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PROGRAM LIBRARY

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TITLE	PULMONARY RESISTANCE
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SUMMARY

A system of programs is described which, adapted from DEC's Advanced Signal Averager, allows accurate measurement of mean pulmonary arterial flow and pressure, left atrial pressure and intrapleural pressure. From these data, obtained by use of appropriate electromagnetic flow and suitable pressure transducers, the system calculates total and arteriolar resistances and right ventricular work. This information, together with the digitized average wave forms, is written on dectape.

In addition, a program is included with the system, which measures cardiac output on-line from an indicator dilution curve by the Stewart-Hamilton[1] method.

The system is capable of interfacing with the Advanced Averager, so that the options available in the signal averager system are retained.

Hardware required is as follows: PDP8/I with EAE and 8K core; disc or dectape; a second dectape (for dectape systems); and LAB-8 peripherals.

The programs of the system are written in PAL8 assembly language and use PS/8 or OS/8 as their basic operating system.

PULMONARY RESISTANCE

INTRODUCTION

In order to assess the status of the pulmonary vascular bed, we wished to average four analog signals, representing pulmonary arterial flow and pulmonary arterial, left atrial and pleural pressures, using the R-wave of the electrocardiogram as the synch pulse to initiate the average wave form. Pulmonary arterial flow was to be measured by an electromagnetic flowmeter around the pulmonary artery, and the pressures by suitably placed catheters and pressure transducers. Furthermore, we wished to manipulate the digitized data to obtain the vascular resistances,

$$R_1 = \int_o^T \Delta p(t)dt \Big/ \int_o^T q(t)dt$$

and

$$R_2 = \int_o^T \left[\Delta p(t)/q(t)\right]dt \qquad ,$$

and right ventricular work, $\omega = \int_o^T p(t)\cdot q(t)dt$, where $p(t)$ = pressure; $q(t)$ = flow; $\Delta p(t)$ = pressure gradient; and T = length of average cardiac cycle. It is necessary, of course, that the flow and pressure measuring systems have frequency-response characteristics such that the manipulations above are valid.

Unfortunately, the young animals we were studying were subject to sinus arrhythmia and, although DEC's Advanced Signal Averager was capable of sampling and averaging these data, it lost data in the face of irregularly-appearing synch pulses or of widely varying pulse rates. Consequently, a system was developed which avoided these pitfalls and yet interfaced with the Advanced Averager to allow calculation of confidence limits and trend functions on the averaged wave forms.

Since, in spite of its drawbacks[2,3], the indicator dilution method is often used in calculating cardiac output, we also interfaced the programs above with a program to calculate cardiac output from a dye-dilution curve on-line.

The resulting system is useful in measuring these steady-state moieties and in digitizing average wave forms for more complex analysis. This system is described in this paper.

The programs comprising the system may be classified as follows: (1) The controlling program with its collection of subroutines; (2) the sampling, averaging and dectape-writing programs; (3) a program to process on-line a dye-dilution curve; (4) a compiler to preset certain timing and averaging parameters; and (5) the various patches to handle the interfacing between the Pulmonary Vascular Resistance system and the Advanced Averager. These programs are described in detail below. OS/8 or PS/8 is used to interface the programs, and a knowledge of DEC's PS/8 system is presumed in the descriptions which follow.[4,5]

The system requires a PDP8/I or E computer with 8K core, AXØ8 Laboratory Peripheral, Extended Arithmetic Element, a disc or dectape transport as the system device for PS/8 or OS/8 and a dectape transport as a separate storage device.

BUILDING THE SYSTEM

Source tapes (ASCII format) are provided for the various programs of the system and are assembled by PAL8 and loaded according to the following schemes:

1. Controlling Program:
   a. DEFS: definitions for the system
   b. PZERO: the initial page Ø (field Ø) of the system
   c. SUBR: the subroutines called by the various programs of the system, obtained by combining the following source tapes: SUB1, SUB2, SUB3, SUB4, SUB5.
   d. CONT1, CONT2: the controlling program.

Assemble (PAL8) as follows:

```
*CONT, <DEFS, PZERO, SUBR, CONT1, CONT2
```

Load with ABSLDR

```
• SAVE SYS RESIST Ø-7577; 4ØØ=3ØØ1
```

Load again with ABSLDR

```
• SAVE SYS CONT 4ØØ-7577; 6ØØ=3ØØ1
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2. The sampling, averaging and data-writing programs:
   a. Sampler: SAMP:

Assemble: SAMP, <DEFS, PZERO, SUBR, SAMP

Load with ABSLDR

```
• SAVE SYS SAMP 6ØØØ-7577; 6ØØØ=1ØØØ
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b. Averaging-data-writing program: MEAN:

Assemble: MEAN, <DEFS, PZERO, SUBR, MEAN

Load with ABSLDR

• SAVE SYS MEAN 6ØØØ-7577, 174ØØ-17577; 66ØØ=1ØØØ

c. A program to read the dectape data files: READER:

Assemble: READER, <DEFS, PZERO, SUBR, READER

Load with ABSLDR

• SAVE SYS READER Ø-7577; 6ØØ=1ØØØ

3. The Dye-dilution program: GRND:

Assemble: GRND, <DEFS, PZERO, SUBR, GRND1, GRND2

Load with ABSLDR

• SAVE SYS GRND 4ØØ-7577; 4ØØ=1ØØØ

4. The compiler: CMPILR:

Assemble: CMPILR, <DEFS, PZERO, SUBR, CMPILR

Load with ABSLDR

• SAVE SYS CMPILR Ø-7577; 4ØØ=2ØØ1

5. The patches to interface between Resistance and Advanced Averager (and allow a stand-alone PS/8 adapted Advanced Averager):

a. Patch for Signal Averager, Sect 1 (Compiler): S1PTCH

Assemble: S1PTCH, <S1PTCH

Load after Signal Averager, Sect 1 (DEC-LB-U17C-PB)

• SAVE SYS SAV1 Ø-7577; 577=Ø

b. Patch for Signal Averager, Sect 2 (Timing section): S2PTCH

Assemble: S2PTCH, <S2PTCH

Load after Signal Averager, Sect 2 (DEC-LB-U17C-PB)

• SAVE SYS SAV2 7ØØØ-7577; 6777=1ØØØ

This section is used when a stand-alone Advanced Averager is needed and does not interface with the Resistance system.

c. Patch for Signal Averager, Sect 3 (Sampler): S3PTCH

Assemble and load after Sect 3 binary tape.

• SAVE SYS SAV3 64ØØ-7577; 6527=1ØØØ

d. Patch for Signal Averager, Sect 4 (Averager): S4PTCH

Assemble and load after Sect 4 binary tape.

• SAVE SYS SAV4 64ØØ-7577; 6777=1ØØØ

e. Patch for Signal Averager, Sect 5 (Calculator): S5PTCH

Assemble and load after Sect 5 binary tape.

• SAVE SYS SAV5 64ØØ-7577; 6377=1ØØØ

f. Patch for compiled output tape of Signal Averager, Sect 1: SØPTCH.

Run SAV1 and prepare a compiled paper tape according to the specifications desired. If, after the paper tape is punched, the message, "INSUFFICIENT MEMORY," appears on the screen of the AXØ8, destroy the paper tape. It would be fatal to the system. The message, "SYNCH ON CHANNEL '__'", indicates that the paper tape is safe. Load it into core and follow with the binary tape, SØPTCH, prepared from the source tape provided. Then save the file on DTA1 (dectape transport #1) giving it a file name according to the scheme outlined below (see "Preparation of Dectape Library"):

• SAVE DTA1 SMØN Ø-7577, 1ØØØØ-17577; 151=1ØØØ

where M and N are integers coded according to the rules outlined in "Preparation of Dectape Library".

g. Finally, a core control block dummy program for the bootstrap which returns from signal averager to the Resistance System: CNTBLK:

Assemble: CNTBLK, <CNTBLK

Load with ABSLDR

• SAVE SYS CNTBLK Ø-377; 35Ø=2ØØ1

PREPARATION OF DECTAPE LIBRARY

The system may be initiated by the command, R CMPILR, whereupon certain questions concerning synch channel assignment and timing information are to be answered. In order to avoid the necessity of this dialogue during every experiment, CMPILR can be used to prepare a library of compiled files on dectape, each one of which contains given timing parameters. These files are labelled by the user as R1ØØ, R2ØØ, etc. The system may then be initiated by the command, R RESIST, with the library dectape in transport #1 and the particular timing file which is desired may be selected.

Once operating, the Resistance System interfaces with the Signal Averager through the CNTRL/U (↑U) key of the teletype. Striking this key while the controlling section of the Resistance System is running causes Section 3 of Advanced Averager to be brought into core and run. The operator may then call in Advanced Averager, Sections 4 and 5 for processing of the data obtained by Section 3 and may return to the Resistance System from Section 3 by use of the ↑U key. This allows the accurate averaging of the Resistance System to be combined with the great versatility of the Advanced Averager (confidence limits, trend function, synch delay, high resolution epochs, etc.).

In order to accomplish this, it is necessary to coordinate the timing and synch channel parameters of the two systems. For each R1ØØ, R2ØØ, etc. file, the user must prepare at least one compiled signal averager compiled tape which contains the same answers for synch channel assignment and length of the sampling interval. These signal averager compiled files are then added to the library dectape and from this tape a single resistance and corresponding signal averager file is chosen at run-time by the controlling program of the Resistance System.

a. Preparation of timing files for Resistance System:

The user puts the library dectape in DTA1, with the transport on "Write Enabled." Giving the command, .R CMPILR, starts the compilation. After the identifying message is shown, the user strikes carriage return (CR) to proceed. The program asks "EKG on S '__'". The user answers with the number "1" or "2", and S1 or S2 is assigned to the electrocardiogram. During the dialogue between the program and the user, the user's answers are echoed on the CRT of the AXØ8, but not on the teletype. The "Rub-out" key of the teletype may be used to erase an answer. When blanks are to be filled in by the user, the line-feed key (LF) will erase all answers and restore blanks. CNTRL/C (↑C) will return to the PS/8 monitor, and carriage return (CR) is used to record the answer and move on to the next question.

Following the user's answer to the first question, the opposite synch channel ("2" or "1") is automatically assigned to the synch to be used during a green-dye curve. CMPILR then asks "AVERAGE '____' SWEEPS". The user's answer to this question determines the number of cardiac cycles used in computing the averages.

CMPILR then asks the two questions which determine the sampling interval used in its digitizing of the wave-forms. The first is: "'____' DATA PTS/SWEEP". The answer should be below 512. Answers over 512 are ignored and cause the message, "INSUFFIC MEMORY" to appear. If this occurs, the user must strike CR to repeat the dialogue from the question, "AVERAGE '____' SWEEPS". If the answer is below 512, the next question is: "MIN HT RATE: '____'/MIN". The answer to this question determines the minimal heart rate, below which data at the end of diastole are lost by the sampling program. (Unlike Advanced Averager, the Resistance System has a variable length buffer, the maximum length of which is determined by the answers to this and the preceding questions). CMPILR then uses the answers to these two questions to compute the sampling interval to be used subsequently. If this interval is so short that processing of the interrupts is not possible before the next sample (below 670 microseconds) or so high that the RC clock of the AXØ8 cannot be set (over 2.0 sec) CMPILR repeats the questions, and the operator must choose more suitable answers.

If the sampling interval is acceptable CMPILR then displays the length of the averaging epoch in the message "SAMP LENGTH=xxxx SEC". The user should record this information in order to prepare signal averager tapes with identical timing information (see below). At this point, the user may strike CR to continue or, if he wishes to return to the previous questions, he may strike LF. (Generally when there is a question on display without blank spaces to be filled, LF indicates "No" or rejection of the statement; and CR indicates "Yes" or acceptance of the statement).

CMPILR then asks: "COMPILE?" If the user wishes, he may answer with LF ("No") and the Resistance System is initiated with his previous answers in core. In this instance, the ↑U pseudointerrupt is disabled and no interfacing with Advanced Averager is possible (↑U acts as the "Rub-out" key). If CR is answered to the question ("Yes"), CMPILR asks "R# '_' ØØ", and the operator assigns a decimal number, 1-9, to the file, whereupon (after CR is struck) the pertinent information is written in a file on DTA1. The operator should write down his answers to CMPILR's dialogue, so that suitable signal averager compiled tapes may be made.

After creating the particular file, CMPILR asks "DO ANOTHER?" CR means "Yes" and returns to the first CMPILR question; LF signifies "No" and the PS/8 Monitor is brought into core, the teletype responding with ".".

b. Preparation of timing and parameter files for the Advanced Averager System:

The conversation between the user and Advanced Averager, Section 1, is well described in DEC-LB-T30B-D. For each file compiled by CMPILR, there must be at least one file created by Advanced Averager, Section 1, which contains identical synch channel assignment and an identical ratio of epoch length/number of data points per epoch. Thus, if the user creates a resistance file, called R1ØØ, he must create at least one signal averager file of the " ØØ" series which has the same answer to "SYNCH ON CHAN: '_'" as did the resistance file and in which the answers to the questions "DATA PTS: '____'" and "LENGTH: '____' '_' SEC" give the same ratio as did the answers to "'____' DATA PTS/SWEEP" and "SAMP LENGTH= XXXX SEC" in the conversation with CMPILR. The file will later be named "S1Ø_" where the blank can be any digit Ø-9. The remaining answers to Sect 1, Signal Averager may vary according to the user's preference and the available core. (Note: The patch to Section 1, Signal Averager, is arranged to permit use of PS/8 with 8K core only--users with more than 8K of core, must modify this patch to protect the top page in each field of core, since presently only the top pages of fields Ø and 1 are protected). Thus, for each timing schedule in the Resistance System, there are ten possible schema of Signal Averaging. The exact one employed is to be selected at run-time (see below).

After answering the appropriate questions posed by Signal Averager, Section 1, the user is presented with the question, "COMPILE CONTROL TAPE: '_'". Answering "N" (No) chains Section 1 to Section 2 and the user may thus have a stand-alone Signal Averager system operating under PS/8. Answering "Y" (Yes) with setting of the switch register as described in the manual for Advanced Averager causes paper tape to be punched.

After the tape is punched one of two messages appear on the screen of the AXØ5. "INSUFFICIENT MEMORY" is an indication that the choice of various options (number of channels, trend function, high resolution, etc.) have caused the buffer to overload the top page of Field 1 and that the tape is accordingly fatal. The paper tape should be destroyed. CR in response to the message will cause Signal Averager, Section 1, to obtain new information. This process is then repeated until the compiled tape is safe. The message "SYNCH ON CHANNEL '_'" is an indication that the tape is safe and may be used to load the library dectape.

Once the compiled paper tape is deemed satisfactory, its binary segment should be loaded into core, followed by the binary file SØPTCH.BN. This can be accomplished with ABSLDR as follows:

```
• R ABSLDR
* PTR:, SYS:SØPTCH$
•
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After the period is typed by ABSLDR, then save the file as follows on DTA1:

```
• SAVE DTA1 SMØN Ø-7577, 1ØØØØ-17577; 151=1ØØØ
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The user assigns the numbers M and N as follows: M is the number of the corresponding "R" file in the Library: RMØØ. N is any digit Ø-9.

Repeating this process the user may build up on a dectape up to nine different "R" files with specific EKG channel assignments and timing parameters and, for each "R" file, one to ten corresponding "S" files with identical channel assignments and sampling intervals and with varying options as to channels displayed, statistical parameters, etc. This Library tape may then be used at run-time to avoid the necessity of repeating the process each time an experiment is done.

RUN-TIME: METHODS OF MEASUREMENT

The Resistance system assumes that the experiments are managed and the analog channels are assigned in the following manner:

a. Synch assignments:

The output of an electrocardiogram suitably amplified, is connected to either S1 or S2 Schmitt trigger input of the AX05. The other Schmitt trigger of the AX08 is used to receive a signal for the initiation of the green-dye curve.

b. Pressure and flow measurements:

Signals from three pressure transducers, suitably amplified, are brought to analog channels 1-3 of the AX08, Channel 1 being assigned to pulmonary arterial pressure, channel 2 to left atrial and channel 3 to pleural pressure. If desired, the last one or two pressures may be omitted, and the system will still run. At the beginning of the experiment these channels are calibrated by imposing a known pressure signal to channels 1-3. (See below).

Channel 0 of the AX08 is used for input from an electromagnetic flowmeter attached to the main pulmonary artery. Each run (measurement of flow and pressures) consists of an initial zero run during which the pressure transducers are opened to ambient air and the flowmeter set to its electronic zero setting. After the zero run, the actual pressure and flow measurement follows. As many as 99 runs may be obtained in a single experiment.

c. To perform a dye curve, the output from a densitometer, suitably amplifed, is attached to channel 1 of the AX08. Calibration of the densitometer is done at the beginning of the experiment. A volumetric syringe, used for all the dye curves, is filled with indocyanine green (Hynson, Westcott & Dunning:Becton Dickenson dye cartridge; volume of "cartridge" is approximately 3/4 ,or 1¼ ml). This syringe is emptied into 10.0 ml of the animal's blood, to which 0.5 ml of heparin has been added. It is important to avoid lipo-hepin or other heparin preparations containing a reducing substance, such as sodium bisulfite, as these interfere with the colorimetric analysis by the densitometer. A 1:10 dilution of this mixture is obtained and used for the calibration level. Heparinized blood, to which no dye has been added, is used for the zero level. The "zero level" blood is drawn through the densitometer as the instrument is balanced, the Schmitt trigger of the AX08 is fired and then the dye-containing blood is drawn through the densitometer, to complete calibration. For each subsequent green-dye curve, the same volumetric syringe is used to deliver a bolus of dye into the pulmonary artery as the Schmitt trigger of the AX08 is fired and blood from the aorta is drawn through the densitometer.

Many densitometers have an electronic "check" signal, which is a standard output from the densitometer, used to check for any change of amplifier settings between calibration and the actual dye curve. Immediately prior to green-dye calibration and to each dye curve, the program asks the operator for a zero level of the densitometer and for a "check" level and incorporates this information into the calculation of cardiac output. If the investigator's densitometer is not so equipped, he may ignore these requests and the program will run without this information. (See below).

RUNNING THE SYSTEM

1. Preliminary: The flowmeter and pressure transducers are connected as above to the AX08 through a suitable amplifying system. The EKG and green-dye signal outputs are connected to the Schmitt triggers of the AX08. At the time of performance of a green-dye calibration or curve, the densitometer output is to be connected to channel 1 of the AX08. Finally, the date is entered in the PS/8 - OS/8 system by the command in the teletype, • DATE XX/XX/XX.

2. Timing parameters, experimental information: The system may be started in one of two ways: (1) by the command • R CMPILR, answering CMPILR's questions as above and by

striking LF to answer the question, "COMPILE?" If this route is taken, no library tapes are required, the necessary information having been obtained by CMPILR. No interfacing with the Advanced Averager is possible, however, the ↑U key merely acting as a "Rub-out". (2) The command, •R RESIST, may be used to start the system. In this case an identifying message appears, and striking CR allows the program to proceed. The program then asks, "R '_'ØØ". The user should answer with the number (1-9) of the resistance compiled file he wishes (making certain that the Dectape Library desired is on DTA 1). The program responds with the question, "SXØ'_'", where X is the answer chosen for the previous question. The user should answer with the number (0-9) of the corresponding Advanced Averager compiled file. The program then reads the desired information from DTA1. Subsequent use of ↑U will cause the appropriate Advanced Averager to be run.

After the above information is obtained by either route of entry to the controlling program, the question, "EXPT #: '__'; '___'", appears on the screen of the AX08. The first entry of the experiment number must be a letter (A-Z); the remaining entries may be letters or numbers (0-9). After the first two entries, CR must be struck to proceed to the last three entries. "Rub-out" may be used to replace an incorrect entry; LF erases all the entries. When the experiment number is satisfactory, striking CR on the teletype records the answer. The program then asks, "AGE ANIM: '____' WKS." The user should answer with the appropriate decimal integer (fractions not permitted). CR causes the answer to be recorded. On the same display, the question "WGT:'______' KG" may then be answered with the appropriate number. The decimal point must be included in answering the latter question. Fractions are permitted.

The program then types out the information above, formatting a title page for the experiment. In the event that the operator failed to enter the data on the system, the message "DATE?" appears on the screen. CR then causes return to the keyboard monitor, so that the system may be restarted after the proper date is entered.

3. Adjusting the clock and synch levels: The display, "TIMING...", then appears. After CR is struck, a cross-hair pattern appears on the screen, the center portion of which may be moved by adjustment of the coarse and fine controls of the RC clock of the AX08. A fuller description of this is given in the description of Advanced Averager (DEC-LB-T30B-D).When the alignment is satisfactory, the user should strike CR. It may be necessary to hold the carriage return key for a brief instant to proceed. The RC clock is now set so that its interrupt fires at intervals equal to the sampling

interval specified in the compiled tapes set up by CMPILR and Advanced Averager, Section 1.

Next the message, "ADJUST SYNC AND ANALOG", appears. After CR is struck, the raw input from analog channel 0 appears (pulmonary arterial flow). If the channel number appears briefly, but then no input appears, the knob next to the EKG synch input on the AX08 must be adjusted to allow firing of the Schmitt trigger. When this level is satisfactory, the input signal will be displayed. Any clipping of the signal may be rectified by adjustment of the recorder's and flowmeter's outputs. By striking CR, the user may similarly adjust the output of channels 1 to 3. After channel 3 (pleural-pressure) is adjusted, the output of channel 1 will appear in response to synchs from the Schmitt trigger assigned to green-dye signal. This Schmitt trigger can then be adjusted. After it is satisfactory the user should strike CR.

4. Data tape: The message, "DTA1=DATA; 2 INFO WDS", appears on the screen. The user should then remove the Library tape from dectape transport #1 and replace it with the dectape upon which data is to be written. This tape should have been prepared with room for two extra information words in its directory (date and age of animal). This may be done by use of the PIP options, Z=2 or S=2. Finally, the dectape transport should be

placed in "WRITE ENABLED" mode. If CR is struck, the resistance and green-dye programs are operational.

The operator then directs the controlling program by conversation with the AX08 screen, answering the appropriate questions as they appear. Generally, unless otherwise specified, CR indicates "Yes" and LF "No".

5. The Resistance Section: Calibration: The first question of this section, "ANOTHER RUN: Y OR N '_'", is answered in the affirmative. The program then asks, "R=RUN; C=CALIB:'_'".

Calibration must be carried out before any calculation of resistances can be done (otherwise all answers will be zero--the calibration factors for the resistance runs are set at zero initially). The user answers "C" to the questions above, strikes CR and is confronted with the question, "R=RES; G=GRND '_'", to which he answers "R", if he wishes to calibrate the flowmeter and pressure transducers, or "G", if he wishes to calibrate the densitometer.

i) Flowmeter and pressure transducer calibration: Answering "R" to the question above gives the message "ZERO' on the screen. The pressure gauges should then be opened to ambient air and the flowmeter set on its electronic zero. The user strikes CR, whereupon the sampling program is brought into core and run. Four wave forms (constant signals corresponding to zero) appear on the screen. When the signals are satisfactory, the operator strikes CR, whereupon the teletype signals the beginning of an averaging by typing "<". If undisturbed, the program will then average for the number of cardiac cycles specified in the CMPILR program ("AVERAGE '____' SWEEPS) and will automatically calculate the zero levels and return to the controlling program's question "OK? Y OR N '_'", after typing ">" to signify that the averaging was complete. If the user is impatient and wishes to average less than the pre-set number of cycles, he may strike control/P (↑P) which immediately terminates averaging and proceeds to the question above. Answering this question with "N", returns to the "ZERO" message; a "Y" answer records the zero readings in memory and gives the display, "RUN". The user types CR, closing the pressure gauges and delivering the calibration levels to the flowmeter and to the three pressure transducers. These four calibration levels are then displayed. When all is well, the user should type CR to begin averaging these signals. The ↑P key has the same function as above. After the calibration averages have been computed (and the zero levels subtracted) the message, "OK? Y OR N '_'", reappears. If "N" is answered, the program recycles from the "ZERO" point. If "Y" is answered, the computer has the average displacements corresponding to the calibration flow and pressures in memory, and it is then necessary to tell it what these calibration flow and pressures were, so that it may calculate the calibration factors.

"CALIB EM: Y OR N? '_'" is the first message to appear. If the electromagnetic flowmeter has already been calibrated (not applicable to the first calibration of the experiment), the user may answer "N" and the program proceeds to inquire about the pressure calibration. Otherwise the message, "IN VITRO?", appears in response to a "Y" answer. Answering LF (No), causes the system to search for the answer to a previously run green-dye cardiac output. If there is such an answer in core, it is used for calculating the calibration factor for the flowmeter. If not, the question is repeated. A CR answer (Yes) to the question, "IN VITRO?", leads to the display, "Q= '____' L/MIN". The user enters the flow corresponding to the flowmeter's deflection level during calibration, including the decimal point. This flow would correspond either to the manufacturer's information or to the investigator's result in an in vitro calibration of the flowmeter. The user then strikes CR to record the answer.

The message, "CHAN 1 = ____ MM HG", appears. This is answered with the decimal integer corresponding to the calibration pressure used for the pulmonary arterial transducer. Similar questions are answered for channels 2-3.

Following the answer to channel 3, the four calibration factors are displayed on the screen. If they are satisfactory, the user strikes CR and they are typed out and stored in core. If not, the user may strike LF and the entire calibration procedure is repeated.

Following print-out of the calibration factors, the message, "R=RUN; C=CALIB: '_'", reappears.

ii) Green-dye calibration: Answering "C" to the question above and "G" to the subsequent question, "R=RES; G=GRND '_'", gives the display "GRNDYE-CAL", to which the user answers with CR. At this point the signal from analog channel 1 appears, along with the message "ZERO=XXXX". The user should connect the output of the densitometer to analog channel 1 of the AX08, and zero the densitometer. When the display level is satisfactory, CR is struck, the display remains the same, but the message, "CHECK=XXXX", appears. Many densitometers are provided with an electronic check level. The user should then turn on this known output from the densitometer and, when the level is satisfactory on the display, strike CR. This procedure, used with each subsequent green-dye curve, serves as a protection against changes in the densitometer level between calibration and a given green-dye curve. If no such device is available on the user's densitometer, striking CR with the display at the zero level will cause the multiplication factor, ZERO/CHECK, to be set at 1, and calibration can proceed.

The next display to appear shows the densitometer output (chan 1 - AX08), along with a cursor which may be moved up or down by the knob alongside analog Channel 0 of the AX08 (knob=channel 34 of AX08), and the message, "ZERO=XXXX", which records the level of the cursor.

The user should balance the densitometer during aspiration of the blank blood sample. When it is balanced, the green-dye synch signal is given to the computer and the dye-containing blood sample is drawn through the densitometer. This causes the calibration deflection to appear in the AX08 screen. As soon as the maximum level is reached, blood sampling may be stopped, but the user should wait until the full curve is written across the entire screen of the AX08. The cursor must then be set to the zero level of the curve. Striking CR causes the program to calculate the maximum deflection, subtract the zero cursor reading and store the answer as the calibration deflection. The message, "R=RUN; C=CALIB: '_'", then reappears and the densitometer is calibrated.

6. Resistance Section: Obtaining Data: Once the system is calibrated, it may be used to obtain up to 99 "runs" of pulmonary vascular resistance and up to 99 green-dye curves, each one giving typed answers and being written on dectape. After each run, the system returns to the display, "ANOTHER RUN: Y OR N? '_'". Answering "Y" to this question gives the question "R=RUN; C=CALIB: '_'", and an additional resistance run or green-dye curve may be done. Answering "N" causes the program to format off the typed page and return to the PS/8 monitor. At any time in the dialogue or during a green-dye curve, the user may strike control/Z (↑Z) and the message "ANOTHER RUN: Y OR N? '_'" appears, the interrupted dialogue being aborted. Striking ↑C on the teletype at these times returns to the PS/8 monitor without formatting a teletype page. Should the user wish to turn on the signal averager during this dialogue, he may strike ↑U and Advanced Averager, Section 3 will be brought into core and run on the parameters contained in the selected compiled signal averager file. (See below for details). If the investigator wishes to recalibrate, he may do so by answering "C" to the question "R=RUN; C=CALIB: '_'". In that case, new calibration factors replace the old ones.

Following each resistance run or green-dye curve, the answers (weight of animal, number of samples in average, sampling interval, calibration factors, means, cardiac output, etc.) and the digitized wave forms are written on the DTA1 dectape in a file labelled by the experiment number given earlier in the dialogue and with the extension "R" (resistance) or "G" (green-dye curve) and the number of the set or curve (1-99).

i) Resistance Runs: If the operator answers "R" to the question "R=RES; G=GRND: '_'", the message, "ZERO", appears on the screen. He should then type CR, zeroing the three pressure transducers and the flowmeter, as described under calibration. When zero levels appear satisfactory on the screen, the user should type CR and the averaging process for zeroes begins. After averaging is complete, the message "OK: Y OR N? '_'", appears, which should be answered as described in the calibration description. If the answer is "Y", the message, "RUN", appears. The pressure transducers and flowmeter should be set to record and CR typed.

At this point the raw wave-forms corresponding to the four channels appear on the screen. Several options are available to the operator at this point: (1) LF causes the raw wave forms to appear (even if the program is averaging); (2) "X" expands the view scale, displaying 2x the previous signal--this key may be struck several times, further to expand the scale; (3) "C" causes the view scale to contract by a factor of 2 and may be struck repeatedly;

(4) LF after several "X" or "C" returns the view scale to the original level; (5) CR initiates the averaging process, indicating so by typing "<" and continues averaging for the preset number of sweeps, whereupon the program types ">" and returns to the question "OK: Y OR N? '_'". The averaging process may be aborted either by typing LF (in which case the sampling program returns to the raw input display) or by typing ↑P (in which case the averaging is terminated and calculation begins with the particular number of sweeps current at the time the key was struck). This ↑P option operates only during the averaging process.

At the conclusion of the averaging process, the answers and digitized wave-forms are written on dectape, DTA1, and the message, "OK: Y OR N? '_'", appears. Typing "N" causes the resistance set counter to be decremented by one, so that a subsequent resistance run overwrites the unsatisfactory one. Typing "Y" causes the four averages to be displayed on the screen. If the user does not like them, he may type LF, and the resistance set counter is decremented by one. Typing CR causes the set number, number of sweeps, cardiac rate and means to be typed, followed by the cardiac index (cardiac output divided by weight) and the indexed resistances. These resistances are given by the following formulae:

(a) Total resistance = $[\int P_{PA}(t)\,dt]/[\text{cardiac index}]$

(b) Arteriolar resistance =

$$[\int (P_{PA}(t) - P_{LA}(t))dt]/[\text{cardiac index}]$$

(c) Integrated total resistance =

$$[\int (P_{PA}(t))/Q(t))dt] * \text{weight}$$

(d) Integrated arteriolar resistance =

$$[\int (P_{PA}(t) - P_{LA}(t))/Q(t)dt] * \text{weight}$$

Right ventricular work is given as:

$$\text{Work} = [\int P_{PA}(t) * Q(t)dt]/\text{weight}$$

Units for resistances are mm Hg/L/min/kg and for work are mm Hg * L/min/kg.

ii) Green-dye curves: Typing "R" to the question, "R=RUN; C=CALIB: '_'", and "G" to the subsequent question, "R=RES; G=GRND: '_'", causes the program to run a green-dye curve. The display "GRND-CRV" appears, to which the operator responds with CR. Next the message "ZERO=XXXX" appears along with the output of channel 1. The user connects the densitometer to analog channel 1 of the AX08, levels the zero reading on the densitometer and strikes CR. The message "CHECK=XXXX" appears, to which the user responds as described under calibration.

The display with the cursor and the message "ZERO=XXXX" appears in answer to CR after the last step. At this point, aortic blood is sampled through the densitometer, the densitometer is balanced at the zero level and the bolus of dye is injected into the pulmonary artery, the time of injection being noted by the green-dye synch signal. Note: The program will sample the green-dye curve <u>only</u> if the synch signal has been delivered. Continued aortic sampling will give the green-dye curve on the display. After the curve has been written completely across the screen, the user sets the cursor to the curve's baseline and strikes CR.

The process of calculating cardiac output is slow. During this phase, the curve is displayed along with two messages: "Q1=XXXX" and "Q=XXXX". After a few moments a number appears in the message, "Q1=XXXX". This is the cardiac output calculated by the following method:

Area = A1 + A2, where A1 = area under curve from zero point to "downslope" (see Fig. 1), calculated by Simpson's rule. A2 = 2X area from "downslope" (0.8 x true maximum) to point 2 (0.4 x true maximum).

Then Q1=15*[Cal Check/Curve Check]*[Calibration Deflection]/Area

This flow approximates cardiac output quite closely.

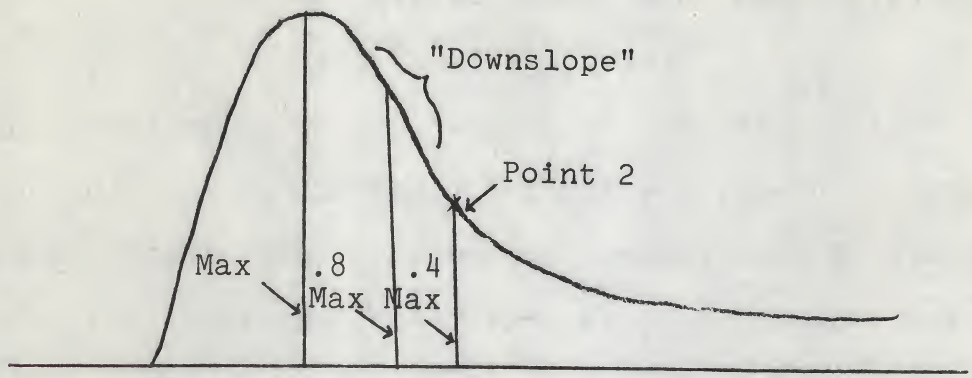


FIG. 1

After appearance of this answer, the program calculates area A2 by obtaining the natural logarithm of each deflection from "downslope" to the end of the curve. A straight-line is then fitted to the points, log deflection vs time, from "downslope" to "point 2". The equation for this straight-line is then used to compute theoretic points from "point 2" to the end of sampling. If all actual points lie above the theoretic points, then recirculation is judged to have already occurred, and the fitted line is used to calculate the area under the negative exponential curve from "downslope" to infinity. If such is not the case, the program fits to one additional point, repeats the process, and checks for recirculation. This process is continued until recirculation appears or the points are exhausted. The area under the negative exponential from "downslope" to infinity is then substituted for A_2

in the estimate of area under the green-dye curve, and Q is calculated in a manner similar to Q1.

This portion of the program can be quite time-consuming for some curves. During the time that it is going on, the display of the green-dye curve is altered from "downslope" to the end of the curve, while the logarithms are calculated and the least squares fitting process undergone. After the program has settled the recirculation question, the answer for cardiac output is written on the "Q=XXXX L/MIN" part of the display. The program then restores the original points of the curve for "downslope" to the end of the curve, which process is visible on the display of the curve.

If the curve is not satisfactory, and the operator wishes, he may abort the curve by striking ↑Z on the teletype. The message "ANOTHER RUN: Y OR N? '_'", will then appear. If the curve and answers are satisfactory, the user may strike CR, whereupon the answers are written on the teletype and answers and wave form of the curve are written on dectape transport #1 and the message "ANOTHER RUN: Y OR N?'_'", appears.

7. Resistance Section: Interfacing with Advanced Averager: At any time when the messages: "ANOTHER RUN: Y OR N? '_'", "R=RUN; C=CALIB: '_'", "R=RESIS; G=GRND: '_'", "OK: Y OR N? '_'", "ZERO", or "RUN" are on the screen, the operator may strike ↑U

to call in Advanced Averager, Section 3. This works only if the system was started with the command •R RESIST and a compiled file for Advanced Averager was loaded from the Library tape. At other times and under other conditions, the ↑U pseudo-interrupt either has no effect or acts as a rub-out.

Once Advanced Averager, Section 3, is running, the display and calculations possible will, of course, be those selected in the compiled file for Advanced Averager. The directions for running the Advanced Averager are exactly those described in DEC Manual DEC-LB-T30B-D, except that to progress from Section 3 to Section 4, the user need only strike ↑P, and the loading and running of Section 4 is automatic. Similarly, Section 4 automatically chains to Section 5 and upon completion of Section 5, ↑P causes Section 3 to run again.

With Section 3 running, two curves of exit are possible. ↑C gives the keyboard monitor, effectively terminating the experiment. ↑U causes the controlling section of the Resistance system to run, asking the question "ANOTHER RUN: Y OR N?'_'".

THE READER

Also provided is a program, called reader, whose function is to read the data tape produced by the Resistance System. With the desired dectape on a transport, this program is initiated by the command •R READER. An identifying message appears, to which the operator responds with CR. The message "DTA '_'" then appears on the AX05 screen. The user answers with the number of the dectape transport to be used. The same message reappears, so that the user may search several dectapes for the desired file. Answering with CR instead of a number terminates this portion of the program and causes the question "FILE # '__'; '___'; '_'. '__'" to appear on the screen. The user responds to this request with the file name of the desired answer tape, as coded by the Resistance system, e.g., AA; 001; R.01. A CR should be given before each segment of the file-name.

The program then searches the directory of the first dectape number given for the desired file. If it is not there, the program types "NOT ON DTA #X" and searches the next dectape transport indicated. Finding the desired file, the program then types out the following information: File number, date file created, age of animal, weight of animal. For a resistance run, the answers obtained by the resistance system are then typed out. For a green-dye curve, those answers peculiar to the green-dye curve are given on the teletype.

Finally, the program returns to the keyboard monitor of the PS/8 system, leaving in core the digitized wave-forms of the flow and pressures (for a resistance run) or of the green-dye curve (for a green-dye run).

The format for the digitized wave-forms of the resistance run as written in core by the Mean program of the Resistance System, written in the dectape answer file and as put into core by the Reader program is as follows:

Locations 307-6177, Field Ø
Locations Ø-7377, Field 1

Point #1 of sweep:

- No. times entries made in averaging for point #1
- Exponent of 2, High order mantissa, Low order mantissa — pulm art flow in floating point (L/min)
- Exp, High order, Low order — pulm art pressure (mm Hg)
- Exp, High order, Low order — left atrial pressure (mm Hg)
- Exp, High order, Low order — pleural pressure (mm Hg)
- No. times entries made: Point #2
- ⋮

.
.
.
.
.
.

No. times entries made: last point of sweep

Exp of pulm art flow

.
.
.
.
.
.

Low order of pleural pressure

0

0

.
.
.
.
.
.

0 (to end of buffer)

The answer buffer for the resistance system begins at location 200, Field 0 and extends to location 264, and is written in the first block of the answer file in dectape:

<u>Location</u>:	<u>Entry</u>:
200:	Weight of animal (floating format)
203:	Sampling interval in microsecs (floating format)
206:	No. points in resistance buffer (integer format)
207:	Last cardiac output by greendye (floating format)
212:	Last cardiac output by greendye - shortcut (floating format)
215:	No. points in average - resistance (integer format)
216-231:	Calibration factors, Channels Ø-3 (floating format)
232-245:	Means-resistance, Channels Ø-3 (floating format)
246-264:	Arteriolar Resistance, Total Resistance, Arteriolar R2 Integral, Total R2 Integral, Right Ventricular Work (floating format).

For a green-dye curve, the digitized wave-form is written in loc 0-7377 of Field 1 and restored to these locations by the Reader program, and consists of the sampled points seriatim in floating point format.

The answer buffer for a green-dye curve begins at location 200, field 0 and extends to location 253, Field 0 and is likewise written in the first block of the answer file:

Location	Entry
200-231:	Weight of animal, etc., as in Resistance System
232:	Time interval - green-dye curve (sec) -floating point
235-236:	Curve check and calibration check - integer format
237:	Calibration Factor - integer format
240:	Take-off of curve from baseline in number time increments - floating point
243:	Number time increments from takeoff point to beginning of negative exponential fit - floating point
246:	Number time increments from takeoff point to recirculation - floating point
251:	Sum squares of least square fit - floating point format.

The date of the file-creation is stored as the first extra information word in the directory and the age of the animal is the second extra information word. This enables cross-indexing of the files according to date and age and the user may easily write a program to collect all files of a given date or age. Please see listing of Reader program for the means of accessing these extra information words.

REFERENCES

1. Hamilton, W.F., Moore, J.W., Kinsman, J.M. and Sparling, R.G.: Simulataneous determination of the pulmonary and systemic circulation times in man and of a figure related to the cardiac output. Am. J. Physiol. 84:338-344, 1928.

2. Jacobs, R.R., Schmitz, U., Heyden, W.C., Roding, B. and Schenk, W.G.,Jr.: Determination of the accuracies of the dye dilution and electromagnetic flowmeter methods of measuring blood flow. J. Thor. and Cardiovas. Surg. 58:601-608, 1969.

3. Sato, T.: A critical study of Hamilton-Stewart's principle for the analysis of hemodynamics--a mathematical analysis. Japanese J. Physiol. 13:260, 1963.

4. PS/8 Programming System: DEC-08-MEXA-D.

5. PS/8 System User's Guide: DEC-08-MEXA-D and OS/8 System User's Guide: DEC-S8-OSUMA-8-D.

APPENDIX 1

DETAILED DESCRIPTION OF COMPONENT PROGRAMS OF SYSTEM

I. GENERAL SCHEMA:

The system is composed of the following programs:

1. Compiler (CMPILR):

Obtains timing and synch information, checking each against availability of channels and core, and putting information on page 0 of field 0. Capable of chaining to Controlling Program or of writing information on Dectape as desired by user.

2. Controlling Program (CONT):

Entered initially, this program obtains proper Resistance and Advanced Averager compiled tapes from library tape of dectape and puts former into core (page 0 of field 0) and writes latter on system device as a file, SZER.

Program then obtains information concerning experiment and data from user and from PS/8 system respectively, and allows proper setting of RC clock of AX08 and of synch and analog levels of AX08.

The heart of the controlling section then interfaces with the user and calls in various programs to do sampling, green-dye curve, etc., as desired by the user, typing out the answers for the resistance runs as indicated.

3. Sampling Program (SAMP):

This program is called by the controlling program and handles the task of A-to-D conversion and sampling. It is capable of sampling the raw signals and displaying them or of cumulating them in preparation for averaging. Finished, SAMP chains to MEAN.

4. The Mean Program (MEAN):

This program has two functions. First, entered from SAMP, it massages the digitized cumulative wave forms in core to average each point and multiply by the suitable calibration factor, leaving the floating point average of each point in core according to the schema described above (see Reader). Secondly, it writes the answers and these digitized waves on the answer file on dectape transport #1, performing this function both for a resistance run and for a green-dye curve.

5. Green-dye Program (GRND):

This program handles calibration of the densitometer or performance of a green-dye curve as dictated by the controlling program. Finished, it types its answers and chains to the Mean Program.

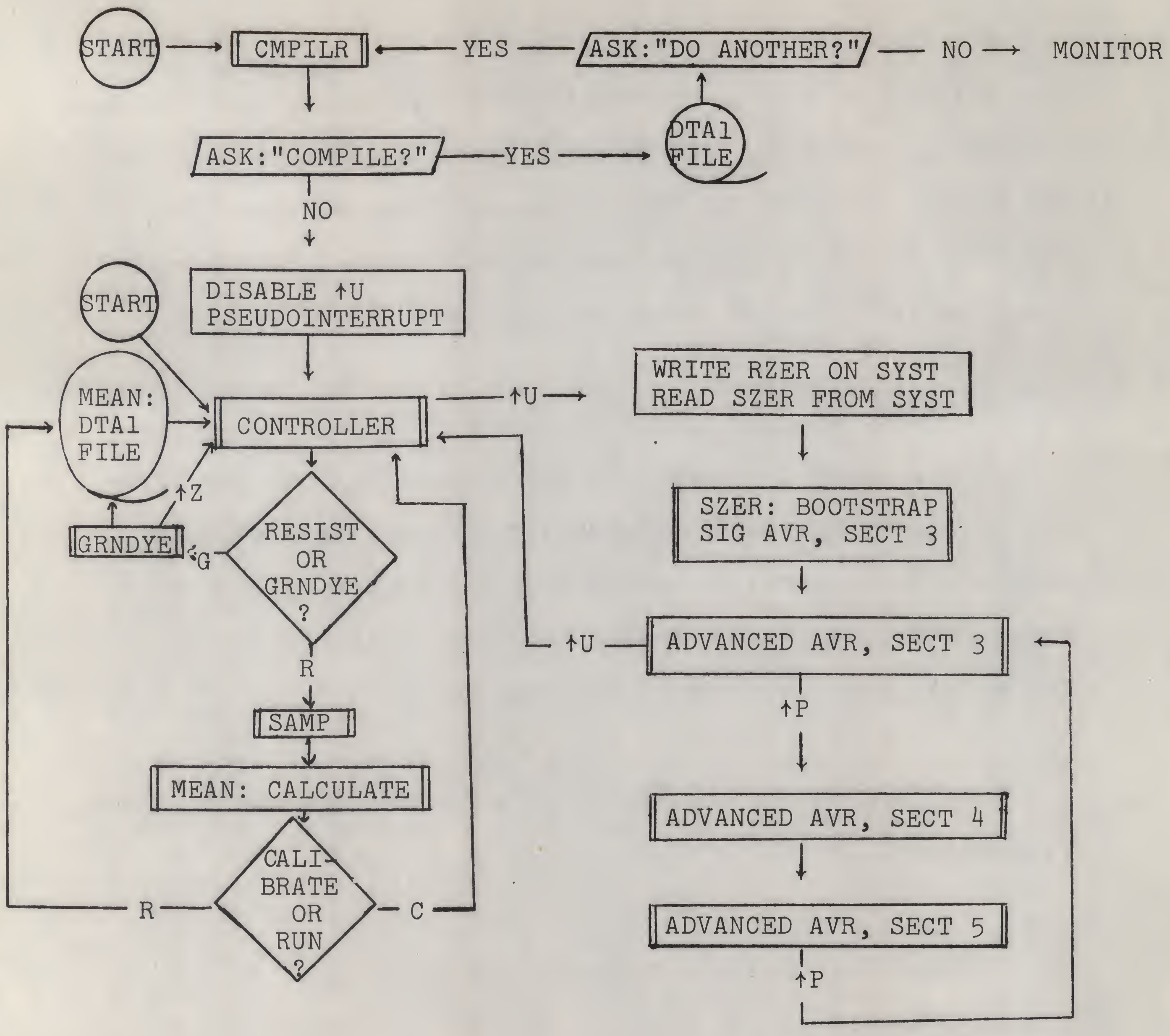
6. SZER:

Written on the system device by the initial portion of the controlling program, this program contains the compiled information necessary to run the particular Advanced Averager schema selected by the user and also includes a bootstrap to load and run Advanced Averager, Section 3.

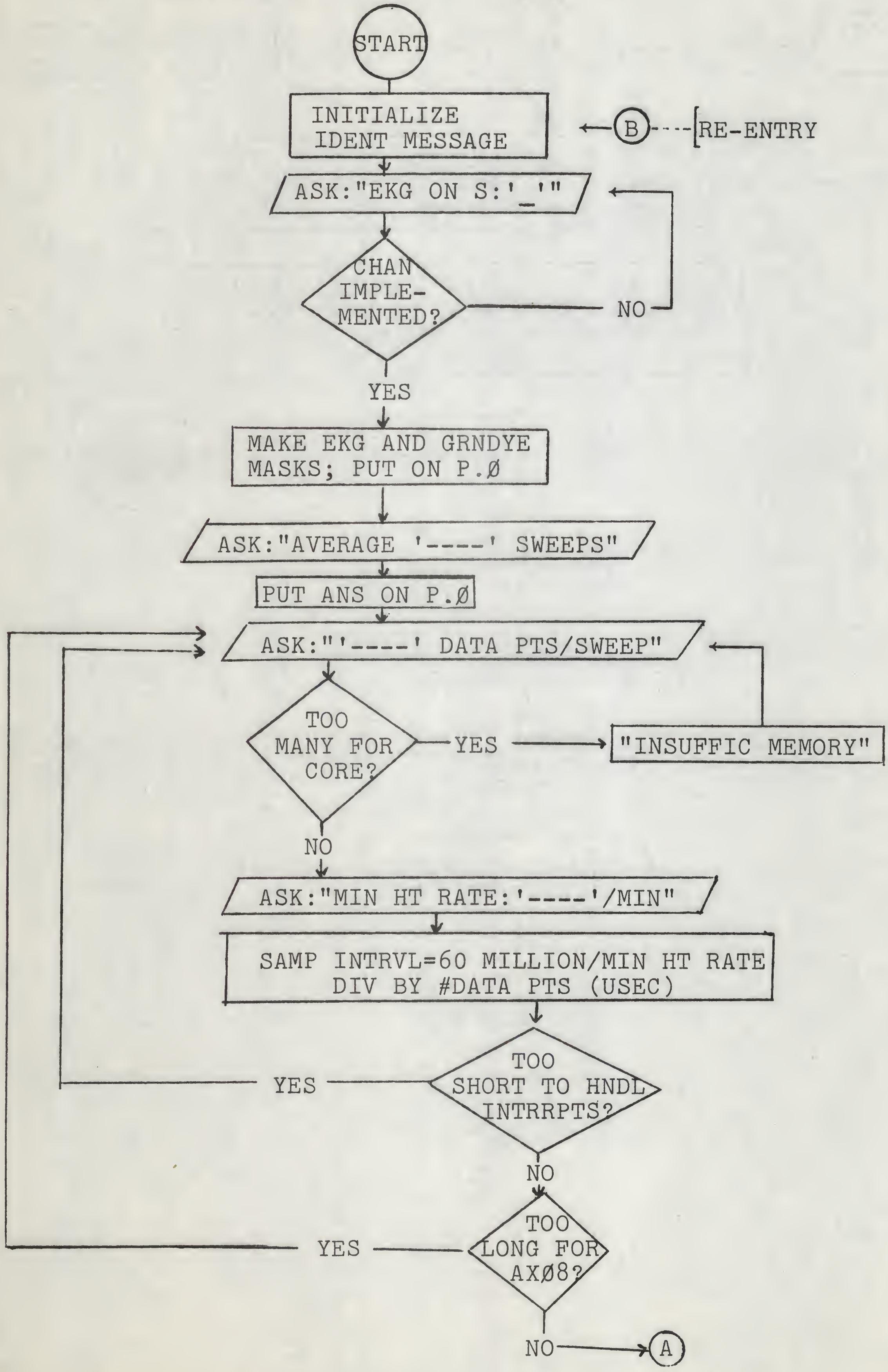
7. RZER:

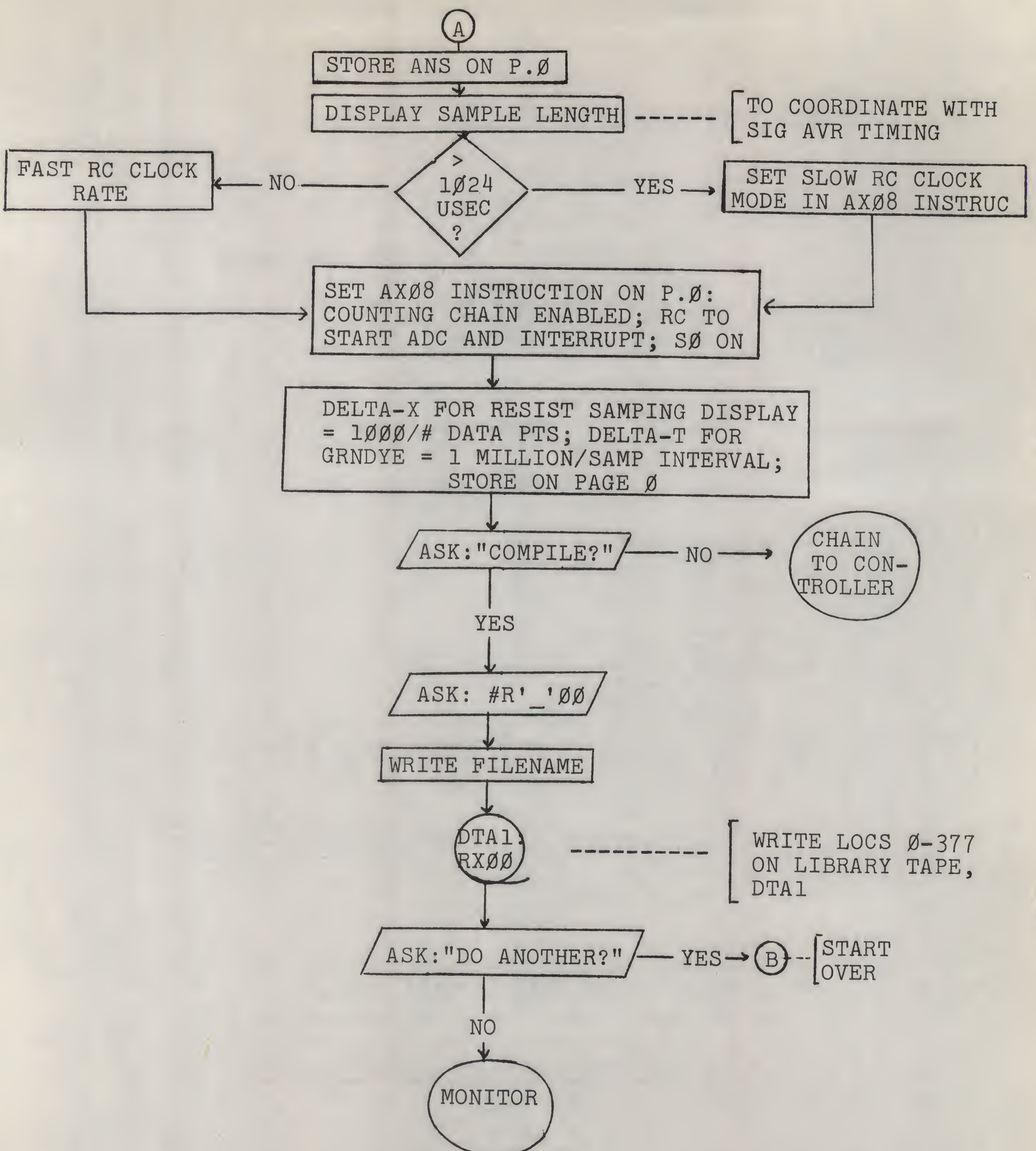
This program is written by the controlling program after the ↑U pseudointerrupt and consists of the page 0 and page 1 information acquired by the Controlling Program plus a bootstrap to reload and run the Controlling Program upon ↑U pseudointerrupt in Advanced Averager, Section 3.

8. These interconnections are summarized in the following flow sheet.


START
CMPILR
YES
ASK:"DO ANOTHER?"
NO
MONITOR
ASK:"COMPILE?"
YES
DTA1 FILE
NO
START
DISABLE ↑U PSEUDOINTERRUPT
MEAN: DTA1 FILE
CONTROLLER
↑U
WRITE RZER ON SYST READ SZER FROM SYST
↑Z
GRNDYE
G
RESIST OR GRNDYE ?
SZER: BOOTSTRAP SIG AVR, SECT 3
↑U
ADVANCED AVR, SECT 3
R
↑P
SAMP
MEAN: CALCULATE
ADVANCED AVR, SECT 4
R
CALI-BRATE OR RUN ?
C
ADVANCED AVR, SECT 5
↑P

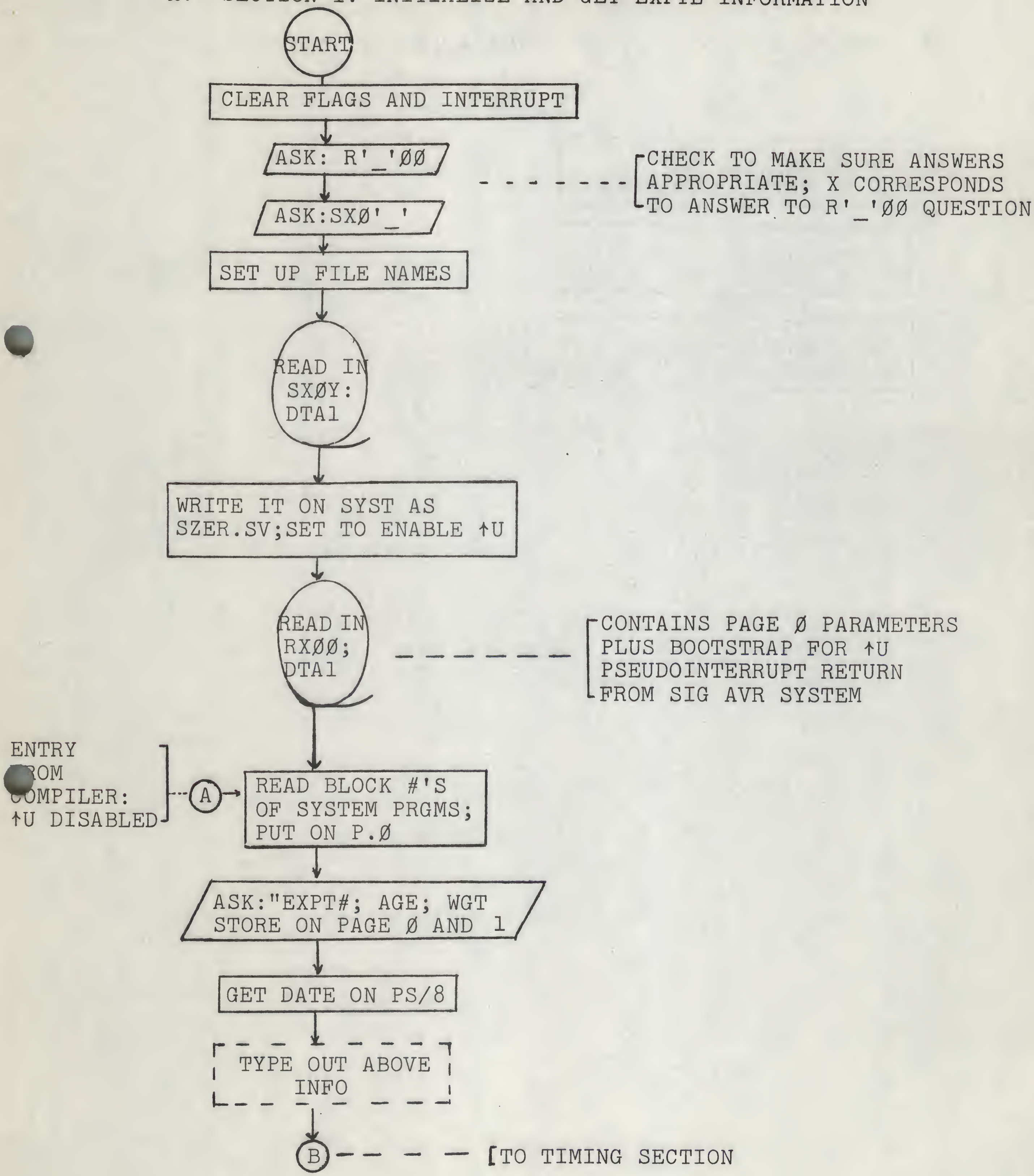
II. COMPILING PROGRAM: CMPILR:



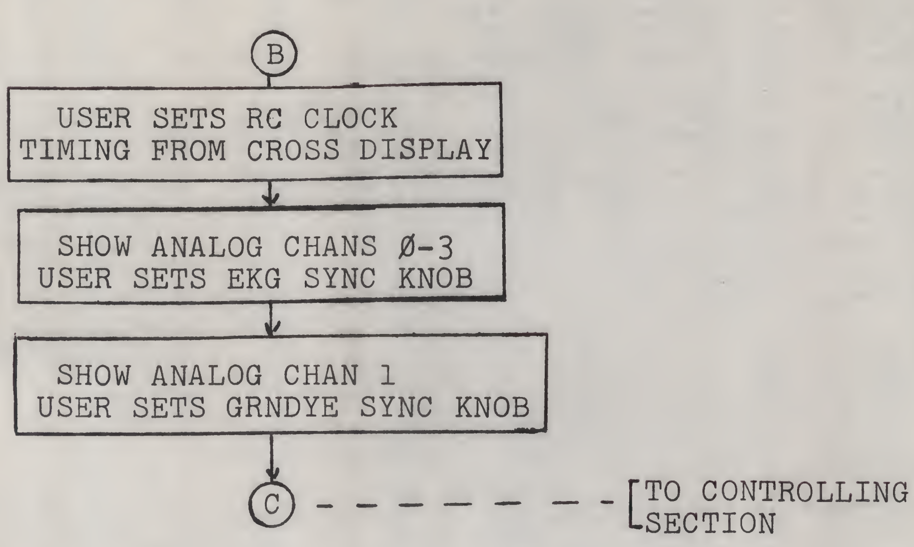

A
STORE ANS ON P.Ø
DISPLAY SAMPLE LENGTH
TO COORDINATE WITH SIG AVR TIMING
> 1Ø24 USEC ?
NO
FAST RC CLOCK RATE
YES
SET SLOW RC CLOCK MODE IN AXØ8 INSTRUC
SET AXØ8 INSTRUCTION ON P.Ø: COUNTING CHAIN ENABLED; RC TO START ADC AND INTERRUPT; SØ ON
DELTA-X FOR RESIST SAMPING DISPLAY = 1ØØØ/# DATA PTS; DELTA-T FOR GRNDYE = 1 MILLION/SAMP INTERVAL; STORE ON PAGE Ø
ASK:"COMPILE?"
NO
CHAIN TO CONTROLLER
YES
ASK: #R'_'ØØ
WRITE FILENAME
DTA1: RXØØ
WRITE LOCS Ø-377 ON LIBRARY TAPE, DTA1
ASK:"DO ANOTHER?"
YES
B
START OVER
NO
MONITOR

III. CONTROLLING PROGRAM: CONT:

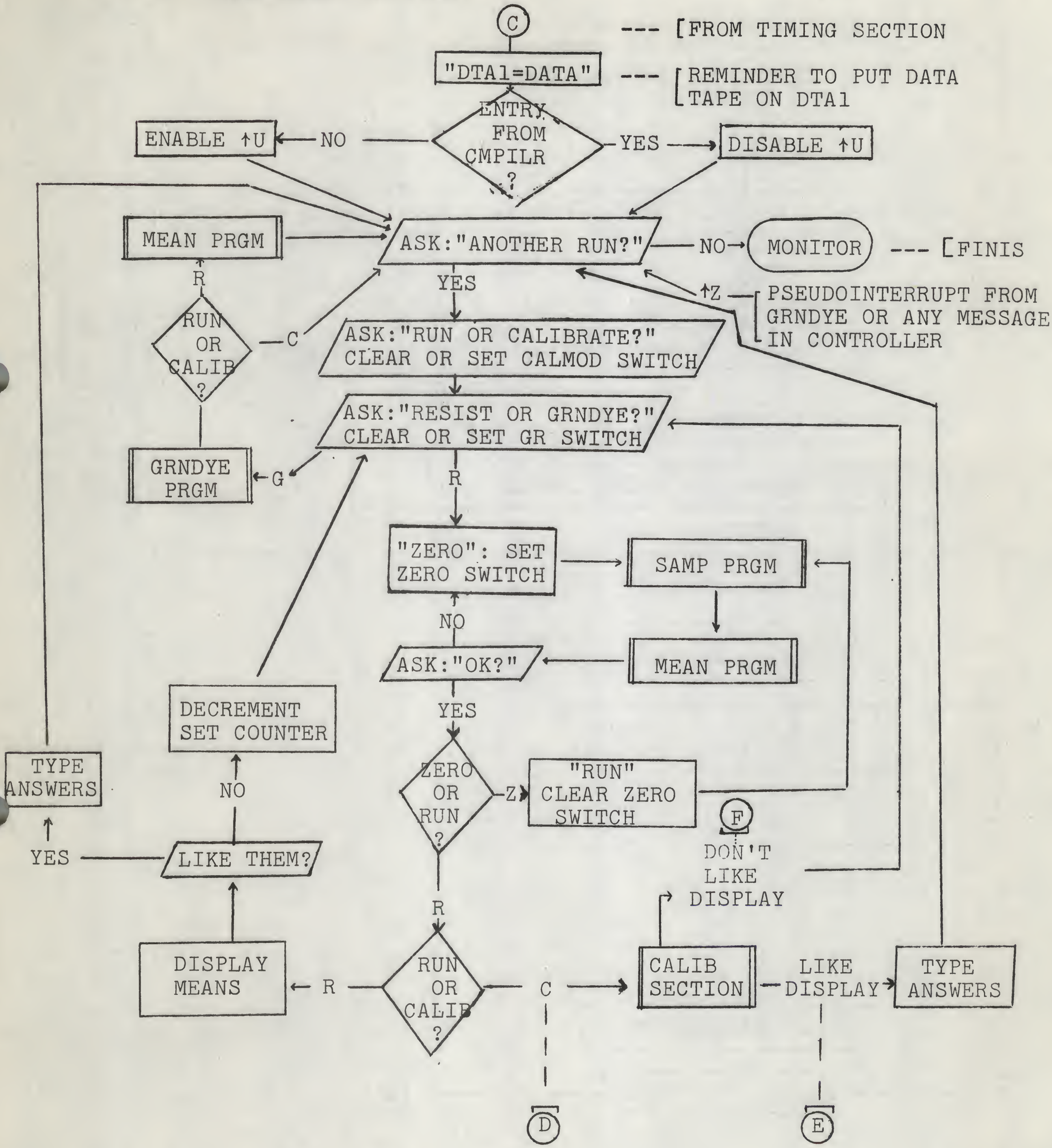
A. SECTION 1: INITIALIZE AND GET EXPTL INFORMATION



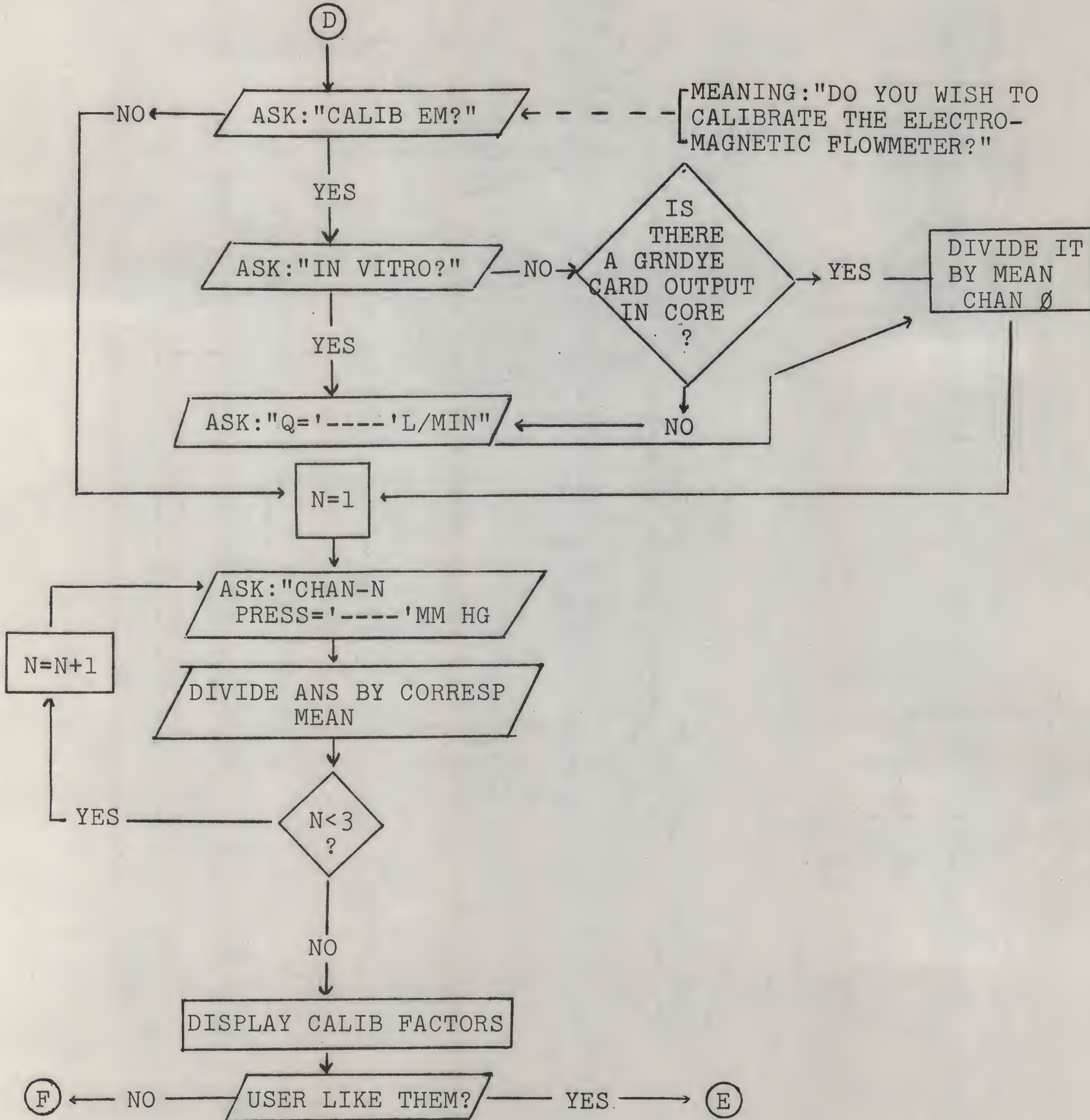
B. TIMING SECTION: AS IN SIGNAL AVERAGER, SECTION 2:



C. CONTROLLING SECTION:

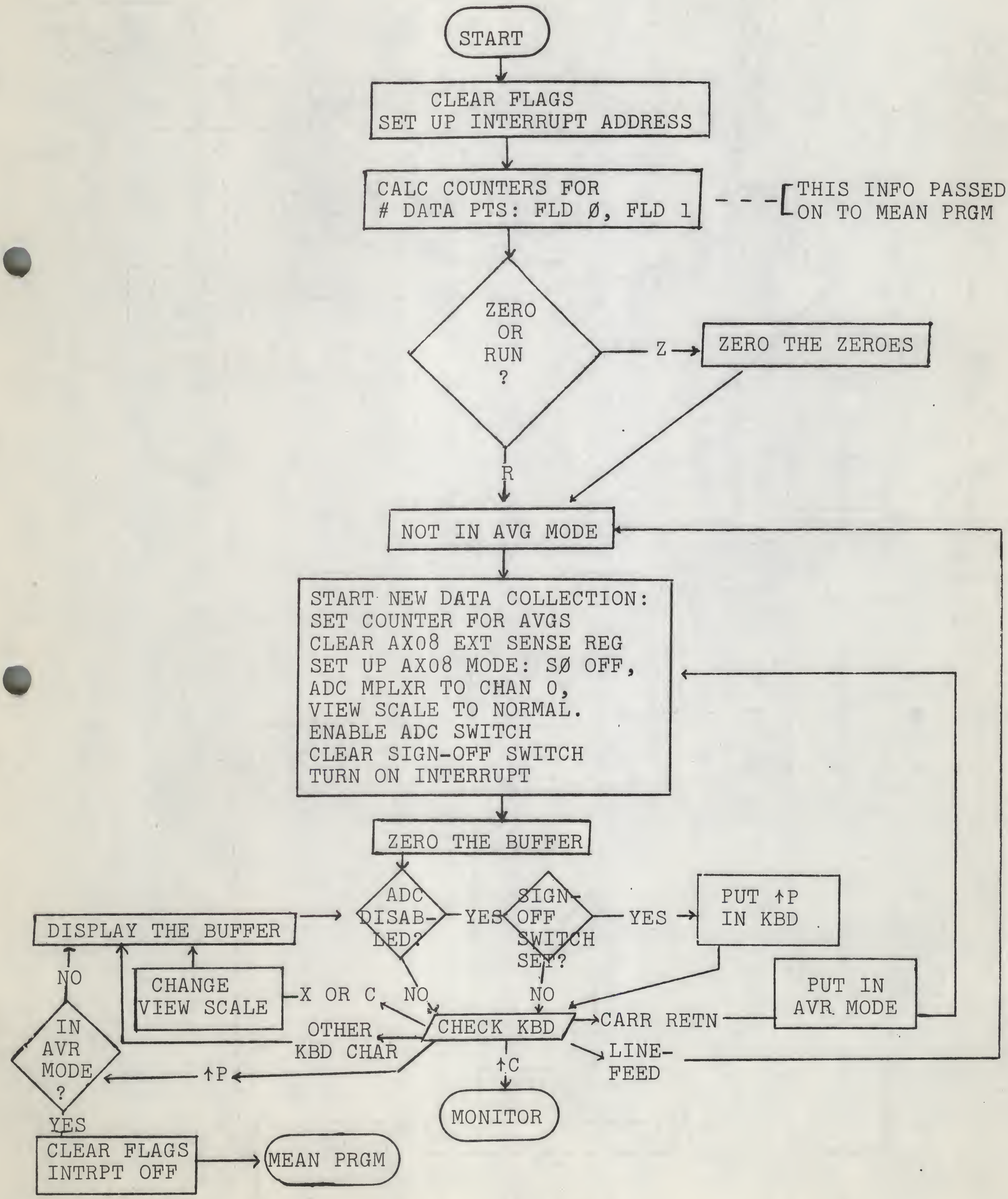


D. DETAILS OF CALIB SECTION:

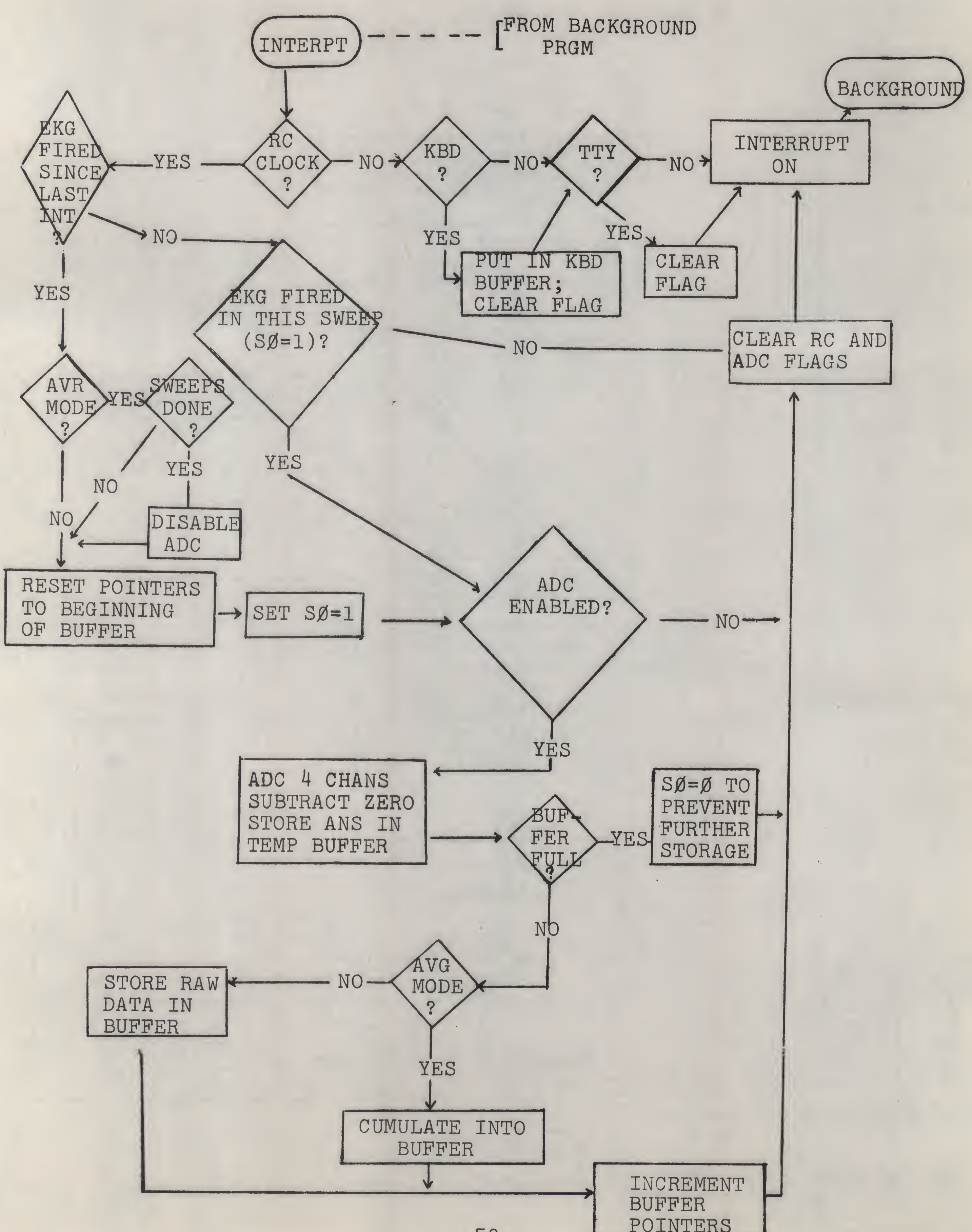


IV. ADC SAMPLING PROGRAM: SAMP:

A. BACKGROUND PROGRAM:



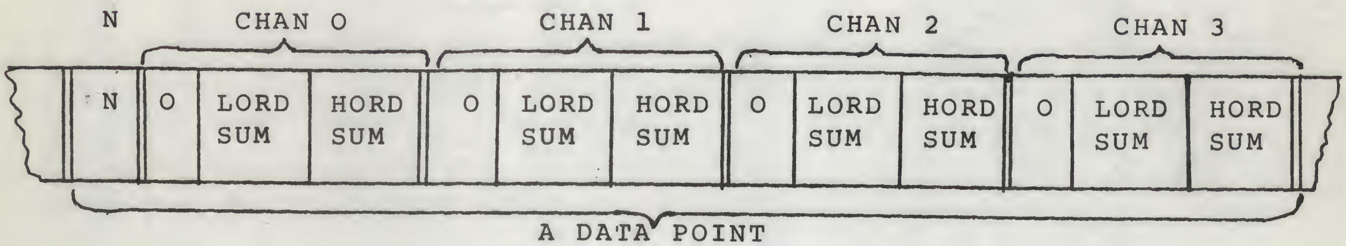
B. INTERRUPT SCHEME:



C. BUFFER SCHEME:

Field Ø: Locs 3Ø7 - 5777

Field 1: Locs Ø - 7377



1. Raw Input:

   N=0 for all data points

   1st Loc of each channel = 0 for all data points

   LORD SUM (Low-order) = 0 for all data points

   HORD SUM (High-order) contains raw input for particular channel

2. Average Mode:

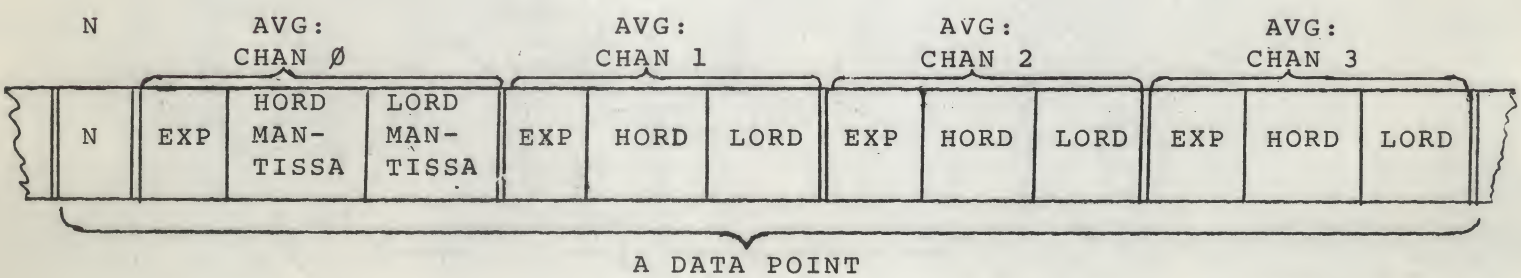
   N contains # entries made into cumulate register

   1st Loc of each channel = 0 for all data points

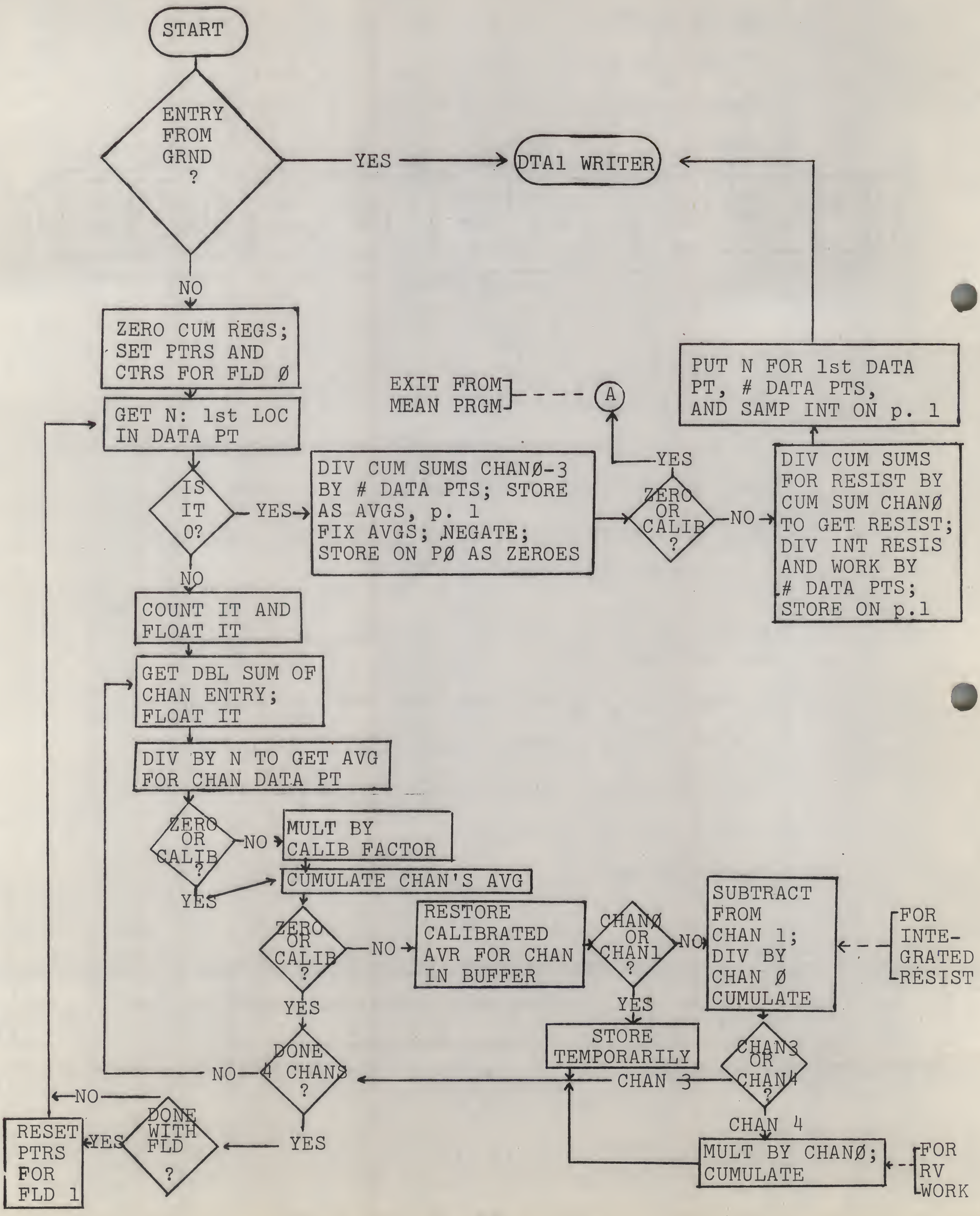
   LORD-HORD SUM = double precision cumulate register

V. MEAN-DTA1 WRITING PROGRAM:

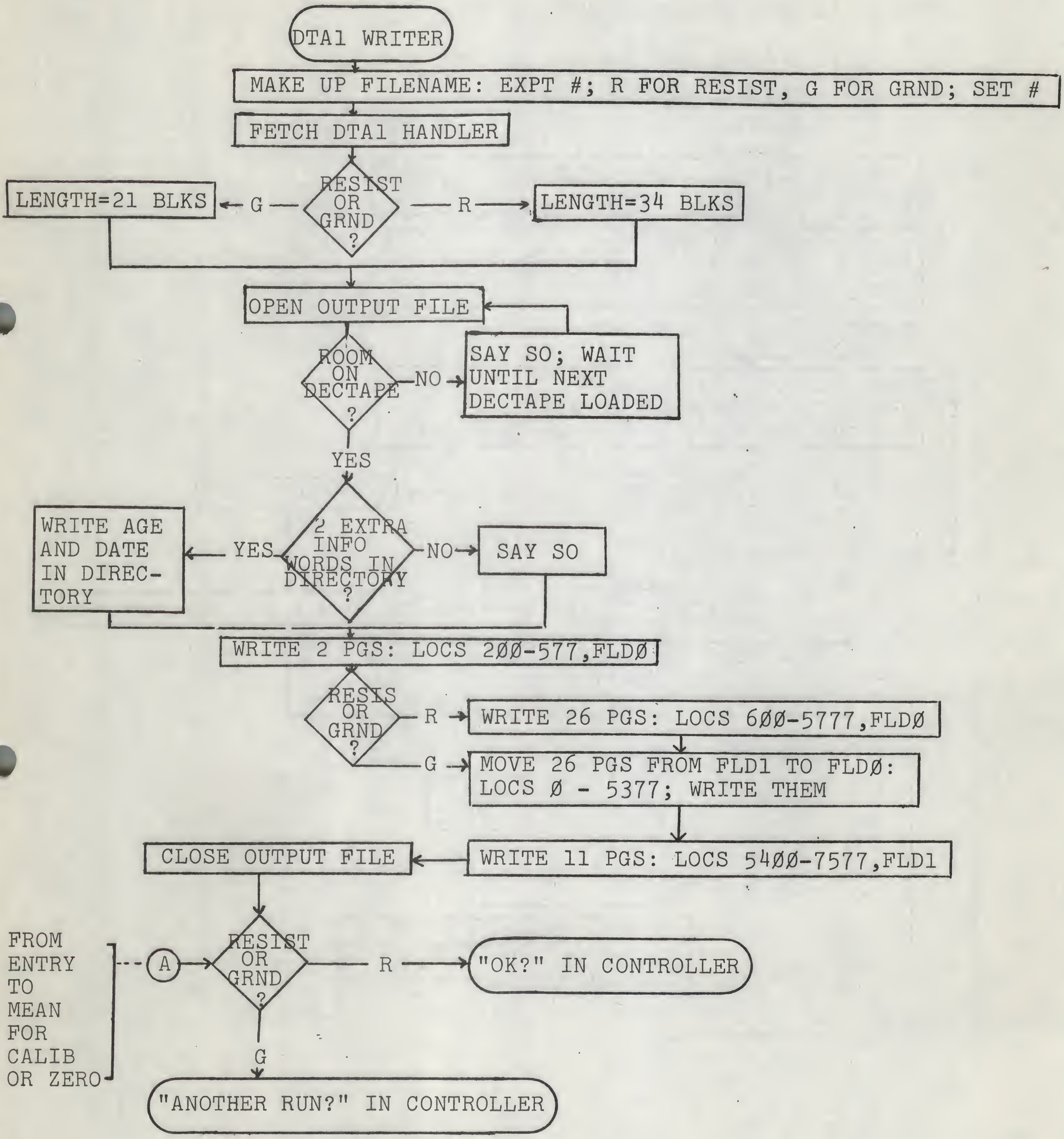
A. BUFFER SCHEME:



B. FLOW CHART: AVERAGING SECTION:



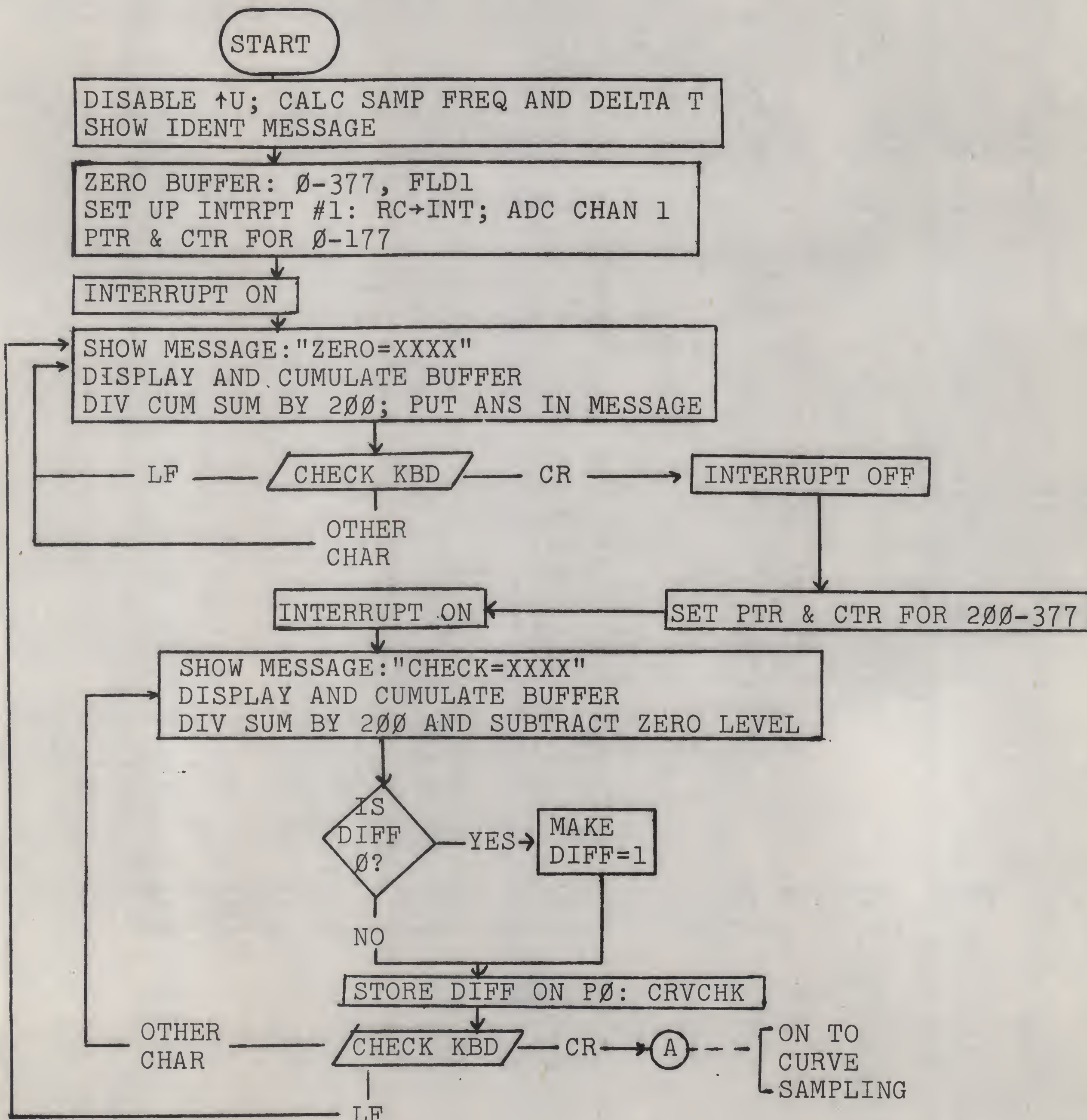
C. DTA1 - WRITING SECTION:



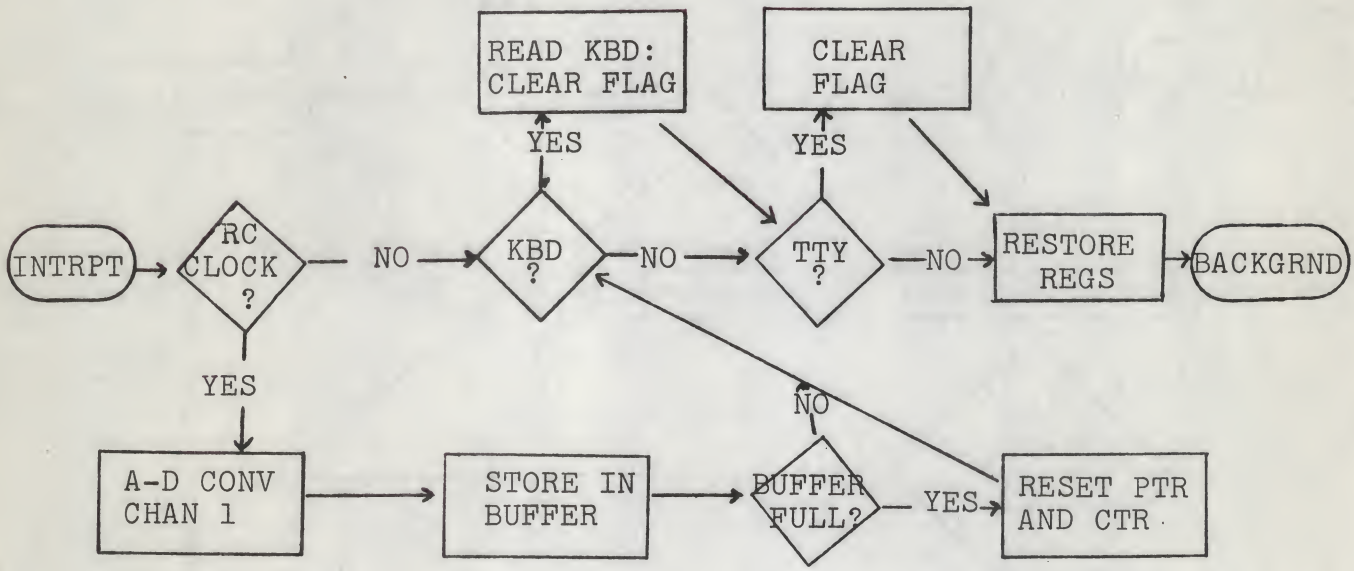
VI. GREENDYE PROGRAM:

A. GETTING "CHECK" LEVEL:

1. BACKGROUND PRGM:

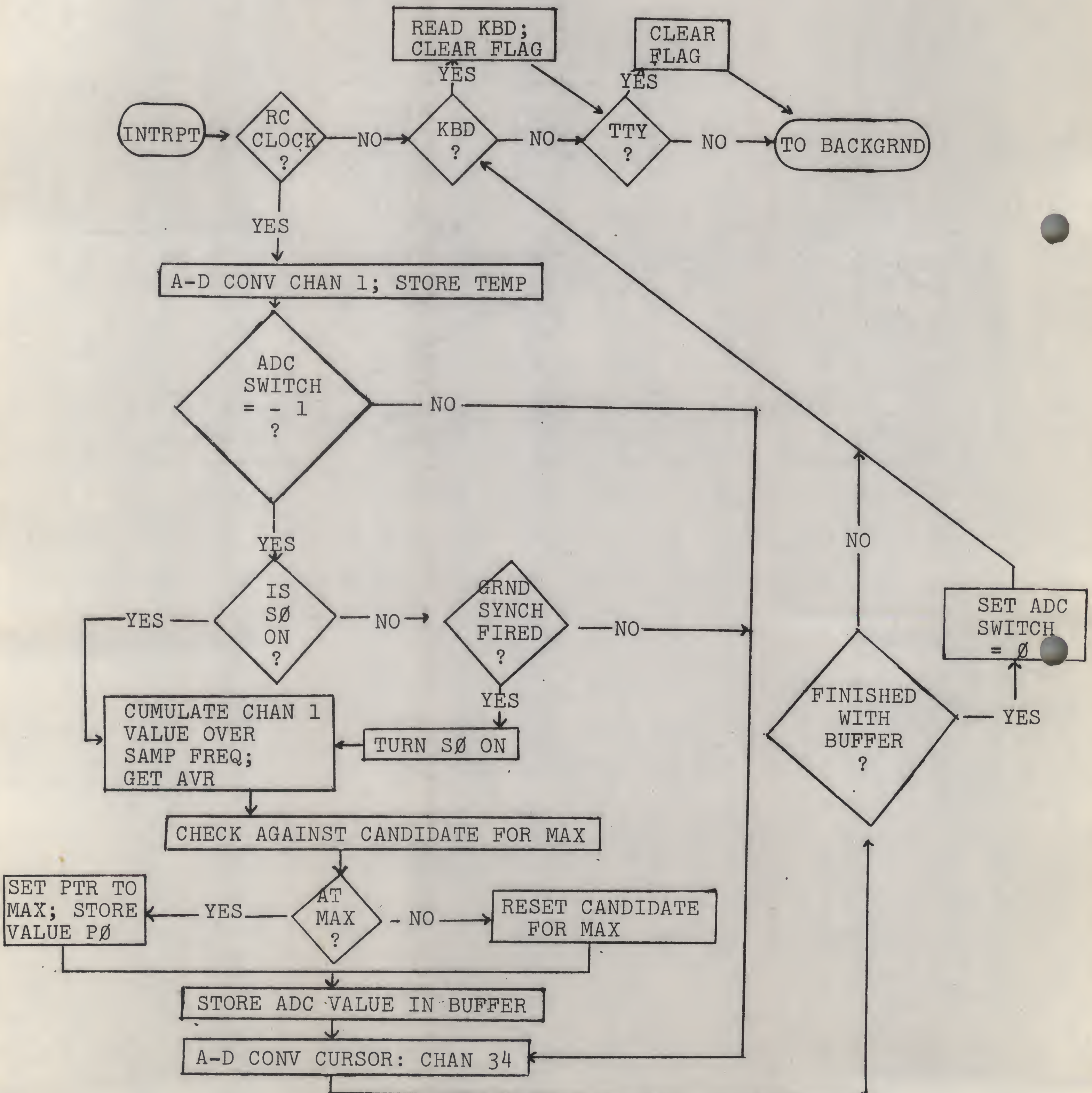


2. INTERRUPT SCHEME #1:

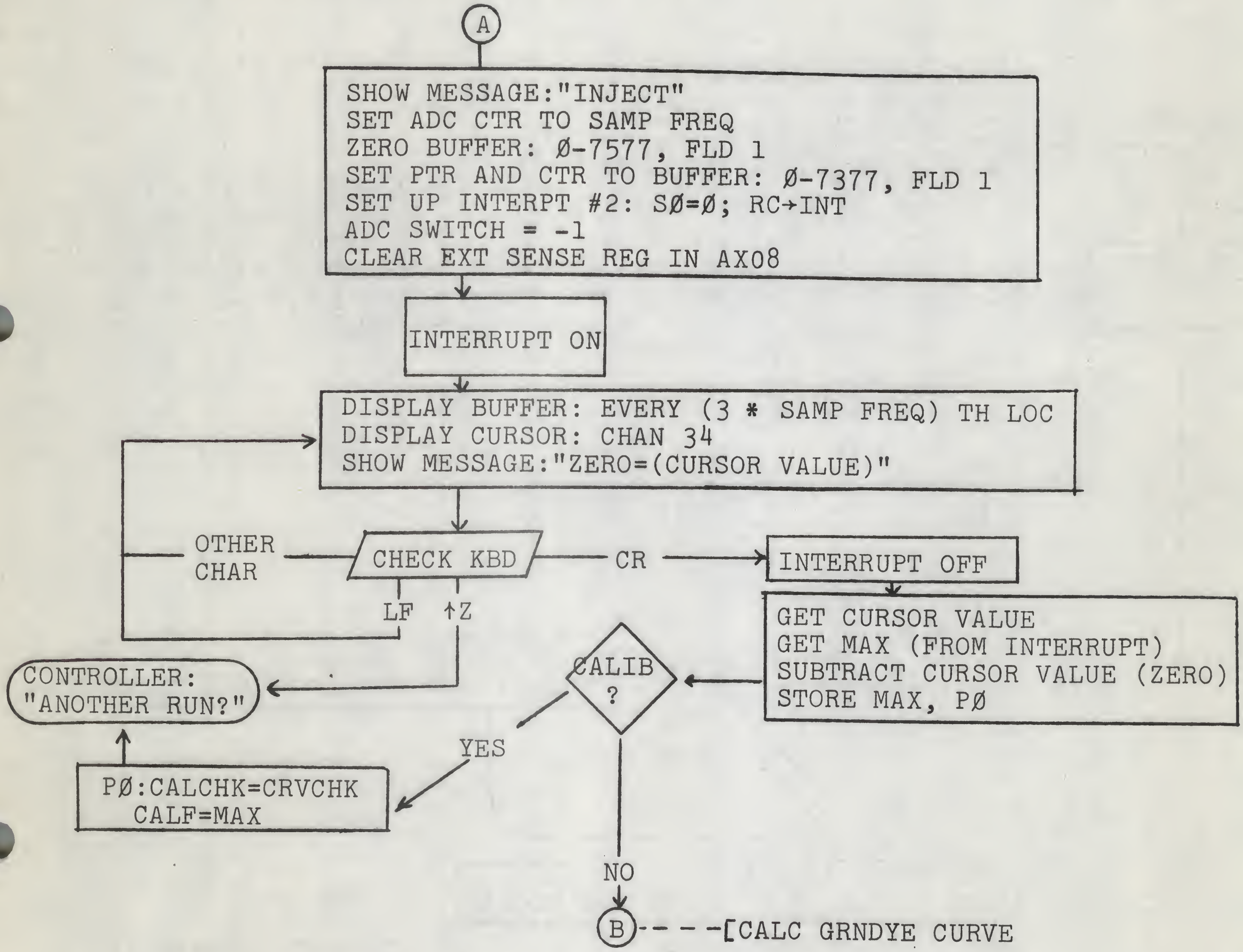


B. SAMPLING CHAN 1 TO GET GRNDYE CURVE:

1. INTERRUPT SCHEME #2:

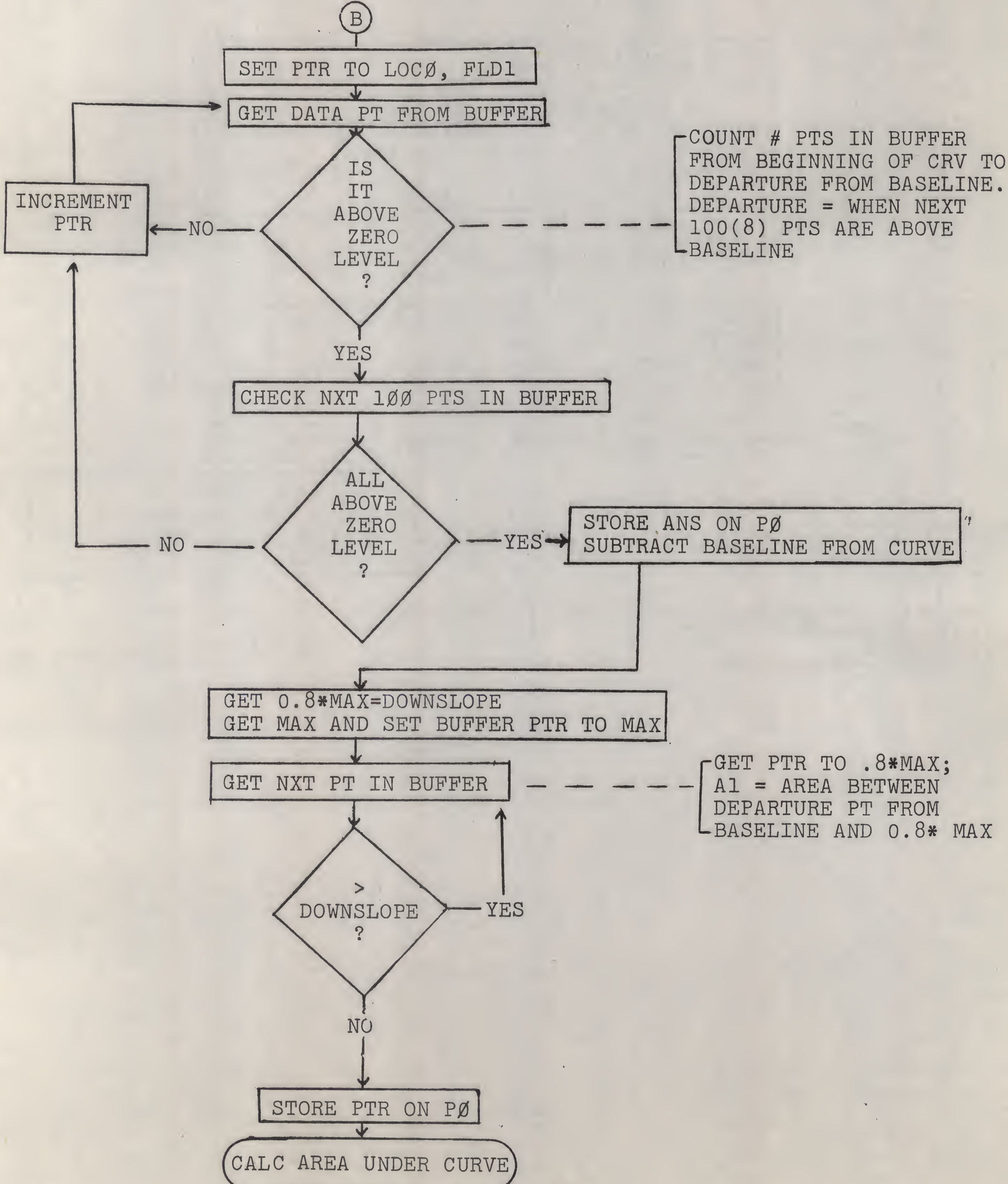


2. BACKGRND PRGM:



C. CALCULATION OF GREENDYE CURVE:

1. OBTAIN POINTERS FOR A1&A2:



2. Calculation of Area:

This is done by breaking down the area under the theoretic experimental curve into two parts: (1) A1 = area under actual curve from the point of departure of the curve from baseline (set by the "zero" cursor) to the point past the maximum where the ordinate (deflection) is 80% of maximum; A2 = area under the theoretic curve from the 80% of maximum point (downslope) to infinity. By logic as outlined in Section 1 above, the program, having calculated the maximum value and its location in buffer (interrupt scheme #2) and having been given (from the cursor level) the level of the baseline, first obtains a pointer to the departure point and a pointer to the location in buffer for "downslope".

A1 is calculated by Simpson's rule on the unaltered data in buffer from the departure point to downslope. This calculation uses the following formulae:

(1) For even number of points:

A1 = (1/3)*[2*SUM + 4*D(D-1)+D(D)]

(2) For odd number of points:

A1 = (1/12)*[8*SUM + 15*D(D-2)+12*D(D-1)+5*D(D)]

where

D(D) = deflection at "downslope"

SUM = cumulative sum from D(1) [first point after departure from baseline] to D(D-2) for even or D(D-3) for odd.

A2 is calculated by two methods: (1) a shortcut method whereby the area from "downslope" to the point where the deflection = 50% of "downslope" is doubled to approximate the area from "downslope" to infinity under the theoretic negative exponential curve; the flow calculated with this method of calculating A2 is called Q1; and (2) a least squares fit to the curve log(deflection) vs x from "downslope" to the point of recirculation. The latter is calculated by finding the natural logarithm of each point from "downslope" to the end of the curve. Then a least squares fit is obtained for this straight-line from "downslope" to the point where the deflection = 50% of downslope. From the formula for this straight-line, the theoretic points are calculated from here to the end of the curve and are compared with the logarithms of the actual deflections. If all actual points lie above corresponding theoretic points, recirculation is said to have occurred, the least squares fit is accepted and A2 is calculated from it. Otherwise, the process is recycled, the program adding the next point beyond 50% of downslope to the least squares fit, and so forth.

During these calculations the buffer (every third point) is displayed along with the messages "Q1=xxxx" and "Q=xxxx", giving the values of cardiac output by the alternate method and the method of least squares, respectively. This display occurs during an interrupt, the background program being the calculating program described above.

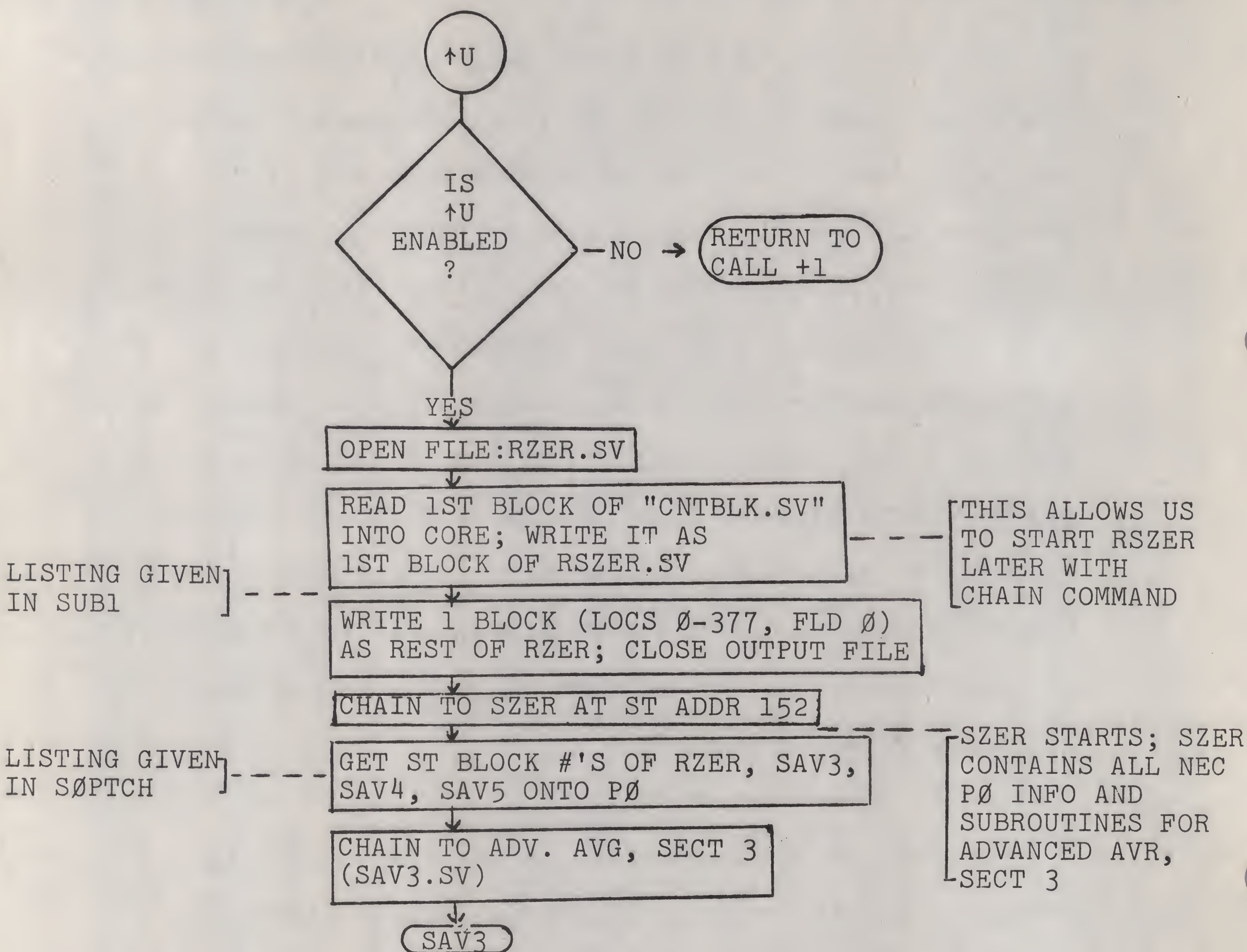
3. Buffer:

Initially, the buffer (locs Ø-7377, Field 1) contains the data sampled by A-D conversion of Channel 1 in the following format: a integer representing the value, followed by two entries of 0, to represent a single sample from the beginning of the curve to its end, whereupon the remainder of Field 1 (74ØØ-7577) contains all Ø's. During calculation for least squares fit, the portion of the curve from "downslope" to the end of the curve is written (as log deflection) in standard floating point format [loc 1 = exponent to base 2; loc 2 = high order mantissa; loc 3 = low order mantissa]. After calculation of cardiac output, this portion of buffer is reconverted to the original format.

Finally, before the buffer is written in DTA1 by the mean program, the individual entries from beginning to end are floated. The end of the curve is recognizable, since subsequent entries are Ø.

VII. MANAGEMENT OF ↑U PSEUDOINTERRUPT:

A. FROM CONTROLLING PROGRAM TO SECT 3, ADVANCED AVERAGER:



B. FROM ADVANCED AVERAGER, SECT 3 TO CONTROLLER: