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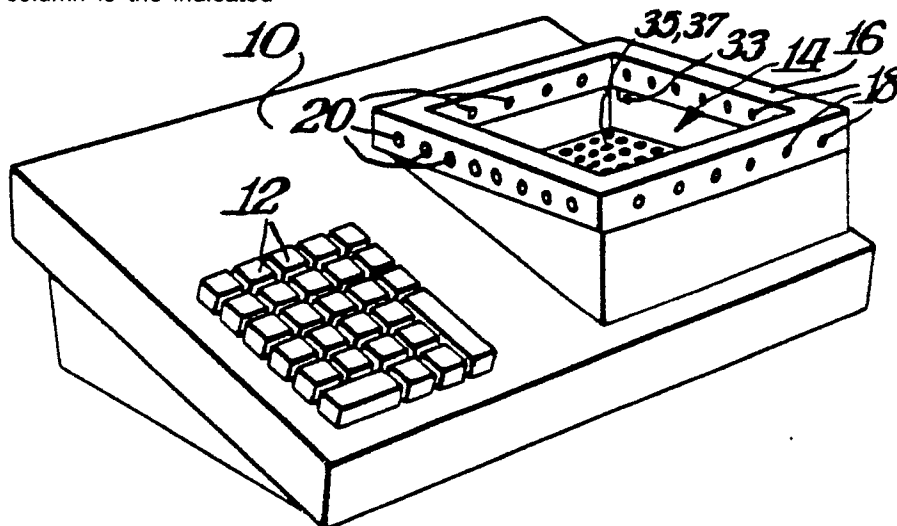
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**Location identifying means.**

A system for positively identifying which one of a plurality of receptacles has received a sample is disclosed. It includes means for sequentially sensing the presence, along rows and columns, of tubes for dispensing samples. The receptacle at the intersection of the sensed row and column is the indicated one.

*Fig. 1.*



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## LOCATION IDENTIFYING MEANS

### BACKGROUND OF THE INVENTION

With the increased utilization of analytical and clinical instruments there is a decided trend toward automatic sample handling. With such automatic sample handling the user typically will place the patient or other sample into various receptacles of a rack or tray or plate for later automatic analysis.

The plate may then be manipulated to position the respective receptacles in the plate under a sampling position at which a needle is introduced into the open receptacle, the sample withdrawn, and dispensed into the testing instrument for processing. More recently with the advent of microprocessor control of several mechanisms the sampling needle has been positioned and manipulated into each of the respective receptacles to withdraw a sample for processing.

Whichever system is used, a weak spot in automatic sample handling is the inability to ensure the technician or the user has placed the sample in a designated receptacle and has not placed two or more samples in a single receptacle. The receptacles can be numbered trusting the technician to place a sample in the proper numbered position. Being fallible, the technician can just as easily place the sample in the wrong receptacle. This is particularly true when microtiter plates are used.

Microtiter plates typically are plastic plates having a plurality of receptacles located in rows and columns. Since the size of the plate is small and the size of each receptacle even smaller, it is difficult for the technician to use a pipet or other dispensing device such as syringe to introduce the various samples to be analyzed into the proper receptacles. It is very easy for the technician to improperly dispense a sample and thereby lose track of a particular patient sample. In fact most systems in use today rely heavily upon the integrity of the technician to insure that such confusion and mispositioning does not take place.

Experience has shown that this is not always the case. The human factor being present always affords the opportunity for a sample to be misplaced or even to have two samples placed in a single receptacle causing unnecessary confusion and a requirement that samples be run a second time. All this adds to the inconvenience of the patient and those requiring the results of the test. Also if samples are mixed up, considerable danger to the patient could result.

### SUMMARY OF THE INVENTION

Many of these disadvantages of the prior art are alleviated or reduced by a system which positively identifies the actual receptacle location of a sample which is introduced into one of a plurality of receptacles disposed in an array of rows and columns. The samples, of course, are introduced into the respective receptacles by some sort of a dispensing tube such as a pipet, syringe or the like by a human or robotic operator. The system for identifying such receptacle locations comprises first means for sensing the presence of the dispensing tube contiguous any of the rows of the receptacles, second means for sensing the presence of the dispensing tube contiguous any of the columns of receptacles, and means responsive to each of the first and second means for providing a signal indicative of the location of the receptacle lying at the intersection of the row and column in which the presence of a dispensing tube was sensed, thereby positively identifying the position of a receptacle associated with the sample dispenser tube. Preferably the presence of a dispensing tube is sensed only if the tube is contiguous a row or column continuously for a predetermined period of time. Additionally a means are provided that are responsive to the signal for providing a visual indication of the location of the sensed receptacle.

The first and second means each comprises a light emitting diode and a light detector positioned at opposite ends of each row and column, each light-emitting diode being activated in sequence. Preferably the detectors are observed in a similar sequence. This has the advantage of reducing power required and also reducing the complexity of the system that would be required for a simultaneous sensing of all the rows and columns. Sequential sensing provides entirely sufficient speed when dealing with a human operator. Finally means are included to illuminate a desired receptacle in which a sample is to be placed to aid the technician. Thus even if the sample is introduced into the wrong receptacle, the location of the sample is detected and recorded.

### BRIEF DESCRIPTION OF THE DRAWINGS

The invention may be more fully understood from the following detailed description thereof taken in connection with accompanying drawings which form a part of this application and in which:

FIG. 1 is a pictorial representation of an instrument constructed in accordance with this invention for accommodating a microtiter plate and automatically ascertaining the location of the receptacles in the plate in which samples are introduced;

FIGS. 2A, 2B, and 2C are plan, front and side elevational views of the microtiter plate;

FIG. 3 is block diagram of a system for positively identifying the receptacle location of samples constructed in accordance with this invention;

FIGS. 4A and 4B are certain schematics used at a workstation to cooperate with the sensors for each microtiter plate depicted in FIGS. 2A-C;

FIGS. 5A-L are a series of flowcharts describing the sequencing of the microprocessor used in the workstation circuits; and

FIGS. 6A-D are flowcharts depicting the operation of the system of FIG. 1.

### DESCRIPTION OF THE PREFERRED EMBODIMENT

A typical environment in which the system of this invention may be used is seen most clearly in the pictorial representation of FIG. 1. This figure shows an instrument 10 having a keyboard 12 and a cavity 14 adapted to receive a microtiter plate or other matrix type device capable of providing or holding receptacles adapted to receive samples to be analyzed. At the top of the cavity 14 there is a ring or frame 16 mounting on two adjacent sides infrared, light-emitting sources such as light-emitting diodes 18 (LED) and on the remaining, adjacent two sides corresponding light detectors 20. The diodes and detectors define a matrix or array configuration with the points of intersection of the paths between the respective diodes and detectors corresponding to the receptacle positions on the microtiter plate.

The microtiter plate is seen more clearly in FIG. 2. While a microtiter plate is shown, it is apparent that this could just as well be racks or a tray of some type holding various receptacles, either fixed or movable, adapted to receive samples to be analyzed. The only criteria is that the various receptacles should be arranged in rows and columns so that their positions might be sensed by light from the preferably orthogonally directed LEDs 18 and detectors 20.

The microtiter plate itself preferably is constructed of molded plastic defining a plurality of receptacles 24 arranged as noted in rows and columns. The top of the receptacles 24 is covered by a thin film 26 such as an ionomer resin which may be preslit as at 29 to provide an access for each of the receptacles 24. One side of the micro-

titer plate preferably has a barcode label 31 attached thereto for identification purposes. Furthermore the receptacle 14 (FIG. 1) has a barcode reader 33 of known type for sensing the barcode. It will be noted that the LEDs 18 and detectors 20 are in a plane above that of the microtiter plate 22.

As may be seen most clearly in FIG. 1, the bottom surface of the cavity 14 contains a number of orifices 35 in which are positioned visible light-emitting diodes 37. Each diode 37 corresponds to one of the receptacles 24 of the microtiter plate. This will facilitate, as will be described hereinafter, the illumination of a particular receptacle in which the sample is to be placed. There may be a microtiter plate sensor (an optical sensor) positioned to sense the presence of the microtiter plate in the cavity 14. For the sake of clarity the sensor is not shown.

There may be seen in FIG. 3, a diagram of the sample entry controller, shown in FIG. 1, which permits the positive identification of the receptacle location of an introduced sample. Thus the controller 10 includes a microprocessor 34 which may be a Motorola MC68701. The microprocessor is connected to operate infrared LED multiplexing circuitry which includes the LEDs 18 and the detectors 20 (FIG. 1). The microprocessor 34 also is connected to drive infrared LED multiplexing circuitry 36 which drives the LEDs 18 and detectors 20 (FIG. 1) and provides a return signal denoting the receptacle location in which a sample actually is introduced. At the same time visible LED multiplexing circuitry 40 controlled by the microprocessor is connected to drive the sample entry visible LED matrix 37 (FIG. 1). A keyboard interface 44 is coupled to the keyboard 12 (FIG. 1).

Finally an RS 485 interface 42 is connected through flex couplings J6 and J10 to a higher level host computer 50 and to the barcode reader 33 (FIG. 1).

The sample entry controller 10 has circuitry shown in FIGS. 4A and 4B adapted to operate with a six column, eight row microtiter plate, by way of example. The function of these workstation electronics, including the microprocessor 34, is to drive the various visible LED arrays 37 and the IR LED matrix 18 with its associated detectors 20. In addition, the microprocessor controls the plate sensor 32 and interacts with the keyboard 12. There are a total of 14 IR LEDs 18 and a corresponding 14 detectors 20. Eight of each are arranged along opposite sides of the matrix holder 16 (FIG. 1). Six of each are arranged along opposite, but orthogonal sides of the matrix holder to define the matrix with forty-eight intersections corresponding to the receptacles of the microtiter plate.

The microprocessor 34 is a single chip computer consisting of 29 parallel I/O lines, 128 bytes of ram, 2048 bytes of UV erasable ROM, and a serial communications interface. The microprocessor controls, as noted, two sets of multiplexers used to control the LEDs used in the system, i.e., the multiplexer system is one which turns the various LEDs and corresponding detectors on one at a time. They're turned on and off at a rate faster than that to which the human eye can respond so they appear continuously "on" to the observer. Since the LEDs are "on" one at a time, the power consumption for the panel is reduced.

Since the IR LEDs and their corresponding detectors are opposite each other in the orthogonal grid configuration as noted, the microprocessor is fast enough to illuminate an LED while looking at its corresponding detector's output. The microprocessor can then check the next location and so on until a positive response is found, i.e., the beam is disturbed, and the row or column location disturbed by the sample dispenser is located.

The microprocessor select switch IR LED will be "on" by setting addresses IRAD01-3. These output lines are coupled through suitable buffers 54 which convert TTL logic used in the microprocessor to the MOS levels used for CMOS switches. The outputs indicated as MIRAD0-3 control multiplexers 56 which are nothing more than analog switches to selectively connect the outputs of the detectors 20 sequentially to provide an output signal from the common terminal of the multiplexers 56. This output signal is connected to an amplifier 58. Voltage amplifiers 60 and comparator 62 provide an output "sense" signal which is coupled back to the microprocessor. This output signal is high if there is no change in the light passing from the actuated IR LED to its corresponding detector. On the other hand the output sense signal will be low if there is a change, i.e., there is a disturbance in the infrared beam passing from the LED to its detector.

The microprocessor also supplies six address lines VRAD0-2 and VCAD0-2 for the control of the selection of a single visible LED 37. These address lines, operate through decoders to address one of the eight rows (VRA0-7) of LEDs 37 and one of the six columns (VCA1-7) of LEDs 37. When one row is selected and one column is selected their intersection will result in one light 37 being illuminated.

The microprocessor also communicates with a higher level computer 50 over an RS 485 interface line 42 denoted by the block 42. This higher level computer commands the microprocessor as to which receptacle should be loaded, when to read the barcode, and when the operations are complete. These commands are all two letter commands followed by alphanumeric data if necessary.

These commands will be explained further with reference to flowcharts of FIG. 6. The keyboard 12 is connected to the input KBD1-8 of the microprocessor. The signals may be appropriately pulled up by 4.7 K ohm resistors and fed into the third port of the microprocessor. The information is strobed into the processor memory by the KBSTRB line connected to port 20 of the processor.

## OPERATION

In a typical operation, for example, the samples are loaded into the respective receptacles of a microtiter plate by a pipette, syringe, or other suitable dispensing device. The plate sensor detects the presence of the plate. One of the visible LEDs 37 indicates a particular receptacle in which the sample is to be loaded by highlighting this desired receptacle from below through the clear plastic microtiter plate. At the same time, the orthogonal grid of infrared LEDs and detectors are positioned around the perimeter of the cavity 14 in a plane above the microtiter plate. Thus when the loading device such as a pipet or syringe or the like breaks the infrared path of an LED/detector pair, the microprocessor which is constantly cycling through all of the IR positions will detect this beam disturbance. The microprocessor also determines which receptacle position has actually been loaded, i.e., whether it be the one highlighted or not. This actual position is compared to the desired position, i.e. the position of the visible LED that was lit and the user queried as to whether the loading was intended or not. The microtiter plate has a barcode reader which is read by the computer and recorded so that it may be transmitted to the host computer 50 (FIG. 3) for updating and continued use of the microtiter plate.

The operation of the workstation itself will be better understood with reference to the flow diagram of FIGS. 5. The first step (FIG. 5A) is to configure the peripheral hardware that is connected to the microprocessor. This requires the proper setting up of the serial interface parameters, the resetting of all array addresses for the light emitting diodes, and the checking of all random access memory (RAM). The next step is to set up a background routine which will cycle through the addressing of the infrared light emitting diodes. This will occur in the interrupt handler software. Every 20 milliseconds an interrupt will occur and at that time the software will update an address counter to select the next LED.

The interrupt handler will also check the infrared (IR) detectors for a beam disturbance. The handler will record the location of the disturbance, and flag the main routine that this has happened.

This may not be clear at present, but later in the discussion it will be clear how the software uses this information to determine where the user injected the sample.

The software now waits in a loop for a command to be entered by the computer or the user. If a command is not entered it remains in this loop forever. The only work being accomplished by the microprocessor is the servicing of the aforementioned interrupt. The flow out of this test routine has two possible paths (FIG. 5B). The user command entry is via a keyboard; therefore the computer must monitor the keyboard until information the user wants to enter is obtained.

Once the user entry is obtained the command must be decoded. Either the task is performed or the required information is sent to the host computer. The host computer is the alternate way of entering a command. The information is received by the microprocessor over an RS485 communications link. It is decoded and stored into a buffer until the entire command sequence is sent. Then a lookup table of valid commands is checked to see what the next task is. This routine is called DO COMMAND.

This routine goes through all possible command strings and either sends the program flow to accomplish a task, if a match is determined, or to the next command check. If all commands are checked and a valid match is not obtained, then the software flags the host computer with an error message (FIG. 5I and 5F). There are numerous error messages that can be sent to the host computer. The types are:

- 01 no microtiter plate installed
- 02 wrong well loaded, well ID detected
- 03 long load of microtiter plate
- 04 illegal command received from host
- 05 command buffer full - illegal user entry

Therefore, the type error that was just explained would result in an error code 4 being transmitted to the host computer.

At this point the software should actually have a valid command. Each one of the commands will be discussed in full (FIG. 5C). The first to be discussed is the plate input (PI) routine which allows the user to install a microtiter plate. The first step at the sample entry station is for the user to install a microtiter plate for the samples to be loaded. This can be done at any time, but for description sake, the host computer will coordinate this activity.

The first step of this activity is a valid PI command to be received from the host computer 50. The software transfers the flow to the PI routine (FIG. 5K) and monitor port 10 of the microprocessor. This port is used for many purposes but bit 8 is used to read the output of an IR sensor 32 (FIG.

4A) which is set in the cavity 14 (FIG. 1) at the optimum height to measure if a microtiter plate was installed properly. If this bit is set then the plate is in. Otherwise the software increments a counter. The counter is then checked to see if it is at the maximum. The counter at maximum indicates that the user has taken too long to install a plate. This results in an error 3 being sent to the host computer.

The normal exit, bit 8 set ... return, sends back an acknowledge signal to the host computer of the successful entry. The other capability that exists is the multiple feedback from the interrupt service routine. The background program is running constantly, and if a plate is installed all beams should be disturbed very close together. This information can be used as a check of the plate-in sensor 32 for correct operation.

The plate is now installed and the host computer knows that it is installed. The next step is the identification of the sample plate. The host computer will initiate this process by sending a BC command (FIG. 5E). The BC command tells the software to read the barcode tape 31 that is on the side of the microtiter plate 22 (FIG. 2A). Each plate has a unique barcode. This allows for all sample plates to be distinguished from one another.

The BC command also tells the software to send a command over another RS485 line to the barcode reader. The barcode reader initiates a read and after a successful one sends the valid barcode back to the workstation microprocessor. This requires that the workstation software look for a start character, which typically for barcode is an asterisk. The information following the asterisk will be stored in a buffer until the second asterisk is received. At this time the software has received a complete barcode. The information is moved from the temporary buffer that it was stored in, to a transmit buffer. The transmit routine is called, which allows for the transfer of any information in the transmit buffer to the host computer.

The host computer now has the information necessary to look up the data base for that particular plate. The plate being new will allow the user to enter samples into anyone of the 48 available receptacles. If the microtiter plate was previously used, the host computer would interrogate the database for that plate and determine the next available sample receptacle. Either way, the computer will enter the well number of the microtiter plate to be loaded.

The workstation software then will receive a command WN (FIGS. 5L and 5M) followed by two numbers. These two numbers represent the next receptacle that the host computer would like loaded. This does not mean that the user must enter sample into this receptacle, but it is desirable. The

receptacle is illuminated by the software sending a visible LED (VLED) address out to the visible LED selection logic. This will backlight the desired receptacle to be loaded.

The user will then take a sample and introduce it via a pipet or syringe into the lighted receptacle. The background routine will detect which set of orthogonal beams were disturbed, and set a flag in memory with the receptacle number. This information will then be sent back to the host computer either saying that the proper receptacle was loaded, or the number of the receptacle that actually was loaded.

This background program is designed to illuminate only one IR LED at any particular time. The software then monitors the detector response directly across from the LED. If a positive response is obtained, the software will then scan the opposite axis LEDs and detectors to obtain the other axis coordinate. This will now correspond to an actual receptacle position.

The samples can be repetitively entered until the user desires to stop. At this point the host computer 50 will request the workstation to inform the user to remove the plate. This is done by command routine RP (FIG. 5H). This routine flashes all the visible LEDs which indicates to the user to remove the plate. The software monitors the plate present sensor to determine when the user removes the plate. The microprocessor then sends back an acknowledge signal to the host computer for further operations with respect to this sample plate. A clear command CL (FIG. 5G) is sent and illumination in the sample cavity is removed.

This concludes the explanation of the simple sample entry software package. The software is relatively simple but allows for positive sample placement, and communications of sample entry parameters to a larger host computer. This circuitry and software does provide a cost effective means of positive sample entry into a chemical instrument.

With reference to FIGS. 6 there is shown a typical flow diagram of the manner in which the higher level or host computer 50 operates the entire system.

At the beginning of the program a command is sent to the workstation called PI which is (microtiter) plate insert as described above. Until there is a positive response back from the workstation, the host system 50 will stay in that loop continuously. Once it has finally received the sample plate (here a microtiter plate) it goes into a routine called get plate number from workstation. The host system then issues a BC command which is a barcode read command to the workstation. The workstation initiates the reading process and once it has gotten a valid barcode it returns that informa-

tion back to the host computer 50 and the host displays that plate number. The user if desired can compare the displayed plate number with the expected plate number just for another level of security in the system. When the host computes 50 receives the barcode number it associates a certain database with that plate. All of the plates have a unique number. Now it checks the database to see what is the next available receptacle in the microtiter plate. In the event that it's a brand new one of course it would be receptacle number 1. It displays the target well on the CRT screen of the host computer and it also sends the WN command to the workstation.

The WN command is followed by a two-digit number which is the receptacle that the user is to load. The workstation then illuminates the visible LED underneath that receptacle. The user on prompting inserts a sample into that receptacle thus breaking the orthogonal infrared beams as explained above. The workstation indicates the receptacle receiving the sample is right or wrong. All well illumination is removed-CL routine. Once the beam is broken, the workstation sends back a positive update and the databases are brought up to present and then the operator is prompted to remove the plate and that's when a RP command is sent to the workstation. If it was the wrong receptacle, the workstation will send the receptacle number where the sample was deposited. Then the host computer can update its database to reflect the actual receptacle. Now the system prompts the operator to get the patient I.D. number. At this point the user puts in a request for the test that they would like run on that sample. The RP command illuminates all visible LEDs underneath the plate and the user knows then to pull out the plate. The host computer displays "remove plate" on the CRT, and it waits for a positive response from that back from the workstation. Sample processing begins.

There has thus been described a relatively simple system which serves in a user friendly manner to assist the technician or user in applying samples into a sample holder in an appropriate manner and checking to insure the samples are properly inserted as instructed. A plastic receptacle is illuminated to show the user where to insert the sample and a relatively simple infrared LED-detector matrix is used to sense and determine whether or not the sample has been properly inserted into the desired receptacle. If not, the actual receptacle receiving the sample is sensed. Keyboard interfacing is provided as well as interfacing with a host computer. It is to be understood that whereas infrared diodes are illustrated, visible LEDs may be

used just as well. Also other sample introducing devices may be used as desired. Instead of a microtiter plate, a plurality of receptacles in racks or the like may be used.

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## Claims

1. A system for positively identifying which one of a plurality of receptacles, disposed in an orthogonal array of rows and columns has received a sample dispensing tube, the system comprising: first means for sensing the presence of the dispensing tube contiguous any of the rows of receptacles, 10

second means for sensing the presence of the dispensing tube contiguous any of the columns of receptacles. 15

means responsive to each of the first and second means for providing a signal indicative of the location of the receptacle lying at the intersection of a row and column in which the presence of a dispensing tube was sensed, thereby positively sensing the position of a receptacle associated with the sample dispenser tube. 20

2. The system of claim 1 wherein the dispensing tubes presence is sensed only if the tube is contiguous a row or column continuously for a predetermined period of time. 25

3. The system of claim 2 which include means responsive to the signal for providing a visual indication of the location of the sensed receptacle. 30

4. The system of claim 3 wherein the first and second means each comprise a light emitting diode and a light detector positioned at opposite ends of each row and column, each light emitting diode being activated in sequence. 35

5. The system of claim 4 which also included means to illuminate a receptacle in which a sample is to be placed. 40

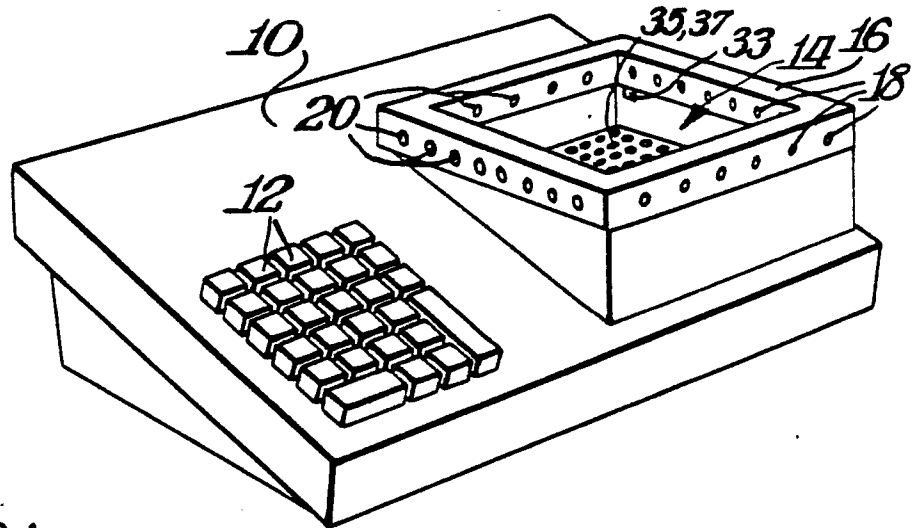
6. The system of claim 1 which include means responsive to the signal for providing a visual indication of the location of the sensed receptacle.

7. The system of claim 1 wherein the first and second means each comprise a light emitting diode and a light detector positioned at opposite ends of each row and column, each light emitting diode being activated in sequence. 45

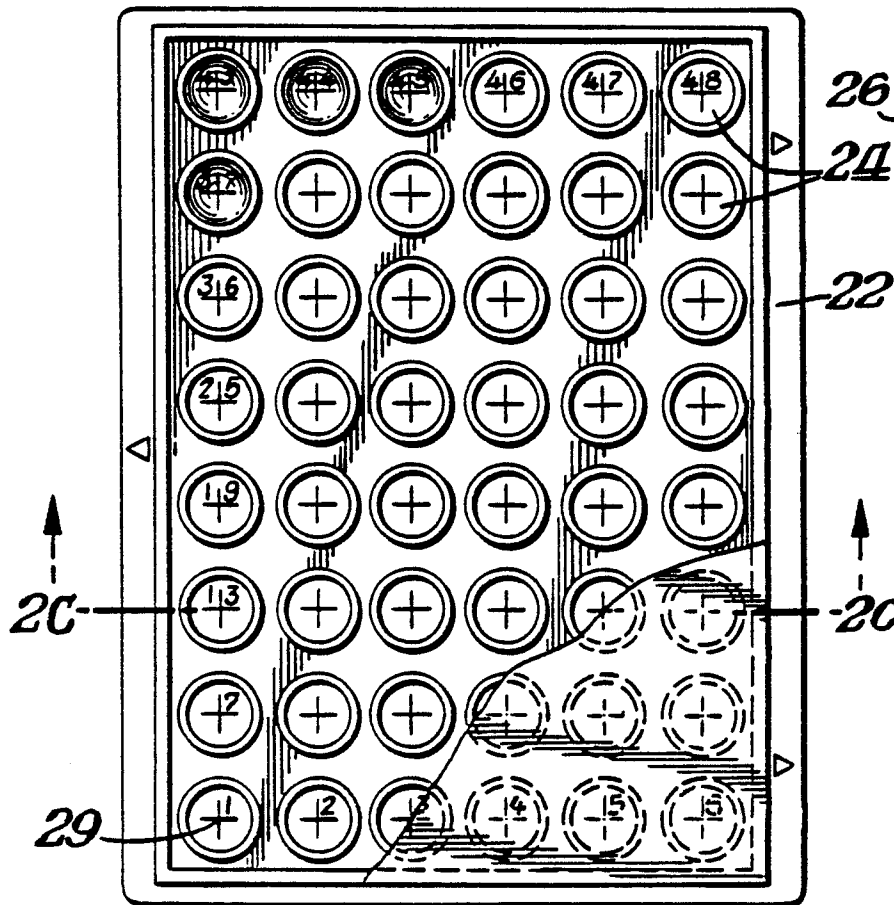
8. The system of claim 1 which also included means to illuminate a receptacle in which a sample is to be placed. 50

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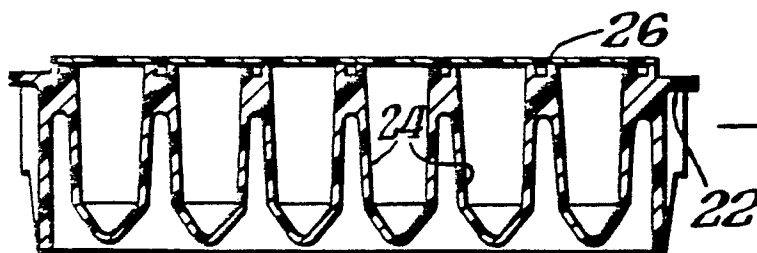
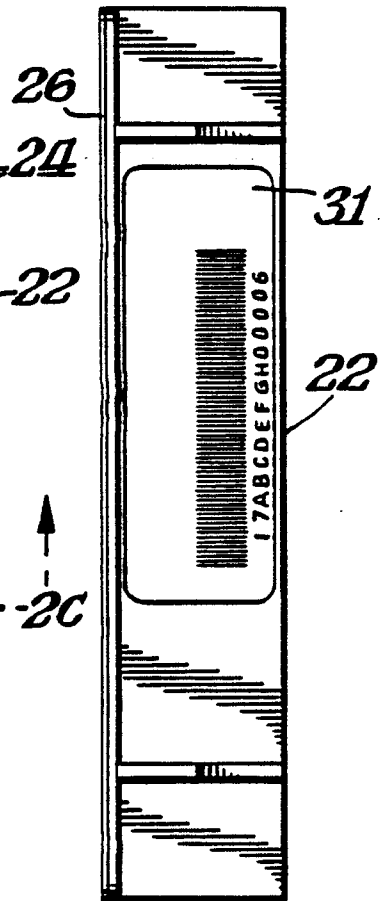
*Fig. 1.*



*Fig. 2A.*



*Fig. 2B.*



*Fig. 2C.*

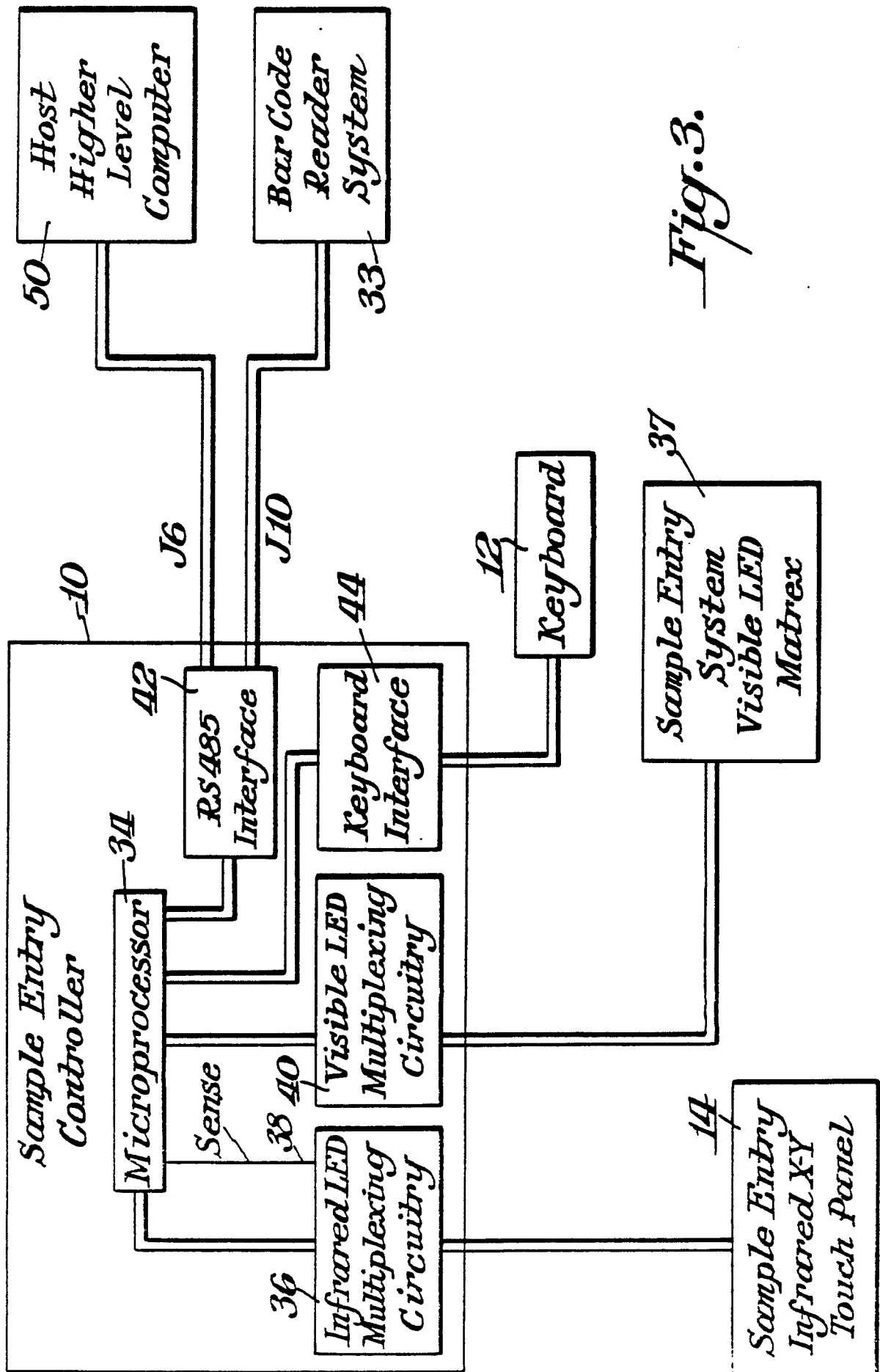
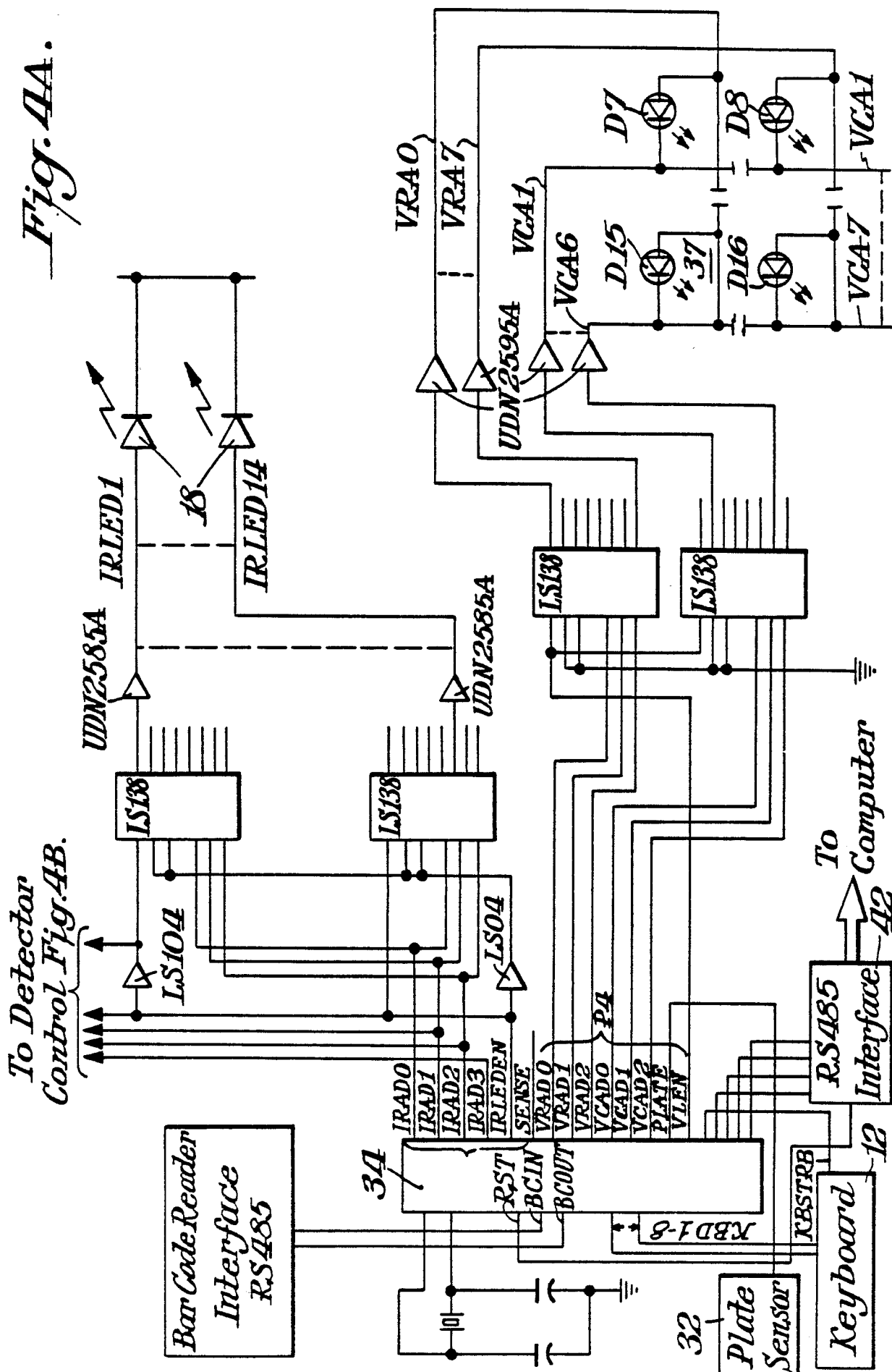


Fig. 3.

Fig. 4A.



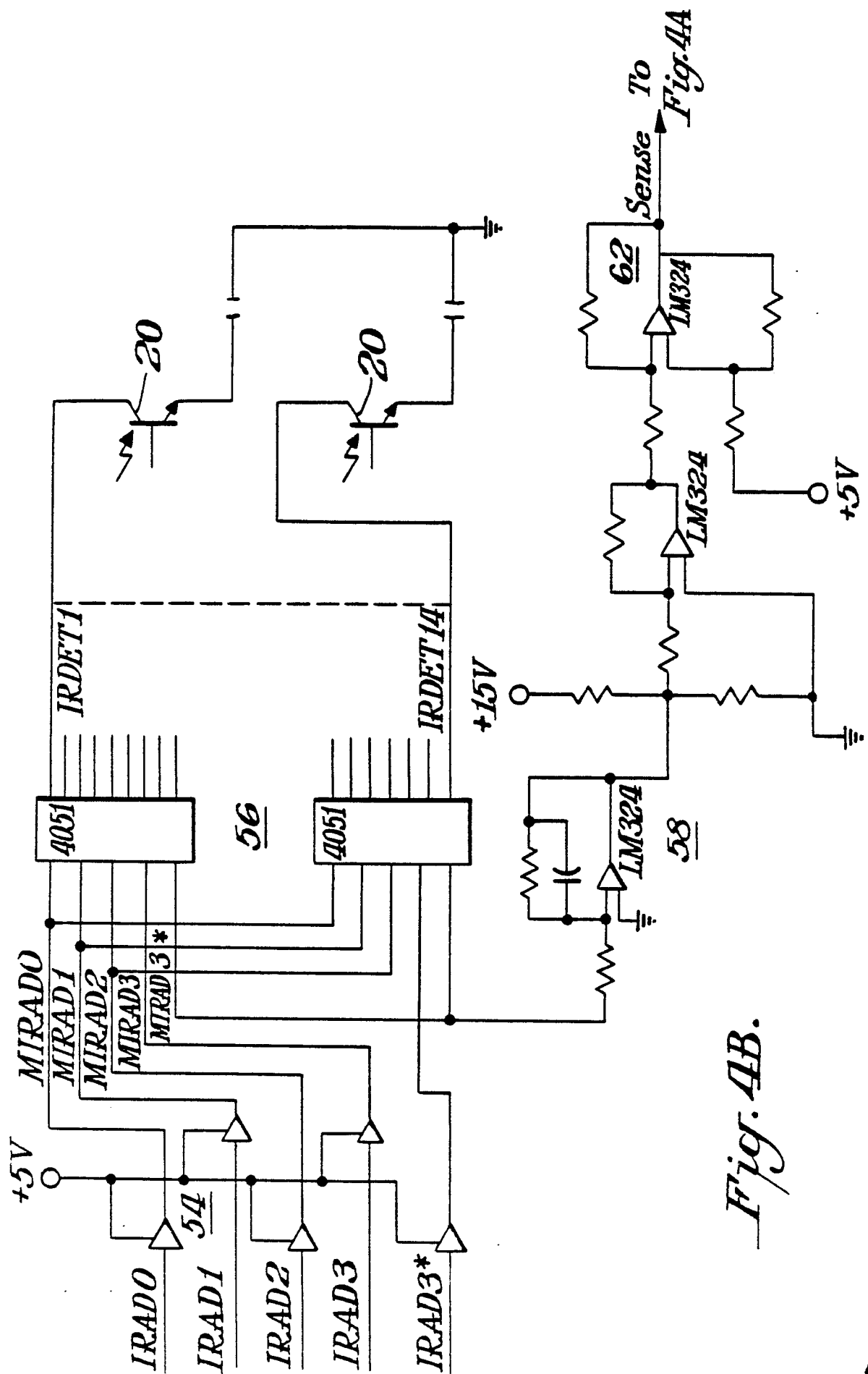
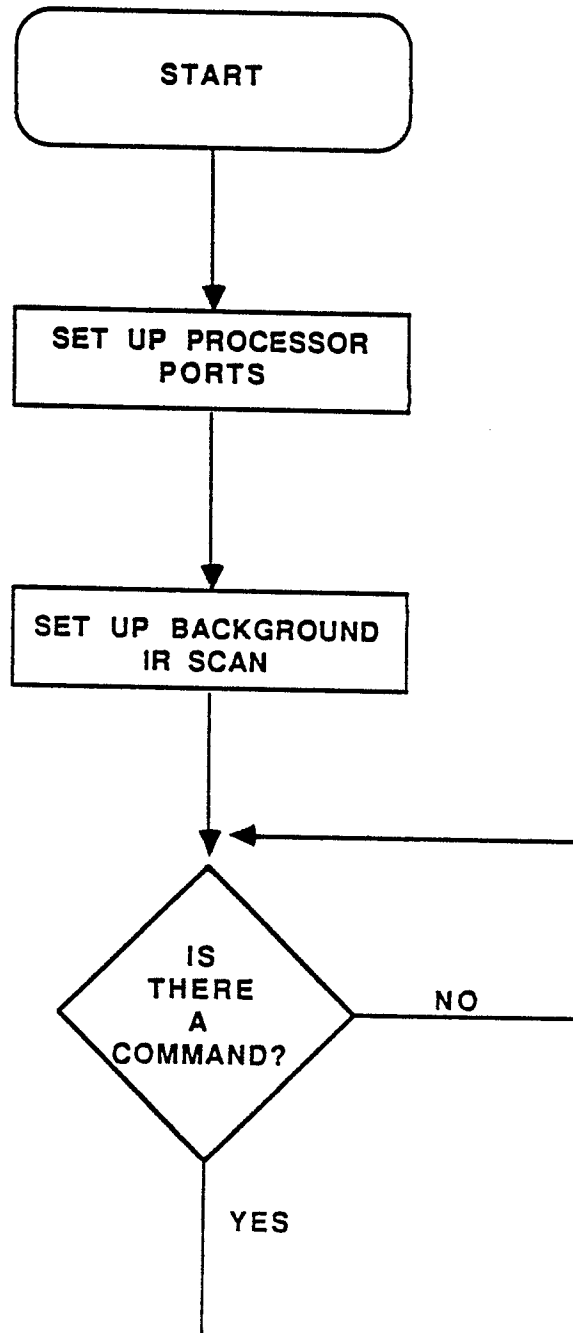
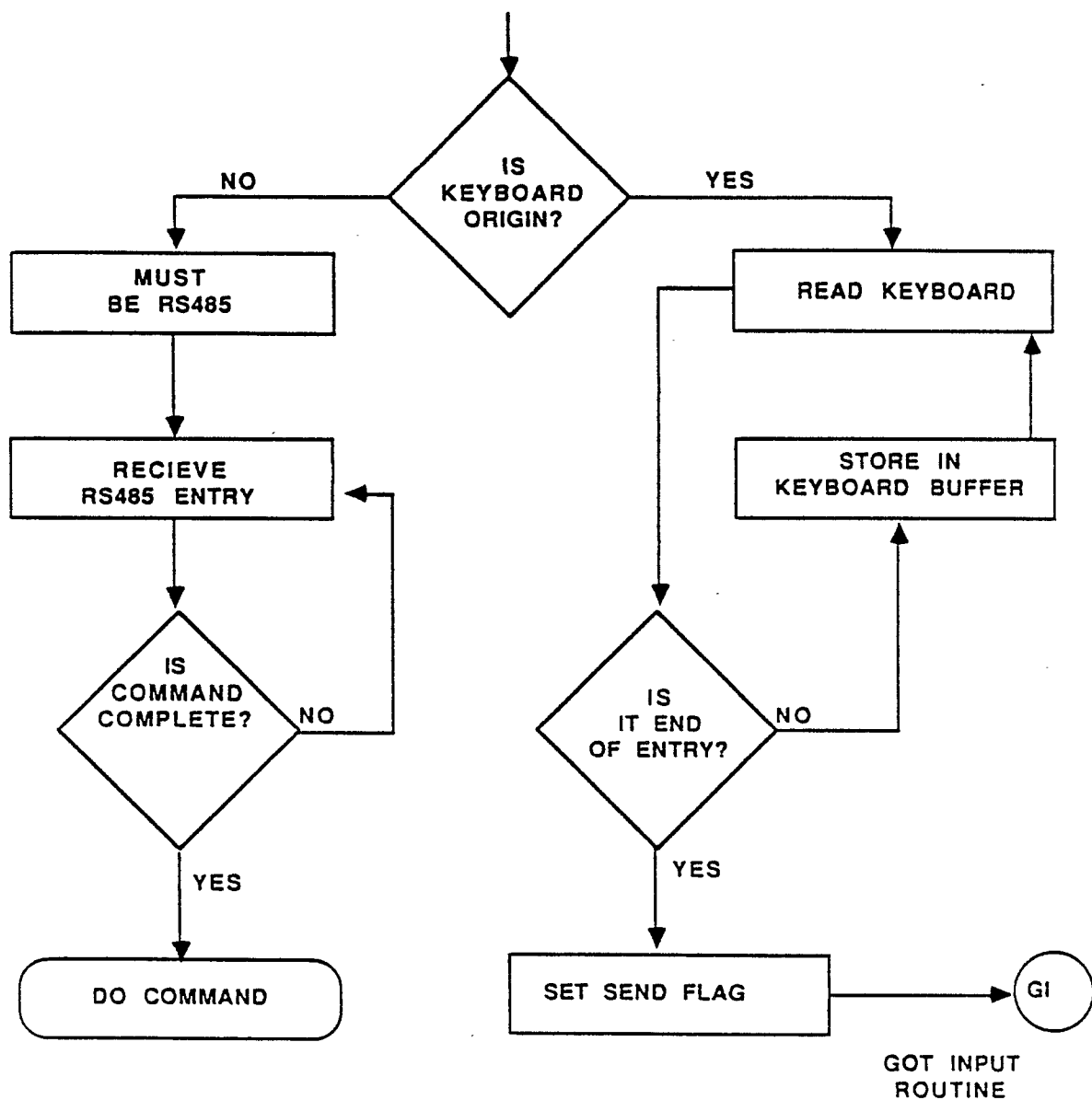
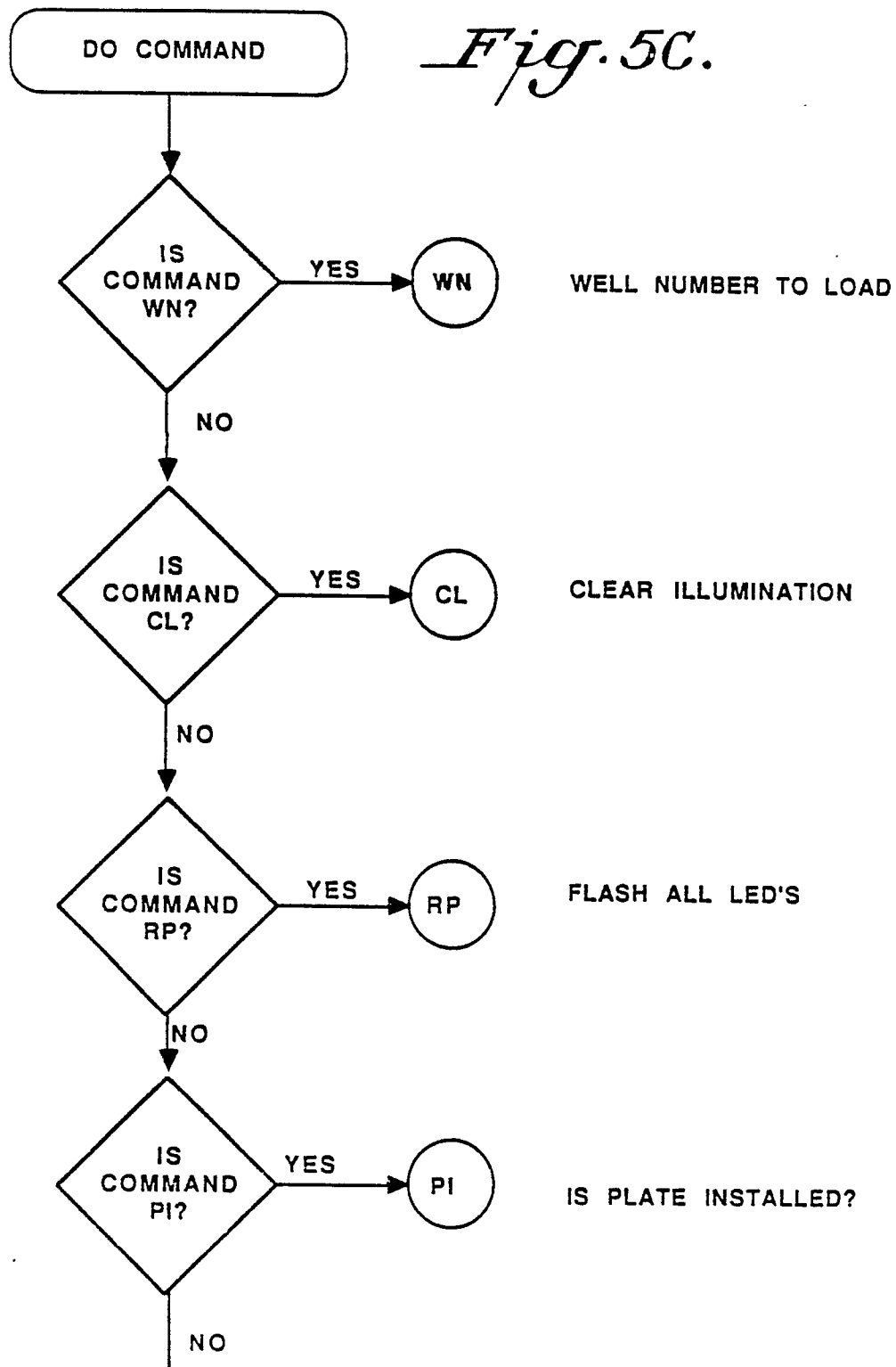
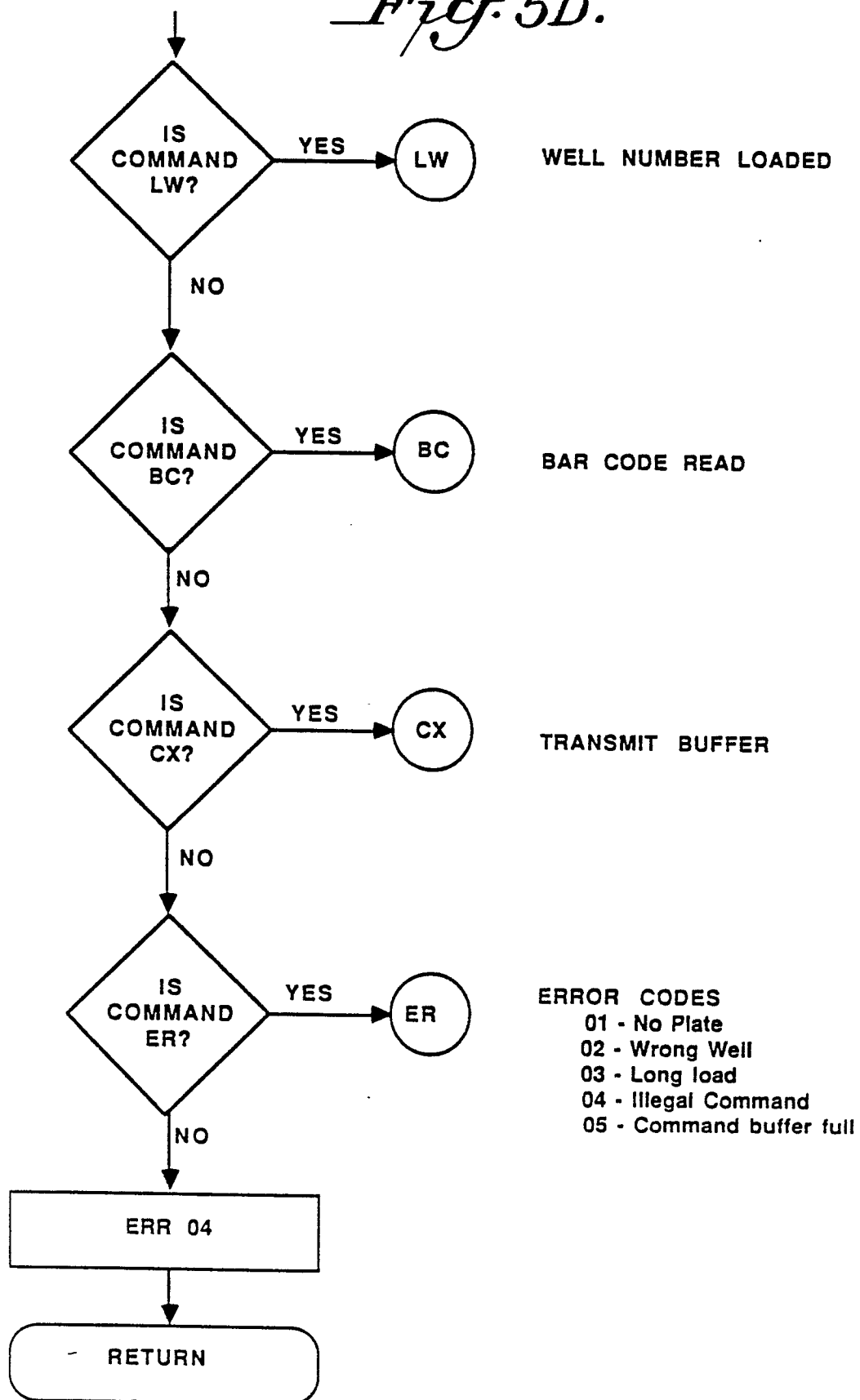


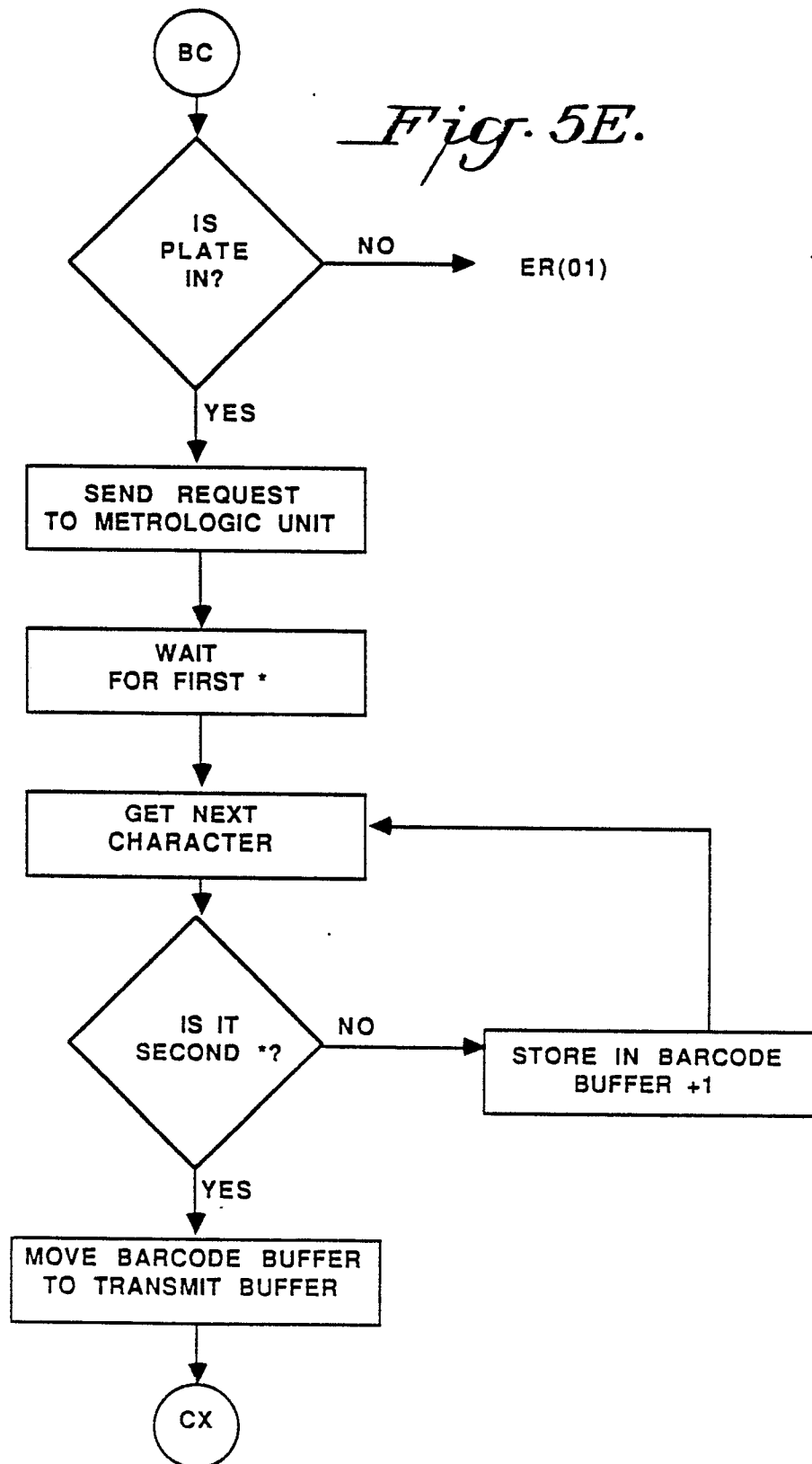
Fig. 4B.

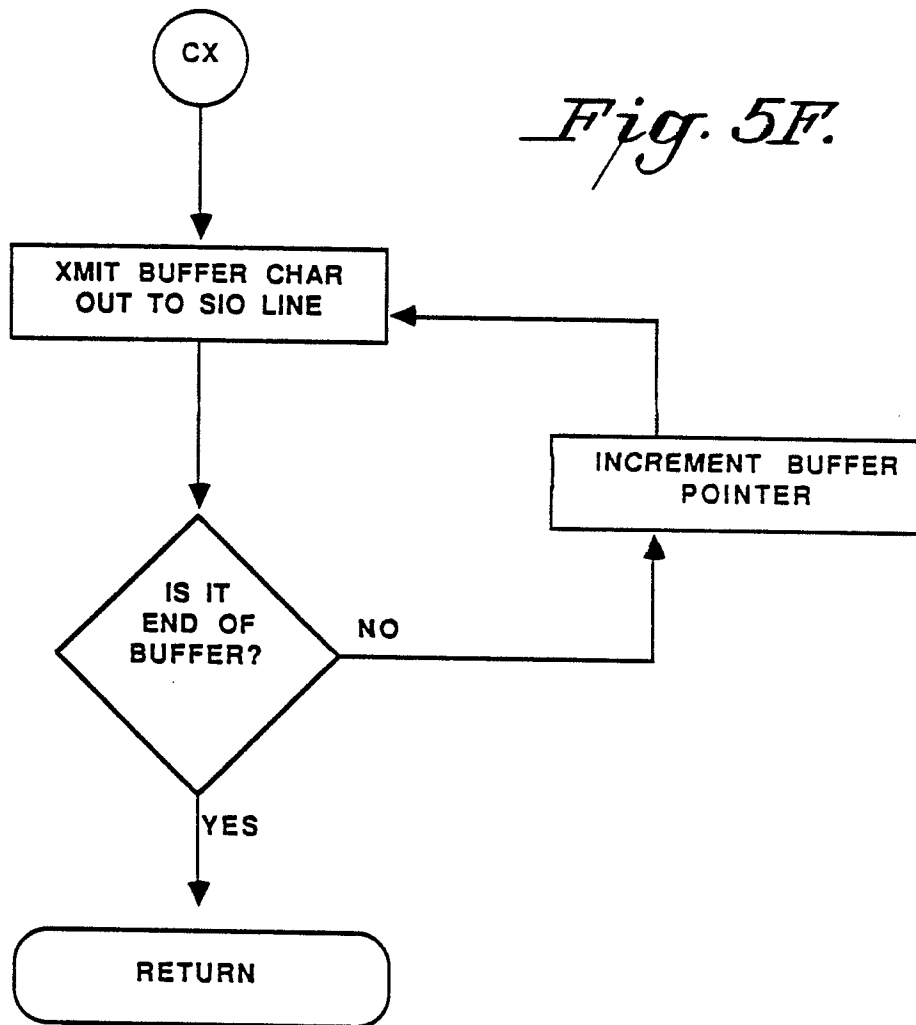
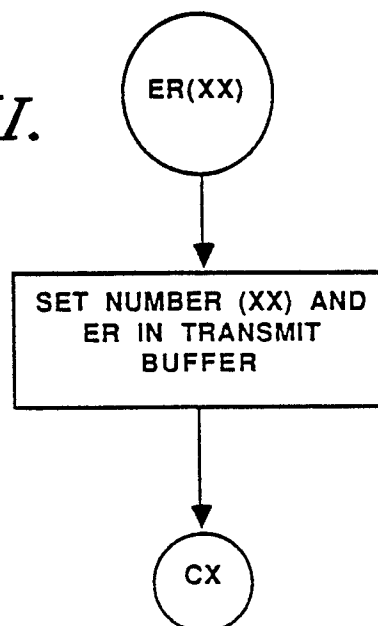
*Fig. 5A.*

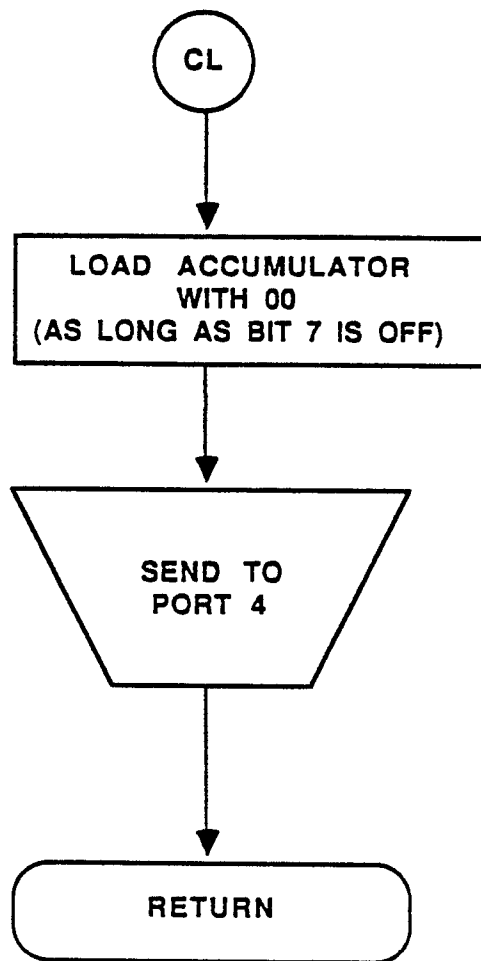
*Fig. 5B.*



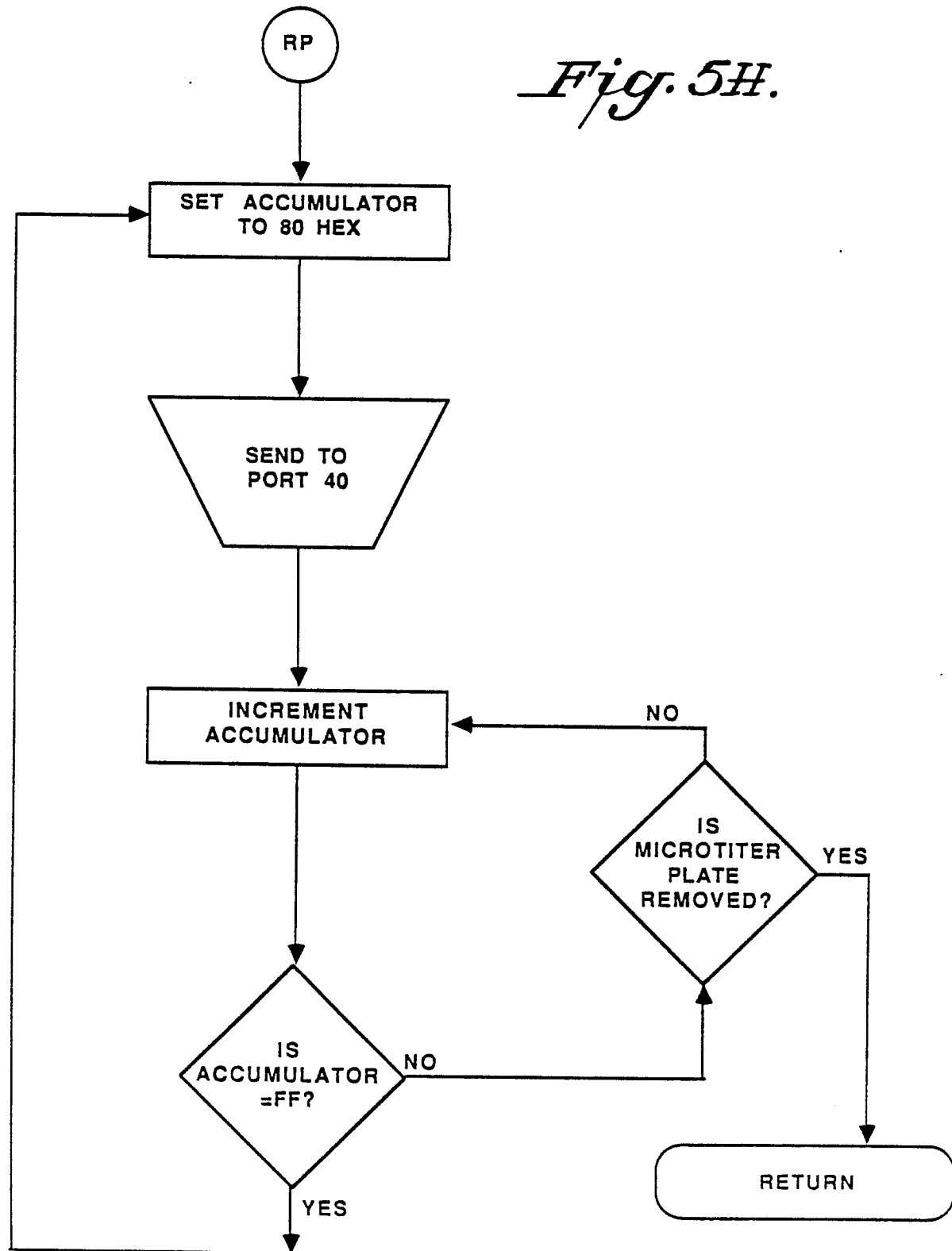
*Fig. 5D.*

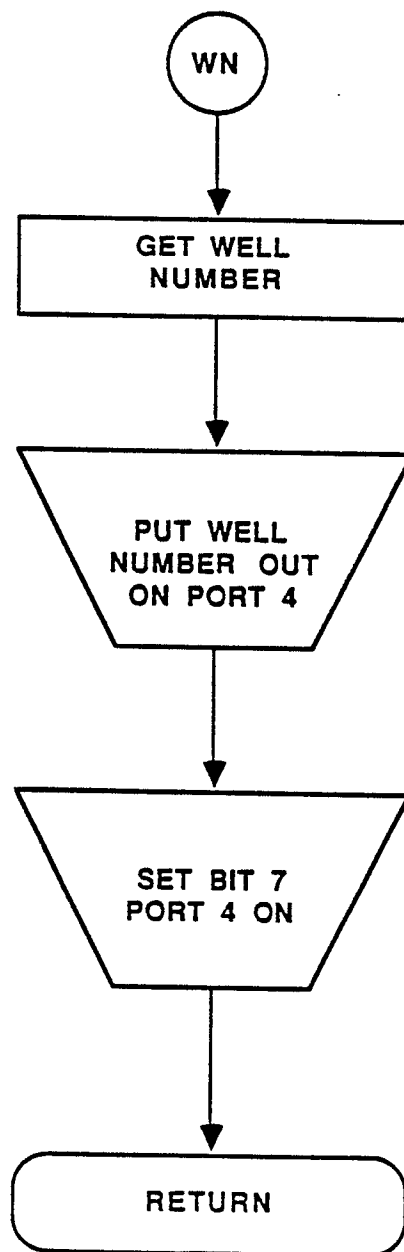
*Fig. 5E.*

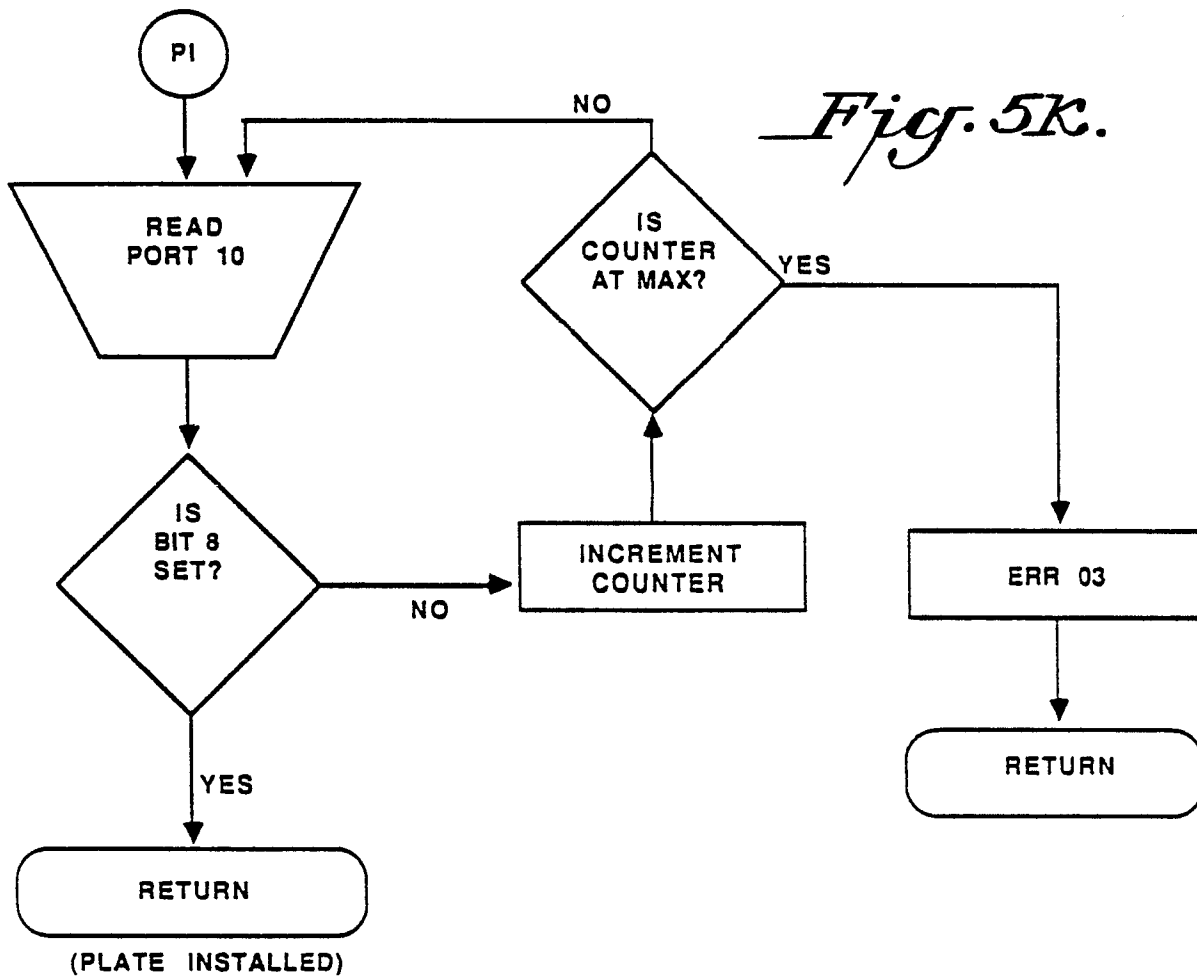
*Fig. 5F.**Fig. 5I.*

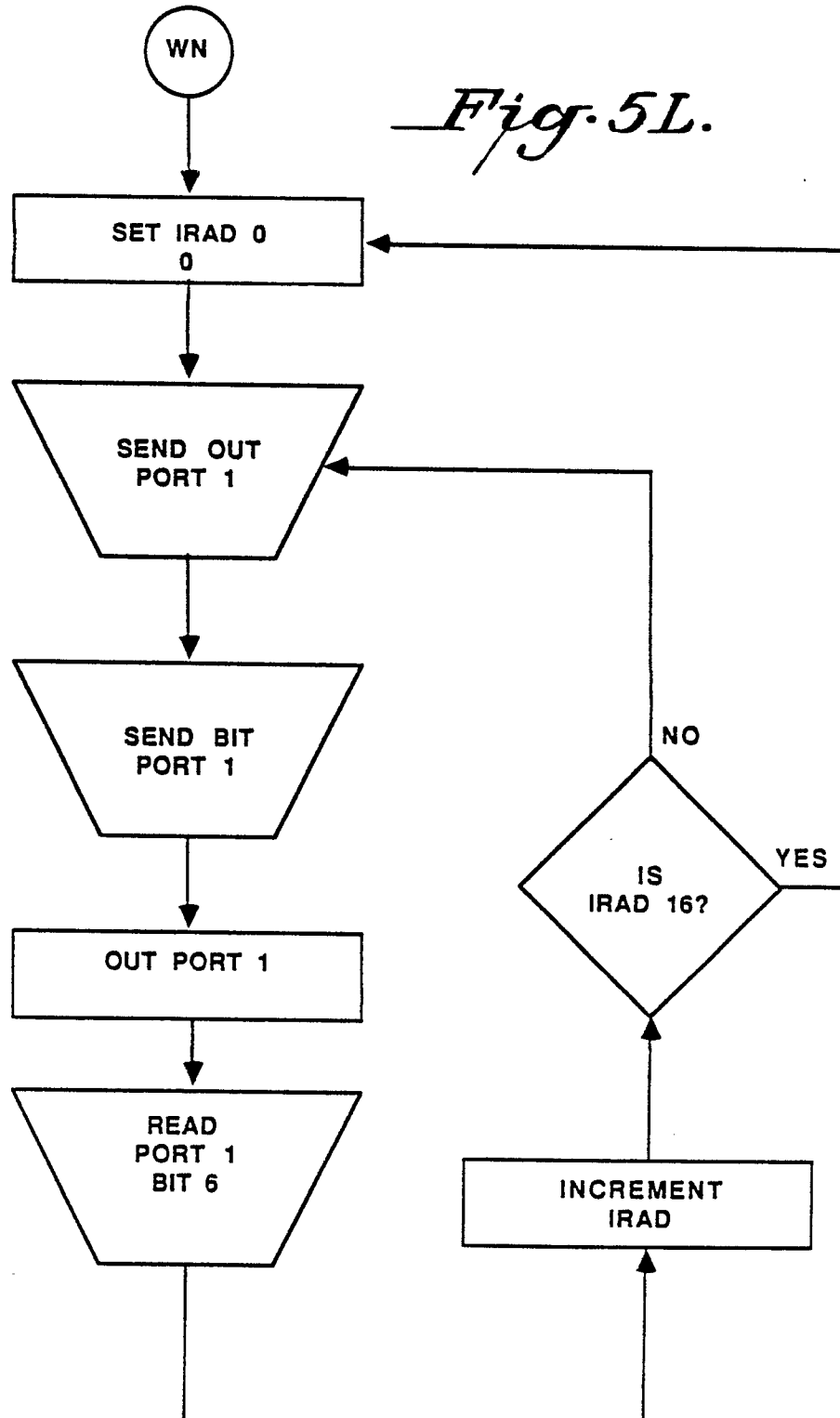


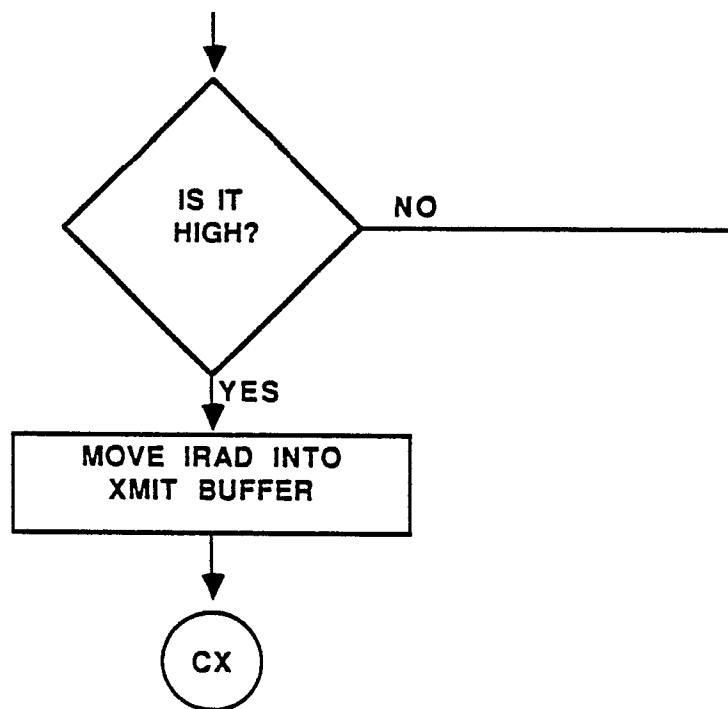
*Fig. 5G.*

*Fig. 5H.*

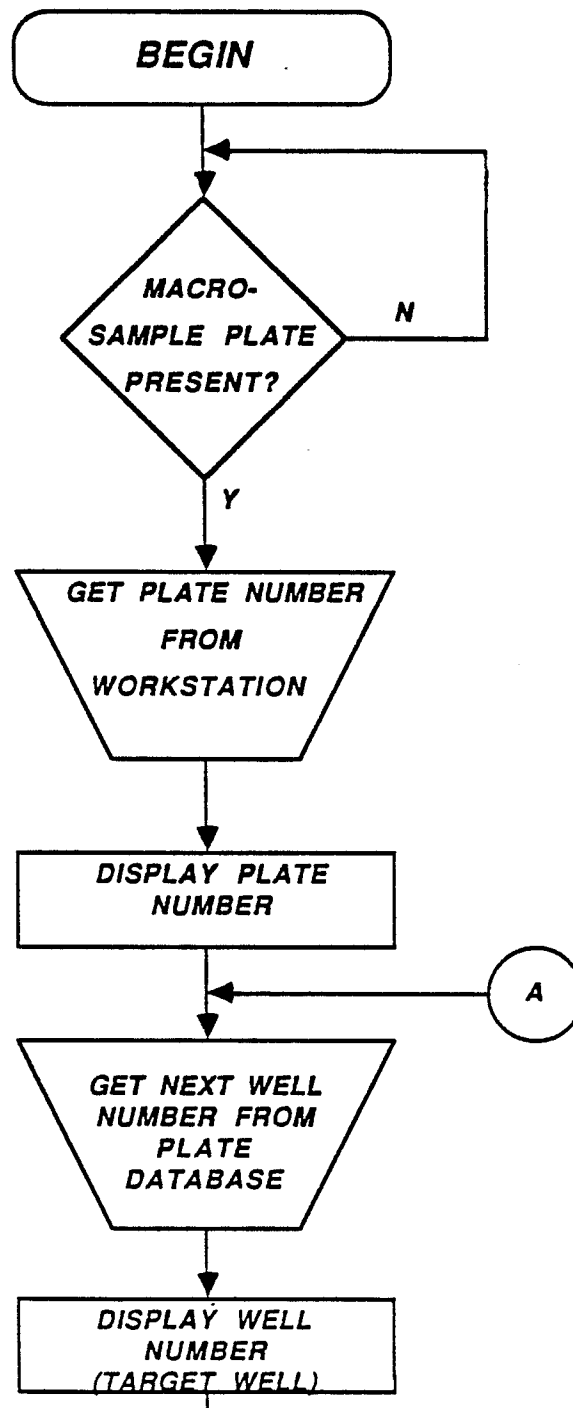
*Fig. 5J.*

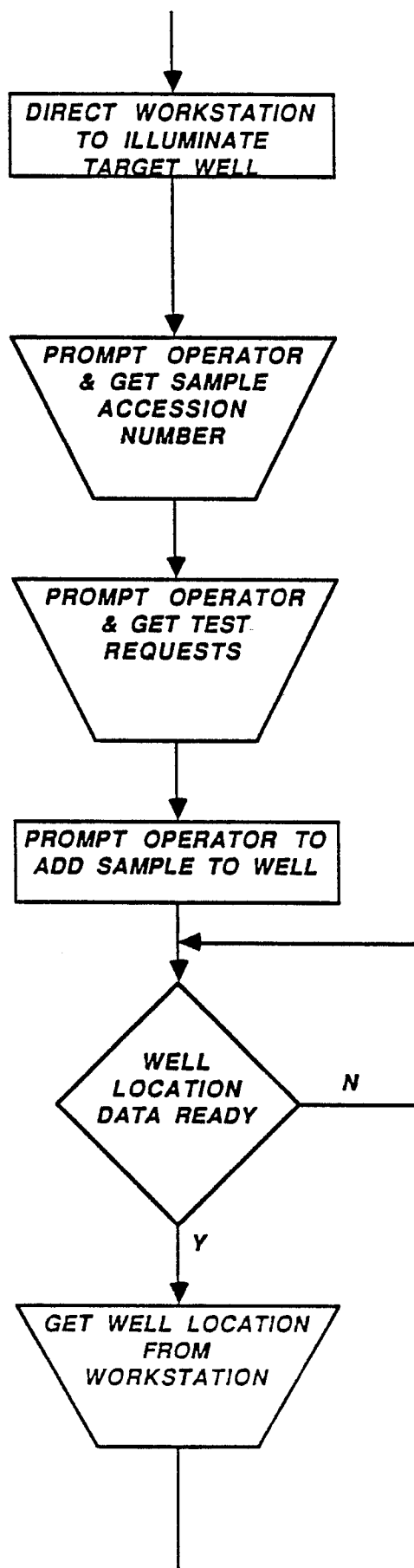


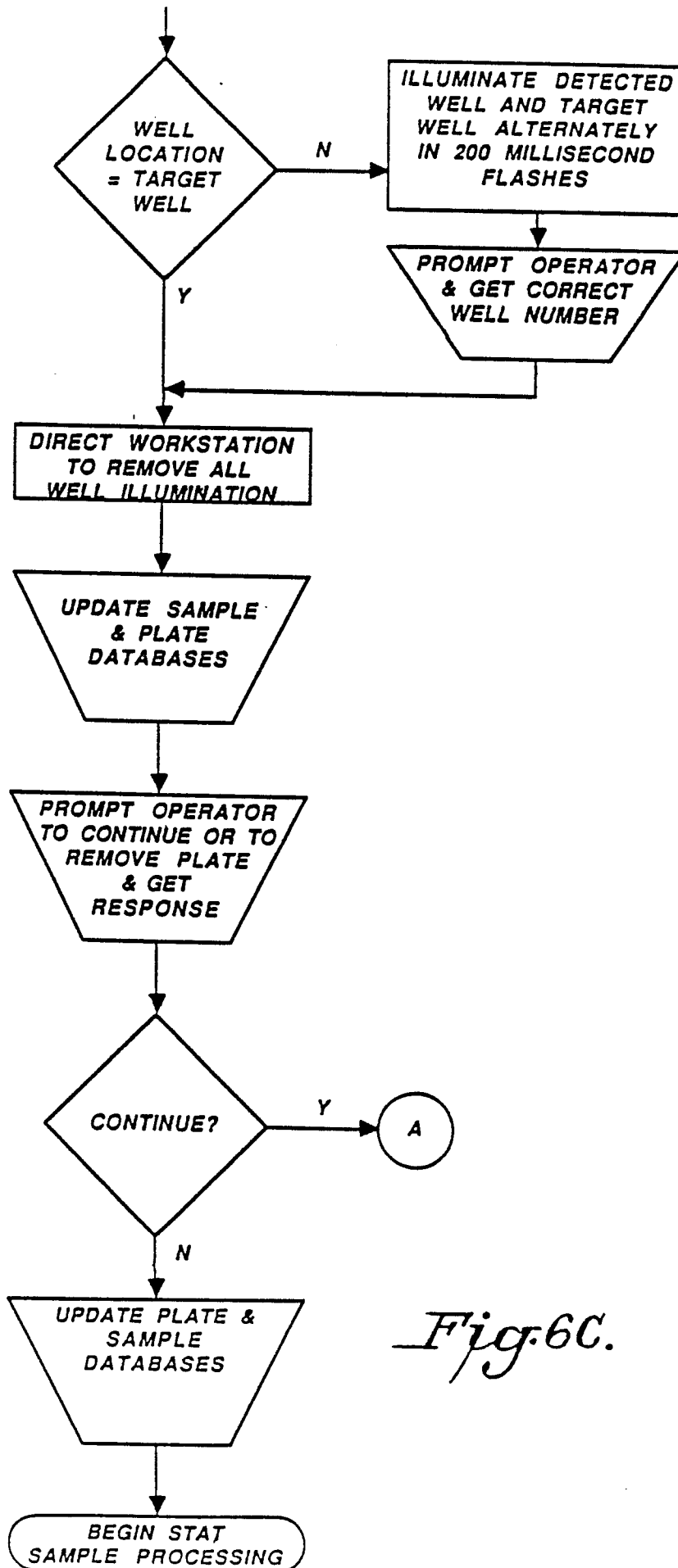
*Fig. 5L.*



*Fig. 5M.*

*Fig. 6A.*

*Fig. 6B.*

*Fig. 6C.*