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A COMPUTERIZED METHOD FOR ACQUISITION AND ANALYSIS OF FLOW-VOLU--ETC(U)
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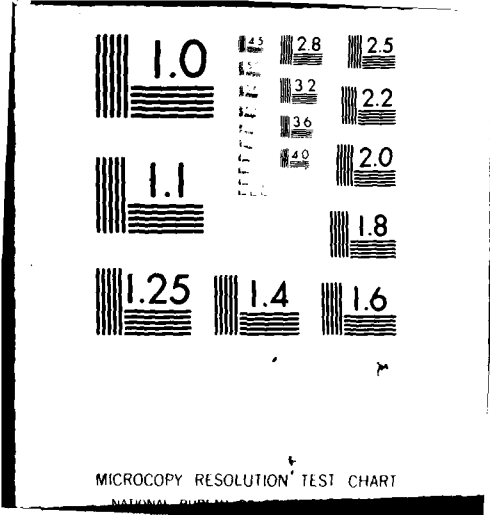
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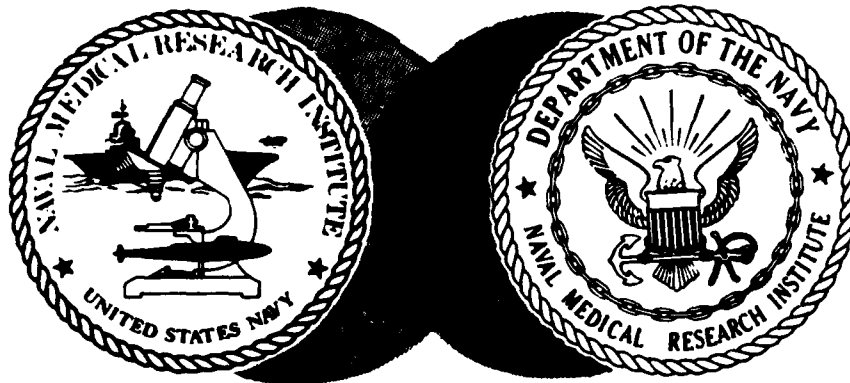
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A COMPUTERIZED METHOD FOR ACQUISITION
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I. INTRODUCTION

The Maximal Expiratory Flow-Volume Loop is a simple, non-invasive test of pulmonary function in which instantaneous maximal expired air-flow is plotted against expired volume. A typical flow-volume loop is shown in Figure 1. Volume in ml is plotted on the x-axis versus air-flow in l/s on the y-axis. Maximal inspiration from residual volume (RV) to total lung capacity (TLC) is shown in the upper portion of the curve with positive values for flow. Maximal expiration is shown in the lower portion of the curve with negative values for flow. Figure 1 illustrates the four measurements made from the flow-volume loop: the Forced Expiratory Vital Capacity (FEV), the Peak Expiratory Flow (PEF), instantaneous airflow after 50% of the vital capacity has been expired (\dot{V}_{MAX50}) and instantaneous airflow after 75% of the vital capacity has been expired (\dot{V}_{MAX75}). Theoretical considerations and experimental observations have demonstrated that, during the first 20% of expired vital capacity, flow is effort dependent, while flows at lower lung volumes (\dot{V}_{MAX50} and \dot{V}_{MAX75}) are effort independent (Mead, Turner, Macklem, and Little, 1967; Hyatt, Schilder, and Fry, 1958; Pride, Permutt, and Riley, 1967). Instantaneous flows at low lung volumes have been shown to provide information useful in assessing the function of small airways (<2mm diameter) of the lung (Gelb and Zamel, 1973; Gelb, Gold, Wright, Bruch, and Nadel, 1973).

While the test is simple for the subject to perform, data reduction may be quite time-consuming if multiple flow-volume loops are obtained. The methods of data acquisition and analysis are important determinants of the error of the measurements. Accurate recording of flow-volume loops

requires instruments with a frequency response >12 Hz, which is beyond that of the usual X-Y recorder (Ferris, 1978). One approach to this problem has been to record the primary signals on analog tape for later slow playback into an X-Y recorder. Data reduction is then performed using the hard-copy X-Y plot. This procedure has several disadvantages: it is time-consuming, acquisition of accurate calibration signals is cumbersome, analog tape recorders are often subject to considerable drift, and data reduction from the hard-copy of an X-Y recorder limits the resolution of flow and volume measurements.

We describe herein an alternate method of recording and reducing flow-volume data. Data acquisition is performed using a digital oscilloscope with a high frequency response. Accurate calibration signals can be easily recorded using the same instrument. Subsequent data reduction is performed with a PDP 11/70 computer which allows simple and precise data analysis.

The results of a statistical analysis of control data from an experimental study in which this method was used are described to illustrate its precision.

II. METHODS

Airflow is measured with a #4 Fleisch pneumotachograph. Calibration of this device against a constant flow from a Tissot spirometer revealed it to be linear over a range of 0.1 l/s to 16 l/s with a mean error of $<.015$ l/s. Pressure drop across the pneumotachograph is sensed with a Validyne ± 2 cm H_2O transducer. The analog signal from the transducer is amplified with a Validyne CD-12 amplifier and fed into the Y-channel of a Nicolet digital oscilloscope. The geometry of the pneumotachograph

required for a linear response introduces considerable dead-space into the system. Thus, in order to avoid CO₂ accumulation, a constant flow of approximately 1.25 l/s is continually applied to the pneumotachograph and the signal from this bias flow is zero suppressed. The bias flow is generated using a reciprocating piston vacuum pump. The variance in bias flow produced by this pump accounted for <1.25% of the flow signal in the range of interest. Calibration flows of zero and 1.0 l/s are fed separately into the oscilloscope and stored in memory as described below.

Volume is measured with the subject seated in an air-conditioned, pressure-compensated volume plethysmograph (Mead, 1960). The signal from the plethysmograph is the X-channel input of the Nicolet digital oscilloscope. Tests revealed that although the volume response of the plethysmograph is non-linear, volume can be accurately determined using a polynomial (of degree 9) calibration equation.

Ten healthy, non-smoking males served as subjects in the experimental study in which various pulmonary function measurements, including flow-volume loops, were made immediately before and at 1, 2, 3, 6, 7, and 23 hours following a dry hyperbaric exposure in air at 8.6 ATA for 10 min. Control measurements were made at similar times on a separate day when no dive was made. At each hour, 3-5 replications of the flow-volume loop were recorded. Instruments were calibrated prior to pre-dive measurements and immediately prior to the 1st, 5th, and 23rd hour post-dive measurements.

III. DATA ACQUISITION SYSTEM

A semi-automated system acquires and stores data from the transducers of the body plethysmograph. The hardware required for data

acquisition and storage consists of a Nicolet digital storage oscilloscope (Model 2090) and a Hewlett-Packard desktop computer (Model 9825A) with associated peripheral equipment. For the flow-volume loop calculations a PDP 11/70 digital computer and a Tektronix graphics display terminal (Model 4014) are used.

The analog signals from the volume and flow transducers of the plethysmograph are fed into the Nicolet oscilloscope, which digitizes them using an internal analog-to-digital (A/D) convertor. The resulting data are stored in the instrument and simultaneously displayed on its screen. With an output range of 0 to 4096 units, the A/D convertor has a voltage resolution of <5 mv at ± 10 V full-scale and <2 mv on the ± 4 V scale. Since the memory holds a total of 4096 data points, the oscilloscope can take a reading once each 10 ms for a maneuver requiring ~40 s to perform. This sample rate gives sufficiently accurate reproduction of the original signal trace.

Before data from another maneuver can be acquired by the digital oscilloscope, its memory must be cleared and the current contents transferred to a permanent storage medium. This and other control functions are performed by the desktop computer. The software uses the 32-character alphanumeric display of the HP 9825A to prompt the operator to enter, via the built-in keyboard, a header file containing information about the subject (ID number, sex, age, race, height, weight), experimental details (barometric pressure, room temperature, control or experiment designator, pre- or post-treatment designator, etc.) and additional comments as needed for later identification, inspection and statistical analysis of the data. When data transfer is initiated by operator command, the internal real-time clock of the HP 9825A is read. The time (month:day:hour:minute:second format) is added to the information already included in the header and this expanded version is

recorded on a digital tape cassette. The flow-volume data from the Nicolet is then transmitted via an IEEE-488 interface bus to the computer and recorded on the cassette. The time required to go from initiation of transfer to a state of readiness for the next acquisition is ~10 seconds. Thirty-two (32) memory transfers can be stored on each cassette. The software automatically records each data set on the next available tape file and prompts the operator when a new cassette is needed.

The HP 9825A is a convenient real-time controller for the data acquisition process due to its small physical size and the ease with which it can be made to interact with even relatively unskilled operators. It does lack, however, the large memory capacity, high computational speed, and sophisticated graphics terminal needed to perform the complex data manipulations of flow-volume loop calculations. Thus, when several cassettes have been recorded, the data are transferred to disks on the PDP 11/70 via the IEEE-488 bus. The HP 9825A, which controls this procedure, automatically transfers all the data files on a cassette, prompts the operator to insert the next tape in the series, and sends an "end-of-file" statement to the PDP 11/70 when all the data from a given experiment have been transferred.

Thus the advantages of digital data acquisition and transfer are achieved through use of the HP 9825A. Its portability and facility in directly communicating with the PDP 11/70 permit access to the substantial computational power of this larger computer without requiring the latter to be near the experiment site or connected "on-line" to the experimental apparatus. Though this acquisition system has been described in connection with flow-volume loop measurements, it can be used to obtain data from other lung function maneuvers, including FRC, closing volume, and pressure-volume curves.

IV. DATA ANALYSIS

The data analysis program is written in FORTRAN for a PDP 11/70 using the RSX-11 operating system and requires a Tektronics 4014 graphics display terminal. The contribution to the data analysis of this storage tube display terminal is its cursor capability. This feature allows the operator to visually select specific data points as they are displayed on the screen. The program uses data transferred from the Hewlett-Packard desktop computer to calculate flow-volume parameters.

When the program starts, it requests an input file name (the file containing the raw data to be analyzed) and an output file name (the new file in which the calculated flow-volume results will be stored). If a previous analysis session was interrupted, the program will not prompt for these names; they are stored in a "trail file" containing information necessary for the program to re-start itself at the point at which it was stopped.

The next query is whether or not a regression equation is to be used to determine volume. If the volume transducer is non-linear (as it was for the experiments reported in this paper), then the relationship between actual volume measured and transducer output must be found. This previously determined calibration equation is incorporated into the program and a "Yes" (Y) answer causes it to be applied to all calculations of volume. "No" (N) indicates a linear relation exists between transducer input and output and a scale factor included in the analysis software is used.

The input file is structured in groups called records, with each record consisting of two parts, the header and the actual experimental data. Part of the information in the header is used to determine the flow scale factor, and most of the header is incorporated into the output file.

The input file may contain many records, some with data from lung function measurements other than flow-volume loops. The header provides the information necessary for the program to select the appropriate records, which consist of flow calibration and flow-volume data records.

In order to determine the correct scale factor for flow, the program proceeds as follows. Input file headers are searched until the first flow (low) calibration file is found. The program defaults to a flow value (F_L) of zero, but the operator is given the opportunity to change this to any other value (liters/second) that may have been used. The flow signal (f_L in unscaled Nicolet units) is plotted versus time (Nicolet units) on the graphics terminal (Fig. 2). The operator can eliminate obvious artifacts by selecting a minimum and a maximum time, t_1 and t_2 , respectively. The portion of the calibration data between t_1 and t_2 is averaged to reduce random noise effects and a single unscaled transducer output value is obtained. To set t_1 , the cursor on the terminal display is moved to the appropriate position and "L" is typed. Similarly, t_2 is indicated by the location of the cursor when "H" is entered on the keyboard. Typing "Q" causes the program to average the data. If "Q" is entered with neither t_1 nor t_2 being set, the software uses all the points shown on the screen. It then finds and displays the corresponding flow (high) calibration file (Fig. 3), which is analyzed similarly to the low calibration data and has a default value of 1 liter/sec.

Once both calibration outputs have been determined, the flow scale factor is given by:

$$S_F = (F_H - F_L)/(f_H - f_L) \quad (1)$$

S_F = flow scale factor (liters/sec-Nicolet unit)
 f_H = transducer output at high calibration flow (Nicolet units)
 F_H = calibration (high) flow (liters/sec)
 f_L = transducer output at low calibration flow (Nicolet units)
 F_L = calibration (low) flow (liters/sec)

Again using the information in the headers, the program identifies the flow-volume data file associated with the calibration files just processed and plots on the terminal a properly scaled flow-volume trace (Fig. 4). Flow (liters/sec) is shown on the y-axis as a function of volume (ml) on the x-axis. The operator is then asked whether or not this curve is to be accepted for more analysis. If not, the next calibration file is found and the process thus far described is repeated. If the curve is accepted, the values of FVC, \dot{V}_{MAX75} , \dot{V}_{MAX50} , and PF are computed. (It has been shown that a portion of the variability of maximal expiratory flow measurements is due to an oscillation of flow of uncertain origin (Clement and Van De Woestijne, 1971). In order to decrease this variability flow values at 75% and 50% of FVC are obtained by unweighted averaging of seven adjacent data points centered on the specified volume). These values are displayed on the graphics terminal and their corresponding positions indicated on the plot by dashed lines (Fig. 1). The operator again can either accept or reject the curve and its calculated parameters. Accepted values are stored in a temporary file.

The program next queries whether there are more flow-volume loops in the same group. As long as the answer is "yes", the program proceeds to the

next calibration file-data file combination and calculates FVC, \dot{V}_{MAX75} , \dot{V}_{MAX50} , and PF. When all the data for a given group are analyzed, the vital capacity of each curve in the temporary file is compared with the maximum FVC stored there. For the curves having a vital capacity $\geq 95\%$ of the maximum, each of the four calculated parameters is stored in the permanent output file. Data for loops with a smaller value of FVC are rejected.

The operator is asked to enter an identification number for the group of curves whose analysis has just been completed. The program next asks whether or not to stop. "Yes" causes the appropriate information to be stored in the trail file so that the data analysis later can be resumed at the same point in the input file at which it is being stopped. If the user indicates that he does not wish to stop, the program proceeds to the next group of curves and starts again with the calibration routine. If no calibration data are available, the software defaults to the most recent values, which are contained in the trail file. The program overrides the operator and stops itself if no unanalyzed flow-volume curves exist in the input data file.

When all the flow-volume data in a given file are processed, the user is left with an output file containing the values of vital capacity, flow at 75% and 50% of vital capacity, and peak flow for all loops that were not rejected during the analysis. The calculated parameters for each group of curves are identified by a header containing information required for later statistical analyses.

V. STATISTICAL ANALYSIS

A. MEAN ERROR OF REPLICATION

Peak flow is largely effort dependent, and therefore much of the

variability of the measurement is due to variations in the effort put forth by the subject. For this reason, the peak flow measurement has limited usefulness in the evaluation of respiratory mechanics. In particular, the peak flow measurement yields no information concerning the function of small airways of the lung. We have not, therefore, attempted to estimate the precision with which our methods measure peak flow.

Control data from all 10 subjects were analyzed to determine if FVC, \dot{V}_{MAX50} , or \dot{V}_{MAX75} varied significantly with time. Data were analyzed with a linear model which estimates distinct intercepts and slopes for each subject. Parameters were estimated by a least squares-method using a FORTRAN version of the iterative parameter estimation program of (Bailey and Homer, 1971).

The results of the analysis are presented in Table 1. The F values in the table are a measure of the degree to which error is minimized by having the algorithm estimate a slope for each subject, as compared to the null hypothesis of zero slopes. As shown in Table 1, for FVC, \dot{V}_{MAX50} , and \dot{V}_{MAX75} total error is significantly reduced by a model which assumes that these measurements vary linearly with time.

For the determination of mean error of replication, we have examined the residual error after time effect has been eliminated by the linear model. The mean error of replication is given by:

$$\begin{array}{l} \text{MEAN ERROR OF} \\ \text{REPLICATION} \end{array} = \sqrt{\frac{\text{RESIDUAL ERROR}}{\text{DEGREES OF FREEDOM}}} \quad (2)$$

TABLE 1

FLOW-VOLUME MEASUREMENTS AS A LINEAR FUNCTION OF TIME

MEASUREMENT	F	df Numerator	df Denominator	P
FVC	2.154	10	175	.015
\dot{V}_{MAX50}	2.925	10	175	<.001
\dot{V}_{MAX75}	1.959	10	175	.026

The percent error of replication is then obtained by dividing the mean error of replication by the grand mean of the measurement for all 10 subjects. The results of this analysis are shown in Table 2. The mean percentage errors of replication for FVC, \dot{V}_{MAX50} , and \dot{V}_{MAX75} are 2.09%, 6.75%, and 9.69%, respectively.

B. β -ERRORS AND POWER

The precision of the measurements derived from the flow-volume loop may be better appreciated by examining the power of the measurements in an experimental design which employs self-pairing. Table 3 lists coefficients of variation (CV, standard deviation divided by mean value) for each of the three measurements in each subject, along with the mean coefficients of variation for all 10 subjects. For all three measurements, coefficients of variation exhibit little intersubject variation. Therefore, mean values of CV were used in the calculation of β -errors and power of the flow-volume measurements.

For an experimental design employing self-pairing of n subjects, the relevant variance is intrasubject variance. Taking the mean coefficient of variation as an estimate of this variance, and taking the mean of the variable under consideration as 1, the equation

$$\bar{X} = z_{\alpha} (\overline{CV}/\sqrt{n}) + 1 \quad (3)$$

specifies the relative value of the variable required for significance at the α -level, where z_{α} is the standard normal deviate corresponding to the α -error.

TABLE 2
MEAN ERRORS OF REPLICATION

MEASUREMENT	RESIDUAL ERROR	df	MEAN ERROR OF REPLICATION	GRAND MEAN	% ERROR OF REPLICATION
FVC	2665670	175	123.4 ml	5820.3 ml	2.09
V _{MAX} 50	22.769	175	.361 l/s	5.523 l/s	6.75
V _{MAX} 75	7.047	175	.201 l/s	2.138 l/s	9.69

TABLE 3

COEFFICIENTS OF VARIATION FOR FLOW-VOLUME MEASUREMENTS

SUBJECT	FVC	\dot{V}_{MAX50}	\dot{V}_{MAX75}
WN	.0164	.0452	.0862
RE	.0167	.0888	.0841
GG	.0131	.0759	.0910
MW	.0372	.0472	.0806
DS	.0111	.0891	.0998
TG	.0286	.0537	.0860
PC	.0212	.0792	.1306
JS	.0130	.0833	.1327
WB	.0190	.0760	.0772
\bar{CV}	.0209	.0652	.0855

The standard normal deviate corresponding to the β -error (Z_β) is given by:

$$Z_\beta = \frac{(\mu_1 - \bar{X})}{\overline{CV}/\sqrt{n}} \quad (4)$$

where μ_1 is the population mean under the alternative hypothesis. The power of the test is then given by $1 - (\beta\text{-error})$.

The results of the calculations for the 3 measurements derived from the flow-volume loop are shown in Table 4 for two different alternative hypotheses. In the first portion of the table, the power of each measurement is shown for α -levels of .05 and .01. Under the assumption that the true population mean (μ_1) is 20% lower than the mean (μ_0) specified under the null hypothesis, a power of $>.999$ is attained for all three measurements. This indicates that there is a 99.9% chance of detecting a 20% reduction of mean FVC, $\dot{V}\text{MAX}50$, or $\dot{V}\text{MAX}75$ for a given subject.

The second portion of the table lists the power of each measurement under the alternative hypothesis that the true population mean is 10% lower than that specified by the null hypothesis. The table reveals that at an α -level of .01, the power of the FVC and $\dot{V}\text{MAX}75$ measurements are >0.999 and 0.989 respectively. The power of the $\dot{V}\text{MAX}75$ measurement under these conditions is .873. These results show that the $\dot{V}\text{MAX}75$ measurement is the least precise of the three measurements, which agrees with the determination of mean error of replication described above.

The effect of decreasing the specified α -level is to increase the confidence that any observed difference between treatment and control groups is not due to random sampling error. To use other terminology,

TABLE 4
 β -ERRORS AND POWER OF FLOW-VOLUME LOOP MEASUREMENTS*

$H_A: \mu_1 = .8\mu_0$ **						
$\alpha = .05$			$\alpha = .01$			
	.05 LEVEL	β -ERROR	POWER	.01 LEVEL	β -ERROR	POWER
FVC	.9870	<.001	>.999	.9831	<.001	>.999
VMAX50	.9596	<.001	>.999	.9472	<.001	>.999
VMAX75	.9470	<.001	>.999	.9308	<.001	>.999

$H_A: \mu_1 = .9\mu_0$						
$\alpha = .05$			$\alpha = .01$			
	.05 LEVEL	β -ERROR	POWER	.01 LEVEL	β -ERROR	POWER
FVC	.9870	<.001	>.999	.9831	<.001	>.999
VMAX50	.9596	.002	.998	.9472	.011	.989
VMAX75	.9470	.041	.959	.9308	.127	.873

* ALL CALCULATIONS ASSUME AN N OF 10

** H_A : = ALTERNATIVE HYPOTHESIS
 μ_1 = POPULATION MEAN SPECIFIED BY ALTERNATIVE HYPOTHESIS
 μ_0 = POPULATION MEAN SPECIFIED BY NULL HYPOTHESIS

decreasing tolerance for false positive results increases the specificity of the measurement. The increased specificity however leads to a decreased sensitivity (larger β -error) in the measurement. That is to say, as the specificity is increased, there is a progressively greater risk of failing to detect a true difference in population means. For the VMAX75 measurement, if one wishes to be confident that any observed differences between treatment and control groups could occur only once in a hundred times due to random sampling error, then one has an 87.3% chance of detecting a 10% difference in means between treatment and control measurements.

The results in Table 4 were calculated assuming a sample size of 10. As can be seen from Equation 4, a larger sample size will result in a smaller β -error and a corresponding increase in the power of the measurement.

VI. DISCUSSION

The method described in this report is an integrated, computer-assisted system for the acquisition and analysis of data from flow-volume loops. As such, it has a number of advantages over more conventional techniques for performing this pulmonary function test.

Direct digital acquisition of data eliminates the noise and drift problems inherent in analog tape recorders. It further improves the accuracy and resolution of signals by removing the need to re-record the data on an X-Y plotter and by making unnecessary the usual manual measurements on the resulting hard copy. The method also precludes the often encountered difficulty of making both calibration and data signals fit on the same plotter scale.

Semi-automation of the data system greatly reduces the amount of manual "bookkeeping" required. It has the added advantages of allowing the operator to concentrate more fully on the proper performance of the test and of preventing errors due to human carelessness in the data log and the headers.

Computer assistance simplifies analysis and decreases the time required for the data reduction process. It allows calibration data to be easily examined and thus aids detection of errors that occur during calibration. In addition, this method allows straightforward application of non-linear transducers.

The most important benefit of this system is the considerable precision with which measurements can be made. As indicated by the statistical analysis of the sample data, the probability of detecting a 10% change in the mean of FVC, \dot{V}_{MAX50} , or \dot{V}_{MAX75} is quite high (99.9%, 98.9%, and 87.3%, respectively, for the data presented here). Thus the method described in this report has a high probability of finding clinically important changes in the parameters derived from flow-volume loops.

GLOSSARY OF SYMBOLS AND TERMS

TLC	Volume remaining in the lungs at the end of a maximal inspiration.
RV	Volume remaining in the lungs at the end of a maximal expiration.
FVC	Forced expiratory vital capacity, i.e. the maximal volume of gas which can be forcibly exhaled from TLC.
PF	Peak expiratory flow.
\dot{V}_{MAX50}	Instantaneous flow after 50% of the vital capacity has been

expired.

VMAX75

Instantaneous flow after 75% of the vital capacity has been expired.

α -ERROR

The probability that an observed difference in means is due to random sampling error.

β -ERROR

The probability of failing to detect a true difference of population means.

Z_{β}

Standard normal deviate corresponding to the β -error.

H_0

Null hypothesis.

H_A

Alternative hypothesis.

μ_0

Population mean specified by the null hypothesis.

μ_1

Population mean specified by the alternative hypothesis.

CV

Mean coefficient of variation, i.e. the mean value of the quotient: (1 standard deviation of X)/(mean value of X).

df

Degrees of freedom.

F

Variance ratio.

Nicolet Unit

For unscaled flow and volume values, the integer output by the A/D convertor:

(input voltage)(4096)/(A/D full-scale voltage).

For unscaled time units, the sequential number of the data point.

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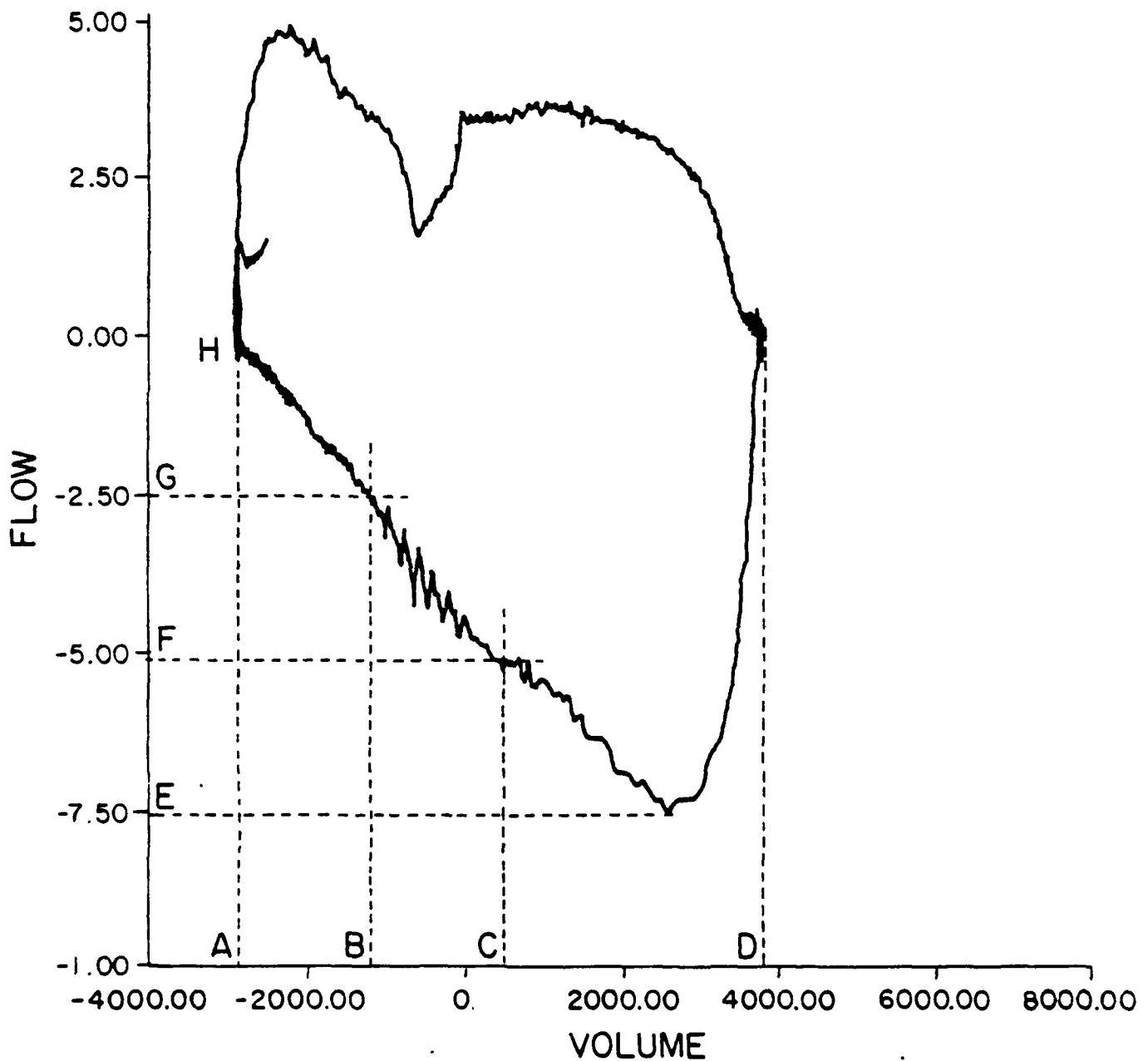


Fig. 1. A typical flow-volume loop. Flow (l/s) is plotted on the vertical axis vs. volume (ml) on the x-axis. Flow begins at residual volume (H) and proceeds in a clockwise direction. All volume measurements reflect relative distances along the x-axis. The zero point on the volume axis is a set-point in the plethysmograph for for measuring FRC (functional residual capacity), and has no meaning for the flow-volume loop measurements.

A = residual volume (RV)
 B = volume at which 75% of FVC is expired
 C = volume at which 50% of FVC is expired
 D = total lung capacity (TLC)

E = peak expiratory flow (PEF)
 F = \dot{V}_{MAX50}
 G = \dot{V}_{MAX75}
 (D-A) = FVC

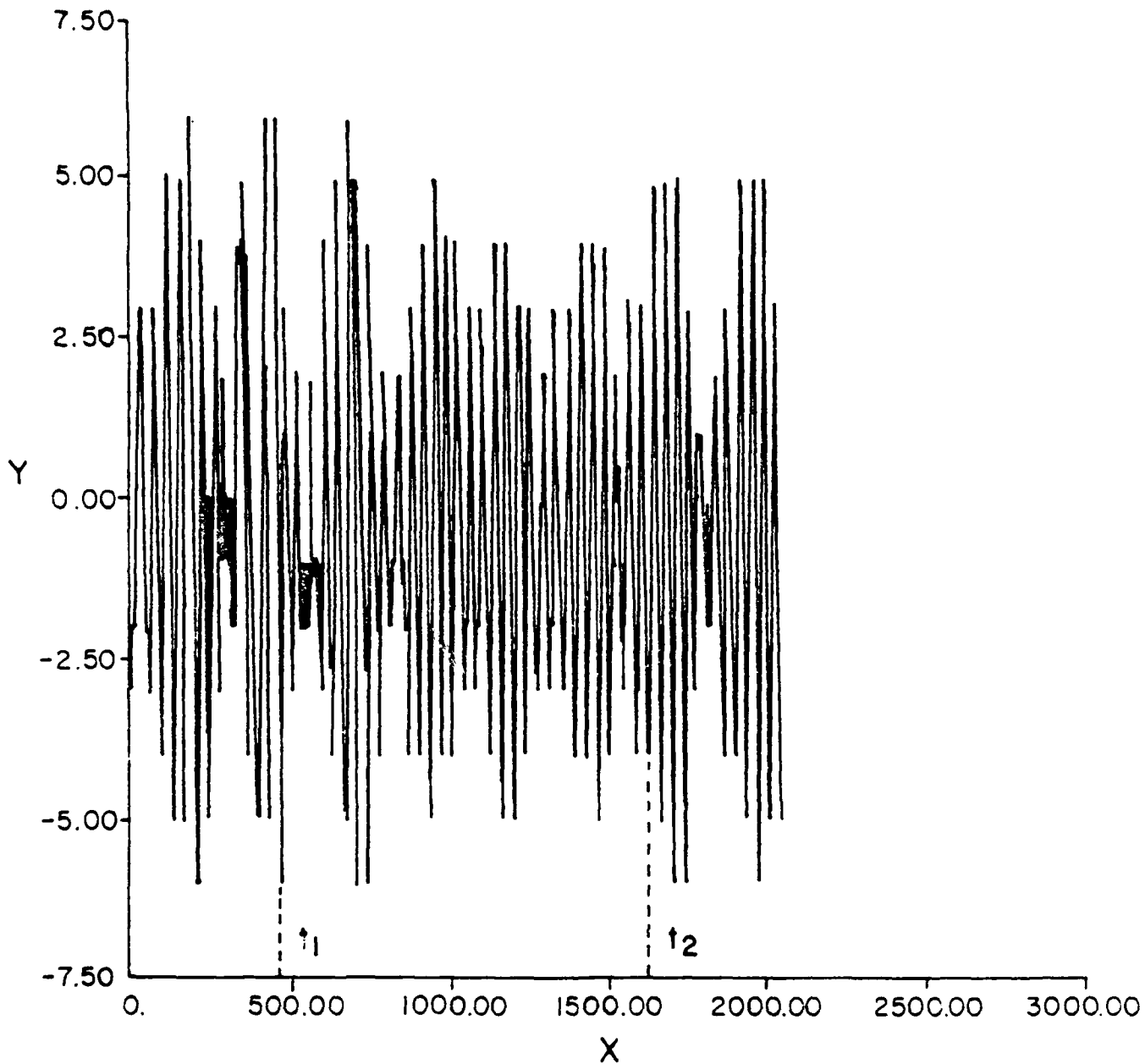


Fig. 2. A typical flow (low) calibration file as displayed on the graphics terminal. The positions of t_1 and t_2 are shown for illustration only since there are no obvious artifacts in the data. Flow (Nicolet units) on the vertical axis is plotted against time (Nicolet units). The magnitude of the noise is exaggerated by the expanded vertical scale; for reference, a flow of 1 l/s is represented by 200 Nicolet units. A time unit is equivalent to 10 ms.

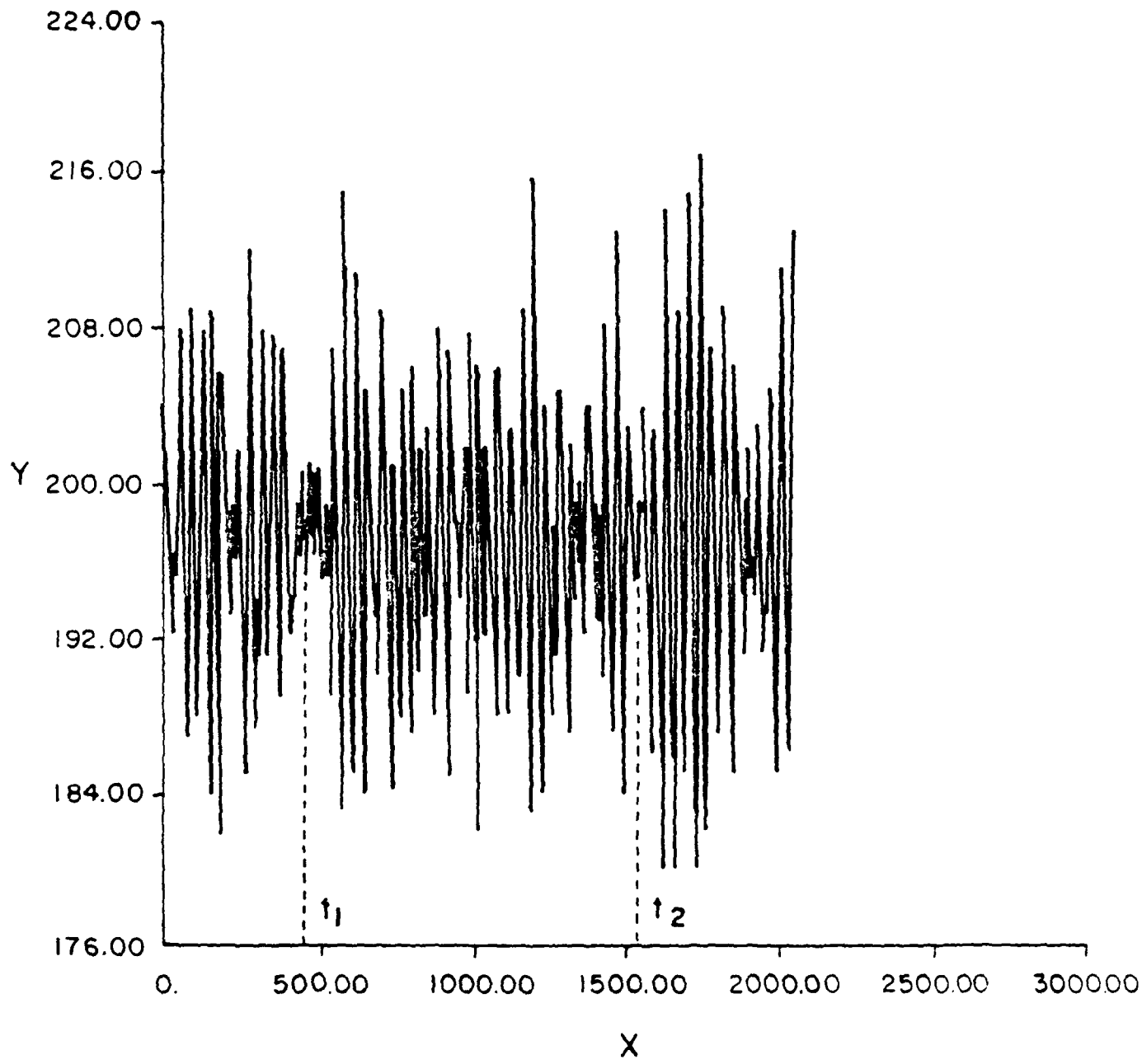


Fig. 3. A typical flow (high) calibration file with t_1 and t_2 shown for illustration only. Flow (Nicolet units) is plotted on the vertical axis and time (Nicolet units) for a flow of 1 l/s; each time unit represents 10 ms. Note that the signal noise is exaggerated by the zero-suppression and expanded scale of the vertical axis.

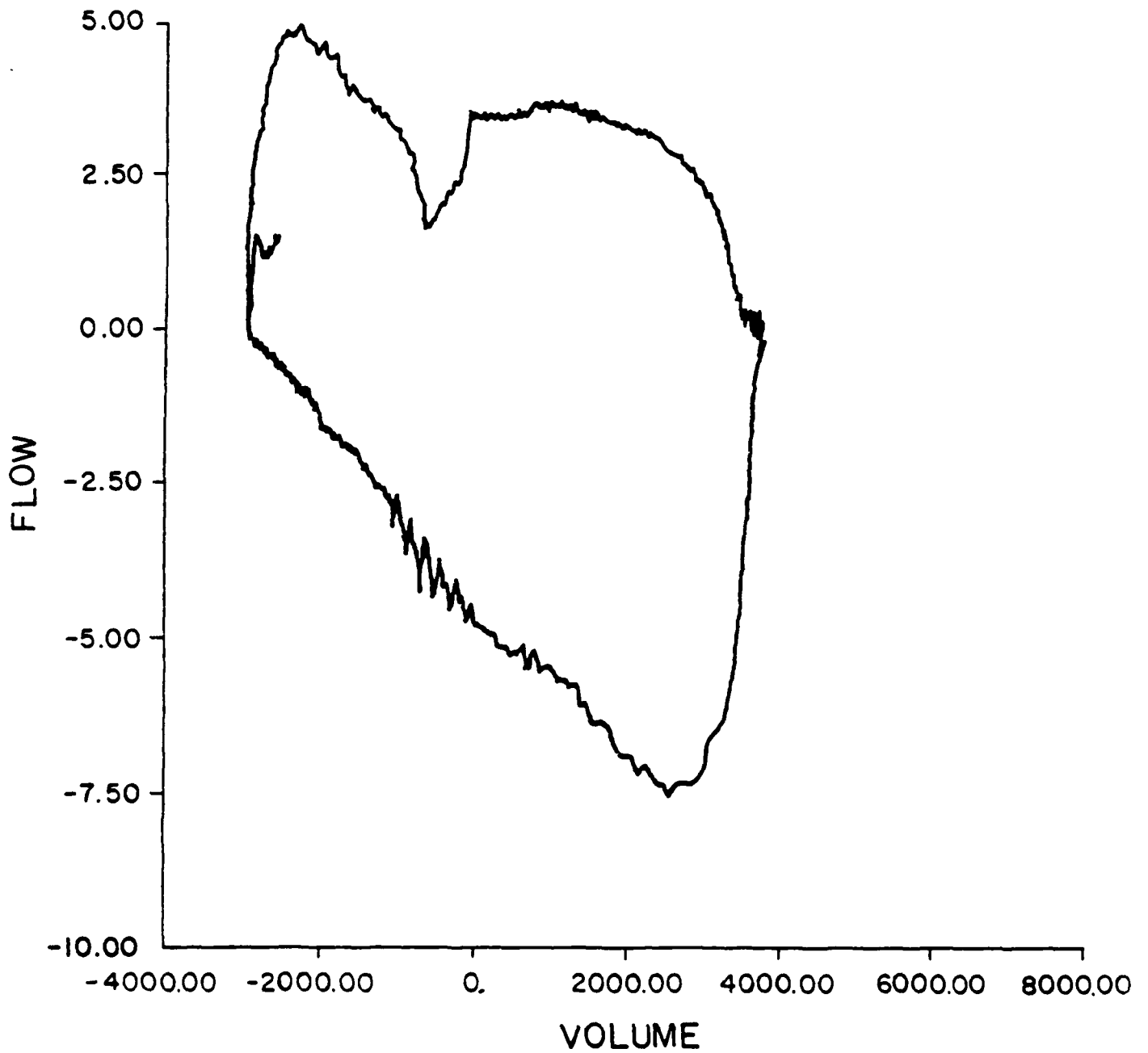


Fig. 4. A typical flow-volume loop as displayed on the graphics terminal. Flow (l/s) is plotted on the vertical axis vs. volume (ml).

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