# Modelling and control of the respiratory system of the newborn with RDS

by

Kamel Ammour


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## Abstract

The aim of the dissertation is to develop a detailed mathematical model of the neonatal respiratory system, to write simulation programs based on this model, and examine the behaviour, in simulation, of a 'robust' digital control algorithm.

Infants born prematurely often suffer from the condition known as 'Respiratory Distress Syndrome' (RDS) whereby insufficient oxygen reaches the arterial blood due to the immaturity of the respiratory system. The usual form of treatment for those babies who can breathe autonomously is to surround them in an oxygen-rich atmosphere in an incubator and head box. This therapy has to be managed very carefully in order to avoid dangerous episodes of hypoxia and hyperoxia which can, in extreme cases, lead to brain damage or blindness. Recent studies have demonstrated the feasibility of using feedback control of the insired oxygen concentration using an arterial oxygen sensor and a microcomputer.

## Glossary

| | |
|---|---|
| **Alveolus** | An air cell in the lung |
| **Alectalsis** | Failure of air entering lung immediately |
| **Hypoxia** | Lack of oxygen |
| **Hyperoxia** | Excessiveness of oxygen |
| **RDS** | Respiratory distress syndrome, a condition in which difficulty in breathing is caused in newly born babies |
| **Surfactant** | A wetting agent; a substance, such as a detergent, that reduces surface tension. A surfactant is secreted by the cells (pneumocytes) lining the alveoli of the lungs to prevent the alveolar walls from sticking together. In its absence, as in the immature lungs of premature babies and in some diseases, the lungs tend to collapse. |

## Acknowledgements

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I am grateful to my typist, Mrs. Marcia Robertson for her good work.

# Chapter One

Cause and effect dealing with sick infants particularly with RDS and analysis of various mechanical phenomena occurring in the lung.

## 1.1 Respiration in the fetus/newborn. (1), (2)

### a) Respiration in the fetus.

In the fetus the respiration function deals with the placenta as the organ for gas exchange rather than with lungs.

In the fetus, completely surrounded by amniotic fluid, the lungs have no gas exchange function, and $O_2$ and $CO_2$ are transferred to and from maternal blood and fetal blood in near-contact in the placenta. The mother's heart pumps arterial blood through her aorta and uterine arteries into the spinal arteries of the placenta. From these it surges into intervillous sinusoids. The fetal heart pumps blood through its aorta and umbilical arteries to cotyledon arteries in the placenta. From these blood flows into the fetal placental capillary loops, which dip into the intervillous spaces and sinusoids fed with maternal blood.

### b) Respiration in the newborn

At birth, the umbilical cord is cut and the newborn infant can no longer depend on the maternal circulation; it must breathe soon or die. Now the gas exchange occurs in the lungs, between air and blood separated by alveolocapillary membranes.

With the first breath a reserve volume of air (the functional residual capacity (FRC) is built up in the lung. The newborn lung expands fully within a few minutes and its FRC is then reasonably stable.

The lungs do not empty completely during the expiration and it establishes about one half of the neonatal residual volume with the first breath.

c) Respiration in the premature baby

As we know the lungs are the last organ to be developed in the fetus. So for the neonatal baby, born say after seven months of gestation, the lungs are not already developed completely, hence the baby finds a difficulty to breath and the most noticeable thing is that for the first expiration the lungs deflate almost thoroughly and that means its FRC is equal to zero. So the small alveoli cannot remain open, hence the small alveoli collapse, shunting blood through lung regions in which gas exchange does not occur and this has an effect that the infant appears exhausted, becomes flaccid and unresponsive and dies if there is no oxygen ventilation supply. And this is called the respiratory distress syndrome which result from asphyxia and atelectalsis. So many alveoli fail to function because of what is called atelectalsis or collapse.

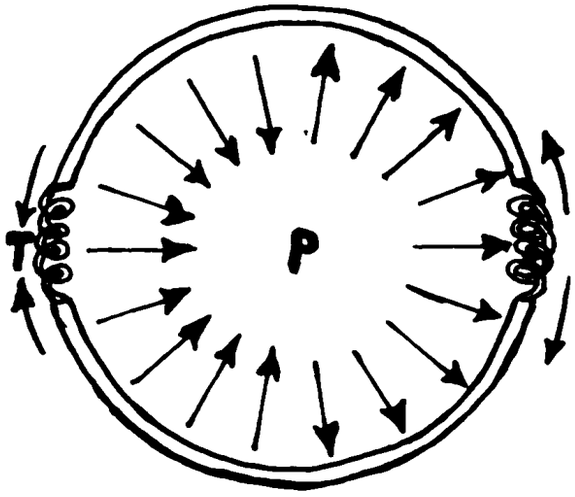
1.2 Surface tension (1), (4)

1.2.1 Definition

Surface tension is a manifestation of attracting forces

between atoms or molecules.

Tension and pressure are often used synonymously. So we speak of $PO_2$ as the partial pressure of $O_2$ or the tension of $O_2$. However, surface tension has the units of force per unit of length; pressure has the units of force per unit of area. The pressure in a bubble is related with the surface tension according to the Laplace equation: $P = \frac{2T}{R}$ where P is the pressure within the bubble, T is the surface tension of the liquid and R is radius of the bubble.




Tension and pressure in a sphere

### 1.2.2 Effect of surface tension

For many years it was believed that the recoil of the lung was due entirely to stretching of the yellow elastic fibres present in the lung, parenchyma. However, in 1929, Von Neergaard showed that the pressure required to enlarge the lung with fluid under static conditions, was less than half that required to inflate an air-filled lung.

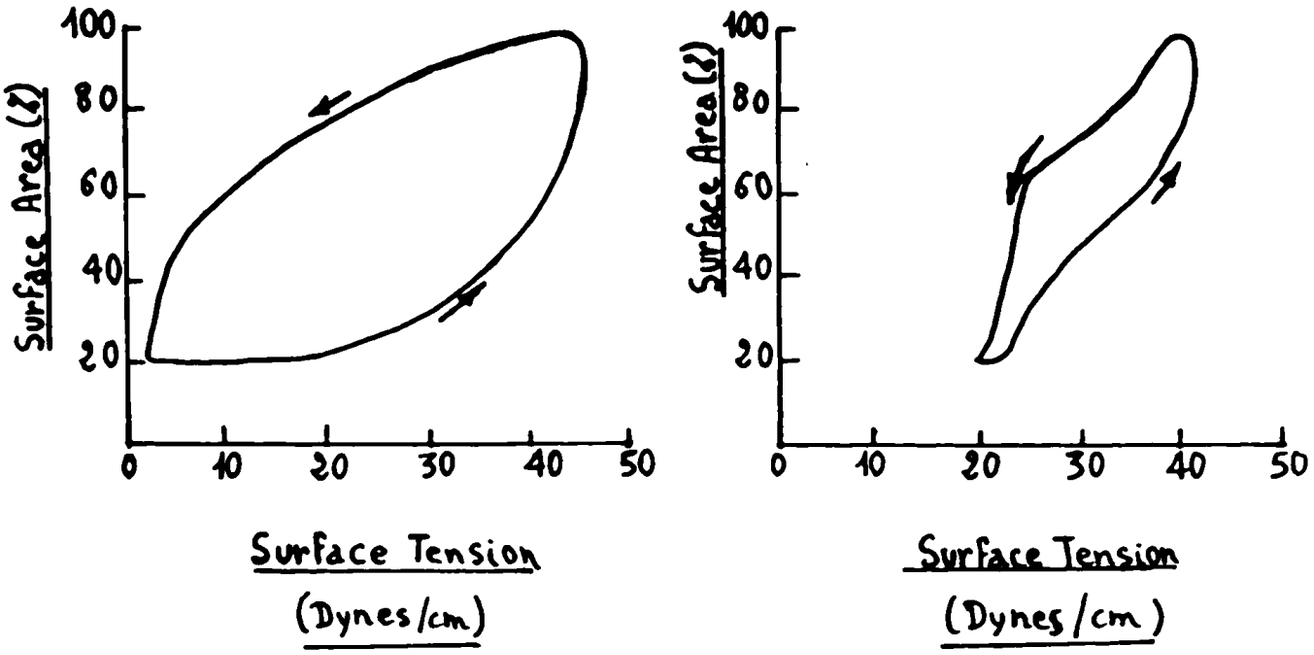
Von Neergaard correctly deduced that each of the hundreds of million of alveoli has a liquid-air interface, which tends to retract or recoil just as a bubble does. The sum of these recoil pressures for the whole lung, provides just as much or more, recoil as do the elastic fibres.

He concluded that much of the elastic recoil was due to surface tension acting throughout the vast air/liquid lining the alveoli.

Surface tension at an air/liquid interface produces forces which tend to reduce the area of the interface.

Alveolus with a low surface tension requires a low air pressure to maintain a given volume; one with a high surface tension requires a large counter pressure. Therefore low surface tension reduces the muscular effort necessary to ventilate the lungs and keep them aerated.

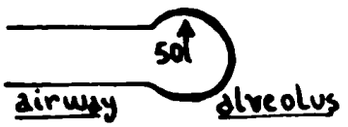
### 1.2.3 Surface tension of lungs for a normal infant and infant with respiratory distress syndrome.




At the left is the normal lung extracts which at compression of film to 20% of original surface the minimal surface tension is about 2 dynes/cm.

At the right is the extract from lung of a newborn baby who died of the respiratory distress syndrome, his minimal surface tension is 20 dynes/cm.

Normal infant

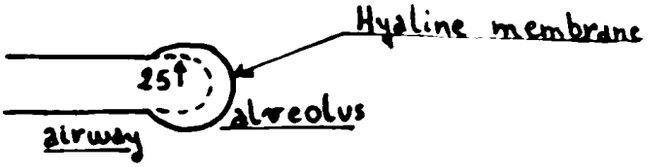



Pressure $= \frac{2 \times \text{Tension}}{\text{Radius}}$

$= \frac{2 \times 5 \text{ (Dynes/cm)}}{50 \text{ (Microns)}}$

$= 2$ cm. Water

Respiratory Distress. Newborn




Pressure $= \frac{2 \times \text{Tension}}{\text{Radius}}$

$= \frac{2 \times 25}{25}$

$= 20$ cm water

At the left normal infant. A transpulmonary pressure of only 2cm $H_2O$ is needed to inflate a deflated alveolus with a radius of 50u and a minimal surface tension of 5 dynes/cm.

At the right infant with respiratory distress; 20cm $H_2O$ is required to inflate the smaller alveolus with a high minimal surface tension (50 dynes/cm).

The infant must make a maximal effort with each breath to inflate the alveolus.

The strange features of the surface tension of the alveolar lining fluid are due to the presence of a surface-active material or surfactant.

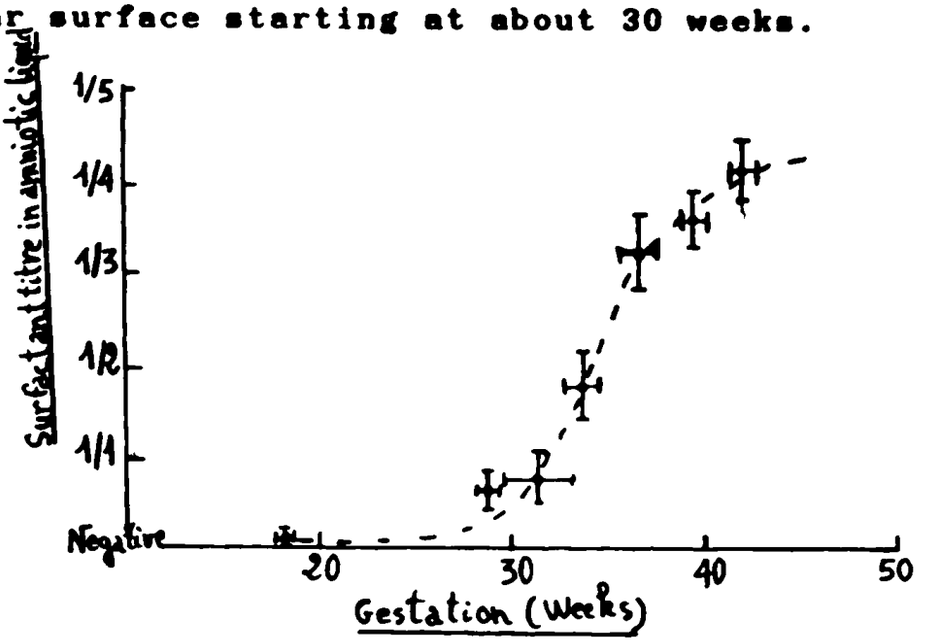
1.3 Surfactant (3), (2). (4)

1.3.1 Surfactant

Surfactant is synthesised by the alveolar type II cells and delivered to the alveolar surface where it forms a surface film with special physical properties allowing the lungs to retain air, even when the transpulmonary pressure is very low.

Surfactant appears in the lungs relatively late in

gestation, there is a stage of tissue storage starting at 24 weeks in fetus followed by a stage of delivery to the alveolar surface starting at about 30 weeks.




This fig show : Surfactant in humain amniotic fluid. Increase in surfactant with advancing gestation, in the humain shown by rise in dilution at which its presence is detectable by Clements's shake

### 1.3.2 Surfactant deficiency

Surfactant deficiency increases surface tension within the alveoli; hence, a greater transpulmonary pressure is required to inflate the lung.

Surfactant deficiency also reduces lung compliance (see 1.7) increases work of breathing, causes alveolar hypoventilation.

Without surfactant, small alveoli cannot remain open at the relatively low transpulmonary pressures that open and maintain larger alveoli.

Pulmonary transudation is also influenced by surfactant activity. Surface tension causes a pressure gradient across the alveolar-capillary membrane (of the order of 0.4 KPa) which, together with the above - atmospheric pressure in the pulmonary capillaries (about 0.7 KPa) tends to favour transudation. These pressures are counteracted by the osmotic pressure of the plasma proteins (about 3.5 KPa) so that transudation does not normally occur. Diminished surfactant activity would elevate the pressure gradient across the alveolar-capillary membrane and, if sufficiently severe, would tip the balance in favour of transudation. This may be the cause of the hyaline membrane in the respiratory distress syndrome of the newborn.

The respiratory distress syndrome is a condition affecting the newborn infant which is associated with rapid distressed breathing and indrawing of thoracic soft tissues; it does not recover within 24hr of birth and no cause other than surfactant deficiency can be inferred.

The immediate cause of the atelectasis is without question, inability to form a normal film of surfactant.

Recovery from RDS must be mainly due to development of the capacity to produce surfactant.

Inactivation by fibrogen was suggested as a cause of surfactant deficiency by Taylor and Abrams. According to Taylor and Abrams, the main cause of surfactant deficiency in the newborn baby cold be leakage of protein into air spaces.

## 1.4 Lung volume and its subdivisions (2), (1), (4)

### 1.4.1 Lung volume

The lung is divided in four volumes.

a) Tidal volume (VT) is the volume of gas added to and then removed from the lungs with each breath it is usually 500 to 600 ml. Tidal volume comprises the volume entering the alveoli (350 to 450 ml) plus the volume remaining in the airway (150 to 175 ml) per breath with exercise tidal volume increase.

b) Inspiratory reserve volume (IRV)

IRV is the maximum amount of gas that can be inspired from the end-inspiratory position, it is the reserve available for increasing tidal volume.

IRV decreases as tidal volume increases.

IRV reflects the balance between lung and chest elasticity, muscle strength, thoracic mobility, midposition, and tidal volume.

c) Expiratory reserve volume (ERV)

ERV is the maximal volume of gas that can be expired from the end-expiratory level it measures reserve expiratory capability.

IRV reflects thoracic and abdominal muscle strength, thoracic mobility, and the balance of elastic forces that determine midposition at the end of spontaneous expiration.

d) Residual volume (RV)

RV is the volume of gas remaining in the lungs at the end of a maximal expiration. It reflects the balance of elastic

forces of lung and thorax, muscle strength affecting expiratory reserve volume.

1.4.2 Lung capacities

As the subdivision of the lung volume, the lung capacities can also be subdivised into 4 capacities and they are as follows:

a) Total lung capacity (TLC): the amount of gas contained in the lung at the end of a maximal inspiration, it involves IC and FRC or VC and RV and comprise the four volumes IRV + TV + ERV + RV

TLC is affected.

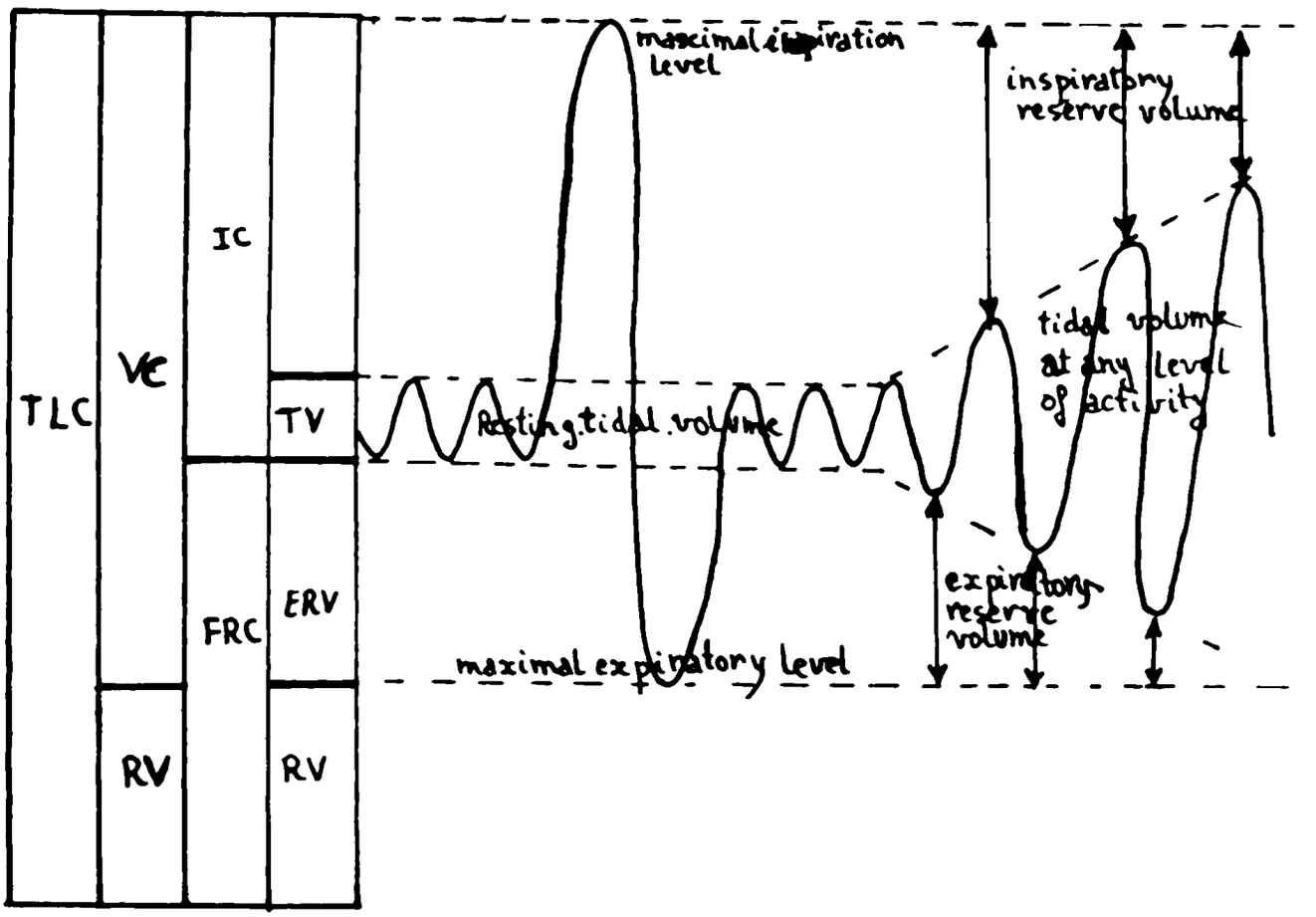
b) Vital capacity (VC): is the maximal volume of gas that can be expelled from the lungs by forceful effort following a maximal inspiration.

VC comprises IRV, TV and ERV.

c) Inspiratory capacity (IC) is the maximal volume of gas that can be inspired from the resting expiratory level.

d) Functional residual capacity (FRC) is the volume of gas remaining in the lungs at the resting expiratory level. FRC comprises ERV and RV.

**The figure below is the resume of what we have said.**

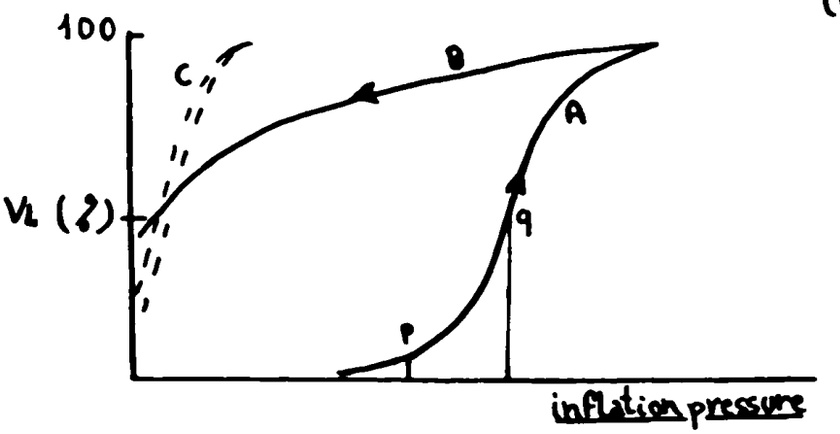



Subdivisions of the lung volume & capacity

1.5 The lung inflation for normal and abnormal baby with RDS: (3)

The comparison between the lung inflation for normal and premature baby with RDS is given by the four all together figures below

1.5.1 Normal baby:




(VL %) = Lung volume as percentage of its maximum

A is the Static inflation curve

B is the Static deflation curve

C is liquid expansion curve

Fig 1

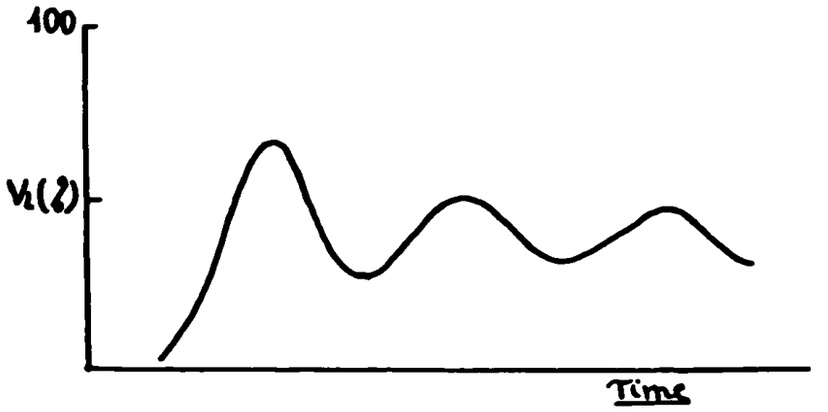



Fig 2

The static inflation curve A in fig 1 consists of three distinct regions. In the first up to P, virtually no air enters the lung; in the second between P and Q the curve is concave upwards; in the third, above an inflexion point, it is convex upwards. This shape can be explained by the need to apply a critical pressure to open peripheral lung units. In the first region, the transpulmonary pressure is

insufficient to open any signficant proportion of the lung. In the second region, viewed through the dissecting microscope; peripheral air spaces are seen to open sharply, one after another, the largest first, the smallest last. In the third region, the convex shape of the curve is due to increasing expansion of already open air spaces. The deflation curve (D) differs from the inflation curve.

Transpulmonary pressure has to be reduced at P level or less before any substantial volume of air leaves the lung.

At the end of the normal expiration (low transpulmonary pressure) much more air remains in the lungs; this is the functioning residual volume FRC. So during lung deflation, low pressures are sufficient to hold air in the lungs because a special surface film (surfactant) is present which reduces surface tension to a very low value when the lung surface is compressed dynamically.

If we take curve C we notice that when we use liquid to expand the lung, there is no air-liquid interface, and much lower pressures are sufficient to expand the lung.

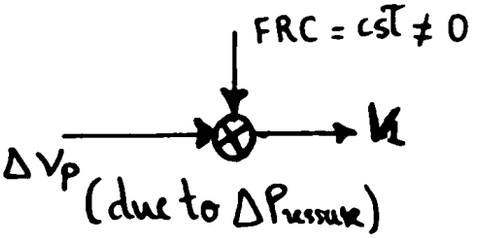
And this is obtained thanks to the surfactant which leads the surface tension to a low level hence a low air pressure is required to maintain a given volume.

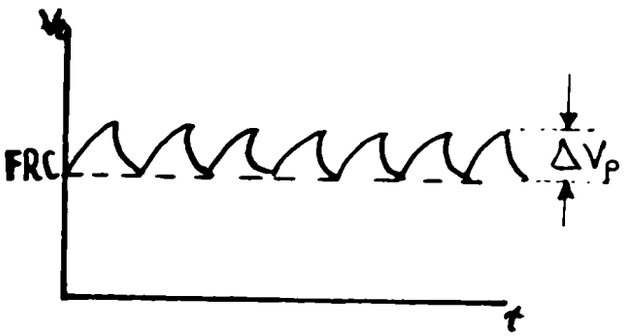
The fig 2 shows the variation of the volume VL(%) during spontaneous breath.

At the beginning there is what we call the first breathing and the lung volume rises from the zero level to more than the resting tidal volume, after for the next breathings the

volume will fluctuate over a certain level which we call FRC (ERV + RV) and it stabilises at this level and never drops to zero level.

So for the simulation of the volume we have like bias resulting from FRC and alteration due to the breathing or variation of Pressure.




### 1.5.2 Abnormal baby with RDS

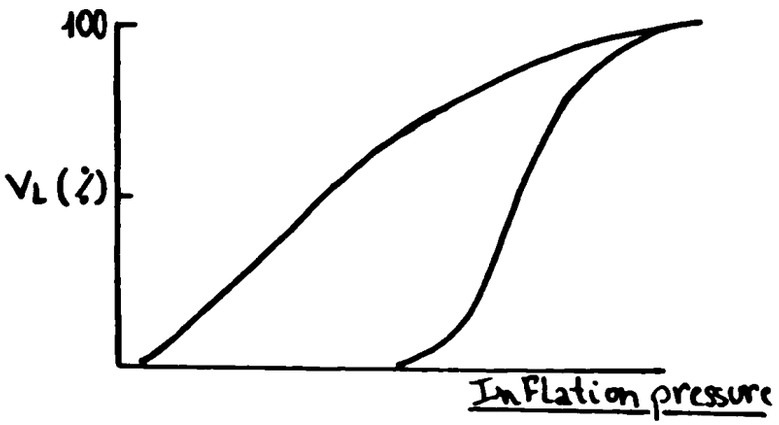



Fig 3

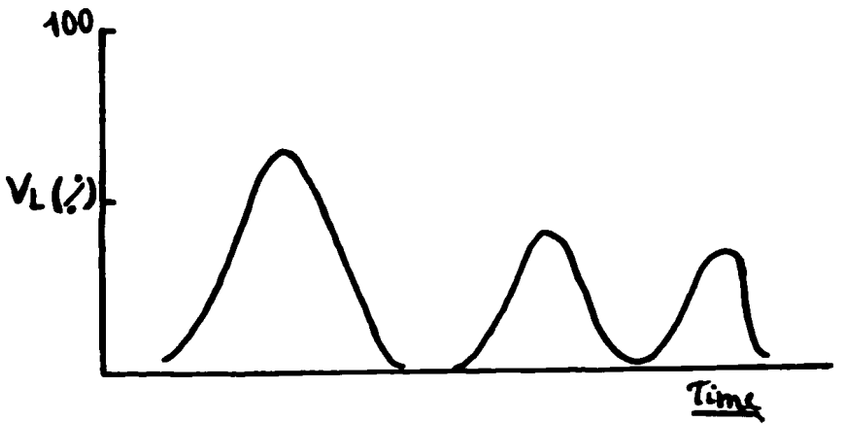
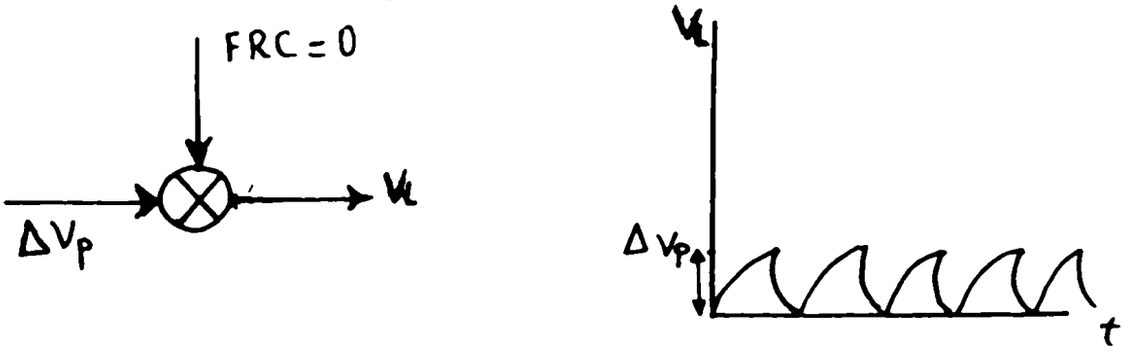



Fig 4

The curve of lung inflation of the immature baby is similar to that of mature baby except that the former needs higher opening pressures.

The deflation curve, however is different; the immature lung empties more or less completely at low pressures, and virtually no FRC is formed (fig 3).

After the first inflation of the mature lung, subsequent breathes can be achieved without the need for high opening pressures; but the immature lung, lacking surfactant has to be reopened with each breath (fig 4). So if we simulate the lung volume of the premature baby, there is no bias because of the non existing of FRC, so there is only alteration due to the deep breathing.




1.6 <u>FRC: its formation, its effect and the factors which influence it</u> (1), (4).

1.6.1 <u>the formation of FRC</u>.

According to Karlberg et al, the volume of the first inspiration varies from 12 to 67 ml, and the volume remaining in the lungs varies from 4 to 30 ml (i.e. approximately 1 - 10 ml/Kg body weight). This is the first stage in forming a Functional Residual Capacity (FRC), the

critical event in lung aeration; but after the first breath only 30%, at most, of the established FRC is present. According to Klaus et al who measured FRC by the Dubois, plethysmograph method, it averages about 17 ml/Kg at 0-10 min, 22 ml/Kg at 11-20 min and 32 ml/Kg at 21-30 min, after which no further increases take place. Genbelle et al obtained a value of 30 ml/Kg by the gas dilution method, and also found no increase after 1 hour of age; on the other hand, Koch found an increase of about 15% in FRC between 1-2 hr and 24 hr; Karlberg et al observed no tendency for the FRC to get bigger during the first few breaths, so we must assume it is added to only gradually; probably a little more lung gets aerated each time the infant takes a big breath and cries.

1.6.2 the effect of the FRC

The FRC acts as a buffer against extreme changes in alveolar $PO_2$ with each breath. If there were no FRC, alveolar $PO_2$ would decrease to that of venousblood in the pulmonary capillaries at end expiration and rise to near 19.6 KPa with deep inspiration; Blood $PO_2$ and content would also fluctuate widely with each breath. The size of the FRC is important when a rapid change in alveolar gas composition is necessary. For example, if a patient breathes 100% $O_2$ instead of air, he will achieve a high alveolar $O_2$ concentration more slowly if his FRC is large than if it is small.

1.6.3 The factors which influence the FRC

1.6.3.1 Body size

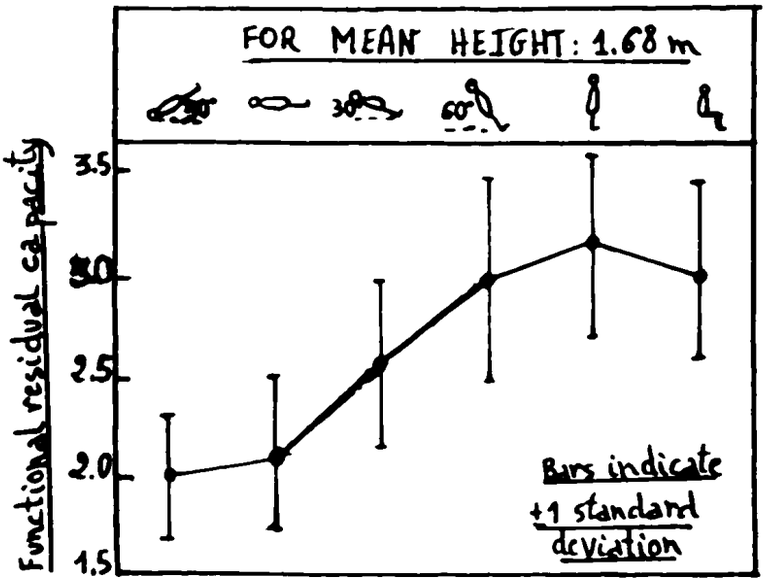
Most authors relate FRC to height, the relationship being linear throughout the range of normal height. Estimates range from an increase of FRC of 32 ml/cm additional height (Cotes, 1975) to 51 ml/cm (Bates, Macklem and Christie, 1971). Obesity causes a marked reduction in FRC compared with lean subjects of the same height.

1.6.3.2 Sex

For the same body height, females have a FRC about 10 per cent less than the corresponding value in males (Bates, Macklem and Christie, 1971).

1.6.3.3. Posture

A very large number of studies have been reported giving a difference between upright and supine within the range 500 - 1000 ml (Whitfield, Waterhouse and Arnott, 1950; Craig, Wahba and Don 1971; Craig et al, 1971).




Functional residual capacity in various body position

1.6.3.4 Anaesthesia

The reduction in FRC correlates well with an increase in the alveolar-arterial $PO_2$ gradient during anaesthesia with spontaneous breathing (Hickey et al, 1973) anaesthesia with artificial ventilation (Hewlett et al, 1974).

1.6.3.5 Surfactant deficiency

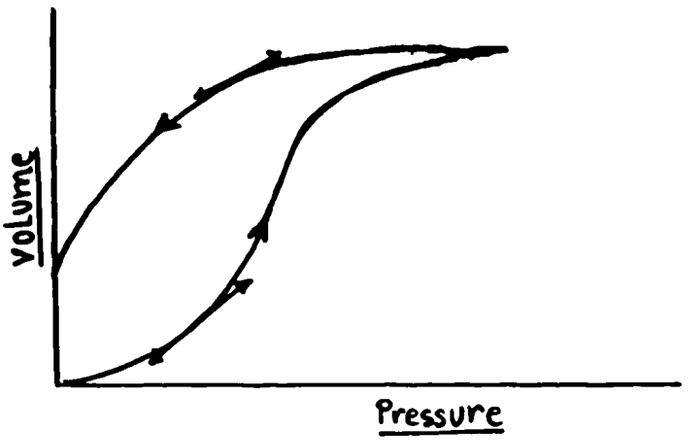
The non existence of FRC is due to surfactant deficiency which has a big effect on the surface tension.

1.7 Compliance and its importance in physical interpretation of the lung respiration (2), (5).

1.7.1 Definition:

Compliance describes the property of elasticity or distensibility of the lungs and chest wall it expresses the ease with which lung volume is changed.

So the more elasticity of the lung leads to the more higher compliance.




The slope (of the fig above) volume over pressure defines

the dynamic compliance.

Therefore the dynamic compliance is equal to: $Cd = \left.\frac{VL}{P_{Tp}}\right|_{\dot{V}L=0}$

Where $\Delta VL$ is the change in the lung volume under a variation of the transpulmonary pressure $\Delta P_{Tp}$ at zero airflow conditions.

Therefore the higher the compliance, the larger the delivered volume per unit of pressure.

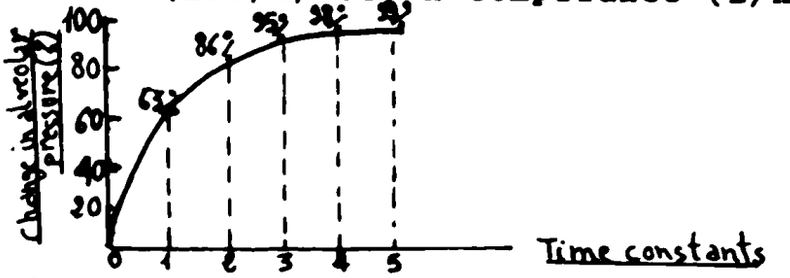
1.7.2 Its importance in physical interpretation

In addition to the pressure required to overcome the elasticity of the respiratory system, pressure is needed to force gas through the airways (airway resistance) and exceed the viscous resistance of the lung tissue (tissue resistance). We define a dynamic resistance which is a property of the inherent capacity of the lungs to resist airflow and is expressed as the ratio of the change in transpulmonary pressure ($\Delta P_{Tp}$) and the change in total airflow ($\Delta \dot{V}L$) at a certain level of lung volume (VL)

Therefore $Rd = \left.\frac{\Delta P_{Tp}}{\Delta \dot{V}L}\right|_{VL = cst}$

Compliance and resistance can be used to define a time constant for the lung. The time constant of the respiratory system is a measure of the time (expressed in seconds) necessary for the alveolar pressure to reach 63 per cent of the change in airway pressure and is defined as the product of resistance and compliance, as follows:

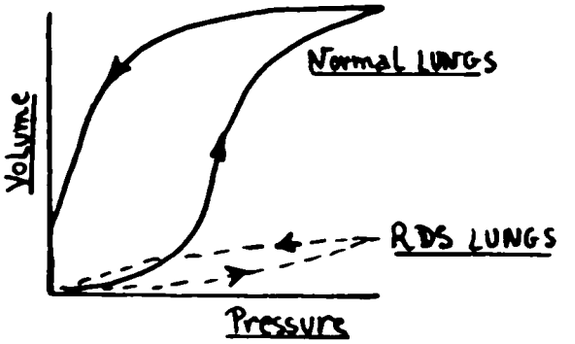
Time cst (sec) = Resistance (KPa/L/sec) x compliance (L/KPa)




Since the lung of baby with RDS has a smaller compliance (see 1.7.3), its time constant and corresponding time for pressure equilibration will be shorter therefore lungs with decreased compliance will complete inflation and deflation in a shorter time than normal lungs.

1.7.3 Factors which influence the compliance

Surfactant deficiency reduces lung compliance




The slope of the relationship volume, pressure is the compliance.

From the curves we notice that the compliance in normal baby is higher than in abnormal baby with RDS.

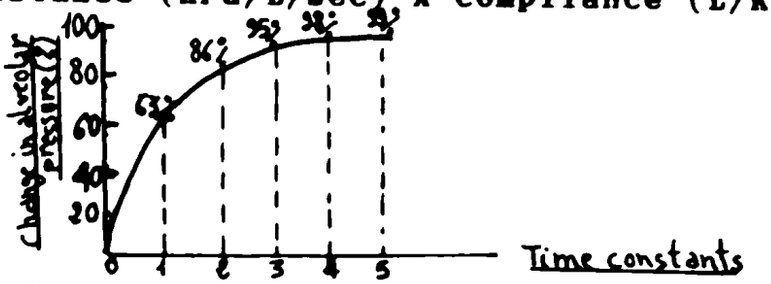
Remarks: The recovery from RDS is confirmed by the increasing of the compliance.

1.7.4 Effect due to the decrease or increase of the compliance.

1.7.4.1 Decreased lung compliance (case of RDS)

Decreased lung compliance is a serious problem which is related with inspiration difficulty. As compliance

Time cst (sec) = Resistance (KPa/L/sec) x compliance (L/KPa)

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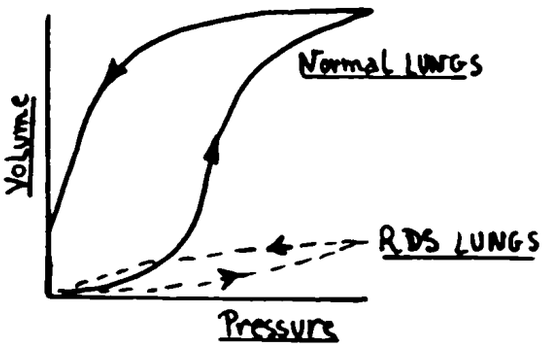



The slope of the relationship volume, pressure is the compliance.

From the curves we notice that the compliance in normal baby is higher than in abnormal baby with RDS.

Remarks: The recovery from RDS is confirmed by the increasing of the compliance.

1.7.4 Effect due to the decrease or increase of the compliance.

1.7.4.1 Decreased lung compliance (case of RDS)

Decreased lung compliance is a serious problem which is related with inspiration difficulty. As compliance

decreases, a greater transpulmonary pressure change is required to produce a given volume change. The greater inspiratory effort needed to produce this change means that the work of breathing increases as compliance decreases, and as a result, alveolar hypoventilation develops, ventilation-perfusion mismatching increases, and lung diffusion-perfusion relationships become grossly abnormal.

1.7.4.2 Increased lung compliance

An increase of lung compliance might appear advantageous because such a lung can be inflated with less effort. On the contrary, increased lung compliance is a serious problem. Increased compliance reduces transpulmonary pressure, the force that holds small airways open. The patient with increased lung compliance breathes with his lungs more fully inflated so there is a limitation in expiratory flow rate. Increasing compliance ultimately causes lung failure.

1.8 Airways for human lung and its subdivision (1), (5), (3)

The lung starts as a single small bag which grows and divides into a lot of branches. The single trachea leads into some 23 sequential generations of dichotomous branching (see table 1). These branches can be classified into 3 groups:

Generations 0 through 16 are purely conducting
17 through 19 are partly conducting and partly diffusing
and generations 20 through 23 are all diffusing airways.

The inspired air can avoid participating in gas exchange with the blood either by remaining in the conducting airway

**TABLE 1**

**Dimensions of Human Airway Model "A"**
**Average Adult Lung with Volume 4,800 ml at About ⅔ Maximal Inflation***

| Generation z | Number per Generation n(z) | Diameter d(z) (cm) | Length l(z) (cm) | Total Cross Section S(z) ($cm^2$) | Total Volume V(z) ($cm^3$) | Accumulated Volume $\sum_{l=0}^{z} V(l)$ ($cm^3$) |
|---|---|---|---|---|---|---|
| 0 | 1 | 1.8 | 12.0 | 2.54 | 30.50 | 30.5 |
| 1 | 2 | 1.22 | 4.76 | 2.33 | 11.25 | 41.8 |
| 2 | 4 | 0.83 | 1.90 | 2.13 | 3.97 | 45.8 |
| 3 | 8 | 0.56 | 0.76 | 2.00 | 1.52 | 47.2 |
| 4 | 16 | 0.45 | 1.27 | 2.48 | 3.46 | 50.7 |
| 5 | 32 | 0.35 | 1.07 | 3.11 | 3.30 | 54.0 |
| 6 | 64 | 0.28 | 0.90 | 3.96 | 3.53 | 57.5 |
| 7 | 128 | 0.23 | 0.76 | 5.10 | 3.85 | 61.4 |
| 8 | 256 | 0.186 | 0.64 | 6.95 | 4.45 | 65.8 |
| 9 | 512 | 0.154 | 0.54 | 9.56 | 5.17 | 71.0 |
| 10 | 1,024 | 0.130 | 0.46 | 13.4 | 6.21 | 77.2 |
| 11 | 2,048 | 0.109 | 0.39 | 19.6 | 7.56 | 84.8 |
| 12 | 4,096 | 0.095 | 0.33 | 28.8 | 9.82 | 94.6 |
| 13 | 8,192 | 0.082 | 0.27 | 44.5 | 12.45 | 106.0 |
| 14 | 16,384 | 0.074 | 0.23 | 69.4 | 16.40 | 123.4 |
| 15 | 32,768 | 0.066 | 0.20 | 113.0 | 21.70 | 145.1 |
| 16 | 65,536 | 0.060 | 0.165 | 180.0 | 29.70 | 174.8 |
| 17 | 131,072 | 0.054 | 0.141 | 300.0 | 41.80 | 216.6 |
| 18 | 262,144 | 0.050 | 0.117 | 534.0 | 61.10 | 277.7 |
| 19 | 524,288 | 0.047 | 0.099 | 944.0 | 93.20 | 370.9 |
| 20 | 1,048,576 | 0.045 | 0.083 | 1,600.0 | 139.50 | 510.4 |
| 21 | 2,097,152 | 0.043 | 0.070 | 3,220.0 | 224.30 | 734.7 |
| 22 | 4,194,304 | 0.041 | 0.059 | 5,880.0 | 350.00 | 1,084.7 |
| 23† | 8,388,608 | 0.041 | 0.050‡ | 11,800.0 | 591.00 | 1,675.0 |

* From E. R. Weibel, *Morphometry of the Human Lung* New York: Academic Press, Inc., and Heidelberg, Germany: Springer-Verlag, 1963.

‡ Adjusted for complete generation.

TABLE 2—CLASSIFICATION AND APPROXIMATE DIMENSIONS OF AIRWAYS OF ADULT HUMAN LUNG (INFLATED TO ABOUT ¾ OF TLC)*

| COMMON NAME | NUMERICAL ORDER OR GENERATION | NO. OF EACH | DIAMETER (MM) | LENGTH (MM) | TOTAL CROSS-SECTIONAL AREA ($CM^2$) | DESCRIPTION AND COMMENT |
|---|---|---|---|---|---|---|
| Trachea | 0 | 1 | 18 | 120 | 2.5 | Main cartilaginous airway; partly in thorax. |
| Main bronchus | 1 | 2 | 12 | 47.6 | 2.3 | First branching of airway; one to each lung; in lung root; cartilage. |
| Lobar bronchus | 2 | 4 | 8 | 19.0 | 2.1 | Named for each lobe; cartilage. |
| Segmental bronchus | 3 | 8 | 6 | 7.6 | 2.0 | Named for radiographical and surgical anatomy; cartilage. |
| Subsegmental bronchus | 4 | 16 | 4 | 12.7 | 2.4 | Last generally named bronchi; may be referred to as medium-sized bronchi; cartilage. |
| Small bronchi | 5–10 | 1,024† | 1.3† | 4.6† | 13.4† | Not generally named; contain decreasing amounts of cartilage. Beyond this level airways enter the lobules as defined by a strong elastic lobular limiting membrane. |
| Bronchioles | 11–13 | 8,192† | 0.8† | 2.7† | 44.5† | Not named, contain no cartilage, mucus-secreting elements or cilia. Tightly embedded in lung tissue. |
| Terminal bronchioles | 14–15 | 32,768† | 0.7† | 2.0† | 113.0† | Generally 2 or 3 orders so designated; morphology not significantly different from orders 11–13. |
| Respiratory bronchioles | 16–18 | 262,144† | 0.5† | 1.2† | 534.0† | Definite class; bronchiolar cuboidal epithelium present but scattered alveoli are present giving these airways a gas exchange function. Order 16 often called first-order respiratory bronchiole, 17 second-order and 18 third-order. |
| Alveolar ducts | 19–22 | 4,194,304† | 0.4† | 0.8† | 5,880.0† | No bronchiolar epithelium; have no surface except connective tissue framework; open into alveoli. |
| Alveolar sacs | 23 | 8,388,608 | 0.4 | 0.6 | 11,800.0 | No reason to assign a special name; are really short alveolar ducts. |
| Alveoli | 24 | 300,000,000 | 0.2 | | | Pulmonary capillaries are in the septae that form the alveoli. |

*Adapted from Staub, N. C.: Anesthesiology 24:831, 1963, and Weibel, E. R.: *Morphometry of the Human Lung* (Berlin: Springer, 1963). The number of airways in each generation is based on regular dichotomous branching. This is not strictly true; for example, there are 5 lobar branches (1 to each lobe), not 4.

†Numbers refer to last generation in each group.

(generations 0 to 16) or by reaching non perfused alveoli. The former deals with the anatomical dead space (Vcds) and the latter deals with the alveolar dead space (VAds) and can be described in simular manner by the venous blood which avoids participating in gas exchange.

1.8.1 Dead space

1.8.1.1 anatomical dead space (Vcds conducting dead space volume).

The anatomical dead space is that part of the inspired tidal volume which is unchanged at the beginning of expiration, and it is given by the equation:

$$Vcds = (VT - \dot{V}A/f)$$

where VT is the tidal gas

$\dot{V}A$ is rate of alveolar gas flow

f is the breathing frequency

1.8.1.1.1 Factors affecting anatomic dead space.

The anatomic dead space is about one fifth of the tidal volume.

The anatomic dead space is affected by:

a) the size of subject: the Vcds is based on body height.

b) Vcds increases slightly with age.

c) Position of the neck and jaw has a pronounced effect on the anatomical dead space, and studies by Nunn, Campbell and Peckett (1959) have indicated the following mean values in three conscious subjects

| | |
|---|---|
| neck extended, jaw protruded | 143 ml |
| normal position | 119 ml |

neck flexed, chin depressed 73 ml

d) Posture influences the anatomical dead space.

Fowler (1950 ) quotes the following mean values:

| | |
|---|---|
| sitting | 147 ml |
| semi-reclining | 124 ml |
| supine | 101 ml |

1.8.1.2 Alveolar dead space VAdS

Alveolar dead space may be defined as that part of the inspired gas which passes through the anatomical dead space to mix with gas at the alveolar level, but which does not take part in gas exchange.

$VAds = (\dot{V}A - \dot{V}e)/f$

where $\dot{V}A$ is alveolar ventilation rate

$\dot{V}e$ (effective ventilation) is that portion which reaches perfused alveoli and undergoes gas exchange with the blood.

f is the breathing frequency

Alveolar dead space is influenced by the failure of alveolar perfusion.

VAds is too small to be measured in healthy subjects, particularly young people, but can become large enough to interfere with alveolar ventilation in patients with RDS.

1.9 Type of air flow (2), (4), (1), (5)

Gas flows from a region of high pressure to one of lower pressure. The rate flow is function of the pressure difference and the resistance to gas flow of the connecting passage. The relationship between driving pressure and air flow for a given gas can be characterized by the use of an equation called the mechanical energy balance:

$$Pi - Po = \Delta P = \rho \dot{V}^2/2 \left[ \frac{1}{Ao^2} - \frac{1}{Ai^2} \right] + \Sigma \lambda$$

where Pi is inflow pressure, Po is outflow pressure, $\Delta P$ is driving pressure, $\rho$ is gas density, $\dot{V}$ is airflow rate, Ao is exit cross-sectional area, Ai is entrance cross-sectional area, and $\Sigma \lambda$ is sum of the serial mechanical energy losses caused by frictional or viscous effects. This energy balance describes the effect of airways and gas composition on the air flow that results from a given driving pressure. Changes of gas composition alter gas density and viscosity effects, and changes of airway dimensions or shape alter frictional effects on gas flow. The first term on the right side of the equation expresses the effect of differences between entrance and exit cross-sectional areas on the Kinetic energy of the system. It can be ignored in this application because the airflow rate during breathing is not great enough to produce a large Kinetic energy effect. This leaves the more simple equation : $\Delta P = \Sigma \lambda$

The remaining term on the right side represents a complicated function of the physical properties of the gas, the geometry of the airway passages, and the gas flow rate. The precise relationship between pressure difference and gas flow rate depends upon the nature of the flow which is usually described as being either laminar or turbulent. In most situations, the flow is transitional, being partly laminar and partly turbulent. The flow pattern may vary

between different regions of the respiratory tract, for instance, there may be laminar flow in the trachea while there is turbulent flow in the larynx.

Reynold's number, NR, provides a criterion for determining whether flow is laminar or turbulent.

Reynold's number is given by: $NR = \frac{\rho . \bar{V} D}{u}$

Where $\rho$ is the fluid density

$u$ is the fluid viscosity

$\bar{V}$ is the mean linear velocity

$D$ is the tube diameter

If NR < 2000 the flow pattern is laminar

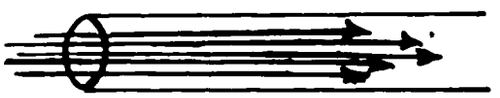
If NR > 2000 turbulent flow develops

Hence we define the critical volocity by:

$$\bar{V}c = \frac{2000}{D} \frac{u}{\rho}$$

1.9.1 Laminar flow

As gas flows slowly and steadily through a straight smooth, rigid, large-calibre, cylindric tube, a laminar (streamlined) flow pattern develops.



The driving pressure required in this case, is proportional to the air flow

$$\Delta P = K_1 \dot{V}$$

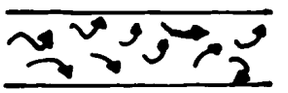
where $K_1$ is a cst that includes the influence of viscosity.

$$K_1 = 8 N L / \pi r^4$$

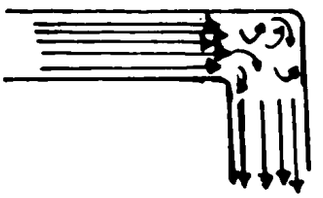
where N, L and r are: the gas viscosity, length of passageway, radius of passage way respectively.

1.9.2 Turbulent flow

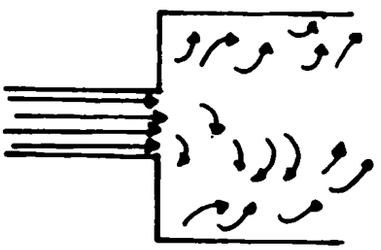
Turbulent flow will arise in a long, straight, unbranched tube if the flow rate is high enough or when the diameter or the direction of a tube is change abruptly.



High flow rate



Sharp angles



Change in diameter

Branches

the driving pressure required in this case is as follows:

$$\Delta P = K_2 = \dot{V}^2$$

where $K_2$ is a constant that includes the influence of density.

The effect of turbulent flow is that no new gas can reach the end of a tube until the volume of gas which has entered the tube is close to the geometrical volume of the tube. And this has as a result that the effective dead space is thus maximal when flow is turbulent.

When the air flow is a combination of laminar and turbulent flow $\Delta P$ will equal to: $\Delta P = K_1 \dot{V} + K_2 \dot{V}^2$


1.10 Total respiratory resistance (1), (4), (2)

Resistance means opposition to motion. Because motion involves friction, resistance occurs in any part of the respiratory system that moves or in which air movement occurs.

$$R = \frac{\Delta P}{\dot{V}}$$

1.10.1 Airway resistance

The airway component includes friction between the gas molecules and the walls of the airways plus the internal friction between the gas molecules themselves (viscosity). In subjects at rest it constitutes the remaining 80% of total respiratory resistance.

The airway resistance Raw involves three resistances in series:

Raw = Rn + RL + RE

where Rn is the resistance across the nose.

$$Rn = \frac{\text{Atmospheric pressure - pressure in the nasopharynx}}{\text{Flow}}$$

RL is the resistance through the larynx

$$RL = \frac{\text{Pressure in the larynx - pressure at the bifurcation of the trachea}}{\text{flow}}$$

RE is the resistance across an endotracheal tube

$$RE = \frac{\text{Pressure at one end}}{\text{------}} - \frac{\text{pressure at the other}}{\text{flow}}$$

Lung volume decreases as the airways resistance is increased since it opposed to the flow. The airways resistance also influences the FRC.

The FRC is reduced as the airways resistance is increased.

1.10.2 Tissue resistance

The tissue resistance is a frictional resistance due to the displacement of the tissues of the lung, and it occurs only during motion; hence this resistance is reduced to zero at each end inspiration and end expiration.

The tissues resistance is about 20% of the total pulmonary resistance and it depends on the velocity of motion and is a factor during both inspiration and expiration.

The tissues resistance and airways resistance are additive.

It means by that if the greater elastic force is dissipated in overcoming frictional resistance in the tissues during expiration, the less is the elastic force available for overcoming airway resistance.

1.10.3 Dynamic resistance

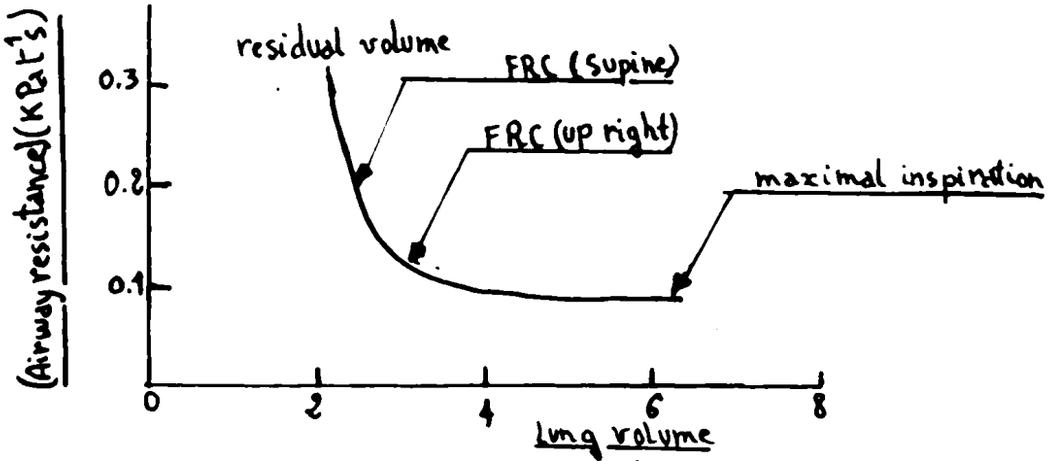
see (1.7.2)

1.11 Closing volume: (4), (5)

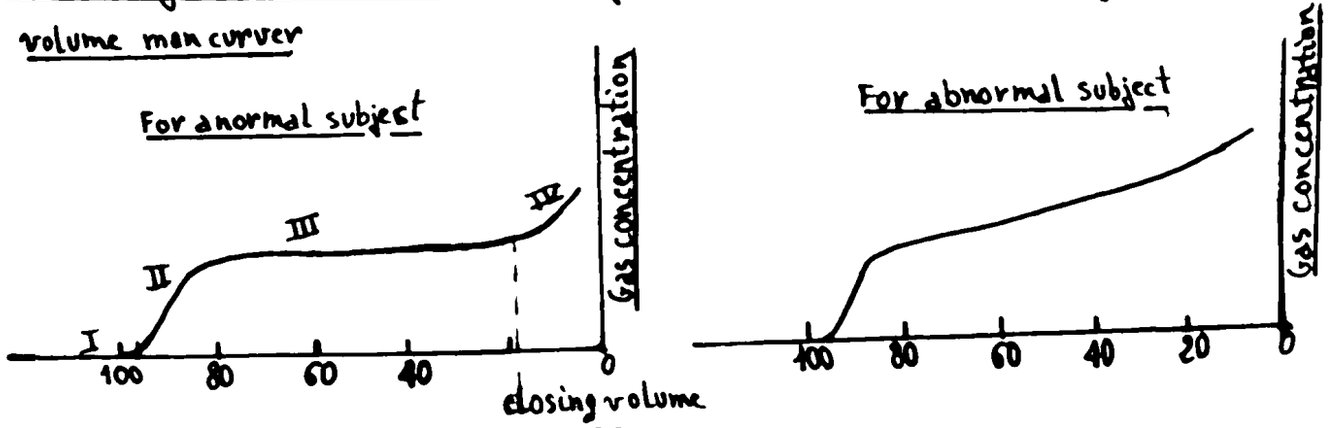
When the lung volume is reduced, there is a reduction in the size of all air-containing parts. Thus the alveoli and their ducts diminish in size and the airways in the dependent parts are always those which are most likely to close.

The closing volume is reached when the airways resistance increases and reaches a certain level.

An increase of FRC due to positive end-expiratory pressure will tend to decrease airway closure.




the two fig below show us the expired gas concentration for the closing volume man curver

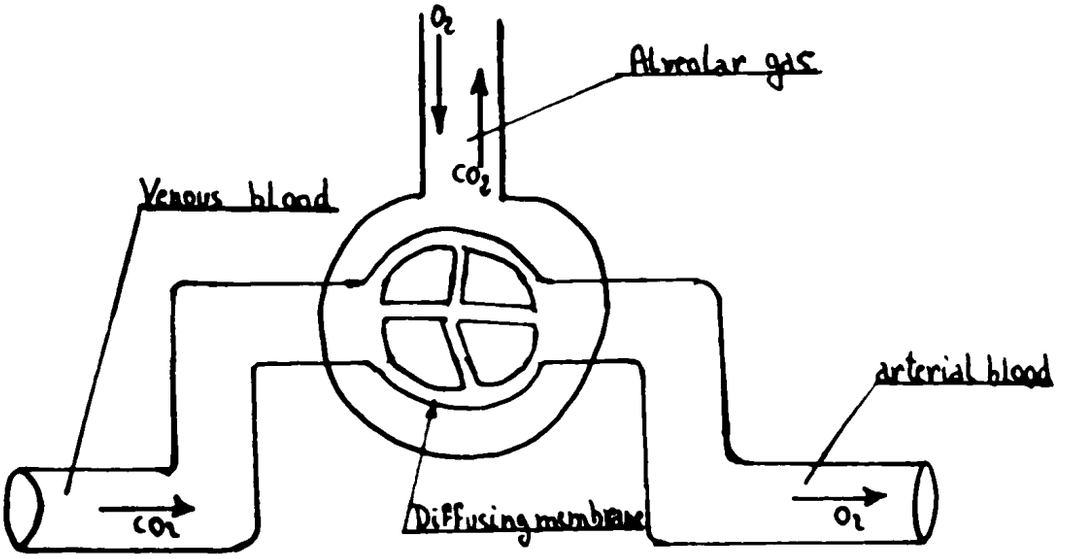


For a normal subject we are interested in the phase IV, the lung volume at which the sharp slope increases in concentration is observed is defined as closing volume. In the abnormal subject we haven't got the phase III (normal subject) which rise very slowly, but instead we have got a curve which vary more rapidly.

1.12 Alveolar capillary diffusion (2)

The most tremendous phenomena which occurs in the respiratory system cycle is that which happens in the alveolar capillary membrane. This latter behaves like a filter between alveolar oxygen and capillary $CO_2$.

The exchange of gas between alveolus and capillary is as follows:




Gas exchange in the alveolar capillary membrane

The venous blood conveys $CO_2$ and alveolar gas conveys $O_2$ towards the alveolar capillary membrane where gas exchange occurs.

Here $CO_2$ diffuse toward the alveole and $O_2$ diffuse toward the arterial blood.

The quantity of diffusion of both $O_2$ and $CO_2$ depends on certain criteria like membrane area, diffusion distance, liquid viscosity, transmembrane pressure difference etc.....

All factors which affect the rate of gas diffusion across the alveolarcapillary membrane can be represented by the following equation.

$$\dot{v} \propto \frac{Cs.T.A.dP}{\sqrt{MW}.L.\eta}$$

where $\dot{V}$ is the volumetric rate of gas transfer by diffusion, Cs is the solubility coefficient, T is the absolute temperature, A is the area of the gas-exchange membrane, dP is the difference in gas pressure across the diffusion path, MW is the molecular weight of the gas, L is the length of diffusion pathway, and $\eta$ is the viscosity of the liquid.

All the factors are comprehensifs, may be the diffusion distance factors is the only one which is not, so what does it mean diffusion distance. The diffusion distance is the length of the pathway between the alveolus and the haemoglobin molecule within the erythrocyte.

### 1.12.1 Pulmonary diffusing capacity

Gas transfer between alveoli and pulmonary capillary blood obeys the fundamental law of diffusion:

$$\frac{dV}{dt} = DL\,(P_1 - P_2)$$

where $\frac{dV}{dt}$ is the rate of transfer of $O_2$ or $CO_2$ (depending on which gas we are interested) per minute across the membrane.

$D_L$ is the diffusion coefficient of the gas considered in this membrane.

(P1 - P2) is the pressure difference of this gas between the two sides of this membrane.

$$DL \propto \frac{Cs.A}{\sqrt{MW}.L}$$

$\frac{1}{DL}$ can be written as trois resistances in series.

$$\frac{1}{DL} = \frac{1}{DA} + \frac{1}{DM} + \frac{1}{Db}$$

where DL is a measure of the conductance across the lung.

$$DL = \frac{\dot{V}}{PA - P\bar{V}}$$

where $P\bar{V}$ is the pressure of $O_2$ in the end capillary.

$\frac{1}{DA}$ is the resistance in the alveoli

$\frac{1}{DM}$ is the resistance across the alveolar capillary membrane

$\frac{1}{Db}$ is the resistance associated with the rate limitation of

$O_2$ removal by haemoglobin.

and can be written as:

$$\frac{1}{Db} = \frac{1}{\theta\ Vc}$$

where $\theta$ is a term for the reaction rate of $O_2$ with haemoglobin and Vc is capillary blood volume.

1.12.2 Factors influencing the pulmonary diffusing capacity.

a) Body position: DL is greater in the lying position by 15% to 20% over that measured with the subject upright.

b) Body size

DL increases during growth

c) Physical exercise

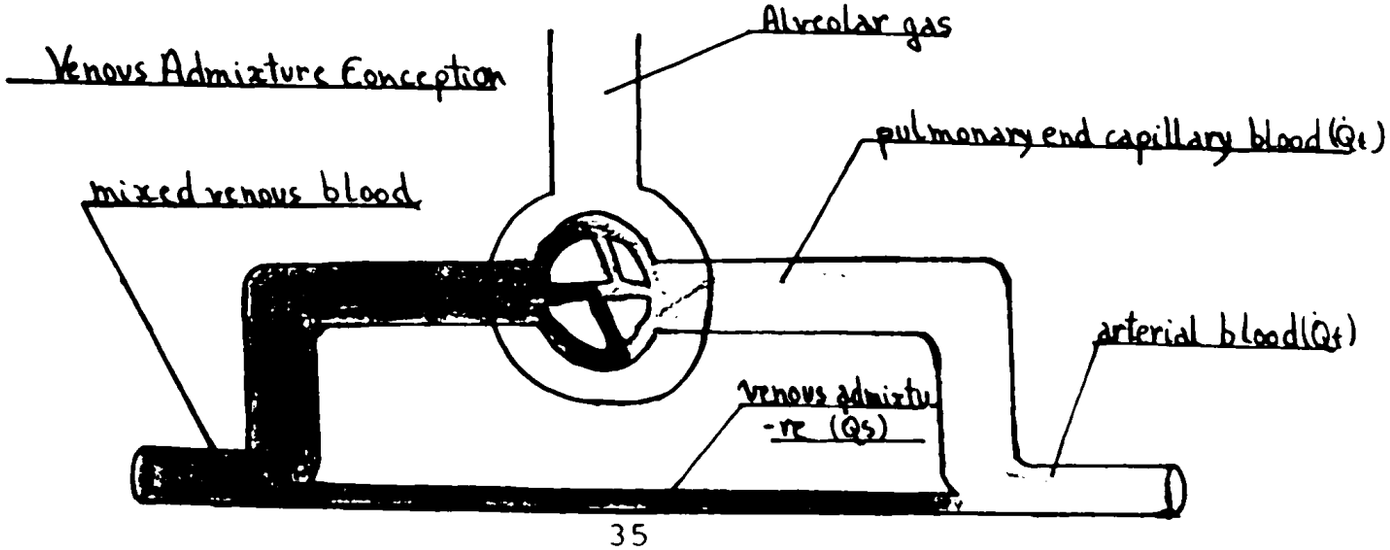
DL of healthy subjects increases by 25% to 35% during muscular exercise

d) Pulmonary disease

Mismatching of ventilation with perfusion reduces the effective, or functioning membrane area for gas transfer. So leads to a reduction in DL.

1.13 The concept of venous admixture (4), (3)

Venous admixture is the degree of admixture of mixed venous blood with pulmonary end-capillary blood.



### 1.13.1 Shunt (Sh)

The venous admixture affects the difference observed between the arterial and pulmonary end-capillary pressure denoted by $(P_{ECO_2} - P_{aO_2})$

More the venous admixture increases more this difference increases. So we define a new parameter (shunt) which is sensible at this difference. The shunt (Sh) is defined as the ratio between venous admixture ($\dot{Q}s$) and the total cardiac output ($\dot{Q}t$).

$$\text{Therefore } Sh = \frac{\dot{Q}s}{\dot{Q}t}$$

we know that:

Pulmonary capillary blood flow + venous admixture = cardiac output

$$\dot{Q}c + \dot{Q}s = \dot{Q}t \quad (1)$$

as we know also that:

The amount of oxygen in one minute's flow through the shunt plus the amount of oxygen in one minute's flow through the pulmonary capillaries are equal to the total amount of oxygen in one minute's flow of arterial blood.

$$C\bar{V}O_2 \cdot \dot{Q}S + C'CO_2 \cdot \dot{Q}C = CaO_2 \cdot \dot{Q}t \quad (2)$$

where $C\bar{V}O_2$, $C'CO_2$ and $CaO_2$ are the concentrations of oxygen respectively in mixed venous blood, in pulmonary end-capillary blood and in arterial blood.

From 1 and 2 we can establish the equation of the shunt as

$$Sh = \frac{\dot{Q}s}{\dot{Q}t} = \frac{C'CO_2 - CaO_2}{C'CO_2 - C\bar{V}O_2}$$

The shunt can vary from a small value (e.g. 0.01) to a high value (e.g. 0.5) according to whether the baby is normal or abnormal with RDS.

For a high value of Sh (e.g. 0.5) (baby with RDS) the baby needs an artificial ventilation so he must be supplied with high oxygen concentration in order to survive.

When the baby recovers from RDS, his shunt reduces dramatically and in that case he will not need an artifical ventilation.

When a baby has not got a high shunt, a high concentration of inspired oxygen can be fatal for the retina of the premature baby and a form of blindness can appear in this surviving of premature baby.

When a baby has got a shunt more than 0.6 or 0.7 he will probably die as the gas exchange in the alveolar capillary membrane cannot be done or very very small amount of gas exchange can occur.

1.13.2 Scatter of $\dot{V}/\dot{Q}$ ratio

The ventilation perfusion ratio denoted by ($\dot{V}/\dot{Q}$) has an effect on the gas exchange. Indeed the alveoli can be divided in several regions. Nonperfused alveoli and which is called alveolar dead space.

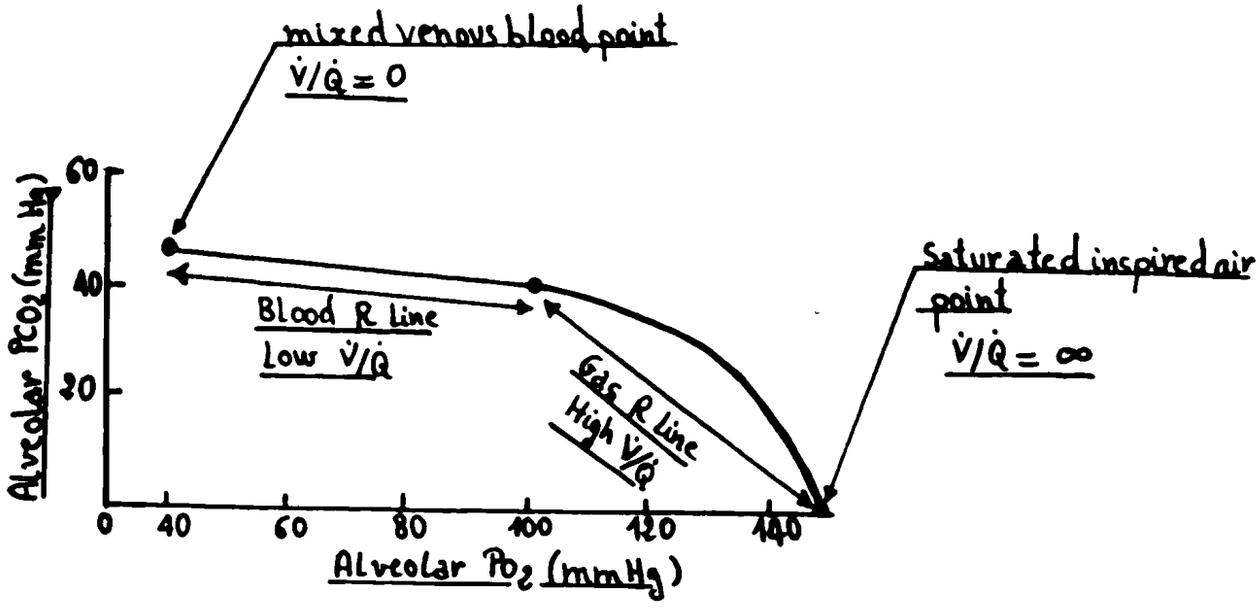
Here the ratio $\dot{V}/\dot{Q} = \infty$ as there is only a portion of inspired flow.

Non ventilated alveoli which is called alveolar shunt

Here the ratio $\dot{V}/\dot{Q} = 0$ as there is only blood flow.

Region where the gas exchange occurs and here $\frac{\dot{V}}{\dot{Q}}$ varies from 0.85 to 0.5 depending on how close to the membrane this region considered is.

The ratio $\frac{\dot{V}}{\dot{Q}}$ can inform us about the relation between Alveolar $PCO_2$ and $PO_2$ see fig. below.




R is the respiratory exchange ratio

$$\frac{\dot{V}}{\dot{Q}} = \frac{0.86\,(CaO_2 - C\bar{v}O_2)R}{PAO_2}$$ { see (ch modelling)

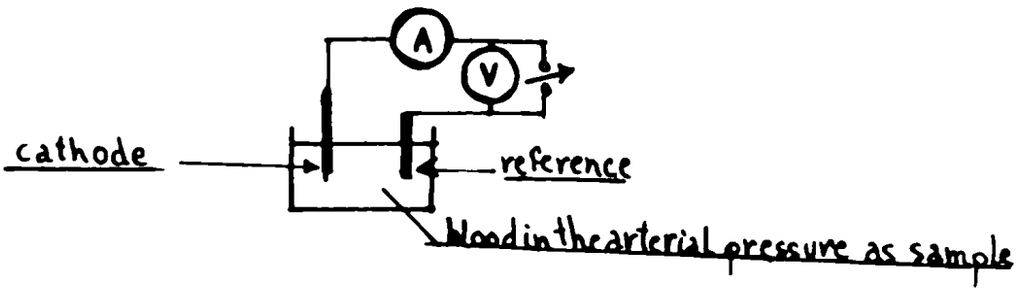
1.14 Sensor principles (7)

In order to control the inspired oxygen concentration to be supplied to the newborn suffering from RDS, we must sample the arterial oxygen pressure so that it will be between the

secure limits avoiding by that, blindness (high $PaO_2$), and brain damage (low $PaO_2$).

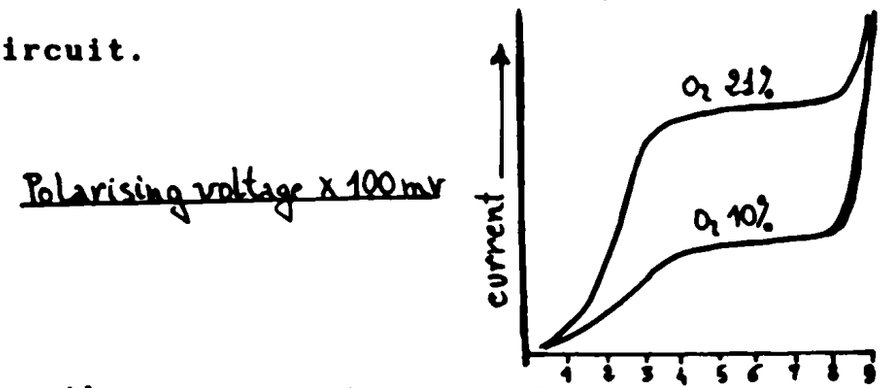
To do that we must search for a device which is sensitive to oxygen concentration in the arterial blood as input and gives a corresponding voltage as output. This device exists and is called catheter.

1.14.1 Basic principles




Simplest arrangement for polarographic oxygen measurment

The simplest arrangement for the polagraphic oxygen electrode consists of a noble-methal cathode polarised at a negative potential with respect to a reference electrode. Oxygen in the vicinity of the cathode surface is reduced when an appropriate polarising potential is applied, giving rise to a current which may be measured in the external circuit.




In the range of the polarographic plateau, current is practically independent of polarising voltage and is said to be diffusion-limited.

There is a steady state between the rate of arrival and consumption of oxygen at the cathode surface, this is the ideal operating condition in which current is directly related to oxygen partial pressure.

## Chapter Two

Modelling of the respiratory system.

### 2.1 An adaptive analogue tracker for automatic measurement of lung parameters. (8)

The adaptive electronic tracker is able to monitor continuously the mechanical properties of the respiratory system. It is capable of tracking the rapid changes in lung parameters as the frequency of breathing changes. The design of the adaptive tracker is based on equation-error formulation and the global asymptotic stability of the adaptive tracking equations is guaranteed.

#### 2.1.1 Mathematical lung model

The mathematical model for the lung, relating inspired airflow, lung volume, and pressure is described by:

$$P_m - P_p = RV + EV \qquad (1)$$

where $P_m$ = mouth pressure

$P_p$ = intrapleural pressure

$R$ = resistance of airways and lung tissue

$E$ = elastance of the lung and chest wall

$V$ = airflow into the lung

$V$ = lung volume

In order to determine R and E we have to measure $P_m$, $P_p$, V and V which is not easy to behold. Also since the noise corrupts this pressure and the airflow is partly laminar and partly turbulent.

This model is poor during the forced expiration of normal subjects and during normal expiration of subjects suffering

from chronic obstructive lung disorders.

This model is poor when the airflow is high because the flow is then turbulent and it is more accurate to model the lung by the equation

$$Pm - Pp = R_1 \dot{V} + R_2 \dot{V}^2 + EV$$

where $R_2$ is a resistance term to account for turbulent flow.

As Pp is difficult and dangerous to measure, the intraoesophageal pressure Po is measured and taken instead. Pm, Po and $\dot{V}$ can be measured unlike V which is not accessible. However a good estimate of the lung volume can be obtained by a direct integration of the airflow $\dot{V}$ which is reset during expiration and this can be done by taking an integrate/reset amplifier.

If we start at to, P, $\dot{V}$ and V which represent the pressure, flow and lung volume are as follows:

$$\left.\begin{aligned} P(t) &= Kp\,[\{Pm(t) - Po(t)\} - \{Pm(to) - Po(to)\}] \\ \dot{V}(t) &= K\dot{v}\,\{\dot{V}(t) - \dot{V}(to)\} \\ V(t) &= Kv \int \dot{V}(t)\,dt \end{aligned}\right\} \quad (2')$$

where: Kp = gain of the preamplifier and pressure transducer

$K\dot{V}$ = gain of the preamplifier and flow transducer

KV = gain of the lung volume integrate/reset amplifier

Therefore $P(t) = Rs\dot{V}(t) + Es\,V(t)$ (2)

where $Rs = \frac{RKp}{Ki}$ and $Es = \frac{Ekp}{KvK\dot{v}}$

To identify the lung parameters a response-error formulation is used. The model parameters $\alpha_i$ are adjusted according to

steepest-descent law

$$\dot{\alpha}_i = -K \frac{dF}{d\alpha_i}$$ where F is a performance criterion which is a quadratic function of the response error and K is the adaptive gain.

The response error system has the advantage that only the system input and output need to be measured.

The lung parameters Rs and Es are estimated respectively by $\hat{R}s$ and $\hat{E}s$ so that the error equation is generated:

$\varepsilon = P - \hat{R}s\dot{V} - \hat{E}sV$ ③

2 and 3 give: $\varepsilon = (Rs - \hat{R}s)\dot{V} + (Es - \hat{E}s)V$

or $\varepsilon = \tilde{R}s\dot{V} + \tilde{E}sV$ ④ where $\tilde{R}s = (Rs - \hat{R}s)$ and $\tilde{E}s = (Es - \hat{E}s)$

$\tilde{R}s$ and $\tilde{E}s$ are the instantaneous deviation in tracking respectively Rs and Es.

Equation 4 can be written in vector form as

$\varepsilon = \theta . \tilde{X}$

where $\tilde{X}T = (\tilde{R}s\tilde{E}s)$ and $\theta = (\dot{V}V)$

$\tilde{X} = X - \hat{X}$

the parameters adjustment law can be written as:

$$\frac{d\hat{X}}{dt} = -M \frac{dF(\varepsilon)}{d\hat{X}}$$

where F $(\varepsilon)$ is the error performance criterion which is chosen here to be $F(\varepsilon) = \frac{1}{2}\varepsilon^2$

[M] is (2 x 2) positive definite diagonal matrix defined as the gain matrix

as $\tilde{X} = X - \hat{X}$ & $\varepsilon = \theta\tilde{X}$ } Therefore $d\tilde{X} = -d\hat{X}$

Therefore $d\hat{X} = -\theta^{-T} d\varepsilon$

Therefore $$\frac{d\hat{X}}{dt} = -M\frac{dF(\xi)}{d\hat{X}} = -M\frac{dF(\xi)}{-(B^{-T})d\xi} = M\,\Theta^{T}\frac{dF(\xi)}{d\xi}$$

which give finally.

$$\begin{bmatrix} \frac{d\hat{R}s}{dt} \\ \frac{d\hat{E}s}{dt} \end{bmatrix} = \begin{bmatrix} m_1 & 0 \\ 0 & m_2 \end{bmatrix} \begin{bmatrix} \dot{V} \\ V \end{bmatrix} \xi \qquad (5)$$

5 is the parameters adjustment law in vector matrix form.

If we make the substitutions below.

$$X_1 = Rs/\sqrt{m_1},\ X_2 = Es/\sqrt{m_2}$$

$$\hat{X}_1 = \hat{R}s/\sqrt{m_1},\ \hat{X}_2 = \hat{E}s/\sqrt{m_2}$$

$$h_1 = \dot{V}\sqrt{m_1},\ h_2 = V\sqrt{m_2}$$

$$\tilde{X}i = Xi - \hat{X}i;\ i = 1,2$$

Therefore $\xi = h_1\tilde{X}_1 + h_2\tilde{X}_2$

Therefore equation 5 will give

$$\begin{bmatrix} \frac{d\hat{X}_1}{dt} \\ \frac{d\hat{X}_2}{dt} \end{bmatrix} = \begin{bmatrix} h_1 \\ h_2 \end{bmatrix} \xi \qquad (6)$$

as $\tilde{X} = X - \hat{X}$

$\dot{\tilde{X}} = \dot{X} - \dot{\hat{X}}$

Therefore $$\begin{bmatrix} \frac{d\tilde{X}_1}{dt} \\ \frac{d\tilde{X}_2}{dt} \end{bmatrix} = \begin{bmatrix} \dot{X}_1 \\ \dot{X}_2 \end{bmatrix} - \begin{bmatrix} h_1 \\ h_2 \end{bmatrix} \zeta \qquad (7)$$

which can be written as

$$\dot{\tilde{X}} = \dot{X} - H\zeta \qquad (8)$$

the equation above is asymptotically stable in the large, hence the null solution

$\tilde{X} = 0$ is an asymptotically stable equilibrium point in the parameters deviation plane.

This can be proved by taking Lyapunov function:

$$V(\tilde{X}) = \frac{1}{2} \tilde{X}^T \tilde{X} = \frac{1}{2} (\tilde{X}_1^2 + \tilde{X}_2^2)$$

which is positive definite $V(0) = 0$ and $V(\tilde{X})>0$ for $\tilde{X} \neq 0$

By taking its derivative

$$\dot{V}(\tilde{X}) = -(\tilde{X}^T H^T); (H.\tilde{X}) = -\zeta^2$$

$\dot{V}(\tilde{X})$ is negative semi definite unless $H.\tilde{X}= 0$, this is realisable if H and $\tilde{X}$ are orthogonal.

Therefore the system is asymptotically stable provided that H and $\tilde{x}$ are not orthogonal.

Furthermore $V(\tilde{X}) \rightarrow \infty$ as $\tilde{X} \rightarrow \infty$ therefore the null solution $\tilde{X} = 0$ is asymptotically stable in the large.

2.1.2 Electronic design of the tracker

The electronic tracker consists of three main parts.

1. The preamplifiers and filtering stage which consist of buffers, variable-gain amplifiers, 2nd-order Butterworth

Lowpass filters with a cut off frequency of 5.0HZ, overload and underload indicators.

2. This is the signal conditioning stage for generating the signals given by 2'

   It consists of a compute-reset integrator, a track-hold amplifier, a compute-reset amplifier and zero-crossing comparator with exponentially decaying hysteresis.

3. This is the adaptive circuit which implemented equation 3 in the forward path and equation 5 in feedback paths. It consists of two compute hold integrators, four internally trimmed linear multipliers, and a summing amplifier.

2.2 Modelling of the respiratory system (5)

The respiratory system involves the pulmonary system, the circulatory system and the metabolic system.

The pulmonary system includes the airway (trachea, larynx etc ...) and the lung. It starts from the noze and finishes at the alveolar capillary membrane where there is a gas exchange $O_2$ and $CO_2$.

The function of the pulmonary system is to lead the oxygen from noze to the alveolar capillary membrane and to convey the $CO_2$ from this membrane to the outside of the human body during expiration.

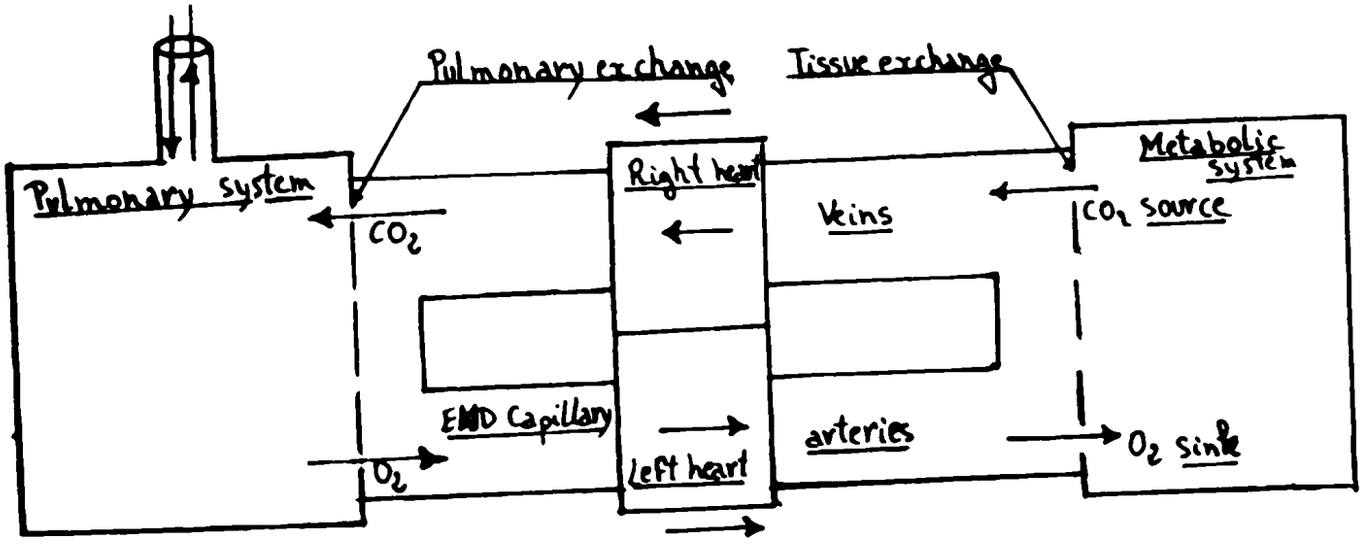
This membrane allows the leakage of $O_2$ to the other side of this membrane (capillary) and permits the diffusion of $CO_2$ in the opposite direction.

The circulatory system involves the right and left heart, the veins and the arteries. The function of this system resembles that of two bus stations connected by two buses moving in opposite direction and driving on two different roads.

The left heart pumps the arterial blood which conveys the $O_2$ from the end capillary to the tissues and the right heart pumps the venous blood which leads the $CO_2$ from the tissues towards the end capillary.

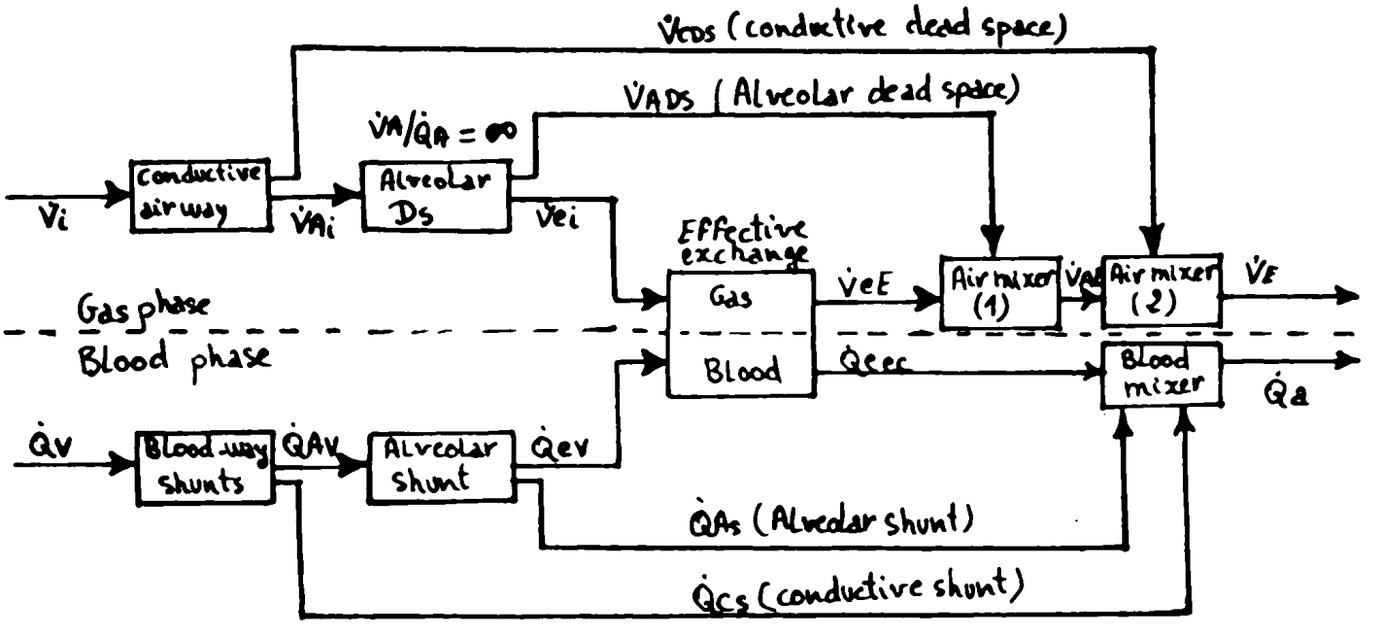
The metabolic system is where the reaction occurs, there the $O_2$ transforms into $CO_2$. So $O_2$ feeds the tissues and the tissues expulse the rubbish which is the $CO_2$.

The figure below clarifies what has been said:




Respiratory gas transport

### 2.2.1 Block diagram of the respiratory system:




The block diagram of the respiratory system comprises two phases, Gas phase and Blood phase.

#### 2.2.1.1 Gas phase:

When a person inspires, his total inspired volume flow ($\dot{V}i$) goes via the conductive airway. One portion of $\dot{V}i$ remains in the conductive airway and it is called conductive dead space ($\dot{V}cds$). The other portion $\dot{V}Ai$ (inspired alveolar volume flow) is at its round divided in two volumes. Alveolar dead space ($\dot{V}Ads$) which avoids the participation in gas exchange, and effective volume flow ($\dot{V}ei$) which undergoes gas exchange

with the blood. Here the effective volume gives oxygen ($O_2$) to the blood and takes $CO_2$.

When this person expires, his expired effective volume flow ($\dot{V}eE$) mixes with $\dot{V}Ads$ and gives the total expired alveolar volume flow ($\dot{V}AE$).

$\dot{V}AE$ will mix with $\dot{V}cds$ during its flow via the conductive airway for finally giving the total expired volume flow which is gas outside the human body.

2.2.1.2 Blood phase:

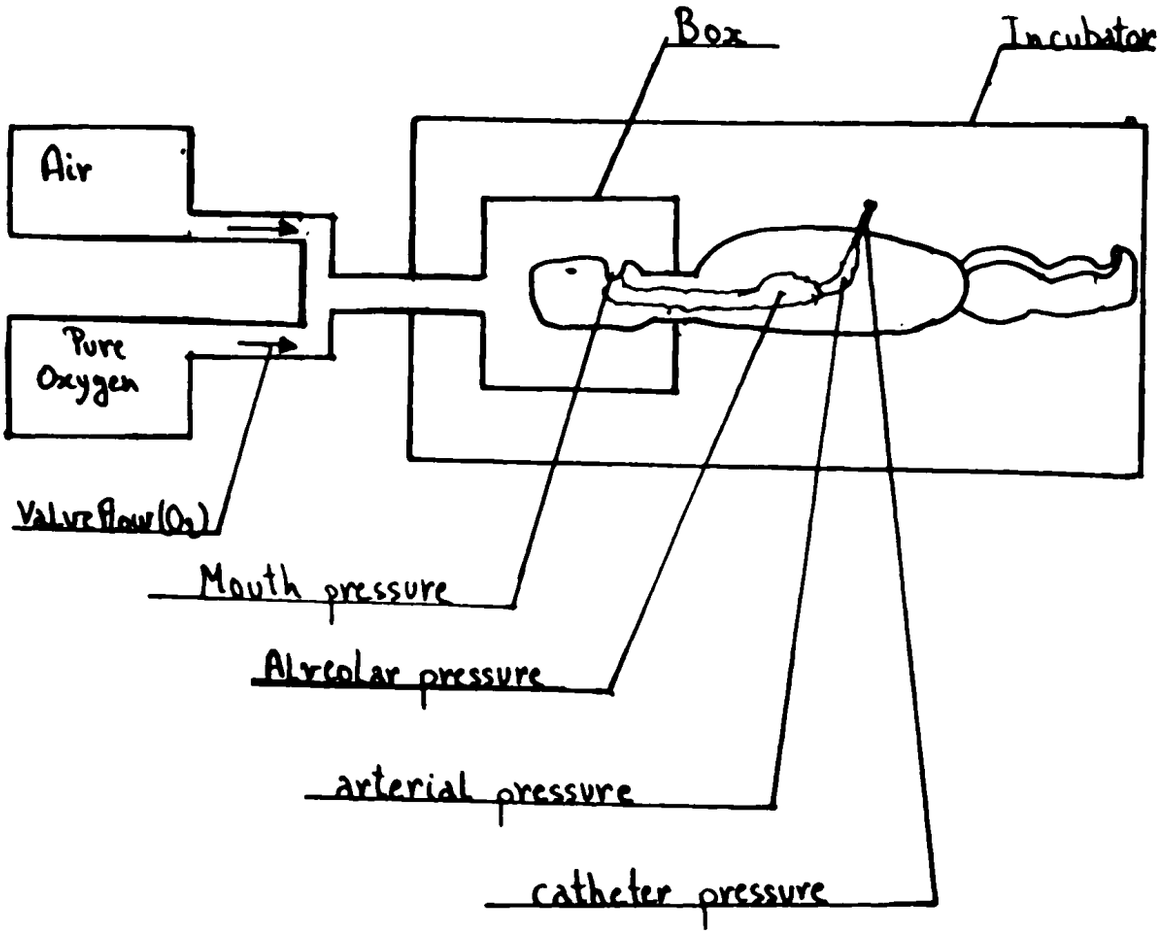
On the other hand the total flow rate venous blood ($\dot{Q}V$) conveys $CO_2$ from the tissues to the alveolar capillary membrane unlike $\dot{V}i$ which conveys $O_2$ to this membrane.

Before reaching this membrane $\dot{Q}V$ is divided on conductive shunt ($\dot{Q}cs$) which by passes the alveoli thoroughly, and alveolar capillary flow ($\dot{Q}Av$).

This latter at his round is divided on two portions. One is the alveolar shunt ($\dot{Q}As$) which reaches nonventilated alveoli and does not participate in the gas exchange unlike the second portion which is called effective blood flow ($\dot{Q}eV$).

After the settlement of the gas exchange the effective and capillary blood flow ($\dot{Q}eec$) which conveys $O_2$ will mix with $\dot{Q}As$ and Qcs in order to give the arterial blood flow ($\dot{Q}a$).

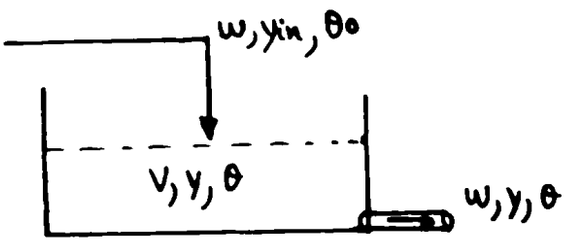
## 2.3 Modelling of the system "valve flow - mouth pressure - Alveolar - Arterial pressure - catheter pressure" (3), (4), (9)




### 2.3.1 Val flow - mouth pressure

Let us denote val flow by V and mouth pressure by $F_1$.

We assume the box is similar to a tank



Where W is the volumetric flow rate of the feed of concentration Yin

$\theta$ is the temperature of the system; $\theta \approx \theta^{\circ}$

V is the volume of the tank

then the material-balance equation is as follow:

$$\frac{V\,dY}{dt} = W(Yin - Y) - V\,Kr\,Y \qquad (1)$$

$$\text{with } Kr = re^{-E/R\theta}$$

where E = energy of activation ) all these are constant
R = gas constant ) for a given system
r = a coefficient )

From 1 we can have

$$\frac{dY}{dt} = \frac{W}{V}(Yin - Y) - Kr\,Y$$

If we take $\frac{W}{V} = K_1$ and $Kr = K_2$ we will get

$kr = k_2$ is related with the transformation of $O_2$ in $CO_2$ by the means of the baby

$k_1$ is related with the valve flow rate.

*Remarks: All concentration until now are partial

Therefore $Cair + CCO_2 + CO_2 = 1$ in the box

from 3 using Laplace transform we will have:

$$SY = K_1 Yin - K_1 Y - K_2 Y$$

$$\text{Therefore } Y(S + K_1 + K_2) = K_1 Yin$$

$$\text{Therefore } Y/Yin = K_1/(S + K_1 + K_2) \qquad (4)$$

If we take into consideration the time delay due to the flow to go through the pipe the transfer function 4 will be

$$Y/Yin = (K_1 e^{-\tau S}) / (S + K_1 + K_2) \quad (5)$$

where $\tau$ is time delay $\tau = 1/V$ where v is the velocity of $O_2$ to travel the pipe of length l

Now we are going to change surroundings from the box area to the baby respiratory area. The notion of concentration partial will have no sense, since we pass from one area to another area. Therefore we must transfer the concentration to the pressure absolute. In order to do that we have to multiply y by $P_1$, where $P_1$ is the total pressure in the box. Multiplying 5 by $P_1$ we will get:

$$\frac{Y P_1}{Yin} = \frac{P_1 K_1 e^{-\tau S}}{S + K_1 + K_2}$$

For computation program purpose, let $\tau$ = T3 and Yin = V

Therefore

$$\frac{F_1}{V} = \frac{P_1 K_1 e^{-T3\,S}}{S + K_1 + K_2} \quad (6)$$

where $F_1 = Y P_1$ is the Pressure in the mouth of the baby

## 2.3.2 Mouth pressure - Alveolar pressure relationship

The alveolar pressure (PA) is related to the mouth pressure by the formula overleaf.

$$\ln\left(1 - \frac{PA}{F_1}\right) = -t/RC \qquad (7)$$

where C is the dynamic compliance and R is the dynamic flow resistance

Therefore, $\frac{PA(t)}{F_1(t)} = 1 - e^{-t/RC}$ for a step response

The Laplace transform is given by

$$\frac{PA(S)}{F_1(S)} = \frac{1}{S} - \frac{1}{S + \frac{1}{RC}} = \frac{1}{S} \cdot \frac{1}{1 + RCS}$$

$$\frac{PA(S)}{F_1(S)} = \frac{1}{S} g(S) \text{ for a step response}$$

For pulse response $\frac{PA(S)}{F_1(S)} = g(S) = \frac{1}{1 + RCS}$ (8)

For Program purpose PA is denoted by $P_3$

Let $RC = T_1$

Therefore $\frac{P_3}{F_1} = \frac{1}{1 + T_1 S}$ (9)

In real life not all the volume of the inspired flow goes straight to the alveolar but there is some which remains in the dead space (trachea etc....) and participates in the expired flow.

Normal person breathes about 600 ml of air and about 200 ml go to the dead space.

Therefore, there is a ratio K = air in the alveolar over air inspired.

$$\text{Therefore} \quad \frac{P_3}{F_1} = \frac{K}{1 + T_1 S} \qquad (10)$$

### 2.3.3 Alveolar pressure - arterial pressure relationship

The equation given the relationship between end capillary oxygen concentration and end capillary oxygen pressure is as follows:

$$CECO_2 = Hb \times Q \times 1.34 + 0.0031 \times PECO_2 \qquad (11)$$

Also the equation relating the arterial pressure and arterial concentration pressure is given by:

$$CaO_2 = Hb \times Q \times 1.34 + 0.0031 \times PaO_2 \qquad (12)$$

Hence the difference between end capillary concentration and arterial oxygen concentration using 11 and 12 is equal to:

$$CECO_2 - CaO_2 = 0.0031(PECO_2 - PaO_2) \qquad (13)$$

This difference is also given by the formula below:

$$CECO_2 - CaO_2 = \frac{\dot{V}O_2}{\dot{Q}t} \quad \frac{\dot{Q}S/\dot{Q}t}{1 - \dot{Q}S/\dot{Q}t} \qquad (14)$$

where $\dot{V}O_2$ is the oxygen consumption

$\dot{Q}S$ is the venous admixture

$\dot{Q}t$ is the cardia output

From 14 and 13 we will have:

$$0.0031\ (PECO_2 - PaO_2) = \frac{\dot{V}O_2}{\dot{Q}t} \quad \frac{\dot{Q}S/\dot{Q}t}{1 - \dot{Q}S/\dot{Q}t} \qquad (15)$$

Let $\frac{\dot{Q}S}{\dot{Q}t} = Sh$ (shunt)

and let $\frac{\dot{V}O_2}{\dot{Q}t}$ = L scater ratio

Therefore $PECO_2 - PaO_2 = \frac{L\ Sh}{1 - Sh} \frac{1}{0.0031}$ (mmHg) =

$= \frac{L\ Sh}{1 - Sh} \frac{1}{0.0031} \frac{1}{7.6}$ (KPa)

$$PECO_2 - PaO_2 = \frac{L\ Sh}{1 - Sh} 42.4448 \qquad (16)$$

Or $PECO_2 = PAO_2 - 1$ (mmHg) (17) and 1 mmHg = 0.1316 KPa

Therefore $PAO_2 - 0.1316 - PaO_2 = \frac{L\ Sh}{1 - Sh} 42.4448$

Therefore $PaO_2 = PAO_2 - \frac{L\ Sh}{1 - Sh} 42.4448 - 0.1316$ (18)

The shunt (Sh) deals with the state of the baby

For a normal baby or normal man, Sh varies from 0.01 to 0.1 at most.

For a baby with RDS Sh varies from 0.3 to 0.5.

The parameter L depends a lot from the inspired oxygen concentration.

2.3.3.1 Choice of L

L can be chosen by two methods.

2.3.3.1.1 Using a formula 19

$$R = \frac{\dot{V}CO_2}{\dot{V}O_2}$$

R is the respiratory exchange ratio

$\dot{V}$ is the gas volume per unit time

$$\frac{\dot{V}A}{\dot{Q}} = 8.63 \quad \frac{(C\bar{V}O_2 - CaCO_2)}{PACO_2}$$

where $\dot{V}A$ is the means expired alveolar ventilation

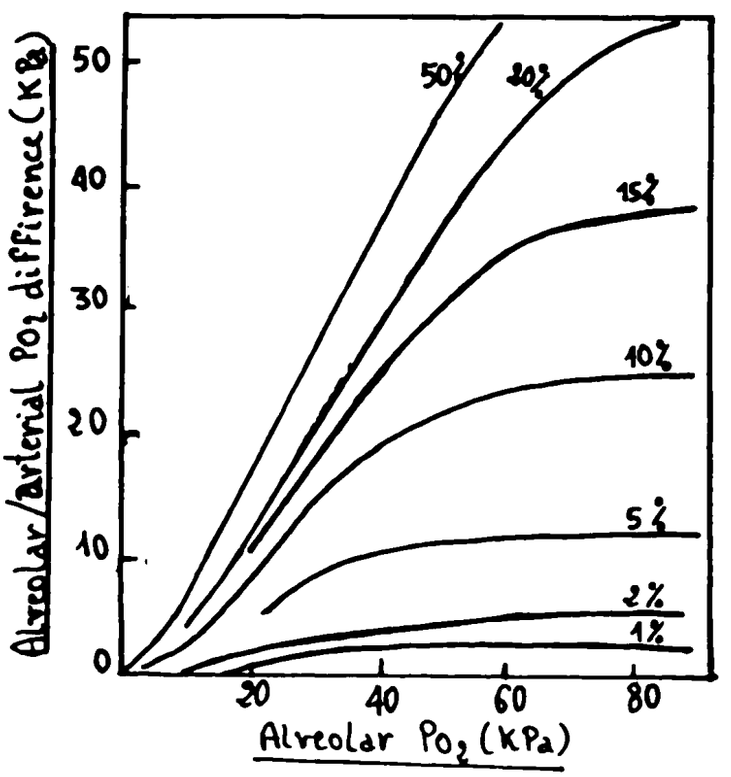
or $L = \frac{\dot{V}O_2}{\dot{Q}}$ and if we assume that $\dot{V}A \approx \dot{V}CO_2$, then

$$L = \frac{\dot{V}CO_2}{\dot{Q}R} = L = \frac{\dot{V}A}{\dot{Q}R} = (8.63) \quad \frac{(C\bar{V}CO_2 - CaCO_2)}{(R)\,(PA.CO_2)} \qquad (19)$$

where $C\bar{V}CO_2$ is the concentration of $CO_2$ in mixed venous.
In this method there is a lot of variables unknown, hence we leave this method.

2.3.3.1.2 <u>Using a graph</u>

I deduce L from the graph below:



this curve gives $PAO_2 - PaO_2$ as a function of $PAO_2$

$$PAO_2 - PaO_2 = f(PAO_2)$$

or equation 18 is: $PaO_2 = PAO_2 - [L\ Sh/(1-Sh)]x\ 42.4448 - 0.1316$

Therefore, $PAO_2 - PaO_2 = [L\ Sh/(1-Sh)]x\ 42.4448 + 0.1316$ 18

For Sh = 50% 18 gives $PAO_2 - PaO_2 = Lx42.4448 + 0.1316$

or from the graph we notice for Sh = 0.5 that: $PAO_2 - PaO_2 = cst\ PAO_2$

and in this case cst deduced from the curve, is 0.7

Therefore, for Sh = 0.5, $L = \frac{0.7}{42.4448}\ PAO_2$

for Sh = 0.01 we have $PAO_2 - PaO_2 = L\ 0.01\ x\ 42.4448 + 0.1316$

if we take also $L = \frac{0.7}{42.4448}\ PAO_2$ we will have

$$PAO_2 - PaO_2 = 0.007\ PAO_2 + 0.1316$$

So for larger Sh and smaller Sh this deduction is efficient but for Sh medium, it will be like we take the tangent of the curves.

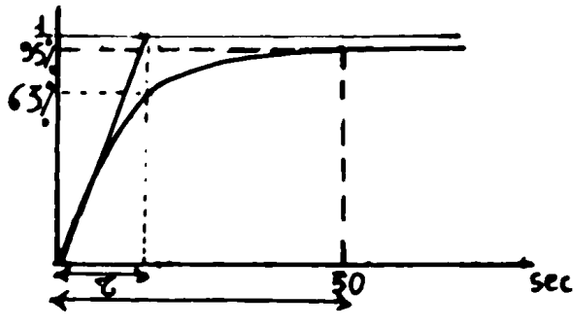
For program purposes we label $PaO_2$ by $P_5$

$$P_5 = P_3 - [L\ Sh/(1-Sh)]x\ 42.4448 - 0.1316 \qquad 20$$

with $L = \frac{0.7}{42.4448}\ x\ P_3$

### 2.3.4 Arterial Pressure - cath. pressure.

The catheter which we use takes about 50s to stabilise $[Pc(t)/Pa(t)] = 1 - e^{-t/\tau}$ for a domaine time.




By Laplace transform we will have

$$\frac{Pc(S)}{Pa(S)} = \frac{1}{S}\cdot\frac{1}{S+1/\tau} = \frac{1}{S}\cdot\frac{1}{S\tau+1}$$

For a pulse response $\dfrac{Pc(S)}{Pa(S)} = \dfrac{1}{S\tau+1}$

For program using, take Pc as $P_6$ and $\tau$ as $T_4$

$$\frac{P_6}{P_5} = \frac{1}{ST_4 + 1} \qquad (21)$$

### 2.3.5 Valve flow - cath. pressure relationship.

$$\frac{P_3}{V} = \frac{F_1}{V}\times\frac{P_3}{F_1} = \frac{P_1 k_1 e^{-T3}}{S + k_1 + k_2}\cdot\frac{K}{1 + T_1 S}$$

$$P_5 = P_3 - [L\,Sh/(1-Sh)]\times 42.4448 - 0.1316$$

$$P_5 = \frac{VK}{1+T_1 S}\cdot\frac{P_1 k_1 e^{-T3}}{S+k_1+k_2} - \frac{L\,Sh \times 42.4448 - 0.1316}{1-Sh}$$

$$P_6 = \frac{1}{ST_4 + 1} P_5$$

$$P_6 = \left[\frac{K_1}{1+T_1 S}\left(\frac{P_1 K_1 e^{-T3}}{S + K_1 + K_2} - \frac{V}{1-Sh}\right)\right]\frac{L\ Sh \times 42.4448 - 0.1316}{ST_4 + 1}$$

with $L = (0.7/42.4448)\ P_3$

2.3.6 Approximation of the Parameter value

$P_1$ : is the total pressure in the vicinity of the mouth (KPa)

$P_1 \approx 1\ atm = 10^5\ Pa = 100\ KPa$

T1 = RC (compliance x resistance) in second

T1 = 0.05 sec for baby with RDS and may vary little bit from baby to baby.

T3 = is the delay due to the oxygen to traverse the pipe

$$T3 = \frac{1}{v}\ (\text{in second}) \quad ; \quad T3 \approx 0.5\ sec$$

$K_1 = \frac{w}{v}$ flow rate over volume of the box; its unit is:

ml/ml sec = 1/sec

$$k_1 = \frac{10}{60x2} \quad 0.08\ sec^{-1}$$

$k_2$ = Kr shows us the degree of the reaction by sec = $(sec^{-1})$

$$k_2 \approx \frac{0.234}{0.275}\left(\frac{\dot{V}CO_2}{\dot{V}O_2}\right)\frac{1}{60} \approx 0.014\ sec^{-1}$$

K is the ratio between $\frac{\dot{V}O_2 \text{ used (consumption)}}{\dot{V}O_2 \text{ inspired}}$

$$\approx \frac{400}{600} \approx 0.667$$

$T_4$ is time cst for the catheter to reach 63% of the arterial pressure

we have $\frac{PC}{Pa} = 1 - e^{-t/T4}$

For t = 50s: $\frac{Pc}{Pa} \approx 0.95$

$0.95 = 1 - e^{-50/T4}$ Therefore $1 - 0.95 = 0.05 = e^{-50/T4}$

Therefore $\text{Log } 0.05 = -\frac{50}{T4}$

Therefore T4 = - 50/Log 0.05 = 16.69 sec

2.4 Influence and importance of the respiratory frequency, inspiration expiration (I : E) ratio and peak airway pressure (3), (10)

In babies with RDS, it was demonstrated that the improvements in arterial $PO_2$ could be achieved by slowing the respiratory frequency, raising in peak airway pressure, increasing the relative duration of inspiration (I : E) ratio, increasing inspired oxygen concentration and use of a positive end-expiratory.

The improvement in oxygenation from the use of a high I : E ratio and positive end-expiratory pressure can be explained

by the lung being held open for a major part of the breathing cycle.

The increase of I : E ratio is usually the more effective in severe case of surfactant deficiency, because the opening pressure of large parts of the lungs is beyond the reached of a practicable end-expiratory pressure.

However the use of a prolonged inspiratory phase and end-expiratory is safe only when the lung compliance is very low. Because in the recovering phase of RDS the transmission of the ventilator pressure to extrapulmonary, intrathoracic structures slows down the venous return and reduces cardia output. Hence the use of a prolonged I : E ratio and end-expiratory pressure are inappropriate and may embarrass the circulation.

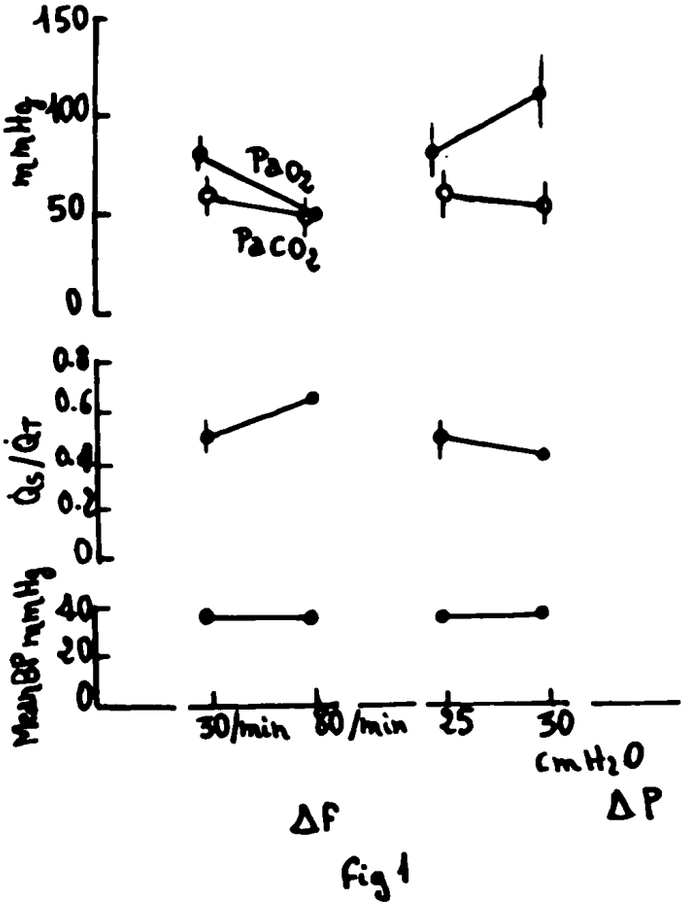



fig 1

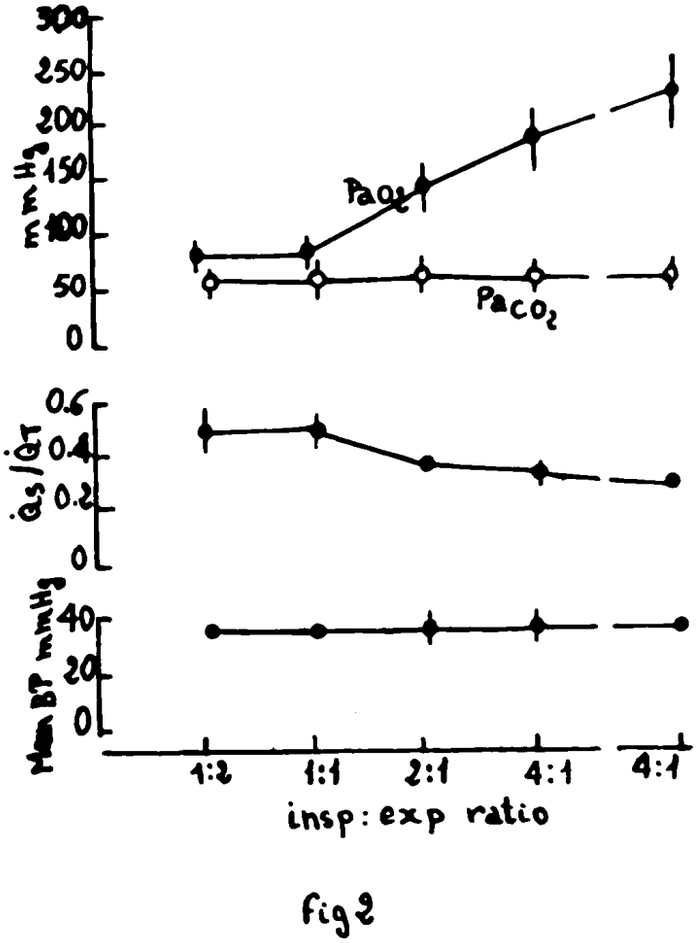



fig 2

Fig 1 shows us the effect of varying respiratory frequency and peak airway pressure on arterial oxygen tension ($PaO_2$), calculated right - to left shunt ($\dot{Q}S/\dot{Q}T$) and mean arterial blood pressure (MBP).

Fig 2 illustrates the effect of altering I : E ratio on arterial blood pressure, right-to-left shunt, and mean arterial blood pressure.

# Chapter Three

## Simulation Results

### 3.1 Computer Simulation Program

This program will simulate the whole system starting from the valve flow taking as input and finishing at the catheter taking as output.

The equation of the whole system to simulate is given by 22 in 2.3.5; and all the constant parameters ($P_1$, $K_1$, $K_2$, $T_3$, $T_1$, $T_4$, K) are given and define in 2.3.6.

This program is running for different values of the shunt (S) and val-flow (V) which are defined also in chp 2, and it simulates the valve flow, the mouth pressure, alveolar pressure, arterial pressure and catheter pressure. The unit taken for the all pressure is the (KPa) Kilo Pascal.

Remarks: In clinical work the catheter measurement unit is the volt.

The catheter is a sort of apparatus which transforms the pressure into voltage.

The relationship between the voltage and the catheter pressure is linear.

The starting point for the mouth pressure and alveolar pressure is taken as 10KPa and the arterial pressure and catheter pressure is taken as 3.4KPa unless the value of the shunt is less than 0.3 where both of the arterial and catheter pressure have the starting point as 10KPa.

Also the computer program will give the statics pressure for all the simulating variables after 50s of running program.

```
 10 PAGE
 20 PRINT "MODELLING OF THE SYSTEM; INCUBATOR-HUMAN
    RESPIRATORY"
 30 PRINT
 40 PRINT
 50 PRINT
 60 REM: MODELLING OF THE SYSTEM INCUBATOR - RESPIRATORY
    SYSTEM
 70 REM: INITIALISATION
 80 LET @1=50
 90 LET F1=P3=10
100 LET P5=P6=3.4
110 REM; STORRING OF THE PARAMETERS
120 READ P1,K1,K2,T3,T1,T4,K
130 REM: STORRING OF THE PARAMETERS
140 DATA 100,8.00000E-02,1.40000E-02,.5,5.00000E-02,16.69,
    .667
150 LET T=Y0=0
160 DIM (100)
170 REM: N MUST BE LESS THAN 100
180 LET N=M2=5
190 LET @0=.1
200 REM: DELAY=N*@0
210 MAT A=ZER
220 LET M1=1
230 PRINT "INPUT S"
240 INPUT S
250 IF S>.5 THEN STOP
260 IF S<.3 THEN LET P5=P6=10
270 PRINT "INPUT THE VAL FLOW (V)"
280 PRINT "NOTICE V IS BETWEEN 0 AND 1"
290 INPUT V
300 PAGE
310 LET T=0
320 FOR B=0 TO 50 STEP 10
330 LINE B,2.00000E-02,B,-2.00000E-02
340 ANNOT B,-5.00000E-02,B
350 NEXT B
360 ANNOT 45,-5.00000E-02,"SEC"
370 FOR C=0 TO 1 STEP .1
380 LINE -.8,C,.8,C
390 ANNOT -4,C,C*100
400 NEXT C
410 ANNOT .1,1,"KPA"
420 ANNOT -45, .8,"P1=";P1;"KPA"
430 ANNOT -45, .7,"K1=";K1
440 ANNOT -45, .6,"K2=";K2
450 ANNOT -45, .5,"T3=";T3
460 ANNOT -45, .4,"T1=";T1
470 ANNOT -45, .3,"T4=";T4
480 ANNOT -45, .2,"K=";K
490 ANNOT -45, .1, "SHUNT (S)=";S
```

```
500 ANNOT -45, 0,"VAL FLOW(V)=";V
510 DYNAMIC
520 EQUATIONS
530 INDVAR T
540 REM: V IS THE VALVE FLOW, F1 IS THE INSIRED FLOW
550 REM: P3 IS THE ALVEOLAR PRESSURE, P5 IS THE ARTERIAL
    PRESSURE
560 REM: P6 IS THE CATHETER PRESSURE ON KPA
570 DER F1=F2
580 F2=-F1*(K1 + K2) + YO
590 DER P3=P4
600 P4=(F1*K-P3)/T1
610 L=(.7/42.4448)xP3
620 P5=(P3-L*S*42.4448/(1-S))-.1316
630 DER P6=((P5/T4)-(P6/T4)
640 Y=V*P1*K1
650 DISPLAY V,F1/100,P3/100,P5/100,P6/100
660 EQUEND
670 IF T>@1 THEN GOTO 750
680 LET YO=A(M1)
690 LET M1=M1+1
700 IF M1>15 THEN LET M1=1
710 LET A(M2)=Y
720 LET M2=M2+1
730 IF M2>15 THEN LET M2=1
740 DYNEND
750 ANNOT 25,V,"V(%)=";*100
760 ANNOT -45,-.5,"VAL FLOW","MOUTH PRE","ALV PRE","ART
    PRE", "CATH PRE"
770 ANNOT -45,-.6,V,F1,P32,P5,P6
780 FOR B=0 TO 50 STEP 10
790 LINE B,2.00000E-02,B,-2.00000E-02
800 ANNOT B,-5.00000E-02,B
810 NEXT B
820 REM: REINITIALISATION
830 LET F1=P3=10
840 LET P5=P6=3.4
850 PRINT "PRESS NOMBER LESS THAN 5 TO CONT"
860 INPUT Z
870 IF Z>5 THEN STOP
880 PAGE
890 GOTO 230
```

### 3.2 Computers simulation results

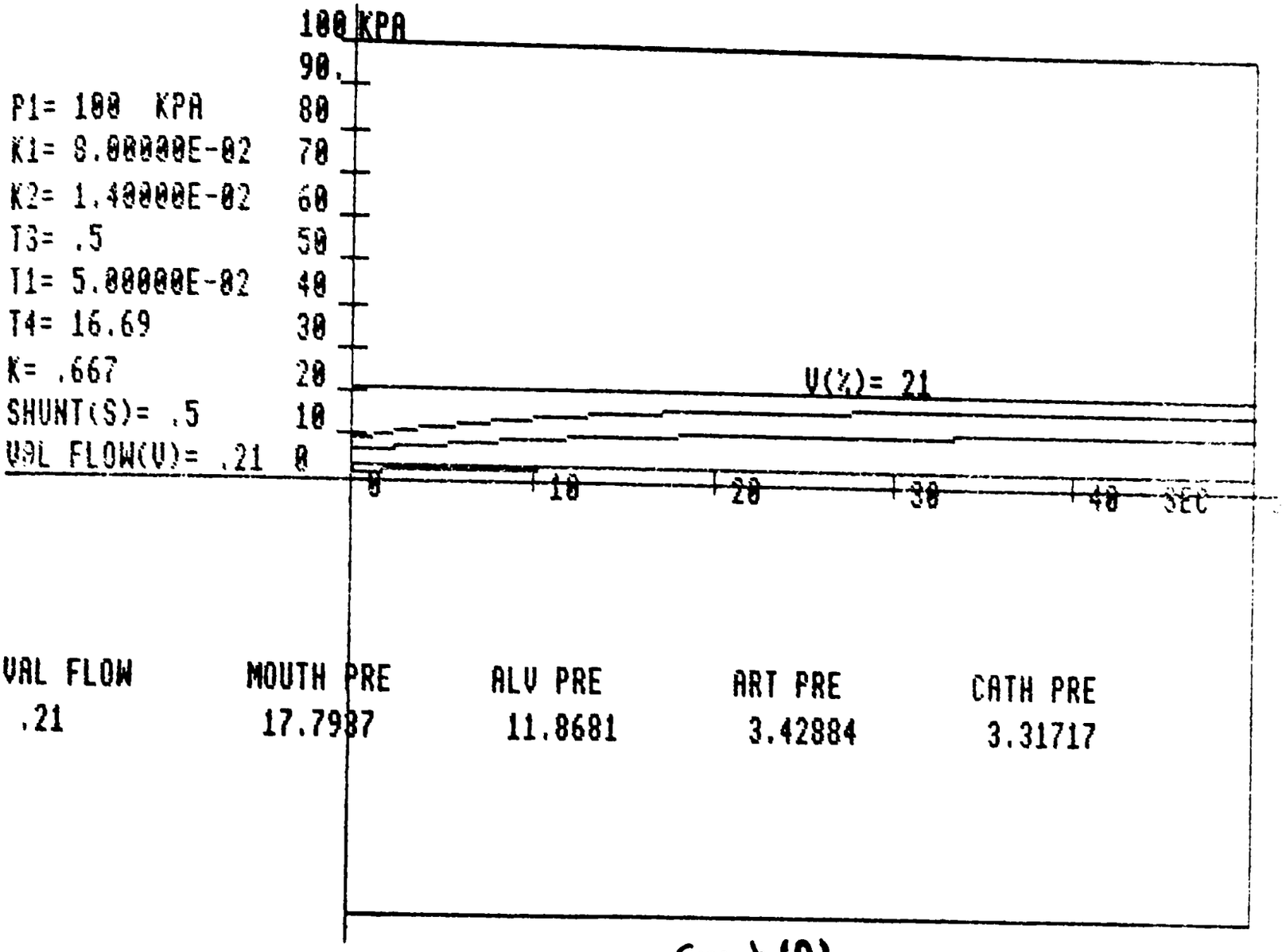
The results for arterial pressure for a given value of the shunt (Sh) and valflow (V) is as follows:

→ ventilation increases with RDS →

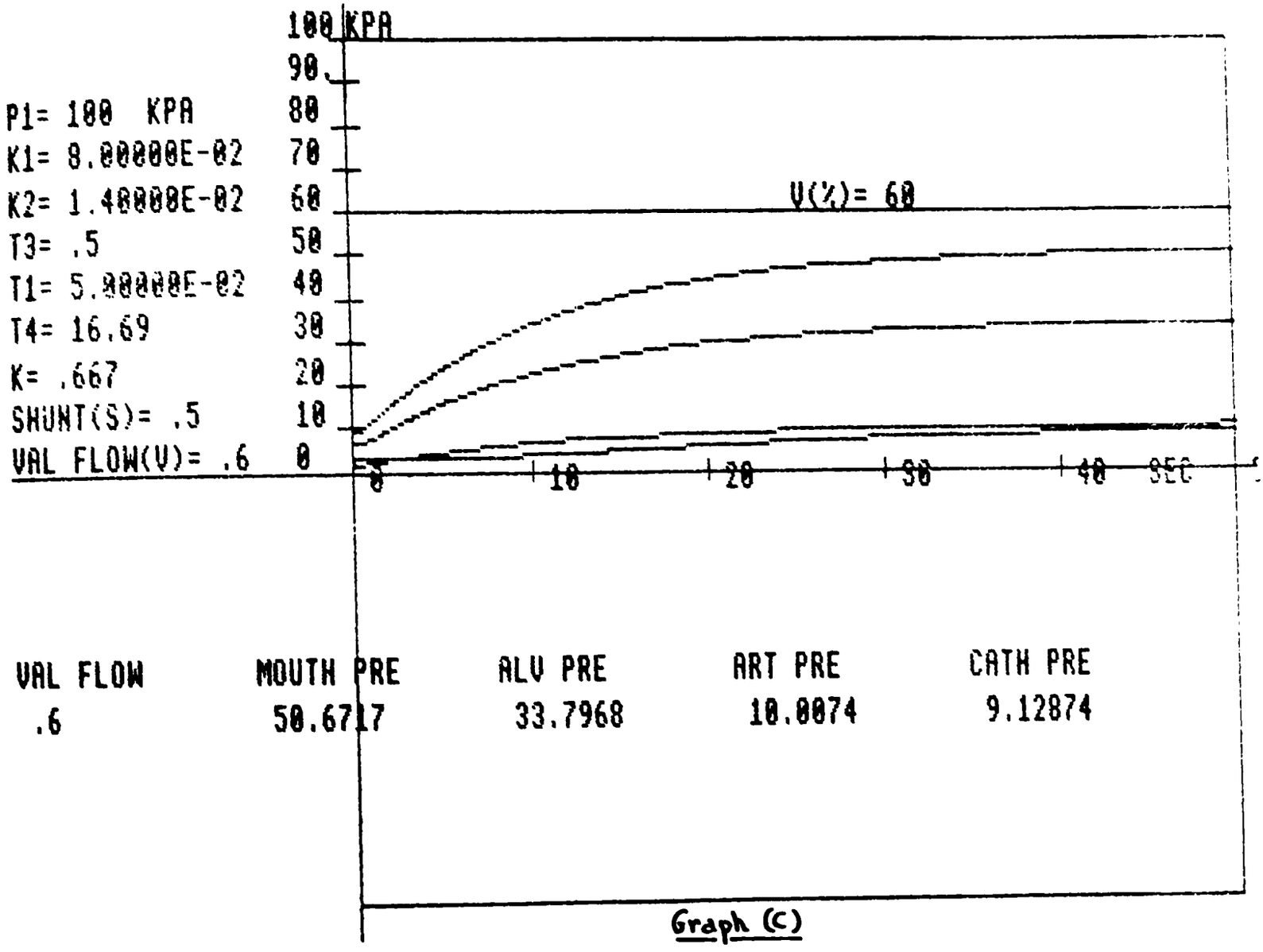
shunt decreases when the babies recover from RDS ↓

| Shunt (Sh) \ Valve flow (V) | without ventilation 0.21 | with ventilation 0.3 | with ventilation 0.35 | with ventilation 0.4 | with ventilation 0.6 | with ventilation 0.7 | with ventilation 0.95 |
|---|---|---|---|---|---|---|---|
| 0.5 | Graph (A) 3.42884 | | Graph (B) 5.79038 | | Graph (C) 10.0078 | Graph (D) 11.6943 | Graph (E) 15.9113 |
| 0.4 | | | | Graph (F) 11.8958 | | | |
| 0.3 | | Graph (G) 11.7184 | | | | Graph (H) 27.4621 | |
| 0.2 | Graph (I) 9.65961 | | Graph (J) 16.1539 | | | | |
| 0.01 | Graph (K) 11.6526 | | | | | Gragh (L) 39.0092 | |

Arterial pressure values (KPA) after 50 sec of running Program

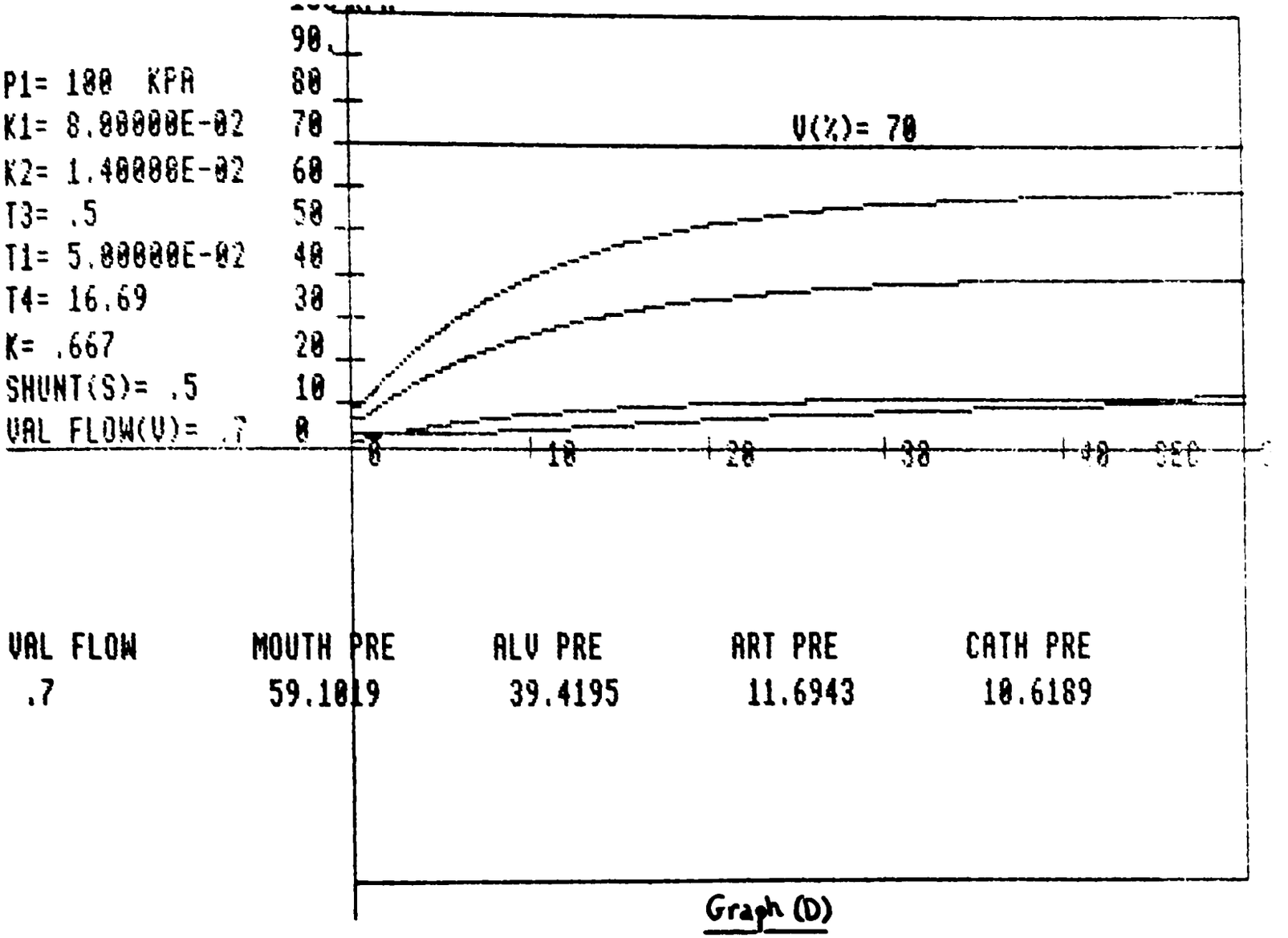

100 KPA
90.
80
70
60
50
40
30
20
10
0
P1= 100 KPA
K1= 8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= .5
VAL FLOW(V)= .21
V(%)= 21
0
10
20
30
40
SEC
VAL FLOW
.21
MOUTH PRE
17.7987
ALV PRE
11.8681
ART PRE
3.42884
CATH PRE
3.31717

Graph (A)

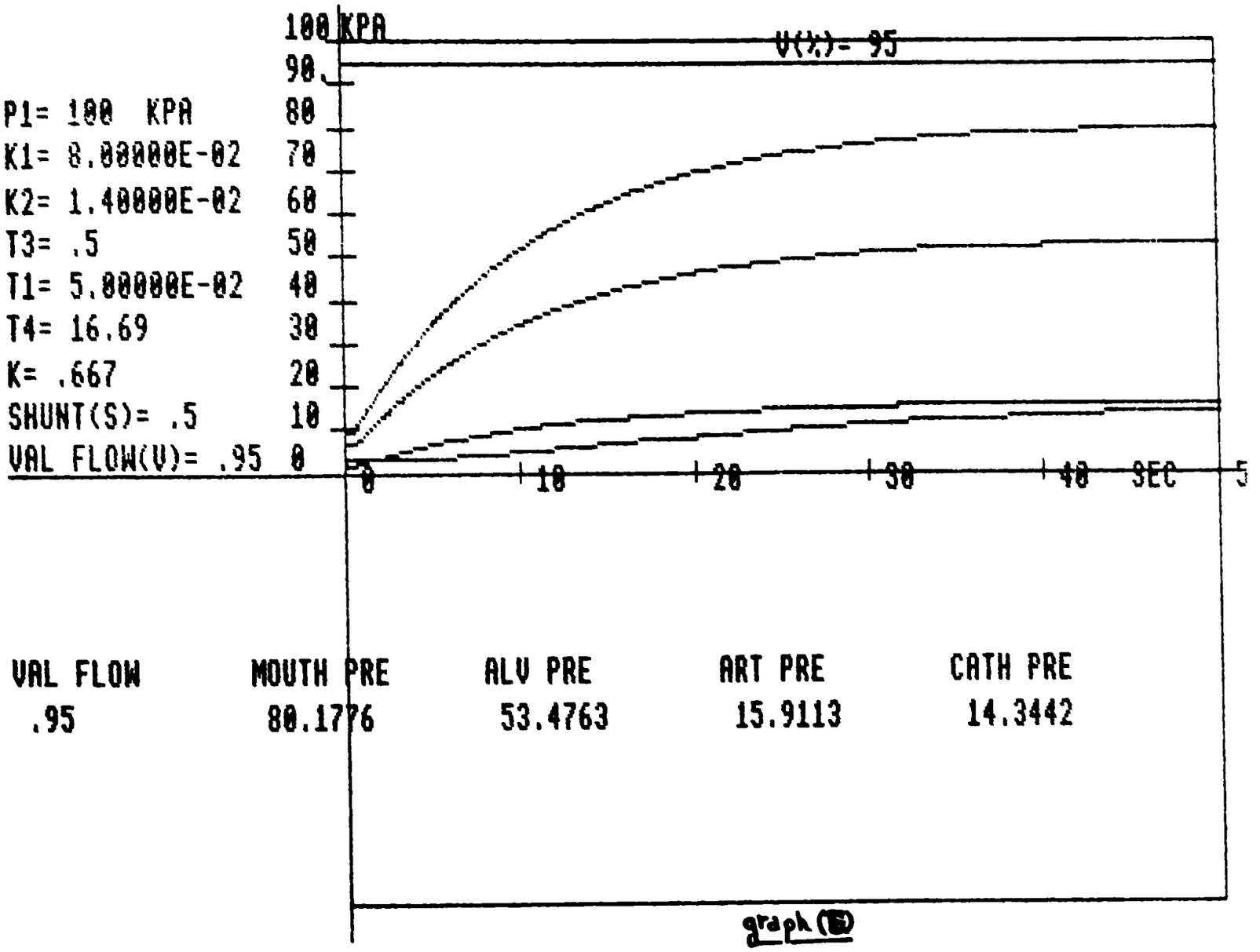



| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .6 | 50.6717 | 33.7968 | 10.0074 | 9.12874 |

Graph (C)

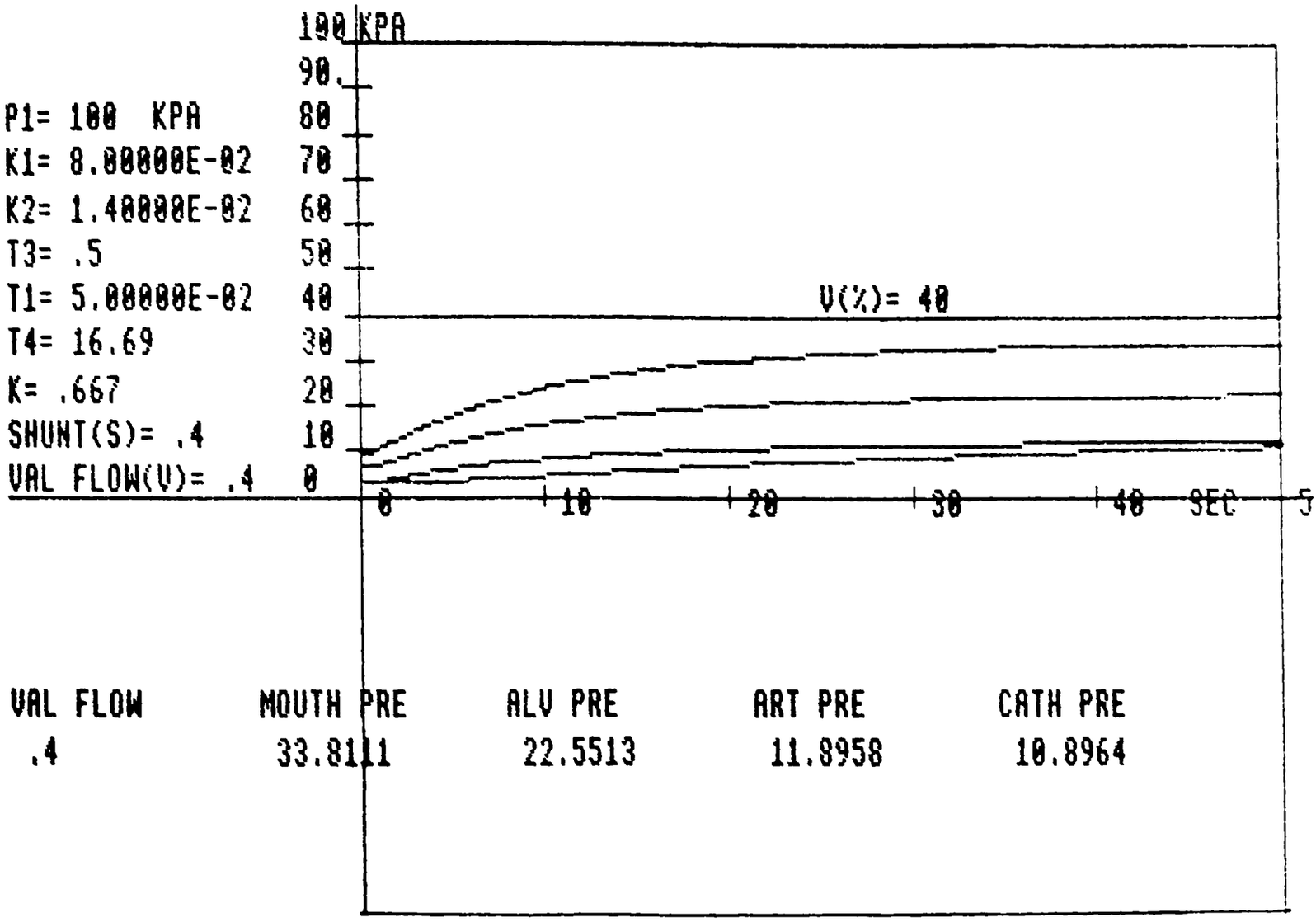

P1= 100 KPA
K1= 8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= .5
VAL FLOW(V)= .7
90
80
70
60
50
40
30
20
10
0
V(%)= 70
0
10
20
30
40
VAL FLOW
MOUTH PRE
ALV PRE
ART PRE
CATH PRE
.7
59.1019
39.4195
11.6943
10.6189

Graph (D)



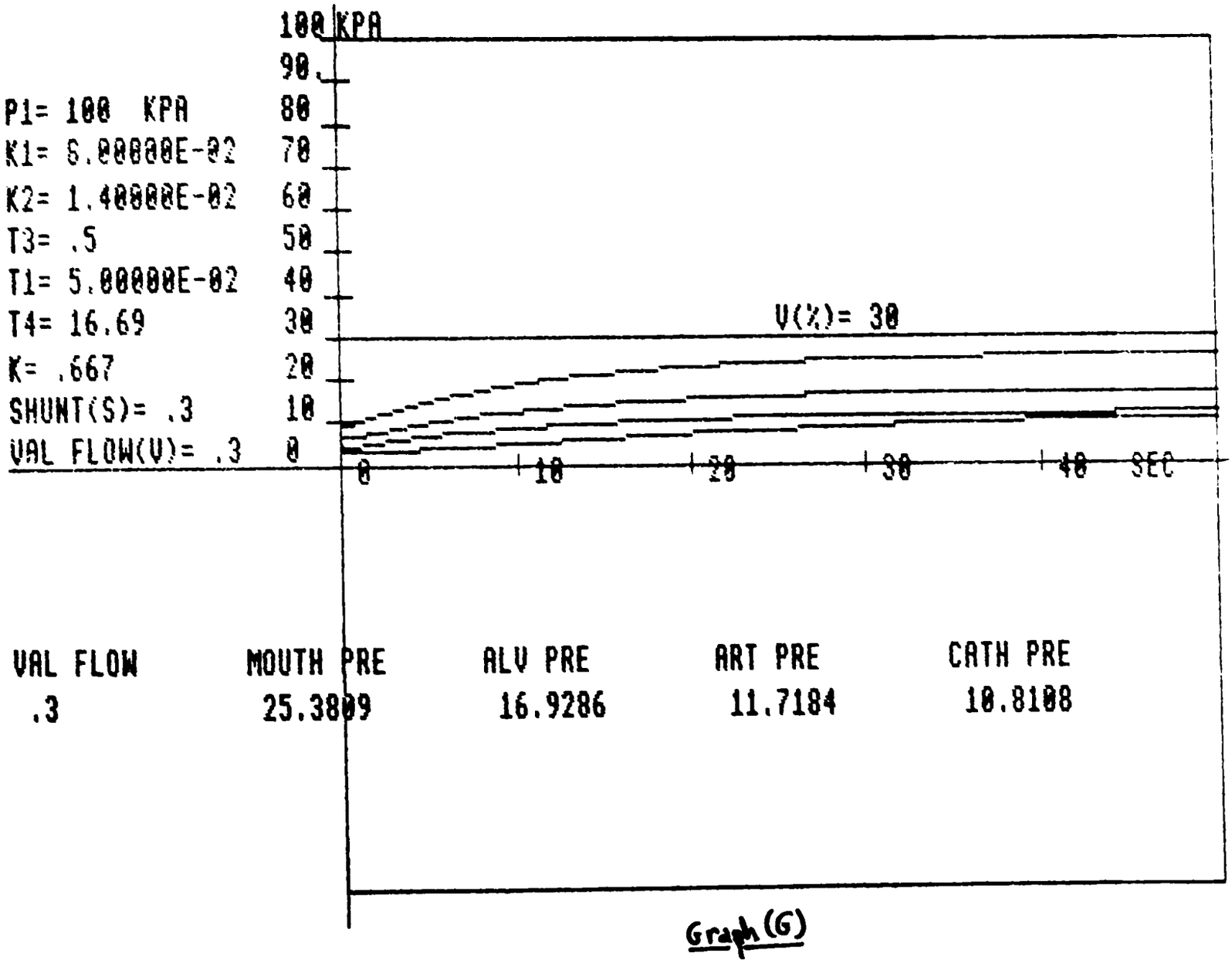

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .95 | 80.1776 | 53.4763 | 15.9113 | 14.3442 |

graph (15)



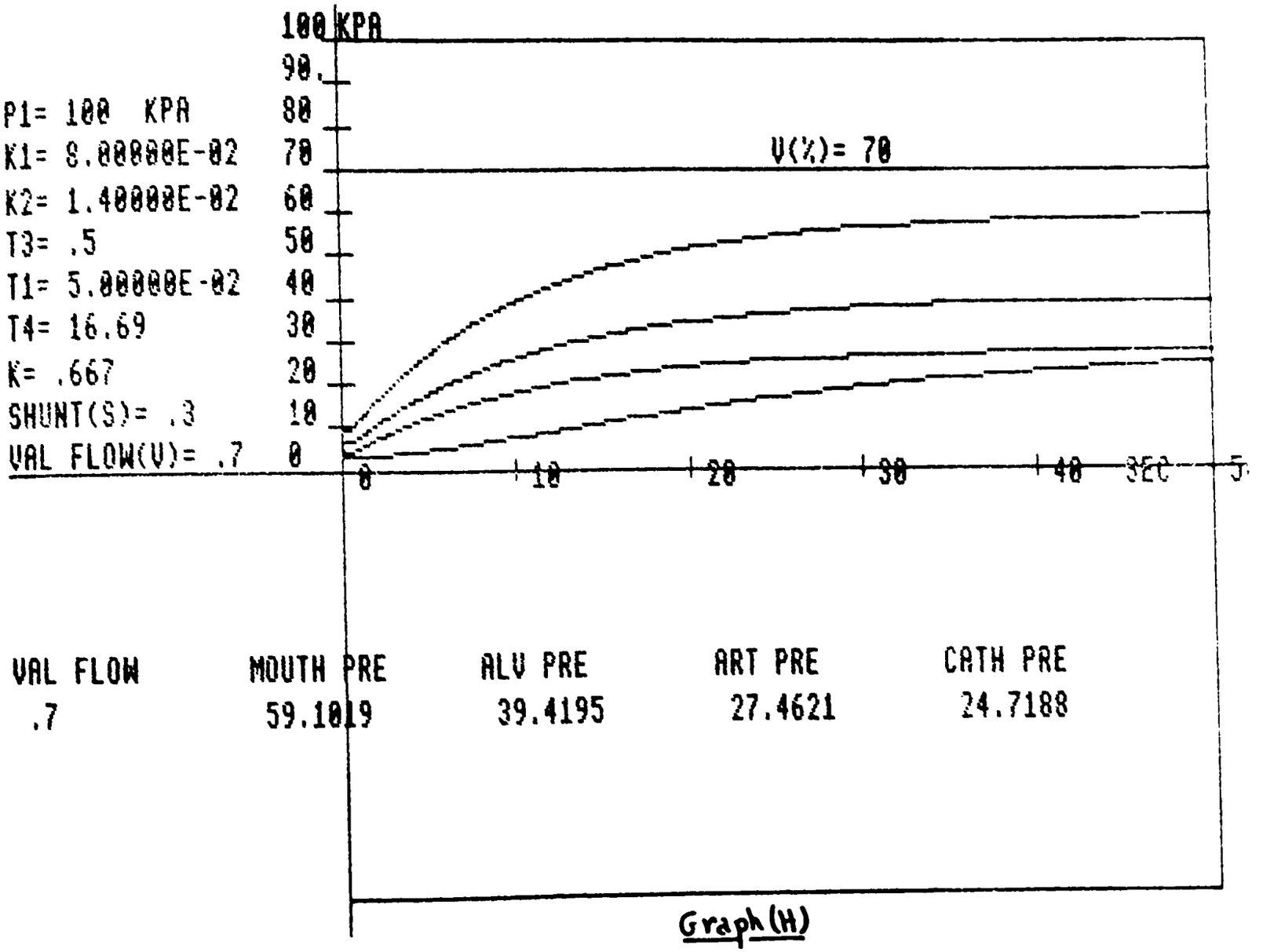

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .4 | 33.8111 | 22.5513 | 11.8958 | 10.8964 |

graph (F)



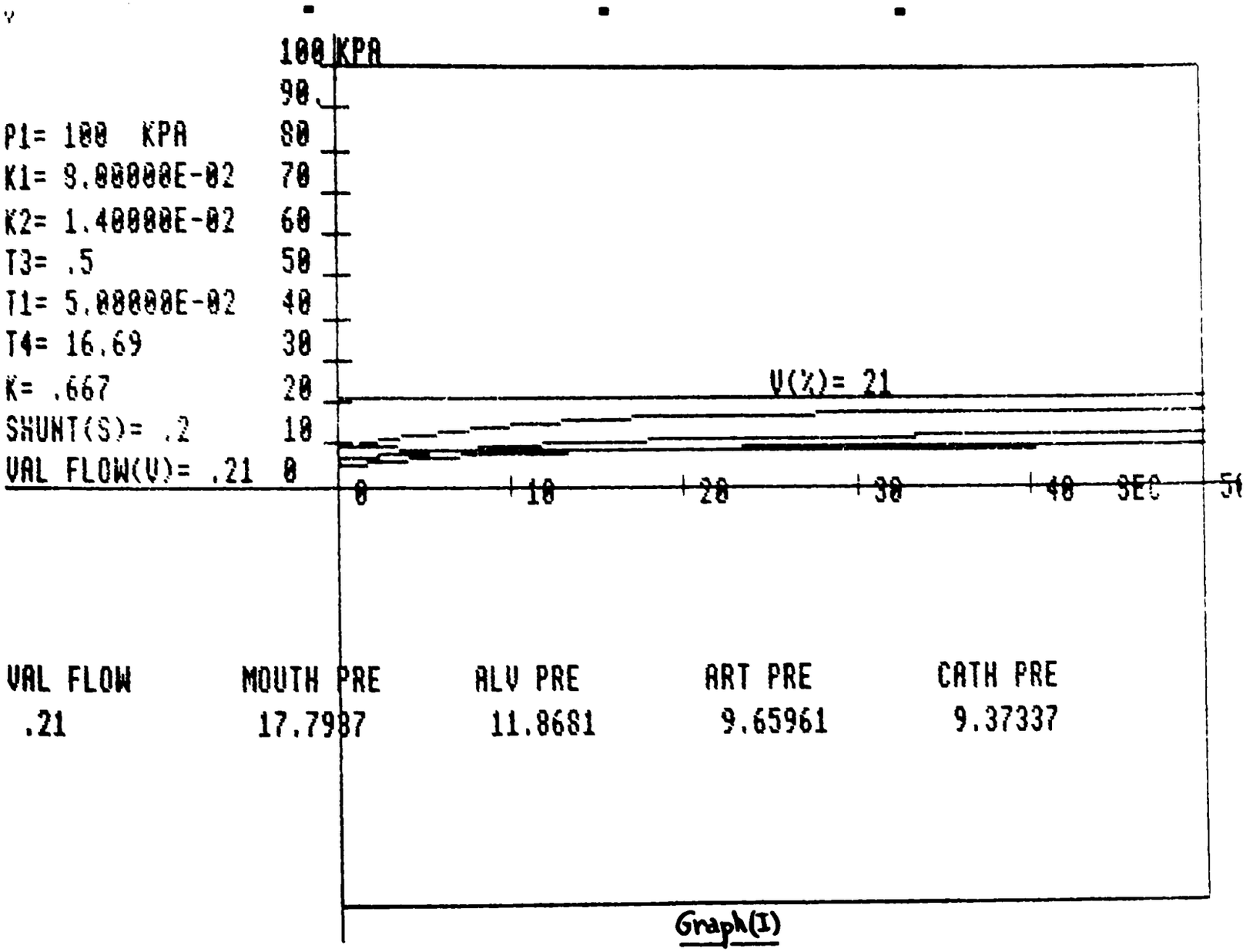

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .3 | 25.3809 | 16.9286 | 11.7184 | 10.8108 |

Graph (G)

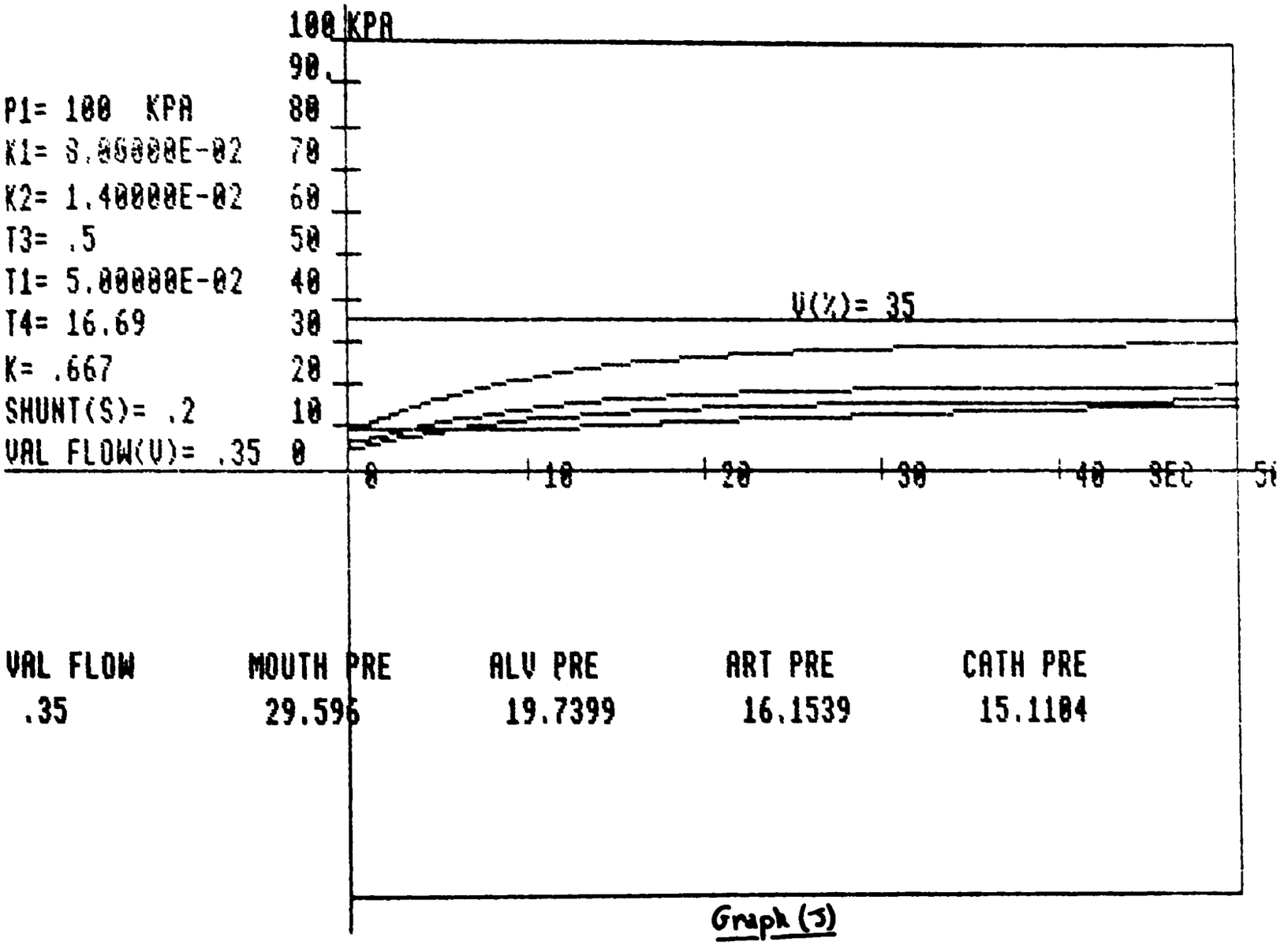



| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .7 | 59.1019 | 39.4195 | 27.4621 | 24.7188 |

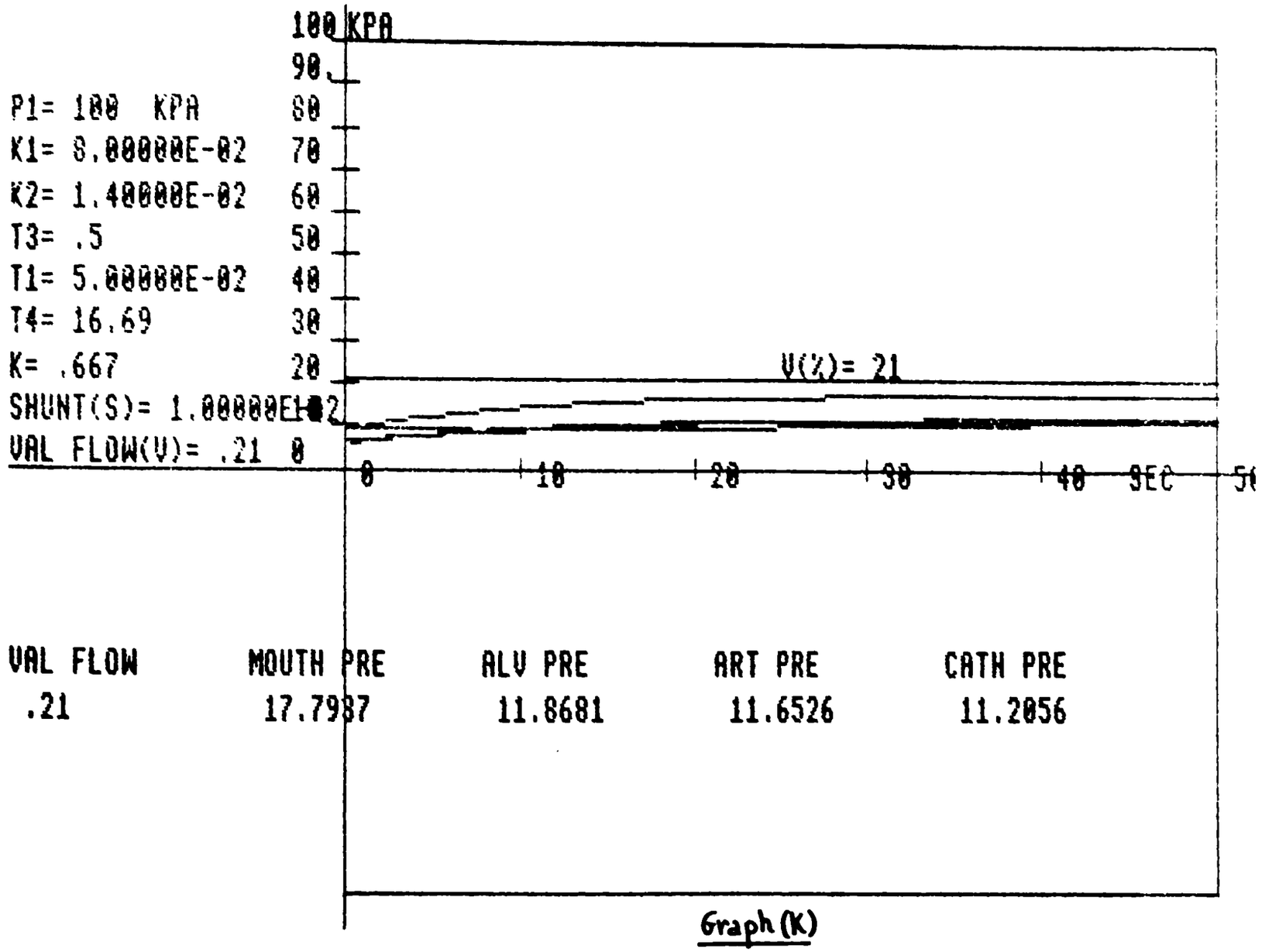
Graph(H)


100 KPA
90
80
70
60
50
40
30
20
10
0
P1= 100 KPA
K1= 9.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= .2
VAL FLOW(V)= .21
V(%)= 21
10
20
30
40
SEC
VAL FLOW
MOUTH PRE
ALV PRE
ART PRE
CATH PRE
.21
17.7987
11.8681
9.65961
9.37337

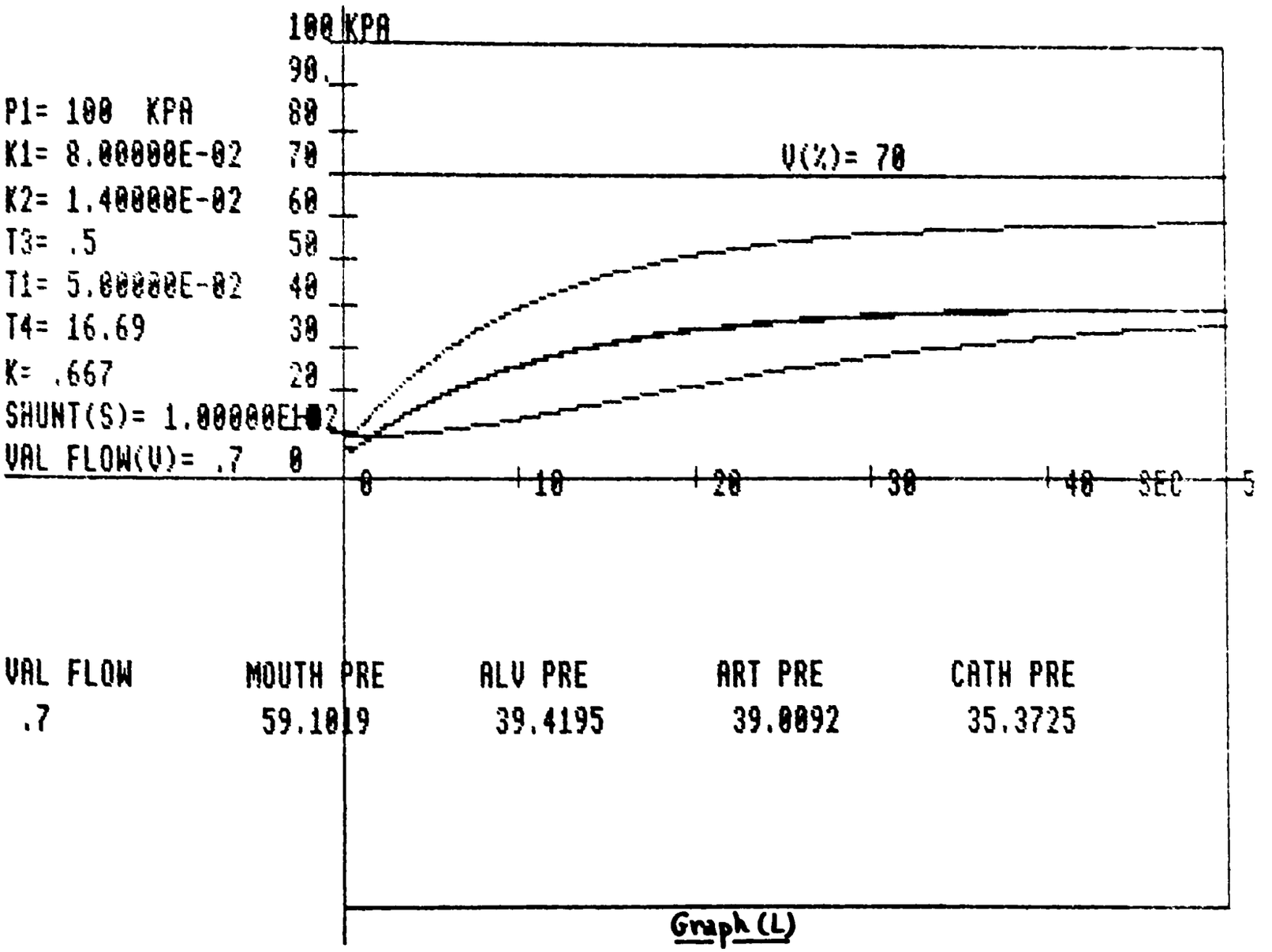
Graph(I)


100 KPA
90
80
70
60
50
40
30
20
10
0
P1= 100 KPA
K1= 3.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= .2
VAL FLOW(V)= .35
V(%)= 35
0
10
20
30
40
SEC
VAL FLOW
.35
MOUTH PRE
29.596
ALV PRE
19.7399
ART PRE
16.1539
CATH PRE
15.1104

Graph (3)


100 KPA
90
80
70
60
50
40
30
20
0
P1= 100 KPA
K1= 8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= 1.00000E+02
VAL FLOW(V)= .21
V(%)= 21
10
20
30
40
SEC
VAL FLOW
.21
MOUTH PRE
17.7987
ALV PRE
11.8681
ART PRE
11.6526
CATH PRE
11.2056

Graph (K)


100 KPA
90
80
70
60
50
40
30
20
10
0
P1= 100 KPA
K1= 8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= 16.69
K= .667
SHUNT(S)= 1.00000E-02
VAL FLOW(V)= .7
V(%)= 70
0
10
20
30
40
SEC
VAL FLOW
MOUTH PRE
ALV PRE
ART PRE
CATH PRE
.7
59.1019
39.4195
39.0092
35.3725

Graph (L)

**Conclusion:** When the baby suffers from RDS we have to supply him with oxygen. In that case we have to increase the valve oxygen flow until his arterial pressure reaches 10KPa.
Arterial pressure less than 8KPa or more than 12KPa, is a diagnostic of a baby which is in a dangerous state.
The less or the more arterial pressure reflects that the baby is getting worse. When the baby is recovering from RDS (his shunt is decreasing) we have to decrease the valve oxygen flow (always the valve oxygen flow value must correspond to an arterial pressure about 10KPa).
**Remarks:** the shunt value is a kind of tool which notify us about the baby state. It shows us how much the baby suffers from RDS. The more this value is big the more the baby suffers from RDS.

# Chapter Four

## Simulation of Astron controller

4.1 Diagram block of the whole system (Astron controller + the system valveflow - catheter-pressure). We use the Astron controller in order to control the oxygen valve flow by increasing or by decreasing its level according to oxygen valve flow value needed to stabilise the arterial pressure at 10KPa.

The Astron controller equation used is as follows:

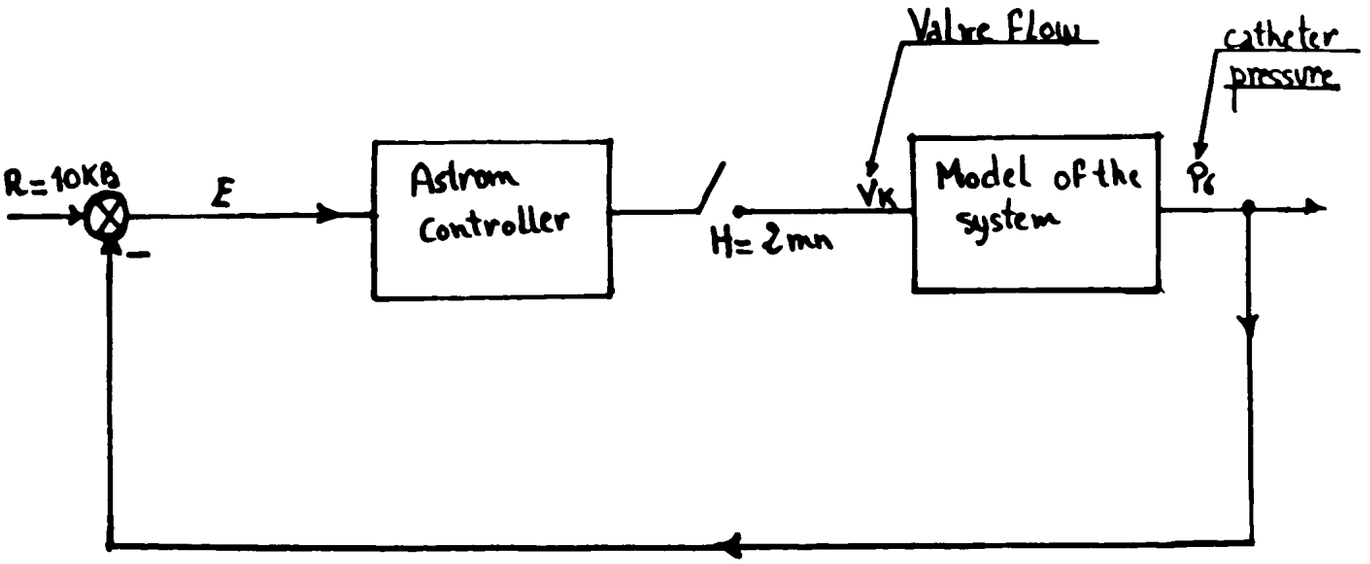
$$V_k = V_{k-1} + E/W$$

where $V_k$ is the valve flow value at loop k.

E is the error between the set point (10KPa) and the catheter pressure

W is the integration gain

H is sampling time



## 4.2 Computer simulation program

This program is simular to the first program but it includes the Astron contoller.

In this program we want to see the influence on the arterial pressure after 10mm of simulation by choosing a different value of the integrator gain (W) and by taking a different starting point of the valve flow. And we want also to see the final valve flow corresponding to this arterial pressure. And finally we want to see the effect of the noise on the arterial pressure.

This latter can be done by taking $K_1$ and $K_2$ random rather than to take them constant.

To do that we have to insert the lines 503 and 505 between 500 and 510 so we will have:

```
500 DYNAMIC
503 K1 = 0.08 + D * RND(0-1)
505 K2 = 0.014 + G* RND(0-1)
```

The noise deals with the agitation of the baby (by crying etc..) which is related straightly with $K_1$ and $K_2$. Because when cries he needs more oxygen so the rate flow increases making $K_1$ bigger, as $K_1$ is equal to rate flow over volume of the box which is constant.

Also the reaction of the transformation of $O_2$ in $CO_2$ also increase so $K_2$.

```
 10 PAGE
 20 PRINT "MODELLING AND CONTROL OF THE SYSTEM: VALVE FLOW -
    ARTERIAL PRESSURE
 30 PRINT
 40 PRINT
 50 PRINT
 60 REM:  MODELLING OF THE SYSTEM ... INCUBATOR - RESPIRATORY
          SYSTEM
 70 REM:  INITIALISATION
 80 LET @1=600
 90 LET V=.21
100 LET F1=P3=10
105 LET P5=P6=3.4
107 REM:  W IS THE INTGRATER CST OF THE ASTROM CONTROLLER"
108 PRINT "INPUT W'
109 INPUT W
112 REM R IS THE POINT SET
114 LET R=10
120 REM: STORRING OF THE PARAMETERS
130 READ P1,K1,K2,T3,T1,T4,K
140 DATA 100,8.00000E-02,1.40000E-02,.5,5.00000E-02,16.9,.677
150 LET T=Y0=0
160 DIM A(100)
170 REM: N MUST BE LESS THAN 100
180 LET N=M2=5
190 LET @0=.1
200 REM: DELAY=N*@0
210 REM: TIME SAMPED =H1*@0
220 LET H1=1200
230 LET H=0
240 MAT A=ZER
250 LET M1=1
260 PRINT "INPUT S"
270 INPUT S
274 IF S<.3 THEN LET P5=P6=10
280 IF S>.5 THEN STOP
290 PAGE
300 LET T=0
310 FOR B=0 TO 600 STEP 120
320 LINE B,2.00000E-02,B,-200000E-02
330 ANNOT B,-5.00000E-02,B/60
340 NEXT B
350 ANNOT 550,-5.00000E-02,"MIN"
360 FOR C=0 TO 1 STEP .1
370 LINE -8,C,8,C
380 ANNOT -40,C,C*100
390 NEXT C
400 ANNOT 8,1,"KPA"
410 ANNOT -600,.8,"P1=;P1;"KPA"
420 ANNOT -600,.7,"K1=";K1
430 ANNOT -600,.6,"K2=";K2
440 ANNOT -600,.5,"T3=";T3
450 ANNOT -600,.4,"T1=";T1
```

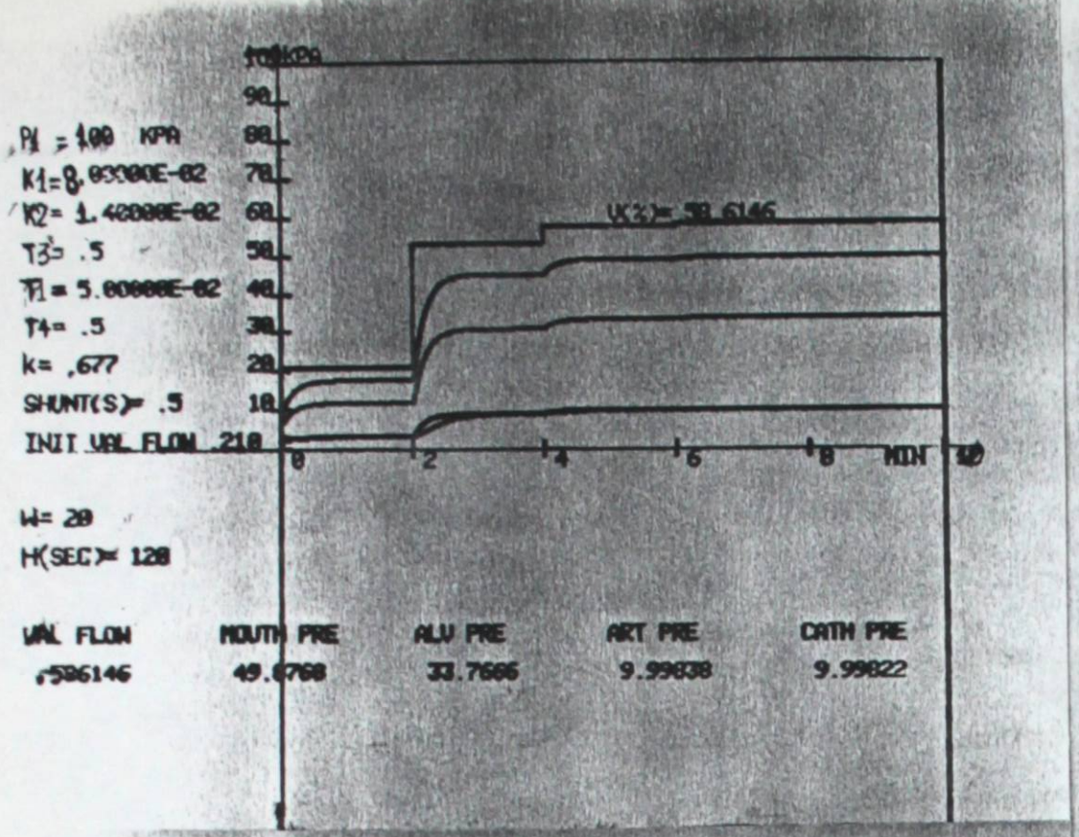
```
460 ANNOT -600,.3,"T4=";T3
470 ANNOT -600,.2,"K=";K
480 ANNOT -600,.1,"SHUNT(S)=";S
490 ANNOT -600,0,"INIT VAL FLOW';V
495 ANNOT -600,-.2,"W=";W
497 ANNOT -600,-.3,"H(SEC)=";H1*@0
500 DYNAMIC
510 LET H=H+1
520 IF H<H1 THEN 560
530 LET R=R-P6
540 LET V=V+R/W
550 LET H=0
560 EQUATIONS
570 INDVAR T
580 REM : V IS THE VALVE FLOW ,F1 IS THE INSPIRED FLOW
590 REM : P3 IS THE ALVEOLAR PRESSURE,  P5 IS THE  ARTERIAL
          PRESSURE
600 REM : P6 IS THE CATHETER PRESSURE ON PKA
610 DER F1=F2
620 F2=-F1*(K1+K2)+YO
630 DER P3=P4
640 P4=(F1*K-P3)/T1
650 L=(.7/42.4448)*P3
660 P5=(P3-L*S*42.4448/(1-S))-.1316
670 DER P6=((P5/T4)-(P6/T4))
680 Y=V*P1*K1
690 DISPLAY V,F1/100,P3/100,P5/100,P6/100
700 EQUEND
710 IF T>@1 THEN GOTO 790
720 LET KYO=A(M1)
730 LET M1=M1+1
740 IF M1>15 THEN LET M1=1
750 LET A(M2)=Y
760 LET M2=M2+1
770 IF M2>15 THEN LET M2=1
780 DYNEND
790 ANNOT 300,V,"V(%)=";V*100
800  ANNOT  -450,-.5,"VAL  FLOW","MOUTH  PRE","ALV  PRE","ART
PRE","CATH PRE"
810 ANNOT -450,-.6,V,F1,P3,P5,P6
820 REM : "PRESS ANY KEYS LESS THEN 5 TO CONT"
830 INPUT Z
840 PAGE
850 IF Z>5 THEN STOP
860 REM REINITIALISATION
870 LET F1=P3=10
873 LET P5=P6=3.4
875 LET V=.21
880 GOTO 260
```

## 4.3 Computer simulation results

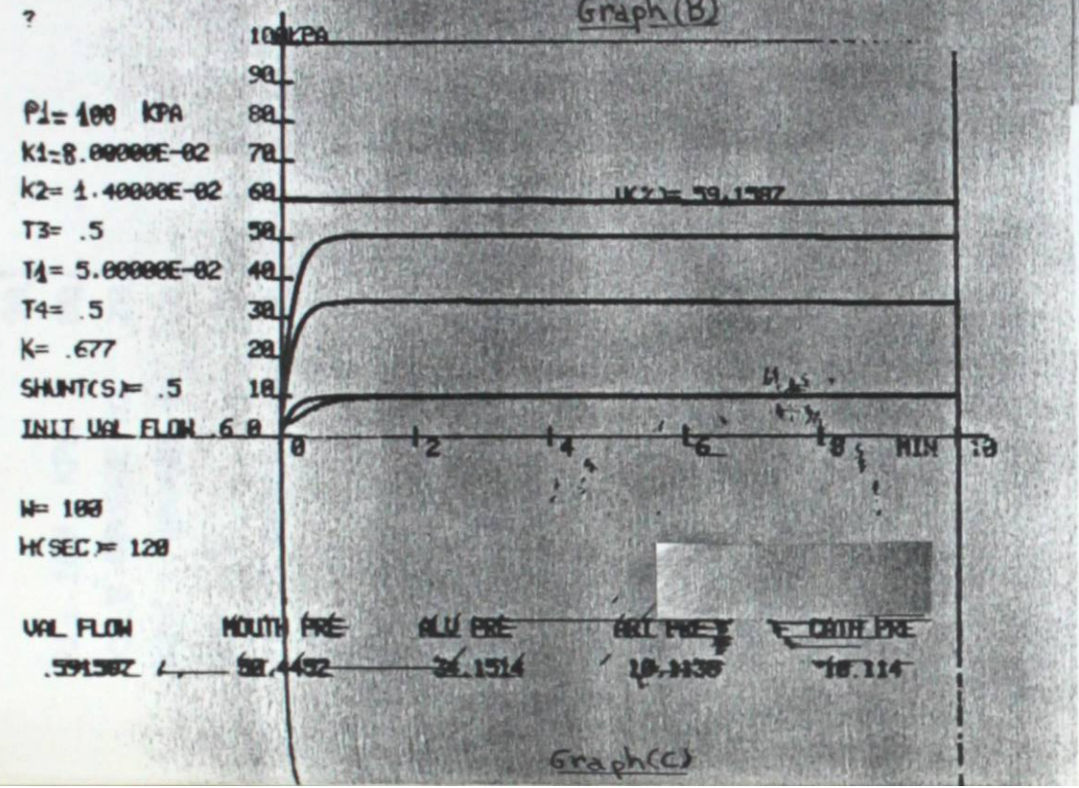
| For $K_1$ and $K_2$ = constant | Initial Valve-Flow = 0.21 W = 100 | Initial valve-Flow = 0.21 W = 20 | Initial Valve-Flow = 0.3 W = 100 | Initial valve-Flow = 0.6 W = 100 |
|---|---|---|---|---|
| Shunt = 0.5 | art pres = 6.95765kPa Final valve Flow = 0.440579 Graph (A) | art pres = 9.99838 Final valve Flow = 0.586146 Graph (B) | | art pres = 10.1138 Final valve Flow = 0.591589 Graph (C) |
| Shunt = 0.4 | art pres = 9.15481kPa Final valve Flow = 0.310665 Graph (D) | art pres = 9.71682 Final valve Flow = 0.33466 Graph (E) | | |
| Shunt = 0.3 | art pres = 9.79081 Final valve Flow = 0.248116 Graph (F) | art pres = 9.8528 Final valve Flow = 0.214865 Graph (G) | art pres = 10.2507 Final valve Flow = 0.254908 Graph (H) | |
| Shunt = 0.2 | art pres = 9.9828 Final valve Flow = 0.213029 Graph (I) | art pres = 9.9301 Final valve Flow = 0.21 Graph (J) | | |
| Shunt = 0.01 | art pres = 10.0628 Final valve Flow = 0.177563 Graph (K) | art pres = 10.0135 Final valve Flow = 0.179943 Graph (L) | | |
| For $K_1$ and $K_2$ Random | | | | |
| shunt (Sh) = 0.5 {D = 0.08 {G = 0.05 | | art pres = 10.016 Final valve Flow = 0.660083 Graph (M) | | art pres = 9.5542 Final valve Flow = 0.634663 Graph (N) |
| Shunt (Sh) = 0.5 {D = 0.8 {G = 0.14 | | art pres = 10.0316 Final valve Flow = 0.533344 Graph (P) | | art pres = 10.4394 Final valve Flow = 0.589239 Graph (O) |

Arterial pressure and final valve flow For 10mn of simulation

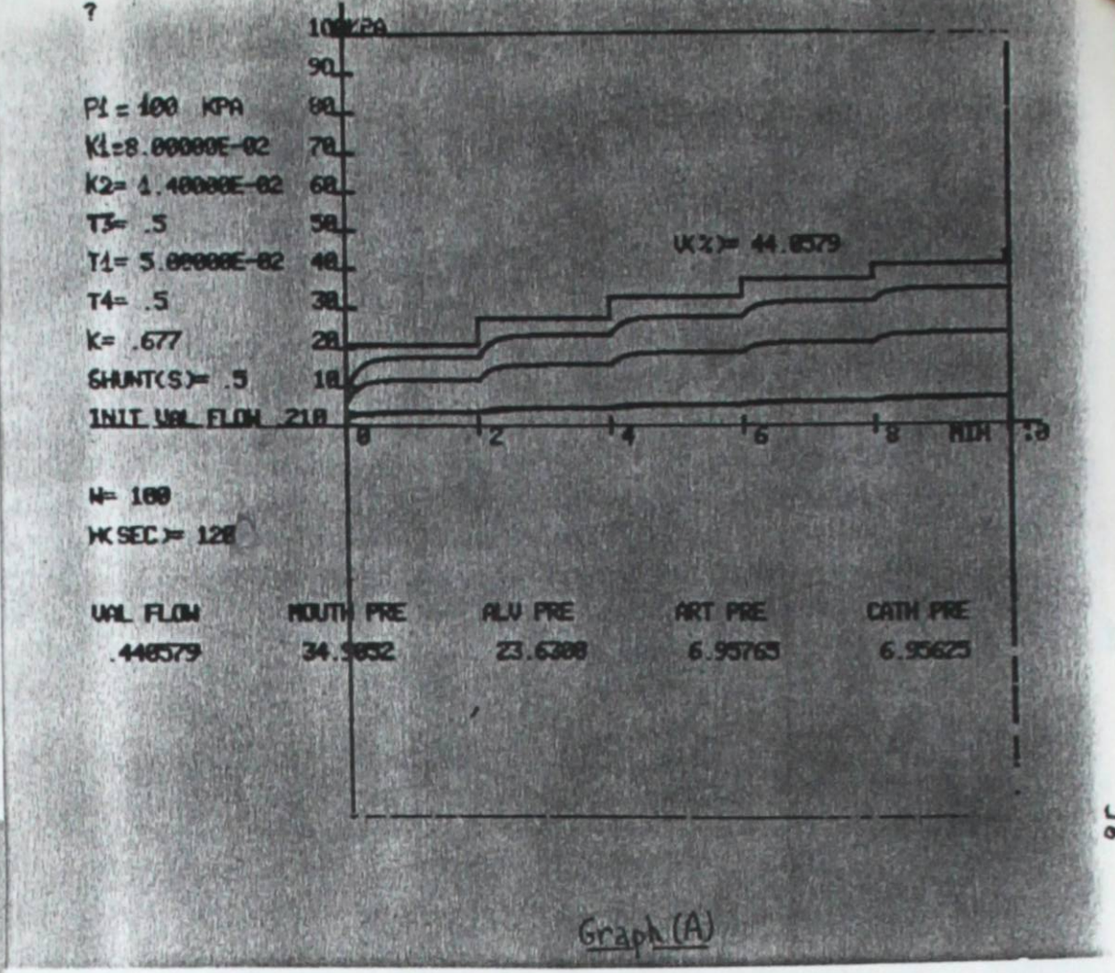
★ Remark: the values of the final valve flow of the graph G, J and L are differents of those in the computer simulation results
The values in the computer simulation results are just before the fifth sampling.
the values of the graph G, J and L are just after the fith sampling.



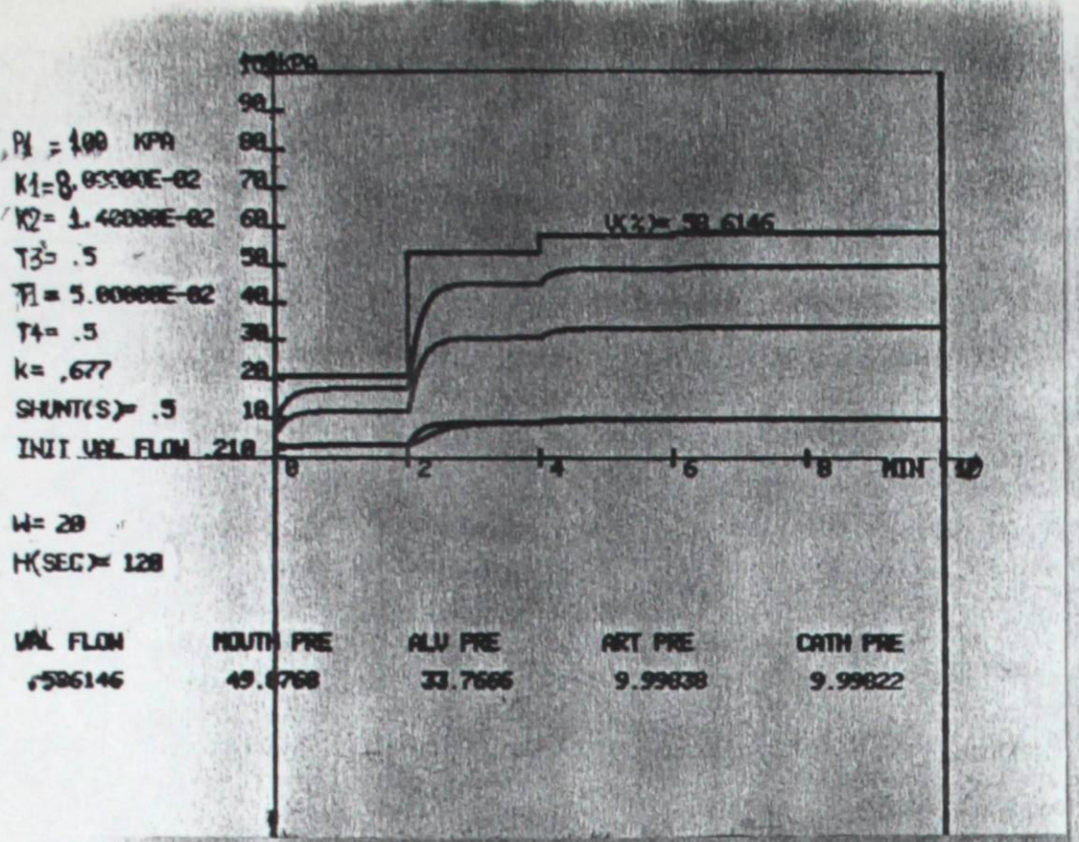

Graph (B)

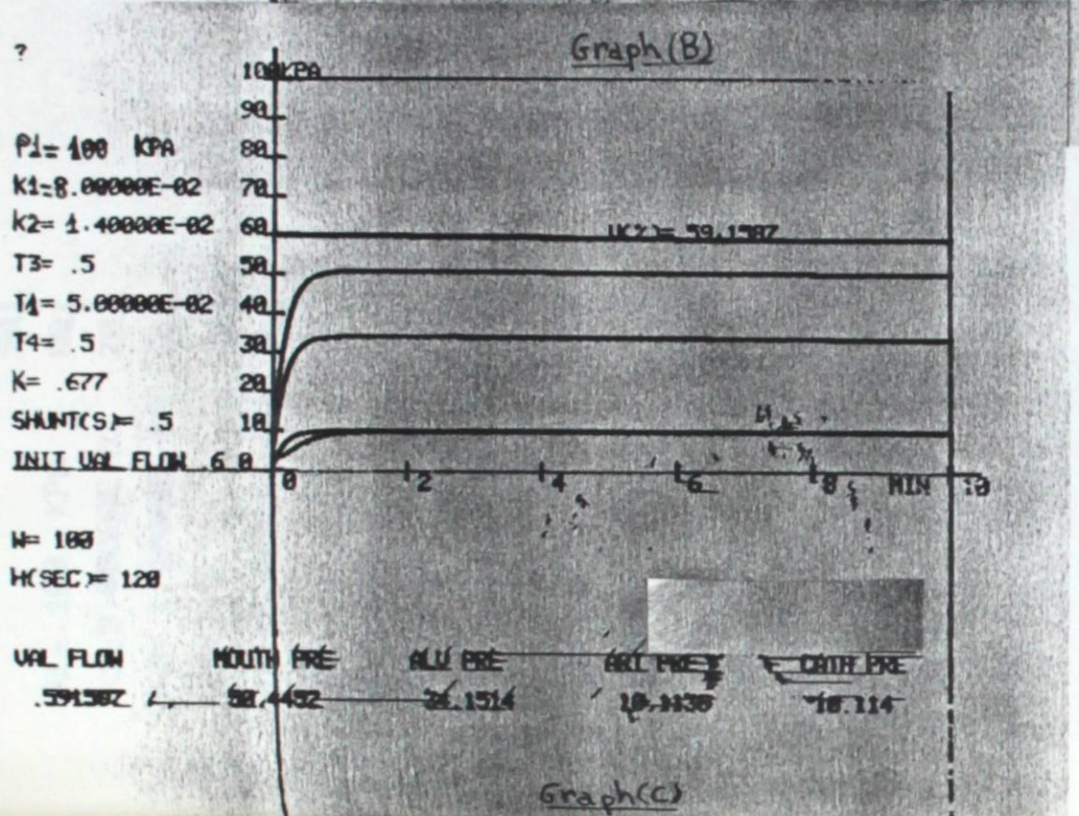



Graph(C)



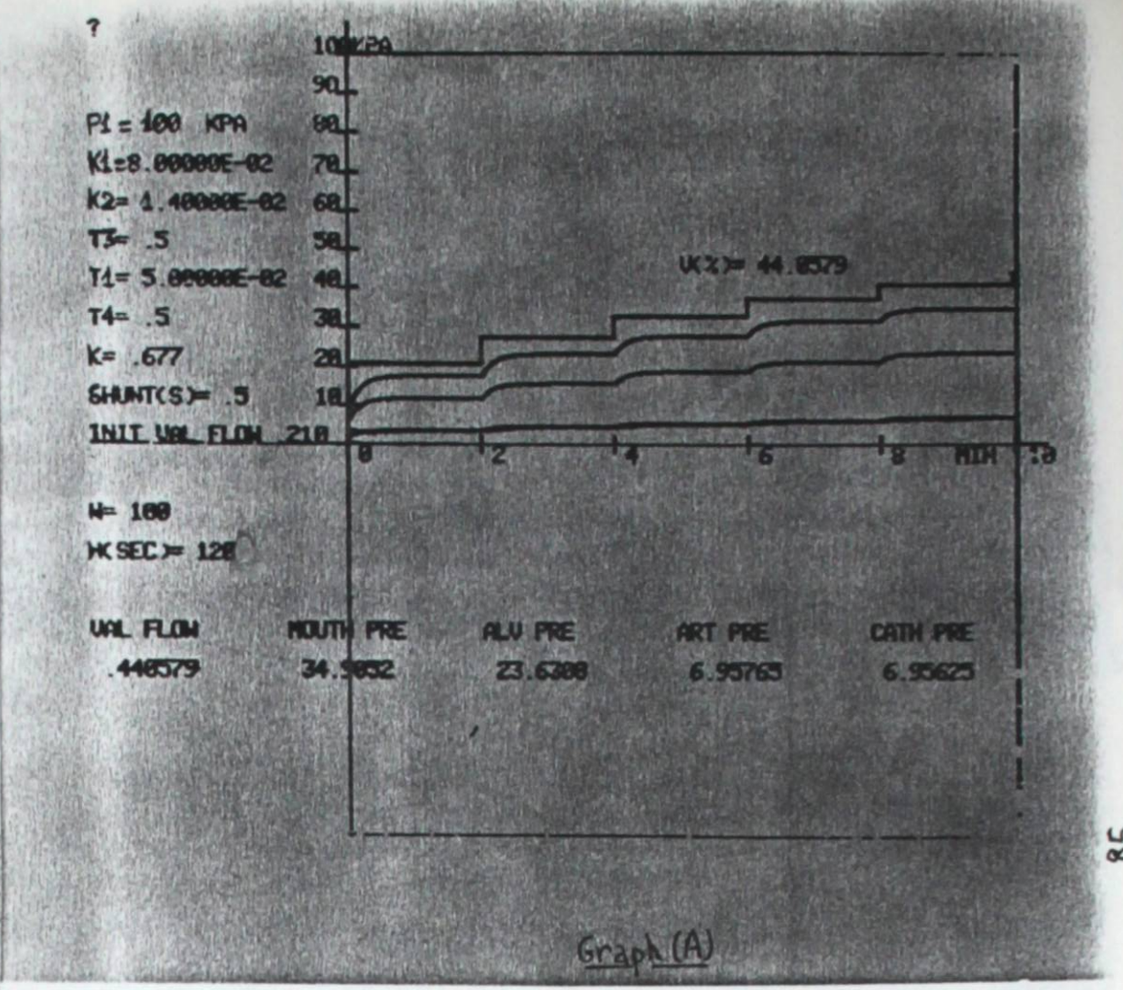

Graph (A)



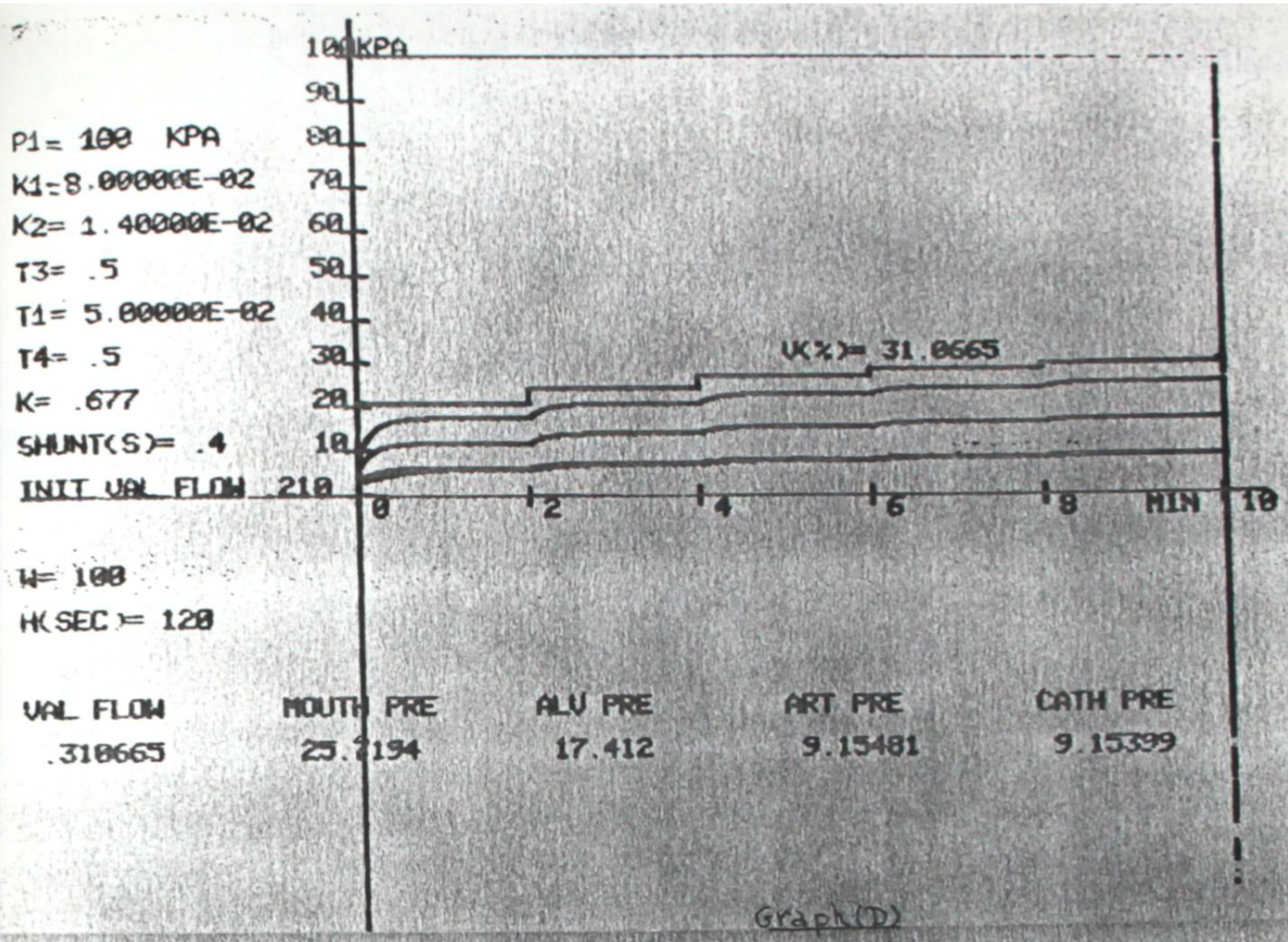




Graph(B)

Graph(C)




Graph(A)

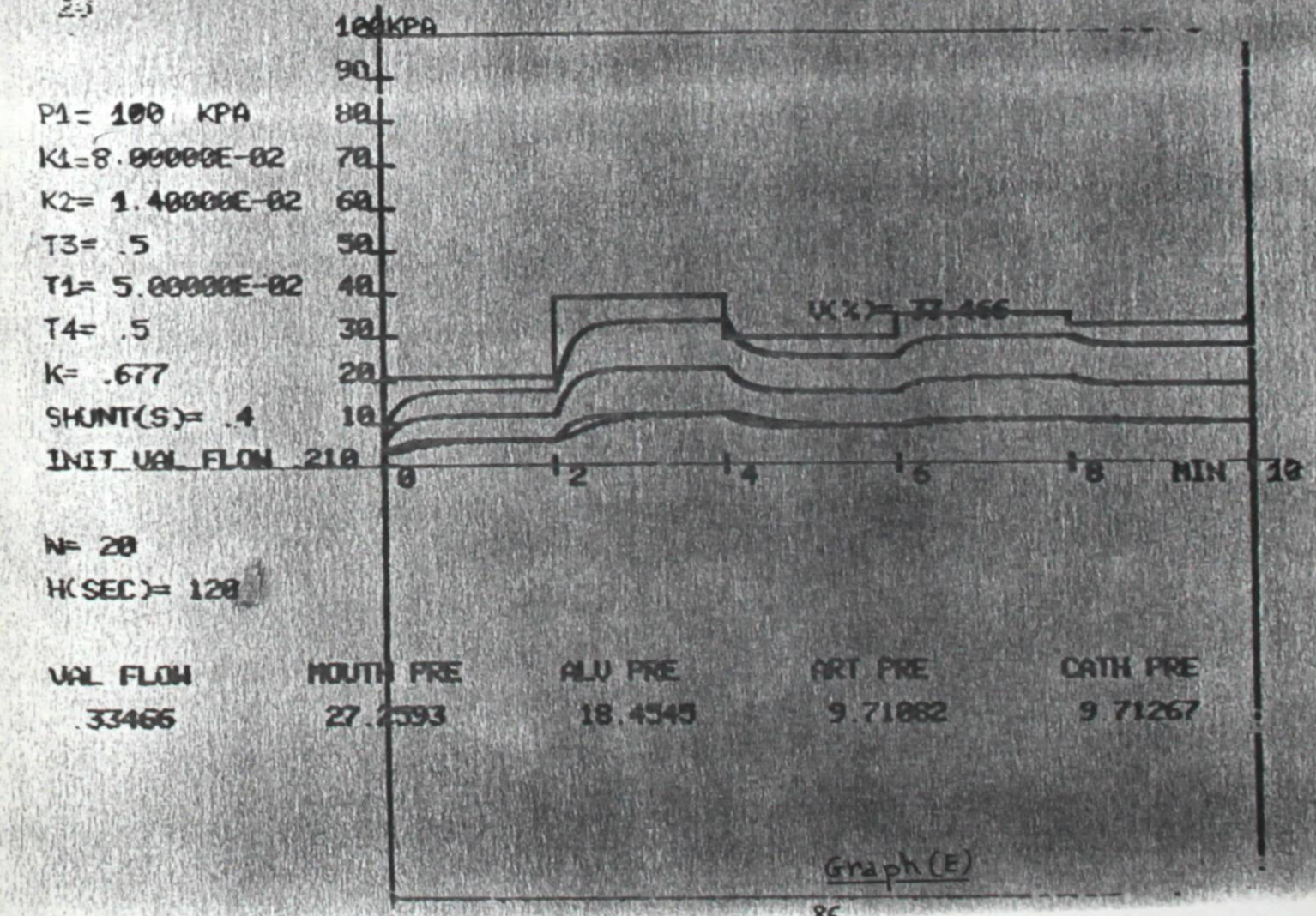



P1= 100 KPA
K1=8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= .5
K= .677
SHUNT(S)= .4
INIT VAL FLOW 210

N= 100
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .310665 | 25.2194 | 17.412 | 9.15481 | 9.15399 |

Graph(D)

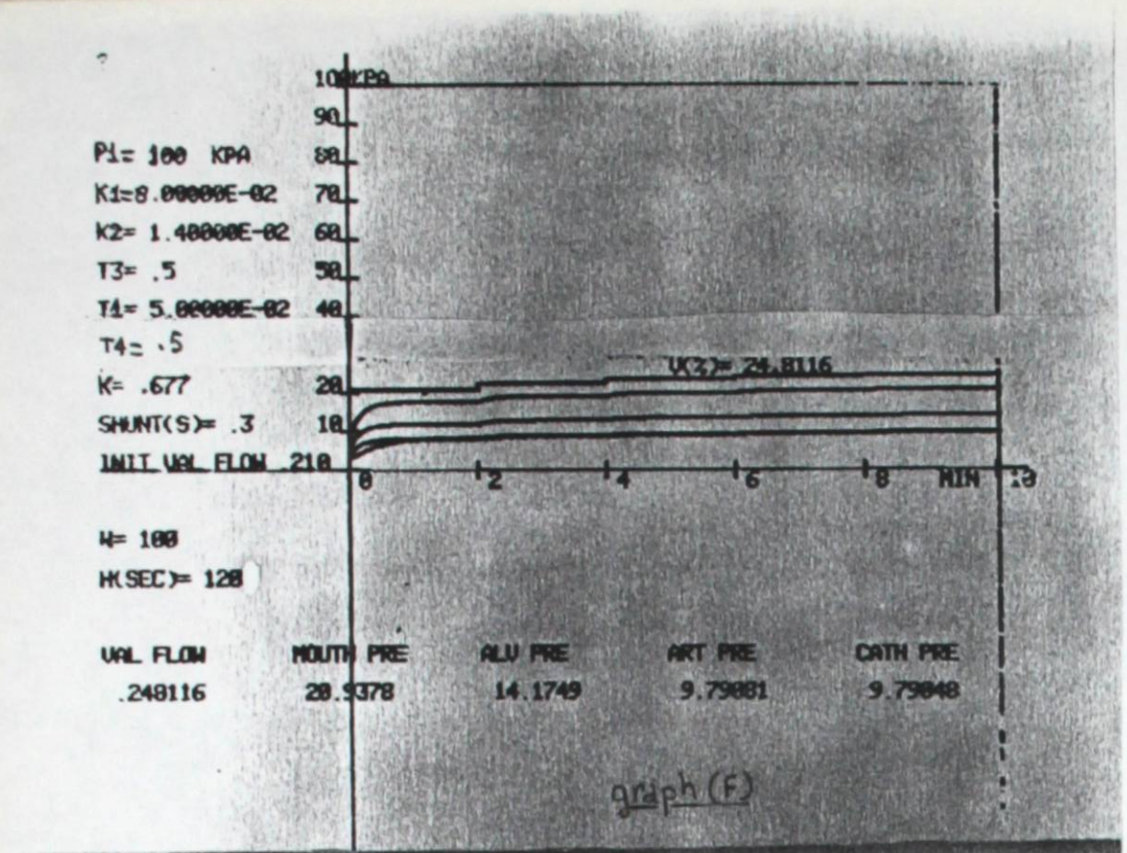



P1= 100 KPA
K1=8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= .5
K= .677
SHUNT(S)= .4
INIT VAL FLOW 210

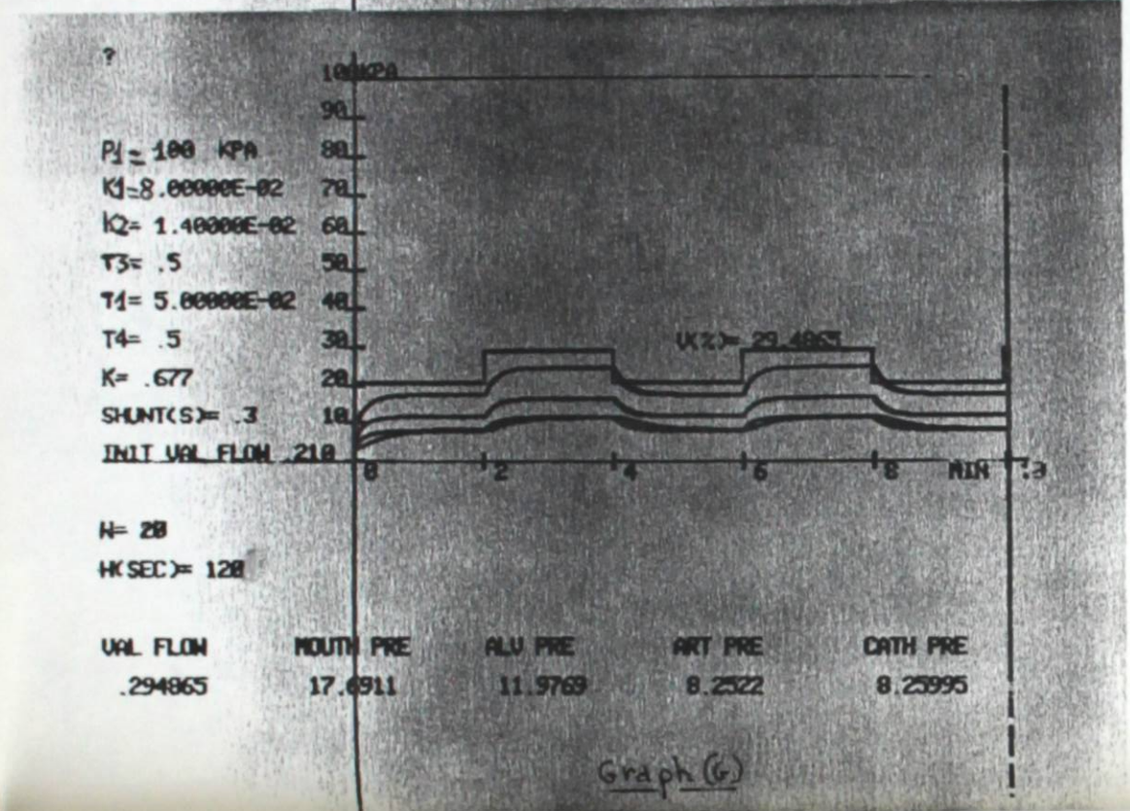
N= 20
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .33466 | 27.2593 | 18.4545 | 9.71882 | 9.71267 |

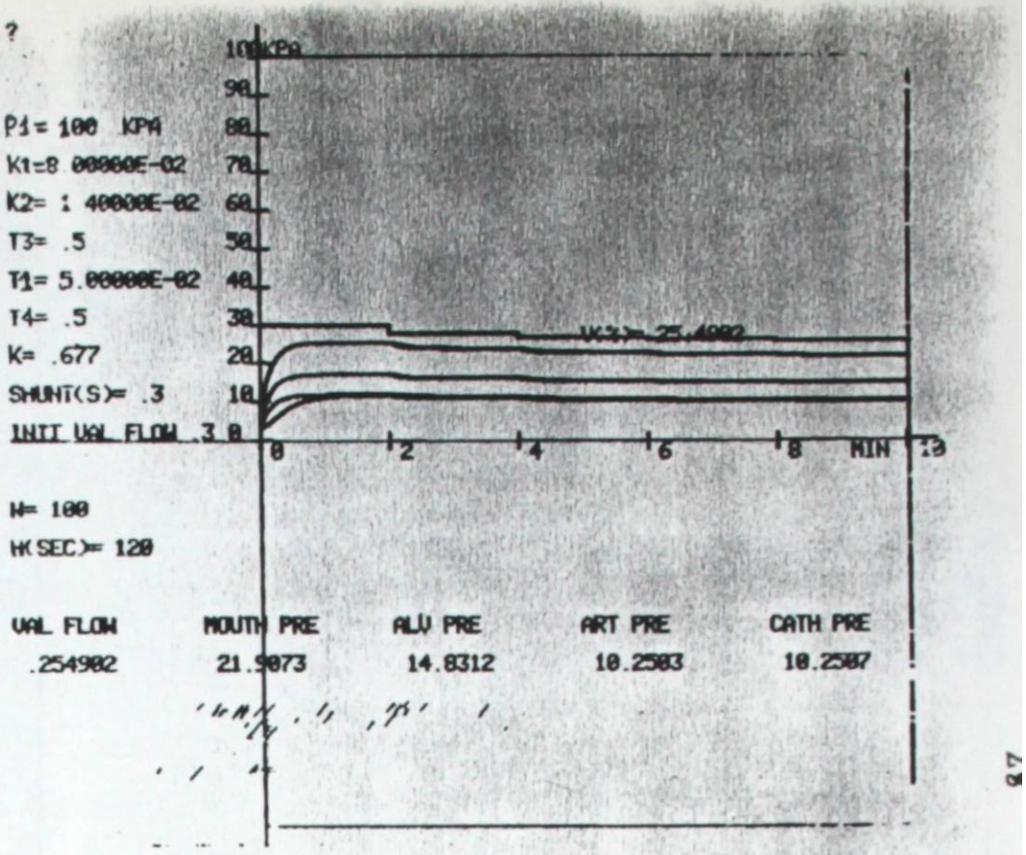
Graph(E)




graph (F)



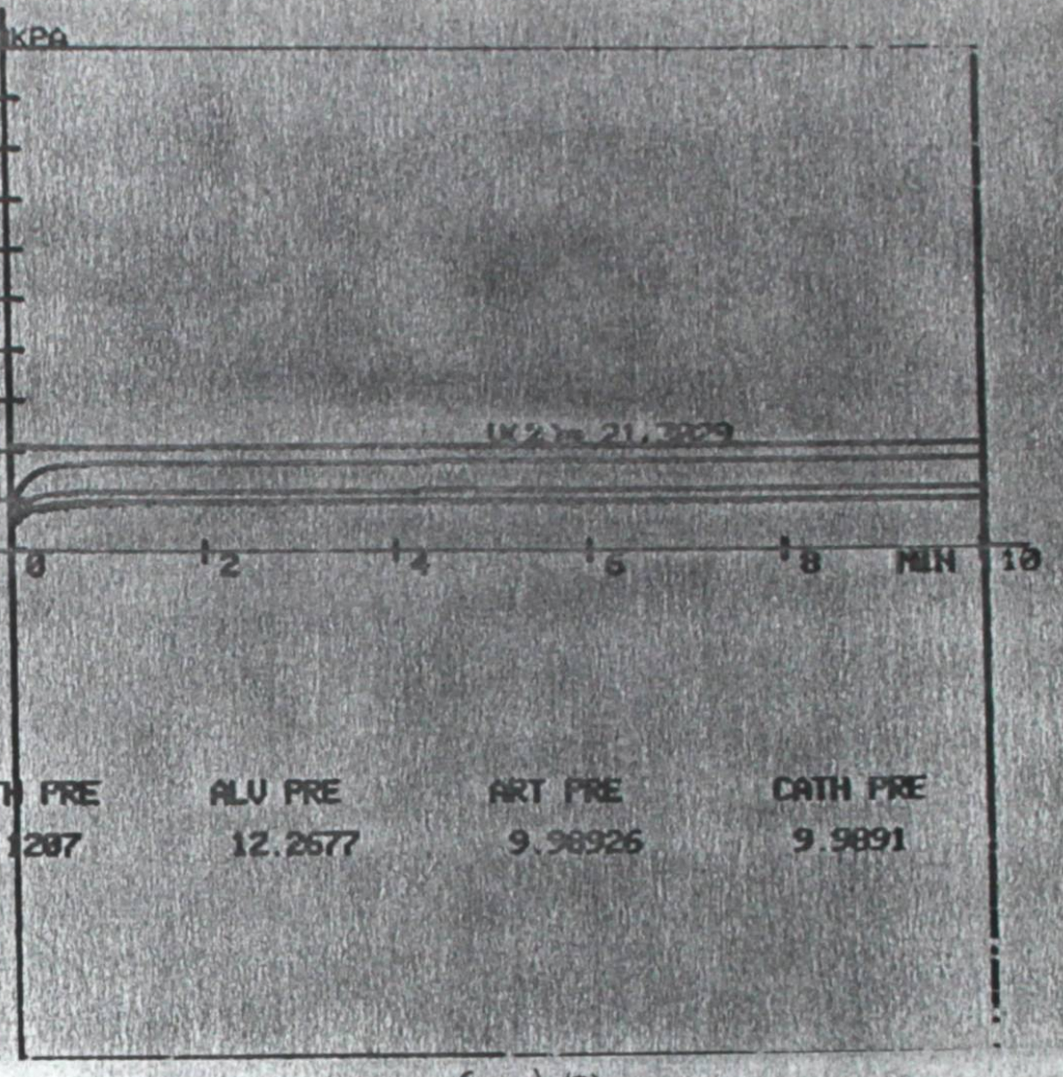

Graph (G)




Graph (H)

?

P1= 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= .2
INIT VAL FLOW .210



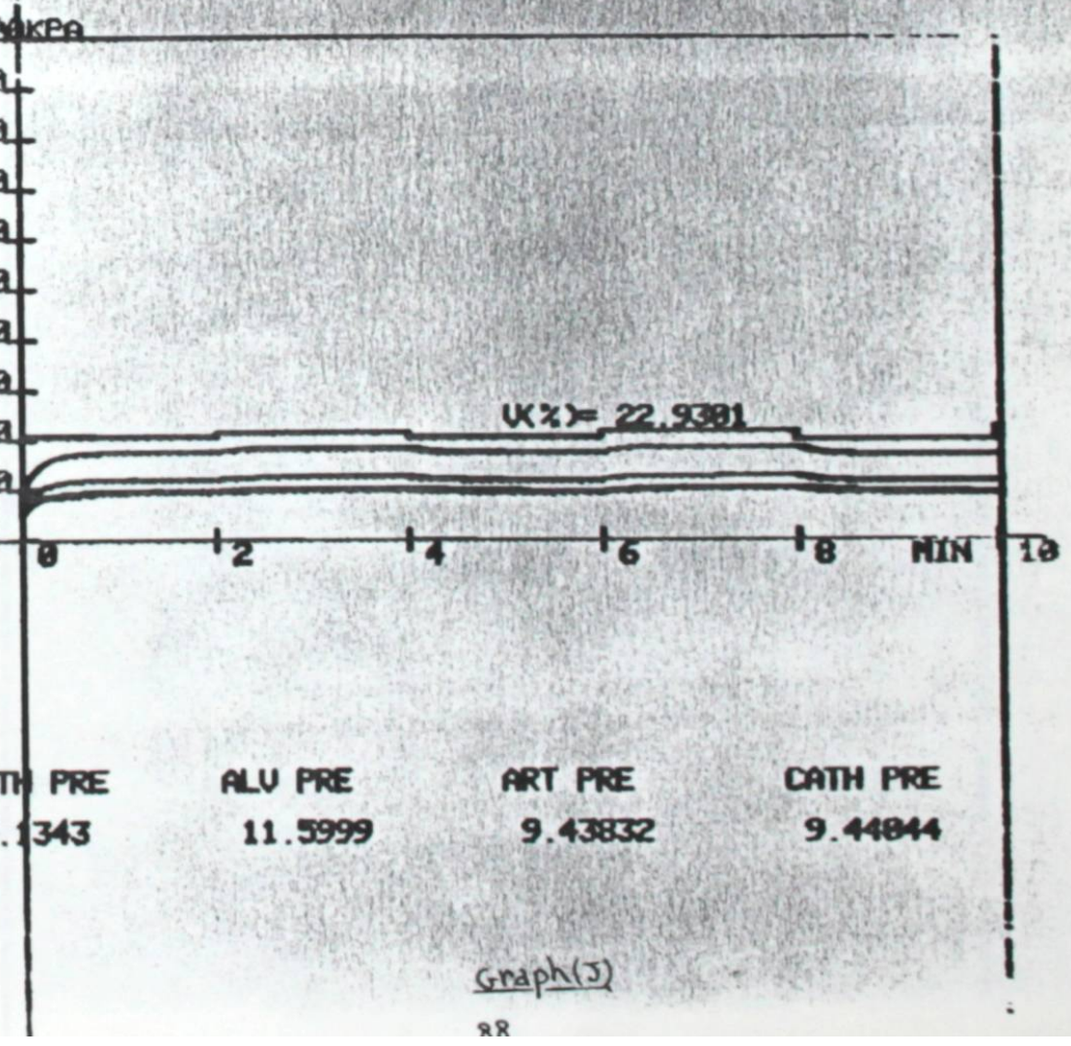

N= 100
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .213829 | 18.1207 | 12.2677 | 9.98926 | 9.9891 |

Graph (I)

?

P1= 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= .2
INIT VAL FLOW .210




N= 20
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .229301 | 17.1343 | 11.5999 | 9.43832 | 9.44844 |

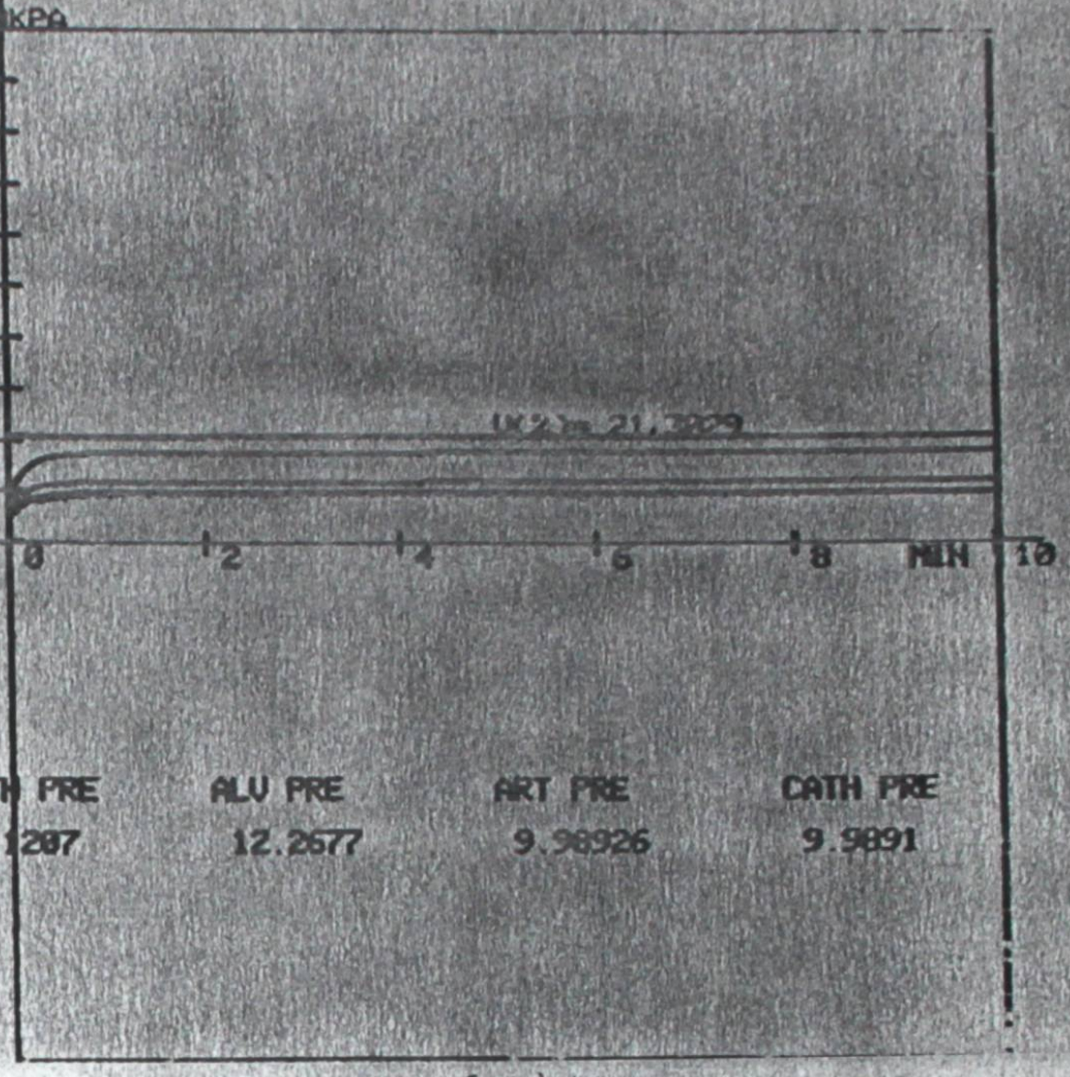
Graph(J)

?

P1= 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= .2
INIT VAL FLOW .210

N= 100
HK(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .213829 | 18.1207 | 12.2677 | 9.98926 | 9.9891 |



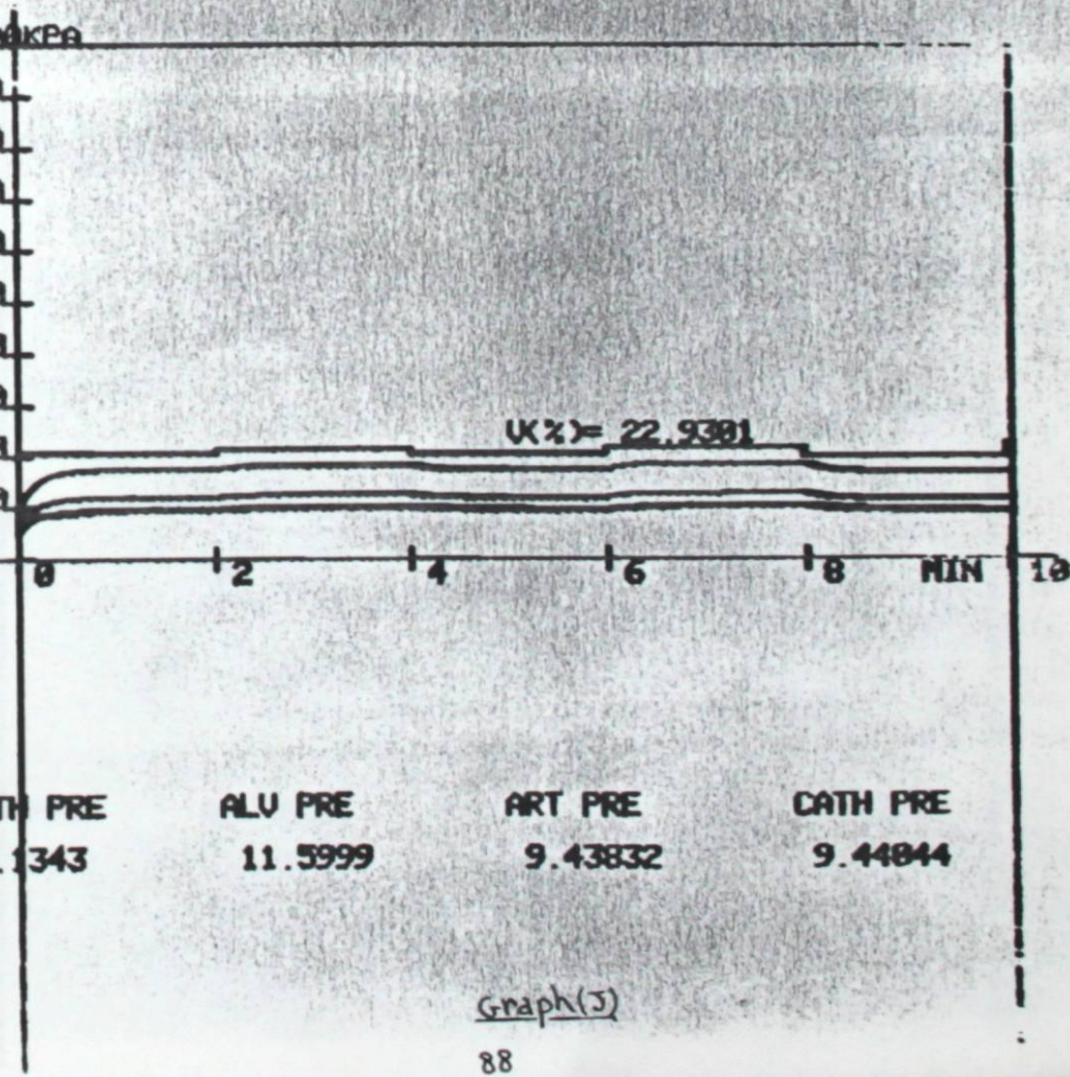

Graph (I)

?

P1= 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= .2
INIT VAL FLOW .210

N= 20
HK(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .229301 | 17.1343 | 11.5999 | 9.43832 | 9.44044 |



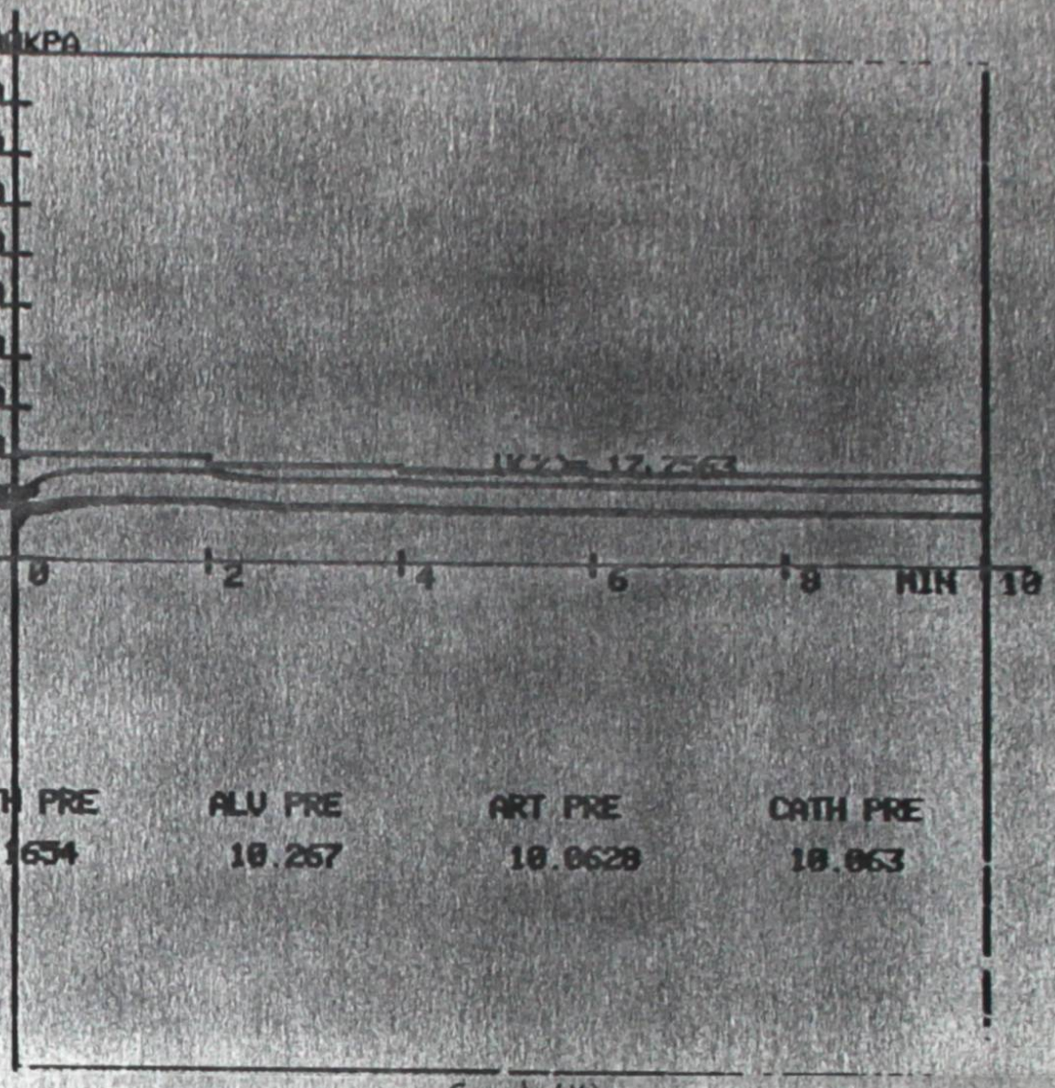

Graph(J)

?

P1 = 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= 1.000000E-02
INIT VAL FLOW .210

W= 100
HK SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .177563 | 15.1654 | 10.267 | 10.0628 | 10.063 |



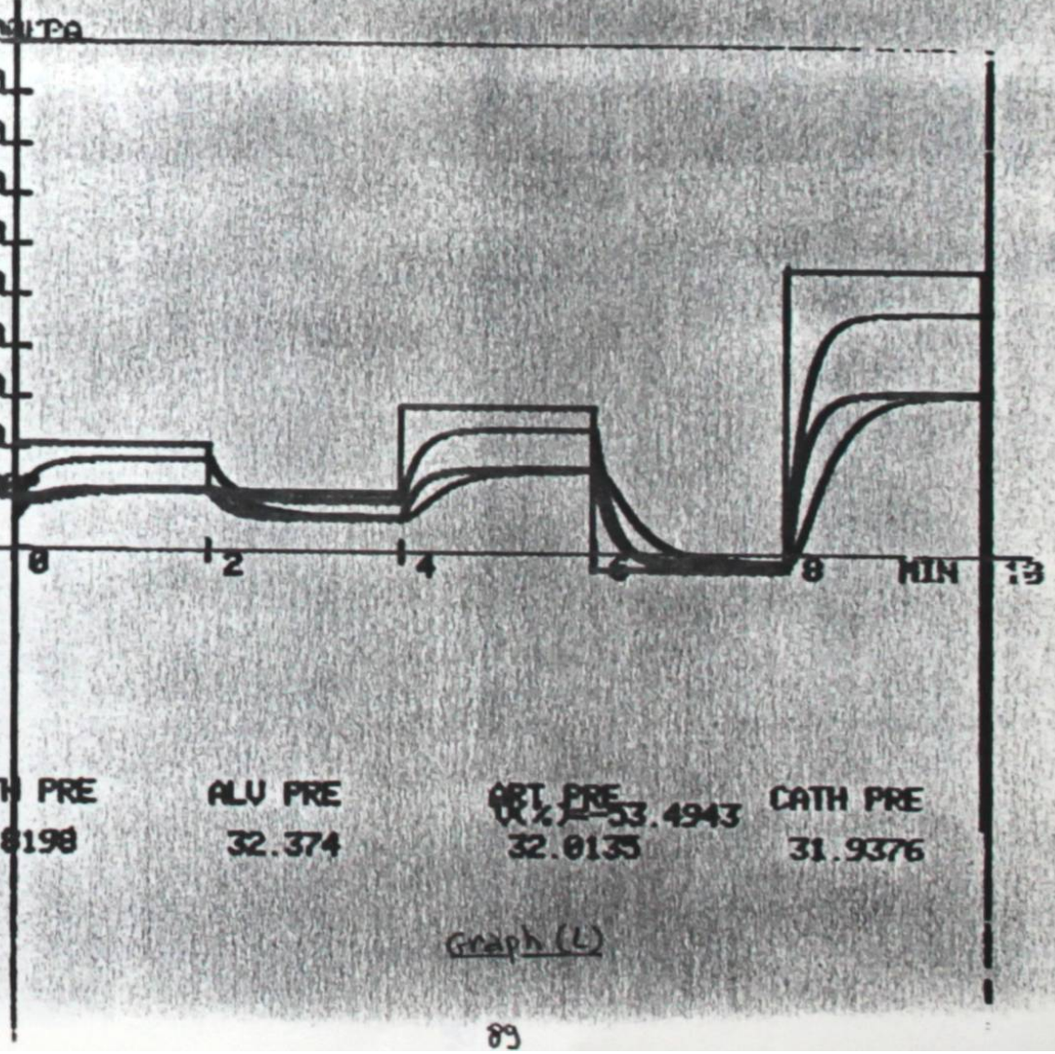

Graph (K)

:

P1 = 100 KPA
K1=8.000000E-02
K2= 1.400000E-02
T3= .5
T1= 5.000000E-02
T4= .5
K= .677
SHUNT(S)= 1.000000E-02
INIT VAL FLOW .210

W= 20
HK SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| -.534943 | 47.8198 | 32.374 | 32.0135 | 31.9376 |



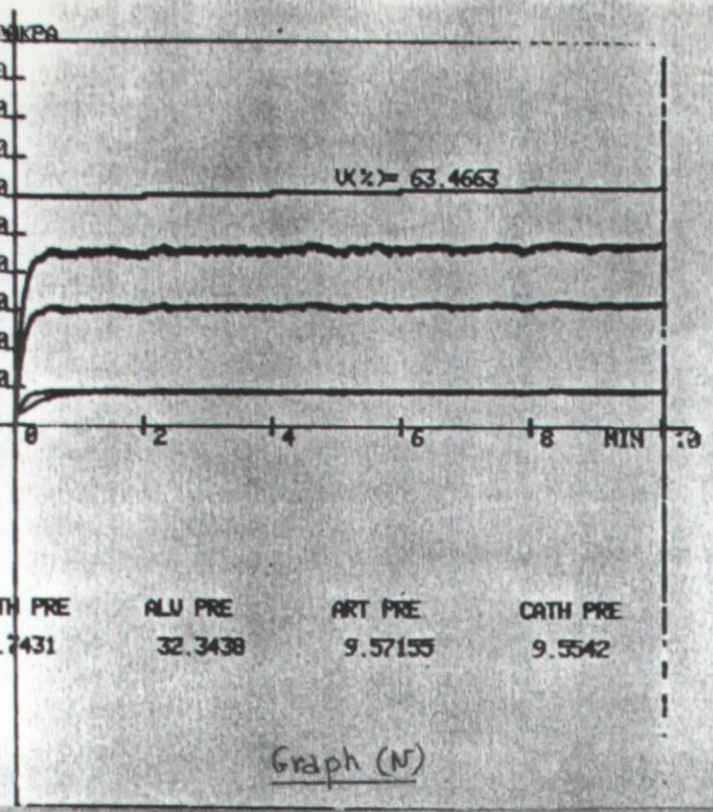

Graph (L)

?

P1 = 100 KPA
K1=8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= .5
K= .677
SHUNT(S)= .5
INIT VAL FLOW .6 0

W= 100
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .634663 | 47.7431 | 32.3438 | 9.57155 | 9.5542 |

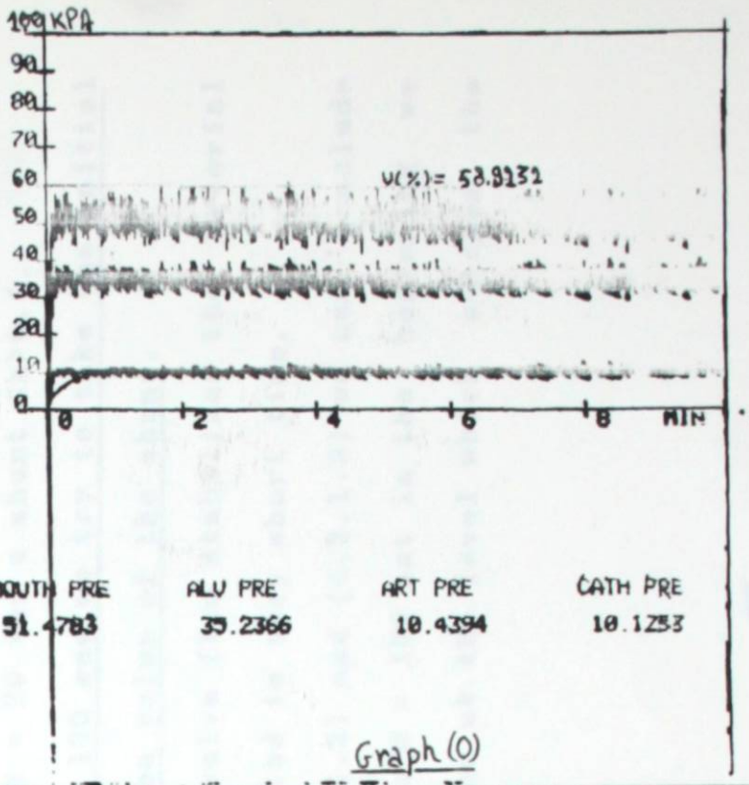



Graph (N)

P1 = 100 KPA
K1 = 8.00000E-02
K2 = 1.40000E-02
T3 = .5
T1 = 5.00000E-02
T4 = .5
K = .677
SHUNT(S) = .5
INIT VAL FLOW .6

W = 100
H(SEC) = 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .589232 | 51.4783 | 35.2366 | 10.4394 | 10.1253 |



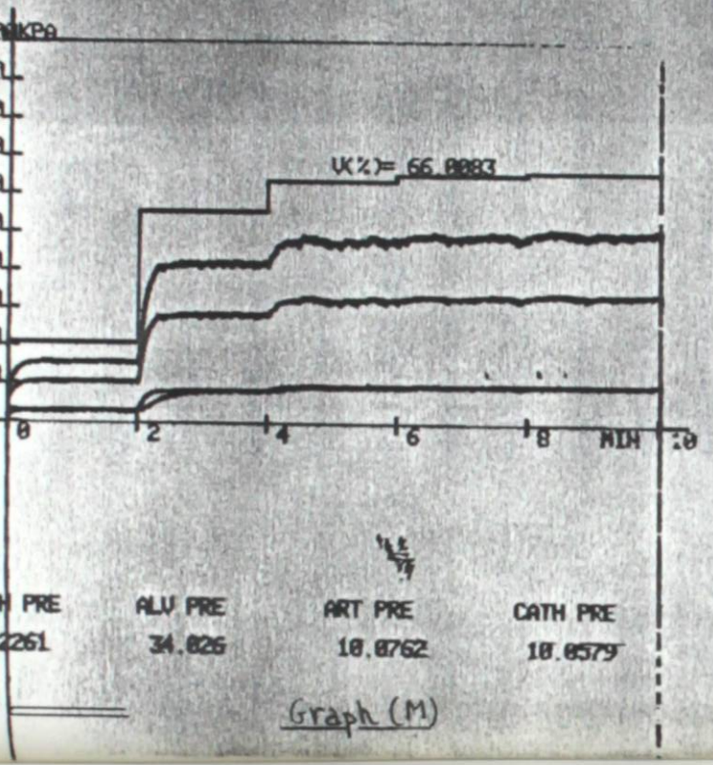

Graph (O)

?

P1 = 100 KPA
K1=8.00000E-02
K2= 1.40000E-02
T3= .5
T1= 5.00000E-02
T4= .5
K= .677
SHUNT(S)= .5
INIT VAL FLOW .210

W= 20
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| .660883 | 50.2261 | 34.826 | 10.0762 | 10.0579 |

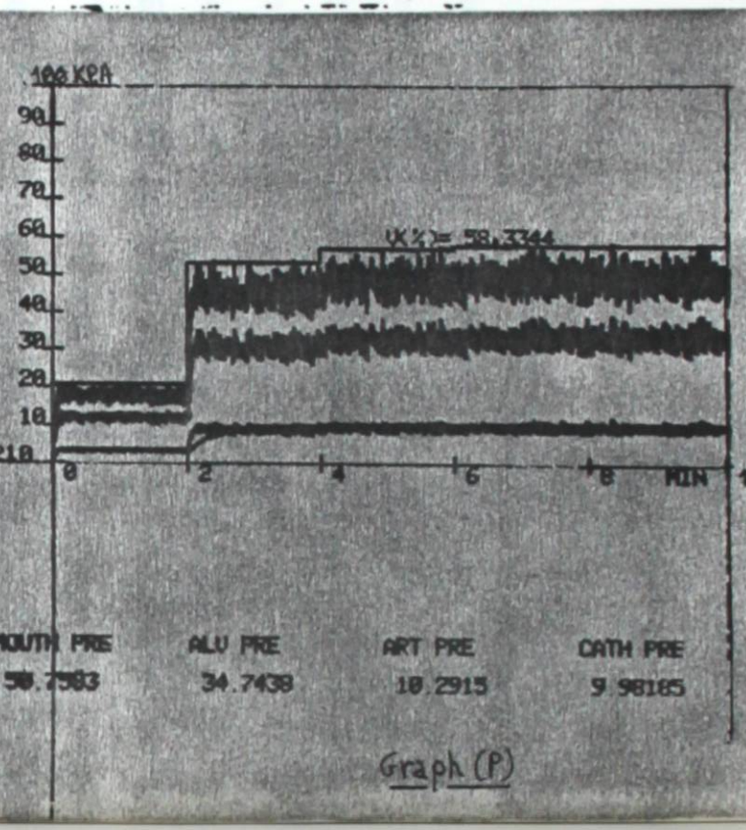



Graph (M)

P1 = 100 KPA
K1=8.00000E-02
K2 =1.40000E-02
T3 = .5
T1= 5.00000E-02
T4 = .5
K= .677
SHUNT(S = .5
INIT VAL FLOW .210

W= 20
H(SEC)= 120

| VAL FLOW | MOUTH PRE | ALV PRE | ART PRE | CATH PRE |
|---|---|---|---|---|
| 563344 | 50.2583 | 34.7439 | 10.2915 | 9.98185 |




Graph (P)

4.3.1 Case where $K_1$ and $K_2$ are not affected by the noise.

4.3.1.1 For W = 20 and initial flow = 0.21

When the shunt decreases from 0.5 to 0.01 we notice that the valve flow curves go from the underdamping (which stabilises the arterial pressure at the needed value after only 4mn) to the unstable curve.

4.3.1.2 For W = 100 and initial flow = 0.21

When the shunt increases from 0.01 to 0.5 we notice that the valve flow curves go from the critical (which stabilises the arterial pressure at the needed value only after 20 sec approximately) to the underdamping which stabilises the arterial pressure at 10 KPa after more than 15 mn.

In this case all the curves are stable but more the shunt is high more the arterial pressure curve takes a long time to reach its target.

From (4.3.1.1) and (4.3.1.2) we can conclude that it is better for an intitial flow of 0.21 to take W = 100 for a shunt Sh<0.3 and to take W = 20 for a shunt Sh>0.4.

4.3.1.3 Here we take W = 100 and we try to take the initial valve flow according to the value of the shunt.

Here we notice that the valve flow stabilises the arterial pressure at the value wanted in very short time.

From (4.3.1.1) and (4.3.1.2) and (4.3.1.3) we can conclude that it is better to take W = 100 but in the beginning we must open the valve flow at the level which matches the shunt value.

4.3.2 Case where $K_1$ and $K_2$ are affected by the noise

We notice in this case that the value of the valve flow is increased slightly comparing with those findings before for the same value of the shunt

($K_1$ = 0.08 + D * RND (0-1)

($K_2$ = 0.014 + G *RND (0-1)

For the curve correspondant (D = 0.08 and G = 0.05) and (D = 0.8 and G = 0.14)

4.3.3 Conclusion: In order to have the arterial pressure the nearest possible from 10KPa. In a short time, it is recommended to run the first program (without controller) in order to find the bias (the better value of the valve flow according to the shunt value which makes the arterial pressure in the vicinity of 10KPa). Afer run the second program (with the controller) and take W = 100.

## References


1. Julius H. Comroe. Physiology of respiration. 1
2. N. Balfour Slonim. Lyle H. Hamilton. Respiratory physiology. 2
3. L.B. Strang. Neonatal Respiration. Physiological and clinical studies. 3
4. J.F. Nunn. Applied respiratory physiology. 4
5. Fred S. Grodins. Stanley M. Yamashiro. Modern concepts in medical physiology. Respiratory function of the lung and its control. 5
6. Waldemar A. Carlo and Richard J. Martin. Principles of Neo-Natal assisted ventilation. 6
7. Peter Rolfe. IEE Medical Monographs. Arterial oxygen measurement in the newborn with intra-vascular transducers. 7
8. M. D. Nada. D.A. Linkers. An adaptive analogue tracker for automatic measurement of lung parameters. 8
9. Yasundo Takahashi. Control and dynamic systems.
10. E.O.R. Reynolds. Effect of alterations in mechanical ventilator settings on pulmonary gas exchange in hyaline membrane disease. 10
11. A. Sano. M. Kikucki. Adaptive control of arterial oxygen pressure of newborn infants under incubator oxygen treatments.