INFORMATION TO USERS

This reproduction was made from a copy of a document sent to us for microfilming. While the most advanced technology has been used to photograph and reproduce this document, the quality of the reproduction is heavily dependent upon the quality of the material submitted.

The following explanation of techniques is provided to help clarify markings or notations which may appear on this reproduction.

1. The sign or "target" for pages apparently lacking from the document photographed is "Missing Page(s)". If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting through an image and duplicating adjacent pages to assure complete continuity.

2. When an image on the film is obliterated with a round black mark, it is an indication of either blurred copy because of movement during exposure, duplicate copy, or copyrighted materials that should not have been filmed. For blurred pages, a good image of the page can be found in the adjacent frame. If copyrighted materials were deleted, a target note will appear listing the pages in the adjacent frame.

3. When a map, drawing or chart, etc., is part of the material being photographed, a definite method of "sectioning" the material has been followed. It is customary to begin filming at the upper left hand corner of a large sheet and to continue from left to right in equal sections with small overlaps. If necessary, sectioning is continued again—beginning below the first row and continuing on until complete.

4. For illustrations that cannot be satisfactorily reproduced by xerographic means, photographic prints can be purchased at additional cost and inserted into your xerographic copy. These prints are available upon request from the Dissertations Customer Services Department.

5. Some pages in any document may have indistinct print. In all cases the best available copy has been filmed.

University Microfilms International
300 N. Zeeb Road
Ann Arbor, MI 48106

LAURIA, MICHAEL JOSEPH

A SYSTEM FOR REAL-TIME ANALYSIS OF ANESTHETIC GASES.

THE UNIVERSITY OF ARIZONA, M.S., 1982

PLEASE NOTE:

In all cases this material has been filmed in the best possible way from the available copy. Problems encountered with this document have been identified here with a check mark __✓__.

1. Glossy photographs or pages _____
2. Colored illustrations, paper or print _____
3. Photographs with dark background _____
4. Illustrations are poor copy _____
5. Pages with black marks, not original copy _____
6. Print shows through as there is text on both sides of page _____
7. Indistinct, broken or small print on several pages ✓
8. Print exceeds margin requirements _____
9. Tightly bound copy with print lost in spine _____
10. Computer printout pages with indistinct print ✓
11. Page(s) _____ lacking when material received, and not available from school or author.
12. Page(s) _____ seem to be missing in numbering only as text follows.
13. Two pages numbered _____. Text follows.
14. Curling and wrinkled pages _____
15. Other _____

University
Microfilms
International

A SYSTEM FOR REAL-TIME ANALYSIS OF ANESTHETIC GASES

by

Michael Joseph Lauria

A Thesis Submitted to the Faculty of the

DEPARTMENT OF ELECTRICAL ENGINEERING

In Partial Fulfillment of the Requirements
For the Degree of

MASTER OF SCIENCE

In the Graduate College

THE UNIVERSITY OF ARIZONA

1 9 8 2

STATEMENT BY AUTHOR

This thesis has been submitted in partial fulfillment of requirements for an advanced degree at The University of Arizona and is deposited in the University Library to be made available to borrowers under rules of the Library.

Brief quotations from this thesis are allowable without special permission, provided that accurate acknowledgment of source is made. Requests for permission for extended quotation from or reproduction of this manuscript in whole or in part may be granted by the head of the major department or the Dean of the Graduate College when in his judgment the proposed use of the material is in the interests of scholarship. In all other instances, however, permission must be obtained from the author.

SIGNED: Michael Lawrie

APPROVAL BY THESIS DIRECTOR

This thesis has been approved on the date shown below:

Kenneth C. Mylrea

K. C. MYLREA
Associate Professor of
Electrical Engineering

July 29, 1982
Date

ACKNOWLEDGMENTS

I would like to thank Jerry M. Calkins, Kenneth C. Mylrea, Reynolds J. Sanders, Charles K. Waterson, Richard C. Watt and the entire Advanced Biotechnology Group in the Department of Anesthesiology at the University of Arizona Hospital for their support and for the use of their facilities. I will always remember and appreciate their patience and understanding.

TABLE OF CONTENTS

TABLE OF CONTENTS--Continued

LIST OF ILLUSTRATIONS

LIST OF TABLES

ABSTRACT

A system for real-time analysis of anesthetic gases was designed and implemented using commercially available devices. The system provides breath-by-breath determination of inspired and end-tidal concentration, their ratio, inspired and expired volume, respiratory rate, the single breath uptake of anesthetic, the cumulative uptake of anesthetic, and the time and the square root of time elapsed during anesthesia delivery. Mean differences between precalculated values and the same values measured by the system for each parameter, with the exception of cumulative uptake, were 5% or less of the precalculated value. Cumulative uptake had a worst case difference between the precalculated value and the measured value of 10.6% of the precalculated value. Breath-by-breath analysis is only possible when there is at least a two second apnea period between breaths. The maximum respiratory rate recommended for use of this system is twelve breaths per minute.

CHAPTER 1

INTRODUCTION AND BACKGROUND

Within recent years, surgical operations have grown increasingly complex and often require several hours to complete. In addition, advances in medicine have provided the anesthesiologist with patients who, because they are more elderly, more severely ill or both, have a less predictable physiological behavior when subjected to general anesthesia. In order to assess the physiological effects of anesthesia, the anesthesiologist usually relies upon interpretation of vital signs such as blood pressure, heart rate, response to a surgical stimulus and gas delivery system settings when making clinical judgments regarding anesthesia delivery. Presently, there is no suitable and routinely available operating room device that can predict the effect or provide quantitative information regarding transfer of anesthetic agent into or out of the patient. Therefore, a more accurate and efficient means of determining anesthetic uptake for patients who receive general anesthesia has become a greater concern for the anesthesiologist. The purpose of this project is to design and implement a system which can provide breath-by-breath analysis and quantification of anesthetic gas transport. It is felt that if such an information system were available, more precise control and closer physiologic surveillance is possible for the clinical practice of anesthesia.

History of Respiratory Gas Analysis and Interpretation

Historically, analyses of respiratory gases such as oxygen and carbon dioxide have proved to be significant in making physiological assessments. These earlier studies involved development of various measurement techniques which were used to determine metabolic rate, respiratory dead space, the effects of analgesic drugs on respiration and the significance of end-tidal CO_2. One early application of gas analysis was to determine changes in respiratory dead space caused by the drug atropine (Severinghuas and Stuffel 1955). In this study, a nitrogen gas analyzer was used to produce washout curves so that dead space could be calculated using Fowler's method (West 1974, pp. 19-20). Another study concerned with the effects of hypothermia on CO_2 production used an infrared CO_2 gas analyzer and a spirometer to measure the volume of CO_2 produced before and after hypothermia (Severinghaus, Stuffel and Bradley 1957). Indirect measurement of metabolic rate was also accomplished by measurement of oxygen consumption (Guyton and Farrish 1959). A rapid oxygen analyzer was used in a breathing system which maintained a constant flow of an oxygen-containing gas. Animals inhaled the oxygen gas mixture and returned expired CO_2 to the flowing gas mixture in the breathing system. The rate of O_2 consumption was determined from the difference between the inhaled O_2 concentration and the O_2 concentration measured downstream from the point of respiratory gas exchange multiplied by the flow rate of the gas in the breathing system. Since it is well known that one liter of O_2 consumed by the body

corresponds to approximately 4.8 KCAL of heat released in the oxidation of nutrients, a good approximation of total body metabolism was provided by this measurement system.

The first computer analysis of respiratory gases was performed by Noe (1963). In this study, pneumotachography was used to measure respiratory flow and an infrared analyzer was used for continuous measurement of expired CO_2. Both analog and digital computers were employed in creating concentration versus volume curves from single breath time analysis of CO_2 concentration and respiratory flow. This system was used to determine respiratory dead space, CO_2 production and pulmonary function in both healthy and diseased patients.

The effect of analgesic drugs on respiration has also been an area of application for gas analysis. Jennett (1968) used a pneumotachograph, an infrared CO_2 analyzer, a paramagnetic O_2 analyzer and a Douglas bag for collecting gas samples so that mean O_2 and CO_2 concentrations could be determined. Her system provided measurements of oxygen consumption, carbon dioxide production, respiratory exchange ratio and metabolic rate so that the effects of analgesic drugs could be quantitated. Nunn and Hill (1968) used spirometry and infrared CO_2 analysis to determine the effects of inhaled anesthetic agents on respiratory dead space and CO_2 partial pressure. This study used the simultaneous recordings produced by the spirometer and the CO_2 analyzer to produce concentration versus expired volume relationships which can be used to determine respiratory dead space.

Jeretin, Martinez and Wandycz (1971) developed a carbon dioxide mixing chamber that provided an alternative to cumbersome spirometers and Douglas bags that were typically used for measuring mean expired CO_2 and tidal volume. The primary purpose of their work was to demonstrate a simple and accurate device that could provide continuous measurement of mean expired carbon dioxide. It could also provide the data necessary for calculation of dead space and CO_2 production. The accuracy of the mixing chamber was determined by comparative measurements made with a Douglas bag.

The significance of interpreting end-tidal CO_2 during anesthesia was pointed out by Takki, Aromaa and Kauste (1972). The primary purpose of their study was to determine if various types of artificial ventilation induced hypocapnia which could lead to harmful side-effects such as metabolic acidosis, impaired tissue oxygenation due to shifting of the oxyhemoglobin dissociation curve, decreased cerebral blood flow and decreased cardiac output and stroke volume. The data in their study was acquired by a comparison of CO_2 levels in the blood versus expired concentrations of CO_2 provided by an infrared gas analyzer.

The more recent work in respiratory gas analysis has involved applications of microcomputers to perform on-line analysis of oxygen consumption and carbon dioxide production. Noe et al. (1980) developed a system which used an infrared CO_2 analyzer, a polarographic O_2 analyzer, a pneumotachograph and a digital microcomputer with an analog to digital converter. Flow rates and gas concentrations were recorded and played back into the computer which sampled the recordings at a 40 Hz rate. The

delay between flow and concentration signals was determined for each case. The digitized data was processed by multiplying each flow sample by its corresponding concentration sample and using Euler's method to obtain the total O_2 consumed and the CO_2 produced. An initial calibration recording was required before data processing could proceed. Another system recently developed for measuring pulmonary gas exchange (Ramanathan et al. 1982) measured O_2 consumption and CO_2 production in a Bain circuit. A polarographic O_2 analyzer and an infrared CO_2 analyzer were employed, but analysis of waveforms included only mean values of respiratory flow and concentration.

One trend observed from these studies is the continuing and growing interest in developing faster, more accurate and reliable methods of performing on-line measurements of gas transfer, end-tidal concentrations and other physiological variables. Another important trend is the growing use of more modern technology in implementing such methodologies for usage in the clinical environment. It is also apparent that methods for quantifying anesthetic gas transfer can be developed using measurement techniques similar to those previously discussed for O_2 and CO_2. However, none of these studies discussed this possibility and neither of the two recent studies involving on-line computer analysis mentioned *in vitro* verification of the accuracy of their methods.

This method for determining gas transfer in this project was similar to that used by Noe et al. (1980) except that in this case, a system for determining the breath-by-breath uptake of volatile anesthetic agents was developed. This system also provides measurements of other

important physiological parameters not included in Noe's work such as on-line measurement of tidal volume, respiratory rate, inspired and end-tidal concentrations of anesthetic, and the cumulative uptake of anesthetic agent measured from the start of induction. The accuracy of the output parameters provided by this system were determined *in vitro* with the aid of both electrical and mechanical test systems.

Reasons for Analysis and Interpretation of Anesthetic Gases

In order to properly discuss the reasons for analysis and interpretation of anesthetic gases, a brief review of some of the key factors involved with anesthesia delivery will be presented.

The overall goal of the anesthesiologist in delivering general anesthesia is to raise the concentration of the anesthetic in the arterial blood high enough to provide an unconscious and pain free state. Since no simple method exists to determine this effect, an indirect technique of gas analysis has been employed to establish a reference level. Minimum alveolar concentration (MAC) is the alveolar anesthetic concentration at standard atmospheric pressure and body temperature that produces immobility in fifty percent of the patients exposed to a noxious stimulus (Eger 1978, pp. 1-2). Therefore, MAC is a measure of the potency of a particular anesthetic agent and is used as a guideline in determining the concentration of anesthetic vapor that should be delivered to a patient. Although MAC is an alveolar value, it is usually estimated in percent of inspired gas since alveolar concentration is difficult to measure routinely. It is necessary to deliver higher concentrations for agents with higher MAC values in order to fully anesthetize the patient.

Likewise, the anesthesiologist must be careful not to deliver high concentrations for agents with lower MAC values for fear of seriously endangering the well-being of the patient.

Anesthetic uptake is determined from the conservation of mass principle. In this case, uptake of anesthetic by the patient must equal the difference between the amount of anesthetic inspired by the patient and the amount of anesthetic expired by the patient. This is simply a statement of mass balance between the anesthesia delivery system and the patient assuming that they are the only components involved with the exchange of mass in a lossless system. The amount and rate of anesthetic uptake are a function of tidal volume (V_T), alveolar volume (V_A), dead space volume (V_D), cardiac output (Q), respiratory rate (RR) and inspired, alveolar, arterial and venous concentration (C_{IN}, C_A, Ca and Cv respectively). Note that a complete list of the symbols used in this chapter and the following chapters is provided in Appendix E. Figure 1.1 shows the interaction of these factors. $C_{IN} \times V_T$ gives the amount of anesthetic gas delivered to the lung per breath while the amount exhaled from the lung in a single breath is $C_A \times V_A + C_{IN} \times V_D$. The difference between the amount of anesthetic inhaled and the amount exhaled is defined as the uptake (U). The rate of uptake ($\dot{U}$) is simply U x RR and is related to cardiac output by the equation

$$\dot{U} = (Ca - Cv) \times Q. \qquad (1)$$

This equation presupposes that the transport of anesthetic between the blood and the lung is carried out by diffusion. In order for

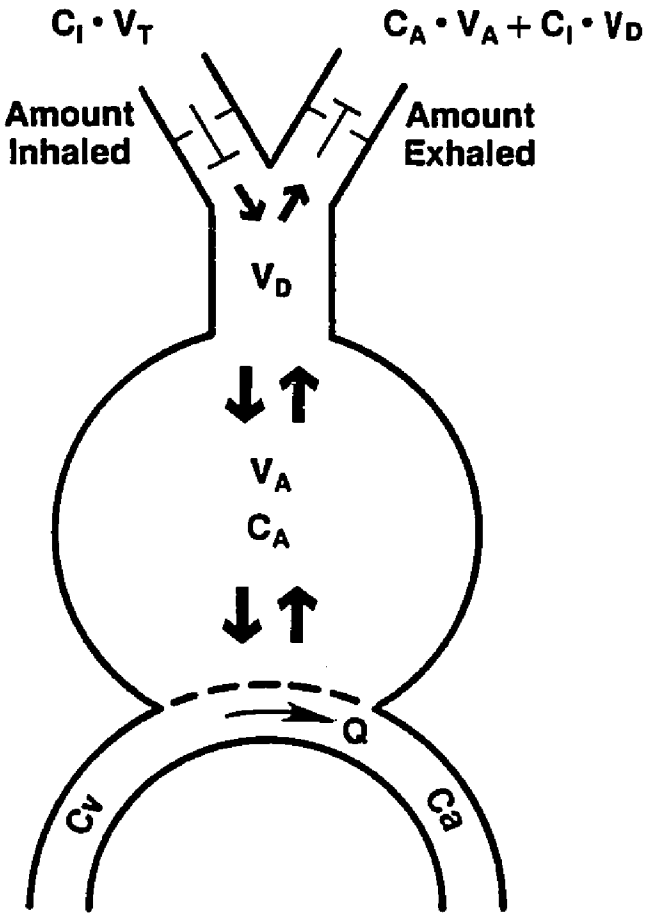


Figure 1.1. Lung-vascular transport model illustrating some of the factors involved with anesthetic uptake.

diffusion to occur, there must be a concentration difference between the inspired gas and the venous blood. Since the area for gas exchange between the lung and pulmonary blood is very large, diffusion occurs rapidly. Under normal physiological conditions, an equilibrium will occur between the lung and the blood before the start of expiration. Respiratory physiology demonstrates that when this occurs, the alveolar concentration is always proportional to the arterial concentration. The ratio between these two parameters is defined as the in vivo blood-gas partition coefficient which may be considered a constant for an individual although it may vary from person to person. Therefore, determination of the alveolar concentration provides an indirect measurement of the concentration of anesthetic in the blood.

Equation (1) shows the relationship between the rate of anesthetic uptake and the patient's cardiac output. The only parameter that cannot be determined by analysis of anesthetic gas transfer is the venous concentration which can only be determined by taking samples of the venous blood.

Patients with health problems such as obesity, pulmonary dysfunction or extremes of age often have complications involving anesthetic uptake and distribution due to their physiological condition. These may affect one or more of the factors mentioned above.

Little research has been done to determine if on-line quantitative information regarding anesthetic uptake is useful to the anesthesiologist. However, physiological theory and empirical studies have indicated some important parameters that should be monitored during

anesthetic delivery. For example, alveolar anesthetic concentration is proportional to the end-tidal concentration, which is the widely accepted physiological term for the concentration measured at the end of expiration. The proportionality constant depends upon the ratio of dead space to tidal volume. Referring to Figure 1.1, note that the amount of exhaled anesthetic is the sum of two terms, the dead space term ($C_{IN} \times V_D$) and the alveolar term ($C_A \times V_A$). This implies that the expired concentration is a mixture of the inspired concentration and the alveolar concentration. If V_D is small compared to V_A, then there is only a brief period of mixing between alveolar and dead space gas and the end-tidal concentration is approximately equal to the alveolar concentration. On the other hand, if V_D is large when compared to V_A, then there will be a significant amount of mixing between the alveolar and dead space gas and the end-tidal concentration will be significantly different from the alveolar concentration. This is often the case for patients with diseased lungs. However, for healthy patients, determining end-tidal concentration provides an indirect measure of anesthetic concentration in the blood and may be used to predict the rate at which blood concentration level changes with time. Over a short period of time the dead space to tidal volume ratio (V_D/V_T) is usually constant even in a patient with lung disease. Prior determination of this ratio may allow for useful measurement of end-tidal concentration.

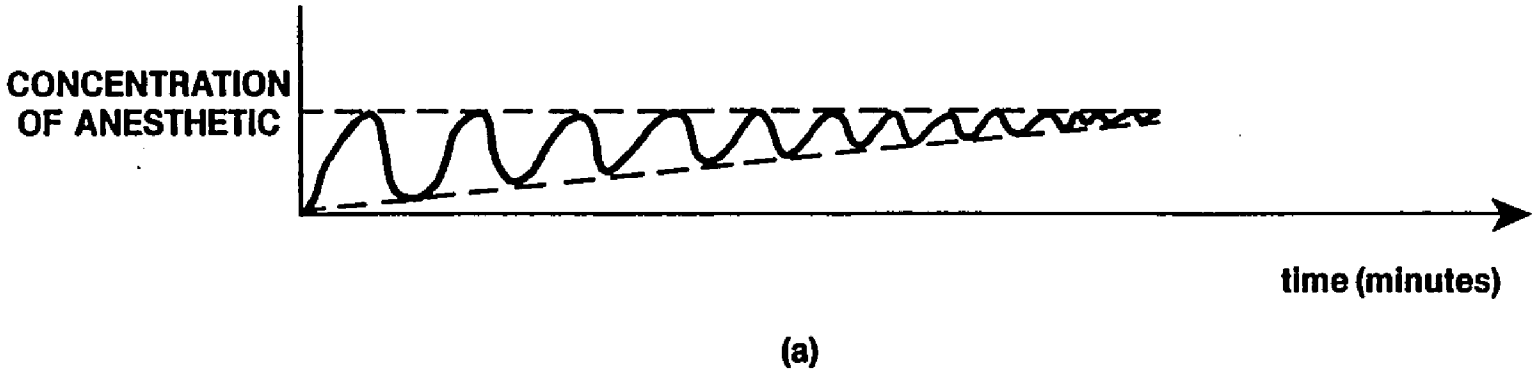
One important physiological model for anesthetic uptake was developed by Eger (1978, pp. 113-120). In this model, it is assumed that the anesthesia delivery system has reached a steady-state and the

concentration of anesthetic delivered to the patient is a constant. Figure 1.2 demonstrates the change in end-tidal concentration over time when inspired concentration is constant. The periodic curves represent actual fluctuations in anesthetic level measured at the mouth of the patient. The dashed lines represent inspired and end-tidal concentration levels. End-tidal concentration will always asymptotically approach the inspired concentration for both induction and emergence.

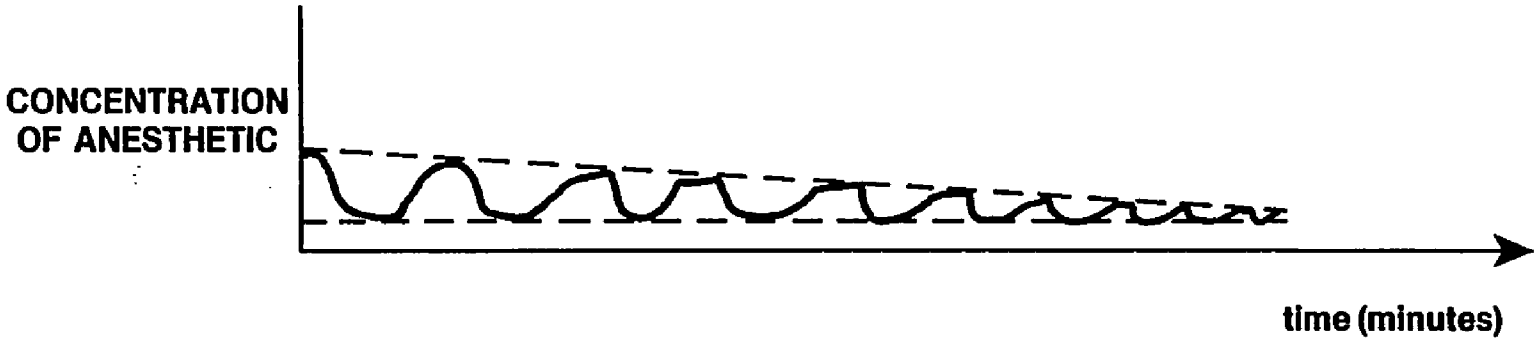
Eger (1978) also articulated the "concentration effect" which states that the higher the inspired concentration, the more rapid the rise in end-tidal concentration. This effect may be observed by periodically deriving the ratio of end-tidal to inspired concentration and determining its time rate of change. Since the rate of anesthetic uptake decreases with increasing alveolar concentration, determining end-tidal concentrations and the end-tidal to inspired concentration ratio can aid the anesthesiologist in predicting the patient's anesthetic uptake.

Another empirical model of anesthetic uptake is the square root of time model which is the basis of the investigations carried out by Lowe and Ernst (1981, pp. 67-89). Their work deals with the significance of both the instantaneous uptake and the cumulative uptake of anesthetic and their relationship to anesthetic dosage and the depth of anesthetic. The significance of determining cumulative uptake stems from the empirical relationship:

$$\text{Cumulative uptake} = 2 \times Ca \times Q \times (t)^{\frac{1}{2}} \quad . \qquad (2)$$



(a)



(b)

Figure 1.2. Concentration vs. time curves.

(a) Induction.
(b) Emergence.

Ca and Q are the same as previously defined, t is the total time elapsed during anesthesia delivery and the constant (2) has the units of $(\text{minutes})^{\frac{1}{2}}$/volume percent in order to make the equation dimensionally correct. This relationship is subject to many constraints such as the amount of fat in the patient's body and the condition of the patient's heart and lungs. However, this relationship can still be used to provide an approximation of the patient's cardiac output when other parameters are consistent. For example, since end-tidal concentration is proportional to alveolar concentration which is proportional to arterial concentration, end-tidal concentration is proportional to the arterial concentration with the blood-gas partition coefficient as the portionality constant whenever (V_D/V_T) is small. Therefore, by measuring t and the cumulative uptake, cardiac output can be determined using Eq. (2) and a good approximation of the blood-gas partition coefficient. It should also be noted that, unlike Eger's model, this model considers the total time of induction, including the time prior to the anesthesia delivery reaching a steady state, and makes no assumptions regarding the level of inspired concentration.

The previous work done in respiratory gas analysis, especially the work done by Noe et al. (1980), demonstrated the feasibility of making on-line continuous measurements of parameters such as O_2 consumption and CO_2 production. The major goal of this project is to provide this same type of measurement for anesthetic agents. Other parameters such as tidal volume, end-tidal and inspired anesthetic concentration, the ratio of end-tidal to inspired concentration and the cumulative uptake of

anesthetic, measured from the time the measurement system was activated, are also provided since they are relevant to the discussions and models of anesthetic uptake previously discussed.

Flexibility and modularity were also important considerations of the system design so that the system could be used in various situations and be easily modified without any extensive redesign. The output parameters provided by the system should be within at least 5% of their true value since the anesthesiologist is usually provided this level of accuracy by other instruments commonly used in the clinical environment. The system design is limited to performing breath-by-breath analysis on normal adult patients who have at least a two second apnea period between breaths.

CHAPTER 2

SYSTEM DESIGN

Figure 2.1 is a block diagram of a conventional circle system for anesthesia delivery. Oxygen, nitrous oxide and anesthetic vapor are provided to the system by the gas flowing from the oxygen and nitrous oxide supplies through the anesthetic vaporizer and into the circle. A single direction of flow in the circle is accomplished by the pair of unidirectional valves V_1 and V_2. This arrangement prevents rebreathing of carbon dioxide while unused anesthetic vapor, oxygen and nitrous oxide are cycled back to the patient through the CO_2 absorber. The reservoir bag enables the circle system to deliver the larger gas volumes necessary during peak flow periods of respiration.

Figure 2.2 is a block diagram of the monitoring system and its relationship to the patient and the anesthesia delivery system. The sensing devices that provide respiratory flow and anesthetic concentration information are typically placed between the Y-piece of the delivery system and the mouth of the patient and should be as close to the patient as possible (i.e., directly connected to the endotracheal tube or mask). The patient, either spontaneously or with the aid of a ventilator, cycles anesthetic-containing gas back and forth through the flow and concentration transducers. Signals representing flow and concentration are produced by the flow meter and anesthetic gas analyzer which are in turn

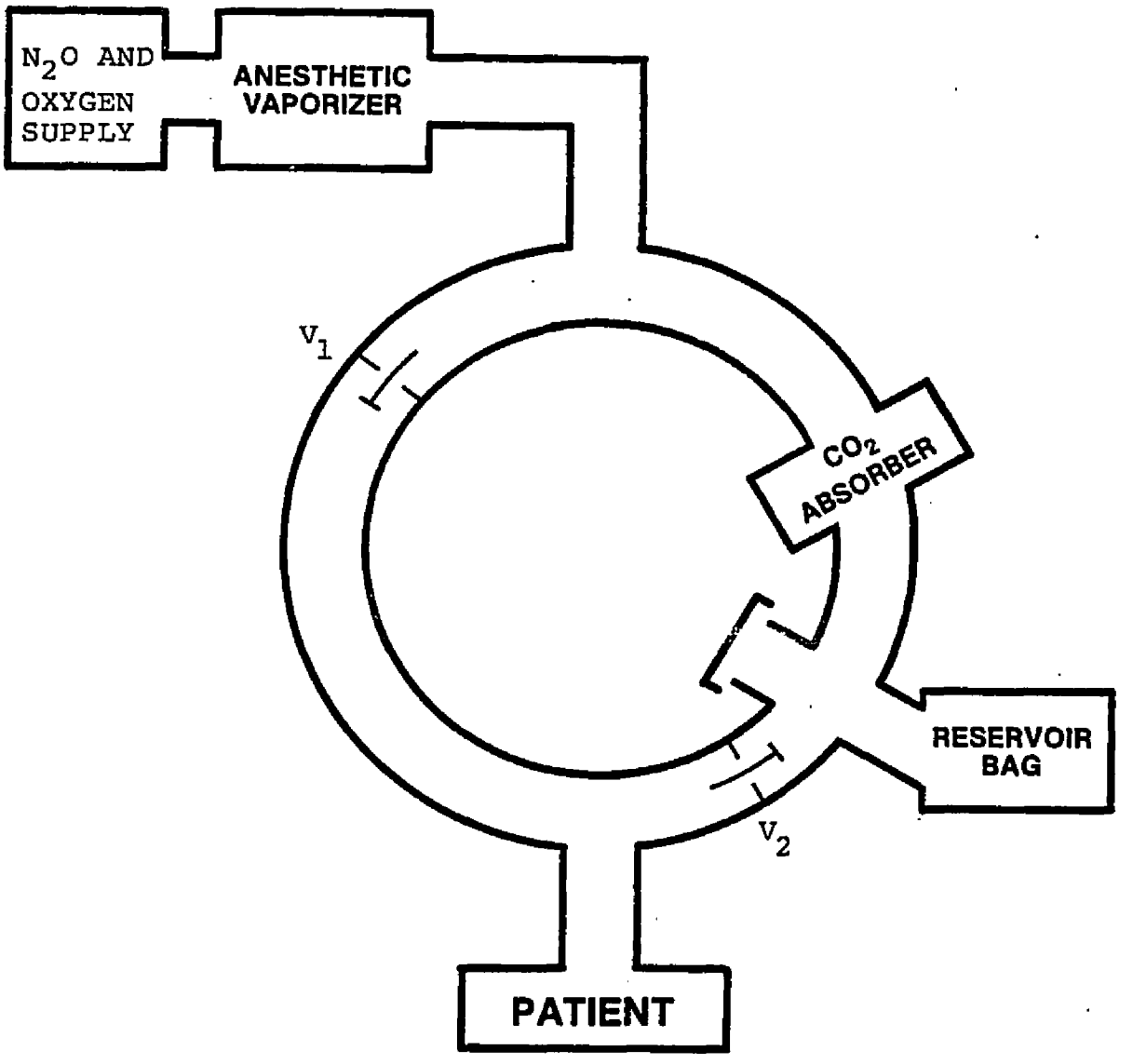


Figure 2.1. Block diagram of conventional circle system for anesthesia delivery.

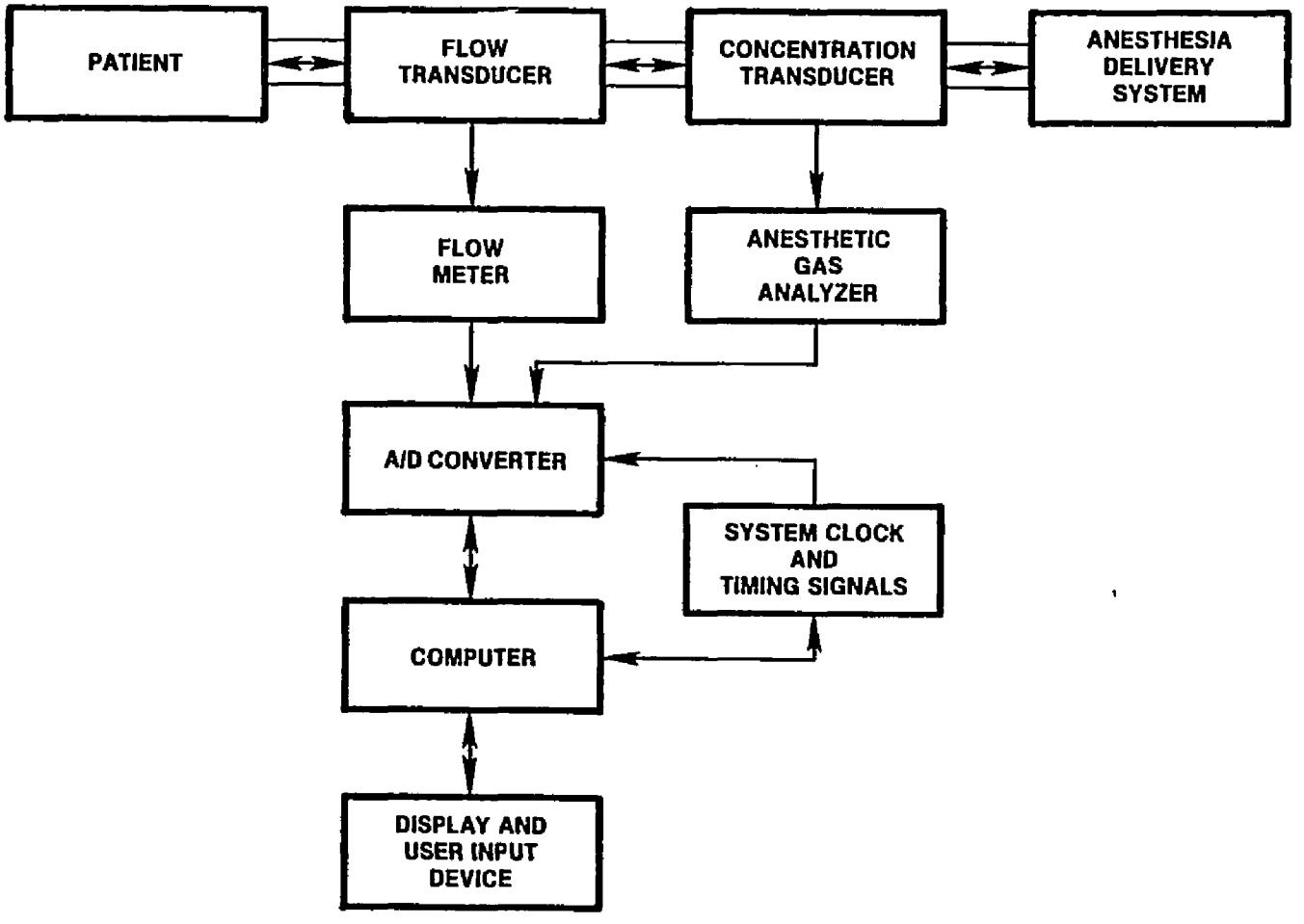


Figure 2.2. Block diagram of monitoring system and its relationship to the patient and the anesthesia delivery system.

digitized by the analog-to-digital converter for computer input. Timing signals are provided by the system clock so that data can be attained at a predetermined rate. Acquisition and processing of data is controlled by an algorithm stored in computer memory. User control information may start and stop the system or provide parameters to computer memory which can be used by the system control algorithm. The arrows in Figure 2.2 indicate direction of information flow.

System Operation

The output of the flow meter is used to determine the onset of inspiration, the start of expiration and the end of the respiratory cycle. During the respiratory cycle, flow and concentration samples are stored in computer memory for processing. At the end of the cycle, the system ceases to acquire flow data while the accumulated single breath data is being processed. The gas analyzer used had a response time delay of 0.2 to 0.7 seconds; therefore, the concentration data becomes available to the computer some time after the start of the respiratory cycle and continues until the same time delay has elapsed after completion of the respiratory cycle. The computer processes the data and displays the results one second later. The system then returns to testing flow data for the start of respiration and the entire process is repeated. Figure 2.3 is a flow chart illustrating the sequence of operations carried out by the system. Details concerning system operation are presented in Chapter 3.

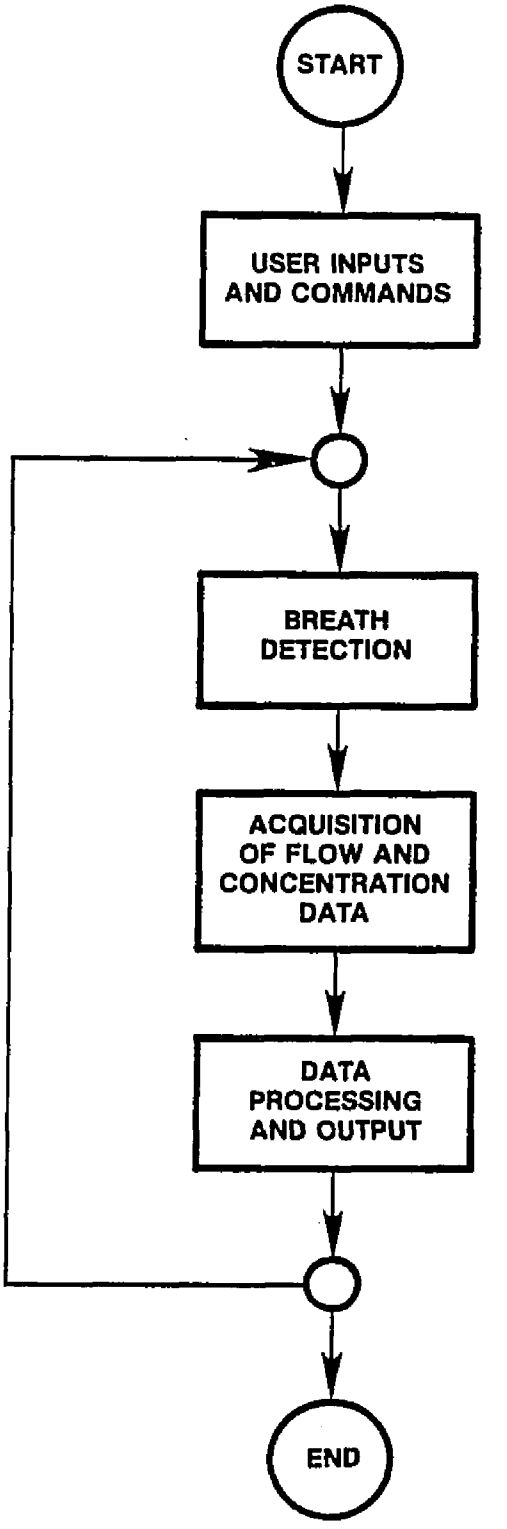


Figure 2.3. System control algorithm.

System Input and Output Specifications

Listed below are the outputs provided by the system:

1) inspired and end-tidal concentrations of anesthetic (volume percent);
2) the ratio of end-tidal to inspired concentration;
3) respiratory rate (breaths per minute);
4) the breath uptake of anesthetic (milliliters of vapor per breath);
5) the cumulative uptake of anesthetic (milliliters of vapor);
6) the inspired and expired tidal volumes (liters);
7) time and square root of time elapsed since the start of anesthesia delivery (minutes and $(\text{minutes})^{\frac{1}{2}}$);
8) an apnea alarm in which the delay between the cessation of breathing and activation of the alarm is preset by the user. When the delay is exceeded, the words APNEA ALARM! are continuously displayed until a breath is detected.

This system requires only two physiological inputs from the patient: respiratory flow and anesthetic concentration measured at the patient's mouth. User inputs for the system are as follows:

1) the apnea alarm delay value, which is an integer representing hundredths of a second;
2) the delay time between the flow measuring device and the anesthetic gas analyzer, which is also an integer value in hundredths of a second (this value may be determined by the system via a user option);

3) a flow calibration factor which is the number of liters per minute passing through the flow transducer head that produces a one volt output from the flow meter (a real number with the units of liters per minute per volt);
4) a concentration calibration factor which is the concentration sensed by the gas analyzer transducer or sampling chamber that produces a one volt output from the analyzer (a real number with the units of percent anesthetic concentration per volt);
5) a start and a stop command.

Discussion of System Design

The major purpose of this system is to provide a breath-by-breath analysis of anesthetic gases. However, the system is sequential in that the processing and display of data must take place before the next breath can be sampled and analyzed. Therefore, an apnea time between breaths is required if the system is to function correctly. Since there is usually an apnea time between breaths of approximately two seconds or more for normal voluntary breathing or when respiration is accomplished with the aid of a mechanical ventilator, the question remains whether this is time enough for processing and outputting of data to be completed. The equation which describes this situation is

$$Ta = Td + Tp + To \tag{3}$$

where Ta is the apnea time between breaths, Td is the time delay between the anesthetic gas analyzer and the flow meter, Tp is the processing time and To is the time required to output the results. Tp + To is usually no

longer than one second with the aid of high speed computers, buffered peripherals and efficient data processing algorithms. The gas analyzer chosen to implement this system (the Engstrom EMMA) has a specified response time of 0.2 to 0.7 seconds; therefore, this system should have no problems when used for analyzing a normal adult patient with an apnea period between breaths of two seconds or longer. Assuming that a respiratory cycle is approximately two to three seconds long, the maximum respiratory rate that can be used with this system is about twelve to fifteen breaths per minute. Small children and other rapidly breathing patients would require a system which can provide breath-by-breath analysis within fractions of a second. This could be accomplished by multiprocessing, which is the use of separate microprocessors each dedicated to a specific task (i.e., data acquisition, processing data, control of displays and management of calibration procedures).

CHAPTER 3

SYSTEM REALIZATION

The system discussed and illustrated in Chapter 2 was realized with the following components:

1) the EMMA anesthetic gas analyzer (Engstrom Medical, Bromma, Sweden) which employs a coated vibrating adsorption crystal to detect anesthetic concentration;
2) the McGaw VR-1 Respiratory Therapy Unit (American Edwards Laboratories, Santa Anna, California) which uses the differential pressure produced by a pneumotachograph to measure respiratory flow;
3) the LSI-11 mini-computer system with the ADV11 analog to digital converter and the KWV11 programmable real-time clock (Digital Equipment Corp., Maynard, Massachusetts);
4) the Tektronix FG501 oscillator (Tektronix Corp., Beaverton, OR).

The system configuration using these components is shown in Figure 3.1. This configuration implements the block diagram of Figure 2.2 with system operation and control accomplished in the manner outlined in Figure 2.3.

Software Implementation

All source code developed for this system was written in FORTRAN IV for the LSI-11 mini-computer. Compilation of FORTRAN source code and

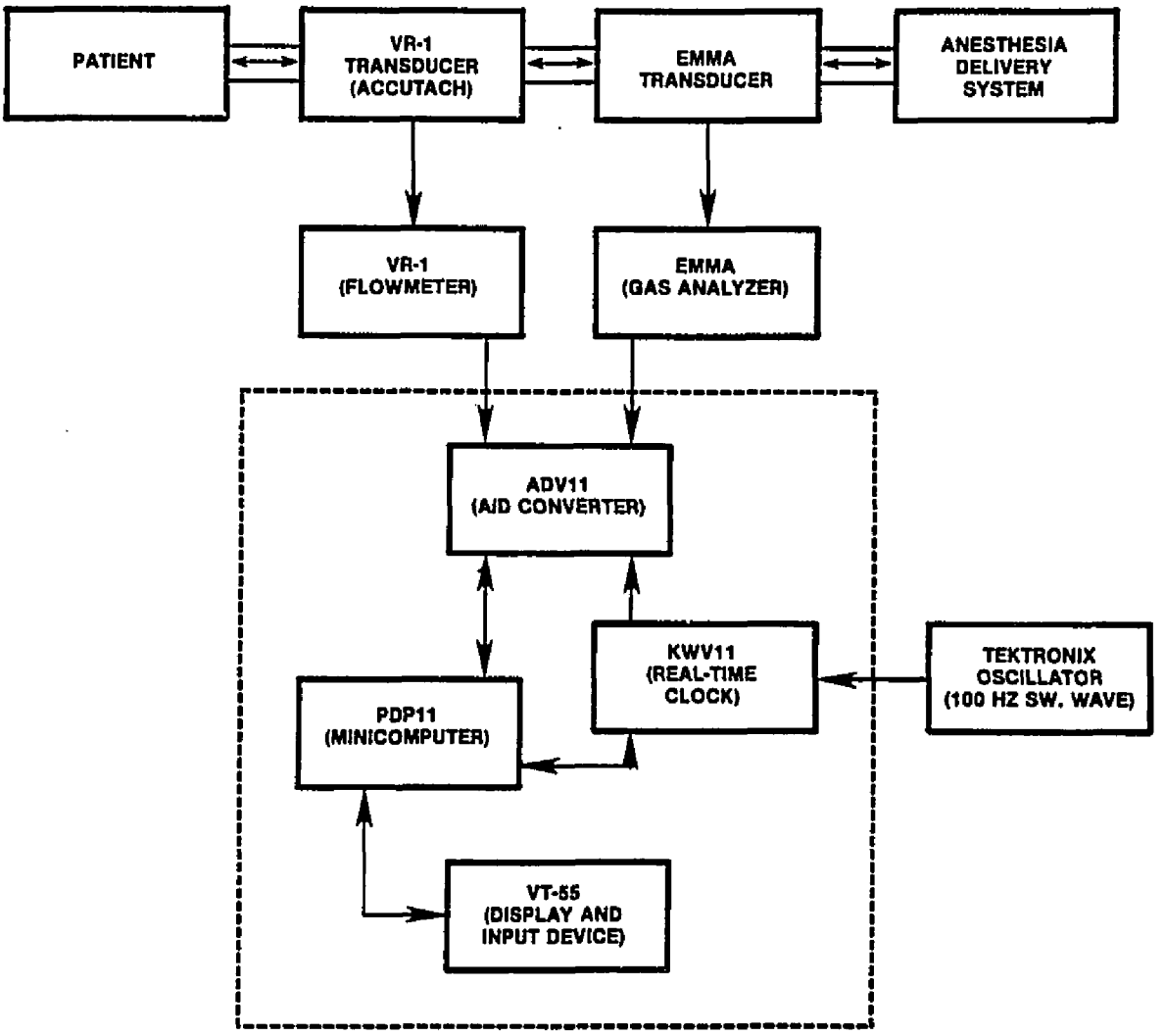


Figure 3.1. Block diagram showing the relationship of components for realization of the system.

linkage of the LSI-11 system library and designer written software modules was accomplished by the software compiler and linker developed by the Digital Equipment Corporation for the RT-11 operating system. Flow charts for the six software modules, MONITR, USEROP, LAGCAL, DETECT, ACQUIR and PROCES, used to implement the system functions outlined in Figure 2.3 are listed in Appendix B. Source code for each of the six modules is listed in Appendix C. The following subsections will describe each of the software modules.

The Main Calling Program - MONITR

MONITR is composed of four major subroutines that

1) interact with the user to obtain information (USEROP),
2) detect the onset of respiration (DETECT),
3) acquire and store data samples of the respiratory and concentration waveforms corresponding to a single breath (ACQUIR) and
4) process the acquired data and display the results (PROCES).

In addition, MONITR also contains subroutines that set and read the real-time clock. After completion of the data acquisition subroutine, MONITR checks the number of data samples acquired to determine if a "valid breath" has occurred. A breath is considered "valid" if the inspiratory half of its respiratory cycle is at least a tenth of a second long.

User Input and Command Subroutine - USEROP

This subroutine requests from the operator the information discussed in Chapter 2 (System Inputs and Outputs section) and describes the form in which the data is to be entered. It also allows the user to

implement a special function which automatically calculates the time delay between the respiratory and concentration waveforms received from their respective devices. The subroutine which accomplishes this function is called LAGCAL. LAGCAL simultaneously samples both the flow and concentration waveforms from the start of a respiratory cycle. When the cycle is completed, the operator is asked whether this has been done during induction or emergence. For either case, the time corresponding to the end of inspiration is determined during the course of the respiratory cycle and stored as an integer variable. For induction, the subroutine searches the buffer containing the concentration data samples to determine which sample corresponds to the end of the inspiratory plateau (i.e., the largest concentration sample that was acquired at the latest point in time). The delay is then the difference between the time when this data sample was taken and the time corresponding to the end of inspiration. For emergence, the subroutine operates in a similar manner except that the time corresponding to the end of the inspiratory valley (i.e., the smallest concentration sample that occurred at the latest point in time) is substituted for the time corresponding to the end of the inspiratory plateau. The measurement made by the LAGCAL subroutine is illustrated in Figure 3.2 as the real-time interval between the zero-crossing in the respiratory flow waveform and the end of the inspiratory plateau in the concentration waveform. It should be noted that the LAGCAL subroutine is limited to calculating time delays that are no greater than one half of the respiratory cycle.

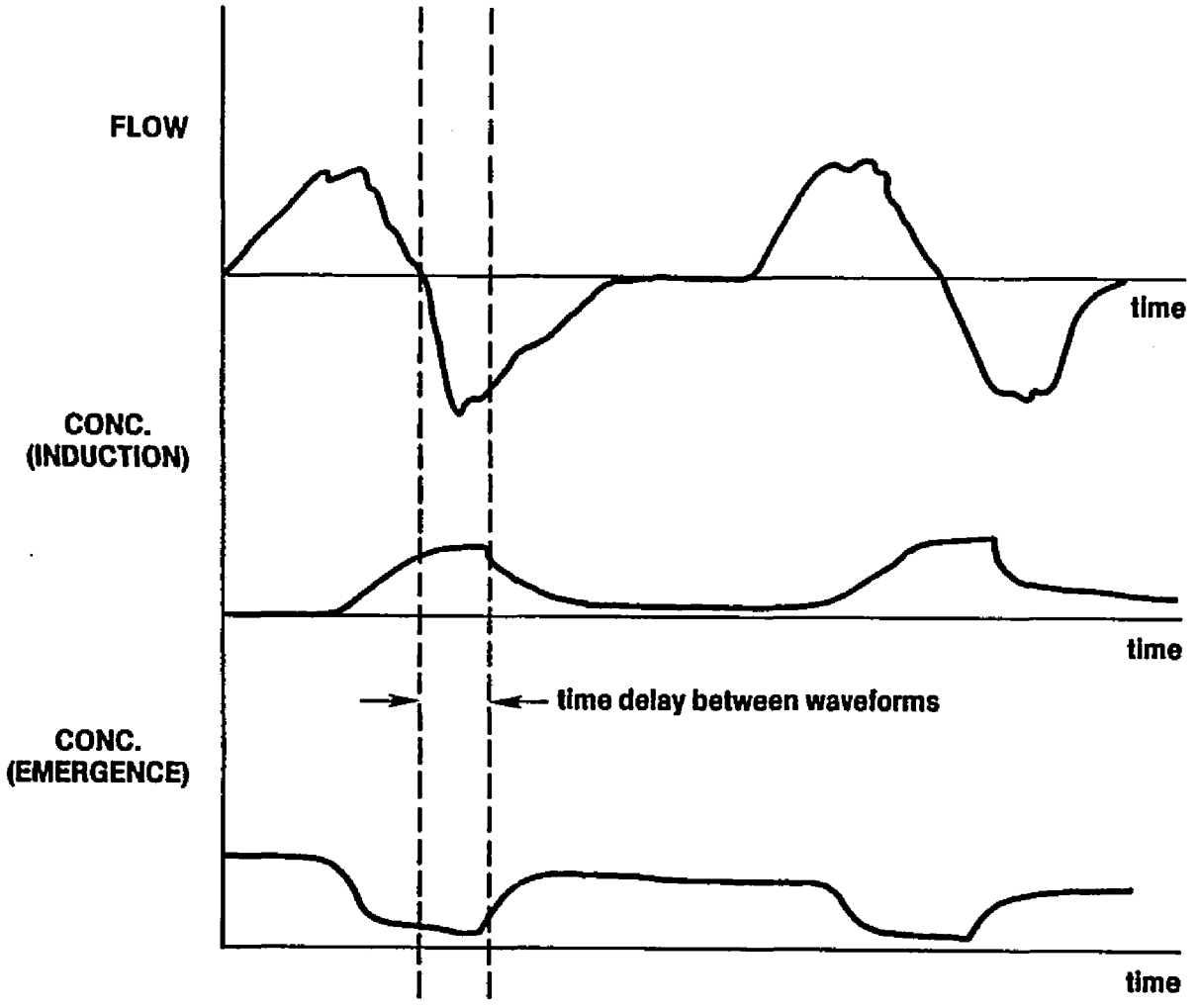


Figure 3.2. Illustration of how LAGCAL determines the delay between the flow and concentration waveforms.

Information regarding system usage is fully outlined in Appendix A which contains a set of user instructions for operating this system. Discussions of breath detection and data acquisition will be outlined in the next two subsections.

Onset of Respiration Detection Subroutine - DETECT

The function of this subroutine is to detect the start of a respiratory cycle. It accomplishes this by using the FORTRAN library routine RTS (real-time sampling) in the interrupt driven sampling mode using Schmitt trigger number 1 as an input for the interrupt signals provided by the 100 Hz square wave oscillator. For more details regarding the use and function of this library routine, see DECLAB-03 FORTRAN Extensions User's Guide (Digital Equipment Corporation 1978).

DETECT first takes a flow sample and checks to see if it is greater than the value that corresponds to a minimal amount of inspiratory flow (approximately 0.05 volts) which now will be called the positive threshold (inspiratory flow will correspond to a positive direction and therefore a positive voltage produced by the flow meter). If the first flow sample obtained is below this threshold, DETECT continues to take flow samples until a sample exceeds the positive threshold. If the first flow sample obtained is above the positive threshold, then the subroutine continues to take samples until a sample is acquired that is below the positive threshold. DETECT then proceeds in the manner described above until the positive threshold is once again exceeded. In either case, it is an upward crossing of the positive threshold that marks the onset of respiration. The data acquisition routine will be

called immediately after such an event. Breath detection is implemented in this way so that an entire respiratory cycle can be sampled instead of attempting to handle cycles that have already started. This method is effective in synchronizing the system to the patient. Figure 3.3 demonstrates that the start of a breath will not be acknowledged by the DETECT subroutine until an upward crossing of the positive threshold has occurred.

Another function of DETECT is to check for the possibility of patient apnea. It accomplishes this by summing the number of samples it has taken while waiting for a breath to begin and comparing this sum to the apnea alarm value preset by the user.

Data Acquisition Subroutine - ACQUIR

The primary purpose of this subroutine is to acquire all flow and concentration data and store it in buffers for processing. This subroutine, like DETECT, acquires data samples with the aid of the FORTRAN library subroutine RTS. Flow sampling starts immediately. Once the number of samples acquired corresponds to the time delay between the flow meter and gas analyzer, the subroutine will start acquiring concentration samples. The first flow sample whose value is below the positive threshold will be used to mark the end of inspiration and the time corresponding to when this sample was acquired will be stored as the variable INEND. Sampling of both flow and concentration continues until a flow sample is acquired that upwardly crosses the negative threshold (this corresponds to what was defined for the positive threshold except that -0.05 is the voltage representing the least detectable amount of

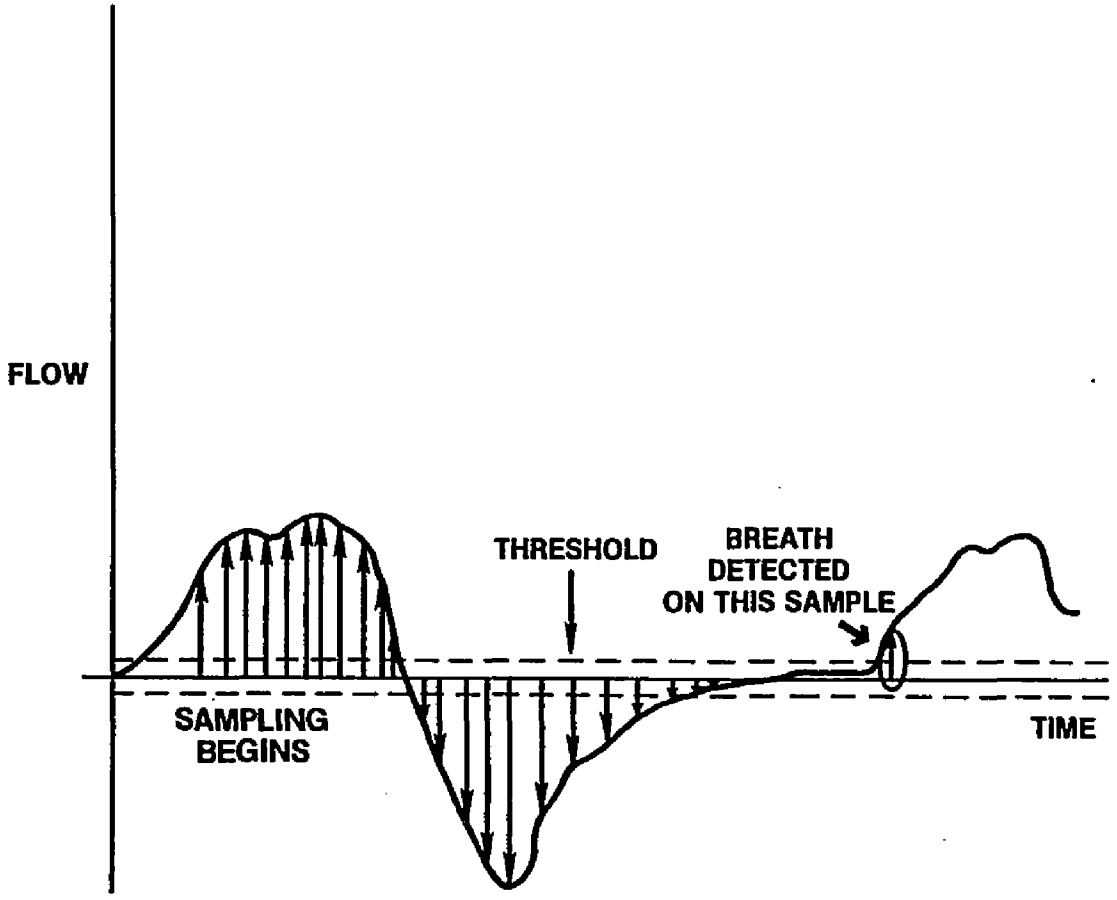


Figure 3.3. Illustration of the breath detection algorithm.

expiratory flow). The time corresponding to this flow sample is stored as variable EXEND which marks the end of the respiratory cycle. Flow sampling then ceases but sampling of concentration continues until the number of concentration samples equals the number of flow samples.

Respiratory measurements using pneumotachography have a frequency range from 0 to 40 Hz (Webster 1978, pp. 7-8). The Nyquist criterion states that a sampling rate of at least twice the highest frequency component of the signal being sampled is required to avoid serious loss of information. Therefore, 100 Hz was chosen as the sampling frequency in order to meet this minimum requirement and to provide some margin of safety. The buffers used to store the data samples are 1000 words each in length which allows for a respiratory cycle of up to ten seconds in duration.

When ACQUIR is finished gathering data it returns to the main program where the data processing subroutine is then called. Figure 3.4 illustrates the points on the respiratory waveform that ACQUIR interprets as the end of inspiration and expiration. ACQUIR also assists the main program in checking for valid breaths by returning a count of the number of flow samples acquired.

Data Processing and Output Subroutine - PROCES

This subroutine processes the data samples provided by the ACQUIR subroutine and displays the results to the operator as specified in Chapter 2. All data samples must be converted to their voltage equivalents. This system employs a twelve bit A/D converter which implies that there are 2^{12} or 4096 possible output values provided by the converter to

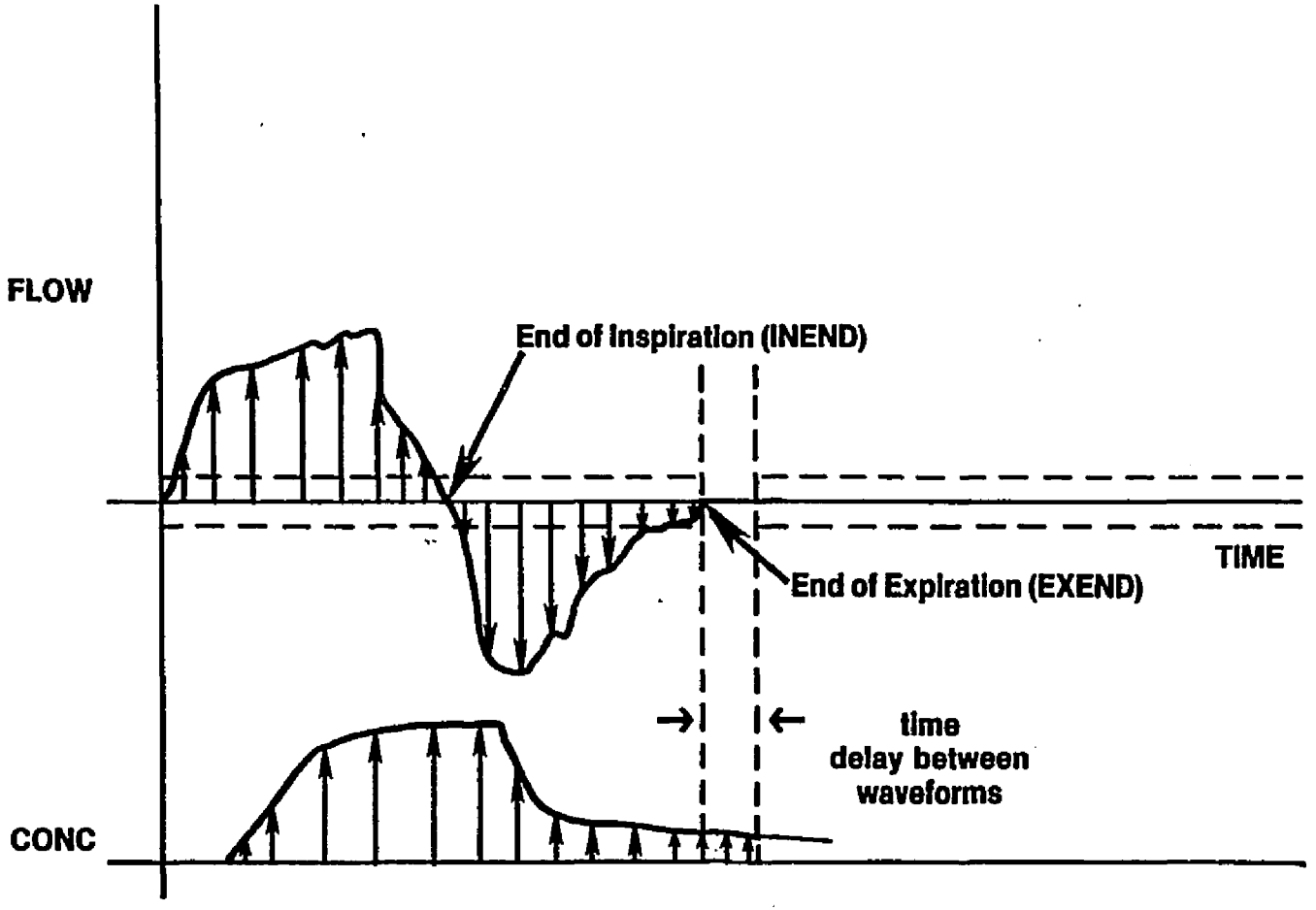


Figure 3.4. Illustration of the ACQUIR subroutine.

the computer. The specified input range of the converter is from +5 to -5 volts where 4095 corresponds to a +5 volt input and 0 corresponds to a -5 volt input. Assuming that the A/D converter provides a linear output response to all voltages within the specified input range, the equation for transforming a digital output value to an analog input voltage can be approximated by a simple linear relationship

$$A = D \times 10/4095 - 5 \tag{4}$$

where A is the analog voltage and D is the digital value. The value of the slope and the intercept in Eq. (4) were derived from the input and output specifications of the A/D converter.

The next step is to multiply the voltage obtained in the above equation by the proper calibration value that was provided by the user during the USEROP subroutine (i.e., the flow calibration value (FLCAL) for flow samples and the concentration calibration value (CONCAL) for concentration samples). Flow samples are stored in a buffer labeled IFLOW while concentration samples are stored in a buffer labeled ICONC.

A summary of the equations used to calculate inspired concentration (C_{IN}), end-tidal concentration (C_{ET}), the ratio of end-tidal to inspired concentration (RATIO), the respiratory rate (RR), the inspired volume (V_{IN}), the expired volume (V_{EX}), the single-breath uptake of anesthetic (U) and the cumulative uptake are derived and presented in the following section. When data processing is completed, PROCES displays the results and returns to the main program MONITR.

A Summary of the Calculations Performed by the PROCES Subroutine

Inspired and end-tidal concentration are determined by using Eq. (4) to convert the last inspired and last expired concentration ($INCONC_{INEND}$ and $ICONC_{EXEND}$) samples to their analog input voltage equivalents and multiplying both by concentration calibration factor (CONCAL)

$$C_{IN} = (ICONC_{INEND} \times 10/4095 - 5) \times CONCAL; \quad (5)$$

$$C_{ET} = (ICONC_{EXEND} \times 10/4095 - 5) \times CONCAL. \quad (6)$$

Therefore, the ratio of end-tidal to inspired concentration is simply

$$RATIO = C_{ET}/C_{IN} . \quad (7)$$

Respiratory rate is calculated using both the starting time of the breath presently being analyzed (ITIME) and the starting time of the previously analyzed breath (TIME0)

$$RR = 1/(ITIME - TIME0) . \quad (8)$$

Inspired and expired volume are simply the time integration of respiratory flow. For inspired volume, the integration limits are from the start of the respiratory cycle until the end of inspiration. For expired volume, the integration limits are from the end of inspiration to the end of expiration

$$V_{IN} = \int_{ITIME}^{INEND} F(t)\, dt \quad (9)$$

$$V_{EX} = \int_{INEND}^{EXEND} F(t)\, dt \qquad (10)$$

where V_{IN} is the inspired volume, V_{EX} is the expired volume, F is respiratory flow, t is time and ITIME, INEND and EXEND are as previously defined. The integrations in Eqs. (9) and (10) can be approximated using the set of flow samples gathered by the data acquisition routine (ACQUIR) and by employing the trapezoidal rule

$$V_{IN} = 0.01 \times FLCAL \times \sum_{i=ITIME}^{INEND} (IFLOW(i) \times 10/4095 - 5) \qquad (9a)$$

$$V_{EX} = 0.01 \times FLCAL \times \sum_{i=INEND}^{EXEND} (IFLOW(i) \times 10/4095 - 5) \qquad (10a)$$

where 0.01 seconds is the time interval between samples, FLCAL is the flow calibration factor, IFLOW is the buffer that stores the flow samples and all other variables are the same as previously defined.

The calculation of the anesthetic uptake for a single breath is similar to the calculations for inspired and expired volume except that anesthetic concentration is included as a factor. The integration in this case starts at the beginning of the respiratory cycle to the end of expiration

$$U = \int_{ITIME}^{EXEND} F(t) \times C(t - Td)\, dt \qquad (11)$$

where C is the concentration, U is the single breath uptake, Td is the time delay between the respiratory and concentration waveforms and all other variables are the same as previously defined. Once again by using the flow and concentration samples gathered by the data acquisition routine (ACQUIR) and the trapezoidal rule, the single breath uptake can be approximated by the following equation:

$$U = 0.01 \times FLCAL \times CONCAL \times \sum_{i=ITIME}^{EXEND} \{(IFLOW(i) \times 10/4095 - 5) \times (ICONC(I) \times 10/4095 - 5)\} \quad (11a)$$

where all the variables in Eq. (11a) are the same as previously defined. Note that the time delay between respiratory and concentration waveforms (Td) is not included in Eq. (11a) since acquisition of concentration samples did not begin until after the time delay (Td) had elapsed as previously discussed in the section describing the ACQUIR subroutine. Cumulative uptake is simply the summation of all the single breath uptakes.

The relationship between Eq. (11a) and the definition of the single breath uptake of anesthetic described in Chapter 1 can be illustrated by separating the right side of Eq. (11a) into two terms

$$U = 0.01 \times FLCAL \times CONCAL \times \sum_{i=ITIME}^{EXEND} \{(IFLOW(i) \times 10/4095 - 5) \times (ICONC(i) \times 10/4095 - 5)\} + 0.01 \times FLCAL \times CONCAL$$

(continued)

$$x \{(IFLOW(i) \times 10/4095 - 5) \times (ICONC(i) \times 10/4095 - 5)\}. \quad (12)$$

The first term on the right side of Eq. (12) is essentially $C_{IN} \times V_T$ while the second term is the same as $C_A \times V_A + C_{IN} \times V_D$ which were the same terms describing the conservation of mass principle discussed in Chapter 1 and illustrated in Figure 1.1. The plus sign connecting these two terms is due to the fact that in this system inspiratory flow is assumed to be in the positive direction and expiratory flow in the negative direction. If respiratory flow was only assigned an absolute value, then the two terms would have a negative sign between them. Since there is no actual calculation of V_D made by this system, it is necessary to take continuous samples of concentration in order to account for the mixing of alveolar and dead space gas. This is also true during the inspiratory half of the respiratory cycle since the concentration of gas entering the patient does not immediately rise to the level of anesthetic concentration in the delivery system due to the time it takes to fill the tube connecting the patient to the delivery system.

CHAPTER 4

METHODS OF SYSTEM EVALUATION

The system described in Chapter 3 was tested by two different methods. The first method used electrical analog signals to simulate respiratory and concentration waveforms with the purpose of testing the system's computer hardware and software. The second method employed mechanical test systems which simulated the breathing of anesthetic gas by a patient. The EMMA and VR-1 provided the respiratory and concentration waveforms generated by the mechanical test systems.

Electrical Analog Simulation Tests

For this set of tests, sine waves were used to simulate respiratory flow waveforms and square waves were used to simulate concentration waveforms. Figure 4.1 compares actual flow and concentration waveforms to the electrical analog signals used in this simulation. Although the simulation waveforms are not congruent with the physiological waveforms, they do provide an adequate representation that can be used to test computer hardware and softwave.

Equipment

A Hewlett-Packard 3694A instrumentation recorder, a Tektronix FG 501 oscillator, a 741 operational amplifier, a 1N 4005 signal diode, a 2 kilo-ohm potentiometer and a Tektronix T922 dual channel oscilloscope were used to implement the block diagram of Figure 4.2. The recorder was

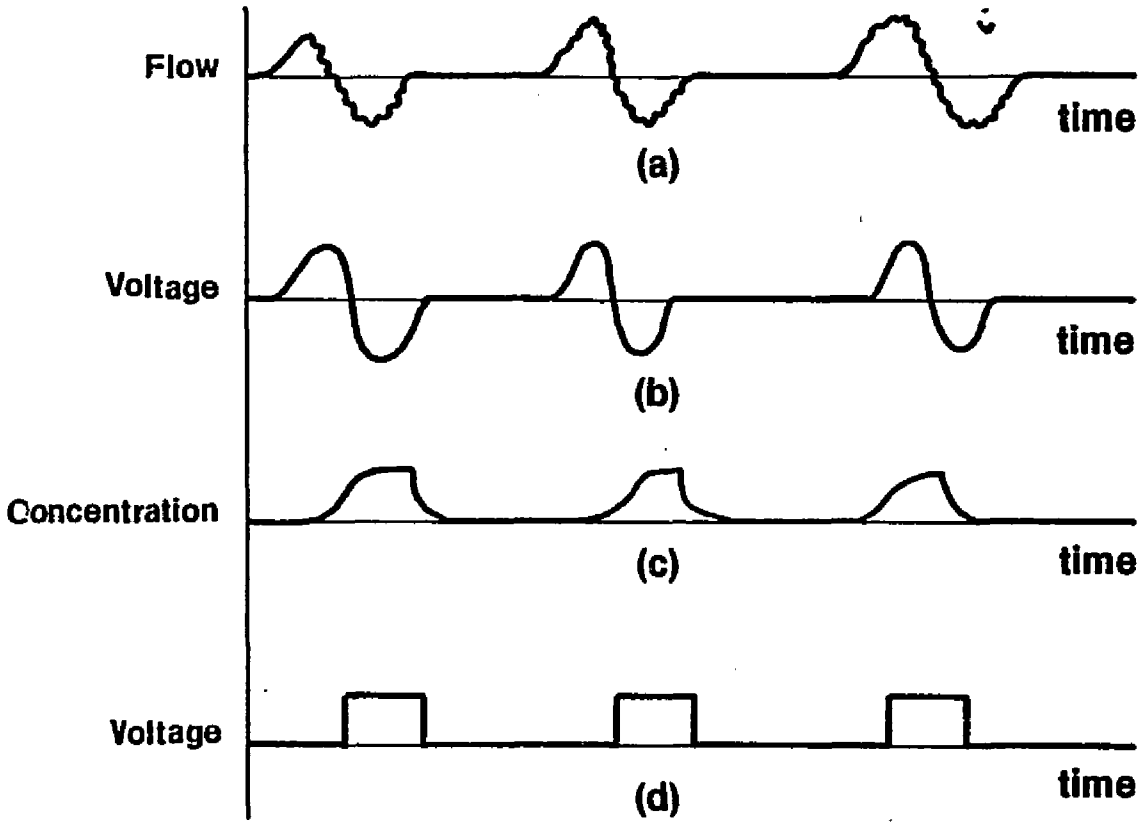


Figure 4.1. Comparison of actual waveforms to those used for simulation.

(a) Actual respiratory waveform.
(b) Waveform used to simulate respiratory flow.
(c) Actual concentration waveform.
(d) Waveform used to simulate concentration waveform.

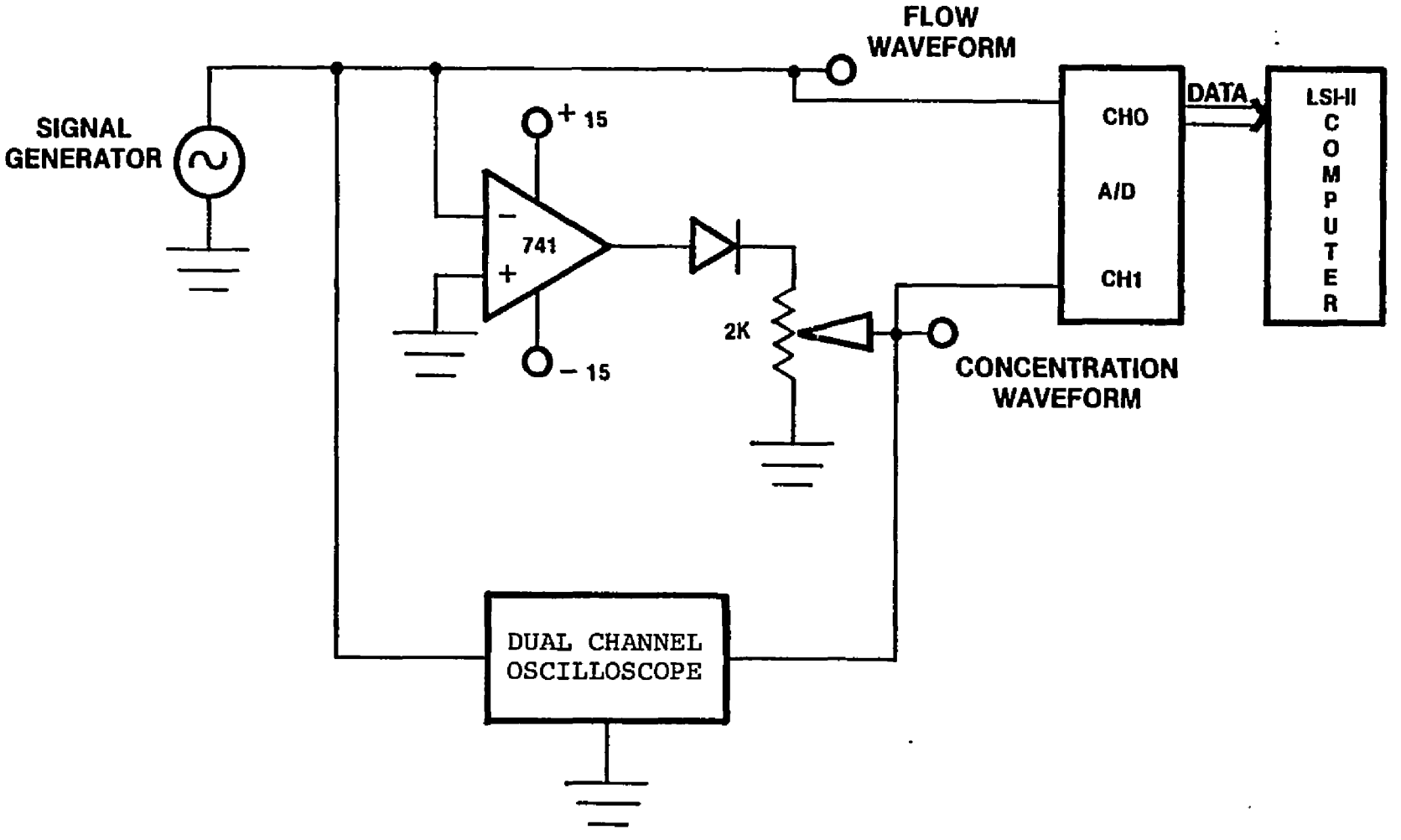


Figure 4.2. Test system used for electrical analog simulation.

calibrated using its own internally generated signals and appropriately adjusting input levels until its meter indicated the correct signal level. The oscilloscope was calibrated by its own internal 60 Hz calibration signal.

Recordings of sine waves produced by the oscillator were made and these recordings were used as the signal generator in Figure 4.2. In order to more closely simulate actual respiratory waveforms, time intervals were made between sine waves by erasing portions of the tape. The sine waves cause the output of the open-loop operational amplifier to be at +15 volts when the sine wave is in the negative half of its cycle and -15 volts when the sine wave is in the positive half of its cycle. The diode rectifies the square wave appearing at the output of the amplifier so that only the positive half of the cycle appears across the 2k potentiometer. The 2k potentiometer can then be adjusted to produce the desired magnitude of the concentration waveform. The magnitude and duration of the waveforms are monitored and measured by the oscilloscope. The markings on the oscilloscope display were used to make measurements and the worst case error in reading these markings is assumed to be less than 5%.

Values of tidal volume were determined by calculating the areas under the curve of a sine wave for a half cycle. For example, the area under a half of a sine wave is always the product of its period and amplitude divided by 3.14; therefore, for an amplitude of 1 volt and a period of 1 second, the area under half of the sine wave curve will be 0.318 volt-seconds. This was converted to liters by using a flow

calibration value of 60 liters per minute per volt which is the same as 1 liter per second per. Values of breath uptake were calculated similarly except that the magnitude of the square wave corresponding to the inspiratory half of the cycle was multiplied by the expected value for the inspiratory volume. Since the half of the square wave corresponding to the expiratory half of the cycle was always approximately zero, expiratory volume did not figure in the calculation of the expected value. Expected values for inspired and end-tidal concentration were determined directly from the oscilloscope readings. Respiratory rate was determined directly from the time between the start of two successive respiratory cycles.

This type of preliminary testing is essential so that problems related to computer hardware or software can be isolated from problems caused by the flow or gas sensing devices.

Mechanical Simulation Test Systems

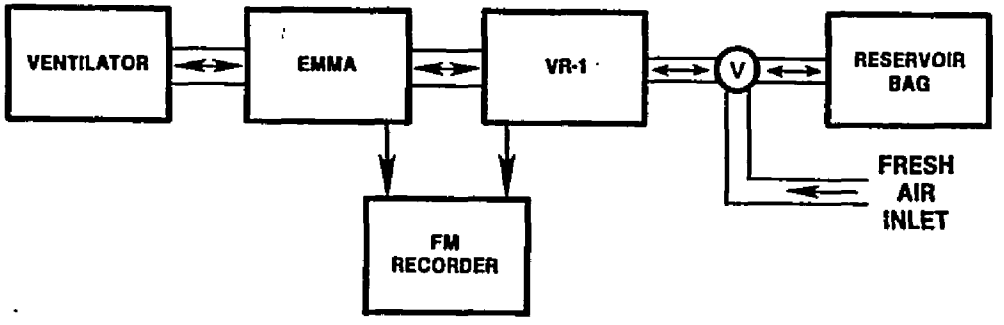
Three types of testing were done with mechanical simulation systems: 1) steady-state tests, which employed a closed system to simulate the situation of zero anesthetic uptake (patient end-tidal concentration equal to inspired concentration); 2) single breath uptake, tests which involved an open system to simulate large inhalations of anesthetic vapor; and 3) volume dilution tests, which simulated multiple breath uptake by using a ventilator to mix a pre-measured volume of air into a system filled with an anesthetic gas of known concentration until a final concentration was obtained.

Steady State Tests

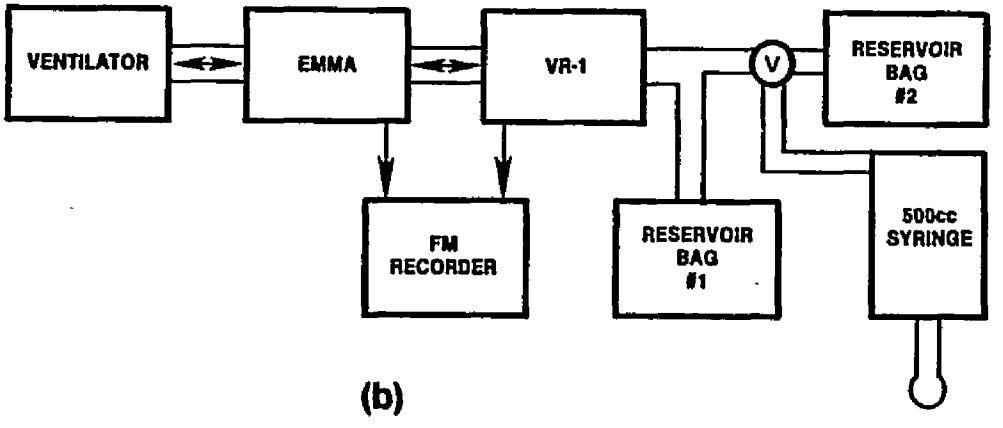
Equipment

A Harvard animal ventilator, a VR-1 respiratory therapy unit, an Engstrom EMMA anesthetic gas analyzer, a one liter rebreathing bag, a HP 3694A instrumentation recorder and a three-way Ohio ventilator valve were used to implement the steady state mechanical simulation system. Figure 4.3a is a block diagram illustrating the configuration of these components. The recorder was calibrated as previously described. The VR-1 was calibrated by continuously passing a 500 cc volume of air through the VR-1 transducer with the aid of a McGaw 500 cc syringe pump. Adjustments were made to the zero and span controls on the VR-1 until a reading of 0.50 liters appeared on the VR-1 output display for both the inspired and expired volumes. The analog output on the back of the VR-1 corresponding to respiratory flow was also calibrated to determine the number of liters per minute that produced a one volt output. A calibrated flow meter with a one liter per minute resolution was used to estimate flow. Although the analog output from the VR-1 was somewhat noisy, it still provided a linear change in voltage corresponding to changes in flow through the VR-1 transducer when tested in the range from +30 to -30 liters per minute.

The ventilator was calibrated against the previously calibrated VR-1. The tidal volume setting on the ventilator was varied from 100 to 500 cc in 100 cc increments. The tidal volume produced by the ventilator at each increment was recorded. The VR-1 can determine tidal volume within a resolution of 5 cc.



(a)



(b)

Figure 4.3. Mechanical simulation systems.

(a) Used for steady-state and single-breath uptake tests.
(b) Used to measure multiple breath uptake by means of volume dilution.

The EMMA was calibrated in the manner specified by the manufacturer when a calibrated anesthetic test gas is used as a reference. The first step was to zero the meter on the EMMA while 100% O_2 flowed through the transducer. Following this a 2 ± .05% halothane in O_2 mixture (Matheson Test Gas Inc., Rahway, New Jersey) was passed through the transducer at a rate of 4 liters per minute. While the calibrated gas was passing through the transducer, the gain potentiometer on the side of the EMMA was adjusted until the meter on the front panel read 2%. After completing this procedure, the function switch on the EMMA front panel was placed in the calibrate position and the meter reading was recorded so that calibration would not have to be repeated. Note that this particular calibration setting corresponds to a particular transducer. If a different transducer is used, it too must be calibrated as previously described or by using an already calibrated transducer as a reference.

Procedure

The system was flushed and filled with an anesthetic gas (either halothane or enflurane) of known concentration. The valve V remained closed to the fresh air inlet at all times. The gas in the test system was periodically cycled back and forth by the ventilator while recordings of flow and concentration were made. These recordings were later played back into their respective A/D channels. The meter on the front panel of the EMMA could be read with a resolution of 0.05% anesthetic vapor. Respiratory rate was determined by direct measurement with a clock that

provided a resolution of 0.5 seconds. Since no anesthetic or any other gas enters or leaves the system, no uptake or loss of anesthetic should occur.

The purpose of these tests is to determine how well the system performs during an equilibrium situation. It measures the system's ability to calculate tidal volume, to determine inspired and end-tidal concentration, to calculate uptake and to measure respiratory rate.

Single Breath Uptake Tests

Equipment

The equipment used in this set of tests is the same as that used in steady state tests with the exception of the valve V in Figure 4.3a. In this case, V is implemented by two unidirectional valves, one which opens when flow is from left to right and the other which opens when flow is from right to left. Calibration procedures are the same as previously discussed.

For these tests, it was necessary to measure the volume of the connecting tubing between the transducers and the unidirectional valves. This was accomplished by filling the tubing with water and then pouring the water into a graduated cylinder. This volume was measured to be 20 ± 1 cc.

Procedure

The procedures employed for these tests were the same as those for the steady state tests except that only single breaths were recorded and the arrangement of the unidirectional valves simulated the opening

of V in Figure 4.3a to entrain fresh air during the expiratory half of the respiratory cycle. Assuming that inspiratory flow is from left to right and that the valve which opens when flow exists in this direction is connected to the reservoir bag, the ventilator fills the bag with anesthetic vapor during inspiration. During this time, the EMMA detects the anesthetic concentration of the gas used to fill the test system while the VR-1 measures inspiratory flow. Assuming that expiratory flow is from right to left and that the valve which opens when flow is in this direction is connected to the fresh air inlet, the EMMA measures the anesthetic concentration of the incoming fresh air mixed with the gas left in the connecting tubing between the valves and transducers. This gas left in the connecting tubing will be called the "dead space" gas.

This system simulates a respiratory cycle which has a constant inspired concentration during inspiration with a transition from the inspired level to virtually zero end-tidal concentration during expiration. The equation which describes this is derived from the conservation of mass principle discussed in Chapter 1 where the difference between the inspired and expired amounts of anesthetic is defined as the single breath uptake

$$U = C_{IN} \times V_{IN} - C_{IN} \times V_D \qquad (13)$$

where C_{IN} is the inspired concentration, V_{IN} is the inspired volume and V_D is the dead space volume. Note that this equation assumes that the fresh air entrained during expiration contains no anesthetic vapor.

Volume Dilution Tests

Equipment

The equipment used in these tests was the same as that used in the steady state tests except that a one liter bag and a 500 cc syringe pump were added. The configuration of this test system is shown in Figure 4.3b. Equipment was calibrated as previously described.

Procedure

The procedure used in these tests was similar to that described for the steady state tests except that V closes off reservoir bag #2 and the 500 cc syringe pump from the rest of the system while it is being flushed and filled with anesthetic-containing gas. When this is completed reservoir bag #2 is filled with fresh air from the 500 cc syringe pump The ventilator then cycles gas back and forth through the system while V is opened to allow mixing between the fresh air and the anesthetic containing gas. This causes a gradual decrease in concentration until a final equilibrium concentration is achieved.

The primary purpose of this type of testing is to simulate anesthetic induction so that an evaluation of the system's ability to determine cumulative uptake can be made. The equation that predicts the cumulative uptake of anesthetic simulated by volume dilution is derived as follows:

$$\text{Uptake (1st breath)} = C0 \times V - C1 \times V$$

$$\text{Uptake (2nd breath)} = C1 \times V - C2 \times V$$

$$\vdots$$

$$\text{Uptake (nth breath)} = Cn\text{-}1 \times V - Cn \times V$$

where V_{IN} is the inspired volume, V_{EX} is the expired volume and the C's are levels of anesthetic concentration. Assuming that V_{IN} equals V_{EX} which will simply be called V_T, the cumulative uptake for all n breaths can be written as

$$\text{Cumulative Uptake} = U_T \times (CO - Cn) \tag{14}$$

where CO is the initial concentration of anesthetic in the test system and Cn is the final concentration of anesthetic in the test system. The final concentration of anesthetic in the test system can be predicted from the equation for the conservation of mass within this system

$$V_{INT} \times C_{INT} = V_{FIN} \times C_{FIN} \tag{15}$$

where V_{INT} is the initial volume in the system, C_{INT} is the initial concentration, V_{FIN} is the final volume, and C_{FIN} is the final concentration. Note that the derivation of Eq. (14) assumes that the concentration in the test system jumps from one discrete level to the next during each respiratory cycle. This is not what actually occurs since the mixing of gases in the test system is actually a continuous function of time. The equation also neglects any mixing that occurs as a result of diffusion. Therefore, Eq. (14) is only an approximation of the cumulative uptake of anesthetic.

Tests for the Delay Calculation Routine and the Apnea Alarm

The delay calculation subroutine was tested by both electrical analog signals and actual respiratory and concentration waveforms produced by the VR-1 and the EMMA.

Equipment

Testing done with electrical analog signals used the same equipment called out for the electrical analog signal simulation tests previously described. Testing done using waveforms produced by the VR-1 and EMMA used the test equipment called out for the single breath uptake tests and a Gould strip chart recorder. An additional EMMA transducer was used so that two different time delays could be measured.

Calibration of equipment used in the previously described tests was the same. The speed of the strip chart recorder was checked by a stop watch after being allowed to run at a rate of 5 millimeters per second. A metric ruler was used to verify that the proper length of paper passed by a predetermined reference point. The ruler provided a resolution of 0.5 millimeters.

Procedure

Since the square waves produced by the test set-up of Figure 4.2 always lag the sine waves produced by the signal generator by one-half of a cycle, the delay time between waveforms is always one-half the period of the sine wave. The period of the sine wave can easily be measured by the oscilloscope of Figure 4.2. Periods of one second and two seconds were tried.

Simultaneous strip chart recordings of respiratory and concentration waveforms were made from the test set-up of Figure 4.3a. One set of recordings was made from one transducer while another set of recordings was made from a second transducer with a different response

time. The delay between the respiratory and concentration waveforms was measured directly from the strip chart recordings.

Apnea Alarm Tests

The apnea alarm was tested by simply starting the system without providing a respiratory waveform to the appropriate A/D channel. A stop watch with a resolution of 0.5 seconds was used to directly measure the time it took for the alarm message to appear on the screen.

Tests for Measuring the Elapsed Time and its Square Root

Elapsed time and the square root of elapsed time were recorded during electrical analog simulation tests and compared to the time measured by a clock which was external to the computer system. Readings were taken every minute for 15 minutes and rounded off to the nearest minute. Four trials were performed in this manner. Square roots of time produced by the system were rounded off to the nearest tenth of a root minute and compared to the expected square root of time read from the external clock.

Statistical Evaluation of Data

Means and standard deviations determined from the observations made during all of the previously described tests were calculated by the MINC-11 minicomputer using the application packages provided by the Digital Equipment Corporation. In all cases, at least ten observations of a single trial were made so that means and standard deviations could be considered statistically significant except in the case of the volume

dilution tests since conditions for each trial were difficult to repeat. Actual calculations performed by the applications package are the same as those found in most standard texts (Miller and Freund 1977, pp 289-305). Mean differences between calculated and measured values were determined for the trial which had the largest standard deviation in each of the previously described tests. The 95% confidence interval about each of these mean differences was also calculated using the standard deviation for that trial and a table of t-test values which can be found in Miller and Freund on page 462.

CHAPTER 5

RESULTS

The electrical analog signal tests were divided into two cases. In the first case, inspired and expired volume were held constant while varying inspired concentration and respiratory rate. In the second case, inspired concentration was held constant while varying tidal volume and respiratory rate. There were six trials for each case and ten observations were made for each trial. The mean difference between the calculated and measured value for the trial which had the largest standard deviation for a particular parameter is presented as a measure of system accuracy. The 95% confidence interval about the mean difference is also provided as a measure of the repeatability of this value. Table 1 summarizes the results of the electrical analog simulation tests for inspired and expired volume, single breath uptake, inspired concentration and respiratory rate. The case and trial used to determine the accuracy and repeatability along with the calculated value for the parameter are also given in Table 1. The complete listing of data for the electrical analog signal simulation tests is given in Table D.1 in Appendix D. Mean differences between calculated and measured values were 5% or less of the calculated value for all parameters tested.

There were four separate trials made for the steady state tests with twelve observations per trial. Both concentration and tidal volume were varied for each trial. Table 2 summarizes the results of these tests

Table 1. Results of the electrical analog signal simulation tests.

Mean differences were determined for the trial which had the largest standard deviation for that particular parameter.

Parameter	Calculated Value	Case	Trial	Mean Difference	95% Confidence Interval
V_{IN}	0.318L	1	4	-.002L	±.002L
V_{EX}	1.272L	2	6	.003L	±.001L
C_{IN}	3.00%	1	2	.025%	±.004%
U	4.77ml	1	4	-.061ml	±.023ml
RR	6.0 breaths/ minute	1	4	-0.3 breaths/ minute	±0.1 breaths/ minute

Table 2. Results of the steady state tests.

Mean differences were determined for the trial which had the largest standard deviation for that particular parameter.

Parameter	Calculated Value	Trial	Mean Difference	95% Conficence Interval
V_{IN}	.520L	1	-.003L	±.005L
V_{EX}	.520L	1	.011L	±.011L
C_{IN}	1.20%	1	.02%	±.015%
C_{ET}	1.20%	1	.01%	±.015%
RATIO	1.00	1	.01	±.015
RR	6.0 breaths/ minute	1	0.3 breaths/ minute	±.15 breaths/ minute

for inspired and expired volume, inspired and end-tidal concentration, the ratio of end-tidal to inspired concentration and the respiratory rate in the same way Table 1 summarized the results of the electrical analog simulation tests except that there were no separate cases. Table D.2 in Appendix D provides a complete listing of the data taken during the steady state mechanical simulation tests. Mean differences between calculated and measured values were 5% or less of the calculated value for all parameters tested.

There were also four trials made for the single breath uptake tests. Ten observations were made for the first two trials, twelve observations were made for the third trial and eleven observations were made for the fourth trial. Both inspired concentration and tidal volume were varied for each trial. Table 3 summarizes the results of these tests for inspired and expired volume, inspired concentration and single breath uptake in the same way Table 2 summarized the results of the steady state tests. Table D.3 in Appendix D provides a complete listing of the data taken during the single breath uptake mechanical simulation tests. Mean differences between calculated and expected values were 2% or less of the calculated value for all parameters tested.

Six trials for the volume dilution tests were made and only one observation for each trial was made since it was difficult to independently repeat each trial. The mean difference between the calculated and measured value of cumulative uptake for all six of these trials was -0.13 ml with a 95% confidence interval of .12 ml. The mean difference between the calculated and measured value for all of these trials was

Table 3. Results of the single breath uptake tests.

Mean differences were determined for the trial which had the largest standard deviation for that particular parameter.

Parameter	Calculated Value	Trial	Mean Difference	95% Confidence Interval
V_{IN}	.300L	3	-.005L	±.001L
V_{EX}	.300L	3	.005L	±.001L
U	3.06ml	4	-.035ml	±.011ml
C_{IN}	2.00%	4	-.04%	±.01%

10.6% or less of the calculated value. Table D.4 in Appendix D provides a complete list of the data taken during the volume dilution mechanical simulation tests.

Calculation of the delay between respiratory and concentration waveforms was tested in two waves. In the first case, two trials with ten observations per trial were made using the electrical analog simulation system. In the second case, two trials with ten observations were made using the single breath uptake mechanical simulation system. Four separate trials were made to test the apnea alarm with ten observations per trial. In each trial, the apnea alarm setting was varied to test a range of values from 5 to 30 seconds. There were also four separate trials to test the measurement of elapsed time and its square root. In each trial, elapsed time was recorded each minute and compared to the measured value for 15 minutes. Table 4 summarizes the results of these

Table 4. Results of additional tests for the time delay between flow and concentration, the apnea alarm delay, elapsed time and square root of elapsed time.

Mean differences were determined for the trial which had the largest standard deviation for that particular parameter.

Parameter	Calculated Value	Case	Trial	Mean Difference	95% Confidence Interval
Td	0.50 sec	1	1	0.02 sec	± .01 sec
Apnea Alarm	5.0 sec	-	1	0.0 sec	±0.0
t	1 min	-	1	0 min	±0 min
$\sqrt{t}$	1.0 $(min)^{\frac{1}{2}}$	-	1	0.0 $(min)^{\frac{1}{2}}$	±0.0 $(min)^{\frac{1}{2}}$

three tests in the same way Table 1 summarized the results of the electrical analog simulation tests. The mean difference between the calculated and measured values was 4% or less of the calculated value for the time delay calculation tests while there was no detectable difference between calculated and expected values for any observation made during both the apnea alarm tests and the elapsed time tests. Tables D.5, D.6 and D.7 in Appendix D provide a complete listing of the data taken during the delay calculation, apnea alarm and elapsed time tests, respectively.

CHAPTER 6

DISCUSSION OF RESULTS

The results presented in Table 1 indicate that the computer hardwave and software function correctly since the mean differences between the calculated and expected values for inspired and expired volume, inspired concentration and single breath uptake were all 2% or less of the calculated value. Respiratory rate had the largest mean difference between calculated and measured values (5% of the calculated value). This was the result of errors in determining the calculated values from the oscilloscope readings which only provided a resolution of 5%.

In Table 2, the mean difference between the calculated and expected value for expired volume was considerably larger than that in Table 1. One possible reason for this is that the VR-1 had a tendency to drift and frequently required a zero baseline adjustment. However, the reason for this drift being in the same direction is not known. Though no actual data was taken on this phenomenon, the front panel indicators of the VR-1 consistently showed an expiratory volume that was larger than the inspiratory volume whenever the device was clinically used as a respiratory monitor. Another possible reason for the discrepancy between inspired and expired volume may have been due to the build-up of pressure biases in the test system itself which could cause volume changes to the gas in the test system. Although no data was taken for the pressure in the test system, a pressure gage was used to monitor pressure and the

peak inspiratory and expiratory pressures during the respiratory cycle were observed to be approximately equal. Temperature in the laboratory was constant throughout all the tests and is not considered to be a factor which could affect volume measurements.

The data gathered for the single breath uptake tests also indicated a discrepancy between inspired and expired volume though the mean differences between the calculated and measured values for expired volume was smaller than in the steady state test. The mean difference between calculated and measured values for single breath uptake indicated that the EMMA worked well when used in the system.

Unlike the VR-1 which regularly required calibration, the EMMA was observed to maintain its calibration for months only requiring an occasional zero adjustment. However, two problems were observed with the EMMA: it did not accurately measure humidified gas and sharp changes in flow through its transducer caused abrupt changes in meter readings and the analog output signal. The first problem is due to adsorption of water vapor by the vibrating crystal in the EMMA transducer. The effect of water vapor adsorption is specified by the manufacturer to be 0.15% halothane for gas saturated at 25° Centigrade (see page 10 of the EMMA service manual). The other problem is not documented by the manufacturer. However, it can be conjectured that this problem is the result of the transducer's temperature sensitivity. A device developed by Cooper et al. (1981), which detects anesthetic concentration by means of an adsorption crystal, required that its transducer be held at a constant temperature so that the device would maintain calibration. However,

their study did not specify the effects of temperature changes on device calibration. Assuming that the EMMA transducer also has an internal heating mechanism, sharp changes in flow would reduce the transducer temperature. This would cause the heating mechanism to turn on until the transducer returned to its normal operating temperature. While the transducer temperature is changing, fluctuations in the output signal occur due to a shift in device calibration. However, neither of these problems appeared to severely affect the single breath uptake tests since only dry gases were used and the respiratory waveforms produced by the Harvard ventilator were relatively smooth and approximately sinusoidal.

The volume dilution tests had the largest mean difference in terms of percent of the calculated value. One reason for this is due to the summing of errors caused by the inspired and expired volume discrepancy. Since the expired volume was always larger than the inspired volume, the calculated value derived from Eq. (14) would always predict a value larger than the measured value. Another reason for the large inaccuracies that occurred in the volume dilution tests may be due to the fact that Eq. (14) does not account for all the dynamics in the test system. For example, mixing due to diffusion or the continuous change in concentration that occurs during each respiratory cycle. Volume dilution tests were difficult to repeat since they required filling the test system to the same volume, pressure and anesthetic concentration. The equipment available did not allow this to be done within a reasonable accuracy.

To properly assess the system's ability to determine cumulative uptake, it appears necessary to design an alternative test system where the uptake of anesthetic on a per breath basis can be accurately predicted. One possiblity is to design a system which functions similarly to the system used to determine single breath uptakes, except that this system would allow for continuous breaths of a fixed inspired concentration and return a known amount of anesthetic vapor during expiration. This system would have to perform this function on a continuous basis in order to properly test the system's ability to determine cumulative uptake.

A more stable flow meter would also be useful in order to reduce the effects of bias which were induced by the VR-1. It is preferable that such a flow meter employ pneumotachography as a means of transducing flow to an analog voltage so that it could readily be applied to clinical testing. The output of the flow meter should also have a low pass filter to cut off any signals that exceed 40 Hz which is considered the upper frequency limit of respiratory waveforms produced by pneumotachography as discussed in Chapter 3.

Clinical evaluations would also require finding a suitable replacement for the EMMA or modifying the EMMA so that the problems previously discussed would not affect system performance. If a replacement for the EMMA was chosen, it would require a response time of one second or less in order that the system function within the design goals specified in Chapter 2. It would be preferable that such a device have an in-line transducer in order to facilitate usage in the clinical

environment by decreasing the lag time between the respiratory and concentration waveforms.

It should also be noted that this system does not advise the user of the case when a respiratory cycle begins while the system is still processing and displaying data for the user. This problem may be solved by adding a special interrupt mechanism which communicates to the central processing unit that such a situation has occurred. A message can then be typed out to the system user that not enough time is being allowed between breaths.

CHAPTER 7

CONCLUSIONS

A system for real-time analysis of anesthetic gases was designed and implemented using commercially available devices. The system provides breath-by-breath determination of inspired and end-tidal concentration, their ratio, inspired and expired volume, respiratory rate, the single breath uptake of anesthetic, the cumulative uptake of anesthetic, and the time and the square root of time elapsed during anesthesia delivery. Accuracy was defined as the mean difference between the calculated value and the corresponding value measured by the system for the trial with the largest standard deviation. With the exception of cumulative uptake, all parameters had a mean difference between the calculated and measured value which was 5% or less of the calculated value. Cumulative uptake had a worst case difference between the calculated and measured value which was 10.6% of the calculated value. Breath-by-breath analysis is only possible with this system when there is an apnea period between breaths of two seconds or longer. The maximum respiratory rate recommended for system use is twelve breaths per minute.

Only in vitro laboratory tests were made since the system is not yet ready for clinical evaluation. Additional laboratory testing to better characterize the system is needed before any animal studies or clinical evaluations can be performed. The flow meter and anesthetic gas analyzer presently used need to be replaced with components that will

function properly when subjected to actual physiological conditions. A smaller and easier to handle computer system will also have to be used in order to make the system portable. This system design could also be applied to O_2 and CO_2 analysis for determination of metabolic rate and other studies related to O_2 consumption and CO_2 production.

Improved laboratory test systems need to be designed before further testing is to be done. Such test systems need to be properly characterized so that reliable prediction of test parameters can be made. Such a test system is needed primarily for determining how well the system determines cumulative uptake.

CHAPTER 8

FUTURE CONSIDERATIONS

Figure 8.1 is a block diagram of an alternative to the system described in Chapter 2. Such a system can perform the tasks of data acquisition, processing and display simultaneously. For example, the acquisition module can be taking data samples while the processing module performs calculations and the display module is providing the results of the last set of data to the user. Although the displayed results are two breaths behind the present respiratory cycle, this normally does not pose a problem in most anesthetic delivery situations.

The advantage of such a system can be seen by examining Eq. (3). The terms Tp and To are virtually eliminated; therefore, only the response time of the gas analyzer determines the required apnea period between breaths. Implementation of such a system would require sophisticated interfacing techniques that would allow memory to be shared between modules. Despite this, it may prove to be an interesting means of implementing a clinically applicable system for analysis of anesthetic gases. With advances being made in the area of anesthetic gas analyzers, it is possible that a future system of this type would have few limitations in the clinical environment. The only major restriction of such a system would be its cost since all the components outlined in Figure 8.1 would be expensive when implemented in the form of hardware and the price of

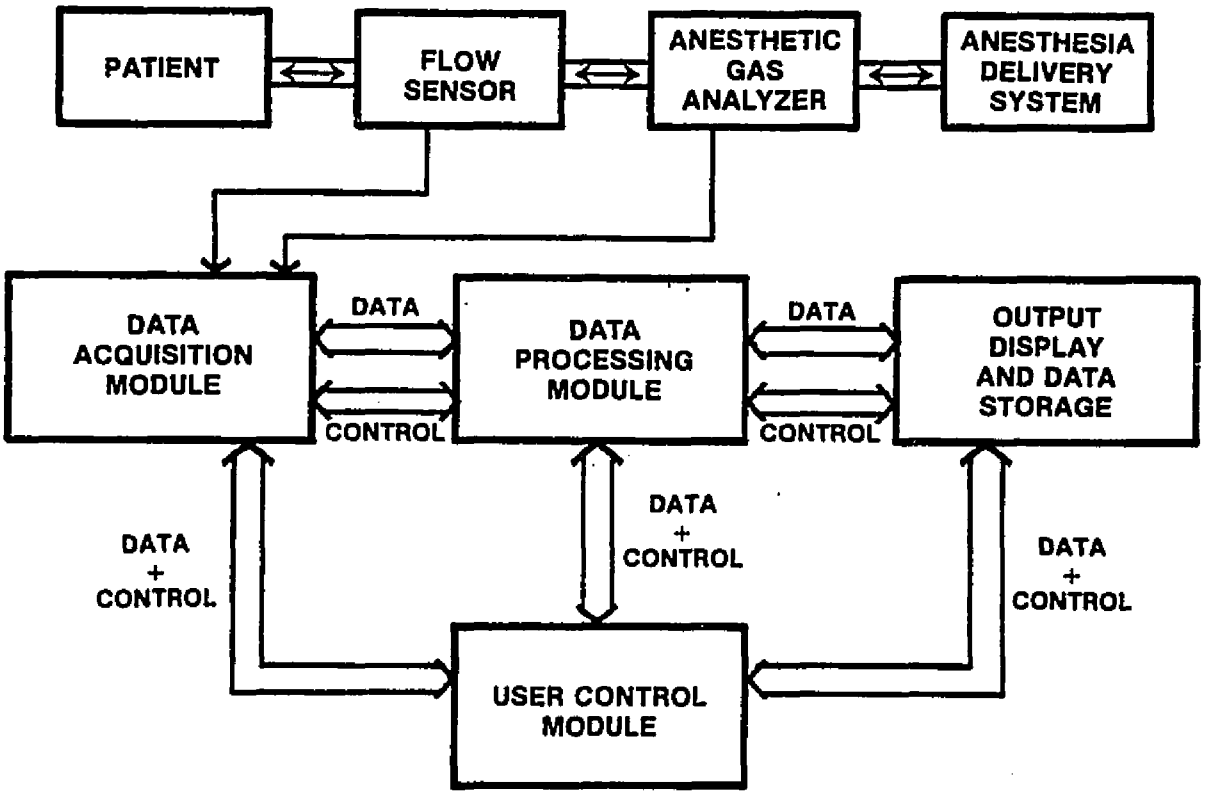


Figure 8.1. Block diagram of a future anesthesia monitoring system that employs four independent modules which perform simultaneous tasks.

software development would also be considerable for a system of this complexity.

Such a system can also make itself useful in driving on-line graphic displays which can provide the anesthesiologist with uptake curves, square-root of time model regression lines and other useful visual information. The advantages of systems that can perform tasks simultaneously have yet to be fully explored.

APPENDIX A

SYSTEM USER INSTRUCTIONS

To start the system, enter R_MONITR. A request for the apnea alarm value will be typed on the CRT terminal. For this request, an integer value ranging from 0 to 9999 must be entered. There are no default values. This value will represent hundredths of a second and sets the system's apnea alarm to this value. For example, if 2500 were entered, an apnea alarm message would be typed on the CRT screen if a respiratory cycle were not detected within 25.00 seconds.

The next request typed on the screen will ask the operator if a delay calculation is desired. This corresponds to the delay between the flow and concentration waveforms at the A/D converter. If such a calculation is desired, a message asking the user to enter a 0 when the respiratory waveform and its corresponding concentration waveform are ready to be sampled and processed by the system. After the system acquires the data corresponding to these waveforms, the user is asked if the situation was analogous to anesthetic induction or emergence. In either case, the system will output the delay value and proceed to ask the user for other information. If no delay calculation is warranted, the user must enter the delay value as an integer corresponding to hundredths of a second it must be in the range of 0 to 999.

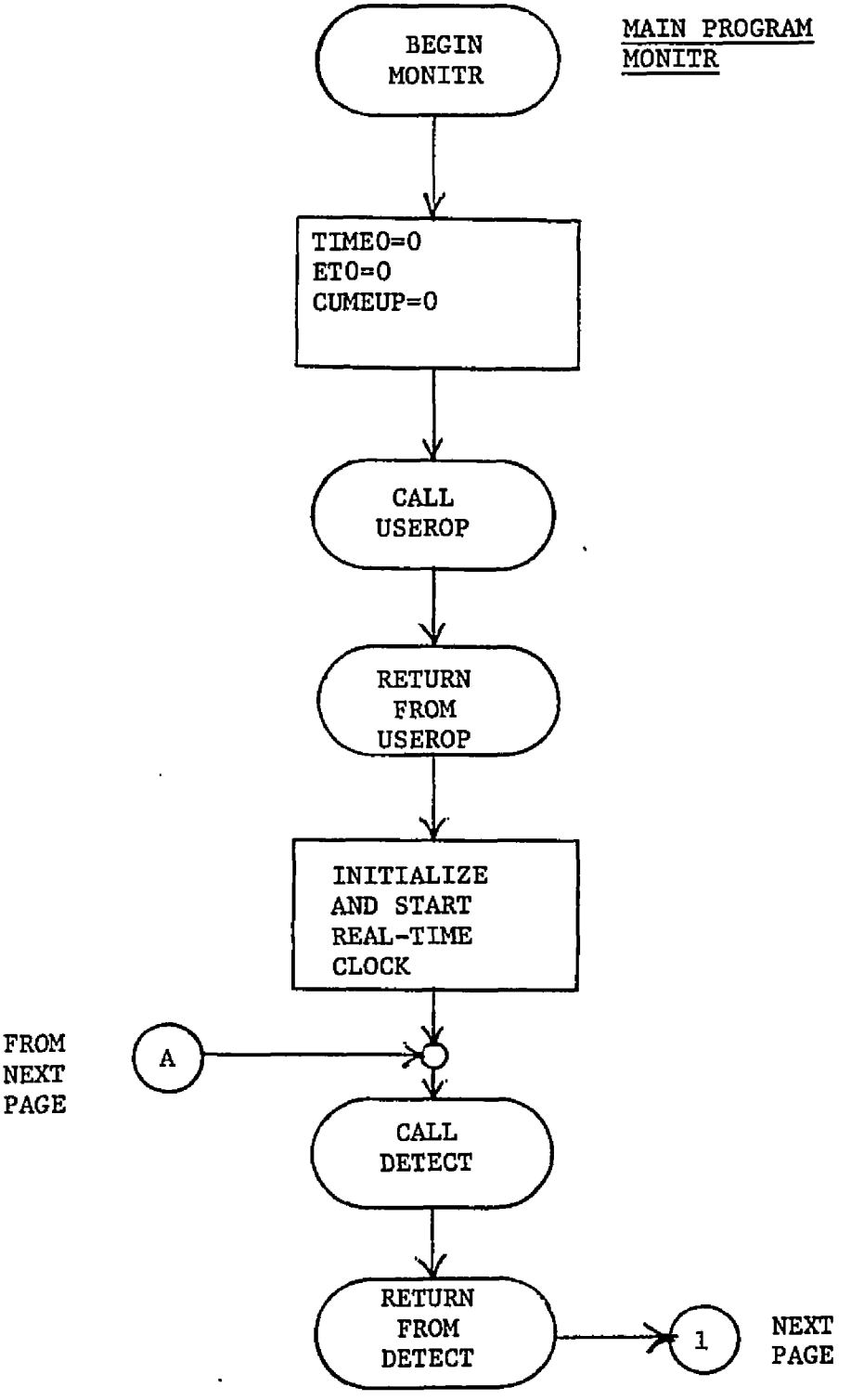
The following requests typed out by the system ask for the flow and concentration calibration values which are real numbers that may be of any value but must include a decimal point. These values are obtained by the user by direct calibration of the flow meter and gas analyzer (i.e., determine what flow or concentration produces a one volt output). The user should also check that both these devices are properly biased (i.e., produce zero volt outputs when their flow and concentration inputs are zero).

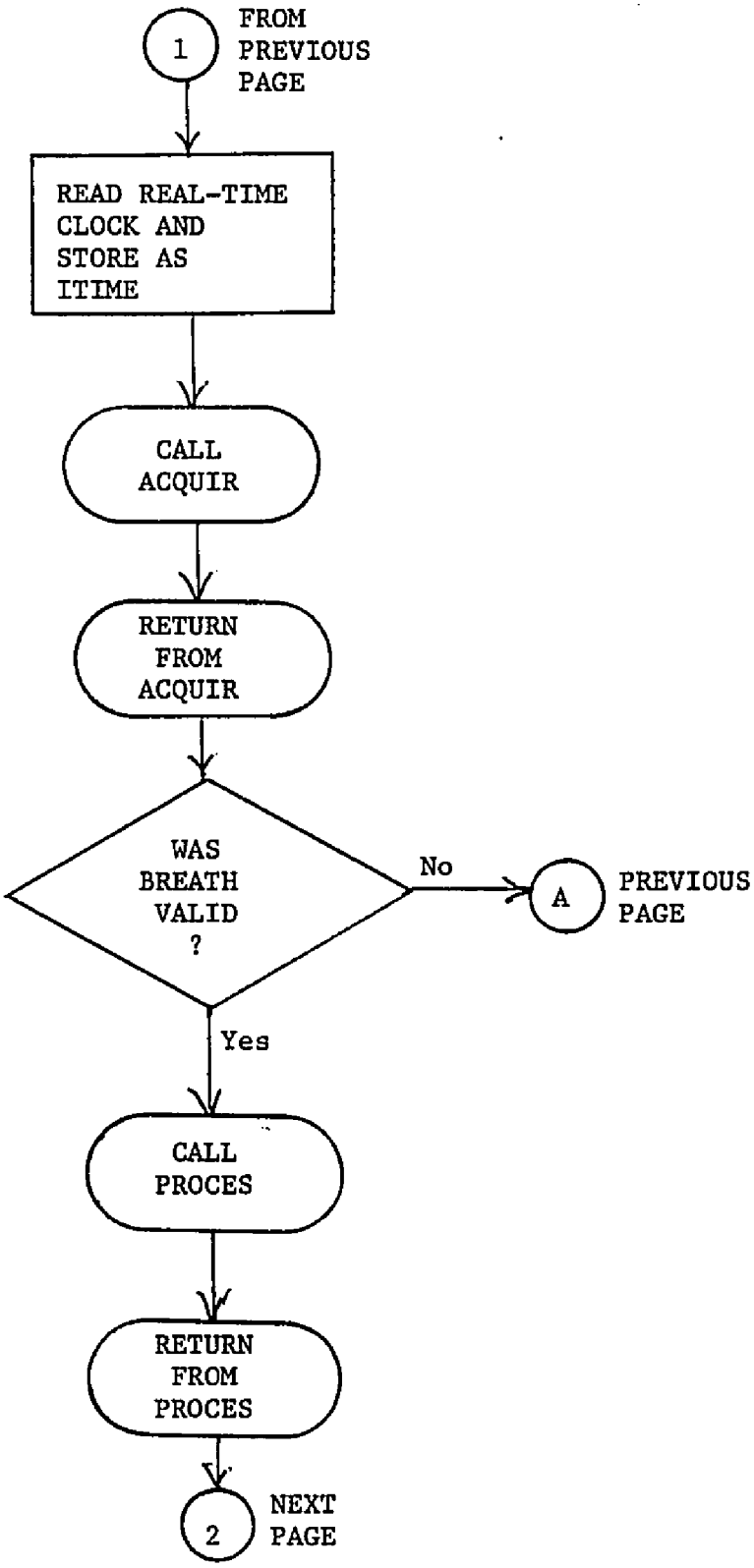
Finally, the user can either start the system or re-enter the data described above. Once the system has started, it can only be stopped by a "control C" command. Outputs delivered to the CRT screen can be stopped with a "control S" command. In this case, the system proceeds as normal but the output is suppressed until a "control Q" command is entered. The operator should always check to see if

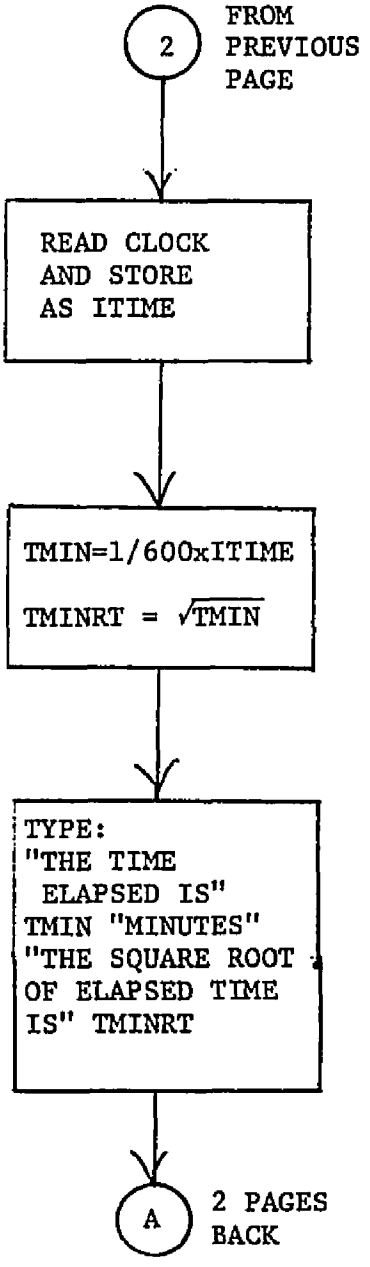
1) the 100 Hz oscillator is connected to ST1;
2) the analog output of the flow meter is connected to CH0;
3) the analog output of the gas analyzer is connected to CH1;
4) the reference connection of all the devices above should be connected to HQ GND (high quality ground).

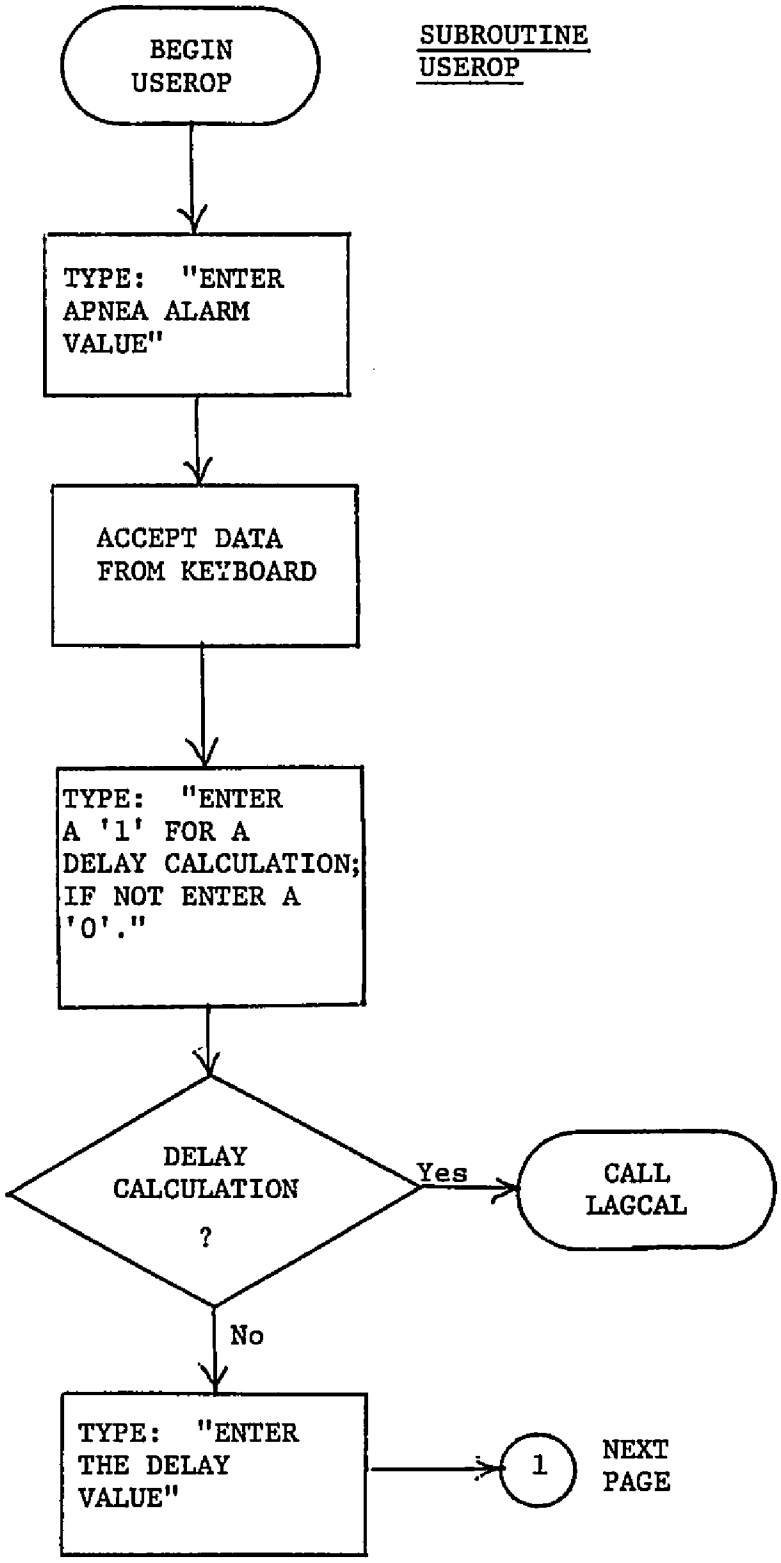
APPENDIX B

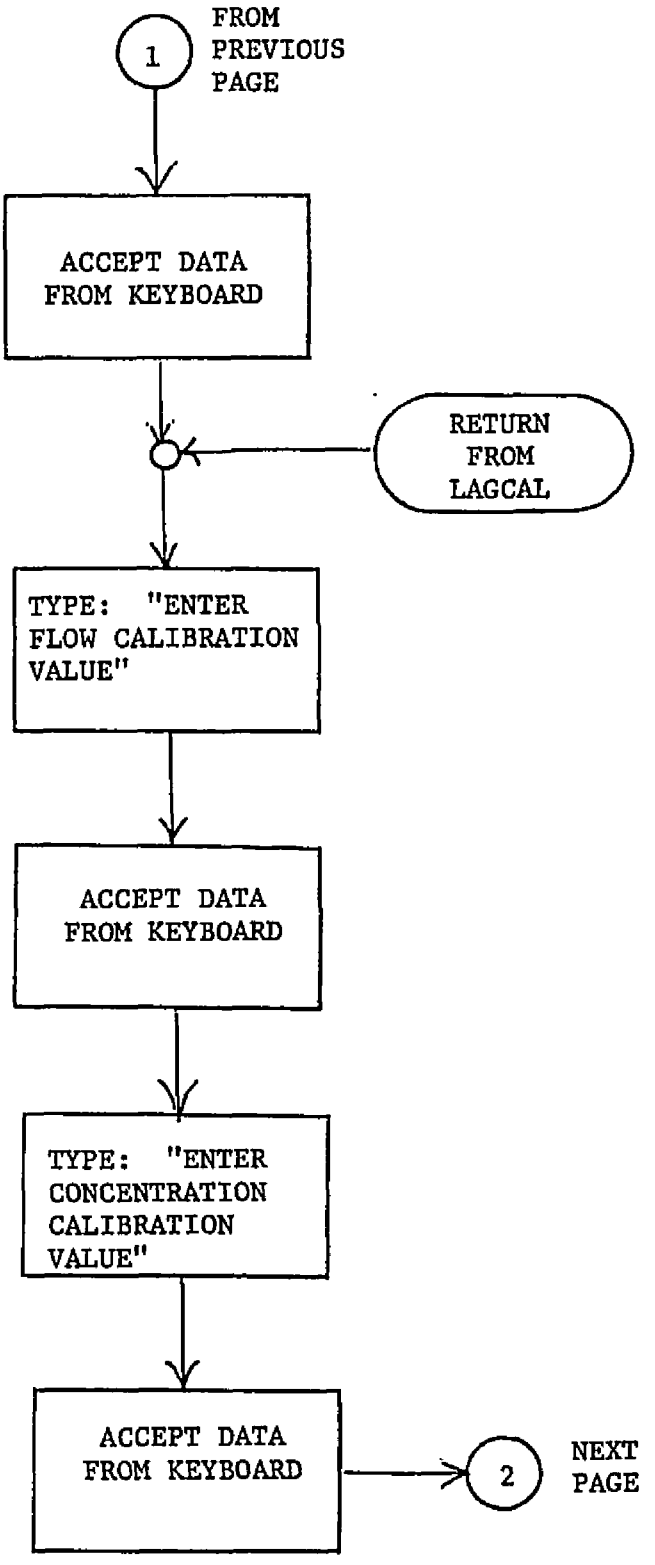
FLOW CHARTS OF THE SIX SOFTWARE MODULES USED TO IMPLEMENT THE SYSTEM

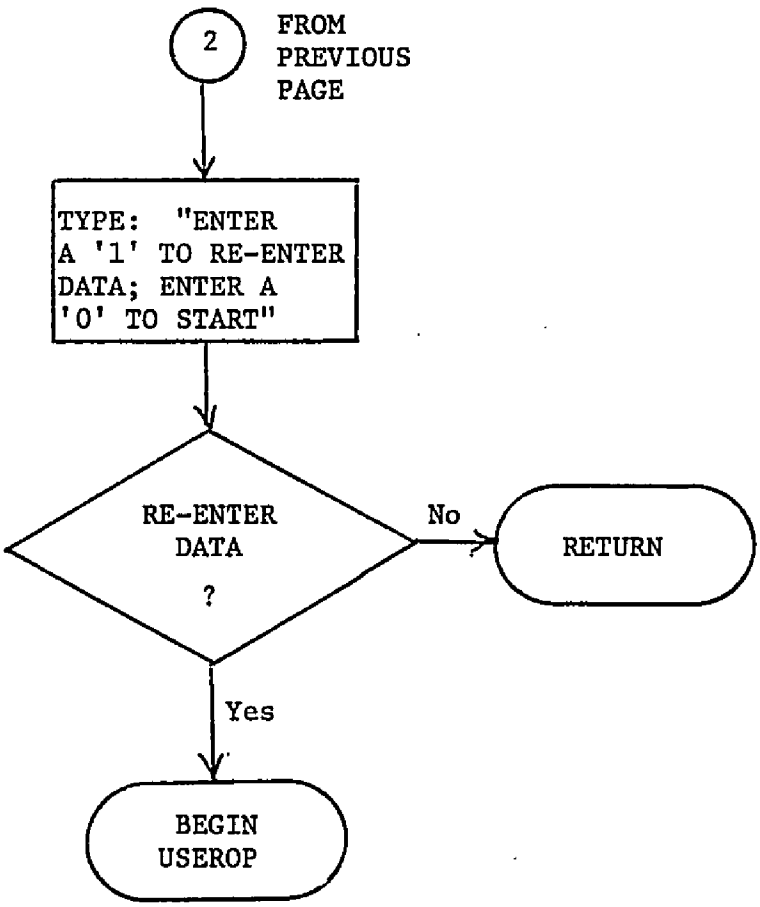

BEGIN MONITR
MAIN PROGRAM MONITR
TIME0=0
ET0=0
CUMEUP=0
CALL USEROP
RETURN FROM USEROP
INITIALIZE AND START REAL-TIME CLOCK
FROM NEXT PAGE
A
CALL DETECT
RETURN FROM DETECT
1
NEXT PAGE

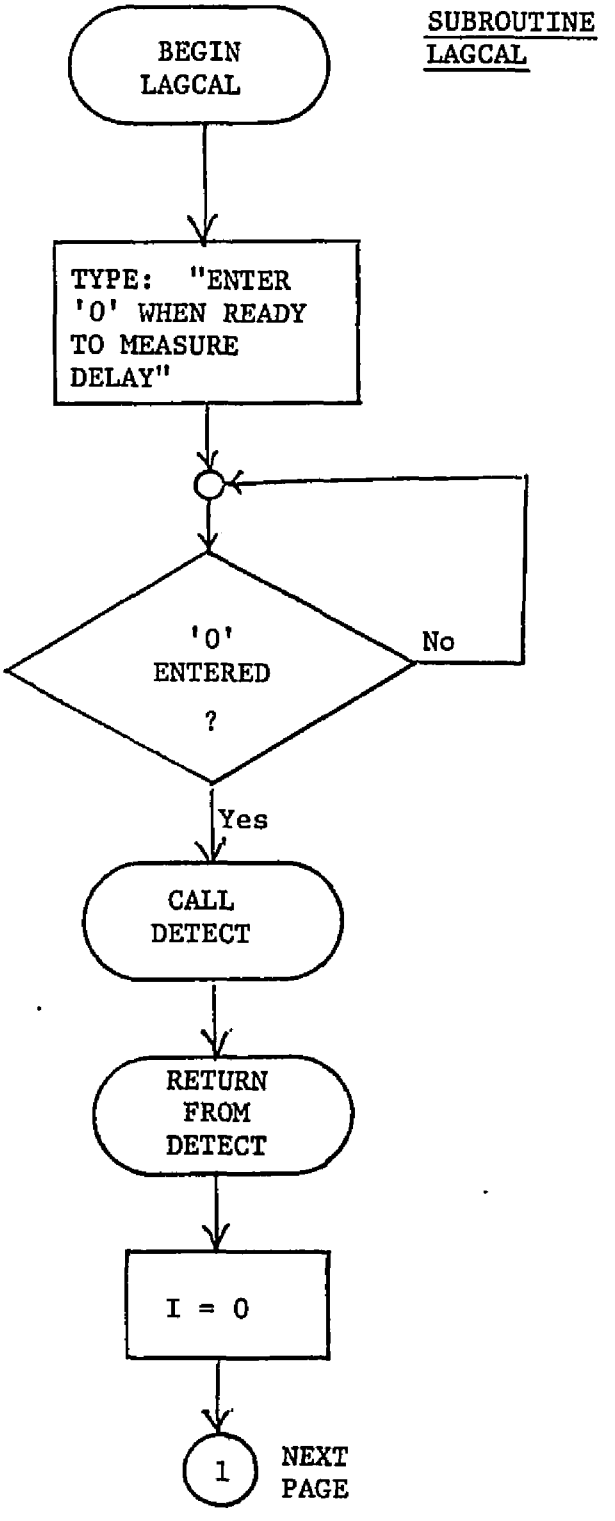

1
FROM PREVIOUS PAGE
READ REAL-TIME CLOCK AND STORE AS ITIME
CALL ACQUIR
RETURN FROM ACQUIR
WAS BREATH VALID ?
No
A
PREVIOUS PAGE
Yes
CALL PROCES
RETURN FROM PROCES
2
NEXT PAGE

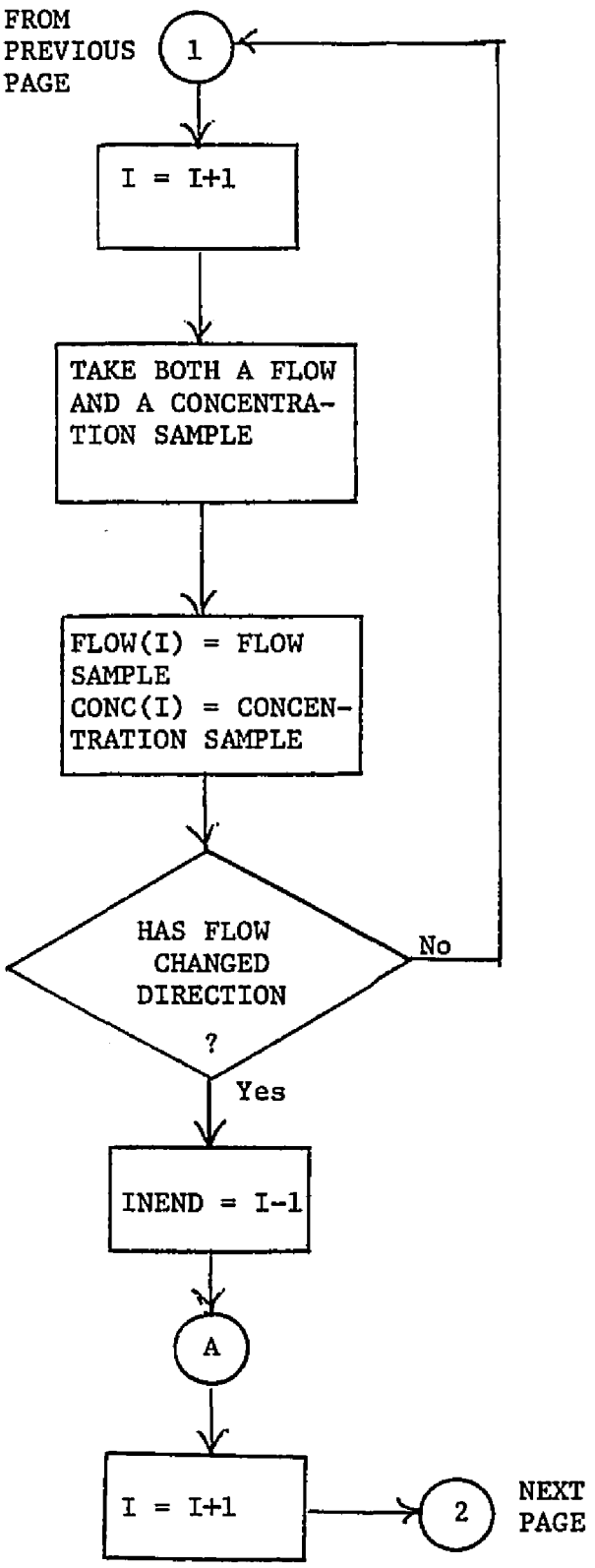

2
FROM
PREVIOUS
PAGE
READ CLOCK
AND STORE
AS ITIME
TMIN=1/600xITIME
TMINRT = √TMIN
TYPE:
"THE TIME
ELAPSED IS"
TMIN "MINUTES"
"THE SQUARE ROOT
OF ELAPSED TIME
IS" TMINRT
A
2 PAGES
BACK

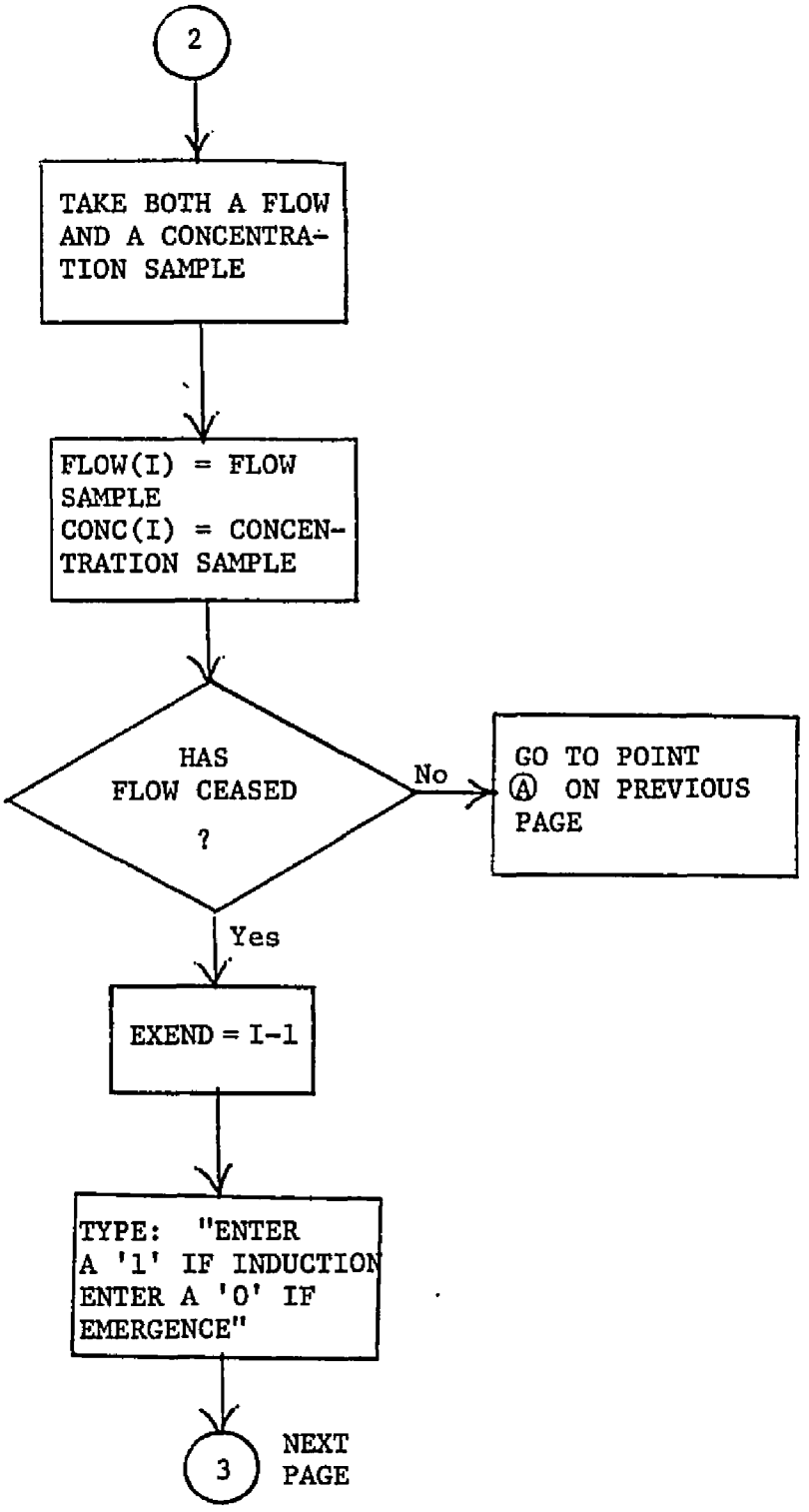

BEGIN USEROP
SUBROUTINE USEROP
TYPE: "ENTER APNEA ALARM VALUE"
ACCEPT DATA FROM KEYBOARD
TYPE: "ENTER A '1' FOR A DELAY CALCULATION; IF NOT ENTER A '0'."
DELAY CALCULATION ?
Yes
CALL LAGCAL
No
TYPE: "ENTER THE DELAY VALUE"
1
NEXT PAGE

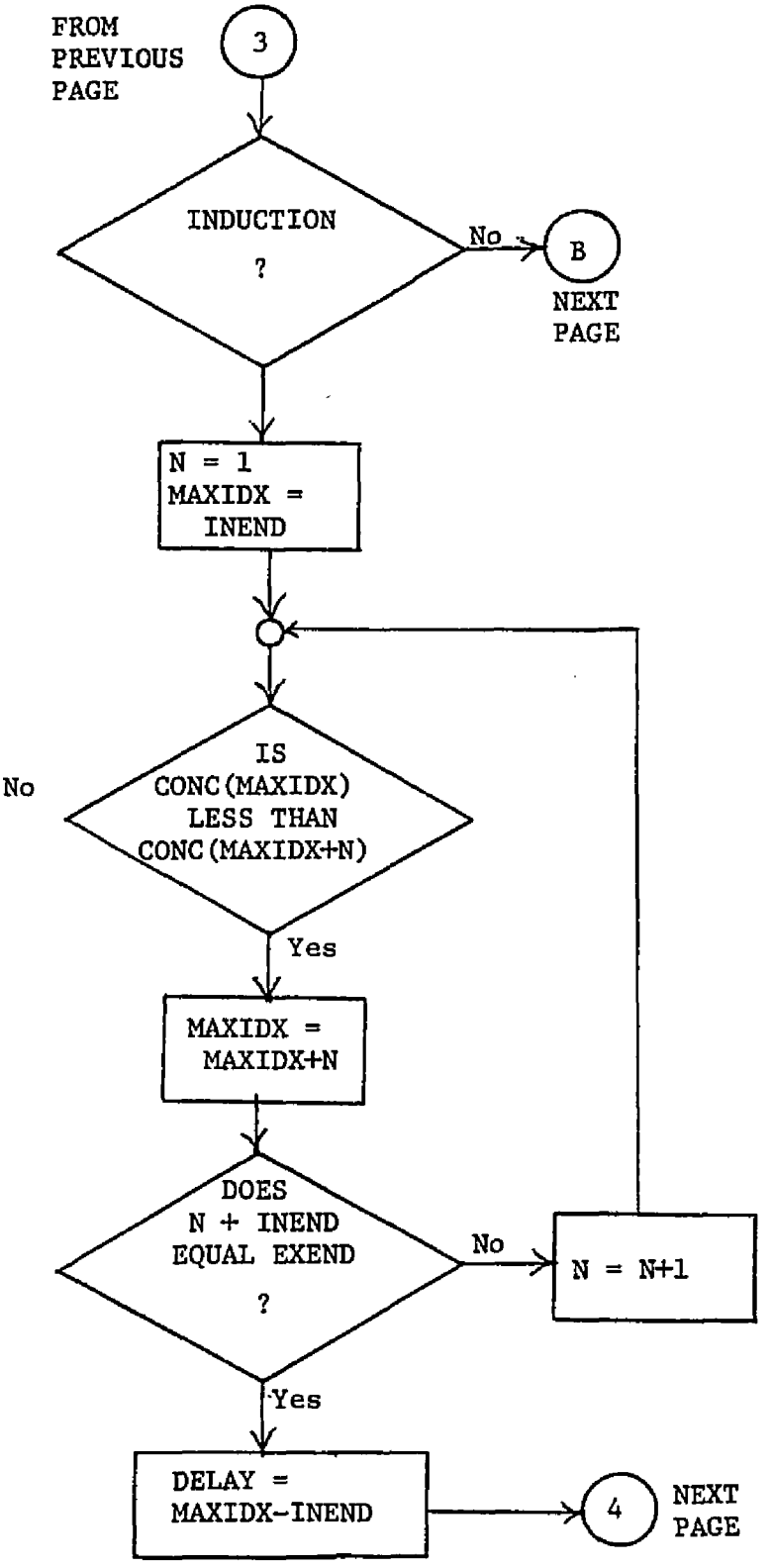

1
FROM PREVIOUS PAGE
ACCEPT DATA FROM KEYBOARD
RETURN FROM LAGCAL
TYPE: "ENTER FLOW CALIBRATION VALUE"
ACCEPT DATA FROM KEYBOARD
TYPE: "ENTER CONCENTRATION CALIBRATION VALUE"
ACCEPT DATA FROM KEYBOARD
2
NEXT PAGE

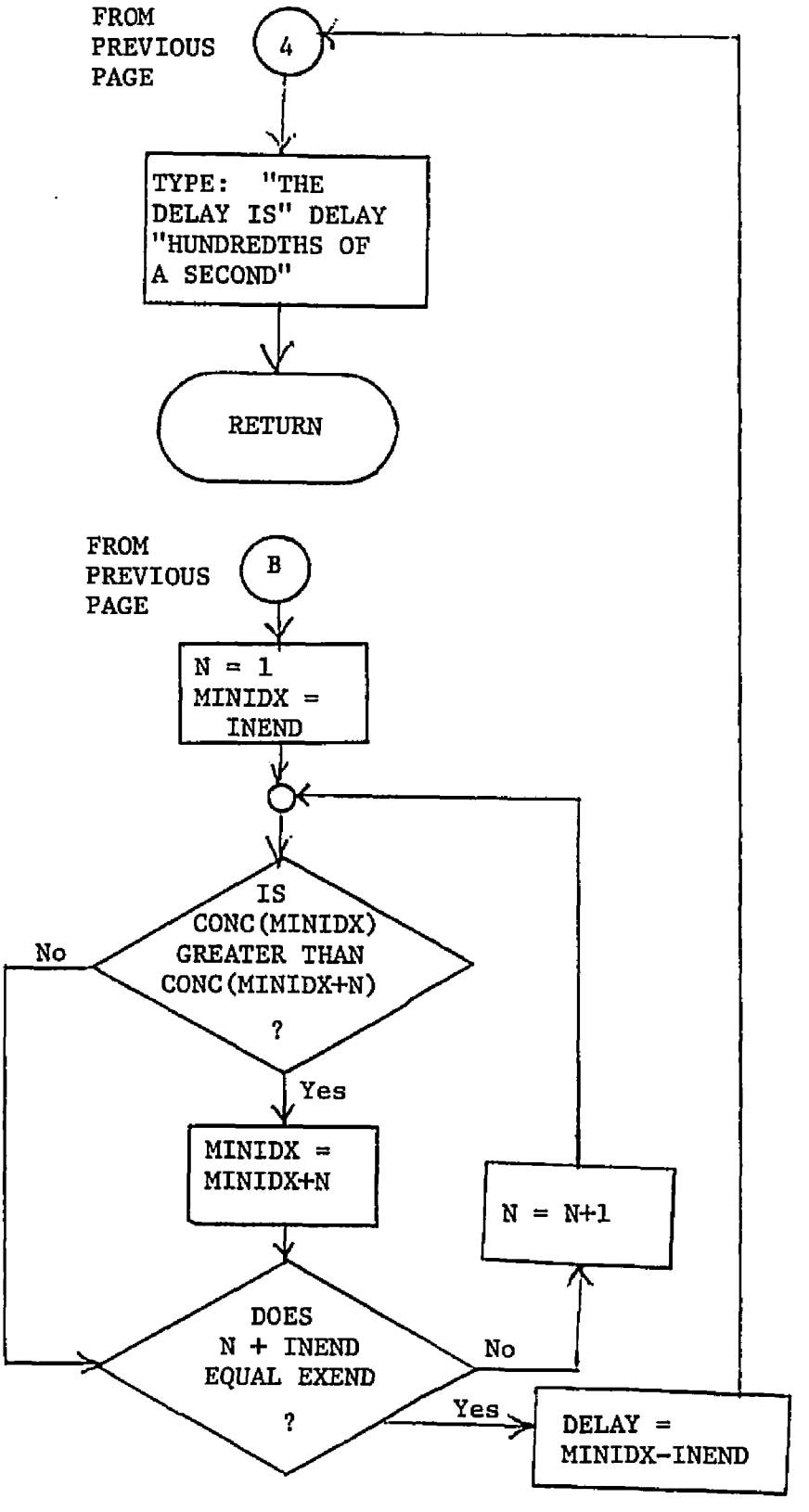

2
FROM
PREVIOUS
PAGE
TYPE: "ENTER
A '1' TO RE-ENTER
DATA; ENTER A
'0' TO START"
RE-ENTER
DATA
?
No
RETURN
Yes
BEGIN
USEROP

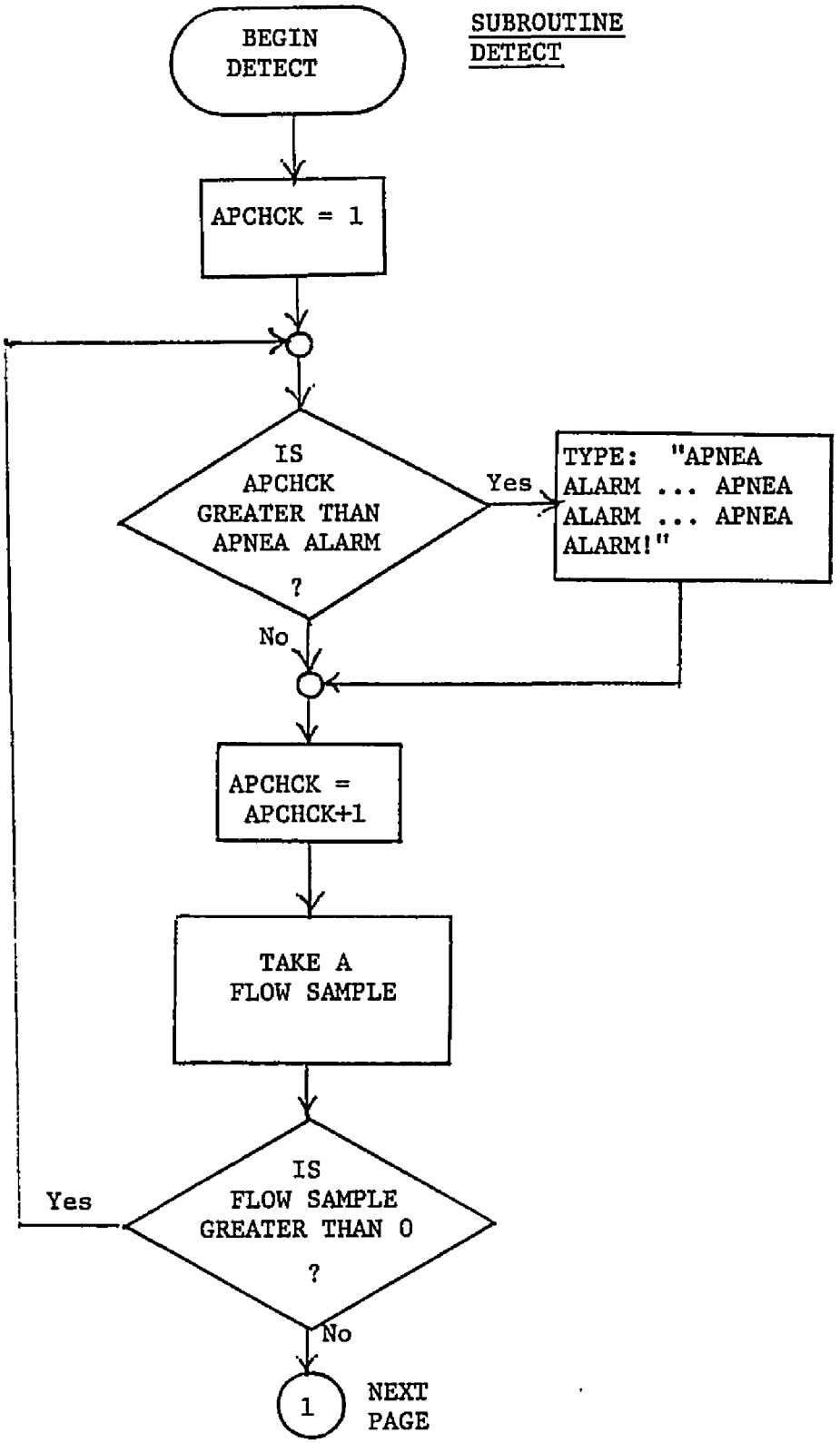

SUBROUTINE
LAGCAL
BEGIN
LAGCAL
TYPE: "ENTER
'0' WHEN READY
TO MEASURE
DELAY"
'0'
ENTERED
?
No
Yes
CALL
DETECT
RETURN
FROM
DETECT
I = 0
1
NEXT
PAGE

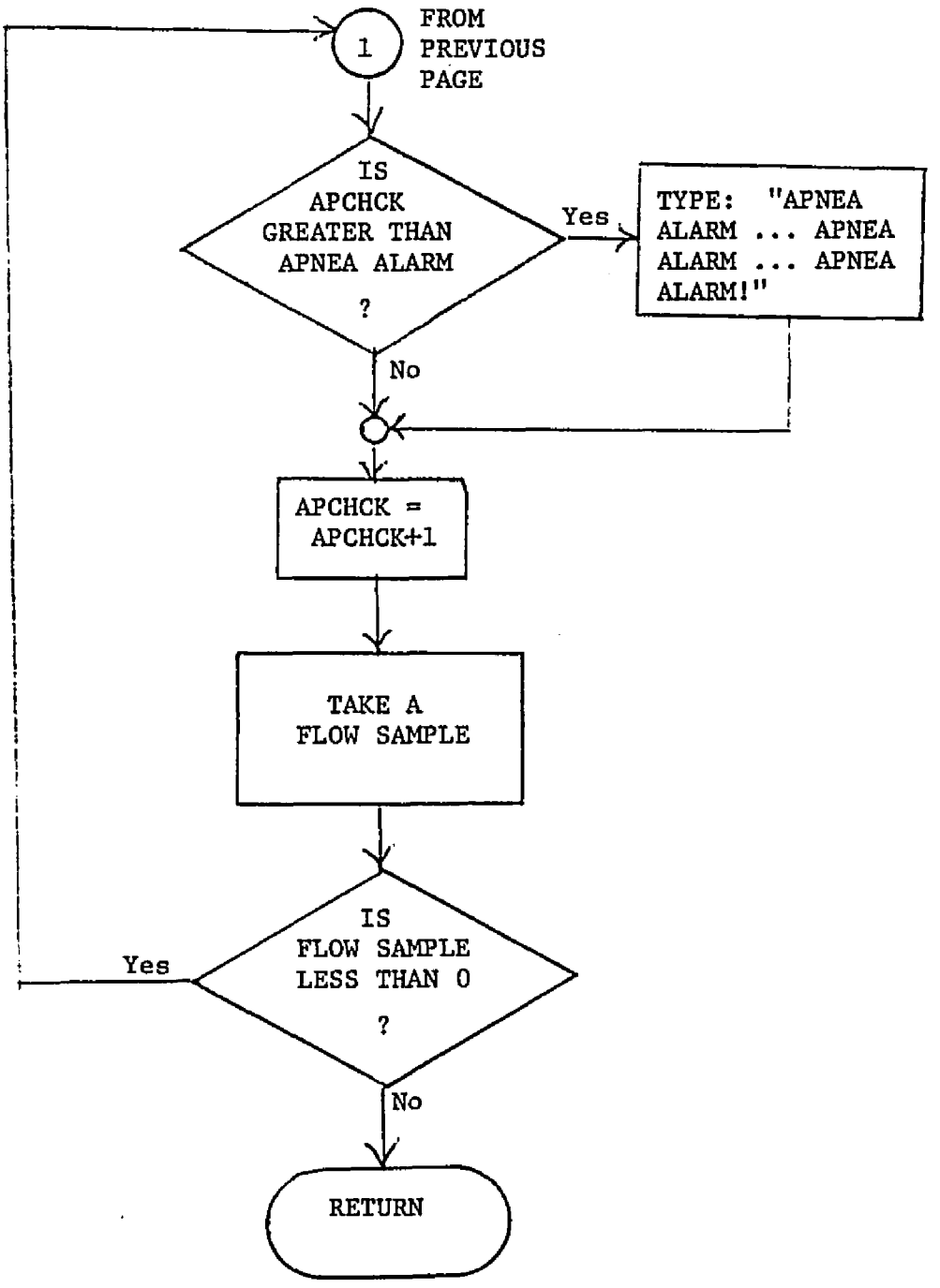

FROM
PREVIOUS
PAGE
1
I = I+1
TAKE BOTH A FLOW
AND A CONCENTRA-
TION SAMPLE
FLOW(I) = FLOW
SAMPLE
CONC(I) = CONCEN-
TRATION SAMPLE
HAS FLOW
CHANGED
DIRECTION
?
No
Yes
INEND = I-1
A
I = I+1
2
NEXT
PAGE

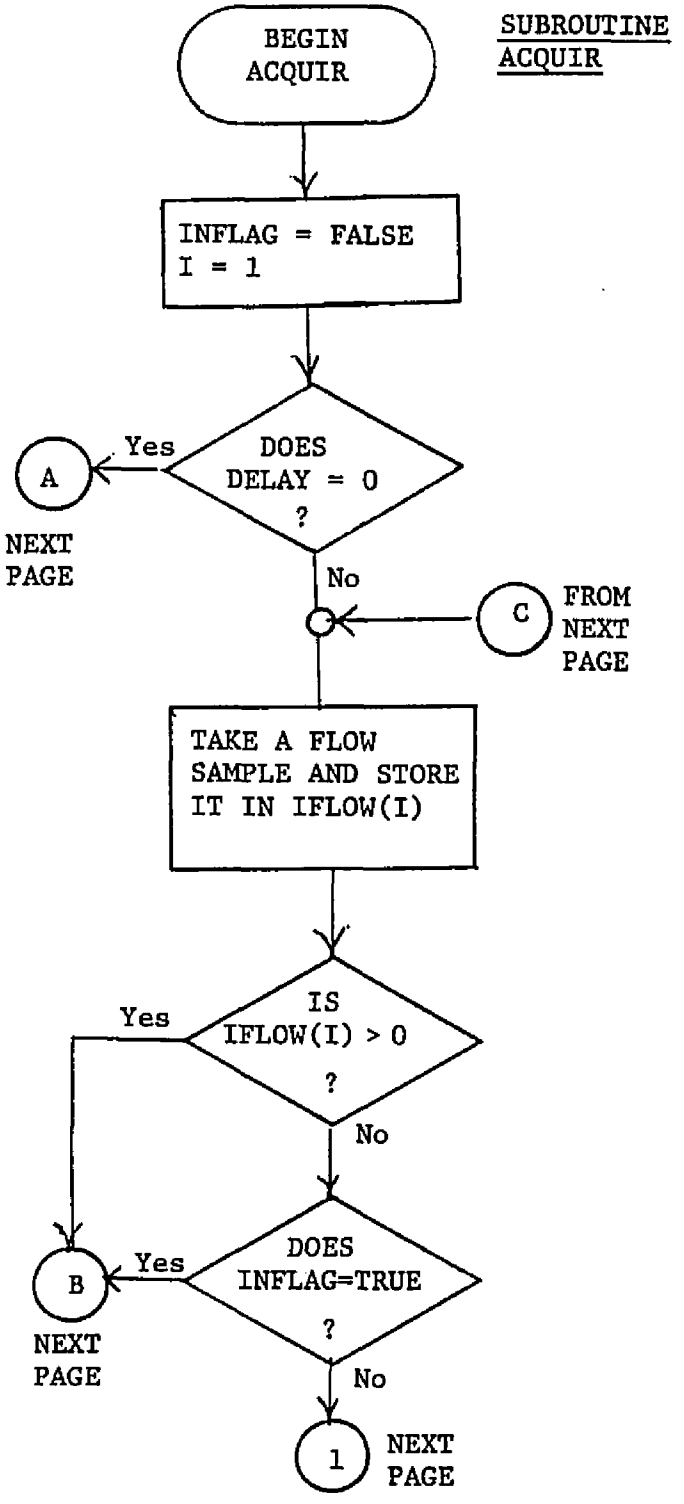

2
TAKE BOTH A FLOW AND A CONCENTRATION SAMPLE
FLOW(I) = FLOW SAMPLE
CONC(I) = CONCENTRATION SAMPLE
HAS FLOW CEASED ?
No
GO TO POINT Ⓐ ON PREVIOUS PAGE
Yes
EXEND = I-1
TYPE: "ENTER A '1' IF INDUCTION ENTER A '0' IF EMERGENCE"
3
NEXT PAGE

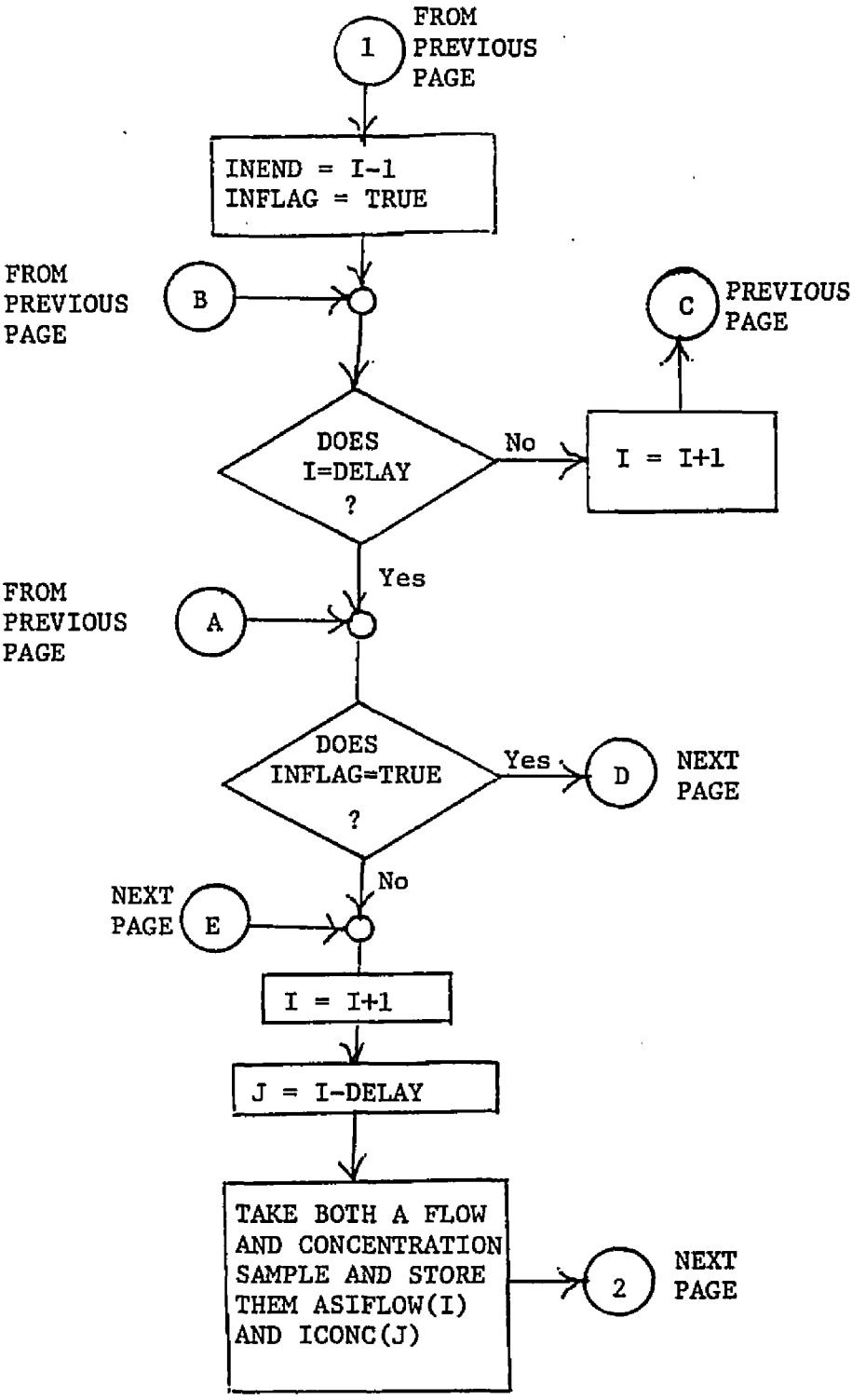

FROM
PREVIOUS
PAGE
3
INDUCTION
?
No
B
NEXT
PAGE
N = 1
MAXIDX =
INEND
No
IS
CONC(MAXIDX)
LESS THAN
CONC(MAXIDX+N)
Yes
MAXIDX =
MAXIDX+N
DOES
N + INEND
EQUAL EXEND
?
No
N = N+1
Yes
DELAY =
MAXIDX-INEND
4
NEXT
PAGE

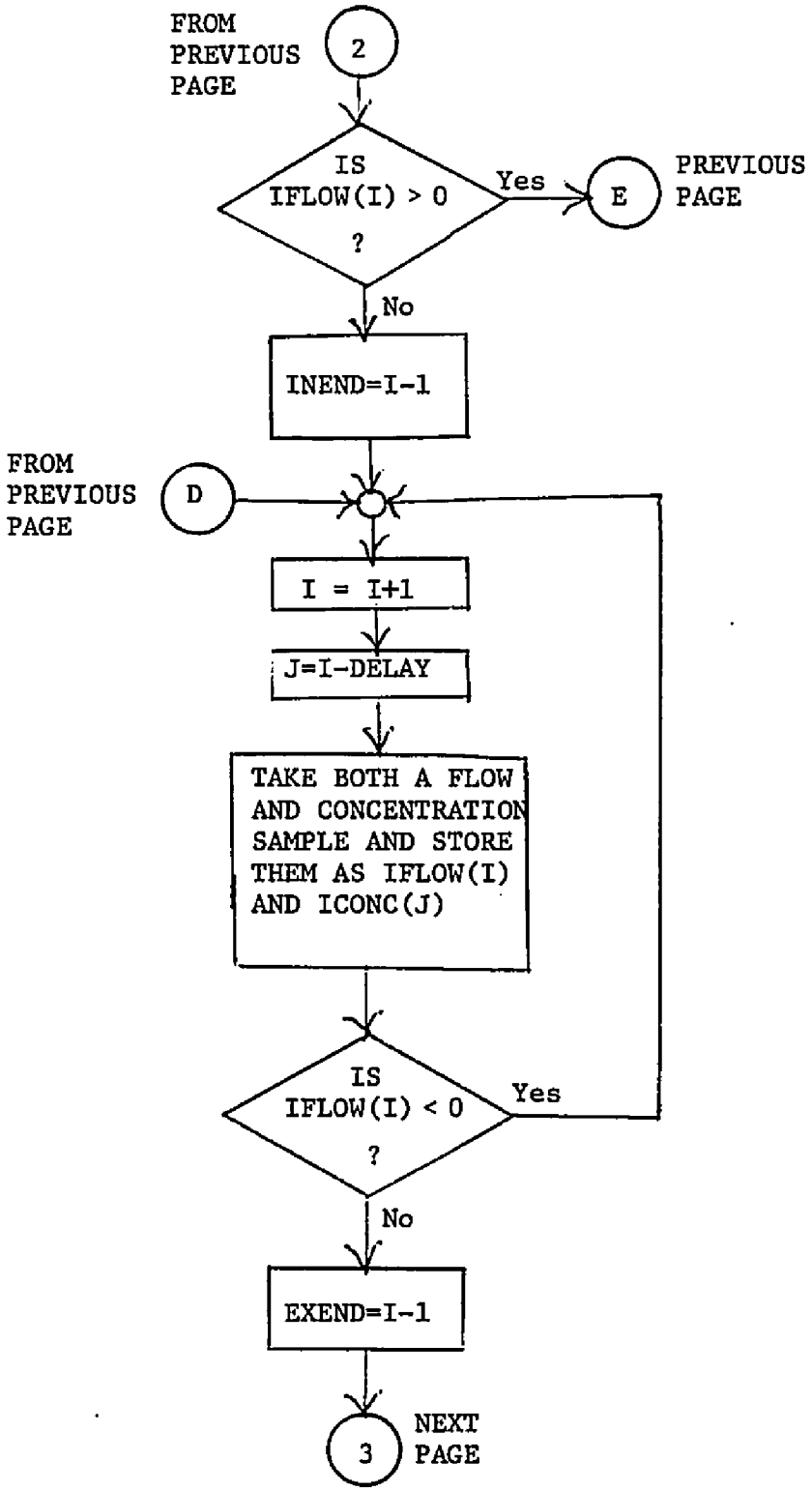

FROM PREVIOUS PAGE
4
TYPE: "THE DELAY IS" DELAY "HUNDREDTHS OF A SECOND"
RETURN
FROM PREVIOUS PAGE
B
N = 1
MINIDX = INEND
IS CONC(MINIDX) GREATER THAN CONC(MINIDX+N) ?
No
Yes
MINIDX = MINIDX+N
N = N+1
DOES N + INEND EQUAL EXEND ?
No
Yes
DELAY = MINIDX-INEND

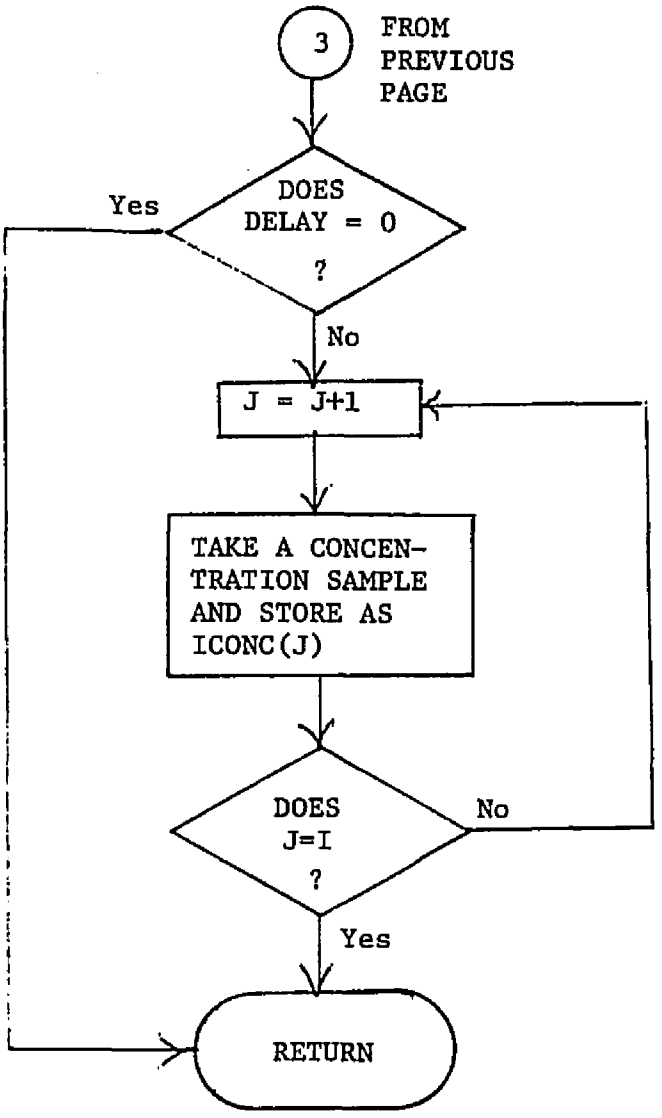

BEGIN
DETECT
SUBROUTINE
DETECT
APCHCK = 1
IS
APCHCK
GREATER THAN
APNEA ALARM
?
Yes
TYPE: "APNEA
ALARM ... APNEA
ALARM ... APNEA
ALARM!"
No
APCHCK =
APCHCK+1
TAKE A
FLOW SAMPLE
IS
FLOW SAMPLE
GREATER THAN 0
?
Yes
No
1
NEXT
PAGE

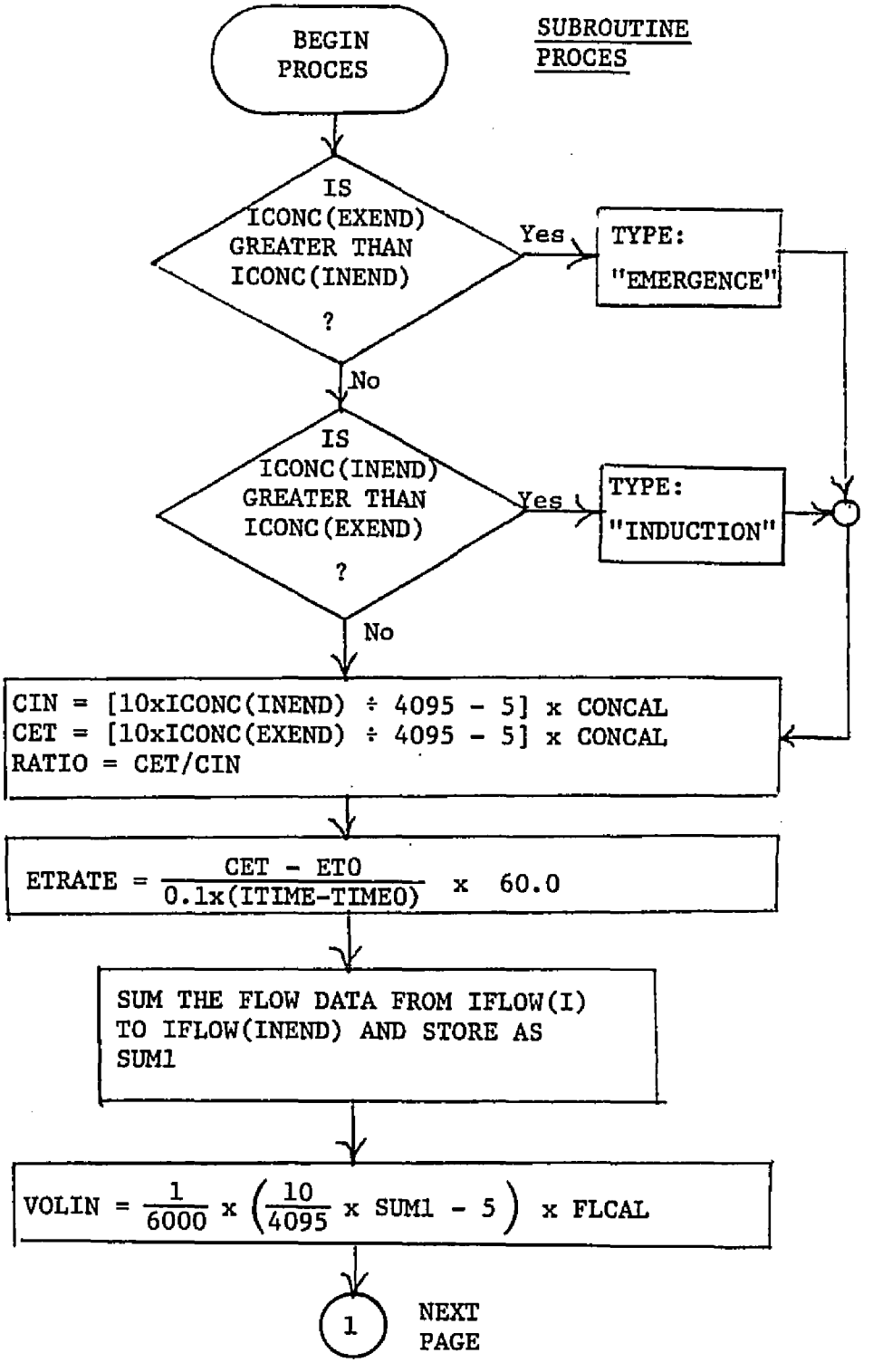

1
FROM
PREVIOUS
PAGE
IS
APCHCK
GREATER THAN
APNEA ALARM
?
Yes
TYPE: "APNEA
ALARM ... APNEA
ALARM ... APNEA
ALARM!"
No
APCHCK =
APCHCK+1
TAKE A
FLOW SAMPLE
IS
FLOW SAMPLE
LESS THAN 0
?
Yes
No
RETURN

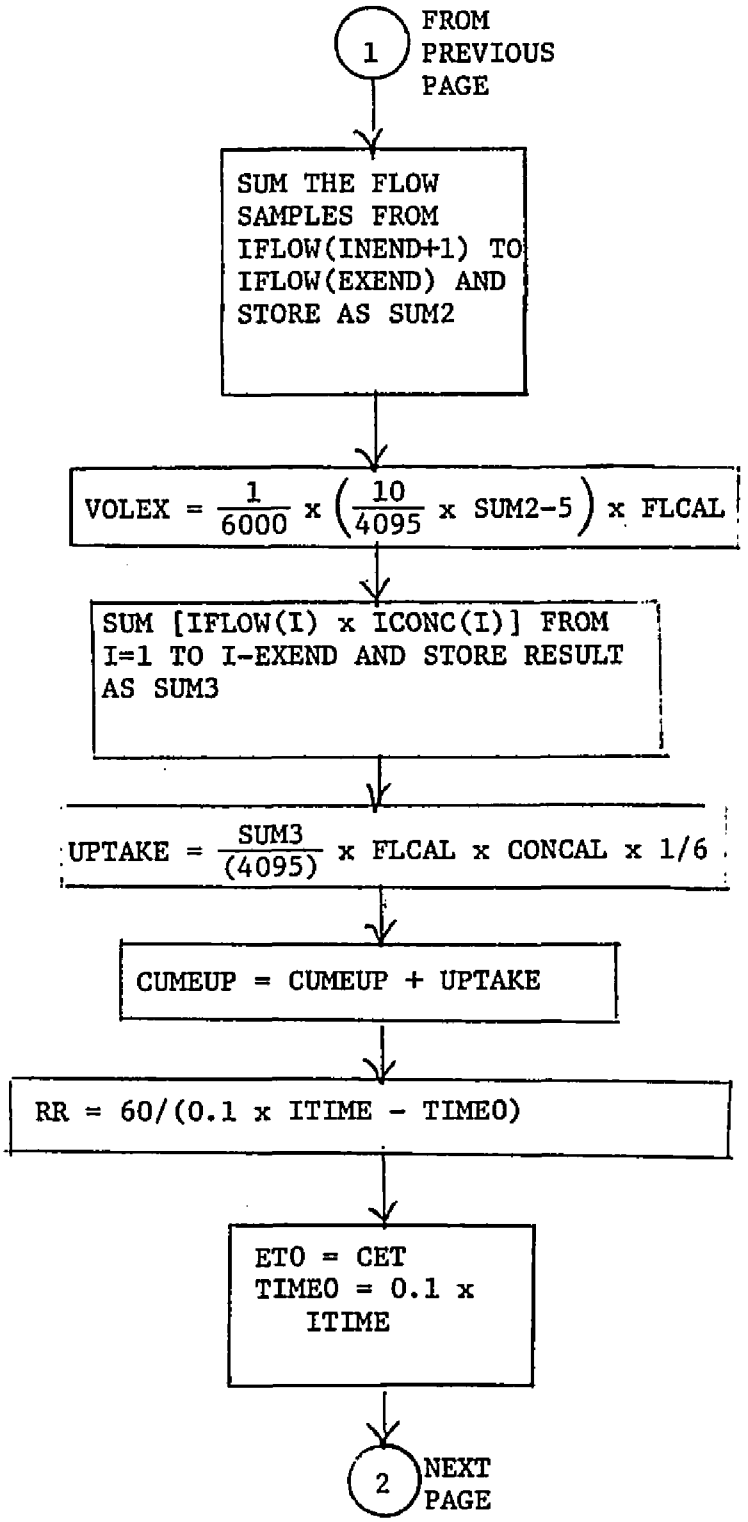

BEGIN ACQUIR
SUBROUTINE ACQUIR
INFLAG = FALSE
I = 1
DOES DELAY = 0 ?
Yes
A
NEXT PAGE
No
C
FROM NEXT PAGE
TAKE A FLOW SAMPLE AND STORE IT IN IFLOW(I)
IS IFLOW(I) > 0 ?
Yes
No
DOES INFLAG=TRUE ?
Yes
B
NEXT PAGE
No
1
NEXT PAGE

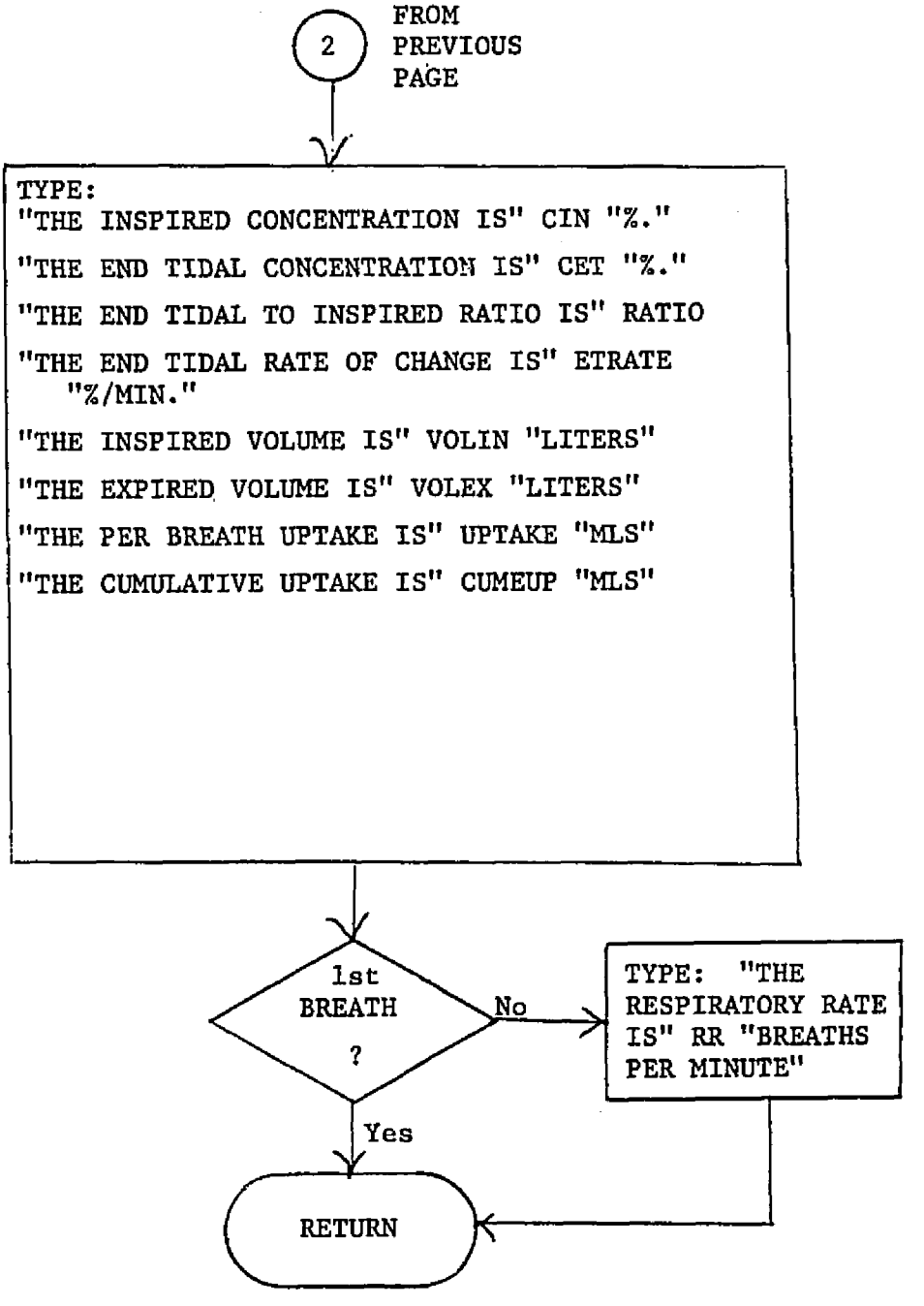

1
FROM PREVIOUS PAGE
INEND = I-1
INFLAG = TRUE
FROM PREVIOUS PAGE
B
C
PREVIOUS PAGE
DOES I=DELAY ?
No
I = I+1
Yes
FROM PREVIOUS PAGE
A
DOES INFLAG=TRUE ?
Yes
D
NEXT PAGE
No
NEXT PAGE
E
I = I+1
J = I-DELAY
TAKE BOTH A FLOW AND CONCENTRATION SAMPLE AND STORE THEM ASIFLOW(I) AND ICONC(J)
2
NEXT PAGE


FROM PREVIOUS PAGE
2
IS IFLOW(I) > 0 ?
Yes
E
PREVIOUS PAGE
No
INEND=I-1
FROM PREVIOUS PAGE
D
I = I+1
J=I-DELAY
TAKE BOTH A FLOW AND CONCENTRATION SAMPLE AND STORE THEM AS IFLOW(I) AND ICONC(J)
IS IFLOW(I) < 0 ?
Yes
No
EXEND=I-1
3
NEXT PAGE


3
FROM
PREVIOUS
PAGE
DOES
DELAY = 0
?
Yes
No
J = J+1
TAKE A CONCEN-
TRATION SAMPLE
AND STORE AS
ICONC(J)
DOES
J=I
?
No
Yes
RETURN


BEGIN PROCES
SUBROUTINE PROCES
IS ICONC(EXEND) GREATER THAN ICONC(INEND) ?
Yes
TYPE: "EMERGENCE"
No
IS ICONC(INEND) GREATER THAN ICONC(EXEND) ?
Yes
TYPE: "INDUCTION"
No
CIN = [10xICONC(INEND) ÷ 4095 - 5] x CONCAL
CET = [10xICONC(EXEND) ÷ 4095 - 5] x CONCAL
RATIO = CET/CIN
ETRATE = (CET - ETO) / (0.1x(ITIME-TIMEO)) x 60.0
SUM THE FLOW DATA FROM IFLOW(I) TO IFLOW(INEND) AND STORE AS SUM1
VOLIN = 1/6000 x (10/4095 x SUM1 - 5) x FLCAL
1
NEXT PAGE


1
FROM PREVIOUS PAGE
SUM THE FLOW SAMPLES FROM IFLOW(INEND+1) TO IFLOW(EXEND) AND STORE AS SUM2
VOLEX = 1/6000 x (10/4095 x SUM2-5) x FLCAL
SUM [IFLOW(I) x ICONC(I)] FROM I=1 TO I-EXEND AND STORE RESULT AS SUM3
UPTAKE = SUM3/(4095) x FLCAL x CONCAL x 1/6
CUMEUP = CUMEUP + UPTAKE
RR = 60/(0.1 x ITIME - TIME0)
ET0 = CET
TIME0 = 0.1 x ITIME
2
NEXT PAGE


2
FROM PREVIOUS PAGE
TYPE:
"THE INSPIRED CONCENTRATION IS" CIN "%."
"THE END TIDAL CONCENTRATION IS" CET "%."
"THE END TIDAL TO INSPIRED RATIO IS" RATIO
"THE END TIDAL RATE OF CHANGE IS" ETRATE "%/MIN."
"THE INSPIRED VOLUME IS" VOLIN "LITERS"
"THE EXPIRED VOLUME IS" VOLEX "LITERS"
"THE PER BREATH UPTAKE IS" UPTAKE "MLS"
"THE CUMULATIVE UPTAKE IS" CUMEUP "MLS"
1st BREATH ?
No
TYPE: "THE RESPIRATORY RATE IS" RR "BREATHS PER MINUTE"
Yes
RETURN

APPENDIX C

FORTRAN SOURCE CODE

```
      PROGRAM MONITR
C  THIS IS THE MAIN CALLING PROGRAM FOR THE ANESTHESIA MONITORING SYSTEM
      COMMON /BLCK1/IFLOW(1000),ICONC(1000)/BLCK2/INEND,EXEND
      COMMON /BLCK4/DELAY/BLCK3/APNEA/BLCK5/ITIME/BLCK6/TIME0,ET0,CUMEUP
      COMMON /BLCK7/FLCAL,CONCAL
      INTEGER EXEND,DELAY,APNEA
      DATA TIME0,ET0,CUMEUP/0.0,0.0,0.0/
      CALL USEROP                          !GET DATA FROM USER
      ICMF1=0
      CALL SETR(5,17,10.0,ICMF1)           !START THE SOFTWARE CLOCK
      TYPE *,' CALLING DETECT '
   10 CALL DETECT                          !FIND THE START OF A BREATH
      ITIME=IDOR(0,-1,'177777,,IVAR)       !READ THE TIME ON THE CLOCK
      CALL ACQUIR                 !ACQUIRE FLOW AND CONCENTRATION DATA
      IF(INEND.LT.20.OR.EXEND.LT.20)GO TO 10
      TYPE *,' RETURNED FROM ACQUIR '
      CALL PROCES                 !PROCESS AND OUTPUT THE ACQUIRED DATA
      TYPE *,' RETURNED FROM PROCES '
      ITIME=IDOR(0,-1,'177777,,IVAR)       !READ THE CLOCK FOR OUTPUT TO USER
      TMIN=(.1/60.0)*FLOAT(ITIME)
      TMINRT=SQRT(TMIN)
      TYPE *,' THE TIME ELAPSED IS ',TMIN,' MINUTES '
      TYPE *,' THE SQUARE ROOT OF ELAPSED TIME IS ',TMINRT,' MIN**1/2 '
      GO TO 10                             !GO BACK TO DETECT
      END
```

```
      SUBROUTINE USEROP
C  THE PURPOSE OF THIS ROUTINE IS TO ACQUIRE THE NECESSARY DATA FROM THE
C  USER THAT WILL BE USED IN DATA ACQUISITION AND PROCESSING
      COMMON /BLCK3/APNEA/BLCK4/DELAY/BLCK7/FLCAL,CONCAL
      INTEGER APNEA,DELAY
   10 TYPE *,' ENTER THE APNEA ALARM VALUE IN HUNDRETHS OF A SECOND.'
      ACCEPT *,APNEA
      TYPE *,' ENTER A 1 TO DETERMINE THE DELAY,OTHERWISE ENTER A 0'
      ACCEPT *,J
      IF(J.EQ.1)CALL LAGCAL   !CALCULATES THE DELAY
      IF(J.EQ.0)TYPE *,' ENTER THE DELAY VALUE IN HUNDRETHS OF A SECOND'
      IF(J.EQ.1)GO TO 20
      ACCEPT *,DELAY
   20 TYPE *,' ENTER THE FLOW CALIBRATION VALUE IN LITERS/MIN PER VOLT '
      ACCEPT *,FLCAL
      TYPE *,' ENTER THE CONCENTRATION CALIBRATION VALUE IN % PER VOLT '
      ACCEPT *,CONCAL
      TYPE *,' ENTER A 1 TO RE-ENTER THE DATA, ENTER A 0 TO START
     1 MONITOR'
      ACCEPT *,K
      IF(K.EQ.1)GO TO 10
      RETURN
      END
```

```
      SUBROUTINE LAGCAL
C  THIS ROUTINE CALCULATES THE DELAY BETWEEN THE FLOW METER AND THE
C  ANESTHETIC GAS ANALYZER
      COMMON /BLCK3/APNEA/BLCK4/DELAY
      INTEGER APNEA,DELAY,EXEND
      DIMENSION IBUF(2),IFL(1000),IC(1000)
      TYPE *,' ENTER 0  WHEN READY TO DETERMINE THE DELAY'
      ACCEPT *,M
      CALL DETECT      !FIND THE START OF A BREATH
      I=0
   10 I=I+1
      ICMF=0
C  ACQUIRE FLOW AND CONCENTRATION SAMPLES
      CALL RTS(IBUF,2,,1,0,2,,0,ICMF,IBEF)
    1 IF(ICMF.EQ.0)GO TO 1     !WAIT FOR COMPLETION OF SAMPLING
      IFL(I)=IBUF(1)           !STORE SAMPLES IN BUFFERS
      IC(I)=IBUF(2)
C  CHECK FOR THE END OF INSPIRATION
      IF(IFL(I).GT.2047)GO TO 10
C  STORE THE INDEX OF THE FLOW BUFFER ELEMENT CORRESPONDING TO THE
C  END OF INSPIRATION
      INEND=I-1
   20 I=I+1
      ICMF=0
      CALL RTS(IBUF,2,,1,0,2,,0,ICMF,IBEF)
    2 IF(ICMF.EQ.0)GO TO 2
      IFL(I)=IBUF(1)
      IC(I)=IBUF(2)
C  CHECK FOR THE END OF EXPIRATION
      IF(IFL(I).LT.2038)GO TO 20
C  STORE THE INDEX OF THE FLOW BUFFER ELEMENT CORRESPONDING TO THE
C  END OF EXPIRATION
      EXEND=I-1
      TYPE *,' ENTER A 1 IF INDUCTION, OTHERWISE ENTER 0'
      ACCEPT *,J
      MAXIDX=INEND     !USE INEND AS A REFERENCE
      IF(J.NE.1)GO TO 30
      DO 100 N=INEND,EXEND
C  DETERMINE THE LAST MAXIMUM ELEMENT IN THE CONCENTRATION BUFFER
C  AND STORE ITS INDEX AS MAXIDX IN THE CASE OF INDUCTION
      IF(IC(MAXIDX).LT.IC(I)+4)MAXIDX=I
  100 CONTINUE
      GO TO 40
   30 DO 200 N=INEND,EXEND
C  DETERMINE THE LAST MINIMUM ELEMENT INT HE CONCENTRATION BUFFER
C  AND STORE ITS INDEX AS MAXIDX IN THE CASE OF EMERGENCE
      IF(IC(MAXIDX).GT.IC(I)-4)MAXIDX=I
  200 CONTINUE
C  THE DIFFERENCE BETWEEN MAXIDX AND INEND IS THE DELAY
   40 DELAY=MAXIDX-INEND
      TYPE *,' THE DELAY IS ',DELAY,' HUNDRETHS OF A SECOND '
      RETURN
      END
```

```
      SUBROUTINE DETECT
C  THIS ROUTINE DETECTS THE START OF A RESPIRATORY CYCLE
      COMMON /BLCK3/APNEA
      INTEGER APNEA,APCHCK,IBUF(1)
D     TYPE *,' STARTED DETECT '
      APCHCK=1                  !INITIALIZE THE COUNTER
C  CHECK FOR APNEA CONDITION
   20 IF(APCHCK.GT.APNEA)TYPE 110
      APCHCK=APCHCK+1
      ICMF=0
C  TAKE A FLOW SAMPLE
      CALL RTS(IBUF,1,,,0,,,0,ICMF,IBEF)
    1 IF(ICMF.EQ.0)GO TO 1
C  SEE IF SAMPLE IS INSPIRATORY HALF OF THE CYCLE
      IF(IBUF(1).GT.2052)GO TO 20
C  IF NOT CHECK FOR APNEA CONDITION AND SAMPLE LOOKING FOR THE
C  START OF RESPIRATORY CYCLE
   30 IF(APCHCK.GT.APNEA)TYPE 110
      APCHCK=APCHCK+1
      ICMF=0
      CALL RTS(IBUF,1,,,0,,,0,ICMF,IBEF)
    2 IF(ICMF.EQ.0)GO TO 2
C  CHECK TO SEE IF SAMPLE IS ABOVE INSPIRED FLOW THRESHOLD
      IF(IBUF(1).LT.2052)GO TO 30
C  AT THIS POINT A BREATH HAS BEEN DETECTED
      RETURN
  110 FORMAT('         APNEA ALARM!!...          APNEA ALARM!!...  ')
      END
```

```
      SUBROUTINE ACQUIR
C  THIS ROUTINES ACQUIRES THE FLOW AND CONCENTRATION DATA CORRESPONDING
C  TO A SINGLE BREATH.IT ALSO DETERMINES THE END OF INSPIRATION AND EXPIRATION
      COMMON /BLCK4/DELAY
      COMMON /BLCK1/IFLOW,ICONC/BLCK2/INEND,EXEND
      DIMENSION IFLOW(1000),ICONC(1000),IBUF(1),IBFC(2)
      INTEGER EXEND,DELAY
      LOGICAL INFLAG
C  INITIALIZE THE VARIABLES
      INFLAG=.FALSE.
C  START DATA ACQUISITION AND CHECK FOR THE END OF INSPIRATION
C  CONTINUE UNTIL THE END OF DELAY
      I=1
      IF(DELAY.EQ.0)GO TO 15
      DO 10 I=1,DELAY
      ICMF=0
      CALL RTS(IBUF,1,,,0,,,0,ICMF,IBEF)
    1 IF(ICMF.EQ.0)GO TO 1
      IFLOW(I)=IBUF(1)
C  CHECK FOR THE END OF INSPIRATION
      IF(IFLOW(I).GT.2047)GO TO 10
      IF(INFLAG)GO TO 10
C  STORE THE INDEX OF THE ELEMENT CORRESPONDING TO THE
C  END OF INSPIRATION
      INEND=I-1
C  SET THE END OF INSPIRATION FLAG
      INFLAG=.TRUE.
   10 CONTINUE
      IF(INFLAG)GO TO 20
C  THIS SECTION ACQUIRES BOTH FLOW AND CONCENTRATION DATA AND
C  LOOKS FOR THE END OF INSPIRATION IF INFLAG WAS NEVER SET
   15 ICMF=0
      CALL RTS(IBFC,2,,1,0,2,,0,ICMF,IBEF)
    2 IF(ICMF.EQ.0)GO TO 2
      IFLOW(I)=IBFC(1)
      J=I-DELAY
      ICONC(J)=IBFC(2)
      I=I+1
      IF(IFLOW(I-1).GT.2047)GO TO 15
      INEND=I-1
C  THIS SECTION TAKES FLOW AND CONCENTRATION SAMPLES AND
C  LOOKS FOR THE END OF EXPIRATION
   20 ICMF=0
      CALL RTS(IBFC,2,,1,0,2,,0,ICMF,IBEF)
    3 IF(ICMF.EQ.0)GO TO 3
      IFLOW(I)=IBFC(1)
      J=I-DELAY
      ICONC(J)=IBFC(2)
      I=I+1
      IF(IFLOW(I-1).LT.2038)GO TO 20
      EXEND=I-1
C  THE NEXT FEW LINES PICK-UP THE LAGGING CONCENTRATION DATA
      IF(DELAY.EQ.0)GO TO 30
   25 J=J+1
      ICMF=0
      CALL RTS(IBUF,1,,,1,,,0,ICMF,IBEF)
    4 IF(ICMF.EQ.0)GO TO 4
      ICONC(J)=IBUF(1)+2
      IF(J.LT.I-1)GO TO 25
   30 TYPE *,' FINISHED ACQUIRING DATA '
      RETURN
      END
```

```
      SUBROUTINE PROCES
C
C  THIS ROUTINE PROCESSES AND OUTPUTS THE DATA ACQUIRED BY THE PREVIOUS
C  ROUTINES CALLED BY MONITR
C
      COMMON /BLCK1/IFLOW(1000),ICONC(1000)/BLCK2/INEND,EXEND/BLCK4/DELAY
      COMMON /BLCK5/ITIME/BLCK6/TIME0,ET0,CUMEUP/BLCK7/FLCAL,CONCAL
      INTEGER EXEND,DELAY
C  DETERMINE AND OUTPUT WHETHER THE PATIENT IS IN AN INDUCTANCE OR EMERGENCE
C  STATE FOR THIS BREATH
      TYPE *,INEND,EXEND
      TYPE *,' STARTED PROCES '
      IF(ICONC(EXEND).GT.ICONC(INEND))TYPE *,' EMERGENCE '
      IF(ICONC(INEND).GT.ICONC(EXEND))TYPE *,' INDUCTION '
C  NOW DETERMINE THE INSPIRED, EXPIRED AND RATIO CONCENTRATIONS
      CIN=(10.0*FLOAT(ICONC(INEND))/4095.0-5.0)*CONCAL
      CET=(10.0*FLOAT(ICONC(EXEND))/4095.0-5.0)*CONCAL
      RATIO=CET/CIN
C  NOW CALCULATE THE TIME RATE OF END TIDAL CHANGE
      ETRATE=((CET-ET0)/(0.1*FLOAT(ITIME)-TIME0)*60.0)
C  NOW CALCULATE THE VOLUMES
      SUM=0.0
      DO 10 I=1,INEND
   10 SUM=SUM+(10.0*FLOAT(IFLOW(I))/4095.0-5.0)
D     TYPE *,' SUM 1 IS ',SUM
      VOLIN=0.01*SUM*FLCAL/60.0
      SUM2=0.0
      ISTART=INEND+1
      DO 20 J=ISTART,EXEND
   20 SUM2=SUM2+(10.0*FLOAT(IFLOW(J))/4095.0-5.0)
D     TYPE *,' SUM2 IS ',SUM2
      VOLEX=0.01*SUM2*FLCAL/60.0
C  NOW WE WANT TO CALCULATE THE TOTAL MASS UPTAKE
      SUM=0.0
      DO 30 K=1,EXEND
   30 SUM=SUM+(FLOAT(ICONC(K))-2047.5)*(FLOAT(IFLOW(K))-2047.5)
      UPTAKE=(SUM/4095.0**2)*FLCAL*CONCAL*10.0/60.0
      CUMEUP=CUMEUP+UPTAKE
      RR=60.0/(0.1*FLOAT(ITIME)-TIME0)
C  NOW OUTPUT THE RESULTS
      TYPE *,' THE INSPIRED CONCENTRATION IS ',CIN,' % '
      TYPE *,' THE END TIDAL CONCENTRATION IS ',CET,' % '
      TYPE *,' THE END TIDAL TO INSPIRED RATIO IS ',RATIO
      TYPE *,' THE END TIDAL RATE OF CHANGE IS ',ETRATE,' %/MIN '
      TYPE *,' THE INSPIRED VOLUME IS ',VOLIN,' LITERS '
      TYPE *,' THE EXPIRED VOLUME IS ',VOLEX,' LITERS '
      TYPE *,' THE PER BREATH UPTAKE IS ',UPTAKE,' MLS '
      TYPE *,' THE CUMULATIVE UPTAKE IS ',CUMEUP,' MLS '
      IF(TIME0.NE.0.0)TYPE 100,RR
      ET0=CET
      TIME0=0.1*FLOAT(ITIME)
      RETURN
  100 FORMAT(' THE RESPIRATORY RATE IS ',F6.2,' BREATHS/MIN ')
      END
```

APPENDIX D

A COMPLETE LISTING OF EXPERIMENTAL DATA

Table D.1. Electrical analog simulation data.

Case 1: FLOW = IV peak sine wave

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 1: Concentration = 0 to 4v square wave						
1	.317	.317	4.00	-.02	12.73	5.9
2	.316	.316	3.99	-.03	12.71	5.8
3	.316	.316	4.00	-.02	12.71	5.8
4	.316	.316	4.00	-.02	12.70	6.0
5	.316	.317	4.00	-.02	12.68	5.9
6	.315	.317	4.00	-.02	12.68	6.0
7	.315	.317	4.00	-.02	12.68	5.9
8	.316	.317	4.00	-.03	12.67	5.8
9	.316	.317	4.00	-.02	12.67	5.9
10	.316	.317	4.00	-.03	12.67	6.0
Mean	0.316	0.317	4.00	-.023	12.69	5.9
S.D.	0.001	0.000	0.00	.005	0.022	0.1
Trial 2: 3v-0v square wave for concentration waveform						
1	.315	.317	3.03	-.01	9.59	12.0
2	.315	.317	3.02	-.01	9.59	12.0
3	.315	.318	3.03	-.01	9.59	12.0
4	.315	.318	3.02	-.01	9.60	11.9
5	.315	.318	3.03	-.01	9.59	12.0
6	.315	.317	3.02	-.01	9.59	12.0
7	.315	.318	3.02	-.01	9.59	12.0
8	.315	.317	3.03	-.01	9.60	12.0
9	.315	.317	3.02	-.01	9.59	12.0
10	.314	.317	3.03	-.01	9.58	12.0
Mean	.315	.3174	3.025	-.01	9.591	12.0
S.D.	.000	.0005	.005	.00	.005	0.0

Table D.1.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 3: Concentration = 0 to 2v square wave						
1	.315	.318	2.01	-.01	6.38	9.8
2	.315	.318	2.01	-.01	6.37	9.9
3	.314	.317	2.01	-.01	6.37	9.9
4	.315	.318	2.01	-.01	6.38	9.8
5	.314	.317	2.01	-.01	6.38	9.7
6	.315	.318	2.01	-.01	6.37	9.8
7	.314	.318	2.01	-.01	6.37	9.8
8	.315	.318	2.01	-.01	6.37	9.7
9	.314	.318	2.01	-.01	6.35	9.8
10	.315	.318	2.01	-.01	6.37	9.8
Mean	.3146	.3178	2.01	-.01	6.37	9.8
S.D.	.0005	.0004	.00	.00	0.01	0.1
Trial 4: Concentration = 0 to 1.5v square wave						
1	.314	.319	1.48	-.01	4.68	5.4
2	.313	.318	1.48	-.01	4.68	5.6
3	.313	.317	1.48	-.01	4.67	5.6
4	.313	.317	1.48	-.01	4.66	5.7
5	.317	.317	1.48	-.01	4.73	5.7
6	.318	.317	1.48	-.01	4.74	5.8
7	.318	.317	1.48	-.01	4.73	5.7
8	.317	.317	1.48	-.01	4.73	5.7
9	.318	.317	1.48	-.01	4.73	5.7
10	.317	.317	1.48	-.01	4.74	5.6
Mean	.316	.317	1.48	-.01	4.71	5.7
S.D.	.002	.001	.00	.00	0.03	0.2

Table D.1.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 5: Concentration = 0 to 1v square wave						
1	.316	.317	.99	-.01	3.13	11.8
2	.316	.317	.99	-.01	3.13	12.0
3	.316	.318	.99	-.01	3.13	12.0
4	.316	.317	.99	-.01	3.14	12.1
5	.316	.318	.99	-.01	3.13	12.0
6	.316	.318	.99	-.01	3.13	12.1
7	.315	.318	.99	-.01	3.14	12.1
8	.316	.318	.99	.00	3.13	12.0
9	.316	.318	.99	.00	3.13	12.0
10	.316	.318	.99	.00	3.13	12.0
Mean	.316	.318	.99	.01	3.132	12.0
S.D.	.0003	.0005	.00	.00	.004	0.1
Trial 6: Concentration = 0 to 0.5v square wave						
1	.316	.318	0.48	-.00	1.53	10.0
2	.316	.318	0.48	.00	1.53	9.8
3	.316	.318	0.48	.00	1.53	9.8
4	.316	.318	0.48	.00	1.53	9.9
5	.315	.318	0.48	.00	1.53	9.9
6	.316	.318	0.48	.00	1.53	10.0
7	.316	.318	0.48	.00	1.53	9.9
8	.315	.318	0.48	.00	1.53	9.9
9	.315	.318	0.48	.00	1.52	10.0
10	.315	.318	0.48	.00	1.53	9.9
Mean	.3156	.318	0.48	.00	1.53	9.9
S.D.	.0005	.000	.00	.00	.00	0.1

Table D.1.--Continued

Case 2: Concentration = 0 to 1 volt square wave

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 1: Flow = 0.5v peak sine wave						
1	.153	.162	.99	-.01	1.53	7.8
2	.152	.163	.99	-.01	1.53	7.8
3	.154	.162	.99	-.01	1.54	7.9
4	.153	.162	.99	-.01	1.53	7.8
5	.153	.163	.99	-.01	1.53	7.8
6	.155	.160	.99	-.01	1.55	7.8
7	.153	.161	.99	-.01	1.53	7.8
8	.153	.163	.99	-.01	1.53	7.8
9	.152	.163	.99	-.01	1.52	7.8
10	.152	.163	.99	-.01	1.53	7.8
Mean	.153	.162	.99	-.01	1.53	7.8
S.D.	.001	.001	.00	.00	.01	0.0
Trial 2: Flow = 1 volt peak sine wave						
1	.316	.317	.99	-.01	3.14	5.0
2	.316	.318	.99	-.01	3.14	4.8
3	.315	.318	.99	-.01	3.13	4.8
4	.316	.318	.99	-.01	3.14	4.9
5	.315	.317	.99	-.01	3.13	4.9
6	.316	.318	.99	-.01	3.14	4.9
7	.315	.317	.99	-.01	3.13	5.0
8	.315	.318	.99	-.01	3.13	4.9
9	.316	.318	.99	-.01	3.14	4.9
10	.315	.318	.99	-.01	3.13	4.9
Mean	.3155	.3177	.99	-.01	3.135	4.9
S.D.	.0005	.0005	.00	.00	.005	0.1

Table D.1.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 3: Flow = 1.5 volt peak sine wave						
1	.481	.488	.99	-.01	4.81	12.0
2	.482	.488	.99	-.01	4.82	11.9
3	.482	.489	.99	-.01	4.82	11.9
4	.482	.490	.99	-.01	4.82	11.9
5	.481	.489	.99	-.01	4.81	11.9
6	.480	.488	.99	-.01	4.81	11.9
7	.482	.489	.99	-.01	4.82	11.9
8	.481	.490	.99	-.01	4.81	11.9
9	.482	.489	.99	-.01	4.82	11.9
10	.482	.489	.99	-.01	4.82	11.9
Mean	.4815	.4889	.99	-.01	4.816	11.9
S.D.	.0007	.0007	.00	.00	.005	0.0
Trial 4: Flow = 2 volt peak sine wave						
1	.640	.651	.99	-.01	6.39	10.0
2	.641	.652	.99	-.01	6.40	10.1
3	.641	.652	.99	-.01	6.40	10.1
4	.641	.652	.99	-.01	6.41	10.0
5	.640	.652	.99	-.01	6.39	10.1
6	.641	.651	.99	-.01	6.40	10.2
7	.642	.650	.99	-.01	6.41	10.1
8	.641	.651	.99	-.01	6.40	10.1
9	.641	.652	.99	-.01	6.40	10.1
10	.639	.652	.99	-.01	6.39	10.1
Mean	.641	.6515	.99	-.01	6.40	10.1
S.D.	.001	.0007	.00	.00	.01	0.1

Table D.1.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 5: Flow = 3 volt peak sine wave						
1	.966	.961	.99	-.01	9.63	5.9
2	.966	.962	.99	-.01	9.63	6.0
3	.965	.962	.99	-.01	9.62	5.9
4	.965	.962	.99	-.01	9.62	5.8
5	.966	.962	.99	-.01	9.63	6.0
6	.965	.962	.99	-.01	9.62	5.9
7	.964	.962	.99	-.01	9.61	5.9
8	.964	.963	.99	-.01	9.61	5.9
9	.965	.962	.99	-.01	9.62	5.9
10	.965	.962	.99	-.01	9.62	5.9
Mean	.965	.962	.99	-.01	9.62	5.9
S.D.	.0007	.0003	.00	.00	.006	0.1
Trial 6: Flow = 4 volt peak sine wave						
1	1.275	1.274	.99	-.01	12.74	8.8
2	1.275	1.276	.99	-.01	12.74	8.8
3	1.276	1.277	.99	-.01	12.75	8.9
4	1.275	1.275	.99	-.01	12.74	8.7
5	1.274	1.275	.99	-.01	12.73	8.9
6	1.275	1.274	.99	-.01	12.74	8.8
7	1.276	1.275	.99	-.01	12.75	8.8
8	1.276	1.275	.99	-.01	12.75	8.8
9	1.276	1.276	.99	-.01	12.75	8.7
10	1.275	1.276	.99	-.01	12.74	8.8
Mean	1.275	1.275	.99	-.01	12.74	8.8
S.D.	.006	.001	.00	.00	.007	0.1

Table D.2. Steady state mechanical simulation data.

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 1						
1	.514	.531	1.21	1.22.	-.158	5.5
2	.529	.529	1.24	1.22	.067	5.6
3	.512	.533	1.21	1.18	-.194	5.5
4	.514	.532	1.21	1.23	-.169	5.9
5	.525	.529	1.21	1.22	.009	5.7
6	.513	.532	1.25	1.21	-.165	5.8
7	.514	.531	1.20	1.21	.009	5.8
8	.529	.529	1.21	1.22	-.194	5.7
9	.512	.533	1.24	1.23	.067	5.6
10	.514	.532	1.21	1.18	-.158	5.7
11	.525	.529	1.25	1.22	-.169	5.7
12	.513	.532	1.20	1.22	-.165	5.7
Mean	.523	.531	1.22	1.21	-.102	5.7
S.D.	.007	.002	.02	.02	.110	0.2
Trial 2						
1	.410	.420	1.11	1.12	-.07	
2	.409	.419	1.12	1.12	-.03	
3	.405	.418	1.12	1.12	-.01	
4	.410	.419	1.12	1.12	-.10	
5	.410	.417	1.11	1.11	-.03	
6	.408	.419	1.12	1.12	-.04	
7	.407	.418	1.12	1.13	-.11	
8	.409	.418	1.11	1.12	-.11	
9	.410	.419	1.12	1.11	.00	
10	.409	.418	1.11	1.12	-.04	
11	.410	.418	1.12	1.12	-.03	
12	.409	.419	1.12	1.12	-.01	
Mean	.409	.419	1.12	1.12	-.048	
S.D.	.002	.001	.005	.01	.050	

Table D.2.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)	R.R. (Breaths/Min.)
Trial 3						
1	.296	.301	.91	.90	-.08	12.3
2	.295	.302	.93	.91	-.07	12.4
3	.295	.301	.93	.92	-.05	12.5
4	.294	.302	.92	.92	-.06	12.0
5	.295	.302	.89	.90	-.07	12.2
6	.294	.304	.90	.90	-.03	12.2
7	.294	.303	.91	.92	-.04	12.3
8	.295	.302	.92	.91	-.02	12.3
9	.296	.301	.93	.92	-.01	12.2
10	.294	.302	.92	.91	-.05	12.2
11	.295	.302	.91	.92	-.02	12.3
12	.294	.303	.92	.92	-.03	12.3
Mean	.295	.302	.916	.91	-.044	12.3
S.D.	.001	.001	.012	.01	.023	0.2
Trial 4						
1	.197	.211	1.51	1.50	-.03	10.1
2	.198	.210	1.53	1.52	-.04	10.2
3	.196	.209	1.52	1.51	-.02	10.1
4	.198	.209	1.50	1.50	-.01	10.1
5	.195	.212	1.52	1.52	-.02	10.0
6	.196	.211	1.52	1.51	-.03	10.0
7	.197	.210	1.51	1.50	-.03	10.2
8	.197	.210	1.49	1.50	-.03	10.3
9	.198	.209	1.50	1.51	-.02	10.1
10	.195	.212	1.51	1.50	-.04	10.0
11	.196	.211	1.52	1.51	-.03	10.0
12	.198	.209	1.50	1.49	-.02	10.1
Mean	.197	.210	1.51	1.51	-.024	10.1
S.D.	.001	.001	.01	.01	.009	0.0

Table D.3. Single breath uptake data.

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)
Trial 1					
1	.522	.523	0.83	.03	4.08
2	.521	.523	0.83	.03	4.08
3	.521	.521	0.82	.01	4.07
4	.523	.523	0.83	.02	4.09
5	.523	.523	0.83	.01	4.08
6	.523	.523	0.81	.02	4.08
7	.524	.524	0.80	.01	4.09
8	.522	.523	0.83	.01	4.07
9	.523	.524	0.81	.01	4.08
10	.522	.523	0.80	.00	4.07
Mean	.523	.523	0.82	.01	4.08
S.D.	.001	.001	0.01	.01	.01
Trial 2					
1	.406	.410	0.92	.03	3.61
2	.404	.409	0.91	.07	3.58
3	.404	.409	0.93	.08	3.60
4	.405	.410	0.92	.07	3.61
5	.406	.410	0.92	.05	3.62
6	.404	.409	0.92	.06	3.59
7	.406	.410	0.93	.03	3.61
8	.405	.410	0.91	.04	3.60
9	.406	.410	0.93	.02	3.62
10	.404	.409	0.91	.03	3.58
Mean	.405	.410	0.92	.05	3.60
S.D.	.001	.001	.01	.02	.014

Table D.3.--Continued

Observation No.	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	Uptake (ml)
Trial 3					
1	.296	.305	1.97	0.04	5.55
2	.297	.303	1.96	0.05	5.56
3	.296	.304	1.95	0.04	5.54
4	.298	.303	1.97	0.04	5.55
5	.295	.304	1.98	0.03	5.54
6	.295	.306	1.96	0.04	5.55
7	.295	.306	1.95	0.04	5.54
8	.294	.307	1.96	0.05	5.53
9	.295	.306	1.95	0.05	5.54
10	.296	.304	1.95	0.04	5.54
11	.294	.307	1.96	0.05	5.53
12	.295	.306	1.95	0.03	5.54
Mean	.2955	.3053	1.96	0.04	5.54
S.D.	.0012	.0014	.01	0.01	0.01
Trial 4					
1	.196	.203	1.68	0.03	3.01
2	.197	.203	1.67	0.04	3.03
3	.196	.204	1.68	0.04	3.04
4	.196	.203	1.67	0.04	3.02
5	.196	.203	1.68	0.05	3.03
6	.197	.203	1.68	0.03	3.04
7	.196	.204	1.67	0.03	3.03
8	.197	.203	1.67	0.04	3.02
9	.195	.204	1.67	0.05	3.05
10	.196	.203	1.69	0.04	3.00
11	.195	.204	1.69	0.03	3.01
12	.195	.204	1.68	0.04	3.01
Mean	.196	.2034	1.67	0.04	3.025
S.D.	.001	.0005	.01	0.01	.015

Note: "dead space" for all trials was approximately 20 cc.

Table D.4. Volume dilution test data.

Breath #	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	R	Uptake (ml)
Trial 1 - Expected Cumulative Uptake was 1.5 ml						
1	.495	.505	1.31	1.12	.855	0.93
2	.496	.505	1.13	1.09	.965	0.19
3	.495	.505	1.09	1.05	.963	0.19
4	.494	.506	1.05	1.02	.971	0.15
					Cumulative Uptake =	1.46 ml
Trial 2 - Expected Cumulative Uptake was 1.4 ml						
1	.400	.407	1.20	1.00	.83	0.80
2	.399	.406	1.00	0.95	.95	0.19
3	.400	.407	0.95	0.90	.95	0.19
4	.398	.408	0.84	0.87	.98	0.08
					Cumulative Uptake =	1.26 ml
Trial 3 - Expected Cumulative Uptake was 1.8 ml						
1	.399	.407	1.50	1.26	.84	0.95
2	.398	.408	1.25	1.17	.94	0.31
3	.398	.408	1.16	1.10	.95	0.23
4	.397	.409	1.10	1.05	.95	0.19
5	.398	.408	1.05	1.04	.99	0.03
					Cumulative Uptake =	1.71 ml
Trial 4 - Expected Cumulative Uptake was 0.90 ml						
1	.296	.305	1.01	0.83	.82	0.52
2	.295	.306	0.82	0.77	.94	0.14
3	.295	.306	0.77	0.73	.95	0.11
4	.294	.307	0.73	0.70	.96	0.08
5	.295	.306	0.70	0.68	.97	0.04
					Cumulative Uptake =	0.89 ml

Table D.4.--Continued

Breath #	V_{IN}(L)	V_{EX}(L)	C_{IN}(%)	C_{ET}(%)	R	Uptake (ml)
Trial 5 - Expected Cumulative Uptake was 1.9 ml						
1	.296	.305	1.71	1.34	.70	1.08
2	.296	.305	1.33	1.21	.91	0.34
3	.295	.306	1.21	1.16	.96	0.14
4	.296	.305	1.15	1.11	.97	0.11
5	.297	.305	1.11	1.09	.98	0.05
6	.296	.305	1.09	1.08	.99	0.02
					Cumulative Uptake =	1.74 ml
Trial 6 - Expected Cumulative Uptake was 3.0 ml						
1	.496	.504	2.01	1.55	.77	2.08
2	.494	.505	1.53	1.46	.95	0.34
3	.495	.504	1.46	1.42	.97	0.19
4	.495	.504	1.42	1.41	.99	0.05
					Cumulative Uptake =	2.68 ml

Table D.5. Delay calculation data.

Trial 1		Trial 2	
Observation No.	Delay Observation	Observation No.	Delay Observation
Case 1		Case 1	
1	0.51	1	0.26
2	0.52	2	0.25
3	0.52	3	0.25
4	0.51	4	0.26
5	0.52	5	0.26
6	0.52	6	0.26
7	0.52	7	0.26
8	0.52	8	0.26
9	0.51	9	0.26
10	0.52	10	0.26
Mean	0.52	Mean	0.26
S.D.	0.01	S.D.	0.00
Case 2		Case 2	
1	0.41	1	0.21
2	0.40	2	0.21
3	0.40	3	0.20
4	0.40	4	0.20
5	0.41	5	0.21
6	0.40	6	0.21
7	0.41	7	0.20
8	0.41	8	0.20
9	0.41	9	0.21
10	0.41	10	0.21
Mean	0.41	Mean	0.21
S.D.	0.01	S.D.	0.01

Table D.6. Apnea alarm test data.

Trial 1		Trial 2	
Observation No.	Delay Observation	Observation No.	Delay Observation
1	5	1	10
2	5	2	10
3	5	3	10
4	5	4	10
5	5	5	10
6	5	6	10
7	5	7	10
8	5	8	10
9	5	9	10
10	5	10	10
Mean	5	Mean	10
S.D.	0	S.D.	0

Trial 3		Trial 4	
Observation No.	Delay Observation	Observation No.	Delay Observation
1	20	1	30
2	20	2	30
3	20	3	30
4	20	4	30
5	20	5	30
6	20	6	30
7	20	7	30
8	20	8	30
9	20	9	30
10	20	10	30
Mean	20	Mean	30
S.D.	0	S.D.	0

Table D.7. Elapsed time and square root of elapsed time data.

	Minutes	Measured Elapsed Time	Square Root
Trial 1	1	1	1.0
	2	2	1.4
	3	3	1.7
	4	4	2
	5	5	2.2
	6	6	2.4
	7	7	2.6
	8	8	2.8
	9	9	3.0
	10	10	3.2
	11	11	3.3
	12	12	3.5
	13	13	3.6
	14	14	3.7
	15	15	3.9

Trials 2, 3 and 4 had the same results as Trial 1.

APPENDIX E

LIST OF SYMBOLS

A - an analog input voltage (volts)

C - concentration (volume percent)

C_A - alveolar concentration (volume percent)

Ca - arterial concentration (volume percent)

C_{ET} - end-tidal concentration (volume percent)

C_{FIN} - final concentration (volume percent)

C_{IN} - inspired concentration (volume percent)

C_{INT} - initial concentration (volume percent)

C_v - venous concentration (volume percent)

CO_2 - carbon dioxide

D - a digital output from an A/D converter

EXEND - the time corresponding to the end of expiration (minutes)

F - respiratory flow (Liters per minute)

ICONC - the buffer which stores concentration samples

IFLOW - the buffer which stores flow samples

INEND - the time corresponding to the end of inspiration (minutes)

ITIME - the time corresponding to the start of a respiratory cycle (minutes)

O_2 - oxygen

Q - cardiac output (Liters per minute)

RR - respiratory rate (breaths per minute)

RATIO - the ratio end-tidal to inspired concentration

t - time measured from when the system is turned on (minutes)

Ta - apnea period between respiratory cycles (seconds)

Td - the time delay interval between the respiratory flow and concentration waveforms (seconds)

To - the time it takes to output data (seconds)

Tp - the time it takes to process data (seconds)

U - uptake of anesthetic for a single breath (milliliters)

$\dot{U}$ - the rate of anesthetic uptake (milliliters per minute)

V_A - alveolar volume (Liters)

V_D - dead space volume (Liters)

V_E - expired volume (Liters)

V_I - inspired volume (Liters)

V_{INT} - initial volume (Liters)

V_T - tidal volume (Liters)

$\sum_{i=1}^{n}$ - the summation of the i subscript variable from 1 to n

$\int_{t_o}^{t_n} f(t)\,dt$ - the integration of f(t) from t_o to t_n

REFERENCES

Cooper, J. B., J. H. Edmonson, D. M. Joseph and R. S. Newbower, "Piezo-electric Sorption Anesthetic Sensor," I.E.E.E. Transactions on Biomedical Engineering, February 1981.

Digital Equipment Corporation, DECLAB-03 FORTRAN Extension User's Guide, Maynard, MA, February 1978.

Eger, E. I., II, Anesthetic Uptake and Action, Williams and Wilkins, Baltimore, MD, 1978, pp. 113-120.

Guyton, A. C. and C. A. Farrish, "A Rapidly Responding Continuous Oxygen Consumption Recorder," J. of Appl. Physiology 14:143, 1959.

Jennet, Sheila, "Assessment of Respiratory Effects of Analgesic Drugs," British J. of Anesthesiology 40:746, 1968.

Jeretin, S., L. R. Martinez and T. Wandycz, "A carbon dioxide mixing chamber - a simple device for continuous measurement of Expired Carbon Dioxide," Anaesthesia, Volume 34, No. 5, May 1971.

Lowe, H. J. and E. A. Ernst, The Quantitative Practice of Anesthesia, Williams and Wilkins, Baltimore, MD, 1981, pp. 67-89.

Miller, I. and J. E. Freund, Probability and Statistics for Engineers, Prentice-Hall, Englewood Cliffs, NJ, 1977, pp. 289-305.

Noe, F. E., "Computer Analysis of Curves from an Infrared CO_2 Analyzer and Screen-Type Airflow Meter," J. of Appl. Physiology 18(I):149-157, 1963.

Noe, F. E., A. J. Whittey, K. R. Davies and B. L. Wickham, "Noninvasive Measurement of Pulmonary Gas Exchange during General Anesthesia," Anesthesia and Analgesia 59:263-269, 1980.

Nunn, J. F. and D. W. Hill, "Respiratory Dead Space and Arterial to End-Tidal CO_2 Tension differences in Anesthetized Man," J. of Appl. Physiology 15(3):383-389, 1968.

Ramanathan, S., J. Chalon, T. Salyanarayana, J. Arismendy and H. Turndorb, "Continuous and Simultaneous On-Line Measurements of $\dot{V}_{O2}$ and $\dot{V}_{CO2}$ during Endo-racheal Anesthesia," Anesthesia and Analgesia 61: 362-365, 1982.

Severinghaus, J. W. and M. Stuffel, "Respiratory Dead Space Increase Following Atropine in Man, and Atropine, Vagal or Ganglionic Blockade and Hypothermia in Dogs," J. of Appl. Physiology 8(I): 81-87, 1955.

Severinghaus, J. W., M. Stuffel and A. F. Bradley, "Alveolar Dead Space and Arterial to End-Tidal Carbon Dioxide Differences during Hypothermia in Dog and Man," J. of Appl. Physiology 10(3):349-355, 1957.

Takki, S., V. Aromaa and A. Kauste, "The validity and usefulness of the End-Tidal pCO_2 during Anaesthesia," Annals of Clinical Research 4:278-284, 1972.

Webster, J. C., ed., Medical Instrumentation - Applications and Design, Houghton Mifflin Company, Boston, 1978, pp. 7-8.

West, J. B., Respiratory Physiology - the essentials, Williams and Wilkins, Baltimore, MD, 1974, pp. 19-20.