7Φ   V = C * P1 * X
8Φ   T2 = (V - C2)/.1 - T1
9Φ   F = 6Φ/(T1 + T2)
1ΦΦ  Y = 1 - EXP (-2 * T2)/T)
11Φ  W = F * (P1 *V - V↑2/.2*Y)
12Φ  Z = R1 * V *EXP (-T2/T)
13Φ  P2 = F/6Φ * (P1*T1 -Z)
14Φ  IF W>3Φ,4Φ,5Φ.6Φ.7Φ.8Φ.9Φ.1ΦΦ THEN GO TO 18Φ
15Φ  IF W<25.35.45.55.65.75.85.95 THEN GO TO 18Φ
16Φ  IF S>P2 THEN 17Φ ELSE GO TO 18Φ
17Φ  S = P2 : W12 =W : P12 = P1: V12 = T12 = T1 :
     T13 = T2 : F12 = F
18Φ  NEXT T1
19Φ  NEXT P1
2ΦΦ  P3 = P12 * (1-K * EXP (- T12/T))
21Φ  V2 = P12/R
22Φ  DEF FNR (x) = INT (x * 1ΦΦΦ + Φ.5)/1ΦΦΦ
23Φ  PRINT TAB(4) "W": FNR (W12), =, FNR(S): TAB (35)
     P1 = ": FNR (P12)
24Φ  PRINT
25Φ  PRINT TAB(4) "V = ": FNR(V12),"T1 = ": FNR(T12): TAB(35)
     "T2 = ": FNR(T13)
     PRINT TAB(4) "F: FNR(F12), "V2 = ": FNR(V2): TAB(35)
     "P3 = ": FNR(P3)
     END
```

TABLE 2.5: VENTILATORY PARAMETERS FOR RECTANGULAR PRESSURE INPUT

S/NO	W_e	P_{ap}	T_I	T_e	f	V	P_I	V_{max}	$\bar{P}_A$
	1cm.H2O	CmH2O	Seconds	Seconds	Breath/ minute	ℓ	CmH2O	l/S	CmH2O
1-	30	5.125	0.45	2.714	18.965	0.464	5.725	2.120	0.814
2-	40	6.043	0.325	3.269	16.693	0.507	7.250	2.685	0.656
3-	50	7.296	0.275	4.075	13.794	0.583	9.125	3.380	0.577
4-	60	8.718	0.250	5.018	11.390	0.675	11.175	4.139	0.530
5-	70	9.845	0.225	5.631	10.246	0.734	12.975	4.806	0.499
6-	80	10.682	0.200	5.920	9.804	0.760	14.525	5.380	0.475
7-	90	11.231	0.175	5.893	9.887	0.755	15.825	5.861	0.456
8-	100	12.864	0.175	6.990	8.374	0.865	18.125	6.713	0.443

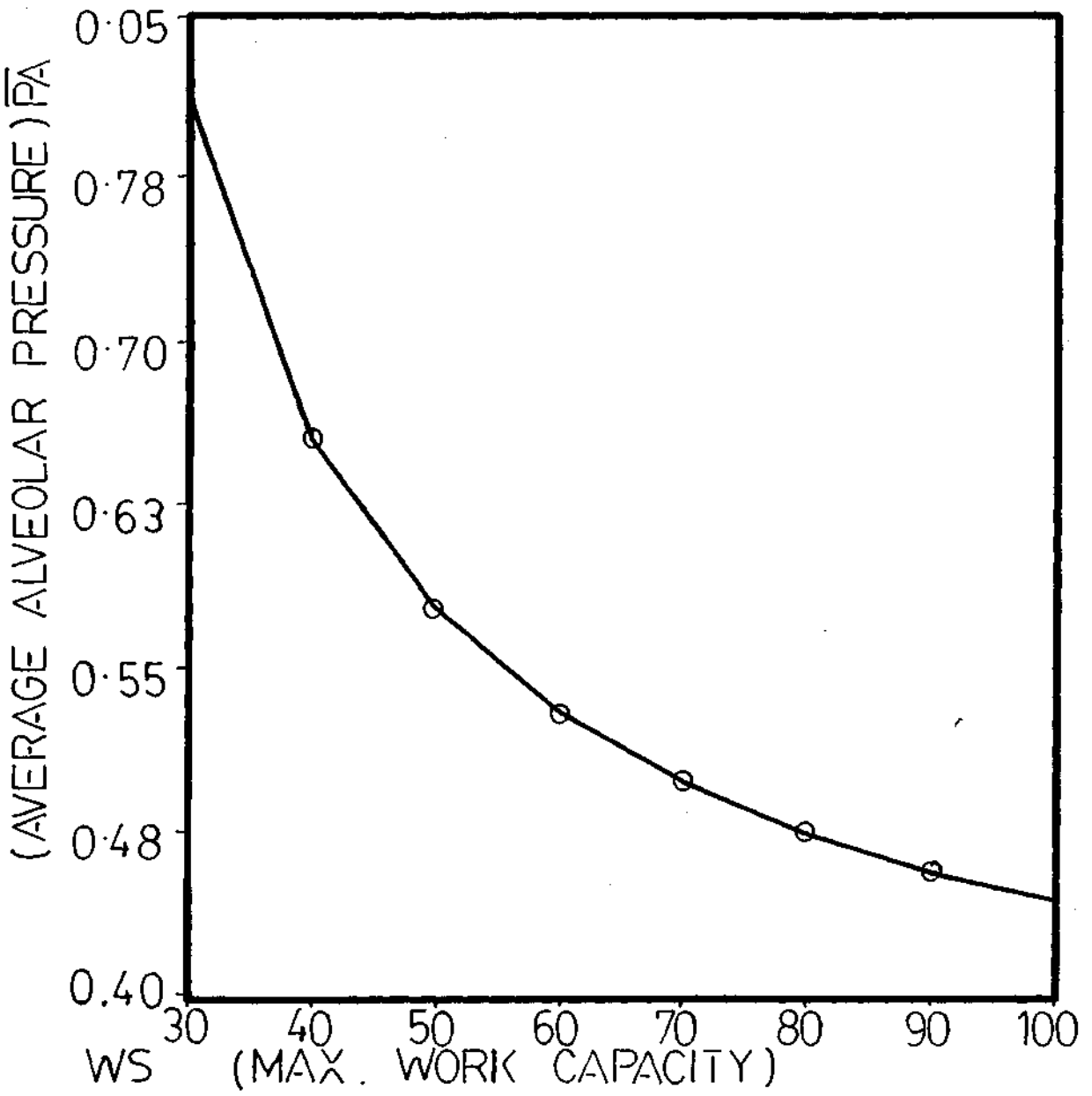


Fig:2.3. Rectangular Pressure Input .

2.5.2: RAMP PRESSURE INPUT

```
5    REM *** RAMP PRESSURE *** INPUT ***
1Ø   S = 9999
2Ø   T = .27 : R1 = 1.5: C2 = .48 : R = 2.7 : C = .1
     k =  .555
3Ø   W12 = Ø: P12 = Ø : V12 = Ø:T12 = Ø: T13 = Ø: F12 = Ø
4Ø   FOR P1 = 11 TO 12 STEP .Ø25
5Ø   FOR T1 = .5 TO .6 STEP .025
6Ø   X = 1 -(T/T1) * (1 - EXP (-T1/T))
7Ø   V = C * P1 * X
8Ø   T2 = (V - C2)/.1 -T1
9Ø   F = 6Ø/(T1+T2)
1ØØ  Y = (P1/T1)^2 * C * (T1^2/2 +T * (T1 + T)
     *EXP (-T1/T) -T^2)
1Ø5  Y1 = V^2/.2 * (1 - EXP((-2*T2)/T)
11Ø  W = F*(Y - Y1)
12Ø  Z = R1 * V * EXP (-T2/T)
13Ø  P2 = F/6Ø * ((P1*T1)/2 -Z)
14Ø  IF W > 3Ø, 4Ø, 5Ø, 6Ø, 7Ø, 8Ø, 9Ø, 1ØØ, THEN 18Ø
15Ø  IF W<25, 35, 45, 55, 65, 75, 85, 95, THEN 18Ø
16Ø  IF S>P2 THEN 17Ø ELSE GOTO 18Ø
17Ø  S = P2: W12 = W: P12 = P1: V12 = V1: T12 =T1
     T13 = T2 : F12 = F
18Ø  NEXT T1
19Ø  NEXT P1
195  Z1 = 1 - (R1/T12) * (T/R) (1-EXP (-T12/T))
2ØØ  P3 = P12/Z1
```

```
220  FNR (X) = INT (X*1000 +0.5)/1000
230  PRINT TAB(4) "W = "FNR(W13), "P2 = ", FNR(S)
     TAB(35) "P1 = ", FNR (P12)
240  PRINT
250  PRINT  TAB(4) "V =  " FNR (V12), "T1  = ", FNR (T12):
     TAB(35) "T2 = ", FNR (T13)
260  PRINT
270  PRINT TAB(4) "F = ", FNR(F12), ``V² = ``, FNR(V₂):
     TAB(35) ``P3 = '', FNR(P3)
280  END
```

TABLE 2.6: VENTILATORY PARAMETERS FOR RAMP PRESSURE INPUT

S/NO	WS	P_{ap}	T_i	T_e	f	v	p_i	V_{max}	$\overline{P_a}$
	1.Ce H20	Cm.H20	Seconds	Seconds	breath/ minute	ℓ	Cm H20	l/S	CmH20
1-	30	8.458	0.525	4.259	12.542	0.626	11.200	4.148	0.615
2-	40	9.885	0.425	4.907	11.252	0.681	13.725	5.083	0.547
3-	50	11.703	0.375	5.831	9.669	0.725	16.725	6.194	0.505
4-	60	12.913	0.325	6.178	9.226	0.798	19.075	7.065	0.477
5-	70	14.621	0.300	6.939	8.290	0.872	22.000	8.148	0.456
6-	80	16.044	0.275	7.424	7.793	0.918	24.625	9.120	0.440
7-	90	17.186	0.250	7.645	7.600	0.937	26.950	9.981	0.427
8-	100	18.03	0.225	7.603	7.665	0.931	28.950	10.722	0.416

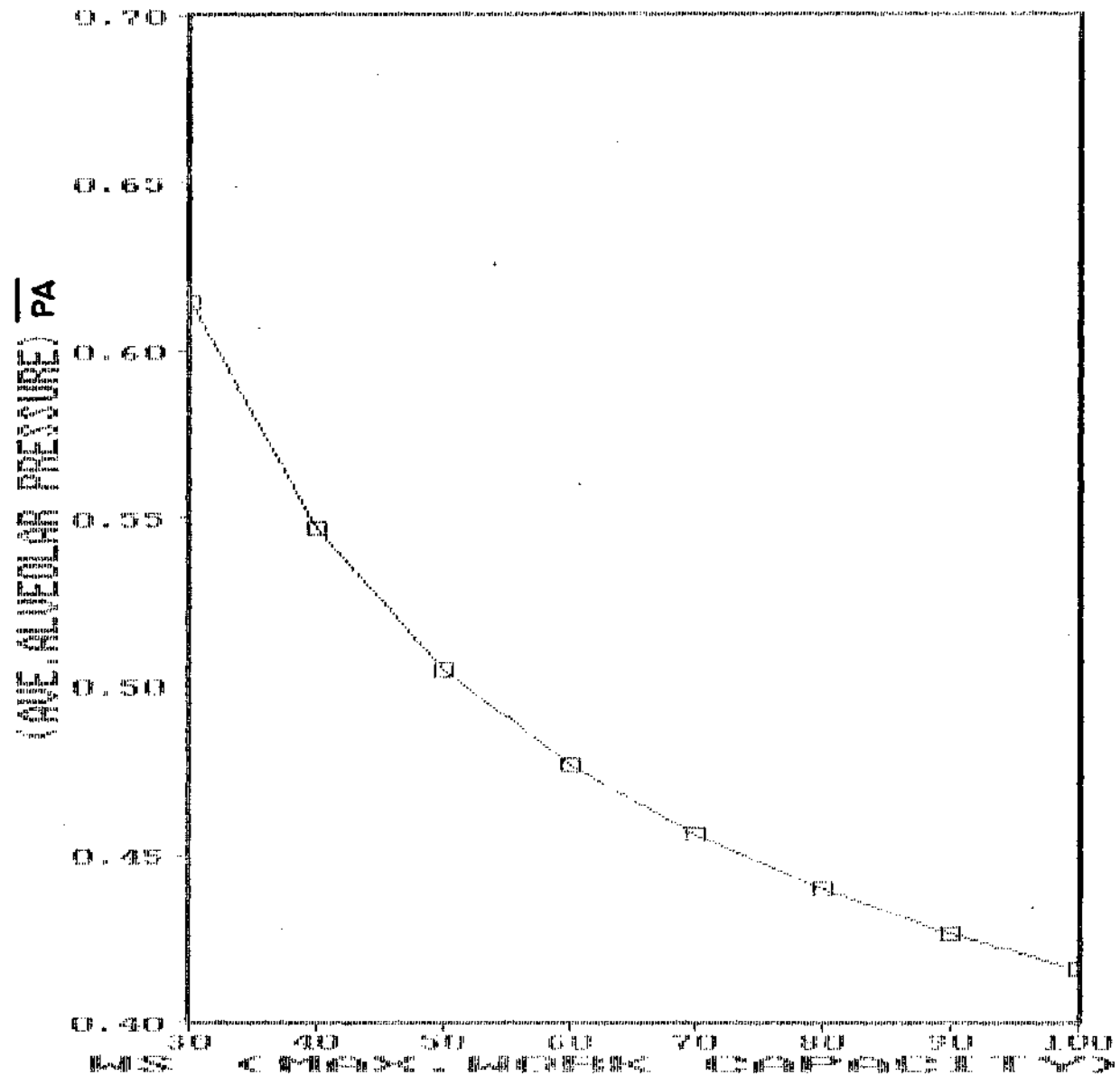


FIG. 2·4 : RAMP PRESSURE INPUT

5.3: SINE PRESSURE INPUT

```
10  REM *** SINE PRESSURE INPUT
20  S = 9999
30  T = 27: R1 = 1.5: C2 = .148: R = 2.7: C = .1: B = 6
40  W12 = Ø: P12 = Ø: V12 = Ø: T13 = Ø
50  G = (B*C)/(1 + B 2*T 2)
60  D = (B*C)/(1 + T 2*B*2) .5
70  M = ATN (B * T)
80  FOR P1 = 7 TO 8 STEP .025
90  FOR T1 = .4 TO .5 STEP .025
100 X = D/B * (Sin (B*T1 -M) + Sin (M))
110 X1 = T*G*(1 - EXP (-T1/T))
120 V = P1 (X - X1)
130 T2 = (V - C2)/.1 - T1
140 F = 60/(T1 +T2)
150 Y = (P1 2 * D)/(4*B)*((COS(M)
      - cos (2*B*T1 - M)) + 2*B*T1 Sin(M))
160 Y1 = (P1 2*B*G)/(B 2 + 1/T 2)
170 Y2 = cos(B*T1) - Sin (B*T1)
180 Y3 = EXP(-T1/T) * ((COS(B*T1))
      - (Sin (B*T1)/(B*T)) - 1
190 Y4 = V 2/(2*C) * (1 -EXP((-2*T2)/T))
200 W = F*(Y + Y1 * Y3 - Y4)
210 Z = (P1/B) * (1 - cos(B*T1))
220 Z1 = (R1*V* EXP(-T2/T))
230 E2 = (F/60) * (Z - Z1)
240 IF W > 30,40,50,60,70,80,90,100 THEN 280
250 IF W < 25, 35, 45, 55, 65, 75, 85, 95, THEN 280
```

```
260  IF S>P2 THEN 270 ELSE GOTO 280
270  S = P2: W12 = W: P12 = P1: V12 = V: T12 = T1: T13 =
     T2: =F
280  NEXT T1
290  NEXT P1
300  Z2 = (Sin (B*T12) + R1*G*EXP(-T12/T))
310  Z3 = R1* D * cos (B*T12 - M)
320  P3 = P12 * (Z2 -Z3)
330  V2 = P12/R
340  DEF FNR (X2) = INT (X2 * 1000 + 0.5)/1000
350  PRINT  TAB(4)  "W =  ",  FNR(W12), "P2  = ",  FNR(S):
     TAB(35) "P1 = ": FNR (P12)
360  PRINT
370  PRINT TAB(4) "V = ", FNR (V12), "T1 = ", FNR(T12)
     TAB(35) "T2 = ", FNR (T13)
380  PRINT
390  PRINT TAB(4) "F = ", FNR (F12), "V2 = ", FNR(V2):
     TAB (35) "P2 = " : FNR (P3)
400  END
```

TABLE 2.7 VENTILATORY PARAMETERS FOR SINE PRESSURE INPUT

S NO	W_a	P_{av}	T_i	T_a	f	V_t	P_t	V_{max}	$\overline{P_A}$
	Cm H_2O	Cm H20	Seconds	Seconds	breath/ min	ℓ	Cm H20	L/S	CmH20
1-	30	5.13	0.4	3.045	17.41	0.493	7.975	2.954	0.670
2-	40	7.72	0.4	5.531	10.117	0.741	12.00	4.444	0.586
3-	50	12.864	0.325	8.104	7.118	0.991	17.825	6.602	0.483
4-	60	15.877	0.325	10.425	5.582	1.223	22.000	8.148	0.467
5-	70	17.006	0.375	13.257	4.401	1.511	24.900	9.222	0.496
6-	80	22.102	0.325	15.219	3.680	1.701	30.625	11.343	0.450
7-	90	28.189	0.275	17.196	3.452	1.886	39.975	14.806	0.414
8-	100	35.189	0.25	20.134	2.943	2.186	51.975	19.250	0.395

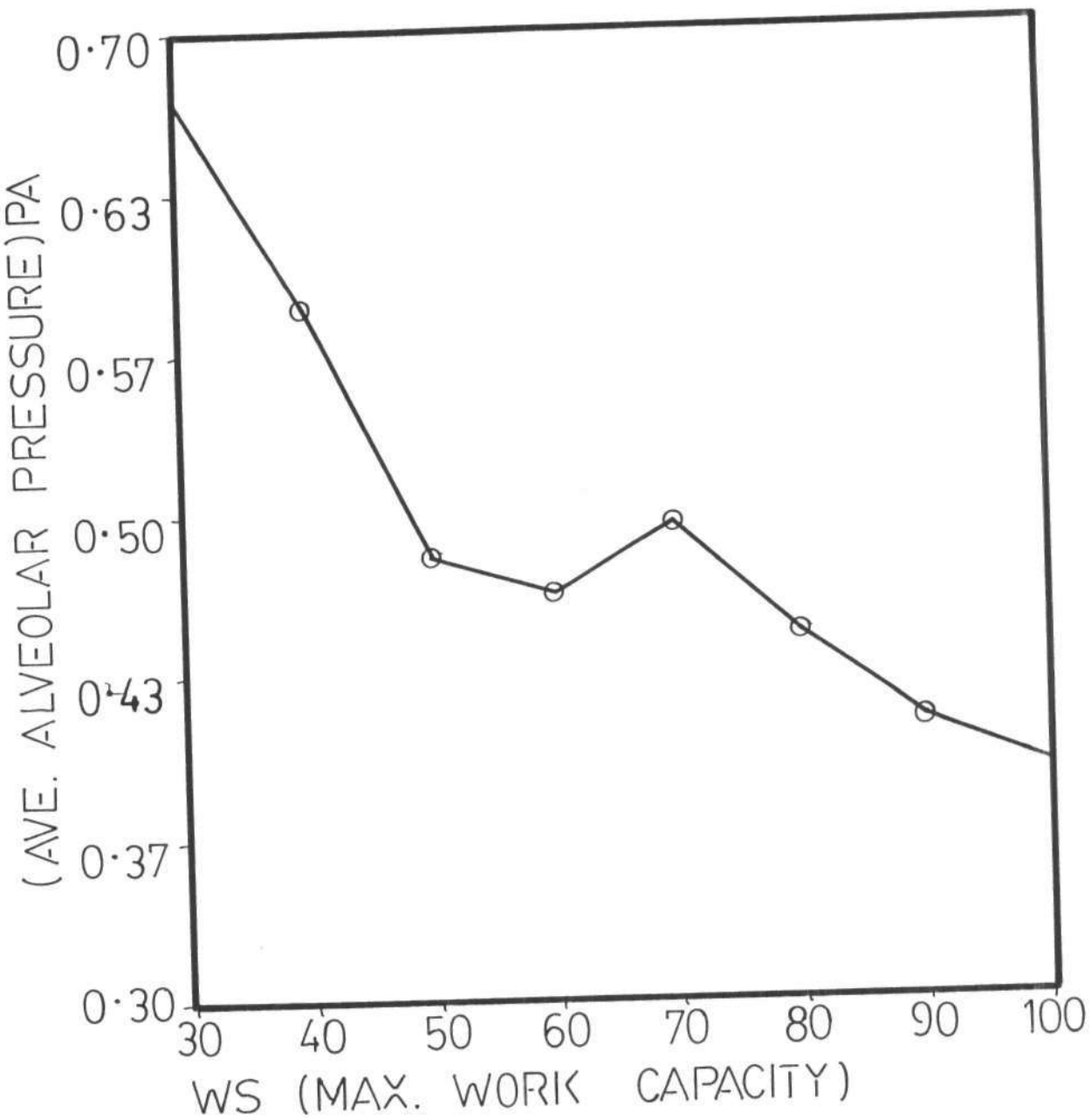


Fig: 2.5. Sine Pressure Input .

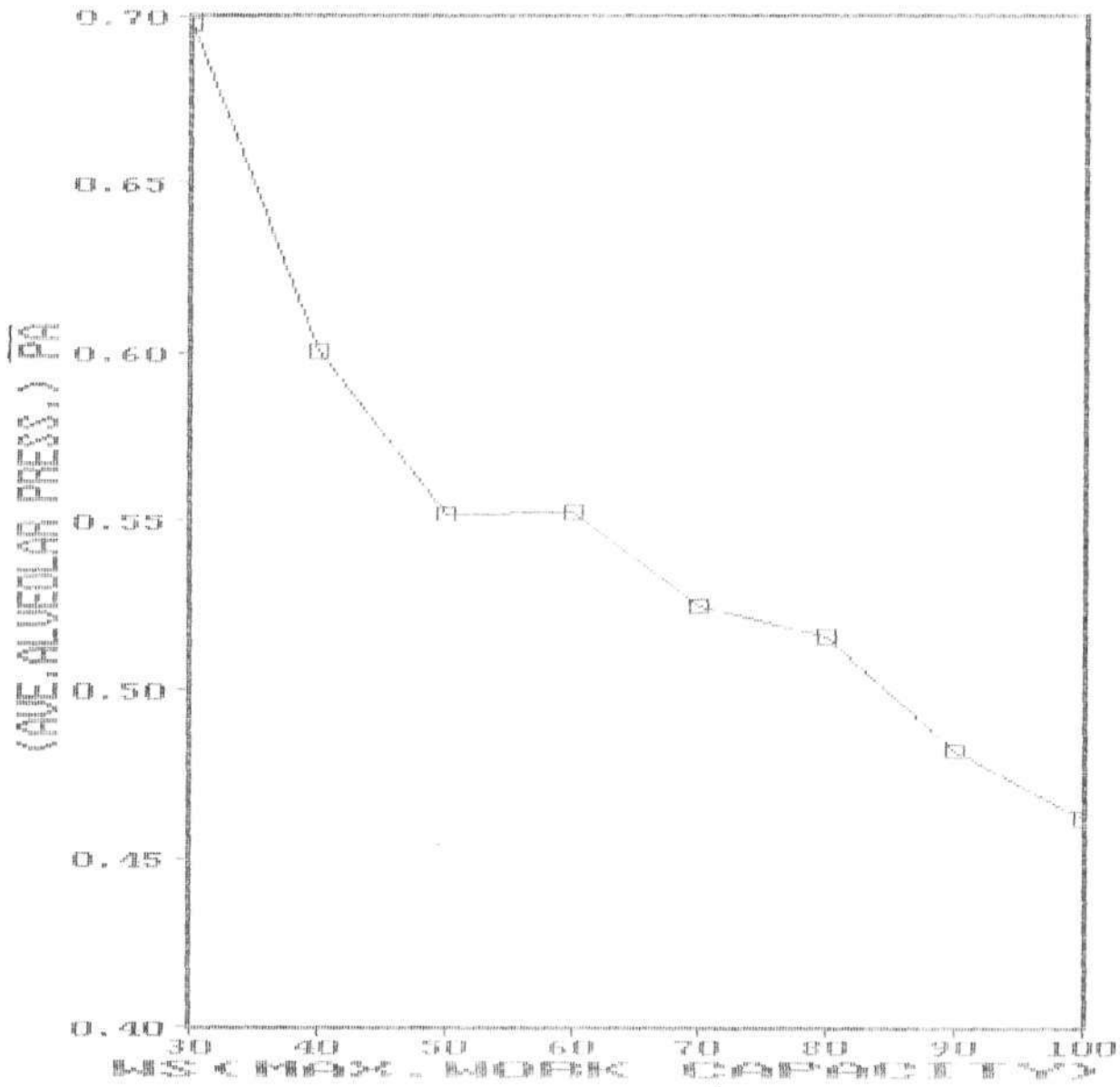
2.5.4 GAMMA PRESSURE INPUT:

```
5    REM *** GAMMA PRESSURE INPUT ***
10   S = 9999
20   T = .27: R1 = 1.5: C2 = .148: R = 2.7: C = .1
     K = .555: b = 3.73: a = 2
30   FOR P1 = 21 TO 22 STEMP .025
40   FOR T1 = .4 TO .5 STEP .025
50   X = EXP(-b * T1)
60   X1 = EXP(-a * T1) * (1 + T1 * (a-b))
70   X2 = (P1 * a)/(R*(a-b)^2)
80   V = X2 * (X - X1)
90   T2 = (V -C2)/.1 - T1
100  F = 60/(T1 + T2)
110  Y = (b/(a+b)^2) * EXP(-(a+b)*T1) * ((a+b) * T1 + 1)
120  Y1 = (a-b)/2* T12^2 * EXP(-2*a*T1) + T1/2 * EXP
     (-2a*T1)
130  Y2 = 1/(4*a) * EXP(-2*a*T1)
140  Y3 = (a - b)^2/(4*a*(a+b)^2)
150  Y4 = V^2/(2*C) * (1 - EXP ((-2*T2)/T))
16   Y5 = (P1 * a)↑2/(R*(a - b)^2
170  W = F * (Y5 * (Y - Y1 - Y2 + Y3) - Y4
180  Z = (P1 * a * (2*K - 1))/(a-b)^2 * EXP(-b*T1)
       + P1/a - R1 * V*EXP (-T2/T)
190  Z1 = P1/(a - b) * EXP (-a*T1)
200  Z2 = 1/(a*(a - b)) * (2*a*b -b*b -2*a*a*K)
     + T1 * (b - 2 * a * K)
210  P2 = F/60 * (Z +Z1 * Z2)
220  IF W > 30 THEN 260
230  IF W <29 THEN 260
```

```
240  IF S > P2 THEN 250 ELSE GOTO 260
250  S = P2 : W12 = W : P12 = P1 : V12 = V : T12 = T1
     :T13 = T2 : F12 = F
260  NEXT T1
270  NEXT P1
280  Z3 = ((P12 * a * b)/(a - b)^2* (1 - k)
290  Z4 = EXP (-b/a) -EXP (-1)
300  Z5 = P12 (b - a*K)/(a - b) * EXP(-1)
310  P3 = (Z3*Z4) - Z5
320  V2 = P12/R
330  DEF FNR(X3) = INT (X3*1000 + 0.5)/1000
340  PRINT TAB(4) "W = ", FNR(W12), "P2 = ", FNR(S),
     TAB (35) "P1 = ", FNR (p12)
350  PRINT
370  PRINT TAB(4) "V", FNR(V12), "T1 = ", FNR(T12):
     TAB(35) "T2 =", FNR(T13)
380  PRINT TAB(4) "F = ", FNR (F12): "V2 = ", FNR (V2):
     TAB(35) "P3 = ", FNR (P3)
390  END
```

TABLE 2.8: VENTILATORY PARAMETERS FOR GAMMA PRESSURE INPUT

S/NO	W_a	P_{ao}	T_i	T_a	f	V_t	P_i	V_{max}	$\overline{P_a}$
	I.CmH20	CmH20	Second	Second	breath/ minute	l	Cm H20	l/S	CmH20
1-	30	7.060	0.425	3.090	17.069	0.500	22.000	8.148	0.697
2-	40	10.269	0.375	4.559	12.160	0.641	32.000	11.852	0.601
3-	50	13.149	0.325	5.193	10.874	0.700	40.975	15.176	0.552
4-	60	15.074	0.225	3.248	17.275	0.495	46.975	17.398	0.553
5-	70	18.853	0.200	3.536	16.061	0.522	58.750	21.759	0.525
6-	80	22.455	0.175	3.414	16.718	0.507	69.975	25.917	0.516
7-	90	27.180	0.175	4.481	12.888	0.614	84.700	31.370	0.482
8-	100	31.528	0.175	5.462	10.644	0.712	98.250	36.389	0.462



FIG·2·6 : GAMMA PRESSURE INPUT

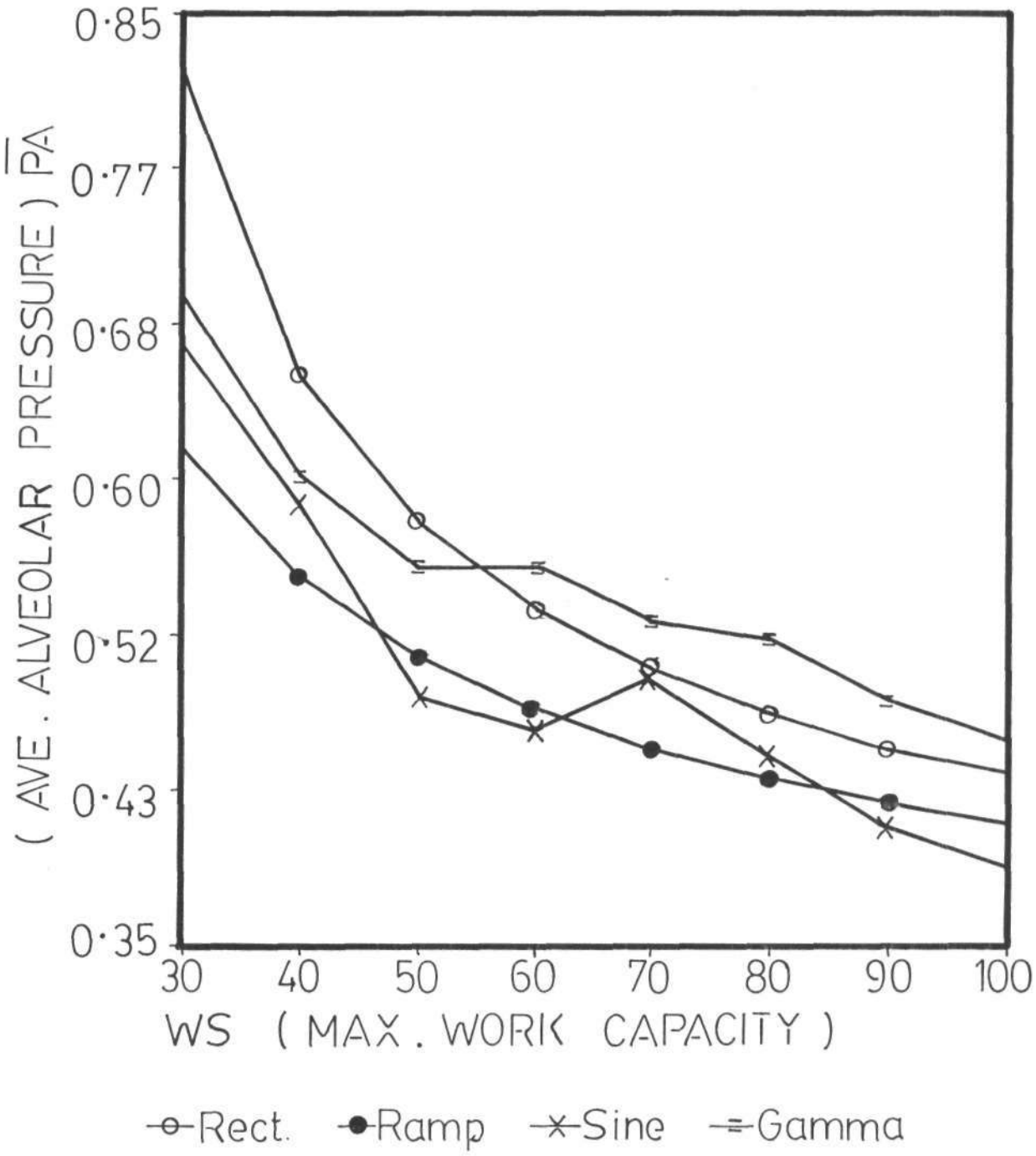


Fig: 2.7. Comparative Analysis of Ramp, Rectangular, Sine & Gamma Pressures Input .

2.6 "RESULT AND DISCUSSION"

The respiratory mechanical parameters R_a, R_b and C may differ from patient to patient. Table (2.3) shows the values of these parameters for a patient in need of controlled ventilation.

Using optimization techniques, the values of T_i and P_{ap} - the basic design parameters of the ventilator are calculated for a given value of the work capacity of the patient W_s. These in turn, give the values of other parameters such as T_e, f, P_i, V, V_{max} and $\overline{P_A}$. In table (2.5 - 2.8), the optimum values of the parameters for Rectangular, Ramp, Sine and Gamma distribution pressure inputs respectively are presented. Each row of the table gives optimum values of the ventilator parameters for which the average alveolar pressure $\overline{P_A}$ is minimum, and the ventilatory work W_s is constrained within the permissible work capacity of the patient. For example for a patient with W_s = 40 litres CM. H20 for the rectangular input wave form, the optimal parameters are given in row 2 of table (2.5) with the minimum value of the average alveolar pressure as 0.656 Cm H20. If a healthier patient, say with W_s = 90 litres Cm H20 is to be provided with (IPPV), the ventilator parameters must be set according to row 7 of table 2.5, in which the minimum average alveolar pressure is given as 0.456 Cm H20.

2.7 COMPARISON OF THE RESULTS FOR DIFFERENT WAVE FORMS:

In tables (2.5) and (2.6) for the Rectangular and Ramp input pressures wave forms the variation of average alveolar pressure with patient!s work rate capacity Ws is given. Comparing the results for these wave forms, it is observed that the average alveolar pressure which is an important parameter for the circulatory system is not much affected by the shape of the input pressure wave form. The inspiratory time T_i for Rectangular pressure input is less than for the Ramp pressure input. It is opined that with short inspiratory periods, the physiological dead space increases and the muscles have to do more work against both elastic and non-elastic resistance[6,31]. It may not be possible to achieve the desired gas transfer to and from the blood in a short inspiratory period. The rapid introduction of air into the lungs increases the abnormal distribution of air into the alveoli resulting in an over-ventilation of unperfused alveoli. Since the ramp input pressure has greater inspiratory period as compared to rectangular input pressure we conclude that the ramp wave form is better than the rectangular wave form. The only advantage with rectangular input is the low peak alveolar pressure P_{ap}. The P_{ap} for the ramp input pressure is slightly more than the one for rectangular input pressure but is still within the safe limits. It shows that ramp pressure wave form is generally a better choice than the rectangular wave form.

In Table (2.7) and (2.8), the results for the sine input and Gamma input pressure wave forms respectively are tabulated. The variation in average alveolar pressure for sine wave form is less than that of the Gamma distribution wave form and the inspiratory period for sine wave form is greater than that for the Gamma distribution. The peak alveolar pressure in Tables (2.7) and (2.8) do not show much difference. We conclude that the sine pressure input is a better choice than the Gamma pressure input. We have also observed that by increasing the value of the constant in the sine pressure input the inspiratory period T_1 decreases and the peak alveolar pressure increases which shows that by increasing the value of β the model becomes less useful. If we decrease the value of β, T_1 increases and average alveolar pressure $\bar{P}_A$ also increases which is also not useful.

In Gamma input wave form by changing the value of the constant(α) the same results are obtained as in the sine pressure input by changing the value of β.

2.8 CONCLUSION:

Figures (2.7) show that out of all the four models namely Rectangular, Ramp, Sine and Gamma pressures input the ramp pressure input gives more satisfactory values of the parameters.

Therefore at the time of haemodialysis the artificial ventilator (IPPV) must be set according to the parameters given in Table (2.6), which was obtained as a result of computer generated out put of the mathematical modelling as outlined in the equations derived in thesis.

CHAPTER THREE

OPTIMAL CONTROL OF PATIENTS ARTIFICIAL KIDNEY WITH DIALYSATE RECYCLE

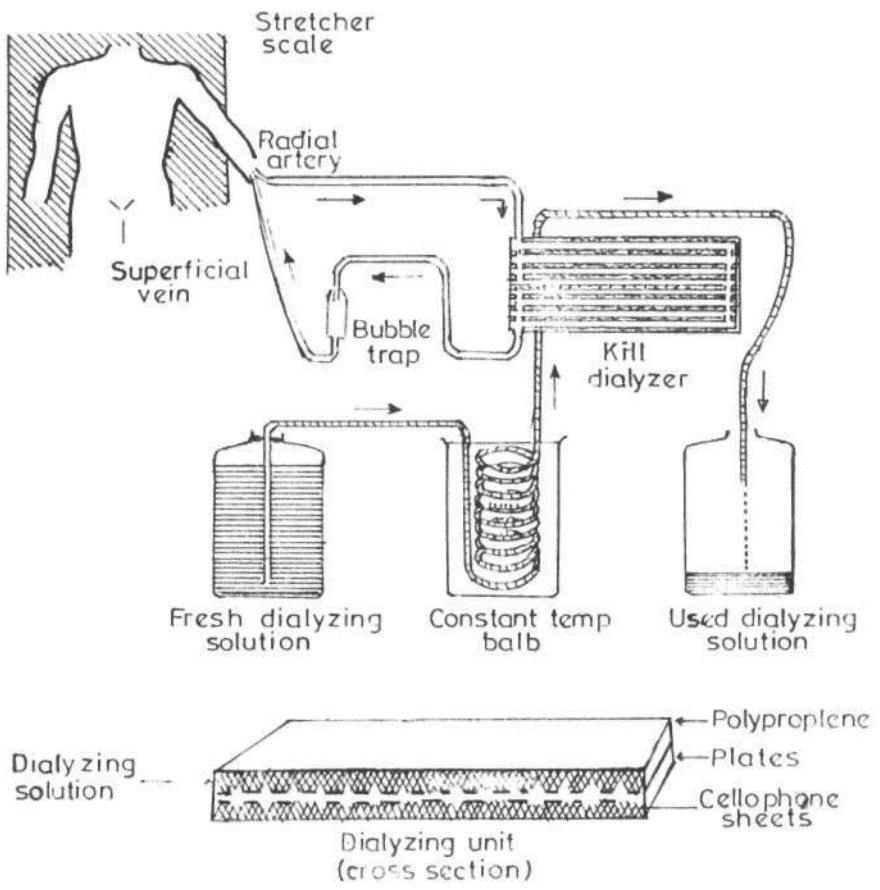
3.1 INTRODUCTION:

Among the various methods of blood purification, haemodialysis has proved to be a clinically satisfactory method of treatment for patients with end stage of renal failure. Despite satisfactory results, it is still far from an optimal procedure and is both time consuming and expensive. The planning of haemodialysis therapy for individuals is done largely on empirical grounds. The physicians are not even aware, except in a general sense, as to what are the various parameters of the dialyser operation and how they affect the patients dialysis.

In haemodialysis Figure (3.1)[7] the patient's blood is circulated extra corporeally through a dialyser for up to 12 hours. The exchange of solutes takes place through a semi permeable membrane between the blood and dialysate because of difference in concentration. Fig (3.2) shows the variation of the over all mass transfer resistance to urea transport as a function of dialysate flow rate for a kill type of artificial kidney. For each dialysate flow rate there is an associated overall mass transfer resistance, which decreases as the dialysate flow rate increases.

Since it is desirable to remove as much biological waste as possible, one way of reducing the dialysis time is to feed fresh dialysate at large rates. However this not only demands high cost but also if maintained a characteristic disorder termed as disequilibrium syndrome is developed in large number of patients. After two to three hours of dialysis, these patients develop headache, nausea and vomiting, and this condition persists throughout the dialysis, leaving the patient weak and exhausted. Many investigators believe that this disequilibrium syndrome is related to an increase in cerebro spinal fluid (CSF) pressure which occurs during dialysis and is thought to be due to an osmotic imbalance between the blood plasma and (CSF). It has been suggested that this imbalance is a result of urea being removed from the plasma at a rate greater than that at which it should be removed from the (CSF).

Cooper, et al[2], showed that by recycling a portion of the dialysate, the amount of fresh dialysate can be reduced substantially with comparable reduction in dialysis time. The effect of dialysate recycling rate and fresh make up rate on the rate of dialysis has been studied by Gupte, et al[8], King[20], et al investigated the effect of blood flow rate on dialysis and found that it is an effective parameters in controlling the dialysis.



FIG·3·1 : SCHEMATIC DIAGRAM OF THE ARTIFICIAL KIDNEY

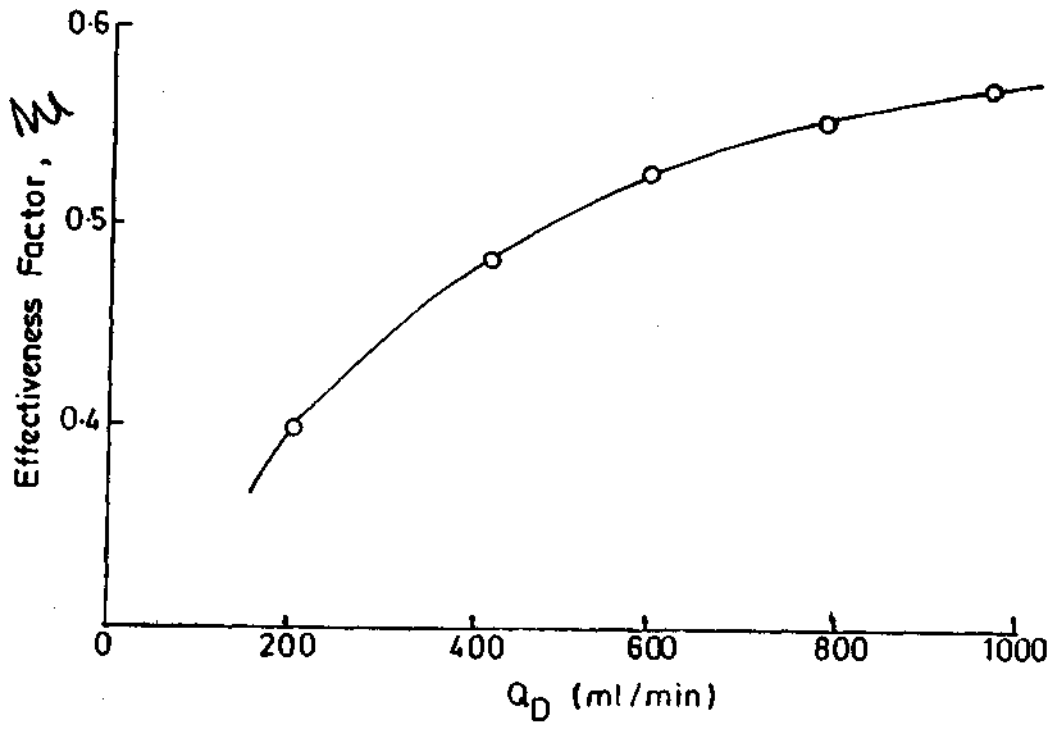
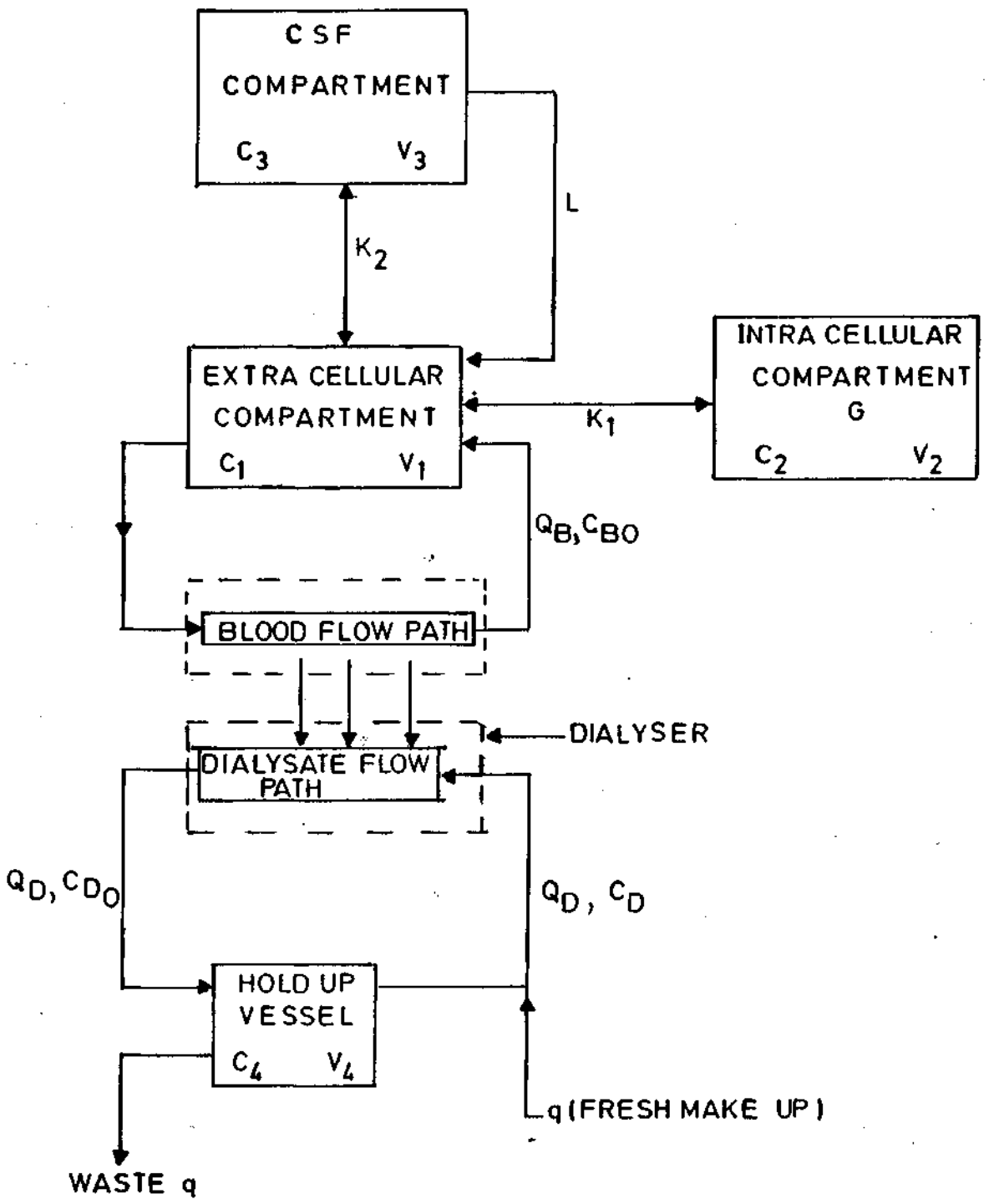


FIG. 32 : EFFECTIVENESS FACTOR FOR KILL DIALYSER

3.2: PATIENT ARTIFICIAL KIDNEY MODEL:

Figure (3.3) is a schematic diagram of the patient coupled to an artificial kidney system. The body fluids are treated as three compartments with uniform mixing. It is assumed that all the cells can be lumped together as the cellular compartment. The blood plasma and the interstitial are lumped together as extra cellular compartment. The brain fluid compartment is added to study the occurrence of disequilibrium syndrome.

The generation of waste solutes is assumed to be in the intracellular compartment at a constant rate G. It exchanges mass with extra cellular compartment by diffusion (K_1). The (CSF) compartment exchanges mass with extra cellular compartment through diffusion (K_2) and bulk flow (L). Blood leaves the patient at concentration C_1 and flow rate Q_B flows to the artificial Kidney where it is dialysed and returns to the patient at the same flow rate but at a new, lower concentration C_{BO}. The membrane in the dialyser is characterised by a mass transfer resistance (K). Fresh dialysate bleeds into the circulating system at a rate (q) and mixes with the recycling dialysate to form a stream of concentration C_D and flow rate Q_D. The concentration of the dialysate leaving the kidney increases to C_{DO}. A portion of the exit stream equal to the make up is discarded at a rate q and concentration C_4 from a well stirred hold up vessel of volume V_4. The recycled portion flows from the vessel to the point where it mixes with fresh dialysate and the cycle begins all over again.



FIG·3·3 : SCHEMATIC DIAGRAM OF PATIENT - ARTIFICIAL KIDNEY SYSTEM WITH DIALYSATE – RE CYCLE

TABLE 3.1 SYMBOLS AND NOTATIONS

NO	QUANTITY	SYMBOLS	UNITS
1	Area of the Membrane	A	m^2
2	Concentrations of extracellular	C_1	g/litre
3	Concentration of intracellular	C_2	g/litre
4	Concentration of Cerebro Spinal Fluid	C_3	g/litre
5	Concentration of hold up vessel	C_4	g/litre
6	Concentration of Urea in dialysate stream at the dialyser inlet.	C_0	g/litre
7	Concentration of Urea in dialysate stream at the dialyser outlet.	C_{00}	g/litre
8	Urea generation rate due to metabolic pressure	G	g/h
9	Performance index	j	
10	Feed back gain matrix	F	
11	Over all mass transfer of the membrane in dialyser	K	Cm/h
12	Mass transfer coefficient for transport between extracellular to intracellular pools	K_1	litres/h
13	Mass transfer coefficient for transport between extracellular to CSF pools	K_2	litres/h
14	Bulk flow rate of fluid from CSF pool	L	litres/h
15	Proportionality constant relating concentration difference to CSF pressure.	P_0	mmH2O/g/litre
16	Fresh make up rate of the dialysate	q	litres/h
17	Blood flow rate	Q_B	litre/h
18	Recycling rate of dialysate	Q_D	litre/h
19	Weighting matrix on state variable	Q	
20	Weighting matrix on control variable	R	
21	Time	t	
22	Discrete time interval	T	
23	Effectiveness factor deviation from its desired state value.	u	

NO	QUANTITY	SYMBOLS	UNITS
24	Optimal Control Vector	u^*	
25	Volume of extracellular pool	V_1	litres
26	Volume of intra cellular pool	V_2	litres
27	Volume of CFS pool	V_3	litres
28	Volume of hold up vessel	V_4	litres
29	State variable	X	
30	Concentration deviation of pool i, from its desired steady state value.	X_i	g/litre
31	Measured variable	Y	
32	Effectiveness factor of the dialyser	ξ	

TABLE #.3.2 NUMERICAL VALUES OF THE SYSTEM PARAMETERS OF AN ADULT PATIENT

AGE		40 Years
WEIGHT		70kg
SEX		Male
V_1	=	15 litres
V_2	=	25 litres
V_3	=	0.135 litres
V_4	=	150 litres
Q_B	=	12 litres/h
qss	=	36 litres/h
K_1	=	56.7 litres/h
K_2	=	0.085 litres/h
L	=	0.00197 litres/h
G	=	0.312 g/h
C_{1ss}	=	20mg%
C_{4ss}	=	10mg%

3.3 MATHEMATICAL MODELLING:

Around extra cellular compartment.

$$V_1\frac{dC_1}{dt}=k_1(C_2-C_1)+k_2(C_3-C_1)+LC_3+Q_B(C_{BO}-C_1) \quad \ldots(3.1)$$

Around intra cellular compartment.

$$V_2\frac{dC_2}{dt}=G+k_1(C_1-C_2) \quad \ldots\ldots(3.2)$$

Around cerebro spinal fluid compartment.

$$V_3\frac{dC_3}{dt}=k_2(C_1-C_3)-LC_3. \quad \ldots\ldots(3.3)$$

Around dialysate hold up vessel,

$$V_4 \frac{dC_4}{dt} = Q_D C_{DO} - Q_D C_4 \qquad \text{.....(3.4)}$$

Around kidney,

$$Q_B (C_1 - C_{BO}) = Q_D \ (C_{D_o} - C_D) \qquad \text{.....(3.5)}$$

Around fresh dialysate mixing point,

$$(Q_D - q)\, C_4 = Q_D C_D . \qquad \text{....(3.6)}$$

3.2.1 PERFORMANCE EQUATIONS OF THE DIALYSER

$$D = \frac{Q_B (C_1 - C_{BO})}{(C_1 - C_D)} \qquad \text{....(3.7)}$$

where D is the dialysance and for counter current flow can be calculated from

$$\frac{D}{Q_B} = \xi = 1 - EXP\left[\frac{KA}{QB}\left(1 - \frac{Q_B}{Q_D}\right)\right]$$

$$\left[\frac{Q_B}{Q_D} - EXP\ \left(\frac{KA}{Q_B}\left(1 - \frac{Q_B}{Q_D}\right)\right)\right]^{-1} \qquad \text{....(3.8)}$$

Where $\xi = \frac{D}{QB}$ *is the efficiency of the dialyser.*

Using the algebraic Eqs. (3.5-3.7) to eliminate the secondary variables C_{BO}, C_D and restricting the equations to single

derivative terms Eqs. (3.1-3.8) are reduced to a set of first order differential equations. This process is shown below.

From Eq. (3.7)

$$\frac{D}{Q_B}=\frac{C_1-C_{BO}}{C_1-C_D}=\xi, \quad C_{BO} = C_1 - \xi C_1 + \xi C_D$$

Introducing in the above the value of $C_D = \frac{(Q_D-g)\,C_4}{Q_D}$

From Eq. (3.6), we have,

$$C_{BO}=C_1-\xi C_1+\frac{\xi (Q_D-q)\,C_4}{Q_D}$$

Putting this value of C_{BO} in Eq. (3.1)

$$V_1\frac{dc_1}{dt}=K_1(C_2-C_1)+K_2(C_3-C_1)+LC_3-Q_B\xi C_1$$

$$+Q_B\xi C_4-\frac{Q_B}{Q_D}\xi qC_4 \qquad \ldots.(3.9)$$

From Eq. (3.5)

$$C_{DO}=C_D+\frac{Q_B}{Q_D}(C_1-C_{BO})$$

or

$$C_{DO}=C_4-\frac{qC_4}{Q_D}+\xi C_1\frac{Q_B}{Q_D}-\frac{Q_B}{Q_D}\xi C_4+\xi\frac{Q_B}{Q_D^2}qC_4.$$

By putting this value of C_{DO} in Eq. (3.4) we have.

$$v_4\frac{dc_4}{dt} = Q_B\xi C_1 - Q_B\,\xi C_4 + \frac{Q_B}{Q_n}\xi\, q\, C_4 - qC_4 \qquad \ldots.(3.10)$$

We introduce new variables

$X_1 = C_1 - C_{1ss}$ where 1 = 1.2.3.4.

$U_1 = Q_B - Q_{Bss}$

$U_2 = q - q_{ss}$

which express deviation from the desired steady state value of

(1) C_{1ss} which is the desired steady state urea concentration in the 1th compartment.

(2) ξ_{ss} and Q_{Bss} which are the desired steady state values of effectiveness and blood flow rate respectively.

These are now introduced in Eq s. (3.9, 3.2, 3.3, 3.10) to give

$$v_1\frac{d}{dt}(X_1+C_1ss) = K_1(X_2 + C_2ss - X_1C_1ss) + K_2\,(X_3 + C_3ss - X_1 - C_1ss)$$

$$+L(X_3+C_{3ss}) - \xi\,(U_1+Q_{Bss})\,(X_1+C_{1ss}) + \xi\,(U_1+Q_{Bss})\,(X_4+C_{4ss})$$

$$-\frac{(U_1+Q_{Bss})}{Q_D}\,\xi\,(U_2+q_{ss})\,(X_4+C_{4ss})$$

Noticing that the steady state values also satisfy the same differential Eq. (3.9). we have.

$$\frac{dx1}{dt} = \frac{K1}{V1}(x2-x1) + \frac{k2}{v1}(x3-x1) + \frac{L}{V1}x_3$$

$$-\frac{\xi}{V1}\ (U1+Q_{Bss})\ (x1+C1_{ss})+\frac{\xi}{V1}\ (U_1+Q_{Bss})\ (x_1+C_{1ss})$$

$$-\frac{\xi}{V1QD}\ (U1+Q_{Bss})\ (x4+C_{4ss})\ (U_2+q_{ss}))\qquad\qquad ....(3.11)$$

Similarly by the same substitution in Eqs. (3.2, 3.3 and 3.10), we arrive at,

$$\frac{d}{dt}\ (x2+C_{2SS})=G+\frac{K1}{V2}\ (X_1+C_{1ss}-X_2-C_{2ss})$$

or

$$\frac{dx2}{dt}=\frac{K1}{V2}\ (X1-X2)\qquad\qquad ....(3.12)$$

and

$$V_3\frac{d}{dt}\ (X_3+C_{3SS})=K_2\ (X1+C_{1SS}-X_2-C_{2SS})-L(X_3+C_{3SS})$$

or

$$\frac{dx3}{dt}=\frac{K_2}{V_3}\ (X_1-X_3)-\frac{L}{V_3}\ X_3\qquad\qquad ....(3.13)$$

and

$$V_4\ \frac{d}{dt}\ (X_4+C_{4SS})=\xi\ (U_1+Q_{BSS})\ (X_1+C_{1SS})\ -\ \xi\ (U_1+Q_{BSS})\ (X_4+C_4SS)$$

$$+\frac{U_1+Q_{BSS}}{Q_D}\xi\ (X_4+C_{4SS})\ (U_2+q_{ss})\ -\ (U_2+q_{ss})\ (X_4+C_4ss)$$

or

$$\frac{dx4}{dt}=\frac{\xi}{V_4}\ (((U_1+Q_{BSS})(X_1+C_{1SS}))\frac{-\xi}{V_4}(((U_1+Q_{BSS})(X_4+C_{4SS}));$$

$$+\ \frac{\xi}{V_4Q_D}\ (((U_1+Q_{BSS})\ (X_4+C_4SS)\ (U_2+q_{SS}))$$

$$- \frac{1}{V_4}\left((U_2+q_{SS})(X_4+C_4SS)\right) \qquad \ldots(3.14)$$

An additional Equation for CSF pressure deviation is included,

$$Y_3 = P_0(X_3 - X_1) \qquad \ldots(3.15)$$

Eqs.(3.11) to (3.14) are the system state equations, The actual measured variable are,

$$Y = \begin{bmatrix} X_1 \\ X_2 \\ \\ X_3 \\ X_4 \end{bmatrix}$$

or interms of the state variables and a measurement matrix C

$$Y = C\ X$$

where,

$$C = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ \\ -PO & 0 & PO & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \qquad \ldots(3.16)$$

The system of Eqs. (3.11 - 3.14) after linearization may be represented in the matrix (Vector) form as,

$$X(t) = Ax(t) + B\ u(t) \qquad \ldots(3.17)$$

where A and B are (4x4) coefficient matrix and (4x2) control matrix respectively. These are given by,

$$A = \begin{bmatrix} \frac{(-K_1 - K_2 - \xi Q_{BSS})}{V_1} & \frac{K_1}{V_1} & \frac{K_2+L}{V_1} & \frac{\xi Q_{BSS}}{V_1} & (1-\frac{q_{ss}}{Q_D}) \\ \\ \frac{K_1}{V_1} & \frac{-K_1}{V_2} & 0 & 0 & \\ \\ \frac{K_2}{V_3} & 0 & \frac{(-K_2+L)}{V_3} & 0 & \\ \\ \frac{\xi Q_{BSS}}{V_4} & 0 & 0 & \frac{\xi Q_{BSS}}{V_4}(\frac{q_s s}{Q_D} - 1) & \frac{-q_{ss}}{V_4} \end{bmatrix}$$

$$\ldots(3.18)$$

$$B = \begin{bmatrix} \frac{-\xi}{V_1}\left(C_{1_{ss}} - C_{4_{ss}} + \frac{C_{4_{ss}}}{Q_D} q_{ss}\right) & \frac{-\xi}{V_1 Q_D} C_4 SS\, Q_{sss} \\ 0 & 0 \\ 0 & 0 \\ \frac{\xi}{V_4}\left(C_{1_{ss}} C_{4_{ss}} + \frac{C_{4_{ss}}}{Q_4} q_{ss}\right) & \frac{\xi}{V_4 Q_D} Q_{sss} C_{4_{ss}} - \frac{1}{V_4} C_{4_R} \end{bmatrix} \quad \ldots(3.19)$$

In addition clinical operation with artificial kidney the blood samples are obtained periodically at both input and output ends of the dialyser in order to estimate the current state of the patient. These samples are regularly analysed for the concentration of the blood urea nitrogen (BUN). However the analysis of these samples takes a minimum of 20 min so that a continuous time control and monitoring of the patient is difficult and it is desirable to have a discrete control policy.

Eq.(3.17) is discretized as

$$\dot{x}(t) = A\, x(t) + BU(O) \quad \ldots(3.20)$$

where O and t correspond to kth and (k+1)th step respectively.

Let us assume the solution of the differential equation (3.20) in the form,

$$x(t) = e^{At}\, x(O) + D(t)\, U(O) \quad \ldots(3.21)$$

That gives

$$\dot{x}(t) = A\left[e^{At}\, x(0)\right] + \dot{D}(t)U(0) \qquad \ldots(3.22)$$

Again from Eq. (3.21)

$$e^{At}\, x(0) = x(t) - D(t)\, U(0)$$

putting this value in Eq. (3.22)

$$\dot{X}(t) = A\,[x(t) - D(t)\, U(0)] + \dot{D}(t)\, U(0) \qquad \ldots(3.23)$$

In Eqs.(3.17) and (3.23) we compare the coefficient of U(0) to find

$$\dot{D}(t) - A\, D(t) = B \qquad \ldots(3.24)$$

As a differential Equation for D(t) in Eq. (3.21) which has the solution

$$D(t) = A^{-1}\,(e^{At} - I)B \qquad \ldots(3.25)$$

as is verified below. Differentiating Eq. (3.25)

$$\dot{D}(t) = A^{-1}\,(A\, e^{At})B = e^{At}\, B$$

Also from Eq. (3.25)

$$e^{At}\, B = A\, D(t) + B$$

or $\dot{D}(t) = A\, D(t) + B$

Thus Eq. (3.21) gives the solution to Eq.(3.20) where D(t) is given by Eq. (3.25).

The Eq.(3.21) now generalizes to.

$$x(k+1) = \emptyset\, x\,(k) + \Delta U(k) \qquad \ldots(3.26)$$

Where x(k), x(k+1) represent x(t) at the kth and (k+1) st sampling instant respectively.

In the above $\emptyset$ and Δ are state and control transition matrices for the discrete system and may be obtained in terms of A and B as,

$$\Phi = \sum_{i=0}^{\infty} \frac{A^i\, T^i}{i!}$$

$$\Phi = I+AT = + \frac{A^2T^2}{2!} + \frac{A^3T^3}{3!} + \quad \ldots.(3.27)$$

and $\Delta = A^{-1}(e^{AT}-I)B$

$$\Delta = (T+\frac{AT^2}{2!} + \frac{A^2T^3}{3!} + \quad \ldots..(3.28)$$

Where T represents the sampling period.

3.4 NUMERICAL TECHNIQUE FOR THE SOLUTION OF THE PROBLEM:

In this section an optimal control policy pertaining to the blood flow rate and fresh dialysate make-up rate for a dialyser with re-circulating dialysate is obtained.

The system parameters for an adult patient and of a kill dialyser are given in table (3.2). for a sampling period of ½ hour, the system state and control transition matrices A and B in Eqs. (3.18 - 3.19). we form diagonalise A by a similarity transformation S which gives,

$$S^{-1}(AT)S = (A_D\ T)$$

where A_D is diagonal form of A.

Again,

$$\phi = e^{AT} = S\left(e^{(AD)^T}\right)S^{-1} \quad \ldots.(3.29)$$

Note that

S is the matrix containing normalized eigen vectors of the matrix A as its columns.

Now from values in Table (3.2),

$$A = \begin{bmatrix} -4.3853 & 3.7800 & 0.00579 & 0.4560 \\ 2.2680 & -2.9680 & 0 & 0 \\ 0.6296 & 0 & -0.64422 & 0 \\ 0.0900 & 0 & 0 & -0.4284 \end{bmatrix}$$

The eigen values and the normalized eigen vectors of the matrix A are

$$\lambda_1 = -6.4451,\ x_1 = \begin{bmatrix} -0.87477 \\ 0.47496 \\ 0.09496 \\ 0.01308 \end{bmatrix}$$

$$\lambda_2 = -0.4744,\ x_2 = \begin{bmatrix} -0.22267 \\ -0.28158 \\ -0.82582 \\ 0.43489 \end{bmatrix}$$

$$\lambda_3 = -0.6469,\ x_3 = \begin{bmatrix} -0.00425 \\ -0.00595 \\ 0.99997 \\ 0.00175 \end{bmatrix}$$

and

$$\lambda_4 = -0.1594,\ x_4 = \begin{bmatrix} 0.50279 \\ 0.554079 \\ 0.65301 \\ 0.16824 \end{bmatrix}$$

where λ_1, λ_2, λ_3, and λ_4 are eigen values and x_1, x_2, x_3, and x_4 are their corresponding normalized eigen vectors,

Thus,

$$S = \begin{bmatrix} -0.87477 & -0.22267 & -0.00425 & 0.50279 \\ 0.47496 & -0.28158 & -0.00505 & 0.54079 \\ 0.09496 & -0.82582 & 0.99997 & 0.65301 \\ 0.01308 & 0.43489 & 0.00175 & 0.16824 \end{bmatrix}$$

The inverse of the matrix X s is given by,

$$S^{-1} = \begin{bmatrix} -0.76589 & 0.69308 & 0.00076 & 0.05804 \\ -0.19425 & -0.40941 & -0.00663 & 1.92225 \\ -0.45758 & -0.06711 & 0.99004 & 0.95479 \\ 0.56646 & 1.01548 & 0.00677 & 0.96041 \end{bmatrix}$$

Or

$$AS = \begin{bmatrix} 5.65560 & 0.10527 & 0.02251 & -0.05332 \\ -3.06119 & 0.13359 & -0.02316 & -0.08618 \\ -0.61197 & 0.39181 & -0.6468 & -0.10412 \\ -0.50502 & -0.20635 & -0.00113 & -0.0269 \end{bmatrix}$$

Finally

$$AD=S^{-1}AS= \begin{bmatrix} -6.44513 & 0 & 0 & 0 \\ 0 & -0.47445 & 0 & 0 \\ 0 & 0 & -0.64690 & 0 \\ 0 & 0 & 0 & -0.15944 \end{bmatrix}$$

which gives

$$\Phi = \begin{bmatrix} 0.32522 & 0.51995 & 0.00123 & 0.10237 \\ 0.31349 & 0.61574 & 0.00060 & 0.04961 \\ 0.13408 & 0.11637 & 0.72483 & 0.01788 \\ 0.02038 & 0.01631 & 0.00003 & 0.80987 \end{bmatrix}$$

and

$$\Delta = \begin{bmatrix} -1.30006E-4 & -5.3196E-5 \\ -6.03752E-5 & -2.28535E-5 \\ -2.18255E-5 & -8.14075E-6 \\ 3.15915E-5 & -1.70435E-4 \end{bmatrix}$$

3.5 COMPUTER PROGRAMME TO FIND THE VALUES OF PHI(♦) AND DELTA (Δ):

```
1♦   REM      TO FIND AUTOMATIC VALUES OF PHI AND DELTA
2♦   DIM      A(1♦,1♦), S(1♦,1♦), B(1♦,1♦), C(1♦,1♦),
              S1(1♦,1♦), D(1♦,1♦), E(1♦,1♦), S2(5,5)
3♦   DIM      Q(5,5), A1(5,5), A2(5,5), B1(5,5), U(4,4),
              SUB(5,5), P(5,5), DELTA (5,5)
4♦            PRINT "ENTER M AND N OF MAT A"
5♦   INPUT    M, N
6♦   FOR I    = 1 TOM M
7♦   FOR J    = 1 TO N
8♦   READ     A(I,J)
9♦   LET      A1 (I,J) = A(I,J)
1♦♦  NEXT J   : NEXT I
11♦  DEFN FNR (XI = INT (X1 * 1♦♦♦♦♦♦ + 0.5)/1♦♦♦♦♦♦
12♦  PRINT    "THIS IS THE BEGINNING OF THE INPUT DATA TO
              THE COMPUTER"
13♦  PRINT    "THIS IS A MATRIX"
14♦  FOR      I = 1 TO N
15♦  FOR      J = 1 TO N
16♦  PRINT    "A(" , I , J , ") = " ' FNR (A(J,J))
```

```
17ϕ  NEXT      J : NEXT I
18ϕ  FOR       K = I TO N
19ϕ  FOR       L = 1 TO M
20ϕ  READ      S(K.L)
21ϕ  S₂(K.L)   = S(K.L)
22ϕ  NEXT L : NEXT K.
23ϕ  PRINT     "THIS IS S MATRIX"
24ϕ  FOR       I = 1 TO N
25ϕ  FOR       J = 1 TO N
26ϕ  PRINT     " S (" . I . J . ") = ".FNR(S(I.J))
27ϕ  NEXT      J : NEXT I
28ϕ  PRINT     "THIS IS THE PRODUCT B=A*S"
29ϕ  FOR       I = 1 TO N
31ϕ  FOR       J = 1 TO N
32ϕ  B(I.J) = 0.0
33ϕ  FOR       K = 1 TO M
34ϕ  B(I.J)    = B(I.J) + A(I.J) * S(K.J)
35ϕ  NEXT K:   NEXT I
36ϕ  PRINT     "B(". I. J. ") - " . FNR(B(I.J))
37ϕ  NEXT J :  NEXT I
38ϕ  PRINT
39ϕ  PRINT "THIS IS THE B MATRIX ENTERED AS B1 - MATRIX"
40ϕ  FOR       I = 1 TO N
41ϕ  FOR       J = 1 TO 2
42ϕ  READ      B1 (I.J)
43ϕ  PRINT     "B1(" . I . J. ") = ". FNR (B1(I.J))
44ϕ  NEXT      J
45ϕ  NEXT      I
```

```
46ϕ  DATA      -4.3853.  3.78ϕϕ.ϕ.ϕϕ579.ϕ.456ϕ. 2.268ϕ.  -
               2.268ϕ.  ϕ.  ϕ.  ϕ.629ϕ.  ϕ.  -ϕ.64422.  ϕ.
               ϕ.ϕ9ϕϕ. ϕ.ϕ. -ϕ.42 84
47ϕ  DATA      -ϕ.87477. -ϕ.22267. -ϕ.ϕϕ425. 0.5ϕ279
               ϕ.47496. -ϕ.28158. -ϕ.ϕϕ595. ϕ.54ϕ79    ϕ
               ϕ.ϕ9496. -ϕ.92582.  ϕ.99997.  .653ϕ1
                ϕ.ϕ1308   ϕ.43489.  0.ϕϕ175. ϕ.16824
48ϕ  DATA      -ϕ.ϕϕϕ51. -ϕ.ϕϕϕ16. ϕ. ϕ. ϕ. ϕ
                ϕ.ϕϕϕϕ7. -ϕ.ϕϕϕ37
49ϕ  REM       *** INVERT THE S- MATRIX ***
5ϕϕ  GOSUB     125ϕ
51ϕ  REM       *** PERFORM THE PRODUCT S1 AS ***
52ϕ  PRINT     "THIS IS THE PRODUCT S1 AS"
53ϕ  FOR       I = 1 TO N
54ϕ  FOR       J = 1 TO N
55ϕ  C(1.J)    = ϕ.ϕ
56ϕ  FOR       K = 1 TO M
57ϕ  C(I.J)    = C(I.J) + SI(I.K) *B(K.J)
58ϕ  NEXT K
59ϕ  NEXT J.   NEXT I
6ϕϕ  FOR       I = 1 TO N
61ϕ  FOR       J = 1 TO N
62ϕ  IF        I <> J THEN C(I.J) = ϕ.ϕ
63ϕ  PRINT     "C(": I: J: ") = ".. FNR (c(J.J))
64ϕ  NEXT J
65ϕ  NEXT I
66ϕ  PRINT
67ϕ  REM       ** PERFORM THE EXP PRODUCT OF
```

```
                    D(I.J) = EXP (C (I.J)) * T **
68ϕ  PRINT          "THIS IS THE PRODUCT D = EXP (AD)T"
69ϕ  LET            T = ϕ.5
70ϕ  FOR            I = 1 TO N
71ϕ  FOR            J = 1 TO M
72ϕ  IF             j < > I THEN 75ϕ
73ϕ  D(I.J) =       2.71828 + (C(I.J)*T)
74ϕ  PRINT          "D(". I: j: ") = ". FNR(D(I.J))
75ϕ  NEXT J
76ϕ  NEXT I
77ϕ  PRINT
78ϕ  PRINT          "THIS IS THE S * EXP (AD)T MATRIX"
79ϕ  FOR I = 1 TO N
80ϕ  FOR J = 1 TO N
81ϕ  LET E(I.J) = ϕ.ϕ
82ϕ  FOR K = 1 TO M
83ϕ  E(I.J) = E(I.J) + S2 (I.K) * D (K.J)
84ϕ  NEXT K
85ϕ  PRINT "E (". I. J. ") = ". FNR(E(I.J))
86ϕ  NEXT J: NEXT I
87ϕ  PRINT
88ϕ  PRINT           "THIS IS THE MATRIX = Q = S*EXP
                    (AD)T * SI"
89ϕ  FOR            K = 1 TO N
90ϕ  FOR            L = I TO N
91ϕ  LET            Q (K.L) = ϕ.ϕ
92ϕ  FOR            I = 1 TO M
93ϕ  Q (K.L) = Q (K.L) + E (K.I) * SI(I.L)
```

```
94ϕ  NEXT L
95ϕ  PRINT      "Q(",K,L,") = ", FNR(Q(K,L))
96ϕ  NEXT L      : NEXT K
97ϕ  GO SUB 15 1ϕ
98ϕ  FOR I = 1 TO N
99ϕ  FOR J = 1 TO N
100ϕ U(I,J) = ϕ.ϕ
101ϕ U(I,I) = 1.ϕ
102ϕ NEXT J : NEXT I
103ϕ FOR K = 1 TO N
104ϕ FOR L = 1 TO N
105ϕ SUB(K,L) = Q(K,L) - U(K,L)
106ϕ PRINT "SUB(", K, L, ") = ", SUB(K,L)
107ϕ NEXT L : NEXT K
108ϕ FOR I = 1 TO N
109  FOR J = 1 TO N
111ϕ P(I,J) = ϕ.ϕ
112ϕ P(I,J) = P(I,J) + A2 (I,K) * SUB(K,J)
113ϕ NEXT K
114ϕ PRINT "P(",I, J, ") = ", P(I,J)
115ϕ NEXT J : NEXT I
116ϕ PRINT      "THIS IS THE DELTA MATRIX"
117ϕ FOR 1 = I TO N
118ϕ FOR J = 1 TO 2
119ϕ DELTA (I,J) = ϕ.ϕ
120ϕ FOR K = 1 TO N
121ϕ DELTA (I,J) = DELTA (I,J) + P(I,K) *B1(K,J)
122ϕ NEXT K.
```

```
123ϕ NEXT J: NEXT I
124ϕ END
125ϕ REM ** START THE INVERSION HERE **
126ϕ FOR P = 1 TO N
127ϕ FOR R = 1 TO N
128ϕ IF R = P THEN GOTO 133ϕ
129ϕ FOR C = 1 TO N
130ϕ IF C = P THEN GOTO 132ϕ
131ϕ S(R,C) = S(R,C) - (S(R,P)) * S(P,C)/S(P,P)
132ϕ NEXT C
133ϕ NEXT R
134ϕ S(P,P) = -1/S(P,P)
135ϕ FOR I = 1 TO N
136ϕ IF I = P THEN 139ϕ
137ϕ S(I,P) = S(I,P) * S(P,P)
138ϕ S(P,I) = S(P,I) * S(P,P)
139ϕ NEXT I
14ϕϕ NEXT P
141ϕ FOR R = 1 TO N
142ϕ FOR C = 1 TO N
143ϕ SI(R,C) = -S(R,C) : NEXT R
144ϕ NEXT C : NEXT R
145ϕ PRINT "INVERTED S-MATRIX"
146ϕ FOR  R = 1 TO N
147ϕ FOR  C = 1 TO N
148ϕ PRINT "S1 (": R: C: ")": FNR(S₁(R,C))
149ϕ NEXT C : NEXT R
15ϕϕ END
```

```
151ϕ FOR  P = 1 TO N
152ϕ FOR  R = 1 TO N
153ϕ IF   R = P THEN GOTO 158ϕ
154ϕ FOR  C = 1 TO N
155ϕ IF   C = P THEN GOTO 159ϕ
156ϕ A1   (R,C) = A1(R,C) - A1(R,P) *A1(P,C) A1(P,P)
157ϕ NEXT C
158ϕ NEXT R
159ϕ A1(P,P) = -1/A1(P,P)
16ϕϕ FOR  I = 1 TO N
161ϕ IF   I = P THEN 158ϕ
162ϕ A1   (I,P) = A1(I,P) *A1(P,P)
163ϕ A1   (P,I) = A1(P,I) *A1(P,P)
164ϕ NEXT I
165ϕ NEXT P
166ϕ FOR  R = 1 TO N
167ϕ FOR  C = 1 TO N
168ϕ A2   (R,C) = -A1 (R,C)
169ϕ NEXT C: NEXT R
17ϕϕ PRINT "INVERTED A MATRIX"
171ϕ PRINT
172ϕ FOR  R = 1 TO N
173ϕ FOR  C = 1 TO N
174ϕ PRINT "A2 (";R;C;") = ";FNR(A2(R,C))
175ϕ NEXT C: NEXT R
176ϕ RETURN
177ϕ END
```

3.6 THE LINEAR DISCRETE - TIME OPTIMAL REGULATOR PROBLEM:

Consider the discrete - time linear system

$$x(i+1) = A(i)x(i) + B(i)\,U(i) \qquad \ldots(3.30)$$

Where $x(i_o) = x_o$ $\qquad \ldots(3.31)$

with controlled variables

$$z(i) = Dix(i) \qquad \ldots(3.32)$$

consider the criterion

$$\sum_{i=i_o}^{i_1-1} [z^T(i+1)R3(i+1)z(i+1) + U^T(i)R2(i)U(i)] + X^T(i1)P1X(i1) \qquad \ldots(3.33)$$

Where $R_3(i+1) > o$ and $R_2(i) > o$ for $i = io, io+1, \ldots i_1-1$

and $P_1 \geq o$

i.e R_2, R_3 are positive definite (with all eigen values positive) and P_1 is non negative definite (i.e all eigen values are positive or zero. Then the problem of determining the input U(i)

for, $i = i_o, i_o+1, i_o+2, \ldots, i_1-1$.

is called the discrete time deterministic linear optimal - regulator problem.[10]

If all matrices occurring in the problem formulation are constant we refer to it as the time - invariant discrete time linear optimal regulator problem. It is noted that the terms following the summation sign in the criterion do not have the same index. This is motivated as follows.

The initial value of the controlled variable z(io) depends entirely upon the initial state x(io) and cannot be changed. Therefore there is no point in including a term which

$z(i_0)$ in the criterion. Similarly the final values of the input $U(i_1)$ affects only the system behaviour beyond the terminal instant i_1. therefore the term involving $U(i_1)$ can be excluded as well.

It is also noted that the controlled variable does not contain a direct link in the problem formulation of Eq(3.30). The omission of a direct link can be motivated by the fact that usually some freedom exists in selecting the controlled variable, so that often it is justifiable to make the instant at which the controlled is to be controlled coincide with the sampling instants. In this case no direct link enters into controlled variable regulator problems where the controlled variables does not have a direct link, however, are easily converted to the formulation of problem.

In deriving the optimal control law, our approach is different from the continuous time case where we use elementary calculus of variation. Here we invoked dynamic programming.

Let us define the scaler function $\sigma[X(i),i]$ as follows:

$$\sigma[x(i),i] = \begin{cases} \min_{U(i),\ldots,U(i_1-1)} \left\{ \sum_{j=1}^{i_1-1} [z^T(j+1)R_2(j+1)z(i+1) \right. \\ \quad + U^T(j)R_2(j)U(j)] \\ \quad \left. + X^T(i)P1\,X(i) \right\} \\ \text{for } i = i_0, i_0+1, \ldots i_1 - 1 \\ X^T(i_1)\,P1\,X(i_1) \text{ for } i = i_1 \end{cases} \quad \ldots(3.34)$$

We see that $\sigma[x(i),i]$ represents the minimal value of the criterion, computed over the period i, i+1, ...i1 - when at the instant i the system is in the state x(i). We derive an iterative equation for this function. Consider the instant (i-1). Then if the input u(i - 1) is arbitrarily selected, but $u(i), u(i+1), \ldots u(i_1-1)$ <u>are chosen optimally WITH RESPECT TO THE STATE AT TIME i</u>, we can write for the criterion over the period $i-1, i, \ldots, i_1$.

$$\sum_{j=i-1}^{i_1-1}[z^T(j+1)R_3(j+1)z(j+1) + U^T(j)R_2(j)U(j)]$$
$$+ x^T(i1)\,P1\,X(i1)$$
$$= Z^T(i)R_3(i)\,Z(i) + U^T(i-1)R_2(i-1)U(i-1)$$
$$+ \quad \sigma[x(i),i] \ldots (3.35)$$

obviously to determine U°(i-1), the optimal input at time (i-1). We must choose U(i-1) so that the expressions,

$Z^T(i)R_3\,z(i) + U^T(i-1)\,R_2\,U(i-1) + \sigma[x(i),i]$

is minimised. ...(3.36)

The minimal value of (3.36) must be the minimal value of the criterion evaluated over the control periods i-1, $i,\ldots(i_1-1)$ consequently we have the equality.

$$\sigma[x(i-1),\ i-1] = \min_{u(i-1)} \{ Z^T(i)R_3(i)\,Z\,(i)$$
$$+ U^T\,(i-1)R_2(i-1)\,U(i-1) + \sigma[x(i),i]\}$$

From (3.30) and (3.32) ...(3.37)

$$X(i+1) = A(i)x(i) + B(i)U(i)$$
$$X(i) = A(i-1)x(i-1) + B(i-1)U(i-1)$$
$$Z(i) = D(i)\,x\,(i)$$

Putting these values in Eq. (3.37),

$$\sigma[x(i-1),\ i-1] = \min_{u(i-1)} \{[D(i)\ x(i)]^T R_3(i)x(i) + U^T(i-1)R_2(i-1)U(i-1) = \sigma[x(i),\ i]\}$$

$$= \min_{u(i-1)} [\{ A(i-1)\ X(i-1) + B(i-1)U(i-1)\}D(i)]^T$$

$$[R_3(i)D(i)A(i-1)X(i-1) + B(i-1)U(i-1)]$$

$$+ U^T(i-1)R_2\ x(i-1) + U(i-1)$$

$$+ \sigma[A(i-1)\ x(i-1) + B(i-i)\ U(i-1),\ i]$$

$$[x(i-1),\ i-1] = \min_{u(i-1)} [\{A(i-1)\ X(i-1) + B(i-1)u(i-1)\}^T$$

$$x\ R_1(i)\ \{A(i-1)x(i-1) + B(i-1)\ u(i-1)\}$$

$$+ u^T(i-1)R_2(i-1)u(i-1)$$

$$+ \sigma\{A(i=1)x(i-1) + B(i-1)u(i-1),\ i\})]$$

where $R_1(i) = D^T(i)\ R_3(i)\ D(i)$

Rationalizing the notation this expression becomes

$$[x,\ i-1] = \min_{u} \{\left[A(i-1)x + B(i-1)u\right]^T$$

$$R_1(i)\ \left[A(i-1)x + B(i-1)u\right] + u^T R_2(i-1)u$$

$$+ \sigma[(A(i-1)x + B(i-1)u),\ i]\} \qquad \ldots(3.38)$$

This is an iterative equation in the function $\sigma[x,i]$. It can be solved in the order $\sigma[x,\ i_1]$, $\sigma[x,\ i_1-1]$, $\sigma[x,\ i_1-2]$ ....since $[x,\ i_1]$ is given by (3.34)

Let us attempt to find a solution of the form

$$\sigma[x,i] = x^T P(i)x \qquad \ldots(3.39)$$

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Where P(i), i = i_0, i_0 +1, ...i_1, is a sequence of matrices to be determined. From Eq. (3.34) we see that

$$P(i_1) = P(i) \qquad \ldots(3.40)$$

Now from Eq. (3.39)

$$\sigma[(A(i-1)x + B(i-1)u, i] = [A(i-1)x + B(i-1)u]^T P(i)x$$

Putting this value in Eq (3.38),

$$\sigma[x, i-1] = u^{min} \{[A(i-1)x + B(i-1)u]^T R_1(i) [A(i-1)x+B(i-1)u] + u^T R_2(i-1)u$$

$$+ [A(i-1)x + B(i-1)u]^T P(i)[A(i-1)x + B(i-1) u]\}$$

$$\sigma[x,i-1] = u^{min} x \{x^T A^T (i-1)R_1(i)A(i-1)x + x^T A^T(i-1)R_1(i-1)x$$

$$x B(i-1)u + u^T B^T(i-1)R_1(i)A(i)(i-1)x$$

$$+ u^T B^T(i-1)R_1(i)B(i-1)u$$

$$+ U^T R_2(i-1)u + x^T A^T(i-1)P(i)A(i-1)x$$

$$+ x^T A^T(i-1)P(i)B(i-1)u$$

$$+ U^T B^T(i-1)P(i)A(i-1)x + u^T B^T(i-1)P(i)B(i-1)u\}$$

$$\sigma[x,i-1] = \min_U \{x^T A^T(i-1)R_1(i)A(i-1) + x^T A^T(i-1)R_1(i)B(i-1)u$$

$$+ u^T B^T(i-1)R_1(i)A(i-1)x + u^T B^T(i-1)rR_1(i)B(i-1)u$$

$$+ u^T R_2(i-1)u + x^T A^T(i-1)\ P(i)A(i-1)x$$

$$+ x^T A^T(i-1)\ P(i)B(i-1)u$$

$$+ u^T B^T(i-1)\ P(i)A(i-1)x$$

$$+ U^T B^T(i-1)\ P\ (i)\ B(i-1)\ U\} \qquad \ldots(3.41)$$

Now

$$\frac{d}{dxJ}(x^T Ax)\ \ \frac{d}{dxj}(x_I A_{iJ}\ x_J)$$

$$= \quad x_I A_{ij} + A_{ji}\ x_i$$

$$= \quad (A^T)_{ji}{}^T i + A_{ji}\ x_i$$

$$= \quad (A^T + A)x_i$$

$$= \quad ((A^T+A)x)_j$$

i.e

$$\frac{d}{dx}\ (x^T Ax) = (A^T+A)\,x$$

similarly

$$\frac{d}{dx_1}(x^T Ay) = X_1\ A_{IJ}\ Y_J$$

$$= Aij\ Y_i = (Ay)_i$$

OR

$$\frac{d}{dx_1}(x^T Ay)\quad (Ay)_1$$

$$\frac{\partial}{\partial x_1}\ (y^T AX)_1 = (A^T\ AY)_1$$

Differentiating (3.41) with respect to u.

$$\frac{\partial\sigma[x, i-1]}{\partial u}$$

$$= [A^T(i-1)R1(i)B(i-1)]^T x + B^T(i-1)R1(i)A(i-1)x$$

$$+ [(B^T(i-1)R1(i)B(i-1)) + (B^T(i-1)R1(i)B(i-1))^T]u$$

$$+ [R2(i-1) + R2^T(i-1)]u + o$$

$$+ [A^T(i-1)P(i)B(i-1)]^T x + B^T(i-1)P(i)A(i-1)x$$

$$+ [(B^T(i-1)P(i)B(i-1) + (B^T(i-1)P(i)B(i-1))^T]u$$

Rearranging the terms in the above, we have.

$$\frac{\partial\sigma[x, i-1]}{\partial u}$$

$$= \{B^T(i-1)R1^T(i)A(i-1)x + B^T(i-1)R1(i)A(i-1)x$$

$$+ B^T(i-1)R1(i)B(i-1)u + B^T(i-1)R1^T(i)B(i-1)u$$

$$+ R2(i-1)u + R2^{T}(i-1)u + B^{T}(i-1)P^{T}(i)A(i-1)x$$

$$+ B^{T}(i-1)P(i)A(i-1)x + B^{T}(i-1)P(i)B(i-1)u$$

$$+ B^{T}(i-1)P^{T}(i)B(i-1)u\}$$

At minimum

$$\frac{\partial \sigma[x, i-1]}{\partial u} = O$$

i.e

$$[B^{T}(i-1)R1(i)B(i-1) + B^{T}(i-1)R1^{T}(i)B(i-1) + R2(i-1)+R2^{T}(i-1)$$

$$+ B^{T}(i-1)P(i)B(i-1) + B^{T}(i-1)P^{T}(i)B(i-1)]u(i-1)$$

$$= -[B^{T}(i-1)R1^{T}(i)A(i-1)x(i-1)$$

$$+ B^{T}(i-1)R1(i)A(i-1)x(i-1)$$

$$+ B^{T}(i-1)P^{T}(i)A(i-1)x(i-1)$$

$$+B^{T}(i-1)P(i)A(i-1)x(i-1)].$$

Since R1, P1(i) are symmetric matrices,

$$U(i-1) = -\{[B^{T}(i-1)B(i-1) + R2(i-1)+B^{T}(i)B(i-1)]^{-1}$$

$$x[B^{T}(i-1)R1(i)A(i-1) + B^{T}(i-1)P(i)A(i-1)]x(i-1)\}$$

or

$$U(i-1) = -F(i-1)\ x\ (i-1). \qquad \ldots(3.42)$$

Where the feed back gain matrix F(i-1) follows from,

$$F(i-) = (B^{T}(i-1)B(-1) + R2(i-1)+B^{T}(i-1)P(i)B(i-1)\}^{-1}x$$

$$x\ (B^{T}(i-1)R1(i)A(i-1) + B^{T}(i-1)P(i)A(i-1)\}$$

or

$$F(i-1) = [R2(i-1)+B^{T}(i-1)\{R1(i)+P(i)\}B(i-1)]^{-1}x$$

$$B^{T}(i-1)[R1(i) + P(i)]A(i-1) \qquad \ldots(3.43)$$

Where $i = i_0 + 1, \ldots , i_1$

From Eq. (3.39)

$$o[x(i-1), i-1] = x^{T}(i-1)P(i-1)X(i-1). \qquad \ldots(3.44)$$

Inserting the value of u(i-1) given in Eqs. ((3.42) & (3.43))

into Eq. (3.41), equating the two values of o[x(i-1), i-1]in Eqs. (3.41), (3.44) and simplifying which involves cancellation, we get,

$$x^T(i-1)P(i-1)x(i-1) = x^T(i-1)A^T(i-1)R1(i)A(i-1)x(i-1)$$
$$-x^T(i-1)A^T(i-1)R1(i)B(i-1)F(i-1)x(i-1)$$
$$+x^T(i-1)A^T(i-1)P(i)A(i-1)x(i-1)$$
$$-x^T(i-1)A^T(i-1)P(i)B(i-1)F(i-1)x(i-1)$$

or

$$P(i-1) = A^T(i-1)\,[R1(i)+P(i)][A(i-1) - B(i-1)\,F(i-1)] \quad \ldots(3.45)$$

Where $i = i_0+1, \ldots, i_1$

The recursion scheme given in Eqs. (3.42 - 3.45) is a backward recursion scheme.

To solve our problem, we will be using the above recursion scheme in forward order by replacing the index i by $i_1 - i$ where i_1 is the largest value of i. Then we will have,

$$P(i) \rightarrow P(i1-i)$$
$$P(i-1) \rightarrow p(i1 - i+1)$$

By using new index k, Eq. (3.42) becomes

$$U(K) = - F(K)\, x\, (K) \quad \ldots(3.46)$$

Whereas Eg. (3.43) takes the form

$$F(K) = [\Delta^T(c^TQC + J\,(K-1)\,\Delta+R]^{-1}\Delta^T(C^TQC+J(k-1)\emptyset. \quad \ldots(3.47)$$

For our problem, B(i-1) represents Δ

$B^T(I-1)$ " " Δ^T

R1(i) represents C^TQC,

R2(i-1) represents R, A(i-1) represents $\emptyset$ and P represents J.

Where,

$$Q = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} = I,$$

$$R = \begin{bmatrix} 0.4 & & 0.0 \\ 0.0 & & 0.05 \end{bmatrix},$$

and

$$C = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ -P0 & 0 & P0 & 0 \\ 0 & 0 & 1 & 0 \end{bmatrix}.$$

Finally Eg. (3.45) appears as

$$J(K) = \emptyset^{T} (C^{T}QC+J(K-1)) (\emptyset - \Delta F(K)) \qquad ...(3.48)$$

The procedure for computing the feed back gain matrix F is summarized below

Starting with J_0 = O, Eq. (3.47) is used to calculate F1, and then, Eq. (3.48) is used for calculating J1 with specific values of Q and R given above.

Once J1 is known, the sequence can be repeated for F2 and J2 then continuing F3, J3, ..., Fp,JP Where p is the number of samples. Now Eq. (3.46) along with starting value x(0) yields U(o); in turn the discrete time system Eq. (3.26) yield for K = O and given x(0) and u(0), the state x (1). once x(1) is know, Eq. (3.45) is used in the form

$$U^{t}(1) = - F1\ x(1)$$

to calculate u(1), Eq.(3.26) with x(1) and u (1) then yields x(2). This is repeated for all P stages to yields $u^t(2)$,, x(3), $u^t(3)$, x(4) ... $u^t(P-1)$,x(p) in their order.

The numerical magnitude of control period (discrete time interval, T) strongly influences the feed back matrix and the resulting control response. This follows because the sampling period determines the time interval over which the control is held constant. More over, as the sampling period is decreased, the control trajectory approaches that for the continuous time system. It takes significantly longer computation time to compute the optimal policies. After several test runs, a control period of 0.5 hour is found adequate from experimental point of view.

The weighting matrices Q and R have the property of weighting the objective of returning the Urea concentration in the body fluid compartments to the desired values quickly, while not allowing too high CSF pressure over shoot. The weighting matrix R on the control is selected to keep the control within allowable ranges.

The weighting matrices used for these results have already been mentioned.

Fig (3.4) shows the optimal values of the control variables as a function of time. The discrete sampling period is chosen to be 0.5 hours, therefore, to implement this

policy. the fresh make up rate of dialysate and the blood flow rate are to be changed accordingly.

Fig (3.5) shown the response of the system as obtained with the application of the above policy, After 12 hours of treatment time, the urea concentration in the extra cellular compartment decays to 0.142g/ℓ when compared with the standard No RECYCLE 500ml/min make up RATE, this result into a 11.2% reduction in dialysis time and 37.1% reduction in the amount of fresh dialysate feed.

The implementation of the policy is relatively a minor change in the aperational procedure. The blood flow rate values can be obtained the need of on external pump and which patient can tolerate under normal conditions .

3.7 COMPUTER PROGRAMME AND RESULTS

There are six routines or in the APL terminology, 'functions'. (It is worth mentioning that this nomenclatures make sense: a computer programme effects a mapping from one set to another).

Four of the functions are simply transliterations of the corresponding equations. I cite them in order:

```
VX←U XFN X∅
*REDUSES EQUATION 1
```

```
     *REQUIRES CLOBAL VARIABLES PHI AND Δ
     X ← (PHI +.× X⍵) + Δ + .× DΔ
(1)  X(K+1) ←Ø X(k) + Du(k)
     ΔD - F DFN X
     * REALISES EQUATION 2
     U← F+.×XΔ
(2)  u(k) = -F(k) x(k)
     ΔJ←F JFN J Ø
     *REALISES EQUATION 3.
     *REQUIRES CLOBAL VARIABLES PHI.C.Q.D.
     J ← (Ø PHI) +.×((ØC)+.×Q+.×C)+JØ)+.×PHI-D+.×FΔ

(3)  Jk = ØT(CT QC +)K-1)(Ø - ΔFk)
     *F ←FFN J : Z
     *REALISES EQUATION 4.
     *REQUIRES GLOBAL VARIABLES PHI. C. Q. D. R.
     *USES THE INTERMEDIATE LOCAL VARIABLE Z
      FOR CONVENIENCE AND TIDINESS.
      Z←J + (ØC) +.×Q+.× C
      F ← (CØΔ) + × z+.×PHI) R+(ØA)+.×Z+.×Δ Δ
(4)       Fk ← |ΔT(CTQC + Jk-1)Δ+R|-1ΔT(CTQC + Jk-1)Ø
```

At this point. some revision of APL notation is in order.

1. .`ØC'MEANS `transpose of C'.
2. .`A+.×B' gives the traditional matrix inner product of A with B.
3. ⌹ A' gives the invirse of A (if A is non-singular).

'B ÷ A' solves the system of linear equations with coefficient matrix A and 'right side' B.

4. Any varible existing in the workspace is accessible to a function as a 'global variable'. However, naming a varriable in the header line of a function, as we have done in the Z in FFN, bakes it local, in accessible from outside.

There are two functions, GRANDI and XUFN, which do not correspond directly with any of the numbered equations and which use loops.

```
ΔFM ← GRANDI P; K; J
* PRODUCES ARRAY FM OF F'S AND THE
* GLOBAL VECTOR JX OF J'S.
*USES MANY GLOBAL VARIABLES: PHI, C, Q, D, R, J Ø
FM ← ( .2, 4) P K ←O  CREATES AN INITIAL
B x 2 x 4 ARRAY OF ZEROES, FM.
JV ← J Ø MAKES A VECTOR OF JØ.
Lo: → (p < K←K+1)/L1
WE BRANCH TO LI WHEN K>P.
FM [K;;] ← F ← FFN J
JV ← JV, J ← F FN J
→ LO  CLOSING THE LOOP.
LI :  'THE  F AND J ARRAYS HAVE BEEN MADE'Δ
ΔXA ← F XUFN xØ , k , x , u
A  PRODUCES Δ SEQUENCE OF X's AS Δ 24 x 4
A MATRIX, FOR COMPARISON AND STUDY.
XΔ ← (24 4)* k ← o
```

```
LO : → (24 ≤K←K+1)/LI
D ← F [K.,] UFN X
→ LO
LI : 'FINISHED!'▲
```

As you can plainly see, GRANDI and XUFN tell the equation implementations what they are to do.

TABLE 3.3: VARIATION IN BLOOD FLOW AND DIALYSATE FLOW

NO	TIME (HOURS)	U^t_1	U^t_2	Q_B, ℓ/h BLOOD FLOW RATE	q, ℓ/h DIALYSATE FLOW RATE
1	0.5	0.009	0.031	15.009	36.031
2-	1.0	-0.037	-0.178	14.963	35.822
3-	1.5	-0.082	-0.471	14.918	35.529
4-	2.0	-0.116	-0.762	14.884	35.238
5-	2.5	-0.137	-0.999	14.863	35.001
6-	3.0	-0.147	-1.166	14.853	34.834
7-	3.5	-0.150	-1.264	14.850	34.736
8-	4.0	-0.148	-1.306	14.852	34.694
9-	4.5	-0.144	-1.304	14.856	34.696
10-	5.0	-0.138	-1.272	14.862	34.728
11-	5.5	-0.132	-1.221	14.868	34.779
12-	6.0	-0.125	-1.158	14.875	34.842
13-	6.5	-0.118	-1.089	14.882	34.911
14-	7.0	-0.111	-1.019	14.889	34.981
15-	7.5	-0.105	-0.948	14.895	35.052
16-	8.0	-0.098	-0.881	14.902	35.119
17-	8.5	-0.092	-0.616	14.908	35.184
18-	9.0	-0.086	-0.755	14.915	35.245
19-	9.5	-0.080	-0.698	14.920	35.302
20-	10.0	-0.075	-0.645	14.925	35.355
21-	10.5	-0.070	-0.595	14.930	35.405
22-	11.0	-0.065	-0.549	14.935	35.451
23-	11.5	-0.060	-0.507	14.940	35.493
24-	12.0	-0.056	-0.468	14.944	35.532

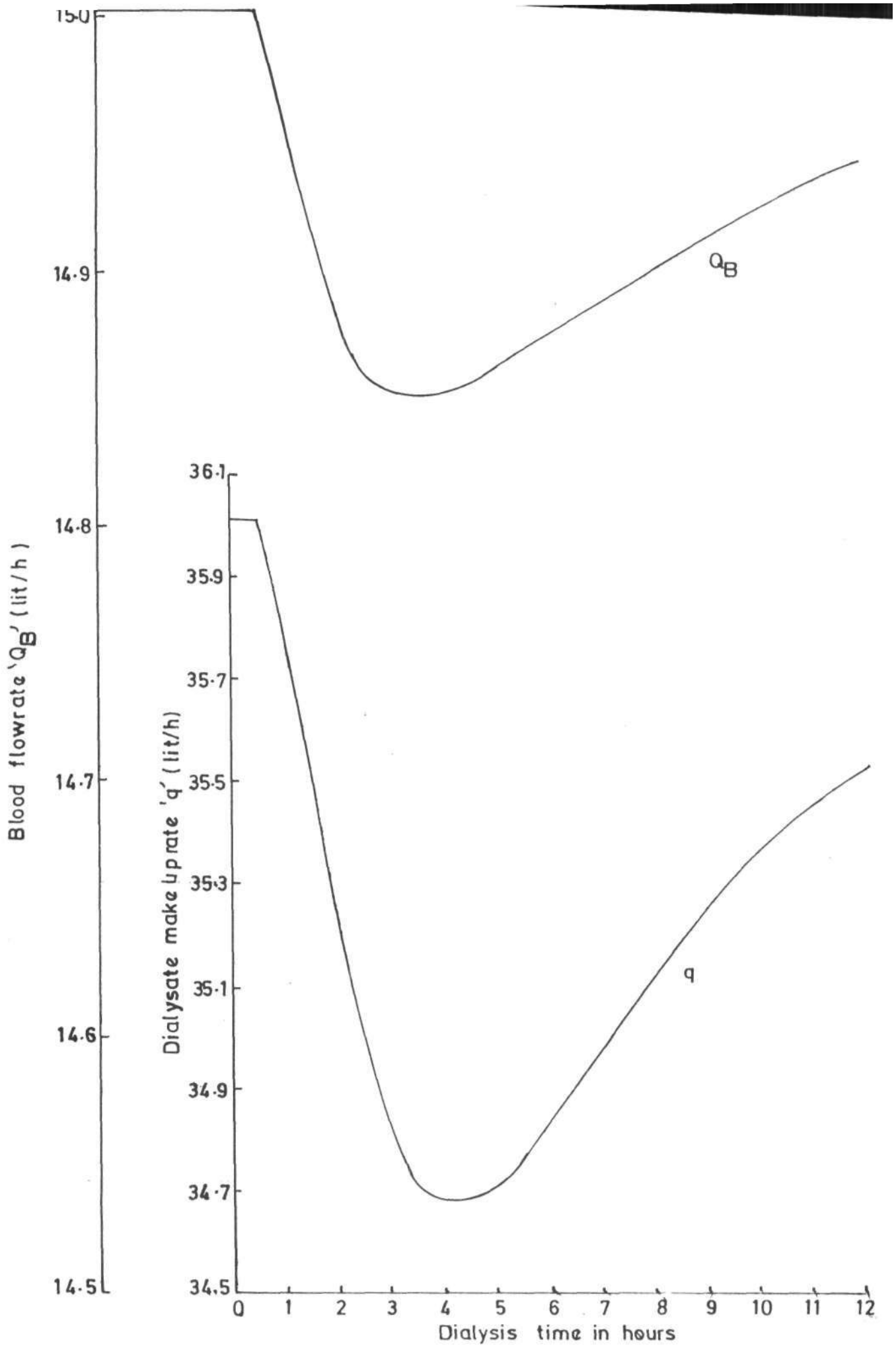
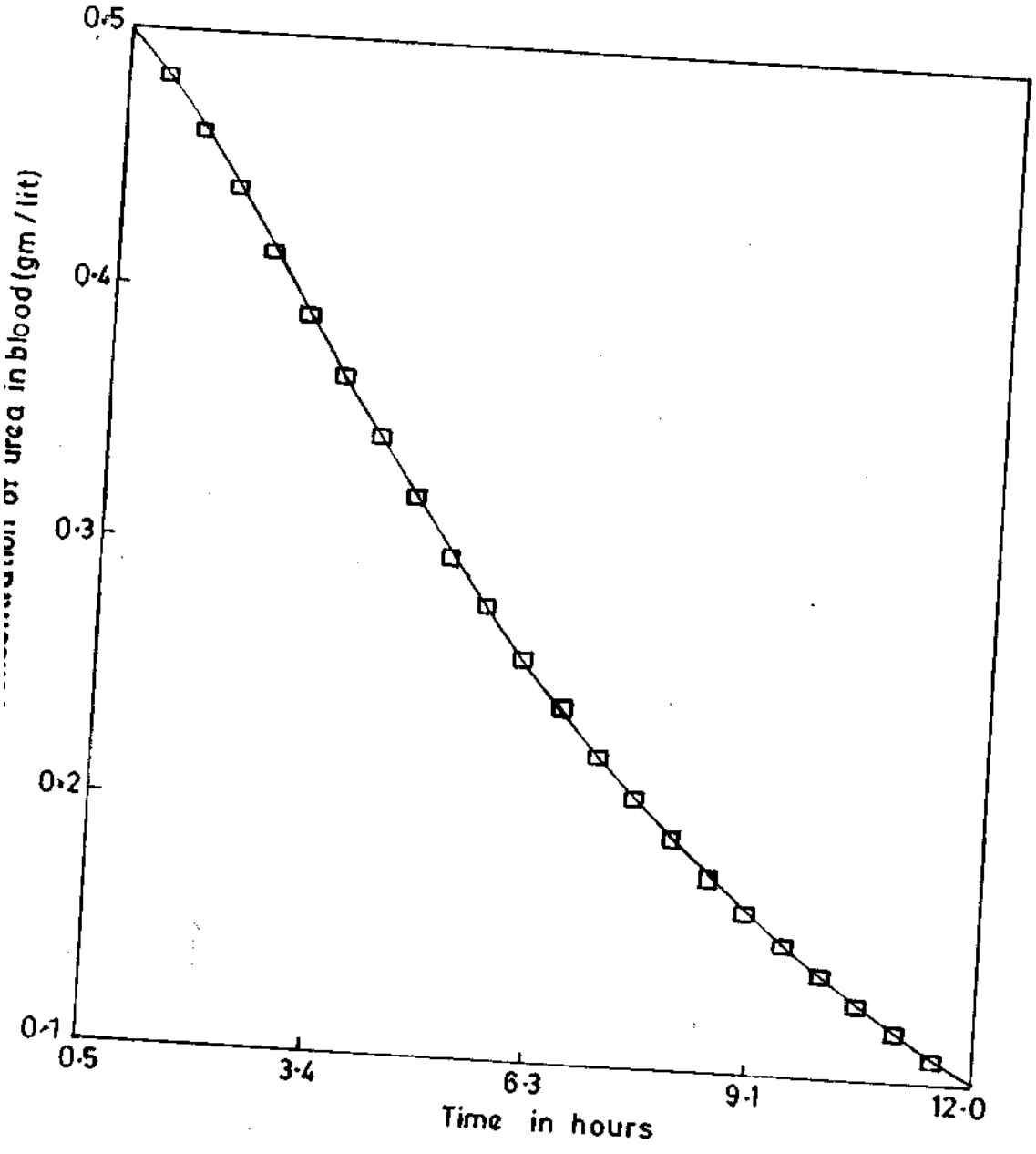


FIG.3·4:OPTIMAL VALUES OF CONTROL VARIABLES AS FUCTIONS OF DIALYSIS TIME

TABLE 3.4: DECAY OF CONCENTRATIONS DURING THE DIALYSIS

NO	TIME (HOURS)	X_1	X_4	C_1 g/ℓ	C_4 g/ℓ
1-	0.5	0.480	0.504	0.523	0.544
2-	1.0	0.463	0.426	0.506	0.466
3-	1.5	0.443	0.362	0.486	0.402
4-	2.0	0.421	0.310	0.465	0.350
5-	2.5	0.399	0.267	0.441	0.307
6-	3.0	0.376	0.231	0.419	0.271
7-	3.5	0.353	0.202	0.396	0.242
8-	4.0	0.330	0.177	0.373	0.217
9-	4.5	0.309	0.156	0.352	0.196
10-	5.0	0.288	0.138	0.331	0.178
11-	5.5	0.268	0.123	0.311	0.163
12-	6.0	0.249	0.100	0.292	0.140
13-	6.5	0.232	0.099	0.275	0.139
14-	7.0	0.215	0.089	0.259	0.129
15-	7.5	0.199	0.080	0.243	0.120
16-	8.0	0.185	0.073	0.229	0.113
17-	8.5	0.171	0.066	0.214	0.106
18-	9.0	0.158	0.060	0.202	0.100
19-	9.5	0.147	0.055	0.180	0.095
20-	10.0	0.136	0.050	0.179	0.090
21-	10.5	0.125	0.046	0.169	0.086
22-	11.0	0.116	0.042	0.159	0.082
23-	11.5	0.107	0.038	0.150	0.078
24-	12.0	0.099	0.035	0.142	0.075



FIG·3.5: DECAY OF CONCENTRATION OF UREA IN EXTRACELLULAR COMPARTMENT WITH DIALYSIS TIME

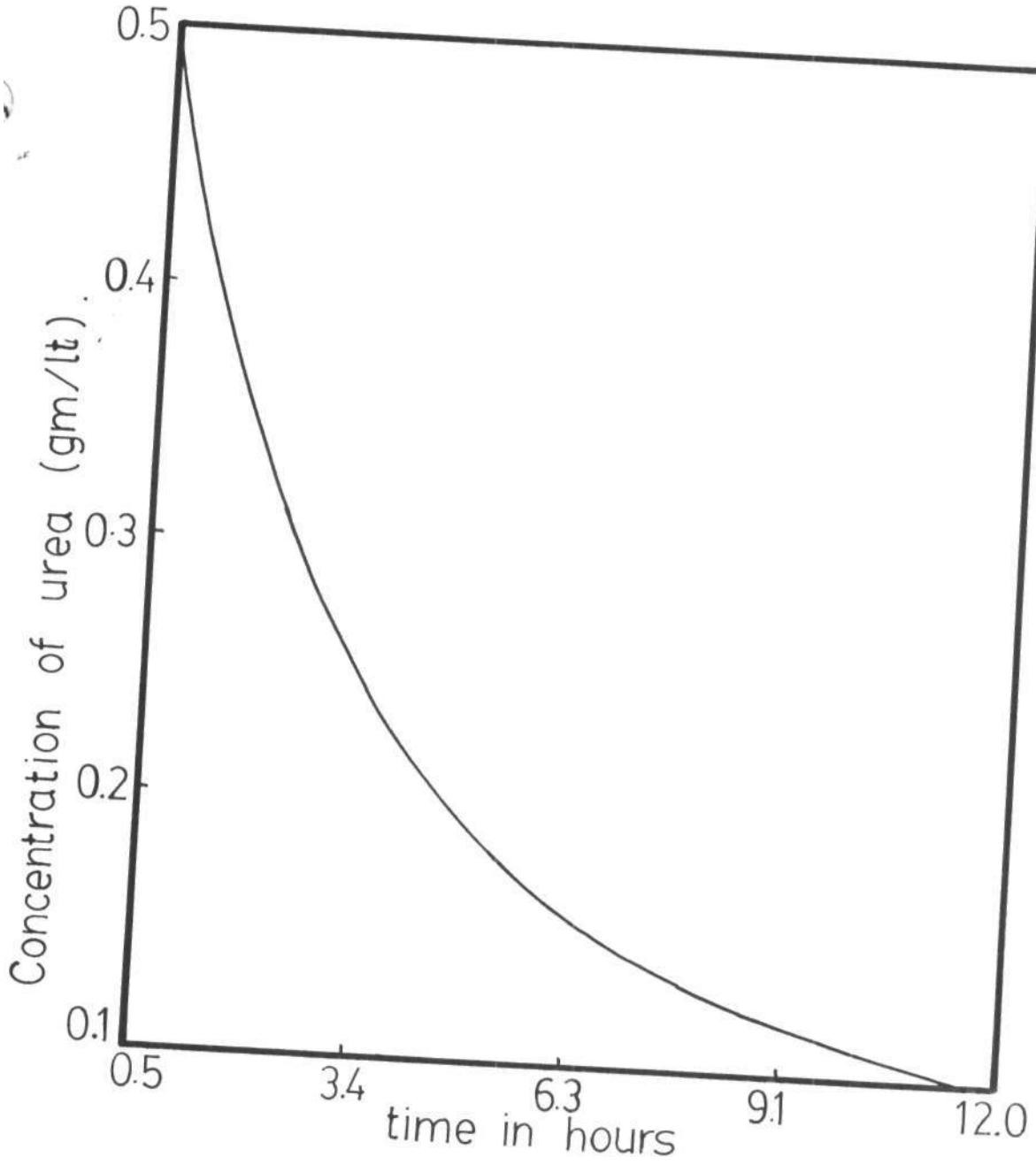


Fig 3.6: DECAY OF CONCENTRATION OF UREA IN HOLDUP VESSEL.

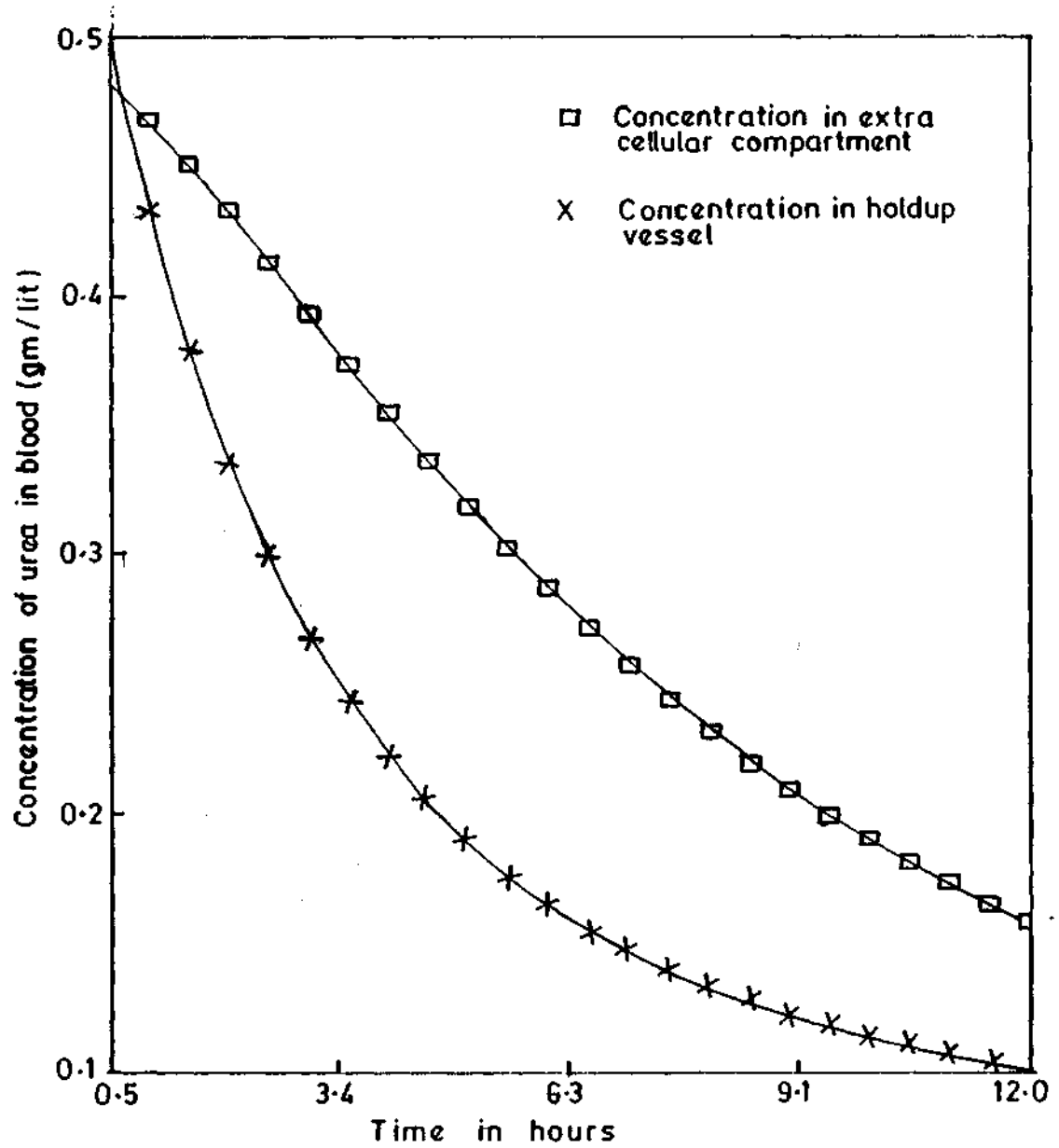


FIG.3.7: SIMULATED DECAY OF CONCENTRATION OF UREA IN BLOOD WITH DIALYSIS TIME

This mathematical model is useful not only in planning therapy in a dialysis centre, but also in establishing the limits for dialyser operating variables for home dialysis.

It is observed that for constant values of fresh make up, as the dialysate recycle rate is increased from 500ml/min to 2500ml/min, the dialysis time is shortened by about 2.5 hours. When used with a fresh make up supply at 500ml/min, it takes much less than 12 hours to bring the urea level to normal value which is 0.2066q/litre. This may enable the dialysis facility at a medical centre, to be utilized twice in 24 hours, thus reducing the unit dialysis cost. A considereable saving in the dialysate cost may be realised by reducing the dialysate make up rate to 200 from 500 ml/min compared with the normal operating procedure, the penalty for the cost reduction is 3.5 hours, which may be reduced to 1.5 hours by a suitable recycling. Increasing the fresh make up rate to 1000 ml/min, cuts the dealysis time by an additonal hour, but the cost increment is, however fairly increased.

3.8 DISCUSSION:

In this chapter, a mathetical model which describes the transport of urea between the body fluid comparments during hemodialysis has been presented. The model also shows the

several of the operating parameters of the dialysis system. With the model it is possible to estimate the effects of changes in artificial kidney operating variables upon the rate of solute removal from the body. For example, figures (3.4) and (3.7) ... show the effect of changes in the dialyser. Thus one can predict the time required to achieve a given final plasma concentration as a function of blood pump or dialysate pump settings. Although certain factors ssuch as, water transfer and simultaneous diffusion of other solutes have been neglected.

This model adequatelv represents the artificail kidney patient system for the removal of urea. This work shows that by controlling the parameters of the dialyser operation, the time end cost of dialysis can be reduced. This study permits the physician to consider the results of various treatment schemes without actually running a dialysis.

Recycling the dialysate yields reduction in dialysis time, the time reduction in this model may not be large but with the daily operating schedule of a dialysis centre, the cost savings for the patient may be substantial. This work is particularly suitable to a home patient as using smaller dialysate make up rate in a recycle system will reduce the cost at the expense of a slightly longer dialysis.

tation time. permitting the use of this method as a medical diagnostic aid.

A model of urea transfer from the body containing an extracellular, an interacellular and a cerebrospinal fluid compartment has been discussed.

A patient artificial kidney system has been presented by.
(i) a three compartment distribution model urea.
(ii) dialysis characteristic of the artificial kidney.

The rate of urea loss is optimized by varying both the dialysate flow (Q_D) and the flow of patients blood (QB) through the artificial kidney.
Simultaneous variation of Q_B and Q_D results in shortening of dialysis time without achieving high CSF to plasma concentration - gradients.

This study has served to show how the operation of a dialyser with suitable recycling of dialysate leads to shorter dialysis and costs. Although the proposed policy does not result in very large saving in terms of treatment time, when considered in conjuction with daily operating schedule of a dialysis centre. the potential cost savings for the patient are substantial. The present policy is suitable for home dialysis in particular. since the control of fresh make up rate of dialysate feed in the proposed recycle system reduces

the cost subtantially at the expense of a slight increase in dialysis time.

4.2 RECOMMENDATION FOR FURTHER WORK.

The present investigation has succeded in minimizing the cost and dialysis time. However, the scheme here in is based on the minimization of urea gradient between CSF and plasma only and does no account for the clearance of middle molecular weight molecules. Therefore for the further study which in addition to the above can include the clearance of middle molecular weight molecules as well. This might lead to the optimization of total dialysis process.

There is need to correlate the predicted results of the present analysis with the data obtained on the dialysis patients.

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